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Das Portal der wissenschaftlichen Medizin

S3-Leitlinie
„Screening, Diagnose und Behandlung alkoholbezogener Störungen"

AWMF-Register Nr. 076-001

Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde (DGPPN)

Deutsche Gesellschaft für Suchtforschung und Suchttherapie e.V. (DG-SUCHT)

Tabellenband
(Aktualisierte Version 2020)

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Tabellenband

AMSTAR-2 Bewertungen der Systematischen Reviews

Agabio, R., Trogu, E., & Pani, P. P. (2018). Antidepressants for the treatment of people with co-occurring depression and alcohol dependence. Cochrane database of systematic reviews.			
	YES	Partial YES	NO
Did the research question and inclusion criteria for the review include the components of PICO	X		
Did the report of the reviews contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	X		
Did the review authors explain their selection of the study designs for inclusion in the review?	X		
Did the review authors use a comprehensive literature search strategy?	X		
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Did the review authors describe the included studies in adequate detail?	X		
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If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	-		
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Boffo, M., Zerhouni, O., Gronau, Q.F., van Beek, R.J., Nikolaou, K., Marsman, M. & Wiers, R.W. (2019). Cognitive bias modification for behavior change in alcohol and smoking addiction. Bayesiana meta-analysis of individual participant data. Neuropsychology Review, 29 (1), 52-78.			
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Bonnet, U., & Scherbaum, N. (2017). How addictive are gabapentin and pregabalin? A systematic review. European neuropsychopharmacology, 27(12), 1185-1215.			
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Cafferky, B. M., Mendez, M., Anderson, J. R., & Stith, S. M. (2018). Substance use and intimate partner violence: A meta-analytic review. Psychology of Violence, 8(1), 110-131.			
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Calabria, B., Shakeshaft, A. P., & Havard, A. (2011). A systematic and methodological review of interventions for young people experiencing alcohol-related harm. Addiction, 106(8), 1406-1418.			
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Devries, K. M., Child, J. C., Bacchus, L. J., Mak, J., Falder, G., Graham, K., ... & Heise, L. (2014). Intimate partner violence victimization and alcohol consumption in women: A systematic review and meta-analysis. Addiction, 109(3), 379-391.			
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Duke, A. A., Smith, K. M., Oberleitner, L., Westphal, A., & McKee, S. A. (2018). Alcohol, drugs, and violence: A meta-meta-analysis. Psychology of violence, 8(2), 238-249			
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Finnerup, N. B., Attal, N., Haroutounian, S., McNicol, E., Baron, R., Dworkin, R. H., ... & Kamerman, P. R. (2015). Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. The Lancet Neurology, 14(2), 162-173.			
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Foran, H. M., & O'Leary, K. D. (2008). Alcohol and intimate partner violence: A meta-analytic review. Clinical psychology review, 28(7), 1222-1234.			
	YES	Partial YES	NO
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Jones, E.B. & Sharpe, L. (2017). Cognitive bias modification: A review of Metaanalyses. Journal of Affective Disorders, 223, 175-183.			
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If meta-analysis was performed did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	-		
Did the review authors account RoB in individual studies when interpreting/ discussing the results of the review?	X		
Did the review authors provide satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	X		
If they performed quantitive synthesis did the review authors carry out an adequate investigation of publication bias and discuss its likely impact on the results of the review?	X		
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	X		

Kohler, S., & Hofmann, A. (2015). Can motivational interviewing in emergency care reduce alcohol consumption in young people? A systematic review and meta-analysis. Alcohol and Alcoholism, 50(2), 107-117.			
	YES	Partial YES	NO
Did the research question and inclusion criteria for the review include the components of PICO	X		
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Mdege, N. D., & Watson, J. (2013b). Predictors of study setting (primary care vs. hospital setting) among studies of the effectiveness of brief interventions among heavy alcohol users: A systematic review. Drug and alcohol review, 32(4), 368-380.			
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Ntais, C., Pakos, E., Kyzas, P., & Ioannidis, J. P. (2005). Benzodiazepines for alcohol withdrawal. Cochrane Database of Systematic Reviews, (3).			
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Palpacuer, C., Duprez, R., Huneau, A., Locher, C., Boussageon, R., Laviolle, B., & Naudet, F. (2018). Pharmacologically controlled drinking in the treatment of alcohol dependence or alcohol use disorders: a systematic review with direct and network meta-analyses on nalmefene, naltrexone, acamprosate, baclofen and topiramate. Addiction, 113(2), 220-237.			
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Did the research question and inclusion criteria for the review include the components of PICO	X		
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Pennay, A., Cameron, J., Reichert, T., Strickland, H., Lee, N. K., Hall, K., & Lubman, D. I. (2011). A systematic review of interventions for co-occurring substance use disorder and borderline personality disorder. Journal of Substance Abuse Treatment, 41(4), 363-373			
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Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	X		

Riper, H., Andersson, G., Hunter, S. B., de Wit, J., Berking, M., & Cuijpers, P. (2014). Treatment of comorbid alcohol use disorders and depression with cognitive-behavioural therapy and motivational interviewing: A meta-analysis. Addiction, 109(3), 394-406.			
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Riper, H., Hoogendoorn, A., Cuijpers, P., Karyotaki, E., Boumparis, N., Mira, A., ... & Blankers, M. (2018). Effectiveness and treatment moderators of internet interventions for adult problem drinking: An individual patient data meta-analysis of 19 randomised controlled trials. PLoS medicine, 15(12).			
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Roberts, N. P., Roberts, P. A., Jones, N., & Bisson, J. I. (2015). Psychological interventions for post-traumatic stress disorder and comorbid substance use disorder: A systematic review and meta-analysis. Clinical psychology review, 38, 25-38.			
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Saarto, T., & Wiffen, P. J. (2010). Antidepressants for neuropathic pain: a Cochrane review. Journal of Neurology, Neurosurgery & Psychiatry, 81(12), 1372-1373.			
	YES	**Partial YES**	**NO**
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Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	**X**		

Samson, J. E., & McHugh, R. M. (2019). Brief Alcohol Interventions for Adolescents and Young Adults in Emergency Department Settings: A Descriptive Review and Meta-analysis. Adolescent Research Review, 4(3), 313-327.			
	YES	**Partial YES**	**NO**
Did the research question and inclusion criteria for the review include the components of PICO	**X**		
Did the report of the reviews contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	**X**		
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Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	**x**		

Simioni, N., Cottencin, O., & Rolland, B. (2015). Interventions for increasing subsequent alcohol treatment utilisation among patients with alcohol use disorders from somatic inpatient settings: a systematic review. Alcohol and Alcoholism, 50(4), 420-429.			
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Did the research question and inclusion criteria for the review include the components of PICO	X		
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Sundström, C., Blankers, M., & Khadjesari, Z. (2017). Computer-based interventions for problematic alcohol use: a review of systematic reviews. International journal of behavioral medicine, 24(5), 646-658.			
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Tanner-Smith, E. E., & Lipsey, M. W. (2015). Brief alcohol interventions for adolescents and young adults: A systematic review and meta-analysis. Journal of substance abuse treatment, 51, 1-18.			
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Tansil, K. A., Esser, M. B., Sandhu, P., Reynolds, J. A., Elder, R. W., Williamson, R. S., ... & Hungerford, D. W. (2016). Alcohol electronic screening and brief intervention: a Community Guide systematic review. American journal of preventive medicine, 51(5), 801-811.			
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Tiet, Q. Q., & Mausbach, B. (2007). Treatments for patients with dual diagnosis: a review. Alcoholism: Clinical and Experimental Research, 31(4), 513-536.			
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Torrens, M., Fonseca, F., Mateu, G., & Farré, M. (2005). Efficacy of antidepressants in substance use disorders with and without comorbid depression: a systematic review and meta-analysis. Drug and Alcohol Dependence, 78(1), 1-22.			
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Tripodi, S. J., Bender, K., Litschge, C., & Vaughn, M. G. (2010). Interventions for reducing adolescent alcohol abuse: a meta-analytic review. Archives of pediatrics & adolescent medicine, 164(1), 85-91.			
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Did the review authors report on the sources of funding for the studies included in the review?	X		
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	-		
If meta-analysis was performed did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	-		
Did the review authors account RoB in individual studies when interpreting/ discussing the results of the review?	X		
Did the review authors provide satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	X		
If they performed quantitive synthesis did the review authors carry out an adequate investigation of publication bias and discuss its likely impact on the results of the review?	X		
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	X		

Turnbull, C., & Osborn, D. A. (2012). Home visits during pregnancy and after birth for women with an alcohol or drug problem. Cochrane Database of Systematic Reviews, (1).			
	YES	Partial YES	NO
Did the research question and inclusion criteria for the review include the components of PICO	X		
Did the report of the reviews contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	X		
Did the review authors explain their selection of the study designs for inclusion in the review?	X		

Did the review authors use a comprehensive literature search strategy?	X		
Did the review authors perform study selection in duplicate?	X		
Did the review authors perform data extraction in duplicate?	X		
Did the review authors provide a list of excluded studies and justify the exclusions?	X		
Did the review authors describe the included studies in adequate detail?	X		
Did the review authors us a satisfactory technique for assessing the risk of bias in individual studies that were included in the review?	X		
Did the review authors report on the sources of funding for the studies included in the review?	X		
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	-		
If meta-analysis was performed did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	-		
Did the review authors account RoB in individual studies when interpreting/ discussing the results of the review?	X		
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If they performed quantitive synthesis did the review authors carry out an adequate investigation of publication bias and discuss its likely impact on the results of the review?	X		
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	X		

van Emmerik-van Oortmerssen, K., van de Glind, G., van den Brink, W., Smit, F., Crunelle, C. L., Swets, M., & Schoevers, R. A. (2012). Prevalence of attention-deficit hyperactivity disorder in substance use disorder patients: a meta-analysis and meta-regression analysis. Drug and Alcohol Dependence, 122(1-2), 11-19.			
	YES	Partial YES	NO
Did the research question and inclusion criteria for the review include the components of PICO	X		
Did the report of the reviews contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	X		
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Did the review authors perform study selection in duplicate?	X		
Did the review authors perform data extraction in duplicate?	X		
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If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	X		
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If they performed quantitive synthesis did the review authors carry out an adequate investigation of publication bias and discuss its likely impact on the results of the review?	X		
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	X		

Webb, G., Shakeshaft, A., Sanson-Fisher, R., & Havard, A. (2009). A systematic review of work-place interventions for alcohol-related problems. Addiction, 104(3), 365-377.			
	YES	Partial YES	NO

Did the research question and inclusion criteria for the review include the components of PICO	X		
Did the report of the reviews contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	X		
Did the review authors explain their selection of the study designs for inclusion in the review?	X		
Did the review authors use a comprehensive literature search strategy?	X		
Did the review authors perform study selection in duplicate?	X		
Did the review authors perform data extraction in duplicate?	X		
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Did the review authors describe the included studies in adequate detail?	X		
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Did the review authors report on the sources of funding for the studies included in the review?	X		
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	-		
If meta-analysis was performed did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	-		
Did the review authors account RoB in individual studies when interpreting/ discussing the results of the review?	X		
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If they performed quantitive synthesis did the review authors carry out an adequate investigation of publication bias and discuss its likely impact on the results of the review?	X		
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	X		

Wilson, I. M., Graham, K., & Taft, A. (2014). Alcohol interventions, alcohol policy and intimate partner violence: a systematic review. BMC public health, 14(1).			
	YES	Partial YES	NO
Did the research question and inclusion criteria for the review include the components of PICO	X		
Did the report of the reviews contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	X		
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If they performed quantitive synthesis did the review authors carry out an adequate investigation of publication bias and discuss its likely impact on the results of the review?	X		
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	X		

Yuma-Guerrero, P. J., Lawson, K. A., Velasquez, M. M., Von Sternberg, K., Maxson, T., & Garcia, N. (2012). Screening, brief intervention, and referral for alcohol use in adolescents: a systematic review. Pediatrics, 130(1), 115-12			
	YES	**Partial YES**	**NO**
Did the research question and inclusion criteria for the review include the components of PICO	**X**		
Did the report of the reviews contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	**X**		
Did the review authors explain their selection of the study designs for inclusion in the review?	**X**		
Did the review authors use a comprehensive literature search strategy?	**X**		
Did the review authors perform study selection in duplicate?	**X**		
Did the review authors perform data extraction in duplicate?	**X**		
Did the review authors provide a list of excluded studies and justify the exclusions?			**X**
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Did the review authors us a satisfactory technique for assessing the risk of bias in individual studies that were included in the review?		**X**	
Did the review authors report on the sources of funding for the studies included in the review?		**X**	
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	**-**		
If meta-analysis was performed did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	**-**		
Did the review authors account RoB in individual studies when interpreting/ discussing the results of the review?	**X**		
Did the review authors provide satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	**X**		
If they performed quantitive synthesis did the review authors carry out an adequate investigation of publication bias and discuss its likely impact on the results of the review?	**X**		
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	**X**		

Tabellenband

Evidenztabellen der Systematischen Reviews (Cochrane Library)

Title	Alcoholics Anonymous and other 12-step programs for alcohol dependence		
First Author	Ferri, M., 2006	Source	16856072
Level of evidence	Ia	Study type	Systematic Review
Study information	3.417 people Randomized controlled trials comparing AA or other TSF programs to other psychological treatments or no treatment. Where available observational studies with control groups will be considered and separately analysed. Search in the specialized Register of Trials of the Cochrane Group on Drugs and Alcohol, the Cochrane Central Register of Controlled Trials (CENTRAL), MED LINE from 1966, EMBASE from1980, CINAHL from 1982, PsychINFO from 1967. Searches were updated in February 2005. Authors also inspected lists of references for relevant studies.		
Intervention	Experimental Intervention: Twelve-step programs (Alcoholics Anonymous and other Twelve Step Facilitation (TSF) programs; Control group - no intervention; other interventions (e.g. Motivational Enhancement Therapy (MET), Cognitive-behavioural coping skills training (CBT), Relapse Prevention Therapy (RPT) or Twelve-Step program variants (e.g. spiritual, non-spiritual, professionally led, lay led).		
Outcome and effect size	Results • AA may help patients to accept treatment and keep patients in treatment more than alternative treatments, though the evidence for this is from one small study that combined AA with other interventions and should not be regarded as conclusive. • Other studies reported similar retention rates regardless of treatment group • Three studies compared AA combined with other interventions against other treatments and found few differences in the amount of drinks and percentage of drinking days. • Severity of addiction and drinking consequence did not seem to be differentially influenced by TSF versus comparison treatment interventions, and no conclusive differences in treatment drop-out rates were reported. • Included studies did not allow a conclusive assessment of the effect of TSF in promoting complete abstinence. Authors' conclusions: No experimental studies unequivocally demonstrated the effectiveness of AA or TSF approaches for reducing alcohol dependence or problems. One large study focused on the prognostic factors associated with interventions that were assumed to be successful rather than on the effectiveness of interventions themselves, so more efficacy studies are needed.		
Comments	Outcomes: • reducing alcohol intake, • achieving abstinence, • maintaining abstinence, • improving the quality of life of affected people and their families, • reducing alcohol associated accidents and health problems Patients/ Settings • Inpatient detoxification (Brown, 2002) • Patients who applied for outpatient rehabilitation (Davis, 2002) • outpatient therapy or aftercare (Cloud, 2004; MATCH, 1998) • Inpatients (Kahler, 2004). • Men with alcohol problems and their wives (McCrady, 1996) • Work setting (Walsh, 1991) • Hospital-based program vs. community based 12-step program (Zemore, 2004) Limitations: • Studies were conducted in Canada and in the USA. • Methods and procedures of randomization are not described in any report or publication and could not be assessed. •Allocation concealment was never mentioned in any report or publication of the included studies.		
References	Brown 2002a, Brown 2002b, Cloud 2004, Davis 2002,Kahler 2004, McCrady 1996, McCrady 2004, Project MATCH research group 1997, Project MATCH research group 1998a, Project MATCH Research Group 1998b, Walsh 1991, Zemore 2004a, Zemore 2004b		

Title	Acamprosate for alcohol dependence		
First Author	Rösner, S., 2010	Source	20824837
Level of evidence	Ia	Study type	Systematic Review
Study information	24 RCTs with 6.915 participants Systematic search in: Cochrane Drugs and Alcohol Group, PubMed, EMBASE, CINAHL and unpublished Studies (until January 2009)		
Intervention	Experimental intervention: Acamprosate Control intervention: Placebo: 21 Studies Control intervention: Naltrexone: 3 Studies		
Outcome and effect size	1.Acamprosate vs. Placebo: a) Significantly reduced the risk of any drinking RR=0.86 (95% CI [0.81 l 0.91]); NNT=9.09 (95% CI [6.66 l 14.28]) b) Significantly increased the cumulative abstinence duration MD=10.94 (95% CI [5.08 l 16.81]) c) Secondary outcomes (gammaglutamyltransferase, heavy drinking) did not reach statistical significance. d) Diarrhea was the only side effect that was more frequently reported under acamprosate than placebo RD=0.11 (95% CI [0.09 l 0.13]); NNTB=9.09 (95% CI [7.69 l 11.11]). e) Effects of industry sponsored trials RR=0.88 (95% CI [0.80 l 0.97]) did not significantly differ from those of non-profit funded trials RR=0.88 (95% CI [0.81 l 0.96]). f) Linear regression test did not indicate a significant risk of publication bias (p=0.861). 2.Acamprosate versus naltrexone: Three trials compared acamprosate and naltrexone and did not indicate a superiority of one or the other drug on return to any drinking, return to heavy drinking and cumulative abstinence duration. 3. Author`s conclusions: Acamprosate appears to be an effective and safe treatment strategy for supporting continuous abstinence after detoxification in alcohol dependent patients. Even though the sizes of treatment effects appear to be rather moderate in their magnitude, they should be valued against the background of the relapsing nature of alcoholism and the limited therapeutic options currently available for its treatment.		
Comments	23 studies were conducted in an outpatient setting, one study was conducted in an inpatient setting, 19 studies from Europe, 2 studies from USA, 1 study from South Korea, 1 study from Australia, 1 study from Brazil		
References	Anton 2006, Baltieri 2003, Barrias 1997, Besson 1998, Borg 2003, Chick 2000, Geerlings 1997, Gual 2001, Kiefer 2003, Ladewig 1993, Lhuintre 1985, Lhuintre 1990, Mason 2006, Morley 2006, Namkoong 2003, Niederhofer 2002, Paille 1995, Pelc 1992, Pelc 1997, Poldrugo 1997, Rousseaux 1996, Sass 1996, Tempesta 2000, Whitworth 1996		

Title	Alcohol and drug screening of occupational drivers for preventing injury		
First Author	Cashman, C. M., 2009	Source	19370641
Level of evidence	IV	Study type	Systematic Review
Study information	Two interrupted time-series studies Study 1: From 1983-1996 (115.019 employees in five large interstate transport companies) Study 2: From 1984-1997 (Unclear number of truck drivers) Searched in: MEDLINE, EMBASE, The Cochrane Library, Cochrane Occupational Health Field's specialised register, DARE, PsychINFO, ERIC, ETOH, CISDOC, NIOSHTIC, TRANSPORT, Zetoc, Science Citation Index and Social Science Citation index and HSELINE. (all to June 2007)		
Intervention	1. Experimental Intervention: Implementation of legislation for mandatory random drug testing and mandatory random and for-cause alcohol testing. 2. Control Intervention No alcohol or drug testing 3. Experimental Intervention: Mandatory random drug testing (federal injury data that covered all truck drivers of interstate carriers)		
Outcome and effect size	In one study mandatory random and for-cause alcohol testing was associated with a significant decrease in the level of injuries immediately following the intervention (-1.25 injuries/100		

	person years, 95% CI [-2.29|-0.21]) but did not significantly affect the existing long-term downward trend (-0.28 injuries/100 person years/year, 95% CI [-0.78|0.21]). Mandatory random drug testing was significantly associated with an immediate change in injury level following the intervention (1.26 injuries/100 person years, 95% CI [0.36|2.16]) in one study, and in the second study there was no significant effect (-1.36/injuries/100 person years, 95% CI [-1.69|0.41]). In the long term, random drug testing was associated with a significant increase in the downward trend (-0.19 injuries/100 person years/year, 95% CI [-0.30|-0.07]) in one study, the other study was also associated with a significant improvement in the long-term downward trend (-0.83 fatal accidents/100 million vehicle miles/year, 95% CI [-1.08|-0.58]). Authors' conclusions: There is insufficient evidence to advise for or against the use of drug and alcohol testing of occupational drivers for preventing injuries as a sole, effective, long-term solution in the context of workplace culture, peer interaction and other local factors. Cluster-randomised trials are needed to better address the effects of interventions for injury prevention in this occupational setting.
Comments	• Only small number of time-series studies from USA. • No randomized-controlled trials available
References	Swena 1999, Spicer 2005

Title	**Alcohol ignition interlock programs for reducing drink driving recidivism**		
First Author	**Willis, C., 2004**	**Source**	**15495082**
Level of evidence	Ib	**Study type**	Systematic Review
Study information	One randomised controlled trial (RCT) and ten controlled trials were identified, and also three ongoing trials. Data regarding recidivism while the interlock is installed in the vehicle; after the interlock has been removed from the vehicle and total recidivism during the study were extracted and entered into analyses using RevMan. Searched in: The Cochrane Injuries Group's Specialised register (Sept 2002), MEDLINE (1966 to August 2002), PubMed (to Aug 2002), EMBASE (1980 to Sept 2002), TRANSPORT (1988 to 2002 issue 06), CENTRAL (The Cochrane Library 2002, Issue 3), The Science Citation Index (1980 to Sept 2002) National Research Register (2002, issue 3). Search in the Internet using various search engines.		
Intervention	1. Experimental Intervention: Interlock is installed in the vehicle as part of an educational / interventional program 2. Control Intervention Not clearly described		
Outcome and effect size	1.Recidivism while the interlock is installed in the vehicle The RCT showed that the interlock program was effective while the device was installed in the vehicle; relative risk 0.36 (95% CI [0.21|0.63]). Controlled trials support this conclusion, with a general trend − in both first-time and repeat offenders − towards lower recidivism rates when the interlock device is installed. 2. Recidivism after the interlock has been removed from the vehicle: Neither the RCT nor the controlled trials provide evidence for any effectiveness of the program continuing once the device has been removed. Authors' conclusions: In order to eliminate potential selection bias, more RCTs need to be conducted in this area so that effectiveness, as well as efficacy, can be ascertained. The interlock program appears to be effective while the device is installed in the vehicle of the offender. Studies need to address ways of improving recidivism rates in the long term, as the major challenges are participation rates, compliance and durability.		
Comments	• Only small number of trials from USA. • Studies are rather old • The RCT is limited to those offenders who had demonstrated an ability to comply with prescribed treatments and were approved for relicensing by the state's Medical Advisory Board. Therefore, this study does not evaluate the effectiveness of the interlock on the less motivated repeat drink driver, as there is a selection bias towards those offenders who had overcome their drink driving habit.		
References	Beck 1999, Dussault 2000, Frank 2002, Jones 1993, Lucke 2001, Marine 2000, Marine 2001,		

	Marques 1995, Morse 1992, Popkin, 1993, Raub 2001, The EMT group 1990, Tippetts 1998, Vezina 2002, Voas 1999, Voas 2002

Title	**Anticonvulsants for alcohol withdrawal.**		
First Author	**Minozzi, S., 2010**	**Source**	**20238337**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	56 RCT with 4.076 participants Systematic research in Cochrane Drugs and Alcohol Group, PubMed, EMBASE, CINAHL (to December 2009)		
Intervention	Experimental intervention: Anticonvulsant alone or in combination with other drugs Control intervention: Placebo; other pharmacological interventions		
Outcome and effect size	1. Anticonvulsant versus placebo: No statistically significant differences for the six outcomes considered 2. Anticonvulsant versus other drug: 19 outcomes considered, results favour anticonvulsants only in the comparison carbamazepine versus benzodiazepine (oxazepam and lorazepam) for alcohol withdrawal symptoms (CIWA-Ar score): 3 studies, 262 participants, MD=-1.04 (95% CI [-1.89|-0.20]), none of the other comparisons reached statistical significance. 3. Comparing different anticonvulsants: No statistically significant differences in the two outcomes considered. 4. Comparing anticonvulsants plus other drugs versus other: drugs (3 outcomes considered), results from one study, 72 participants, favour paraldehyde plus chloral hydrate versus chlordiazepoxide, for the severe life-threatening side effects, RR=0.12 (95% CI [0.03|0.44]). 5. Conclusions: Results of this review do not provide sufficient evidence in favour of anticonvulsants for the treatment of AWS. There are some suggestions that carbamazepine may actually be more effective in treating some aspects of alcohol withdrawal when compared to benzodiazepines, the current first-line regimen for alcohol withdrawal syndrome. Anticonvulsants seem to have limited side effects, although adverse effects are not rigorously reported in the analysed trials.		
Comments	33 studies from Europe, 18 studies from North America, 4 studies from Australia / New Zealand, 1 study from Asia Limitations: • Some studies are rather old, have a small sample size and methodological limitations (randomization, patient allocation is unclear, information about follow-ups is missing) • Heterogeneity in populations, • No information about dose-response effects • Differences in patient co-morbidity		
References	1.Anticonvulsants versus placebo (17 studies) Alldredge 1988, Bjorkqvist 1976, Blanchard 1985, Bonnet 2003, Burroughs 1985a, Chance 1991, Gann 2004, Glatt 1966, Golbert 1967, Koethe 2007, Krupitsky 2007, Lambie 1980, Murphy 1983, Rathlev 1994, Reoux 2001, Sampliner 1974, Stanhope 1989 2.Anticonvulsants versus other drugs (32 studies) Agricola 1982, Borg 1986, Borg 1986, Burroughs 1985a, Burroughs 1985a, Burroughs 1985b, Burroughs 1985b, Choi 2005, Dencker 1978; Elsing 1996, Elsing 2009 Golbert 1967, Kaim 1972, Kaim 1972, Kalyoncu 1996, Koppi 1987, Kramp 1978, Krupitsky 2007, Lapierre 1983, Longo 2002, Lucht 2003, Madden 1969, Malcolm 1989, Malcolm 2002, Malcolm 2007, Manhem 1985, McGrath 1975, Murphy 1983, Nimmerichter 2002, Radouco-Thomas 1989, Robinson 1989, Santo 1985, Stuppaeck 1992, Stuppaeck 1998, Thompson 1975, Tubridy 1988 3.Different anticonvulsants (10 studies) Flygering 1984, Golbert 1967, Kaim 1972, Krupitsky 2007, Krupitsky 2007, Mariani 2006, Ritola 1981, Rosenthal 1998, Schik 2005, Seifert 2004, Teijeiro 1975, 4. Anticonvulsant in combination with other drugs (6 studies) Balldin 1986, Golbert 1967, Lucht 2003, Myrick 2000, Spies 1996, Spies 1996, Rothstein 1973 5. Anticonvulsant in combination with other drugs versus other anticonvulsant (1 study) Croissant 2009		

Title	Baclofen for alcohol withdrawal		
First Author	Liu, J., 2019	Source	28822350
Level of evidence	Ib	Study type	Systematic Review
Study information	1 RCT with 37 participants Systematic Research in: Cochrane Central Register of Controlled Trials (September 2010), MEDLINE (1966 to September 2010), EMBASE (1980 to September 2010) und CINAHL (1982 to September 2010. We also searched the following registers of ongoing trials, e.g. Clinicaltrials.gov, Controlled trials.com, EUDRACT, etc.		
Intervention	Experimental Intervention: Baclofen Control intervention: Placebo or other drugs (e.g. benzodiazepines)		
Outcome and effect size	1. Baclofen vs. placebo: No studies available 2. Baclofen vs. benzodiazepines: There was only one study, which was eligible according to the inclusion criteria. In the study, all 37 patients completed, with no dropouts in either group, and no difference in the patients compliance to treatment was found between groups. 3. CIWA-Ar score and its 4 sub scales (anxiety, agitation, sweating and tremors): Both baclofen and diazepam treatments significantly decreased the CIWA-Ar score, with no significant differences between the 2 treatments. Although baclofen was slightly slower than diazepam, as indicated by significantly higher scores on days 2 and 3 in the baclofen versus the diazepam group, on subsequent days the efficacy of baclofen and diazepam was comparable. 4. Sweating score: Mean baseline sweating score was significantly higher in the baclofen than in the diazepam group. Both drug treatments significantly decreased the sweating score when analysed separately, with no significant differences between the 2 treatments. 5. Tremor score: Mean baseline tremor score did not differ between the 2 groups; both drug treatments significantly decreased the tremor score, without differences between treatments. 6. Anxiety: Mean baseline anxiety score was significantly higher in the baclofen than in the diazepam group; both drug treatments decreased anxiety score, with no significant differences between the 2 treatments. 7. Agitation score: Mean baseline agitation score was significantly higher in the baclofen than in the diazepam-group; both drug treatments decreased the agitation score. 8. Changes in AST, ALT, GGT and MCV: A reduction in AST, ALT, GGT and MCV value was found in both baclofen and diazepam treated patient groups. 9. Side effects: No side effects were reported by either baclofen or diazepam-treated patients. On discontinuation of treatment, no withdrawal symptoms or side effects were observed. Authors` conclusions: The evidence of recommending baclofen for AWS is insufficient. Better designed RCTs are demanded to further prove its efficacy and safety.		
Comments	1 study from Italy		
References	Addolorato 2006		

Title	Benzodiazepines for alcohol withdrawal		
First Author	Amato, L., 2010	Source	20238336
Level of evidence	Ia	Study type	Systematic Review
Study information	64 studies with 4.309 participants Systematic research in: Cochrane Drugs and Alcohol Group' Register of Trials (December 2009), PubMed, EMBASE, CINAHL (January 1966 to December 2009), EconLIT (1969 to December 2009		
Intervention	Experimental intervention: Benzodiazepines alone or in combination with other drugs Control intervention: Placebo; other pharmacological interventions		
Outcome and effect size	1. Benzodiazepines versus placebo: Benzodiazepines performed better for seizures, 3 studies, 324 participants, RR=0.16, 95% CI [0.04|0.69]), no statistically significant difference for the other outcomes considered.		

	2. Benzodiazepines versus other drugs: There is a trend in favour of benzodiazepines for seizure and delirium control, severe life threatening side effect, dropouts, dropouts due to side effects and patient's global assessment score. A trend in favour of control group was observed for CIWA-Ar scores at 48 hours and at the end of treatment. The results reach statistical significance only in one study, with 61 participants, results on Hamilton anxiety rating scale favour control MD=-1.60, 95% CI [-2.59|-0.61]) 3.Comparing different benzodiazepines among themselves: Results never reached statistical significance but chlordiazepoxide performed better 4. Benzodiazepine plus other drug versus other drug: Results never reached statistical significance 5. Fixed-schedule versus symptom-triggered regimens: Results from a single study, with 159 participants, favour symptom-triggered regimens MD=-1.10, 95% CI [-3.27, 1.07] for CIWA-Ar scores at the end of treatment. Differences in isolated trials should be interpreted very cautiously. 6. Authors' conclusions: Benzodiazepines showed a protective benefit against alcohol withdrawal symptoms, in particular seizures, when compared to placebo and a potentially protective benefit for many outcomes when compared with other drugs. Nevertheless, no definite conclusion about the effectiveness and safety of benzodiazepines was possible, because of the heterogeneity of the trials both in interventions and the assessment of outcomes.
Comments	26 studies from Europe, 32 from North America, 3 from Asia, 2 from South Africa 1 from Australia Limitations • Small sample sizes • Data on safety outcomes are sparse and fragmented. • Although a significant number of trends has emerged, most of these were small and the data for most outcomes did not reach statistical significance, indicating the need for larger, well-designed studies in this field.
References	1.Benzodiazepines versus Placebo: (11 studies) Adinoff 1994, Burroughs 1985a, Kaim 1969, Kaim 1972, Krupitsky 2007, Martin 1975, McLendon 1980, Mielke 1976, Naranjo 1983; Sellers 1977, Sellers 1983 2.Benzodiazepines versus other drugs: (42 studies) Addolorato 1999, Addolorato 2006, Adinoff 1994, Bailly 1992, Baumgartner 1987, Baumgartner 1991, Borg 1986, Burroughs 1985a, Burroughs 1985b, Choi 2005, Dion 1968, Favre 2005, Funderburk 1978, Gillman 2004, Gillmer 1973, Golbert 1967, Kaim 1969, Kaim 1972, Kalyoncu 1996, Kramp 1978, Krupitsky 2007, Lapierre 1983, Lenzenhuber 1999, Lepola 1984, Longo 2002, Lucht 2003, Malcolm 1989, Malcolm 2002, Malcolm 2007, McGrath 1975, Nava 2007, Overall 1973, Palestine 1976, Pena-Ramos 1977, Pena-Ramos 1979, Radouco-Thomas 1989, Runion 1978, Sellers 1977, Stuppaeck 1992; Tubridy 1988, Worner 1994 3. Comparing different benzodiazepines among themselves (18 studies) Adinoff 1994, Anton 1997, Brown 1972, Day 2004, Jauhar 2000, Kolin 1981, Kumar 2009, Martin 1975, McLendon 1980; Mendels 1985, Mielke 1976, Miller 1984, Mukherjee 1983, O'Brien 1983, Ritson 1986, Saletu 1983, Solomon 1983, Wilson 1985 4.Benzodiazepines plus other drug versus other drug (3 studies) Dion 1968, Sellers 1977, Spies 1996 5.Fixed-schedule versus symptom-triggered regimens (3 studies) Daeppen 2002, Saitz 1994, Spies 2003

Title	**Brief interventions for heavy alcohol users admitted to general hospital wards.**		
First Author	**McQueen, J., 2011**	**Source**	**21833953**
Level of evidence	Ib	**Study type**	Systematic Review
Study information	14 RCTs and CTs involving 4.041 adults and adolescents (16 years or older) admitted to general inpatient hospital care for any reason other than specifically for alcohol treatment Search geschaeftsstelle@dgps.de in the Cochrane Drug and Alcohol Group Register of Trials (March 2011) the Cochrane Central Register of Controlled Trials (The Cochrane Library March 2011), MEDLINE January 1966-March 2011, CINAHL 1982-March 2011,		

	EMBASE 1980-March 2011 and www.clinicaltrial s.gov to April 2011 and performed some relevant handsearching
Intervention	1. Experimental Intervention: Brief interventions (of up to 3 sessions) 2. Control Intervention No or usual care
Outcome and effect size	1 Brief intervention(s) versus control (assessment/no-intervention or standard treatment) a) Reduction in alcohol consumption Patients receiving brief interventions have a greater reduction in alcohol consumption compared to those in control groups at six month, MD=-69.43 (95% CI [-128.14|-10.72]) and nine months follow up, MD=-182.88 (95% CI [-360.00|-5.76]), but this is not maintained at one year. Self-reports of reduction of alcohol consumption at 1 year were found in favour of brief interventions, SMD=-0.26 (95% CI [-0.50|-0.03]). b) Secondary outcomes In addition there were significantly fewer deaths in the groups receiving brief interventions than in control groups at 6 months, RR=0.42 (95% CI [0.19|0.94]) and one year follow up, RR=0.60 (95% CI [0.40|0.91]). Furthermore, screening, asking participants about their drinking patterns, may also have a positive impact on alcohol consumption levels and changes in drinking behaviour. Authors' conclusions The main results of this review indicate that there are benefits to delivering brief interventions to heavy alcohol users admitted to general hospital wards in terms of reduction in alcohol consumption and death rates. However, these findings are based on studies involving mainly male participants. Further research is required determine the optimal content and treatment exposure of brief interventions within general hospital settings and whether they are likely to be more successful in patients with certain characteristics.
Comments	• Mainly male adults (16 years or older) identified as heavy drinkers in hospital • Mainly studies from the UK and USA • Brief interventions consisted of all, or any, of the following: Self-efficacy enhancement, skills based counselling, brief motivational counselling, brief advice, education leaflets, telephone calls, feedback letter.
References	Antti-Poika 1988, Chick 1985, Freyer-Adam 2008, Gentilello 1999, Heather 1996, Holloway 2007, Liu 2011, McManus 2003, McQueen 2006, Saitz 2007, Schermer 2006, Sommers 2006, Tsai 2009, Watson 1999

Title	**Effectiveness of brief alcohol interventions in primary care populations.**		
First Author	**Kaner, E. F., 2018**	**Source**	**17443541**
Level of evidence	Ib	**Study type**	Systematic Review
Study information	Meta-analysis of 22 RCTs with 7.619 participants Search in the Cochrane Drug and Alcohol Group specialised register (February 2006), MEDLINE (1966 to February 2006), EMBASE (1980 to February 2006), CINAHL (1982 to February 2006), PsycINFO (1840 to February 2006), Science Citation Index (1970 to February 2006), Social Science Citation Index (1970 to February 2006), Alcohol and Alcohol Problems Science Database (1972 to 2003), reference lists of articles.		
Intervention	1.Experimental Intervention: Brief interventions 2.Control group No or usual care		
Outcome and effect size	Brief intervention versus control group a) Alcohol consumption: Lower alcohol consumption in the intervention group than the control group after follow-up of one year or longer (mean difference: -38 grams/week, 95% CI [-54|-23]) although there was substantial heterogeneity between trials (I2=57%). b) Gender differences: Sub-group analysis (8 studies, 2.307 participants) confirmed the benefit of brief intervention in men (mean difference: -57 grams/week, 95% CI [-89|-25], I2=56%), but not in women (mean difference: -10 grams/week, 95% CI [-48|29], I2=45%). c) Treatment duration:		

	Meta-regression showed little evidence of a greater reduction in alcohol consumption with longer treatment exposure or among trials which were less clinically representative. Extended intervention was associated with a non-significantly greater reduction in alcohol consumption than brief intervention (mean difference=-28grams/week, 95% CI [-62|6], I2=0%) Authors' conclusions: Overall, brief interventions lowered alcohol consumption. When data were available by gender, the effect was clear in men at one year of follow up, but not in women. Longer duration of counselling probably has little additional effect. The lack of evidence of any difference in outcomes between efficacy and effectiveness trials suggests that the current literature is relevant to routine primary care. There is a clear need for more evaluative research on brief interventions with women, younger people and those from cultural minority groups. In addition, there is a need for more research in transitional and developing countries. However, given the large number of trials of brief alcohol intervention showing a positive impact in men, there is no need for more of the same before such interventions are delivered in primary care. Longer treatment appeared to have little effect in significantly improving outcomes. Moreover, there is some suggestion that screening alone may result in alcohol consumption reduction, and this should be investigated further. Finally, future research direction should focus on implementation issues including a more precise specification of brief intervention components.
Comments	Gender differences are found
References	Aalto 2000, Aalto 2001, Altisent 1997, Anderson 1992, Chang 1997, Cordoba 1998, Crawford 2004, Curry 2003, Diez 2002, Fernandez 1997, Fleming 1997, Fleming 1999, Fleming 2000, Fleming 2002, Fleming 2004, Grossberg 2004, Gentillelo 1999, Gordon 2003, Heather 1987, Huas 2002, Israel 1996, Kunz 2004, Lock 2006, Longabaugh 2001, Maisto 2001, McIntosh 1997, Ockene 1999, Reiff-Hekking 2005, Richmond 1995, Rodriguez 2003, Rodriguez-Martos 2005, Rodriguez-Martos 2006, Romelsjo 1989, Scott 1991, Senft 1997, Seppa 1992, Tomson 1998, Wallace 1988

Title	**Brief interventions for heavy alcohol users admitted to general hospital wards**		
First Author	**McQueen, J., 2011**	**Source**	**21833953**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	14 RCTs and CTs involving 4.041 adults and adolescents (16 years or older) admitted to general inpatient hospital care for any reason other than specifically for alcohol treatment Search geschaeftsstelle@dgps.de in the Cochrane Drug and Alcohol Group Register of Trials (March 2011) the Cochrane Central Register of Controlled Trials (The Cochrane Library March 2011), MEDLINE January 1966 -March 2011, CINAHL 1982 - March 2011, EMBASE 1980- March 2011 and www.clinicaltrials.gov to April 2011 and performed some relevant handsearching		
Intervention	1. Experimental Intervention: Brief interventions (of up to 3 sessions) 2. Control Intervention: No or usual care		
Outcome and effect size	Brief intervention(s) versus control (assessment/no-intervention or standard treatment) a) Reduction in alcohol consumption: Patients receiving brief interventions have a greater reduction in alcohol consumption compared to those in control groups at six month, MD=-69.43 (95% CI [-128.14|-10.72]) and nine months follow up, MD=-182.88 (95% CI [-360.00|-5.76]) but this is not maintained at one year. Self-reports of reduction of alcohol consumption at 1 year were found in favour of brief interventions, SMD=-0.26 (95% CI [-0.50|-0.03]). b) Secondary outcomes: In addition there were significantly fewer deaths in the groups receiving brief interventions than in control groups at 6 months, RR=0.42 (95% CI [0.19|0.94]) and one year follow up, RR=0.60 (95% CI [0.40|0.91]). Furthermore screening, asking participants about their drinking patterns, may also have a positive impact on alcohol consumption levels and changes in drinking behaviour. Authors' conclusions: The main results of this review indicate that there are benefits to delivering brief		

	interventions to heavy alcohol users admitted to general hospital wards in terms of reduction in alcohol consumption and death rates. However, these findings are based on studies involving mainly male participants. Further research is required determine the optimal content and treatment exposure of brief interventions within general hospital settings and whether they are likely to be more successful in patients with certain characteristics.
Comments	• Mainly male adults (16 years or older) identified as heavy drinkers in hospital • Mainly studies from the UK and USA • Brief interventions consisted of all, or any, of the following: Self-efficacy enhancement, skills based counselling, brief motivational counselling, brief advice, education leaflets, telephone calls, feedback letter.
References	Antti-Poika 1988, Chick 1985, Freyer-Adam 2008, Gentilello 1999, Heather 1996, Holloway 2007, Liu 2011, McManus 2003, McQueen 2006, Saitz 2007, Schermer 2006, Sommers 2006, Tsai 2009, Watson 1999

Title	**Case management for persons with substance use disorders**		
First Author	**Hesse, M., 2007**	**Source**	**17943902**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	15 RCTs with 6.694 participants with at least one alcohol or drug related problem. Search in the Cochrane Controlled Trials Register (Cochrane Library, issue 4, 2006), MEDLINE (1966-2006), EMBASE (1980-2006), LILACS (1982-2006), PsycINFO (1973-2006), Biological Abstracts (1982-2000). Reference searching; personal communication; conference abstracts; book chapters on case management.		
Intervention	1.Experimental Intervention: Case management (brokerage case management model, intensive case management model, the strengths-based case management model, assertive community treatment: case management with access to vouchers for free MMT and case management without access to vouchers for MMT 2.Control intervention Treatment as usual or another treatment mode		
Outcome and effect size	1.Case management versus treatment as usual: • Concerning primary outcomes, eight comparisons from seven studies were available for illicit drug use. The overall effect size was SMD=0.12 (95% CI [-0.06|0.29], Z=1.27, p=0.20). Heterogeneity for drug abuse was significant (F 2(7)=23.25, p=0.002, I2=69.9%). The fail-safe number of studies was 0, as the result was non-significant. • Alcohol use was available for two studies. The effect was SMD=0.01 (Z=0.03, ns). • Outcomes concerning legal problems were reported by four studies. The overall effect size was non-significant (SMD=0.05, 95% CI [0.05|0.159], Z=1.00, p=0.32), and heterogeneity was non-significant (F 2(3)=0.06, p=0.97, I2=0%). All comparisons favoured case management with similar small effect sizes. • Psychiatric symptoms were reported by two studies, showing no difference between experimental and control. The effect was small and non-significant (SMD=0.01, 95% CI [-0.23|0.26]; Z=0.10, p=0.92). • The effect size for illicit drug use was not significant, and small (standardized mean difference (SMD)=0.12, 95% CI [0.09|0.29], p=0.20). Substantial heterogeneity was found (I2=69.9%). 2. Linkage to other treatment services: • Linkage to other treatment services was reported in 10 studies with 3132 patients. The effect size for linkage was moderate (SMD=0.42, 95% CI [0.21|0.62), p<0.001), but substantial heterogeneity was found (I2=85.2%). • Moderator analyses suggested that a part of the heterogeneity found in linkage studies could be explained by the presence or absence of a treatment manual for case management. 3. Case management versus other treatments: • A single, large trial of case management with two arms showed that case management was superior to psycho-education and drug counselling in reducing drug use. • One study reported alcohol use outcomes (Sorensen, 2003), and the results favoured		

	control, but was non-significant (SMD=0.21, 95% CI [0.11|0.53]). 4. Manualised: versus non-manualised case management Additional analysis of the studies suggested that the use of a manual to guide the delivery of case management could increase linkage. Authors' conclusions: There is current evidence supporting that case management can enhance linkage with other services. However, evidence that case management reduces drug use or produces other beneficial outcome is not conclusive.
Comments	Setting One study was conducted in Europe; all other studies were from North America Participants • Opiate dependent persons requiring or receiving substitution treatment (Corsi, 2007; Coviello, 2006; Naber, 2006a, 2006b; Sorensen, 2005a, 2005b; Zanis, 1996) • Mixed population of drug abusers (mainly opiate and cocaine/crack abusers) (Martin, 1993; Morgenstern, 2006; Rapp, 1998, 2006; Rhodes, 1997; Scott, 2002; Sorensen, 2003). • Two studies were conducted in criminal justice settings (Martin, 1993; Rhodes, 1997). • Three studies targeted homeless substance abusers: two predominantly consisted of alcohol abusers (Braucht, 1995; Cox, 1998), and one recruited substance abusers (mainly alcoholics) with co-occurring mental disorders (Morse, 2006). • Substantial heterogeneity was found
References	Braucht 1995, Calsyn, 2005, Corsi 2007, Coviello 2006, Cox 1998, Martin 1993, Martin 1997, Masson 2004, Morgenstern 2006, Morse 2006, Naber 2006a, Naber 2006b, Rapp 1998, Rapp 2006, Rhodes 1997, Scott 2002, Siegal 1996, Siegal 2002, Sorensen 2003, Sorensen 2005a, Sorensen 2005b, Zanis 1996

Title	**Colchicine for alcoholic and non-alcoholic liver fibrosis and cirrhosis**		
First Author	**Rambaldi, A., 2001**	**Source**	**11318982**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	15 RCTs with 1.714 participants Systematic search in: The Cochrane Hepato-Biliary Group Controlled Trials Register, The Cochrane Controlled Trials Register on The Cochrane Library; MEDLINE: EMBASE, Science Citation Index (September 2004).		
Intervention	Experimental intervention: Colchicine Control intervention: Placebo: 21 studies Control intervention: Naltrexon: 3 studies		
Outcome and effect size	1. Colchicine versus placebo: No significant effects of intervention on mortality (relative risks (RR)=1.00, 95% CI [0.87|1.16]), liver-related mortality (RR=1.08, 95% CI [0.88|1.33]), complications (RR=1.01, 95% CI [0.74|1.38]), liver biochemistry, liver histology, or alcohol consumption (RR=1.03, 95% CI [0.77|1.39]). 2. Adverse events: Colchicine was associated with a significantly increased risk of serious adverse events (RR=8.38, 95% CI [1.08|65.2]) and non-serious adverse events (RR=4.35, 95% CI [2.16|8.77]). Authors` conclusions: Colchicine should not be used for alcoholic, viral, or cryptogenic liver fibrosis or liver cirrhosis outside randomised clinical trials.		
Comments	• Included studies are rather old • The dosage was 1mg colchicine five days a week in the majority of the trials. Some used the same dosage but for six or seven days a week. Only one trial used colchicine 1.2mg per day. • The treatment duration varied from one month to 55 months with a median of 18 months in the 15 trials. • The entry criteria in the randomised clinical trials varied, but the inclusion criteria made it highly likely that all patients did in fact have fibrosis or cirrhosis of the liver.		
References	Akriviadis 1990, Angelico 2000, Buligescu 1990, Colman 1998, Cortez-Pinto 2002, Gültepe		

	1994, Kershenobich 1988, Lin 1996, Morgan 2002, Parise 1995, Reinhardt 1986, Sáinz 1992, Trande 1996, Trinchet 1989, Wang 1994

Title	**Gamma-hydroxybutyrate (GHB) for treatment of alcohol withdrawal and prevention of relapses.**		
First Author	**Leone, M. A., 2010**	**Source**	**20166080**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	13 studies (randomized controlled trials (RCT), controlled clinical trials (CCT), and controlled prospective studies (CPS)) with 4.309 participants Search in: The Cochrane Drugs and Alcohol Group's Register of Trials (October 2008), PubMed, EMBASE, CINAHL (January 2005 to October 2008), EconLIT (1969 to February 2008), and reference lists of retrieved articles.		
Intervention	Experimental intervention: GHB alone or in combination with other drugs Control intervention: Placebo; other pharmaceutical interventions		
Outcome and effect size	<u>1. GHB 50mg vs. placebo:</u> For alcohol withdrawal syndrome, comparing GHB 50mg versus placebo, results from 1 study (23 participants) favour GHB for withdrawal symptoms: MD=-12.1 (95% CI [-15.9|-8.29]), but tolerated side effects were more frequent in the GHB group: RR=16.2 (95% CI [1.04|254.9]; based on 7 of 11 patients in the GHB group developing transitory vertigo compared to none in the placebo group). At mid-term, comparing GHB 50mg/day with placebo, 1 study (71 participants, 3 months follow-up) favour GHB for abstinence rate (RR=5.35, 95% CI [1.28|22.4]), controlled drinking (RR=2.13, 95% CI [1.07|5.54]), relapses (RR=0.36, 95% CI [0.21|0.63]), and number of daily drinks (MD=-4.60, 95% CI [-6.18|-3.02]). <u>2. GHB 50mg versus Clomethiazole:</u> In the comparison of GHB 50mg versus Clomethiazole, results from 1 study (21 participants) favour GHB for withdrawal symptoms: MD=-3.40 (95% CI [-5.09|-1.71]). <u>3. GHB 50mg versus Clomethiazole:</u> For GHB 100mg versus Clomethiazole, results from 1 study (98 participants) favour Clomethiazole for side effects: RR=1.84 (95% CI [1.19|2.85]). <u>4. GHB versus other pharmaceutical interventions:</u> On abstinence, GHB performed better than Naltrexone (NTX) (2 studies, 64 participants) (RR=2.59, 95% CI [1.35|4.98] at 3 months) and better than Disulfiram (1 study, 59 participants) (RR=1.66, 95% CI [0.99|2.80] at 12 months, slightly significant). <u>5. GHB plus other drug versus other pharmaceutical interventions:</u> The combination of GHB and NTX was better than NTX for abstinence (RR=12.3, 95% CI [1.79|83.9] at 3 months; 1 study, 35 participants). The combination of NTX, GHB and Escitalopram was better than Escitalopram alone for abstinence (RR=2.02 95% CI [0.03|3.94] at 3 months; RR=4.58, 95% CI [1.28|16.5] at 6 months; 1 study, 23 participants). <u>6. Alcohol Craving Scale:</u> For Alcohol Craving Scale, results favour GHB over placebo (MD=-4.50, 95% CI [-5.81|-3.19] at 3 months; 1 study, 71 participants) and over Disulfiram at 12 months (MD=-1.40, 95% CI [-1.86|-0.94], from 1 study with 41 participants). All other comparisons and outcomes did not show significant differences. <u>Authors' conclusions:</u> There is insufficient randomised evidence to be confident of a difference between GHB and placebo, or to determine reliably if GHB is more or less effective than other drugs for the treatment of alcohol withdrawal or the prevention of relapses. The small amount of randomised evidence available suggests that GHB 50mg may be more effective than placebo in the treatment of AWS, and in preventing relapses and craving in previously detoxified alcoholics during the first 3 months of follow-up. This review does not provide evidence in favour or against GHB compared to benzodiazepines and Clomethiazole for treatment of AWS; but, again based on a small amount of randomised evidence, GHB appears better than NTX and Disulfiram in maintaining abstinence and preventing craving in the medium term (3 to 12months). The review does not provide evidence of a difference in side effects between GHB and benzodiazepines, NTX or Disulfiram. These findings should be considered alongside concerns that have been raised about GHB regarding the risk of		

	developing addiction, and the misuse or abuse of the drug, suggesting to use GHB only under strict medical surveillance.
Comments	Thirteen RCTs were included, 11 of which had been conducted in Italy.
References	Addolorato 1999a, Caputo 2003, Caputo 2007, Ceccanti 1996, Di Bello 1995, Elsing 1996, Ferri 1991, Gallimberti 1989, Gallimberti 1992, Nava 2006, Nava 2007, Nimmerrichter 2002, Stella 2008

Title	**Home visits during pregnancy and after birth for women with an alcohol or drug problem.**		
First Author	**Doggett, C., 2005**	**Source**	
Level of evidence	Ia	**Study type**	Systematic Review
Study information	Six studies (709 women) using random or quasi-random allocation of pregnant or postpartum women with a drug or alcohol problem to home visits. Trials enrolling high-risk women of whom more than 50% were reported to use drugs or alcohol were also eligible. Search in the Cochrane Pregnancy and Childbirth Trials Register (30 April 2004), CENTRAL (The Cochrane Library, Issue 2, 2004), MEDLINE (1966 to April 2004), EMBASE (1980 to week 16, 2004), CINAHL (1982 to April 2004), PsycINFO (1974 to April 2004), citations from previous reviews and trials, and contacted expert informants.		
Intervention	1. Intervention: Home visits after birth 2. Control Group: No home visits		
Outcome and effect size	1. Home visits after birth versus no home visits a) Drug and alcohol related outcomes: • There were no significant differences in continued illicit drug use (2 studies, 248 women; relative risk (RR) =0.95, 95% CI [0.75|1.20]), • continued alcohol use (RR=1.08, 95% CI 0.83|1.41) • Failure to enroll in a drug treatment program (2 studies, 211 women; RR=0.45, 95% CI [0.10|1.94]). b) Pregnancy and puerperium outcomes: • As no study provided a significant antenatal intervention, the risk of adverse pregnancy and delivery outcomes were not reported. c) Infant/child outcomes: • There was no significant difference in the Bayley MDI (3 studies, 199 infants; weighted mean difference (WMD)=2.89, 95% CI [-1.17|6.95]) • or Psychomotor Index (WMD=3.14, 95% CI [-0.03|6.32]). • Other outcomes reported by one study only included breastfeeding at six months (RR=1.00, 95% CI 0.81|1.23), incomplete six-month infant vaccination schedule (RR=1.07, 95% CI [0.58|1.96]), non-accidental injury and non-voluntary foster care (RR=0.16, 95% CI [0.02|1.23]), failure to use postpartum contraception (RR=0.41, 95% CI [0.20|0.82]), child behavioural problems (RR=0.46, 95% CI [0.21|1.01]), and involvement with child protective services (RR=0.38, 95% CI [0.20|0.74]). Authors' conclusions: A review of trials found evidence that home visits after the birth increased the engagement of these women in drug treatment services but there were insufficient data to say if this improved the health of the baby or mother. Further research is needed, with visits starting during pregnancy. There is insufficient evidence to recommend the routine use of home visits for women with a drug or alcohol problem. Further large, high-quality trials are needed, and women's views on home visiting need to be assessed.		
Comments	• Studies are relatively small, with many studies also having large losses to follow-up. • None provided a significant antenatal component of home visits. • The visitors included community health nurses, paediatric nurses, trained counsellors, paraprofessional advocates, midwives and lay African-American women. Subgroup analyses performed: • timing of intervention: pregnancy (early and late), after birth, pregnancy and period after birth; • duration of intervention (e.g. less than six months; at least six months); • intensity or frequency of intervention • person/s doing the visit: team or individual social worker, counsellor, nurse, or trained lay		

	worker; • content of visits: such as pregnancy care, drug and alcohol interventions, counselling, parent craft, life skills etc., non-judgemental and supportive versus directive; • effect of modifying factors: such as alcohol problem and/or methadone stabilised, methadone and continued drug abuse, heroin abuse, polydrug abuse or other drug abuse co-existence of domestic violence or mental illness, partner with partner with drug or alcohol problem, separation of infant from mother
References	Black 1994, Butz 1998, Dakof 2003, Grant 1996, Quinlivan 2000; Schuler 2000

Title	**Motivational interviewing for substance abuse.**		
First Author	**Smedslund, G., 2011**	**Source**	**21563163**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	57 studies were RCTs, and two studies were quasi-RCTs with a total of 13.342 persons dependent or abusing substance. Only studies were included that had checked video or sound recordings of the therapies in order to be certain that what was given really was MI. Search in 18 electronic databases, 5 web sites, 4 mailing lists, and reference lists from included studies and reviews. Search dates were November 30, 2010 for Cochrane Library, Medline, Embase and PsychINFO.		
Intervention	1. Interventions: MI or motivational enhancement therapy (typically lasting for 1-4 sessions) 2. Control Group: No-treatment control; treatment as usual, assessment and feedback, other active treatment. Within each category, computed meta-analyses were made separately for post-intervention, short, medium and long follow-ups.		
Outcome and effect size	1. MI versus no-treatment control: Compared to no treatment control MI showed a significant effect on substance use which was strongest at post-intervention SMD=0.79, (95% CI [0.48|1.09]) and weaker at short SMD=0.17 (95% CI [0.09|0.26]], and medium follow-up SMD=0.15 (95% CI [0.04|0.25]). For long follow-up, the effect was not significant SMD=0.06 (95% CI [-0.16|0.28]). 2. MI versus treatment as usual: There were no significant differences for either follow-up post-intervention, short and medium follow up. 3. MI versus assessment and feedback: MI did better for medium follow-up SMD=0.38 (95% CI [0.10|0.66]). For short follow-up, there was no significant effect. 4. MI versus other active interventions: There were no significant effects for either follow-up. There was not enough data to conclude about effects of MI on the secondary outcomes. Authors' conclusions: MI can reduce the extent of substance abuse compared to no intervention. However, it seems that other active treatments, treatment as usual and being assessed and receiving feedback can be as effective as motivational interviewing. There was not enough data to conclude about the effects of MI on retention in treatment, readiness to change, or repeat convictions. The evidence is mostly of low quality, it forces us to be careful about our conclusions. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.		
Comments	• For 29 studies the allocation generation method is unclear. • A minority of 2 studies have not used adequate generation of allocation. • For most of the studies there is an inadequate description of what, if anything, was done to conceal the allocation (n=50) and were therefore judged as having unclear risk of bias. • In psychological therapies like MI, it is not possible to blind the people giving the intervention. • It is also not generally possible to blind the participants • In 27 of the 59 studies we believe that there was a high risk of bias because participants and/or providers knew who were in the intervention group. • In the majority of studies (n=31) it was unclear whether the assessors were blinded. In 22		

	studies the assessors appear to have been adequately blinded.
References	Adamson 2008, Anton 2005, Baros 2007, Baker 2009, Ball 2007a, Ball 2007b, Barnett 2007, Bauer 2007, Bazargan-Hejazi 2005, Bell 2007, Bernstein 2009, Bien 1993, Borsari 2005, Brown 2010, Capone 2009, Carey 2006, Carroll 1998, Carroll 2006a, Carroll 2006b, Carroll 2009, Chanut 2007, Connors 2002, Copeland 2001a, Copeland 2001b, D'Amico 2008, De Wildt 2002, Emmen 2005, Feldstein 2007, Freyer-Adam 2008, Gordon 2003, Kadden 2007, Litt 2005, Litt 2008, Kahler 2004, Kavanagh 2004, Kay-Lambkin 2009, Kelly 2000, Maisto 2001, Marijuana TP 2004, Marsden 2006, Martin 2008, Martino 2006, Mastroleo 2010, MATCH 1993, MATCH 1997, MATCH 1998a, MATCH 1998b, MATCH 1998c, MATCH 1998d, McCambridge 2008, Miller 2003, Morgenstern 2009, Naar-King 2006a, Naar-King 2006b, Naar-King 2006c, Naar-King 2007, Olmstead 2007, Orford 2009a, Orford 2009, Parsons 2009,Peterson 2006, Rohsenow 2004, Saitz 2007, Schaus 2009, Sellman 2001, Stein 2002, Stein 2009, Stein 2010, Stephens 2007, Stern Stotts 1997, Stotts 1999, Stotts 2001, Stotts 2006, Thevos 2001, Thush 2009, Tonigan 2002, UKATT 2005a, UKATT 2005b, UKATT 2008, Villanueva 2007, Walitzer 2008, Walker 2006, Walters 2009, White 2006, Winhusen 2008, Winters 2007, Wood 2007, Wu 2008, Zywiak 2002

Title	**Milk thistle for alcoholic and/or hepatitis B or C virus liver diseases.**		
First Author	**Rambaldi, A., 2005**	**Source**	**17943794**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	13 randomised clinical trials assessed milk thistle in 915 patients with alcoholic and/or hepatitis B or C virus liver diseases. Search in: The Cochrane Hepato-Biliary Group Controlled Trials Register, The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and full text searches were combined (December 2003).		
Intervention	Experimental Intervention: Milk thistle or milk thistle constituents Control intervention: Placebo; no intervention		
Outcome and effect size	1. Methodological Quality: The methodological quality was low: only 23% of the trials reported adequate allocation concealment and only 46% were considered adequately double-blinded. 2. Experimental intervention vs. control intervention: a.) Milk thistle versus placebo or no intervention had no significant effect on mortality (RR=0.78, 95% CI [0.53|1.15]), complications of liver disease (RR=0.95, 95% CI [0.83|1.09]), or liver histology. b.) Liver-related mortality was significantly reduced by milk thistle in all trials (RR=0.50, 95% CI [0.29|0.88]), but not in high-quality trials (RR=0.57, 95% CI [0.28|1.19]). c.) Milk thistle was not associated with a significantly increased risk of adverse events (RR=0.83, 95% CI [0.46|1.50]). 3. Authors' conclusions: Our results question the beneficial effects of milk thistle for patients with alcoholic and/or hepatitis B or C virus liver diseases and highlight the lack of high-quality evidence to support this intervention. Adequately conducted and reported randomised clinical trials on milk thistle versus placebo are needed.		
Comments	Included studies are rather old (1980-2002).		
References	Bunout 1992, Buzzelli 1993, Buzzelli 1994, Fehér 1989, Ferenci 1989, Fintelmann 1980, Láng 1990, Lirussi 2002, Lucena 2002, Magliulo 1978, Parés 1998, Salmi 1982, Salvagnini 1985, Trinchet 1989, Velussi 1997		

Title	**Opioid antagonists for alcohol dependence**		
First Author	**Rösner, S., 2010**	**Source**	**21154349**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	50 RCTs with 7.793 patients Search in: Cochrane Drugs and Alcohol Group (CDAG) Specialized Register, PubMed, EMBASE and CINAHL until January 2010.		

Intervention	Experimental Intervention: • Naltrexone • Injectable naltrexone • Naltrexone in combination with other pharmaceutical interventions Control intervention: Placebo, other pharmaceutical interventions
Outcome and effect size	1. Naltrexone vs. placebo: a) Naltrexone reduced the risk of heavy drinking to 83% of the risk in the placebo group RR=0.83 (95% CI [0.76|0.90]) and decreased drinking days by about 4%, MD=-3.89 (95% CI [-5.75|-2.04]). b) Significant effects were also demonstrated for the secondary outcomes of the review including heavy drinking days, MD=-3.25 (95% CI [-5.51|-0.99]), consumed amount of alcohol, MD=-10.83 (95% CI [-19.69|-1.97]) and gamma-glutamyltransferase, MD=-10.37 (95% CI [-18.99|-1.75]). Side effects of naltrexone were mainly gastrointestinal problems (e.g. nausea: RD=0.10; 95% CI [0.07|0.13]) and sedative effects (e.g. daytime sleepiness: RD=0.09; 95% CI [0.05|0.14]). 2. Injectable naltrexone: a) Subgroup analyses of extended-release formulations of naltrexone compared to placebo indicate that injected naltrexone reduced the risk of any drinking after detoxification to 92% of the placebo group RR=0.92 (95% CI [0.84|1.00]), the percentage of drinking days by about 9% MD=-8.54 (95% CI [-15.77|-1.31]), and the percentage of heavy drinking days by about 3% M=-3.05 (95% CI [-8.46|2.35]). b) Extended-release naltrexone caused significantly more often daytime sleepiness than placebo RD=0.22 (95% CI [0.02|0.42]), decreased appetite RD=0.08 (95% CI [0.04|0.11]), dizziness RD=0.08 (95% CI [0.04|0.12]), fatigue RD=0.06 (95% CI [0.01|0.10]), and vomiting RD=0.06 (95% CI [0.02|0.11]). c) Early drop-out due to side effects were more frequent in the extended-release naltrexone group than in the placebo group RR=1.57 (95% CI [0.92|2.69]), while the risk of dropping out irrespective of reasons slightly differed between injectable naltrexone 3. Naltrexone vs. acamprosate: a) Results from 3 clinical trials did not indicate a significant difference between both substances in any of the primary outcomes. b) For the risk to return to heavy drinking RR=0.96 (95% CI [0.87|1.06]), the risk to return to any drinking RR=0.97 (95% CI [0.91|1.04]) a non-significant trend favouring naltrexone compared to acamprosate was found. In contrast, drinking days were non-significantly higher under naltrexone compared to acamprosate MD=3.06 (95% CI [-7.42|13.53]). Naltrexone was associated with a higher risk of nausea RD=0.08 (95% CI [0.03|0.13]) and somnolence RD=0.07 (95% CI [0.01 to 0.13]) compared to acamprosate, while acamprosate caused more often diarrhoea RD=-0.27 (95% CI [-0.34|-0.20]). c) Naltrexone had a 31% higher risk of terminating the study early because of adverse events than acamprosate RR=1.31 (95% CI [0.63|2.73]). In contrast, the risk of dropping out from a study irrespective of drop-out reasons was 8% lower in the naltrexone than in the acamprosate RR=0.92 (95% CI [0.77|1.10]). 4.) Naltrexone versus apripiprazole, nefazodone or topiramate: a) Summarized effects for naltrexone versus aripiprazole, nefazodone and the anticonvulsant topiramate, based on one study at a time, showed a non-significant superiority of active control compared to naltrexone. b) The only side-effects, which significantly differed between groups was decreased appetite and insomnia, which were documented more frequently in the naltrexone than in the nefazodone group (decreased appetite: RD=0.22; 95% CI [0.07|0.38]; NNTH=4.54; insomnia: RD=0.23; 95% CI [0.06|0.41]; NH=4.35). c) Drop-out risks were 4%, 51% and 12% higher under naltrexone than aripiprazole (RR=1.04; 95% CI [0.42|2.57]), nefazodone (RR=1.51; 95% CI [0.90|2.53]) and topiramate (RR=1.12; 95% CI [0.68|1.83]). 5. Naltrexone + acamprosate versus placebo: a) The combination of naltrexone and acamprosate, tested in two RCTs was shown to

	reduce the risk to return to heavy drinking and to any drinking by about 30% (heavy drinking: RR=0.71; 95% CI [0.38|1.35]; any drinking: RR=0.70; 95% CI [0.35|1.39]) compared to placebo; drinking days were lowered by two percent (MD=-2.20; 95% CI [6.30|1.90]) and GGT values by about nine units per liter(MD=-8.70; 95% CI [-24.86|7.46]). None of the effects reached statistical significance. b) Compared to placebo, the combined therapy with naltrexone and acamprosate caused significantly more often decreased appetite (RD=0.11; 95% CI [0.05|0.17]; NNTH=9.09), diarrhea (RD=0.20; 95% CI [0.13|0.27]; NNTH=5), nausea (RD=0.20; 95% CI [0.14|0.26]; NNTH=5) and vomiting (RD=0.09; 95% CI [0.03|0.14]; NNTH=11.1). The risk to drop-out due to adverse events was higher in the combined therapy group than in the placebo group (RR=3.75; 95% CI [1.33|10.55]), while the risk of dropping out irrespective of reasons was higher in the placebo group (RR=0.83; 95% CI [0.28|2.49]). <u>6. Naltrexone + acamprosate versus naltrexone</u> a) When compared to naltrexone alone, effects of combined treatment with naltrexone and acamprosate turned out be lower in their magnitude than compared to placebo for most outcomes: The risk reduction for return to heavy drinking was 3% (RR=0.97; 95% CI [0.75|1.26]), for any drinking 12% (RR=0.88; 95% CI [0.61|1.28]), while drinking days were decreased by about 1% (MD=-1.10; 95% CI [-5.21|3.01]). None of the primary outcomes reached statistical significance. A significant effect was demonstrated for the GGT, assessed in one trial only, which was lower in the naltrexone than in the combined treatment group (MD=10.7; 95% CI [1.87|19.93]). b) The combination of acamprosate and naltrexone induced significantly more often diarrhea (RD=0.37; 95% CI [0.10|0.65]; NNTH=2.70) and nausea (RD=0.09; 95% CI [0.02|0.16]; NNTH=11.1) than naltrexone alone. The risk of dropping out because of side effects (RR=1.07; 95% CI [0.55|2.08]) and the risk of terminating the study early irrespective of reasons (RR=1.03; 95% CI [0.95|1.43]) were non-significantly higher in the combined treatment group than in the naltrexone group. <u>7. Naltrexone + ondansetrone / sertraline versus placebo</u> a) Combinations of naltrexone with either ondansetrone or sertraline have both been shown to significantly reduce drinking days and consumed amount per drinking day: In the trial with ondansetron, patients drank alcohol on about 25% days less than those treated with placebo (MD=-23.80; 95% CI [-58.13|10.53]); in the trial with sertraline, the effect was lower (MD=-10.6; 95% CI [-12.06|-9.14]), but reached statistical significance. The same applies to consumed amount per drinking day, which reduced at about 50grams in the ondansetron trial (MD=-50.70; 95% CI [-81.53|-19.87]) and 28grams in the sertraline trial (MD=-10.6; 95% CI [-12.06|-9.14]) in comparison to placebo. b) For the combination with sertraline, a significant effect was also demonstrated on heavy drinking days (MD=-8.20; 95% CI [-9.61|-6.79]). c) Sertraline was associated significantly more often with sleepiness (RR=0.40; 95% CI [0.18|0.62]), nausea (RR=0.29; 95% CI [0.06|0.51]) and dizziness (RR=0.25; 95% CI [0.03|0.47]). <u>8. Nalmefene versus placebo Treatment phase</u> a) None of the effects reached statistical significance. <u>9. Effects of industry-sponsored studies</u>, RR=0.90 (95% CI [0.78|1.05]) did not significantly differ from those of non-profit funded trials, RR=0.84 (95% CI [0.77|0.91]) and the linear regression test did not indicate publication bias (p=0.765). <u>Authors' conclusions</u> Naltrexone appears to be an effective and safe strategy in alcoholism treatment. Even though the sizes of treatment effects might appear moderate in their magnitudes, these should be valued against the background of the relapsing nature of alcoholism and the limited therapeutic options currently available for its treatment.
Comments	Various features of the study design, which have been implemented in the naltrexone and nalmefene trials included in the review, ensure a high methodological quality of the primary database.

References	Ahmadi 2002, Anton 1999, Anton 2004, Anton 2005, Anton 2006, Auriacombe 2000, Balldin 2003, Baltieri 2008, Brown 2009, Chick 2000, de Goes e Castro 2004, Galarza 1997, Garbutt 2005, Gastpar 2002, Guardia 2002, Heinälä 2001, Hersh 1998, Huang 2005, Johnson 2000, Johnson 2004, Kiefer 2003, Killeeen 2004, Kranzler 1998, Kranzler 2000, Kranzler 2004, Krystal 2001, Latt 2002, Lee 2001, Martinotti 2008, Mason 1994, Mason 1999, Monterosso 2001, Monti 2001, Morley 2006, Morris 2001, O'Malley 1992, O'Malley 2007, O'Malley 2008, Oslin 1997, Oslin 2005, Oslin 2008, Petrakis 2004, Petrakis 2005, Pettinati 2008a, Pettinati 2008b, Schmitz 2004, Schmitz 2009, Volpicelli 1992, Volpicelli 1997, ZióÅ,kowski 2000

Title	**Psychosocial interventions for women enrolled in alcohol treatment during pregnancy**		
First Author	**Lui, S., 2008**	**Source**	**18646166**
Level of evidence	n.a.	**Study type**	Systematic Review
Study information	No article met the inclusion criteria. Search in the Cochrane Drugs and Alcohol Group's Trial register (December 2007); MEDLINE (1950-2007); PsychINFO (1806 to 2007); EMBASE (1974 to 2007); CINAHL (1982-2007)		
Intervention	1. Intervention: Any psychosocial intervention 2. Control group: Pharmacological interventions or placebo or non-intervention or another psychosocial intervention for treating alcohol dependence in pregnancy		
Outcome and effect size	Results: The search strategy identified 958 citations. 17 citations were deemed relevant for full text review, an additional 9 articles were retrieved through hand searching references, for a total of 26 articles. Following full text review no articles met the inclusion criteria. Data extraction and assessment of methodological quality were therefore not possible. Authors' conclusions: The review question remains unanswered as there were no randomised control trials found relevant to the topic. There is a need for high quality randomised controlled trials to determine the effectiveness of psychosocial interventions in pregnant women enrolled in alcohol treatment programs.		
Comments	n.a.		
References	n.a.		

Title	**Psychological and/or educational interventions for reducing alcohol consumption in pregnant women and women planning pregnancy**		
First Author	**Stade, B. C., 2009**	**Source**	**19370597**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	Four RCTs (715 women Who were less than 28 weeks pregnant and who were consuming some alcohol) Search in: The Cochrane Pregnancy and Childbirth Group's Trials Register (August 2008), CENTRAL (The Cochrane Library 2007, Issue 4), MEDLINE (1966 to November 2007), EMBASE (1980 to November 2007), CINAHL (1982 to November 2007), Counsel.Lit (1980 to November 2007), PsychLIT (1974 to November 2007) and PsychINFO (1967 to November 2007) and check for cited references from retrieved articles		
Intervention	1. Intervention: Psychological and educational interventions (ranging from a 10-minute education session and provision of a self-help-manual through to an hour-long motivational interview with reinforcement at each prenatal visit) for reducing consumption of alcohol among pregnant women, or women planning for pregnancy. 2. Control group: Women in the control groups generally received routine care, which may have included advice on reducing alcohol		
Outcome and effect size	1. Psychological and/or educational interventions versus control group: Results from individual studies suggest that interventions may encourage women to abstain from alcohol in pregnancy. There was very little information provided on the effects of interventions on the health of mothers and babies.		

	Authors' conclusions: The evidence from the limited number of studies suggests that psychological and educational interventions may result in increased abstinence from alcohol, and a reduction in alcohol consumption among pregnant women. However, results were not consistent, and the paucity of studies, the number of total participants, the high risk of bias of some of the studies, and the complexity of interventions limits our ability to determine the type of intervention which would be most effective in increasing abstinence from, or reducing the consumption of, alcohol among pregnant women.
Comments	• No meta-analysis was performed as the interventions and outcomes measured in the studies were not sufficiently similar. • For most outcomes there were no significant differences between groups; and results relating to abstaining or reducing alcohol consumption were mixed. • All studies were carried out in the USA.
References	Chang 1999, Handmaker 1999a, O'Connor 2007, Reynolds 1995

Title	**Psychotropic analgesic nitrous oxide for alcoholic withdrawal states**		
First Author	**Gillmann, M. A., 2007**	**Source**	**17443576**
Level of evidence	Ia	**Study type**	Systematic Review
Study information	5 RCTs, 212 participants, were included. Search in: Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 2, 2005), MEDLINE, EMBASE, CINAHL (all to May 2005)		
Intervention	Experimental intervention: PAN Control intervention: Oxygen (placebo) and/or benzodiazepine regimens		
Outcome and effect size	1. Improvement of scores as measured on a modified Gross Scale: PAN showed improvement of symptoms (RR=1.35; 95% CI 1.01|1.79), of the amount and duration of sedative medication and of psychomotor function (WMD=-8.71; 95% CI -13.71|-3.71). 2. Improvement of depression and anxiety: At one hour post intervention, no significant differences were found for depression (WMD=-2.40; 95% CI -8.70|3.89) and anxiety (WMD=-3.70; 95% CI -10.53|3.12). 3. Adverse effects: None of the included studies reported any significant adverse effects of any treatment Authors' conclusions: Results indicate that PAN may be an effective treatment of the mild to moderate alcoholic withdrawal state. The rapidity of the therapeutic effect of PAN therapy coupled with the minimal sedative requirements, may enable patients to enter the psychological treatment phase more quickly than those on sedative regimens, accelerating the patients' recovery. Our review does not provide strong evidence due to the small sample sizes of the included trials. Neither does the review indicate any causes for concern that PAN is more harmful than the benzodiazepines. Clinicians wishing to use PAN may initially wish to do so within trial settings. Further high quality trials should be done to confirm these findings and to investigate whether the PAN therapy has fewer adverse effects than other treatments for the alcohol withdrawal states. Studies to investigate the possible cost-effectiveness of PAN by reducing costly hospital admissions and decreasing post administration supervision also need to be performed.		
	The review does not provide strong evidence due to the small sample sizes of the included trials. Limitations • Two studies published in journals and three dissertations were included. • All studies were conducted in South Africa and only included male, mainly white, participants. • Studies are old, have small sample sizes • Allocation concealment was unclear or not reported • Due to the difference between measured outcomes in each trial, it was not possible to conduct meta-analyses for most outcomes		
References	De Rooster 1983, Fey 1993, Gillman 1986a, Gillman 2004, Janks 1994		

Title	**Efficacy and safety of pharmacological interventions for the treatment of the Alcohol Withdrawal Syndrome**		
First Author	**Amato, L., 2011**	**Source**	**21678378**
Level of evidence	Ib	**Study type**	Systematic Review
Study information	5 reviews, 114 studies, 7333 participants Search in the Cochrane Database of Systematic Reviews (30 November 2010). Two authors independently screened, extracted data, summarised key characteristics of the included reviews and assessed their quality using AMSTAR; the quality of the evidence was summarised according to the GRADE methodology.		
Intervention	Experimental intervention: Benzodiazepines, anticonvulsants, Baclofen, GHB and PAN (psychotropic analgesic nitrous oxide) Control intervention: Placebo; other drugs		
Outcome and effect size	Experimental intervention: Benzodiazepines, anticonvulsants, Baclofen, GHB and PAN (psychotropic analgesic nitrous oxide) Control intervention: Placebo; other drugs when compared to placebo and a potentially protective benefit for many outcomes when compared with antipsychotics. Nevertheless, no definite conclusions about the effectiveness and safety of benzodiazepines were possible, because of the heterogeneity of the trials both in interventions and in the assessment of outcomes. Data on potential harms are sparse and fragmented. Results do not provide sufficient evidence in favour of anticonvulsants for the treatment of AWS, but anticonvulsants seem to have limited side effects. There is also not enough evidence of effectiveness and safety of baclofen, because only one study consider this treatment and of GHB for which no strong differences were observed in the comparisons with placebo, benzodiazepines and anticonvulsants.		
Comments	Heterogeneity of the trials in patient populations (age, gender, nationality, severity of symptoms, treatment setting,) interventions and in the assessment of outcomes		
References	Amato 2010, Gillman 2007, Leone 2010, Liu 2011, Minozzi 2010		

Title	**Pharmacologic Interventions for Pregnant Women Enrolled in Alcohol Treatment**		
First Author	**Smith, E. J., 2009**	**Source**	**19588428**
Level of evidence	n.a.	**Study type**	Systematic Review
Study information	No studies could be included Search in: Cochrane Drugs and Alcohol Group's Trial register (August 2008), MEDLINE (1.1950|6.2008), EMBASE (1.1974-8.2008); CINAHL (1.1982-6.2008); PsycInfo (1.1806-6.2008), and reference lists of articles.		
Intervention	Experimental condition: Pharmacologic intervention Control condition: Other pharmacologic treatment alone or in association with psychosocial treatment, placebo, non-intervention or psychosocial intervention.		
Outcome and effect size	Following full text review no articles met the inclusion criteria. Data extraction and assessment of methodological quality were therefore not possible. Authors' conclusions: The review question remains unanswered as there were no randomised control trials found relevant to the topic. There is a need for high quality research to determine the effectiveness of pharmacologic interventions in pregnant women enrolled in alcohol treatment program.		
Comments	Thirty-one of the retrieved for full text review were excluded because they were not the correct study design. A majority of the articles we found described cohorts, case series or case reports concerning the effects of drinking or pharmacologic interventions on the foetus. Many articles did not provide a control group with which to compare the results. Other articles were excluded because they were review articles. The references of these articles were searched for potentially relevant articles. Some of these reviews explained the limitations in implementing drug trials in pregnant women.		
References	No studies included.		

Title	S-adenosyl-L-methionine for alcoholic liver diseases		
First Author	Rambaldi, A., 2006	Source	16625556
Level of evidence	Ia	Study type	Systematic Review
Study information	9 RCTs with 434 patients with alcoholic liver diseases. Search in The Cochrane Hepato-Biliary Group Controlled Trials Register (May 2005), The Cochrane Central Register of Controlled Trials in The Cochrane Library (Issue 2, 2005), MEDLINE (1950 to May 2005), EMBASE (1980 to May 2005), and Science Citation Index Expanded (searched May 2005). (Mai 2005).		
Intervention	Experimental intervention: S-adenosyl-L-methionine (SAMe) Control intervention: Placebo; other pharmacological interventions [Other interventions allowed if applied in both groups]		
Outcome and effect size	1. No significant effects of SAMe on: • All-cause mortality (RR=0.62, 95% CI [0.30|1.26]), • Liver-related mortality (RR=0.68, 95% [CI 0.31|1.48]), • All-cause mortality or liver transplantation (RR=0.55; 95% CI [0.27|1.09]), or complications (RR=1.35, 95% CI [0.84|2.16]). The analysis is based mostly on one trial only. 2. Adverse effects: SAMe was not significantly associated with non-serious adverse events (RR=4.92; 95% CI [0.59|40.89]) and no serious adverse events were reported. Authors' conclusions We could not find evidence supporting or refuting the use of SAMe for patients with alcoholic liver diseases. We need more long-term, high-quality randomised trials on SAMe for these patients before SAMe may be recommended for clinical practice.		
Comments	The methodological quality regarding randomisation was generally low, but 8 out of 9 trials were placebo controlled. Only one trial including 123 patients with alcoholic cirrhosis used adequate methodology and reported clearly on all-cause mortality and liver transplantation. Heterogeneity in patient populations. Studies are rather old.		
References	Altomare 1988, Chawla 1999, Cibin 1988, Corrales 1991, Diaz Belmont 1996, Loguercio 1994b Mato 1999b, Trespi 1997, Vendemiale 1989b,		

Title	Social norms interventions to reduce alcohol misuse in University or College students		
First Author	Moreira, M. T., 2009	Source	19588402
Level of evidence	Ia	Study type	Systematic Review
Study information	Twenty-two RCTs or cluster RCTs (7.275 participants). Search in: Cochrane Drugs and Alcohol Group Register of Trials; Central; MEDLINE; EMBASE; PsyInfo; CINAHL (up to March 2008).		
Intervention	1. Intervention: a) Universal personalized normative feedback to individuals, where all students are asked to participate regardless of drinker status or risk level b) Targeted interventions focusing on members of a particular group, such as first-year students, fraternity and sorority members, athletes, members of an academic class, or individuals who are deemed to be at higher risk of alcohol problems c) Social Norms Marketing Campaigns, e.g. community-wide electronic and/or print media campaigns that refer to normative drinking patterns. 2. Control intervention: No social norms intervention, assessment only, questionnaire used to measure alcohol consumption or alternative educational or psychosocial intervention assessment only, questionnaire used to measure alcohol consumption or alternative educational or psychosocial intervention		
Outcome and effect size	1. Alcohol related problems: Significant reduction with Web/computer feedback (WF) (SMD=-0.31, 95% CI [-0.59|-0.02]), three studies, 278 participants. No significant effect of mailed feedback (MF), individual face-to-face feedback (IFF) or group face-to-face feedback (GFF). 2. Peak Blood Alcohol Content (BAC): Significant reduction with WF (SMD=-0.77, 95% CI [-1.25|-0.28]), two studies, 198		

	participants. No significant effect of MF or IFF. 3. Drinking Frequency: Significant reduction with WF (SMD=-0.38, 95% Cl [-0.63|-0.13]), two studies, 243 participants and IFF (SMD=-0.39, 95% Cl [-0.66|-0.12]), two studies, 217 participants. No significant effect of MF. 4. Drinking Quantity: Significant reduction with WF (SMD=-0.35, 95% Cl [-0.51|-0.18]), five studies, 556 participants and GFF (SMD=-0.32, 95% Cl [-0.63|-0.02 9) three studies, 173 participants. No significant effect of MF or IF. 5. Binge drinking: Significant reduction with WF (SMD=-0.47, 95% Cl [-0.92|-0.03]) one study, 80 participants, IFF (SMD=-0.25, 95% Cl [-0.49|-0.02]) three studies, 278 participants and GFF (SMD=-0.38, 95% Cl [-0.62|-0.14]) four studies, 264 participants. No significant effect for MF. BAC: No significant effect of MF and IFF 6. Drinking norms: Significant reduction with WF (SMD=-0.75, 95% Cl [-0.98|-0.52]) three studies, 312 participants. Authors' conclusions: WF and IFF are probably effective in reducing alcohol misuse. No direct comparisons of WF against IFF were found, but WF impacted across a broader set of outcomes and is less costly so therefore might be preferred. Significant effects were more apparent for short-term outcomes (up to three months). For mailed and group feedback, and social norms marketing campaigns, the results are on the whole not significant and therefore cannot be recommended.
Comments	Several sources of potential bias in the individual studies were detected: • lack of blinding of students or researchers, • use of self-reported outcome measures. Only a few studies reported how important aspects of study design were conducted, such as concealment of treatment allocation and handling of missing data, making it difficult to assess the risk of bias. Lack of adequate allocation concealment, blinding and analysis is associated with overestimation of intervention effects, and therefore we cannot rule out the possibility that the effects observed in this review may be exaggerated due to methodological limitations
References	Baer 2001, Borsari 2000, Borsari 2005, Carey 2006, Collins 2002, DeJong 2006, DeJong 2008, Juárez 2006, Kypri 2004, Kypri 2005, Kypri 2008, Lewis 2007a, Lewis 2007a, Female Lewis 2007a, Male Lewis 2007b, Marlatt 1998, McNally 2003, Michael 2006, Murphy 2001, Neal 2004, Neighbors 2006, Walters 2000, Walters 2007, Werch 2000

Title	**Thiamine for Wernicke-Korsakoff Syndrome in people at risk from alcohol abuse**		
First Author	**Day, E., 2004**	**Source**	**14974055**
Level of evidence	Ib	**Study type**	Systematic Review
Study information	1 RCT with 107 participants Search in: The Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG), The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS were searched on 22 January 2008 using the terms: thiamin* OR aneurin*. The CDCIG Specialized Register contains records from all major health care databases (The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS) The search in August 2005 retrieved no new studies for inclusion; the latest search of January 2008 retrieved one possible study for inclusion, which was excluded.		
Intervention	Experimental Intervention: 1. Thiamine or thiamine-containing products at any dose and in any formulation (oral, intramuscular or intravenous) Control intervention: Placebo, other interventions or no treatment		
Outcome and effect size	1. Comparison of five doses of intramuscular thiamine and measurement of outcomes after 2 days of treatment. • Lowest dose (5mg/day) was compared with each of the other four doses. There was a		

	significant difference in favour of the 200mg/day compared with the 5mg/day dose in the number of trials taken to reach criterion on a delayed alternation test (MD=-17.90, 95% CI [-35.4|-0.40], p=0.04). No significant differences emerged in comparing the other doses with 5mg/day. • The pattern of results did not present a simple dose-response relationship. The study had methodological shortcomings in design and the presentation of results that limited further analysis. <u>Authors' conclusions</u> There is insufficient evidence from randomized controlled clinical trials to guide clinicians in the dose, frequency, route or duration of thiamine treatment for prophylaxis against or treatment of WKS due to alcohol abuse.
Comments	2 studies met the inclusion criteria for the review, one of which was unpublished. They involved a total of 177 participants, and both were randomized double-blind placebo-controlled trials. However, one study was very small (n=8) and contained insufficient data for quantitative analysis. <u>Risk of bias</u> • Method used to generate random allocation is not reported. • Both studies were described as double-blind, but neither of the reports described precautions taken to minimize detection bias. • Unclear losses to follow up • Relatively small size of each treatment group, •High rate of non-completion
References	Ambrose, 2001 Nichols, unpublished

Tabellenband

Evidenztabellen der PubMed-Recherche

2. Screening und Diagnostik

Title	Alcohol Biomarker Screening in Medical and Surgical Settings		
First Author	Miller, P. M., 2006	Source	16441267
Level of evidence	3a	Study type	Review on alcohol use biomarkers
Study quality	Sensitivity and specificity of CDT, GGT, MCV, alone and in combination with CAGE in GI tract cancer patients at admission, before surgery. No effect sizes, no overall evaluation of Sensitivity, specificity, pos. and neg. PV		
Participants			
Patient characteristics	Sensitivity of several markers in surgical, liver cirrhosis, patients Heavy alcohol consumption causes or aggravates many common medical conditions including hypertension (HTN), stroke, heart disease, pancreatitis, liver disease, oral cancer, and breast cancer.		
Intervention	Article highlights the proceedings of a symposium presented at the 28th Annual Meeting of the Research Society on Alcoholism in Santa Barbara, CA, on June 28, 2005.		
Comparison	n. a.		
Length of follow-up	Assessment perioperatively in surgical settings		
Outcome and effect size	Excessive drinking also contributes significantly to medical complications in trauma and surgical patients. GGT and %CDT and their combination, have been used in medical and surgical settings to detect heavy drinking, predict medical complications, and provide an objective risk factor for alcohol-related diseases (Miller, 2004; Miller et al., 2005). This symposium includes presentations on 4 recent studies examining the utility of alcohol biomarkers in different medical/surgical settings (i.e., primary health care, critical surgical care) and with different disease states (i.e., HTN, hepatitis C). The potential of alcohol biomarkers in enhancing the quality of medical care and reducing its cost will be discussed.		
Funding	RSA conference		
Comments	Selected review of authors, no systematic review		

Title	ROC analysis of alcoholism markers – 100% specificity		
First Author	Brinkmann, B., 2000	Source	11009066
Level of evidence	2b	Study type	Comparison of cohorts
Study quality	Moderate sample size; Males and females were investigated in all subgroups; assessment of a broad range of biomarkers, methods well-described; ROC-Analyses conducted		
Participants	341 blood samples from alcoholic s and nonalcoholic.		
Patient characteristics	Non-alcoholics divided into (A) 33 persons with no ethanol consumption during the past year and (B) 60 persons with daily consumption less than 40 g ethanol. Alcoholics were divided into (C) 177 persons with no ethanol at the time of admission/first blood sampling (withdrawal therapy) and (D) 71 persons with positive ethanol levels on admission / first blood sampling.		
Intervention	Measure of Methanol (MeOH), Sum of acetone + 2-propanol (A + 2P), G-Glutamyltransferase (G-GT),Carbohydrate deficient transferrin (CDT) in “Alcoholics” Computation of Alc-Index=0.1121 × [MeOH] + 0.4082 × [A + 2P] + 0.0907 × [G-GT] + 0.1254 × [CDT] -7.7736		
Comparison	Nonalcoholics		
Length of follow-up	Cross-Sectional study??		
Outcome and effect size	All markers showed different extents of overlap between the collectives of alcoholics and nonalcoholics. By logistic regression, a formula was developed combining these markers with different mathematical weights. Thus an “Alc-Index” could be calculated for each individual. The ROC curve connecting all individual values gives an ideal form with 100% specificity and nearly 93% sensitivity. The threshold between the collectives of alcoholics and non-alcoholics was defined by the Alc-Index value 1.7. This was associated with no false positives among the nonalcoholics while nearly 93% of the alcoholics exceeded this index.		
Funding	This study was sponsored by the Bund gegen Alkohol und Drogen im Straßenverkehr e.V		

Comments	Overall, well-conducted study, Introduction of the “Alc-Index” (combination of 4 biomarkers).

Title	**Combining carbohydrate-deficient transferrin and gamma-glutamyltransferase to increase diagnostic accuracy for problem drinking**		
First Author	**Chen, J., 2003**	**Source**	**14633645**
Level of evidence	1a	**Study type**	Cohort study, group comparison
Study quality	Large international sample, subjects were well-defined. AUDADIS Interview. The algorithm derived by Sillanaukee and Olsson was tested and compared with new algorithms derived by logistic regression and discriminant analysis. ROC analyses conducted. Analyses controlled for sex and BMI.		
Participants	1684 subjects, WHO-ISBRA-study		
Patient characteristics	Alcohol-consuming individuals, international emergency room sample		
Intervention	Measurement for combining results of GGT, AST and CDT and lnCDT, lnGGT and lnAST		
Comparison	Non-drinkers, light/moderate drinkers (at least once per month and <210g/week for men, <140g/week for women), heavy drinkers (>210 g/week for men, >140g/week for women and no past treatment for an alcohol-related problem), and alcohol-dependent persons.		
Length of follow-up	Cross-sectional study		
Outcome and effect size	The results of our discriminant analysis support the findings of Sillanaukee and Olsson (2001) that using the levels of CDT and GGT in combination may provide a better indicator for the diagnosis of problem drinking (defined as consumption of >=60g ethanol per day), than either test alone. For men, combining lnCDT and lnGGT provided the best accuracy for detecting daily consumption of 60g ethanol or more in the past 30 days. For women, GGT alone provided the best accuracy for that consumption level. Clinical variables added significantly to the diagnostic accuracy of the models for both men and women, and conversely the test results modified the probability of problem drinking as assessed from clinical data alone. A graphic method was produced to help clinicians estimate probabilities for consumption of 60g or more per day. Conclusions: Combining biochemical markers enhances detection of problem drinking in men but not in women. Information on clinical variables increases the ability to correctly detect problem drinking.		
Funding	WHO/ISBRA study group member s: B. Tabakoff WHO support. The work was funded in Australia by the National Health and Medical Research Council.		
Comments	Large international sample, replication of previous results regarding combined measures (CDT and GGT combination, ALC-Index), gender-specific sensitivity/specificity analyses.		

Title	**Comparison of self-reports and biological measures for alcohol, tobacco, and illicit drugs consumption in psychiatric inpatients**		
First Author	**de Beaurepaire, R., 2007**	**Source**	**17596918**
Level of evidence	1b	**Study type**	Cohort study
Study quality	Biological measures (urine cotinine, cannabis, opiates, cocaine, amphetamines and barbiturates; blood carbohydrate-deficient transferrin [CDT] and gamma-glutamyl transferase [GGT])		
Participants	486		
Patient characteristics	Psychiatric inpatients: diagnostic groups according to primary diagnosis ‘‘Schizoph.’’: corresponding to the group ‘‘schizophrenia and other psychotic disorders’’ of the DSM-IV; ‘‘Mood disorders’’: corresponding to the group ‘‘mood disorders’’ of the DSM-IV; ‘‘Drinkers with problems’’: patients hospitalized for alcohol detoxification whatever the psychiatric comorbidities; ‘‘Personality disorders’’: personality disorders according to the DSM-IV; ‘‘Other’’: other patients.		
Intervention	Biological measures: urine cotinine, cannabis, opiates, cocaine, amphetamines and barbiturates; blood carbohydrate-deficient transferrin [CDT] and gamma-glutamyl transferase [GGT])		
Comparison	Self-reports (free interview)		
Length of follow-up	Cross-sectional study		

Outcome and effect size	The results show a low correlation between biological measures and self-reported consumption of alcohol and illicit drugs. Fifty-two percent of the patients under-reported their consumption of illicit drugs (kappa=.47). Patients with schizophrenia and personality disorders were more likely to disclose their illicit drug consumption relative to patients suffering from mood disorders and alcohol dependence. Fifty-six percent of patients underreported alcohol use, as evaluated by CDT (kappa=.2), and 37% underreported when using the CDT+GGT measure as an indicator. Smoking appeared to be reported adequately. In the study we observed a strong negative correlation between cannabis use and age, a strong correlation between tobacco and cannabis use, and correlations between tobacco, cannabis and alcohol consumption.
Funding	This work was supported by the MILDT (Mission interministérielle de lutte contre les drogues et la toxicomanie, Paris, France) and by the Ligue contre le cancer (Paris, France).
Comments	This study is the first to compare self-reports and biological measures of alcohol, tobacco and illicit drug uses in a large sample of inpatients suffering from various categories of psychiatric illnesses, allowing for cross-diagnosis comparisons. Screening for alcohol and substance use in psychiatric populations

Title	**Comparison of the combined marker GGT-CDT and the conventional laboratory markers of alcohol abuse in heavy drinkers, moderate drinkers and abstainers**		
First Author	**Hietala, J., 2006**	**Source**	**16799164**
Level of evidence	2b	**Study type**	Comparison of cohorts
Study quality	Patients well-characterized; moderate to small sample size; lab measures well conducted		
Participants	165 and 86 reference individuals		
Patient characteristics	165 heavy drinkers, consuming 40-540g of ethanol per day, and 86 reference individuals who were either moderate drinkers (n=51) or abstainers (n=35).		
Intervention	Measures of GGT–CDT and compare with the conventional markers of alcohol abuse including ASAT, ALAT, MCV in heavy drinkers.		
Comparison	Moderate drinkers or abstainers		
Length of follow-up	Cross-sectional study??		
Outcome and effect size	The sensitivity of GGT–CDT (90%) in correctly classifying heavy drinkers exceeded that of CDT (63%), GGT (58%), mean corpuscular volume (MCV) (45%), aspartate aminotransferase (AST) (47%), and alanine aminotransferase (ALT) (50%), being also essentially similar for alcoholics with (93%) or without (88%) liver disease.		
Funding	Not reported		
Comments	Well-conducted study, patient sample well-characterized; sensitivity reported also for subjects with and without liver disease.		

Title	**Combinations of carbohydrate-deficient transferrin, mean corpuscular erythrocyte volume, gamma-glutamyltransferase, homocysteine and folate increase the significance of biological markers in alcohol dependent patients**		
First Author	**Rinck, D., 2007**	**Source**	**17234365**
Level of evidence	1b	**Study type**	Cohort study
Study quality	good		
Participants	Group A: 177; Group B/ control group: 181		
Patient characteristics	Group A: 33 women, 144 men; fulfilled criteria for alcohol dependence according to ICD-10. Mean age 44. They were included at the day of admission to a closed detoxification unit. Group B: control group, social drinkers, volunteers, screened for alcohol consumption and alcohol drinking patterns using structured interview (FEG). None was drinking more than 30g ethanol per week. Mean age: 30 years		
Intervention	Blood samples: folate, GGT, plasma homocysteine, MCV, %CDT were analysed.		
Comparison	To advance the clinical diagnostic pattern of identifying alcohol dependent patients using a combination of established laboratory markers and new biomarkers for alcoholism.		
Length of follow-up	None		
Outcome and effect size	MCV: sensitivity 76% (95% CI [69|82]), specificity (95% CI [92.9|98.8]), Positive predictive value (PPV) 71.7% (95% CI [67|76.4]), Negative Predictive Value (NPV) 97.3%		

	CDT: sensitivity 84.4% (95% CI [78.2|89.3]), specificity 95% (CI 90.7|97.7]), PPV 65.2% (95% CI [60.3|70.1]), NPV 98.2% Homocysteine: sensitivity 67% (CI 59.6|73.9]), specificity 83.3% (95% CI [77.1|88.5]), PPV 30.9% (95% CI [26.1|35.7]), NPV 95.8% Folate: sensitivity 21.1%, (95% CI [15.5|28]), specificity 97.8% (95% CI [94.4|99.4]), PPV 51.5% (95% CI [46.3|56.7]), NPV 91.8% GGT: sensitivity 54.2% (95% CI [46.6|61.6]), specificity 92.8% (95% CI [88|96.1]), PPV 45.5% (95% CI [40.3|50.6]), NPV 94.8% Combination of different markers led to a significant elevation in sensitivity. Best value for men: combination of MCV, CDT, GGT and homofysteine, and folate has a sensitivity of 98.6% and a specificity of 86.4%. Best value for women: combination of MCV and CDT: sensitivity of 94.1% and specificity of 96%.
Funding	Support by a grant from Axis Shield, Norway.
Comments	Evaluation of combined markers in a moderate sample size, reports sensitivity and specificity measures.

Title	**Improved diagnostic classification of alcohol abusers by combining carbohydrate-deficient transferrin and gamma-glutamyltransferase**		
First Author	**Sillanaukee, P., 2001**	**Source**	**11274018**
Level of evidence	1b	**Study type**	Combination of several cohort studies alcohol abusers vs. social drinkers
Study quality	Six data sets based on clinical studies done in Germany (studies 1 and 4), Spain (study 2), France (study 3), Finland (study 5), and Japan (study 6). Large sample, males and females investigated; ROC analyses performed		
Participants	n=1412 from 6 studies		
Patient characteristics	An analysis of six different clinical studies on alcohol abusers and social drinkers.		
Intervention	Measurement of CDT, GGT, ASAT, ALAT, MCV, lnCDT, lnGGT, g-CDT=0.8 x ln(GGT) + 1.3 x ln(CDT) in “alcohol abusers”		
Comparison	Social drinkers		
Length of follow-up	Cross-sectional studies?		
Outcome and effect size	The total error rate among males and females was lowest for g-CDT. In the present study, the average sensitivity and specificity for males were, respectively, 75% and 93% for g-CDT, 58% and 94% for CDT, and 55% and 90% for GGT. The average sensitivity and specificity for females were, respectively, 68% and 96% for g-CDT, 40% and 94% for CDT, and 52% and 96% for GGT. This indicates a significant improvement in classification using only two markers. The sensitivity and specificity values are quite similar for GGT and CDT. Among subjects with liver disease, the specificity of the two markers is similar.		
Funding	Not reported		
Comments	Large international sample, ROC analysis indicating the strength of a combined measure.		

Title	**Biological markers of problem drinking in homeless patients**		
First Author	**Thiesen, H., 2010**	**Source**	**19917520**
Level of evidence	1b	**Study type**	Cohort study
Study quality	Concentrations of carbohydrate-deficient transferrin (%CDT), γ-glutamyl transferase (γGT), aspartate amino-transferase (ASAT), and mean corpuscular volume (MCV), together with a combined index of the %CDT and γGT, the Antilla Index (AI)		
Participants	104		
Patient characteristics	Homeless subjects with (n=87) or without (n=24) problem drinking according to the Fast Alcohol Screening Test.		
Intervention	“Alcohol problem”		
Comparison	“No alcohol problem”		
Length of follow-up			
Outcome and effect size	Concentrations of all markers were significantly higher in the alcoholic patients than in		

	other homeless patients. The best agreement between liver markers and self-reported status was found between the combined %CDT and γGT index (kappa=0.61, p<0.001, sensitivity=63%, specificity=94%).
Funding	The study was funded through intramural sources from the Centre for Alcohol and Drug Research under the University of Aarhus. The center is funded by the Danish government based on five-year grants from the Danish National Budget.
Comments	The combined AI is a relatively efficient measure of current drinking in homeless populations.

Title	**Biochemical measures in the diagnosis of alcohol dependence using discriminant analysis**		
First Author	**Vaswani, M., 2005**	**Source**	**16272676**
Level of evidence	2b	**Study type**	Cohort case control study
Study quality	Statistics: sensitivity, specificity, positive, negative predictive value, discriminant analysis		
Participants	100 subjects with alcohol dependence vs. 70 healthy controls		
Patient characteristics	Alcohol-dependent individuals vs. healthy controls		
Intervention	Total cholesterol (TC), APOB, LDL/HDL based on ASAT and GGT in AD patients		
Comparison	Same procedure in controls		
Length of follow-up	Cross-sectional study (?)		
Outcome and effect size	Sensitivity LDL-C 94.6, spec: 46%; TC, VLDL-C, LDL/HDL-C, APOA1, APOA1/APOB sensitivity >80%, spec: 25-45.8%; positive PV and negative PV was 39.6-94.67% and 52% to 73.7%. Diagnostic accuracy varied from 44.4% APOB to 69.4% TC. Sens: ASAT 75.3%, GGT 74.2%, spec: 88% and 100%. Sens ADH and ALAT: 61% and 67%, positive PV and negative PV range between 66-100% and 51-56%. All four markers diagnostic accuracy: 56% to 85.3% Discriminant analysis: 84.5% were classified on TC, APOB and LDL/HDL and 89.1% on ASAT and GGT.		
Funding	Not reported.		
Comments	TC, APO-B, LDL/HDL and ASAT and GGT are able to discriminate between AD and control samples		

Title	**Opportunistic screening for alcohol use disorders in primary care: comparative study**		
First Author	**Coulton, S., 2006**	**Source**	**16488896**
Level of evidence	2b	**Study type**	Cohort study
Study quality	Male primary care attendees aged 18 or over who completed an alcohol use disorders identification test (AUDIT) questionnaire.		
Participants	194		
Patient characteristics	Primary care attendees		
Intervention	AUDIT Scores and measures of GGT, ASAT, per cent CDT, and MCV. Hazardous alcohol consumption, weekly binge consumption, and monthly binge consumption were ascertained using the time line follow back method over the previous 180 days. Alcohol dependence was determined using the DSM IV. Unit costs were established from published resource references and from actual costs of analysing the biochemical tests		
Comparison	Alcohol consumer vs. non-consumers		
Length of follow-up			
Outcome and effect size	A significant correlation was observed between alcohol consumption and score on the alcohol use disorders identification test (Pearson's correlation coefficient r=0.74) and measures of GGT (r=0.20) and % CDT (r=0.36) but not ASAT (r=0.08) or erythrocyte mean cell volume (r=0.02). The AUDIT exhibited significantly higher sensitivity, specificity, and positive predictive value than all of the biochemical markers for hazardous consumption (69%, 98%, and 95%), weekly binge consumption (75%, 90%, and 71%), monthly binge consumption (66%, 97%, and 91%), and alcohol dependence (84%, 83%, and 41%). The questionnaire was also more cost efficient, with a lower cost per true positive for all consumption outcomes.		
Funding	Funding: The study was funded as part of the stepped care treatment evaluation in primary care funded by the Welsh Office of Research and Development. The authors have no		

	connection with this organization beyond the recipients of the original grant.
Comments	The alcohol use disorders identification test questionnaire is an efficient and cost efficient diagnostic tool for routine screening for alcohol use disorders in primary care.

Title	**Validity of carbohydrate-deficient transferrin (%CDT), gamma-glutamyltransferase (gamma-GT) and mean corpuscular erythrocyte volume (MCV) as biomarkers for chronic alcohol abuse: a study in patients with alcohol dependence and liver disorders of non-alcoholic and alcoholic origin**		
First Author	**Hock, B., 2005**	**Source**	**16185209**
Level of evidence	1b	**Study type**	Case-Control cohort study
Study quality	GGT, %CDT, MCV AUDIT		
Participants	216		
Patient characteristics	Well-characterized collectives of alcohol-dependent patients with current consumption (ALC patients n= 101) and relevant control groups (115 social drinkers, 46 patients with unspecifically increased y-GT. SI hepatitis patients and 20/51 patients with non-alcohol/ alcohol-dependent liver cirrhosis) were included into the study.		
Intervention	Alcohol-dependent individuals		
Comparison	Social drinkers		
Length of follow-up	Cross-Sectional study (?)		
Outcome and effect size	Median AUDIT scores of patients without/with regular heavy drinking were 1-3/27. The following medtans/95th percentiles were obtained for %CDT: social drinkers 2.2/3.0, patients with unspecifically increased y-GT 2.1/3.0 hepatitis 2.0/4.4, non-alcohol-dependent liver cirrhosis 2.4/4.8, alcohol-dependent liver cirrhosis 3.0/5.9, ALC patients 3.9/14.9. Differences between patients without and with alcohol abuse were highly significant (p<0.001). No differences in CDT values were found between males and females. There was no correlation between %CDT values, y-GT, MCV and the amount of alcohol consumed in ALC patients: 3.0% CDT (95th percentile social drinkers) is proposed as cut-off for the test used (Tina-quant* %CDT 2nd-generation). At this cut-off the sensitivity for ALC patients was 73.3% whereas y-GT/MCV had a sensitivity of 71.3%/64.4%. Multivariate analysis performed at 95% specificity resulted in an improvement of the sensitivity by combining %CDT with y-GT (83.2%). A further enhancement of the sensitivity to 88.1%) was obtained by combination of %CDT, y-GT and MCV. The diagnostic specificity of %CDT calculated at the cut-off of 3%, was 93.5% in patients with unspecifically increased y-GT, 88.2% in hepatitis patients and 70.0% in patients with non-alcohol-dependent liver cirrhosis. %CDT was more specific in these patient, collectives than MCV, and especially more than y-GT especially in hepatitis 52.9% and 35 % in non-alcohol-dependent liver cirrhosis.		
Funding	The study was supported with an unrestricted educational grant by Roche Diagnostics GmbH, Mannheim, Germany. No personal grant was given to any of the co-workers.		
Comments	Common Standard measures are compared in a moderate size clinical sample		

Title	**Measurement of direct ethanol metabolites suggests higher rate of alcohol use among pregnant women than found with the AUDIT--a pilot study in a population-based sample of Swedish women**		
First Author	**Wurst, F. M., 2008**	**Source**	**18221928**
Level of evidence	2b	**Study type**	Cohort study
Study quality	Direct biomarkers and AUDIT measures in a moderate special sample of pregnant women		
Participants	Study population: 103 pregnant women		
Patient characteristics	Women in pregnancy		
Intervention	AUDIT, urine and hair samples, neonatal outcomes collected and investigated for eTG, FAEE		
Comparison	Personal reports, AUDIT vs. biomarkers		
Length of follow-up	Cross-sectional		
Outcome and effect size	1 of 103 urine samples (ETG) and 19 hair samples (16 EtG, 3 FAEE) were positively tested; 26 subjects were identified as potential consumers (AUDIT and markers combined); N=6 on AUDIT only; 14 subjects on hair EtG only, 3 positive on Hair FAEE; 3 on combined AUDIT		

	and any biomarker; 7 positive ETG or FAEE individuals, only 1 admitted ongoing alcohol intake (AUDIT)
Funding	Grant from Systembolagets forsnings fond, Sweden.
Comments	Special sample, combination of interview and direct biomarkers.

Title	**Ethyl glucuronide in hair compared with traditional alcohol biomarkers--a pilot study of heavy drinkers referred to an alcohol detoxification unit**		
First Author	**Høiseth, G., 2009**	**Source**	**19298326**
Level of evidence	1b	**Study type**	Cohort study
Study quality	adequate design		
Participants	16		
Patient characteristics	12 men, 4 women, history of alcohol ingestion; patient were recruited directly after admission to a withdrawal clinic. Mean age 49 years +/-7 years. 3 Patients suffered from hepatitis and 1 from pancreatitis.		
Intervention	1) Estimated daily intake of ethanol (EDI) during the last 3 months. 2) Details information of alcohol ingestion in the last 24h. 3) Collection of serum samples to measure AST; ALT, GGT, CDT. 4) Hair: 3cm as close as possible to the skin (200mg); Hair ethyl glucuronide was determined using a previously published method (Morini et. al, 2006).		
Comparison	To investigate the sensitivity of ethylglucuronide in hair compared to CDT, AST, GGT, ALT		
Length of follow-up	None		
Outcome and effect size	The mean estimated daily intake (EDI) over the previous 3 months was 206 +/-136g pure alcohol. The sensitivity to detect heavily alcohol use was for %CDT 64%, for AST 67%, for ALT 67%, for GGT 93% and for ethylglucuronide in hair 94%. There was no correlation between the quantitative values of EDI and %CDT (r=-0.26), AST (r=0.20), ALT (r=0.14) and GGT. There was a positive, statistically significant correlation between EDI and the level of EtG in hair.		
Funding	none declared		
Comments			

Title	**Determination of ethyl glucuronide in nails by liquid chromatography tandem mass spectrometry as a potential new biomarker for chronic alcohol abuse and binge drinking behavior**		
First Author	**Morini, L., 2012**	**Source**	**22193819**
Level of evidence	3b	**Study type**	Cohort study
Study quality	Not good as nails do not reflect a specific time window. No information about any influencing factors.		
Participants	15		
Patient characteristics	9 men, 6 women, age between 15 and 65 years.		
Intervention	1) Self report of alcohol intake in g/day. 2) Ethyl glucuronide in nails: fingernails (30mg) were collected with scissors by clipping the 1-2mm distal segment. Nails were collected every 10 days, up to five times per subject.		
Comparison	Development and validation of a liquid chromatography tandem mass spectrometry (LC-MS/MS) method to determine EtG concentrations in nails and to evaluate the sensitivity and specificity of this test to discriminate between chronic excessive alcohol consumption and binge drinking behavior.		
Length of follow-up	None		
Outcome and effect size	EtG concentration in nails ranged between 12.3pg/mg and 92.6pg/mg. 5 were EtG positive. These 5 participants declared an alcohol consumption between 10 and more than 60g/day.		
Funding	none declared		
Comments			

Title	**Ethyl Glucuronide, Ethyl Sulfate, and Ethanol in Urine After Intensive Exposure to High Ethanol Content Mouthwash**

First Author	Reisfield, G. M, 2011	Source	21619720
Level of evidence	1b	Study type	Cohort study
Study quality	Very good quality		
Participants	10		
Patient characteristics	Volunteers, no history of ethanol use disorders, no history of sensitivity to ethanol, hepatic or renal dysfunction, diabetes mellitus and symptoms of urinary tract infection. They abstained from ethanol use for 5 days prior to the study.		
Intervention	Gargle with mouthwash (20ml of Listerine unflavored product, 26.9% ethanol) 4 times daily for 3 1/4 days. Post gargle specimens were collected at 2, 4, and 6 hours after the final gargle of the study. 1) BrAC compared to arterial blood alcohol concentration (ABAC) 2) Intake of 0.60g alcohol per kg bodyweight during a maximum time of 15 minutes. Fasting for 2h before the experiment. BrAC was measured using a prototype breath analyzer (Servotek). The analyzer utilizes absorption of infrared radiation. The breath analyzer uses ratios between alcohol and water concentrations rather than absolute concentrations for its calculations. Determination of ethylglucuronide, ethylsulfate and ethanol in urine.		
Comparison	To determine the degree of ethanol absorption and the resultant formation and urinary excretion of its conjugated metabolites following intensive use of high ethanol content mouthwash.		
Length of follow-up	None		
Outcome and effect size	1) No detectable EtG in urine at the beginning of the study -all volunteers abstained from ethanol for 5 days. 2) 1 positive EtG results (173ng/ml). This was a 2h post gargle specimen on the final day of the study. 3) EtS was detected in the urine of 7 of 10 participants, but it was not detected in the single specimen with detectable EtG. Max. EtS concentration was 104ng/ml		
Funding	none declared		
Comments			

Title	Urinary Ethyl Glucuronide and Ethyl Sulfate Testing for Recent Drinking in Alcohol-Dependent Outpatients Treated With Acamprosate or Placebo		
First Author	Dahl, H., 2011	Source	21616946
Level of evidence	1b	Study type	Cohort study
Study quality	good design, adequate number, good reference standard, double blind, randomized		
Participants	56, 26 women, 30 men		
Patient characteristics	Treatment seeking persons, recruited via advertisement, mean age 50 years; DSM IV criteria for alcohol dependence		
Intervention	Urinary EtG and EtS using liquid chromatography-mass spectrometry method, self-reports		
Comparison	To compare urinary EtG and EtS testing with self-reports as ways to detect drinking in alcohol-dependent subjects participating in a randomized double-blind evaluation to determine the effect of 21-days acamprosate medication, alcohol-cue reactivity and alcohol priming.		
Length of follow-up	None		
Outcome and effect size	Patients were randomized to 21 days of either acamprosate or placebo treatment. No significant difference between the treatment groups regarding the reduction of positive urine tests (30% of reduction in the acamprosate medication and 33% in the placebo group). In 26 of the 63 EtG and EtS positive cases (41.3%) the patient admitted alcohol consumption on the previous day. The self-reported quantity of drinking over the past 3 days prior to urine sampling showed a good correlation with the EtG ($r=0.662$, $p<0.001$) and EtS ($r=0.716$, $p<0.001$).		
Funding	Financial support was provided through the regional agreement on medical training and clinical research between Stockholm County Council and the Karolinksy Institutet, and the Swedish Science Council.		
Comments			

Title	Urinary Ethyl Glucuronide and Ethyl Sulfate Testing for Detection of Recent Drinking in an Outpatient Treatment Program for Alcohol and Drug Dependence		
First Author	Dahl, H., 2011	Source	21339184
Level of evidence	2b	Study type	Cohort study
Study quality	good design, adequate number, good reference standard		
Participants	n=24 (3 women, 21 men)		
Patient characteristics	Outpatients: n=8 treatment for alcohol, n=10 treatment for drug dependence, n=6 patients in methadone maintenance therapy.		
Intervention	Twice weekly urine samples; one single question about any drinking in the past 3 days. Urinary EtG and EtS were determined by liquid chromatography-mass spectrometry		
Comparison	To evaluate the extra information obtained about recent drinking, when introducing urinary EtG and EtS testing into routine practice in outpatient treatment programs for alcohol and drug dependence		
Length of follow-up	None		
Outcome and effect size	214 urinary samples collected. 211 self-reports collected. In 21% of the cases, alcohol intake was admitted in good agreement with EtG/EtS results (83.5-89.1%).		
Funding	Financial support was provided through the regional agreement on medical training and clinical research between Stockholm County Council and the Karolinska Institutet.		
Comments	No correlation between self reprot and EtG/EtS results. Good: different paitent population		

Title	Clinical Application of Ethyl Glucuronide Testing in the U.S. Army		
First Author	Lande, R. G., 2011	Source	21218309
Level of evidence	3b	Study type	Cohort study, retrospective chart review
Study quality	Poor, no reference standard was applied.		
Participants	328 service members with 1.852 urine samples		
Patient characteristics	All services members referred to the Walter Reed Army Medical Center's Army Substance Abuse Program. Enrollment in this program followed a clinician's confirmation of a substance abuse or dependence diagnosis after completing a comprehensive evaluation.		
Intervention	Scheduled and unscheduled ethylglurunoide testing in urine. Alcohol Use Disorders Identification Test (AUDIT) was applied at the beginning with cut off of 8 or more for men and 4 or more for women.		
Comparison	To examine the clinical characteristics of ethyl glucuronide testing among service members referred to a military substance abuse program.		
Length of follow-up	None		
Outcome and effect size	Among all participants 45 (17.2%) had a positive UEtG level. Of those, (19/45; 42.2%) half were between 1000 and 9999ng/ml. A statistically significant decline in EtG levels occurred with serial testing over time. The observed agreement between the AUDIT and the initial ethyl glucuronide level was moderate, with 61%. Of the 159 participants screened negative by the AUDIT, 135 tested negative by initial EtG. This showed a good negative predictive value whereby a negative AUDIT has an 85.5% chance of predicting an initial negative EtG level. The positive predictive value of the AUDIT was poor in predicting a positive EtG level. Of the 101 positive AUDIT scores, only 22 (21.8%) participants were positive by the initial EtG test.		
Funding			
Comments			

Title	Determination of Ethyl Glucuronide in Hair Samples of Chinese People by Protein Precipitation (PPT) and Large Volume Injection-Gas Chromatography-Tandem Mass Spectrometry (LVI-GC/MS/MS)		
First Author	Shi, Y., 2010	Source	20977979
Level of evidence	2b	Study type	Cohort study
Study quality	good, relatively low number of volunteers		
Participants	21		

Patient characteristics	Chinese volunteers, 15 clear alcohol consumption history, 6 were children as absolute teetotalers no bleaching, dyeing, or any other cosmetic treatment
Intervention	Ethyl glucuronide in hair: determination by LVI-GC/MS/MS all hair specimens were pretreated with protein-precipitation (PPT). PPT is likely to enhance sample recovery for EtG detection in hair.
Comparison	To develop and validate a sensitive, precise and specific analytical method for the determination of EtG in hair samples.
Length of follow-up	None
Outcome and effect size	All EtG positives reported ethanol intake, no EtG in children (defined as teetotalers). EtG concentration in positive samples ranged from 10 to 78pg/mg in hair with an increase in average daily alcohol consumption, the concentration of EtG in hair also exhibited a corresponding increase. In six cases EtG in hair was low despite a known history of alcohol abuse.
Funding	Support from the National Basic Research Training Fund, National Institute scientific program and the National Natural Science Foundation
Comments	Results regarding influence of hair colors are based on 2 cases. Primarily a method paper, however a finding is that EtG in hair is possible to determine in Chinese population.

Title	**Urinary Ethylglucuronide Assessment in Patients Treated With Disulfiram: A Tool to Improve Verification of Abstention and Safety**		
First Author	**Mutschler, J., 2010**	**Source**	**20975547**
Level of evidence	1b	**Study type**	Cohort study
Study quality	adequate design		
Participants	51		
Patient characteristics	30 men, 21 women; all fulfilled diagnostic criteria for alcohol dependence (ICD 10, DSM-IV); treated with Disulfiram (dosage 1.5g/kg body weight); patient were in outpatient treatment. Mean age: 47.74 years. Mean criteria (ICD-10): 5.8 +/-0.49. Previous alcohol intake was 292 +/-94.44g ethanol per day.		
Intervention	1) Ethyl glucuronie in urine determined by LC/MS-MS. Detection limit was 0.1mg/l 2) breathalyzer		
Comparison	To examine ethyl glucuronide in urine as a tool to verify abstention in patients treated with supervised disulfiram		
Length of follow-up	None		
Outcome and effect size	Ethyl glucuronide: 3 positive with no alcohol-disulfiram reaction. Breathalyzer results were negative for all.		
Funding	Supported by the Central Institute of Mental Health, Mannheim		
Comments	No EtG results are given.		

Title	**Ethyl Glucuronide and Ethyl Sulfate in Urine After Consumption of Various Beverages and Foods--Misleading Results?**		
First Author	**Musshoff, F., 2010**	**Source**	**20838803**
Level of evidence	1b	**Study type**	Cohort study
Study quality	Good design for a drinking experiment, interesting results, adequate discussion		
Participants	19		
Patient characteristics	12 women, 7 men, age range 19 to 40; 80 hours of abstinence from alcohol beverages.		
Intervention	Drinking experiment: Group 1: between 2.0 and 3.0l of a so called non-alcoholic beer (max 4g ethanol per litre); Group 2: between 1.1 and 2.0l of apple juice (max. 3g ethanol per litre); Group 3: between 1.5 and 2.0 l of grape juice (max. 7.9g ethanol per litre); Group 4: between 750 and 1.320 g sauerkraut (min. 2% wine); Group 5: between 670 and 690g of matured peeled bananas. • Determination of Ethylglucuronide (EtG): urine was collected every 1 to 2h in the first 8h after ingestion. • Determination of Ethyl sulfate (EtS) in urine		
Comparison	To evaluate other possible sources of ethanol and therefore for positive EtG and EtS		

	results.
Length of follow-up	None
Outcome and effect size	1) Non-alcoholic beer: Using a cut-off of 0.1mg/L, positive EtG findings were revealed after the ingestion of a lot of non-alcoholic beer up to 13h later (EtG ranged from 0.211 to 0.512mg/l). EtS peak concentration ranged from 0.134 to 0.169mg/l. The concentrations peaked between 5.0 and 7.5h after drinking. EtG and EtS were detectable for up to 26h and 25h. A cut-off level of 0.5mg/l was exceeded in a period of 5 to 7h after drinking. 2) Apple juice: no elevated EtG or EtS concentrations. 3) Grape Juice: no elevated EtG concentrations. EtS was positive with peak concentrations between 0.107 and 0.648mg/l. EtS detectable for up to 35h. 4) Sauerkraut: only one case EtG positive. This participant ate 750g sauerkraut - EtG peak concentration of 0.2mg/l was measured 2h after ingestion. 5) Matured bananas: Consumption of 670 to 690g bananas (ethanol dose 3.5g). Urinary peak concentration of EtG ranged from 0.04 to 0.12mg/l. EtS peak concentration up to 0.055mg/l. EtS and EtG detectable for up to 24h and 20h, respectively. Conclusion: a 0.1mg/l cutoff is useful – however, a 24h waiting period should be used to avoid not false-positive results.
Funding	None declared
Comments	

Title	**Ethyl Glucuronide Concentrations in Oral Fluid, Blood, and Urine After Volunteers Drank 0.5 and 1.0g/kg Doses of Ethanol**		
First Author	**Høiseth, G., 2010**	**Source**	**20663284**
Level of evidence	2c	**Study type**	Cohort study
Study quality	Adequate design, fair interpretation		
Participants	113 men, 8 women		
Patient characteristics	Healthy volunteers, median age 22y.		
Intervention	Ethyl glucuronide and ethanol in oral fluid (saliva), blood and urine. Oral fluid was collected by Statsure Saliva Sampler. EtG was measured using a UPLC-MS-MS method.		
Comparison	To investigate the concentrations of EtG in oral fluid, blood and urine after 2 doses of ethanol		
Length of follow-up	None		
Outcome and effect size	The detection time for EtG was median 11.5h in oral fluid. According to this, the detection time for EtG in oral fluid is therefore only a few hours longer than for ethanol itsself and represents limited additional value. Dose dependent relationship for EtG kinetics in blood, urine and oral fluid.		
Funding	Sponsored by the Research Council of Norway.		
Comments			

Title	**Levels of Ethyl Glucuronide and Ethyl Sulfate in Oral Fluid, Blood, and Urine After Use of Mouthwash and Ingestion of Nonalcoholic Wine**		
First Author	**Høiseth, G., 2010**	**Source**	**20223100**
Level of evidence	1b	**Study type**	Cohort study
Study quality	Adequate design of the experiment		
Participants	12		
Patient characteristics	healthy volunteers, 4 men, 8 women with a median age of 22 years and mean body mass index of 22.0kg/m^2. Social drinkers with a median use of 12 standard drinks/month and had abstained from alcohol during the week preceding the study, according to self-reports.		
Intervention	1) Ethylglucuronide in oral fluid, blood and urine. 2) Ethylsulfate in blood and urine 3) Measurement of ethanol in oral fluid, blood and urine. EtG and EtS in blood and urine were determined by UPLC-MS/MS. Experiment: 1) mouthwash: 8 times 2) one bottle (7.5dL) nonalcoholic wine which contained 3.0mg/l EtG and 1.5mg/l EtS.		

	3) one gulp (dose 1.8g ethanol) vodka containing 60% alcohol
Comparison	to investigate the concentrations of ethyl glucuronide (EtG) in oral fluid and both EtG and ethyl sulfate (EtS) in blood and urine following intense use of mouthwash and ingestion of nonalcoholic wine
Length of follow-up	None
Outcome and effect size	All samples of blood and oral fluid were negative for ethanol, EtG and EtS in all three groups. All samples were negative for ethanol in all three groups. In the group ingesting nonalcoholic wine, all three subjects were negative for EtG in urine but positive for EtS (up to 2.15mg/l). Of the four subjects ingesting 3.75ml vodka in one gulp, two subjects showed positive samples of EtG and EtS in urine. All subjects using mouthwash were negative for EtG and EtS.
Funding	Sponsored by the Research Council of Norway.
Comments	

Title	**Serum/whole Blood Concentration Ratio for Ethylglucuronide and Ethyl Sulfate**		
First Author	**Høiseth, G., 2009**	**Source**	**19470223**
Level of evidence	1b	**Study type**	Cohort study
Study quality	good design, relatively low number of patients		
Participants	13		
Patient characteristics	Patients at admission to an alcohol rehabilitation clinic. 9 men and 4 women. Median age was 47 years. Median weight was 78kg.		
Intervention	Two blood samples collected at the same time: 1) ethylglucuronide 2) ethyl sulfate		
Comparison	To determine the Serum/Blood (S/B) ratio for ethyl glucuronide and ethyl sulfate in samples from patients at admission to an alcohol rehabilitation clinic.		
Length of follow-up	None		
Outcome and effect size	The median concentration of EtG in blood was 2.69mg/l and in serum 4.59mg/l. Regarding the S/B ratio the median value for EtG was 1.69 and the range was 1.33-1.90. There was no correlation between the absolute levels of EtG in blood or serum and the S/B ratio. The median concentration of EtS in blood was 1.13mg/l and in serum 1.56mg/l. Regarding the S/B ratio the median value for EtS was 1.30, and the range was 1.08-1.47. There was no correlation between the absolute levels of EtS in blood or serum and the S/B ratio.		
Funding	None declared		
Comments			

Title	**False-positive Ethyl Glucuronide Immunoassay Screening Associated With Chloral Hydrate Medication as Confirmed by LC-MS/MS and Self-Medication**		
First Author	**Arndt, T., 2009**	**Source**	19084359
Level of evidence	3b	**Study type**	Case-Control study
Study quality	Good design, only 2 participants, important topic		
Participants	2		
Patient characteristics	Patient: 1 woman, 35 years old, on medication with burprenorphine, levetiracetam, gabapentin, clomethiazole, chloral hydrate; Proband: 1 woman, healthy, without any medication taking in a self-medication experiment a single dose of 500mg chloral hydrate after 5 days of ethanol abstinence		
Intervention	Ethyglucuronide, Ethyl sulphate		
Comparison	Self-medication of chloral hydrate, measurement of EtG using DRI-EtG enzyme immunoassay and LC-MS/MS		
Length of follow-up	None		
Outcome and effect size	Trichloroethyl glucuronide as an important chloral hydrate metabolite remains the most probable cross reacting substance with the DRI EtG immunoassay. It is recommended that positive EtG immunoassay results always be confirmed by a more specific technique such as LC-MS/MS, including ethyl sulfate as a second minor ethanol metabolite.		
Funding	Not declared		
Comments	Use of spiked urine samples to rule out interference of medication		

Title	**Detection Times for Urinary Ethyl Glucuronide and Ethyl Sulfate in Heavy Drinkers During Alcohol Detoxification**		
First Author	**Helander, A., 2009**	**Source**	**18971292**
Level of evidence	2b	**Study type**	Cohort study
Study quality	relevant topic, good design		
Participants	32		
Patient characteristics	Randomly selected alcohol-dependent patients (meeting DSM-IV criteria), being hospitalized for alcohol detoxification.		
Intervention	Breath alcohol concentration, urinary ethyl glucuronide, UEtS measured by LC-MS and for EtG also DRI-EtG EIA (immunochemical assay)		
Comparison	To establish the detection windows for EtG and EtS in urine in alcohol patients during alcohol detoxification and to examine factors that could possibly be of influence.		
Length of follow-up	None		
Outcome and effect size	The detection time for urinary EtG was weakly correlated (r=0.434; p=0.013) with the initial alcohol concentration. For EtG the individual time range until return to below the applied cut-off limit (<5mg/l) was 40 to 130 hours with a similar time course observed for EtS. EtG and EtS remained detectable in urine for several days.		
Funding	Financial support: through the regional agreement on medical training and clinical research between Stockholm County Council and the Karolinska Institutet.		
Comments			

Title	**Comparison of Ethyl Glucuronide in Hair With Phosphatidylethanol in Whole Blood as Post-Mortem Markers of Alcohol Abuse**		
First Author	**Bendroth, P., 2008**	**Source**	**18023314**
Level of evidence	3b	**Study type**	Cohort study
Study quality	Study quality is good, however not consistently applied reference standard. In vitro formation of PEth was not excluded by determination of blood alcohol. Diagnostic criteria of alcohol abuse are not in accordance with the ICD-10.		
Participants	70		
Patient characteristics	51 men, 19 women; consecutive medicolegal autopsies, age between 18 and 70 year, exclusion criteria: sampling complication, severe putrefaction		
Intervention	Ethyl glucuronide in hair using LC-MS/MS, Phospathidylethanol in whole blood using HPLC; Liver histology; anamnestic evidence of alcohol abuse were obtained from the database of the Swedish National Board of Forensic Medicine, police reports and medical records.		
Comparison	Comparison of EtG in hair, PEth in femoral whole blood as well as with traditional indicators of alcohol abuse such as liver histology and anamnestic evidence.		
Length of follow-up	None		
Outcome and effect size	Positive cases: for EtG in hair 49 cases; for PEth 36 cases. Of the positive cases, 39 showed EtG levels above the cut-off limit and 29 cases were above cut-off for PEth levels. Only EtG positive were 15 cases compared to four cases with a positive PEth. Among 45 positive cases, 87% and 64% were positive for EtG and PEth, whereas only 27% had a confirmed liver histology of abuse.		
Funding	not declared		
Comments			

Title	**Urinary Ethyl Glucuronide Testing Detects Alcohol Consumption in Alcoholic Liver Disease Patients Awaiting Liver Transplantation**		
First Author	**Erim, Y., 2007**	**Source**	**17457868**
Level of evidence	2b	**Study type**	Cohort study
Study quality	Good study design, important topic, external reference standard not optimum (no TLFB)		
Participants	n=18 (9 men, 9 women)		
Patient characteristics	Mean age 51 years; All patients are alcohol liver disease candidates for liver transplantation. Participants of group therapy (12 sessions, psychoeducation, etc.; aim was to reach abstinence); Of all 18, 10 met ICD10 criteria for an alcohol dependence syndrome		

	and 2 for harmful alcohol use. 13 reported being abstinent for less than 6 months.
Intervention	Breathalyzer device - measured at the beginning of every session; Urinary EtG on voluntary basis - determined using liquid chromatography mass spectrometry.
Comparison	To compare urinary EtG measurement with breath alcohol testing and self-report as ways to disclose recent drinking in ALD patients undergoing addiction group therapy before liver transplantation
Length of follow-up	None
Outcome and effect size	1) no self-report about alcohol intake 2) 127 breath tests were performed. 1 was positive. 3) 96 urine tests of 9 patients. 24 (25%) were positive. Half of the liver transplant candidates had been drinking alcohol at least once during the period of the group therapy - this was not identified by the breath alcohol testing.
Funding	None declared
Comments	

Title	**Ethyl Glucuronide in Hair: Is It a Reliable Marker of Chronic High Levels of Alcohol Consumption?**		
First Author	**Politi, L., 2006**	**Source**	**16968341**
Level of evidence	1b	**Study type**	Cohort study
Study quality	Good study design and quality, however, external reference standard not optimum.		
Participants	22 alcoholics, 21 volunteers		
Patient characteristics	Group A: known alcoholics at the beginning of an in-patient withdrawal treatment. 13 females, 9 males. Age range between 29-62 years. Group B: 21 volunteers. Nine females, ranging in age from 28 to 53 years, body weight from 47 to 70kg.		
Intervention	Ethyl glucuronide in hair using liquid chromatography-electrospray tandem mass spectrometry (LC-ESI-MS-MS), ethanol daily intake (EDI)		
Comparison	To correlate EtG hair concentration with ethanol use, hair samples from different users were collected together with all the information available about the donors drinking habits		
Length of follow-up	None		
Outcome and effect size	Current known alcoholism had ethyl glucuronide hair concentration in the range 4.0-434.4pg/mg. HEtG was not detected in hair samples from teetotalers (n=7); all volunteers reporting an EDI of at least 30g tested positive for EtG (cut off 4pg/mg). All volunteers declaring an ethanol daily intake higher than 40g tested positive for EtG (cut-off 5pg/mg). No false negatives were found. EDI and EtG results correlated.		
Funding	None declared		
Comments			

Title	**Ethyl Sulfate: A Metabolite of Ethanol in Humans and a Potential Biomarker of Acute Alcohol Intake**		
First Author	**Helander, A., 2005**	**Source**	**16105250**
Level of evidence	4	**Study type**	Cohort study
Study quality	Not good, no information available regarding the characterization of the patients		
Participants	9 healthy individuals and 354 clinical urine samples from the routine laboratory		
Patient characteristics	No information available.		
Intervention	UEtG and UEtS measured by LC-MS and LC-MS/MS methods		
Comparison	To confirm the identity of EtS in human urine after alcohol intake; to compare the urinary excretion characteristics with that of ethanol and EtG, and evaluate if EtS may also be useful as biomarker.		
Length of follow-up	None		
Outcome and effect size	1) Of 352, 86 (24%) were positive for both EtG and EtS. 2) Of 93 positive samples, 92.5% were positive for both. 3) Urinary excretion time was dependent on the dose of ethanol ingested. EtG and EtS was detectable more than 12 and more than 24 hours.		
Funding	Financial support in part by a grant from the Karolinska Institutet.		
Comments	No information about false-positives; in vitro formation, bacterial degradation cannot be		

	excluded.

Title	Breath Alcohol Analysis Incorporating Standardization to Water Vapour Is as Precise as Blood Alcohol Analysis		
First Author	Grubb, D., 2012	Source	21943631
Level of evidence	2b	Study type	Cohort study
Study quality	Good design, low number of participants		
Participants	12 healthy individuals (7 men, 5 women)		
Patient characteristics	Paid volunteers, ages ranged from 18 to 57 years		
Intervention	Breathe alcohol analysis with contact free exhalations. Blood alcohol concentration		
Comparison	To compare the precision of novel breath analyzer utilizing standardisation of the BrAC to the alveolar-air water vapour concentration with the precision of arterial blood alcohol concentration (ABAC)-determinations.		
Length of follow-up	None		
Outcome and effect size	The precision of breath alcohol analysis was as good as the precision of blood alcohol analysis (CV 2.4% vs. 2.38%; p=0.43). A 95% confidence interval for the difference between the CV values was -0.38% to 0.33%.		
Funding	In part supported by Servotek AB, Sweden and by grants from "Anna och Edwin Bergers Stiftelse"		
Comments			

Title	Factors Contributing to the Variability Observed in Duplicate Forensic Breath Alcohol Measurement		
First Author	Gullberg, R. G., 2011	Source	21378437
Level of evidence	2c	Study type	Retrospective analysis of data sets
Study quality	Big data set		
Participants	Data set of 91.108		
Patient characteristics	Data sets consisting of breath alcohol tests from persons arrested for driving while intoxicated were obtained from four jurisdictions during specific time periods.		
Intervention	Breath tests		
Comparison	To investigate and quantify through appropriate multivariate statistical analyses those factors contributing significantly to the variation observed in breath alcohol measurement		
Length of follow-up	None		
Outcome and effect size	The breath alcohol concentration was the most statistically and practically significant predictor of absolute difference between the duplicate results. Subject manipulation of exhalation time and volume have a very small systematic effect on estimated breath alcohol concentration.		
Funding	None declared		
Comments			

Title	The Relationship of Normal Body Temperature, End-Expired Breath Temperature, and BAC/BrAC Ratio in 98 Physically Fit Human Test Subjects		
First Author	Cowan, J. M., 2010	Source	20529457
Level of evidence	2b	Study type	Cohort study
Study quality	Good reference standard		
Participants	n=98 (14 women, 84 men)		
Patient characteristics	Physically fit volunteers, drinking 3 equal portions of whiskey (50.5% ethanol by volume) mixed with a carbonated beverage at 15 min intervals to produce a peak BrAC of at least 0.06g/210l.		
Intervention	1) Breath alcohol concentration using Intoyilyzer 8000 specially equipped and calibrated at the factory to measure the temperature of the breath sample.		

	2) Blood sample which was analyzed by headspace gas chromatography for blood alcohol concentration. 3) Body temperature: oral, tympanic, temporal.
Comparison	To examine the relationships between: 1) normal body temperature and end-expired breath temperature, 2) venous BAC/end-expired BrAC ratio, 3) breath temperature and BAC/BrAC ration, and 4) body temperature and BAC/BrAC ratio.
Length of follow-up	None
Outcome and effect size	The BAC exceeded the BrAC for every subject. BAC/BrAC ratios: no difference for men and women. The correlation between BAC and BrAC was high (r=0.938, p<0.001). The correlations between body temperature and end-expired breath temperature, body temperature and BAC/BrAC ratio, and breath temperature and BAC/BrAC were much lower. For physically fit subjects studied, their BrAC results were consistently lower than their BAC results, and these results were very well-correlated.
Funding	None declared
Comments	

Title	**Random Alcohol Testing Reduced Alcohol-Involved Fatal Crashes of Drivers of Large Trucks**		
First Author	**Snowden, C. B., 2007**	**Source**	**17690795**
Level of evidence	2b	**Study type**	Retrospective analysis of data, cross-sectional
Study quality	Good design, high number, limited by retrospective nature		
Participants	71.606 truck drivers, 32.0647 passenger car drivers		
Patient characteristics	Pooled cross-sectional data collected in the Fatality Analysis Reporting System (FARS) of USA, a census of all motor vehicle crashes on public roadways in the US between 1988 and 2003. All are large truck drivers between 21-65 years old		
Intervention	Random alcohol testing for transportation workers was introduced in 1994. The tests are unannounced. Blood alcohol concentration is determined.		
Comparison	To examine the impact of random alcohol testing on the likelihood that the driver of a large truck involved in a fatal motor vehicle crash was alcohol-involved.		
Length of follow-up	None		
Outcome and effect size	Overall, 3.3% of drivers of large trucks and 34.3% of passenger car drivers in fatal crashes were alcohol involved. Alcohol involvement among drivers of large trucks declined from 5.5% in 1988 to 2.0% in 2003. The decline for passenger car drivers was from 38.3% in 1988 to 30.7% in 2003.		
Funding	The research was supported by the Center for Substance Abuse Prevention		
Comments	Contributes to the sparse literature about random alcohol testing in truck drivers / safety sensitive occupations.		

Title	**Use of blood alcohol concentration in resuscitation room patients**		
First Author	**Csipke, E., 2007**	**Source**	**17652671**
Level of evidence	2b	**Study type**	Cohort study/ observational study
Study quality	Good design, interesting aspects covered, additional biomarker testing would further improve quality		
Participants	n=273 (158 male, mean age 62 years)		
Patient characteristics	Patients were treated in the resuscitation room. Of the 273, 242 with medical complaints, 29 with surgical complaints. No data were available for the 2 remaining patients.		
Intervention	1) Blood alcohol concentration was measured by an automated enzymatic method, DRI Ethyl Alcohol Assay. 2) Paddington Alcohol Test (PAT) five item questionnaire about the maximum units consumed. It is positive for men drinking more than 8 units and women more than 6 units in a single session, at least once a week, or in anyone who believed their attendance was alcohol related. 3) Patient Attitude Questionnaire: four item questionnaire. Specifically for use on subsequent admission to a ward.		

Comparison	BAC comparison to questionnaire results, and attitudes to BAC testing
Length of follow-up	None
Outcome and effect size	1) BAC results ranged from 0-440mg/100ml. 32 had evidence of alcohol use (BAC>10mg), 25 had a BAC>80mg/100ml. Mean alcohol concentration among those who did consume alcohol was 170mg/100ml (SD=115.38). 1 in 10 had a BAC of>80mg/100ml. 2) PAT results: 30 were positive. 2/3 who were positive in PAT had BAC<80mg/100ml. 60% with BAC>80mg/100ml scored negative in PAT. 3) Patient attitude questionnaire: 264 (97%) patients reported that implementing BAC testing as a routine procedure would be acceptable.
Funding	The study was funded by St. Mary's Paddington Charitable Trust.
Comments	

Title	**Elimination rates of breath alcohol**		
First Author	**Pavlic, M., 2007**	**Source**	**17064864**
Level of evidence	1b	**Study type**	Cohort study
Study quality	Good design, adequate interpretation		
Participants	59		
Patient characteristics	32 men, 27 women, mean age 29.1 years. BMI between 17.6 and 28.7 (M=21.8). Self-estimated alcohol intake 20g-400g ethanol per week.		
Intervention	Drinking experiment 2 hours leading to 1.07 +/-0.23g ethanol per kg body weight. -> Determination of BrAC: started 30 min after stopping to drink; performed every 30min -> blood samples: venous blood alcohol concentration (BAC) Measurement and blood drawing were performed up to 5h after drinking.		
Comparison	To contribute to the establishment of scientifically acceptable BrAC elimination rates for back calculations observing adequate statistical scopes.		
Length of follow-up	None		
Outcome and effect size	After 33min: mean BAC 0.993 +/-0.28g/l. elimination rate: overall 0.169g/l. Significant difference between men and women (p<0.05); women 0.179g/l vs. men 0.162g/l. BrAC: after 33min 0.455 +/-0.119mg/l. overall elimination rate for BrAC 0.08mg/l. Significant differences for men and women (p<0.04). Elimination rate for women 0.087mg/l vs. 0.078. The blood/breath alcohol conversion factor Q varies over time. After 34 minutes the mean BAC/BrAC conversion factors Q is 2169, after 306 minutes it is 2707.		
Funding	None declared		
Comments	Of relevance in Austria since venipuncture is not accepted in the context of driving under influence.		

Title	**Breath alcohol concentration determined with a new analyzer using free exhalation predicts almost precisely the arterial blood alcohol concentration**		
First Author	**Lindberg, L., 2007**	**Source**	**16978819**
Level of evidence	1b	**Study type**	Cohort study, drinking experiment
Study quality	Interesting design (BrAC, ABAC, VBAC), new methodology, adequate interpretation, funding by company		
Participants	15		
Patient characteristics	Healthy paid volunteers, age: 26-67 years. Moderate drinkers accustomed to consuming alcohol beverages		
Intervention	1) BrAC compared to arterial blood alcohol concentration (ABAC) 2) intake of 0.60g alcohol per kg bodyweight during a maximum time of 15 minutes. Fasting for 2 h before the experiment. BrAC was measured using a prototype breath analyzer (Servotek). The analyzer utilizes absorption of infrared radiation. The breath analyzer uses ratios between alcohol and water concentrations rather than absolute concentrations for its calculations.		
Comparison	To evaluate the performance of this new BrAC instrument by comparing standardized alcohol concentration in freely expired breath with arterial (ABAC) and venous (VBAC) blood alcohol concentration.		
Length of follow-up	None		
Outcome and effect size	The ABAC/BrAC ratio was 2251 +/-46 in the post-absorptive phase and the mean bias		

	between ABAC and BrACx 2251 was 0.0035g/l with 95% limits of agreement of 0.0033 and -0.026. The ABAC and BrACx2251 were highly correlated (r=0.998, p<0.001) and the regression relationship indicated excellent agreement and no fixed or proportional bias. The VBAC and BrAC ratio never stabilized and varied continuously. The new breath analyzer using free exhalation has a high precision for in vivo testing. Furthermore, there is a big difference between ABAC and VBAC.
Funding	The work was supported in part by Servotek AB, Arlöv, Sweden.
Comments	

Title	**Relationship between blood alcohol concentration and carbohydrate-deficient transferrin among drivers**		
First Author	**Appenzeller, B. M., 2005**	**Source**	**16002036**
Level of evidence	2b	**Study type**	Cohort study
Study quality	Adequate design, fair interpretation, additional biomarkers and self-reports would improve quality		
Participants	408		
Patient characteristics	341 men, 67 women. Sample is one third of a total of 1.260 drivers apprehended in this period. This group was representative in terms of Blood Alcohol Concentration, age and gender. Age median for men was 37 years, for women 41 years.		
Intervention	Blood alcohol concentration, Carbohydrate-deficient Transferrin (CDT) determined in blood using HS-GC/FID method.		
Comparison	BAC with CDT		
Length of follow-up	None		
Outcome and effect size	The percentage of specimens with CDT≥3% was close to 0 in drivers with BAC under 0.5g/l and reached 47 and 67% when BAC was between 3 and 3.5g/l and above 3.5g/l, respectively showing an increasing frequency of chronic alcohol abuse with respect to increasing BAC ranges. The percentage of BAC≥0.8g/l was 69.4% among drivers with CDT <1% and 97.1% for those with CDT≥3.		
Funding	SAN-02-001 Luxembourg Ministry of Health		
Comments			

Title	**Levels and types of alcohol biomarkers in DUI and clinic samples for estimating workplace alcohol problems**		
First Author	**Margues, P. R., 2012**	**Source**	**22311827**
Level of evidence	5	**Study type**	Review, not systematic
Study quality	Poor, compilation of data from different sources resulting in recommendation for biomarker use. No systematic research strategy. No reason for including the studies is given.		
Participants	8 studies		
Patient characteristics	All studies included represent uniform measurement approaches. Population of the studies: 6 categories: •abstinent, •general population, •dui overall sample average, •DUI high risk group, •alcohol clinic outpatient, •alcohol clinic inpatients		
Intervention	Comparison of 5 biomarkers in the 6 categories of samples: Biomarkers: •PEth micromol/l , •GGT U/l, •%CDT , •y%CDT, •Hair EtG pg/mg		
Comparison	To address what levels of different alcohol biomarkers might be indicative of problem drinking among employees at the workplace		
Length of follow-up	None		
Outcome and effect size	Alcohol biomarkers can improve detection by extending the timeframe for estimating problematic exposure levels. An established high-sensitivity proxy for alcohol driving risk proclivity is used: an average 8 months of failed blood alcohol concentration (BAC) breath tests from alcohol ignition interlock devices.		
Funding	Supported by the National Institute on Alcohol Abuse and Alcoholism.		
Comments			

Title	**Abstinence monitoring of suspected drinking drivers: ethyl glucuronide in hair versus CDT**		
First Author	**Linigier, B., 2010**	**Source**	**20373230**
Level of evidence	1b	**Study type**	Cohort study, retrospective
Study quality	Good, however, different time spans are reflected by the two markers.		
Participants	154		
Patient characteristics	all were in the context of suspected relevant alcohol problems with regard to driving		
Intervention	• Determination of Ethyl glucuronide in hair • CDT measurements by an immunochemical method and by HPLC. • Self-report of abstinence		
Comparison	Etyhl glucuronide determinations in the hair of self-reported teetotalers were reviewed and compared with carbohydrate-deficient (CDT) blood tests by immunochemistry and high performance liquid chromatograph y (HPLC)		
Length of follow-up	None		
Outcome and effect size	• 70 samples were EtG negative. • 84 had positive EtG in Hair (HEtG) levels Of those 84, 39 (46%) had elevated CDT levels determined by immunochemical method and 15 (18%) elevated CDT levels determined by HPLC. • of negative EtG: 27 (39%) had elevated CDT levels determined by the immunochemical method and 3 (4%) elevated CDT levels determined by HPLC. • 27 with an elevated immunochemical CDT value were negative in EtG; however, 5 of them had liver disease. 4 of them also hat cosmetically treated hair (bleached, toned, dyed, double process) which may lead to a reduction of as much as 75 percent in the EtG concentration.		
Funding	none declared		
Comments			
Title	**Alcohol biomarkers as tools to guide and support decisions about intoxicated driver risk**		
First Author	**Bean, P., 2009**	**Source**	**19916121**
Level of evidence	1b	**Study type**	Pilot study
Study quality	Very good reference standards and design, good interpretation, good number of participants		
Participants	200		
Patient characteristics	All are third and fourth repeat offenders. They must comply the following criteria: • have experienced the previous DUI within 5 years of the current arrest, • show a BAC greater than 0.15 at the time of the arrests • have a family member or partner concerned with their current use of alcohol • received a diagnosis of suspected alcohol dependence at the assessment of interview.		
Intervention	• Time Line Follow Back: alcohol consumption last 30 days. • Blood samples: CDT, EDAC (early detection of alcohol consumption). The routine panels include: aspartate aminotransferase (AST), albumin, phorous, ratio of blood urea nitrogen/creatinine, high-density lipoprotein (HDL), monocytes, hematocrit, magnesium, cholesterol, gamma glutamyltransferase (GGT), platelets, iron, white blood cells, total bilirubin, direct bilirubin, bilirubin ratio, lactate dehydrogenase, chloride, sodium and alkaline phosphatase.		
Comparison	Whether biomarkers can help the assessor identify high risk drivers who continue to drink heavily after their arrest and detect relapses in drivers enrolled in their drivers safety plans		
Length of follow-up	Assessment at baseline, follow-up: 3, 6 and 12 months		
Outcome and effect size	1. Baseline: When each biomarker was used alone, the EDAC test identified 35 (18%) of the drivers as heavy drinkers compared to 9 (5%) identified by the CDT test and 16 (8%) identified by the GGT test. Best combination was found when combining the EDAC with the CDT (20% identified). Regarding TLFB (self-report) 37 (19%) reported consumption of at least one drink the month prior the assessment. 50% of the drivers (4/8) who tested positive by the CDT test at baseline also tested positive by the EDAC test. However 80% who tested positive in the EDAC were not identified as heavy drinkers by the CDT test. The best detection rate was achieved with the EDAC-CDT combination, which captured heavy drinking in 20%; most of whom (68%) denied drinking at the assessment interview. 2. Follow up: (Monitoring abstinence) 20% experienced a relapse.		

Funding	none declared
Comments	

Title	**Comparison of ethyl glucuronide in hair with carbohydrate-deficient transferrin in serum as markers of chronic high levels of alcohol consumption**		
First Author	**Morini, L., 2009**	**Source**	**19410394**
Level of evidence	2b	**Study type**	Cohort study
Study quality	Not good, results are not comprehensible for CDT as they do not use the same samples to determine CDT with 2 different methods.		
Participants	86		
Patient characteristics	48 men, 38 women, teetotalers, social drinkers, heavy drinkers at the beginning of withdrawal treatment		
Intervention	1) ethanol daily intake (EDI) within the last 2 weeks and 3 months 2) questions about hair natural color, hair hygienic habits and cosmetic treatments (perm, dyeing, or bleaching) 3) Blood samples for CDT (CDT-immunonephelometric or CDT-HPLC - DAD) 4) hair sampling for determination of ethyl glucuronide in hair: 3 cm proximal segment		
Comparison	To compare sensitivity and specificity of EtG in hair and CDT in serum as markers of heavy drinking		
Length of follow-up	None		
Outcome and effect size	EDI: median 111g ethanol/d for 2 weeks; 109g ethanol/day for 3 months, HEtG: range from LOD (2 and 3pg/mg hair) to 890.5pg/mg. CDT range 0.7% to 11.9% - both methods do differ. With a cut off of 27pg/mg HEtG, HEtG detected all consuming more than 60g/day (according to EDI): sensitivity 1.0, specificity 0.93 CDT with a cut off at 2.5%: sensitivity 0.44, specificity 0.93. Sensitivity: HEtG twice as sensitive as CDT. Regarding specificity: same results for CDT and HEtG.		
Funding	None declared		
Comments			

Title	**Combinations of carbohydrate-deficient transferrin, mean corpuscular erythrocyte volume, gamma-glutamyltransferase, homocysteine and folate increase the significance of biological markers in alcohol dependent patients**		
First Author	**Rinck, D., 2007**	**Source**	**17234365**
Level of evidence	1b	**Study type**	Cohort study
Study quality	Good reference standard, good design, adequate interpretation, adequate number of patients and controls		
Participants	Group A: 177 Group B/control group: 181		
Patient characteristics	Group A: 33 women, 144 men; fulfilled criteria for alcohol dependence according to ICD-10. Mean age: 44 years. They were included at the day of admission to a closed detoxification unit. Group B: control group, social drinkers, volunteers, screened for alcohol consumption and alcohol drinking patterns using structured interview (FEG). None was drinking more than 30 g ethanol per week. Mean age: 30 years		
Intervention	Blood samples: folates, GGT, plasma homocysteine, MCV, %CDT were analyzed.		
Comparison	To advance the clinical diagnostic pattern of identifying alcohol dependent patients using a combination of established laboratory markers and new biomarkers for alcoholism.		
Length of follow-up	None		
Outcome and effect size	MCV: sensitivity 76% (95% CI [69|82]), specificity (95% CI [92.9|98.8]), positive predictive value (PPV) 71.7% (95% CI [67|76.4]), negative predictive value (NPV) 97.3% CDT: sensitivity 84.4% (95% CI [78.2|89.3]), specificity 95% (95% CI [90.7|97.7]), PPV 65.2 % (60.3-70.1%), NPV 98.2% Homocysteine: sensitivity 67% (95% CI [59.6|73.9]), specificity 83.3% (95% CI [77.1|88.5]), PPV 30.9% (95% CI [26.1|35.7]), NPV 95.8% Folate: sensitivity 21.1%, (95% CI [15.5|28]), specificity 97.8% (95% CI [94.4|99.4]), PPV		

	51.5% (95% CI [46.3|56.7]), NPV 91.8% GGT: sensitivity 54.2% (95% CI [46.6|61.6]), specificity 92.8% (95% CI [88|96.1]), PPV 45.5% (95% CI [40.3|50.6]), NPV 94.8% Combination of different markers led to a significant elevation in sensitivity. Best value for men: combination of MCV, CDT, GGT and homocysteine, and folate has a sensitivity of 98.6% and a specificity of 86.4%. Best value for women: combination of MCV and CDT: sensitivity of 94.1% and specificity of 96%.
Funding	Support by a grant from Axis Shield, Norway
Comments	

Title	**Phosphatidylethanol (PEth) concentrations in blood are correlated to reported alcohol intake in alcohol-dependent patients**		
First Author	**Aradottir, S., 2006**	**Source**	**16624837**
Level of evidence	2b	**Study type**	Cohort study
Study quality	Good design, adequate number of participants, good reference standard		
Participants	Group A: 66 outpatients, Group B: 78 inpatients		
Patient characteristics	Group A: 55 men, 11 women, actively drinking patients, mean age was 49.1±9.9 years. Group B: 68 men, 10 women, admitted to the detoxification unit of Hospital. Mean age was 52.9 ± 8.5 years.		
Intervention	PEth analysis: HPLC method; GGT: enzymatic colorimetric assay, different cut-offs applied; CDT: HPLC method; MCV: automated techniques. Time Line Follow Back to obtain estimations of the alcohol consumption during the previous 14 days.		
Comparison	Correlation to ethanol intake and diagnostic sensitivity of the markers		
Length of follow-up	None		
Outcome and effect size	PEth, CDT and GGT correlated to ethanol intake, with the strongest correlation found for PEth. The diagnostic sensitivity for PEth was 99%, and for other markers it varied between 40 and 77%. Only the combination of CDT and GGT reached a sensitivity of 94%. Correlation between PEth and CDT (p>0.001), PEth and GGT (p< 0.001), no correlation between PEth and MCV. Correlation between GGT and MCV (p<0.001). No correlation between CDT and GGT or MCV.		
Funding	Financial support from the Swedish Medical Research Council, the Swedish Alcohol Research Fund, the Royal Physiographic Society in Lund and the Medical Faculty of Lund University		
Comments			

Title	**Effectiveness of pharmacist counseling combined with nicotine replacement therapy: a pragmatic randomized trial with 6,987 smokers**		
First Author	**Costello, M. J., 2011**	**Source**	**21153694**
Level of evidence	2b	**Study type**	RCT
Study quality	Medium		
Participants	N=6967		
Patient characteristics	Smokers		
Intervention	Two models of a pharmacist-led behavioral intervention		
Comparison			
Length of follow-up	5 weeks		
Outcome and effect size	Quit rates were significantly higher among Group A, 3-session completers (27.7%; n=478) compared to Group B participants (18.0%; n=604).		
Funding	The STOP Study was funded by the Ontario Ministry of Health Promotion (awarded to P. Selby)		
Comments			

Title	**Ethyl glucuronide concentration in hair for detecting heavy drinking and/or abstinence: a meta-analysis**		
First Author	**Boscolo-Berto, R., 2013**	**Source**	**23250386**

Level of evidence	Ia	**Study type**	MA following a systematic review
Study quality	good		
Participants	15 studies, n=770		
Patient characteristics	social drinkers (daily>0<60) , heavy drinkers (daily>60), teetotalers (0)		
Intervention	hair ETG, cut offs <7pg/mg (non-use) and >30pg/mg (heavy use)		
Comparison	hair ETG differences between groups, assessment also in terms of recently described cut offs		
Length of follow-up	N.A.		
Outcome and effect size	Partial overlap between teetotalers and social drinkers (related to 7pg/mg cut off) and between social and heavy drinkers (related to 30pg/mg cut off); 7pg/mg cut off may only be used for suspecting active use, not for proving abstinence; 30pg/mg cut off limits false negative effect in differentiating heavy from social drinkers.		
Funding	nothing declared		
Comments	Larger and well-designed population studies are required to draw any definitive conclusion		

Title	**Hair ethyl glucuronide levels as a marker for alcohol use and abuse: A review of the current state of the art**		
First Author	**Crunelle, C. L., 2013**	**Source**	**24239414**
Level of evidence	2c	**Study type**	Review
Study quality	Moderate		
Participants	Techniques=19 papers; Interpretation=23 papers; hair EtG as marker=11 papers		
Patient characteristics	Alcohol dependents, social drinkers, control group		
Intervention	Summary of techniques for hair ETG analyses		
Comparison	N.A.		
Length of follow-up	N.A.		
Outcome and effect size	Description of different methods (GC, LC, EIA) but no comparisons provided. Data interpretation dependent on hair length, pigmentation cosmetic treatments, alcohol consumption profiles, gender, metabolism profiles. ETG as marker: authors refer to the study by Boscolo-Berto.		
Funding	nothing declared		
Comments	EtG quantification in hair is a useful tool for the objective detection of alcohol consumption over extended time periods, but care should be taken when interpreting the result. Altogether this paper is of limited relevance.		

Title	**Inhalation of Alcohol Vapor: Measurement and Implications**		
First Author	**McLean, R. R., 2017**	**Source**	**28054395**
Level of evidence	2a	**Study type**	Meta-analyses
Study quality	good but very small		
Participants	N=21 studies: 14 with occupational exposure, 6 in laboratory tests, 1 with e-cigarette		
Patient characteristics	Persons without special risk factors: employees ore those willing to participate in lab tests		
Intervention	Exposure by hand sanitizer, at workplace or in laboratory to alcohol containing fluids per inhalation or use of alcohol vapor containing e-cigarette		
Comparison	Pre-post Blood alcohol concentration (BAC) and breath alcohol concentration (BrAC) urinary alcohol metabolites, ethyl glucuronide (β-D-6-glucuronide or EtG) and ethyl sulfate (EtS),		
Length of follow-up	None, measurement during up to 4 hours after exposure		
Outcome and effect size	BAC and BrAC showed measurable after exposition: incidental exposure to alcohol vapor from hand sanitizer corresponds to inconsistent or extremely small increases in BrAC and BAC biomarkers. After an 8 hour shift with regular use elevated EtG levels up to 2.100 ng/ml, positive EtG levels in 90% of participants with a mean EtG of 278 ng/ml, Positive urine EtS was present in 72% of the sample with a mean value of 9ng/ml (range=0 to 84ng/ml). Effects mostly subclinical. Puffing from an e-liquid with 23% alcohol was associated with diminished performance on the Purdue Pegboard Dexterity Test, in 3 out		

	of 8 persons EtG levels increased from undetectable to average 371 ng/ml after one session
Funding	Non-commercial: MIRECC and NIH, USA
Comments	No relevant dermal resorption in the studies, no inclusion of vulnerable populations, mainly occupational with hand sanitizers

Title	**Phosphatidylethanol (PEth) Is Superior to Carbohydrate-Deficient Transferrin and γ-glutamyltransferase as an Alcohol Marker and Is a Reliable Estimate of Alcohol Consumption Level**		
First Author	**Walther, L., 2015**	**Source**	**26503066**
Level of evidence	1b	**Study type**	RCT with parallel evaluation of different measurements
Study quality	Good		
Participants	N= 160 enrolled, 115 completed (76 men, 39 women)		
Patient characteristics	Alcohol dependent patients within a RCT for pharmacotherapy, 30-70 years old		
Intervention	Therapy with vareniclin vs. placebo		
Comparison	Diaries about alcohol consumption with PEth, CDT, GGT, AST, ALT at 5 time points. AUDIT and AUDIT-C only before intervention, continuous diary		
Length of follow-up	14 weeks		
Outcome and effect size	PEth rs=0.56 and CDT rs=0.35 with diary, PEth rs=0.23 and CDT rs=0.22 with retrospective consumption (AUDTT), At all consumption levels, PEth had the highest sensitivity of all biomarkers studied. rs=0.63 between the 2 alcohol biomarkers PEth and CDT. PEth values can be translated into an approximate level of alcohol consumption and PEth appears to be a more reliable measure of alcohol consumption than self-reports. At baseline CDT was increased in 42% (n=113), GGT in 15% (n=114), AST in 18% (n=114), and ALT in 9% (n=114), PEth (≥0.02mol/l) in all cases.		
Funding	Pfizer, Sweden, and U.K, Swedish Medical Research Council, also Astra Zeneca's postdoc program, Wilhelm & Martina Lundgren Foundation, SVLS (The Swedish Society of Medicine), Lindhes advokatbyr a, Capios Research Foundation, Tore Nilsons Foundation, SRA (National Alcohol Retailing Monopoly Council for Alcohol Research), Fredrik & Ingrid Thurings Foundation, Svenska Lundbeckstiftelsen, Hj€arnfonden (Swedish Brain Foundation), Magnus Bergvalls Foundation, Skane County Council0s Research and Development Foundation, and Gyllenstierna Krapperups Foundation		
Comments	Results at week 6 used for calculation of correlations between markers and diary		

Title	**Biomarkers for the Detection of Prenatal Alcohol Exposure: A Review**		
First Author	**Bager, H., 2017**	**Source**	**28098942**
Level of evidence	2a	**Study type**	Systematic review
Study quality	Good		
Participants	53 articles selected for data extraction; several thousand participants		
Patient characteristics	Most studies on maternal material, only few on fetal/newborn material (hair, placenta, meconium (majority of studies), nails, blood		
Intervention	Summary of techniques for measurement of EtG (and EtS), FAEEs, PEth		
Comparison	Differeces between different types of consumption over different periods of time		
Length of follow-up	N.A.		
Outcome and effect size	Various techniques and material described; results not directly comparable; strong support for the use of direct ethanol metabloites such as EtG, FAEEs and Peth for screening of alcohol intake during pregnancy; no Effect sizes		
Funding	No COI		
Comments	Testing with respective biomarkers recommended during pregnancy		

Title	**Biomolecules and Biomarkers Used in Diagnosis of Alcohol Drinking and in Monitoring Therapeutic Interventions**		
First Author	**Nanau, R. M., 2015**	**Source**	**26131978**

Level of evidence	2c	**Study type**	Authors state it was a systematic review, however, no respective details are given → rather narrative review
Study quality	Moderate		
Participants	Not reported		
Patient characteristics	Various populations including healthy volunteers, control groups, patients etc		
Intervention	N.A.		
Comparison	N.A.		
Length of follow-up	N.A.		
Outcome and effect size	"There is a clear need for an assay standardization to ensure the use of these biochemical tests as routine biomarkers." No conclusions regarding clinical aspects, no condensed recommendations, no effect sizes.		
Funding	Authors declared to have none, however they declare that the paper was funded by In vitro, a private company, details see next column		
Comments	Manuela G. Neuman is Founder and CEO In Vitro Drug Safety and Biotechnology, Toronto Canada. In Vitro Drug Safety And Biotechnology Inc. is a privately held company in Toronto, ON and is a Single Location business categorized under Commercial Biotechnical Research. Current estimates show this company has an annual revenue of 461120 and employs a staff of approximately 4. (data from google search, performed Jan 30, 2020)		

Title	**Biomarkers of Alcohol Consumption and Related Liver Disease**		
First Author	**Niemelä, O., 2010**	**Source**	**20470213**
Level of evidence	2a	**Study type**	Systematic review
Study quality	Review of “recent literature” on the interpretation of biomarkers and liver status in response to ethanol intake. No flow-chart, no heterogeneity measures, no meta-statistics. Review of “recent literature” on the interpretation of biomarkers and liver status in response to ethanol intake.		
Participants	n. a.		
Patient characteristics	Patients with alcohol intake and liver diseases and associated disorders		
Intervention	All available biomarkers/lab markers for liver disease and alcohol intake are systematically presented, including analytical method		
Comparison	n. a.		
Length of follow-up	n. a.		
Outcome and effect size	Information on the specific role of ethanol consumption behind hepatotoxicity may be obtained through measurements of blood ethanol and its specific metabolites (ETG, phosphatidylethanol, protein-acetaldehyde condensates). Recent studies have indicated that being overweight is another increasingly common cause of abnormal liver enzyme levels and adiposity may also increase the impact of ethanol consumption on liver pathology. Interestingly, increased liver enzyme activities in circulation may reflect not only hepatic function but can also serve as indicators of general health and the status of oxidative stress in vivo. ALT and GGT activities predict insulin resistance, metabolic syndrome, mortality from coronary heart diseases and even mortality from all causes. If the upper reference limits for liver enzyme activities were defined based on the data obtained from normal weight abstainers, the clinical value of liver enzyme measurements as screening tools and in patient follow-up could be significantly improved.		
Funding	Useful review, in particular providing a stepwise approach in individuals with alcohol intake and liver disease		
Comments	Useful review, in particular providing a stepwise approach in individuals with alcohol intake and liver disease		

Title	**Diagnostic Characteristics and Application of Alcohol Biomarkers**		
First Author	**Topic, A., 2013**	**Source**	**23724610**
Level of evidence	2a	**Study type**	Systematic review
Study quality	Review of all available laboratory markers on alcohol use. No flow-chart, no heterogeneity		

	measures, no meta-statistics. Review of all available laboratory markers on alcohol use. No flow-chart, no heterogeneity measures, no meta-statistics.
Participants	n. a.
Patient characteristics	Any subject with alcohol consumption
Intervention	All available biomarkers/lab markers are systematically presented, including analytical method
Comparison	n. a.
Length of follow-up	n. a.
Outcome and effect size	Alcohol biomarkers traditionally used in clinical practice [blood alcohol concentration (BAC), gamma-glutamyl transferase (GGT), carbohydrate-deficient transferrin (CDT), the ratio GGT/CDT, alanine aminotransferase (ALT), aspartate amino-transferase (AST), the ratio AST/ALT, mean corpuscular volume (MCV), phosphatidyl-ethanol (PEth)] are well validated. They are used as screening/monitoring markers of acute/chronic excessive alcohol intake, alcoholism in pregnancy, and other disorders/ conditions related to alcohol abuse. Numerous potential alcohol biomarkers have been discovered, but few are validated. Significant progress has been made in the development of sensitive and practical alcohol transdermal devices that can instantly/continuously measure BAC through human skin. Transdermal sensing of alcohol may become a valuable method for monitoring abstinence.
Funding	This work was supported by grants 173008 and III 41 018 from the Ministry of Education and Science, Republic of Serbia
Comments	Useful review, in particular providing a comprehensive view on lab markers and new aspects of transdermal systems of alcohol detection

Title	**Non-oxidative Ethanol Metabolites as a Measure of Alcohol Intake**		
First Author	**Maenhout, T. M., 2013**	**Source**	**23178443**
Level of evidence	2a	**Study type**	Systematic review
Study quality	Review of the use, and psychometric properties of direct and indirect alcohol markers (traditional and direct biomarkers). No flow-chart, no heterogeneity measures, no meta-statistics.		
Participants	n. a.		
Patient characteristics	Patients/Persons with alcohol use or alcohol use disorders		
Intervention	All available lab markers, in particular direct alcohol markers are presented.		
Comparison	n. a.		
Length of follow-up	n. a.		
Outcome and effect size	Although non-oxidative ethanol metabolites are known for decades, significant advances in analytical techniques, particularly mass spectrometry, were required before accurate and reliable methods for the measurement in biological samples were achieved. As non-invasive markers, EtG and EtS in urine or hair could have a role in screening, diagnosis and monitoring treatment in selected groups of subjects or in general population studies. Due to their intermediate normalization rates, they could fill the gap between direct ethanol measurement and chronic alcohol biomarkers such as CDT and GGT. Additionally, these biomarkers offer a high ethanol-specificity in combination with approximately a two-fold higher sensitivity in comparison with CDT. In case of Forensic use of direct ethanol metabolites, caution has to be taken in interpretation and pre-analytical pitfalls should be considered. PEth seems to be a good candidate as a new alcohol marker due to the high sensitivity and high specificity, but further investigation has to be performed with respect to the determination of applicable cut-off values and interpretation in clinical and forensic situations. FAEE, EtG and EtS in hair have large advantages in comparison to other alcohol markers with respect to specificity since they contain the ethyl group of ethanol and with respect to the longer detection window because of the storage in the steadily growing hair matrix. Future research will focus on further standardization of the analytical methods and implementation of non-oxidative ethanol metabolites in a clinical and especially in a forensic context.		
Funding	n. a.		
Comments	Useful review, in particular providing thorough information on new direct alcohol marker		

Title	Biomarker-Based Approaches for Assessing Alcohol Use Disorders		
First Author	Niemelä, O., 2016	Source	26828506
Level of evidence	2a	Study type	Systematic review
Study quality	A systematic review of the current methods used to measure biomarkers of alcohol consumption was conducted using PubMed and Google Scholar databases (2010–2015).No flow-chart, no heterogeneity measures, no meta-statistics.		
Participants	n. a.		
Patient characteristics	Patients/Persons with alcohol use or alcohol use disorders		
Intervention	All available lab markers, in particular direct alcohol markers are presented.		
Comparison	n. a.		
Length of follow-up	n. a.		
Outcome and effect size	A more systematic use of biomarkers of alcohol consumption, including EtG and CDT or GT-CDT, improves the possibilities for early intervention in alcohol use disorders. Increased activities of serum liver-derived enzymes, LT and GGT, are useful screening tools for liver affection but also prognostic indices of simultaneous extra-hepatic risks, such as metabolic syndrome, and cardio-or cerebrovascular events. GGT levels are linked with the status of oxidative stress, which is a key mechanism by which ethanol use promotes tissue injury.		
Funding	Review of literature regarding direct and indirect biomarkers, including Biomarker Abbreviation, Biological Sample Type and Marker Characteristics. Also, biomarkers of hepatic fibrogenesis are included.		
Comments			

3.1 Kurzinterventionen

Title	Randomized controlled trial of a brief intervention for unhealthy alcohol use in hospitalized Taiwanese men.		
First Author	Liu, S.-I., 2011	Source	21205050
Level of evidence	1b	Study type	RCT
Study quality	high quality; standardized treatment protocol, extensive training (5 days) of interventionists		
Participants	N=616, alcohol dependent patients N=305		
Patient characteristics	Men aged 18–65years admitted to medical or surgical wards in a medical center were approached to participate in the study. Unhealthy alcohol use was divided into (I) heavy drinking, defined as more than 14 drinks week (168g of alcohol) per week in the previous 30 days. Without meeting the criteria for alcohol abuse or dependence, (II) alcohol abuse and, (III) alcohol dependence		
Intervention	BI was based on MI and consisted of two sessions of 30 minutes each, 1 week apart, in conjunction with a brochure which the interventionist reviewed individually with the participants and encouraged them to use as a reference for cutting back or stopping alcohol use		
Comparison	Treatment as usual		
Length of follow-up	Follow-up by telephone at 4, 9 and 12 months		
Outcome and effect size	The intervention group consumed significantly less alcohol than the control group among both unhealthy drinkers and the subgroup of alcohol-dependent participants over 12 months Significantly more participants with alcohol use disorders in the intervention than in the control group (8.3%, vs. 2.1%) consulted specialists by 12 months. Groups did not differ in alcohol-related problems and health-care utilization at follow-up		
Funding	Department of Health, Republic of China (DOH93-TD-M-113-019; and DOH95-TD-M-113-037).		
Comments			

Title	Alcohol screening and brief intervention in primary care: Absence of evidence for efficacy in people with dependence or very heavy drinking.		
First Author	Saitz, R., 2010	Source	20973848
Level of evidence	1b	Study type	Systematic Review

Study quality	High quality; included reviews through 2006; an additional electronic literature search was conducted through 2009; clear search strategy; clear information about inclusion and exclusion of studies: focus only on dependence. Therefore only two studies identified
Participants	N=199
Patient characteristics	Men and women and age not clearly specified; only outpatient primary care settings;
Intervention	In one study including dependent alcoholics 10-15min BI by resident physician. In the other study including dependent alcoholics the BI was done by an experienced addiction psychiatrist, and duration was not specified
Comparison	One study: compared with six weekly 90 min educational sessions. other: not specified
Length of follow-up	One study: 18 months. Other: not specified.
Outcome and effect size	Absence of evidence for the efficacy of BI among primary-care patients with screening-identified alcohol dependence
Funding	NIAAA and NIDA
Comments	

Title	**The effectiveness of brief intervention among injured patients with alcohol dependence: who benefits from brief interventions?**		
First Author	**Field, C., 2010**	**Source**	**20493644**
Level of evidence	1b	**Study type**	RCT
Study quality	extensive training of clinicians; monitoring of treatment fidelity;		
Participants	N=1336		
Patient characteristics	Trauma care setting; male: 82%, 44% (n=588) met criteria for alcohol dependence at baseline. Of the patients eligible for follow-up, 77% completed a 6 month assessment and 66% completed a 12 month assessment		
Intervention	Brief MI (BMI)		
Comparison	treatment as usual (handout) plus assessment		
Length of follow-up	follow-up assessment s by telephone at 6 and 12 months		
Outcome and effect size	consistent interaction between BMI and alcohol dependence status, which indicated higher reductions in volume per week at 6 and 12 months follow-up (ß=-0.56, p=0.03, ß=-0.63, p=0.02, respectively), maximum amount at 6 months (ß=-0.31, p=0.04), and decreases in percent days abstinent at 12 months (ß=0.11, p=0.007) and alcohol problems at 12 months (ß=-2.7, p=0.04) among patients with alcohol dependence receiving BMI. In addition, patients with alcohol dependence at baseline that received BMI were .59 (95% CI [0.39|0.91]) times less likely to meet criteria for alcohol dependence at six months		
Funding	NIAAA		
Comments			

Title	**Approach to treatment of mental illness and substance dependence in remote Indigenous communities: results of a mixed methods study.**		
First Author	**Nagel, T., 2009**	**Source**	**19664081**
Level of evidence	1b	**Study type**	RCT
Study quality	No diagnostic of alcohol dependence; authors used a cut-off of 3 on the severity of dependence scale as indicative of cannabis and alcohol dependence; only 8 subjects with alcohol consumption and without cannabis consumption at baseline approx. one third of the sample were abstinent at baseline		
Participants	N=49 (average SDS-Scale alcohol: 6.9; alcohol consumers at baseline: n=31)		
Patient characteristics	49 Patients of health centers in remote Indigenous communities with "chronic mental illness"		
Intervention	The intervention consisted of two one-hour treatment sessions two to six weeks apart, which integrated problem-solving, motivational therapy and self-management principles.		
Comparison	Controls received the same Intervention with a delay of 6 months		
Length of follow-up	6, 12 and 18 months		
Outcome and effect size	There was significant advantage for treatment for alcohol dependence (p=0.05), with		

	response also evident in cannabis dependence (p=0.064) and with changes in substance dependence sustained over time.
Funding	Dpt. of Health and Community Services, National Health and Medical Research Council and Cooperative Research Centre for Aboriginal Health
Comments	All individuals were initially treated in a mental health center and carers/family members were also included in the intervention

Title	**Some medical inpatients with unhealthy alcohol use may benefit from brief intervention.**		
First Author	**Saitz, R., 2009**	**Source**	**19371494**
Level of evidence	1b	**Study type**	RCT
Study quality	study of good quality, clear procedures, valid instruments 12-month-follow-up rate 84%		
Participants	N=341 Dependent alcoholics: 261 (76 women)		
Patient characteristics	341 adult subjects (99 women) from the medicine service of a large, urban teaching hospital. Eligibility criteria included current (past-month) drinking of risky amounts (defined for eligibility as >14 standard drinks per week or ≥5 drinks per occasion for men; >11 drinks per week or ≥4 drinks per occasion for women and people age ≥66 years		
Intervention	Subjects were randomized to the control or intervention group. Intervention subjects were assigned to 30 minutes of brief motivational counseling that was based on the principles of motivational interviewing. Sessions were conducted by counseling and clinical psychology doctoral students whom we trained and included feedback, an open discussion (lasting about 20 minutes), and construction of a change plan.		
Comparison	Control subjects received usual care (i.e., they were told their screening results and advised they could discuss their alcohol use with their physicians).		
Length of follow-up	3 and 12 months		
Outcome and effect size	Evidence in self-reported receipt of alcohol treatment in the past 3 months among subjects with alcohol dependence and change in the mean number of drinks per day from enrollment to 3 and 12 months in subjects with dependence is moderated by gender and age. Women and younger (<40) men are more likely to profit from BI.		
Funding	not reported		
Comments			

Title	**Evaluation of a telephone-based stepped care intervention for alcohol-related disorders: a randomized controlled trial.**		
First Author	**Bischof, G., 2008**	**Source**	**18054443**
Level of evidence	1b	**Study type**	RCT
Study quality	study of good quality, clear procedures, valid instruments 12-month-follow-up rate 91.7%		
Participants	N=408		
Patient characteristics	Primary care (GPs) patients meeting criteria for alcohol dependence , abuse, at-risk consumption, (average consumption of >20/30g of alcohol per day for women/men within the last 4 weeks, or regular heavy drinking episodes		
Intervention	(binge drinking), defined as >60/80g of alcohol for women/men on at least two occasions within the last 4 weeks) Exclusion criteria were acute or terminal illness, severe drug dependence , not having a telephone, not understanding or speaking German sufficiently, unable to read, being in alcohol specific treatment, and no alcohol consumption in the last 4 weeks.		
Comparison	Eligible participants were randomly assigned to one of three conditions: (1) stepped care (SC): a computerize d intervention plus up to three 40-min telephone-based interventions depending on the success of the previous intervention; (2) full-care (FC): a computerized intervention plus a fixed number of four 30-min telephone-based interventions that equals the maximum of the stepped care intervention; (3) an untreated control group (CG).		
Length of follow-up	booklet on health behavior		
Outcome and effect size	follow-up assessments by telephone at 6 and 12 months		
Funding	Decrease of alcohol use (39.5%) compared to the control group in at-risk drinkers and		

	alcohol abusers; no effects of BI in alcohol dependent patients
Comments	federal government (BMBF)

Title	**Randomized-controlled trial of a telephone and mail intervention for alcohol use disorders: three-month drinking outcomes.**		
First Author	**Brown, R., 2007**	**Source**	**17550366**
Level of evidence	1b	**Study type**	RCT (12 months)
Study quality	extensive training of clinicians; monitoring of treatment fidelity, good follow-up rate (83,5% in men, 84.5% in women)		
Participants	N=897 (EG: N=445 vs. N=452)		
Patient characteristics	Primary care patients aged between 21 and 59 years meeting DSM-IV criteria for alcohol abuse or dependence and no alcohol treatment in the past 3 months. EG vs. CG: female: n=246 (55.3%) vs. n=251 (55.5%); alcohol dependence: n=214 (48.1%) vs. n=211 (46.7%)		
Intervention	Up to six sessions of protocol-driven telephone counseling based on principles of motivational interviewing and stages of readiness to change		
Comparison	Control subjects received a pamphlet on healthy lifestyles.		
Length of follow-up	Follow-up assessments by telephone at 3 months		
Outcome and effect size	Male experimental subjects (N=199) manifested a 30.6% decline in risky drinking days, Compared with a 8.3% decline in controls (N=201, p<0.001). The total consumption declined by 17.3% compared with 12.9% by controls (p=0.001). Female experimental subjects (N=246) manifested a 17.2% decrease in risky drinking days compared with an 11.5% decrease by controls (N=251; p=NS) and a 13.9% decline in total consumption compared with 11.0% by controls (p=NS). Greater numbers of telephone counseling sessions were associated		
Funding	Medicine and Public Health. Pilot study work was supported by the American Academy of Family Physicians Foundation		
Comments			

Title	**A randomized controlled trial of goal choice interventions for alcohol use disorders among men who have sex with men (MSM).**		
First Author	**Morgenstern, J., 2007**	**Source**	**17295566**
Level of evidence	1b	**Study type**	RCT between 2 different types of Intervention (MI vs. MI+CBT); self-selected untreated "controls"
Study quality	Study of moderate quality: no randomized control group, small sample size, no proactive recruitment		
Participants	MI alone n=42, MI+CBT n=47		
Patient characteristics	HIV-negative MSM with current AUD (N=198) were recruited using a wide variety of targeted outreach and media recruitment strategies. Participants (n=89) accepted treatment and were randomized to either 4 sessions of motivational interviewing (MI) or 12 sessions of combined MI and coping skills training (MI+CBT). Other participants (n=109) declined treatment but were followed, forming a non-help-seeking group (NHS)		
Intervention	MI+CBT consisted of 12 weekly sessions. All treatment sessions were videotaped. MI consisted of 4 sessions delivered over 12 weeks, similar to the design of motivational enhancement therapy (MET) in Project MATCH (Project MATCH Research Group, 1993).		
Comparison	Untreated controls initially not interested in treatment received assessment only.		
Length of follow-up	12 week, 12 months		
Outcome and effect size	MI yielded significantly better drinking outcomes during the 12-week treatment period than MI +CBT, but post-treatment outcomes were equivalent. NHS also reduced their drinking significantly (no sig. differences compared to treatment condition). Authors conclude that this reduction was caused by a substantial proportion ("one third") of controls that received alcohol-related treatment between baseline and 12-months f-u.		
Funding	NIAAA		
Comments			

Title	**Brief intervention for medical inpatients with unhealthy alcohol use: a randomized, controlled trial.**		
First Author	**Saitz, R., 2007**	**Source**	**17283347**
Level of evidence	1b	**Study type**	RCT
Study quality	study of good quality, clear procedures, valid instruments 12-month-follow-up rate 84%		
Participants	N=341 Dependent alcoholics: 261 (76 women)		
Patient characteristics	341 adult subjects (99 women) from the medicine service of a large, urban teaching hospital. Eligibility criteria included current (past-month) drinking of risky amounts (defined for eligibility as >14 standard drinks per week or ≥5 drinks per occasion for men; >11 drinks per week or ≥4 drinks per occasion for women and people age ≥66 years);		
Intervention	A 30-minute session of motivational counseling given by trained counselors during a patient's hospitalization (n=172).		
Comparison	Control subjects (n=169) received usual care (i.e., they were told their screening results and advised they could discuss their alcohol use with their physicians).		
Length of follow-up	3 and 12 months		
Outcome and effect size	Evidence in self-reported receipt of alcohol treatment in the past 3 months among subjects with alcohol dependence and change in the mean number of drinks per day from enrollment to 3 and 12 months in all subjects. Main result: Brief intervention is insufficient for linking medical inpatients with treatment for alcohol dependence and for changing alcohol consumption in all patients with unhealthy alcohol use		
Funding	NIAAA & NCRR		
Comments			

Title	**The efficacy of motivation al interviewing as a brief intervention for excessive drinking: a meta-analytic review**		
First Author	**Vasilaki, E., 2006**	**Source**	**16547122**
Level of evidence	1a	**Study type**	meta-analytic review of MI intervention sin RCTs
Study quality	High quality using a well reported and valid methodological quality score for each selected study. Analysis of effect sizes using Coe's effect size calculator. Two different design types: (I) MI vs a no-treatment control, and (II) MI vs a comparison treatment.		
Participants	A total of 2767 participants were included in the 15 brief intervention trials analysed.		
Patient characteristics	Various settings: college students, outpatient community settings, emergency room or clinic settings, specialist substance-abuse treatment agencies.		
Intervention	various BMI approaches (not further specified) from 15 up to 240 minutes conducted by students, nurses, clinicians and researchers		
Comparison	(I) MI vs a no-treatment control, and (II) MI vs a comparison treatment.		
Length of follow-up	Up to six months		
Outcome and effect size	Nine studies compared brief MI with a no-treatment (NT) control group. Five studies compared brief MI with treatment as usual/brief advice/standard care, one with directive-confrontation al counselling, one with educational intervention, one with skill-based counselling (SBC), and one with cognitive behavioral treatment. Aggregated effect size was 0.18 (95% CI [0.07|0.29]) compared to non-intervention. When follow-up period was shorter than 3 months, the ES was greater 0.60 (95% CI [0.36| 0.83]). Compared to other treatments, aggregated effect size was 0.43 (95% CI [0.17|0.70]). MI is more effective with young adults who are heavy-or low-dependent drinkers than with older drinkers or those with a more severe drinking problem and is more cost-effective than more extensive treatments		
Funding	not reported		
Comments			

Title	**Evaluation of a brief intervention in an inner-city emergency department.**		
First Author	**Bazargan-Hejazi, S., 2005**	**Source**	**15988430**

Level of evidence	1b	**Study type**	RCT
Study quality	Study of medium quality; Systematic screening with high participation rate (98%); Low follow-up rates (63%), High refusal rate (40%) in eligible subjects. No independent randomization (each second participant was allocated to the opposite condition than the preceding participant)		
Participants	N=295 ED patients screening positive on the CAGE. without alcohol counselling in the previous 12 months		
Patient characteristics	emergency department		
Intervention	MI (15 to 20 minutes)		
Comparison	health information		
Length of follow-up	in-person follow-up assessments at 3 months		
Outcome and effect size	Among the 185 patients followed up, 64% of the intervention group versus 80% of the control group scored greater than 7 on the follow-up AUDIT (scored on a scale of 1 to 40; p<.05, odds ratio OR=2.35, 95% CI [1.21|4.55]). Multinomial logistic regression analysis demonstrates, after controlling for demographic characteristic s and other independent variables, that assignment to intervention status decreased the odds of at-risk (moderate) drinking as defined by AUDIT scores of 7 to 18 (OR=0.42, p<0.05, 95% CI [0.19|0.91]) but did not affect patients with AUDIT scores in the 19 to 40 range		
Funding	NIAAA, NIH		
Comments	Limitation: it's not clear whether controls received a BI from their physician or GP. Intervention and control group decreased their drinking, but there is no significant difference between groups.		

Title	**A theory-based intervention to reduce alcohol drinking in excess of guideline limits among undergraduate students.**		
First Author	**Hagger, M., 2012**	**Source**	**22233103**
Level of evidence	2b	**Study type**	RCT
Study quality	Study of medium quality. Strengths: deduction of the interventions (theory based) and study question: What kind of intervention/s (single or in combination) exactly shows effects? Limitations: cluster randomization based on academic department low participation rate, low follow up rate of 43,86 % and complete cases of 33,57% respectively; and brief follow up period of 1 month		
Participants	E-mail-invitations to 2.500 students; 709 filled in questionnaire. Final sample of 638. Follow up rate of 43.86%, however excessive amount of data missing from 73 persons, who have been excluded, therefore: complete cases for follow up: N=238 (33.6%)		
Patient characteristics	Undergraduate students from 19 departments in the university of Nottingham / UK. Mean age: 20.4 years; males N=295; females N=414. No obvious in-/exclusion criteria 7.3% did not drink at all. Web-based intervention with incentives		
Intervention	Participants have been randomized to one of the following four groups according to their university department: 1. Mental simulation only 2. Implementation intervention only 3. Mental simulation PLUS implementation intention intervention 4. control group		
Comparison	Assessment only		
Length of follow-up	1 month		
Outcome and effect size	Intention to treat analyses revealed significant main effects for mental simulation on number of units of alcohol consumed (F(1, 227)=6.15, p<0.05, 2 p=0.01) and number of heavy episodic drinking occasions (F(1, 227)=4.27, p<.05, 2 p=0.01).Participants receiving the mental simulation condition reported significantly fewer units consumed (M=42.11, SD=42.54) and heavy episodic drinking occasions (M=3.24, SD=4.34) relative to those that did not receive the manipulation (units of alcohol, M=47.77, SD=41.84; heavy episodic drinking occasions, M=3.81, SD=4.87).		
Funding	European Research Advisory Board		
Comments	Short Follow-up period, low response rate at follow-up		

Title	**Effectiveness of a brief intervention using mental simulation s in reducing alcohol consumption in corporate employees**

First Author	Hagger, M., 2011	Source	21749236
Level of evidence	2b	Study type	
Study quality	Good response in eligible participants, good sample size, low follow-up rates (52.5/60.6%), short follow-up period of one month.		
Participants	281 out of 330 eligible corporate employees allocated to intervention (n=142) and control group (n=139)		
Patient characteristics	Corporate employees (18 years or older) who volunteered to participate in a ‘‘health survey". Of the 10 companies initially approached, three consented to their employees’ participation in the study		
Intervention	Mental simulation manipulation. Participants were presented with an introductory passage of text about alcohol intake and the health benefits of keeping alcohol intake within guideline limits suggesting participants to set themselves a goal of keeping their alcohol intake within guideline limits based on World Health Organization recommend actions. The following simulation exercise asks participants to visualize achieving the goal of keeping alcohol in safe limits. The instructions were followed by a series of blank, ruled lines for participants to write down their responses.		
Comparison	Assessment only		
Length of follow-up	1 month		
Outcome and effect size	The analysis with units of alcohol consumed as the dependent variable revealed a significant main effect for intervention condition (ANCOVA; p<0.05). The analysis with frequency of binge-drinking occasions as the dependent variable revealed no significant main effects. Participants receiving the mental simulation manipulation consumed significantly fewer units of alcohol at follow-up (M=7.24, SD=6.49) relative to participants allocated to the control condition (M=9.30, SD=8.55). There were also significant effects for the baseline number of units (F(1, 149)=50.68, p 5 0.01, Z2 p=0.25), FAST score (F(1, 149)=11.56, p=0.01, Z2 p=0.07) and the intention (F(1, 149)=3.82, p=0.05, Z2 p=0.03) and subjective norm (F(1, 149)=4.53, p 5 0.05, Z2 p=0.03).		
Funding	The European Foundation for Alcohol Research (www.erab.org)		
Comments	Only limited evidence due to inclusion of all employees irrespective of their alcohol consumption. Low response at follow up and short follow-up period.		

Title	Curbing alcohol use in male adults through computer generated personalized advice: randomized controlled trial.		
First Author	Boon, B., 2011	Source	21719412
Level of evidence	1b	Study type	RCT
Study quality	Overall good, good follow-up participation (89%, 91%), but baseline attrition not well documented, highly selective subsample. Participants initially blinded to real purpose of study.		
Participants	N= 450 (Intervention n=230, control n=220)		
Patient characteristics	Participants were males, aged 18 to 65 years, screened positive for risky drinking (>20 units of alcohol per week) and/or binge drinking (>5 units of alcohol at a single occasion at least 1 day per week) in the past 6 months. Selected with a screener from a sampling frame of 25.000 households and of a sample recruited through advertisement in national newspapers		
Intervention	Online personalized feedback including normative feedback on drinking, consequences of drinking, advice on how to reduce alcohol intake in their specific situation, etc., approx. 10 minutes		
Comparison	information-only control: standard brochure (Facts about alcohol)		
Length of follow-up	1 and 6 months		
Outcome and effect size	Participants drinking to below the threshold at 1-month follow-up (Intention-to-treat): Intervention 42% vs. controls 31%, (OR=1.7, 95% CI [1.13|2.46], NNT=8.6, $\chi 2$=6.7, p=0.01). 6-month follow-up 46% vs. C 37% (OR=1.4, 95% CI [0.97|2.06], $\chi 2$=3.3, p=0.07).		
Funding	Netherlands Health Research Council		
Comments	Binge-drinkers not distinguished from risky drinkers, no explicit binge-drinking outcome.		

Title	**Motivation al interviewing + feedback intervention to reduce alcohol-exposed pregnancy risk among college binge drinkers: determinants and patterns of response**		
First Author	**Ceperich, S. D., 2011**	**Source**	**21318412**
Level of evidence	1b	**Study type**	RCT
Study quality	Good. Good follow-up participation (91%). But small and highly selective sample in response to mailings and flyers posted on campus etc.		
Participants	N=228 (Intervention n=114, Controls n=114)		
Patient characteristics	Female, 18 to 24 year old students from a mid-Atlantic urban university at risk for alcohol exposed pregnancy (AEP, having sexual intercourse with a man in the past 90 days, using contraception ineffectively) AND drinking at risk levels (5+ drinks per occasion at least once in the past 90 days or 8+ drinks per week).		
Intervention	BALANCE (Birth Control and Alcohol Awareness: Negotiating Choices Effectively) counseling: single 60 to 75-minute session of personalized feedback and based on Motivational Interviewing, following a semistructured counseling manual		
Comparison	Minimal treatment controls: information pamphlet about women's health.		
Length of follow-up	4 months		
Outcome and effect size	AEP risk difference: 14.7% (I: 20.2% vs. C: 34.9%), $\chi 2=5.51$, $p<0.02$, risk drinking difference: 11.3% (I: 65.3% vs C: 77.6%), $\chi 2=3.12$, $p<0.08$		
Funding	Cooperative agreement MM-0044-02 between the AAMC, CDC, and VCU. Investigator effort was also supported by NIMH K01 MH01688 and NIAAA R01 AA14356		
Comments	1-month outcomes reported in Ingersoll et al., 2005 Not exclusively binge-drinkers.		

Title	**Electronic screening and brief intervention for risky drinking in Swedish university students – a randomized controlled trial.**		
First Author	**Ekman, D. S., 2011**	**Source**	**21316157**
Level of evidence	2b	**Study type**	RCT
Study quality	Not good. Very poor follow-up participation (37%, 24%), analyses based on 6-months follow-up participant only.		
Participants	N=654 (330 vs. 324). But: Analyses based on n=158 (80 vs. 78)		
Patient characteristics	Third-semester students with weekly alcohol use 120 g alcohol+ (women)/ 180 g+ (men) OR ≥2 heavy episodic drinking (HED) occasions (48g+/ 60g+) in past month, 98% binge-drinkers		
Intervention	Extensive normative feedback: Same three statements as comparison group plus more comprehensive normative feedback with information describing participants' alcohol use compared with peers at the university, and, if applicable, advice on reducing any unhealthy levels of consumption. The personalized advice consisted of 12 possible statements or suggestions about the student's alcohol habits.		
Comparison	Very brief feedback consisting of three statements on weekly consumption, frequency of HED, and highest BAC and comparison against safe drinking limits acc. To Swedish Institute for Public Health		
Length of follow-up	3 and 6 months		
Outcome and effect size	No sign. Between group differences regarding HED occasions (34% vs. 27% reduction: weekly consumption (19% vs. -6% reduction), peak BAC (12% vs. 15% reduction), change from risky to non-risky (25% vs. 30%).		
Funding	Within the economical frames of the author's employment at Linköping University. No specific research funding agency contributed to the study		
Comments	Unknown, whether the 55% not agreeing to participate in follow-up also received intervention		

Title	**Reducing high-risk drinking in mandated college students: evaluation of two personalized normative feedback interventions.**		
First Author	**Doumas, D. M., 2011**	**Source**	**21295938**
Level of evidence	2b	**Study type**	RCT
Study quality	Not so good. Small sample, poor follow-up participation (62%).		
Participants	Total N=135 (n=81 vs. 54)		

Patient characteristics	mandated college students, aged 18 to 24 years, 70% male, 84% Caucasian
Intervention	Counselor guided web-based personalized normative feedback (CWF) In addition to SWF, review of feedback with a MI trained counselor. Feedback based on MI principles and techniques, including expressing empathy, developing discrepancy, avoiding argumentation, rolling with resistance, supporting self-efficacy. Counselor and participant reviewed personalized feedback, discussing the participant's drinking profile in relation to peer norms and risk of later problems
Comparison	Self-guided web-based personalized normative feedback (SWF).Based on E-Chug, a brief Web-based program designed to reduce high-risk drinking by providing personalized feedback and normative data regarding drinking and the risks associated with drinking. 30 minutes to complete
Length of follow-up	M=8 months
Outcome and effect size	CWF significantly greater reductions in weekly drinking quantity (17% reduction vs. 34% increase, Wilks' Λ=0.94, F(1, 81)=4.94, p<0.03, η2=0.06) and binge drinking frequency (no change vs. 90% increase, Wilks' Λ=0.95, F(1, 81)=3.91, p<0.05, η2=0.05) than SWF group.
Funding	No information in article
Comments	No untreated controls

Title	**Online alcohol interventions: a systematic review.**		
First Author	**White, A., 2010**	**Source**	**21169175**
Level of evidence	1a	**Study type**	Systematic review
Study quality	High quality study. Strengths: clear objective (to review the efficacy of online interventions for alc. misuse); search strategy stated. Limitation: if any, single studies not well described		
Participants	Literature search identified 31 studies. 17 met inclusion criteria. Out of these 17:12 conducted with university students; 11 specifically focused on at-risk, heavy or binge drinkers. 12 studies predominantly involving brief personalize d feedback interventions. sample sizes ranged from 40 to 3.216 (median 196)		
Patient characteristics	12 out of 17 studies targeted students; however 2 targeted general company employees and 3 community members. Age of participants: students between 18 and 25; other studies mean age 43.1. Percentage of females ranged from 27.6% to 77.9% (mean 54.5%)		
Intervention	12/17 studies evaluated the impact of brief personalized feedback and 7/17 examined an online multi-module information/ education treatment (often incorporating personalized feedback)		
Comparison	Control groups typically received psychoeducational resources (10/17) or completed an online assessment.		
Length of follow-up	Posttreatment assessments were conducted anywhere from 1 week to 12 months, with several studies conducting assessments at multiple time points. Across the 17 studies, 7 had a maximum FU period of a month, 4 had a max. 3-months FU and 3 followed participants to 6 months, one to 12-months post intervention. Retention rates of 83.5% for the IG and 86.3% for the CG.		
Outcome and effect size	Effect sizes could be extracted from 8 of the 17 studies. In relation to alc. units per week /month and based on 5 RCTs where a measure of alc. units per week/month could be extracted, differential effect sizes to posttreatment ranged from 0.02 to 0.81 (M=0.42, Mdn=0.54). Pre-post effect sizes for brief personalized Feedback ranged from 0.02 to 0.81, and in 2 multi-session modularized interventions, a pre-post effect size of 0.56 was obtained in both. Pre-post differential effect sizes for peak blood alcohol concentration s (BAC) ranged from 0.22 to 0.88, with a mean effect size of 0.66		
Funding	Australian Commonwealth Department of Health and Ageing		
Comments	Review provides evidence for effectiveness of online alcohol intervention s. Restrictions: most data come from student samples, number of studies for computing effect sizes was limited		

Title	**Can stand-alone computer-based interventions reduce alcohol consumption? A systematic review.**		
First Author	**Khadjesari, Z., 2011**	**Source**	**21083832**

Level of evidence	1a	**Study type**	Systematic review and meta-analysis
Study quality	High quality. PRISMA standards applied.		
Participants	Twenty four studies included, 19 pooled for meta-analysis. Twenty studies reported a sample size of fewer than 300 participants, six of which had fewer than 100 participants. The smallest sample size was 40, reported in two studies while the largest comprised more than 1000.		
Patient characteristics	RTC's were included in adult populations (aged 18 years and over) with any level of alcohol consumption. This review included studies that measured a change in alcohol consumption. A reduction in alcohol consumption was considered a positive behaviour change. Students were the most commonly studied population group (n=18), with three studies of adult problem drinkers from the general population, two of workplace employees and one of emergency department attendees. Eight studies appeared to screen for hazardous drinking, either in the form of binge drinking, total number of drinks per week, Alcohol Use Disorders Identification Test (AUDIT) cut-off score (generally reported as8) or some combination of these. The other studies used either a lower cut-off score or did not restrict inclusion based on alcohol intake.		
Intervention	Eligible computer-based interventions were those considered behavioural interventions, aimed at bringing about positive behaviour change, adapted for a computer-based format. Inclusion was restricted to stand-alone (non-guided) computer-based interventions. Eligible studies compared computer-based interventions with either a minimally active (e.g. assessment-only, usual care, generic non-tailored information or educational materials) or an active comparator group (e.g. brief intervention)		
Comparison	The majority of studies (n= 22) compared a computer-based intervention with a minimally active comparator group. Minimally active comparators consisted mainly of assessment with some factual information about the harms of excess alcohol consumption, or a waiting-list design. Three studies compared a computer-based intervention with an active comparator group. Active comparator groups consisted of an in-person motivational interview, cognitive behaviour therapy and an expectancy challenge.		
Length of follow-up	Twelve studies measured short-term outcomes (less than 3 months), nine measured medium-term outcomes (3–6 months) and three measured long-term outcomes (longer than 6 months). The shortest length of follow-up was 2 weeks and the longest was 12 months.		
Outcome and effect size	The meta-analyses suggested that computer-based interventions were more effective than minimally active comparator groups (e.g. assessment-only) at reducing alcohol consumed per week in student (Test for overall effect: Z=3.65; p=0.0003; mean difference: -19,42 g/week) and non-student populations (Test for overall effect: Z=2.69; p=0.007; mean difference: -119,94 g/week). However, most studies used the mean to summarize skewed data which could be misleading in small samples. A sensitivity analysis of those studies that used suitable measures of central tendency found that there was no difference between intervention and minimally active comparator groups in alcohol consumed per week by students.		
Funding			
Comments	Studies included cover a broad spectrum of unhealthy alcohol consumption and are not restricted to binge drinking. This is also true for outcome variables. The vast majority of studies comes from student samples		

Title	**Efficacy of web-based personalized normative feedback: a two-year randomize d controlled trial.**		
First Author	**Neighbors, C., 2010**	**Source**	**20873892**
Level of evidence	2b	**Study type**	RCT
Study quality	High quality. Long follow-up period. However, only 51% of invited participants completed assessment. Sophisticated statistical analysis.		
Participants	818 college freshman; 163-164 allocated to five conditions.		
Patient characteristics	Freshmen students at a large university. Of the 2.095 students who completed the screening questionnaire, 898 (56.68% female) met the drinking eligibility criteria of at least five/four drinks for men/women, respectively, on one or more occasions during the past		

	month and were invited to complete the baseline assessment
Intervention	Participants were randomly assigned to (a) single exposure to personal norms feedback (PNF) following the baseline assessment; and (b) biannual exposure of PNF delivered following baseline and after the 6, 12, and 18-month assessment s. Participants receiving feedback were also randomly assigned to receive either (a) gender-specific or (b) gender-nonspecific normative feedback
Comparison	Attention control (non-personalized information).
Length of follow-up	Follow-up assessments at 6, 12, 18, and 24 months post baseline
Outcome and effect size	Results from hierarchical generalized linear models provided modest effects on weekly drinking and alcohol-related problems but not on heavy episodic drinking. Relative to control, gender-specific biannual PNF was associated with reductions over time in weekly drinking (d=-0.16, 95% CI [-0.02|-0.31]), and this effect was partially mediated by changes in perceived norms. For women, but not men, gender-specific biannual PNF was associated with reductions over time in alcohol-related problems relative to control (d=-0.29, 95% CI [-0.15|-0.58]). Few other effects were evident.
Funding	In part by National Institute on Alcohol Abuse and Alcoholism
Comments	Only 51% of invited participants completed assessment. Results are restricted to college students. Long follow-up periods. Results speak in favor of gender-specific normative feedback and longer intervention periods in web-based interventions. Changes are modest

Title	**Efficacy of brief motivation al intervention in reducing binge drinking in young men: A randomized controlled trial.**		
First Author	**Daeppen, J.-B., 2011**	**Source**	**20729010**
Level of evidence	1b	**Study type**	RCT
Study quality	Good, randomization status revealed after assessment, blinded interviewers, computer assisted Interview, good follow-up participation (88%).		
Participants	N=269 Binge-drinkers (intervention: n=125,Controls: 146)		
Patient characteristics	Random sample of a census of men included during army conscription (which is mandatory for 20-year-old males in Switzerland) Binge: 60g+ per occasion at least once a month.		
Intervention	Single face-to-face BMI session, trained master level psychologist, menu of MI elements, supervision e.g. audio-taped sessions, with emphasis on counsellors' style according to MI spirit, principles, e.g. emphasis, collaboration, evocation, autonomy support, etc. Mean length of intervention was 15.8 (±5.5) minutes		
Comparison	Untreated controls, assessment only		
Length of follow-up	6 months		
Outcome and effect size	Binge drinking occasions per month: Incidence rate ratio=0.82 (95 % CI [0.64|1.05], p=0.12) Drinks per week: Incidence rate ratio=0.80 (95 % CI [0.66|0.98], p=0.03)		
Funding	La Commission cantonale de la dîme de l'alcool (CCDA)		
Comments	All conscripts received an intervention, regardless of their drinking status. Table includes numbers and results for binge-drinkers only (Among non-bingers, BMI did not contribute to the maintenance of low-risk drinking).		

Title	**A brief motivational interview in a pediatric emergency department, plus 10-day telephone follow-up, increases attempts to quit drinking among youth and young adults who screen positive for problematic drinking**		
First Author	**Bernstein, J., 2010**	**Source**	**20670329**
Level of evidence	2b	**Study type**	RCT
Study quality	Good, interviewers blinded, 71% of eligibles randomized, follow-up participation ok (69-74%)		
Participants	N= 853 (Intervention n=283, Assessment Control n=284,Minimal Assessment Control n=286)		
Patient characteristics	14–21 year olds presenting to the pediatric ED (87% ≥18 years), with binge drinking (5+/ 4+ in 2 hours for men/ women) or high-risk behaviors in conjunction with alcohol use (e.g. unplanned/ unprotected sex, riding with a drunk driver, injury, fighting, car crash, or an arrest) and ⁄or AUDIT score 4+/ 8+ for 14–17/ 18–21 year olds. Median number of binge		

	episodes per month=1, 45% men
Intervention	20-to 30-minute peer-structured motivational conversation delivered by a peer educator, referral to community resources and treatment if indicated, plus a 5-to 10-minute ''booster'' telephone call after 10 days.
Comparison	Minimal Assessment Controls: brief handout, advice, list of help facilities, and appointment for follow-up in 1 year. Assessment Controls: standard assessment instruments, for re-assessment after 3 and 12 months.
Length of follow-up	3 and 12 months
Outcome and effect size	Exceeded 5+/ 4+ drinks (dichotomous): 3-month: AOR (I vs. AC)=1.10 (95% CI [0.73–1.66]) p=0.653 12-month: AOR=1.02 (95% CI [0.69–1.51]) p=0.929 Interaction p-value=0.768, main effect p-value=0.731
Funding	NIAAA P60AA1375 9, NIAAA Youth Alcohol Prevention Center
Comments	Not exclusively binge-drinkers. No effect on other measures of drinking consumption.

Title	**RCT of effectiveness of motivation al enhancement therapy delivered by nurses for hazardous drinkers in primary care units in Thailand.**		
First Author	**Noknoy, S., 2010**	**Source**	**20236990**
Level of evidence	2b	**Study type**	RCT
Study quality	Well-done study, however small sample size and predominantly male participants (91%) strength: high follow up rates		
Participants	Of 117 subjects, 59 had been randomized to the intervention group and 58 to the control group		
Patient characteristics	Consecutive attenders aged between 18 and 65 years at Primary Care Units (PCU) in Thailand All patients who had an AUDIT score ≥8, without obvious exclusion criteria, were invited to participate in the study. 91% male		
Intervention	Three nurse-based sessions (day 1, at 2 weeks and at 6 weeks after the baseline), each comprising ∼15 min. Intervention is based on principles of MET and tailored to stages of change		
Comparison	Assessment only		
Length of follow-up	6 weeks, 3 months and 6 months		
Outcome and effect size	Significantly reduced frequency of binge drinking in past week at 3 months (p=0.002, 0.29 vs 1.36) but not at 3 weeks (p=0.066; .60 cs. 1.20) and 6 months (p=0.121; 0.45 vs. 0.95). Significantly reduced drinks per week at 3 months (p=0.005, 6.49 vs. 17.00) and 6 months (p=0.0351; 4.72 vs. 11.24).		
Funding	Thai Health Promotion Foundation		
Comments	Not all patients had been binge drinking at baseline (inclusion criterion AUDIT 8 or more points)		

Title	**Efficacy of physician-delivered brief counseling intervention for binge drinkers**		
First Author	**Rubio, G., 2010**	**Source**	**20102995**
Level of evidence	1b	**Study type**	RCT
Study quality	Study with high quality; inclusion of binge drinkers only; large sample size		
Participants	752 subjects met all inclusion criteria and were randomized into an experimental group (n=371) and a control group (n=381)		
Patient characteristics	Patients from primary care centers located in Madrid and 74 family physicians were selected for this study. Binge drinkers were defined as men/women who had drunk 5/4 or more standard drinks per occasion (12.8g of alcohol per drink) on 1 or more occasions in the previous month. Patients with binge drinking and AUDIT score 15 or lower were included (261 female, 491 male). Exclusion of alcohol dependent patients.		
Intervention	Two 10-to 15-minutes counseling sessions 4 weeks apart within the context of routine patient care by a physician using a scripted workbook. The intervention workbook included educational material, a list of methods for cutting down drinking, a treatment contract, and cognitive behavioral exercises. An office nurse contacted the patients 2 and 8 weeks after the initial counseling sessions to reinforce the face-to-face sessions.		

Comparison	A booklet on general health issues
Length of follow-up	12 months
Outcome and effect size	At the end of the follow-up period, 48% of the experimental group subjects had no binge episodes, versus 33% of controls (p=0.001). The subjects of the experimental group also reduced weekly drinking by a mean 3.0 drinks more per week than controls (p=0.001). No effect size reported.
Funding	Grants FCM/03 and FCM/04 (Fundacion Cerebro y Mente) and Instituto de Salud Carlos III, Centro de Investigación en Red de Salud Mental, CIBERSAM
Comments	This study is of special importance since it included only binge drinkers whereas other studies mostly have mixed samples.

Title	**Randomized controlled trial of proactive web-based alcohol screening and brief intervention for university students.**		
First Author	**Kypri, K., 2009**	**Source**	**19752409**
Level of evidence	1b	**Study type**	RCT
Study quality	Study of high quality. Strengths: high number of participants; blind researchers. Limitation: high rate of non-responders		
Participants	N=13.000 students were approached via e-mail; N=7.237 answered; N=2.435 included because of criterion of harmful drinking (8 or more on AUDIT) N=2.050 finished		
Patient characteristics	Participants have been undergraduates of an Australian university, aged 17 to 24 years, Mean age.: 19.7 years; female: 45.5%; mean AUDIT score 14.2		
Intervention	10 minutes of web-based motivational assessment and personalized feedback: 5 topics: explanation of AUDIT score; estimated BAC; monetary expenditure; comparison with other students; hyperlinks help lines; optional: tips for reducing		
Comparison	Received only screening		
Length of follow-up	After 1 month and 6 months		
Outcome and effect size	After one month, IG drank less often (rate ratio 0.89; less alc. overall (0.83; 10 vs. 8 drinks per week) than CG. No differences in binge drinking. At 6 months, intervention effects persisted for drinking frequency (0.91) and overall volume (0.89; 11 vs. 9 drinks per week) but not for other variables. No effect sizes reported.		
Funding	In part by grant 15166 from the Western Australian Health Promotion Foundation (Healthway)		
Comments	Limited evidence by high rate of non-responders		

Title	**Brief intervention for hazardous and harmful drinkers in the emergency department.**		
First Author	**D'Onofrio, G., 2008**	**Source**	**18436340**
Level of evidence	1b	**Study type**	RCT
Study quality	Good. Good follow-up participation (95%, 92%). Blinded follow-up interviewers		
Participants	N=484 (n=247 each group)		
Patient characteristics	ED patients 18+ who screened above NIAAA guidelines for “low-risk” drinking or presented with an alcohol-related injury, 68% men, exclusion of AUDIT 20+.		
Intervention	A Brief (5-10 minutes) Negotiation Interview (performed by emergency practitioners), manual-guided intervention using techniques based on motivational interviewing, brief advice, and behavioral contracting. Four primary steps: (1) raise the subject of alcohol; (2) provide feedback by reviewing the patient’s screening data, make a connection between alcohol and the visit/illness or injury if possible, NIAAA guidelines for low-risk drinking; (3) enhance motivation; and (4) negotiate and advise by summarizing the patient’s reasons for change and negotiating a drinking goal. Patients are then asked to complete and sign a drinking agreement.		
Comparison	Scripted Discharge Instructions (<1 minute), incl. a recommendation to decrease alcohol intake (and, if appropriate, use seatbelts, exercise regularly, and stop smoking). A handout was provided with more information related to all identified health risks.		
Length of follow-up	6 and 12 months		
Outcome and effect size	Non-significant treatment effects: mean number of drinks per week (p=0.4), binge-drinking episodes per month (p=0.7), proportion of low-risk drinkers (p=0.6)		

Funding	National Institute on Alcohol Abuse and Alcoholism grant R01 AA12417-01A1 National Institute on Drug Abuse grant K23 DA15144, and Robert Wood Johnson Generalist Physician Faculty Scholar Award
Comments	No untreated controls, binge-drinkers not distinguished from risky drinkers.

Title	**Motivation al interviewing with underage college drinkers: a preliminary look at the role of empathy and alliance.**		
First Author	**Feldstein, S. W., 2007**	**Source**	**17891666**
Level of evidence	2b	**Study type**	RCT
Study quality	Good follow-up participation (93%), but small, highly selective sample.		
Participants	N= 55 (n=40 vs.15)		
Patient characteristics	Psychology students with heavy drinking (RAPI 3+ points OR at least one binge in the last 2 weeks), 78% women		
Intervention	One 45-minute session MI by doctoral students who had completed the MI ‘‘Training for Trainers’’ workshop		
Comparison	Untreated controls		
Length of follow-up	2 months (93%)		
Outcome and effect size	No significant time by group interaction effect F(2, 47)=2.51, p=0.09 But: MI Group (d=-0.49, M=0.77, 95% CI [0.01|1.02]) had substantially better effect sizes for reductions of binge drinking than controls (d=-0.21, M=1.27, 95% CI [0.32|1.12]).		
Funding	UNM’s Graduate Research and Travel Award		
Comments	Binge-drinkers not distinguished from risky drinkers. Aimed to study empathy and alliance		

Title	**Screening and brief intervention targeting risky drinkers in Danish general practice--a pragmatic controlled trial.**		
First Author	**Beich, A., 2007**	**Source**	**17855332**
Level of evidence	2b	**Study type**	RCT
Study quality	‘Pragmatic’ controlled trial. Selective sample of general practices. Poor follow-up participation (61%). Blinding was not feasible, either for patients and GPs, or for outcome assessment and statistical analysis.		
Participants	N=329 Binge-Drinkers (160 vs. 149) of 906 risky drinkers		
Patient characteristics	GP patients in Denmark aged 18-64, with AUDIT 8-21 and maximum of 35 drinks per week, not been transferred for alcohol treatment , recruited out of 6897 adult patients from 39 GPs, 67% male		
Intervention	Brief (10 min) intervention, based on the ‘drink-less’ protocol (WHO collaborative study on brief interventions, 2001). Feedback on present drinking, advice on reducing drinking with suggestions on how to do it, a self-help booklet, and an open invitation for a follow-up consultation at the earliest convenience . GPs were asked to suggest (and schedule) an appointment. Doctor’s manual, brief flip chart. GPs had received a full-day training course on FRAMES and on how to handle resistance		
Comparison	untreated control group, screening only		
Length of follow-up	12-14 months		
Outcome and effect size	Binge drinking (6+ drinks per occasion at least weekly): Men: ARR=0.08 (95% CI [-0.02|0.18)=32/31 vs 20/114, p=0.13 Women: adverse effects ARR=−0.30 (95% CI [-0.47|0.09). 2/28 vs. 13/35, p=0.007		
Funding	Danish Ministry and Board of Health, Association of County Councils in Denmark, Laegevidens kabens Fremme		
Comments	Not exclusively binge-drinkers, but 82/69% of men/women binged monthly, severe alcohol problems excluded. Binge-drinking was investigated as secondary outcomes. Other (primary) outcomes such as at risk drinking, e.g. usual consumption above /below weekly limits: no effect.		

Title	**Brief motivational intervention and alcohol expectancy challenge with heavy drinking college students: a randomized factorial study.**

First Author	Wood, M.,2007	Source	17658696
Level of evidence	2b	Study type	RCT
Study quality	Study of good quality and sophisticated outcome analysis, however restricted to college students and mixed inclusion criteria (binge drinking, high quantity-frequency, and alcohol-related consequences)		
Participants	345 college students		
Patient characteristics	Students were recruited via posted flyers and advertisements during the early weeks of several successive semesters in the school newspaper. Inclusion criteria, either: (a) heavy drinker status (14 or more drinks per week for men, 10 per week for women); (b) at least one episode of heavy episodic drinking in the past 30 days; and (c) endorsement of at least two alcohol related consequences in the past year. Students, who reported more than 40 drinks per week and/or exhibited moderate to severe dependence, were excluded.		
Intervention	a) Brief motivational intervention (BMI) lasting between 45 and 60 min. b) alcohol expectancy challenge (AEC). Two sessions, held approximately one week apart, 8–10 participants The two sessions followed the same basic format, namely a placebo manipulation followed by an interactive discussion regarding alcohol expectancies, but differed according to content. The first session focused on the positive and negative dose-related effects of alcohol in relation to social situations, while the second session focused on sexual contexts. c) BMI plus AEC		
Comparison	Assessment only		
Length of follow-up	1, 3 and 6 months		
Outcome and effect size	Both BMI (β=-0.23, p<0.05) and AEC (β=-0.28, p<0.01) produced initial significant decreases in the Slope of Heavy Drinking, while AEC was significantly positively associated with the Quadratic Binge Drinking factor, indicating significant intervention decay. For BMI, d was 0.19 at one month, increased to .26 at three months, and decreased to 0.18 by six months. For AEC, d was 0.15 at one month, increased to 0.22 at three months and had diminished completely (d=0.00) by six months		
Funding	National Institute on Alcohol Abuse and Alcoholism		
Comments	Only short-term effects could be observed (in especially for AEC). The study is restricted to college students. The sample is mixed with respect to inclusion criteria (high quantity-frequency, alcohol-related consequences, and binge drinking)		

Title	A randomize d trial of motivation al interviewing and feedback with heavy drinking college students		
First Author	Juárez, P., 2006	Source	17345916
Level of evidence	2b	Study type	RCT
Study quality	Study of good quality, however small sample size and short follow-up, Strength: comparison of two (single or combined) interventions. especially for our question: target group binge drinkers		
Participants	640 students screened. 202 met criterion of heavy drinking. Final sample size of 122 students. FU rate: 73%		
Patient characteristics	Inclusion criterion: at least one occasion of heavy drinking within the previous two weeks (5 or more drinks for men; 4 for women) mean age: 19.43 years females: 52,5% mostly White/non-Hispanic (56,6%) or Hispanic (30.3%) 80,3% were freshman or sophomores they were screened from introductionally or advanced psychology classes at a Southwester n university in New Mexico.		
Intervention	The two interventions to be tested were: 1. MI - here modified MET-MATCH (1995) 2.Feedback (FB) -here according to Check up to Go ("eCHUG) five groups have been compared: 1. MI plus FB 2. MI only 3. FB by e-mail 4. MI plus e-mailed FB 5. control group		
Comparison	Assessment only		
Length of follow-up	Approx. 2 months after baseline assessment, participants completed identical measures to baseline and were interviewed individually about their frequency and quantity of alc. consumption in the two past months, using a modified timeline procedure that lasted 5 to 10 min.		
Outcome and effect size	All five groups reduced their consumption, peak BAC, consequence s and dependence symptoms. For females, there were reductions in consequence s and dependence symptoms in groups that received feedback, as compared to groups that did not receive		

	feedback. For females, there was an effect of the feedback (effect sizes (η^2) 0.22 for dependence symptoms and 0.20 for alcohol related consequence s), but there was no overall effect of MI on any outcome measure.
Funding	Supported in part by grant T32-AA07465 from the National Institute on Alcohol Abuse and Alcoholism
Comments	The study is underpowered and comparisons between intervention groups and control group have to be interpreted with caution. In addition, the follow-up period is rather short

Title	**A controlled trial of web-based feedback for heavy drinking college students**		
First Author	**Walters, S., 2007**	**Source**	**17136461**
Level of evidence	2b	**Study type**	RCT
Study quality	Study of good quality, however a selective sample (universities` freshman). Limitations: captured sample of convenience; relatively short follow-ups and relatively high rate of attrition; Strengths: standardized randomization and intervention; intent to treat analysis		
Participants	N=351 students who completed baseline assessment. 106 out of them met inclusion criterion of at least one heavy drinking episode in the previous month (5 and 4 drinks respectively) 106 (100%) at baseline 76 (71%) at 8 week FU 82 (77.4%) at 16 weeks FU; not mentioned how many allocated to CG and IG		
Patient characteristics	Approx. half female (48.1%) and mostly Caucasian (72.7%) first year students at a large university in Southern US; participation was open to all first-year students, regardless of their drinking status; no further details		
Intervention	Web-based intervention. After assessment, the IG received immediately a personalized feedback called "Check up to go-e-CHUG" • summary of frequency and quantity • comparison to US norms • estimated level of risk • money spent • cigarettes per month • advice and local referral information		
Comparison	Assessment-only		
Length of follow-up	8 weeks and 16 weeks		
Outcome and effect size	At 8 weeks, the IG showed significant decrease in drinks per week and peak BAC over control. By 16 weeks, the CG also declined to a point where there were no differences between groups. e.g. drinks per week at baseline: IG=8.92 and CG=7.7; after 16 weeks: IG=3.17 and CG=2.98.No effect sizes reported.		
Funding	supported by a PRIME grant from the University of Texas School of Public Health		
Comments	Findings are quite restricted due to convenience sample and short follow-up. Only short-term efficacy. No harm to abstainers and light drinkers; The correction of the normative perception seems to play an important role.		

Title	**The efficacy of two brief intervention strategies among injured, at-risk drinkers in the emergency department: impact of tailored messaging and brief advice.**		
First Author	**Blow, F., 2006**	**Source**	**16736077**
Level of evidence	1b	**Study type**	RCT
Study quality	Good, systematic screening, good follow-up participation (>85%), no information on blinding.		
Participants	N=575 (Tailored booklet & advice n=129, Tailored booklet, no advice n=121, Generic booklet & advice n=124, Generic booklet, no advice n=120)		
Patient characteristics	Injured 18+ patients presenting to an ED identified through screening as at-risk drinkers (men <65 y: 15+ per week & 5+ per occasion at least 4x past month, women <65 y & men 65+ y: 12+ per week & 4+ per occ., women 65+ 9+ per day & 4+ per occ.),71% men, mean 28 years old		
Intervention	a)tailored message booklet with brief advice, b)generic message booklet with brief advice, c)tailored message booklet only,		

	Advice by research social workers trained in principles, including those encompassed in FRAMES (Feedback, Responsibility, Advice, Menu, Empathy, Self-Efficacy). Tailoring of booklets included e.g. participant's injury & drinking in comparison to others of same gender and age, age and gender-safer drinking limits, potential benefits of changing alcohol use. Generic booklet contained standard graphics/ text
Comparison	Generic booklet only
Length of follow-up	3 and 12 months
Outcome and effect size	Heavy episodic drinking: significant difference in each of the four groups in mean changes of number of heavy episodic drinking per month from baseline to 12-month follow-up: -1.3 to -2.8 (ps 0.01<0.001). No significant impact of tailored vs. generic message.
Funding	National Institute on Alcohol Abuse and Alcoholism grant AA11629.
Comments	No untreated controls. Not exclusively binge-drinkers.

Title	**Two brief alcohol interventions for mandated college students.**		
First Author	**Borsari, B., 2005**	**Source**	**16187809**
Level of evidence	2b	**Study type**	RCT
Study quality	Good. Good follow-up participation (94%, 89%). But small sample.		
Participants	N=64 (Intervention n=34, Controls n=30)		
Patient characteristics	Mandated College Students with two or more binge episodes past month, 83% male, 100% Binge-drinkers,		
Intervention	In-person brief motivational interview (BMI; Person. Feedback, educational information, harm reduction model, MI principles, M=62 minutes)		
Comparison	An alcohol education session (AE). Information and effects were discussed no personal information were elicited, M=46 minutes		
Length of follow-up	3 and 6 months		
Outcome and effect size	No significant Time x group effect for all four drinking variables, but: sign. Time x group interaction for alcohol-related problems ($F(2, 123)=4.09$, $p<0.05$ in favour of BMI), numerically larger reduction of typical BAC after BMI than AE (30% vs. 11%).		
Funding	National Institute on Alcohol Abuse and Alcoholism Grants F31-AA05571 to Brian Borsari and R01-AA12518 to Kate B. Carey		
Comments	No untreated Controls		

Title	**Reducing alcohol-exposed pregnancy risk in college women: initial outcomes of a clinical trial of a motivation al intervention.**		
First Author	**Ingersoll, K., 2005**	**Source**	**16183466**
Level of evidence	1b	**Study type**	RCT
Study quality	Good. Good follow-up participation (87%), but small and highly selective sample in response to mailings and flyers posted on campus etc.		
Participants	N=228 (Intervention n=114, Controls n=114)		
Patient characteristics	Female, 18 to 24 year old students from a mid-Atlantic urban university at risk for alcohol exposed pregnancy (AEP, having sexual intercourse with a man in the past 90 days, using contraception ineffectively) AND drinking at risk levels (5+ drinks per occasion at least once in the past 90 days or 8+ drinks per week).		
Intervention	BALANCE (Birth Control and Alcohol Awareness: Negotiating Choices Effectively) counseling: single 60 to 75-minute session of personalized feedback and based on Motivational Interviewing, following a semistructured counseling manual.		
Comparison	Minimal treatment controls: information pamphlet about women's health.		
Length of follow-up	1 month		
Outcome and effect size	No risk drinking: 29% intervention vs. 15% controls, $\chi2(1)=5.72$, $p<0.02$. Change in number of binges in past month: 0.2 vs. -2.2, $t=3.08$, $p<.07$ AEP risk: 46 vs. 26%, $\chi2=8.15$, $p<0.005$.		
Funding	Cooperative agreement between the Association of American Medical Colleges, Centers for Disease Control, and the Virginia Commonwealth University, MM-0044-02, and NIMH K01 MH01688.		
Comments	4-months outcomes reported in Ceperich & Ingersoll 2011. Not exclusively binge-drinkers,		

	but 82/ 69% of men/ women binge at least monthly. More severe alcohol problems excluded. Binge drinking was investigated as secondary

Title	**Psychological Interventions for Alcohol Misuse Among People With Co-Occurring Depression or Anxiety Disorders: A Systematic Review**		
First Author	**Baker, A. L., 2012**	**Source**	**21890213**
Level of evidence	1a	**Study type**	Systematic review
Study quality			
Participants	8 RCTs		
Patient characteristics	Individuals with depressive or anxiety disorders		
Intervention	Brief interventions, MI, CBT, MI/CBT, IPT, brief supportive psychotherapy		
Comparison	Active controls, education, treatment as usual		
Length of follow-up			
Outcome and effect size	Motivational interviewing and cognitive–behavioral interventions were associated with significant reductions in alcohol consumption and depressive and/or anxiety symptoms. Although brief interventions were associated with significant improvements in both mental health and alcohol use variables, longer interventions produced even better outcomes.		
Funding	National Health and Medical Research Council, Queensland University of Technology, Australian Postgraduate Awards		
Comments			

Title	**A systematic review of psychological interventions for excessive alcohol consumption among people with psychotic disorders**		
First Author	**Baker, A. L., 2012**	**Source**	**21890213**
Level of evidence	1a	**Study type**	Systematic review
Study quality			
Participants	7 RCTs		
Patient characteristics	individuals with psychotic disorders		
Intervention	Assessment interviews, brief motivational interventions, and lengthier cognitive behavior therapy		
Comparison	Treatment as usual, education, standard interview		
Length of follow-up			
Outcome and effect size	Assessment interviews, brief motivational interventions, and lengthier cognitive behavior therapy have been associated with reductions in alcohol consumption among people with psychosis. While brief interventions (i.e. 1-2 sessions) were generally as effective as longer duration psychological interventions (i.e. 10 sessions) for reducing alcohol consumption, longer interventions provided additional benefits for depression, functioning, and other alcohol outcomes.		
Funding	National Health and Medical Research Council, Queensland University of Technology		
Comments			

Title	**The Effect of Brief Interventions for Alcohol Among People With Comorbid Mental Health Conditions: A Systematic Review of Randomized Trials and Narrative Synthesis**		
First Author	**Boniface, S., 2018**	**Source**	**29293882**
Level of evidence	1a	**Study type**	Systematic Review
Study quality			
Participants	17 RCTs		
Patient characteristics	Adults with risky alcohol consumption and comorbid mental health conditions		
Intervention	Brief interventions		
Comparison	(minimally) active controls		
Length of follow-up			
Outcome and effect size	Where BI was compared with a minimally active control, BI was associated with a significant reduction in alcohol consumption in four out of nine RCTs in common mental		

	disorders and two out of five RCTs in severe mental illness. Where BI was compared with active comparator groups (such as motivational interviewing or cognitive behavioural therapy), findings were also mixed.
Funding	National Institute for Health Research, Biomedical Research Centre for Mental Health, King's Improvement Science, King's Health Partners, Guy's and St Thomas' Charity, Maudsley Charity, Health Foundation
Comments	

Title	**Psychosocial Interventions for People With Both Severe Mental Illness and Substance Misuse**		
First Author	**Hunt, G. E., 2013**	**Source**	**24092525**
Level of evidence	1a	**Study type**	Systematic review
Study quality			
Participants	8 RCTs (n=509)		
Patient characteristics	people with a severe mental illness		
Intervention	motivational interviewing		
Comparison	treatment as usual		
Length of follow-up			
Outcome and effect size	Some differences, favouring treatment, were observed in abstaining from alcohol (n=28, 1 RCT, RR=0.36, 95% CI [0.17|0.75], very low quality of evidence) but no other substances (n=89, 1 RCT, RR=-0.07, 95% CI [-0.56|0.42], very low quality of evidence).		
Funding	The Cochrane Collaboration		
Comments			

Title	**Effectiveness of brief interventions in primary health care settings to decrease alcohol consumption by adult non-dependent drinkers: a systematic review of systematic reviews**		
First Author	**Alvarez-Bueno, 2013**	**Source**	**25514547**
Level of evidence	1a	**Study type**	Systematic review of systematic reviews
Study quality	Included SR ranging from 7 to 11 fulfilled AMSTAR-criteria out of 11. Alvarez-Bueno 2015 did not report a detailed preregistrated protocoll, no comprehensive literature search, did not report the excludud SR's, nor discuss systematically risk of bias, nor Publication bias, No discussion of CoI.		
Participants	7 SR, Range of size: from 2.716 Patients, 7 Studies (1999) to 7.619 pts., 22 Studies included (2007)		
Patient characteristics	Primary health care setting. Adults 17-70 y. o. Non-alcoholic adult drinkers		
Intervention	Brief (or extended) interventions, 3-5-90 min with or without follow-up sessions		
Comparison	usual care or brief or extended interventions with differences in intensity		
Length of follow-up	6-12 months		
Outcome and effect size	Reduction in the weekly alcohol consumption that ranged from 19 to 51g in the BI groups compared with other intervention strategies. Brief interventions have a moderate effect on reducing alcohol consumption among excessive drinkers or people who consume excessive amounts of alcohol and as a consequence these interventions increased the number of people drinking alcohol below established limits of risk. Brief interventions with multiple contacts or follow-up sessions are the most effective. The 5 to 15 min intervention reported more effectiveness than longer intervention or usual care. Finally, overall, the effectiveness of the BI integrating follow-up sessions showed better results than those consisting of a single session.		
Funding	Network for Prevention and Health Promotion in Primary Care (redIAPP, RD12/0005) grant and a research project grant (PI12/01914) from the Instituto de Salud Carlos III (Institute of Health Carlos III) of the Ministry of Economy and Competitiveness (Spain), co-financed with European Union ERDF funds.		
Comments	Elsevir.		

Title	**Efficacy of brief interventions for hazardous drinkers in primary care: systematic review and meta-analyses**		
First Author	**Ballesteros, 2004**	**Source**	**15100612**
Level of evidence	1a	**Study type**	Systematic review and meta-analyses
Study quality	AMSTAR 9		
Participants	13 (12 RCT) studies, n=4353		
Patient characteristics	Hazardous drinkers not satisfying criteria for alcohol dependence. Primary care setting. Age 15-70 y.		
Intervention	MI, one session 3-5min; Or: BI, 10-15minwith follow-up sessions of 3-5min; OR: Extended Intervention, BI with 10-15 min follow-up sessions		
Comparison	"CTRL, no specific advice on alcohol consumption to participants from their primary care providers except if required by the health problem reported or if requested by the patient); Minimal intervention (MI, a unique session of general advice on alcohol consumption lasting ~3-5 min but without stressing strategies to decrease consumption);"		
Length of follow-up	6 -12/ up to 18 months		
Outcome and effect size	No clear evidence of a dose-effect relationship was found. BIs outperformed minimal interventions and usual care (random effects model OR=1.55, 95% CI [1.27|1.90], RD =0.11, 95% CI [0.06|0.16], NNT=10, 95% CI [7|17]). ...The heterogeneity between individual estimates was accounted for by the type of hazardous drinkers (heavy versus moderate) and by the characteristics of the included individuals (treatment seekers versus non treatment seekers). No evidence of publication bias. Support of a moderate efficacy of BIs.		
Funding	not given		
Comments	Enough information was given in text or tables to extract data to carry out an ITT analyses.		

Title	**Reduction of alcohol consumption by brief alcohol intervention in primary care: systematic review and meta-analysis.**		
First Author	**Bertholet, 2005**	**Source**	**15883236**
Level of evidence	1a	**Study type**	Systematic review and meta-analysis
Study quality	No detailed a Priori Protokoll. No discussion of CoI.		
Participants	19 trials, 5639 individuals.		
Patient characteristics	"Outpatients who were actively attending primary care centers or seeing providers, Age 15-70 y. Studies involving alcohol treatment–seeking patients were excluded."		
Intervention	(1) Intervention delivered individually that focused on alcohol consumption with a face-to-face component during the initial session, and (2) intervention defined as “brief intervention” or “motivational intervention” or reporting the use of feedback or advice to reduce alcohol consumption.		
Comparison	N=14: UC, usual care without explicit mention of advice regarding alcohol use, or no intervention. N=5: Intervention <5 min		
Length of follow-up	6-12-48 months		
Outcome and effect size	The definitions and measures of outcomes such as binge drinking, well-being, and problems related to alcohol drinking were too heterogeneous to allow results to be pooled. 17 trials reported a measure of alcohol consumption, of which 8 reported a significant effect of intervention. The adjusted ITT analysis showed a mean pooled difference of -38 g of ethanol (~4 drinks)/week, 95% CI [-51|-24]) in favor of the BAI group. Evidence of other outcome measures was inconclusive.		
Funding	Funding/Support: This study was supported by the Clinical Epidemiology Center and the Alcohol Treatment Center, University Hospital, Lausanne, Switzerland		
Comments			

Title	**The effectiveness of electronic screening and brief intervention for reducing levels of alcohol consumption: a systematic review and meta-analysis**

First Author	Donoghue, 2014	Source	24892426
Level of evidence	1a	Study type	systematic review and meta-analysis
Study quality	With most studies included in this review assessed as being adequate in terms of their methodological quality. Quality of SR: no detailed a priori protocol, Noneligibility: one researcher only, no unpublished data considered, excluded studies not listed, a very general description of the risk of bias. No discussion of CoI.		
Participants	23 studies included for qualitative, 17 studies included for quantitative analysis. Range of n's: 12/12 -1251/84		
Patient characteristics	Participants were identified, through screening, as consuming alcohol to a hazardous level. Student populations (13/17, 76%). 10/17 in the USA.		
Intervention	eSBI: an electronic intervention aimed at providing information and advice designed to achieve a reduction in hazardous/harmful alcohol consumption with no substantial face-to-face therapeutic component. Computer-or Web-based. With assessment followed by personalized and/or normative feedback.		
Comparison	Assessment with no further feedback; 4 studies included w. general information on alcohol consumption.		
Length of follow-up	1 -6 months, attrition rate 1 to 50%		
Outcome and effect size	Mean difference in grams of ethanol consumed per week between those receiving an eSBI versus controls at up to 3 months (mean difference -32.74, 95% CI [-56.80|-8.68], z=2.67, p=0.01), 3 to less than 6 months (mean difference -17.33, 95% CI [-31.82|-2.84], z=2.34, p=0.02), and from 6 months to less than 12 months follow-up (mean difference -14.91, 95% CI [-25.56|-4.26], z=2.74, p=0.01). No statistically significant difference was found at a follow-up period of 12 months or greater (mean difference -7.46, 95% CI [-25.34|10.43], z=0.82, p=0.41).		
Funding	Conflicts of Interest: None declared. Funded by the NIH Research (NIHR) Programme Grants for Applied Research. CD is funded by: NIHR Biomedical Research Centre for Mental Health at S. London, Maudsley NHS Foundation Trust, King's College London, by the NIHR Collaborations for Leadership in Applied Health Research & Care S. London at King's College Hospital NHS Foundation Trust. TP is funded by a NIHR Clinical Doctoral Research Fellowship.		
Comments			

Title	Effectiveness of physician-based interventions with problem drinkers: a review		
First Author	Kahan, 1995	Source	7697578
Level of evidence	1a	Study type	Systematic review
Study quality	Data not extracted. No discussion of CoI.		
Participants	11 trials		
Patient characteristics	All trials examining the effectiveness of interventions by physicians in reducing alcohol consumption among problem drinkers attending a health-care facility		
Intervention	physician-based interventions feasible, practical 30 in or less		
Comparison	In at least two of the trials some subjects in the control group also received counselling on alcohol, and most trials did not even attempt to ascertain the degree of control-group contamination by outside interventions of this kind. Several of the studies did not use a pure control group but instead used a group that received minimal intervention in the form of advice to cut down on their drinking given by letter 22 or verbally by their general practitioner.		
Length of follow-up	Data not extracted		
Outcome and effect size	The four trials with the highest validity scores showed that men in the intervention groups reduced their weekly alcohol consumption by five to seven standard drinks more than the men in the control groups. Results for women were inconsistent. No convincing evidence of declines in alcohol-related morbidity among men or women was found.		
Funding			
Comments	1995		

Title	**A systematic review of the impact of brief interventions on substance use and co-morbid physical and mental health conditions**		
First Author	**Kaner, 2012**	**Source**	
Level of evidence	1a	**Study type**	Systematic review
Study quality	No bias discussed. No list of excluded studies. No preregistered protocol. No information on funding given, no discussion of CoI.		
Participants	14 trials		
Patient characteristics	"Individuals with recognised co-morbidity is involving physical or psychological conditions. 4 trials included patients using many substances though primarily illicit drugs, two related specifically to alcohol misuse and two to tobacco use"		
Intervention	brief interventions, individually delivered on a face-to-face basis		
Comparison	"Control conditions also varied but were generally treated as usual or the provision of written information.1 study: this trial was comparable to brief intervention in other studies."		
Length of follow-up	8 weeks - 1 year		
Outcome and effect size	Heterogenous finding in respect to comorbity, intervention, control condition and outcomes (drugs, alcohol, tobacco). Findings were most positive for brief intervention targeting physical health and substance use outcomes, mixed regarding mental health and substance use and least strong for dual substance use.		
Funding	Not mentioned		
Comments	Design of SR: substance use and co-morbid physical and mental health conditions.		

Title	**Social norms interventions to reduce alcohol misuse in university or college students**		
First Author	**Moreira, 2019**	**Source**	**19588402**
Level of evidence	1a	**Study type**	Systematic review
Study quality	Cochrane		
Participants	Twenty-two studies were included (7,275 participants).		
Patient characteristics	15 to 24 years students (universities, colleges) where all students are asked to participate regardless of drinker status or risk level, or: Targeted interventions focusing on members of a particular group, such as first-year students, fraternity and sorority embers, athletes, members of an academic class, or individuals who are deemed to be at higher risk of alcohol problems		
Intervention	Social normative intervention, 45-175 min, 1 or 2 sessions.		
Comparison	vs no intervention, alcohol education leaflet or other non-normative feedback intervention		
Length of follow-up	1 week -4 years		
Outcome and effect size	"Alcohol related problems: Significant reduction with Web/computer feedback (WF) (SMD=-0.31, 95% CI [-0.59|-0.02]), three studies, 278 participants. No significant eMect of mailed feedback (MF), individual face-to-face feedback (IFF) or group face-to-face feedback (GFF). Peak Blood Alcohol Content (BAC): Significant reduction with WF (SMD=-0.77, 95% CI [-1.25|-0.28]), two studies, 198 participants. No significant eMect of MF or IFF. Drinking Frequency: Significant reduction with WF (SMD=-0.38, 95% CI [-0.63|-0.13]), two studies, 243 participants and IFF (SMD=-0.39, 95% CI [-0.66|-0.12]), two studies, 217 participants. No significant eMect of MF. Drinking Quantity: Significant reduction with WF (SMD=-0.42 , 95% CI [-0.51|-0.18]), five studies, 556 participants and GFF (SMD=-0.32, 95% CI [-0.63|-0.02]) three studies, 173 participants. No significant eMect of MF or IF.Binge drinking: Significant reduction with WF (SMD=-0.47, 95% CI [-0.92|-0.03]) one study, 80 participants, IFF (SMD=-0.25, 95% CI [-0.49|-0.02]) three studies, 278 participants and GFF (SMD=-0.38, 95% CI [-0.62|-0.14]) four studies, 264 participants. No significant eMect for MF. BAC: No significant effect of MF and IFF Drinking norms: Significant reduction with WF (SMD=-0.75, 95% CI [-0.98 |-0.52]) three studies, 312 participants."		
Funding	"One authors department has received funding from the alcohol industry for unrelated prevention research. Oxford Brookes University-School of Health and Social Care, UK. FCT-Fundação ciência e tecnologia, Portugal. AERC -Alcohol Education and Research Council, UK. ERAB -European Research Advisory Board, Belgium."		
Comments	Cochrane		

Title	**Brief interventions for alcohol problems: a meta-analytic review of controlled investigations in treatment-seeking and non-treatment-seeking populations**		
First Author	**Moyer, 2002**	**Source**	**11964101**
Level of evidence	1a	**Study type**	meta-analytic review
Study quality	Low, no detailed search strategy, no bias addressed, no description of included studies, no reasons given for exclusion		
Participants	"Studies in non-treatment-seeking samples (n=34) and in those comparing brief interventions with extended treatment in treatment-seeking samples (n=20). N/study: not given."		
Patient characteristics	"'problem drinkers', 'heavy drinkers' and 'non-problem drinking', in treatment-seeking; and non-treatment-seeking populations"		
Intervention	Brief interventions for alcohol use disorders		
Comparison	control or extended treatment conditions		
Length of follow-up	<3–>12 months		
Outcome and effect size	"Effect sizes for multiple drinking-related outcomes at multiple follow-up points, and took into account the critical distinction between treatment-seeking and non-treatment-seeking samples. For studies of the first type, small to medium aggregate effect sizes in favor of brief interventions emerged across different follow-up points. At follow-up after, the effect for brief interventions compared to control conditions was significantly larger when individuals with more severe alcohol problems were excluded. For studies of the second type, the effect sizes were largely not significantly different from zero. This review summarizes additional positive evidence for brief interventions compared to control conditions typically delivered by health-care professionals to non-treatment-seeking samples. The results concur with previous reviews that found little difference between brief and extended treatment conditions. Because the evidence regarding brief interventions comes from different types of investigation with different samples, generalizations should be restricted to the populations, treatment characteristics and contexts represented in those studies."		
Funding	"This work was supported by National Institute on Alcohol Abuse and Alcoholism grant AA08689, the VA Quality Enhancement Research Initiative and the VA Mental Health Strategic Healthcare Group."		
Comments			

Title	**A systematic review of emergency care brief alcohol interventions for injury patients**		
First Author	**Nilsen, 2008**	**Source**	**18083321**
Level of evidence	1a	**Study type**	Systematic review
Study quality	No a priori defined search strategy, no search by two independent researcher, no grey literature, no ref of excluded studies, No assessment of bias, no CoI addressed		
Participants	14 studies, 12 studies that compared pre-and post-BI results, n= 85 to 1,139		
Patient characteristics	to injury patients in emergency care		
Intervention	Effectiveness of brief alcohol interventions		
Comparison	control group (CG) conditions; 4 studies compared BI-groups of varying intensity		
Length of follow-up	3-12 month-, one study Driving under influence: 3 y		
Outcome and effect size	"BI vs CC: small to medium aggregate effect sizes in favor of BI emerged across different follow-up points. At follow-up after >3-6 months, the effect for BI vs. CC compared to control conditions was significantly larger when individuals with more severe alcohol problems were excluded. BI vs extended interventions: type, the effect sizes were largely not significantly different from zero."		
Funding	This work was supported by National Institute on		
Comments			

Title	**Technology-Based Alcohol Interventions in Primary Care: Systematic Review**

First Author	Ramsey, 2019	Source	30958270
Level of evidence	1a	Study type	Systematic Review
Study quality	studies were rated on risk of bias and found to be predominantly low risk (n=18), followed by moderate risk (n=16), and high risk (n=8)		
Participants	42 studies (among them 28 RCTs)		
Patient characteristics	at-risk drinkers in primary care		
Intervention			
Comparison			
Length of follow-up			
Outcome and effect size	Of the 24 studies with primary or secondary efficacy outcomes related to drinking and drinking-related harms, 17 (71%) reported reduced drinking or harm in all primary and secondary efficacy outcomes. Furthermore, of the 31 studies with direct comparisons with treatment as usual (TAU), 13 (42%) reported that at least half of the primary and secondary efficacy outcomes of the technology-based interventions were superior to TAU. High efficacy was associated with provider involvement and the reported use of an implementation strategy to deliver the technology-based intervention.		
Funding	Alcohol Abuse and Alcoholism grant AA08689, the VA		
Comments			

Title	Motivational interviewing for substance abuse		
First Author	Smedslund, 2011	Source	21563163
Level of evidence	1a	Study type	Systematic review and Meta-Analysis
Study quality			
Participants	59 RCTs		
Patient characteristics	Randomized controlled trials with persons dependent or abusing substances		
Intervention	Motivational Interviewing		
Comparison	no-treatment control, treatment as usual, assessment and feedback, other active treatment.		
Length of follow-up			
Outcome and effect size	Compared to no treatment control MI showed a significant effect on substance use which was strongest at post-intervention SMD=0.79, (95% CI [0.48|1.09]) and weaker at short SMD=0.17 (95% CI [0.09|0.26]), and medium follow-up SMD=0.15 (95% CI [[0.04|0.25]).For long follow-up, the effect was not significant SMD=0.06(95% CI [-0.16|0.28]). There were no significant differences between MI and treatment as usual for either follow-up post-intervention, short and medium follow up. MI did better than assessment and feedback for medium follow-up SMD=0.38 (95% CI [0.10|0.66]).For short follow-up, there was no significant effect. For other active intervention there were no significant effects for either follow-up. There was not enough data to conclude about effects of MI on the secondary outcomes.		
Funding	Quality Enhancement Research Initiative and the VA		
Comments			

Title	Behavioral counseling interventions in primary care to reduce risky/harmful alcohol use by adults: a summary of the evidence for the U.S. Preventive Services Task Force		
First Author	Whitlock, 2004	Source	20722127
Level of evidence	1a	Study type	Systematic review
Study quality	Only studies included that met predefined quality criteria		
Participants	15 high quality intervention studies		
Patient characteristics	risky and harmful drinking adults		
Intervention	1) “very brief interventions” (1 session, up to 5 minutes long) 2) “brief interventions” (1 session, up to 15 minutes long), 3) “brief multicontact interventions” initial session up to 15 minutes long, plus follow-up contacts		
Comparison	assessment only		

Length of follow-up	
Outcome and effect size	Six to 12 months after good-quality, brief, multicontact behavioral counseling interventions (those with up to 15 minutes of initial contact and at least 1 follow-up), participants reduced the average number of drinks per week by 13% to 34% more than controls did, and the proportion of participants drinking at moderate or safe levels was 10% to 19% greater compared with controls. One study reported maintenance of improved drinking patterns for 48 months.
Funding	Mental Health Strategic Healthcare Group.
Comments	

Title	**Effectiveness of SBIRT for Alcohol Use Disorders in the Emergency Department: A Systematic Review**		
First Author	**Barata, 2017**	**Source**	**29085549**
Level of evidence	1a	**Study type**	Systematic review
Study quality			
Participants	35 RCTs		
Patient characteristics	Emergency Department patients identified through screening who are at risk for AUD		
Intervention	Brief intervention (BI) and brief motivational intervention (BMI) strategies		
Comparison	control intervention or usual care		
Length of follow-up			
Outcome and effect size	Thirteen studies enrolling a total of 5.261 participants reported significant differences between control and intervention groups in their main alcohol-outcome criteria of number of drink days and number of units per drink day. Sixteen studies showed a reduction of alcohol consumption in both the control and intervention groups; of those, seven studies did not identify a significant intervention effect for the main outcome criteria, but nine observed some significant differences between BI and control conditions for specific subgroups (i.e., adolescents and adolescents with prior history of drinking and driving; women 22 years old or younger; low or moderate drinkers); or secondary outcome criteria (e.g. reduction in driving while intoxicated).		
Funding	North Shore University Hospital, Department of Emergency Medicine, Manhasset, New York		
Comments			

Title	**Use of non-face-to-face modalities for emergency department screening, brief intervention, and referral to treatment (ED-SBIRT) for high-risk alcohol use: A scoping review**		
First Author	**Biroscak, 2019**	**Source**	**30829126**
Level of evidence	1a	**Study type**	Scoping Review
Study quality			
Participants	28 RCTs, 2 Pre-post studies		
Patient characteristics	Emergency Department patients (including adolescents) identified through screening with high-risk alcohol use patterns as well as study participants targeted for primary public health prevention (e.g., adolescent ED patients)		
Intervention	Non-face-to-face modalities of BI		
Comparison	Control intervention or usual care		
Length of follow-up	Main results were mixed with respect to showing evidence of EDSBIRT intervention effects.		
Outcome and effect size	"Effort on the manuscript by B.J.B. was supported by the National Institute on Minority Health and Health Disparities of the National Institutes of Health (NIH) Loan Repayment Program (LRP) under award number L60MD009893-01. Effort on the manuscript by F.E.V. was supported by the National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health, Office of the Director, National Institutes of Health (OD), Office of Behavioral and Social Sciences Research (OBSSR) under award number R01AA022083. The funding organization had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication."		

Funding	
Comments	

Title	**The effect of brief interventions for alcohol among people with comorbid mental health conditions: a systematic review of randomized trials and narrative synthesis**		
First Author	**Boniface, 2018**	**Source**	**29293882**
Level of evidence	1a	**Study type**	Systematic Review
Study quality			
Participants	17 RCTs		
Patient characteristics	adults with risky alcohol consumption and comorbid mental health conditions		
Intervention	brief interventions		
Comparison	(minimally) active controls		
Length of follow-up			
Outcome and effect size	Where BI was compared with a minimally active control, BI was associated with a significant reduction in alcohol consumption in four out of nine RCTs in common mental disorders and two out of five RCTs in severe mental illness. Where BI was compared with active comparator groups (such as motivational interviewing or cognitive behavioural therapy), findings were also mixed.		
Funding	National Institute for Health Research, Biomedical Research Centre for Mental Health, King's Improvement Science, King's Health Partners, Guy's and St Thomas' Charity, Maudsley Charity, Health Foundation		
Comments			

Title	**A realist review of brief interventions for alcohol misuse delivered in emergency departments.**		
First Author	**Davey, 2015**	**Source**	**25875021**
Level of evidence	1a	**Study type**	Systematic Review
Study quality			
Participants	18 RCTs, 17 Pre-/Post, 2 Reviews, 1 Meta-Analyse, 1 Symposiums-Presentation		
Patient characteristics	ED patients aged 18-64 yrs.		
Intervention	"BIs for alcohol use among adult populations conducted in ED; defined as a single session lasting between 5 and 30 min; however, some BIs were as long as 60 min and were included as long as it involved only one session"		
Comparison	Standard care/usual care (15 studies), active treatment (7 studies; e.g. longer feedback, extended counseling, tailored advice)		
Length of follow-up			
Outcome and effect size	At 12-month follow-up, most studies did not find significant differences between groups with regard to alcohol consumption Identified Context-Mechanism-Outcome configurations: (1) engagement in and retention of BI materials, (2) resolving ambivalence, (3) increased insight/awareness, and (4) increased perceived self-efficacy/empowerment in using one's skills. It is through these mechanisms that patients achieve desirable outcomes from a BI, including an increase in motivation to change, thereby leading to decreased alcohol use and alcohol-related consequences. These processes are more likely to occur when the severity of patients' alcohol use is moderate, when in contemplation stage of change at admission, and when patients enter the ED with a (moderate) injury attributed to alcohol use and have a heightened (but not too high) emotional state upon ED admission.		
Funding	Department of Psychology, Ryerson University, Toronto, Canada. There is no funding agency to acknowledge. This project was completed with no granting agency.		
Comments			

Title	**Electronic Interventions for Alcohol Misuse and Alcohol Use Disorders: A Systematic Review**

First Author	Dedert, 2015	Source	26237752
Level of evidence		Study type	Systematic review and meta-analysis of RCTs with n>=50
Study quality	Risk of bias in adult studies: 3-low, 7-moderate, 4-high. Risk of bias in student studies: 5-low, 8-moderate, 1-high.		
Participants	Total: 28 RCTs (n=14 college student populations, n=14 non-college adults)		
Patient characteristics	Adults who misused alcohol or had an AUD.		
Intervention	"Level of human support: “minimal” support: 17 RCTs, “low” non-counseling support: 8, “moderate or high”: 3. Most trials examined a 1-time intervention (n=19), delivered online or at a desktop computer (n=24), that compared a person's alcohol consumption with his or her peer group norm (n=19). The modal intervention was a single session, 5 trials 2-5 sessions, 1 trial 62 sessions, and 3 trials unlimited access. E-intervention component was personalized normative feedback (8 adult trials, 12 student trials), goal setting (7 adult trials, 3 student trials), psychoeducation (9 adult trials, 7 student trials), and coping skills training (3 adult trials, 2 student trials). "		
Comparison	E-interventions versus inactive controls		
Length of follow-up	6 months and longer		
Outcome and effect size	Significantly reduced alcohol use in student samples after 6 months (MD=-11.7, 95% CI [-19.3|-4.1]), not after 12 months. Marginally reduced alcohol use in adult sample after 6 months (MD=-25.0; 95% CI [-51.9|-1.9]) , not after 12 months There was no statistically significant effect on meeting drinking limit guidelines in adults or on binge-drinking episodes or social consequences of alcohol in college students.		
Funding	Primary funding source of review: U.S. Department of Veterans Affairs.		
Comments			

Title	Brief in Person Interventions for Adolescents and Young Adults Following Alcohol-Related Events in Emergency Care: A Systematic Review and European Evidence Synthesis		
First Author	Diestelkamp, 2016	Source	26314693
Level of evidence	1a	Study type	Systematic Review
Study quality			
Participants	7 RCTs (N=1125) , 6 practice projects, 1 nonrandomised pilot study + 1 observational study		
Patient characteristics	"Study participants are aged between 12 and 25 years and are treated in an emergency care setting (inpatient or outpatient) following an alcohol-related event; Outcome measures address 1 or more of the following: alcohol consumption, alcohol-related risk behaviours, alcohol-related negative consequences and/or seeking of further alcohol treatment or counselling;"		
Intervention	"The intervention is a brief intervention (maximum 60 min) consisting of a maximum of 3 sessions with a minimum of 1 session delivered in the ED; is focused on alcohol use and is delivered in person"		
Comparison	"The control condition consists either of no treatment, standard care, an intervention other than a BI or a BI of different intensity"		
Length of follow-up			
Outcome and effect size	Six RCTs found reductions of alcohol use for all participants. Four RCTs found effects on alcohol consumption, alcohol-related risk-behavior or referral to treatment. Heterogeneity of study designs and effects limit conclusions on effectiveness of BIs for young ED patients following an alcohol-related event.		
Funding	"Supported by the German Federal Ministry of Education and Research (grant number 01KQ1002B) and aims at strengthening health care regions in Germany by establishing new transsectoral cooperations and implement and evaluate selected innovations."		
Comments			

Title	Variance in the Efficacy of Brief Interventions to Reduce Hazardous and Harmful Alcohol Consumption Between Injury and Noninjury Patients in Emergency Departments: A Systematic Review and Meta-Analysis of Randomized Controlled Trials		
First Author	Elzerbi, 2017	Source	28669555

Level of evidence	1a	**Study type**	Systematic Review
Study quality			
Participants	23 RCTs, N=15.173		
Patient characteristics	"ED patients aged 16-64 yrs. not seeking treatment for alcohol use and meeting a minimum criterion of hazardous or harmful drinking (hazardous and harmful drinking was understood as regular average consumption of 20 to 40 g and >40 g of alcohol per day for women and 40 to 60 g and >60 g per day for men, respectively. Trials were excluded that focused exclusively on dependent drinkers"		
Intervention	"brief intervention was defined as no more than 4 sessions, each session lasting no longer than 45 minutes and delivered face-to-face, by short message service, detailed health information workbooks, over the telephone or electronically) and was delivered by non-specialist personnel and carried out in non-specialist settings"		
Comparison	"Comparator control groups varied from “screening only” and “assessment only” to “treatment as usual”, “evaluation only”, or “minimal intervention” (such as the provision of an information leaflet). Trials were excluded that focused exclusively on dependent drinkers."		
Length of follow-up			
Outcome and effect size	"At 6-month follow-up, an effect in favor of brief intervention over control was identified for targeted injury studies. For pooled non-injury-specific studies, small benefits of brief intervention were evident at less than or equal to 5-month follow-up, at 6-month follow–up and at 12-month follow-up. Meta-analysis identified noninjury-specific studies as associated with better response to brief intervention than targeted injury studies."		
Funding	"National Addiction Centre, Addictions Department, Institute of Psychiatry, Psychology and Neuroscience, King’s College London, London, UK"		
Comments			

Title	**Social norms information for alcohol misuse in university and college students**		
First Author	**Foxcroft, 2015**	**Source**	**25622306**
Level of evidence		**Study type**	Systematic review of RCTs with individual or cluster designs
Study quality	Good. RCTs high risk of bias particularly with regards to blinding of participants/ personnel and incomplete outcome data		
Participants	Total: 70 studies (n=44.958 participants). Meta-analyses: 63 studies (n=42.784 participants).		
Patient characteristics	University and college students. 43 at-risk samples, 6 mandate samples, 26 samples derived from all available students		
Intervention	Social norms interventions delivered by mailed normative feedback (MF); web/computer normative feedback (WF); individual face-to-face normative feedback (IFF); group face-to-face normative feedback (GFF); and normative marketing campaign (MC). Interventions varied from no face-to-face contact session (paper or web feedback) to one or two face-to-face contact sessions with duration ranging from 45 minutes (Neal 2004) to 175 minutes (Michael 2006). Some studies involved a booster session a erth initial intervention, providing students with personalized normative feedback at later time points		
Comparison	Control intervention: Interventions with no social norms component including no intervention or minimal intervention in the form of a leaflet, or an educational or psychosocial intervention without a social norms component.		
Length of follow-up	Mainly somewhere between immediate post intervention to 12 months. 24 months: 3 RCTs, 36 months 2 RCTs, 48 months 1 RCT.		
Outcome and effect size	Over the longer-term, after four or more months of follow-up, there was a small effect of social norms information on binge drinking (pooled across delivery modes: SMD=-0.06, 95% CI [-0.11|-0.02] (participants=11.292; studies=16; moderate quality evidence), drinking quantity (pooled across delivery modes: SMD=-0.08, 95% CI [-0.12|-0.04] (participants=21.169; studies=32; moderate quality evidence), and peak BAC (pooled across delivery modes: SMD=-0.08, 95% CI [-0.17|0.00] (participants=7198; studies=11; low quality evidence). For these outcomes, effects were not any different across the different delivery modes.		
Funding	The U.S. National Institutes of Health provided funding for just under half (33/70) of the		

	studies included in this review. Eighteen studies provided no information about funding, and only 13 papers had a clear conflict of interest statement.
Comments	

Title	**Motivational interviewing for the prevention of alcohol misuse in young adults**		
First Author	**Foxcroft, 2016**	**Source**	**27426026**
Level of evidence		**Study type**	Systematic review of randomized controlled trials
Study quality	low and moderate quality studies		
Participants	Total: 84 trials (n=22872 participants). Higher risk samples: 70 trials.		
Patient characteristics	Young adults up to the age of 25 years. Some trials also included adolescents (aged 15+). Most trials (70) targeted participants at-risk (positive screen).		
Intervention	MIs are defined as a one or more session approach including MI principles (adopting an empathic non-judgemental stance, listening reflectively, developing discrepancy, rolling with resistance and avoiding argument, supporting efficacy to change) as the core of the intervention as well as a feedback element or other non-MI techniques. At least 65 of the trials investigated MI as part of brief alcohol interventions.		
Comparison	MI versus no intervention/ assessment only. MI versus alternative interventions.		
Length of follow-up	Studies with follow-up periods of at least four months were of more interest in assessing the sustainability of intervention effects and were also less susceptible to short-term reporting or publication bias.		
Outcome and effect size	Long-term (→ 4 months): Effects in favour of MI for the quantity of alcohol consumed (standardized mean difference (SMD)=-0.11, 95% CI [-0.15|-0.06]; moderate quality evidence); frequency of alcohol consumption (SMD=-0.14, 95% CI [-0.2|-0.07]; moderate quality evidence); and peak blood alcohol concentration, or BAC (SMD=-0.12, 95% CI [-0.20 |0.05]; moderate quality evidence). Binge-Drinking: no effects for binge drinking (SMD=-0.04, 95% CI [-0.09|0.02], moderate quality evidence) or for average BAC (SMD=-0.05, 95% CI [-0.18|0.08]; moderate quality evidence). Further analyses showed that there was no clear relationship between the duration of the MI intervention (in minutes) and effect size. Subgroup analyses revealed no clear subgroup effects for longer-term outcomes (four or more months) for assessment only versus alternative intervention controls; for university/college vs other settings; or for higher risk vs all/low risk participants.		
Funding	"The US National Institutes of Health provided funding for half (42/84) of the studies included in this review. Twenty-nine studies provided no information about funding, and only eight papers had a clear conflict of interest statement."		
Comments			

Title	**Brief intervention and decrease of alcohol consumption among women: a systematic review**		
First Author	**Gebara, 2013**	**Source**	**24016074**
Level of evidence		**Study type**	RCTs, systematic review.
Study quality			
Participants	36 Studien		
Patient characteristics	15 Studien nur Frauen, 10 Studien Männer und Frauen, 10 Studien Studenten und Studentinnen, 1 Studien allgemeine Bevölkerung		
Intervention	Kurzintervention: 36 articles that met the following inclusion criteria: a) performed and/or evaluated the effectiveness of a BI; b) performed a BI toward alcohol consumption (no other drugs); c) presented women as part of the studied sample		
Comparison	es soll genauer bestimmt werden, ob BI auch bei Frauen gleich gut wirken		
Length of follow-up	3, 6 und 12 Monate		
Outcome and effect size	In general, the results indicated a decrease in alcohol consumption among women following BI, both in the number of days of consumption and the number of doses, suggesting that the impact on the woman's reproductive health and the lower social acceptance of female consumption can be aspects favorable for the effectiveness of BI in this population		

Funding	nach einer Kurzintervention ist in der Regel eine Reduktion sowohl der Menge als auch der Trinktage zu beobachten, kann aber nicht systematisch belegt werden.
Comments	

Title	**Specialty substance use disorder services following brief alcohol intervention: a meta-analysis of randomized controlled trials**		
First Author	**Glass, 2015**	**Source**	**25913697**
Level of evidence	1a	**Study type**	Systematic review and meta-analysis of RCTs in general health-care settings with adult and adolescent samples
Study quality	13 Studies included, 9 meta-analyzed		
Participants			
Patient characteristics	"Adult and Adolescent samples, exclusion of studies in which the outcome consisted of attendance at treatment sessions that were delivered by clinical research interventionists as part of the research study"		
Intervention	"The majority of interventions involved brief advice or a motivational interview ; several offered additional counseling or booster intervention sessions and one intervention had no in-person contact and simply mailed a letter to participants requesting they make an appointment with a specialist"		
Comparison	Mostly assessment only or non-alcohol specific health advice, one study with brief advice + 2 booster sessions		
Length of follow-up	"Follow-up periods ranged from 3 to 18 months, except for one study that had a 10-year follow-up."		
Outcome and effect size	"Thirteen RCTs met inclusion criteria and nine were meta-analyzed (n= 993 and n= 937 intervention and control group participants, respectively). In our main analyses the pooled risk ratio (RR) was 1.08, 95% CI [0.92|1.28]. Five studies compared referral-specific interventions with a control condition without such interventions (pooled RR=1.08, 95% CI [0.81|1.43]). Other subgroup analyses of studies with common characteristics (e.g. age, setting, severity, risk of bias) yielded non-statistically significant results."		
Funding	Not reported		
Comments			

Title	**Are nurse-conducted brief interventions (NCBIs) efficacious for hazardous or harmful alcohol use? A systematic review**		
First Author	**Joseph, 2014**	**Source**	**24645911**
Level of evidence		**Study type**	RCTs, systematic review.
Study quality	Studien recht heterogen,		
Participants	11 RCTs, 2676 participants (2098 men and 578 women)		
Patient characteristics	"Total of 2.676 participants (2.098 men and 578 women) were included in the 11 NCBI trials analysed. The mean age of the participants was 37.47 years (SD=13.88). Of the 2.676 participants, 1.986 completed the follow-up assessment and three trials reported a follow-up rate of less than 70%. Follow-up length varied with the trials ranging from 3 months to 2 years. Problemtrinker."		
Intervention	alkoholbezogene Kurzinterventionen von Pflegepersonal im Vergleich mit anderen Bedingungen		
Comparison	Interventionen durch Pflegekräfte		
Length of follow-up	3 Monate bis 2 Jahre		
Outcome and effect size	"Eleven trials were found meeting inclusion criteria, comparing nurse-conducted brief interventions with a control group or with other treatments. Five trials reported a statistically significant reduction in alcohol consumption in the intervention group with 6–12-month follow-up period and two trials concluded that brief interventions delivered by nurses were as efficacious as by physicians." The findings of included studies in the present review do not provide a unique result because of different outcome measures such as reduction in the percentages of hazardous drinkers, changes in AUDIT scores, alcohol-related problems, number of drinking days, number of abstinent days and binge drinking episodes. Also secondary outcome measures of two trials showed no improvement in the number of standard drinks taken each		

	drinking day (Goodall et al. 2008), and alcohol consumption in a typical week (Smith et al. 2003) in the treatment group as compared with the control group.
Funding	
Comments	Common methodological problems were attrition, short follow ups, lack of collateral or objective (e.g. serum and breath analyses) verification, non-blinded follow ups, and lack of parallel eplication with separate research teams.

Title	**Personalized digital interventions for reducing hazardous and harmful alcohol consumption in community-dwelling populations**		
First Author	**Kaner, 2017**	**Source**	**28944453**
Level of evidence	1a	**Study type**	Systematic review and meta-analyses of randomized controlled trials
Study quality	Good. Moderate-quality trials, substantial heterogeneity among trials		
Participants	Total: 57 trials (n=34.390 participants). Primary meta-analysis: 41 trials (n=19.241 participants). Binge-drinking frequency meta-analysis: 15 trials (n=3.587). Delivery mode meta-analysis: 5 trials (n=390)		
Patient characteristics	People living in the community whose alcohol consumption had been screened as hazardous or harmful and who were directed toward any digital intervention including web-based, mobile phone text messaging, smartphone apps, social networking, or stand-alone computer-based technologies. No restrictions to age.		
Intervention	Digital interventions: Interventions were digital, defined as being delivered primarily through a programmable computer or mobile device (laptop, phone or tablet), and were responsive to user input to generate personalised content which aimed to change the participants' alcohol-related behaviours. Interventions were not restricted to those accessible online (CD-ROM also included). Not explicitly brief intervention.		
Comparison	Digital interventions vs. no interventions. Digital intervention vs. face-to-face interventions (5 trials, n=390).		
Length of follow-up	Longest follow-up time; range: 1-24 months; median=3 months.		
Outcome and effect size	Primary meta-analysis: Participants using a digital intervention drank approximately 23g alcohol weekly (95% CI [15|30]) less than participants who received no or minimal interventions. Binge-drinking meta-analysis: The estimated difference between the digital intervention and no or minimal intervention arms in the number of binges per week was -0.24 (95% CI [-0.35|-0.13]), The risk ratio of being a binge drinker at the time of longest follow-up among those randomised to a digital intervention relative to those randomised to a control or minimal intervention condition was 0.98 (95% CI [0.97|1.00]). Delivery mode meta-analysis: No difference in alcohol consumption at end of follow up (MD=0.52 g/week, 95% CI [-24.59|25.63]; low-quality evidence).		
Funding	56% of the trials were funded by government or research foundation funds; 11% by personal awards such as PhD fellowships; and 33% did not report sources of funding.		
Comments			

Title	**Effectiveness of brief alcohol interventions in primary care populations**		
First Author	**Kaner, 2018**	**Source**	**17443541**
Level of evidence	1a	**Study type**	Systematic review and meta-analyses of randomized controlled trials
Study quality	Good. Moderate-quality trials, substantial heterogeneity among trials		
Participants	Total: 69 trials (n=33642 participants); Primary meta-analysis: 34 trials (n=15197). Binge-drinking frequency meta-analysis: 15 trials (n=6946). Binge-drinking percentage meta-analysis: 10 trials (n=4456)		
Patient characteristics	Primary care populations: Participants recruited in general practice (38 trials), emergency care (27 trials), college health clinics (2 trials), public sexual health clinic (1 trial), veterans' affair medical center (1 trial). Few studies targeted particular age groups: adolescents or young adults (6 studies, 9%) and older adults (4 studies, 6%). Mean baseline alcohol consumption was 244 g/week (30.5 standard UK units) among the studies that reported		

	these data.
Intervention	"Brief intervention: a single session and up to 5 sessions of verbally-delivered information, advice or counselling that was designed to achieve a reduction in risky alcohol consumption, alcohol-related problems, or both. Extended intervention: more than five sessions or total combined session durations was more than 60 minutes. "
Comparison	Brief intervention vs. minimal or no intervention (61 trials). Extended interventions vs. brief (4 trials), minimal/ no intervention (7 trials).
Length of follow-up	Primary meta-analysis: 12 months
Outcome and effect size	Primary meta-analysis: Alcohol per week reduced by 20g in BI groups compared to minimal or no intervention interventions (95% CI [-28|-12]). Binge-drinking meta-analyses: Moderate-quality evidence of a very small impact on binge drinking frequency (MD=-0.08 binges/week, 95% CI [-0.14|-0.02]). Sign reduction in the percentage of binge drinkers at 12 months (-7%, 95% (CI [-12|-2], substantial heterogeneity); no difference between brief and extended interventions.
Funding	Sources of funding were reported by 60 studies (87%). With two exceptions, studies were funded by government institutes, research bodies or charitable foundations. One study was partly funded by a pharmaceutical company and a brewers association, another by a company developing diagnostic testing equipment.
Comments	Background Text: No difference between efficacy and effectiveness findings; Effective in Emergency setting but lower impact than in GP setting (mean difference -10g/week, 95% CI [-18|-2] vs. -26 g/week, 95% CI [-37|-14]). Five studies reported adverse effects (very low-quality evidence): No adverse effects (2 trials); increased binge drinking for women (1 trial), adverse events related to driving outcomes but equivalent in both study arms (2 trials).

Title	**Interventions to prevent and reduce excessive alcohol consumption in older people: a systematic review and meta-analysis**		
First Author	**Kelly, 2018**	**Source**	**28985250**
Level of evidence		**Study type**	RCTs, meta-analysis
Study quality	Angesichts der Heterogenität und der geringen Anzahl der Studien sollten die Ergebnisse vorsichtig interpretiert werden.		
Participants	13 Studien		
Patient characteristics	Prävention oder Reduktion kritischen Alkoholkonsums bei älteren Menschen (über 55 J.) fanden sich 10 Studien zu dem Personenkreis mit kritischem oder schädlichem (harmful or hazardous) Alkoholgebrauch. Ausgeschlossen wurden Studien mit alkoholabhängigen Menschen.		
Intervention	Kurzintervention bei Älteren		
Comparison			
Length of follow-up	3 bis 6 Monate, max. ein Jahr		
Outcome and effect size	Im Ergebnis finden sich bei den Kurzinterventionen positive Effekte wie Verringerungen des Risiko-Scores und/oder Trinkmengenreduktion – aufrechterhalten über ein Jahr –, jedoch ohne signifikante Unterschiede zu den Kontrollgruppen, bei denen schon bei einfachen Interventionen wie Flyer oder Rückmeldungen zum Trinkverhalten eine Verringerung der Trinkmenge berichtet wurde. Nur zweimal wurde nach Geschlecht getrennt ausgewertet: Es fanden sich keine signifikanten Unterschiede in den Ergebnismaßen bezüglich Geschlecht. Soweit möglich wurden die Daten einer Meta-Analyse unterzogen, 8 Studien mit 3.591 Teilnehmern wurden eingeschlossen. In der Meta-Analyse (5 Studien mit Kurzintervention) fand sich ein signifikanter Effekt nach 3 bis 6 Monaten auf die Trinkmenge (mittlere Standard-Differenz SMD=-0,17 (95% CI [-0,30|-0,04]). In der Meta-Analyse (5 Studien mit Kurzintervention) fand sich ein signifikanter Effekt nach 3 bis 6 Monaten auf die Trinkmenge (mittlere Standard-Differenz SMD=-0,17 (95% CI [-30|-0,04])		
Funding			
Comments			

Title	**Can stand-alone computer-based interventions reduce alcohol consumption? A systematic review**		
First Author	**Khadjesari ,2011**	**Source**	**21083832**
Level of evidence	1a	**Study type**	Systematic review and meta-analysis of RCTs
Study quality	High quality. PRISMA standards applied.		
Participants	"24 studies included, 19 pooled for meta-analysis. Range of sample size: 40-1.000. 20 studies with n<300) "		
Patient characteristics	"Adult populations (aged ≥18 years) with any level of alcohol consumption; studies that measured a change in alcohol consumption. A reduction in alcohol consumption was considered a positive behaviour change. Students (n=18), adult problem drinkers from the general population (n=3), work-place employees (n=2), emergency department attendees (n=1). Eight studies appeared to screen for hazardous drinking, either in the form of binge drinking, total number of drinks per week, Alcohol Use Disorders Identification Test (AUDIT) cut-off score (generally reported as8) or some combination of these. The other studies used either a lower cut-off score or did not restrict inclusion based on alcohol intake "		
Intervention	"Eligible computer-based interventions were those considered behavioural interventions, aimed at bringing about positive behaviour change, adapted for a computer-based format. Inclusion was restricted to stand-alone (non-guided) computer-based interventions. Most studies delivered the intervention via the internet (n=14). One study sent tailored text-messages to handheld computers, while the others were available from a computer in a fixed location. Most interventions were accessed from computers at a location determined by the researchers (n=16); the remainder were able to access the intervention online at a location and time convenient to them."		
Comparison	Computer-based interventions versus minimally active group (e.g. assessment-only, usual care, generic non-tailored information or educational materials, n=22 RCTs). Computer-based interventions versus active comparator group (e.g. brief intervention, n=3 RCTs).		
Length of follow-up	"Short-term (<3 months, 12 RCTs), medium-term (3-6 months, 9 RCTs), long-term (>6 months, 9 RCTs). Range: 2 weeks to 12 months."		
Outcome and effect size	Computer-based interventions were more effective than minimally active comparator groups (e.g. assessment-only) at reducing alcohol consumed per week in student and non-student populations. However, most studies used the mean to summarize skewed data, which could be misleading in small samples. A sensitivity analysis of those studies that used suitable measures of central tendency found that there was no difference between intervention and minimally active comparator groups in alcohol consumed per week by students. Participants receiving a computer-based intervention appeared to reduce their frequency of binge drinking compared with those receiving a minimally active comparator (mean difference=-0.23 days per week; 95% CI [-0.47|0.00]; p=0.05).		
Funding	None reported.		
Comments	"Studies included cover a broad spectrum of unhealthy alcohol consumption and are not restricted to binge drinking. This is also true for outcome variables. Majority student samples."		

Title	**Systematic Review on the Effectiveness of Brief Interventions for Alcohol Misuse among Adults in Emergency Departments**		
First Author	**Landy, 2016**	**Source**	**26482134**
Level of evidence	1a	**Study type**	Systematic Review
Study quality			
Participants	34 RCTs		
Patient characteristics	ED patients aged 18-65 yrs.		
Intervention	Single session typically lasting 5-30 minutes, a few studies lasted as long as 60 minutes		
Comparison	Control intervention or usual care		
Length of follow-up			
Outcome and effect size	All studies reported a significant reduction in alcohol consumption at 3 months post-BI, with some studies finding significant differences between the BI and control groups, and other studies finding significant decreases in both conditions but no between-groups		

	differences. The majority of studies did not find significant between-group differences at 6 and 12 months post-BI with regard to decreases in alcohol consumption. Individuals who received a BI were significantly less likely to have an alcohol-related injury at 6 or 12 months post-BI than individuals who did not receive a BI. BIs are unlikely to reduce subsequent hospitalizations however, they may be effective in reducing risky driving and motor vehicle crashes associated with alcohol use, which can result in hospitalization.
Funding	
Comments	

Title	**Review article: Effectiveness of ultra-brief interventions in the emergency department to reduce alcohol consumption: A systematic review**		
First Author	**McGinnes, 2016**	**Source**	**27459669**
Level of evidence	1a	**Study type**	Systematic Review
Study quality			
Participants	13 RCTs		
Patient characteristics	"Adults and adolescents with drinking behaviour, dysfunctional drinking patterns or symptoms of an alcohol-related disorder attending an ED "		
Intervention	"Any face-to-face interaction of 10 min or less or any non-face-to-face intervention involving technology"		
Comparison	"screening only, assessment only or minimal intervention that included the provision of written information or standard care"		
Length of follow-up			
Outcome and effect size	Outcomes of interest were frequency of alcohol consumption, quantity of alcohol consumed, binge drinking and ED representation. Thirteen studies (nine single center and four multicenter) were included. Six studies showed a significant reduction in the quantity consumed with intermediate effect size at 3 months (d=0.40) and small effect size at 12 months (d=0.15). Two studies showed a significant reduction in binge drinking with small effect size at 3 months (d=0.12) and 12 months (d=0.09). No studies showed an effect on frequency of alcohol consumption or ED representation. Heterogeneity in study design, definition of risky, harmful or hazardous alcohol use, intervention types, outcomes, outcome timeframes and outcome measures prevented the performance of quantitative meta-analysis. Despite its limited effectiveness in reducing alcohol use in the short-term, with the large number of people attending EDs with risky drinking, the use of an effective ultra-BI would have the potential to have a measurable population effect.		
Funding	"The present study was funded by a grant from the Australasian College for Emergency Medicine."		
Comments	"Three studies showed a significant reduction in binge drinking (Table 3). D'Onofrioet al. randomised patients to a BNI conducted by trained ED staff, with or without a telephone booster at 1 month or standard care. A significant treatment effect was shown at 12 months with both BNI and BNI plus booster groups having fewer binge drinking days in the past 28 days than the standard care group. BNI compared with standard care showed a small effect size (d=-0.09). In a pilot study, Suffoletto et al. randomised patients with hazardous alcohol use to a weekly text message with generic assessment or personalised feedback with goal setting or control. At 3 months, the personalised feedback group showed a significant difference in change in number of heavy drinking days in the past month. However, this difference was between the intervention and assessment group only. Comparison of the intervention group with the control group showed an intermediate effect size (d=-0.46) whereas the intervention group compared with the assessment group showed a large effect (d=-0.95). Suffoletto et al. randomised patients attending the ED with an AUDIT-C score ≥3 for women and≥4 for men to a text message intervention with or without feedback or control. At 3 months, the text message with feedback group was 2.4 times more likely not to report any binge drinking in the past 30 days than the control group. Comparison of the text message with feedback group with the control group showed a small effect (d=0.12) whereas the text message group without feedback compared with the control group showed a small positive effect (d=0.12). The text message with feedback group compared with the text message without feedback showed a small effect size (d=-0.22)."		

Title	Brief interventions for heavy alcohol users admitted to general hospital wards		
First Author	McQueen, 2011	Source	21833953
Level of evidence	1a	Study type	Systematic review and meta-analyses of controlled trials
Study quality	Methodological quality of trials was mixed, heterogeneity.		
Participants	Total: 14 trials (n=4.041 participants). Primary meta-analyses: 8 trials. Meta-analysis on number of binges: 1 trial. Meta-analysis on Heavy drinking days per week: 1 trial.		
Patient characteristics	Heavy alcohol users admitted to general hospital wards, aged 16+ years. Mainly male.		
Intervention	Brief intervention: a single session or up to three sessions involving an individual patient and health care practitioner (e.g. nurses, physicians, psychologists, alcohol counsellors, graduates/students, social workers) comprising information and advice, often using counselling type skills to encourage a reduction in alcohol consumption and related problems. Control groups were defined as assessment only (screening) or treatment as usual including provision of leaflets.		
Comparison	Brief intervention(s) versus control.		
Length of follow-up	4, 6, 9 and 12 months		
Outcome and effect size	Primary meta-analysis: Patients receiving brief interventions have a greater reduction in alcohol consumption compared to those in control groups at six month (4 trials, MD=-69.43; 95% CI [-128.14|-10.72]) and nine months follow up (1 trial, MD=-182.88 (95% CI [-360.00|-5.76]) but this is not maintained at one year (4 trials). Self-reports of reduction of alcohol consumption at 1 year were found in favour of brief interventions (SMD=-0.26, 95% CI [-0.50|-0.03]). In addition there were significantly fewer deaths in the groups receiving brief interventions than in control groups at 6 months (RR=0.42, 95% CI [0.19|0.94]) and one year follow up (RR=0.60, 95% CI [0.40|0.91]). Number of binge episodes past month: No significant differences between control and brief intervention groups (1 trial; RR=0.99 (95% CI [0.83|1.19]). Number of heavy drinking days per week: Significant differences in favour of the brief intervention group at all time points (1 trial; month 4: MD=-0.56; 95% CI [-1.02| -0.10]; month 9: MD=-0.78, 95% CI [-1.32|-0.24]; month 12: MD=-0.71, 95% CI [-1.26|-0.16]).		
Funding	Not reported.		
Comments	Findings based on small number of trials (2 trials concerning binge/heavy episodic drinking).		

Title	Interventions for reducing alcohol consumption among general hospital inpatient heavy alcohol users: A systematic review.		
First Author	Mdege, 2013	Source	23474201
Level of evidence		Study type	RCTs, systematic review.
Study quality			
Participants	22 studies which met the inclusion criteria enrolled 5307 participants in total		
Patient characteristics	Ausschluss von schwer Abhängigen eine Variante; auch keine Studien mit pharmakologischer Intervention.		
Intervention	There is growing interest in pro-active detection and provision of interventions for heavy alcohol use in the general hospital inpatient population.		
Comparison	"Effectiveness of interventions in reducing alcohol consumption among general hospital inpatient heavy alcohol users."		
Length of follow-up	mindestens 12 Monate		
Outcome and effect size	Results from single session brief interventions and self-help literature showed no clear benefit on alcohol consumption outcomes, with indications of benefit from some studies but not others. However, results suggest brief interventions of more than one session could be beneficial on reducing alcohol consumption, especially for non-dependent patients. No active intervention was found superior over another on alcohol consumption and other outcomes. No intervention effect concerning binge-drinking found.		

Funding	
Comments	Nach meiner Einschätzung geht es mehr um den Vergleich von Klinik und Hausarzt/Ambulanz und BI; BI in primery care settings effektiver

Title	**A Systematic Review of Digital and Computer-Based Alcohol Intervention Programs in Primary Care.**		
First Author	**Nair, 2015**	**Source**	**26373848**
Level of evidence	1a	**Study type**	Systematic Review
Study quality	Lower: only 66% RCTs (10/15), 4/15 descriptive studies, 1/15 quasi-experimental design		
Participants	15 trials		
Patient characteristics	Participants were recruited from either emergency departments (ED, n=6), General Practices (GP, n=5) or from university or college health clinics (n=4)		
Intervention	Only digital or computer-based interventions, such as programs implemented via laptops, computer touch-screen kiosks or mobiles, were included. There were no restrictions on type of intervention included, however most programs were designed to simply assess risk level of drinking and provide feedback to patients. All intervention programs in this review aimed to reduce alcohol consumption.		
Comparison	"No restriction on type of comparator group. However most studies utilised a control group which did not receive any personalized feedback on their risk level of drinking, for example no feedback or a generic health pamphlet. Brief vs. extended intervention"		
Length of follow-up	1.5 to 12 months		
Outcome and effect size	"Of the 15 trials, nine found the intervention group had significantly decreased alcohol consumption between 1.5-and 6-month follow-up occasions. Three of these nine trials showed lasting effects up to 12 months post baseline. One of the four trials which focused on extended interventions found the extended program resulted in improved drinking outcomes compared to the brief intervention. Some studies also resulted in less binge drinking and alcohol-related consequences at follow up."		
Funding	The National Drug and Alcohol Research Centre is funded by the Australian Government Department of Health and Maree Teesson is funded on Australia National Health and Medical Research Council Research Fellowship.		
Comments			

Title	**Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force**		
First Author	**O'Connor, 2018**	**Source**	**30422198**
Level of evidence	1a	**Study type**	Systematic review and meta-analysis of randomized clinical trials and nonrandomized controlled intervention studies
Study quality	Good. Review intended to include good-quality studies only.		
Participants	Total: 68 intervention trials (n=36.528 participants). Primary meta-analysis on drinks per week: 32 trials (n=15.974). Meta-analysis on heavy use episodes: 12 trials (n=8.108 participants).		
Patient characteristics	Adolescents and adults recruited through screening (at least 50%) from primary care or a health care system or from other settings that applied an intervention that could feasibly be implemented in or referred from primary care.		
Intervention	Counseling in screen-detected persons (web-based interventions not excluded): Most interventions involved 1-2 sessions (90% 4 or fewer) with a medium of 30 minutes of contact time (88% 2 hrs or less). Almost all interventions involved at least basic education; general feedback how the participant's drinking compared with recommended limits, and suggestions about how to reduce alcohol use. Many used a SBIRT (screening, brief intervention, and referral to treatment) approach. The most commonly reported intervention element was the use of personalized normative feedback (62%) and motivational techniques in combination with personalized normative feedback.		
Comparison	Intervention(s) versus control.		
Length of follow-up	6-12 months		

Outcome and effect size	Counseling interventions were associated with a decrease in drinks per week (weighted mean difference, -1.6, 95% CI [-2.2|-1.0]; 32 studies [37 effects; n=15.974]), the proportion exceeding recommended drinking limits (OR=0.60, 95% CI [0.53|0.67]; 15 studies (16 effects; n=9.760)), and the proportion reporting a heavy use episode (OR=0.67, 95% CI [0.58|0.77]; 12 studies (14 effects; n=8.108)), and an increase in the proportion of pregnant women reporting abstinence (OR=2.26, 95% CI [1.43|3.56]; 5 studies (n=796)) after 6 to 12 months.
Funding	Review was funded by the Agency for Healthcare Research and Quality, US Department of Health and Human Services. Funding of included trials not reported.
Comments	OLDER ADULTS impact depends on outcome!!!! Only 6 of the included trials (n=3.650) reported on harms. In all cases, authors reported no harms. Further, no pattern of unexpected paradoxical increases in alcohol use was noted with these interventions. Despite heterogenous study characteristics, in most terms rather homogenous findings.

Title	**The impact of brief alcohol interventions in primary healthcare: a systematic review of reviews**		
First Author	**O'Donnell , 2014**	**Source**	**24232177**
Level of evidence		**Study type**	systematic review of reviews
Study quality			
Participants	Twenty-four systematic reviews met the eligibility criteria (covering a total of 56 randomized controlled trials		
Patient characteristics	"viele unterschiedliche Studien und deshalb sehr verschiedene Gruppen, die untersucht wurden. Tabelle 1 im Review gibt den Überblick! Begrenzung der Reviews: For example, there were limited data available on the effectiveness of brief alcohol intervention in different models of primary healthcare systems, beyond the broad comparison on geographic grounds. Second, in basing our conclusions on the findings of previous systematic reviews, this review is necessarily limited by individual authors' decisions regarding the exclusion/inclusion of particular studies, further confounded by the fact that the standard of reporting, analysis and interpretation, whilst generally high, varied across the included papers. Third, our reliance on previous systematic reviews limits the immediacy of our findings as the most recent primary research is not included."		
Intervention	four questions: (a) does the cumulative evidence base continue to show that brief alcohol intervention is effective when delivered in primary healthcare settings? (b) is brief alcohol intervention equally effective across different countries and different healthcare systems? (c) is the brief alcohol intervention evidence base applicable across different population groups? and (d) what is the optimum length, frequency and content of brief alcohol intervention, and for how long is it effective?		
Comparison	"provide a structured, comprehensive summary of the evidence base on the effectiveness of brief alcohol intervention in primary healthcare"		
Length of follow-up			
Outcome and effect size	Brief intervention was effective for addressing hazardous and harmful drinking in primary healthcare, particularly in middle-aged, male drinkers. Across the included studies, it was consistently reported that brief intervention was effective for addressing hazardous and harmful drinking in primary healthcare, particularly in middle-aged, male drinkers. Evidence gaps included: brief intervention effectiveness in key groups (women, older and younger drinkers, minority ethnic groups, dependent/co-morbid drinkers and those living in transitional and developing countries); This overview highlights the large volume of primarily positive evidence supporting brief alcohol intervention effects as well as some unanswered questions with regards to the effectiveness of brief alcohol intervention across different cultural settings and in specific population groups, and in respect of the optimum content of brief interventions that might benefit from further research.		
Funding			
Comments	"Kurze Interventionen der Kontrollbedingungen bewirken Ähnliches:Thus the mere fact of enrolment in a brief intervention trial may be associated with positive behaviour change due to a general 'Hawthorn Effect', whereby increased attention or scrutiny influences drinking, or volunteering in itself means that the individual has started a change process.--- Nevertheless, the cumulative (pooled) analyses reported in successive systematic reviews		

	reveal positive brief intervention effects over and above those seen in control conditions who typically received assessment only, treatment as usual or written advice."

Title	**How effective are brief interventions in reducing alcohol consumption: do the setting, practitioner group and content matter?**		
First Author	**Platt, 2016**	**Source**	**27515753**
Level of evidence		**Study type**	systematic review and Meta-Regression analysis
Study quality	RCTs, multilevel meta-analysis		
Participants	52 trials were included contributing data on 29.891 individuals		
Patient characteristics	Patienten ab 16 J. im Gesundheitswesen; Ausschluss schwer Kranker und Patienten von Alkohol-Suchtkliniken; Ausschluss schwangerer Frauen		
Intervention	Kurzintervention in Bezug auf Alkoholkonsum		
Comparison	Kontrollgruppendesign, Vergleich von Settings		
Length of follow-up	unterschiedlich, ab 3 Monaten, oft 6 oder 12 Monate bis zu 36 Monate		
Outcome and effect size	"geringfügige, aber signifikante Ergebnisse. Es spielte in manchen Studien der Untersucher eine Rolle: Die Interventionen, die vom Pflegekräften durchgeführt wurden, hatten den höchsten Effekt (d=-0.23, 95% CI [-0.33|0.13]). Setting: In universitären Umfeld und im Hausarzt/Ambulanzbereich durchgeführte Interventionen erzielten geringe, aber signifikante Effekte (d=-0.20, 95% CI [-0.39|-0.09]) bzw. (d=-0.20, 95% CI [-0.27|-0.13]). Interventionen, die in kommunalen Einrichtungen wie Militär, Justizbereich, oder mit zielgerichteter Rekrutierung erfolgten, schienen nicht effektiv zu sein (d=-0.03, 95% CI [-0.16|0.10])"		
Funding			
Comments			

Title	**Effectiveness and treatment moderators of internet interventions for adult problem drinking: An individual patient data meta-analysis of 19 randomised controlled trials**		
First Author	**Riper, 2018**	**Source**	**30562347**
Level of evidence	1a	**Study type**	Individual patient data meta-analysis of RCTs
Study quality	High quality. Drop-out rate 43 %; limited to first follow-ups.		
Participants	Total: 19 RCTs (n=14.198 participants; n=.8095 participants with post-data included in individual patient data meta-analysis)		
Patient characteristics	Adult population (aged ≥18 years) with quantifiable levels of alcohol consumption that exceeded recommendations for low-risk drinking. Mean age 41 years (SD=13), 52% male. Mean weekly standard unit level 38.1 (SD=26.9). The mean full AUDIT score (n=9 trials) was 15.0 (SD=6.8), indicating hazardous or harmful alcohol use. Of the participants for which a full AUDIT score was available, 22.2% (n=678) scored above 20, indicating a risk of alcohol dependence.		
Intervention	Internet-based alcohol interventions (iAIs)		
Comparison	Internet-based alcohol interventions (iAIs) versus controls. Plus investigation of diverse moderators: Human-guided versus unguided interventions; single versus multiple sessions; personal and normative feedback only versus integrated therapeutic principles		
Length of follow-up	First follow-up data (Follow-up perdiods not associated with main outcomes)		
Outcome and effect size	The overall difference in mean weekly alcohol reduction was significant and in favour of the iAI condition (b=-5.02 SUs, 95% CI [-7.57|-2.48], p<0.001. Our results show that internet-based alcohol interventions in both community and healthcare populations are effective in reducing mean weekly alcohol consumption and in achieving adherence to low-risk drinking limits. Participants above age 55 were significantly more likely to drink within limits than younger participants (OR=1.68, 95% CI [1.22 |2.30], p=0.001). Human-supported interventions were superior to fully automated ones on both outcome measures. Waitlist control in RCTs was associated with significantly better treatment outcomes than the use of other types of control (comparative reduction: -9.27 Sus. Women decreased their mean weekly alcohol consumption less than men (around 2 SUs). Both men and women from different age groups and with different drinking profiles, including heavy drinking and binge-only drinking, can benefit from internet alcohol		

	interventions.
Funding	The authors did not receive specific funding for this work.
Comments	

Title	**Brief Alcohol Interventions for Adolescents and Young Adults in Emergency Department Settings: A Descriptive Review and Meta-analysis**		
First Author	**Samson, 2019**	**Source**	
Level of evidence	1a	**Study type**	Systematic Review + Meta-Analyse
Study quality			
Participants	11 RCTs		
Patient characteristics	ED Patients aged 12-25 yrs. Screening positive for risky alcohol consumption (incl. HED).		
Intervention	"Any form of brief alcohol intervention for adolescents or young adults 25 or younger, delivered in emergency department settings. Eligible interventions could include up to 5 h of contact time, and involved any actions expected to reduce participants' alcohol consumption"		
Comparison	no-treatment control, wait-list control, or some form of treatment as usual comparison conditions		
Length of follow-up			
Outcome and effect size	Quantitative analyses suggested that current research, on average, finds very little evidence that interventions in emergency department settings are efficacious, regardless of variations in the study and the intervention. It must be noted that this result is contrary to that reported in the parent study (Tanner-Smith and Lipsey 2015). Including personalized feedback was the only component identified that was related to an average effect size significantly greater than zero (k=8, g=0.07, 95% CI [0.00| 0.14]), but this result was not replicated in sensitivity analysis – likely because of one study with a strong, negative effect.		
Funding	"This work uses data collected with support from the National Institute on Alcohol Abuse and Alcoholism award number R01AA020286. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Alcohol Abuse and Alcoholism or the National Institutes of Health."		
Comments			

Title	**Alcohol screening and brief intervention in workplace settings and social services: a comparison of literature**		
First Author	**Schulte, 2014**	**Source**	**25339914**
Level of evidence	2a	**Study type**	Systematic Review
Study quality			
Participants	9 RCT´s		
Patient characteristics	Workplace Interventions for employees with risky drinking patterns		
Intervention	Alcohol screening and brief intervention, in some studies face to face and web-based		
Comparison	brief intervention vs assessment only or treatment as usual		
Length of follow-up			
Outcome and effect size	In all 9 studies there could be shown positive effects; the evidence of effectiveness was shown in reduction of alcohol consumption, drinking days or peak drinks per occasion. 8 from 9 studies showed partly significant better results in the intervention group, one study (Hermannsson) showed a significant reduction in both groups.		
Funding	BISTAIRS Research Project of the European Union		
Comments			

Title	**Interventions for increasing subsequent alcohol treatment utilization among patients with alcohol use disorders from somatic inpatient settings: a systematic review**		
First Author	**Simoni, 2015**	**Source**	**25780027**
Level of evidence		**Study type**	Systematic Review

Study quality	5 RCTs
Participants	5 RCTs including 1113 individuals with AUDs
Patient characteristics	Adult inpatient population (aged ≥18 years) with AUDs
Intervention	Single session (2 studies), Multi-session inpatient advice (1 study), 2 studies inpatient BI plus post discharge sessions
Comparison	No intervention (n=3), Usual Care (n=2)
Length of follow-up	16 weeks to 18 months
Outcome and effect size	"No evidence of efficacy in increasing subsequent treatment utilization was reported for inpatient BIs alone, but interventions with post-discharge sessions might be beneficial. Increased treatment utilisation was generally associated with favourable drinking outcomes. Given the small number of included studies and the presence of several alternative methodological explanations for the present findings, no firm conclusions could be drawn on efficacious interventions for increasing subsequent treatment utilisation among somatic inpatients with AUDs. "
Funding	Publication project sponsored by “le Conseil Régional du Nord-Pas-de-Calais” and “l’Agence Régionale de Santé du Nord-Pas-de-Calais”
Comments	

Title	**Computer-Based Interventions for Problematic Alcohol Use: a Review of Systematic Reviews**		
First Author	**Sundstrom, 2017**	**Source**	**27757844**
Level of evidence	1a	**Study type**	Systematic review of systematic reviews
Study quality	No meta-analysis.		
Participants	Total: 14 systematic reviews		
Patient characteristics	Mixed		
Intervention	Computer-based interventions, not explicitly brief interventions.		
Comparison	computer-based interventions versus controls		
Length of follow-up	Mostly 6 months and less		
Outcome and effect size	It was generally reported that computer-based alcohol interventions were effective in reducing alcohol consumption, with mostly small effect sizes. There were indications that longer, multisession interventions are more effective than shorter or single session interventions. Furthermore, effects seem to decay over time and may disappear completely after more than 12months, although few studies include such long follow-ups. Binge-drinking: The impact of interventions on frequency of binge drinking and harm is not clear: In student populations three reviews presented effect sizes on binge drinking: no significant reduction (at >5 weeks) with a minimal effect size (d=0.10, 95 % CI [0.00|0.20), significant reduction with a small to medium effect size (d=-0.35, 95 % CI [-0.64|-0.06) found no effect.		
Funding	No funding reported.		
Comments			

Title	**Brief Alcohol Interventions for Adolescents and Young Adults: A Systematic Review and Meta-analysis**		
First Author	**Tanner-Smith, 2015**	**Source**	**25300577**
Level of evidence	1a	**Study type**	Systematic Review + Meta-Analyse
Study quality	158 RCTs		
Participants			
Patient characteristics	Participants aged 11-25 yrs. In all settings (ED, university, self-administered etc.)		
Intervention	"BI defined as brief contact time generally one to five sessions–with a provider such as a physician, nurse, psychologist, counselor, or other service professional including a discussion of alcohol consumption, feedback on risk or levels of use, comparisons to local or national norms, information on potential harms, or coping strategies and goal-setting plans for dealing with drinking situations. Interventions could target any risk level (universal, selective, or indicated) of participants, as long as they involved five or fewer hours of total contact time and four or fewer weeks between the first and last intervention		

	session (excluding booster sessions)."
Comparison	"Comparison conditions of no treatment, a wait-list control, or some form of routine treatment as usual (i.e., services the participants would have received even in the absence of the brief intervention). Studies that compared two types of interventions were not eligible. "
Length of follow-up	
Outcome and effect size	Overall, brief alcohol interventions led to significant reductions in alcohol consumption and alcohol-related problems among adolescents ($\bar{g}$=0.27 and $\bar{g}$=0.19) and young adults ($\bar{g}$= 0.17 and $\bar{g}$= 0.11). These effects persisted for up to one year after intervention and did not vary across participant demographics, intervention length, or intervention format. However, certain intervention modalities (e.g., motivational interviewing) and components (e.g., decisional balance, goal-setting exercises) were associated with larger effects. We conclude that brief alcohol interventions yield beneficial effects on alcohol-related outcomes for adolescents and young adults that are modest but potentially worthwhile given their brevity and low cost.
Funding	"This work was supported by Award Number R01AA020286 from the National Institute on Alcohol Abuse and Alcoholism."
Comments	

Title	**Alcohol Electronic Screening and Brief Intervention: A Community Guide Systematic Review**		
First Author	**Tansil, 2016**	**Source**	**27745678**
Level of evidence		**Study type**	Systematic review of randomized controlled trials
Study quality	Majority of studies fair quality of execution		
Participants	Total: 31 studies with 34 study arms. Excessive drinkers 24 studies (28 study arms).		
Patient characteristics	People with excessive alcohol consumption or alcohol-related harms from high-income countries; half of the studies conducted in university settings; studies targeting treatment seekers were not included.		
Intervention	"At a minimum, e-SBI involves: 1. Screening individuals for excessive drinking, and 2. Delivering a brief intervention (BI), which provides personalized feedback about the risks and consequences of excessive drinking. Personalized feedback can be fully automated (e.g., computer-based); interactive (e.g., provided by a person via telephone); or partially automated and interactive. At least one part of the BI must be delivered by an electronic device. The BI provided using e-SBI techniques may also include other common elements of traditional ASBI. One such element is motivational feedback, which has two levels: Low-level motivational feedback includes general advice on how to reduce excessive alcohol consumption; high-level feedback provides more individually tailored messages based on factors such as readiness to change or developing personal goals. Another element is normative feedback, comparing an individual's own alcohol consumption with that of others (e.g., college students in the same school). Over 80% of the BI were delivered solely through automated methods. Overall, 42% of the BI included high-level motivational feedback."		
Comparison	Electronic Screening and Brief intervention versus controls.		
Length of follow-up	>1 month		
Outcome and effect size	Summary effect estimates showed reductions in all alcohol consumption outcomes. Among excessive drinkers, the largest and most consistent changes were in frequency (median -16.5%, 95% CI [-35.6|-11.8] reduction in episodes/month) and intensity of binge drinking (median -23.9%, 95% CI [-51.3|-2.1] reduction in peak alcohol consumption). Peak alcohol consumption also declined in studies that included binge and non-binge drinkers in the intervention condition.		
Funding	No funding reported		
Comments			

Title	**The efficacy of Motivational Interviewing as a brief intervention for excessive drinking: A meta-analytic review**

First Author	Vasilaki, 2006	Source	16547122
Level of evidence		Study type	Systematic review and meta-analysis of RCTs
Study quality	7/15 trials with excellent methodology.		
Participants	Total: 15 RCTs (n=2767 participants; MI vs. no treatment: 9 RCTs, MI versus other treatment: 9 RCTs).		
Patient characteristics	"Outpatient community samples 5 RCTs; emergency-room or clinic patients with alcohol-related problems e.g. physical injury 4 RCTs; student samples 4 RCTs. Mean age 31.8 (SD=10.3) years; 69% males: 36.0% dependent drinkers."		
Intervention	Brief intervention delivered according to the principles of MI on the basis of Miller and Rollnick's (2002) definition of MI. Even the briefest interventions (30 min), as long as they claimed to adopt the principles and techniques of MI as described by Miller and Rollnick (1991) and delivered a face-to-face intervention rather than one by computer or telephone.		
Comparison			
Length of follow-up			
Outcome and effect size	In addition, examining participants' age as a predictor of treatment outcome, they found that clients who consumed high levels of alcohol and who were older at baseline were significantly more likely to reduce the number of binge episodes during the post-treatment period.		
Funding			
Comments	"Only one study reported unfavourable results for MI (Maisto et al., 2001)."		

Title	Online alcohol interventions: a systematic review.		
First Author	White, 2010	Source	21169175
Level of evidence	1a	Study type	Systematic Review
Study quality	High quality. Strengths: clear objective: search strategy reported. Limitation: single studies not described in detail		
Participants	17 studies; Sample sizes ranged from 40 to 3.216 (median n=196)		
Patient characteristics	University students (12 studies); general company employees (2 studies); community members (3 studies). Age range: 18-25 (student samples) and mean age 43.1 (other studies). Percentage of females ranged from 27.6% to 77.9% (mean 54.5%)		
Intervention	"12/17 studies evaluated the impact of brief personalized feedback and 7/17 examined an online multi-module information/ education treatment (often incorporating personalized feedback)"		
Comparison	Control groups typically received psychoeducational resources (10/17) or completed an online assessment.		
Length of follow-up	"Posttreatment assessments were conducted anywhere from 1 week to 12 months, with several studies conducting assessments at multiple time points. Across the 17 studies, 7 had a maximum FU period of a month, 4 had a max. 3-months FU and 3 followed participants to 6 months, one to 12-months post intervention. Retention rates of 83,5% for the IG and 86,3% for the CG."		
Outcome and effect size	"Effect sizes could be extracted from 8 of the 17 studies. In relation to alc. units per week /month and based on 5 RCTs where a measure of alc. units per week/month could be extracted, differential effect sizes to posttreatment ranged from 0.02 to 0.81 (mean 0.42, median 0.54). Pre-post effect sizes for brief personalized Feedback ranged from 0.02 to 0.81, and in 2 multi-session modularized interventions, a pre-post effect size of 0.56 was obtained in both. Pre-post"		
Funding	Australian Commonwealth Department of Health and Ageing		
Comments	"Review provides evidence for effectiveness of online alcohol interventions. Restrictions: most data come from student samples, number of studies for computing effect sizes was limited."		

Title	Screening, Brief Intervention, and Referral for Alcohol Use in Adolescents: A Systematic Review.

First Author	Yuma-Guerrero, 2012	Source	22665407
Level of evidence	1a	Study type	Systematic Review
Study quality			
Participants	7 RCTs		
Patient characteristics	"Adolescent patients in acute care settings. All studies took place in the emergency departments of level I trauma centers. Ages of patients included in the studies varied widely; the study with the youngest age boundary included patients 12 to 20 years of age, and the study with the highest age boundary included patients 18 to 24 years of age."		
Intervention	"All but one of the studies used motivational interviewing (MI) as the foundation for the intervention. The remaining study delivered the intervention through an interactive computer program based on social learning theory."		
Comparison	Standard care, feedback only, Booklet		
Length of follow-up			
Outcome and effect size	Four of the 7 studies reviewed demonstrated a significant intervention effect; however, no one intervention reduced both alcohol consumption and alcohol-related consequences. Two of these 4 studies only included patients ages 18 and older. Subgroup analyses with adolescents engaged in risky alcohol-related behaviors, conducted in 2 of the studies, showed significant intervention effects. Five studies showed positive consumption and/or consequences for all study participants regardless of condition, suggesting that an emergent injury and/or the screening process may have a protective effect.		
Funding	No external funding		
Comments			

Title	Alcohol screening and brief intervention in primary care: Absence of evidence for efficacy in people with dependence or very heavy drinking		
First Author	Saitz, 2011	Source	20973848
Level of evidence	1a	Study type	Systematic Review
Study quality	"high quality; included reviews through 2006; an additional electronic literature search was conducted through 2009; clear search strategy; clear information about inclusion and exclusion of studies: focus only on dependence. Therefore only two studies identified."		
Participants	N=199		
Patient characteristics	Men and women and age not clearly specified; only outpatient primary care settings;		
Intervention	"In one study including dependent alcoholics 10–15 min BI by resident physician. In the other study including dependent alcoholics the BI was done by an experienced addiction psychiatrist, and duration was not specified. "		
Comparison	"One study: compared with six weekly 90 min educational sessions. other: not specified"		
Length of follow-up	"One study: 18 months. other: not specified"		
Outcome and effect size	Absence of evidence for the efficacy of BI among primary care patients with screening identified alcohol dependence		
Funding	NIAAA and NIDA		
Comments			

Title	A systematic review of work-place interventions for alcohol-related problems		
First Author	Webb, 2009	Source	19207344
Level of evidence	1a	Study type	Systematic Review
Study quality	High quality; systematic review and evaluation of methodological quality of studies included.		
Participants	10 Studies including 4 RCTs		
Patient characteristics	Recruitment not clearly specified in all studies; one study identified participants via screening. For alcohol measures, seven studies used self-report measures only one used company records only, one used a combination of self-report, biochemical testing (gamma glutamic transferase and carbohydrate-deficient transferrin) and company records and one		

	did not specify how alcohol data were collected
Intervention	Interventions (1-3 sessions depending on study) comprised three broad types of strategies: psychosocial skills training, brief intervention, including feedback of results of self-reported drinking, life-style factors and general health checks and alcohol education delivered via an internet website. The psychosocial interventions included peer referral 14, 20, team building and stress management and skills derived from the social learning model. For health checks, topics covered in addition to alcohol were smoking, exercise, diet, weight, stress, depression, blood pressure, cholesterol, diabetes, cancer, safety and preventive health-care risks.
Comparison	One study: health education class, 3 studies: no intervention
Length of follow-up	
Outcome and effect size	Weaknesses in all studies related to representativeness of samples, consent and participation rates, blinding, post-test time-frames, contamination and reliability, and validity of measures used. All except one study reported statistically significant differences in measures such as reduced alcohol consumption, binge drinking and alcohol problems.
Funding	Alcohol Education and Rehabilitation Foundation of Australia
Comments	

Title	**Screening and Brief Interventions for Prevention and Early Identification of Alcohol Use Disorders in Adults and Young People**		
First Author	**Jackson, 2010**	**Source**	
Level of evidence	1a	**Study type**	Systematic Review of systematic reviews
Study quality	High quality; systematic rating of methodological quality		
Participants	27 systematic reviews digital n=390		
Patient characteristics	Recruitment heterogeneous; mostly participants recruited via screening, mostly exclusion of individuals showing signs of alcohol dependence.		
Intervention	"Heterogeneous Interventions mainly conducted in the US. Interventions included very brief intervention (e.g. simple advice) to extended brief interventions (consisted of 2 to 7 sessions with a duration of initial and booster sessions of 15 to 50 min or 10 to 15 min in 1 session with number of specific booster sessions of 10 to 15 min duration)."		
Comparison	Mostly no intervention.		
Length of follow-up	heterogeneous		
Outcome and effect size	"Evidence has been identified for the positive impact of brief interventions for alcohol misuse on alcohol consumption, mortality, morbidity, alcohol-related injuries, alcohol-related social consequences, and healthcare resource use. Whilst the majority of studies were conducted in primary care, limited evidence was also identified for other healthcare settings. One systematic review presenting information on the effectiveness of brief interventions for alcohol misuse in non-healthcare settings was identified. Brief interventions were shown to be effective in both men and women. Study populations were made up primarily of adult populations. However, the limited evidence identified for the effectiveness of brief interventions in young people was inconclusive. Study participants were predominantly Caucasian in origin. Socioeconomic status was not shown to influence the effectiveness of brief interventions. The relationship between the level of alcohol dependence and the effectiveness of brief interventions was unclear. One review put forward limited evidence of the effectiveness of brief interventions in patients with a dual diagnosis of a psychiatric condition and alcohol misuse. Limited evidence suggests that even very brief interventions may be effective in reducing negative alcohol-related outcomes. The benefit arising from increased exposure or the incorporation of motivational interviewing principles was unclear."		
Funding	"School of Health and Related Research (ScHARR), in the Faculty of Medicine, Dentistry and Health, University of Sheffield"		
Comments			

1.4 Arzneimittel zur Entzugsbehandlung

Title	**Gamma-hydroxybutyrate reduces both withdrawal syndrome and hypercortisolism in severe abstinent alcoholics: an open study vs. diazepam**		
First Author	**Nava, F., 2007**	**Source**	**17613965**
Level of evidence	3b	**Study type**	open randomized study
Study quality	low		
Participants	N=42		
Patient characteristics	alcoholic inpatients we performed		
Intervention	Both diazepam (0.5mg/kg bodyweight, q.i.d.) and GHB (50mg/kg bodyweight, q.i.d.) were orally administered for three weeks		
Comparison	To compare the effects of diazepam and gamma-hydroxybutyrate (GHB) on the suppression of severe alcohol withdrawal syndrome and hypercortisolism		
Length of follow-up	no		
Outcome and effect size	During all study period, GHB was more able than diazepam in reducing both withdrawal syndrome ($p<0.01$) and hypercortisolism ($p<0.01$).		
Funding	Supported by the Italian Ministry of Health and by the Regional Authority of Lombardia and Veneto		
Comments	only abstract evaluated		

Title	**A double-blind evaluation of gabapentin on alcohol effects and drinking in a clinical laboratory paradigm**		
First Author	**Myrick, H., 2007**	**Source**	**17250613**
Level of evidence	2b	**Study type**	RCT
Study quality	Sub-acute human laboratory study		
Participants	N=35 non-treatment-seeking alcoholic subjects, outpatients		
Patient characteristics	The average subject was 33 years old, male (94%), and Caucasian (80%). There were no differences between the 2 groups on any demographic variables and both groups had similar drinking during the 5-day natural observation period.		
Intervention	Double-blind treatment with up to 1,200 mg of gabapentin (n=18) or placebo (n=17) for 8 days.		
Comparison	The safety and tolerability of gabapentin were monitored in the natural environment during the first 5 days of medication treatment and during a free-choice limited access consumption paradigm following an initial drink of alcohol in a bar–lab setting on Day 7.		
Length of follow-up	No		
Outcome and effect size	There was no overall effect of gabapentin on drinking or craving; however, it was tolerated (e.g., mood and sedation) as well as placebo over 5 days of natural drinking. Peak blood alcohol averaged about 23mg% (maximum 34mg%) in the placebo group and about 19mg% (maximum 33mg%) in the gabapentin group ($F=0.07$, $p=0.79$). There was no effect of gabapentin on alcohol stimulation ($p=0.75$) or sedation ($p=0.99$).		
Funding	No information		
Comments	The results of this natural drinking and clinical laboratory study support the potential safety and tolerability of the anticonvulsant gabapentin if used in the treatment of alcohol withdrawal or alcohol relapse prevention. The lack of interaction with alcohol is of clinical significance considering the extent of outpatient treatment of alcoholism and comorbid psychiatric conditions Limitation: N<50		

Title	**A randomized, open-label, controlled trial of gabapentin and phenobarbital in the treatment of alcohol withdrawal**		
First Author	**Mariani, J. J., 2006**	**Source**	**16449096**
Level of evidence	2b	**Study type**	RCT
Study quality	Moderate		
Participants	N=27		
Patient characteristics	Adult Inpatients seeking treatment with no obvious demographic or alcohol history-differences in both treatment groups. Exception: the patients receiving gabapentin were in		

	more severe withdrawal on admission. Percent of subjects with history of alcohol withdrawal seizures: 36% (GP), 23% (P). Mean baseline CIWA score 18-20 in both groups.
Intervention	Not blinded treatment with 1200mg GP/d vs. 60mg phenobarbital dosed down within 4 days to 600mg GP vs. 30mg phenobarbital
Comparison	Comparisons of the mean daily CIWA and craving scale rating scale scores.
Length of follow-up	No follow-up
Outcome and effect size	There were no significant differences in the proportion of treatment completers between treatment groups (p=0.70) or the proportion of patients in each group requiring rescue medication for breakthrough signs and symptoms of alcohol withdrawal (p=0.45). There were no significant treatment differences in withdrawal symptoms or psychologic al distress. No withdrawal seizures or symptoms of alcohol withdrawal delirium occurred in either treatment group.
Funding	Supported by the Beth Israel Medical Center Department of Psychiatry
Comments	The results of this study suggest that gabapentin may be equivalent to phenobarbital in the treatment of alcohol withdrawal. Limitation: Not blinded, N<50

Title	**A retrospective chart review comparing tiagabine and benzodiazepines for the treatment of alcohol withdrawal**		
First Author	**Myrick, H., 2005**	**Source**	**16480168**
Level of evidence	4	**Study type**	Retrospective chart review
Study quality	Low quality, N=13		
Participants	N =13		
Patient characteristics	All patients who received tiagabine (n=7) were seen clinically over the course of treatment for dual psychiatric and substance abuse disorders. Another group of subjects (n=6) initially presented for a double-blind, controlled trial comparing gabapentin and lorazepam and either declined to enroll or met exclusion criteria. This group of subjects was treated with oxazepam (n=5) or lorazepam (n=1). CIWA-baseline- scores between 14 and 16.		
Intervention	Tiagabine doses were initiated at 2mg BID (twice a day) to 4mg BID. Oxazepam doses were initiated at 30mg BID to 30mg QID (four times a day) for the first day of treatment. One patient received 2mg of lorazepam QID on the first day of treatment. All doses were tapered over five days of treatment.		
Comparison	Compares treatment outcomes for patients (N=13) treated for alcohol withdrawal with either the anticonvulsant tiagabine or the benzodiazepines oxazepam and lorazepam.		
Length of follow-up	6 months		
Outcome and effect size	Both benzodiazepines and tiagabine appeared to reduce CIWA-Ar scores at about the same magnitude (F(1,8)=1.19, p<0.31).		
Funding	National Science Foundation Training Grant, NIH Undergraduate Student Training Grant DBI- 0097842, and NIAAA Grant AA10761		
Comments			

Title	**An ethanol protocol to prevent alcohol withdrawal syndrome**		
First Author	**Dissanaike, S., 2006**	**Source**	**16864031**
Level of evidence	3b	**Study type**	Group 1: retrospective chart review Group2: prospective protocol case-control study
Study quality	Moderate quality		
Participants	Group 1: N=92; Group 2: N=68		
Patient characteristics	Surgical patients. Group 1: retrospective chart review. Group 2 consisted of all patients treated prospectively with this protocol Both groups had similar demographics and consisted primarily of male trauma victims.		
Intervention	Group2: a protocol for the initiation, dosage, and weaning of intravenous ethanol in patients at risk for AWS, based on blood alcohol levels and clinical assessment of withdrawal symptoms and signs.		
Comparison	Less AWS-symptoms in Group 2 (prospective with protocol) and more referral in rehabilitation in Group 2		

Length of follow-up	no
Outcome and effect size	Intravenous ethanol was very variable in dosage, duration, and indication. The protocol decreased the duration of treatment between the two groups from 7 days to a mean of 3 days. The failure rate dropped from 20% to 7%. Referral to the substance abuse clinic rose from 7.6% to 20%. The only complication was asymptomatic hyponatremia in one patient.
Funding	No information
Comments	

Title	**Antiglutamatergic strategies for ethanol detoxification: comparison with placebo and diazepam**		
First Author	**Krupitsky, E. M., 2007**	**Source**	**17374039**
Level of evidence	1b	**Study type**	placebo-controlled randomized single-blinded
Study quality	Study of good quality, clear procedures		
Participants	N=127 (N=25 (placebo), N=25 (diazepam), N=25 (lamorigine), N=26 (Memantine), N=26 (topiramate))		
Patient characteristics	Male alcohol-dependent inpatients, baseline CIWA: 12-14		
Intervention	Subjects were assigned to 1 of 5 treatments for 7 days: placebo, diazepam 10mg TID, lamotrigine 25mg QID, memantine 10mg TID, or topiramate 25mg QID. Additional diazepam was administered when the assigned medication failed to suppress withdrawal symptoms adequately.		
Comparison	3x10mg Diazepam=4x25mg, Lamotrigin=3x10mg, Mamantine=4x25mg, Topiramate > Placebo		
Length of follow-up	No		
Outcome and effect size	All active medications significantly reduced observer-rated (F(4, 122)=3.85, p=0.006) and self-rated withdrawal severity (F(4, 122)=8.93, p<0.001), dysphoric mood (F(4, 114)=9.28, p<0.001), and supplementary diazepam administration (Fisher exact test: p<0.0001). Compared with placebo. The active medications did not differ from diazepam (Fisher exact test: p=0.40).		
Funding	Civilian Research Development Fund (CRDF) • NIAAA (R21- AA014543-01A1, KO5 AA 14906-01, I-P50 AA-12870- 04) • U.S. Department of Veterans Affairs		
Comments	The trial may indicate that different antiglutamatergic drugs may reduce AWS. Limitation: Low power! 5 arms and N=26 in each group. Open trial, not blinded.		

Title	**Baclofen in the treatment of alcohol withdrawal syndrome: a comparative study vs diazepam**		
First Author	**Addolorato, G., 2006**	**Source**	**16490478**
Level of evidence	2b	**Study type**	RCT
Study quality	Study of good quality, clear procedures		
Participants	N=37		
Patient characteristics	At baseline, mean total CIWA-Ar score (i.e. the sum of all items) was significantly higher in baclofen than diazepam group.		
Intervention	Baclofen (30mg/day for 10 consecutive days) was orally administered to 18 patients (15 males, 3 females; median age: 46.5 years). Diazepam (0.5-0.75mg/kg/day for 6 consecutive days, tapering the dose by 25% daily from day 7 to day 10) was orally administered to 19 patients (17 men, 2 women; median age: 42.0 years)		
Comparison	When CIWA-Ar subscales for sweating, tremors, anxiety and agitation were evaluated singly, treatment with baclofen and diazepam resulted in a significant decrease in sweating, tremors and anxiety score, without significant differences between the 2 drug treatments. Both treatments decreased the agitation score, although diazepam was slightly more rapid than baclofen.		
Length of follow-up	No		
Outcome and effect size	Both baclofen and diazepam significantly decreased CIWA-Ar score, without significant differences between the 2 treatments (F[1,140)=2.81, p>0.05). A reduction in AST, ALT,		

	GGT and MCV value was found in both baclofen- and diazepam- treated patient groups. No side effects were reported by either baclofen- or diazepam- treated patients.
Funding	Partially supported by a grant from "Associazione Ricerca in Medicina," Rome-Bologna, Italy
Comments	Limitationen: N<50

Title	**Comparison of intravenous ethanol versus diazepam for alcohol withdrawal prophylaxis in the trauma ICU: results of a randomized trial**		
First Author	**Weinberg, J. A., 2008**	**Source**	**18188105**
Level of evidence	2b	**Study type**	RCT
Study quality	low		
Participants	N=50		
Patient characteristics	Trauma patients admitted to the ICU with a history of chronic daily alcohol consumption greater than or equal to five beverage equivalents per day.		
Intervention	Were prospectively randomized to one of two 4-day prophylactic regimens: intravenous ethanol infusion (EtOH) versus scheduled-dose diazepam (BENZO).		
Comparison	Patients were evaluated with the Riker sedation-agitation scale, a 7-point instrument for the subjective assessment of both sedation (1 - unarousable) and agitation (7 - dangerous agitation).		
Length of follow-up	No		
Outcome and effect size	Concerning the prophylaxis of AWS, intravenous ethanol offers no advantage over diazepam with respect to efficacy or adverse sedative effects (p=n.s.).		
Funding	No information		
Comments			

Title	**Inappropriate use of symptom-triggered therapy for alcohol withdrawal in the general hospital**		
First Author	**Hecksel, K. A., 2008**	**Source**	**18315992**
Level of evidence	2b	**Study type**	Randomized study
Study quality	Low		
Participants	N=124		
Patient characteristics	Hospitalized medical and surgical patients.		
Intervention	observation		
Comparison	Of the 124 randomly selected patients, only 60 (48%) met both inclusion criteria. Of the remaining 64 patients, 9 (14%) were drinkers but could not communicate, and 35 (55%) could communicate but had not been drinking. Twenty (31%) met neither criterion.		
Length of follow-up	No		
Outcome and effect size	Fewer than half of the randomly selected patients met both of the inclusion criteria for the CIWA-Ar instrument. Significant association between postoperative status (p=0.01), liver disease (p=0.02) retained significance to predict appropriate ness. 7 of 11 patients who experienced adverse events had received STT according to the CIWA-Ar protocol (p=0.05). Significant association between adverse events and a history of alcohol dependence or AWS.		
Funding	No information		
Comments			

Title	**Oxcarbazepine versus carbamazepine in the treatment of alcohol withdrawal**		
First Author	**Schik, G., 2005**	**Source**	**16109591**
Level of evidence	2b	**Study type**	Single-blinded and randomized pilot study
Study quality	low		
Participants	N=29		
Patient characteristics	Inpatients seeking withdrawal treatment. Baseline CIWA in CBZ-group (13-16) > than in the Oxcarbazepine-group (4-6).		

Intervention	The CBZ group received 600mg of carbamazepine on days 1-3, 300mg CBZ on day 4 and a last dose of 100 mg on day 5. Corresponding to the equivalent dosing of CBZ to OXC of 1:1.5 (Smith, 2001), the OXC group received 900mg of oxcarbazepine on days 1 to 3, 450mg OXC on day 4 and a final dose of 150mg OXC on day 5. Except for day 5, the medication was given in three daily doses.
Comparison	CBZ vs. Oxcarbazepine
Length of follow-up	No
Outcome and effect size	The oxcarbazepine group showed a significant decrease of withdrawal symptoms and reported significantly less 'craving for alcohol' compared to the carbamazepine group (p=0.011). Subjectively experienced side effects, normalization of vegetative parameters and improvement in the cognitive processing speed did not reveal differences for both groups.
Funding	No information
Comments	Limitation: Low baseline-AWS in oxcarbazepine-group

Title	**Oxcarbazepine-efficacy and tolerability during treatment of alcohol withdrawal: a double-blind, randomized, placebo-controlled multicenter pilot study**		
First Author	**Koethe, D., 2007**	**Source**	**17511748**
Level of evidence	1b	**Study type**	RCT, 4-site, double-blind, randomized, placebo- controlled pilot study
Study quality	Study of good quality, clear procedures.		
Participants	N=50		
Patient characteristics	Inpatients seeking withdrawal-treatment.		
Intervention	Oxcarbazepine vs placebo. No initial group differences were found.		
Comparison	The amount of rescue medication of clomethiazole (CLO) capsules needed was chosen as the primary variable		
Length of follow-up	No		
Outcome and effect size	No differences were found in the need for rescue medication CLO (p=0.69), decrease of withdrawal symptoms (p=0.54), or craving for alcohol (p=0.20) between the OXC and the placebo group. Subjectively experienced side effects, normalization of vegetative parameters (p=0.28), craving (p=0.20), or improvement of psychopathological parameters (p=0.28) were not different between the groups. 1 subject in each group experienced an epileptic seizure.		
Funding	Novartis Pharma GmbH		
Comments			

Title	**Self-reported sleep, sleepiness, and repeated alcohol withdrawals: a randomized, double blind, controlled comparison of lorazepam vs gabapentin**		
First Author	**Malcolm, R., 2007**	**Source**	**17557449**
Level of evidence	1b	**Study type**	RCT
Study quality	Study of good quality, clear procedures.		
Participants	N=101		
Patient characteristics	Outpatients in treatment for alcohol withdrawal, 25% females, 15% African Americans, 3% Native Americans, and 1% Hispanic Americans.		
Intervention	4-day fixed-dose taper of gabapentin or lorazepam		
Comparison	Self-reported daytime sleepiness using the Epworth Sleepiness Scale. Self-reports of depression (Beck Depression Inventory), daily alcohol withdrawal using the Clinical Institute Withdrawal Assessment for Alcohol. Patients receiving 600mg, 900mg and 1200mg gabapentin did not differ and are combined in the analysis.		
Length of follow-up	8 days		
Outcome and effect size	During treatment for alcohol withdrawal, gabapentin as compared to standard therapy with lorazepam was superior on multiple sleep measures, in patients who had previous withdrawals.		
Funding	Supported by the National Institute on Alcohol Abuse and Alcoholism (NIAAA)		
Comments			

Title	Alcohol withdrawal pharmacotherapy for inpatients with medical comorbidity		
First Author	Weaver, M. F., 2006	Source	16785215
Level of evidence	2b	Study type	Clinical trial, cohort study
Study quality	Moderate		
Participants	N=183		
Patient characteristics	Patients hospitalized on general medical wards at a university medical center		
Intervention	Subjects in the ST arm received lorazepam doses based on CIWA-Ar score. Subjects in the FS arm received scheduled lorazepam with tapering over 4 days.		
Comparison	To determine whether there is a difference between symptom-triggered (ST) and fixed-schedule (FS) dosing of lorazepam		
Length of follow-up	No		
Outcome and effect size	No statistically significant difference in change of CIWA-Ar scores for the first 2 days between FS and ST groups (p=0.88). Symptom- triggered dosing for alcohol withdrawal for general medicine inpatients resulted in less lorazepam given with similar reduction in CIWA-Ar scores for the first 2 days, but a higher proportion of protocol errors.		
Funding	Funded by a Mentored Clinical Scientist Development Award (K23 AA00 222) from the NIAAA		
Comments			

Title	Alcohol withdrawal syndrome: symptom-triggered versus fixed-schedule treatment in an outpatient setting		
First Author	Elholm, B., 2011	Source	21414950
Level of evidence	1b	Study type	RCT; 5-site, double-blind, randomized, placebo- controlled study
Study quality	Study of good quality, clear procedures		
Participants	N=163		
Patient characteristics	Outpatients seeking withdrawal-treatment		
Intervention	randomized 1:1 to either a symptom-triggered self-medication or tapered dose, using chlordiazepoxide		
Comparison	Comparison of alcohol withdrawal symptoms, amount of medication, duration of symptoms, time to relapse and patient satisfaction		
Length of follow-up	10 days, one year		
Outcome and effect size	Time to SAWS score <12 (p=0.924) or <6 (p=0.091) did not differ between the two treatment groups. No differences regarding median cumulated dose of chlordiazepoxide, relapse, well-being, satisfaction, abstinence after one year.		
Funding	Danish Ministry of Health		
Comments	Results suggest that outpatient treatment is effective and in a specialized setting. Symptom-triggered medication is as effective and safe as the standard fixed- schedule treatment in outpatients.		

Title	Levetiracetam for the treatment of alcohol withdrawal syndrome: a multicenter, prospective, randomized, placebo-controlled trial		
First Author	Richter, C., 2010	Source	21105289
Level of evidence	1b	Study type	RCT; 5-site, double-blind, randomized, placebo-controlled study
Study quality	Study of good quality, clear procedures		
Participants	N=106		
Patient characteristics	Inpatients seeking withdrawal-treatment		
Intervention	Randomized to either Levetiracetam (administered in a fixed dose schedule over 6 days) or placebo. Diazepam was added symptom triggered as rescue medication.		
Comparison	Group comparison of the overall needed symptom triggered daily and weekly dose of diazepam, Alcohol withdrawal symptoms over time. Adherence, Safety, QoL, Craving,		

	Anxiety, Depression.
Length of follow-up	7 days
Outcome and effect size	The number of patients who developed severe withdrawal syndromes did not differ significantly between placebo or levetiracetam group (18.4% vs 20.3%). The mean diazepam use between day 1 and day 8 did also not differ (44.7mg in the levetiracetam and 38.6mg in the placebo group, p=0.522). Tolerability and safety data were similar in the LV group when compared with placebo.
Funding	UCB-Pharma
Comments	Results do not support an own or additional effect of LV on the reduction of alcohol withdrawal symptoms. Study design does not give information about a possible effect of early monotherapeutic treatment on AWS and on withdrawal seizures

Title	**Zonisamide versus diazepam in the treatment of alcohol withdrawal syndrome**		
First Author	**Rubio, G., 2010**	**Source**	**20927698**
Level of evidence	2b?	**Study type**	3-week, randomized, flexible-dose open, controlled pilot trial
Study quality	Moderate		
Participants	N=40		
Patient characteristics	Inpatients seeking withdrawal-treatment		
Intervention	Zonisamide 400-600mg/day (week 1), tapering to a minimum dose of 100-300mg/ day (week 3) or Diazepam (from 130-50mg/ day tapering to 5-15mg/ day).		
Comparison	Comparison of AWS during treatment with Zonisamid vs. Diazepam		
Length of follow-up	Day 7, 14, 21		
Outcome and effect size	• Similar reduction of AWS-symptoms during the first 14 days in both groups [F(9,29)=4.83; p<0.001). • Similar scores for craving, anxiety and depression without significant effect for group (F(2,37)=1.58, p=0.28). • Less side effects in the Zonisamid group (p=0.004). • Lower craving scores (t(39)=2.87, p<0.01), withdrawal symptoms (t(39)=14.32, p<0.001), anxiety symptoms (t(39)=19.31, p<0.001) and depressive symptoms (t(39)=4.63, p<0.001) after 3 weeks in the Zonisamid group.		
Funding	No information		
Comments	Zonisamid might also be a anticonvulsive drug for the treatment of acute AWS		

Title	**A prospective, randomized, trial of phenobarbital versus benzodiazepines for acute alcohol withdrawal**		
First Author	**Hendey, G. W., 2011**	**Source**	**20825805**
Level of evidence	1b	**Study type**	RCT; 2-site prospective, randomized, double blind trial
Study quality	Moderate		
Participants	N=44		
Patient characteristics	Inpatients in the emergency department with beginning alcohol withdrawal syndrome		
Intervention	Intravenous phenobarbital (mean, 509 mg) or i.v. lorazepam (mean, 4.2mg). At discharge, LZ patients received chlordiazepoxide (Librium), and PB patients received placebo		
Comparison	To compare the effect of intravenous phenobarbital (PB) versus intravenous lorazepam (LZ) plus oral chlordiazepoxid regarding the reduction of alcohol withdrawal symptoms after 48 hours and time in the emergency department (ED)		
Length of follow-up	48 hours		
Outcome and effect size	There were no differences between PB and LZ in baseline CIWA scores (p=0.3), discharge scores (p=0.04), ED length of stay (p=0.8), admissions (p=0.8) or 48-hour follow-up CIWA scores (p=0.6).		
Funding	No information		
Comments	Phenobarbit al and LZ were similarly effective in the treatment of mild/moderate alcohol		

	withdrawal in the Emergency Department and at 48 hours. But: low number of patients, need of intensive care. Difficult combination with lorazepam i.v. plus oral Chlordiazepoxid.

Title	**Pregabalin, tiapride and lorazepam in alcohol withdrawal syndrome: a multicentre, randomized, single-blind comparison trial**		
First Author	**Martinotti, G., 2010**	**Source**	**20078487**
Level of evidence	2b	**Study type**	
Study quality	Good quality, clear procedure		
Participants	N=111 (divided in 3 groups)		
Patient characteristics	Day clinic patients with AWS.		
Intervention	Maximum doses of pregabalin (450mg/day) vs. tiapride (800mg/day) vs. lorazepam (10mg/day)		
Comparison	To compare lorazepam with pregabalin and tiapride in the treatment of alcohol withdrawal syndrome (AWS). Medication was administered symptom triggered. Outcome measures were the reduction of withdrawal symptoms, the number of days remaining in treatment and the maintenance of abstinence.		
Length of follow-up	14 days		
Outcome and effect size	All the medications in the trial showed evidence of safety and efficacy in the treatment of uncomplicated forms of AWS. The number of subjects remaining alcohol free for the entire study period [pregabalin: 23 (62.2%); tiapride: 14 (37.8%); lorazepam: 21 (56.8%)] was significantly different in the three treatment groups, with a higher number in the pregabalin group (x2=4.19, p=0.04). Significant differences between groups of treatment were found with regard to items 9 (headache, fullness in head) and 10 (orientation and clouding of sensorium) of CIWA with a higher reduction for pregabalin group (Kruskal–Wallis test=7.5, p=0.02; 8.8, p=0.01).		
Funding	None		
Comments	Pregabalin may be considered as a potentially useful drug for treatment of AWS.		

Title	**Oxcarbazepine in combination with Tiaprid in inpatient alcohol-withdrawal--a RCT**		
First Author	**Croissant, B., 2009**	**Source**	**19724979**
Level of evidence	2b	**Study type**	RCT-randomized, open-label, parallel-group, clinical trial
Study quality	Moderate		
Participants	N=60		
Patient characteristics	Inpatients with alcohol dependence seeking withdrawal-treatment		
Intervention	Starting dose: 600mg Oxcarbamazepine plus 1200mg tiaprid/day vs. 2 cps. Clomethiazole every 4 hrs.		
Comparison	To compare a combination of oxcarbazepine (OXC)/ tiaprid (TIA) vs. clomethiazole (CLO) in alcohol withdrawal.		
Length of follow-up	6-8 days		
Outcome and effect size	Severity of alcohol withdrawal syndrome comparable between OXC/TIA and CLO-patients. Significantly more patients in the OXC/TIA-group (48.1%) displayed no AE compared to the CLO-group (24.1%). No significant differences between groups regarding total number of recorded adverse events (AEs).		
Funding	No information		
Comments	• OXC/TIA could have the potential to become a promising alternative for alcohol dependent patients unable to undergo inpatient withdrawal therapy with CLO. • Should be tested in daily care and outpatients settings.		

Title	**Efficacy of a combination of flumazenil and gabapentin in the treatment of alcohol dependence: relationship to alcohol withdrawal symptoms**		
First Author	**Anton, R. F., 2009**	**Source**	**19593171**
Level of evidence	1b	**Study type**	Double blind prospective controlled

Study quality	Good quality
Participants	N=60
Patient characteristics	Alcoholics who did and did not exhibit pretreatment alcohol withdrawal (AW) symptoms.
Intervention	Of those in the low AW (Alcohol withdrawal) group, 18 received placebos and 26 received active flumazenil/gabapentin. Of those in the high AW group, 9 received placebo and 7 received active flumazenil/ gabapentin. 0.1mg (1mL) of flumazenil/placebo.
Comparison	Sixty alcohol-dependent individuals (44 with low AW and 16 with high AW) were randomized to compare FMZ (2mg of incremental bolus for 20 minutes for 2 consecutive days) and GBP (up to 1200mg nightly for 39 days) or their inactive placebos.
Length of follow-up	48hrs to 6 weeks
Outcome and effect size	In those patients with high AW but not in those with a mild AW greater improvement in AW symptoms was observed in the active medication group compared with the placebo group. Patients in the high AW group had also more Percent days abstinent during treatment and time to first heavy drinking
Funding	Supported by a grant from Hythiam Inc.
Comments	These results suggest a differential response to FMZ/GBP treatment, depending on pre-treatment AW status (high or low).

Title	**A double-blind trial of gabapentin versus lorazepam in the treatment of alcohol withdrawal**		
First Author	**Myrick, H., 2009**	**Source**	**19485969**
Level of evidence	1b	**Study type**	RCT-prospective double blind, dose-response trial
Study quality	Good quality, clear procedure		
Participants	N=74		
Patient characteristics	Patients with alcohol withdrawal symptoms (CIWA-Ar ≥10) seeking outpatient treatment		
Intervention	2 doses of gabapentin (900mg tapering to 600mg or 1200 tapering to 800mg) or lorazepam (6mg tapering to 4mg) for 4 days		
Comparison	Comparison of alcohol withdrawal symptoms, alcohol drinking and craving during and immediately after outpatient treatment with high dose Gabapentin, moderate dose gabapentin or Lorazepam.		
Length of follow-up	Days 1 to 4 with follow up until day 12		
Outcome and effect size	High-dose gabapentin was statistically superior but clinically similar to lorazepam in reducing withdrawal symptoms. During treatment, lorazepam treated participants had higher probabilities of drinking compared to gabapentin-group. Post-treatment, gabapentin-treated patients had less probability of drinking during the follow-up compared to the lorazepam-treated participants. The gabapentin groups also had less craving, anxiety, and sedation compared to lorazepam.		
Funding	NIAAA grants and VA Medical Research		
Comments	High dose Gabapentin was effective for outpatient treatment of alcohol withdrawal and reduced the probability of drinking during alcohol withdrawal and in the immediate post-withdrawal week compared to lorazepam. Cave: gabapentin group with 600mg was stopped based on lack of efficacy and clinical complication.		

Title	**Proof-of-concept human laboratory study for protracted abstinence in alcohol dependence: effects of gabapentin**		
First Author	**Mason, B. J., 2009**	**Source**	**18855801**
Level of evidence	2b	**Study type**	Early Phase II proof-of-concept human laboratory cue-reactivity study
Study quality	Good quality, clear procedure, preclinical trial		
Participants	N=33		
Patient characteristics	Paid volunteers with current Diagnostic and Statistical Manual of Mental Disorders-IV alcohol dependence and a strength of craving rating 1 SD or greater for alcohol than water cues.		
Intervention	gabapentin 1200mg vs. placebo		
Comparison	To compare symptoms of craving and disturbances in sleep and mood after one week		

	treatment with Gabapentin (1200mg/day) vs. placebo.
Length of follow-up	1 week
Outcome and effect size	Gabapentin was associated with significantly greater reductions than placebo on several measures of subjective craving for alcohol as well as for affectively evoked craving. Gabapentin was also associated with significant improvement of sleep quality.
Funding	NIAAA
Comments	Only proof-of-concept with short treatment duration! Results suggest that gabapentin may be effective for treating the protracted abstinence phase in alcohol dependence.

Title	**Gamma-hydroxybutyric acid versus clomethiazole for the treatment of alcohol withdrawal syndrome in a medical intensive care unit: an open, single-center randomized study**		
First Author	**Elsing, C., 2009**	**Source**	**19462303**
Level of evidence	2b	**Study type**	Open, single-center randomized study
Study quality	Moderate		
Participants	N=26		
Patient characteristics	Alcoholic patients with severe AWS and concomitant medical diseases treated in an Intensive care unit.		
Intervention	Clomethiazole given orally in a dosage of 250 mg every 4 hours as a liquid or GHB i.v. (initially 30mg/kg body weight followed by 15mg/kg BW).		
Comparison	To compare four major AWS symptoms (tremor, sweating, nausea, restlessness) between clomethiazole and GHB treated patients.		
Length of follow-up	7 hrs.		
Outcome and effect size	GHB was more effective in treating AWS symptoms in the first 7 hrs with a greater decrease of AWS symptoms. No influence on duration of ICU stay. No serious side effects.		
Funding	No information		
Comments			

Title	**A randomized, double-blind comparison of lorazepam and chlordiazepoxide in patients with uncomplicated alcohol withdrawal**		
First Author	**Kumar, C. N., 2009**	**Source**	**19371497**
Level of evidence	1b	**Study type**	RCT double-blind
Study quality	Good quality		
Participants	N=100		
Patient characteristics	Male inpatients in a state of moderately severe, uncomplicated alcohol withdrawal at screening		
Intervention	Lorazepam (8mg/day) or chlordiazepoxide (80mg/day) with dosing down-titrated to zero in a fixed-dose schedule.		
Comparison	To compare withdrawal symptoms according to CIWA-Ar between Lorazepam and Chlordiazepoxid treated patients.		
Length of follow-up	8 days, follow-up 4 days later		
Outcome and effect size	No significant difference in f alcohol withdrawal severity between Lorazepam and chlordiazepoxide in reducing symptoms of alcohol withdrawal. Irritability and dizziness were more common with lorazepam (2.9% vs 0.4%, 0.9% vs 0.0%), and palpitations were more common with chlordiazepoxide (0.9% vs 0.0%)		
Funding	None		
Comments			

3.5 Körperliche Komplikationen

Title	**Alcoholism, peripheral neuropathy (PNP) and cardiovascular autonomic neuropathy (CAN)**		
First Author	**Agelink, 1998**	**Source**	**9879694**
Level of evidence	2b	**Study type**	Case control
Study quality	medium		
Participants	N=115		
Patient characteristics	35 strictly selected, detoxified alcoholics (DSM-III-R), and 80 well matched healthy controls		
Intervention			

Comparison	
Length of follow-up	
Outcome and effect size	Our findings provide reason to suspect that the total lifetime dose of alcohol and the duration of alcohol dependence are the most important factors contributing to the pathogenesis of both PNP and sympathetic dysfunction
Funding	
Comments	

Title	**Peripheral neuropathy in chronic alcoholism: a retrospective cross-sectional study in 76 subjects**		
First Author	**Ammendola, 2001**	**Source**	**11373267**
Level of evidence	2b	**Study type**	Cohort study
Study quality	medium		
Participants	N=76		
Patient characteristics	alcoholics with PNP		
Intervention	A consecutive sample of 76 chronic alcoholic patients was studied clinically, biochemically and electrophysiologically to assess clinical and/or subclinical signs of alcohol-related neuropathy as well as the most important and disputed risk factors for neuropathy such as age, parental history of alcoholism, nutritional status, alcoholic disease duration and total lifetime dose of ethanol (TLDE)		
Comparison	retrospektive Betrachtung;		
Length of follow-up			
Outcome and effect size	positive family history of alcoholism, but above all alcoholic disease duration and TLDE, could be more important factors than malnutrition in determining neuropathy		
Funding			
Comments			

Title	**Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis.**		
First Author	**Finnerup, 2015**	**Source**	**25575710**
Level of evidence	1b	**Study type**	Systematic Review
Study quality	high		
Participants	229 Studies		
Patient characteristics	Pt with PNP		
Intervention			
Comparison	Trial outcomes were generally modest: in particular, combined NNTs were 6.4 (95% CI [5.2|8.4]) for serotonin-noradrenaline reuptake inhibitors, mainly including duloxetine (nine of 14 studies); 7.7 (95% CI [6.5|9.4]) for pregabalin; 7.2 (95% CI [5.9|9.21]) for gabapentin, including gabapentin extended release and enacarbil; and 10.6 (95% CI [7.4|19.0]) for capsaicin high-concentration patches. NNTs were lower for tricyclic antidepressants, strong opioids, tramadol, and botulinum toxin A, and undetermined for lidocaine patches. Based on GRADE, final quality of evidence was moderate or high for all treatments apart from lidocaine patches; tolerability and safety, and values and preferences were higher for topical drugs; and cost was lower for tricyclic antidepressants and tramadol.		
Length of follow-up			
Outcome and effect size	These findings permitted a strong recommendation for use and proposal as first-line treatment in neuropathic pain for tricyclic antidepressants, serotonin-noradrenaline reuptake inhibitors, pregabalin, and gabapentin; a weak recommendation for use and proposal as second line for lidocaine patches, capsaicin high-concentration patches, and tramadol; and a weak recommendation for use and proposal as third line for strong opioids and botulinum toxin A. Topical agents and botulinum toxin A are recommended for peripheral neuropathic pain only.		
Funding	Role of the funding source: The study was partially funded by NeuPSIG. NA, NF, PK, RB, AR, MH, BHS are members of NeuPSIG management committee. No author was paid to write		

	this article by a pharmaceutical company or other agency. The corresponding author and all co-authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.
Comments	

Title	**Revisiting the evidence for neuropathy caused by pyridoxine deficiency and excess.**		
First Author	**Ghavanini**	**Source**	**25137514**
Level of evidence	2b	**Study type**	Systematic Review
Study quality	medium		
Participants	36 Studien; N=660		
Patient characteristics	Pt who took Pyridoxin		
Intervention	SR; However, neurological practitioners frequently discourage patients from taking pyridoxine in excess of 50mg/d given concerns around the development of a toxic sensory neuronopathy. There is no systematic review to support either of the 2 practices. To address this gap in knowledge, we reviewed the available literature on neuropathy attributed to pyridoxine deficiency and excess.		
Comparison			
Length of follow-up			
Outcome and effect size	Based on the current limited data, it can be concluded that very low doses of daily pyridoxine are required to prevent peripheral neuropathy. There is inadequate evidence to support routine pyridoxine supplementation in patients with disorders of peripheral nervous system. Supplementation with pyridoxine at doses greater than 50 mg/d for extended duration may be harmful and should be discouraged.		
Funding	Role of the funding source: The study was partially funded by NeuPSIG. NA, NF, PK, RB, AR, MH, BHS are members of NeuPSIG management committee. No author was paid to write this article by a pharmaceutical company or other agency. The corresponding author and all co-authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.		
Comments			

Title	**The course of alcoholic-nutritional peripheral neuropathy.**		
First Author	**Hawley, 1982**	**Source**	**6293240**
Level of evidence	2c	**Study type**	Outcome Research
Study quality	poor quality prognostic cohort study		
Participants	n=24 (ITT n=63)		
Patient characteristics	pt with alcoholic-nutritional peripheral neuropathy		
Intervention	abstinence		
Comparison			
Length of follow-up	2 to 72 months (mean 33)		
Outcome and effect size	11 of the patients were able to stop drinking alcohol. Initial subjective improvement was seen within the first week or two, but substantial improvement was not seen for 5 to 6 months. Most leg motor nerve velocity improved at a mean rate of increase of 0.12 M/sec per abstinent month. Large motor units and slowed nerve conduction persisted in "cured" patients. The largest motor units detected in the legs grew, despite alcohol intake.		
Funding			
Comments	25 Jahre alt, kleine Fallzahl, zeigt aber dass es unter Abstinenz besser wird		

Title	**Alcohol-related peripheral neuropathy: a systematic review and meta-analysis.**		
First Author	**Julian, 2019**	**Source**	**30467601**
Level of evidence	1b	**Study type**	Systematic Review
Study quality	medium		

Participants	N=2.590
Patient characteristics	Alcoholics with PNP
Intervention	
Comparison	87 articles were included in this review, 29 case-control studies, 52 prospective/ retrospective cohort studies and 2 randomized control trials, 1 cross sectional study, and 3 population-based studies.
Length of follow-up	
Outcome and effect size	The prevalence of peripheral neuropathy amongst chronic alcohol abusers is 46.3% (95% CI [35.7|57.3]) when confirmed via nerve conduction studies. Alcohol-related peripheral neuropathy generally presents as a progressive, predominantly sensory axonal length-dependent neuropathy. The most important risk factor for alcohol-related peripheral neuropathy is the total lifetime dose of ethanol, although other risk factors have been identified including genetic, male gender, and type of alcohol consumed. At present, it is unclear what the pathogenetic mechanisms for the development of neuropathy amongst those who chronically abuse alcohol are, and therefore, it is unknown whether it is attributed to the direct toxic effects of ethanol or another currently unidentified factor. There is presently sparse data to support a particular management strategy in alcohol-related peripheral neuropathy, but the limited data available appears to support the use of vitamin supplementation, particularly of B-vitamin regimens inclusive of thiamine.
Funding	This review did not receive funding. Dr. Zis is sincerely thankful to the Ryder Briggs Fund. This is a summary of independent research carried out at the NIHR Sheffield Biomedical Research Centre (Translational Neuroscience).
Comments	heterogene Studiendesigns im SR, daher "medium" quality und "nur" 1b

Title	**Treatment of alcoholic polyneuropathy with vitamin B complex: a randomised controlled trial.**		
First Author	**Peters, 2006**	**Source**	**16926172**
Level of evidence	2b	**Study type**	RCT
Study quality	medium		
Participants	N=325		
Patient characteristics	325 patients with sensory symptoms and signs of alcoholic polyneuropathy.		
Intervention			
Comparison	Patients were randomised to the ‘old formulation’ (i.e. vitamins B1, B2, B6, and B12), ‘new formulation’ [i.e. identical to the ‘old formulation’ with additional folic acid (vitamin B9)], or placebo in a 1:1:1 ratio.		
Length of follow-up	12-week treatment period		
Outcome and effect size	Therapeutic efficacy was assessed in 253 patients by measuring vibration perception threshold (biothesiometry), intensity of pain, sensory function, co-ordination, and reflex responses. Patients treated with the ‘new formulation’ or ‘old formulation’ showed significant improvement in the primary efficacy endpoint (vibration perception threshold at the big toe) and secondary efficacy endpoints in comparison to placebo. The active treatment groups were comparable to placebo in terms of safety.		
Funding	Conflicts of interests — The trial was sponsored by Laboratoires SMB, Belgium, of which F.V., S.D.N., D.M. and M.C. are employees. No other author had a financial interest in the investigational product. No other conflict of interest declared.		
Comments	Specific vitamin B complex (with and without folic acid) significantly improved symptoms of alcoholic polyneuropathy over a 12-week treatment period.		

Title	**Antidepressants for neuropathic pain: a Cochrane review.**		
First Author	**Saarto & Wiffen, 2010**	**Source**	**22786518**
Level of evidence	1b	**Study type**	Systematic Review
Study quality	medium		
Participants	66 reports; 3.293 participants		
Patient characteristics	Pt with neuropathic pain of different ethiology		

Intervention	treatment with different AD
Comparison	
Length of follow-up	
Outcome and effect size	Antidepressants are effective for a variety of neuropathic pains. Both TCAs and venlafaxine have a NNT of approximately 3.
Funding	
Comments	

Title	**Alcoholic polyneuropathy: a clinical and epidemiological study.**		
First Author	**Vittadini, 2001**	**Source**	**11524304**
Level of evidence	2b	**Study type**	Cohort Study
Study quality	medium		
Participants	N=236		
Patient characteristics	Alcoholics with PNP; Verschiedene Schweregrade und Konsummuster		
Intervention	Retrospective analysis		
Comparison			
Length of follow-up			
Outcome and effect size	Significant correlations were found between polyneuropathy, the duration of alcoholism, the type of alcoholic beverage consumed (wine) and the presence of liver disease and macrocytosis.		
Funding			
Comments			

Title	**Drinking pattern and alcohol-related medical disorders.**		
First Author	**Wetterling, 1999**	**Source**	**10414607**
Level of evidence	2b	**Study type**	Cohort study
Study quality	High		
Participants	N=241		
Patient characteristics	Chronic alcoholics admitted for detoxification		
Intervention	Retrospective analysis		
Comparison	History of alcohol abuse as well as drinking behaviour in the last 6 months were assessed by a semi-structured interview. Findings included intensive clinical examination with abdominal ultrasound in most subjects.		
Length of follow-up			
Outcome and effect size	The heavy drinkers suffered more often from pancreatitis, oesophageal varices, polyneuropathy or erectile dysfunction than episodic drinkers. They also showed more upper gastrointestinal disorders, although the estimated life-time alcohol intake was comparable to continuous drinkers. No difference relating to withdrawal delirium or seizures could be found between the groups of alcoholics		
Funding	BMFF; No.07EB9421, 07FDA01; Bonn Germany		
Comments			

Title	**Opioid Misuse as a Predictor of Alcohol Treatment Outcomes in the COMBINE Study: Mediation by Medication Adherence.**		
First Author	**Witkiewitz, 2018**	**Source**	**29873089**
Level of evidence	1b	**Study type**	RCT
Study quality	High		
Participants	N=1383		
Patient characteristics	alcoholics as part of the COMBINE Study		
Intervention			
Comparison	9 treatment groups/ 16 weeks		

Length of follow-up	16 weeks
Outcome and effect size	Baseline opioid misuse significantly predicted the time-to-first heavy drinking day (OR=1.38 [95%CI [1.13|1.64], p=0.001) and a higher probability of being in a heavier and more frequent drinking profile at the end of treatment (OR=2.90 [95% CI [1.43|5.90],
Funding	Funding: This research was supported by grants funded by the National Institutes of Health R01 AA022328 and R01 AA025539 (Witkiewitz, PI) and R34 AT08398 (Vowles, PI). The content is solely the responsibility of the authors and does not necessarily reflect the views of NIH.
Comments	Opioid misuse and other drug use were associated with poorer an AUD treatment outcome, which was mediated by medication adherence. Clinicians and researchers should assess opioid misuse and other drug use in patients undergoing AUD treatment.

Title	**Benfotiamine in treatment of alcoholic polyneuropathy: an 8-week randomized controlled study (BAP I Study).**		
First Author	**Woelk, 1998**	**Source**	**9872352**
Level of evidence	2a	**Study type**	Case control
Study quality	Medium		
Participants	N = 84		
Patient characteristics	out-patients with severe symptoms of alcoholic polyneuropathy		
Intervention	three-armed, randomized, multicentre, placebo-controlled double-blind study		
Comparison	The efficacy of benfotiamine vs a combination containing benfotiamine and vitamins B6 and B12 in out-patients with severe symptoms of alcoholic polyneuropathy (Benfotiamine in treatment of Alcoholic Polyneuropathy, BAP I). 3-armig: Placebo, Benfotiamin und Formula		
Length of follow-up	8 weeks		
Outcome and effect size	Benfotiamine led to significant improvement of alcoholic polyneuropathy.		
Funding			
Comments			

Title	**How addictive are gabapentin and pregabalin? A systematic review**		
First Author	**Bonnet, 2017**	**Source**	**28988943**
Level of evidence	1b	**Study type**	SR
Study quality	high		
Participants	106 Studien		
Patient characteristics	Pt. mit verschiedenen SUD		
Intervention			
Comparison	We did not find convincing evidence of a vigorous addictive power of gabapentinoids which is primarily suggested from their limited rewarding properties, marginal notes on relapses, and the very few cases with gabapentinoid-related behavioral dependence symptoms (ICD-10) in patients without a prior abuse history (N=4). In support, there was no publication about people who sought treatment for the use of gabapentinoids. Pregabalin appeared to be somewhat more addictive than gabapentin regarding the magnitude of behavioral dependence symptoms, transitions from prescription to self-administration, and the durability of the self-administrations.		
Length of follow-up			
Outcome and effect size	The principal population at risk for addiction of gabapentinoids consists of patients with other current or past substance use disorders (SUD), mostly opioid and multi-drug users, who preferred pregabalin. Pure overdoses of gabapentinoids appeared to be relative safe but can become lethal (pregabalin > gabapentin) in mixture with other psychoactive drugs, especially opioids again and sedatives. Based upon these results, we compared the addiction risks of gabapentin and pregabalin with those of traditional psychoactive substances and recommend that in patients with a history of SUD, gabapentinoids should be avoided or if indispensable, administered with caution by using a strict therapeutic and prescription monitoring.		

Funding	No funding
Comments	

3.6. Komorbide psychische Störungen

3.6.2 Schizophrenie

Title	**A systematic review of psychological interventions for excessive alcohol consumption among people with psychotic disorders**		
First Author	**Baker, A. L., 2012**	**Source**	**22632145**
Level of evidence	1a	**Study type**	Meta-analysis of 7 RCTs
Study quality	Adequate study selection process: systematic literature search during Jan. 2010 → identification of 429 papers → extraction of 26 potentially relevant studies → exclusion of 19 studies due to methodological issues. Narrative review and calculation of effect sizes (Cohen´s d) for alcohol use outcomes using Comprehensive Meta-analysis (Biostat) and STATA/SE 11 (Stata-Corp). No calculation of an overall effect size because of substantial diversity in participants, type of treatment und alcohol use measures. Assessment of methodological quality of studies by means of the validated Physiotherapy Evidence Database (PEDro) scale.		
Participants	N=7 RCTs with a total of n=942 Studies evaluated: Baker 2002a+b, Graeber 2003, Martino 2006, Baker 2006, Kemp 2007, Craig 2008, Barrowclough 2010		
Patient characteristics	Patients with psychotic disorders (schizophrenia, schizoaffective, psychotic mood disorders, bipolar disorders) and comorbid alcohol use disorder (AUD) (Graeber et al., 2003) or substance use disorders (SUD) (the remaining 6 studies). In the six studies with SUD secondary subgroup analyses were performed with the data of the AUD patients. In-patients (N=1), in- and out-patients (N=2), out-patients (N=4)		
Intervention	1 to 3 sessions MI (Motivational Interviewing) (N=3) or a combination of MI and CBT (Cognitive behavioral therapy) over 4-6 sessions (N=1), or 10 sessions (N=1), or over a period of 12 or 18 months (N=2).		
Comparison	TAU (Treatment as Usual) or psychoeduc ation or “standard psychiatric interviews” same length as intervention.		
Length of follow-up	3 months to 18 months		
Outcome and effect size	1 or 2 sessions MI had no advantage compared to the control condition. 3 sessions MI had more abstinent days compared to the control condition (small pure AUD sample with n=30, psychoeducation as control condition, Graeber 2003). Size effect small to moderate. 2 studies with an MI+CBT intervention showed no difference in alcohol use parameters between intervention and control, but the intervention groups showed more improvement in affective or psychotic symptoms. The remaining 2 studies with an MI+CBT intervention showed an advantage for the intervention. Size effect moderate.		
Funding	NHMRC Fellowship QUT Vice Chancellor´s Senior Research Fellowship Australian Postgraduate Awards		
Comments			

Title	**A pilot study comparing motivational interviewing and an educational intervention in patients with schizophrenia and alcohol use disorders (Evaluated in the meta-analysis of Baker et al., 2012)**		
First Author	**Graeber, D. A., 2003**	**Source**	**12836801**
Level of evidence	1b	**Study type**	RCT
Study quality	Composite PEDro score 5 (total 9). Low drop-out rate. Groups dissimilar at baseline, no ITT analysis, assessors were not blinded, no verification of self-report alcohol use, no ratings of treatment adherence/fidelity. Small sample size, almost only males, possible therapist effect.		
Participants	N=30		
Patient characteristics	In- and out-patients with schizophrenia and comorbid alcohol use disorder (AUD) male: 96,7% mean age: 44		
Intervention	MI 3 x 1-hour weekly individual sessions, delivered by a psychologist		
Comparison	Psychoeducation 3 x 1- hour weekly individual sessions, delivered by a social worker		
Length of follow-up	24 weeks (Assessments after 4, 8 and 24 weeks). 93% at all time points		
Outcome and effect size	MI had more abstinent days during follow-up. Size effect small to moderate. No difference		

	on drinking intensity.
Funding	
Comments	

Title	**Motivational interviewing among psychiatric in-patients with substance use disorders / Evaluation of a motivational interview for substance use within psychiatric in-patient services (Evaluated in the meta-analysis of Baker et al., 2012)**		
First Author	**Baker, A., 2002**	**Source**	**12197863**
Level of evidence	2b	**Study type**	RCT
Study quality	Composite PEDro score 6 (total 9). Groups similar at baseline, blinded assessors. No ITT analysis, no verification of self-report alcohol/drug use, no ratings of treatment adherence/fidelity.		
Participants	N=160		
Patient characteristics	In-patients with psychotic disorders (37% schizophrenia, 29.6% mood, 12.3% other, 19.8% none) and comorbid SUD (54.4% alcohol, 50.8% cannabis, 21.9% amphetamines, 12.5% heroin, 11.3% tranquilizers) male: 81.3% mean age: 31, criteria for alcohol consumption: >4 drinks per day for men, >2 drinks per day for women		
Intervention	MI 1 x 30-45 Min. individual session, delivered by a psychologist		
Comparison	TAU		
Length of follow-up	12 months (Assessments after 3m (70%), 6m (73.1%) and 12m (71.9%)). All follow-ups 55,6%		
Outcome and effect size	Alcohol use (standard drinks per day) reduced for the whole sample. No differences between intervention and control group.		
Funding	Research into Drug Abuse grant from the Commonwealth Department Of Health and Aged Care.		
Comments	Secondary subgroup analyses on alcohol outcomes among the patients who reported excessive alcohol use at baseline.		

Title	**Cognitive-behavioural therapy for substance use disorders in people with psychotic disorders: Randomised controlled trial (Evaluated in the meta-analysis of Baker et al., 2012)**		
First Author	**Baker, A., 2006**	**Source**	**16648530**
Level of evidence	2b	**Study type**	RCT
Study quality	Composite PEDro score 6 (total 9). Groups dissimilar at baseline, no ITT analysis, not clear whether assessors were blinded. No verification of self-report alcohol/drug use, no ratings of treatment adherence/fidelity.		
Participants	N=130		
Patient characteristics	Out-patients with psychotic disorders (62.2% schizophrenia, 12.6% schizoaffective, 9.2% bipolar, 4.2% affective) and comorbid SUD (67.3% alcohol, 73.1% cannabis, 47% amphetamines) male: 78.2% mean age: 28		
Intervention	Combination of MI + CBT, 10 x 60 min. weekly individual sessions, delivered by a psychologist.		
Comparison	TAU		
Length of follow-up	12 months: Assessments after 15 weeks (93%), 6 months (94.6%) and 12 months (80%)		
Outcome and effect size	Substantial reduction in drinking in the entire sample. No differences between intervention and control group. In parallel, improvement of mania and negative symptoms for the entire sample. MI + CBT intervention group showed better improvement in depression at 6 m and general functioning at 12 m.		
Funding	National Health and Medical Research Council (NHMRC)		
Comments	Secondary subgroup analyses on alcohol outcomes among the patients who reported excessive alcohol use at baseline.		

Title	**A randomized controlled pilot study of motivational interviewing for patients with psychotic and drug use disorders (Evaluated in the meta-analysis of Baker et al., 2012)**

First Author	Martino, S., 2006	Source	16968350
Level of evidence	2b	Study type	RCT
Study quality	Composite PEDro score 5 (total 9). ITT analysis, verification of self-report on alcohol/drug use by means of urine screens and collateral reports, treatment adherence and competence with videotaped sessions. Groups dissimilar at baseline, assessors were not blinded.		
Participants	N=44		
Patient characteristics	In- and out-patients with psychotic disorders (43% schizophrenia, 34% schizoaffective, 23% psychotic NOS) and comorbid SUD (47.7% alcohol, 50% cannabis, 54.5% cocaine) male: 73% mean age: 32.		
Intervention	MI 2 x 60 min. individual sessions, delivered by a psychologist or social worker.		
Comparison	"Standard psychiatric interview" 2 x 60 min individual sessions, delivered by a psychologist or social worker.		
Length of follow-up	12 weeks: Assessments after 4, 8 and 12 weeks, 77% at all time points.		
Outcome and effect size	Reduction in days of use per month for the entire sample. No differences between intervention and control group.		
Funding	NIDA		
Comments	Secondary subgroup analyses on alcohol outcomes among the patients who reported excessive alcohol use at baseline		

Title	Stop Using Stuff: trial of a drug and alcohol intervention for young people with comorbid mental illness and drug and alcohol problems (Evaluated in the meta-analysis of Baker et al., 2012)		
First Author	Kemp, R., 2007	Source	17852064
Level of evidence	2b	Study type	RCT
Study quality	Composite PEDro score 5 (total 9). Groups dissimilar at baseline, no ITT analysis, assessors were not blinded. No verification of self-report alcohol/drug use, no ratings of treatment adherence/fidelity. Very small sample size.		
Participants	N=19		
Patient characteristics	Out-patients with psychotic disorders (% of specific diagnoses not reported) and comorbid SUD (% of specific diagnoses not reported) male: 70% mean age: 21		
Intervention	Combination of MI + CBT, 4-6 individual sessions, delivered by clinic staff.		
Comparison	TAU		
Length of follow-up	6 months (84.2%)		
Outcome and effect size	Reduction of frequency, but not quantity of alcohol use for the entire sample. Greater reduction of frequency of alcohol use in the intervention group. Size effect moderate. Also, MI + CBT intervention group showed better improvement in self-efficacy.		
Funding			
Comments	Secondary subgroup analyses on alcohol outcomes among the patients who reported excessive alcohol use at baseline.		

Title	Integrated care for co-occurring disorders: psychiatric symptoms, social functioning, and service costs at 18 months (Evaluated in the meta-analysis of Baker et al., 2012)		
First Author	Craig, T. K., 2008	Source	18308908
Level of evidence	2b	Study type	RCT
Study quality	Composite PEDro score 7 (total 9). Groups similar at baseline. No ITT analysis, assessors were not blinded. No verification of self-report alcohol/drug use, no ratings of treatment adherence/fidelity. Low follow-up rate, diagnoses from clinical notes, cluster randomization with possible contamination between conditions.		
Participants	N=232		
Patient characteristics	Out-patients with psychotic disorders (schizophrenia, schizoaffective, delusional, bipolar with psychotic symptoms, % not reported) and comorbid SUD (33% alcohol only, 22% cannabis only, 13% alcohol and cannabis, 24% stimulants, 8% others) male: 84.1% mean age: 39		
Intervention	Combination of MI + CBT, delivered by clinical case managers (63% nurses) over 18		

	months. Number of sessions not reported.
Comparison	TAU
Length of follow-up	18 months (66.4%)
Outcome and effect size	Slight, non- significant reduction in alcohol use for the entire sample. No difference between intervention and control group. The MI + CBT intervention group showed lower psychiatric symptom scores at 18 months.
Funding	Bethlem and Maudsley National Health Service Trust
Comments	Outcomes among the patients who reported excessive alcohol use at baseline.

Title	**Integrated motivational interviewing and cognitive behavioural therapy for people with psychosis and comorbid substance misuse: randomised controlled trial (Evaluated in the meta-analysis of Baker et al., 2012)**		
First Author	**Barrowclough, C., 2010**	**Source**	**21106618**
Level of evidence	2b	**Study type**	RCT
Study quality	Composite PEDro score 9 (total 9). Groups similar at baseline, ITT analysis, assessors were blinded, verification of self-report alcohol/drug use by means of case coordinator reports. No ratings of treatment adherence/fidelity.		
Participants	N=327 with SUD, out of which n=142 had AUD (alcohol use disorder) only.		
Patient characteristics	Out-patients with psychotic disorders (81.7% schizophrenia, 8.3% schizoaffective, 8.9% psychotic NOS, 1.2% schizophreniform) and comorbid SUD (48% alcohol only, 35.5% drug only, 16.5% both) male: 86.5% mean age: 38		
Intervention	Combination of MI + CBT, delivered in individual sessions by psychologists, nurse therapists and a social worker usually in the patient´s home over 12 months. Up to 26 x 60 min. sessions. Mean number of sessions attended: 16.7±8.3		
Comparison	TAU		
Length of follow-up	18 months: Assessments after 6 m (90.5%), 12m (82.3%), 18m (79.5%)		
Outcome and effect size	The MI + CBT intervention group had lower substance use per occasion of use. The subgroup with AUD only reported more days abstinent in the intervention vs. control condition.		
Funding	UK Medical Research Council, Department of Health		
Comments	Secondary subgroup analyses on alcohol outcomes among the patients who reported excessive alcohol use at baseline. Rates of abstinence not reported separately for alcohol use.		

Title	**A randomized trial of clozapine vs. other antipsychotics for cannabis use disorder in patients with schizophrenia**		
First Author	**Brunette, M. F., 2015**	**Source**	**25914610**
Level of evidence	2b	**Study type**	RCT
Study quality			
Participants	N=31		
Patient characteristics	Treatment resistant patients with psychotic disorders and comorbid cannabis use disorder (CUD)		
Intervention	Treatment resistant patients were randomized either to switch to clozapine or to continuation of their previous antipsychotic medication		
Comparison	Continuation of previous antipsychotic medication		
Length of follow-up	3 months (90.3%)		
Outcome and effect size	Improvement of psychiatric symptoms and reduction of cannabis use in intervention group But: No difference concomitant alcohol use between intervention and control group		
Funding	NIDA		
Comments	Secondary analysis on parameters of alcohol use		

Title	**Long-acting Injectable Risperidone Compared With Zuclopenthixol in the Treatment of Schizophrenia With Substance Abuse Comorbidity**		
First Author	**Rubio, G., 2006**	**Source**	**16933590**

Level of evidence	2b	**Study type**	RCT
Study quality	Open study, but blinded assessors. Objective main outcome parameter: percentage of positive urine tests during follow-up period. Low drop-out rate (9/115). ITT analysis with LOCF.		
Participants	N=115		
Patient characteristics	In-patients with schizophrenia and comorbid SUD (87.8% alcohol, 71.3% cannabis, 26% cocaine) male: 96.7% mean age: 35.7 Selection/inclusion of patients during in-hospital stay, after psychosis was stabilized. Patients stayed in hospital another 7-15 days after they were randomized. Thereafter, they were referred to the outpatient center.		
Intervention	Risperidone depot i.m. + CBT		
Comparison	Zuclopenthixol depot i.m. + CBT		
Length of follow-up	6 months (92%). Weekly visits with urine tests for alcohol, opiates, cocaine and cannabis. Psychiatric assessments at 2, 4 and 6 months.		
Outcome and effect size	Less positive urine tests in the risperidone depot group. Stronger reductions in psychiatric symptoms (PANSS Scale) and better compliance (attendance of more CBT program sessions) in the risperidone depot group.		
Funding	Fundación Cerebro y Mente		
Comments	No separate outcome data on alcohol use parameters, but high percentage of AUD in the sample (87.8%). Hence, high probability that results are relevant for AUD.		

Title	**Naltrexone Augmentation of Neuroleptic Treatment in Alcohol Abusing Patients With Schizophrenia**		
First Author	**Petrakis, I. L., 2004**	**Source**	**14634716**
Level of evidence	1b	**Study type**	RCT, double-blind, placebo-controlled
Study quality	Verification of self-reports on alcohol use by means of breathalyzer readings at every visit.		
Participants	N=31		
Patient characteristics	Out-patients with schizophrenia (58.1%) or schizoaffective disorder (41.9%) and comorbid alcohol use disorder (AUD). Male: 100%, mean age: 46		
Intervention	Naltrexone on top to antipsychotic medication + CBT		
Comparison	Placebo on top to antipsychotic medication + CBT		
Length of follow-up	12 weeks, (80.6%) weekly visits		
Outcome and effect size	Fewer drinking days, fewer heavy drinking days, and less craving in the naltrexone group. No difference in side effects between groups. No influence of naltrexone on symptoms of schizophrenia		
Funding	NARSAD, NIAAA, Veterans Affairs MERIT grant, VA-Yale Alcoholism Research Center, VISN I MIRECC		
Comments			

Title	**Effects of Acamprosate on Cognition in a Treatment Study of Patients With Schizophrenia Spectrum Disorders and Comorbid Alcohol Dependence**		
First Author	**Ralevski, E., 2011**	**Source**	**21716064**
Level of evidence	2b	**Study type**	RCT
Study quality	double-blind, no verification of self-report alcohol use		
Participants	N=23		
Patient characteristics	Out-patients with schizophrenia spectrum disorder (specific diagnoses not reported) and comorbid alcohol dependence male: 82.6% mean age: 50.7.		
Intervention	Acamprosate + CBT		
Comparison	Placebo + CBT		
Length of follow-up	12 weeks, Weekly assessments, 74% completed at least 8 weeks. 65% completed all 12 weeks of treatment.		
Outcome and effect size	Decrease in alcohol consumption in both groups, no difference between acamprosate and placebo. No significant change in cognitive functioning, no difference between acamprosate and placebo in any cognitive domain.		
Funding	Forest Laboratories, VA Alcohol Center, Mental Illness Research Education and clinical Center (MIRECC)		

Comments	Main finding: Acamprosate had no adverse effects on cognition and did not influence psychotic symptoms (good tolerability)

Title	**A Systematic Review of Psychosocial Research on Psychosocial Interventions for People With Co-Occurring Severe Mental and Substance Use Disorders**		
First Author	**Drake, R. E., 2008**	**Source**	**17574803**
Level of evidence	1a	**Study type**	Systematic, qualitative, narrative review of 22 RCTs and 23 quasi-experimental studies with comparison groups.
Study quality	Acceptable study selection process: systematic literature search → exclusion of studies with n<10 and pre-post studies unless they involved A-B-A designs. No calculation of effect sizes, no assessment of methodological quality of studies.		
Participants	N=22 RCTs with a total of n=2.044, N=23 quasi experimental studies with a total of n=9.509		
Patient characteristics	Patients with severe mental disorder (mostly schizophrenia and schizoaffective disorder, in some studies also severe depressive and bipolar disorders) and comorbid substance use disorder (SUD). Only two studies with comorbid alcohol use disorder (AUD): Graeber et al. (2003), Hulse & Trait (2002), both RCTs with n=30 and n=120, resp.		
Intervention	Various integrated interventions: Psychotherapeutic interventions (individual, group, or family) (N=20, out of which 15 RCTs): MI, or CBT, or a combination of MI and CBT, or a combination of MI and contingency management, or contingency management, or a combination of MI, CBT and family therapy, or supportive group therapy and psychoeducation. Case management (integrated intensive case management with or without ACT) (N=11, out of which 6 RCTs). Integrated residential treatment and outpatient rehab programs (N=13, out of which1 RCT). Legal interventions (N=5, out of which 1 RCT)		
Comparison	Various comparison interventions		
Length of follow-up	1 month to 3 years		
Outcome and effect size	Advantage of Intervention with regard to substance use and/or mental health outcomes in trials with: • Psychotherapeutic interventions: 16 out of 20 trials • Case management: 7 out of 11 trials • Residential and outpatient rehab programs: 11 out of 13 trials No advantage of Intervention in legal trials (4 out of 5 trials negative)		
Funding	West Foundation		
Comments	Only two studies with comorbid alcohol use disorder (AUD): • Graeber et al. (2003): RCT, n=30 with schizophrenia and AUD, MI vs. psychoeducation, with advantage of intervention. This paper is included in the review of Baker et al. (2012). • Hulse & Trait (2002): RCT, n=120 with “acute psychiatric diagnosis” and AUD, MI vs. information packet, with advantage of intervention. This paper is not included in the review of Baker et al. (2012).		

Title	**Clozapine Use in Patients With Schizophrenia and a Comorbid Substance Use Disorder: A Systematic Review**		
First Author	**Arranz, B., 2017**	**Source**	**29273271**
Level of evidence	2a? 3a?	**Study type**	Systematic review of studies of different types (RCTs, blinded and open-label, cohort and case control studies, cross-sectional and observational studies). Five out of 14 studies included specific evaluation of AU/AUD
Study quality	Medium		

Participants	N=14, out of which N=5 with evaluation of AUD:
	a) Drake et al. (2000): open label prospective multisite, n=151;
	b) Brunette et al. (2006): prospective single-blind, n=95
	c) Swanson et al. (2007): prospective observational multisite, n=362;
	d) Kim et al. (2008): prospective naturalistic, n=61;
	e) Brunette et al. (2011): RCT single-blind, n=31		

Patient characteristics	a + b) schizophrenia or schizoaffective disorder and SUD outpatients; c + d) schizophrenia		

	and SUD, in- and outpatients; e) schizophrenia or schizoaffective disorder and SUD
Intervention	a, b, d and e) Clozapine; c) SGAs (CLO, RIS or OLA)
Comparison	a) Drake et al. (2000): FGAs; b) Brunette et al. (2006): other APs (mainly FGAs, eight cases with other SGAs); c) Swanson et al. (2007): second arm: FGAs, third arm: AP free d) Kim et al. (2008): Risperidone; e) Brunette et al. (2011): other APs (FGAs and SGAs)
Length of follow-up	a) 3 years; b) 2 years; c) 3 years; d) 2 years; e) 12 weeks
Outcome and effect size	a and b) Clozapine was superior to FGA in improving AUD (clinician rating scales and interviews); c) SGAs incl. Clozapine were superior to FGAs and absence of APs in self-reported alcohol use; d) no difference in self-reported alcohol use; e) no difference in self-reported alcohol use (heavy drinking days per week; breathanalyzer). No report on effect sizes
Funding	No funding
Comments	

Title	**Treatment of Substance Use Disorders With Co-Occurring Severe Mental Health Disorders**		
First Author	**Murthy, P., 2019**	**Source**	**31157674**
Level of evidence	3a?	**Study type**	Systematic review of studies of different types (reviews, meta-analyses, RCTs, blinded and open-label, cohort and case control studies, secondary analyses).
Study quality	narrative review		
Participants	N=43; few studies with populations with SMI and specifically AUD (Sawicka et al., 2017; Serrita et al., 2019); not clear how many / which other studies included specific evaluation of AUD.		
Patient characteristics	SMI and SUD		
Intervention	Various pharmacological and psychosocial interventions		
Comparison	Various controls		
Length of follow-up	No details given		
Outcome and effect size	Pharmacological interventions: Reviews by Bennett et al. (2017), Temmingh et al. (2018): Open-label trials and RCTs demonstrate the comparative efficacy of CLO, OLA and RIS over other APs in respect to SUD outcomes (no specific statement in respect to AUD). No difference between the SGAs in respect to SUD with the exception of cannabis UD. Lynn-Star et al. (2018) (secondary analysis of the PRIDE study): The depot antipsychotic paliperidone war superior to oral antipsychotics in several outcome measures in patients with SCH and SUD (no report on use of specific substances). Review by Sawicka et al. (2017): Naltrexon leads to reductions in drinking days and number of drinks consumed in patients with SMI and AUD. Serrita et al. (2019), small RCT placebo-controlled glycin vs. PLA in patients with SCH/Schizoaffective Disorder and AUD: no difference. Psychosocial interventions: No studies referring specifically to SCH and AUD.		
Funding	No funding		
Comments	In respect to psychosocial interventions an integrated approach and early start in the course of treatment are recommended. No specific comments/recommendations regarding SCH and AUD.		

Title	**Naltrexone Efficacy in Treating Alcohol-Use Disorder in Individuals With Comorbid Psychosis: A Systematic Review**		
First Author	**Sawicka, M., 2017**	**Source**	**28959434**
Level of evidence		**Study type**	Systematic review of RCTs and non-RCTs
Study quality	"N=9 nine reports (five journal articles and four detailed poster presentation abstracts): 4 RCTs and 5 non-RCTs (1 retrospective chart review, 4 prospective open label studies, one of which without control) with a total of 798 participants with SMI and AUD, out of which n=273 with psychotic disorder and AUD."		
Participants	"n=273 with schizophrenia or schizoaffective disorder and AUD. The average age of participants, where provided, was 44.24. 87% of participants were male."		
Patient characteristics	Naltrexone in 8 out of 9 studies, concurrent antipsychotic medication in 4 out of 9 studies,		

	concurrent psychosocial intervention.
Intervention	Three different comparisons: a) placebo (4 studies); b) another pharmaceutical agent (acamposate, disulfiram, combinations, 4 studies); c) baseline drinking behaviour (3 studies, one of which utilized the long-acting injectable form of naltrexone)
Comparison	8 to 24 weeks
Length of follow-up	a) Naltrexone vs. placebo: Overall, superiority of naltrexone in self-reported outcomes; b) Naltrexone vs. acamprosate: Overall, superiority of naltrexone in self-reported outcomes (Bratu and Sopterean, 2014); naltrexone vs. disulfiram: no group difference in self-reported drinking outcomes, but in one study more discontinuations with disulfiram because of side effects (Vasile et al., 2013); c) Reduction or self-reported drinking outcomes in one retrospective chart review study ((Maxwell and Shinderman, 2000) and two prospective open-label studies (Batki et al., 2007, 2010), one of which with the long-acting injectable form of naltrexone. No report of effect sizes. Inconclusive evidence on effects of naltrexone on general psychopathology.
Outcome and effect size	
Funding	
Comments	

Title	**Long-acting Injectable vs. Oral Risperidone for Schizophrenia and Co-Occurring Alcohol Use Disorder: A Randomized Trial**		
First Author	**Green, A. I., 2015**	**Source**	**26302441**
Level of evidence	1b	**Study type**	RCT; prescription open-label, blinded ratings
Study quality	high		
Participants	N=95		
Patient characteristics	SCH or schizoaffective disorder and AUD outpatients; mean age 42 y, m:f 77:33; most participants with alcohol dependence (rather than abuse); on average 2 heavy drinking days per week		
Intervention	Risperidone LAI every two weeks		
Comparison	Risperidone orally daily		
Length of follow-up	6 months		
Outcome and effect size	Self-reported alcohol use (Timeline Follow-Back procedure) and Breathanalyzer Primary outcome: Statistical trend for less heavy drinking days per week with LAI risperidone. Secondary outcomes: less drinking days per week with LAI risperidone; no group differences for number of drinks per week and global Alcohol Use Scale score. Medication adherence was better with LAI risperidone. No group differences in psychotic symptoms and global functioning (PANSS, GAF, CGI)		
Funding	Investigator-initial study funded by Janssen		
Comments	SCH patients with AUD appear to continue drinking some alcohol while taking either form of risperidone. Nonetheless, the authors suggest that injectable risperidone may have (limited) advantages and may be a better choice than the oral form for these dual diagnosis patients.		

Title	**Randomized Trial of the Effect of Four Second-Generation Antipsychotics and One First-Generation Antipsychotic on Cigarette Smoking, Alcohol, and Drug Use in Chronic Schizophrenia**		
First Author	**Mohamed, S., 2015**	**Source**	**26075840**
Level of evidence	1b	**Study type**	RCT
Study quality	secondary analysis of data from a high quality study		
Participants	N=1432		
Patient characteristics	Patients with SCH, average age 40.6 years, 74.2% male		
Intervention	Four second-generation antipsychotic drugs (olanzapine, risperidone quetiapine, and ziprasidone) and one first-generation antipsychotic (perphenazine)		
Comparison	four second-generation antipsychotic drugs (olanzapine, risperidone quetiapine, and		

	ziprasidone) and one first-generation antipsychotic (perphenazine)
Length of follow-up	18 months
Outcome and effect size	Significant effects of time showing reduction in substance use over the 18 months; no evidence that any antipsychotic was superior to any other in a secondary analysis of data on substance use outcomes (nicotine, alcohol, illicit drugs)
Funding	NIMH
Comments	Secondary analysis of data from the CATIE study:

3.6.3 Depression

Title	**Antidepressants for Major Depressive Disorder and Dysthymic Disorder in Patients With Comorbid Alcohol Use Disorders: A Meta-Analysis of Placebo-Controlled Randomized Trials**		
First Author	**Iovieno, N., 2011**	**Source**	**21536001**
Level of evidence	1a	**Study type**	Meta-analysis
Study quality	Literature search, 1980-2009		
Participants	N=11, studies included		
Patient characteristics	MDD, Dysthymia, +/- Alcohol dependence		
Intervention	Pharmacotherapy with various antidepressants, psychotherapy		
Comparison	Placebo, TAU		
Length of follow-up	6 to 24 weeks		
Outcome and effect size	AD + MDD: Efficacy of all antidepressants 57.8% vs. 47.1%, ES=0.24 SSRI alone: 59.3% vs. 51.1% ES=0.17, Heterogeneity RR AD vs. PLO p=.105. Also SSRI vs. PLO p=.38 Heavy drinking days: AD vs. PLO p=.274; Heterogeneity: p=0.56		
Funding	None mentioned		
Comments	Most recent meta-analysis. Meta-analysis with metaregression including pharmacological and psychotherapy studies, analyses of heterogeneity coefficients		

Title	**Efficacy of Antidepressants in Substance Use Disorders With and Without Comorbid Depression. A Systematic Review and Meta-Analysis**		
First Author	**Torrens, M., 2005**	**Source**	**15769553**
Level of evidence	1a	**Study type**	Meta-analysis
Study quality	Systematic review, separate analysis for alcohol, opioid, cocaine and other drug dependence		
Participants	N=9 studies included		
Patient characteristics	MDD and Alcohol and substance use disorders		
Intervention	Pharmacotherapy with various antidepressants. SSRI → depression in comorbidity: z=1.3, p=0.19 Other AD → depression in comorbidity: z=2.49, p=0.01 SSRI → alcohol consumption in comorbidity: z=0.20, p=0.84 Other AD → z=1.44, p=0.15		
Comparison	Placebo		
Length of follow-up	Variable, 6-24 weeks		
Outcome and effect size	MDD better with SSRIs 4 studies (Overall OR=1.85, 95% CI [0.73|4.68], ES=0.34) and in 3 studies other antidepressants (Overall OR=4.15, 95% CI [1.35|12.75], ES=0.78). No alcohol intake improvement in 3 SSRI studies (Overall OR=0.93, 95% CI [0.45|1.91] ES=-0.04) and in 3 studies with other antidepressants (Overall OR=1.99, 95% CI [0.78|5.08], ES=0.38)		
Funding	This study was supported in part by grant G03/005 and C03/06 from Fondo de Investigación Sanitaria (FIS), Madrid, Spain.		
Comments	Medication but not psychotherapy evaluated;		

Title	**Treatment of Depression in Patients With Alcohol or Other Drug Dependence: A Meta-Analysis**		
First Author	**Nunes, E. V., 2004**	**Source**	**15100209**

Level of evidence	1a	Study type	Meta-analysis
Study quality	PubMed, MEDLINE, and Cochrane databases from 1970 through December 2003 were searched using the keywords antidepressant treatment or treatment depressed in conjunction with each of the following words: *alcohol dependence, benzodiazepine dependence, opiate dependence, cocaine dependence, marijuana dependence, and methadone.*		
Participants	14 of which were selected for this analysis and included 848 patients		
Patient characteristics	MDD and Alcohol and substance use disorders		
Intervention	5 studies of tricyclic antidepressants, 7 of selective serotonin re-uptake inhibitors, and 2 from other classes		
Comparison	Placebo		
Length of follow-up	6 to 24 weeks		
Outcome and effect size	Depression overall: n=827, ES=0.38 (95% CI [0.18|0.58[) Alcohol and Substance use overall: n=785, ES=0.25 (95% CI [0.08|0.42])		
Funding	National Institute on Drug Abuse and the New York State Psychiatric Institute provided only salary support		
Comments	First meta-analysis on the topic, included studies on alcohol AND substance use disorders, no overall statistics on alcohol and substance use disorders separated		

Title	**Meta-analysis of Supplemental Treatment for Depressive and Anxiety Disorders in Patients Being Treated for Alcohol Dependence**		
First Author	**Hobbs, J. D. J., 2011**	**Source**	**21679263**
Level of evidence	1a	**Study type**	Meta-analysis
Study quality	Study inclusion: random assignment		
Participants	15 studies included, 12 pharmacological		
Patient characteristics	DSM III or later alcohol dependence or alcohol abuse; AND Anxiety or disorder depressive disorder, including major depression, dysthymia and depression NOS.		
Intervention	Pharmacological or psychotherapy		
Comparison	Control TAU or placebo		
Length of follow-up	Variable, at least once within 12 month		
Outcome and effect size	We found a pooled effect size (d) of ES=0.32 for internalizing outcomes and ES=0.22 for a composite of alcohol outcomes. There was also a trend for the studies with better internalizing disorder outcomes to have better alcohol outcomes.		
Funding	Grant R01-015069 from the National Institute on Alcohol Abuse and Alcoholism		
Comments	Overall ES not differentiated between anxiety and depression; However, single studies and ES are presented.		

Title	**Treatments for Patients With Dual Diagnosis: A Review**		
First Author	**Tiet, Q. Q., 2007**	**Source**	**17374031**
Level of evidence	1a	**Study type**	Meta-analysis and systematic review
Study quality	Study inclusion: effect sizes (Cohen's d) for the main psychiatric and substance use outcomes		
Participants	59 studies, 15 on depression/bipolar disorders and ASUD		
Patient characteristics	Comorbid, treatment, intervention, therapy, depression, anxiety, schizophrenia, psychotic/psychosis, severe mental illness, alcohol, drug, and substance		
Intervention	Pharmacological or psychotherapy		
Comparison	Control TAU or placebo		
Length of follow-up	6-53 weeks (depression and bipolar + ASUD)		
Outcome and effect size	Existing efficacious treatments for reducing psychiatric symptoms (e.g., TCA for depressive symptoms) also tend to work in dual-diagnosis patients, (2) existing efficacious treatments for reducing substance use (e.g., relapse prevention) also decrease substance use in dually diagnosed patients, and (3) the efficacy of integrated treatment is still unclear, with only weak evidence currently suggesting that integrated treatment are better than ''treatment as usual,''		

Funding	None
Comments	No overall statistics, however depression and bipolar + ASUD studies and ES are reported.

Title	**Cognitive-behavioral Treatment for Depression in Alcoholism**		
First Author	**Brown, R. A., 1997**	**Source**	**9337490**
Level of evidence	2b	**Study type**	Comparison study, not randomized
Study quality	No untreated control group, study completion 91%, initial abstinence required		
Participants	N=19 vs. N=16		
Patient characteristics	DSM-III-R Alcohol dependence, BDI>9, BDI, HAMD, POMS, TLFB interview		
Intervention	ADTS (abstinence-oriented therapy) + CBT		
Comparison	ADTS + "Relaxation training"		
Length of follow-up	8 Sessions á 45 min, follow-up 6 Month		
Outcome and effect size	HAMD ES=0.69, POMS Depression ES=1.02, %days abstinent ES=0.59; drinks per day ES=0.71		
Funding	Research grant from the Department of Psychiatry Brown University.		
Comments	Initial Study on CBT in comorbid alcohol-dependent individuals		

Title	**Effectiveness of Brief Alcohol Interventions for General Practice Patients With Problematic Drinking Behavior and Comorbid Anxiety or Depressive Disorders**		
First Author	**Grothues, J. M., 2008**	**Source**	**18207336**
Level of evidence	3	**Study type**	Cohort study
Study quality	Patients in GP, 88 participants were diagnosed with comorbid anxiety and/or depressive disorders		
Participants	408		
Patient characteristics	Patients with alcohol use disorders or at-risk drinking or binge drinking. 88 participants were diagnosed with comorbid anxiety and/or depressive disorders.		
Intervention	Brief interventions (BIs)		
Comparison	-		
Length of follow-up	12-month follow-up		
Outcome and effect size	BI were significantly related to reduction of drinking in the non-comorbid (-2.64 g/alcohol vs. -8.61 g/alcohol; p=.03) but not in the comorbid sub-sample (-22.06 g/alcohol vs. -22.09 g/alcohol; p=.76). Compared to non-comorbid participants, a significantly higher reduction of drinking was found for comorbid individuals (-6.55 g/alcohol vs. -22.08 g/alcohol; p=.01).		
Funding			
Comments	Only study on BI in comorbid individuals		

Title	**A Randomized Controlled Trial of Cognitive-Behavioral Treatment for Depression Versus Relaxation Training for Alcohol-Dependent Individuals With Elevated Depressive Symptoms**		
First Author	**Brown, R. A., 2011**	**Source**	**21388602**
Level of evidence	1b	**Study type**	RCT
Study quality	Randomized controlled study, no comparison group without treatment > 90% study completers, abstinence required.		
Participants	CBT-D (n=81) or RTC (n=84).		
Patient characteristics	DSM IV diagnosis of AD, MDD, BDI > 15; Measures: BDI, SCID-P, TLFB interview		
Intervention	ADTS + CBT		
Comparison	ADTS + Relaxation training		
Length of follow-up	8 Sessions à 45 min, up to 12 Month		
Outcome and effect size	No significant differences in drinking and depression outcomes ES: Results are presented in figures no numbers		
Funding	NIAAA grant AA10958		

Comments	Larger study, same design as Brown et al. (1997), but no efficacy reported.

Title	**Clinician-assisted Computerised Versus Therapist-Delivered Treatment for Depressive and Addictive Disorders: A Randomised Controlled Trial**		
First Author	**Kay-Lambkin, F., 2011**	**Source**	**21806518**
Level of evidence	2a	**Study type**	Randomized trail
Study quality	69% follow-up rate		
Participants	274		
Patient characteristics	DSM IV diagnosis of MD, AUD (alcohol misuse/dependence) and cannabis misuse/dependence; Measures: SCID, BDI II, DIPS, OTI		
Intervention	Integrated cognitive behaviour therapy/ motivational interviewing (CBT/MI) and clinician-assisted computerised [CAC] treatment		
Comparison	Person-centered therapy (PCT)		
Length of follow-up	3 months		
Outcome and effect size	Alcohol consumption (abstinence: CAC 13%, CBT: 8%, RCT 6%; ES1=0.46; ES2=0.16; 50% reduction of use: CAC: 45%, CBT: 41%, RCT: 17%, ES1=0.76; ES2=0.67). Change in depression (no depression: CAC 19%, CBT 16%, RCT: 10%, ES1=0.41; ES2=0.29).		
Funding	Grant from the Alcohol Education and Rehabilitation Foundation Australia		
Comments	First study on computerised CBT		

Title	**Pilot Study of Interpersonal Psychotherapy Versus Supportive Psychotherapy for Dysthymic Patients With Secondary Alcohol Abuse or Dependence**		
First Author	**Markowitz, J. C., 2008**	**Source**	**18552624**
Level of evidence	2b	**Study type**	Randomized trail
Study quality	IPT-D (N=14), BSP (N=12), fifty-four percent had current major depression. Study completers: (IPT=8, (57% BSP=10, 83%). Measures: SCID, SCID-II, 24-item HAMD, BDI, CDRS; AA-meetings, breathalyzer test.		
Participants	N=26		
Patient characteristics	Primary DSM-IV dysthymic disorder with early onset (before age 21), and DSM-IV alcohol abuse defined by SCID interview; score >13 on the HAM-D24, and GAF score >61. Alcohol abuse had to be judged clinically secondary (viz., later in onset) to dysthymic disorder.		
Intervention	IPT-D, IPT adapted for dysthymic disorder		
Comparison	BSP brief supportive psychotherapy		
Length of follow-up	16 weeks		
Outcome and effect size	Mood symptoms: W 1-16, IPT BSP HamD 1.15 0.77, BDI 1.38 0.64, CDRS 1.03 0.69 Percentage of days abstinent in prior month: IPT all vs LOCF= 0.21; 0.10; BSP all vs. LOCF: 0.54 vs 0.52		
Funding	National Institute of Mental Health		
Comments	Only study on IPT and supportive therapy		

Title	**Placebo-controlled Trial of Fluoxetine as an Adjunct to Relapse Prevention in Alcoholics**		
First Author	**Kranzler, H. R., 1995**	**Source**	**7864265**
Level of evidence	1b	**Study type**	RCT
Study quality	Placebo controlled, medication + “relapse prevention” (RP), abstinence required? Study completion rate: 95/101 (94%). Measures: TLFB, BDI, HAMD, MAST.		
Participants	101		
Patient characteristics	DSM-III-R, Alcohol dependence DIS, diagnosis of anxiety and mood disorders		
Intervention	Fluoxetine up to 60mg/d + RP		
Comparison	Placebo + RP		
Length of follow-up	12 weeks		
Outcome and effect size	“Depression” outcome: No time x med effect on BDI. Drinking outcomes: Abstinence: Wilcoxon (Gehan) statistic=0.26, df=1, p=0.61.		

	Side effects: decrease in sexual interest and performance and by the poorer compliance with medication in the fluoxetine-treated group.
Funding	NIAAA AA-03510, AA-07290, and AA-00143
Comments	First study, post-hoc analysis of depression

Title	**Placebo-controlled Study of Sertraline in Depressed Recently Abstinent Alcoholics**		
First Author	**Roy, A., 1998**	**Source**	**9787889**
Level of evidence	2b	**Study type**	RCT
Study quality	Randomized study, completers 21/36: 58% abstinence required, placebo-controlled. Measures: BDI, HAMD-24, CGI.		
Participants	N=36 randomized		
Patient characteristics	DSM-III-R alcohol dependence, MDD		
Intervention	Sertraline 100mg/d		
Comparison	Placebo		
Length of follow-up	6 weeks		
Outcome and effect size	HAMD* ES=1.06, BDI* ES=0.76. Alcohol consumption patterns not evaluated. Side effects: No patient was removed because of side effects.		
Funding	Department of Veterans Affairs Medical Center		
Comments	Depression evaluation only		

Title	**Fluoxetine Versus Placebo in Depressed Alcoholics: A 1-year Follow-Up Study**		
First Author	**Cornelius, J. R., 2000**	**Source**	**10795957**
Level of evidence	1b	**Study type**	RCT
Study quality	RCT, abstinence required, study completer rate ~90% (HAM-D24), the Beck Depression Inventory (BDI), and the Global Assessment Scale (GAS); weekly ratings drinking timeline follow back method and the Addiction Severity Index (ASI).		
Participants	N=51		
Patient characteristics	DSM-III-R alcohol dependence, MDD		
Intervention	Fluoxetine 25mg/d (n=25)		
Comparison	Placebo (n=26)		
Length of follow-up	12 weeks		
Outcome and effect size	Depression HAMD* ES=0.57, BDI ES=0.45 Drinking outcomes: *Cumulative Drinks ES=0.76 *Cumulative drinking Days ES=0.57 *Drinks per drinking day ES=0.68 *Cumulative days heavy drinking ES=0.81 *Number of weeks to first heavy drinking ES=0.73 Weeks to first drink ES=0.38 However, the proportion of subjects who were completely abstinent during the 12-week study was low in both groups: 28% (n=7) in Fluoxetine and 15% in the placebo group (n=4). Side effects: “Fluoxetine was well tolerated”.		
Funding	National Institute on Alcohol Abuse and Alcoholism and Mental Health Clinical Research Center.		
Comments	Only study which reported effects of SSRI on both affective and drinking symptoms		

Title	**Double-blind Clinical Trial of Sertraline Treatment for Alcohol Dependence**		
First Author	**Pettinati, H. M., 2001**	**Source**	**11270910**
Level of evidence	2b	**Study type**	RCT
Study quality	RCT, abstinence not required, completer rate: 29/47 in comorbid depression group (61%). Measures: SCID, HAMD-24, BDI, timeline follow-back (TLFB)		

Participants	53 (+ 47 non-depressed)
Patient characteristics	DSM-III-R Alcohol dependence, MDD
Intervention	Sertraline 200mg/d, n=26; completed n=12
Comparison	Placebo n=27, completed n=17
Length of follow-up	14 weeks
Outcome and effect size	Depression: 1) HAM-D ES -0.21 (2) BDI ES -0.20 Alcohol use patterns: (1) Percent Days Drinking ES - 0.36 (2) Weeks relapse ES -0.10 Side effects: The most prevalent examples of subject reports included in "sexual disturbance" were decreased libido and anorgasmia. Gastrointestinal distress (e.g., nausea, diarrhea) and dry mouth were also reported frequently, but these complaints did not differ significantly between the sertraline and placebo groups.
Funding	NIAAA grant (R01- AA09544 Pettinati K02-AA 00239 Kranzler), VAS Veterans Affairs Medical Center.
Comments	First study no effect at all on depression and alcohol use with SSRI

Title	**Sertraline for the Prevention of Relapse in Detoxicated Alcohol Dependent Patients With a Comorbid Depressive Disorder: A Randomized Controlled Trial**		
First Author	**Gual, A., 2003**	**Source**	**14633652**
Level of evidence	2b	**Study type**	RCT
Study quality	RCT, placebo controlled, abstinence required, completer rate: 54.5% sertraline and 56.4% in placebo group; Measures: MADRS, HAMD, SF-36, WHO-ART system for SAEs.		
Participants	39+44		
Patient characteristics	DSM-IV Alcohol dependence, MDD, DD or both		
Intervention	Sertraline 50-150mg/d n= 44, 24 completers		
Comparison	Placebo, n= 39, 22 completers		
Length of follow-up	24 weeks		
Outcome and effect size	(1) HAM-D not assessed (2) SF-36 Mental Health ES=0.48 Alcohol use outcome: (1) Days to relapse n.s. ES=-0.17 (2) Cumulative days of abstinence n.s. ES=-0.04 MADRS > 26: "improvement" p=0.04; "response" n.s., "remission" p=0.04 Results are shown in figures not numbers. Also all variables for MADRS < 26 n.s. Side effects: The most frequently reported adverse events were Headache, 'flu-like' symptoms and dizziness. No difference between the two treatment groups was observed in the incidence of any of these adverse events. The incidence of gastrointestinal adverse events was low (~10% of patients).		
Funding	NIAAA grant (R01- AA09544 Pettinati K02-AA 00239 Kranzler) VAS, Veterans Affairs Medical Center.		
Comments	Depression HAMD, MADRS outcome not reported, all other outcome parameters not significant.		

Title	**Sertraline Treatment of Co-Occurring Alcohol Dependence and Major Depression**		
First Author	**Kranzler, H. R., 2006**	**Source**	**16415699**
Level of evidence	2b	**Study type**	RCT
Study quality	Placebo controlled, abstinence required, Study completion rate Group A S: 58.7% P:56.0%, Group B S: 55.7%, P: 78.3% Measures: DSM-IV MDD Symptom Checklist, DSM-IV AD Symptom Checklist, HAM-D, Clinical Global Impression (CGI), AD Scale, Time-Line Follow Back Questionnaire, Beck Depression Inventory (BDI)		
Participants	N=328		
Patient characteristics	DSM IV Alcohol dependence, MDD and HAMD > 17 vs. < 17 (A vs. B)		
Intervention	Sertraline (at a maximum dose of 200 mg/d)		

Comparison	Placebo
Length of follow-up	10 weeks
Outcome and effect size	HAMD ES outcome: -0.025; Group A vs. B 50% HAMD reduction: (54.8% vs. 67.4%; x2=5.07, p=0.024) ES=-0.30 BDI reduction Group B: 42% vs. 54.9%; x2=4.34, p=0.04, ES=-0.29. Drinking outcome: P vs. S Group A: 3.5% more days abstinent (95% CI [3.7|10.7], p=0.34), P vs. S Group B: 3.2%, (95% CI [4.8|11.3], p=0.43). Group B: standard drinks per week 8.5±12.1, 5.5±6.7, ES=0.306 Side effects: Overall, 138 patients (86.3%) who received sertraline treatment reported one or more treatment emergent adverse events, compared with 143 patients (83.6%) who received placebo. Significant difference: constipation sertraline, 19.4%; placebo, 4.7%; x2 1=15.79, p<0.001.
Funding	Pfizer Pharmaceuticals supported the conduct of this study. Manuscript preparation was supported by NIH grant
Comments	RCT, moderate N, low retention rates

Title	**Lithium Treatment of Depressed and Nondepressed Alcoholics**		
First Author	**Dorus, W., 1989**	**Source**	**2504944**
Level of evidence	2b	**Study type**	RCT
Study quality	RCT, abstinence required, 172 alcoholics (60.1%) without depression and 108 alcoholics (63.2%) with depression completed the study. Measures: DIS, BIS, Lithium Plasma level Drinking measures		
Participants	457		
Patient characteristics	Alcoholics either without depression or with a history of major depression, current major depression, or dysthymic disorder were studied.		
Intervention	lithium carbonate		
Comparison	Placebo		
Length of follow-up	12 months		
Outcome and effect size	No significant effect for depression (52 weeks): BDI p=0.22; (ES BDI=0.24) nor alcohol use patterns (ES heavy drinking days during last 4 weeks: 0.29) Abstinence: .67; alc-rel. hospitalizations .43. Side effects: depressed AD group + Li++ had significantly more diarrhea, shakiness, gait disturbance.		
Funding	VA Research Service, Ciba-Geigy		
Comments	Moderate number of patients, negative results		

Title	**Double-blind, Randomized Comparison of Memantine and Escitalopram for the Treatment of Major Depressive Disorder Comorbid With Alcohol Dependence**		
First Author	**Muhonen, L. H., 2008**	**Source**	**18348597**
Level of evidence	2b	**Study type**	RCT
Study quality	No placebo control, head to head study, abstinence not required. Study completion 58/80 (72.5%). Measures: SCID, MADRS, HAMA, SOFAS, CERAD, MMSE, BDI, BAI, VAS, AUDIT Lab tests: CDT, GGT, ALAT, ASAT		
Participants	N=80 randomized		
Patient characteristics	DSM IV Alcohol dependence, MDD Outpatients		
Intervention	Escitalopram 20mg/d, 29 study completers		
Comparison	Memantine 20mg/d, 29 study completers		
Length of follow-up	26 weeks		
Outcome and effect size	Depression M-group: MADRS 25.8±4.4 to 12.7±7.0, BDI 27.7±8.4 to 15.3±11.1, F=138.04, p<0.001, ES1=0.76, ES2=0.53. Depression ESC-group: MADRS 26.8±4.1 to 11.5±6.6, BDI 27.6±6.8 to 14.3±11.8, F=25.77, p<0.001, ES1=0.81, ES2=0.57. Alcohol outcome: Abstinence baseline M: 56.4%, E: 57.5%;		

	1-3 month: M: 43.6%, E: 45.0%; ES (baseline 1)=-0.20; ES2=-0.20; 12 month: (M: 12.1%, E: 12.5%) ES1=-0.85 ES2=-0.59. Side effects: 7 patients discontinued d. t. AE 4 in M and 3 in E Groups. Side effects: somnolence (M 36%, E 34%), headache (M 36%, E 29%). SAE: 3 died, not related to study med; 2 in M-group (suicide, hyperglycmia) and 1 in E-group (intox by street drugs).
Funding	National Public health institute, Finland
Comments	New compounds in treatment of alcohol dep. And depression, low number of subjects. ES for alcohol intake difficult to compute since abstinence is significantly decreasing during follow-up

Title	**Naltrexone Versus Acamprosate in the Treatment of Alcohol Dependence: A Multi-Centre, Randomized, Double-Blind, Placebo-Controlled Trial**		
First Author	**Morley, K. C., 2006**	**Source**	**16968347**
Level of evidence	2B	**Study type**	RCT
Study quality	Placebo controlled, abstinence required, Study completion rate: n=61 (40, 66%) placebo, n=53 (36, 68%) naltrexone, n=55 (41, 75%) acamprosate Measures: CIDI, Alcohol Dependence Scale (ADS), Penn Alcohol Craving Scale (PACS), ALAT or (GGT), Short Form-12 Health Survey (SF-12), Depression Anxiety Stress Scale (DASS), SOCRATES. Pill count was assessed in the medical reviews.		
Participants	169		
Patient characteristics	(DSM-IV) diagnosis of alcohol dependence or abuse Stratification according to no depression vs. clinically relevant levels of depression		
Intervention	naltrexone (50mg/day), acamprosate (1998mg/day)		
Comparison	placebo		
Length of follow-up	12 weeks		
Outcome and effect size	(a) 'no depression' (n=56) and (b) 'clinically relevant levels' of depression (n=111). ITT 'no depression', significant treatment effects (Breslow test=8.88, p=0.01; ES=0.64) NTX v. PBO (Breslow test, p=0.03) and NTX and acamprosate (Breslow test, p=0.004). There was no significant difference between treatments in the number of days to first relapse for the subsample of subjects with 'clinically relevant depression' (Breslow test=0.50, p=0.78, ES=0.06). Side effects: There were significant treatment differences with respect to number of subjects experiencing headaches (F(2,90)=3.76, p<0.05) and somnolence (F(2,89)=4.71, p<0.05). Post-hoc analyses revealed that, compared to the acamprosate group, subjects randomized to placebo were significantly more likely to report headache while subjects randomized to naltrexone were significantly more likely to experience somnolence than both placebo and acamprosate groups.		
Funding	National Health and Medical Research Council of Australia and the University of Sydney Sesqui Fund.		
Comments	Results regarding drinking outcome in relevant vs. no depression demonstrate d in figures only, but not text.		

Title	**Naltrexone and Disulfiram in Patients With Alcohol Dependence and Current Depression**		
First Author	**Petrakis, I., 2007**	**Source**	**17414239**
Level of evidence	IB	**Study type**	RCT
Study quality	Placebo-controlled, open randomization to disulfiram or no disulfiram, and (2) double-blind randomization to naltrexone or placebo. Abstinence required (stable medication, 2 weeks) Study retention rate: D, ND (1): 21/28 29/37 (2): 39/43 17/23 (3): 29/34 21/25 (4): 25/34 24/30 82%, 79%		
Participants	n=254		

Patient characteristics	DSM-IV alcohol dependence (n=254); DSM IV major depression (n=139, 54.7%)
Intervention	(1) naltrexone alone, (2) placebo alone, (3) disulfiram and naltrexone, and (4) disulfiram and placebo
Comparison	Placebo
Length of follow-up	12-week
Outcome and effect size	Drinking outcomes naltrexone or disulfiram reported significantly fewer drinking days per week (F(1,2810)=5.71, p=0.02) and more consecutive days of abstinence (F(1,246)=4.49, p=0.04). ES=0.38 vs. placebo. Disulfiram-treated subjects who had depression reported significantly lower OCDS (Craving) scores over time than those on naltrexone (z=-2.77, p=0.01). ES=-.48 vs. placebo All other drinking variables: no significant differences across groups. Depression HAMD outcome: pre-post ES (1): 10.7 (5.6), 7.76 (5.15), 0.54; (2): 10.3 (5.9), 7.46 (5.81), 0.48; (3): 10.5 (5.5), 6.34 (6.16), 0.71; (4): 9.1 (5.6), 6.60 (5.45), 0.45. Test by diagnosis: -6.72, p<0.001 Side effects: There were no differences in side effect clusters reported by the group of subjects with current depression and those without. There were no significant interactions between the presence or absence of current depression and the medication condition on any of the side effect clusters. There were 6 serious adverse events in subjects with current major depression of a total of 14 for the entire sample. 9 The adverse events in the subjects with current depression included 2 deaths (1 NTX group, 1 placebo group), 3 psychiatric hospitalizations (2 disulfiram/placebo group, 1 placebo group), and 1 medical hospitalization for acute axonal neuropathy disulfiram/placebo). The deaths were thought to be cardiac but determined not to be study related.
Funding	Veterans Affairs Merit grant (I.P.)
Comments	ES best for NTX or Disulfiram regarding drinking days or consecutive days of abstinence; Craving better in disulfiram-treated depressed subjects; Depression best ES in subjects with Disulfiram and NTX.

Title	**A Double-Blind, Placebo-Controlled Trial of Sertraline in Depressed Adolescent Alcoholics: A Pilot Study**		
First Author	**Deas, D., 2000**	**Source**	**12404308**
Level of evidence	2b	**Study type**	RCT
Study quality	Placebo-controlled trial of sertraline plus cognitive behavior group therapy. Abstinence required? Study completion rate: 9/10? Measures HAMD, alcohol use measures (percent drinking days, drinks per drinking day)		
Participants	10		
Patient characteristics	Primary depression and comorbid alcohol use disorder treatment-seeking adolescents		
Intervention	Sertraline (max. 100 mg/d) plus cognitive behavior group therapy		
Comparison	Placebo + CBGT		
Length of follow-up	12 weeks		
Outcome and effect size	Both groups showed a significant reduction in depression scores with an average reduction between baseline and endpoint HAM-D score of -9.8 F(1,8)=26.14, p≤0.001), although there were no significant group differences. There was an overall reduction in Percent Days Drinking (PDD); (F(1,8)=8.90, p<0.02) and in Drinks Per Drinking Day (DDD); (F(1,8)=20.48, p<0.002)		
Funding	?		
Comments	Pilot study in adolescents, no full article available. No group differences between intervention and control condition.		

Title	**Placebo-controlled Trial of Fluoxetine as an Adjunct to Relapse Prevention in Alcoholics**		
First Author	**Kranzler, H. R., 1995**	**Source**	**7864265**
Level of evidence	1b	**Study type**	RCT
Study quality	Placebo-controlled, medication + “relapse prevention” (RP). Abstinence required? Study completion rate: 95/101(94%)		

Participants	101
Patient characteristics	DSM-III-R, Alcohol dependence DIS diagnosis of anxiety and mood disorders
Intervention	Fluoxetine up to 60mg/d + RP
Comparison	Placebo + RP
Length of follow-up	12 weeks
Outcome and effect size	"Depression" outcome: No time x med effect on BDI Drinking outcomes Abstinence: Wilcoxon (Gehan) statistic=0.26, df=1, p=0.61. Side effects: Chi-square analysis revealed that the only adverse effect that differed significantly in frequency between groups was less sexual interest or performance (x2=3.81, df=1, p=0.05).
Funding	NIAAA AA-03510, AA-07290, and AA- 00143
Comments	First study, post-hoc analysis of depression

Title	**Sertraline and Cognitive Behavioral Therapy for Depressed Alcoholics: Results of a Placebo-Controlled Trial**		
First Author	**Moak, D. H., 2003**	**Source**	**14624185**
Level of evidence	2a	**Study type**	RCT
Study quality	Placebo controlled, medication + CBT study, abstinence required Study completion rate: 57 of the 82 subjects (70%) Measures: HAM-D-21, SCID, (BDI), (OCDS), Alcohol Dependence Scale (ADS), Form 90 modification (TLFB)		
Participants	82		
Patient characteristics	DSM-III-R, alcohol dependence, abuse MDD or dysthymia		
Intervention	Sertraline 200mg/d + CBT, n=38		
Comparison	Placebo + CBT, n=44		
Length of follow-up	12 weeks		
Outcome and effect size	Depression females: *HAMD ES=0.76, *BDI ES=1.09; males: HAMD=0.01 Drinking outcomes ES 1) Time to first heavy drinking day 0.10, 2) Time to first drink NC 3) Drinks per Drinking Day 0.50 (4) Percent Days Abstinent 0.02. <u>Side effects:</u> In the sertraline group, 32 of 38 subjects (84%) were able to tolerate the full dosage of 200 mg. The mean daily dosage for sertraline subjects was 186 mg. Reasons for dosage reduction were nausea (3 subjects), diarrhea (1 subject), insomnia (1 subject), and decreased libido (1 subject who stopped medication). One subject in the placebo group stopped medication and dropped out of the study because of irritability attributed to study medication. Serious adverse events occurred in 4 subjects.		
Funding	NIAAA grant AA10476, Pfizer supported medications		
Comments	Differential Gender effects of combined treatment		

Title	**Clinical Outcomes of an Integrated Treatment for Depression and Substance Use Disorders**		
First Author	**Lydecker, K. P., 2010**	**Source**	**20853931**
Level of evidence	2a	**Study type**	RCT
Study quality	Abstinence not required randomisation. Study completers: T 99/I 107; 24 weeks: 79/87 (80%/83%); 12 month FU: 66/69 67%/65%). 89% in ICBT and 81% in TSF alcohol dependent. Measures: SCID, TLFB, HAMD-21, ASI, AA-affiliation scale		
Participants	206		
Patient characteristics	(1) DSM-IV diagnosis of alcohol, cannabinol, stimulant dependence (2) DSM-IV diagnosis of lifetime major depressive disorder (3) Recent substance use (past 90 days) and elevated depressive symptoms (HAMD Rating >20). Most participants were prescribed an antidepressant (80-90%)		
Intervention	Integrated Cognitive Behavioral Therapy plus standard pharmacotherapy (92-98% AD, ICBT+P). Substance abuse medications across study periods were 2.7%.		

Comparison	Twelve Step Facilitation Therapy plus standard pharmacotherapy (92-98% AD TSF+P). Substance abuse medications across study periods was 2.7%
Length of follow-up	24 weeks. Follow-up at 3, 6, 9, and 12 months post-treatment.
Outcome and effect size	ICBT+P was found to provide superior 18-month substance use outcomes than TSF. TSF+P vs. ICBT+P: 56% (46.67) vs. 74% (65.82) at intake; 23% (14.35) vs. 27% (18.37) at 6 months; 25% (16.37) vs. 20% (12.30) at 12 months. ES 6m=0.32; ES 12m=0.53 HAMD: TSF+P Intake 27.5±13.1 → 19±10.9 → 21.1±10.6; ICBT+P: 28.6±11.4 → 24.5±10.3 → 22.5±9.8 ES I vs. T: -0.08 (intake) ; -0.51 (6 months); -0.13 (12 months) ES over time T: 0.71 (6m vs. intake); 0.53 (12m vs. intake) ES over time I: 0.68 (6m vs. intake); 0.57 (12m vs. intake) Side effects: Across the two groups, there were no adverse events that occurred as a result of treatment.
Funding	VA Medical Research Merit Review Grant awarded to Dr. Sandra A. Brown and VA Merit Review Entry Program Grant awarded to Dr. Susan Tate.
Comments	Group differences for alcohol use patterns but not depression; no clear differentiation between AUD and SUD, majority of subjects met AUD criteria.

Title	**Treatment of Late-Life Depression Complicated by Alcohol Dependence**		
First Author	**Oslin, D. W., 2005**	**Source**	**15956269**
Level of evidence	IB	**Study type**	RCT
Study quality	No placebo control, combination medication study, abstinence required. Study completion 89.2% for the placebo group and 81.1% for the naltrexone group. Measures: Assessment for Treatment Emergent Effects (SAFTEE), HAMD; MMSE, TLFB, ASI, SF36		
Participants	N=74, randomized		
Patient characteristics	DSM-IV Alcohol dependence, Depressive disorder; Subjects older than 55 years.		
Intervention	Naltrexone (50mg/d) + sertraline(100mg/d) + supportive therapy, n=37		
Comparison	Placebo + sertraline (100mg/d) + supportive therapy, n=37		
Length of follow-up	12 weeks		
Outcome and effect size	Depression outcomes: HAMD<10: ES=-0.09; *HAMD<8: ES=0.71 Drinking outcomes: Abstinence from Heavy Drinking ES=-0.01 <u>Side effects:</u> none of adverse events were more common in the naltrexone combination group than the placebo group, and none of these symptoms were related to either completion of the trial or adherence to medication.		
Funding	NIMH (#1K08 MH01599-01,#5P30MH 52129) Department of Veterans Affairs MERP Award.		
Comments	Patients older than 55 years of age No effects with NTX and sertraline combinations		

Title	**A Double-Blind, Placebo-Controlled Trial Combining Sertraline and Naltrexone for Treating Co-Occurring Depression and Alcohol Dependence**		
First Author	**Pettinati, H. M., 2010**	**Source**	**20231324**
Level of evidence	2B	**Study type**	RCT
Study quality	Placebo controlled, combination medication + CBT study, abstinence required. Study completion rate: 24/40 Sertraline + Naltrexone (60%), 29/49 Naltrexone (59.1%), 21/40 Sertraline (52.5%), placebo: 23/39 (59%). Measures: SCID-P, HAMD-24, TLFB		
Participants	N=170		
Patient characteristics	DSM-IV Alcohol dependence, Depressive disorder; (HAM-D [17]) score ≥10; consumption of an alcoholic drink on ≥40% of the 90 days before treatment		
Intervention	the combination of sertraline plus naltrexone (N=42) + CBT weekly		
Comparison	Double placebo (N=39) + CBT weekly, Sertraline (200mg/day [N=40]), Naltrexone (100mg/day [N=49]), all + CBT weekly		
Length of follow-up	14 weeks		

Outcome and effect size	Depression NTX + S vs. all others: *HAMD t=2.1, p=0.04; ES=0.44; *Not depressed: χ2=6.2, p=0.01, OR=3.6, ES=0.28 Drinking outcomes: • Time (days) to relapse to heavy drinking t=3.0, p=0.003, ES=0.54. • Patients totally abstinent during treatment χ2=12.1, p<0.001, OR 3.7, ES=0.40. Side effects: Although there were no statistical group differences, the sertraline plus naltrexone group had six more patients discontinue treatment than did the placebo group.
Funding	NIAAA grant R01- AA09544-10 (Dr. Pettinati) and Pfizer Inc. U.S. Pharmaceuticals Group
Comments	Study combining NTX, Sertraline, CBT, efficacy shown for drinking and affective symptoms.

Title	**Imipramine Treatment of Alcoholics With Primary Depression: A Placebo-Controlled Clinical Trial**		
First Author	**McGrath, P. J., 1996**	**Source**	**8611060**
Level of evidence	2b	**Study type**	RCT
Study quality	Randomized study, 51% study completers; outpatients, initial abstinence not required (2 weeks), N=13 drop-out d. t., TCA side effects (sedation) Measures: HAMD, AA attendance, CGI, MAST (Michigan alcohol screening test), plasma levels of TCA		
Participants	N=69, no initial abstinence		
Patient characteristics	DSM-III-R Alcohol dependence, MDD, DD or depression NOS		
Intervention	Imipramine 300mg + relapse prevention n=36		
Comparison	Placebo + relapse prevention n=33		
Length of follow-up	12 weeks		
Outcome and effect size	HAMD* 0.40, no effect: % days drinking 0.08; % days drinking heavily - 0.26; Drinks per drinking day 0.26.		
Funding	NIAAA		
Comments	First study on TCA, effects on depression but not drinking		

Title	**A Double-Blind, Placebo-Controlled Trial of Desipramine for Primary Alcohol Dependence Stratified on the Presence or Absence of Major Depression**		
First Author	**Mason, B. J., 1996**	**Source**	**8598592**
Level of evidence	2b	**Study type**	RCT
Study quality	Randomized study, completers 71%, abstinence required. Treatment satisfaction > in verum vs. Placebo Group Measures: HAMD-24, Alcohol Dependence Scale (ADS), FHAM, plasma level monitoring, jar control.		
Participants	N=71, n=51 analysed		
Patient characteristics	DSM-III-R Alcohol dependence, MDD, DD or depression NOS		
Intervention	Desipramine 200mg depressed n=12, Desipramine non-depressed n=14		
Comparison	Placebo depressed n=10, Placebo non-depressed n=15		
Length of follow-up	26 weeks		
Outcome and effect size	HAMD*ES=0.93; N.S.: days to relapse 0.65, total number of adverse reactions did not differ between verum and placebo-treated patients		
Funding			
Comments	First study on TCA, effects on depression but not drinking		

Title	**Effectiveness and Tolerability of Mirtazapine and Amitriptyline in Alcoholic Patients With Co-Morbid Depressive Disorder: A Randomized, Double-Blind Study**		
First Author	**Altintoprak, A. E., 2008**	**Source**	**18327889**
Level of evidence	2b	**Study type**	RCT
Study quality	Randomized study, Completers 36/44: 81% abstinence required, no placebo control Measures: HAMD-17, STAI, Udvalg for Kliniske Undersogelser Side Effect Rating Scale, MAST		
Participants	N=36 analysed		
Patient characteristics	DSM-IV Alcohol dependence, abuse, MDD or dysthymia		

Intervention	Amitryptilin up to 125-150mg/day, n=16; Mirtazapin to 45-60mg/day, n=20
Comparison	None
Length of follow-up	56 days
Outcome and effect size	(HAMD M: 24.0±4.4 auf 5.4, ES=0.944; A: 23.7±4.8 auf 4.5 ES=0.94) and Craving (CRA Craving Score M: 170.7±26.0 auf 97.3±40.6, ES=0.73; A: 157.7±29.4 auf 99.9±40.2 ES=0.63) No differences between medications. Tremor, constipation, diminished sexual desire, and orthostatic dizziness were more common among the amitriptyline-treated patients.
Funding	Department of Psychiatry, Ege University School of Medicine, Izmir.
Comments	Head to head comparison of two antidepressants

3.6.4. Bipolare Störungen

Title	**Randomized Trial of Integrated Group Therapy Versus Group Drug Counseling for Patients With Bipolar Disorder and Substance Dependence**		
First Author	**Weiss, R., 2007**	**Source**	**17202550**
Level of evidence	2b	**Study type**	RCT
Study quality	RCT, Psychotherapy only, Abstinence? Study completers 24/31 IGT (77%), 17/31 GDC (55%) Outcome: primary outcome: measure number of days of substance use. Measures: ASI, HAMD, YMRS, SCID DSM IV		
Participants	N=62		
Patient characteristics	Current diagnoses of bipolar disorder and substance dependence other than nicotine, DSM–IV Valproate (N=19, 30.6%), lithium (N=15, 24.2%); > 1 Mood stabilizer (N=29, 46.8%)		
Intervention	integrated group therapy (N=31)		
Comparison	group drug counseling (N=31)		
Length of follow-up	20 weeks of integrated group therapy or group drug counseling with 3 months of posttreatment follow- up.		
Outcome and effect size	Intention-to-treat analysis revealed significantly fewer days of substance use for integrated group therapy patients during treatment and follow-up. Also separate analysis regarding alcohol use. No differences were found between groups or over time during treatment or follow-up. However, analysis of HAM-D and Young Mania Rating Scale scores showed more depressive and manic symptoms for integrated group therapy patients during treatment and during follow-up. ES?		
Funding	Grants DA- 09400, DA- 15968, and DA00326 from the National Institute on Drug Abuse		
Comments	17 (27.4%) had alcohol dependence only, and six (9.7%) had drug dependence only. Analysis does not separate subjects with alcohol and other substance use disorders.		

Title	**Treatment response of bipolar and unipolar alcoholics to an inpatient dual diagnosis program**		
First Author	**Farren, C., 2008**	**Source**	**17707085**
Level of evidence	3	**Study type**	Cohort study
Study quality	Abstinence: “completion of alcohol withdrawal“ Study completer rates: 3 months 226 (92%); 6 Months: 160 (68%)		
Participants	N=232		
Patient characteristics	DSM IV Alcohol dependence + bipolar disorders or depression. Depression (N=124) (M=56 F=68) Bipolar (N=102) (M=50 F=52)		
Intervention	FIRESIDE principles for integrated dual diagnosis treatment		
Comparison	No comparison		
Length of follow-up	3 and 6 Month FU		
Outcome and effect size	Depression 3/6 month abstinence: 71.8%, 55.8% Bipolar 3/6 month abstinence: 64.7% 54.1%		
Funding			
Comments	.		

Title	Switching outpatients with bipolar or schizoaffective disorders and substance abuse from their current antipsychotic to aripiprazole.		
First Author	Sherwood Brown, E., 2005	Source	15960570
Level of evidence	3	Study type	Cohort Study
Study quality	Abstinence needed? Study completion rate n=19 (95%)		
Participants	N=20		
Patient characteristics	DSM-IV Abuse or Dependence cocaine, amphetamines, cannabis, opiates, or alcohol DSM-IV Bipolar Disorder, or schizoaffective disorder- bipolar type		
Intervention	Aripiprazole		
Comparison	No comparison		
Length of follow-up	12 weeks		
Outcome and effect size	Significant reduction in HAM-D scores, YMRS scores, and BPRS scores.		
Funding			
Comments	Significant reduction in alcohol craving, dollars per week spent on alcohol, but not days per week of alcohol use. Significant reduction in cocaine craving, but not dollars per week or days used.		

Title	Efficacy of Valproate Maintenance in Patients With Bipolar Disorder and Alcoholism		
First Author	Salloum, I., 2005	Source	15630071
Level of evidence	2b	Study type	RCT
Study quality	Double-blind, placebo-controlled randomized parallel-group trial. Abstinence required (1 week withdrawal) Study completion rate: n=20 (38%) Measures: SCID DSM-IV, ASI, Alcohol Use Inventory, Life-Time Charting of Bipolar Episodes, Bech- Rafaelsen Mania Scale (BRMS), HAMD 25; GAS; TLFB Modified Quantitative Alcohol Inventory/Craving Scales, Weekly Self-Help Activity Quest. Somatic Symptoms Checklist and Medication Adherence Form to assess medication adverse effects and self-report of medication adherence.		
Participants	N= 59		
Patient characteristics	DSM-IV alcohol dependence criteria actively drinking alcohol in the past month, concurrent acute episode of bipolar I disorder (manic, mixed, or depressed).		
Intervention	lithium carbonate + psychosocial interventions, + valproate + CBT		
Comparison	lithium carbonate + psychosocial interventions, + placebo + CBT		
Length of follow-up	24 weeks		
Outcome and effect size	Heavy drinking: Twelve (44%) of 27 valproate group reported heavy drinking days vs. 17 (68%) of 25 placebo group. drinks per heavy drinking day: V: 5.6 [SD=8.9] P: (M=10.2 [SD=10.8] ES=0.64 Time to relapse heavy drinking: V: 93 days (SD=74 days; Mdn=75 days) P: 62 (SD=61 days; Mdn=44 days; log-rank test, 3.90; df=1; p=.048) ES=0.45 Mood outcomes: Mood outcomes: no difference between treatment groups manic (estimate, -0.03; t44.2=-0.16; p=.87) (ES=-0.04); depressive (estimate, 0.12; t44.7=0.91; p=.36) symptoms (ES=0.05).Side effects: There were no serious drug-related adverse events. One subject (randomized to valproate therapy) discontinued due to adverse effects, and another (randomized to placebo) discontinued due to increased liver function test values. Only nausea and vomiting were more common in the valproate group. No difference vs. PLO		
Funding	NIAAA		
Comments	Add on study, Effects on drinking behavior but not affective symptoms.		

Title	A randomized, double-blind, placebo-controlled add-on trial of quetiapine in outpatients with bipolar disorder and alcohol use disorders		
First Author	Sherwood Brown, E., 2008	Source	18312058
Level of evidence	2B	Study type	Add on RCT
Study quality	Abstinence required: Study completion rate: 102 (ITT), 88%		
Participants	N=115		
Patient characteristics	Bipolar I or II, Alcohol use disorder, DSM IIIR		
Intervention	Various Bipolar medication + Quetiapine (600mg/d)		

Comparison	Various Bipolar medication + Placebo
Length of follow-up	12 Weeks
Outcome and effect size	Heavy drinking days per week no differences across groups week 1-12 Depression HAMD: week 1 to 12 Quetiapine group better (F-value: 4.2, df: 1.234; p=0.04) ES=0.41 Mania: no significant group differences
Funding	Asta Zeneca
Comments	Phama-sponsored; overall improvement in depression only, no effect on drinking or mania.

Title	**A Double- Blind, Placebo- Controlled Study With Quetiapine as Adjunct Therapy With Lithium or Divalproex in Bipolar I Patients With Coexisting Alcohol Dependence**		
First Author	**Stedman, M., 2010**	**Source**	**20626727**
Level of evidence	2b	**Study type**	Add on RCT
Study quality	Q: 176; P: 186 ITT population (n=159, quetiapine; n=169, placebo). Study completion rate: 42.0 and 43.0% for quetiapine and placebo, respectively		
Participants	N=362		
Patient characteristics	DSM IV bipolar I and alcohol dependence		
Intervention	Lithium or Valproate + Quetiapine (flexibly dosed between 300-800mg⁄d)		
Comparison	Lithium or Valproate + Placebo		
Length of follow-up	12 weeks		
Outcome and effect size	Drinking: Q vs. P Proportion heavy drinking days 0.66 vs. 0.67 (p=0.93); Number of standard drinks/d 6.99±3.76 vs. 7.17±4.92 → 3.85±0.25 vs. 3.84±0.24; (p=0.95) Affective outcomes, Q vs. P: Mania YMRS 11.6±6.6 → 4.87±0.44 vs. 10.6±7.9 → 4.00±0.43 (p=0.11) Depression, MADRS: 19.0±8.7 → 6.30±0.7 vs. 17.2±8.6 → 6.22±0.68		
Funding	NIAAA, NIDA, NIMH NARSAD, ASTRA Zeneca		
Comments	Overall no significant influence on both drinking behaviors and affective symptoms.		

Title	**A Randomized, Double-Blind, Placebo- Controlled Pilot Study of Naltrexone in Outpatients With Bipolar Disorder and Alcohol Dependence**		
First Author	**Sherwood Brown, E., 2009**	**Source**	**19673746**
Level of evidence	2B	**Study type**	RCT add on
Study quality	Abstinence required? Study completer rate: 23 naltrexone, 27 placebo-randomized; 26 completed (52%)		
Participants	50		
Patient characteristics	DSM IV bipolar I or II disorder (MINI), current mood state of depressed or mixed (meeting criteria for both mania and depression) mood, current alcohol dependence, outpatients		
Intervention	Bipolar medication + CBT + Naltrexon 50mg/d		
Comparison	Bipolar medicatio n + CBT +Placebo		
Length of follow-up	12 weeks		
Outcome and effect size	Decline of drinking was similar in both groups, statistical trend towards NTX group (F=3.3, p=0.07). Prospective overall ES: Percent change of drinking d⁄wk: 0.68 Percent change of heavy drinking d⁄wk: 0.51 # Drinks/drinking: 0.62 HAMD during study period statistical trend for NTX group (overall improvement ES HAMD=0.56); no differences for YMRS between groups.		
Funding	NIH grant AA01538 9.		
Comments	First study using NTX for treatment of comorbid conditions.		

Title	**A randomized, double-blind, placebo-contr. clinical trial acamprosate alcohol- dependent individuals bipolar disorder**		
First Author	**Tolliver, B., 2012**	**Source**	**22329472**
Level of evidence	1b	**Study type**	RCT add on
Study quality	23 (69.7%) completed all active phase visits., Abstinence required 14 vs. 16 in ITT analysis		
Participants	33 (16 in A, 17 in P)		
Patient characteristics	DSM-IV diagnosis of bipolar I or bipolar II disorder and alcohol dependence		
Intervention	add-on acamprosate (1998mg/day) bipolar med: (lithium, valproic acid, carbamazepine,		

	lamotrigine, first or second-generation antipsychotic meds)
Comparison	Placebo bipolar med: (lithium, valproic acid, carbamazepine, lamotrigine, first or second-generation antipsychotic meds)
Length of follow-up	8 weeks + 4 weeks
Outcome and effect size	Drinking outcomes: no statistically significant differences between treatment groups in the time to first drinking day (HR=1.99, 95% CI [0.38|10.36[) or in the time to first heavy drinking day (HR=1.99, 95% CI [0.58|6.88]) CGI scores for substance use severity revealed significantly lower ratings in acamprosate treated subjects in week 7 (OR=32.1, 95% CI [5.0|205.0]) and week 8 (OR=20.4, 95% CI [2.5|164.0]) ES=1.17. Adjusted longitudinal analysis of mood scores, controlling for baseline values as well as group differences in baseline craving, found no effects of acamprosate MADRS (p=0.12) or YMRS (p=0.96) scores across the active phase of the study. No effects of time or treatment x time interactions on either MADRS or YMRS scores were evident. Longitudinal scores on both the MADRS (p<0.0002) and YMRS (p<0.008) were predicted by corresponding scores on each instrument at baseline.
Funding	Investigator-initiated research grant from Forest Laboratories.
Comments	First study using acamprosate + bipolar meds.

3.6.5. Angststörungen

Title	**Meta-analysis of supplemental treatment for depressive and anxiety disorders in patients being treated for alcohol dependence**		
First Author	**Hobbs, J., 2011**	**Source**	**21679263**
Level of evidence	1a	**Study type**	Meta-Analysis
Study quality	Moderate: • Methodology based on past meta- analyses and manuals of meta- analytic strategies. • Effect sizes derived from several different measures of alcohol use, depression, and anxiety • Synthetic effect size for studies with multiple outcomes that accounts for variance of measures		
Participants	N=15 studies		
Patient characteristics	Samples: 18+ years; Current DSM AD or alcohol; currently inpatient AUDtreatment program; Any current DSM anxiety disorder (except simple phobia, PTSD, and OCD) or current DSM depressive disorder Studies: random assignment to treatment vs. an active control condition (placebo/therapy control) for a co-occurring internalizing disorder, follow-up within one year, sufficient information to allow for effect sizes to be calculated for internalizing and AUD outcome effects		
Intervention	Psycho- social and pharmacological treatments vs. an active control condition (placebo /therapy control) for a co-occurring internalizing disorder.		
Comparison	Comparison s on the following outcomes: • Alcohol outcomes (average of all alcohol outcome effect sizes reported, in the respective studies regarding abstinence, frequency, intensity and quantity) • Intern. Outcomes (Hamilton Rating Scale for Anxiety, Social Phobia Inventory, Symptom Checklist – 90, Anxiety Discomfort Scale, Hamilton Rating Scale for Depr., Beck Depr. Inventory, Profile of Mood States, Montgomery and Asberg Depr. Rating Scale.		
Length of follow-up	< 1 year		
Outcome and effect size	• Pooled effect size (d) of .32 for internalizing outcomes and .22 for a composite of on alcohol outcomes • CBT interventions had a pooled estimate of effect size of d=0.66, while medication yielded a smaller estimate pooled effect size of d=0.24. • Studies where anxiety was treated demonstrate d significantly greater pooled effects sizes for the internalizing outcome (d=0.52) than studies where depression was treated (d=0.21). • Trend (p=.09) for better alcohol outcomes in studies with high vs. low effect sizes on the		

	internalizing outcomes. • Neither psychiatric treatment type nor internalizing disorder type impacted alcohol outcomes
Funding	NIAAA
Comments	Idea that disorders belong to same underlying construct („internalizing disorders“). As effect sizes for psychiatric treatment on anxiety were significantly greater than for depression, it may remain important to consider them separately. Treatments for co-occurring internalizing disorders are moderately effective in AUD populations and interventions provide a small but significant boost in the benefit of AUD outcomes. This suggests that adding treatment to existing AUD treatment is probably warranted.

Title	**Anxiety Disorders: Treatable regardless of the Severity of Comorbid Alcohol Dependence**		
First Author	**Schadé, A., 2007**	**Source**	**17356283**
Level of evidence	2b	**Study type**	Secondary analysis of RCT (Schadé et al. 2005;predictors for response in intervention group)
Study quality	Moderate: Mainly self- reported ratings for alcohol outcome. Some differences to CDT levels. Exclusion of patients using SSRI when entering treatment (potential selection). SSRI).		
Participants	N=34 (72% of patients in the intervention group)		
Patient characteristics	Detoxified patients with a primary DSM-IV diagnosis of AD and a comorbid diagnosis of panic disorder with agoraphobia, agoraphobia without panic attacks or social phobia. 66% male, about 50% employed.		
Intervention	CBT for comorbid anxiety disorders in addition to AD treatment. 12 individual weekly 60-min therapy sessions. Major treatment component was cognitive restructuring. In later sessions behavioral experiments During first six CBT sessions all patients continued to receive treatment for their alcohol problem.		
Comparison	Examination of predictors for treatment response		
Length of follow-up	32 weeks after intake		
Outcome and effect size	None of three alcohol severity measures (ASI severity index, ASI heavy drinking days, SCID alcohol dependence criteria) was related to clinically significant change on either Anxiety Discomfort Scale (ADS) Avoidance or Anxiety. Psychologic al distress (SCL-90; ADS Avoidance: OR=0.97, 95% CI [0.95|0.99]; p<.05; ADS Anxiety: OR=0.97, 95% CI [0.95|0.99]), neuroticism (NEO N; ADS Avoidance: OR=0.78, 95% CI [0.61|0.99]; p<.05; ADS Anxiety: OR=1.22, 95% CI [1.01|1.47]), conscientiousness (NEO C; ADS Avoidance: OR=1.07, 95% CI [0.89|1.30]; p<.05; ADS Anxiety: OR=0.78, 95% CI [0.64–0.94]), female gender (ADS Avoidance: OR=14.2, 95% CI [1.41|144.3]; p<.05; ADS Anxiety: OR=1.53, 95% CI [0.35|6.56]) employment (ADS Avoidance: OR=7.5, 95% CI [1.09|51.3]; p<.01; ADS Anxiety: OR=1.28, 95% CI [0.77|2.14]) and age of onset of alcohol dependence (ADS Avoidance: OR=1.25, 95% CI [1.00|1.55]; p<.01; ADS Anxiety: OR=1.03, 95% CI [1.00|1.06]) showed some predictive value.		
Funding	Dutch Organization for Scientific Research (NWO). Dutch Fund for Mental Public Health (NFGV).		
Comments	Even severely alcohol- dependent patients with an anxiety disorder can benefit from CBT. Males with AD and a comorbid anxiety disorder seem to benefit most from CBT if their AD started after age 25, if they are employed and if their general psychopath ology is less severe.		

Title	**The effectiveness of anxiety treatment on alcohol- dependent patients with a comorbid phobic disorder: a randomized controlled trial.**		
First Author	**Schadé, A., 2005**	**Source**	**15897725**
Level of evidence	1b	**Study type**	RCT
Study quality	Moderate: Mainly self- reported ratings for alcohol outcome. Some differences to CDT levels. Exclusion of patients using SSRI when entering treatment (potential selection). SSRI).		

Participants	N=96; N=47 alcohol and anxiety treamten; N=49 alcohol treatment).
Patient characteristics	Detoxified patients with a primary DSM-IV diagnosis of AD and a comorbid diagnosis of panic disorder with agoraphobia, agoraphobia without panic attacks or social phobia.
Intervention	CBT for comorbid anxiety disorders in addition to AD treatment. 12 individual weekly 60-min therapy sessions. Major treatment component was cognitive restructuring. In later sessions behavioral experiments During first six CBT sessions all patients continued to receive treatment for their alcohol problem
Comparison	CBT for comorbid anxiety disorders in addition to AD treatment. Vs. AD treatment alone.
Length of follow-up	32 weeks after intake
Outcome and effect size	Primary outcome: "percentage of patients who suffer from an alcohol relapse during the 32-week period": OR alcohol and anxiety treatment=0.7, 95% CI [0.30|1.65] n.s. Secondary outcome: "anxiety symptoms" at follow-up: Fear Questionnair e total score M=32.7 alc treat. vs. M=.21.9 alc + anxiety treat., p<.001; Anxiety Discomfort Scale (ADS) Avoidance M=21.6 alc treat. vs. M=13.1 alc + anxiety treat., p<.0001; ADS Anxiety M=16.5 alc treat. vs. M=11.0 alc + anxiety treat., p<.001; SCL-90 total M=167.3 alc treat. vs. M=157.8 alc + anxiety treat., p<.04;
Funding	Dutch Organization for Scientific Research (NWO). Dutch Fund for Mental Public Health (NFGV).
Comments	Anxiety treatment for AD patients with a comorbid anxiety disorder can alleviate anxiety symptoms, but no significant effect on the outcome of alcohol treatment.

Title	**Complex Relationship Between Co- occurring Social Anxiety and Alcohol Use Disorders: What Effect Does Treating Social Anxiety Have on Drinking?**		
First Author	**Thomas, S., 2008**	**Source**	**18028529**
Level of evidence	2b	**Study type**	RCT
Study quality	Moderate: Small sample size, Individuals were required to be early in their drinking careers (i.e., no previous alcohol treatment or alcohol detoxificatio n), sample included also patients with alcohol abuse. All were seeking treatment for social anxiety and not for alcohol. Less than 80% could be reached at some Follow-up- points		
Participants	N=42		
Patient characteristics	Patients were recruited from the community About 50% male/female Mean age about 30 yrs. DSM-IV criteria for current social anxiety disorder and alcohol abuse or dependence All had to answer affirmatively that they used alcohol to reduce social fears.		
Intervention	Paroxetine (PAR) or placebo (PLB) for 16 weeks, initiated at 10mg/d with a flexible dosing schedule. Target dose was 60mg/d by week 4. No additional treatment/ psychotherapy was provided in the trial.		
Comparison	Paroxetine (N=20) vs. Placebo (N=22)		
Length of follow-up	16 weeks		
Outcome and effect size	Paroxetine was not different than placebo in changing drinks per drinking day in the past 30 days at follow-up (PAR M=5.88, PLB M=7.0, n.s.), proportion of heavy drinking days (PAR M=0.54, PLB M=0.55, n.s.), or the proportion of abstinent days (PAR M=0.66, PLB M=0.65, n.s.). Paroxetine improved social anxiety more than placebo on the Liebowitz Social Anxiety Scale (LSAS). At week 16, the PAR group demonstrate d a 53% reduction in LSAS scores as compared with a 32% reduction for the PLB group (p=0.02).		
Funding	NIAAA. Glaxo Smith Kline (study meds).		
Comments	.		

3.6.6. Posttraumatische Belastungsstörungen

Title	**Sertraline in the treatment of co-occurring alcohol dependence and PTSD**

First Author	Brady, K., 2005	Source	15770115
Level of evidence	2b	Study type	RCT
Study quality	High: Double-blind, placebo- controlled randomized controlled trial.		
Participants	N=94		
Patient characteristics	Community sample (advertisements). About 50% men/women, rather high education (12-13 yrs.), rather young age (about 36 yrs.). In all patients PTSD as a result of civilian trauma (40% Sex. Abuse, 50% phys. Abuse, 50% childhood trauma)		
Intervention	Patients in active treatment received a fixed dose (150mg/day) of sertraline over a 12 weeks period (SER) or placebo (PLB). Once a week, all patients received 1 hr of individual cognitive behavioral therapy (CBT) targeting alcohol dependence using the Project MATCH CBT manual (Project MATCH Research Group, 1997). The CBT focused only on alcohol use symptoms. PTSD symptoms were not targeted in the CBT.		
Comparison	Comparison of PTSD symptom severity (clinician administered PTSD scale for DSM-IV; CAPS), and Alcohol consumption (Timeline Follow-back method; TLFB)		
Length of follow-up	12 weeks		
Outcome and effect size	Examination of average alcohol consumption during the treatment period revealed no significant differences in the sertraline versus placebo groups (percentage of drinking days: SER 23.0%, PLB 20.4%; average number of drinks consumed per day: SER 2.0, PLB: 1.4; drinks consumed per drinking day: SER 6.8, PLB 6.3; heavy drinking days: SER 10.4, PLB 8.9). Post hoc cluster analysis, showed significant improvement in sertraline-treated participants with less severe AD and early-onset PTSD		
Funding	NIAAA NIDA		
Comments	.		

Title	Symptom Improvement in Co- Occurring PTSD and Alcohol Dependence		
First Author	Back, S., 2006	Source	16971821
Level of evidence	2b	Study type	RCT
Study quality	Double-blind, placebo-controlled randomized controlled trial. Drop-out rate 36%		
Participants	N=94		
Patient characteristics	Community sample (advertisements) About 50% men/women, rather high education (12-13 yrs.), rather young age (about 36 yrs.). In all patients PTSD as a result of civilian trauma (40% Sex. Abuse, 50% phys. Abuse, 50% childhood trauma)months (mean 17.7)		
Intervention	Patients in active treatment received a fixed dose (150 mg/day) of sertraline (SER) over a 12 weeks period or placebo (PLB). Once a week, all patients received 1 hr of individual cognitive behavioral therapy (CBT) targeting alcohol dependence using the Project MATCH CBT manual (Project MATCH Research Group, 1997). The CBT focused only on alcohol use symptoms. PTSD symptoms were not targeted in the CBT.		
Comparison	Comparison of PTSD symptom severity (clinician administered PTSD scale for DSM-IV; CAPS), Alcohol consumption (Timeline Follow-back method; TLFB)		
Length of follow-up	12 weeks		
Outcome and effect size	Study completion rates significantly higher for individuals with improvement in both disorders (Global responders: 100%; Nonresponder 71.4%; Alcohol-Only Responder 54.5%; PTSD-Only Responder 43.8%; p<.001). PTSD treatment responders had significantly fewer percent days drinking (11% vs. 31%; p=0.01), percent heavy drinking days (9% vs. 21%; p=0.01), and average drinks per day (.77 vs. 2.39; p=0.01) as compared with PTSD treatment nonresponders. There were no significant differences in CAPS Scores by alcohol response status. Improvement in hyperarousal symptoms, in particular, was related to substantially improved alcohol use		
Funding	NIAAA NIDA		
Comments	.		

Title	**Naltrexone and disulfiram in patients with alcohol dependence and comorbid post-traumatic stress disorder**		
First Author	**Petrakis, I., 2006**	**Source**	**17008146**
Level of evidence	2b	**Study type**	RCT
Study quality	Moderate: Potentially confounding effect of abstinence and the open administration of disulfiram.Subanalysis of patients with PTSD (93/254)		
Participants	N=93		
Patient characteristics	Inpatients from several clinics affiliated with the New England Mental Illness Research and Education Clinical Center (MIRECC) Alcohol dependence and DSM-IV major axis I disorder diagnosed by SCID. 98% male		
Intervention	Open randomization to Disulfiram (250 mg) or no disulfiram. In addition double- blind randomization to naltrexone (50 mg) or placebo		
Comparison	Comparison of number of drinking days and number of heavy drinking days (defined as 5 or more standard drinks) per week		
Length of follow-up	12 weeks		
Outcome and effect size	Consecutive days of abstinence were higher in individuals receiving naltrexone (68.7), disulfiram (75.1) or both medications (68.2) after 12 weeks of treatment than the placebo group (49.7; p=.01).		
Funding	Veterans Affairs MERIT grant and the VISN I Mental Illness Research Education and Clinical Center (MIRECC)		
Comments	.		

Title	**Noradrenergic vs Serotonergic Antidepressant with or without Naltrexone for Veterans with PTSD and Comorbid Alcohol Dependence**		
First Author	**Petrakis, I., 2012**	**Source**	**22089316**
Level of evidence	2b	**Study type**	RCT
Study quality	Moderate: 70% Follow-up-Rate. The findings may not generalize to women and non- veterans. Age of onset of pathological drinking and of PTSD was not controlled		
Participants	N=88		
Patient characteristics	Male veterans meeting current diagnostic criteria for both alcohol dependence (AD) and PTSD		
Intervention	patients were randomly assigned to one of four groups: paroxetine + naltrexone (PAR/NAL); paroxetine + placebo (PAR/PLB); desipramine + naltrexone (DES/NAL); desipramine + placebo (DES/PLB)		
Comparison	Comparison of PTSD symptom severity (clinician administered PTSD scale for DSM-IV; CAPS), Alcohol Dependence (Alcohol Dependence Scale; ADS). CAPS data were analyzed using change from baseline CAPS scores in the model to control for baseline symptoms of PTSD		
Length of follow-up	12 weeks		
Outcome and effect size	Paroxetine did not show statistical superiority to desipramine for the treatment of PTSD symptoms. There was a significant decrease in CAPS scores over time ($F_{6108.8}$=2.175, p=0.051) and no significant interactions of treatment with time (DES/PAR by time $F_{6108.8}$=1.249, p=0.287; NAL/PLB by time $F_{6108.8}$=0.813, p=0.562), and no significant three-way interaction. Relative to paroxetine, desipramine significantly reduced the percentage of heavy drinking days ($F_{1.84}$=7.22, p=0.009) and drinks.		
Funding	Not declared		
Comments	.		

Title	**Do treatment improvements in PTSD severity affect substance use outcomes? A secondary analysis from a randomized clinical trial in NIDA's Clinical Trials Network**

First Author	Hien, D., 2010	Source	19917596
Level of evidence	2b	Study type	RCT
Study quality	Moderate: 60% Follow-up- Rate. 40% of sample was abstinent at baseline which restricted the variability in alcohol and drug outcomes and could have diluted the overall treatment effect. Particularly true with respect to alcohol outcomes. Findings may not generalize to a primarily alcohol dependent sample.		
Participants	N=353		
Patient characteristics	100% Women Outpatients in 7 community- based treatment programs DSM-IV diagnosis of full or sub-threshold PTSD (either symptom cluster C or D instead of both substance use within the past six months and a current diagnosis of drug or alcohol abuse or dependence. The maximum number of days of use was categorized into three levels: abstinence (no use), light use (used 1-12 days), and heavy use (used 13 or more days [i.e., more than three days per week])		
Intervention	12 Sessions (two per week) of Seeking Safety or Women's Health Education. Seeking Safety (Najavits, 2002) is a short-term manualized therapy using cognitive- behavioral strategies to reduce substance use and the negative impact of trauma exposure. Women's Health Education (Miller et al., 1998) is a psychoeducational intervention that focuses on general health topics pertinent to women.		
Comparison	Comparison of PTSD symptom severity on the Clinician Administere d PTSD Scale (CAPS), a structured interview that measures DSM-IV PTSD diagnosis and the frequency and intensity of symptoms over the past 30 days. Days with alcohol use in the 30 days prior to assessment		
Length of follow-up	3-, 6-, and 12-months post-treatment.		
Outcome and effect size	In the experimental group one unit of improvement on CAPS for heavy substance users at baseline decreased the odds of being in the heavy users group at follow-up by 4.6% (z-score=4.35, p<0.001), 1.3% (z-score=1.49, p=0.13) for light users, and no impact for those abstinent at baseline. In the control group, one unit of improvement on CAPS for heavy substance users at baseline decreased the odds of being in the heavy users group at follow-up by 0.6% (z-score=0.75, p=0.45), 2.3% (z-score=2.60, p=0.009) for light users, and 0.6% (z-score=0.66, p=0.51) for those who were abstinent. The effect of the improvement of Scale scores was significantly different between Seeking Safety heavy substance users and Women's Health Education heavy substance users at baseline (z-score=2.95, p=0.003), but not statistically different between light substance users at baseline (z-score=0.79, p=0.43).		
Funding	NIDA		
Comments	.		

Title	Randomized controlled trial of cognitive behaviour therapy for comorbid post- traumatic stress disorder and alcohol use disorders		
First Author	Sannibale, C., 2013	Source	25328957
Level of evidence	Ib	Study type	RCT
Study quality	High (Randomized controlled trial, 5% Follow-up- Rate)		
Participants	N=62		
Patient characteristics	Outpatients with Alcohol use disorders (95% Alcohol dependent) and comorbid PTSD, 47% male		
Intervention	12 once-weekly individual sessions of either integrated CBT for PTSD and AUD (IT) or CBT for AUD plus supportive counselling (AS). Participants in both conditions received the same AUD treatment, which was based on the Project MATCH CBT manual and the motivationally enhanced Combined Behavioral Intervention Manual (COMBINE). In the IT group this was integrated with a manualized, exposure-based CBT incorporating exposure therapy with cognitive restructuring for PTSD related cognitions		
Comparison	Comparison of PTSD symptom improvement (clinician administered PTSD scale for DSM-IV; CAPS), and Alcohol consumption according to the Timeline Followback method (drinks per drinking day: DDD; proportion of days abstinent: PDA)		

Length of follow-up	5 and 9.16 (SD=3.45) months post- treatment
Outcome and effect size	Reductions in PTSD severity were evident in both groups. IT participants who had received one or more sessions of exposure therapy exhibited a twofold greater rate of clinically significant change in CAPS severity at follow-up than AS participants (IT 60%, AS 39%, odds ratio OR=2.31, 95% CI [1.06|5.01]). There was a significant time x treatment interaction for DDD at the 5-month follow-up with lower consumption among AS (M=6.91, SD=6.22) than IT participants (M=8.81, SD=5.89; p=0.048). Differences by group in PDA were not significant.
Funding	National Health and Medical Research Council, Australia
Comments	.

Title	**A controlled examination of two coping skills for daily alcohol use and PTSD symptom severity among dually diagnosed individuals**		
First Author	**Stappenbeck, C., 2015**	**Source**	**25617814**
Level of evidence	1b	**Study type**	RCT
Study quality	medium		
Participants	N=78		
Patient characteristics	AUD with comorbid PTSD		
Intervention	Cognitive restructuring [CR] single session psychoeducation plus up to 4 coaching calls; Experiential acceptance [EA] single session psychoeducation plus up to 4 coaching calls		
Comparison	Attention control condition single session psychoeducation plus up to 4 coaching calls		
Length of follow-up	5 week daily follow-up assessment		
Outcome and effect size	CR und EA führten gegenüber der Kontrollgruppe zu einer stärkeren Reduktion der Trinkmenge (drinks per day); CR und EA führten zu einem signifikanten Anstieg abstinenter Tage im follow-up-Zeitraum. CR konsumierten weniger Alkohol an einem gegebenen Tag als EA. Hinsichtlich der PTSD-Symptomatik zeigten sich keine Differenzen zwischen EA, CR und Kontrollgruppe.		
Funding	NIH/NIAAA		
Comments	minimale Intervention bei hoch belasteter Klientel		

Title	**Trauma-focused exposure therapy for chronic posttraumatic stress disorder in alcohol and drug dependent patients: A randomized controlled trial.**		
First Author	**Coffey, S., 2016**	**Source**	**27786516**
Level of evidence	1b	**Study type**	RCT
Study quality	high		
Participants	N=126		
Patient characteristics	AUD with comorbid PTSD		
Intervention	Modified prolonged exposure (mPE) plus residential substance abuse treatment as usual (TAU); mPE plus Trauma-focused motivational enhancement therapy for PTSD (MET) plus residential substance abuse treatment as usual (TAU)		
Comparison	Healthy Lifestyle Sessions (HLS) plus residential substance abuse treatment as usual (TAU)		
Length of follow-up	End of treatment, 3 months and 6 months follow-up		
Outcome and effect size	mPE und mPE plus MET führten zu einer signifikant stärkeren PTSD-Symptomreduktion gegenüber der Kontrollguppe; mPE und mPE plus MET unterschieden sich nicht signifikant hinsichtlich der Symptomreduktion. mPE führte zu einer signifikant stärkeren Reduktion depressiver Symptomatik (BDI) bei Therapieende. Alle 3 Therapiebedingungen führten zu einer signifikanten Reduktion des Substanzkonsums (abstinente Tage in den follow-ups; keine signifikaten Unterschiede zwischen den Therapiebedingungen.		
Funding	NIAAA		
Comments			

Title	**Concurrent naltrexone and prolonged exposure therapy for patients with comorbid alcohol dependence and PTSD: a randomized clinical trial**		
First Author	**Foa, E., 2013**	**Source**	**23925619**

Level of evidence	1b	**Study type**	RCT
Study quality	high		
Participants	N=165		
Patient characteristics	AUD with comorbid PTSD		
Intervention	Prolonged Exposure (PE) plus Naltrexone (100mg/d); Prolonged Exposure (PE) plus pill placebo		
Comparison	Supportive Counseling plus Naltrexone (100mg/d); Supportive Counseling plus pill placebo		
Length of follow-up	End of treatment, 6 months follow-up		
Outcome and effect size	In allen Gruppen starke Reduktion der Trinktage; in den Naltrexongruppen signifikant geringere Anzahl von Trinktagen als in den Placebo-Gruppen. Kein signifikanter Unterschied in Reduktion der PTBS-Symptomatik in allen vier Gruppen ohne signifikanten Effekt von PE.		
Funding	NIAAA		
Comments			

3.6.7. Aufmerksamkeitsdefizit/Hperaktivitätsstörung

Title	**Atomoxetine treatment of adults with ADHD and comorbid alcohol use disorders**		
First Author	**Wilens, T., 2008**	**Source**	**18403134**
Level of evidence	2b	**Study type**	RCT
Study quality	Abstinence required “recently abstinent adults“ Retention rate Atomox.: 44%, Placebo: 64% SCID DSM-IV-TR Axis I Disorders HAMD-17, HAMA Measures: ADHD Investigator Symptom Rating Scale (AISRS) Adult ADHD Clinician Diagnostic Scale; CGI-ADHDS, CGI-ADHDS-I (improvement) TLFB, OCDS		
Participants	N=147		
Patient characteristics	ADHD and Alcohol use disorder diagnosis (DSM IV) Outpatients		
Intervention	Atomoxetin max. dose 100mg/d Side effects: There were no serious adverse events reported. Discontinuation rates due to an adverse event were low in both groups and not significantly different. Adverse events significantly more prevalent in atomoxetine-treated subjects: nausea (atomoxetine: 43.3%, placebo: 9.6%; p<.001), dry mouth atomoxetine: 26.9%, placebo: 11.0%; p=.018), decreased appetite (atomo.: 17.9%, placebo: 2.7%; p=.004), dizziness (atomo.: 14.9%, placebo: 2.7%; p=.014), fatigue (atomoxetine: 13.4%, placebo: 2.7%; p=.026), constipation (atomoxetine: 11.9%, placebo: 1.4%; p=.014), urinary hesitation (atomoxetine: 7.5%, placebo: 0%; p=.023), hot flush (atomoxetine: 6.0%, placebo: 0%; p=.050), and paraesthesia (atomoxetine: 6.0%, placebo:0%; p=.050).		
Comparison	Placebo		
Length of follow-up	Altogether 24 weeks 12 weeks double blind, 12 weeks follow-up: all atomoxetin e		
Outcome and effect size	ADHD symptoms were significantly improved in the atomoxetine cohort compared to placebo (AISRS total score mean [S.D.], atomoxetine: -13.63 [11.35], p<0.001; placebo: -8.31 [11.44], p<0.001, difference: p=0.007; effect size=0.48) Kaplan-Meier estimates of the time to initial relapse to heavy drinking showed no difference between treatments (log-rank; p=0.93). Of 68 subjects atomoxetine group: 64 (94.1%) relapsed end of study period 2; and 69/72 (95.8%) placebo subjects had relapsed. Recurrent-event analysis showed atomoxetine-treated subjects had a significantly lower rate of cumulative heavy drinking days by approximately 26% than placebo-treated subjects (atomoxetine, n=68; placebo n=72; event ratio=0.74, p=0.023)		
Funding	Eli Lilly and Company and by a grant to TEW (K24 DA0162 64 & 5U10DA 015831- 0).		
Comments	Only single RCT study with comorbid AHDS and AUD subjects and treatment with Atomoxetine vs. Placebo		

Title	**Clinical guideline 72 Attention deficit hyperactivity disorder ADULTS**		
First Author	**NICE, 2008**	**Source**	

Level of evidence	1a	**Study type**	Clinical Guideline
Study quality	Evidence –based knowledge		
Participants			
Patient characteristics	ADHD only		
Intervention	Several		
Comparison	Several		
Length of follow-up	various		
Outcome and effect size	Drug treatment for adults with ADHD who also misuse substances should only be prescribed by an appropriately qualified healthcare professional with expertise in managing both ADHD and substance misuse. For adults with ADHD and drug or alcohol addiction disorders there should be close liaison between the professional treating the person's ADHD and an addiction specialist.		
Funding	NICE		
Comments	Only guideline for Adult ADHS, largely without recognition of comorbid alcohol use disorders		

Title	**European consensus statement on diagnosis and treatment of adult ADHD**		
First Author	**Kooij, J., 2003**	**Source**	**30453134**
Level of evidence	1a	**Study type**	Konsensus
Study quality	result of three meetings between 2003 and 2009		
Participants			
Patient characteristics	Adult ADHD only		
Intervention	Several		
Comparison	Several		
Length of follow-up	Various		
Outcome and effect size	However, systematic research has not provided a strong evidence base for appreciable improvements in ADHD when treated in the presence of substance use disorders and drug or alcohol abuse disorders should always be targeted as a primary disorder. Treating ADHD in parallel with SUD can however be important in some cases, particularly where ADHD is severe or where there is good understanding and compliance for the treatment program.		
Funding			
Comments	European consensus for Adult ADHS, largely without recognition of comorbid alcohol use disorders		

Title	**Prevalence Estimates of ADHD in a Sample of Inpatients With Alcohol Dependence**		
First Author	**Luderer, M., 2018**	**Source**	**29308693**
Level of evidence	2b	**Study type**	cross sectional study
Study quality	high		
Participants	N=415		
Patient characteristics	alcohol dependent patients in long-term residential treatment		
Intervention	A structured interview (Diagnostic Interview for ADHD in Adults [DIVA]) was conducted on all patients. DIVA results indicating childhood or adulthood ADHD were assessed in successive diagnostic interviews by two expert clinicians.		
Comparison			
Length of follow-up			
Outcome and effect size	415 of 488 patients had completed the entire diagnostic assessment. ADHD prevalence was 20.5%. DIVA results correlated moderately with experts' diagnoses. In patients with ADHD, a higher comorbid illicit substance use was prevalent and alcohol dependence started earlier and was more severe. Conclusion: This study provides the largest sample on ADHD prevalence in alcohol dependent inpatients. Despite great efforts to avoid overestimation, we found every fifth patient to have ADHD. ADHD diagnosis should not be based solely on a structured interview but should be clinically confirmed.		
Funding	None		

Comments	mono-centric but large sample, extensive diagnostic assessment, low dropout rate

Title	**Variability in the prevalence of adult ADHD in treatment seeking substance use disorder patients: Results from an international multi-center study exploring DSM-IV and DSM-5 criteria**		
First Author	**van de Glind, G., 2014**	**Source**	**24156882**
Level of evidence	2b	**Study type**	international multi-center cross sectional study
Study quality	medium		
Participants	N=1.276		
Patient characteristics	substance use disorders		
Intervention	A two stage international multi-center, cross-sectional study in 10 countries, among patients form inpatient and outpatient addiction treatment centers for alcohol and/or drug use disorder patients. A total of 3.558 treatment seeking SUD patients were screened for adult ADHD. A subsample of 1276 subjects, both screen positive and screen negative patients, participated in a structured diagnostic interview.		
Comparison			
Length of follow-up			
Outcome and effect size	"Results: Prevalence of DSM-IV and DSM-5 adult ADHD varied for DSM-IV from 5.4% (95% CI [2.4|8.3]) for Hungary to 31.3% (95% CI [25.2|37.5]) for Norway and for DSM-5 from 7.6% (95% CI [4.1|11.1]) for Hungary to 32.6% (95% CI [26.4|38.8]) for Norway. Using the same assessment procedures in all countries and centers resulted in substantial reduction of the variability in the prevalence of adult ADHD reported in previous studies among SUD patients (2–83% → 5.4-31.3%). The remaining variability was partly explained by primary substance of abuse and by country (Nordic versus non-Nordic countries). Prevalence estimates for DSM-5 were slightly higher than for DSM-IV. ADHD prevalence in alcohol addicted patients was 5-22% in outpatients, 4-14 % in inpatients, using DSM-IV criteria Conclusions: Given the generally high prevalence of adult ADHD, all treatment seeking SUD patients should be screened and, after a confirmed diagnosis, treated for ADHD since the literature indicates poor prognoses of SUD in treatment seeking SUD patients with ADHD."		
Funding	"The Netherlands, Amsterdam: no external funding was obtained. The participating institute, Arkin, paid for the costs involved, and used funding from Fonds Nuts Ohra for this project. Norway, Bergen Clinics Foundation: Main external funding has been the Regional research council for addiction in West Norway (Regionalt kompetansesenter for rusmiddelforskning i Helse Vest (KORFOR)), funding a 50% position. The remaining resources, with staff and infrastructure, have been from the Bergen Clinics Foundation. Norway, Fredrikstad: The IASP was funded by the hospital, Sykehuset Østfold HF, not with money, but with 50% of the salary of the participants, then by two sources outside the hospital: The Regional center of Dual Diagnosis and the social – and Health directory. Sweden, Stockholm: The study was funded by the Stockholm Center for Dependency Disorders. Belgium: Funding of the IASP-project in Belgium: private funding. France, Bordeaux: Research Grant PHRC (2006–2012) from the French Ministry of Health and the French Government Addiction Agency MILDT grant 2010 to M. Auriacombe and by a French National Research Agency PRA-CNRS-CHU-Bordeaux award (2008–2010) to M. Fatséas. Spain, Barcelona: Financial support was received from Plan Nacional sobre Drogas, Ministerio de Sanidad y Política Social (PND 0080/2011), the Agència de Salut Pública de Barcelona and the Departament de Salut. Government of Catalonia. Spain. Switzerland, Bern/Zürich: The IASP in Switzerland was funded by the Swiss Foundation of Alcohol Research (Grant # 209).Hungary, Budapest: There was no direct funding, but the following grant was used: The European Union and the European Social Fund have provided financial support to the project under the grant agreement no. TÁMOP 4.2.1./B-09/1/KMR-2010-0003. Australia: The IASP Screening Phase was funded by a strategic funding faculty grant from the Curtin University of Technology, Perth, Western Australia.		

	USA, Syracuse: no funding was obtained. For coordination of the IASP study, as described in Funding Resources paragraph above, grants were received from pharmaceutical companies (Shire, Eli Lilly and company, Jansen Cilag), from participating institutes and from three not for profit organizations: the Waterloo Foundation, the Noaber Foundation and the Augeo Foundation."		
Comments	very large sample, multi-center, high variability in the prevalence of ADHD, depending on the country, high dropout rate		
Title	**Prevalence of Attention-Deficit Hyperactivity Disorder in Substance Use Disorder Patients: A Meta-Analysis and Meta-Regression Analysis**		
First Author	**van Emmerik-van Oortmerssen, K., 2012**	**Source**	**22209385**
Level of evidence	1a	**Study type**	Meta-Analysis
Study quality	High		
Participants	N=6.689 from 29 studies		
Patient characteristics	substance use disorders		
Intervention	"A literature search was conducted using MEDLINE, PsycINFO and EMBASE. Search terms were ADHD, substance-related disorders, addiction, drug abuse, drug dependence, alcohol abuse, alcoholism, comorbidity, and prevalence. Results were limited to the English language. After assessing the quality of the retrieved studies, 29 studies were selected. Studies in which nicotine was the primary drug of abuse were not included. All relevant data were extracted and analysed in a meta-analysis. A series of meta-regression analyses was performed to evaluate the effect of age, primary substance of abuse, setting and assessment procedure on the prevalence of ADHD in a variety of SUD populations."		
Comparison			
Length of follow-up			
Outcome and effect size	"Overall, 23.1% (95% CI [19.4–27.2]) of all SUD subjects met DSM-criteria for comorbid ADHD. Cocaine dependence was associated with lower ADHD prevalence than alcohol dependence, opioid dependence and other addictions. Studies using the DICA or the SADS-L for the diagnosis of ADHD showed significantly higher comorbidity rates than studies using the KSADS, DISC, DIS or other assessment instruments. Conclusions: ADHD is present in almost one out of every four patients with SUD. The prevalence estimate is dependent on substance of abuse and assessment instrument."		
Funding	none		
Comments			

Title	**International Consensus Statement on Screening, Diagnosis and Treatment of Substance Use Disorder Patients With Comorbid Attention Deficit/Hyperactivity Disorder**		
First Author	**Crunelle, C., 2018**	**Source**	**29510390**
Level of evidence	2a	**Study type**	systematic review + consensus statement
Study quality	high		
Participants	N=212 publications		
Patient characteristics	ADHD and substance use disorders		
Intervention	PubMed, Cinahl and Psychinfo were searched for articles published January 1994 to December 2015 using the terms “drug abuse,” “substance use,” “addiction,” “dependence” and “ADHD,” limited to articles published in English, French and Dutch. Existing guidelines in Clinical Evidence, CEBAM, NHS Guideline finder, Cochrane library, NICE, National Guideline Clearinghouse and GIN database were searched. All retrieved articles and relevant cross-references were reviewed.		
Comparison			
Length of follow-up			
Outcome and effect size	Adult attention deficit/hyperactivity disorder (ADHD) often co-occurs with substance use disorders (SUD) and is associated with early onset and more severe development of SUD and with reduced treatment effectiveness. Screening tools allow for a good recognition of possible ADHD in adults with SUD and should be used routinely, followed by an ADHD diagnostic process initiated as soon as possible. Sensitivity ASRS 67-100%, specificity ASRS		

	66-82%; Simultaneous and integrated treatment of ADHD and SUD, using a combination of pharmaco- and psychotherapy, is recommended. Long-acting methylphenidate, extended-release amphetamines, and atomoxetine with up-titration to higher dosages may be considered in patients unresponsive to standard doses. This paper includes evidence- and consensus-based recommendations developed to provide guidance in the screening, diagnosis and treatment of patients with ADHDSUD comorbidity. The statements in this consensus text are based primarily on scientific evidence from available publications (n=212; online suppl. Material 1, see www.karger.com/doi/10.1159/000487767). When scientific evidence was lacking, a consensus was sought from the opinions of experts in the field, which is stated specifically in the main text when this was the case.
Funding	none reported
Comments	Consensus paper with clinical recommendations by a group of international experts on ADHD and SUD. Systematic review on screening, diagnosis and treatment of ADHD+SUD

Title	**Adult ADHD Screening in Alcohol-Dependent Patients Using the Wender-Utah Rating Scale and the Adult ADHD Self-Report Scale**		
First Author	**Daigre, C., 2015**	**Source**	**24743975**
Level of evidence	2b	**Study type**	cross sectional study, screening
Study quality	medium		
Participants	N=355		
Patient characteristics	alcohol dependent patients in outpatient treatment		
Intervention	Objective: The aim was to analyze the psychometric properties of two screening instruments, Wender-Utah Rating Scale (WURS) that evaluates childhood ADHD and Adult ADHD Self-Report Scales (ASRS) that assesses symptoms in adulthood, in alcohol-dependent patients. Method: A total of 355 outpatients were included. Conners' adult ADHD diagnostic interview results were used as a gold standard in childhood and adulthood ADHD.		
Comparison			
Length of follow-up			
Outcome and effect size	The WURS with a 41 cutoff had a sensitivity of 79.6% and a specificity of 60.3%. The ASRS with a 14 cutoff had a sensitivity of 86.7% and specificity of 66.1%. Analyzing both rating scales in combination, it was observed that patients with positive ASRS and WURS presented a sensitivity of 92.3%. Patients with positive ASRS, but negative WURS, presented a specificity of 73.6%.		
Funding	none		
Comments			

Title	**Screening for Adult attention-deficit/hyperactivity Disorder in Alcohol Dependent Patients: Underreporting of ADHD Symptoms in Self-Report Scales**		
First Author	**Luderer, M., 2019**	**Source**	**30583265**
Level of evidence	2b	**Study type**	cross sectional study, screening
Study quality	High		
Participants	N=404		
Patient characteristics	alcohol dependent patients in long-term residential treatment		
Intervention	Conners' Adult ADHD Rating Scale Screening Self-Rating (CAARS-S-SR) and Adult ADHD Rating Scale (ASRS). Results were compared with ADHD diagnosis obtained from a stepped approach: first, a structured interview (Diagnostic Interview for ADHD in adults 2.0.; DIVA) was applied; second, probable ADHD diagnoses had to be confirmed by two expert clinicians independently.		
Comparison			
Length of follow-up			
Outcome and effect size	At the previously reported cut-off values, ASRS and CAARS-S-SR showed low sensitivities of 57.1 and 70.6%. A high number of false negative results (NPV ASRS: 89.5%; CAARS-S-SR: 92.3%) indicates underreporting of ADHD symptoms. Sensitivity improved at lower cut-off (ASRS ≥ 11; CAARS-S-SR ≥60) or with a combination of both instruments at lower cut-offs.		

	Area Under the Curve (AUC) for the combination of ASRS and CAARS-S-SR was superior to the AUCs of the single questionnaires. Cutoff values should be adjusted to the clinical setting. Clinicians should take into consideration that a negative screening result does not necessarily imply absence of ADHD.
Funding	none
Comments	

Title	**The Clinical Utility of ASRS-v1.1 for Identifying ADHD in Alcoholics Using PRISM as the Reference Standard**		
First Author	**Reyes, M., 2019**	**Source**	**27138328**
Level of evidence	3b	**Study type**	cross sectional study, prevalence and screening
Study quality	Low		
Participants	N=379		
Patient characteristics	alcohol dependent patients in outpatient and inpatient treatment		
Intervention	The objective was to assess the clinical utility of the Adult ADHD Self-Report Scale (ASRS-v1.1) in identifying ADHD in alcoholics using the Psychiatric Research Interview for Substance and Mental Disorders (PRISM) as the diagnostic "gold standard." A secondary analysis of data from 379 treatment-seeking alcoholics who completed the ASRS-v1.1 and the ADHD module of the PRISM was performed.		
Comparison			
Length of follow-up			
Outcome and effect size	The prevalence of ADHD was 7.7% (95% CI [5.4|10.8]). The positive predictive value (PPV) of the ASRS-v1.1 was 18.1% (95% CI [12.4|25.7]) and the negative predictive value (NPV) was 97.6% (95% CI [94.9|98.9]). The ASRS-v1.1 demonstrated a sensitivity of 79.3% (95% CI [61.6|90.2]) and a specificity of 70.3% (95% CI [65.3|74.8]). Conclusion: The ASRS-v1.1 demonstrated acceptable sensitivity and specificity in a sample of treatment-seeking alcoholics when compared with the PRISM as the reference standard for ADHD diagnosis.		
Funding	Samuel C. Johnson Genomics of Addictions Program (and NIAAA funded grant).		
Comments	Secondary analysis on a sample derived from an acamprosate study. Structured interview (PRISM) not used in this population before		

Title	**Langfassung der interdisziplinären evidenz- und konsensbasierten (S3) Leitlinie „Aufmerksamkeitsdefizit-/ Hyperaktivitätsstörung (ADHS) im Kindes-, Jugend- und Erwachsenenalter". AWMF-Registernummer 028-045.**		
First Author	**AWMF, 2018**	**Source**	
Level of evidence	1a	**Study type**	S3 guideline
Study quality	High		
Participants	-		
Patient characteristics	ADHD		
Intervention	-		
Comparison	-		
Length of follow-up	-		
Outcome and effect size	-		
Funding	-		
Comments	-		

Title	**Validity of the Adult ADHD Self-Report Scale (ASRS) as a Screener for Adult ADHD in Treatment Seeking Substance Use Disorder Patients**		
First Author	**van de Glind, G., 2013**	**Source**	**23660242**
Level of evidence	2b	**Study type**	international multi-center cohort study
Study quality	medium		
Participants	N=1.138		
Patient characteristics	substance use disorders		

Intervention	"To detect attention deficit hyperactivity disorder (ADHD) in treatment seeking substance use disorders (SUD) patients, a valid screening instrument is needed. Objectives: To test the performance of the Adult ADHD Self-Report Scale V 1.1(ASRS) for adult ADHD in an international sample of treatment seeking SUD patients for DSM-IV-TR; for the proposed DSM-5 criteria; in different subpopulations, at intake and 1–2 weeks after intake; using different scoring algorithms; and different externalizing disorders as external criterion (including adult ADHD, bipolar disorder, antisocial and borderline personality disorder). Methods: In 1.138 treatment seeking SUD subjects, ASRS performance was determined using diagnoses based on Conner's Adult ADHD Diagnostic Interview for DSM-IV (CAADID) as gold standard."
Comparison	
Length of follow-up	
Outcome and effect size	"The prevalence of adult ADHD was 13.0% (95% CI [11.0|15.0]). The overall positive predictive value (PPV) of the ASRS was 0.26 (95% CI [0.22|0.30]), the negative predictive value (NPV) was 0.97 (95% CI [0.96|0.98]). The sensitivity (0.84, 95% CI [0.76|0.88]) and specificity (0.66, 95% CI [0.63|0.69]) measured at admission were similar to the sensitivity (0.88, 95% CI [0.83|0.93]) and specificity (0.67, 95% CI [0.64|0.70) measured 2 weeks after admission. Sensitivity was similar, but specificity was significantly better in patients with alcohol compared to (illicit) drugs as the primary substance of abuse (0.76 vs. 0.56). ASRS was not a good screener for externalizing disorders other than ADHD. Conclusions: The ASRS is a sensitive screener for identifying possible ADHD cases with very few missed cases among those screening negative in this population."
Funding	For coordination of the IASP study, grants were received from pharmaceutical companies (Shire, Eli Lilly & Company, Jansen Cilag), from participating institutes and from three not for profit organizations: the Waterloo Foundation, the Noaber Foundation and the Augeo Foundation.
Comments	

Title	**ADHS bei erwachsenen Patienten mit Substanzkonsumstörungen**		
First Author	**Luderer, M., 2019**	**Source**	
Level of evidence	5	**Study type**	narrative review
Study quality	low		
Participants	-		
Patient characteristics	ADHD and substance use disorders		
Intervention	Summary of consensus and guideline recommendations, supplemented with the most recent literature		
Comparison			
Length of follow-up			
Outcome and effect size	In recent years new findings on the comorbidity of ADHD in patients with SUD have emerged. A series of screening and diagnostic instruments have meanwhile been evaluated in this patient group. The consensus paper and various guidelines therefore provide clinicians with specific help in detecting ADHD in patients with SUD and in conducting further diagnostics and treatment of both disorders. For example, the importance of stimulants in the treatment of patients with SUD and ADHD has significantly changed and first studies on psychotherapeutic interventions specific to this comorbidity are now available.		
Funding	none		
Comments			

Title	**Diagnosing ADHD During Active Substance Use: Feasible or Flawed?**		
First Author	**van Emmerik-van Oortmerssen, K., 2017**	**Source**	**28957778**

Level of evidence	2b	**Study type**	cohort study, diagnostic validity of ADHD in non-abstinent patients with SUD
Study quality	Low		
Participants	N=127		
Patient characteristics	ADHD and substance use disorders		
Intervention	Prospective test-retest study in a SUD treatment center among 127 treatment seeking adult SUD patients with a comorbid diagnosis of adult ADHD. Conners' Adult ADHD Diagnostic Interview for DSM-IV was administered at intake and after four SUD treatment sessions.		
Comparison			
Length of follow-up			
Outcome and effect size	The mean time interval between intake and retest assessment was 78 days (SD=32; range 31-248). At the second ADHD assessment, substance use had decreased to about 50% of baseline consumption. Of the 127 patients with an initial diagnosis of ADHD, 121 patients (95.3%) still fulfilled DSM-IV adult ADHD criteria at re-diagnosis. Subtyping of ADHD was less stable (Cohen's Kappa=0.53). Agreement on the number of childhood and adult ADHD symptoms between both assessments was good (intraclass correlation coefficient of 0.69 and 0.65, respectively). Sensitivity analyses in subgroups of patients who were fully abstinent during the second assessment yielded very similar results. CONCLUSIONS: These findings strongly suggest that a pragmatic approach, in which patients are evaluated for ADHD even when they are not (yet) abstinent, is feasible and justifiable.		
Funding	The data were collected within the framework of a RCT to test the efficacy of the integrated treatment for adult treatment seeking SUD patients with comorbid ADHD. The RCT was supported by Fonds NutsOhra, project number 1001-036.		
Comments	type of substance, frequency of use not reported		

Title	**Atomoxetine Treatment of Adults With ADHD and Comorbid Alcohol Use Disorders**		
First Author	**Wilens, T., 2008**	**Source**	**18403134**
Level of evidence	2b	**Study type**	RCT
Study quality	Medium		
Participants	N=147		
Patient characteristics	ADHD and alcohol use disorders ((DSM IV), Outpatients		
Intervention	Abstinence 4-30 days atomoxetine (25-100mg daily) for 12 weeks. ADHD symptoms were assessed using ADHD Investigator Symptom Rating Scale (AISRS) total score. Time-to-relapse to heavy alcohol use was analyzed using a 2-sided log-rank test based on Kaplan–Meier estimates and cumulative heavy drinking events over time were evaluated post hoc with recurrent-event analysis.		
Comparison	Placebo		
Length of follow-up	12 weeks double blind placebo controlled. Afterwards 12 weeks open label all atomoxetine		
Outcome and effect size	56% drop out in atomoxetine group, 64% in placebo group. ADHD symptoms were significantly improved in the atomoxetine group compared to placebo (difference: p=.007; effect size=0.48). No significant differences between treatment groups occurred in time-to-relapse of heavy drinking (p=0.93). Cumulative heavy drinking days were reduced 26% in atomoxetine-treated subjects versus placebo (event ratio=0.74, p=.023). There were no serious adverse events or specific drug–drug reactions related to current alcohol use.		
Funding	"Eli Lilly and Company and by a grant to TEW (K24 DA0162 64 & 5U10DA 0158310)."		
Comments	mono-centric RCT, heterogeneous sample (abuse and dependence), significant treatment effect only for ADHD symptoms and in a secondary analysis for cumulative heavy drinking days (group differences significant around day 55)		

3.6.8. Persönlichkeitsstörungen

Title	**The prevalence of comorbid alcohol use disorder in the presence of personality disorder: Systematic review and explanatory modelling**		
First Author	**Guy, N., 2018**	**Source**	**29611335**
Level of evidence	1a	**Study type**	SR of prospective cohort studies
Study quality	high		
Participants	16 studies		
Patient characteristics	AUD in PD		
Intervention	Prevalence		
Comparison			
Length of follow-up			
Outcome and effect size	Gepolte Lifetime Prävalenz von AUD bei PS: 58.7%, Lifetime Prävalenz von AUD bei PS allgemein: variierte in populationsbasierten und klinischen Settings zwischen 21% to 47%, People with antisocial PD had the highest lifetime AUD prevalence, at 76.7%, followed by those with borderline PD at 52.2%, while those with other forms of PD, or undifferentiated PD, had a prevalence of 38.9%. 12-monats Prävalenz der AUD s bei BPS: 31.1%, 12-monats Prävalenz der AUDs bei zwanghafter PS : 12.9%.		
Funding			
Comments			

Title	**Personality disorder and alcohol treatment outcome: Systematic review and meta-analysis**		
First Author	**Newton-Howes, G. M., 2017**	**Source**	
Level of evidence	1a	**Study type**	
Study quality	High		
Participants	22 studies with 4861 patients		
Patient characteristics	PD in AUD		
Intervention	Prevalence		
Comparison	Association between personality disorder and the outcome of treatment for AUD.		
Length of follow-up	at least 8 weeks		
Outcome and effect size	Primär Outcome Studie. Prävalenz PS bei AUD allgemein 34-71% (Mdn=55%), Prävalenz der antisozialen PS bei AUD in 8 Studien zwischen: 15-41% (Mdn=28%), Prävalenz der BPS bei AUD in 8 Studien zwischen: 11-27 % (Mdn=18%)		
Funding			
Comments			

Title	**Predictors of Substance Use in Youth With Borderline Personality Disorder**		
First Author	**Scalzo, F., 2018**	**Source**	**28627903**
Level of evidence	2b	**Study type**	cohort study
Study quality	medium		
Participants	117 help-seeking youth aged 15-25 years		
Patient characteristics	AUD in BPD Youth (aged 15-25 years)		
Intervention	Prevalence		
Comparison	This study examined the relationship between substance use and severity of BPD in youth presenting for the first time for treatment (first presentation) of BPD. Hierarchical logistic regression was used to investigate whether the severity of BPD predicted substance use.		
Length of follow-up			
Outcome and effect size	16% of the women and 32 % of the men with BPS also had an AUD. After adjusting for demographic factors and concurrent mental state pathology, BPD independently predicted alcohol dependence, amphetamine use in the previous month, or use of 2 or more illicit substances in the previous month but not daily tobacco use or cannabis use in the previous month.		
Funding			

Comments	

Title	**Alcoholism and personality disorders: an exploratory study**		
First Author	**Echeburúa, E., 2005**	**Source**	**15824064**
Level of evidence	2b	**Study type**	Low quality
Study quality	medium		
Participants	30 consecutively recruited alcohol-dependent patients attending an outpatient clinic		
Patient characteristics	PD in AUD		
Intervention	Prevalence		
Comparison	30 consecutively recruited psychiatric patients with non-addictive disorders and 31 subjects from the general population chosen to match the patient samples for age, gender and socio-economic level.		
Length of follow-up			
Outcome and effect size	Forty percent of the alcohol-dependent patients and 16.6% of the general psychiatric clinical sample (vs. 6.4% of the normative sample) showed at least one personality disorder.		
Funding			
Comments			

Title	**Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions**		
First Author	**Stinson, F. S., 2005**	**Source**	**16157233**
Level of evidence	2b	**Study type**	cohort study
Study quality	medium		
Participants	Face-to-face personal interviews were conducted with 43,093 respondents, in the National Institute on Alcohol Abuse and Alcoholism's (NIAAA) 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions		
Patient characteristics	AUD and PD in U.S. general population		
Intervention	Prevalence		
Comparison			
Length of follow-up			
Outcome and effect size	NESARC: Komorbidität AUD und PS: 28.6%, Antisoziale PS + AUD (12.3%).		
Funding			
Comments			

Title	**Co-occurrence of 12-month alcohol and drug use disorders and personality disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions**		
First Author	**Grant, B. F., 2004**	**Source**	**15066894**
Level of evidence	2b	**Study type**	cohort study
Study quality	medium		
Participants	Face-to-face personal interviews were conducted with 43,093 respondents, in the National Institute on Alcohol Abuse and Alcoholism's (NIAAA) 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions		
Patient characteristics	AUD and PD in U.S. general population		
Intervention	Prevalence		
Comparison			
Length of follow-up			
Outcome and effect size	NESARC: Komorbidität AUD und PS zwischen (24-78%), Antisoziale PS + AUD (12.3%).		
Funding			
Comments			

Title	Comorbidity of alcohol dependence and personality disorders: a comparative study		
First Author	Echeburúa, E., 2007	Source	17766317
Level of evidence	2b	Study type	Low quality
Study quality	medium		
Participants	158 consecutively recruited alcohol-dependent patients attending a psychiatric outpatient clinic		
Patient characteristics	PD in AUD		
Intervention	Prevalence		
Comparison	120 consecutively recruited psychiatric patients with non-addictive disorders, and 103 subjects from the general population chosen to match the patient samples for age, gender and socioeconomic level.		
Length of follow-up			
Outcome and effect size	Of the alcohol-dependent patients, 44.3%, and of the general clinical sample, 21.7% (vs 6.8% of the normative sample) showed at least one personality disorder.		
Funding			
Comments			

Title	Personality disorders in alcohol-dependent individuals: relationship with alcohol dependence severity		
First Author	Preuss, U. W., 2009	Source	19622885
Level of evidence	2b	Study type	Low quality
Study quality	medium		
Participants	1.079 inpatients with DSM-IV AD from three inpatient addiction treatment centers were included		
Patient characteristics	PD in AUD		
Intervention	Prevalence		
Comparison			
Length of follow-up			
Outcome and effect size	PS Prävalenz bei SUD und AUD bei 60%		
Funding			
Comments			

Title	Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication		
First Author	Kessler, R. C., 2005	Source	15939839
Level of evidence	2b	Study type	cohort study
Study quality	medium		
Participants	9.282 English-speaking respondents		
Patient characteristics	AUD and PD in U.S. general population		
Intervention	Prevalence		
Comparison			
Length of follow-up			
Outcome and effect size	OR Komorbidität AUD und Cluster B OR=10.3		
Funding			
Comments			

Title	Personality disorders among patients accessing alcohol detoxification treatment: prevalence and gender differences		
First Author	Picci, R. L., 2012	Source	21821240
Level of evidence	2b	Study type	cohort study

Study quality	medium
Participants	206 patients entering alcohol detoxification treatment
Patient characteristics	PD in AUD
Intervention	Prevalence
Comparison	
Length of follow-up	
Outcome and effect size	PD Prävlenz bei AUD Range 46-86%
Funding	
Comments	

Title	**Personality Disorder and Alcohol Use Disorder: An Overview**		
First Author	**Newton-Howes, G., 2018**	**Source**	**29466805**
Level of evidence	3b	**Study type**	Non-SR, narratives Review
Study quality	Low		
Participants			
Patient characteristics	AUD in PD		
Intervention	Prevalence		
Comparison			
Length of follow-up			
Outcome and effect size	Lifetime Prävalenz von AUD bei antisozialer PS beträgt 77%, Lifetime Prävalenz von AUD bei Borderline PS beträgt > 50 %		
Funding			
Comments			

Title	**Treatment for comorbid borderline personality disorder and alcohol use disorders: a review of the evidence and future recommendations**		
First Author	**Gianoli, M. O., 2012**	**Source**	**22686496**
Level of evidence	3b	**Study type**	Non-SR, narrative review
Study quality	low		
Participants			
Patient characteristics			
Intervention	Prävalenz, Therapieoptionen		
Comparison			
Length of follow-up			
Outcome and effect size	Komorbidität AUD bei BPS: 58.3%, Komorbidität BPS bei AUD: 9.8% to 14.7%.Komorbidität AUD bei BPS bei Frauen: 59%		
Funding			
Comments			

Title	**Suicidal behavior in alcohol-dependent subjects: the role of personality disorders**		
First Author	**Preuss, U. W., 2006**	**Source**	**16634856**
Level of evidence	2b	**Study type**	cohort study
Study quality	medium		
Participants	376 treatment-seeking alcohol-dependent subjects		
Patient characteristics	PD in AUD		
Intervention	Prävalenz; Outcome Suizidalität		
Comparison			
Length of follow-up	55% mit PS		
Outcome and effect size			
Funding			
Comments			

Title	Personality disorders among alcoholic outpatients: prevalence and course in treatment		
First Author	Zikos, E., 2010	Source	20181301
Level of evidence	2b	Study type	cohort study
Study quality	medium		
Participants	Patients with alcohol use disorders (n=165)		
Patient characteristics	PD in AUD		
Intervention	prevalence		
Comparison			
Length of follow-up			
Outcome and effect size	No PD 41% (n=57), Cluster B PD 32% (n=44), and other PD 27% (n=37)		
Funding			
Comments			

Title	Revised NESARC personality disorder diagnoses: gender, prevalence, and comorbidity with substance dependence disorders		
First Author	Trull, T., 2010	Source	20695803
Level of evidence	2b	Study type	cohort study
Study quality	medium		
Participants	Epidemiological study with over 40.000 individuals		
Patient characteristics	AUD and PD in U.S. general population		
Intervention	Prevalence		
Comparison			
Length of follow-up			
Outcome and effect size	NESARC-REVISED: the highest comorbidity rates for lifetime alcohol dependence were observed among those with antisocial (49.19% wave 1; 52.09% wave 2), 2 histrionic (49.79%), and borderline (47.41%) PDs		
Funding			
Comments			

Title	Varieties of impulsivity in males with alcohol dependence: the role of Cluster-B personality disorder		
First Author	Rubio, G., 2007	Source	17850221
Level of evidence	1b	Study type	RCT
Study quality	high		
Participants	247 males with alcohol-dependence recruited from 2 alcoholism treatment centers		
Patient characteristics	PD in AUD		
Intervention	Experiment		
Comparison	A matched nonsubstance-abusing comparison group (n=96)		
Length of follow-up			
Outcome and effect size	Deficits in inhibitory control might be specific for AntPD and BPDs in AUD.		
Funding			
Comments			

Title	Patients with addiction and personality disorder: Treatment outcomes and clinical implications		
First Author	van den Bosch, L. M., 2007	Source	17143086
Level of evidence	3b	Study type	non-SR, narrative Review
Study quality	low		
Participants			
Patient characteristics			

Intervention	Psychotherapy
Comparison	
Length of follow-up	
Outcome and effect size	Integrated treatment programs are lacking and research is still too limited
Funding	
Comments	

Title	**Out-patient behaviour therapy in alcoholism: impact of personality disorders and cognitive impairments**		
First Author	**Wölwer, W., 2001**	**Source**	**11202126**
Level of evidence	1b	**Study type**	RCT
Study quality	high		
Participants	120 alcoholics were assigned randomly to one of three out-patient treatment programs		
Patient characteristics	'AUD with / without PD'		
Intervention	psychotherapy, 'coping skills training' and 'cognitive behaviour therapy'		
Comparison	Specific treatment vs. unspecific supportive control		
Length of follow-up	6-month treatment period		
Outcome and effect size	Alcoholic patients relapsing within 6 months after detoxification showed a higher rate of personality disorders (especially antisocial and borderline) and slightly more cognitive deficits (especially in verbal memory and visuomotor functions) than abstainers even before therapy.		
Funding			
Comments			

Title	**Dynamic deconstructive psychotherapy versus optimized community care for borderline personality disorder co-occurring with alcohol use disorders: a 30-month follow-up**		
First Author	**Gregory, R., 2010**	**Source**	**20386259**
Level of evidence	1b	**Study type**	RCT
Study quality	high		
Participants	30 patients, either treatment with DDP (n=15) or to optimized community care (OCC; n=15).		
Patient characteristics	AUD with BPD		
Intervention	Psychotherapie, dynamic deconstructive psychotherapy (DDP)		
Comparison	DDP vs. TAU		
Length of follow-up	12-month randomized controlled trial of DDP versus optimized community care (OCC), 18 months of naturalistic follow-up.		
Outcome and effect size	Patients with DDP achieved significantly greater improvement in core BPD symptoms, depression, parasuicide, and recreational drug use over the 30-month study		
Funding			
Comments			

Title	**Personality-guided treatment for alcohol dependence: a quasi-randomized experiment**		
First Author	**Nielsen, P., 2007**	**Source**	**17882606**
Level of evidence	1b	**Study type**	RCT
Study quality	high		
Participants	n= 108 with AUD, n=47 mit PETAD und n=61 controls		
Patient characteristics	AUD (1/2 mit PD)		
Intervention	Psychotherapy, Personality-Guided Treatment for Alcohol Dependence (PETAD)		
Comparison	PETAD vs. TAU		
Length of follow-up	12-week treatment, 6-month follow-up		
Outcome and effect size	PETAD was associated with better retention, longer time to first relapse, and less time spent drinking post-treatment, although few differences reached statistical significance		

Funding	
Comments	

Title	**The impact of personality disorders on alcohol-use outcomes in a pharmacotherapy trial for alcohol dependence and comorbid Axis I disorders**		
First Author	**Ralevski, E., 2007**	**Source**	**18058408**
Level of evidence	2b	**Study type**	RCT low quality
Study quality	medium		
Participants	254 patients with AUD		
Patient characteristics	PD in AUD		
Intervention	Pharmacotherapy		
Comparison	Comparing pharmacotherapy in patients with ASPD vs. those without, and patients with BPD vs. those without		
Length of follow-up	12-week medication trial for treatment of their alcohol dependence		
Outcome and effect size	Disulfiram und Naltrexon bei Rückfallprophylaxe bei Komorbidität gleich wirksam wie bei AUD allein.		
Funding			
Comments			

Title	**Supervised disulfiram in relapse prevention in alcohol-dependent patients suffering from comorbid borderline personality disorder-a case series**		
First Author	**Mutschler, J., 2010**	**Source**	**20107104**
Level of evidence	4	**Study type**	Case series
Study quality	low		
Participants	n=8		
Patient characteristics	AUD with BPD		
Intervention	Pharmacotherapy, Disulfiram		
Comparison	Safety and efficacy in relapse prevention of a series of alcoholics with BPD		
Length of follow-up	A mean period of 9.25 months		
Outcome and effect size	No negative effect through medication with disulfiram; abstinence length under supervised administration: (4.5 to 14 months)		
Funding			
Comments			

Title	**Safety and drinking outcomes among patients with comorbid alcohol dependence and borderline personality disorder treated with high-dose baclofen: a comparative cohort study**		
First Author	**Rolland, B., 2015**	**Source**	**25356633**
Level of evidence	1b	**Study type**	RCT
Study quality	high		
Participants	n=23 AUD + BPD patients		
Patient characteristics	AUD with BPD		
Intervention	Pharmacotherapy, Baclofen		
Comparison	AUD controls (n=46)		
Length of follow-up	1-year course		
Outcome and effect size	The mean rate of heavy drinking days (74.3±25.3 vs. 41.7±33.3%; $p<0.001$), the rate of serious AEs (65.2 vs. 6.5%; $p<0.001$), and the rate of treatment discontinuation after AEs (52.2 vs. 8.6%; $p<0.001$) were significantly higher in BPD.		
Funding			
Comments			

Title	Personality disorders among Danish alcoholics attending outpatient treatment		
First Author	Nordholm, D., 2007	Source	17851244
Level of evidence	3c	Study type	Outcome research
Study quality	medium		
Participants	363 patients who started psychosocial treatment at the outpatient alcohol clinic		
Patient characteristics	PD in AUD		
Intervention	Verlauf/Outcome		
Comparison	Co-morbid personality disorder (PD) of either the cluster B (A+PDB) or cluster C (A+PDC) type		
Length of follow-up	Re-interview 1 year after onset of treatment		
Outcome and effect size	AUD+PD Cluster B were younger and had a longer history of alcohol abuse than A-PD and A+PDC.		
Funding			
Comments			

Title	Personality disorders in early adolescence and the development of later substance use disorders in the general population		
First Author	Cohen, P., 2007	Source	17227697
Level of evidence	1b	Study type	Prospective cohort study
Study quality	high		
Participants	796 participants		
Patient characteristics	PD als Prädiktor für AUD		
Intervention	Verlauf/ Outcome		
Comparison			
Length of follow-up	9 Jahre (mean) Follow-up		
Outcome and effect size	PD and conduct disorder were associated with diagnoses of later AUD. The greatest of these effects were shown for borderline PD and for conduct disorder, the predecessor of adult antisocial PD.		
Funding			
Comments			

Title	New onsets of substance use disorders in borderline personality disorder over 7 years of follow-ups: findings from the Collaborative Longitudinal Personality Disorders Study		
First Author	Walter, M., 2009	Source	19133893
Level of evidence	1b	Study type	Prospective cohort study
Study quality	high		
Participants	175 patients with BPD		
Patient characteristics	Onset of AUD in BPD		
Intervention	Verlauf/ Outcome		
Comparison	Compared with 396 patients with other personality disorder at baseline and at 6, 12, 24, 36, 48, 60, 72 and 84 months.		
Length of follow-up	7 years follow-up		
Outcome and effect size	Incidence of AUD in BPD 13% vs. 6% in other PD		
Funding			
Comments			

Title	The impact of personality disorders on alcohol-use outcomes in a pharmacotherapy trial for alcohol dependence and comorbid Axis I disorders		
First Author	Ralevski, E., 2007	Source	18058408
Level of evidence	2b	Study type	RCT low quality
Study quality	medium		
Participants	254 patients with AUD		

Patient characteristics	PD in AUD
Intervention	Verlauf/ Outcome
Comparison	Comparing patients with ASPD vs. those without, and patients with BPD vs. those without
Length of follow-up	12-week medication trial for treatment of their alcohol dependence
Outcome and effect size	Diagnosis of personality disorder did not adversely affect alcohol outcomes
Funding	
Comments	

Title	**Personality disorder and alcohol treatment outcome: systematic review and meta-analysis**		
First Author	**Newton-Howes, G., 2017**	**Source**	**28385703**
Level of evidence	1a	**Study type**	SR of prospective cohort studies
Study quality	high		
Participants	22 studies with 4.861 patients		
Patient characteristics	PD in AUD		
Intervention	Verlauf / Outcome		
Comparison	Association between personality disorder and the outcome of treatment for AUD.		
Length of follow-up	At least 8 weeks		
Outcome and effect size	AUD Patienten mit PS brechen häufiger Alkoholtherapie ab als AUD Patienten ohne PS.		
Funding			
Comments			

Title	**Poorer Drinking Outcomes with Citalopram Treatment for Alcohol Dependence: A Randomized, Double-Blind, Placebo-Controlled Trial**		
First Author	**Charney, D., 2015**	**Source**	**26208048**
Level of evidence	2b	**Study type**	RCT low quality
Study quality	medium		
Participants	n= 265 AUD (47% with PD)		
Patient characteristics	AUD with/without PD		
Intervention	Verlauf/ Outcome		
Comparison	PD as a predictor for outcome		
Length of follow-up	12 weeks		
Outcome and effect size	AUD Patienten mit PS brechen häufiger Alkoholtherapie ab und weniger abstinente Zeit als AUD Patienten ohne PS		
Funding			
Comments			

Title	**Personality disorder and chronicity of addiction as independent outcome predictors in alcoholism treatment**		
First Author	**Krampe, H., 2006**	**Source**	**16675768**
Level of evidence	2b	**Study type**	cohort study
Study quality	medium		
Participants	110 patients, 71 (or 65 percent) met criteria for at least one comorbid personality disorder		
Patient characteristics	AUD with / without PD		
Intervention	Verlauf/ Outcome		
Comparison	AUD controls (n=46)		
Length of follow-up	4 years		
Outcome and effect size	PS führt zu kürzerer Abstinenzzeit bis zum ersten Rückfall		
Funding			
Comments			

Title	Personality disorders among alcoholic outpatients: prevalence and course in treatment		
First Author	Zikos, E., 2010	Source	20181301
Level of evidence	2b	Study type	cohort study
Study quality	cohort study		
Participants	Patients with alcohol use disorders (n=165)		
Patient characteristics	PD in AUD		
Intervention	Verlauf / Outcome		
Comparison	No PD 41% (n=57), Cluster B PD 32% (n=44), and other PD 27% (n=37).		
Length of follow-up	12 weeks		
Outcome and effect size	The Cluster B PD group showed significantly higher levels of impulsivity at intake, greater likelihood of early treatment dropout, and quicker times to first slip and to relapse.		
Funding			
Comments			

3.6.9. Nikotin

Title	A Controlled Smoking Cessation Trial for Substance-Dependent Inpatients		
First Author	Burling, T., 2001	Source	11393606
Level of evidence	2b	Study type	RCT
Study quality	large, randomized controlled trial with 2 untreated control groups (usual care + treatment refusers), High drop-out rate from 9-week smoking cessation program due to early discharge + program withdrawal (ca. 50%), smoking relapse/abstinence was verified with CO + cotinine Alcohol/drug relapse/abstinence was verified with alcohol-breath test + urinary drug screen		
Participants	n=200		
Patient characteristics	Long-term residential rehabilitation program for homeless veterans (average 3.5 mo.) Current dx of substance dependence disorder (DSM-IV) Had to complete the first 30 days of the inpatient program and not be in danger of imminent discharge. ≥7 cig./day for the previous 6 months (mean 17.7) only 36% of patients with alcohol dependence only 4% woman		
Intervention	2 intensive intervention groups: a. multicomponent smoking tx (MST) + nicotine patch b. multicomponent smoking tx (MST) plus generalization training (+G) plus nicotine patch 2 untreated control groups: a. usual care who requested smoking treatment but did not receive tx b. treatment refusers who declined smoking treatment=concurrent inpatient treatment of alcohol/illicit drugs + nicotine dependence in inpatient residential program for homeless veterans		
Comparison	2 intensive smoking interventions (MST and MST+G) versus usual care (UC) versus treatment refusers (TF)		
Length of follow-up	Smoking outcomes were examined 1, 3, 6, and 12 months after participants (a) attempted to quit smoking, (b) withdrew from smoking treatment, (c) discontinued smoking treatment because of inpatient discharge, or (d) were 5 weeks post study enrollment (for UC and TR participants), drug/alcohol outcomes were evaluated 1, 3, 6, 12 months post discharge from inpatient tx		
Outcome and effect size	• No significant differences in baseline pts characteristics between UC and TR • No significant differences in baseline pts characteristics between intervention groups and UC • Smoking abstinence rates as 7-day point prevalence: Both intervention groups had significantly higher abstinence rates versus UC+TR only at 1 month follow-up postquit ($p<0.001$), but not at 3, 6, 12 monoths follow-up • smoking relapse rates were not significantly different to UC-drug/alcohol abstinence rates as 30-day point prevalence between tx groups (Table 4): significantly higher at all		

	follow-ups for MST versus MST+G but: abstinence + relapse rates were not significantly different versus UC+TR-drug/alcohol relapse rates between tx-groups (Fig.2): were significantly higher at all follow-ups for MST versus MST+G but: abstinence + relapse rates were not significantly different versus UC
Funding	NIDA
Comments	• only 36% alcohol dependent • only combined analyses with illegal drugs • high-dropout rate during tx • special subgroup of alcohol dependent patients: homeless veterans • only 4% woman=reason for 2B level of evidence • since smoking abstinence rates were only significant between tx- and control groups at 1 month, alcohol abstinence rates at 3, 6, 12 months compare groups that

Title	**Simultaneous versus Delayed Treatment of Tobacco Dependence in Alcohol-Dependent Outpatients**		
First Author	**Nieva, G., 2011**	**Source**	**20881400**
Level of evidence	2b	**Study type**	RCT
Study quality	• Calculation of the sample size: for an estimated reduction of 2% in the delayed group and 25% in the concurrent group, two groups of 53 subjects were necessary (with an alpha risk level of 0.05 and 90% capacity to detect the difference). • Very high loss-to-follow-up: 106 were randomized, 92 (87%) started tx, 74 (70%) completed 30d-follow-up, 51 (48%) 90d-follow-up, and 30 (28%) the 180d-follow-up • Smoking verification via self-report + CO + cotinine • Patients lost to follow-up were presumed to be drinking and smoking • Many patients (n=14) did not come to the first visit, even after they had signed the consent form → initially 106 patients • Statistical analysis was carried out according to intention-to-treat criteria: all patients who came to at least the first visit (day 1) were included in the outcome analysis. • pts lost to follow-up were considered to be drinking + smoking		
Participants	N =92		
Patient characteristics	• Smoked - ≥5 cig./d for >1yr (mean 28 cig./d) • FTND 5.6-6.0 • Desire to quit smoking • Current alcohol dependence with drinking (DSM-IV) • Patients could relapse two times before being excluded; a relapser was excluded directly when in hospital detox was necessary • Sociodemographic and baseline clinical data indicated that the groups were equivalent with two exceptions: patients in the delayed group gave more importance to stopping drinking alcohol (t(68)=2.13, p=0.04) and craving for tobacco was higher in the delayed group (t(88)=2.07, p=0.04). • 41.8% needed pharmacological detox with benzodiazepines/ clomethiazole		
Intervention	• simultaneous group: On day 1 start of tobacco + alcohol tx • delayed group: On day 1 start of alcohol tx, on day 180 start of tobacco tx • alcohol tx: alcohol detoxification + standard alcohol tx • smoking tx: **a**. 10 x 30-45 min sessions based on cognitive behavioral therapy with emphasis on skill training, problem-solving strategies and relapse prevention. **b**. all patients received NRT according to FTND scores for ca. 3 months = outpatients receiving either concurrent or delayed smoking cessation tx		
Comparison	For alcohol abstinence: Simultaneous therapy versus untreated control group receiving only alcohol tx at day 180 For smoking abstinence: Simultaneous versus delayed group = days 30, 60, 90 and 180 versus days 210, 240, 270 and 360		
Length of follow-up	• alcohol follow-up for both groups at days 30, 60, 90, and 180 post start of alcohol tx (day1) • smoking cessation follow-up at days 1, 7, 14, 30, 60, 90 and 180 for the simultaneous group and for the delayed group = 6 months later plus 1 day, 7 days, 14 days, 30 days, 60 days, 90 days and 180 days		

Outcome and effect size	To evaluate the effects that providing an intensive tobacco cessation treatment simultaneously with alcohol dependence treatment versus delayed treatment (first alcohol and 6 months later tobacco) has on alcohol and tobacco consumption smoking results are given as 7-day point-prevalence abstinence rates, time-to-first relapse (TFR) for the two substances (defined as abstinence days until first relapse) and cumulative abstinence duration (CAD), which is the total number of abstinence days during the study. Smoking outcomes: a) Smoking abstinence rates tended to be higher for those who were trying to quit simultaneously, but differences were only significant at 3 months (p=0.033; Cohen's d=0.51). Results at 1 month (p=0.213) and 6-months follow-up (p=0.071) were not significant. b) At 180 days, the simultaneous group presented a mean TFR for smoking of 32.3 days (SD=60.1) and a CAD of 31 days (SD=54.4). The mean TFR of the delayed group was 20.2 days (SD=53.2) and the CAD was 19.2 days (SD=51.5). Differences between both groups did not reach significance. • Alcohol Outcomes: Alcohol abstinence rates between groups on days 30, 60, 90 and 180 were nonsignificant. a) no significant differences for TFR on day 180, as means were 84.1 (SD=63.5) and 86.9 (SD=75.2) days for the simultaneous and untreated group (t(78)=0.19, p=0.850), respectively b) no significant differences for cumulative days of abstinence (CAD), as means were 91.1 (SD=66.1) and 87.8 (SD=75.4) days for the simultaneous and untreated group, respectively (t(90)=0.22, p=0.824). c) survival analysis showed no differences between groups (p=0.144).
Funding	Spanish Plan Nacional Sobre Drogas
Comments	only 2b RCT, because: a) intention-to-treat analysis suffers from high loss to follow-up, because these pts were considered relapses to drinking + smoking b) small patient number

Title	**Concurrent brief versus intensive smoking intervention during alcohol dependence treatment.**		
First Author	**Cooney, N., 2007a**	**Source**	**18072840**
Level of evidence	1b	**Study type**	RCT
Study quality	• <20% drop-out at 6 mo. follow- up • Clear randomization procedure • The study was powered to detect moderate (i.e., d=0.3) differences between smoking cessation treatment conditions. • Smoking abstinence verification with self-report + breath CO-levels of <10 ppm. • Alcohol abstinence with self- report only • Multiple t-tests and chi-square analyses were used to determine if the two treatment groups were homogeneous with respect to background variables. Variables examined were sex, age, ethnicity, education, employment status, baseline number of drinks consumed per day, number of smoking quit attempts, cigarettes smoked per day, and baseline FTND. Analyses indicated that the groups were equivalent on all baseline measures. • 133 pt. randomized, but only 118 participated in tx and only these were analyzed.		
Participants	N=118		
Patient characteristics	• Met DSM-IV criteria for alcohol and nicotine dependence during the past three months. • Consumption of ≥10 cig./d., mean 24.8 cig./d, mean FTND: 5.5, mean 28.1 smoking yrs. • Alcohol consumption average: 19.3 (+/-17.1) drinks/d • Exclusion: current illicit drug abuse • The mean number of days of alcohol abstinence of sample at time of enrollment was 9.02 (SD=26.30) • 89% men		
Intervention	• Outpatient substance abuse treatment program for 3 weeks (meetings 5 days/week). • Randomization to a concurrent brief or intensive smoking cessation intervention.		

	• Intensive intervention: 3 x 1h counseling sessions plus eight weeks of nicotine patch therapy. • Brief intervention: 1 x 15min counselling + 1 x 5min follow-up after smoking cessation • Target smoking quit date = 1 week after tx initiation = concurrent outpatient treatment of alcohol + nicotine dependence
Comparison	Comparison of 2 interventions: brief versus intensive smoking cessation tx
Length of follow-up	Follow-up: 14 days, 3 months and 6 months after discharge from 3-week-program
Outcome and effect size	smoking abstinence: 7-day point prevalence rates were significantly higher for intensive (27.5%) versus brief (6.6%) treatment only at 14-day follow-up, but not at 6 months when abstinence rates fell to 9.1% and 2.1%. smoking intervention effect on drinking (Form-90 self-report): a) proportion days heavy drinking (PDHD: >4♀+>6♂ standard drinks/d) 14 days prior to 14-day follow-up and 30 days prior to 3- and 6-month follow-up b) abstinence rates 14 days prior to 14-day follow-up and 30 days prior to 3- and 6-month follow-up = no significant effect of the smoking cessation treatment condition on drinking abstinence Among those assessed at the 14-day follow-up, across both treatment groups, 16% reported not smoking and not drinking, with 76% of participants reporting they were smoking and not drinking. All participants who reported drinking also reported current smoking (8% of the full sample).
Funding	NIAAA
Comments	No untreated control group. Without high smoking abstinence rates, one cannot provide a strong test of the impact of smoking cessation on alcohol outcomes.

Title	**Smoking cessation during alcohol treatment: a randomized trial of combination nicotine patch plus nicotine gum.**		
First Author	**Cooney, N., 2009**	**Source**	**19549054**
Level of evidence	1b	**Study type**	RCT
Study quality	• Small scale randomized placebo-controlled, double-blind study. • Intention to treat analysis: participants with missing data at each time point were coded as smokers. • Randomization computer program that balanced the two groups for hx of previous substance use tx, age, sex, baseline drinks/drinking day, and baseline cig/day. • The average retention across groups for the prolonged CO-verified smoking abstinence outcome measure was 100% at 2 weeks, 91% at 3 months, 82% at 6 months, and 72% at 12 months → 20% loss-to-follow-up but same numbers for both groups • Patients with alcohol abuse were also included • Self-reported, Form-90 + alcohol-breathalyser for alcohol abstinence • Smoking abstinence verification with self-report + breath CO- levels of <10 ppm. • The two treatment groups were balanced with respect to age, sex, race, baseline smoking rate and CO levels, alcohol and drug use, and veteran status. However, among 13 variables examined, Education, baseline FTND, and Center for Epidemiologic Studies Depression Scale (CES-D) scores were significantly different across treatment groups, with the active gum group having a higher level of education, nicotine dependence, and depressive symptoms		
Participants	N=96		
Patient characteristics	• Men and women with alcohol abuse or dependence - Consumption of >15 cig./d for >3yrs • Current motivation to stop drinking and smoking, and to attend a 16 session outpatient treatment program. - Alcohol detoxification, if necessary, was completed outside the treatment protocol prior to enrollment.		
Intervention	• All pts. Received open-label transdermal nicotine patch • Randomized to either receive 2mg nicotine gum or placebo gum. • Both groups were provided behavioral alcohol and smoking treatment delivered during 3 months of weekly outpatient sessions followed by 3 monthly booster sessions.		

	= concurrent alcohol and tobacco treatment for outpatients
Comparison	Comparison of the 2 interventions
Length of follow-up	2 weeks, 3, 6, 12 months
Outcome and effect size	• Smoking relapse was defined as smoking on 7 consecutive days or smoking at least once each week over 2 consecutive weeks. • Prolonged smoking abstinence was defined as an absence of relapse after a 30 day grace period from the target quit date. This translated to 2 months abstinence prior to the 3-month follow-up, 5 months abstinence prior to the 6-month follow-up, and 11-months abstinence prior to the 12-month follow-up. • Patients receiving nicotine patch plus active gum had a significantly better rate of prolonged smoking abstinence at 12 months (13% vs. 0%; p<0.01) but not at 3 (40% Vs. 35%) and 6 months (20% vs 12%) • A Cox proportional hazards regression model of time to smoking relapse was conducted in which time to smoking relapse was evaluated by nicotine replacement treatment condition, and controlling for the set of covariates that differed between treatment conditions (i.e., education level, depression score, Fagerstrom score, and treatment site). The results indicated that, controlling for the covariates, treatment condition was a significant predictor of time to relapse, such that being in the Active Gum condition extended survival [B=-.57, SE=.27, Wald $\chi 2$=4.47, p<.05; hazard ratio=0.57, (95% CI [0.34|0.96]). • Primary alcohol outcome (Form-90) was self-reported continuous alcohol abstinence for 90 days prior to the follow-up time points: 90-day abstinence rates for drinking at 3 months, 6 months, and 12 months were 28%, 32% and 32% for the placebo gum condition and 45%, 38%, and 43% for the active gum condition → no significant effect of treatment and time and treatment x time interaction - no significant difference to time of first drink
Funding	NIAAA
Comments	• No untreated control group • Only difference between groups is nicotine gum versus placebo gum • Also pts with alcohol abuse • 28% loss to follow-up in both groups

Title	**Ethnic differences in alcohol outcomes and the effect of concurrent smoking cessation treatment**		
First Author	**Fu, S., 2008**	**Source**	**17689205**
Level of evidence	1b	**Study type**	Secondary analysis of RCT from Joseph 2004
Study quality	• Study of sufficient patient numbers • Standardized assessments • Excellent characterization of patients and clear statistical procedures • Low follow-up rates for African Americans with 64+74% (CT+DT) at 12 months and 72+76% at 18 months. • Study with power definition: the sample size provided over 90% power to detect a 15% difference in alcohol abstinence, assuming a 50% abstinence rate in the delayed group, and 80% power to detect a 25% increase in the number of drinking days, assuming the mean days of drinking was equal to the standard deviation of the days of drinking in the delayed group. • Alcohol abstinence verification with self-report (timeline follow-back (TLFB)) and breath alcohol conc. and/or collateral interviews • Smoking abstinence verification with self-report, CO-measurement and/or collateral interview • All main analyses were performed by intention-to-treat. • Intention-to-treat analyses considered all participants and assumed non- respondents to be currently smoking and to have used alcohol in the prior 6 months. • A second set of analyses considered only respondents		
Participants	N=499		
Patient characteristics	• DSM-IV diagnosis of alcohol dependence (97%) or abuse (3%) • male: 69%; • ≥5cig./day for at least 1 year, mean 26 cig./d, M_{FTND}=6		

	• Motivated to quit smoking • At least 1 week of alcohol treatment prior to study inclusion • Ca. 50% with additional SUD (THC, cocaine, opioid) • Psychiatric comorbidity in ca. 52% • Significant differences between white and black pts: Higher unemployment rate + lesser education in blacks, 22 vs. 26 cigs./d, higher number of past quit attempts, tried NRT/Bupropion + smoking counselling in whites, higher number of alcohol dependence criteria (SAM-DIS) + alcohol use severity (ADS) in whites, higher number of additional substance use disorder (cocaine + opiate) in blacks
Intervention	• Concurrent tx (CT): NRT + stage-based individual motivational/behavioural counselling during alcohol dependence treatment • Delayed tx (DT): NRT + stage-based individual motivational/behavioural counselling 6 months after alcohol dependence treatment • Mean of 5 individual behavioural counselling sessions • NRT: nicotine patches, for >20 cig./d plus nicotine gums = comparison of concurrent inpatient treatment versus delayed outpatient treatment of alcohol dependent patients
Comparison	Comparison of 381 caucasians versus 78 African Americans in CT and DT treatment
Length of follow-up	• 6, 12, and 18 months after study inclusion for concurrent treatment • But for delayed treatment 6-month follow-up was prior to smoking cessation tx-only 12- and 18-month follow-up was post treatment in the delayed group (Fig.2) • Length of follow-ups are not identical for CT + DT: 6 months CT is equivalent to 12 months DT 12 months CT is equivalent to 16 months DT
Outcome and effect size	• 7-day point prevalent smoking abstinence rates: no significant ethnic differences in smoking cessation outcomes: at 18 months intention-to-treat = 14.4%+10.3% smoking abstinence in Caucasians and African Americans (p=0.604) Primary alcohol tx outcome (intention to treat): Overall (CT+DT) 6-month alcohol abstinence rates at 6 months, 12 months, and 18 months were 46%, 32%, and 40% for African Americans and 51%, 40%, and 47% for Caucasians = nonsignificant • 6 months alcohol abstinence at 6-month follow-up (CT versus untreated smokers): rates of alcohol abstinence were significantly lower in the CT group in caucasinas (p=0.003), but not in African Americans (p=0.68) (Fig.1) • 6-month alcohol abstinence at 12 months and 18 months remained significantly lower for Caucasians in the CT group versus DT group (Fig.1) • Concurrent smoking cessation tx in Caucasians was associated with an estimated 1.74 greater adjusted odds of resumption of alcohol use • Cox analysis shows that time to first use of alcohol was significantly shorter in Caucasians of the CT group versus DT group (HR=1.51,p= 0.004)
Funding	NIAAA, VA
Comments	African Americans group has no significance for German situation, but reduced alcohol abstinence during concurrent smoking cessation therapy in Caucasians is even more pronounced if African Americans are excluded from analysis

Title	**Bupropion and Nicotine Patch as Smoking Cessation Aids in Alcoholics**		
First Author	**Grant, K., 2007**	**Source**	**17889314**
Level of evidence	2b	**Study type**	Randomized, double-blind, placebo-controlled trial
Study quality	• High loss to follow-up at 4 and 9 weeks and 6 months: 93%, 83% and 75% respectively. • Small patient number • Smoking + alcohol verification only via self-report at 4wks, 9wks + 6mo., plus by collateral informants (in 56%) at 6 months. • Low power to detect small differences due to small n-size • 68 patients were enrolled in study, 58 pts. completed baseline assessment=analyzed • Only respondents analysis • Only for the smoking cessation rates, intention to treat analysis was done, where non-responders were assumed to be smoking cigarettes		
Participants	N=58		
Patient characteristics	• Participants were recruited in a naturalistic fashion within one week of entry into multiple levels of alcohol care (residential, intensive outpatient or low intensity outpatient alcohol		

	treatment) in a community and VA setting and received treatment as usual for their alcohol dependence • Participants were randomized in a double blind manner into the treatment or control group. • Smoked ≥20cig./d for >1yr (mean 23+27 cig./d) • FTND 6.0 • Desire to quit smoking • Current active alcohol dependence (DSM-IV) • Exclusion of patients with alcohol withdrawal seizures • 53% had at least one other substance dependence
Intervention	• Treatment group: received bupropion SR 150mg per day for three days to be followed by 150mg twice daily for 60 days (8 weeks) • Control group: received identical placebo capsules • All participants were instructed to begin their capsules 8 days before their quit smoking date. • Both groups received nicotine patches. • Participants were asked to initiate the patches on their targeted quit date and to follow a tapering regimen of 21mg (four weeks), 14mg (two weeks), and 7mg (two weeks). • Participants were asked to attend a single one hour smoking cessation group in which an educational video was shown, followed by a staff-lead discussion of smoking cessation techniques. = outpatients receiving concurrent smoking cessation tx with bupropion/N RT/brief counselling or NRT/brief counselling alone
Comparison	Bupropion + NRT Versus NRT alone
Length of follow-up	8 week treatment = post-tx, 6-month follow-up
Outcome and effect size	Cigarette smoking outcomes using 7-day point prevalence abstinence rates: a) At each follow-up point there was no significant difference in cigarette smoking outcomes between the placebo and bupropion groups b) Although there was no significant difference between the treatment and control groups, high abstinence rates from cigarettes for both groups at 6 months (33% and 22% in respondents and intention to treat analysis) were found. c) Primary outcome of this study indicates that bupropion, when added to nicotine patch therapy, did not improve smoking outcomes in this population of “in treatment” alcoholics. drinking outcomes: a) Continuous abstinence in past 30 days, drinks per day, drinks per drinking day and percent days abstinent in the previous 30 days were not statistically significant in both groups at all follow-ups (Table 4) b) Participants who successfully discontinued smoking at 6 months (N=13) reported 100% continuous abstinence from alcohol for the past 30 days prior to follow-up compared to 63% of non-quitters (p=0.016) (Table 5)
Funding	
Comments	• No untreated control group • Pts had to smoke ≥20 cig./d • Only 2b RCT, because: small patient number, high loss to follow-up, no biochemical validation of abstinence, intention-to-treat analysis was not always done

Title	**Naltrexone and Alcohol Effects on Craving for Cigarettes in Heavy Drinking Smokers**		
First Author	**Green, R., 2019**	**Source**	**30628813**
Level of evidence	1a	**Study type**	Secondary analysis of a larger trial examining pharmacogenetic effects of naltrexone on subjective response to alcohol in individuals of East Asian descent (placebo-controlled trial, non-randomized) to analyze (a) effects of alcohol on basal craving for cigarettes, (b) effects of naltrexone on cigarette craving and alcohol craving during alcohol administration, and (c) relationship between

			craving for alcohol and cigarettes.
Study quality	low (low subject number)		
Participants	n=31		
Patient characteristics	East asian individuals, heavy drinking smokers (inclusion criteria: a) East-Asian ethnicity, b) between the ages of 21 and 55, (c) score of 8 or higher on the Alcohol-Use Disorders Identification Test, indicating a heavy drinking pattern; exclusionary criteria: current major depression with suicidal ideation, lifetime psychotic disorder, lifetime substance use disorder (other than cannabis))		
Intervention	Two counterbalanced intravenous alcohol administration sessions, one after taking naltrexone (50 mg) for five days and one after taking a placebo for five days; self-reported subjective craving for cigarettes and for alcohol recorded during each experimental session		
Comparison	Placebo		
Length of follow-up	5 days		
Outcome and effect size	**Effects of alcohol and naltrexone on urge to smoke cigarettes:** significant main effect of BrAC (b=0.55 +/- 0.08, p < .01) or medication (b=0.52 +/- 0.17, p=0.001) such that naltrexone or medication reduced craving for cigarettes with significant BrAC x medication interaction (b=0.49 +/- 0.15, p<0.01) such that Naltrexone significantly reduced craving for cigarettes across rising BrAC levels as compared to placebo. The only significant covariate included was smoking status, namely regular versus occasional smoker (p<0.01). **Effects of alcohol and naltrexone on urge to drink**: significant main effect of BrAC (b=0.47 +/- 0.08, p<0.01) or medication (b=0.45 +/- 0.19, p=0.02) indicating that urge for alcohol increased across rising BrAC levels but decreased with naltrexone in comparison to placebo. No significant medication x BrAC interaction (b=0.26 +/- 0.16, p=0.11) or covariates (p's=0.12). **Relationship between urge to drink and urge to smoke:** significant main effect of craving for alcohol and cigarettes (b=0.40 +/- 0.06, p<0.01), indicating a coupling of alcohol and cigarette craving. However, there was no BrAC x craving for alcohol interaction (b=0.01 +/- 0.05, p=0.99) or medication x craving for alcohol interaction (b=0.04 +/- 0.15, p=0.79) suggesting that the effect of alcohol craving on cigarette craving does not differ across rising BrAC levels nor is it moderated by medication. The only significant covariate in these models was smoking status, namely whether participants were regular or occasional smokers (p's<0.01). **Summary**: 1.) Cigarette craving increased across rising BrAC, 2a) In comparison to placebo, naltrexone blunted cigarette craving across rising BrAC levels, 2b) Additionally, significant main effect of alcohol administration on craving for alcohol with heavy drinking smokers reporting greater craving for alcohol at higher alcohol administration levels. **Speculation**: the co-occurrence of smoking and drinking may magnify the effects of naltrexone. 3.) Positive relationship between cigarette craving and alcohol craving → The present results indicated that alcohol increases craving for cigarettes and for alcohol, and that naltCraving for cigarettes and alcohol increased significantly throughout the intravenous alcohol administration. A significant breath alcohol concentration (BrAC) × Medication interaction revealed that naltrexone blunted cigarette craving during alcohol administration, compared to placebo. Naltrexone significantly reduced craving for alcohol during alcohol administration in this group of heavy drinking smokers. Alcohol craving significantly predicted cigarette craving, however this effect did not vary across rising alcohol administration or by medication. **Summary**: Naltrexone reduces craving for cigarettes and for alcohol across rising BrAC levels.		
Funding	none		
Comments	medium: cross-over, but not randomized, no funding indicated, low subject number		

Title	**Tobacco Use During a Clinical Trial of Mecamylamine for Alcohol Dependence: Medication Effects on Smoking and Associations With Reductions in Drinking**		
First Author	**Roberts, W., 2018**	**Source**	**30243424**
Level of evidence	1a	**Study type**	Reanalysis of data of a clinical trial to treat alcohol use disorder (AUD) with a nicotinic acetylcholine receptor (nAChR) antagonist to evaluate the effects of

			mecamylamine on smoking and the association between reductions in alcohol use and smoking. Smoking was assessed prior to randomization and tracked throughout the course of the 12-week medication treatment phase. Participants were categorized as treatment responders or non-responders based on their changes in drinking over the course of the clinical trial.
Study quality	medium: cross-over, but not randomized, no funding indicated, low subject number		
Participants	n=76		
Patient characteristics	Subgroup of smokers who participated in the clinical trial of mecamylamine (10 mg/day) to treat their AUD.		
Intervention	Mecamylamine		
Comparison	Placebo		
Length of follow-up	12 weeks		
Outcome and effect size	Reduction in smoking over the course of the clinical trial without significant differences in smoking outcomes between the mecamylamine and placebo groups: no detectable effect of mecylamine on smoking outcomes. Among moderate/high dependence smokers, those who successfully reduced drinking showed a significant reduction in cigarettes smoked per day over the clinical trial → opportunity for patients being treated for AUD to reduce their smoking.		
Funding			
Comments	deals with smoking as outcome variable		

Title	**Pilot Investigation: Randomized-Controlled Analog Trial for Alcohol and Tobacco Smoking Co-Addiction Using Contingency Management**		
First Author	**Orr, M., 2018**	**Source**	**29561290**
Level of evidence	1a	**Study type**	RCT with a 2 x 2 factorial design ([CM vs. noncontingent control (NC) for alcohol] × [CM vs. NC for smoking tobacco])
Study quality	high (RCT)		
Participants	n=43		
Patient characteristics	Heavy drinking smokers		
Intervention	CM for alcohol abstinence, smoking abstinence, both drugs, or neither drug.		
Comparison	NC for alcohol abstinence, smoking abstinence, both drugs, or neither drug		
Length of follow-up			
Outcome and effect size	Alcohol intake (through urinary ethyl glucuronide) and tobacco smoking (through urinary cotinine) as the primary outcomes: Compared with the NC for alcohol and tobacco smoking group, both the CM for the tobacco smoking group (OR 12.03; 95% CI [1.50|96.31]) and the CM for the alcohol group (OR 37.55; 95% CI [4.86|290.17]) submitted significantly more tobacco-abstinent urinalyses. Similarly, compared with the NC for the alcohol and tobacco group, both the CM for smoking (OR 2.57; 95% CI [1.00|6.60]) and the CM for alcohol groups (OR 3.96; 95% CI [1.47|10.62]) submitted significantly more alcohol-abstinent urinalyses: cross-over effects of CM on indirect treatment targets		
Funding			
Comments	Should be taken into account		

Title	**Nicotine-Use/Smoking Is Associated With the Efficacy of Naltrexone in the Treatment of Alcohol Dependence**		
First Author	**Anton, R. F., 2018**	**Source**	**29431852**
Level of evidence	1a	**Study type**	RCT
Study quality	high (RCT)		
Participants	n=146		
Patient characteristics	Individuals meeting DSM-IV criteria for alcohol dependence who were genotyped for the OPRM1 A118G SNP and who did, or did not, use nicotine/cigarettes		
Intervention	Naltrexone (50mg/d)		

Comparison	Placebo
Length of follow-up	16 weeks
Outcome and effect size	Nicotine-use/smoking status significantly interacted with medication in reducing percent heavy drinking days (PHDD) during the trial (p=0.003), such that nicotine-users/smokers showed significantly lower PHDD on naltrexone versus placebo (p=0.0001, Cohen's d=0.89), while nonusers showed no significant difference between naltrexone and placebo (p=0.95, Cohen's d=0.02). Similar effects were shown for drinks per day and percent days drinking. The superiority of naltrexone over placebo on PHDD reduction in nicotine-users/smokers was confirmed with %dCDT (Cohen's d range 0.3 to 0.9 over the study). Naltrexone did not significantly change cigarette use in smokers, and change in use did not influence naltrexone's effect on PHDD: These data confirm past findings that naltrexone is more efficacious in those who use nicotine/cigarettes. Compared to previous work on the OPRM1 A118G SNP, it appears that nicotine-use might be a more salient predictor of naltrexone treatment response. While naltrexone did not change cigarette use during the study, and smoking change was not related to alcohol reduction, it should be noted that participants were not seeking smoking cessation and MM did not address this issue.
Funding	
Comments	Should be taken into account

Title	**A Randomized Trial Evaluating Whether Topiramate Aids Smoking Cessation and Prevents Alcohol Relapse in Recovering Alcohol-Dependent Men**		
First Author	**Anthenelli, R., 2017**	**Source**	**28029173**
Level of evidence	1a	**Study type**	Evaluated topiramate in abstinent alcohol-dependent men to assess whether this medication (I) promotes smoking cessation and (II) prevents alcohol and other drug relapse in the context of smoking cessation treatment.
Study quality	high (RCT)		
Participants	n=129		
Patient characteristics	Alcohol-dependent male smokers (80% with other substance use disorders)		
Intervention	Topiramate 200mg/d		
Comparison	Placebo		
Length of follow-up	24m		
Outcome and effect size	Only a small proportion (7.9%) of topiramate-treated participants were able to quit smoking, and this cessation rate was similar to placebo (10.6%, OR=1.60, 95% CI [0.4|6.5], p=0.51). Roughly 30% of the sample had a documented relapse to drinking or drug use during the study, and these rates were similar in the topiramate (20/63; 31.8%) and placebo groups (18/66; 27.3%; p=0.58). Results of a longitudinal logistic regression model examining time to any alcohol relapse revealed no medication effect. **Summary**: no effect of topiramate neither on smoking cessation nor on alcohol or drug relapse		
Funding			
Comments	Effects of topiramat on alcohol and smocking were studied separately.		

Title	**A Randomized Trial of Contingency Management for Smoking Cessation During Intensive Outpatient Alcohol Treatment**		
First Author	**Cooney, J., 2017**	**Source**	**27542442**
Level of evidence	1a	**Study type**	RCT to evaluate the efficacy of contingency management (CM) for smoking cessation for smokers with alcohol abuse or dependence delivered concurrently with intensive outpatient alcohol treatment. The study also explored the indirect effects of CM smoking treatment and smoking cessation on alcohol and drug use outcomes
Study quality	high (RCT)		
Participants			
Patient characteristics	Alcohol abuse/dependent smokers		

Intervention	Cognitive behavioral therapy plus nicotine replacement therapy plus contingency management (CBT+NRT+CM)
Comparison	Cognitive behavior therapy plus nicotine replacement therapy (CBT+NRT)
Length of follow-up	6 months
Outcome and effect size	Participants in the CBT+NRT+CM condition were significantly more likely to be cigarette abstinent at the end of treatment ($\chi2(1)=8.48$, $p=0.004$) with approximately double the carbon monoxide confirmed quit rate (60%) compared with the CBT+NRT condition (29%). At the one-month and six-month time-points there were nonsignificant differences in smoking abstinence outcomes by condition. Smoking treatment condition did not directly affect alcohol abstinence outcomes, but we observed an indirect effect of smoking treatment on alcohol and drug abstinence at one-month follow-up that was mediated by smoking cessation at the end of treatment. Adding CM to an evidence-based smoking cessation treatment that included medication and behavioral counseling doubled the quit rate at the end of treatment. This finding provides strong evidence for the efficacy of CM for helping alcohol dependent smokers reach the milestone of initial smoking abstinence.
Funding	
Comments	Deals with smoking as outcome variable.

Title	**The Impact of Smoking Very Low Nicotine Content Cigarettes on Alcohol Use**		
First Author	**Dermody, S., 2016**	**Source**	**26916879**
Level of evidence	1a	**Study type**	7-arm, double-blind, randomized clinical trial at 10 U.S.-based sites
Study quality	high (sophisticted study design)		
Participants	n=403		
Patient characteristics	Daily smokers not currently interested in quitting and currently drinking alcohol. Inclusion criteria: ≥ age 18; smoking ≥ 5 CPD; expired carbon monoxide (CO) > 8 ppm; or urine cotinine > 100 ng/ml. Exclusion criteria: intention to quit smoking in next 30 days; regular use of other tobacco products or frequent binge drinking (i.e., > 9 of past 30 days) 1; significant or unstable medical/psychiatric conditions; positive illicit drug toxicology screen other than cannabis; pregnancy		
Intervention	Tobacco smoking with moderate nicotine content (5.2 mg/g nicotine, 9 mg tar) or very low nicotine content (VLNC; 0.4 to 2.4 mg/g, 9 to 13 mg tar)		
Comparison	Normal nicotine content (NNC; 15.8 mg/g, 9 mg tar)		
Length of follow-up	6m		
Outcome and effect size	Alcohol use trajectories: The best-fitting model was piecewise, v2=66.99, p<0.001; RMSEA=0.07 (0.05, 0.09); CFI=0.97; TLI=0.98; AIC=8,115; BIC=8,167. On average, alcohol use increased from baseline to week 2 (SL1=0.08, 99% CI [0.02 | 0.16], p<0.001), with no significant variability (SL1 variance equaled zero); thereafter, it did not change (i.e., weeks 2 to 6; SL2=0.002, 95% CI [0.03 | 0.03], p>0.10), but demonstrated significant variability (SL2 variance=0.04, 99% CI [0.004 | 0.09]). Effect: During the first 2 weeks, the moderate nicotine condition (5.2 mg/g) exhibited a significantly smaller increase in drinking relative to the NNC cigarette condition. The 0.4 mg/g condition demonstrated a qualitatively smaller, but nonsignificant, increase in alcohol use relative to the NNC control condition. During the last 4 weeks, no conditions differed from NNC control, regardless of covariates (ps>0.10). When the intercept for the alcohol use trajectory was centered at week 6, there were no significant differences in week 6 alcohol use between the NNC cigarette and reduced conditions (ps>0.10. The combined VLNC conditions (0.4 to 2.4 mg/g) showed a qualitatively smaller increase during the first 2 weeks compared to the NNC condition (p<0.10) and no difference during the last 4 weeks, regardless of covariates. There were no significant moderators (ps>0.10). **Summary**: Over time, reduced nicotine exposure and smoking rate mediated effects of VLNC cigarette use on reduced alcohol use. There was no evidence of compensatory drinking in response to nicotine reduction or nicotine withdrawal, even among subgroups expected to be at greater risk (e.g., relatively heavier drinkers, highly nicotine-dependent individuals). Compensatory drinking is unlikely to occur in response to switching to VLNC cigarettes. In contrast, reducing the nicotine content of cigarettes may reduce alcohol use		

Funding	
Comments	Should be taken into account

Title	**Defining and Predicting Short-Term Alcohol Use Changes During a Smoking Cessation Attempt**		
First Author	**Berg, K. M., 2015**	**Source**	**25997014**
Level of evidence	1a	**Study type**	Secondary analysis of a randomized, placebo-controlled trial evaluating the efficacy of five tobacco cessation pharmacotherapies
Study quality	high (RCT with high number of participants)		
Participants	n=1301		
Patient characteristics	Participants with smoking and drinking		
Intervention	Fibe tobacco sessation therapies		
Comparison	Placebo		
Length of follow-up	2 weeks after target quit date (TQD)		
Outcome and effect size	Generally, alcohol use decreased post-TQD. Smokers who reported less pre-quit alcohol use, as well as smokers who were female, non-white, and had a history of alcohol dependence tended to use less alcohol post-quit. Pre- and post-quit alcohol use were more strongly related among men and among those without a history of alcohol dependence. Summary: For most smokers, alcohol use decreased following smoking cessation. These results suggest that the expectation should be of decreased alcohol use post cessation. However, attention may be warranted for those who drink higher amounts of alcohol pre-cessation because they may be more likely to drink more in the post-quit period which may influence smoking cessation success.		
Funding			
Comments	Should be taken into account.		

Title	**Concurrent Alcohol and Tobacco Treatment: Effect on Daily Process Measures of Alcohol Relapse Risk**		
First Author	**Cooney, N. L., 2015**	**Source**	**25622198**
Level of evidence	1a	**Study type**	RCT to compare the effects of alcohol treatment along with concurrent smoking treatment or delayed smoking treatment on process measures related to alcohol relapse risk.
Study quality	high (RCT with high number of participants)		
Participants	n=151		
Patient characteristics	Alcohol dependent smokers who were enrolled in an intensive outpatient alcohol treatment program and were interested in smoking cessation		
Intervention	Concurrent smoking cessation (CSC) intervention		
Comparison	Waiting list for delayed smoking cessation (DSC)		
Length of follow-up	13w		
Outcome and effect size	Analysis of smoking abstinence after 2 weeks (end of intensive alcohol treatment) found 50.5% of CSC and 2.2% of DSC participants were classified CO-verified 7-day point prevalence abstinent ($\chi2(1)=32.49$; N=151; $p<0.001$). At 13 weeks, 19.0% of CSC and 0.0% of DSC participants were classified abstinent ($\chi2(1)=8.39$; N=151; $p<0.01$). Analyses of drinking over time from baseline to Month 3 (Week 13) indicated that participants in both treatment conditions dramatically decreased their rates of heavy drinking from 58% PDH to a mean of 3% PDH from Month 1 to Month 3 (F(time; 3,524)=219.00; $p<0.001$), with no significant differences by treatment condition (F(treatment; 1,524)=2.04; $p>0.15$), and no interaction of treatment x time (F(treatment x time; 1,524)=0.16; $p>.90$). Analysis of PDA also indicated that patients in both treatment conditions increased the frequency of alcohol abstinent days from a mean of 40% days abstinent at baseline to a mean of 95% days abstinent across the 3-month follow-up (F(time; 3,526)=207.66; $p<0.001$). Again there were no differences attributable to treatment (F(treatment; 1,526)=1.85; $p>0.15$) and no interaction of treatment x time (F(treatment x time; 1,526)=0.28; $p>0.80$). On daily IVR		

	assessments, CSC participants had significantly lower positive alcohol outcome expectancies relative to DSC participants. Multilevel modeling (MLM) analyses of within-person effects across the 12 weeks of daily monitoring showed that daily smoking abstinence was significantly associated with same day reports of lower alcohol consumption, lower urge to drink, lower negative affect, lower positive alcohol outcome expectancies, greater alcohol abstinence self-efficacy, greater alcohol abstinence readiness to change, and greater perceived self-control demands. Summary: support for recommending smoking intervention concurrent with intensive outpatient alcohol treatment
Funding	Grant R01AA011197 from the National Institute on Alcoholism and Alcohol Abuse to Ned Cooney. Kevin Sevarino's work on this article was also supported by a Mental Illness Research, Education and Clinical Centers (MIRECC) award from the Department of Veterans Affairs
Comments	

Title	**Nicotine Interactions With Low-Dose Alcohol: Pharmacological Influences on Smoking and Drinking Motivation**		
First Author	**Oliver, J. A., 2013**	**Source**	**24364618**
Level of evidence	1a	**Study type**	RCT to test the separate and combined pharmacological effects of nicotine and a low dose of alcohol (equivalent to 1-2 standard drinks) on substance use motivation using a double-blind and fully crossed within-subjects design
Study quality	high (RCT with sufficient number of participants)		
Participants	n=87		
Patient characteristics	Participants with a wide range of smoking and drinking patterns		
Intervention	4 counterbalanced experimental sessions with alcohol or placebo beverage and nicotine or placebo cigarette		
Comparison	Placebo		
Length of follow-up			
Outcome and effect size	Impact of drug administration (alcohol or nicotine) on craving to smoke, craving to drink, affect, and liking of the beverage and cigarette: combined administration produced higher cravings to smoke for the entire sample, as well as higher cravings to drink among women and lighter drinkers. Heavier users of either alcohol or cigarettes also exhibited enhanced sensitivity to the effects of either drug in isolation. Separate, but not interactive, effects of alcohol and nicotine on mood were observed as well as both same-drug and cross-drug effects on beverage and cigarette liking. Summary: interactive pharmacological effects of nicotine and low doses of alcohol play an important role in motivating contemporaneous use and suggest roles for cross-reinforcement and cross-tolerance in the development and maintenance of alcohol and nicotine use and dependence		
Funding			
Comments			

3.6.9 Illegale Drogen

Title	**Treatment of Cocaine and Alcohol Dependence With Psychotherapy and Disulfiram**		
First Author	**Carroll, K. M., 1998**	**Source**	**9692270**
Level of evidence	2b	**Study type**	RCT, single blind
Study quality	high risk of attrition bias (incomplete outcome data), unclear risk of selection bias (random sequence generation and allocation concealment)		
Participants	n=122 in total, n=42 with only psychosocial interventions		
Patient characteristics	Cocaine / alcohol abusers in an outpatient clinic meeting current DSM-3-R criteria for cocaine dependence, and for concurrent alcohol dependence (85%) or alcohol abuse (15%).		
Intervention	one of five treatments delivered over 12 weeks: cognitive behavioral coping skills training		

	(CBCST) plus disulfiram; twelve step facilitation (TSF) plus disulfiram; clinical management (CM) plus disulfiram; CBCST plus no medication (n=24); TSF plus no medication (n=18)
Comparison	CBT vs. TSF vs. CM
Length of follow-up	12-weekly within 12 months
Outcome and effect size	**Comparison of the two psychotherapy-arms:** No significant difference between CBCST and TSF regarding 1a) the number of participants achieving three or more weeks of consecutive alcohol abstinence (risk ratio (RR)=1.96, 95% CI [0.43 | 8.94]) and 1b) the maximum number of weeks of consecutive alcohol abstinence during treatment (mean difference (MD)=0.40, 95% CI [-1.14 | 1.94]) as well as 1c) alcohol abstinence during follow-up after one year (RR=2.38, 95% CI [0.10 | 55.06]); 2.) retention as number of people who completed all treatment sessions (RR=0.89, 95% CI [0.62 | 1.29]), 3a) maximum number of weeks of consecutive abstinence from cocaine (MD=0.80, 95% CI [-0.70 | 2.30]), 3b) and number of participants achieving three or more weeks of consecutive abstinence from cocaine during treatment (RR=1.10, 95% CI [0.42 | 2.88]), as well as 3c) abstinence from cocaine during follow-up after one year (RR=0.39, 95% CI [0.04 | 3.41]). **Study as a whole:** Disulfiram treatment was associated with significantly better retention in treatment, as well as longer duration of abstinence from alcohol and cocaine use. The two active psychotherapies (CBT and TSF) were associated with reduced cocaine use over time compared with supportive psychotherapy (CM). Cocaine and alcohol use were strongly related throughout treatment, particularly for subjects treated with disulfiram. Conclusion: For the large proportion of cocaine-dependent individuals who also abuse alcohol, disulfiram combined with outpatient psychotherapy may be a promising treatment strategy. This study underlines (a) the significance of alcohol use among treatment-seeking cocaine abusers, (b) the promise of the strategy of treating co-morbid disorders among drug-dependent individuals, and (c) the importance of combining psychotherapy and pharmacotherapy in the treatment of drug use disorders.
Funding	National Institutes of Health
Comments	

Title	**Screening and Brief Interventions for Illicit Drug Use and Alcohol Use in Methadone Maintained Opiate-Dependent Patients: Results of a Pilot Cluster Randomized Controlled Trial Feasibility Study**		
First Author	**Darker, C. D., 2016**	**Source**	**27158853**
Level of evidence	2b	**Study type**	Cluster - RCT
Study quality	Unclear risk of bias regarding selection (random sequence generation and allocation concealment) and detection (blindness of participants and personnel not possible for the kind of intervention).		
Participants	n=465, subgroup with alcohol as the target substance BI was given for		
Patient characteristics	Participants with opioid use disorder receiving methadone who also had concurrent problem alcohol use, as determined by positive ASSIST (alcohol, smoking, and substance involvement screening test) - positive cases in 4 addiction treatment centers (opioid agonist clinic)		
Intervention	Single clinician delivered brief intervention (BI)		
Comparison	Treatment as usual (TAU)		
Length of follow-up	3 months		
Outcome and effect size	Statistically significant difference between global risk score for the intervention (x=39.36 +/- 25.91) group and the control group (x=45.27 +/- 27.52) at 3-month follow-up (t(341)=-2.07, p<0.05). No statistically significant difference between BI and TAU regarding AUDIT and ASSIST scores at three months (standardised mean difference (SMD)=0.07, 95% CI [-0.24|0.3]).		
Funding	Health Research Board of Ireland		
Comments			

Title	**Alcohol-related Brief Intervention in Patients Treated for Opiate or Cocaine Dependence: A Randomized Controlled Study**		
First Author	**Feldman, N., 2011**	**Source**	**21849027**
Level of evidence	2b	**Study type**	RCT
Study quality	High risk of detection bias (no blinding assessment), unclear risk of attrition bias (incomplete outcome data)		
Participants	n=110		
Patient characteristics	Among adult outpatients treated for opioid or cocaine dependence in Switzerland those with AUDIT scores that indicated excessive alcohol drinking or dependence i.e. excessive drinking (7 ≤ AUDIT score <13 for men and 6 ≤ AUDIT score <13 for women); and alcohol use disorder (score > 13)		
Intervention	Treatment as usual and brief intervention (n=50)		
Comparison	Treatment as usual (n=60)		
Length of follow-up	3 and 9 months		
Outcome and effect size	No significant difference between BI and TAU regarding decreased alcohol use (RR=1.13, 95% CI [0.67|- 1.93]) and number of drinks per week at month 3 (MD=0.70, 95% CI [-3.85| 5.25]) as well as AUDIT scores (MD=2.30, 95% CI [-0.58|- 5.18]), decreased alcohol use (RR=1.09, 95% CI [0.62|1.92]) and number of drinks per week (MD=-0.30, 95% CI [-4.79|4.19]) at month 9.		
Funding	not reported		
Comments			

Title	**Feasibility of alcohol screening among patients receiving opioid treatment in primary care.**		
First Author	**Henihan, A. M., 2016**	**Source**	**27816057**
Level of evidence	2b	**Study type**	Cluster - RCT
Study quality	High risk of detection bias (outcome assessors not blinded)		
Participants	n=81		
Patient characteristics	Problem alcohol use among people receiving opioid agonist treatment in a primary care setting		
Intervention	Brief intervention (n=34)		
Comparison	Treatment as usual (n=47)		
Length of follow-up	3 months		
Outcome and effect size	Of 149 practices that were invited, 19 (12.8%) agreed to participate. At follow up, 13 (81.3%) practices with 81 (62.8%) patients were retained. Alcohol screening rates in the intervention group were higher at follow up than in the control group (53% versus 26%) as were brief intervention rates (47% versus 19%). No statistically significant difference in AUDIT or ASSIST scores at three months between BI and TAU (standardised mean difference (SMD) 0.07, 95% CI [-0.24|0.3]).		
Funding	Health Research Board of Ireland		
Comments			

Title	**Effect of motivational interviewing on reduction of alcohol use.**		
First Author	**Nyamathi, A., 2010**	**Source**	**19836904**
Level of evidence	2b	**Study type**	open label RCT, 3 arms
Study quality	High risk of detection bias (open label study), unclear risk of attrition bias (incomplete outcome data)		
Participants	n=256		
Patient characteristics	Methadone-maintained (MM) clients reporting moderate-to-heavy alcohol use based on questions from the ASI attending one of five MM outpatient clinics in the Los Angeles area		
Intervention	Nurse-led hepatitis health promotion (HHP; n=87)		
Comparison	MI delivered in group sessions (MI-group; n=79), or MI delivered one-on-one sessions (MI-single, n=90)		

Length of follow-up	6 months
Outcome and effect size	Significant reduction in self-reported alcohol use from a median of 90 drinks/month at baseline to 60 drinks/month at 6-month follow-up (p<0.05) without differences by condition: no significant difference between MI and educational intervention regarding standard drinks consumed per day (MD=-0.20, 95% CI [-1.76 | 1.36]), greater than 50% reduction in number of standard drinks consumed per day (RR=1.01, 95% [CI 0.77 | 1.31]), and abstinence from alcohol over the last 30 days (RR=0.93, 95% CI [0.57 | 1.50]), and retention at the end of treatment (RR=0.96, 95% CI [0.87 | 1.06]), as well as frequency of illicit drug use as measured by Addiction Severity Index (ASI drug; MD=0.00, 95% CI [-0.03 | 0.03]) and frequency for all drugs taken (MD=-0.00, 95% CI [-0.34 | 0.34]).
Funding	National Institutes of Health
Comments	

Title	**A Randomized Trial of a Brief Alcohol Intervention for Needle Exchangers (BRAINE)**		
First Author	**Stein, M. D., 2002**	**Source**	**12084138**
Level of evidence	2b	**Study type**	RCT
Study quality	Unclear risks of bias regarding selection (random sequence generation and allocation concealment) as well as attrition (incomplete outcome data)		
Participants	n=187		
Patient characteristics	AUDIT-positive (>8) active injection drug users		
Intervention	Two 1-hour therapist brief MI sessions following assessment visits, 1 month apart, focusing on alcohol use and HIV risk-taking		
Comparison	Assessment only		
Length of follow-up	6 months		
Outcome and effect size	Significant difference between BMI and assessment only regarding alcohol use as seven or more drinking days' reduction in the past 30 days (RR=1.67, 95% CI [1.08 | 2.60], p=0.02; moderate-quality evidence); no significant difference between Brief motivational interviewing (BMI) versus assessment only control regarding number of days in the past 30 days with alcohol use after one (MD=-0.30, 95% CI [-3.38 | 2.78]) and six months (MD=-1.50, 95% CI [-4.56 | 1.56]), 25 (RR=1.23, 95% CI [0.96 | 1.57]), 50 (RR=1.27, 95% CI [0.96 | 1.68]), and 75% reduction of drinking days in the past 30 days (RR=1.21, 95% CI [0.84 | 1.75]), one or more drinking days´ reduction in the past 30 days (RR=1.12, 95% CI [0.91 | 1.38]) as well as number of people who completed all treatment sessions (RR=0.98, 95% CI 0.94 | 1.02).		
Funding	National Institutes of Health		
Comments			

Title	**Intensive motivational interviewing for women with concurrent alcohol problems and methamphetamine dependence**		
First Author	**Korcha, R. A., 2014**	**Source**	**24074649**
Level of evidence	2b	**Study type**	open label RCT
Study quality	High risk of detection bias (outcome assessment not blinded)		
Participants	n=163		
Patient characteristics	Diagnosis of both methamphetamine use disorder and alcohol abuse/dependence (DSM-IV criteria)		
Intervention	Intensive 9-session version of MI (intensive MI; n=80)		
Comparison	Standard single MI session (Standard MI, n=83)		
Length of follow-up	6 months		
Outcome and effect size	No significant difference between intensive MI and standard MI regarding alcohol Addiction Severity Index at two (MD=0.03, 95% CI [-0.02 | 0.08]), four (MD=-0.01, 95% CI [-0.06 | 0.04]) and six months (MD=-0.02, 95% CI [-0.07 | 0.03]), retention on the study (RR=17.63, 95% CI [1.03 | 300.48]) and days methamphetamine abstinent in the past six months (MD=3.91, 95% CI [-5.28 | 13.10]). Only women with co-occurring alcohol		

	problems in the Intensive MI condition reduced the severity of their alcohol problems significantly more than women in the Standard MI condition with stronger perceived alliance with the therapist being inversely associated with alcohol problem severity scores.
Funding	National Institutes of Health
Comments	

Title	**Psychosocial Interventions to Reduce Alcohol Consumption in Concurrent Problem Alcohol and Illicit Drug Users**		
First Author	**Klimas, J., 2018**	**Source**	**30521696**
Level of evidence	1a	**Study type**	Cochrane review
Study quality	Medium (RCTs, but most of them with high or unclear risk of bias)		
Participants	n=825		
Patient characteristics	People who use illicit drugs (PWIDs) aged at least 18 years with concurrent problem alcohol use		
Intervention	Psychosocial interventions: cognitive-behavioral coping skills training (CBCST, 1 study), twelve-step program (TSP, 1 study), brief intervention (BI, 3 studies), motivational interviewing (MI, 2 studies), and brief motivational interviewing (BMI, 1 study).		
Comparison	Other psychosocial intervention or treatment as usual (TAU)		
Length of follow-up	div.		
Outcome and effect size	- CBCST vs. TSP (1 study, n=41): no significant difference between groups for either of the primary outcomes (alcohol abstinence assessed with Substance Abuse Calendar and breathalyser at one year: risk ratio (RR)=2.38 (95% CI [0.10 | 55.06]); and retention in treatment, measured at end of treatment: RR=0.89 (95% CI [0.62 | 1.29]), or for any of the secondary outcomes reported (very low quality of evidence for the primary outcomes). - BI vs. TAU (3 studies, n=197): no significant difference between groups for either of the primary outcomes (alcohol use, measured as scores on AUDIT or Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) at three months: standardised mean difference (SMD)=0.07 (95% CI [-0.24 | 0.37]); and retention in treatment, measured at three months: RR=0.94 (95% CI [0.78 | 1.13]), or for any of the secondary outcomes reported (low quality of evidence for the primary outcomes). - MI vs. TAU or educational intervention only (3 studies, n=462): no significant difference between groups for either of the primary outcomes (alcohol use, measured as scores on the AUDIT or ASSIST at three months: SMD=0.04 (95% CI [-0.29 | 0.37]); and retention in treatment, measured at three months: RR=0.93 (95% CI [0.60 | 1.43]), or for any of the secondary outcomes reported (low quality of evidence for the primary outcomes). - Brief motivational intervention (BMI) vs. assessment only (1 study, n=187): More people reduced alcohol use (by seven or more days in the past month, measured at six months) in the BMI group than in the control group (RR=1.67; 95% CI [1.08 | 2.60]), no difference between groups for the other primary outcome, retention in treatment, measured at end of treatment: RR=0.98 (95% CI [0.94 | 1.02]), or for any of the secondary outcomes reported (moderate quality of evidence for the primary outcomes). - MI (intensive) vs. MI (1 study, n=163): no significant difference between groups for either of the primary outcomes (alcohol use, measured using the Addiction Severity Index-alcohol score (ASI) at two months: MD=0.03 (95% CI [0.02 | 0.08]); and retention in treatment, measured at end of treatment: RR=17.63 (95% CI [1.03 | 300.48), or for any of the secondary outcomes reported (low quality of evidence for the primary outcomes). => Summary: Low to very low-quality evidence to suggest that there is no difference in effectiveness between different types of psychosocial interventions to reduce alcohol consumption among people who use illicit drugs, and that brief interventions are not superior to assessment-only or to treatment as usual because of the paucity of the data and the low quality of the retrieved studies.		
Funding			
Comments	Good study that should be taken into account because it proves the evidence which is missing elsewhere		

3.7 Alters- und Geschlechtsspezifische Populationen

3.7.1 Kinder und Jugendliche

Title	**A Brief Motivational Interview in a pediatric emergency department, plus 10-day telephone follow-up, increases attempts to quit drinking among youth and young adults who screen positive for problematic drinking.**		
First Author	**Bernstein, J., 2010**	**Source**	**20670329**
Level of evidence	1b	**Study type**	RCT
Study quality	Well documented study		
Participants	Total N=853 with IG n=283 and 2 controls to adjust for assessment reactivity: AC (standard assessed) n=284, and MAC (minimally assessed) n=286		
Patient characteristics	Patients aged 14–21 years, screened positive on the Alcohol Use Disorders Identification Test (AUDIT) or for binge drinking or for high-risk behaviors.		
Intervention	IG) Peer-conducted motivational intervention, referral to community resources and treatment if indicated, and a 10-day booster in addition to assessment		
Comparison	Assessment control (AC): standard assessment and handout on alcohol risks plus list of treatment facilities. Minimum assessment control (MAC): handout and list only		
Length of follow-up	3 and 12-month follow-up (FU)		
Outcome and effect size	According to 3-month FU [12-month FU], a significantly larger proportion of IG made efforts to quit drinking AOR=2.01, p<.001 [AOR=1.77, p<.007] and to be careful about situations when drinking AOR=1.72, p<.026 [AOR=1.66, p<.029], compared to AC; consumption declined in IG and AC from baseline to 3-month to 12-month FU though effects were non-significant, improvements in alcohol-related consequences or in alcohol-related risk behaviours between IG and AC were non-significant. [Self-reports]		
Funding	NIAAA		
Comments			

Title	**Twelve-month follow-up of aftercare for adolescents with alcohol use disorders.**		
First Author	**Burleson, J., 2012**	**Source**	**21868186**
Level of evidence	1b	**Study type**	RCT
Study quality	Length of aftercare interventions not reported; otherwise well documented study		
Participants	Total N=121, Active aftercare: in-person n=38, brief telephone n=42. No-active aftercare (controls) n=41		
Patient characteristics	Adolescents aged 13-18 (M age=16.0, 80% male), diagnosed with AUD		
Intervention	All received CBT, only completers remained in the study: 2 intervention groups: in-person aftercare or brief telephone aftercare; controls: no-active aftercare		
Comparison	Active aftercare (in-person or brief telephone) vs. no-active aftercare		
Length of follow-up	-, 6,and 12-month FU		
Outcome and effect size	Frequency and number of drinks per occasion were outcome measures, both increased in either intervention. In an HLM, within-person and initial status variance [which is equivalent for baseline-adjustment in ANCOVA], were controlled. In the 12-month FU, active aftercare revealed an impact of 0.121 (SE=0.070, p<.085) in decreasing frequency/number of drinks, showing no difference between in-person and brief telephone interventions. As moderators, age of youths and an existing externalizing disorder had strong impacts on drinking behaviour at all time points regardless of condition. [Self-reports]		
Funding	NIAAA		
Comments	.		

Title	**A systematic and methodological review of interventions for young people experiencing alcohol-related harm**

First Author	Calabria, B., 2011	Source	21371154
Level of evidence	1a	Study type	Systematic Review
Study quality	High heterogeneity in included studies, due to biases in studies no effect sizes computed, review is well documented and transparent		
Participants	A total of N=973 patients in 9 studies; n of patients varied from 6 to 282 across included studies.		
Patient characteristics	Search term 'youth', 12-25 years old across studies, 17-90% male, participants had to meet any of four alcohol-related criteria: diagnosis, screening, referral, or high-risk behaviour (s.a. DUI)		
Intervention	Different interventions: 8 counselling-based (CBT, family therapy, MI, CBT-based peer groups, community reinforcement) 1 medically-based (ondansetron)		
Comparison	Not specified in the review; comparisons to wait-list groups or alternative treatment (group or individual treatment)		
Length of follow-up	Not specified in the review		
Outcome and effect size	No meta-analysis conducted due to study heterogeneity and biases (no effect sizes computed), studies reported weak to moderate effects found on alcohol use; authors summarize that the most promising approaches are CBT, family therapy, and community reinforcement. [Miscellaneous outcome measures]		
Funding	Alcohol Education and Rehabilitation Foundation		
Comments	.		

Title	Brief strategic family therapy versus community control: engagement, retention, and an exploration of the moderating role of adolescent symptom severity		
First Author	Coatsworth, J. D., 2001	Source	11676271
Level of evidence	2b	Study type	Randomized-controlled; ITT-analyses
Study quality	Not focused on substance abuse, control condition very unspecific, outcome variables are not related to substance use; no follow-up.		
Participants	104 families; n=71 adolescents in BSFT, n=31 in control condition (CC)		
Patient characteristics	Mean age=13.1 (75% male). 104 African-American and Hispanic families with adolescents revealing externalizing problems or internalizing problems or academic problems or initiation of AOD. Screening via Revised Behavior Problem Checklist (RBPC).		
Intervention	Brief Strategic Family Therapy (BFST), unspecific controls		
Comparison	Combined individual and family-based intervention delivered by a community agency [CC or TAU]		
Length of follow-up	No follow-up		
Outcome and effect size	Retention and engagement rates: Chi2 analysis of engagement rates revealed that BSFT was significantly more successful in engaging cases (43/53; 81%) than CC (31/51; 61%): $\chi2(1; N=104)=5.2$, $p<0.05$. $\chi2$-analysis of retention rates in treatment revealed that, among those engaged, a higher percentage of BSFT cases (31/43; 72%) were retained when compared to CC (13/31: 42%): $\chi2(1; N=74)=6.8$, $p<0.01$. In post-hoc analyses of clinical scales, effect-sizes g and proportions of Reliable Change Improvement were in favour of retained BSFT adolescents [retained CC adolescents]: for Conduct Disorder g=1.02/52% [g=.34/23%] and for Anxiety/Withdrawal g=.56/23% [g=.43/23%]. [Self-reports]		
Funding			
Comments	.		

Title	Assessing the effectiveness of community-based substance abuse treatment for adolescents		
First Author	Dasinger, L. K., 2004	Source	15152707
Level of evidence	1a	Study type	Systematic Review (multi-site, multi-program, TAU)
Study quality	High heterogeneity in included studies, review is well documented and transparent.		
Participants	A total of N=1.057, with n=238 in Long-Term Residential treatment (LTR), n=513 in Short-Term Residential treatment (STR); n=306 in Outpatient or Intensive Outpatient treatment (OP/IOP).		
Patient characteristics	Screenings via DSM-IV-related GAIN interviews; ages and proportion of males not reported		

Intervention	LTR, SRT, OP/IOP are TAU but varying interventions
Comparison	3 types of program lengths in differing modalities are compared
Length of follow-up	12-month follow-up
Outcome and effect size	Primary outcome was AOD use L3M after intake, secondary outcome was relapse, with 'relapse' defined as increase in AOD use within L3M to L12M after intake. Significant reduction rates (p<0.002) in AOD use were found in 7 out of 10 sites, 85% for LTR, 70.9% for STR, 30.0% for OP/IOP. No significant relapse rates were found for one LTR-site (4.2%) and for OP/IOP-sites combined (11.0%). In pairwise t-test comparisons, results for L3M AOD use were in favour [> better than] of LTR > STR > OP/IOP (p<.001), results for L12M AOD use were in favour of LTR > OP/IOP > STR (p<.002). [Self-reports]
Funding	
Comments	.

Title	**A critical review of adolescent substance abuse group treatments.**		
First Author	**Engle, B., 2009**	**Source**	**20183675**
Level of evidence	1a	**Study type**	Systematic Review
Study quality	In included studies, information about treatment factors (group structure and processes) is poor from a group research view. Review is well documented and transparent		
Participants	13 studies including a total N=1.571, with n of patients varying from 13 to 300 across included studies		
Patient characteristics	Inclusion criteria for patients: aged 11-20 years with AOD use disorders (at least abuse), included studies were RCT of group interventions addressing AOD and reporting AOD outcome.		
Intervention	Group interventions such as Motivational Enhancement Therapy (MET), Cognitive Behavioral Therapy (CBT), Adolescent Group Therapy (AGT), Psychoeducational Group (PET), Minnesota 12-Steps, and other group-based treatments		
Comparison	Comparison to wait-list groups or alternative treatment (group or individual treatment).		
Length of follow-up	No FU was in 23% of studies, 6-month FU was in 23%, 7-9 month FU in 23%, 12-month FU in 23%, and 15-month FU in 8% of studies.		
Outcome and effect size	2 out of 13 interventions were "possibly efficacious" in reducing AOD use (frequency of use, reduction amount): Psycho-education Group at 7-month FU and Adolescent Group Therapy AGT at 12-month FU, revealing a "sleeper effect" in efficacy. [Further statistical specifications not given in the review] [Self-reports]		
Funding			
Comments	.		

Title	**Enhancing family therapy: The addition of a community resource specialist.**		
First Author	**Fishman, H.C., 2001**	**Source**	**11215980**
Level of evidence	4	**Study type**	RCT
Study quality	No FU, outcome variable and patients' characteristics not clearly defined (no explicit diagnoses given)		
Participants	131; n=74 in IG, n=57 in controls		
Patient characteristics	High school students with problem behavior from districts of socioeconomic needs, referred to a community agency; 10% AOD use problems; mean age 15.7 years, 50% male, 59% Afro-American		
Intervention	IG: family therapy + community resource specialist (FT+CRS)		
Comparison	FT+CRS vs. FT only		
Length of follow-up	No follow-up		
Outcome and effect size	66% of FT+CRS [28% in FT only] showed improvements in their respective problem behaviours with $\chi^2(3; N=131)=20.75$, $p<0.001$. AOD use was not specified. Outcome was rated by therapists in an 'improved – no change – worsened' graduation. [Expert ratings based on self-reports confirmed by collateral reports]		
Funding			

Comments	.

Title	**Psychotherapies for adolescent substance abusers: A pilot study**		
First Author	**Kaminer, Y., 1998**	**Source**	**9824170**
Level of evidence	1b	**Study type**	RCT
Study quality	Small sample size, otherwise well-reported study, alcohol use not specified		
Participants	N=32		
Patient characteristics	15.4-16.3 years old, 60-63% male, diagnosed with a “psychoactive substance use disorder” (DSM-III-R) plus a comorbid psychiatric disorder (DISC-C interview)		
Intervention	Cognitive Behavioral Therapy (CBT) and Interactional Treatment (IT), both manualized; urinalyses		
Comparison	CBT vs. IT; 12 weeks treatment both conditions		
Length of follow-up	3-month FU		
Outcome and effect size	Primary outcomes were subjects' reports of days and amount of substance use L7D, severity of substance use disorders and related problems as measured by the T-ASI. In ANOVAs, decrease in substance use was in favour of CBT [F(1, 11)=5.39, p=.040]. So was decrease in family problems [F(1, 15)=3.87, p=0.068]. [Self-reports confirmed by urinalyses]		
Funding			
Comments	.		

Title	**Cognitive behavioral coping skills and psychoeducation therapies for adolescent substance abuse**		
First Author	**Kaminer, Y., 2002**	**Source**	**12436013**
Level of evidence	2b	**Study type**	RCT
Study quality	Well reported study		
Participants	N=88		
Patient characteristics	15.4 years old, 70% male, diagnosed with an AUD alone (13%) or AUD+SUD (60%); most carried a comorbid psychiatric disorder (DISC-IV referring to DSM-IV interview)		
Intervention	Cognitive Behavioral Therapy (CBT) and Psychoeducational Therapy (PET); both manualized; urinalyses		
Comparison	CBT vs. PET		
Length of follow-up	3- and 9-month FU		
Outcome and effect size	The T-ASI was used as primary outcome measurement. ANOVAs revealed: At 3 month FU, PET showed more improvement on T-ASI alcohol use severity than CBT (F(1, 62)=3.17, p=0.08), and CBT showed more improvement on T-ASI substance use severity (F(1, 62)=3.53, p=0.065). [Self-reports confirmed by urinalyses]		
Funding			
Comments	.		

Title	**Efficacy of Outpatient Aftercare for Adolescents With Alcohol Use Disorders: A Randomized Controlled Study**		
First Author	**Kaminer, Y., 2008**	**Source**	**18978635**
Level of evidence	1b	**Study type**	RCT
Study quality	Length of aftercare interventions not reported; otherwise well documented study; urinalyses only in patients with substance use, not with alcohol use		
Participants	Total N=144. Active aftercare: in-person, brief telephone. No-active aftercare (controls)		
Patient characteristics	Adolescents aged 13-18 (mean age 15.9 years, 66% male), 79% diagnosed with SUD according to DSM-IV (DISC-IV interview)		
Intervention	All received CBT, only completers remained in the study; 2 intervention groups: in person aftercare or brief telephone aftercare; controls: no active aftercare		
Comparison	Active aftercare (in-person or brief telephone) vs. no-active aftercare		
Length of follow-up	3 and 6-month FU		

Outcome and effect size	Youths in active aftercare reported less number of 'any drinking days' per month (p=0.044) and of 'heavy drinking days' per month (p=0.035). According to GEE-analyses, alcohol abstinence rates decreased more in non-active aftercare (36.6%, i.e. from 63.4% at end of therapy to 26.8% at end of aftercare; Wald $X^2(1)=11.78$, $p<0.001$) than in active aftercare (20.8%, i.e. from 58.3% at end of therapy to 37.5% at end of aftercare; Wald $X^2(1)=5.64$, $p<0.018$). [Self-reports confirmed by urinalyses but for drug use only]
Funding	
Comments	.

Title	**Integrated Family and Cognitive Behavioral Therapy for adolescent substance abusers: A stage I efficacy study**		
First Author	**Latimer, W. W., 2003**	**Source**	**12957348**
Level of evidence	1b	**Study type**	RCT
Study quality	Urinalyses, assessments by clinical team, sessions videotaped and supervised for quality assessment, small sample size		
Participants	Total N=43; IG n=21, controls n=22		
Patient characteristics	Adolescents aged M=16.1, 77% male, each with AOD disorder diagnosis, 81% carried an AUD diagnosis (DICA-IV referring to DSM-IV)		
Intervention	(IG) Integrated Family and Cognitive Behavioral Therapy (IFCBT)=16 weeks with 1 FT session and 2 CBT group sessions per week		
Comparison	Controls: Drugs Harm Psychoeducation (DHPE); 16 weekly 90 min sessions		
Length of follow-up	FU after 1, 3, and 6 months		
Outcome and effect size	ANCOVAs controlling for age, gender, pretreatment and number of participated sessions were conducted. Throughout the 6-month FU period, mean of L30D alcohol use in DHPE was 6.06 and 2.03 in IFCBT [$F(1, 36)=5.53$, $p<0.024$, medium effect size $d=0.56$]. Mean of L30D marihuana use in DHPE was 13.83 and 5.67 in IFCBT [$F(1, 36)=5.79$, $p<0.021$, large effect size $d=0.79$]. [Expert ratings based on self-reports confirmed by collateral reports and urinalyses]		
Funding	Grant by the National Institute on Drug Abuse		
Comments	.		

Title	**Early intervention for adolescent substance abuse: Pretreatment to posttreatment outcomes of a randomized controlled trial comparing multidimensional family therapy and peer group treatment.**		
First Author	**Liddle, H. A., 2004**	**Source**	**15152709**
Level of evidence	1b	**Study type**	RCT
Study quality	Self-report on drug use, short follow-up period (6 weeks). Sessions were videotaped for supervision and quality assessment, small (22) sub-sample of patients with alcohol use problems or AUD		
Participants	Total N=80; MDFT n=39, peer group therapy n=41		
Patient characteristics	Mean age=13.7 (73% male), 42% Hispanic, 38% African-American, 11% Haitian/Jamaican referred from juvenile justice, school, mental health facilities; SUD abuse diagnosis 47%, SUD dependence diagnosis 16%, conduct disorder 39% (and other comorbid disorders)		
Intervention	Multidimensional Family Therapy (MDFT); peer group therapy; both treatments 90 min weekly over 12-16 weeks, both manualized		
Comparison	MDFT against peer group therapy (CBT oriented)		
Length of follow-up	Varying: 6 weeks and at discharge from the institution		
Outcome and effect size	AOD use was measured by TLFB and the 'Parent and Adolescent Interview'. MDFT patients showed "more rapid" decrease in alcohol use than controls ($t=2.01$, $p<0.05$). Cannabis use and delinquent behaviour did not decrease significantly in either treatment group. [Expert ratings based on self-reports confirmed by collateral reports and urinalyses]		
Funding			
Comments	.		

Title	**Multidimensional family therapy for adolescent drug abuse: Results of a randomized clinical trial.**		
First Author	**Liddle, H. A., 2001**	**Source**	**11727882**
Level of evidence	1b	**Study type**	RCT
Study quality	Urinalyses, assessments by clinical team, sessions were supervised for quality assessment. Only the reduction of drug use is reported, not specified in substances		
Participants	Total N=152; MDFT n=47, MEI n=52, AGT n=53		
Patient characteristics	Mean age =15.9 (80% male), 49% African-American, Hispanic, Asian a.o. diagnosed with an AOD use disorder		
Intervention	Multidimensional Family Therapy (MDFT); Adolescent Group Therapy (AGT); Multifamily educational intervention (MEI); each treatment 14-16 weekly sessions over 5-6 months; all treatments manualized		
Comparison	MDFT (IG) against AGT and MEI (2 controls)		
Length of follow-up	6- and 12-month FU		
Outcome and effect size	ANOVA interactions of Time x Treatment were significant in favour of MDFT for less adolescent drug use with $F(6, 240)=2.68$, $p=0.01$ with a small to medium sized effect of $\eta^2=0.05$. So were improvements in family competence with $F(6, 117)=3.66$, $p=0.002$ with a medium sized effect of $\eta^2=0.16$. Alcohol use was not [Expert ratings based on self-reports]		
Funding	Grant by the National Institute on Drug abuse		
Comments	.		

Title	**Brief intervention for harm reduction with alcohol-positive older adolescents in a hospital emergency department.**		
First Author	**Monti, P. M., 1999**	**Source**	**10596521**
Level of evidence	1b	**Study type**	Randomized-controlled; incentives for participants
Study quality	Baseline alcohol use level in the sample was rather low; data of 3 and 6-month FU aggregated		
Participants	Total N=94; MI n=52, SC=42		
Patient characteristics	Adolescents treated for an alcohol-related emergency at ER: intoxication (45%), motor vehicle accident (27%) a.o.		
Intervention	Motivational Interviewing (MI); Standard Care (TAU) handout of recommendations and list of local treatment agencies		
Comparison	MI against TAU		
Length of follow-up	3 and 6-month FU		
Outcome and effect size	Outcomes were in favour of MI: 32% reduction of alcohol consumption, less DUI. In an ANCOVA, MI patients reported fewer alcohol-related problems in the 6 months FU compared with SC patients [$F(1, 78)=4.10$, $p<0.05$, nearly medium sized effect $\eta^2=0.05$]. Logistic Regressions revealed that MI had an almost 4-fold reduced risk of drinking and driving (OR=3.92) and of alcohol-related injuries (OR=3.94). [FU via telephone interview by a trained staff member who had delivered the intervention in the emergency room]		
Funding			
Comments	.		

Title	**Practitioner Review: Adolescent alcohol use disorders: assessment and treatment issues.**		
First Author	**Perepletchikova, F., 2008**	**Source**	**19017028**
Level of evidence	1a	**Study type**	Systematic Review
Study quality	Assessed participants did not have a high severity of alcohol misuse; no effect sizes or outcome measures are reported		
Participants	Total N=2.491 in 21 studies with study-n varying from 10 to 600; n of medically based interventions varied from 10 to 26		
Patient characteristics	Age 11-18 years in 13 studies (62%) males 34-83%; Age 12-22 years in 8 studies (38%) males 50-81%;		
Intervention	MSFT, MST, individual and group CBT, IFCBT, BSFT, medically based		
Comparison	Not specified in the review (comparisons to wait-list groups or alternative treatment can		

	be concluded from this table because of overlap in included studies, but not for medically based interventions)
Length of follow-up	Variety of FU lengths
Outcome and effect size	Authors reported global 'main findings' in terms of reduction of AOD use without further specifications, no meta-analytic statistical comparison is given. Authors state that "the strongest empirical support" seems to be in favour of MDFT and group administered CBT. [Miscellaneous outcome measures]
Funding	
Comments	.

Title	**Efficacy of Brief Strategic Family Therapy in modifying Hispanic adolescent behavior problems and substance use.**		
First Author	**Santisteban, D. A., 2003**	**Source**	**12666468**
Level of evidence	2b	**Study type**	RCT
Study quality	Well documented; sessions were videotaped for supervision and quality assessment; no FU		
Participants	Total N=126, data analyses per protocol (n=85)		
Patient characteristics	Hispanic adolescents aged M=15.6 years (75% male) with AOD problems and problem behaviour		
Intervention	Brief Strategic Family Therapy (BSFT) M=11.2 weekly sessions; non-manualized psycho-educative group M=8.8 weekly sessions		
Comparison	BSFT against psycho-educative group		
Length of follow-up	No FU in this study report		
Outcome and effect size	No FU was conducted; treatment length/dose was statistically controlled. ANOVA interaction of Time x Treatment was significant in favor of BSFT for less adolescent drug use L30D at termination [$F(1, 69)=6.98$, $p<0.05$, medium sized effect of $\eta^2=0.09$]. Less alcohol use was not significant, though there was a small sized effect of $\eta^2=0.03$. Improvements in scales Conduct Disorder and Socialized Aggression were significant at termination in favor of BSFT. [Parent-reports on problem behavior, ASI self-reports on AOD use confirmed by urinalyses]		
Funding			
Comments	.		

Title	**Individual and family motivational interventions for alcohol-positive adolescents treated in an emergency department.**		
First Author	**Spirito, A., 2011**	**Source**	**21383276**
Level of evidence	1b	**Study type**	Randomized-controlled; incentives for participating adolescents and parents
Study quality	IMI+FCU videotaped and treatment adherence rated. Low N at intake, high attrition (25-28%) leading to low statistical power at FU		
Participants	Total N=125 at intake, IMI n=63 and IMI+FCU n=62		
Patient characteristics	Adolescents aged M=15.4 years (45-48% male), 29-39% African-American, Hispanic a.o. with a positive blood alcohol concentration		
Intervention	IG: IMI plus family motivational interview/family check-up (IMI+FCU) additional 60 min. Controls: Brief individual motivational interview 45 min (IMI) only. Both: 5 booster sessions for parents; 3-months FU interviews via telephone, 6- and 12-months in person.		
Comparison	IMI+FCU against IMI only		
Length of follow-up	3-, 6-, 12-month FU		
Outcome and effect size	Chi2 and GEE analyses were conducted on primary outcome measures (frequency, quantity, high-volume drinking). IMI+FCU improved outcome only on high-volume drinking days at 3-month FU (14.6% vs. 32.1%; $\chi^2(1, N=97)=3.89$, $p=0.048$; OR=2.76). Both conditions resulted in a reduction in all drinking outcomes at all FU points ($p<0.001$ each), with the strongest effects at 3 and 6-month FU. [ADQ self-reports on AOD use; parent-reports in FU]		
Funding			

Comments	.

Title	**Conjoint versus one-person family therapy: Some evidence for the effectiveness of conducting family therapy through one person**		
First Author	**Szapocznik, J., 1983**	**Source**	**6655103**
Level of evidence	2b	**Study type**	Randomized-controlled. No FU.
Study quality	Study dates from 1983; not focused on AOD, small sample size		
Participants	Total N=37, CFT n=18, OPFT n=19		
Patient characteristics	Adolescents with behaviour problems and “problematic substance use”; mean age 17.9 years, 78% male		
Intervention	Conjoint Family Therapy (CFT), One-Person Family Therapy (OPFT); a maximum of 12 sessions in both conditions		
Comparison	OPFT against CFT		
Length of follow-up	Length of follow-up not reported		
Outcome and effect size	Patients in the OPFT condition continued to improve slightly in the Drug Abuse scale, whereas patients in the CFT condition were somewhat worse at follow-up [F(2, 36)=3.2, p<0.05]. [PSS self-reports]		
Funding			
Comments	.		

Title	**Motivational enhancement and other brief interventions for adolescent substance abuse: foundations, applications, and evaluations.**		
First Author	**Tevyaw, T. O, 2004**	**Source**	**15488106**
Level of evidence	1a	**Study type**	Systematic Review (narrative)
Study quality	Aims at methodological and translational research issues, treatment results are of lower priority		
Participants	n/a		
Patient characteristics	Adolescents with AOD use		
Intervention	Brief interventions, including Motivational interviewing (MI)		
Comparison	Motivational Interviewing was effective in reducing substance abuse, especially in patients with heavy drinking patterns and low change motivation.		
Length of follow-up	FU varying from 3 to 12 months across studies; one 48-month FU		
Outcome and effect size	Discusses research issues of MI in adolescent AOD use such as treatment engagement. No citable data reported.		
Funding			
Comments	.		

Title	**Interventions for reducing adolescent alcohol abuse a meta-analytic review.**		
First Author	**Tripodi, S. J., 2010**	**Source**	**20048247**
Level of evidence	1a	**Study type**	Meta-analysis
Study quality	Included studies did not specifically focus on AOD use, and in two of the trials, only approximately 50% of the sample met criteria for alcohol dependence or harmful alcohol use.		
Participants	Not explicitly given, ca. N>1.000, varying from 50 days to 12 months		
Patient characteristics	Studies from 1994-2008 included; patients were younger than 19 years, regardless of AOD use severity		
Intervention	Brief interventions, several formats of family-based interventions, several format s of aftercare were compared		
Comparison	Overall effects, family only effects, individual intervention only effects, outcomes for less and more than 6-month FU		
Length of follow-up	30% <6 months, 40% 6 months, 30% 9-12 months or longer.		
Outcome and effect size	Outcome measures were abstinence, frequency of alcohol use, and quantity of alcohol use.		

	Interventions significantly reduce AOD use (Hedges g=-0.61). Stratified analyses revealed larger effects for individual treatment (Hedges g=-0.75) compared with family-based treatment (Hedges g=-0.46). [Miscellaneous outcome measures, interrater agreements 0.76 < ⍰ < 0.78, fail-safe n=1.058 null studies]
Funding	Partly by a grant from the Donald D. Hammill Foundation
Comments	.

Title	**The effectiveness of brief interventions in the clinical setting in reducing alcohol misuse and binge drinking in adolescents: a critical review of the literature.**		
First Author	**Wachtel, T., 2010**	**Source**	**20500302**
Level of evidence	1a	**Study type**	Systematic Review
Study quality	Selective study, as one of selection criteria was if nurses could successfully use brief intervention s in the clinical setting; no studies on family-oriented interventions were included		
Participants	14 studies included those published the past 10 years		
Patient characteristics	Inclusion criteria: RCT, BI specific to alcohol, participants aged 12-25 years		
Intervention	Brief intervention strategies specific to alcohol, or alcohol-risk reduction: Twelve studies used a Motivational Intervention (MI) style of intervention, seven of which reported reduced alcohol frequency and amount.		
Comparison	All studies were controlled; 8 out of 14 were no-intervention controls, one study used two control groups.		
Length of follow-up	Short-term FU (up to six months), medium-term FU (6-12 months), long-term FU (longer than 12 months)		
Outcome and effect size	MI was partially successful mostly in harm minimization. Long-term FU reported significant reductions in alcohol intake and harmful effects. Successful intervention elements are: face-to-face, one-session, brief motivational interviewing, focusing on harm minimization. Two studies specifically found a reduction in binge drinking episodes, and seven reported a decrease in harmful alcohol effects. No meta-analytic statistical comparison is given. [Miscellaneous outcome measures]		
Funding			
Comments	.		

Title	**On the learning curve: Cognitive behavioral therapies for adolescent substance abuse.**		
First Author	**Waldron, H. B., 2004**	**Source**	**15488108**
Level of evidence	1a	**Study type**	Systematic review (synopsis)
Study quality	To some degree well documented study; arguing in favour of CBT as a promising intervention for SUD in youths		
Participants	Varying from 66 to 224 over RCTs and feasibility studies, n=600 in a multi-site study		
Patient characteristics	Adolescents with substance abuse in outpatient care		
Intervention	Variety of CBT-formats: individual, group, family-based, brief 6-session vs. full-term 12-session, and combinations		
Comparison	Family therapy such as MDFT, psycho-educative treatment, other CBT-formats		
Length of follow-up	6-19 months		
Outcome and effect size	Outcomes vary, no specification as to alcohol is given. Summarizing a variety of findings, authors feel that outpatient CBT treatment can be effective in reducing adolescent substance use and related problems. The outcomes appear better than results of US-wide evaluation in standard treatment/TAU. [Miscellaneous outcome measures]		
Funding			
Comments	.		

Title	**Treatment outcomes for adolescent substance abuse at 4- and 7-month assessments.**		
First Author	**Waldron, H. B., 2001**	**Source**	**11680557**

Level of evidence	2b	**Study type**	RCT
Study quality	Unequal number of treatment sessions across conditions; focused on marihuana use.		
Participants	Total N=120; about n=30 in 4 compared conditions		
Patient characteristics	Mean age 15.4-15.8 years (male 71%); mixed ethnicities; illicit substance-abusing adolescents (mainly marihuana); most were mandated to treatment		
Intervention	4 conditions: CBT, Functional Family Therapy FFT, a combination of CBT and family therapy, unspecific group therapy		
Comparison	CBT and CBT + family therapy were more effective than the other 2 interventions		
Length of follow-up	7 months		
Outcome and effect size	Outcome reports did not differentiate between alcohol use and other substance use. In 4-months FU, FFT $F(1, 28)=20.42$, $p<0.001$, $\eta^2=0.42$] and CBT+FT [$F(1, 26)=7.71$, $p<0.01$, $\eta^2=0.30$] were more effective than the other 2 interventions, as L90D substance use as measured by TLFB increased significantly only in these conditions. In 7-months FU, only youths in the unspecific group condition were the most effective [$F(1, 28)=7.72$, $p<0.01$, $\eta^2=0.22$]. [Expert ratings based on self-reports confirmed by collateral reports and urinalyses]		
Funding	Grant by the National Institute on Drug abuse		
Comments	.		

Title	**Effects of a brief intervention for reducing violence and alcohol misuse among adolescents.**		
First Author	**Walton, M. A., 2010**	**Source**	**20682932**
Level of evidence	1b	**Study type**	Randomized-controlled; incentives for participants
Study quality	High attrition, only self-reports		
Participants	Total N=726; IG1=237; IG2=254; controls=235		
Patient characteristics	Emergency department (ED) patients aged 14 to 18 years (44% male, 56% African American) reporting past-year alcohol use and aggression		
Intervention	IG2: 35 min SafERteens (motivational interviewing with skills training & brief intervention for violence and alcohol) delivered in the ED by therapist; IG1: SafERteens delivered by tablet laptop computers; controls: handout of brochure (TAU)		
Comparison	2 SafERteens intervention formats against TAU		
Length of follow-up	3- and 6-month FU after intervention in ED		
Outcome and effect size	Chi^2 and GEE analyses were conducted on primary outcome measures (alcohol consumption via AUDIT-C, Alcohol consequences via POSIT, aggression/aggression consequences by self-constructed scales). In 6-month FU, both therapist (OR=1.75) and computer-based (OR=1.69) brief interventions were effective at reducing alcohol consequences [Wald $X^2(2)=6.82$, $p<0.03$]. None of the GEE models were significant for the alcohol frequency or aggression-related variables. [Self-reports]		
Funding	NIAAA		
Comments	.		

3.7.2 Schwangere/ Erwachsene Frauen

Title	**Home visits during pregnancy and after birth for women with an alcohol or drug problem.**		
First Author	**Doggett, C., 2005**	**Source**	**16235364**
Level of evidence	1a	**Study type**	Systematic Review (Meta-analysis)
Study quality	Well documented		
Participants	Objectives: To determine the effects of home visits during pregnancy and/or after birth for women with a drug or alcohol problem. Data search up to 2004.		
Patient characteristics	Studies using random or quasi-random allocation of pregnant or postpartum women with a drug or alcohol problem to home visits. Trials enrolling high-risk women of whom more than 50% were reported to use drugs or alcohol were also eligible.		
Intervention	Home visits after birth		
Comparison	No home visits		
Length of follow-up	1966-2004		

Outcome and effect size	Meta-analysis in terms of risk ratios. Six studies (709 women) compared home visits after birth with no home visits. None provided a significant antenatal component of home visits.
Funding	
Comments	.

Title	**Learning sobriety together. A randomized clinical trial examining behavioral couples therapy with alcoholic female patients.**		
First Author	**Fals-Stewart, W., 2006**	**Source**	**16822114**
Level of evidence	2b	**Study type**	Randomized controlled, ITT-analysis
Study quality	Well reported study		
Participants	N=138 couples. Women: DSM-IV criteria for alcohol abuse of dependence. Men: No DSM-IV substance use symptoms.		
Patient characteristics	Women: 20-60 years (mean: 33 years). Partner mean age: 35 years. Married or cohabiting women with alcohol use disorders (91% alcohol dependence) and their intimate partners without SUD. Women agreed to abstinence while in treatment. Self-help meetings.		
Intervention	N=46 couples in Behavior Couples Therapy (BCT), manualized: 32 sessions, 12 sessions with couples, 20 sessions with women only – and individual Drug Counseling (IDC).		
Comparison	Comparison group one: N=46 couples in Individual Based Treatment (IBT), manualized: 32 sessions with women only – Individual Drug Counseling (IDC) program, a 12-step facilitation treatment program. Comparison group two: N=46 couples in Psychoeducational/ Attention Control Treatment (PACT), manualized: 32 sessions, 12 sessions with couples in lectures, 20 sessions with women only IDC individualized program.		
Length of follow-up	End of treatment and 1 year after treatment. Attrition rates BCT: 12, IBT: 12; PACT: 11; percentage of abstinent days (PAD) measured 4 times within 12 months.		
Outcome and effect size	During treatment, no significant differences regarding drinking frequency (e.g. PAD) among participants in different conditions. During the 1 year post treatment follow-up, participants in BCT increased their drinking at a significantly slower rate.		
Funding	NIAAA and NIDA		
Comments	.		

Title	**Interventions delivered during antenatal care to reduce alcohol consumption during pregnancy: A systematic review**		
First Author	**Gilinsky, A., 2011**	**Source**	
Level of evidence	1b	**Study type**	Systematic Review (narrative)
Study quality	High heterogeneity in included studies, no effect sizes computed, review is well documented and transparent		
Participants	The aim of this systematic review was to consider additional evidence by including RCTs and non-RCTs to determine whether pregnant women reduced alcohol consumption during pregnancy following interventions delivered during antenatal care.		
Patient characteristics	33 papers in review, 8 papers included in final review (6 RCTs, 2 non-RCTs).		
Intervention	Psychosocial interventions to reduce alcohol consumption or to establish abstinence. Interventions included brief interventions, MI, a self-help manual, supportive counselling, high feedback ultrasound and basic educational interventions		
Comparison	TAU, information letter		
Length of follow-up	During pregnancy and after delivery. Measurement of alcohol consumption via questionnaire and/or TLFB.		
Outcome and effect size	Narrative review. There was some evidence from a small number of studies that single session face-to-face brief interventions resulted in positive effects on the maintenance of alcohol abstinence during pregnancy.		
Funding	NHS Education for Scotland and NHS Tayside		
Comments			

Title	Early Treatment for women with alcohol addiction (EWA) reduces mortality: a randomized controlled trial with long-term register follow-up		
First Author	Gjestad, R., 2011	Source	21273301
Level of evidence	1b	Study type	Long-term follow-up study (Dahlgren et al., 1989), a randomized controlled study.
Study quality	Well-reported study		
Participants	N=200 women, in early phases of alcohol dependence were admitted to study in 1989. Randomization by dates of birth (odd date birth=women only group).		
Patient characteristics	Long-term register follow-up of study subjects from Dahlgren et al., 1989 (EWA). Comparison of mortality rates in intervention and control group.		
Intervention	100 women in EWA, a women-only ward. Treatment duration: at least 1 year. Description of interventions not clear.		
Comparison	100 women in TAU, regular ward together with alcoholic men. Treatment duration: 5 months on average.		
Length of follow-up	In original study: 2 years follow-up. Attrition rate during follow-up: EWA N=25, TAU N=32. In re-analysis: overall observation time 27 years.		
Outcome and effect size	Hazard ratio over time based on Cox regression with time – dependent covariates. Statistical data: mortality status of group members in relation to age at intake, years since intake, survival plots. Results: Significantly lower mortality was found among younger women who participated in EWA compared with those in TAU.		
Funding	Norwegian Research Foundation, Swedish Research Council and Alcohol Research Council of the Swedish Retail Monopoly		
Comments	.		

Title	Engagement and retention in outpatient alcoholism treatment for women.		
First Author	Graff, F. S., 2009	Source	19444731
Level of evidence	2b	Study type	Drop-out analysis to a randomized controlled study (McCrady et al., 2009)
Study quality	Focus on retention in study, well reported study		
Participants	N=102 women and their male partners in a stable heterosexual relationship		
Patient characteristics	Women: current alcohol abuse or dependence diagnosis (DSM-IV, SCID), with a partner who was willing to participate in study and had no mental disorders. No signs of domestic violence in partnership.		
Intervention	50 couples in Alcohol Behavioral Couples Treatment (ABCT): 20 sessions over a 26-week treatment period for both partners, 90 min per session. Manualized treatment including homework as part of treatment protocol addressing women as well as their partners.		
Comparison	52 couples in Alcohol Behavioral Individual Treatment (ABIT): 20 sessions over a 26-week treatment period for women only, 60 min per session. Manualized treatment including homework as part of treatment protocol addressing women as well as their partners.		
Length of follow-up	N=102. Measurement of treatment retention while in treatment: total no of sessions attended within 6 months. Treatment engagement was measured via completion of homework.		
Outcome and effect size	ANOVA, multiple regressions. Women in ABCT attended significantly lesser sessions than women in ABIT. Correlates of treatment retention: women's age, total number of current alcohol dependence symptoms, Dyadic Adjustment Scale (DAS) scores, spouse drinking status. Predictors of treatment retention: relationship satisfaction, spouse drinking and matching of treatment preference with current treatment arrangement.		
Funding	NIAAA		
Comments	.		

Title	The Women's Recovery Group Study: A stage I trial of women-focused group therapy for substance use disorders versus mixed-gender group drug counseling.		
First Author	Greenfield, S. F., 2007	Source	17446014

Level of evidence	2c	**Study type**	Randomized controlled study with partial randomization, stage 1 Behavioral Development Trial
Study quality	Very small sample size, data analysis includes pre-pilot and pilot study subjects. N in control group very small.		
Participants	N=13 in pre-pilot Women's Recovery Group (WRG) in pilot phase, 23 randomized in WRG (N=16) and Group Drug Counseling (GDC) (N=7).		
Patient characteristics	In pre-pilot N=18, eligible 13 and enrolled in WRG, in pilot phase N=42 and 31 eligible, 8 dropped out before randomization, in study N=23. Age of women in the groups differed significantly. No other significant differences between groups.		
Intervention	N=29 (13 pre-pilot + 16 pilot) WRG intervention, 12 sessions (one per week), 90 min per session, manualized (relapse prevention group therapy that utilizes a cognitive behavioural approach), mean age of 29 women in WRG: 45.0 years.		
Comparison	N=7 women (and 10 men) GDC control, 12 sessions (one per week), 90 min per session, type of community substance abuse treatment program. Mean age of women only: 58.3 years.		
Length of follow-up	At end of trial, 6 month post treatment		
Outcome and effect size	No difference at the end of trials between pre-pilot, pilot and control groups. During 6-month post treatment follow-up WRG members demonstrated a pattern of continued reductions in substance use while GDC women did not. In addition, pilot WRG women with alcohol dependence had significantly greater reductions in average drinks/drinking day than GDC women 6 months post treatment ($p<0.03$, effect size=0.81). While satisfaction with both groups was high, women were significantly more satisfied with WRG than GDC ($p<0.009$, effect size=1.11).		
Funding	NIDA		
Comments	.		

Title	**Multi-site randomized trial of behavioral interventions for women with co-occurring PTSD and substance use disorder.**		
First Author	**Hien, D. A., 2009**	**Source**	**19634955**
Level of evidence	1b	**Study type**	Randomized controlled
Study quality	well reported study, ITT		
Participants	N=353 women. Recruitment settings: Women in 7 outpatient community-based treatment programs across the USA.		
Patient characteristics	1.212 women, 370 completed baseline, 353 in study and randomized to SS or WHE. Group characteristics: 18-65 years, mean age 39 years. Inclusion criteria: 1. At least one traumatic event in lifetime (DSM-IV-R) for full or subthreshold PTSD. 2. Use of alcohol or illicit substances within past six months and a current diagnosis of drug or alcohol abuse or dependence. 3. Capable of giving informed consent. Exclusion criteria defined		
Intervention	N=176 Seeking Safety (SS) group and TAU. SS program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics). Mean treatment attendance 6.2±4.5.		
Comparison	N=177 Women's Health Education (WHE) group and TAU. WHE program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics). Mean treatment attendance 6.0±4.3.		
Length of follow-up	1 week post treatment and follow-up 3, 6, and 12 months.		
Outcome and effect size	Generalized linear model, GEE methodology. Results: Large clinically significant reductions in CAPS and PSS-SR symptoms (d=1.94 and d=1.12) but no difference between conditions. Substance use outcomes (self-reported abstinence/ days per week of any substance use) were not significantly different over time between the two treatments and at follow-up showed no significant change from baseline, when 46% of participants were abstinent. Study results do not favour SS over WHE as an adjunct to SUD treatment for women with PTSD.		
Funding	NIDA		
Comments	.		

Title	**The role of alcohol misuse on PTSD outcomes for women in community treatment: A secondary analysis of NIDA's Women and Trauma study.**		
First Author	**Hien, D. A., 2010a**	**Source**	**20537811**
Level of evidence	1b	**Study type**	Reanalysis of a randomized controlled study of Hien et al., 2009
Study quality	Focus on alcohol misusers and non-misusers, well reported study.		
Participants	N=353 women, randomized to Seeking Safety (SS) or Women's Health Education (WHE) group treatment in outpatient substance abuse treatment. Definition of alcohol misuse: daily alcohol use or one day of alcohol intoxication in prior 30 days.		
Patient characteristics	Comparison of women at baseline: alcohol misusers (N=111) vs. non-misusers (N=242). The groups differ significantly from each other on age and education and on PSS-SR total, and cluster C and D.		
Intervention	N=176 Seeking safety (SS) group and TAU. SS program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics).		
Comparison	N=177 Women's Health Education (WHE) group and TAU. WHE program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics).		
Length of follow-up	1 week post treatment and follow-ups at 3, 6, and 12 months.		
Outcome and effect size	Generalized estimating equations were used to examine the effect of baseline alcohol misuse on PTSD outcome measures over time for all randomized participants. For women with alcohol misuse, after treatment week one, PSS-SR scores were significantly lower in the SS intervention during treatment ($\chi2(1)=4.00$, $p<0.05$) and follow-up ($\chi2(1)=4.87$, $p<0.05$) compared to those in the WHE intervention group. Alcohol misusers in SS who had higher baseline hyperarousal severity improved more quickly than those with lower baseline hyperarousal severity during treatment ($\chi2(1)=4.06$, $p<0.05$).		
Funding	NIDA		
Comments	.		

Title	**Do treatment improvements in PTSD severity affect substance use outcomes? A secondary analysis from a randomized clinical trial in NIDA's Clinical Trial Network.**		
First Author	**Hien, D. A., 2010b**	**Source**	**19917596**
Level of evidence	1b	**Study type**	Reanalysis of a randomized controlled study of Hien et al., 2009.
Study quality	Focus on temporal course of improvement in PTSD and SUD symptoms, well reported study.		
Participants	N=353 women, randomized to Seeking Safety (SS) or Women's Health Education (WHE) group treatment in outpatient substance abuse treatment.		
Patient characteristics	To investigate temporal association between improvement in PTSD and substance use severity during the study's treatment phase, four responder categories were defined: non-responder, substance use responder, PTSD responder and global responder.		
Intervention	N=176 SS group and TAU. SS program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics).		
Comparison	N=177 WHE group and TAU. WHE program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics).		
Length of follow-up	1 week post treatment and follow-up at 3, 6, and 12 months.		
Outcome and effect size	A generalized linear model was applied to test the relationship over follow-up. Results: Non-responders, substance use responders and global responders tended to maintain original classification; PTSD responders were significantly more likely to transition to global responders over time, indicating maintained PTSD improvement was associated with subsequent substance use improvement. Trauma-focused treatment was significantly more effective in achieving substance use improvement compared to the WHE group, but only among those who were heavy substance users at baseline and had achieved significant PTSD reductions.		
Funding	NIDA		
Comments	.		

Title	**Attendance and substance use outcomes for the Seeking Safety program: Sometimes less is more.**		
First Author	**Hien, D. A., 2012**	**Source**	**22182262**
Level of evidence	1b	**Study type**	Reanalysis of a randomized controlled study of Hien et al., 2009.
Study quality	Focus on treatment attendance and membership turnover in rolling groups. Well reported study.		
Participants	N=353 women, randomized to Seeking Safety (SS) or Women's Health Education (WHE) group treatment in outpatient substance abuse treatment.		
Patient characteristics	Research questions: 1. Are there different treatment attendance patterns in this sample? 2. If so, does one of the patterns involve titration of treatment? 3. Are there different substance use outcomes by treatment type?		
Intervention	N=176 SS group and TAU. SS program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics).		
Comparison	N=177 WHE groups and TAU. WHE program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics).		
Length of follow-up	1 week post treatment and follow-ups at 3, 6, and 12 months.		
Outcome and effect size	Latent class pattern mixture modelling (LCPMM) to estimate attendance patterns and to test for treatment effects. The optimal number of classes according to a series of two-piece linear probit LCPMM's was 3: completers (probability of attendance rate: 80% and more), droppers (probability of attendance rate: 41 and lower) and titrators (probability of attendance rate: 50%-80%). Among completers, there were significant decreases of alcohol use from baseline to 1-week post treatment, and a non-significant increase between 1-week post and 12 months post under both treatment conditions. Among droppers, there were non-significant increases of alcohol use from baseline to 1-week post and from there to 12 months post under both treatment conditions. Among titrators, results were rather similar, however, those in SS had lower rates of alcohol use from 1-week through 12-month follow-up compared with WHE (b=-0.203 [0.085], t=-2.389, p=0.017). Results suggest that the number of sessions attended might not be as useful as the quality of the participation for this PTSD and SUD population.		
Funding	NIDA		
Comments			

Title	**When should clinicians switch treatments? An application of signal detection theory to two treatments for women with alcohol use disorders.**		
First Author	**Hildebrandt, T., 2010**	**Source**	**20359693**
Level of evidence	2b	**Study type**	Analysis of a specific issue of a randomized controlled study of McGrady et al., 2009
Study quality	Focus on predictive value of weekly within-treatment drinking, well documented study		
Participants	N=102 women and their male partners in a stable heterosexual relationship		
Patient characteristics	Women: current alcohol abuse or dependence diagnosis (DSM-IV, SCID), with a partner who was willing to participate in study and had no mental disorders. No signs of domestic violence in partnership.		
Intervention	N=50 couples in Alcohol Behavioral Couples Treatment (ABCT): 20 sessions over a 26-week treatment period for both partners, 90 min per session. Manualized treatment including homework as part of treatment protocol addressing women as well as their partners.		
Comparison	N=52 couples in Alcohol Behavioral Individual Treatment (ABIT): 20 sessions over a 26-week treatment period for women only, 60 min per session. Manualized treatment including homework as part of treatment protocol addressing women as well as their partners.		
Length of follow-up	N=102. To identify the earliest point in treatment where clinicians could identify treatment non-responders in two treatments: ABCT and ABIT and evaluate the predictive validity of early response over one-year follow-up		
Outcome and effect size	Receiver operator curve (ROC) analyses indicated that failure to achieve or sustain abstinence by the end of treatment and one year follow-up was predicted with reasonable		

	accuracy (AUC=0.80) by week - 4 percent days abstinent (PDA) in ABIT but not in ABCT. The reasons for different earl response outcomes between ABIT and ABCT are not entirely clear and may be due to additional factors.
Funding	NIAAA
Comments	.

Title	**Women's programs versus mixed-gender day treatment: Results from a randomized study**		
First Author	**Kaskutas, L. A., 2005**	**Source**	**15598193**
Level of evidence	2c	**Study type**	RCT
Study quality	Heterogeneous groups; control conditions not well defined.		
Participants	N=122 women. Significant differences at baseline between two subgroups (women focused and women only vs. hospital-based program).		
Patient characteristics	Substance dependent women.		
Intervention	N=31. Community-based women's program (women focused and women only). Length of program: 6 weeks. Intervention not manualized, no description of topics for group and/or individualized intervention.		
Comparison	N=91 in 3 comparison groups. Group 1, N=22 and group 2, N=27 in mixed-gender community-based programs, group 3 N=42 in mixed-gender hospital-based program. Length of programs: group 1: 6 weeks, group 2: 4 weeks, group 3: 3 weeks. Interventions not manualized, no description of topics for group and/or individualized interventions.		
Length of follow-up	Baseline, end of treatment, 6 months and 12 months post treatment.		
Outcome and effect size	No significant differences between women's program only and two of the three mixed gender programs regarding rates of substance use and abstinence. Multivariate data analysis showed significant differences between women's program only and mixed gender hospital program regarding alcohol and other drug abstinence in follow-up (OR=0.17, p=0.021, t=2.06).		
Funding	NIAAA		
Comments	.		

Title	**Adverse events in an integrated trauma-focused intervention for women in community substance abuse treatment.**		
First Author	**Killeen, T., 2008**	**Source**	**18294804**
Level of evidence	1b	**Study type**	Reanalysis of a randomized controlled study of Hien et al., 2009.
Study quality	Focus on measurement of adverse events, well reported study.		
Participants	N=353 women, randomized to Seeking Safety (SS) or Women's Health Education (WHE) group treatment in outpatient substance abuse treatment.		
Patient characteristics	N=353 women. Adverse events (AEs) measurement with questionnaire (SPSS-SR) at baseline, weekly during treatment and 1 week post treatment. Search for AEs in all study documents including case report form. AEs: increased PTSD symptoms, increased depression symptoms, increased alcohol or illicit substance use.		
Intervention	SS group and TAU. SS program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics). Mean treatment attendance 6.2±4.5		
Comparison	N=177 WHE groups and TAU. WHE program: 12 sessions, 75-90 min over 6 weeks. And TAU sessions (participating in meetings of Anonymous Alcoholics). Mean treatment attendance 6.0±4.3		
Length of follow-up	1 week post treatment and follow-up 3, 6, and 12 months.		
Outcome and effect size	Results: No demographic differences between groups at baseline. No difference between study groups of study-related AEs during treatment (20% for SS vs. 14% for WHE, p=0.3). 67% of study-related AEs involved worsening PTSD symptoms or depression; only 10% related increased substance use. In general, study participants did not use substances to cope with increases in PTSD or depression symptoms experienced during treatment.		
Funding	NIDA		
Comments			

Title	Psychosocial interventions for women enrolled in alcohol treatment during pregnancy.		
First Author	Lui, S., 2008	Source	18646166
Level of evidence	1a	Study type	Systematic Review
Study quality	Well documented		
Participants	Objectives: To evaluate the effectiveness of psychosocial interventions in pregnant women enrolled in alcohol treatment programs for improving birth and neonatal outcomes, maternal abstinence and treatment retention		
Patient characteristics	The search strategy identified 958 citations. 26 for review. Following full text review no articles met the inclusion criteria. Data extraction and assessment of methodological quality were therefore not possible.		
Intervention	Any psychosocial intervention in pregnant women enrolled in alcohol treatment programs for improving birth and neonatal outcomes, maternal abstinence and treatment retention.		
Comparison	Pharmacological interventions or placebo or non-intervention or another psychosocial intervention		
Length of follow-up	Not applicable		
Outcome and effect size	The review question remains unanswered as there were no randomized control trials found relevant to the topic. There is a need for high quality randomized controlled trials to determine the effectiveness of psychosocial interventions in pregnant women enrolled in alcohol treatment programs.		
Funding	18646166		
Comments			

Title	A randomized trial of individual and couple behavioral alcohol treatment for women		
First Author	McCrady, B., 2009	Source	19309184
Level of evidence	2b	Study type	RCT
Study quality	Well reported study		
Participants	Women: current alcohol abuse or dependence diagnosis (DSM-IV, SCID), with a partner who was willing to participate in study and had no mental disorders. No signs of domestic violence in partnership.		
Patient characteristics	Eligible: 351 couples, N=109 couples in randomization SCID-Interviews to diagnose alcohol abuse or dependence. In data analysis: 102 couples – 7 women/ couples dropped out of study before start of treatment and could not be located.		
Intervention	N=56 couples in Alcohol Behavioral Couples Treatment (ABCT): 20 sessions over a 26-week treatment period for both partners, 90 min per session. Manualized treatment including homework as part of treatment protocol addressing women as well as their partners.		
Comparison	N=53 couples in Alcohol Behavioral Individual Treatment (ABIT): 20 sessions over a 26-week treatment period for women only, 60 min per session. Manualized treatment including homework as part of treatment protocol addressing women as well as their partners		
Length of follow-up	At three month intervals from baseline up 18 months after end of intervention.		
Outcome and effect size	In analysis: 102 couples; 7 couples never showed up for treatment. Latent growth curve models. Dependent variables: percentage of days abstinent (PDA) and percentage of days of heavy drinking (PDH). During treatment women increased their PDA and decreased their PDH, with significantly greater improvements in ABCT than in ABIT (d=0.59 for PDA; d=0.79 for PDH). Differences favouring ABCT were maintained during follow-up but were not significant (d=0.31 for PDA; d=0.19 for PDH).		
Funding	NIAAA		
Comments			

Title	Psychological and/or educational interventions for reducing alcohol consumption in pregnant women and women planning pregnancy.

First Author	Stade, B. C., 2009	Source	19370597
Level of evidence	1a	Study type	Systematic Review (narrative)
Study quality	Well documented		
Participants	Objectives: To determine the effectiveness of psychological and educational interventions to reduce alcohol consumption during pregnancy in pregnant women or women planning pregnancy.		
Patient characteristics	22 studies for possible inclusion. Four studies included, 715 pregnant women		
Intervention	Randomized controlled trials examining the effectiveness of psychological and educational interventions for reducing consumption of alcohol among pregnant women, or women planning for pregnancy.		
Comparison	Routine care, which may have included advice on reducing alcohol consumption.		
Length of follow-up	Not specified		
Outcome and effect size	The evidence from the limited number of studies suggests that psychological and educational interventions may result in increased abstinence from alcohol, and a reduction in alcohol consumption among pregnant women. However, results were not consistent, and the paucity of studies, the number of total participants, the high risk of bias of some of the studies, and the complexity of interventions limits our ability to determine the type of intervention which would be most effective in increasing abstinence from, or reducing the consumption of alcohol among pregnant women.		
Funding			
Comments			

Title	Home visits during pregnancy and after birth for women with an alcohol or drug problem (Review).		
First Author	Turnbull, C., 2012	Source	22258956
Level of evidence	1a	Study type	Systematic Review (Meta-analysis)
Study quality	Well documented		
Participants	Objectives: To determine the effects of home visits during pregnancy and/or after birth for women with a drug or alcohol problem. Data search up to 2011. 53 studies in review. 46 studies excluded. 7 studies accepted, most of them focusing on illicit drug use. Research group of Streissguth concentrated on alcohol consumption/dependence of mothers – 3 studies, N=96, partial randomization		
Patient characteristics	Home visits after birth		
Intervention	No home-visits		
Comparison	2005-2011		
Length of follow-up	Main results: Three studies compared home visits mostly after birth with no home visits in homes of women with alcohol and drug problems. Visitors included various professions and lay persons. There was no significant difference in continued alcohol use (three studies, 379 women; RR=1.18, 95% CI [0.96|1.46].		
Outcome and effect size			
Funding			
Comments			

Title	A randomized phase I trial of a brief computer-delivered intervention for alcohol use during pregnancy.		
First Author	Tzilos,G. K., 2011	Source	21823917
Level of evidence	1b	Study type	Randomized controlled pilot study (phase 1)
Study quality	Not focused on alcohol dependency but on alcohol consumption during pregnancy, otherwise well documented		
Participants	N=50 pregnant women attending an inner-city prenatal care clinic.		
Patient characteristics	Assessed 314, randomized 50, 27 to intervention, 23 to control. 82% African Americans, mean age 25.7 years.		
Intervention	N=27. Intervention: Computer delivered brief intervention.		
Comparison	N=23. Assessment only.		
Length of follow-up	2 lost for follow-up (could not be reached). Follow-up phone interviews one month after		

	intervention.
Outcome and effect size	Bivariate logistic regression analysis to examine the effect of treatment on alcohol use at follow-up. Ratings of intervention ease of use, helpfulness, and other factors were high (4.7-5.0 on a 1–5 scale). Participants in both conditions significantly decreased alcohol use at follow-up, with no group differences. However, birth weights for infants born to women in the intervention group were significantly higher ($p<0.05$, $d=0.62$).
Funding	
Comments	

Title	**Randomized controlled pilot study of cognitive behavioral therapy in a sample of incarcerated women with substance use disorders and PTSD.**		
First Author	**Zlotnick, C., 2009**	**Source**	**19892078**
Level of evidence	2c	**Study type**	Randomized controlled pilot study in prison.
Study quality	Very small sample, prison study, well documented		
Participants	N=49. Women prisoners who request intensive substance abuse treatment.		
Patient characteristics	N=103 approached for study, N=49 in study and randomized in intervention and control group. Mean age: 34.6 years.		
Intervention	N=27 in Seeking Safety (SS) group intervention program, on a voluntary basis, 90 mi per session, 3 times a week for 6-8 weeks. Also TAU as 12-steps oriented program in psychoeducational format, attendance was obligatory, 3 to 6 months. After release from prison each women was offered weekly individual booster sessions (60 min).		
Comparison	N=22 TAU as 12-steps oriented program in psychoeducation al format; attendance was obligatory, program lasted 3 to 6 months. Weekly individual case management and drug counselling. No offerings after release from prison.		
Length of follow-up	3-6 month post release from prison. Attrition rates in SS 15%, in TAU 5%.		
Outcome and effect size	ANCOVA at 3 and 6 months post release. No difference between study groups on PTSD symptoms, SUD or other measures. Women in both conditions showed significant improvements from intake to later time points on all of these outcomes across time.		
Funding	NIDA		
Comments			

3.7.3 Ältere Menschen

Title	**Integrated speciality mental health care among older minorities improves access but not outcomes: results of the PRISMe study.**		
First Author	**Areán, P. A., 2008**	**Source**	**18727133**
Level of evidence	1b	**Study type**	RCT PRISM-E
Study quality	High methodological standard, well documented study		
Participants	2,022, at-risk drinking: N=559		
Patient characteristics	>65, 1.046 were white, 499 Black, 297 Latino, 112 Asian, and 68 “other”, 73% male, 78% less than high school level of education, average age was 73 (SD=6.1). at-risk drinking, (as in PRISM-E defined)		
Intervention	Integrated care: Primary care clinics requiring MH/SA services on-site, including medication management, psychotherapy (group, individual and family), case management and a brief behavioral alcohol intervention based on Harm Reduction and Motivational Interviewing Techniques. If the patient agreed to treatment, the primary care provider prescribed medication to those patients who wanted to be treated with medication, and referred all patients to the MH/ SA provider in the primary care clinic for follow-up, care management, and/or psychotherapy		
Comparison	Brokerage case management: Patients were initially evaluated by the primary care provider, who referred the patient to a nurse or a medical social worker. Patients received an evaluation of patient need and access use barriers. Patients were linked to social services to overcome access barriers; for instance, transportation services for those who cannot drive. MH/SA services were provided in a separate location from the primary care clinics by licensed MH/SA providers, and included medication management, psychotherapy and Alcoholics Anonymous model treatment for heavy drinking. Specialty MH/SA service providers were instructed to coordinate care with the patient’s primary care providers to		

	the best of their abilities and to complete on-going documentation of service delivery.
Length of follow-up	6 months
Outcome and effect size	Access: No significant interaction between ethnicity and treatment assignment (p-value for interaction of 0.39), and no main effect for access. Time to first mental health visit: Mean time (in days) from baseline evaluation to first mental health visit was shorter in the integrated than in the referral arm, however, other than in the Asian sample, no differences in time to treatment within ethnic group were found. Overall number of visits: Results of the linear regression model of overall number of visits indicated a statistically significant interaction between treatment assignment and ethnicity (p<0.0001). Whites, Blacks, and Latinos in the integrated arm had a greater number of visits than those in referral arm. Clinical Outcomes: There was no statistically significant treatment effect on mean depression, anxiety, drinking or physical disability within each ethnic group. In both treatment arms, all ethnic groups had relatively similar values at 6 months. Mean post treatment depressive, anxiety and alcohol symptoms remained relatively high. However, there was a nonsignificant trend towards greater improvement following alcohol treatment for Whites. Older adults, with the exception of Asian elderly, are more likely to access and use MH/SA services if services are integrated into primary care medicine than if they are offered in specialty mental health care, even if case managers are on hand to facilitate linkage to community services.
Funding	PRISM-E is a collaborative research study funded by the Substance Abuse and Mental Health Services Administration (SAMH SA), including its three centers: the Center for Mental Health Services (CMHS), the Center for Substance Abuse Treatment (CSAT), and the Center for Substance Abuse and Prevention (CSAP). The Department of Veterans Affairs (VA), the Health Resources and Services Administration (HRSA), and the Center s for Medicare and Medica id Services (CMS) provide d additional support and funding
Comments	

Title	**Satisfaction With Mental Health Services in Older Primary Care Patients**		
First Author	**Chen, H., 2006**	**Source**	**16582046**
Level of evidence	1b	**Study type**	RCT, Data from PRISM-E
Study quality	Well done study. But no specific outcome measures for at risk drinking patients >65		
Participants	1,582, at-risk drinking: N=766		
Patient characteristics	24,930 patients >65 were screened 6,430 met criteria for distress or drinking. Of these, 3,205 gave written informed consent to detailed clinical assessment. Subsequently 2,022 patients were enrolled in the study, meeting criteria for a depressive disorder, an anxiety disorder, at-risk drinking of alcohol, or a combination of these conditions. Patients assessed with psychosis or hypo/manic disorder, or in current MH/SA treatment, were excluded. 1,208 (or 1,209, not clear) used the designed services or made the health visit at least once.		
Intervention	IC. At three-month follow up, 87% (N=618 of 709) completed assessments		
Comparison	ESR. At three months 87% (N=434 of 500) of ESR patients completed		
Length of follow-up	3 months		
Outcome and effect size	91% of the study participants rated the quality of the services they received as good or excellent. Almost 90% believed they had “definitely” or “generally” received the service they wanted, but only 73% thought the service had met their needs. Nevertheless, the majority was satisfied or very satisfied both in terms of the amount of help received (94%) and its effect in addressing their emotional problems (83%). Most of them believed that they definitely would go back to use the same service if they needed help again (93.5%) and would recommend the service to others (94.5%). The average of all items of the satisfaction score is 3.34, with 3 being “satisfied” and 4 being “very satisfied.” Those who were assigned to IC generally reported higher satisfaction on all items than those in the ESR model. The effect sizes were modest, and on two of the seven items (i.e., satisfaction with “the amount of help received from the service” and “the service helped deal with emotional problem”), the difference between IC and ESR was not significant.		

	Severity of alcohol drinking measured by SMAST-G were not associated
Funding	The federal Substance Abuse and Mental Health Services Administration (SAMH SA) and its three centers, the Center for Mental Health Services (CMHS), the Center for Substance Abuse Treatment (CSAT), and the Center for Substance Abuse Prevention (CSAP), sponsored and participated in this initiative, with CMHS serving as the lead. The Department of Veterans Affairs (VA), the Health Resources Services Administration (HRSA), and the Center s for Medica re and Medica id Services (CMS) provided additional funding, support, and collaboration
Comments	

Title	**An evaluation of an intervention to assist primary care physicians in screening and educating older patients who use alcohol.**		
First Author	**Fink, A., 2005**	**Source**	**16274375**
Level of evidence	1b	**Study type**	RCT
Study quality	High methodological standard, well documented study		
Participants	N=665		
Patient characteristics	>65, 53% female, mean age 76.6 years old, had consumed at least one alcoholic drink in the previous 3 months		
Intervention	First experimental intervention (combined report): Six physicians and their 198 patients, each of whom received reports of the patients alcohol use, risks, and problems. Patients also received personalized education based on their reports. Second experimental intervention (patient report); Five physicians whose 245 patients received reports, although the physicians did not. Patients also received personalized education. All eligible patients were asked to complete the CARPS at baseline and 12 months later. The CARPS has four components: a self-administered screening survey (the Alcohol-Related Problems Survey), software for scanning patient responses into a database, software for processing the responses and generating printed reports for physicians and patients of patients' drinking risks, and health education		
Comparison	12 physicians and their 222 patients. None of them received reports, nor did the patients receive any education during the study		
Length of follow-up	12 months		
Outcome and effect size	The patient report and combined report interventions were each associated with greater odds of lower-risk drinking at follow-up than usual care (OR=51.59 and 1.23, respectively, p<0.05 for each). The patient report intervention significantly reduced harmful drinking at follow-up from an expected 21% in usual care to 16%, eliminating an estimated 23% ((21%– 16%/21%) of harmful drinking. The patient report intervention also increased nonhazardous drinking from the 52% expected in usual care to 58%. Relative to usual care, patients in the combined report intervention decreased their consumption of alcohol by 1.14 drinks per week (p<0.05). There was no statistically significant evidence (p>0.05) that participants in the patient report intervention differed from usual care in their changes in drinking from baseline to follow-up. These results suggest that older primary care patients can effectively reduce alcohol consumption and alcohol use patterns when given personalized information about their drinking and health. Providing analogous information to physicians, as was done in the combined report intervention, is effective in decreasing total alcohol consumption, but it is no more effective at decreasing the associated risk (as measured by drinking classification) than reports only to patients.		
Funding	Unknown. The study used CARPS (Computerized Alcohol Related Problems Survey), of which copyright is owned by "Arlene Fink Associates". The other author s denied financial interests.		
Comments			

Title	**Harm reduction among at-risk elderly drinkers: a site-specific analysis from the multi-site Primary Care Research in Substance Abuse and Mental Health for Elderly (PRISM-E) study**		
First Author	**Lee, H. S., 2009**	**Source**	**18613283**
Level of evidence	1b	**Study type**	RCT, site study of PRISM-E at 1 site of 10

Study quality	Well done study with small sample, high methodological standard
Participants	34, male: 20, female: 14, mean age: 72,9, White: 17, African American: 12, Other: 5
Patient characteristics	Low income-patients >65, at-risk drinkers →14 drinks per week for men, >12 drinks per week for women, or four or more drinks four or more times during the past 3 months (binge drinking) or use of benzodiazepines or opioids and drinking seven or more drinks per week. Exclusion criteria dementia, severe cognitive impairment, psychosis, acute physical frailty, clients who had receives mental health or substance abuse treatment in the preceding 3 months
Intervention	The substance abuse treatment model was a harm reduction model developed for older adults with alcohol misuse: Motivational Interviewing strategy, three sessions, trained social workers. Alcohol services were provided in a non-profit community-based, non-residential, 8-week, peer-oriented program for adults over age 55, based on the 12-step model of abstinence. Individual and group recovering planning, psychiatric care, addiction education and case management were provided. The program was staffed by staff, faculty, and volunteers from local health and substance abuse clinicians.
Comparison	
Length of follow-up	6 months
Outcome and effect size	Only 20 of the 34 at-risk drinkers (59%) received services by the 6-month time period, significantly more of these individuals were in the integrated care condition (93% vs. 35%, p=0.001). Among at risk drinkers in the integrated care condition, the average number of drinks in the prior week and the average number of binge drinking episodes in the prior 3 months measured at 6 months and at baseline decreased and were significantly different at the two time points (z=2.83 p=0.005, and z=2.98 p=0.003). Among at risk drinkers in the enhanced referral condition, there were no significant differences in any of the clinical outcomes between the two time points. Conclusion: The integration of substance abuse treatment into primary care is a viable method for ensuring older low-income adults access to services.
Funding	PRISM-E is a collaborative research study funded by the Substance Abuse and Mental Health Services Administration (SAMH SA), including its three centers: the Center for Mental Health Services (CMHS), the Center for Substance Abuse Treatment (CSAT), and the Center for Substance Abuse and Prevention (CSAP). The Department of Veterans Affairs (VA), the Health Resources and Services Administration
Comments	

Title	**PRISM-E: comparison of integrated care and enhanced specialty referral in managing at-risk alcohol use.**		
First Author	**Oslin, D. W., 2006**	**Source**	**16816279**
Level of evidence	1b	**Study type**	RCT, PRISM-E study, 9 of 10 sites
Study quality	High methodological standard, well documented study		
Participants	N=560		
Patient characteristics	>65, at-risk drinking: >14 drinks per week for men, >12 drinks per week for women, or four or more drinks four or more times during the past 3 months (binge drinking) ore use of benzodiazepines or opioids and drinking seven or more drinks per week (n=6). 513 (92%) were white, mean age was 72.0 years. 146 (26%) had concurrent depression or anxiety.		
Intervention	Integrated Care Model (IC): N=280. Standardized intervention to include three 20-to 30-minute face-to-face brief alcohol intervention counseling sessions		
Comparison	Enhanced Speciality Referral (ESR) N=280		
Length of follow-up	6 months		
Outcome and effect size	Greater engagement in care in IC (65%), compared with ESR (38%), and a greater number of visits in the IC (p=0.001). In IC 120 participants (43%) received at least one brief alcohol intervention session. Only 24 p. (9%) had the recommended three brief alcohol intervention visits. Overall, drinking measures declined in both models. Average quantity declined by 35% and frequency by 45%. There were no differences in drinking at six months between the two groups. In total, 21% participants reduced their drinking (18% in IC, and 23% in ESR). The average quantity and frequency models show significant time effects, with reduction in drinking by six months for all participants except for those with a dual diagnosis. An important finding from this study is the minimal uptake and		

	implementation of the interventions in both study groups.
Funding	PRISM-E is a collaborative research study funded by the Substance Abuse and Mental Health Services Administration, including its three centers: Center for Mental Health Services, Center for Substance Abuse Treatment, and Center for Substance Abuse and Prevention. The Department of Veterans Affairs, the Health Resources and Services Administration, and the Centers for Medicare & Medicaid Services
Comments	

Title	**Predictors of Adherence Within an Intervention Study of the At-Risk Older Drinker: PRISM-E.**		
First Author	**Zanjani, F., 2006**	**Source**	**17085763**
Level of evidence	1b	**Study type**	RCT, PRISM-E
Study quality	High methodological standard, well documented study		
Participants	N=8367		
Patient characteristics	Persons aged 65 and older who had a primary care appointment during the study period (March, 2000 through August, 2001) with 1 of 8 participating primary care clinics (2 in the VA and 6 in non-VA community practices) were eligible for recruitment (n=8367). From the screening pool, 365 (9%) met the screening criteria for alcohol (consuming more than 7 drinks per week and/or 2 binge episodes in the last 3 months) and were invited to participate in the baseline interview. There were 287 (78%) participants who were able to complete the baseline interview, and from this participant pool, 145 (50%) met at-risk drinking criteria (drinking more than 13 drinks per week for men and 11 drinks per week for women, twice the recommended drinking level for older adults, 26 or having 4 or more drinks [binge drinking] 4 or more times during the prior 3 months) and were invited to participate in treatment (phase 2). Participants who agreed to treatment (n=125, 86%) were then randomized to 1 of 2 treatment models (phase 3). After randomization, participants were monitored for their treatment initiation and 3-, 6-, and 12-month follow up research adherence. Because of concerns of crosstolerability and drug– alcohol interactions, any use of a benzodiazepine or opioid medication and drinking 7 or more drinks per week also qualified as at-risk drinking. Four participants were eligible based on this criterion.		
Intervention	Integrated care included (a) MH (mental health)/SA (substance abuse) services co-located in primary care; (b) verbal and/or written communication about the evaluation and treatment plan between the MH/SA clinician and PCP (primary care physician); and (c) the availability of brief alcohol interventions (BAI) designed for at-risk drinking.		
Comparison	Enhanced referral care included (a) MH/SA evaluation and treatment occurring in a physically separate location by licensed mental health or substance abuse professionals; (b) coordinated follow-up contacts with the primary care clinic if the participant missed the first scheduled visit; and (c) assistance with transportation		
Length of follow-up	12 months		
Outcome and effect size	Participation in Screening interview: Of the 8.367 participants randomly selected for screening, 4.000 (48%) completed the screening process, with 2.095 refusing, 1.340 unable to contact, and 932 ineligibles based on screening criteria. Participants who participated in the screening interview were younger (M=74.8, SD=5.8) than those not screened (M=76.2, SD=6.7; $\chi 2$= 98.11, df=1, odds ratio [OR]=0.96, 95% CI [0.95|0.97], p<0.001). Gender was not associated with being screened, but females more often refused screening (53% vs 46%) and men were more likely to be unable to be contacted (36% vs 18%; $\chi 2$=57.64, df=1, OR=0.55, 95% CI [0.47|0.68], p<0.001). Participation in Randomization Of the 145 participants who met at-risk drinking criteria, 125 (86%) agreed to treatment randomization; there were no significant differences between participants who consented to randomization from those who did not consent. Treatment Initiation Thirty-seven of the 60 participants in integrated care (62%) and 36 of the 65 participants in referral care (55%) initiated treatment. Treatment initiation rates were not statistically different across treatment groups; however, treatment initiation was differentially predicted in the treatment groups. Integrated care participants in the precontemplative and contemplative stage were more likely to initiate treatment (precontemplative 72%; contemplative 75%; action 20%), compared with recontemplative and contemplative participants		

	(precontemplative 41%; contemplative 45%; action 80%) in referral care (χ2=4.06, df=1, β=-1.67, p=0.0438). Integrated care participants with no history or a desire/attempt to cut down on drinking were more likely to initiate treatment (84%), compared with 53% of integrated participants with such a history, 30% of referral care participants with no history, and 70% of referral participants with a history of desires/attempts to cut down on drinking (χ2=11.79, df=1, β=3.23, p=0.0006). Adherence to Research Follow-Up Adherence to research follow-up rates was not statistically different across treatment groups. Three-month research adherence was differentially predicted in treatment groups by binge levels (χ2=4.12, df=1, β=.02, p=0.0423). Integrated care participants who completed the 3-month research interview had the highest binge levels (M=17.4, SD=28.6), compared with participants who refused (M=14.6, SD=27.6) and participants whom we were unable to contact (UTC) (M=8.4, SD=18.5). Referral care participants who were UTC at 3 months had the highest binge levels (M=46.8, SD=41.6), compared with participants who completed the 3-month research interview (M=13.4, SD=26.3) and participants who refused (M=12.2, SD=25.4). Participants in the precontemplative and contemplative stage in integrated care were more likely than those in referral care to initiate treatment. Furthermore, a greater percentage of integrated care participants with no history, compared with a greater percentage of referral care participants with a history of desires/attempts to cut down on drinking, initiated treatment. A comparison between integrated care and referral care groups suggests that integrated care models may have a better capacity to initiate treatment in participants who have not yet recognized the need for/or taken action toward treatment or have a history of experience with alcohol treatment and to enhance research commitment in heavier drinkers. Individuals in integrated care with the highest treatment initiation were in the precontemplative and contemplative stage. However, individuals in referral care with the highest treatment initiation were individuals in the action stage (recognized the need to change alcohol behaviors and already taking steps to improve their drinking behaviors) and individuals who had a history improving or thinking about improving their drinking behaviors. Thus, the integrated model appeared to overcome individual barriers such as a lack of existing/past actions to improve alcohol behaviors and more severe drinking symptomology, which is a crucial component for a successful prevention program. Furthermore, as compared with referral care, the unique components of the integrated care model (e.g., location, brief alcohol treatment model) may make it less difficult for at-risk older individuals to participate in research and treatment.
Funding	
Comments	

Title	**Longitudinal course of substance treatment benefits in older male veteran at-risk drinkers.**		
First Author	**Zanjani, F., 2008**	**Source**	**18245767**
Level of evidence	1b	**Study type**	RCT, part of PRISM-E study at 3 sites of 10
Study quality	High methodological standard, well documented study		
Participants	N=258 (51% of the total multisite sample of randomized at-risk drinkers). Mean age: 71.6. White: 65.8%. Two groups: “problem at-risk drinkers” N=111; “nonproblematic at-risk drinkers” N=147		
Patient characteristics	Male, >65, “At-risk drinking” defined as >13 drinks per week (1.5 times the NIAAA recommended drinking level for older adults) or having four or more drinks (binge drinking) on four or more occasions during the previous 3 months. “Problem at risk drinkers (PD)”: SMAST-G: 3 or >3 “Nonproblematic at-risk drinkers (ND)”: SMAST-G: <3		
Intervention	Integrated Care Model (IC): Mental health and/or substance abuse services collocated within primary care, availability of brief alcohol interventions designed for at-risk drinking.		
Comparison	Enhanced Specialty Referral Model (ESR): Treatment occurring in a separate location by licensed mental health or substance abuse professionals		
Length of follow-up	6 months after 6 month study period		
Outcome and effect size	Treatment engagement: Participants in IC treatment had higher levels of treatment engagement with no PDS (Problem at-risk drinkers) effect at 3 months (p=0.04) and 6 months (p=0.03) but not at 12 months. Drinking scores: PDS effect for binges (p=0.03)		

	indicating that PD showed greater decline in binges as compared to ND. Despite significant reduction in drinking, mean drinking and binge rates for both nonproblematic and problem at-risk drinkers at 12 months were above NIAAA recommended levels for older adults. Interaction effect: Interaction effect (p=0.03) for at-risk drinking at 3 months indicating that, at this time period, fewer problem drinkers than ND were drinking excessively in IC (22% vs 25%), whereas, conversely, more problem drinkers than ND were at-risk in ESR (43% vs 25%). Longitudinal random effect models examining time, treatment, and PDS effect on drink per week, binge drinking, MCS (mental component score), and PCS (physical component score), indicated trends for reduction in drinking over time irrelevant of treatment care assignment. Whereas there were no effects indicating better outcomes for either treatment model, there was evidence of higher treatment engagement in the IC model. However, participation in treatment improved binge drinking reductions for problem drinkers, but treatment engagement appeared to have minimal effect on reductions in the number of drinks per week, regardless of treatment condition. Furthermore, there was no evidence that the implemented treatment models were successful at improving physical or mental functioning.
Funding	PRISM-E is a collaborative research study funded by the Substance Abuse and Mental Health Services Administration (SAMH SA), including its three centers: the Center for Mental Health Services (CMHS), the Center for Substance Abuse Treatment (CSAT), and the Center for Substance Abuse and Prevention (CSAP). The Department of Veterans Affairs (VA), the Health Resources and Services Administration (HRSA), and the Center s for Medicare and Medicaid Services (CMS) provide d additional support and funding. The development of the manuscript was supported by a training grant from the Nation al Institute of Mental Health (NIMH; 5 T32 MH199 31-08A1) awarded to David Oslin.
Comments	

Title	**What Works for Whom and Why: A Narrative Systematic Review of Interventions for Reducing Post-Traumatic Stress Disorder and Problematic Substance Use Among Women With Experiences of Interpersonal Violence**		
First Author	**Bailey, K., 2019**	**Source**	**30797400**
Level of evidence	2a	**Study type**	narrative systematic review and meta-analysis
Study quality	?		
Participants	N=63 studies women only		
Patient characteristics	N=20 controlled trials women only		
Intervention	Subgroups - context - and mechanism of action study		
Comparison			
Length of follow-up			
Outcome and effect size	Safe social support and ongoing risks of violence were identified as contextual factors which may affect treatment outcomes, requiring attention by researchers and treatment providers. Whilst there was some evidence that reduced PTSD correlates with substance use decrease, there may be more than one pathway to substance use reduction among women with PTSD, requiring a focus on emotional regulation. Other 'active mechanisms' included different modalities of coping skills and support to rebuild connection with self and others. Lack of supplementary studies for trials involving past-focused treatment precluded detailed discussion of these models.		
Funding	UK Economics and Social Research Council ref.: (ES/J500057/!)		
Comments			

Title	**Intimate Partner Violence Outcomes in Women With PTSD and Substance Use: A Secondary Analysis of NIDA Clinical Trials Network "Women and Trauma" Multi-site Study**		
First Author	**Cohen, L. R., 2013**	**Source**	**23584194**
Level of evidence	2b	**Study type**	Secondary analysis
Study quality	(high)		
Participants	N=288		

Patient characteristics	see original study of Hien et al. 2009
Intervention	Seeking Safety vs Women's Health Education vs TAU
Comparison	Participants reporting IPV in 12 month follow-up and participants not reporting IPV
Length of follow-up	12 months
Outcome and effect size	Significant risk factors associated with IPV during Baseline abstinence associated with ↓ risk IPV at FU (OR=0.33, p<0.05). FU were: living with someone who has an alcohol problem (OR=3.2), higher total lifetime traumatic exposures (p=0.05), and recent physical/sexual assault (p=0.06). Baseline abstinence associated with ↓ risk IPV at FU (OR=0.33, p<0.05). TX arm not associated with IPV; interaction between TX and baseline abstinence: those abstinent and in SS were less likely (OR=0.24) to experience IPV compared to non-abstinent SS and abstinent WHE.
Funding	Grant from National Drug Abuse Treatment Clinical Trials Networt (CTN) NIDA: U10 DA013035.
Comments	

Title	**Combining Seeking Safety With Sertraline for PTSD and Alcohol Use Disorders: A Randomized Controlled Trial**		
First Author	**Hien, D. A., 2015**	**Source**	**25622199**
Level of evidence	1a	**Study type**	RCT
Study quality	high		
Participants	N=69		
Patient characteristics	81% female; 59% African American) with primarily childhood sexual (46%) and physical (39%) trauma exposure, and drug dependence in addition to AUD		
Intervention	12 sessions of SS with either sertralin (N=32) or placebo (N=37)		
Comparison	PTSD symptom reduction and SUD symptom reduction		
Length of follow-up	6 and 12 months		
Outcome and effect size	Both groups demonstrated significant improvement in PTSD symptoms. The SS plus sertraline group exhibited a significantly greater reduction in PTSD symptoms than the SS plus placebo group at end-of-treatment (MD=-16.15, p=0.04, d=0.83), which was sustained at 6- and 12-month follow-up (MD=-13.81, p=0.04, d=0.71, and MD=-12.72, p=0.05, d=0.65, respectively). Both SS groups improved significantly on AUD severity at all posttreatment time points with no significant differences between SS plus sertraline and SS plus placebo.		
Funding	This study was supported by grant R01AA014341 from the National Institute on Alcohol Abuse and Alcoholism (primary investigator: Denise A. Hien).Dr. Levin currently receives medication from US World Med for an ongoing study that is sponsored by the National Institute on Drug Abuse and served as a consultant to GW Pharmaceuticals, Eli Lily, and served on an advisory board to Shire in 2006-2007.		
Comments			

Title	**Emotion Dysregulation Moderates the Effect of Cognitive Behavior Therapy With Prolonged Exposure for Co-Occurring PTSD and Substance Use Disorders**		
First Author	**Hien, D. A., 2017**	**Source**	**29049902**
Level of evidence	2b	**Study type**	Secondary analysis
Study quality	high		
Participants	n=110		
Patient characteristics	see original study of Ruglass et al. (2017)		
Intervention	see original study of Ruglass et al. (2017)		
Comparison	We examined the moderating impact of overall Emotional Dysregulation (ED) at baseline (DERS total score) on within-treatment change in PTSD symptom severity and days of primary substance use.		
Length of follow-up	see Ruglass et al. (2017)		
Outcome and effect size	Baseline ED severity moderated treatment outcomes such that high ED was associated with greater reduction in PTSD severity among those who received COPE relative to RPT and AMCG. In contrast, low ED was associated with greater reduction in substance use		

	among those in RPT relative to COPE and AMCG. Our secondary analysis suggests that taking difficulties in emotion regulation into consideration can facilitate efforts to individualize and optimize treatment pathways for PTSD+SUD.
Funding	This study was supported by a grant from the National Institute on Drug Abuse (NIDA; R01DA10843; PI: Denise A. Hien, Ph.D.);
Comments	

Title	**Effectiveness of Seeking Safety for Co-Occurring Posttraumatic Stress Disorder and Substance Use**		
First Author	**Lenz, S. A., 2016**	**Source**	
Level of evidence	2b	**Study type**	Meta-analysis
Study quality			
Participants	N=1.997, 12 between group studies		
Patient characteristics	see details in 12 original studies		
Intervention	"Research questions: (a) To what degree is Seeking Safety effective for decreasing the primary symptoms of PTSD? (b) To what degree is Seeking Safety effective for treating the symptoms of co-occurring substance use among individuals with PTSD? and (c) What are the relationships between mean sample age, ethnic identity, and reported trauma-type moderators and aggregated effect size?"		
Comparison	N=846 participants receiving seeking safety treatment, N=955 received an alternative treatment modality, and N=196 received no treatment or were assigned to a wait-list condition vs. other treatments vs. waiting lists.		
Length of follow-up	Depending on studies		
Outcome and effect size	This meta-analysis of studies evaluating the effectiveness of Seeking Safety for reducing the severity of PTSD and co-occurring substance use symptoms yielded mixed, yet promising findings. Among the 12 studies identified, mean effect sizes related to PTSD symptom reduction were robust across comparison group types (i.e., wait list or alternative treatments). On the client level, aspects of client background may mediate treatment effects when compared with alternative treatments - mainly race (and cultural background) and multiple types of trauma vs. one type. Evaluation of mean effect sizes for Seeking Safety interventions for decreasing frequency of substance use yielded no defensible estimations of treatment effect.		
Funding	not reported		
Comments			

Title	**A Randomized Controlled Trial of Treatments for Co-Occurring Substance Use Disorders and Post-Traumatic Stress Disorder**		
First Author	**McGovern, M. P., 2015**	**Source**	**25846251**
Level of evidence	1a	**Study type**	RCT
Study quality	High		
Participants	N=221		
Patient characteristics	59% female, 41% male, mean age 35.3 years, white 95&, alcohol abuse 61%.		
Intervention	We report on a randomized controlled trial comparing the effect of Integrated Cognitive Behavioral Therapy (ICBT) plus standard care, individual addiction counseling plus standard care, and standard care alone on substance use and PTSD symptoms.		
Comparison	Three-group, multi-site randomized controlled trial. ICBT plus standard care (SC) (n=73); Individual Addiction Counseling (IAC) plus SC (n=75), or SC only (n=73).		
Length of follow-up	3 and 6 months		
Outcome and effect size	Primary outcomes: PTSD severity and substance use severity at 6-months. Secondary outcomes: Therapy retention. Findings: PTSD symptoms reduced in all conditions with no difference between them. In analyses of covariance, ICBT produced more favorable outcomes on toxicology than IAC or SC (comparison with IAC: Parameter estimate=1.10, 95% CI [0.17|2.04]; comparison with SC: Parameter estimate=1.13, 95% CI [0.18|2.08]) and had greater reduction in reported drug use than SC (Parameter estimate=-9.92, 95% CI [-18.14|-1.70). ICBT patients had better therapy continuation versus IAC (p<0.001). There		

	were no unexpected or study related adverse events.
Funding	not reported
Comments	

Title	**Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence: a randomized controlled trial.**		
First Author	**Mills, K. L., 2012**	**Source**	**22893166**
Level of evidence	1a	**Study type**	RCT
Study quality	High		
Participants	N=103		
Patient characteristics	62% women, mean age 33.7 years. Australian-born 85%, Aboriginals 6%, alcohol abuse 12% and high percentage of mixed alcohol and drug use.		
Intervention	To determine whether an integrated treatment for PTSD and substance dependence, Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE), can achieve greater reductions in PTSD and substance dependence symptom severity compared with usual treatment for substance dependence.		
Comparison	Participants were randomized to receive COPE plus usual treatment (n=55) or usual treatment alone (control) (n=48). COPE consists of 13 individual 90-minute sessions (i.e. 19.5 hours) with a clinical psychologist.		
Length of follow-up	6 weeks to 9 months		
Outcome and effect size	"From baseline to 9-month follow-up, significant reductions in PTSD symptom severity were found for both the treatment group (MD=-38.24, 95% CI [47.93|-28.54]) and the control group (MD=-22.14, 95% CI [-30.33|-13.95]); however, the treatment group demonstrated a significantly greater reduction in PTSD symptom severity (MD=-16.09, 95% CI [-29.00|-3.19]).No significant between-group difference was found in relation to improvement in severity of substance dependence (0.43 vs 0.52; incidence rate ratio: 0.85, 95% CI [0.60|1.21]), nor were there any significant between-group differences in relation to changes in substance use, depression, or anxiety."		
Funding	This study was funded by Australian National Health and Medical Research Council (NHMRC) project grant 455209. (For more details see Conflict of Interest)		
Comments			

Title	**Efficacy of Integrated Exposure Therapy vs Integrated Coping Skills Therapy for Comorbid Posttraumatic Stress Disorder and Alcohol Use Disorder: A Randomized Clinical Trial**		
First Author	**Norman, S. B., 2019**	**Source**	**31017639**
Level of evidence	1a	**Study type**	RCT
Study quality	High		
Participants	119 veterans		
Patient characteristics	"A total of 119 veterans (mean [SD] age, 41.6 [12.6] years; 107 [89.9%] male) were randomized."		
Intervention	"Veterans underwent I-PE (Concurrent Treatment of PTSD and Substance Use Disorder Using Prolonged Exposure) or I-CS (Seeking Safety) therapy."		
Comparison	3 and 6 months follow-up		
Length of follow-up	Linear mixture models found that PTSD symptoms decreased in both conditions, with a significantly greater decrease for I-PE treatment compared with I-CS treatment (treatment × time interaction, -2.83; $F_{3,233.1}$=4.92; Cohen d=0.41; p=0.002). The percentage of heavy drinking days improved in both conditions but was not statistically different between I-PE and I-CS treatment (treatment × time interaction, 1.8%; $F_{3,209.9}$=0.18; Cohen d=0.04; p=0.91).The I-PE arm had a greater reduction in PTSD symptoms than the I-CS arm and comparable drinking decreases. The study provides evidence that exposure therapy is more efficacious in treating PTSD than a more commonly available integrated treatment without exposure for comorbid PTSD and AUD.		
Outcome and effect size	"This study was supported by VA Clinical Science Research and Development Merit Grant 1I01CX000756 (Dr. S. Norman, principal investigator). Other funding support included training fellowships through the VA Office of Academic Affiliation (Drs. Haller and		

	Colvonen) and T32 fellowship T32AA013525 through the National Institute on Alcohol Abuse and Alcoholism (Dr. Myers and Mr. Lyons)."
Funding	
Comments	

Title	**Psychological interventions for post-traumatic stress disorder and comorbid substance use disorder: A systematic review and meta-analysis**		
First Author	**Roberts, N. P., 2015**	**Source**	**25792193**
Level of evidence	1a	**Study type**	Systematic review and meta-analysis
Study quality	14 RCTs of good methodological quality		
Participants	N=14 RCT-studies, N=1.506 participants		
Patient characteristics	In RCTs number of women varied between 34% and 100%. Measurement: (1) Pre-post PTSD severity, (2) drug and alcohol use, (3) treatment completion. Post measurement: 5-7 months after regular end of treatment.		
Intervention	Seeking safety, individual trauma-focused cognitive-behavioural interventions and non-trauma-focused interventions aimed at reducing traumatic stress symptoms, SUD symptoms or both.		
Comparison			
Length of follow-up	5-7 months (and longer, depending on studies)		
Outcome and effect size	We found evidence to suggest that psychological intervention that includes a trauma-focused component alongside intervention for SUD can help reduce PTSD symptom severity for individuals with PTSD and comorbid SUD. These results need to be interpreted with caution. Treatment effects were small and mostly for PTSD. (...) We found little evidence to support the use of non-trauma-focused group-based interventions.		
Funding	This study was not directly funded but was undertaken whilst Dr. N. Roberts was in receipt of a National Institute of Social Care and Health Research — Academic Health Science Committee (NISCHR AHSC) Clinical Research Fellowship and was supported by the Institute of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine and Cardiff & Vale University Health Board.		
Comments			

Title	**Helping Alliance, Retention, and Treatment Outcomes: A Secondary Analysis From the NIDA Clinical Trials Network Women and Trauma Study**		
First Author	**Ruglass, L. M., 2012**	**Source**	**22475068**
Level of evidence	2b	**Study type**	Secondary analysis
Study quality	(high)		
Participants	N=223		
Patient characteristics	see study of Hien et al., 2009		
Intervention	Seeking Safety vs. Women's Health Education vs. TAU		
Comparison	therapeutic alliance		
Length of follow-up	12 months		
Outcome and effect size	SS had higher alliance than WHE at week 2 (p=0.01); difference was small (SS M=5.33, WHEM=5.15 on 6-point scale, findings at week 6 similar.• ↑ alliance at week 2 was associated with ↓ PTSD severity post-TX (p<0.001) for SS and WHE; this weakened over time.• Alliance at week 2 was associated with # of TX sessions attended (p=0.05) for SS and WHE.• Alliance was not associated with substance use (p=0.59).		
Funding	Not reported		
Comments			

Title	**Concurrent treatment with prolonged exposure for co-occurring full or subthreshold posttraumatic stress disorder and substance use disorders: A randomized clinical trial**		
First Author	**Ruglass, L. M., 2017**	**Source**	**28490022**
Level of evidence	1a	**Study type**	RCT
Study quality	high		

Participants	N=110
Patient characteristics	Participants: N=110; 64% males; 59% African Americans, who met DSM-IV-TR criteria for full or subthreshold PTSD and SUD.
Intervention	Participants were randomly assigned to COPE (N=39), RPT (N=43), or AMCG (N=28).
Comparison	Reduction of PTSD-Symptoms and Reduction of SUD Symptoms.
Length of follow-up	3 months
Outcome and effect size	At end-of-treatment, COPE and RPT demonstrated greater reduction in PTSD symptom severity relative to AMCG (COPE-AMCG=-34.06, p<0.001; RPT-AMCG=-22.58, p=0.002). Although the difference between COPE and RPT was not significant in the complete sample, the subset of participants with full (versus subthreshold) PTSD demonstrated significantly greater reduction of PTSD severity in COPE relative to RPT. Both treatments were superior to AMCG in reducing days of primary substance use (COPE-AMCG=-0.97, p=0.01; RPT-AMCG=-2.07, p<0.001). Relative to COPE, RPT showed significantly more improvement in SUD outcome at end-of-treatment (RPT-COPE=-1.10, p=0.047). At 3-month follow-up, COPE and RPT maintained their treatment gains and were not significantly different in PTSD severity or days of primary substance use.
Funding	This study was supported by a grant from the National Institute on Drug Abuse (NIDA; R01DA10843; PI: Denise A. Hien, Ph.D.).
Comments	

Title	**A Multisite Randomized Controlled Trial of Seeking Safety vs. Relapse Prevention Training for Women With Co-Occurring Posttraumatic Stress Disorder and Substance Use Disorders**		
First Author	**Schäfer, I., 2019**	**Source**	**30815234**
Level of evidence	1a	**Study type**	RCT
Study quality	High		
Participants	N=343		
Patient characteristics	100% women, mean age 40.9 years, means years in school: 10, 78% unemployed etc. Main substance use disorders: alcohol (85%), sedatives (31%), cannabis (49%), other illicit drugs (ca. 25%). Prior in substance abuse treatment: 66%.		
Intervention	Seeking Safety; N=111, 16 sessions a 90 minutes		
Comparison	Relapse Prevention Treatment N=115, TAU N=117		
Length of follow-up	3 and 6 months		
Outcome and effect size	ITT analysis showed similar decreases in PTSD severity among the three conditions. Seeking Safety + TAU showed superior efficacy to TAU alone and equal efficacy to RPT + TAU on depression and emotion regulation.		
Funding	German Federal Ministry of Education and Research (BMBF) Nr01KR1203A.		
Comments			

3.8 Medizinische Rehabilitation

Title	**A double- blind, placebo- controlled trial to assess the efficacy of quetiapine fumarate XR in very heavy- drinking alcohol- dependent patients.**		
First Author	**Litten, R.Z., 2012**	**Source**	**21950727**
Level of evidence	1b	**Study type**	RCT
Study quality	High: individual RCT; double-blind intervention; follow-up		
Participants	N=224		
Patient characteristics	Inpatients		
Intervention	quetiapine vs. placebo and Medical Management behavioral intervention; MM includes assessment of medication side effects, subject education about excessive drinking, abstinence advice, enhancement of adherence to the study medication regimen, support for recovery, and encouragement to attend mutual self- help groups such as Alcoholics Anonymous..		
Comparison	quetiapine vs. placebo and Medical Management behavioral intervention		
Length of follow-up	4-week follow-up		
Outcome measures	percentage heavy-drinking days, percentage days abstinent, drinks per drinking day, drinks per day, percentage very heavy-drinking days, percentage subjects abstinent, and percentage subjects with no heavy-drinking days, craving, depression, anxiety, poor sleep, and quality of life		
Outcome and effect size	No differences between the quetiapine and placebo groups in percentage of heavy-drinking days, or other drinking outcomes. Patients who reduced their drinking prior to randomization had significantly better drinking outcomes during the maintenance phase (p<0.001). Statistically significant adverse events that were more common with quetiapine versus placebo include dizziness (14 vs. 4%), dry mouth (32 vs. 9%), dyspepsia (13 vs. 2%), increased appetite (11 vs. 1%), sedation (15 vs. 3%), and somnolence (34 vs. 9%)		
Comments	.		

Title	**Meta-analysis of supplement al treatment for depressive and anxiety disorders in patients being treated for alcohol dependence.**		
First Author	**Hobbs, .J.D., 2011**	**Source**	**21679263**
Level of evidence	1a	**Study type**	Meta-analysis (15 RCTs)
Study quality	High: Meta-analysis of 15 RCTs		
Participants			
Patient characteristics	AUD		
Intervention	AUD treatment with a psychiatric treatment for co- occurring internalizing disorder		
Comparison	CBT vs. medication		
Length of follow-up	/		
Outcome measures	Anxiety outcomes, alcohol-related outcomes		
Outcome and effect size	CBT intervention had a pooled estimate of effect size of d=0.66, while medication yielded a smaller estimate pooled effect size of d=0.24. Studies in which anxiety was treated also demonstrated significantly greater pooled effects sizes for the internalizing outcome (d=0.52) than was true for studies in which depression was treated (d=0.21). Trend (p=0.09) for better alcohol outcomes in studies with high vs. low effect sizes on the internalizing outcomes.		
Comments	.		

Title	**The efficacy of disulfiram for the treatment of alcohol use disorder.**		
First Author	**Jørgensen, C.H., 2011**	**Source**	**21615426**
Level of evidence	1a	**Study type**	Meta-analysis (11 RCTs)
Study quality	High: large sample size, meta-analysis of 11 RCTs		
Participants	N=1.527		
Patient characteristics	Men & women with AUD (India, USA, Finland, Italy, Austria, DK)		
Intervention	Disulfiram treatment vs. placebo, none or other abstinence-supportive treatments		

Comparison	Disulfiram treatment vs. placebo, none or other abstinence-supportive treatments
Length of follow-up	Up to 12- month follow-up
Outcome and effect size	Disulfiram Versus Other Pharmalogical Abstinence-Supportive Drugs: Four out of six studies reported significantly more abstinent patients among those treated with Disulfiram (respectively, 86 vs. 44%, 88 vs. 46%, 90 vs. 56%, and 79 vs. 52%). Disulfiram Versus Placebo: significantly increased number of abstinent patients among the disulfiram treated (54 vs. 15%). Disulfiram Versus No Treatment: The results revealed in 1 case a significantly increased abstinence in patients treated with disulfiram as all 20 patients treated remained abstinent during the 3 weeks they received the medicine, whereas the control group continued to drink as they used to. Disulfiram had a significantly better effect on abstinence when compared with placebo, none, or other treatment in 6 of the 10 studies.
Comments	.

Title	**Speeches, strangers, and alcohol use: the role of context in social stress response dampening**		
First Author	**Ham, L.S., 2011**	**Source**	**21596011**
Level of evidence	2a	**Study type**	RCT
Study quality	Low: small sample size; students		
Participants	N=68		
Patient characteristics	undergraduates		
Intervention	consume of alcoholic (target BAC=.08%; n=22, consume of vodka), placebo (n=20, participants instructed that they were consuming vodka with juice mixer but actually consumed a drink with little alcohol), or nonalcoholic control (n= 20, participants knowingly consumed a nonalcoholic juice mixture) beverage followed by the anxiety- inducing social tasks (performance-based (a speech) and an interaction- based (a conversation) social situation)		
Comparison	three beverage conditions: alcohol vs. placebo vs. control		
Length of follow-up	/		
Outcome measures	Social Interaction Anxiety Scale (SIAS), Social Phobia Scale (SPS), Rutgers Alcohol Problem Inventory (RAPI), Subjective Units of Discomfort Scale (SUDS), Breath alcohol		
Outcome and effect size	Significant alcohol condition x social task condition x measurement point three-way interaction (F(6, 110)=2.54, p=0.02, hp 2=.12), significant two-way interaction between alcohol condition and measurement point (F(6, 110)=3.62, p=0.003, hp 2=.17), main effects of social task condition (F(1, 57)=5.24, p=0.03, hp 2=.08); For the alcohol (F(3, 17)=4.20, p=0.02, hp 2=.43) and placebo conditions (F(3, 15)=6.14, p=0.006, hp 2=.55), SUDS increased;		
Comments	.		

Title	**Internet therapy versus internet self-help versus no treatment for problematic alcohol use: A randomized controlled trial.**		
First Author	**Blankers, M., 2011**	**Source**	**21534652**
Level of evidence	1b	**Study type**	RCT
Study quality	High: RCT; follow-up		
Participants	N= 205		
Patient characteristics	Male/female, mean age: 42 years		
Intervention	Internet- based therapy (therapy alcohol online; TAO) vs. Internet- based self- help (self-help alcohol online; SAO) vs. untreated waiting-list control group (WL)		
Comparison	Three groups: TAO, SAO, WL		
Length of follow-up	3-month follow-up, 6-month follow-up		
Outcome measures	Primary outcome measures were alcohol consumption and treatment response. Secondary outcome measures included measures of quality- of-life.		
Outcome and effect size	Significant effects for TAO versus WL (p=0.002) and for SAO versus WL (p=0.03) on alcohol consumption at 3 months post randomization. Differences between TAO and SAO were not significant at 3 months post randomization (p=0.11) but were significant at 6 months post randomization (p =.03), with larger effects obtained for TAO		

Comments	.

Title	**Alcohol and depression.**		
First Author	**Boden, J.M., 2011**	**Source**	**21382111**
Level of evidence	2c	**Study type**	Meta-analysis
Study quality	Moderate: studies of literature; no experiment al design; Studies of literature from 1980 to 2010		
Participants	/		
Patient characteristics	/		
Intervention	/		
Comparison	/		
Length of follow-up	/		
Outcome measures	/		
Outcome and effect size	The presence of either disorder doubled the risk of the second disorder, causal linkage between AUD and major depression		
Comments	.		

Title	**Effects of cue- exposure treatment on neural cue reactivity in alcohol dependence: a randomized trial.**		
First Author	**Vollstädt- Klein, S., 2011**	**Source**	**21292243**
Level of evidence	1b	**Study type**	RCT
Study quality	Moderate: low sample size; no follow-up		
Participants	N=30		
Patient characteristics	abstinent alcohol- dependent patients after detoxification treatment		
Intervention	All patients underwent an extended detoxification treatment comprising medically supervised detoxification, health education, and supportive therapy. The CET patients additionally received nine CET sessions over 3 weeks, exposing the patient to his/her preferred alcoholic beverage.		
Comparison	Cue- exposure based extinction training (CET)-group vs. control		
Length of follow-up	Pre/post (2 weeks)		
Outcome measures	Cue-induced fMRI activation to alcohol cues was measured at pretreatment and posttreatment		
Outcome and effect size	There were no brain regions with larger decrease of cue reactivity in the control group relative to the CET group, even with a liberal threshold of $p<0.005$. Lower brain activation in the left ventral striatum in the CET group compared with the control group in the second fMRI session ([x,y,z]=[-20,12,-8], t=2.58, $p<0.048$ FWE-SV- corrected). For the whole patient sample (n=30), a decrease in fMRI brain activation after treatment compared with pretreatment measurement was prominent in the left dorsal striatum ([x,y,z]=[- 8, 0,14], t=3.60, p=0.009 FWE-SV-corrected)		
Comments	.		

Title	**Does family history of alcoholism moderate naltrexone's effects on alcohol use?**		
First Author	**Capone, C., 2011**	**Source**	**21138720**
Level of evidence	2a	**Study type**	RCT
Study quality	High: Study used multilevel modelling to investigate family history of alcoholism (FHA) based on first-degree relatives and gender as moderators of naltrexone' s effects		
Participants	N=603		
Patient characteristics	COMBINE data set		
Intervention	Participants randomized to receive active medication or placebo plus medical management. Three drinking outcomes: percentage of days abstinent, drinks per drinking day, and percentage of heavy drinking days.		
Comparison	FHA vs. no FHA		

Length of follow-up	/
Outcome measures	/
Outcome and effect size	Main effect of FHA on drinks per drinking day (B=2.01, SE=0.91, p=0.03) No other main effects of FHA were observed on drinking outcomes. A significant Naltrexone × Time interaction was observed for percentage of heavy drinking days (B=- 1.61, SE=0.69, p=0.02). No significant Naltrexone × FHA interactions were observed for any of the three outcomes. Gender did not modify these results. Greater FHA was associated with greater alcohol use per drinking occasion.
Comments	.

Title	**Brief alcohol intervention s for mandated college students: comparison of face-to- face counseling and computer- delivered interventions.**		
First Author	**Carey, K.B., 2011**	**Source**	**21059184**
Level of evidence	1b	**Study type**	RCT
Study quality	Moderate: students		
Participants	N= 667		
Patient characteristics	Students		
Intervention	BMI: interventionists provided a personalize d feedback sheet that summarized (a) drinking patterns (contrasted with gender- specific national and local norms), (b) typical and peak BAC, (c) alcohol- related negative consequences and associated risk behaviors; interventionists also (d) prompted personalize d goal setting for risk reduction, and (e) provided tips for safer drinking. Alcohol 101 Plus™: interactive CD-ROM program set on a "virtual campus." Students engage in social decision making at a virtual party, learn about factors affecting their own BAC in a virtual bar, and test their knowledge about alcohol in a game show. Alcohol Edu for Sanctions: five chapters, with quiz questions, interactive exercises, and journaling opportunities		
Comparison	BMI (brief motivational interviewing) vs. Alcohol 101 Plus™ vs. Alcohol Edu for Sanctions vs. delayed control		
Length of follow-up	1-month follow-up, 6- month follow-up, 12-month follow-up		
Outcome measures	Consumption (drinks per heaviest and typical week, heavy drinking frequency, peak and typical blood alcohol concentration), alcohol problems, recidivism		
Outcome and effect size	Piecewise latent growth models characterize d short-term (1-month) and longer-term (1-12 months) change. Female but not male students reduced drinking and problems in the control condition. Males reduced drinking and problems after all interventions relative to control, but did not maintain these gains. Females reduced drinking to a greater extent after a BMI than after either CDI, and maintained reductions relative to baseline across the follow-up year. No differences in recidivism were found		
Comments	.		

Title	**Impact of functional social support for abstinence after inpatient detoxification.**		
First Author	**Mutschler, J., 2010**	**Source**	**20605007**
Level of evidence	2b	**Study type**	Prospective study
Study quality	Moderate: follow-up		
Participants	N=132		
Patient characteristics	alcohol- dependent inpatients after detoxification		
Intervention			
Comparison			
Length of follow-up	Pre/post (12 weeks)		
Outcome measures	Functional social support (FSS) was measured with the Medical Outcome Study (MOS) Social Support Survey at baseline and at the end of the study. Impact of FSS on different alcohol-dependence related variables; FSS levels, perceived practical social support, number of previous inpatient detoxifications		
Outcome and effect size	Significantly higher FSS levels in patients with a current partnership; negative correlation between perceived practical social support and number of previous inpatient		

	detoxifications.
Comments	.

Title	**Depression, craving, and substance use following a randomized trial of mindfulness-based relapse prevention.**		
First Author	**Witkiewitz, K., 2010**	**Source**	**20515211**
Level of evidence	1b	**Study type**	RCT
Study quality	High: follow-up study for MBRP		
Participants	N=168		
Patient characteristics	Individuals with substance use disorders after intensive stabilization		
Intervention	MBRP: skills in cognitive behavioral relapse prevention (e.g., identifying high-risk situations, coping skills training) and mindfulness meditation		
Comparison	Mindfulness-Based Relapse Prevention (MBRP) vs. treatment-as-usual control group		
Length of follow-up	2-month follow-up, 4-month follow-up		
Outcome measures	Substance Use, Alcohol and Drug Craving, Depression		
Outcome and effect size	Craving mediated the relation between depressive symptoms (BDI) and substance use (Time Line Follow Back) among the treatment-as-usual group, but not among MBRP participants. Specifically, MBRP attenuated the relation between post intervention depressive symptoms and craving (Penn Alcohol Craving Scale) two months following the intervention (f2=0.21). This moderation effect predicted substance use four-months following the intervention (f2=0.18).		
Comments	.		

Title	**The effects of current subsyndromal psychiatric symptoms or past psychopathology on alcohol dependence treatment outcomes and acamprosate efficacy.**		
First Author	**Mason, B.J., 2010**	**Source**	
Level of evidence	1b	**Study type**	Meta-analysis
Study quality	moderate: secondary analysis		
Participants	N=601		
Patient characteristics	Inpatients/outpatients		
Intervention			
Comparison	Acamprosate vs. placebo		
Length of follow-up	/		
Outcome measures	Current psychiatric symptoms were assessed using Hamilton Anxiety and Depression (HAM-A, HAM-D) rating scales. Predictors of good response, defined as abstinence for ≥90% of trial duration, were identified using logistic regression. Response rates, rates of controlled drinking, percent days abstinent, percent days controlled drinking		
Outcome and effect size	Two significant independent negative predictors of good response were identified: (1) The “Anxious Mood” item from the 31-item SIGH-AD (odds ratio [OR]=0.61, 95% CI [0.40|0.91], p=0.016); and (2) having at least 1 psychiatric antecedent (OR=0.41, 95% CI [0.20|0.84], p=0.015). The same significant negative predictors were found for other tested outcomes: rates of controlled drinking, percent days abstinent, and percent days controlled drinking. Three independent significant positive predictors of good response were identified: (1) baseline motivation to be abstinent (OR=4.13, 95% CI [2.72|6.26], p<0.001); (2) lower pretreatment drinking intensity (OR=3.04, 95% CI [1.35|6.81], p=0.007); and (3) treatment with acamprosate (OR=1.63, 95% CI [1.07|2.48], p=0.022).		
Comments	Secondary analysis of the first U.S. acamprosate trial		

Title	**Effects of pretreatment and posttreatment depressive symptoms on alcohol consumption following treatment in Project MATCH.**		
First Author	**Gamble, S.A., 2010**	**Source**	**20105416**
Level of evidence	1b	**Study type**	Meta- Analysis
Study quality	High: large sample size, follow- up, Project MATCH		

Participants	N=1726
Patient characteristics	Project MATCH
Intervention	three treatments conducted over a 3-month period: 4 sessions of motivational enhancement therapy vs. 12 sessions of cognitive-behavioral therapy vs. 12 sessions of twelve-step facilitation
Comparison	motivational enhancement therapy vs. cognitive-behavioral therapy vs. twelve-step facilitation
Length of follow-up	6-month follow-up, 12-month follow-up
Outcome measures	Pretreatment and post treatment depression symptoms (BDI), average DDD and PDA to quantify drinking intensity and frequency
Outcome and effect size	Patients with greater baseline depressive symptoms drank more frequently and intensely in the year following treatment than those with fewer baseline depressive symptoms. Patients who experienced greater depressive symptoms in the year following treatment reported fewer days abstinent and consumed more drinks on those nonabstinent days than those with fewer depressive symptoms
Comments	.

Title	**Cost- effectiveness of home visits in the outpatient treatment of patients with alcohol dependence.**		
First Author	**Moraes, E., 2010**	**Source**	**20029212**
Level of evidence	2b	**Study type**	RCT
Study quality	Moderate: no follow-up		
Participants	N=120		
Patient characteristics	Brazilian outpatients		
Intervention	conventional outpatient treatment for alcoholic patients (CT) vs. conventional treatment plus home visits (HV)		
Comparison			
Length of follow-up	/		
Outcome measures	Identification of resources utilized by each intervention, as well as the cost according to National Health System (SUS), Brazilian Medical Association (AMB) tables of fees, and others based on 2005 data. incremental cost- effectiveness ratio (ICER)		
Outcome and effect size	51.8% abstinent cases for HV and 43.1% for CT, a clinically relevant finding. Other outcome measures, such as quality of life, also showed significant improvements that favored HV. The baseline scenario presented an ICER of USD 1,852. Sensitivity analysis showed an ICER of USD 689 (scenario favoring HV) and USD 2.334 (scenario favoring CT).		
Comments	.		

Title	**The role of ethnic matching between patient and provider on the effectiveness of brief alcohol intervention s with Hispanics**		
First Author	**Field, C., 2010**	**Source**	**19951297**
Level of evidence	2b	**Study type**	RCT
Study quality	High; HLM was used to model the effects of treatment, ethnicity and covariates of interest on change in drinking outcomes from baseline to the 6 and 12-month follow-up. Analyses controlled for age, gender, employment status, marital status, education, baseline alcohol use, prior alcohol treatment, type of injury, and injury severity.		
Participants	N=537		
Patient characteristics	Outpatients, Hispanics		
Intervention	Brief motivational intervention (BMI)		
Comparison	Brief motivational intervention vs. TAU		
Length of follow-up	6-month follow-up; 12-month follow-up		
Outcome measures	Drinking outcomes including volume per week, maximum amount, and frequency of 5 or more drinks per occasion.		
Outcome and effect size	Hispanics who received BMI drank significantly less on average in comparison to Hispanics who did not receive BMI (d12=0.13). In addition, Hispanics who were less acculturated drank significantly less on average at 6- and 12-month follow-up than highly acculturated		

	Hispanics (p6=0.02 and p12=0.004, respectively). Hispanics who received BMI drank 5 or more per occasion significantly less often than Hispanics who did not receive brief intervention (d12=0.23). Hispanics who were less acculturated also drank 5 or more drinks per occasion less frequently at 12 months than highly acculturated Hispanics. Match between patient and provider resulted in a significant reduction in drinking outcomes at 12-month follow-up. In addition, there was a tendency for ethnic match to be most beneficial to foreign-born Hispanics and less acculturated Hispanics
Comments	.

Title	**Web-based treatment for rural women with alcohol problems: preliminary findings.**		
First Author	**Finfgeld- Connett, D., 2011**	**Source**	**19901570**
Level of evidence	2c	**Study type**	Field-study
Study quality	Low: small sample size; no generalizability		
Participants	N=46		
Patient characteristics	Outpatients, women		
Intervention	90-day web-based treatment program		
Comparison	Web-based treatment vs. standard care		
Length of follow-up	Pre/post		
Outcome measures	Demographic and participant satisfaction data		
Outcome and effect size	Participants indicated satisfaction with the program, and 83% noted that they would recommend it to a friend		
Comments	Descriptive results		

Title	**Individualized assessment and treatment program for alcohol dependence: results of an initial study to train coping skills.**		
First Author	**Litt, M.D., 2009**	**Source**	**19712124**
Level of evidence	1b	**Study type**	RCT
Study quality	Moderate: initial study		
Participants	N=110		
Patient characteristics	Outpatients, <18 years, alcohol-abuse or -dependence		
Intervention	packaged CBT program (PCBT): based on cognitive-behavioral principles and designed to remediate deficits in skills for coping with interpersonal (e.g., social pressure, conflict with others) and intrapersonal (e.g., craving, anger) antecedents to drinking; Individualized Assessment and Treatment Program (IATP): experience sampling via cellphone to assess coping skills prior to treatment, sessions focused on training four basic coping skills sets in each situation: Avoidance, Escape, Environmental Modification , and Personal Coping		
Comparison	IATP vs. CBT program (PCBT)		
Length of follow-up	Pre/post (12 weeks)		
Outcome measures	Form-90 (drinking data), Drinker Inventory of Consequences (problems related to drinking), Coping Strategies Scale (CSS), Experience Sampling (ES) of situations and coping via Interactive Voice Response (IVR)		
Outcome and effect size	PDA was higher for IATP patients at posttreatment [F(1, 90)=3.78; p<0.05; effect size d=0.40]; higher rate of abstinence in the IATP condition (30% v. 17%), but this was not significant [$\chi 2(1)=1.28$]; PDH yielded a main effect for Time [F(1, 90)=137.18; p<0.001]		
Comments	.		

Title	**Engagement and retention in outpatient alcoholism treatment for women**		
First Author	**Graff, F.S., 2009**	**Source**	**19444731**
Level of evidence	2c	**Study type**	Field study
Study quality	Low: filed- study		
Participants	N=102		

Patient characteristics	Women and their partners; outpatients
Intervention	couples were randomly assigned to either Alcohol Behavioral Individual Treatment (ABIT) or Alcohol Behavioral Couples Treatment (ABCT)
Comparison	Individual vs. couples treatment
Length of follow-up	Pre/post
Outcome measures	Drinking behaviour, readiness for change, homework record, treatment retention
Outcome and effect size	Women in the individual treatment condition attended significantly more sessions than women in the couples condition (t(100)=-1.98; p=0.05).
Comments	.

Title	**Alcohol treatment effects on secondary nondrinking outcomes and quality of life: the COMBINE study.**		
First Author	**LoCastro, J.S., 2009**	**Source**	**19261230**
Level of evidence	1b	**Study type**	RCT
Study quality	High: large sample size		
Participants	N=1226		
Patient characteristics	COMBINE study		
Intervention	eight treatment combination s in which pills (active medications or placebo) were taken by the participants; half of the subjects from each medication group were also randomly assigned to receive a moderate- intensity behavioral intervention, called the combined behavioral intervention		
Comparison	Naltrexone vs. placebo, acamprosate vs. placebo, vs. both medications vs. placebos; medical management alone vs. medical management + combined behavioural intervention		
Length of follow-up	26-week follow-up, 52-week follow-up		
Outcome measures	primary alcohol consumption outcomes: (1) percentage of days abstinent (PDA), (2) percentage of heavy drinking days (PHDD), and (3) drinks per drinking day (DDD); secondary nondrinking outcome dimensions: physical health, psychologic al health, social relationship s, and environment, craving, mutual-help group attendance, percentage of days paid for work, physical health, mental health		
Outcome and effect size	At baseline, a greater number of significant correlations are seen with the DDD drinking variable (ranging from r=0.08, p<0.01, to r=0.25, p<0.001) than with the PHDD or PDS variables. At the16-week, 26-week, and 52-week assessments all three of the drinking outcome variables are significantly correlated with the secondary outcome variables, e.g. a higher PHDD, more DDD, and lower PDA are related to lower quality-of-life measures, more psychiatric symptoms, perceived stress. Significant posttreatment improvements on all secondary outcomes; for most, these changes were maintained over the 26-week and/or 52-week follow-up time periods. combined naltrexone plus combined behavioral intervention group (M [SE]=52.1 [0.46] adjusted; M [SD]=52.2 [0.46] unadjusted) and the drug placebo group with no combined behavioral intervention (M [SD]=53.1 [0.48] adjusted; M [SD]=53.1 [0.48] unadjusted) reported higher physical health than the naltrexone/no combined behavioral intervention (M [SD]=51.0 [0.48] adjusted; M [SD]=51.0 [0.48] unadjusted) or the combined behavioral intervention/ drug placebo groups (M [SD]=51.0 [0.46] adjusted; M [SD]=51.0 [0.46] unadjusted) . This finding suggests that, together, combined behavioral intervention and naltrexone treatment have a greater impact than either one alone for the SF-12v2 physical health dimension.		
Comments	.		

Title	**Characteristics of first- time alcohol treatment seekers: the COMBINE Study.**		
First Author	**Locastro, J.S., 2008**	**Source**	**18925347**
Level of evidence	1b	**Study type**	Meta- analysis
Study quality	High: large sample size		
Participants	N=1.362		
Patient characteristics	COMBINE study; inclusion eligibility criteria: (1) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994) criteria for		

	alcohol dependence; (2) a minimum of 4 days and a maximum of 21 days of abstinence immediately before time of randomization; and (3) more than 14 drinks (females) or 21 drinks (males) per week, with at least 2 heavy drinking days ≤4 drinks/day for females and ≤5 drinks/day for males) during a consecutive 30-day period within the 90 days before baseline evaluation
Intervention	Three prior-treatment groups: (1) treatment naive (n=691, 50.73%), (2) one to two prior treatments (n=380, 27.90%), or (3) three or more prior treatments (n= 291,21.37%)
Comparison	treatment naive vs. one to two prior treatments vs. three or more prior treatments
Length of follow-up	/
Outcome measures	multiple drinking and psychosocial variables
Outcome and effect size	The three treatment groups differed significantly (at p<0.001) from each other on nearly all alcohol consumption and severity measures. The group with three or more prior treatments reported a greater number of drinks per drinking day and drinks per day; participants reporting no prior treatment had the oldest age at onset of problem drinking (mean age=33.58 [16.20]), compared with those who had one-to two prior treatments (mean age=30.92 [13.04]) or those who had three or more prior treatments (mean age=28.86 [14.52]) (p<0.001); being female was found to have the greatest association with the treatment-naive group (p<0.0001)
Comments	.

Title	**Effectiveness of sequential combined treatment in comparison with treatment as usual in preventing relapse in alcohol dependence.**		
First Author	**Neto, D., 2008**	**Source**	**18852481**
Level of evidence	1b	**Study type**	RCT
Study quality	Moderate: follow-up		
Participants	N=209		
Patient characteristics	Outpatient alcohol- dependent patients		
Intervention	Sequential combined treatment (SCT) vs. treatment as usual (TU); SCT: combined family, normative and stepped approach that seeks to maximize the family and social reinforcement for abstinence. Involves another adult person, significant in the life of the alcoholic patient, in affective and logistic terms, preferably living with him. Each patient is followed-up by only one therapist, usually a physician. TU: psychiatrist as the sole therapist		
Comparison	TU vs. SCT		
Length of follow-up	180 days follow-up		
Outcome measures	Primary outcome measure: time to first relapse, defined as the consumption of any amount of alcohol during the 180 days of follow-up. Secondary outcome measures: maximum duration of continuous abstinence (MDCA), cumulative abstinence duration (CAD), quality of life (ARPQ) and blood test markers of alcohol consumption		
Outcome and effect size	The SCT approach was more effective than TU. The Kaplan– Meier abstinent proportion at the end of the 180 days was 78% for the SCT group and 59% for the TU group (p<0.01). The mean time to first relapse was 150 days for SCT and 123 days for TU (p<0.01). The relative risk reduction of relapse was 62% for SCT after adjustment in multiple Cox regression (p<0.01). SCT had more MDCA (p<0.05) and more CAD (p<0.05)		
Comments	.		

Title	**A double-blind, placebo-controlled study of sertraline with naltrexone for alcohol dependence.**		
First Author	**Farren, C.K., 2009**	**Source**	**18644685**
Level of evidence	1b	**Study type**	RCT
Study quality	High: double-blind intervention		
Participants	N=113		
Patient characteristics	Alcohol-dependent patients, abstinent from alcohol between 5 and 30 days		
Intervention	Relapse prevention psychotherapy on a weekly basis + one of the two conditions		

Comparison	Combined use of naltrexone + sertraline vs. naltrexone + placebo sertraline
Length of follow-up	/
Outcome measures	Time to first drink, time to first relapse to heavy drinking, percent days abstinent, number of drinks per drinking day for drinkers, change in Obsessive Compulsive Drinking Scale total scores, medication compliance
Outcome and effect size	No significant difference between groups in time to first relapse to heavy drinking (p=0.13), time to second drink (p=0.13), or in percent days abstinent (p=0.19)
Comments	.

Title	**Evidence- based treatments in the inpatient rehabilitation of alcoholics.**		
First Author	**Schmidt, P., 2008**	**Source**	**18256969**
Level of evidence	2b	**Study type**	Field-study
Study quality	Moderate: no experimental intervention		
Participants	N=5.504		
Patient characteristics	inpatient alcohol rehabilitation, clinic for drug addiction in 2004		
Intervention	Examination of analogy of both treatment elements used in inpatient rehabilitation of alcohol dependents and the published knowledge concerning the effectiveness of therapy elements.		
Comparison	/		
Length of follow-up	/		
Outcome measures	/		
Outcome and effect size	Highest utilization rate resulted for the treatments “information /schooling” with 93.3%. The utilization rate of “cognitive behavioral treatment” was 85.4%, and of “soft skill training” 79.1%. Low utilization rates resulted for “relapse prevention” with 29.6%, “nutrient schooling” (28.9%), “non- smoker training” (17.3%), “motivational enhancement therapy” (14.8 %), and the therapy element “groups of mental comorbidity” (11.2%). 39.5% of the patients received services from the therapy element “psychoanalytic therapy”. On the average, patients took part in 18 treatment offers (SD=6.8). This were treatment offers of 9 (SD=2.1) from a total of 14 evidence based treatment categories, on the average.		
Comments	Only descriptive results		

Title	**Social networks and their influence on drinking behaviors: differences related to cognitive impairment in clients receiving alcoholism treatment**		
First Author	**Buckman, J.F., 2007**	**Source**	**17690808**
Level of evidence	2a	**Study type**	Meta- analysis
Study quality	High: meta- analysis, follow-ups		
Participants	N=1.726		
Patient characteristics	Outpatients, aftercare clients		
Intervention			
Comparison			
Length of follow-up	3-, 6-, 9-,12-, and 15-month follow-ups		
Outcome measures	Social network support: nine variables were derived from the raw data and dichotomized; 9 variables of social support; amount of alcohol consumed, alcohol-related problems, Social network support		
Outcome and effect size	Three independent social support classes (frequent positive, limited positive and negative) were identified. In the outpatient sample, the frequent positive support class had greater cognitive impairment at treatment entry versus other classes, and extent of impairment significantly predicted improved drinking outcomes in this class. In the aftercare sample, the frequent positive and negative support classes had heightened impairment, yet cognitive impairment significantly predicted relatively poorer drinking outcomes in the negative support class only.		
Comments	.		

Title	**Naltrexone and cognitive behavioral coping skills therapy for the treatment of alcohol drinking and eating disorder features in alcohol- dependent women: a randomized controlled trial.**		
First Author	**O'Malley, S.S., 2007**	**Source**	**17374042**
Level of evidence	1b	**Study type**	RCT
Study quality	Moderate: only women		
Participants	N=103		
Patient characteristics	Alcohol-dependent women; outpatients		
Intervention	Naltrexone in combination with Cognitive Behavioral Coping Skills Therapy (CBCST)		
Comparison	CBCST + placebo		
Length of follow-up	Pre/post (12 weeks)		
Outcome measures	Time to first drinking day, time to first day of heavy drinking		
Outcome and effect size	Naltrexone significantly delayed the time to the second (chi2=5.37, p=0.02) and third ($\chi 2$=4.35, p=0.04) drinking days among subjects who did not maintain abstinence from alcohol		
Comments	.		

Title	**Anxiety sensitivity as a prospective predictor of alcohol use disorders.**		
First Author	**Schmidt, N.B., 2007**	**Source**	**17307935**
Level of evidence	2b	**Study type**	Prospective study
Study quality	Low: non clinical setting; young adults		
Participants	N=404		
Patient characteristics	nonclinical sample of young adults		
Intervention	/		
Comparison	/		
Length of follow-up	2-year follow-up		
Outcome measures	Anxiety Sensitivity Index		
Outcome and effect size	AS was uniquely associated with the later development of alcohol use disorder diagnoses		
Comments	.		

Title	**Ear acupuncture for alcohol withdrawal in comparison with aromatherapy: a randomized controlled trial.**		
First Author	**Kunz, S., 2007**	**Source**	**17295728**
Level of evidence	2c	**Study type**	RCT
Study quality	Low: pure results		
Participants	needle acupuncture (n=55) vs. aromatherapy (n=54)		
Patient characteristics	Inpatients undergoing alcohol withdrawal		
Intervention	Both therapies were applied daily during the first 5 consecutive treatment days.		
Comparison	ear acupuncture vs. aromatherapy		
Length of follow-up	Pre/post		
Outcome measures	The rating scale for the assessment of the alcohol-withdrawal syndrome (AWS scale) served as the main dependent variable and was applied daily during the first 5 days of the withdrawal. Further measures included a subjective visual analogue scale of craving and the Self-Assessment Manikin (SAM).		
Outcome and effect size	The groups differed in their initial self- reported arousal, which then served as a covariate in the further analyses. Neither the extent of craving nor of withdrawal symptoms differed between groups over the observation period. Self- rated arousal decreased in response to both treatments from days 1 to 2 (p<0.001) and within single days (p<0.001), and we found a significant interaction between pretreatment versus posttreatment and days (p<0.001). Neither the extent of craving nor of withdrawal symptoms differed between groups over the observation period. Self- rated arousal decreased in response to both treatments		
Comments	.		

Title	**Viewing videotape of themselves while experiencing delirium tremens could reduce the relapse rate in alcohol- dependent patients.**		
First Author	**Mihai, A., 2006**	**Source**	**17222276**
Level of evidence	2b	**Study type**	RCT
Study quality	Low: small sample size		
Participants	N=60		
Patient characteristics	patients with DT and a minimum of 3 years of severe alcohol dependence		
Intervention	Patients were videotaped during the acute phase of Delirium Tremens; individual exposure to videotape and an explanation of the symptoms by a psychiatrist		
Comparison	viewing videotape vs. no videotape experience		
Length of follow-up	6 months		
Outcome measures	relapse, drinking days per week, number of drinks per drinking day		
Outcome and effect size	Patients with videotape experience had a significantly lower relapse rate after the first month (0% versus 20%), 2 months (13.33% versus 46.67%) and 3 months (26.67% versus 53.33%). Patients with videotape experience had less severe relapses and consumed fewer units of alcohol than controls.		
Comments	.		

Title	**Exploration of the relationship between drinking intensity and quality of life.**		
First Author	**Stewart, S.H., 2006**	**Source**	**16966191**
Level of evidence	1b	**Study type**	
Study quality	moderate		
Participants			
Patient characteristics	Project MATCH sample		
Intervention			
Comparison			
Length of follow-up			
Outcome measures	quality of life, drinks per drinking day (DDD)		
Outcome and effect size	Each quality of life indicator improved with decreased DDD. Gender and ethnicity modified the DDD effect for some outcomes, with DDD exerting a greater influence on quality of life in women and non-Hispanic whites.		
Comments	.		

Title	**Antidepressant efficacy and hormonal effects of Sudarshana Kriya Yoga (SKY) in alcohol dependent individuals.**		
First Author	**Vedamurthachar, A., 2006**	**Source**	**16740317**
Level of evidence	2c	**Study type**	RCT
Study quality	Low: small sample size		
Participants	N=60		
Patient characteristics	inpatients		
Intervention	SKY vs. TAU; SKY therapy included alternate day practice of specified breathing exercise under supervision of a trained therapist.		
Comparison	TAU (no SKY)		
Length of follow-up	Before and after the two weeks of intervention; no further follow-up		
Outcome measures	Subjects completed the Beck Depression Inventory (BDI) before and after the two weeks of this intervention. Morning plasma cortisol, ACTH and prolactin too were measured before and at the end of two weeks.		
Outcome and effect size	BDI scores significantly dropped at post- assessment and the drop was more in the SKY group. Drop also occurred in the plasma cortisol as well as ACTH levels differentially; being more in SKY group. Cortisol values dropped in all SKY individuals and in only 22 of the controls ($\chi 2=9.2$, df=1; p=0.005). Percent drop in BDI correlated positively with that of ACTH (r=0.53, p=0.001) an also that of cortisol (r=0.52, p=0.001). Percentage drop in ACTH		

	and cortisol too were correlated (r=0.35, p=0.14). When examined separately the correlation between percentage drop in BDI and that in cortisol was significant (r=0.52, p=0.003) for the SKY group only. In both groups reductions in BDI scores occurred but significantly more so in SKY group. Likewise, in both groups plasma cortisol as well as ACTH fell after two weeks but significantly more so in SKY group. Reduction in BDI scores correlated with that in cortisol in SKY but not in control group.
Comments	.

Title	**Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial.**		
First Author	**Anton, R.F., 2006**	**Source**	
Level of evidence	1b	**Study type**	Meta-analysis
Study quality	High: large sample size		
Participants	N=1.383		
Patient characteristics	COMBINE study, alcohol abstinent participants who met criteria of alcohol- dependence		
Intervention	Eight groups of patients received medical management with 16 weeks of naltrexone (100mg/d) or acamprosate (3g/d), both, and/or both placebos, with or without a combined behavioral intervention (CBI)		
Comparison	combined CBI and naltrexone vs. combined CBI and acamprosate		
Length of follow-up	12-month follow-up		
Outcome measures	Percent days abstinent from alcohol and time to first heavy drinking day		
Outcome and effect size	Patients receiving naltrexone plus medical management, CBI plus medical management and placebos, or both naltrexone and CBI plus medical management had higher percent days abstinent (80.6, 79.2, and 77.1, respectively) than the 75.1 in those receiving placebos and medical management only; significant naltrexone * behavioral intervention interaction (p=.009); Naltrexone also reduced risk of a heavy drinking day (hazard ratio, 0.72; 97.5% CI [0.53|0.98]; p=0.02); those receiving CBI without pills or medical management had lower percent days abstinent (66.6) than those receiving placebo plus medical management alone or placebo plus medical management and CBI (73.8 and 79.8, respectively; p<0.001).		
Comments	.		

Title	**The efficacy of compliance therapy in pharmacotherapy for alcohol dependence: a randomized controlled trial.**		
First Author	**Reid, S.C., 2005**	**Source**	**16459945**
Level of evidence	2b	**Study type**	RCT
Study quality	Moderate: small sample size		
Participants	N=40		
Patient characteristics	Outpatients, men and women, 18- 65 years old, diagnosis of alcohol dependence		
Intervention	All subjects were prescribed acamprosate (Campral) for 4 months. All subjects received usual medical care consisting of seven medical reviews (duration=15 minutes) over 4 months. Compliance therapy consisted of four to six individual sessions (duration=60 minutes) in which beliefs about medication, side effects, ambivalence, the benefits of treatment, treatment maintenance and relapse prevention were addressed and explored with motivational interviewing and cognitive behavior therapy techniques		
Comparison	Usual medical care (n=20) vs. usual medical care plus compliance therapy (n=20).		
Length of follow-up	4 month follow-up		
Outcome measures	Outcome Variables: number of days taking acamprosate, days to first drink, days to first relapse (more than five drinks) and days to first extended relapse (greater than 2 consecutive days of more than five drinks).		
Outcome and effect size	participation in three or more compliance therapy sessions significantly increased the number of days participants took acamprosate (Figure 1) and the number of days to extended relapse (3 or more days of more than five drinks; Figure 2). There was no significant difference between the two groups in the number of days to first drink or days to relapse (Table 2). Post hoc power analyses on the resulting UC and CT survival rates in		

	each of the per-protocol survival analyses suggested that with 50% of the CT group and 25% of the UC group taking acamprosate at 4 months, there was 45% power to declare this size of effect significant. Regarding time to first drink and time to relapse, 15% of the UC and 17% of the CT group had not drunk or relapsed by the end of treatment; there was 1% power to detect this difference. For time to extended relapse, 15% of the UC and 42% of the CT group had not drunk more than five drinks for 3 consecutive days by the end of treatment. The power to detect this difference was 58%.
Comments	.

Title	**Does contingency management affect motivation to change substance use?**		
First Author	**Ledgerwood, D.M., 2006**	**Source**	**16310974**
Level of evidence	2a	**Study type**	RCT
Study quality	Moderate: follow-up		
Participants	N=115		
Patient characteristics	outpatients		
Intervention	Standard treatment was group based and consisted of relapse prevention and coping skills training, AIDS education and 12-step oriented therapy. Contingency management patients were provided with ST, but did not receive the additional educational components. CMpatients earned vouchers or prizes for providing negative breath and urine specimens. Each time a patient provided urine and breath samples that were negative for cocaine, opiates and alcohol, they were eligible for reinforcement (either a voucher or chance to win a prize depending on treatment condition).		
Comparison	three groups: standard treatment (ST), ST plus voucher CM and ST plus prize CM		
Length of follow-up	3-month follow-up		
Outcome measures			
Outcome and effect size	Patients receiving CM were significantly more likely than ST patients to achieve more than 8 consecutive weeks of abstinence during treatment, $\chi 2$ (N=142)=9.13, $p<0.01$. In total, 43.3% (N=45) of CM patients achieved a LDA of more than 8 weeks, compared with 15.7% (N=6) of patients who received only ST. Patients receiving CM were significantly more likely than ST patients to achieve longer abstinence.		
Comments	.		

Title	**Effectiveness of treatment for alcohol problems: findings of the randomized UK alcohol treatment trial (UKATT).**		
First Author	**UKATT Research Team, 2005**	**Source**	**16150764**
Level of evidence	1b	**Study type**	RCT
Study quality	High, effectiveness study		
Participants	N=742		
Patient characteristics	Outpatients; clients who would normally receive an offer of treatment from British treatment sites for alcohol problems		
Intervention	Social behavior and network therapy comprises cognitive and behavioral strategies to help clients build social networks supportive of change (8 sessions over 8-12 weeks); motivational enhancement therapy comprised three 50 minute sessions over eight to 12 weeks; combined counselling in the motivational style with objective feedback		
Comparison	social behavior and network therapy vs. motivational enhancement therapy		
Length of follow-up	3-month follow-up, 12-month follow-up		
Outcome measures	Changes in alcohol consumption, alcohol dependence, and alcohol related problems over 12 months.		
Outcome and effect size	only significant difference we found was that after three months the adjusted mean physical component score of the SF-36 for clients in the social network group exceeded that of the clients in the motivational group by 1.31 (95% CI [0.05|2.57]); Clients in both groups reported that total alcohol consumption had decreased by 48% at three months and by 45% at 12 months and that alcohol related problems had decreased by 44% at three months and by 50% at 12 months.		

Comments	.

Title	**Effects of music therapy on change readiness and craving in patients on a detoxification unit**		
First Author	**Silverman, M. J., 2011**	**Source**	**22506302**
Level of evidence	2b	**Study type**	Randomized three-group design. posttest only design
Study quality			
Participants	N=141		
Patient characteristics	Alcohol (n=77), Heroin (n=32), prescribed drugs (n=13), others (n=18), no response (n=1)		
Intervention	Condition A: rockumentary (n=41), Condition B: verbal therapy (n=43), Condition C: recreational music therapy (n=56)		
Comparison	Verbal therapy, or recreational music therapy condition		
Length of follow-up	Posttest only design		
Outcome measures			
Outcome and effect size	• Correlations between Contemplation and Action were significant at the 2-tailed p<.001 level • Between-group differences were significant, F(4, 256)=4.43, p<0.003, η2=0.065. Between-subjects effects were significant for Contemplation [F(2, 28)=8,89, p<0.001, η2=0.122] and Action [F(2, 128)=3.77, p<0.027,η2=0.052]. • Concerning Contemplation, participants in Condition A had a significantly higher (p<.001) mean than participants in Condition B. Participants in Condition C had a significantly higher (p<0.007) • Participants in the two music therapy conditions (A and C) were not significantly different from one another (p>0.808) • Although participants in both music therapy conditions tended to have slightly lower cravings (Condition A: M=5.63, Condition C: M=5.20) than participants in Condition B (M=7.19), there were no significant differences between groups. • Participant means of post treatment motivation, enjoyment, and helpfulness tended to be slightly higher in the two music therapy conditions than in Condition B (Table 3).		
Funding	No information		
Comments			

Title	**Effects of Live and Educational Music Therapy on Working Alliance and Trust With Patients on Detoxification Unit: A Four-Group Cluster-Randomized Trial**		
First Author	**Silverman, M. J., 2016a**	**Source**	**27487408**
Level of evidence	2b	**Study type**	Four-Group Cluster-Randomized Trial. single-session posttest-only design
Study quality			
Participants	N=130		
Patient characteristics	Alcohol (n=61), Crystal methamphetamine (n=2), Heroin (n=28), Marijuana (n=2), Prescription drug (n=35), no response (n=2)		
Intervention	Condition A: Live educational music therapy (n=37)		
Comparison	Condition B: recorded educational music therapy (n=30), Condition C: education without music (n=30), Condition D: recreational music therapy (n=33)		
Length of follow-up	no follow up		
Outcome measures			
Outcome and effect size	No significant between-group difference in any of the dependent measures. No difference in live versus recorded lyric analysis conditions or educational and recreational interventions. Although not statistically significant, attendance means (depicted in Table 2) tended to be slightly higher during the live educational music therapy condition. Important for this target group and in the practice, “as it may relate to treatment engagement, motivation, and treatment readiness”.		
Funding	The author reports no conflicts of interest. The author alone is responsible for the content and writing of the article.		

Comments	

Title	**Effects of lyric analysis interventions on treatment motivation in patients on a detoxification unit: a randomized effectiveness study**		
First Author	**Silverman, M. J., 2015**	**Source**	**25701046**
Level of evidence	2b	**Study type**	Randomized Effectiveness Study, randomized controlled design
Study quality			
Participants	N=104		
Patient characteristics	Alcohol (n=64), prescription drugs (n=22), heroin (n=15),Crack (n=1) Marihuana (n=1)		
Intervention	Lyric analysis treatment (n=51)		
Comparison	Wait list control group (n=53)		
Length of follow-up	No follow up		
Outcome measures			
Outcome and effect size	Results indicated that participants in the experimental condition had significantly higher problem recognition (F=5.49 p=0.021, η2=0.053, M=-2.86), desire for help (F=4.51 p=0.036, η2=0.044, M=-1.82) and treatment readiness (F=9.72, p=0.002, η2=0.089, M=-2.70) mean scores than participants in the control condition (see Table 3). Relevant for the practice.		
Comments			

Title	**Treating addiction with tunes: a systematic review of music therapy for the treatment of patients with addictions**		
First Author	**Mays, K. L., 2008**	**Source**	**19042198**
Level of evidence	2a	**Study type**	Systematic review
Study quality			
Participants	N=5		
Patient characteristics	Sucht, verschiedene Mittel, 3 Studien klinisch und ambulant		
Intervention	Musiktherapie additional zu anderen Therapien		
Comparison			
Length of follow-up	No follow up		
Outcome measures			
Outcome and effect size	• No consensus in the published literature regarding the effects of music therapy on outcomes for patients with addictions. No study investigated reduction of drug or alcohol consumption or the ability of music therapy to maintain abstinence for sober individuals. • It is clear that a need exists to conduct controlled studies in which the goal is to show that music therapy has an independent effect on outcomes of patients with addictions.		
Comments			

Title	**Effects of Group Songwriting on Motivation and Readiness for Treatment on Patients in Detoxification: a randomized wait-list effectiveness study**		
First Author	**Silverman, M. J., 2012**	**Source**	**23705345**
Level of evidence	2b	**Study type**	Randomized wait-list effectiveness study
Study quality			
Participants	N=99		
Patient characteristics	Alcohol (n=63), Prescription drugs (n=14), Heroin (n=17), Cocaine /Crack (n=3)		
Intervention	Single group songwriting session (n=48)		
Comparison	Wait list control group (n=51)		
Length of follow-up	No follow up		
Outcome measures			
Outcome and effect size	Significant between-group differences were found in motivation (M=1.79, p=0.013) and readiness for treatment (M=3.96, p=0.001) scales. In both the motivation and readiness for treatment scales, the music therapy condition had higher means than the control condition.		

Comments	

Title	**Effects of a Single Lyric Analysis Intervention on Withdrawal and Craving With Inpatients on a Detoxification Unit: A Cluster-Randomized Effectiveness Study**		
First Author	**Silverman, M. J., 2016b**	**Source**	**26800444**
Level of evidence	2b	**Study type**	Cluster-randomized effectiveness study
Study quality	(N=144)		
Participants			
Patient characteristics	Alcohol (n=63), cocaine/crack (n=2), heroin (n=60), prescription drugs (n=14), other (n=1)		
Intervention	Group-based lyric analysis interventions (n=60)		
Comparison	Wait list control group (n=84)		
Length of follow-up	No follow up		
Outcome measures			
Outcome and effect size	Participants in the experimental condition tended to have lower withdrawal (F(1, 141) =3.75, p=0.055, partial η2=0.026, MD=-9.74, 95% CI [-19.69|0.21]) and craving F(1,136)=3.00, p=0.085, partial η2=0.022, MD=-0.093, 95% CI [-1.99|0.13]) means than participants in the control condition. These results, while not statistically significant, are clinically relevant due to the importance of these negative symptoms within the context of the detoxification setting.		
Funding	The author reports no conflicts of interest.		
Comments			

Title	**Can music therapy engage patients in group cognitive behaviour therapy for substance abuse treatment?**		
First Author	**Dingle, G. A., 2008**	**Source**	**18264881**
Level of evidence	2b/3b	**Study type**	Clinical trial
Study quality			
Participants	N=52		
Patient characteristics	Alcohol (n=13), cannabis (n=3) or injecting/polydrug use (n=7), age 17-52 years		
Intervention	7-week trial of music therapy as an adjunct to group cognitive behaviour therapy with.		
Comparison	No control group		
Length of follow-up	No follow up		
Outcome measures			
Outcome and effect size	• Average attendance rate of 75% across the 7-week trial. Attendance rates were generally high from the second session onwards. • Ratings of motivation to participate in the music therapy session were uniformly high, with an overall mean of 4.0 (out of 5), SD=1.20. • Self-rated enjoyment in the session was high, with an overall average of 4.25 (out of 5), SD=0.74. • 83.5% of the sample rating their experience as 'enjoy- able' or 'extremely enjoyable' • Would participate in another music therapy session, 83% of the participants said 'yes'. • Music therapy provides a flexible and enjoyable approach to learning and is able to engage younger, drug-abusing patients equally well as older, alcohol- dependent patients.		
Funding	No funding		
Comments	Only 24 surveys were analysed, men (n=10), women (n=14). Erste Therapie wurde nicht besucht, erst nach Aufklärung durch den MT in Einzeltherapie kamen Patienten. Daten der ersten Messung wurden mitgenommen.		

Title	**Effects of music therapy and music-based interventions in the treatment of substance use disorders: A systematic review**		
First Author	**Hohmann, L., 2017**	**Source**	**29141012**
Level of evidence	3b	**Study type**	Systematic review
Study quality			

Participants	34 quantitative and six qualitative studies
Patient characteristics	Patients with SUD (substance use disorder)
Intervention	Music therapy, Music Based interventions or MP
Comparison	Control group
Length of follow-up	
Outcome measures	
Outcome and effect size	Descriptive data only, due to the diversity of the quantitative studies, effect sizes were not computed. Benefits for MT/MBI for variable locus of control (67% positive effects compared to CG). The variable helpfulness of the intervention, half of the RCTs reported higher values for MT compared to CG. Variables motivation and enjoyment were inconsistent results. Half of the studies of high level evidence of efficacy did not identify statistically significant improvement for MT/ MBI participants. Regarding depression, withdrawal/ craving, participation, and coping skills none of the RCTs reported benefits for MT. Studies examining anxiety, medical symptoms, anger, sadness, and stress were all of low level evidence of efficacy (…) and results can only serve as a base for further research.
Comments	Due to the diversity of the quantitative studies, effect sizes were not computed. We used a descriptive approach to summarize the efficacy evidence of quantitative studies.

Title	**The effect of a lyric analysis intervention on withdrawal symptoms and locus of control in patients on a detoxification unit: A randomized effectiveness study**		
First Author	**Silverman, M. J., 2010**	**Source**	
Level of evidence	2b	**Study type**	randomized effectiveness study
Study quality			
Participants	N=118		
Patient characteristics	Patients in detoxification facility, women (n=56), men (n=57), no response (n=5)		
Intervention	Music therapy: lyric analysis (n=64)		
Comparison	verbal psychotherapy (n=54)		
Length of follow-up	No follow up		
Outcome measures			
Outcome and effect size	Between-group results were not significant. However, the participants in the music therapy condition (M=48.52, SD=34.08) tended to have slightly lower withdrawal scores (p>0.87) compared to CG (M=49.56, SD=37.68). Not significant (p>0.51), MT has slightly higher external locus of control (M=9.75, SD=4.86) than participants in the verbal therapy condition (M=8.38, SD=4.69). Participants from the experimental group made more comments categorized into the "positive change" category.		
Comments			

Title	**Songwriting to Target State Shame, Guilt, and Pride in Adults with Substance Use Disorder on a Detoxification Unit: A Cluster-Randomized Study**		
First Author	**Silverman, M. J., 2019**	**Source**	**30831049**
Level of evidence	2b	**Study type**	A cluster-randomized study
Study quality			
Participants	N=118		
Patient characteristics	Alcohol (n=52), heroin (n=59), prescription (n=10), methamphetamine (n=1); women (n=52), men (n=64)		
Intervention	Experimental (n=58), participants received a group-based blues songwriting protocol targeting state shame, guilt, and pride and then completed the questionnaire.		
Comparison	Control (n=60), control participants completed the questionnaire before receiving an intervention.		
Length of follow-up	No follow up		
Outcome measures			
Outcome and effect size	No significant between-group difference in state shame or guilt, p>0.05. Slightly less state shame and guilt mean scores in experimental group than participants in the control condition.		

	Significant between-group difference in state pride (p<0.012) experimental participants having higher state pride than control participants. ES was small (partial η2=0.053)
Funding	No conflict of interest
Comments	

Title	**The use of art and music therapy in substance abuse treatment programs**		
First Author	**Aletraris, L., 2014**	**Source**	**25514689**
Level of evidence	2c	**Study type**	Quantitative study
Study quality			
Participants	N=299		
Patient characteristics	U.S. substance abuse treatment programs		
Intervention	Art and music therapy		
Comparison			
Length of follow-up			
Outcome measures			
Outcome and effect size	36.8% of programs used art therapy and 14.7% used music therapy, with 11.7% using both. Programs with a higher percentage of female patients were significantly more likely to offer art therapy (OR=1.011). The percentage of adolescent clients was also positively associated with the use of art therapy but this did not reach standard level significance (OR=1.010). Programs that used MET were significantly more likely to offer art therapy (OR=1.682).		
Funding	No conflict of interest		
Comments			

Title	**Effects of music therapy on drug avoidance self-efficacy in patients on a detoxification unit: a three-group randomized effectiveness study**		
First Author	**Silverman, M. J., 2014**	**Source**	**25514686**
Level of evidence	2b	**Study type**	a three-group randomized effectiveness study
Study quality			
Participants	N=131		
Patient characteristics	Patients on a detoxification unit, women (n=59), man (n=70), no response (n=2), Alcohol (n=75), Crack/Cocaine (n=2), Heroin (n=22), prescription drugs (n=31), No response (n=1)		
Intervention	Music therapy-group lyric analysis intervention.		
Comparison	Verbal therapy-group talk therapy session, wait-list-control		
Length of follow-up	No follow up		
Outcome measures			
Outcome and effect size	Concerning drug avoidance self-efficacy and eagerness for treatment, participants in the music therapy condition tended to have higher means (drug avoidance self-efficacy: M=73.04, SD=19.36, eagerness for treatment: M=5.82 SD=1.57) whereas participants in the wait-list control condition (drug avoidance self-efficacy: M=66.38, SD=12.67, eagerness for treatment: M=4.96 SD=2.51) tended to have the lowest means. No significant between-group differences in motivation, treatment eagerness, or drug avoidance self-efficacy.		
Comments	Single session		

Title	**Effectiveness of Psychoanalytic-Interactional Group Therapy vs. Behavioral Group Therapy in Routine Outpatient Treatment of Alcohol-Dependent Patients**		
First Author	**Nyhuis, P. W., 2018**	**Source**	**29016275**
Level of evidence	1b	**Study type**	RCT “quasi-randomisiert”
Study quality	High-medium		
Participants	N=215		
Patient characteristics	F10.2		
Intervention	nach 10-tägiger stationärer Entzugsbehandlung folgte eine 6monatige ambulante		

	Entwöhnungstherapie mit zusätzlichem "clinical care package", alle 4-6 Wochen ein "Arztgespräch"
Comparison	„quasi-randomisiert“: psychoanalytisch interaktionellen Therapie gegenüber der kombinierten behavioralen Intervention. Die eine Gruppe (n=105) erhielt Combined Behavioral Intervention (CBI) (Miller et al., 2004), die andere Gruppe (n=110) erhielt Psychoanalytic Interactional Therapy (PIT) (Heigl-Evers & Ott, 2002)
Length of follow-up	6 Monate
Outcome and effect size	PIT zeigte ein signifikant besseres Ergebnis bezüglich der Rückfallquote (33,6% bei PIT vs. 49,5% bei CBI; p=0,018) / Haltequote (retention rate) bei PIT (81,8%) auch besser als bei CBI (66,7%); Die Abbruchquote war bei der behavioralen Intervention (n=35) signifikant erhöht im Vergleich zu der psychoanalytisch interaktionellen Intervention (n=20, p=0,008).
Funding	Professor N. Scherbaum received honoraria for the participation in Advisory Boards and for holding lectures by the companies AbbVie, Sanofi-Aventis, Mundipharma, Indivior (formerly Reckitt-Benckiser) and Lundbeck in the past three years. Professor F. Schifano is a member of the ACMD UK as well as of the EMA Psychiatry Advisory Board; his brother is an employee of Astra Zeneca Italy. Professor U. Bonnet, Dr. P. W. Nyhuis, Dr. M. Specka, E. Niederhofer, N. Dembski, A. Niederhofer and M. Tenbergen have nothing to declare.
Comments	

Tabellenband

DELBI-Bewertung der internationalen Quell-Leitlinien

(Übernommen aus der Ersterstellung)

1. *DELBI-Bewertung der internationalen Quell-Leitlinien*

DELBI-Domäne 3	**1 2 3 4** **trifft überhaupt nicht zu** / **trifft vollständig zu**
Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115) (NICE, 2011)	
8. Systematische Anwendung von Methoden bei Evidenzsuche	4
9. Auswahlkriterien für Evidenz klar beschrieben	4
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben	4
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt	4
12. Verbindung von Empfehlung und Evidenz	4
13. Externe Begutachtung	4
14. Verfahren zur Aktualisierung der LL angegeben	1
Summe	**25**
Standardisierter Domänenwert	**0,9**
Alcohol-use disorders: Preventing the development of harmful drinking and alcohol dependence (PH 24) (NICE, 2010)	
8. Systematische Anwendung von Methoden bei Evidenzsuche	4
9. Auswahlkriterien für Evidenz klar beschrieben	4
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben	4
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt	4
12. Verbindung von Empfehlung und Evidenz	4
13. Externe Begutachtung	4
14. Verfahren zur Aktualisierung der LL angegeben	4
Summe	**24**
Standardisierter Domänenwert	**0,9**

DELBI-Domäne 3	1	2	3	4
	trifft überhaupt nicht zu			trifft vollständig zu
Alcohol-use disorders: Preventing the development of harmful drinking and alcohol dependence (PH 24) (NICE, 2010)				
8. Systematische Anwendung von Methoden bei Evidenzsuche			3	
9. Auswahlkriterien für Evidenz klar beschrieben			3	
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben			3	
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt			3	
12. Verbindung von Empfehlung und Evidenz			3	
13. Externe Begutachtung				4
14. Verfahren zur Aktualisierung der LL angegeben				4
Summe	**23**			
Standardisierter Domänenwert	**0,8**			
Alcohol use and pregnancy consensus clinical guideline (2010)				
8. Systematische Anwendung von Methoden bei Evidenzsuche			3	
9. Auswahlkriterien für Evidenz klar beschrieben		2		
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben	1			
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt	1			
12. Verbindung von Empfehlung und Evidenz		2		
13. Externe Begutachtung				4
14. Verfahren zur Aktualisierung der LL angegeben	1			
Summe	14			
Standardisierter Domänenwert	0,5			

DELBI-Domäne 3	1 trifft überhaupt nicht zu	2	3	4 trifft vollständig zu
Australian Guidelines to reduce health risks from drinking (2010)				
8. Systematische Anwendung von Methoden bei Evidenzsuche				4
9. Auswahlkriterien für Evidenz klar beschrieben				4
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben				4
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt				4
12. Verbindung von Empfehlung und Evidenz			3	
13. Externe Begutachtung				4
14. Verfahren zur Aktualisierung der LL angegeben				4
Summe	**27**			
Standardisierter Domänenwert	**1,0**			
VA/DoD clinical practice guideline for management of substance use disorders (2008, 2010)				
8. Systematische Anwendung von Methoden bei Evidenzsuche				4
9. Auswahlkriterien für Evidenz klar beschrieben				4
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben				4
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt				4
12. Verbindung von Empfehlung und Evidenz				4
13. Externe Begutachtung				4
14. Verfahren zur Aktualisierung der LL angegeben				4
Summe	**28**			
Standardisierter Domänenwert	**1,0**			

DELBI-Domäne 3	1 trifft überhaupt nicht zu	2	3	4 trifft vollständig zu
Care of HIV-infected substance users (2009)				
8. Systematische Anwendung von Methoden bei Evidenzsuche	1			
9. Auswahlkriterien für Evidenz klar beschrieben	1			
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben	1			
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt	1			
12. Verbindung von Empfehlung und Evidenz	1			
13. Externe Begutachtung	1			
14. Verfahren zur Aktualisierung der LL angegeben	1			
Summe	**7**			
Standardisierter Domänenwert	**0,3**			
Incorporating alcohol pharmacotherapies into medical practice (2009)				
8. Systematische Anwendung von Methoden bei Evidenzsuche	1			
9. Auswahlkriterien für Evidenz klar beschrieben	1			
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben	1			
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt				4
12. Verbindung von Empfehlung und Evidenz	1			
13. Externe Begutachtung				4
14. Verfahren zur Aktualisierung der LL angegeben				4
Summe	**16**			
Standardisierter Domänenwert	**0,6**			

DELBI-Domäne 3	1	2	3	4
	trifft überhaupt nicht zu			trifft vollständig zu
Medical care of HIV-infected substance-using women (2009)				
8. Systematische Anwendung von Methoden bei Evidenzsuche	1			
9. Auswahlkriterien für Evidenz klar beschrieben	1			
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben	1			
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt		2		
12. Verbindung von Empfehlung und Evidenz	1			
13. Externe Begutachtung	1			
14. Verfahren zur Aktualisierung der LL angegeben	1			
Summe	**8**			
Standardisierter Domänenwert	**0,3**			
Clinical management of alcohol use and abuse in HIV-infected patients (2008)				
8. Systematische Anwendung von Methoden bei Evidenzsuche	1			
9. Auswahlkriterien für Evidenz klar beschrieben	1			
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben	1			
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt		2		
12. Verbindung von Empfehlung und Evidenz		2		
13. Externe Begutachtung	1			
14. Verfahren zur Aktualisierung der LL angegeben	1			
Summe	**9**			
Standardisierter Domänenwert	**0,3**			

DELBI-Domäne 3	1 trifft überhaupt nicht zu	2	3	4 trifft vollständig zu
Preventive services for adults (2007; 2010)				
8. Systematische Anwendung von Methoden bei Evidenzsuche			3	
9. Auswahlkriterien für Evidenz klar beschrieben	1			
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben				4
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt		2		
12. Verbindung von Empfehlung und Evidenz		2		
13. Externe Begutachtung	1			
14. Verfahren zur Aktualisierung der LL angegeben				4
Summe	**17**			
Standardisierter Domänenwert	**0,6**			
Counseling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving (2007)				
8. Systematische Anwendung von Methoden bei Evidenzsuche				4
9. Auswahlkriterien für Evidenz klar beschrieben				4
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben				4
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt				4
12. Verbindung von Empfehlung und Evidenz				4
13. Externe Begutachtung				4
14. Verfahren zur Aktualisierung der LL angegeben	1			
Summe	**25**			
Standardisierter Domänenwert	**0,9**			

DELBI-Domäne 3	1	2	3	4
	trifft überhaupt nicht zu			trifft vollständig zu
Treatment of patients with substance use disorders (2006)				
8. Systematische Anwendung von Methoden bei Evidenzsuche				4
9. Auswahlkriterien für Evidenz klar beschrieben				4
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben				4
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt				4
12. Verbindung von Empfehlung und Evidenz				4
13. Externe Begutachtung				4
14. Verfahren zur Aktualisierung der LL angegeben	1			
Summe	**25**			
Standardisierter Domänenwert	**0,9**			
Substance misuse and alcohol use disorders. In: Evidence-based geriatric nursing protocols for best practice (2009)				
8. Systematische Anwendung von Methoden bei Evidenzsuche		2		
9. Auswahlkriterien für Evidenz klar beschrieben	1			
10. Formulierung der für Empfehlungen verwendeten Methoden klar beschrieben		2		
11. Nutzen, Nebenwirkungen & Risiken berücksichtigt	1			
12. Verbindung von Empfehlung und Evidenz	1			
13. Externe Begutachtung				4
14. Verfahren zur Aktualisierung der LL angegeben	1			
Summe	**12**			
Standardisierter Domänenwert	**0,4**			

Tabellenband

Leitlinien-Synopsen

(Übernommen aus der Ersterstellung)

Kapitel „2. Screening und Diagnostik“

Klinische Fragestellung:
„Welche Screening-Instrumente sind jeweils am besten geeignet, um mit einer möglichst hohen Sensitivität (chronischer Alkoholkonsum) und Spezifität (akuter Alkoholkonsum, Abstinenz-Kontrolle) in unterschiedlichen klinischem Umfeld (z.B. Hausarztpraxis, stationäre Aufnahme, Notaufnahme, präoperatives Screening, Intensivstation) Alkoholkonsum nachzuweisen?“

Fragebogen

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommendation	Harmful drinking and alcohol dependence (chapter 1.2.1.4 or 5.26.1.4): Use formal assessment tools to assess the nature and severity of alcohol misuse, including the - AUDIT for identification and as a routine outcome measure - SADQ or LDQ for severity of dependence - Clinical Institute Withdrawal Assessment of Alcohol Scale, revised (CIWA-Ar) for severity of withdrawal - APQ for the nature and extent of the problems arising from alcohol misuse	Statement 3.40 Questionnaire-based screening is accurate, minimally intrusive and has been found to be acceptable to recipients. It is also considerably cheaper than using physiological tests to detect alcohol-related problems (Wallace 2001). Evidence statement 5.5 Only a limited amount of evidence could be identified relating to the performance of alcohol screening questionnaires in hospital settings. The ‘Five-shot questionnaire’ was shown to detect alcohol misuse in adult male inpatients at a cut-off of greater than or equal to 2.5 (one [++] Belgium). AUDIT was effective in screening UK male and female adult general medical admissions for hazardous and harmful alcohol consumption (one [+] UK). AUDIT was also reported to perform effectively among general hospital inpatients (one [++] systematic review).)	3.5 Quantity–frequency estimates is the recommended way to detect levels of consumption in excess of the NHMRC 2009 guidelines in the general population	

		Evidence statement 5.6 Evidence was identified for the use of alcohol screening questionnaires among adults in emergency care settings. One study found that the CAGE questionnaire was effective in screening for a lifetime diagnosis of alcohol dependence in trauma centre patients ([++] USA). AUDIT- C was shown to effectively identify hazardous drinking among male and female adult traffic casualties in an emergency department (one [+] Spain). FAST displayed good screening properties in the identification of alcohol problems among males and females presenting to an A&E setting in the UK (literature review). The 'Paddington alcohol test' has been shown to be rapid, feasible to use, be UK-specific and to have reasonably good screening properties for the detection of alcohol misuse when implemented in response to clinical 'trigger' conditions in A&E care. These are listed as follows: fall; collapse; head injury; assault; accident; unwell; non-specific gastrointestinal conditions; psychiatric; cardiac; repeat attender (three [++] UK).)		
Strength of recommendation / Evidence	Long version: 5.20.2 Evidence summary: Tools are feasible and appropriate to use in a NHS. For case identification and initial assessment of problem severity. narrative review, no systematic reporting of evidence	A, I	(D), (IV) No general statements regarding the use of questionnaires	-
Reference	NICE 2011	NICE 2010	Australian Government Department of Health and Ageing (2009)	Deutsche Rentenversicherung (2011)

Alcohol-use disorders identification test (AUDIT)

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommentation	Harmful drinking and alcohol dependence (chapter 1.2.1.4 or 5.26.1.4 full version): Use formal assessment tools to assess the nature and severity of alcohol misuse, including the: - AUDIT for identification and as a routine outcome measure - SADQ or LDQ for severity of dependence - Clinical Institute Withdrawal Assessment of Alcohol Scale, revised (CIWA-Ar) for severity of withdrawal - APQ for the nature and extent of the problems arising from alcohol misuse.	Evidence statement 5.1 The AUDIT is effective in the identification of hazardous and harmful drinking in adults in primary care (three [++] systematic reviews, one [++] Finland, one [++] UK and one literature review [not graded]). The use of lower thresholds in conjunction with alcohol screening questionnaires was recommended for women (one [++] Finland, one [++] Belgium, one [++] systematic review and one literature review [not graded]). Optimal screening thresholds for the detection of hazardous or harmful drinking using AUDIT appeared to be >=7 or 8 among men (two [++] systematic reviews) and >=6 to 8 among women (one [++] systematic review, one [++] Finland and one literature review [not graded]).Optimal screening thresholds for identifying binge drinking using AUDIT were >= 7 or 8 for adult males (no data available for females) (one [++] Finland). Primary studies included in a systematic review (++) recommended higher AUDIT thresholds for males (5 to 8) than females (2 to 6). 5.5: AUDIT was effective in screening UK male and female adult general medical admissions for hazardous and harmful alcohol consumption (one [+] UK). AUDIT was also reported to perform effectively among general hospital inpatients (one [++] systematic review). Evidence statement 3.41: The AUDIT has been validated in a number of health and social care settings and across a range of drinking	Chapter 3.6 AUDIT is the most sensitive of the currently available screening tools and is recommended for use in the general population.	

		cultures (Reinert and Allen 2007). ..It asks about drinking frequency and intensity and covers experience of alcohol-related problems and signs of possible dependence. AUDIT can detect 92% of genuinely hazardous and harmful drinkers and excludes 93% of those who are not. It is regarded as the 'gold standard' screening questionnaire for detecting hazardous and harmful drinking. Evidence statement 3.41: ...In addition, categories of risk in relation to alcohol consumption may be defined by scores used in the AUDIT. These are as follows: 1–7: low-risk drinking; 8–15: hazardous drinking; 16–19: harmful drinking; 20+: possible dependence.... What action should they take? ... Complete a validated alcohol questionnaire with the adults being screened. Alternatively, if they are competent enough, ask them to fill one in themselves. Use AUDIT to decide whether to offer them a brief intervention (and, if so, what type) or whether to make a referral. If time is limited, use an abbreviated version (such as AUDIT-C, AUDIT-PC, SASQ or FAST). Screening tools should be appropriate to the setting. For instance, in an emergency department FAST or PAT would be most appropriate. ... Use professional judgment as to whether to revise the AUDIT scores downwards when screening: − women, including those who are, or are planning to become pregnant, younger people (under the age of 18). people aged 65 and over, people from some black and minority ethnic groups.		

Strength of recommendation / Evidence	Long version: 5.20.2 Evidence summary: feasible and appropriate to use in a NHS. For case identification and initial assessment of problem severity. No strength of recommendation, no level of evidence (narrative reporting)	A, 1	A, 1	
Reference				

AUDIT-C

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommentation	Evidence statement 5.25.10: Outcome monitoring (addressing assessment- The AUDIT-C (Bush et al., 1998) is a three-item version of the AUDIT which measures only alcohol consumption; that is, frequency of drinking, quantity consumed on a typical occasion and the frequency of heavy episodic drinking (six or more standard drinks on a single occasion). Bush and colleagues (1998) reported that the AUDIT-C performed better than the full AUDIT in detecting heavy drinking and was just as effective as the full AUDIT in identifying active alcohol misuse or dependence. The study also found that using a cut-off of 3 out of a possible 12 points, the AUDIT-C correctly identified 90% of active alcohol abuse/dependence, and 98% of patients drinking heavily. However, other studies have reported that a cut-off of 5 or more for men and 4 or more for women results in the optimal sensitivity and specificity for detecting any alcohol use disorders (Gual et al., 2002; Dawson et al., 2005b). In addition, the AUDIT-C has been found to	Evidence statement 5.2: The evidence for the effectiveness of shorter versions of AUDIT in adults in primary care was variable. Some authors of cross-sectional diagnostic evaluations observed comparable performance between the full AUDIT and shorter versions (two [++] Finland, one [++] Belgium and one [++] USA). Other findings drawn from primary care were more cautious of the utility of the shorter forms of this questionnaire (one [++] systematic review). The optimal screening threshold for the detection of hazardous drinking using AUDIT-C was greater than or equal to three among men and women (one [++] systematic review and one [++] USA). However, thresholds of greater than or equal to five for the detection of heavy drinking among females and greater than or equal to six for identifying bingeing moderate and heavy drinking men were also recommended (one [++] Finland). Primary studies included in a systematic review recommended higher AUDIT-C thresholds for males (three to six) than females (two to five) (one [++]). FAST was described, within a literature review (not graded), as being effective in the		

	be equally effective in detecting alcohol use disorders across ethnic groups (Frank et al., 2008). However, it should be noted that the AUDIT-C has been reported to have a high false positive rate when used as a screening tool (Nordqvist et al., 2004). Nevertheless, the ease of use, and already established relationship between frequency and quantity of drinking with alcohol misuse and dependence give the AUDIT-C credence for the use of outcome monitoring.	detection of alcohol problems at a cut-off point of greater than or equal to one in males and females in a primary care setting in the UK. Evidence statement 3.43: Even with just 10 questions, the full AUDIT questionnaire has been considered too lengthy for use in routine practice. Thus several shorter versions have been developed (*): These comprise between one and four questions. Generally, they are less accurate than the full AUDIT and do not clearly differentiate between hazardous, harmful and possibly dependent drinking.		
Strength of recommendation / Evidence	No strength of recommendation, no level of evidence (narrative reporting)	II and below		
Reference				

AUDIT oder AUDIT-C allen Patienten in allen Settings

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommendation	Harmful drinking and alcohol dependence: Chapter 1.2.1.4 or 5.26.1.4 full version: Use formal assessment tools to assess the nature and severity of alcohol misuse, including: AUDIT for identification and as a routine outcome measure SADQ or LDQ for severity of dependence Clinical Institute Withdrawal Assessment of Alcohol Scale, revised (CIWA-Ar) for severity of withdrawal APQ for the nature and extent of the problems arising from alcohol misuse.	Evidence statement 5.2: The evidence for the effectiveness of shorter versions of AUDIT in adults in primary care was variable. Some authors of cross-sectional diagnostic evaluations observed comparable performance between the full AUDIT and shorter versions (two [++] Finland, one [++] Belgium and one [++] USA). Other findings drawn from primary care were more cautious of the utility of the shorter forms of this questionnaire (one [++] systematic review). The optimal screening threshold for the detection of hazardous drinking using AUDIT-C was greater than or equal to three among men and women (one [++] systematic review and one[++] USA). However, thresholds of greater than or equal to five for the detection of heavy drinking among females and greater than or equal to six for identifying bingeing moderate and heavy drinking men were also recommended (one [++] Finland). Primary studies included in a systematic review recommended higher AUDIT-C thresholds for males (three to six) than females (two to five) (one [++]). FAST was described, within a literature review (not graded), as being effective in the detection of alcohol problems at a cut-off point of greater than or equal	No statement with regard to the short version of AUDIT Evidence statement 3.6: AUDIT is the most sensitive of the currently available screening tools and is recommended for use in the general population.	

		to one in males and females in a primary care setting in the UK. Statement 3.43 Even with just 10 questions, the full AUDIT questionnaire has been considered too lengthy for use in routine practice. Thus several shorter versions have been developed (for details see www.ncl.ac.uk/ihs/assets/pdfs/hmitm/screeningtools.pdf). These comprise between one and four questions. Generally, they are less accurate than the full AUDIT and do not clearly differentiate between hazardous, harmful and possibly dependent drinking.		
Strength of recommendation / Evidence	AUDIT. 5.20.2 Evidence summary (full version): Feasible and appropriate to use in a national health system for case identification and initial assessment of problem severity.	1	1 No statement regarding the short version of AUDIT	
Reference				

Akuter Alkoholkonsum und Zustandsparameter wie EtG oder EtS in Serum und Urin

Guideline	Alcohol-udisorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommendation	Harmful drinking and alcohol dependence: Evidence statement 1.2.2.10: Consider measuring breath alcohol as part of the management of assisted withdrawal. However, breath alcohol should not usually be measured for routine assessment and monitoring in alcohol treatment programs. Evidence statement 1.2.2.9: Consider blood tests to help identify physical health needs, but do not use blood tests routinely for the identification and diagnosis of alcohol use disorders.	Evidence statement 5.10: Laboratory markers are of limited value in the detection of alcohol misuse when compared with alcohol screening questionnaires (two [++] UK, one [++] Belgium and one [+] Germany). However, the use of blood-alcohol concentration testing may complement the use of later questionnaire screening in the identification of alcohol misuse among patients treated in the emergency department resuscitation room (one [++] UK).	Evidence statement 3.8: Direct measures of alcohol in breath and/or blood can be useful markers of recent use and in the assessment of intoxication.	
Strength of recommendation / Evidence	No strength of recommendation, no level of evidence (narrative reporting)	No strength of recommendation, no level of evidence (narrative reporting) markers not mentioned	Level of evidence 2, markers not mentioned	
Reference				

Chronischer Alkoholkonsum und Zustandsmarker (EtG in Haaren und PEth im Blut)

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommendation	Harmful drinking and alcohol dependence: Evidence statement 1.2.2.10: Consider blood tests to help identify physical health needs, but do not use blood tests routinely for the identification and diagnosis of AUD. Evidence statement 5.25.6: Methods of physical investigation: Breath /blood alcohol level Blood/breath alcohol concentration may be a useful part of the clinical assessment in the following areas: Although self- report has been found to be a reliable indicator of levels of alcohol consumption in treatment seeking populations, patients with alcohol in their system at the time of assessment are more likely to underestimate their levels of alcohol consumption (Sobell & Sobell, 2003). Clinicians have a responsibility to discuss drink driving concerns with patients and ... hair and sweat analysis.	Evidence statement 5.10: Laboratory markers are of limited value in the detection of alcohol misuse when compared with alcohol screening questionnaires (two [++] UK, one [++] Belgium and one [+] Germany). However, the use of blood-alcohol concentration testing may complement the use of later questionnaire screening in the identification of alcohol misuse among patients treated in the emergency department resuscitation room (one [++] UK).	Evidence statement 3.8: Direct measures of alcohol in breath and/or blood can be useful markers of recent use an in the assessment of intoxication.	

	As alcohol is rapidly excreted from the body, there is currently no reliable or accurate way of measuring alcohol consumption in the recent past, and the mainstay of outcome measurement is self- report (Sobell & Sobell, 2003). This is less useful for regulatory monitoring purposes and so there is a growing interest by manufacturers in the design biomarkers for recent alcohol consumption. Studies to date focus on hair and skin sweat analysis, but there is currently a lack of evidence to recommend their use in routine clinical care (Pragst & Balikova, 2006)			
Strength of recommendation / Evidence	No strength of recommendation, no level of evidence (narrative reporting) Markers not mentioned	No strength of recommendation, no level of evidence (narrative reporting Markers not mentioned	Strength of recommendatioln: D Markers not mentioned	
Reference				

Chronischer Alkoholkonsum Kombination von indirekten Zustandsmarkern (z.B. GGT&MCV&CDT, Antilla Index, AlcIndex)

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommendation	Harmful drinking and alcohol dependence: Evidence statement 1.2.2.10: Consider blood tests to help identify physical health needs, but do not use blood tests routinely for the identification and diagnosis of alcohol use disorders. Evidence statement 5.25.6 (full version): Methods of physical investigation There are a number of biomarkers suggested to be clinically useful in the assessment of alcohol related physical harm (Allen et al., 2003), monitoring of clinical outcome, and as a motivational enhancement strategy (Miller et al., 1992). However, in people who are seeking treatment for alcohol misuse, biomarkers do not offer any advantage over self- report measures in terms of accuracy of assessing alcohol consumption (Allen et al., 2003; Sobell & Sobell, 2003), and are less sensitive and specific than the AUDIT in screening for alcohol misuse (Drummond & Ghodse, 1999). Advantages of blood investigations as part of the initial assessment include:	Evidence statement 5.10: Laboratory markers are of limited value in the detection of alcohol misuse when compared with alcohol screening questionnaires (two [++] UK, one [++] Belgium and one [+] Germany). However, the use of blood-alcohol concentration testing may complement the use of later questionnaire screening in the identification of alcohol misuse among patients treated in the emergency department resuscitation room (one [++] UK).	Carbohydrate-deficient transferrin should only be used as an adjunct to other screening measures as they have lower sensitivity and specificity in detecting at-risk people than structured questionnaire approaches (such as AUDIT).	

	screening for alcohol related physical conditions that may need further investigation and onward referral Provide baseline measures of alcohol related damage (in some patients) against which to measure improvement and act as motivational enhancement strategy. Objective measurement of outcome, particularly when combined (e.g. CDT and GGT; Allen et al., 2003) and in conjunction with other structured outcome measures (Drummond et al., 2007).			
Strength of recommendation / Evidence	No strength of recommendation, no level of evidence	No strength of recommendation, no level of evidence	Strength of recommendation: A	
Reference				

AUDIT und eine geeignete Kombination von indirekten Zustandsmarkern

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommendation	harmful drinking and alcohol dependence: Evidence statement 1.2.2.10: Consider blood tests to help identify physical health needs, but do not use blood tests routinely for the identification and diagnosis of alcohol use disorders.	Evidence statement 5.10: Laboratory markers are of limited value in the detection of alcohol misuse when compared with alcohol screening questionnaires (two [++] UK, one [++] Belgium and one [+] Germany). However, the use of blood-alcohol concentration testing may complement the use of later questionnaire screening in the identification of alcohol misuse among patients treated in the emergency department resuscitation room (one [++] UK).	Carbohydrate-deficient transferrin) should only be used as an adjunct to other screening measures as they have lower sensitivity and specificity in detecting at-risk people than structured questionnaire approaches (such as AUDIT).	
Strength of recommendation / Evidence	No strength of recommendation, no level of evidence (narrative reporting)	No strength of recommendation, no level of evidence (narrative reporting)	1a, A	
Reference				

Erheben des Alkoholkonsums

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommendation	Table 16: Assessment tools excluded from narrative review: Quantity–Frequency (QF) Methods, Timeline Follow Back (TLFB) (Sobell and colleagues, 1979)	-	Quantity-frequency index (QFI) and Retrospective Diary: A comparison of a 30-day QFI with a 7d retrospective diary and item 3 on AUDIT showed that the QF question was comparable to the AUDIT item in detecting binge drinking (95 percent positive predictive value). All 3 methods were administered using a computer. The retrospective diary requires patients to identify the type and quantity of alcoholic beverage consumed beginning with the previous day and work back through each day of the week. It was less sensitive than the QFI (ranging from 23.1 percent to 36.7 percent) (Shakeshaft et al. 1999). The QF question asked respondents to indicate the number of occasions during the previous 30 days on which they had consumed four different levels of standard drinks (defined by the NHMRC (2001) as 10g of ethanol). Item 3 (AUDIT-3) asks “how often do you have six or more drinks on one occasion?” Possible responses are “never”,	

			“less than monthly”, “monthly”, “weekly”, and “daily or almost daily”. Although the retrospective diary took longer to administer than the QFI (mean completion times of three min, 38 sec and one min, 41 sec respectively) it provides two important pieces of information: weekly and binge consumption. Further, although the retrospective diary was inferior in detecting binge drinking, the QFI underestimated overall drinking relative to the retrospective diary (Shakeshaft 1999).	
Strength of recommendation / Evidence	No strength of recommendation, no level of evidence	No strength of recommendation, no level of evidence	No strength of recommendation, no level of evidence (narrative reporting)	
Reference				

Klassifikationsschemata der International Classification of Diseases (ICD)

Guideline	Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	Alcohol-use disorders: preventing the development of hazardous and harmful drinking - public health guidance (PH 24)	Australian guidelines to reduce health risks from drinking alcohol (2009)	Deutsche Rentenversicherung: Reha-Therapie-standards Alkohol-abhängigkeit – Leitlinie für die medizinische Rehabilitation der RV
Recommendation	Harmful drinking and alcohol dependence: Introduction: -….alcohol dependence is defined in ICD-10 and DSM-IV in categorical alcohol dependence terms for diagnostic and statistical purposes as being either present or absent, in reality dependence exists on a continuum of severity. However, it is helpful from a clinical perspective to subdivide dependence into categories of mild, moderate and severe. People with mild dependence (those scoring 15 or less on the Severity of Alcohol Dependence Questionnaire; SADQ) usually do not need assisted alcohol withdrawal.	Evidence statement 3.42: 'Hazardous' and 'harmful' drinking are medically defined terms that have been used extensively in the scientific literature and in many recommended tools. 'Harmful use of a psychoactive substance' is an official term in the (WHO's ICD 10th revision. 'Hazardous use of a psychoactive substance', while not an alcohol-use disorder in itself, is included in WHO's 'Lexicon of alcohol and drug terms' (1994).	Evidence statement 3.10: Assessment should include patient interview, structured questionnaires, physical examination, clinical investigations and collateral history. The length of the assessment should be balanced against the need to keep the patient in treatment and address immediate concerns (SoR D, LoE: IV) Evidence statement 3.13: Assessment of the patient's alcohol-related problems, diagnosis and severity of dependence should be recorded. (SoR: S) Evidence statement 3.15: Assessment for mental health problems, such as anxiety, depressive symptoms and suicidal risk, should be routine, including mental stage examination. Referral for further specialist assessment may be needed if significant mental problems are suspected. (SoR: S) The Composite International Diagnostic Interview (CIDI) is a standardised and comprehensive interview designed to assess psychological disorders against the International Classification of	Die vorliegenden Reha-Therapie-standards gelten für alle Rehabilitanden mit der folgenden Erstdiagnose (ICD-10-GM) im Entlassungsbericht Deutsche RV 2011. (LoE: Standard)

			Diseases (ICD) and DSM-IV diagnoses (World Health Organisation 1990). It must be administered or supervised by a fully trained mental health professional who has undertaken recognised CIDI training. As well as substance use disorders, it covers eating disorders, organic mental disorders, schizophrenic disorders, paranoid disorders, affective disorders, anxiety disorders, somatisation disorders, dissociative disorders, and psychosexual disorders. WHO also recently produced the World Mental Health (WMH) Survey Initiative version (Kessler and Ustun 2004). However, one study found that CIDI performed poorly, especially in diagnosing social phobia and post-traumatic stress disorder, compared to clinical assessment (Komiti et al. 2001). The CIDI, the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) and the Alcohol Use Disorder and Associated Disabilities Interview Schedule-Alcohol/Drug- Revised (AUDADIS-ADR) all have reasonable test-retest reliability and diagnostic concordance for alcohol dependence, but not for risky alcohol use or abuse.	
Strength of recommendation / Evidence	Clinical practice No strength of recommendation, no level of evidence	Clinical practice No strength of recommendation, no level of evidence	Standard of Care or IV	Clinical practice No strength of recommendation, no level of evidence
Reference				

Kapitel „3.1 Kurzinterventionen“

Klinische Fragestellung:
„Ist allgemein im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	Australian guidelines to reduce health risks from drinking alcohol (2009)	VA/DoD clinical practice guideline (2009)	Incorporating pharmacotherapies into medical practice (2009)	Preventive services for adults (revised 2010)
Recommentation			Twenty seven systematic reviews and meta-analyses have been included in the review of reviews of the effectiveness of brief interventions for alcohol misuse. The quality of reviews was generally of a high standard in terms of study design characteristics and clarity of reporting. Evidence has been identified for the positive impact of brief interventions for alcohol misuse on alcohol consumption, mortality, morbidity, alcohol-related injuries, alcohol- *related social consequences, and healthcare resource use. [1; p. 9]*		The evidence for the efficacy of brief alcohol counselling has been summarized in a Cochrane review (Kaner et al., 2007), and a USPSTF Review (Whitlock et al., 2004), as well as 7 other meta- analyses and reviews (Ballesteros et al., 2004; Bertholet et al., 2005; Bien et al., 1993; Kahan et al., 1995; Moyer et al., 2002; Poikolainen, 1999; Wilk et al., 1997). While none of these reviews were restricted to VA or DoD patients, and no trial has included VA or DoD patients, there is no reason to expect that VA patients would respond differently than other patients to brief intervention given the robust international findings, including studies of older patients (Fleming et al., 1999).		

					A negative review (Beich et al., 2002) made assumptions that recruitment for screening in the real world would be similar to low participation rates in RCTs. In fact, high rates of alcohol screening have been achieved in VA clinical settings (Bradley et al., 2006).		
Strength of recommendation / Evidence			[++]		A/Ia		
Reference			[2, 3-6]		[3, 5, 7, 8-10]		

Guideline	**Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving (2007)**	**Treatment of Patients with substance use disorders (APA, 2006)**	**DRV-Leitlinien**	**S1-Leitlinie Alkoholdelir**	**S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub- stanzen**	**S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho- therapie**	**S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen**	**S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzinterve ntion**	**S2-Leitlinie Postakut-behand-lung alkohol-bezogener Störungen**
Recommendation								Erfolg minimaler bzw. kurzer Interventione n in Settings der medizinische n oder psycho- sozialen Basisversorg ung bzw. spezifischen Zielgruppen nach- gewiesen	
Strength of recommendation / Evidence								I b	
Reference								Acht Studien zwischen 1988 und 2000 [11]	

Klinische Fragestellung:
„Ist bei Riskantem Konsum im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	Australian guidelines to reduce health risks from drinking alcohol (2009)	VA/DoD clinical practice guideline (2009)	Incorporating pharmaco- therapies into medical practice (2009)	Preventive services for adults (revised 2010)
Recommendation			Die unter 1.1 beschriebene Evidenz bezieht sich in der weit überwiegenden Zahl auf riskanten Alkoholkonsum.	-	Die unter 1.1 beschriebene Evidenz bezieht sich in der weit überwiegenden Zahl auf riskanten Alkoholkonsum.		
Strength of recommendation / Evidence			[++]	-	A, Ia		
Reference			s. 1.1	-	s. 1.1		

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving (2007)	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub-stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho- therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkons um: Screening, Diagnostik und Kurzinterven tion	S2-Leitlinie Postakut-behandlung alkohol-bezogener Störungen
Recommendation								Die unter 1.1 beschriebene Evidenz bezieht sich in der weit überwiegende n Zahl auf riskanten Alkoholkonsum	

Strength of recommendation / Evidence								Ia	
Reference								(s. 1.1)	

Klinische Fragestellung:
„Ist bei Rauschtrinken im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	**NICE CG115 (2011)**	**NICE CG100 (2010)**	**NICE PH 24 (2010)**	**Australian guidelines to reduce health risks from drinking alcohol (2009)**	**VA/DoD clinical practice guideline (2009)**	**Incorporating pharmacotherapi es into medical practice (2009)**	**Preventive services for adults (revised 2010)**
Recommendation	Keine Angabe	Keine Angabe	Keine spezifischen Empfehlungen zur Wirksamkeit bei Rauschtrinken	Keine Angabe	Keine spezifischen Empfehlungen zur Wirksamkeit bei Rauschtrinken	Keine Angabe	Keine Angabe
Strength of recommendation / Evidence							
Reference							

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub-stanzen	S2-Leitlinie Therapeu-tische Maß-nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho-therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzinterve ntion	S2-Leitlinie Postakut-behandlung alkohol-bezogener Störungen
Recommendation								Keine spezifischen Empfehlungen zur Wirksamkeit bei Rauschtrinken	
Strength of recommendation / Evidence									
Reference									

Klinische Fragestellung

„Ist bei Abhängigkeit im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	Australian guidelines to reduce health risks from drinking alcohol (2009)	VA/DoD clinical practice guideline (2009)	Incorporating pharmacotherapi es into medical practice (2009)	Preventive services for adults (revised 2010)
Recommendation			Keine spezifischen Empfehlungen zur Wirksamkeit bei Abhängigen. „The relationship between the level of alcohol dependence and the effectiveness of brief interventions was unclear”		Keine spezifischen Empfehlungen zur Wirksamkeit bei Abhängigen.		
Strength of recommendation / Evidence							
Reference			[1, S.9)].				

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho-trope Sub-stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho- therapie	S2-Leitlinie Akut-behandlung alkohol- bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzinterve ntion	S2-Leitlinie Postakut-behand- lung alkohol-bezogener Störungen
Recommendation								„Es fehlen Studien mit Pat. in späteren Stadien der Abhängigkeit. Gegenwärtig keine Schlussfolgerung en hinsichtlich des Zusammenhangs zwischen Schweregrad der Symptomatik einerseits und Erfolg der Intervention andererseits möglich“ [11, S.11]	
Strength of recommendation / Evidence									
Reference									

Klinische Fragestellung:
„Ist bei Frauen und Männern im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	Australian guidelines to reduce health risks from drinking alcohol (2009)	VA/DoD clinical practice guideline (2009)	Incorporating pharmacotherapi es into medical practice (2009)	Preventive services for adults (revised 2010)
Recommendation			“Brief interventions are effective in reducing alcohol consumption in both men and women.” [1, S.19]				
Strength of recommendation / Evidence	-	-	++	-	-	-	-
Reference	-	-	[3, 5, 7, 9, 12-14].	-	-	-	-

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving (2007)	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub- stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho-therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzinterve ntion	S2-Leitlinie Postakut-behand- lung alkohol-bezogener Störungen
Recommendation								Wider-sprüchliche Ergebnisse zum Einfluss des Geschlechts	
Strength of recommendation / Evidence								I a und Ib	

Reference								Fünf Studien zwischen 1997 und 2002 [11, S.10]	

Klinische Fragestellung:

„Ist bei Menschen im höheren Alter im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	**NICE CG115 (2011)**	**NICE CG100 (2010)**	**NICE PH 24 (2010)**	**Australian guidelines to reduce health risks from drinking alcohol (2009)**	**VA/DoD clinical practice guideline (2009)**	**Incorporating pharmacotherapi es into medical practice (2009)**	**Preventive services for adults (revised 2010)**
Recommendation					(…the robust international findings, including studies of older patients (Fleming et al., 1999) no specific clinical recommendation		
Strength of recommendation / Evidence	-	-	-	-	-	-	-
Reference	-	-	-	-	-	-	-

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving (2007)	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub- stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho- therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzinterve ntion	S2-Leitlinie Postakut-behand- lung alkohol-bezogener Störungen
Recommendation								Ja	
Strength of recommendation / Evidence								I b	-
Reference								[15]	-

Klinische Fragestellung

„Ist bei Menschen mit komorbiden psychiatrischen Störungen im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	Australian guidelines to reduce health risks from drinking alcohol (2009)	VA/DoD clinical practice guideline (2009)	Incorporating pharmacotherapi es into medical practice (2009)	Preventive services for adults (revised 2010)
Recommendation							
Strength of recommendation / Evidence							
Reference							

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving (2007)	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub- stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho- therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzinterve ntion	S2-Leitlinie Postakut-behand- lung alkohol-bezogener Störungen
Recommendation									
Strength of recommendation / Evidence									
Reference									

Klinische Fragestellung

„Ist im Setting der primärmedizinischen Versorgung im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	Australian guidelines to reduce health risks from drinking alcohol (2009)	VA/DoD clinical practice guideline (2009)	Incorporating pharmacotherapi es into medical practice (2009)	Preventive services for adults (revised 2010)
Recommendation			“The majority of included studies were also conducted in primary care.” [1, S. 18]		Die erwähnte Evidenz stammt zum weit überwiegenden Teil aus der primär-medizinischen Versorgung		
Strength of recommendation / Evidence			[++]		A/Ia		
Reference			s. 1.1		s. 1.1		

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub- stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho- therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzinterve	S2-Leitlinie Postakut-behand- lung alkohol-bezogener Störungen
Recommendation		Ja						Ja	
Strength of recommendation / Evidence		A / Ia						Ia	
Reference		s. 1.1						s. 1.1	

Klinische Fragestellung:
„Ist am Arbeitsplatz im kontrollierten Vergleich von einer Wirksamkeit verschiedener Kurzinterventionen auszugehen?“

Guideline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	Australian guidelines to reduce health risks from drinking alcohol (2009)	VA/DoD clinical practice guideline (2009)	Incorporating pharmacotherapi es into medical practice (2009)	Preventive services for adults (revised 2010)
Recommendation			A systematic review of brief interventions for alcohol misuse in the workplace presented limited and inconclusive findings for the effectiveness of interventions in this setting. [1, S.18]				
Strength of recommendation / Evidence			-				
Reference			[16]				

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub- stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres-sivem Verhalten in der Psychiatrie und Psycho- therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzintervention	S2-Leitlinie Postakut-behand- lung alkohol-bezogener Störungen
Recommendation									
Strength of recommendation / Evidence									
Reference									

Klinische Fragestellung

„Für welche Verfahren ist, ebenfalls im kontrollierten Vergleich, eine fehlende Wirksamkeit belegt?“

Guideline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	Australian guidelines to reduce health risks from drinking alcohol (2009)	VA/DoD clinical practice guideline (2009)	Incorporating pharmacotherapi es into medical practice (2009)	Preventive services for adults (revised 2010)
Recommendation							
Strength of recommendation / Evidence							
Reference							

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho- trope Sub- stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres-sivem Verhalten in der Psychiatrie und Psycho- therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzintervention	S2-Leitlinie Postakut-behand- lung alkohol-bezogener Störungen
Recommendation	Reduktion des Alkoholkonsum s ist nicht Gegenstand der Empfehlungen								
Strength of recommendation / Evidence									
Reference									

Klinische Fragestellung:
„Für welche Verfahren ist, ebenfalls im kontrollierten Vergleich, eine unerwünschte Wirksamkeit belegt?“

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation						
Strength of recommendation / Evidence						
Reference						

Guideline	Counselling about proper use of motor vehicle occupant restraints and avoidance of alcohol use while driving (2007)	Treatment of Patients with substance use disorders (APA, 2006)	DRV-Leitlinien	S1-Leitlinie Alkoholdelir	S1-Leitlinie Psychische und Verhaltens-störungen durch psycho trope Sub-stanzen	S2-Leitlinie Therapeu- tische Maß- nahmen bei aggres- sivem Verhalten in der Psychiatrie und Psycho- therapie	S2-Leitlinie Akut-behandlung alkohol-bezogener Störungen	S2-Leitlinie Riskanter, schädlicher und abhängiger Alkoholkon sum: Screening, Diagnostik und Kurzintervention	S2-Leitlinie Postakut-behand- lung alkohol-bezogener Störungen
Recommendation									
Strength of recommendation / Evidence									
Reference									

Kapitel „3.2. Körperliche Entgiftung“

Klinische Fragestellung

„Bei welchen Patientengruppen (schädlicher Gebrauch, Abhängigkeit) ist die Durchführung einer körperlichen Entgiftung wirksam und indiziert?“

A) Abhängigkeit

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		- Bei Entzugserscheinun gen können Benzodiazepine, Carbamazepin, Clomethiazol die Alkoholentzugssym ptome inkl. Entzugsanfälle verhindern bzw. verringern - Sie Wirksamkeit zeigt eine Abhängigkeit/steht in Beziehung zur Entzugs- symptomatik (auch in Relation zum Zeitpunkt des letzten Alkoholkonsums und zur Blutalkoholkonzentr ation) und zum individuellen Risiko von Entzugsanfällen bzw. Delirien			As described in DSM-IV-TR and elsewhere (972, 973), <5% of individuals with alcohol withdrawal develop severe symptoms and <3% develop grand mal seizures. In the past, the mortality rate for patients experiencing alcohol with drawal delirium was as high as 20%; currently, it is closer to 1% because of improved diagnosis and medical treatment (972). The presence of a co-occurring medical disorder may also increase the likelihood of a complicated withdrawal syndrome (974–976).	
Strength of recommendation / Evidence		1++				
Reference		26 (Cochrane Database of Systematic Reviews. 2005; CD005063) bis 39 und ff. des Literaturverzeichnis				

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation	wirksam				Wirksamkeit: - die Behandlung alkoholbezogener Störungen ist effektiver als die Nichtbehandlung,		
Strength of recommendation / Evidence	C/IV				A/Ia		
Reference	Fleischmann 2002				Miller et al 1995, Mirin et al 1995, Hox et al 1998		

Klinische Fragestellung:
„Bei welchen Patientengruppen (schädlicher Gebrauch, Abhängigkeit) ist die Durchführung einer körperlichen Entgiftung wirksam und indiziert?“
B) Schädlicher Gebrauch

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		S.32: 2.1.7 Recommendation: R1 For people in acute alcohol withdrawal with, or who are assessed to be at high risk of developing, alcohol withdrawal seizures or delirium tremens, offer admission to hospital for medically assisted alcohol withdrawal. R2 For young people under 16 years who are in acute alcohol withdrawal, offer admission to hospital for physical and psychosocial assessment, in addition to medically assisted alcohol withdrawal. R3 For certain vulnerable people who are in acute alcohol withdrawal (for example, those who are frail, have cognitive impairment or multiple comorbidities, lack social support, have learning difficulties or are 16 or 17 years), consider a lower threshold for admission to hospital for medically assisted alcohol withdrawal. R4 For people who are alcohol dependent but not admitted to hospital, offer advice to avoid a sudden reduction in alcohol intake and information about how to contact local alcohol support services.				

Strength of recommendation / Level of evidence						
Reference						

Klinische Fragestellung

„Inwieweit hängt die Effektivität der körperlichen Entgiftung von folgenden Faktoren ab:

A) Behandlungskomponenten

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		1. - Es gibt keine Studien zum Effektivitäts-vergleich einer Notfallaufnahme vs. einer geplanten Entgiftung. - *Die niedrigschwellige Notaufnahme ist daher unverzichtbar bei plötzlich einsetzenden Entzugserscheinungen und Entzugskomplikationen - *Die geplante Aufnahme hat vor allem Vorteile wegen der höheren Motivation und der Möglichkeit der gezielten Weiterleitung in eine Langzeittherapie. 2. - **Adäquater Gebrauch von Entzugsskalen (CIWA) bei Symptom getriggerten Entzug wichtig 3. - v.a. beim ambulanten und teilstationären Entzug von dem Vorhandensein und der Zugänglichkeit eines 24h Notdienst 4. von der Form (symptomorientiert vs fixes Medikamentenschema): symptomorientierte Medikamentenverabreichung ist der fixen Schemadosierung überlegen bezogen auf Behandlungszeit und Gesamtdosis der verabreichten Mediakmente (Benzodiazepine) bzw. S. 52: Overall, symptom-triggered dosing was associated with significantly lower doses of benzodiazepines than fixed-dosing and with a shorter treatment duration and importantly without an increase in the incidence of seizures or delirium tremens 5. vom eingesetzten Medikament: gleich wirksam sind Benzodiazepine, Carbamazepine, Clomethiazol		- Multiple randomized, controlled trials demonstrate the use of less medication as well as shorter duration of treatment in symptom-triggered detoxification protocols (998, 1001–1003).		

Strength of recommendation / Level of evidence		1. - Expertenmeinung 2. - ** 3 3. - ?? B/III 1+/Level 3				
Reference		Referenz: 26, 28-38				

Guideline	**S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“**	**S2 Leitlinie „Screening, Diagnostik, Kurzintervention“**	**S2 Leitlinie „Alkoholdelir“**	**S2 Leitlinie „Aggressives Verhalten“**	**S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“**	**S1 Leitlinie „Kindesalter“**	**DRV Leitlinien**
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung
„Inwieweit hängt die Effektivität der körperlichen Entgiftung von folgenden Faktoren ab:“
B) Behandlungsort

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		1. - Die Datenlage reicht nicht aus für eine eindeutige/generelle Empfehlung, in welchem Setting behandelt werden sollte! (Seite 42). - Ambulante Behandlungsregime sollten eine über 24h erreichbare/ zugänglich e Versorgungsstruktur anbieten bzw. die Möglichkeit einer stationären Aufnahme bei Komplikationen beinhalten**.** Stationärer Behandlung für Menschen mit drohenden oder akuten Alkoholentzugssyndro men mit der Möglichkeit eines medikamentengestützt en Entzuges und psychosozialer Unterstützung sowie Motivationsarbeit wird empfohlen für: - Patienten mit hohem Risiko für Entzugskrampfanfälle oder ein Delir - Patienten mit somatischen Komorbiditäten, mit schlechtem Allgemeinzustand, mit fehlender oder geringer sozialer Unterstützung, mit kognitiven Störungen, mit geistigen Behinderungen (33) - Junge Patienten bzw. Patienten unter 16 Jahren		Consider ambulatory medically supervised alcohol withdrawal, when indicated	- Behandlungsform (stationär, teilstationär oder ambulant) hängt primär von der Frage ab, was für den Patienten die effektivste aber auch sicherste Behandlungsform darstellt [I]. - Generell muß die Möglichkeit des Übergangs von einer weniger intensiven zur intensiveren Behandlungsform sichergestellt werden [I]. - Die Behandlungsform hängt auch von der Kooperationsfähigkeit und dem Ausmaß der Hochrisikoverhaltens wie vom Ausmaß der benötigten sozialen und strukturellen Unterstützung ab.[I] Ambulant möglich wenn: - geringes Risiko für Entzugskomplikationen klinische Situation	**ambulant:** - mild to moderate symptoms (mild tremors, mild anxiety, headache, diaphoresis, palpitations, anorexia, and gastrointestinal upset) für nichtpharmakologische oder Benzo-Therapie wenn tgl. Kontakt mit Arzt und/oder Unterstützung durch Familie/Freunde **Stationär bei:** - Severe withdrawal symptoms - History of withdrawal seizures or complications - Delirium tremens or history of delirium tremens - Depression with suicidal ideation - Severe coexisting medical or psychiatric conditions - An unstable home situation

		(S.32: 2.1.7 RECOMMENDATION S R1 For people in acute alcohol withdrawal with, or who are assessed to be at high risk of developing, alcohol withdrawal seizures or delirium tremens, offer admission to hospital for medically assisted alcohol withdrawal. R2 For young people under 16 years who are in acute alcohol withdrawal, offer admission to hospital for physical and psychosocial assessment, in addition to medically assisted alcohol withdrawal. R3 For certain vulnerable people who are in acute alcohol withdrawal (for example, those who are frail, have cognitive impairment or multiple comorbidities, lack social support, have learning difficulties or are 16 or 17 years), consider a lower threshold for admission to hospital for medically assisted alcohol withdrawal.R4 For people who are alcohol dependent but not admitted to hospital, offer advice to avoid a sudden reduction in alcohol intake and information about how to contact local alcohol support services. 2. Benzodiazepine u. Carbamazepin sind ambulant oder stationär wirksam, Clomethiazol sollte wegen seiner Eigenschaften/NW nur stationär eingesetzt werden			und Umfeld/ Umgebung keine intensivere Behandlung erfordert [I] - a variety of psychotherapeutic and pharmacological interventions along with behavioral monitoring can be offered [I] - …in a setting that provides frequent clinical assessment and any necessary treatments [I].	

Strength of recommendation / Level of evidence		1. kein Evidenzgrad angegeben, Expertenmeinung/ Kon sens Expertenkonsens		I Good Subst A	I	Expert Opinion (?)

Reference		Referenz: 26 ff		Hayashida et al., 1989 Mayo-Smith, 1997	966. Rychtarik RG, Connors GJ, Whitney RB, McGillicuddy NB, Fitterling JM, Wirtz PW: Treatment settings for persons with alcoholism: evidence for matching clients to inpatient versus outpatient care. J Consult Clin Psychol 2000; 68:277–289 [A–] 967. Fiellin DA, Reid MC, O'Connor PG: Outpatient management of patients with alcohol problems. Ann Intern Med 2000; 133:815-827 [G]	41. Kosten TR, O'Connor PG. Management of drug and alcohol withdrawal. *N Engl J Med* 2003;348:1786-1795. 42. Blondell RD. Ambulatory detoxification of patients with alcohol dependence. *Am Fam Physician* 2005;71:495-502.

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation	1. Im Vergleich des ambulanten und stat Settings wurde bei milder/ moderater Alkoholabhängigkeit nach 6 Monaten kein Unterschied bez. der Abstinenz gefunden Bei lebens- bedrohlichen Delirien, die kompliziert sind durch kardiale und pulmonale Komplikationen und schwere Bewusstseinsstörungen, ist die Behandlung auf der Intensivstation durchzuführen. Es gelten die Regeln der Intensivtherapie. Da eine orale Therapie unzureichend ist, wird als Anti-Delir- Therapie empfohlen: Diazepam 120-240 mg i.v. pro Tag (kontinuierlich oder als Boli) plus Haloperidol 6 x 10 mg i.v. pro Tag (oder plus Dihydrobenzperidol bis 200 mg i.v. pro Tag) oder Midazolam i.v. bis 20 mg pro Stunde, nach Wirkung, plus Dihydrobenzperidol bis 200 2. mg i.v. pro Tag und fakultativ zusätzlich Clonidin initial 0,025 mg i.v. pro Stunde gegeben werden (wobei die Dosis bei Bedarf erhöht werden kann).						
Strength of recommendation / Level of evidence	A/I C/IV						
Reference	1. Hayashida et al 1989 2. AWMF online Leitlinie Neurologie: Alkoholdelir						

Klinische Fragestellung:
„Inwieweit hängt die Effektivität der körperlichen Entgiftung von folgenden Faktoren ab…?“
C) Behandlungsdauer

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		Behandlungsdauer in Abhängigkeit von Dauer der Entzugssymptome variable			- severe alcohol withdrawal syndrome occurs especially within the first several days after cessation or reduction of heavy, prolonged ingestion of alcohol - Patients in severe withdrawal and those with a history of withdrawal-related symptoms may require up to 10 days of treatment before benzodiazepines can be completely withdrawn.	
Strength of recommendation / Level of evidence						
Reference						

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation	Für die Behandlung von chronisch mehrfach beeinträchtigen Alkoholabhängigen (CMA) gilt, daß die besten Ergebnisse nach einer individuell angepaßten Behandlungsdauer von 2-6 Monaten erzielt werden (wonach unter Berücksichtigung ökonomischer Interessen der Kostenträger ein "therapeutisches Zeitfenster" von 30-60 Tagen optimal zu sein scheint [Fleischmann 2002]).						
Strength of recommendation / evidence	C/IV						
Reference	Fleischmann 2002						

Klinische Fragestellung

„Welche Risiken zeigen sich bei einer Behandlung ohne körperliche Entgiftung im Vergleich zu einer Behandlung mit körperlicher Entgiftung?“

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		- das Auftreten von schweren Entzugskompli-kationen wie Entzugs-krampfanfällen bzw. eines Delirs ist erhöht			- For approximately 67% of the patients with mild to moderate withdrawal symptoms, generalized support, reassurance, and frequent monitoring are sufficient treatment (980), although the effectiveness of supportive treatment for these patients relative to pharmacotherapy is not well established (981, 982). - The syndrome of severe alcohol withdrawal occurs especially within the first several days after cessation or reduction of heavy, prolonged ingestion of alcohol; the syndrome includes signs and symptoms such as clouding of consciousness, difficulty in sustaining attention, disorientation, generalized tonic- clonic seizures (grand mal) seizures, respiratory alkalosis, and fever (969– 971). - <5% of individuals with alcohol withdrawal develop severe symptoms and <3% develop grand mal seizures (972, 973). - In the past, the mortality rate for patients experiencing alcohol withdrawal delirium was as high as 20%; currently, it is closer to 1% because of improved diagnosis and medical treatment (972). - The presence of a co-occurring medical disorder may also increase the likelihood of a complicated withdrawal syndrome (974–976). - there is increasing evidence that repeated episodes of (non-treated) alcohol withdrawal may lead to a worsening of future withdrawal episodes (“alcohol withdrawal kindling or sensitization effect”).	

					Thus individuals with multiple previous withdrawals may require more aggressive treatment (977). - patients with hallucinations require pharmacological treatment.	
Strength of recommendation /		1++				
Reference		Referenz: 26 ff				

Guideline	**S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“**	**S2 Leitlinie „Screening, Diagnostik, Kurzintervention“**	**S2 Leitlinie „Alkoholdelir“**	**S2 Leitlinie „Aggressives Verhalten“**	**S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“**	**S1 Leitlinie „Kindesalter“**	**DRV Leitlinien**
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung

„Gibt es auch Hinweise auf eine fehlende oder sogar unerwünschte Wirksamkeit der körperlichen Entgiftung?“

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		1. Inappropriate use of symptom- triggered therapy 2. Clomethiazol sollte wegen seiner Eigenschaften/NW nur stationär eingesetzt werden 3. Nebenwirkungen insbes. bei Enzephalopathie, Atemwegs- bzw. Lebererkrankungen				
Strength of recommendation / Level of evidence		1. 3 2. Expertenkonsens 3. 1++				
Reference		Referenz: 26ff				

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation	Die Eigenschaft von Carbamazepin, die Leukozyten zu vermindern, kann ein zusätzliches Infektionsrisiko für einzelne Patienten darstellen						
Strength of recommendation / Level of evidence	C/IV						
Reference	APA 1995						

Kapitel „3.3. Qualifizierte Entzugsbehandlung“

Klinische Fragestellung

„Welche Wirksamkeit (z.B. Abstinenzrate, Abstinenzzeit, Rückfälle, Vermittlung in Langzeittherapie, stationäre Wiederaufnahme) zeigt eine qualifizierte Entzugsbehandlung im kontrollierten Vergleich mit einer körperlichen Entgiftung bei verschiedenen Patientengruppen?“

A) Abstinenzrate/Rückfallquote

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation						
Strength of recommendation / Level of evidence						
Reference						

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung

„Welche Wirksamkeit (z.B. Abstinenzrate, Abstinenzzeit, Rückfälle, Vermittlung in Langzeittherapie, stationäre Wiederaufnahme) zeigt eine qualifizierte Entzugsbehandlung im kontrollierten Vergleich mit einer körperlichen Entgiftung bei verschiedenen Patientengruppen?“

B) Abstinenzzeit

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation						
Strength of recommendation / Level of evidence						
Reference						

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung

„Welche Wirksamkeit (z.B. Abstinenzrate, Abstinenzzeit, Rückfälle, Vermittlung in Langzeittherapie, stationäre Wiederaufnahme) zeigt eine qualifizierte Entzugsbehandlung im kontrollierten Vergleich mit einer körperlichen Entgiftung bei verschiedenen Patientengruppen?“

C) Wiederaufnahme

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation						
Strength of recommendation / Level of evidence						
Reference						

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung

„Welche Wirksamkeit (z.B. Abstinenzrate, Abstinenzzeit, Rückfälle, Vermittlung in Langzeittherapie, stationäre Wiederaufnahme) zeigt eine qualifizierte Entzugsbehandlung im kontrollierten Vergleich mit einer körperlichen Entgiftung bei verschiedenen Patientengruppen?“

D) Vermittlung in Langzeit/weiterführende Therapie

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation						
Strength of recommendation / Level of evidence						
Reference						

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung:
„Welche Wirksamkeit (z.B. langfristige Abstinenz, Trinkmengenreduktion) zeigt eine qualifizierte Entgiftung im kontrollierten Vergleich mit Langzeittherapien (stationär, ambulant, etc.) bei verschiedenen Patientengruppen?“

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation						
Strength of recommendation / Level of evidence						
Reference						

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung

„Gibt es auch Hinweise auf eine fehlende oder sogar unerwünschte Wirksamkeit der qualifizierten Entzugsbehandlung?“

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation						
Strength of recommendation / Level of evidence						
Reference						

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung

„Anderes: Was sollte eine Alkoholentgiftung beinhalten?!

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation					The treatment of alcohol withdrawal has two major goals: 1) help the patient achieve detoxification in a manner that is as safe and comfortable as possible and 2) enhance the patient's motivation for abstinence and recovery (968).	
Strength of recommendation / Level of evidence						
Reference						

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Kapitel „3.4. Arzneimittel zur Entzugsbehandlung“

Klinische Fragestellung

3.4.1 „Welche Wirksamkeit (positive, fehlende, unerwünschte) zeigen Arzneimittel im kontrollierten Vergleich, wenn sie bei verschiedenen Patientengruppen (z.B. mit Teilaspekten des Entzuges wie Hypertonus, Tremor, Schlafstörungen, Unruhe / mit speziellen Komplikationen wie Entzugskrampfanfällen, Delir / mit Polytoxikomanie) in verschiedenen Settings (z.B. Intensivmedizin) eingesetzt werden?“

A) Benzos

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		►**Benzodiazepines versus placebo** *Alcohol withdrawal seizures:* - A meta-analysis of three studies (Chlordiazepoxide N=2, Lorazepam N=1) found that benzodiazepines were significantly more effective than placebo (RR: 0.16 [95% CI: 0.04 to 0.69] p=0.01). 26. Level 1++ There were no significant differences between benzodiazepines and placebo for therapeutic success, mortality, side effects, discontinuation due to side effects . Level 1++		Use benzodiazepines over nonbenzodiazepine sedativehypnotics for inpatient alcohol withdrawal management. - documented efficacy, and a greater margin of safety. - reduce withdrawal severity, incidence of delirium, and seizures vs. placebo (seizures (risk reduction, 7.7 seizures per 100 patients treated; P=0.003; delirium (risk reduction, 4.9 cases of delirium per 100 patients treated=0.04)	- benzodiazepines effectively reduce withdrawal severity and the incidence of seizures and delirium (991, 992). - Anticonvulsants and benzodiazepines appear to have comparable efficacy in preventing seizures during alcohol withdrawal - commonly used: chlordiazepoxide	

		► **Benzodiazepines versus benzodiazepines** - no differences for alcohol withdrawal seizures, therapeutic success, mortality, side effects, life threatening side effects, discontinuation due to side effects, alcohol withdrawal delirium, Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) score (change from baseline) at 48 hours. CIWA-Ar score (change from baseline) at end of treatment. Level 1++ **Consider offering a benzodiazepine or carbamazepine.** **Delir:** - no papers found in evidence review recommendations are based on experience and consensus. - benzodiazepine (Lorazepam) plus Neuroleptikum (Haloperidol, Olanzapin) **Anfälle** R11: In people with alcohol withdrawal seizures, consider offering a quick-acting benzodiazepine (such as lorazepamj) to reduce the likelihood of further seizures			(50 mg every 2-4 hours),diazepam (10 mg every 2–4 hours), oxazepam (60 mg q2h), and lorazepam (1 mg q2h) (982,998).	
Strength of recommendation / Level of evidence		- 1++ - Für Abschlußempfehlung keine Evidenz angegeben. - für Delir (Expertenmeinung, Konsensus) Für Anfall: 1+		I Good Subst A		

Reference		Ntais C, Pakos E, Kyzas P et al. Benzodiazepines for alcohol withdrawal. Cochrane Database of Systematic Reviews. 2005;CD005063 Produktinfo		Mayo-Smith, 1997 Ntais et al., 2005	Referenz 991, 992, 995, 982, 998	

Guideline	**S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“**	**S2 Leitlinie „Screening, Diagnostik, Kurzintervention“**	**S2 Leitlinie „Alkoholdelir“**	**S2 Leitlinie „Aggressives Verhalten“**	**S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“**	**S1 Leitlinie „Kindesalter“**	**DRV Leitlinien**
Recommendation	**Delirsymptome** (Halluzinationen, Wahnsymptome oder Agitation) können auch durch die Kombination von Antipsychotika vom Butyrophenon-Typ (z.B. Haloperidol) mit Benzo-diazepinen behandelt werden. - Diazepam wird in Dosierungen von 10-60mg/Tag empfohlen		Benzodiazepine (Diazepam, Lorazepam, Chlordiazepoxid) sind wirksam beim Alkoholentzugsdelir				
Strength of recommendation / Level of evidence	A/I		A/Ia				
Reference	Mayo-Smith et al. 1997; APA 1995, AkdÄ 2002; Auch: Bonnet, Schäfer et al Antikonvulsiva in der Behandlung der Alkoholabhängigkeit, Fortschr Neurol Psychiat 2009; 77: 192–2		Bonnet, Schäfer et al Antikonvulsiva in der Behandlung der Alkoholabhängigkeit, Fortschr Neurol Psychiat 2009; 77-192–20:				

Klinische Fragestellung

3.4.1 „Welche Wirksamkeit (positive, fehlende, unerwünschte) zeigen Arzneimittel im kontrollierten Vergleich, wenn sie bei verschiedenen Patientengruppen (z.B. mit Teilaspekten des Entzuges wie Hypertonus, Tremor, Schlafstörungen, Unruhe / mit speziellen Komplikationen wie Entzugskrampfanfällen, Delir / mit Polytoxikomanie) in verschiedenen Settings (z.B. Intensivmedizin) eingesetzt werden?“

B) Clomethiazol (Distraneurin)

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		**Benzodiazepines versus clomethiazole** There were non-significant differences when benzodiazepines was compared with clo-methiazole for: - alcohol withdrawal seizures - therapeutic success - mortality - side effects - life threatening side effects - discontinuation due to side effects. Level 1++ ►**Clomethiazole versus placebo** There were no results reported in the Cochrane systematic review for the outcomes specified 26. Level 1++ - **Clomethiazole** may be offered as an alternative to a benzo-diazepine or carbamazepine. However, it should be used with caution, in inpatient settings only and according to the summary of product characteristics.				
Strength of recommendation / Level of evidence		- 1++ - für Abschluß-empfehlung keine Evidenz angegeben				
Reference		Ntais C, Pakos E, Kyzas P et al. Benzodiazepines for alcohol withdrawal. Cochrane Database of Systematic Reviews. 2005;CD005063; 42-46				

Klinische Fragestellung

3.4.1 „Welche Wirksamkeit (positive, fehlende, unerwünschte) zeigen Arzneimittel im kontrollierten Vergleich, wenn sie bei verschiedenen Patientengruppen (z.B. mit Teilaspekten des Entzuges wie Hypertonus, Tremor, Schlafstörungen, Unruhe / mit speziellen Komplikationen wie Entzugskrampfanfällen, Delir / mit Polytoxikomanie) in verschiedenen Settings (z.B. Intensivmedizin) eingesetzt werden?“

C) Clomethiazol (Distraneurin)

Guideline	**S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“**	**S2 Leitlinie „Screening, Diagnostik, Kurzintervention“**	**S2 Leitlinie „Alkoholdelir“**	**S2 Leitlinie „Aggressives Verhalten“**	**S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“**	**S1 Leitlinie „Kindesalter“**	**DRV Leitlinien**
Recommendation			Clomethiazol ist wirksam beim Alkoholentzugsdelir				
Strength of recommendation / Level of evidence			A/Ia				
Reference			Bonnet, Schäfer et al Antikonvulsiva in der Behandlung der Alkoholabhängigkeit, Fortschr Neurol Psychiat 2009; 77:				

Klinische Fragestellung

3.4.1 „Welche Wirksamkeit (positive, fehlende, unerwünschte) zeigen Arzneimittel im kontrollierten Vergleich, wenn sie bei verschiedenen Patientengruppen (z.B. mit Teilaspekten des Entzuges wie Hypertonus, Tremor, Schlafstörungen, Unruhe / mit speziellen Komplikationen wie Entzugskrampfanfällen, Delir / mit Polytoxikomanie) in verschiedenen Settings (z.B. Intensivmedizin) eingesetzt werden?“

D) Antiepileptika

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		**Benzodiazepines versus carbamazepine:** - There were no significant differences when benzodiazepines were compared with anticonvulsants for: alcohol withdrawal seizures, mortality, side effects, discontinuation due to side effects, alcohol withdrawal delirium, CIWA-Ar score (change from baseline) at 48 hours CIWA-Ar score (change from baseline) at end of treatment **Carbamazepine versus placebo** - No relevant papers were identified. **Consider offering a benzodiazepine or carbamazepine** (für Abschlußempfehlung keine Evidenz angegeben) **Anfälle:** R13: Do not offer phenytoin to treat alcohol withdrawal seizures		- For managing alcohol withdrawal, carbamazepine and vaolproic acid can be used as an effective alternative to benzodiazepines for mild to moderate withdrawal. [B] - They may be considered in patients that cannot use benzodiazepines (e.g., abuse liability or allergy/adverse reactions). [B]	Carbamazepine diminish the severity of alcohol withdrawal symptoms but has not been proven to prevent delirium or seizures - carbamazepine can be used adjunctively but not as monotherapy (992). - Anticonvulsants and benzodiazepines appear to have comparable efficacy in preventing seizures during alcohol withdrawal - other withdrawal symptoms may also be diminished by anticonvulsants particularly in patients with mild to moderate withdrawal, although the evidence for this is mixed (987) and small sample sizes of studies making meta- analysis problematic (1025).	
Strength of recommendation / Level of evidence		1++ Anfälle: 1+		I Fair Subst B		

Reference		Ntais C, Pakos E, Kyzas P et al. Benzodia-zepines for alcohol withdrawal. Cochrane Database of Systematic Reviews. 2005;CD005063		Mayo-Smith, 1997 Polycarpou et al., 2005 Reoux, 2001		

Klinische Fragestellung

3.4.1 „Welche Wirksamkeit (positive, fehlende, unerwünschte) zeigen Arzneimittel im kontrollierten Vergleich, wenn sie bei verschiedenen Patientengruppen (z.B. mit Teilaspekten des Entzuges wie Hypertonus, Tremor, Schlafstörungen, Unruhe / mit speziellen Komplikationen wie Entzugskrampfanfällen, Delir / mit Polytoxikomanie) in verschiedenen Settings (z.B. Intensivmedizin) eingesetzt werden?“

E) Antiepileptika

Guideline	**S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“**	**S2 Leitlinie „Screening, Diagnostik, Kurzintervention“**	**S2 Leitlinie „Alkoholdelir“**	**S2 Leitlinie „Aggressives Verhalten“**	**S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“**	**S1 Leitlinie „Kindesalter“**	**DRV Leitlinien**
Recommendation	Mittels Carbamazepin kann eine milde bis mäßige Entzugssymptomatik vermindert werden. - Carbamazepin sollte in den ersten 48 Stunden auf 400-900 mg/täglich in unretardierter Tablettenform oder als Liquidum aufdosiert werden; danach kann diese Dosis täglich um 200 mg heruntertitriert werden - Auch zur Anfallsprophylaxe kann Carbamazepin eingesetzt werden.						
Strength of recommendation / Level of evidence	C/IV						
Reference	Mayo-Smith et al. 1997; AkdÄ 2002						

Klinische Fragestellung

3.4.1 „Welche Wirksamkeit (positive, fehlende, unerwünschte) zeigen Arzneimittel im kontrollierten Vergleich, wenn sie bei verschiedenen Patientengruppen (z.B. mit Teilaspekten des Entzuges wie Hypertonus, Tremor, Schlafstörungen, Unruhe / mit speziellen Komplikationen wie Entzugskrampfanfällen, Delir / mit Polytoxikomanie) in verschiedenen Settings (z.B. Intensivmedizin) eingesetzt werden?“

F) andere

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation	**Delirsymptome** (Halluzinationen, Wahnsymptome oder Agitation) können auch durch die Kombination von Antipsychotika vom Butyrophenon-Typ (z.B. Haloperidol) mit Benzo-diazepinen behandelt werden. - Dabei sollte Haloperidol in einer Dosis von 0,5- 2 mg oral, i.m. oder i.v. alle 2 Stunden solange notwendig verabreicht werden, wobei die Gesamtdosis meist unter 10 mg pro 24 Stunden, in einigen Fällen aber auch mehr (10-40 mg/Tag und darüber) betragen kann.	**Delir:** - no papers found in evidence review - recommendations are based on experience and consensus. - benzodiazepine (Lorazepam) plus Neuroleptikum (Haloperidol, Olanzapin)		- Other agents, such as beta-blockers, and clonidine, are generally not considered as appropriate monotherapy for alcohol withdrawal, [D] but may be considered in conjunction with benzodiazepines in certain patients. [C] - Use of alcohol as an agent for medically supervised withdrawal is contraindicated. [D]	- ß-blockers reduce signs of autonomic nervous system hyperactivity (e.g., tremor, tachycardia, elevated blood pressure, diaphoresis) and, at higher doses, arrhythmias (1012–1014) - has been shown to reduce tremor, heart rate, and blood pressure (1016, 1017) - beta-blockers and clonidine diminish the severity of alcohol withdrawal symptoms but have not been proven to prevent delirium or seizures - beta-blockers, clonidine and neuroleptics can be used adjunctively but not as monotherapy (992). - Neuroleptics particularly haloperidol are recommended for patients with delirium, delusions, or hallucinations - Because antipsychotic agents are not effective for treating the underlying withdrawal state (992), they should be used as an adjunct to benzodiazepines. the use of intravenous ethanol is not supported by the current published data (1034, 1035).	
Strength of recommendation / Level of evidence	A/I	Delir: Expertenmeinung, Konsensus		C,D	Keine Angabe	

Reference	Mayo-Smith et al. 1997; APA 1995, AkdÄ 2002; Auch: Bonnet, Schäfer et al Antikonvulsiva in der					

Klinische Fragestellung

3.4.1 „Welche Wirksamkeit (positive, fehlende, unerwünschte) zeigen Arzneimittel im kontrollierten Vergleich, wenn sie bei verschiedenen Patientengruppen (z.B. mit Teilaspekten des Entzuges wie Hypertonus, Tremor, Schlafstörungen, Unruhe / mit speziellen Komplikationen wie Entzugskrampfanfällen, Delir / mit Polytoxikomanie) in verschiedenen Settings (z.B. Intensivmedizin) eingesetzt werden?“

G) andere

Guideline	**S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“**	**S2 Leitlinie „Screening, Diagnostik, Kurzintervention“**	**S2 Leitlinie „Alkoholdelir“**	**S2 Leitlinie „Aggressives Verhalten“**	**S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“**	**S1 Leitlinie „Kindesalter“**	**DRV Leitlinien**
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung

„Welche Hinweise auf eine differentielle Indikation gibt es (z.B. bei akuter Alkoholintoxikation, Mischintoxikation, Erregungszuständen, eingeschränkter Leberfunktion, eingeschränkter Nierenfunktion, eingeschränkter Lungenfunktion, chronisch mehrfach Abhängigen, stark reduziertem Allgemeinzustand; Schwangerschaft)?“

Benzodiazepine

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		- Keine Daten zu Komorbiditäten, älteren Patienten, Leberfunktionseinschränkungen, Kognitive Störungen, Enzephalopathie. - Behandlung durch Erfahrenen bei eigeschränkter Leberfunktion - Bevorzugung von Benzodiazepinen mit kurzer Halbwertszeit z.B. Oxazepam bzw. Lorazepam (keine Verstoffwechselung über Leber) - “People with decompensated liver disease who are being treated for acute alcohol withdrawal should be offered advice from a healthcare professional experienced in the management of patients with liver disease.”		Benzodiazepines without active metabolites such as lorazepam or oxazepam may be preferred in patients with liver impairment. [A] Dose and withdrawal scales should be individualized for each patient. Geriatric patients should start with lower doses of benzodiazepines than younger adults. [A]	For patients who have severe hepatic disease, are elderly, or have delirium, dementia, or another cognitive disorder, short-acting benzodiazepines such as oxazepam or lorazepam are preferred by some clinicians and appear to be efficacious. - Lorazepam also has the advantage of being able to be administered parenterally.	
Strength of recommendation / Level of evidence		Expertenmeinung		A		
Reference					Referenz: 1004, 1005	

Klinische Fragestellung

„Welche Hinweise auf eine differentielle Indikation gibt es (z.B. bei akuter Alkoholintoxikation, Mischintoxikation, Erregungszuständen, eingeschränkter Leberfunktion, eingeschränkter Nierenfunktion, eingeschränkter Lungenfunktion, chronisch mehrfach Abhängigen, stark reduziertem Allgemeinzustand; Schwangerschaft)?“

Benzodiazepine

Guideline	**S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“**	**S2 Leitlinie „Screening, Diagnostik, Kurzintervention“**	**S2 Leitlinie „Alkoholdelir“**	**S2 Leitlinie „Aggressives Verhalten“**	**S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“**	**S1 Leitlinie „Kindesalter“**	**DRV Leitlinien**
Recommendation	- Bei Patienten mit schweren Leberschäden, älteren Patienten, Patienten mit organischen psychischen Störungen (Delir, Demenz) sollten kurzwirksame BZD wie Oxazepam oder Lorazepam bevorzugt warden - Bei Patienten mit relevanten körperlichen Erkrankungen sollten Pharmaka allerdings auch bei milden bis moderaten Entzugssyndromen eingesetzt werden						
Strength of recommendation / Level of evidence	C/IV						
Reference	APA 1995 Mayo-Smith et al. 1997						

Klinische Fragestellung
„Welche Hinweise auf eine differentielle Indikation gibt es (z.B. bei akuter Alkoholintoxikation, Mischintoxikation, Erregungszuständen, eingeschränkter Leberfunktion, eingeschränkter Nierenfunktion, eingeschränkter Lungenfunktion, chronisch mehrfach Abhängigen, stark reduziertem Allgemeinzustand; Schwangerschaft)?“

Clomethiazol

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		Keine Daten zu Komorbiditäten, älteren Patienten, Leberfunktionseinschränkungen, Kognitive Störungen, Enzephalopathie. - Bisher nur Empfehlung von kurzwirksamen Benzodiazepinen (Expertenempfehlung). - Hinweise auf Kontraindikationen				
Strength of recommendation / Level of evidence		Expertenempfehlung				
Reference						

Klinische Fragestellung
„Welche Hinweise auf eine differentielle Indikation gibt es (z.B. bei akuter Alkoholintoxikation, Mischintoxikation, Erregungszuständen, eingeschränkter Leberfunktion, eingeschränkter Nierenfunktion, eingeschränkter Lungenfunktion, chronisch mehrfach Abhängigen, stark reduziertem Allgemeinzustand; Schwangerschaft)?“

Clomethiazol

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung

„Welche Hinweise auf eine differentielle Indikation gibt es (z.B. bei akuter Alkoholintoxikation, Mischintoxikation, Erregungszuständen, eingeschränkter Leberfunktion, eingeschränkter Nierenfunktion, eingeschränkter Lungenfunktion, chronisch mehrfach Abhängigen, stark reduziertem Allgemeinzustand; Schwangerschaft)?“

Antiepileptika

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		Keine Daten zu Komorbiditäten, älteren Patienten, Leberfunktionseinschränkungen, Kognitive Störungen, Enzephalopathie. - Bisher nur Empfehlung von kurzwirksamen Benzodiazepinen (Expertenempfehlung).				
Strength of recommendation / Level of evidence						
Reference						

Klinische Fragestellung
„Welche Hinweise auf eine differentielle Indikation gibt es (z.B. bei akuter Alkoholintoxikation, Mischintoxikation, Erregungszuständen, eingeschränkter Leberfunktion, eingeschränkter Nierenfunktion, eingeschränkter Lungenfunktion, chronisch mehrfach Abhängigen, stark reduziertem Allgemeinzustand; Schwangerschaft)?“

Antiepileptika

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung
„Welche Hinweise auf eine differentielle Indikation gibt es (z.B. bei akuter Alkoholintoxikation, Mischintoxikation, Erregungszuständen, eingeschränkter Leberfunktion, eingeschränkter Nierenfunktion, eingeschränkter Lungenfunktion, chronisch mehrfach Abhängigen, stark reduziertem Allgemeinzustand; Schwangerschaft)?“

andere

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-infected patients, USA, (2008)
Recommendation		- Keine Daten zu Komorbiditäten, älteren Patienten, Leberfunktionseinschränkungen, Kognitive Störungen, Enzephalopathie. - Bisher nur Empfehlung von kurzwirksamen Benzodiazepinen (Expertenempfehlung).				
Strength of recommendation / Level of evidence						
Reference						

Klinische Fragestellung

„Welche Hinweise auf eine differentielle Indikation gibt es (z.B. bei akuter Alkoholintoxikation, Mischintoxikation, Erregungszuständen, eingeschränkter Leberfunktion, eingeschränkter Nierenfunktion, eingeschränkter Lungenfunktion, chronisch mehrfach Abhängigen, stark reduziertem Allgemeinzustand; Schwangerschaft)?“

andere

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Klinische Fragestellung
"Anderes"
Symptomgetriggert vs. Fixdosis

Guildeline	NICE CG115 (2011)	NICE CG100 (2010)	NICE PH 24 (2010)	VA/DoD (SUD), USA, Veterans (2009)	Treatment of Patients with SUD, USA, APA (2006)	HIV-in patien (2008
Recommendation		- Nicht ausrechende Evidenz für das "Frontloading". - Symptom-triggered dosing regimen of benzodiazepines is associated with significantly lower doses of benzodiazepines (31) and shorter treatment duration compared to a fixed-dosing regimen (28-30). Symptom- triggered dosing regimen improve patients' physical functioning compared to the fixed-dosing regimen (p<0.01) (28) and it is cost-effective. Eine Empfehlung eines bestimmten Vorgehens erfolgt nicht da es keine gesicherte Überlegenheit gibt. Für alle Entzugsformen, insbesondere aber für die Symptomgetriggerte Behandlung ist ein Fachpersonal mit spezifischen Kenntnissen wichtig Follow a symptom- triggered regime for drug treatment for people in acute alcohol withdrawal who are: in hospital or in other settings where 24-hour assessment and monitoring are available		Use symptom-triggered therapy or gradual dose tapering over several days for alcohol withdrawal management. A. Symptom-triggered therapy where patients are given medication only when signs or symptoms of withdrawal appear (e.g., PRN dosing) [A] B) A pre-determined fixed medication dose with gradual tapering over several days may be considered for some patients, although it is inferior to symptom-triggered therapy. [B]		
Strength of recommendation / Level of evidence		A/1 bis B/3		I Good Subst A		
Reference		Referenz: 28-33		APA, 1995; CSAT, 1995; Hayashida et al., 1989 Mayo-Smith, 1997 Saitz et al., 1994		

Klinische Fragestellung
"Anderes"
Symptomgetriggert vs. Fixdosis

Guideline	S2 Leitlinie „Akutbehandlung Alkoholbezogener Störungen“	S2 Leitlinie „Screening, Diagnostik, Kurzintervention“	S2 Leitlinie „Alkoholdelir“	S2 Leitlinie „Aggressives Verhalten“	S2 Leitlinie „Postakutbehandlung Alkoholbezogener Störungen“	S1 Leitlinie „Kindesalter“	DRV Leitlinien
Recommendation							
Strength of recommendation / Level of evidence							
Reference							

Kapitel “3.7.1 Kinder und Jugendliche“

Psychotherapeutic treatment

Guideline	Evidence level
	(Varying: see near left)
Statement	
6.22 SPECIAL POPULATIONS – CHILDREN AND YOUNG PEOPLE Individual or group CBT: Three reviews. Evidence level Ia. A number of studies which assess the use of individual or group based psychological therapies have been identified and reviewed (Waldron & Kaminer 2004; Perepletchikova et al. 2008; Tripodi et al. 2010). Tripodi and colleagues (2010) conducted a meta-analysis of 16 experimental studies (including 14 RCTs) evaluating interventions both in individual and group format based interventions (brief interventions, CBT [cognitive-behavioural therapy], family-based therapies, multi-component therapies) with a focus on reducing alcohol misuse. However, only few trials included samples of children or young people identified with harmful or dependent drinking, the specific focal point of this guideline: studies with individuals who did not meet criteria for harmful drinking or alcohol dependence (n=1); with participants diagnosed with a significant co-morbid psychiatric disorder (n=2); and in a large fraction of studies, the focus was not specifically on alcohol misuse, but rather on substance misuse more generally (n=7). The results of this meta-analyses showed a significantly large effect in drinking reduction for individual interventions (effect size = -0.75; 95% CI, -1.10 to -0.40). However, the meta-analyses did not distinguish between different types of individual interventions in pooled analyses therefore other reviews which focused on specific interventions were considered (cf. p.346). Brief interventions and motivational interviewing (cf. p.346 et seq.): Both the NICE prevention of alcohol related problems in adults and young people (NICE 2010a) and also the NICE public health guidance on community interventions for vulnerable young adults consider the evidence for brief motivational techniques. The evidence for this is from the adult literature though there is an emerging albeit still limited literature for adolescents where modifications of motivational interviewing or motivational enhancement techniques [MET] for adolescents have shown promise for both evaluation and treatment (Colby et al. 1998; Monti et al. 1999). However, a review by Perepletchikova and colleagues (2008) reported that, in alcohol use disorders, evidence suggests that motivational techniques are more effective when combined with CBT, for example in the Cannabis Youth Trial (CYT; Dennis et al. 2004), although this population were predominately diagnosed as dependent on cannabis. Cognitive behavioural therapy: Waldron and Kaminer (2004), in a review of CBT approaches to substance use disorders (more broad than just alcohol misuse), concluded that individual CBT treatment may be effective in reducing substance misuse as well as other related problems. Interventions with the adolescent alone (for example, CBT or CBT plus MET) have been reported as effective (Dennis et al. 2004; Kaminer & Burleson 1999; Kaminer et al. 1998). However, much of the evidence base is from approaches dealing with co- morbidity such as conduct disorders, and anxiety and affective disorders where information on the extent and severity of alcohol misuse specifically is lacking. Perepletchikova and colleagues (2008) considered 5 studies looking at the effectiveness of CBT in the reduction of alcohol use disorders, three of which were of CBT alone, one evaluated an integrated family and group CBT approach and one looked at efficacy of CBT on reduction of substance use in those with co- morbid conduct disorder. Again it appears that the data is primary concerned with children and young people who did not have a high severity of alcohol misuse. Kaminer and colleagues (2002) in one of the few studies that had a more substantial proportion of participants with alcohol dependence randomized participants to CBT or a psycho- educational	

therapy. Of 88 included participants, 12.5% (n=11) had an alcohol use disorder only and 60% (n=53) had an alcohol disorder as well as a marijuana use disorder. Of these 64 participants with an alcohol use disorder, 58% met criteria for abuse and 42% for dependence (DSM III-R; American Psychiatric Association, 1987). The authors reported that there were reductions across both therapies in alcohol use. At 3-month-FU, alcohol use had improved significantly, and showed continued improvement at 9- month-FU. Substance use also showed a positive trend towards improvement. Kaminer and colleagues (2008) only included participants who meet DSM–IV criteria for alcohol dependence, although 81.8% of the sample also used marijuana. Although the primary focus of co- morbidity has been on individuals with conduct disorder, a few studies have also examined the problems presented by co- occurring common mental health disorders, such as depression and anxiety. One study evaluated the efficacy of an integrated 20-week programme of CBT with case management in a population of substance abusing young people (aged between 15 and 25 years). Sixty-three percent of the sample met criteria for alcohol dependence. Treatment resulted in a significant improvement in abstinence rates as well as a reduction in the number or participants meeting diagnostic thresholds for dependence. These positive effects were also observed at 44 week follow-up. This study (like others) evaluates the effectiveness of psychological interventions for young people include participants whom are over the age of 18 years. However, this age-range makes interpretation of data sets such as this difficult.

Twelve Step Facilitation (TSF): No formal evaluations in alcohol dependent adolescents were identified for TSF.

6.22.7 Multi-component psychological interventions (cf. p.348 et seq.). Meta-analysis. Evidence level Ia Effectiveness of multi-component interventions Meta-analytic results (p.350) “showed that family interventions are more effective than control for reducing both behavioural problems (SMD -0.75; -1.19 to - 0.30) and offending (RR -0.67; 0.42 to 1.07). Furthermore, 10 trials on multi-systemic therapy that met the inclusion criteria for the review were analysed. There was significant heterogeneity for most outcomes; however, there was consistent evidence of a medium effect on reduction in offending outcomes including number of arrests (SMD -0.44; - 0.82 to -0.06) and being arrested (RR 0.65; 0.42 to 1.00). In a recent meta-analysis, Tripodi and colleagues (2010) evaluated six trials of multi-component and family-based interventions in the systematic review. However, none of these trials were focused specifically on alcohol misuse, and in two of the trials, only approximately 50% of the sample met criteria for alcohol dependence and harmful alcohol use. The overall findings were in line with the NICE ASPD guideline (NICE, 2009). The review did however reports that that multi- component family therapies were effective in reducing drinking in adolescents (Hedges g = - 0.46, 95% CI, -0.66 to -0.26). Perepletchikova and colleagues (2008) reviewed the evidence of family therapies specifically on alcohol use, although some of the family therapies did include substance use disorders. The types of family therapies

Further references

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Waldron, H. B., & Kaminer Y. (2004). On the learning curve: Cognitive- behavioral therapies for adolescent substance abuse. Addiction, 99:93–105.

Guideline	**Evidence level**
13 (American Psychiatric Association, 2006)	(Varying, see near left) […] = references not relevant for these guidelines and not given in “Further references” near right
Statement	**Further references**

F. PSYCHOSOCIAL TREATMENTS (p.39) Evidence level Ib
Social Skills training has been successfully used as an adjunct to a more comprehensive treatment plan and can be delivered in a wide variety of outpatient treatment settings. It may be particularly useful in certain dually diagnosed populations, such as patients with schizophrenia […] and adolescents at risk for beginning substance abuse (Griffin, Botvin, Nichols, Doyle 2003).

8. Family therapies (p.43) Evidence level Ib and IIa Controlled studies have shown positive outcomes of involving non-alcohol-abusing family members in the treatment of an alcohol-abusing individual […]. More recent studies have demonstrated the effectiveness of family involvement in substance use disorder treatment for both women and men […], including patients on methadone maintenance […]. Family therapy, often in combination with other
approaches, has also been studied extensively and has shown good evidence for efficacy in adolescents (Liddle, Rowe, Dakof, Ungaro, Henderson 2004; Santisteban, Coatsworth, Perez- Vidal, Kurtines, Schwartz, LaPerriere, Szapocznik 2003; Waldron, Slesnick, Brody, Turner, Peterson 2001). There is also some evidence that these approaches can improve the psychosocial functioning and decrease the likelihood of substance use in children living with a parent abusing alcohol or other substances […].

10. Brief therapies (p.44) Evidence level III
The efficacy of brief interventions has been studied mostly in connection with alcohol use disorders. The interventions were initially designed to facilitate the

treatment of alcohol abuse or dependence in a setting other than a substance abuse treatment facility (e.g., primary care clinic, mental health clinic, EAP) […]. More recent evidence suggests that brief interventions are also effective with other substance use disorders, including cannabis […], opioid […], and nicotine […] dependence and in special populations such as adolescents (Tevyaw, Monti 2004), patients with co-occurring psychiatric and substance use disorders […], and patients in the military […].

CLINICAL FEATURES INFLUENCING TREATMENT
Section 6: Age. a) Children and adolescents (p.66) Evidence level III and Ib Although research data establishing the efficacy of specific treatment modalities for adolescent substance use disorders are sparse, program outcomes for adolescents appear to be enhanced by the availability of treatment that is developmentally appropriate and peer oriented and includes educational, vocational, and recreational services. Corrective experiences in family interaction should be part of the treatment plan (Catalano, Hawkins, Wells, Miller, Brewer 1991). Family therapy also appears to have benefit (Santisteban, Coatsworth, Perez-Vidal, Kurtines, Schwartz, LaPerriere, Szapocznik 2003; Waldron, Slesnick, Brody, Turner, Peterson 2001; Coatsworth, Santisteban, McBride, Szapocznik 2001). Residential facilities are very effective in reducing substance use, but gains are lost when aftercare is not well coordinated (Dasinger, Shane, Martinovich 2004).

Further references

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Guideline	**Evidence level**
14 (Substance Abuse and Mental Health Services Administration U.S., 2006)	n/a
Statement	**Further references**
Chapter 6: Family-Based Services (pp.93–113) Evidence level Ia	

In 1997, Stanton and Shadish conducted a meta-analysis that compared the effectiveness of family education, family therapy, and other forms of family intervention for people with substance use disorders. Stanton et al. suggested in their meta- analysis (1997) that family therapy is more effective than family education groups and other family services for people with substance use disorders.

Chapter 9: Adapting Intensive Outpatient Treatment for Specific Populations (p.172) Family involvement Because outpatient family therapy may offer benefits superior to other outpatient treatments (Williams et al. 2000), IOT [Intensive Outpatient Treatment] providers are encouraged to work with the family as much as possible.

Chapter 9: Adapting Intensive Outpatient Treatment for Specific Populations (p.173).
Evidence level Ib Treatment of the family
Family-oriented interventions have long been used to treat adolescents who abuse substances. Szapocznik and colleagues (1983; 1986) helped establish the effectiveness of family therapy in treating adolescents. The premise of family therapy is that the family plays a role in creating conditions leading to adolescent drug use and that family elements help adolescents recover (Liddle et al. 2001). Evidence shows that youth who receive family therapy have less drug use at treatment completion than those who receive peer group therapy or whose families participate in parent education or a multifamily intervention (Liddle et al. 2001). Family cognitive-behavioral therapy integrates traditional family systems theory with techniques of cognitive-behavioral therapy. This approach considers adolescent substance abuse as a conditioned behavior that is reinforced by cues and contingencies within the family (Latimer et al. 2003).

Chapter 9: Adapting Intensive Outpatient Treatment for Specific Populations
Exhibit 9-3 (cf. p.174)
The Family Intervention Program (Fishman & Andes 2001) partners a family therapist with a community resource specialist. The specialist helps the family establish healthy community networks. Working as a team, the therapist and specialist conduct five family therapy sessions and perform the following:

- Assess the family system; explore the family's resources, concerns, and goals; and create a treatment plan.
- Explore relationships among family members, identify areas of difficulty and stress, and determine the effect on the family system.
- Determine the effect of other systems, such as schools, on the family.
- Focus on the family's concerns and goals and include others who can help resolve problems.

Work on how the family can resolve issues without staff help and develop a follow-up plan.

Further references

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conducting family therapy through one person with drug-abusing adolescents. Journal of Consulting and Clinical Psychology, 54:395–397.
Williams, R. J., Chang, S. Y., & Addiction Centre Adolescent Research Group. (2000). A comprehensive and comparative review of adolescent substance abuse treatment outcome. Clinical Psychology: Science and Practice, 7:138– 166.

Medical treatment

Guideline	Evidence level
1 (NICE CG115, 2011)	(See near left)

Statement

7.1.1 Current practice (p.366) n/a
In particular, many drugs will not have a license for use in adolescents/children or in the elderly but this does not mean they necessarily lack efficacy or are unsafe. Nevertheless, when prescribing in these populations due care must be taken in terms of dosage and monitoring of side effects, as well as potential interactions with other medications or physical morbidity.

7.12 CHILDREN AND YOUNG PEOPLE (p.422 et seq.)
Evidence level Ib

Studies considered
The GDG [Guideline Development Group] were able to identify only three small pilot RCTs in this area for children and young people (Niederhofer, & Staffen, 2003a; Niederhofer et al., 2003b; Niederhofer, & Staffen, 2003c).

Evidence summary
Niederhofer and Staffen (2003a) conducted a double blind placebo controlled study with 26 participants with a DSM–IV diagnosis of chronic or episode alcohol dependence. Participants ranged in age from 16 to 19 years. The participants were randomly allocated to treatment with acamprosate (1332 mg daily) or placebo for 90 days. Participants were assessed at start of treatment, and at 30 and 90 days. Results revealed that the acamprosate group had a significantly higher proportion of days abstinent throughout the 90 days of treatment ($p<0.001$), as well as a higher duration of mean cumulative abstinence ($p<0.01$). There were no significant differences between the two groups with regards to side effects, and diarrhoea was the only reported side effect.

Niederhofer and colleagues (2003b) assessed naltrexone compared with a placebo in a double blind placebo controlled study, with 30 participants ranging in age from 15 to 19 years with a DSM–IV diagnosis of chronic or episodic alcohol dependence. All participants received 50 mg of naltrexone daily and were assessed at the start of treatment and at 30 and 90 days. At the 90 day assessment point, sixty of ninety participants completed treatment. Participants remained abstinent longer than those in the placebo group during 90 days of treatment ($p<0.01$) and had a longer duration of mean cumulative abstinence (69.8 days) than the placebo arm (22.8 days) ($p<0.01$).

Lastly, Niederhofer and Staffen (2003c) compared disulfiram and placebo in a double blind placebo controlled trial with 26 adolescents (age range: 16 to 19 years) with DSM–IV chronic or episodic alcohol dependence. Participants received 200 mg of disulfiram daily and were assessed at the start of treatment, 30 and 90 days. Results indicated that on day 90 of treatment, 2 of the placebo treated patients compared with 7 disulfiram treated patients had been continuously abstinent ($p=0.0063$).

Additionally, the duration of mean cumulative abstinence was	
Further references	
Niederhofer, H., & Staffen, W. (2003a). Acamprosate and its efficacy in treating alcohol dependent adolescents. European Child, & Adolescent Psychiatry, 12:144– 148. Niederhofer, H., Staffen, W., & Mair, A. (2003b). Comparison of naltrexone and placebo in treatment of alcohol dependence of adolescents. Alcoholism Treatment Quarterly, 21(2):87- 95. Niederhofer, H., & Staffen, W. (2003c). Comparison of disulfiram and placebo in treatment of alcohol dependence of adolescents. Drug and Alcohol Review, 22, 295–297.	

Guideline	**Evidence level**
8 (TIP 49; U.S. Department of Health und Human Services, SAMHSA, 2009)	(See near left)
Statement	
Acamprosate Cautions (p.13). Currently not evidence-based. Patient Condition or Circumstance — Treatment Recommendation Moderate renal impairment — Reduce dosage to (creatinine clearance 30–50 one 333 mg tablet mL/min) daily Pregnant or nursing women — Avoid using acamprosate unless potential benefits outweigh risks (Acamprosate is FDA pregnancy category C; it is unknown whether acamprosate is excreted in human milk.) Age 65 or older — Because of a higher risk of diminished renal function in persons 65 or older, perform baseline and frequent renal function tests; acamprosate has not been evaluated for safety or efficacy in geriatric populations Children or adolescents — Prescribe with caution; acamprosate has not been evaluated for safety or efficacy in pediatric or adolescent populations Disulfiram Cautions (p.22)	
Patient Condition or Circumstance	**Treatment Recommendation**
History of cardiac disease, diabetes mellitus, hypothyroidism, epilepsy, cerebral damage, chronic or acute nephritis, hepatic cirrhosis, or hepatic insufficiency	Use with caution. No evidence exists that patients with pre-existing liver disease are more likely to suffer severe hepatotoxicity from disulfiram therapy.
Patients with hepatitis C	According to current available evidence, if baseline transaminase levels are normal or only moderately elevated (less than five times the upper limit of normal), use with careful monitoring of liver function been determined. One study indicates that disulfiram can be safe and effective with adolescents (Niederhofer, & Staffen, 2003c). Administer with caution.
How Is Oral Naltrexone Used? Side Effects, Contraindications, and Cautions (p.30). Evidence level III The results of a recent small, open-label pilot study suggest that naltrexone is well tolerated in adolescents seeking treatment and may reduce alcohol consumption and	

craving (Deas, May, Randall, Johnson, & Anton 2005). Oral Naltrexone Dosages (p.30)

How Is Extended-Release Injectable Naltrexone Used? Side Effects, Contraindications, and Cautions (p.40)
Injectable naltrexone carries the same contraindications as oral naltrexone (see Exhibit 4-3 on page 31) plus those listed in Exhibit 5-2. There are no data on use of naltrexone in children or adolescents; treatment of these populations with naltrexone is not recommended.

Appendix C— Excerpts From Quick Guide for Clinicians Based on TIP 45*Considerations for Specific Populations (p.81)
Adolescents are more likely to drink large quantities of alcohol in a short period of time, making it important that staff be alert to escalating blood alcohol levels. Adolescents are more likely to use drugs they cannot identify, to combine multiple substances with alcohol, to ingest unidentified substances, and to be unwilling to disclose drug use. Asking open-ended questions and using street terminology for drugs can be helpful in both establishing rapport and obtaining an accurate substance use history.

References

Deas, D., May, K., Randall, C. L., Johnson, N. A., & Anton, R. F. (2005). Naltrexone treatment of adolescent alcoholics: An open label pilot study. Journal of Child, & Adolescent Psychopharmacology, 15:723–728.

Psycho-social treatment

Guideline	Evidence level
1 (NICE CG115, 2011)	(Varying; see topic near left)

Statement

2.12.2 Current service provision for children and young people (p.35) Evidence level IV
Treatment variety
Given the co-morbidity noted above, many adolescents having alcohol treatment are often seen in specialist services, such as Youth Offending Teams, or specialist services for young people with conduct disorders, such as the newly-developed multi-systemic therapy teams (Department of Health, 2007), although identification and treatment of their dependence and/or harmful use may not be fully explored. In the US, adolescents with substance- use disorders receive treatment in a variety of settings including community, residential and criminal justice settings, and home-based treatment. However, there is little research evaluating the differences between these settings. As a consequence, there is little clear evidence to determine the most appropriate treatment environments. The American Academy of Child and Adolescent Psychiatry (2001) recommend that factors affecting the choice of setting should include: the need to provide a safe environment; motivation of the adolescent and his/her family to cooperate with treatment; the need for structure and limit-setting; the presence of additional medical or psychiatric conditions and the associated risks; the availability of specific types of treatment settings for adolescents; preferences for treatment in a particular setting; and past treatment failure in a less restrictive/intensive setting.

4 EXPERIENCE OF CARE
4.1 INTRODUCTION (p.65) Evidence level IV
As the guideline also aims to address support needs for families/carers, a thematic analysis was conducted using transcripts from people with parents who misuse alcohol. These were accessed from the National Association for Children of Alcoholics (NACOA) website (www.nacoa.org.uk). NACOA provides information and support to people (whether still in childhood or in adulthood) of parents who misuse alcohol and the website includes personal experiences from such people in narrative form. However, there were some limitations to the thematic analysis. Because the review team relied only on transcripts submitted to NACOA, information on other issues that could be

particularly pertinent for children with parents who misuse alcohol may not have been identified. Moreover, people who have visited the NACOA website to submit their accounts may over- represent a help-seeking population. Finally, while some accounts are based on experiences which occurred recently, others occurred a long time ago; therefore there may be differences in attitudes, information and services available. For these reasons this analysis was not included in Chapter 4, but it can be found in Appendix 14.

4.2.9 Carer experiences (p.75) Evidence level III–IV
Another qualitative study (Gance- Cleveland, 2004) investigated the benefit of a school-based support group for children with parents who misuse alcohol and found that the group helped them to identify commonalities with each other, feel that they were understood, support and challenge each other, and share coping strategies. The children who took part also felt that the group was a trusted and safe place in which they could reveal secrets and feel less isolated and lonely, that it enabled them to be more aware of the impact of addiction on family dynamics, and helped them increase resilience and do better at school (Gance- Cleveland, 2004). In conclusion, talking to others (especially with those who have had similar experiences) was found to be helpful in terms of coping, making friendships and understanding more about alcohol misuse.

4.4 RECOMMENDATIONS (p.81) Evidence level IV
4.4.1.4 When families and carers are involved in supporting a person who misuses alcohol, discuss concerns about the impact of alcohol misuse on themselves and other family members, and: provide written and verbal information on alcohol misuse and its management, including how families and carers can support the service user offer a carer‘s assessment where necessary negotiate with the service user and their family or carer about the family or carer‘s involvement in their care and the sharing of information; make sure the service user‘s, family‘s and carer‘s right to confidentiality is respected.

4.4.1.5 All staff in contact with parents who misuse alcohol and who have care of or regular contact with their children, should: take account of the impact of the parent‘s drinking on the parent-child relationship and the child‘s development, education, mental and physical health, own alcohol use, safety and social network be aware of and comply with the requirements of the Children Act (2004).

Thematic analysis of people with parents who have alcohol problems (pp.547-554)
Evidence IV (narrative study) Introduction: A qualitative analysis was conducted using transcripts from people with parents who have alcohol problems, accessed from the NACOA website.
Methods
Using all the personal experiences available from NACOA submitted from 2004 onwards, the review team analysed 46 48 [sic] accounts from people with parents who misuse alcohol, the large majority of whom were female. All accounts have been published on the website in their original form. The majority are written by people from the UK but there are also some from other countries, such as the US and Australia. Poems and letters were excluded from the analysis. Each transcript was read and re-read and sections of the text were collected under different headings using a qualitative software program (NVivo). Initially the text from the transcripts was divided into three broad headings that emerged from the data: impact of the parent‘s alcohol problems on the child‘s behaviour, thoughts and feelings; impact of the parent‘s alcohol problems on the child‘s psychological state/mental health; and support and services for the family and the child. Under these broad headings specific emergent themes identified separately by two researchers were extracted and regrouped under the subsections below.

Support and services for the family and children of parents who misuse alcohol (p.554 et seq.)
Evidence level IV (narrative study) Summary of thematic analysis (p.557)
There are some overarching themes experienced in childhood by people with parents who misuse alcohol. A dominant theme was that of avoidance and hiding the truth,

which stemmed primarily from shame, fear and wanting a sense of normality. Concealing feelings and thoughts made approaching other people or services for support difficult, when most people just wanted to talk to somebody. This may have been exacerbated by feelings of anxiety and worry, in addition to a sense of guilt, self- blame and heightened responsibility towards the parent. When they did seek help on behalf of their parent, it seemed to occur in quite desperate circumstances, such as getting their parent sectioned. This suggests that children of parents who misuse alcohol do not, or cannot, access the services and support they need easily. There were also overarching themes experienced in adulthood which seemed to originate from childhood experience. Many people struggled to form stable relationships which was often put down to lack of trust and self-isolation, which impacted on work, social life and the ability to maintain a successful relationship with a partner. Such problems could have originated from not being able to form "normal" friendships in childhood. Depression, and to some extent anxiety, emerged as longstanding psychological problems attributed to various childhood experiences as well as personal traits such as low self- esteem. Development of own drinking problem was also a theme, in which alcohol was used to block out negative thoughts and experiences, or even used in an attempt to identify with the parent. There were also a range of common life choices which emerged, predominantly an impact on relationship choices and parenting skills. Some people also reported overcoming adversity by transferring the negative behaviours, thoughts and feelings into the positive ones. There are some limitations to the qualitative analysis for this guideline. As the review team relied only on transcripts submitted to NACOA, information on other issues that could be particularly pertinent for children with parents who misuse alcohol may not have been identified. Moreover, people who have visited the NACOA website to submit their accounts may over- represent a help-seeking population. Finally, while some accounts are based on experiences which occurred recently, others occurred a long time ago; therefore there may be differences in attitudes, information and services available. For these reasons this analysis was not included in Chapter 4.

Further references

Guideline	**Evidence level**
14 (Substance Abuse and Mental Health Services Administration U.S., 2006)	(See near left)

Statement

Chapter 6: Family-Based Services (p.94)
Evidence level Ia
Family involvement in treatment seems to work equally well for adults and adolescents (Stanton, & Shadish 1997)

[No evidence level is given for all of the following]
Chapter 6: Family-Based Services (p.100) Incorporating multifamily groups into IOT [intensive outpatient treatment] has been shown to increase the length of treatment for female clients, increase completion rates for men, and improve family functioning and children's behavior (Boylin, & Doucette, 1997; Meezan, & O'Keefe, 1998).

Chapter 6: Family-Based Services (p.100) Treatment providers report that having more than one generation present in the group can help institute a family's commitment to abstinence and recovery (Conner et al., 1998).

Chapter 9: Adapting Intensive Outpatient Treatment for Specific Populations (p.173) The adolescent community reinforcement approach focuses on teaching adolescents coping skills and changing environmental influences related to continued substance use (Godley et al., 2001).

Chapter 9: Adapting Intensive Outpatient Treatment for Specific Populations (p.173) The family support network intervention increases parental support of an adolescent's

recovery through developing a support group for parents, provides home therapy sessions combined with group sessions, and can be used with any standard adolescent treatment approach (Hamilton et al. 2001).

Chapter 9: Adapting Intensive Outpatient Treatment for Specific Populations (p.174)
Exhibit 9-3
The Family Intervention Program (Fishman, & Andes, 2001.) This approach partners a family therapist with a community resource specialist. The specialist helps the family establish healthy community networks. Working as a team, the therapist and specialist conduct five family therapy sessions and perform the following:
Assess the family system; explore the family's resources, concerns, and goals; and create a treatment plan.
Explore relationships among family members, identify areas of difficulty and stress, and determine the effect on the family system.
Determine the effect of other systems, such as schools, on the family.
Focus on the family's concerns and goals and include others who can help resolve problems.
Work on how the family can resolve issues without staff help and develop a follow-up plan.

Further references

Boylin, W. M., & Doucette, J. (1997). Multifamily therapy in substance abuse treatment with women. American Journal of Family Therapy 25(1):39–47.
Conner, K. R., Shea, R. R., McDermott, M. P., Grolling, R., Tocco, R. V., & Baciewicz, G. (1998). The role of multifamily therapy in promoting retention in treatment of alcohol and cocaine dependence. American Journal on Addictions, 7(1):61–73.
Fishman, H. C., & Andes, F. (2001). Enhancing family therapy: The addition of a community resource specialist. Journal of Marital and Family Therapy 27(1):111-116.)
Godley, S. H., Meyers, R.J., Smith, J. E., Karvinen, T., Titus, J. C., Godley, M. D., Dent, G., Passetti, L., & Kelberg, P. (2001). The adolescent community reinforcement approach for adolescent cannabis users. Cannabis Youth Treatment Series, Volume 4. DHHS Publication No. (SMA) 01-3489. Rockville, MD: Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration.
Hamilton, N. L., Brantley, L. B., Tims, F. M., Angelovich, N., & McDougall, B. (2001) Family Support Network for Adolescent Cannabis Users. Cannabis Youth Treatment Series, Volume 3. DHHS Publication No. (SMA) 01-3488. Rockville, MD: Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration.
Meezan, W., & O'Keefe, M. (1998). Multifamily group therapy: Impact on family functioning and child behavior. Families in Society, 79(1):32–44.
Stanton, M. D., & Shadish, W. R. (1997). Outcome, attrition, and family-couples treatment for drug abuse: A meta-analysis and review of the controlled, comparative studies. Psychological Bulletin, 122(2):170–191.

Differential indication

Guideline	Evidence level
1 (NICE CG115, 2011)	Currently not evidence-based.

Statement

EVALUATING THE ORGANISATION OF CARE FOR PEOPLE WHO MISUSE ALCOHOL

Clinical evidence for case management (p.100) No studies identified which evaluated the efficacy of case management for children and adolescents or older people and met inclusion criteria.

ASSERTIVE COMMUNITY TREATMENT (p.101) No studies identified which evaluated the efficacy of case management for children and adolescents or older people and met inclusion criteria. STEPPED CARE (p.105) No studies identified which evaluated the efficacy of case management for children and young people or older people and meeting inclusion criteria were identified. Residential and community settings for the delivery of interventions for alcohol misuse (p.230) No clinical evidence of different settings in the treatment of alcohol misuse was identified for children, young people or older populations.
Further references
n/a

Guideline	**Evidence level**
2 (NICE, CG100, 2010)	Currently not evidence-based.
Statement	
2.1.6 FROM EVIDENCE TO RECOMMENDATIONS (p.32; no evidence level) All of the studies reviewed were in adult populations although age was not restricted when undertaking the literature search. As such, the GDG [Guideline Development Group] agreed that while the presentation of a young person with alcohol withdrawal is rare, it is associated with a unique set of problems and management should always include addressing any underlying long- term psychosocial issues. The GDG agreed that this population is particularly vulnerable and that admission should be considered at a lower threshold in those under 18 and advised in those under 16 years. The GDG recognizes that intoxication is a more common problem than withdrawal in this age group. 2.1.7 RECOMMENDATIONS (p.32; no evidence level) For young people under 16 years who are in acute alcohol withdrawal, offer admission to hospital for physical and psychosocial assessment, in addition to medically assisted alcohol withdrawal. (p.41) The GDG noted that study sizes were small and heterogeneous with respect to inclusion/ exclusion criteria, and none included young people or older adults in their samples. Therefore, the study populations may not be representative of those presenting to clinical practice, especially as patients with a history of substance misuse or a concurrent medical or psychiatric condition were excluded. (p.70) None of the evidence reviewed included people from the young adult and older adult populations.	
Further references	

Guideline	Evidence level
13 (American Psychiatric Association, 2006)	Levels III and Ib (see near left)
Statement	**Further references**
1. Commonly available treatment settings and services (p.26) Evidence level III The benefit of expanded availability of social services has been demonstrated for adult substance users of both sexes. Community residential facilities show more variability in substance use outcomes for youth and adolescents (Weiner, Abraham, Lyons, 2001); this may be related to inadequate matching of services to individual needs. 2. Commonly available treatment settings and services (p.27) Evidence level Ib Nevertheless, studies show that case management interventions are effective for individuals with an alcohol use disorder (p.79) or co- occurring psychiatric and substance use disorders (p.80) and for adolescents with substance use disorders (Godley, Godley, Dennis, Funk, Passetti, 2002).	
Further references	
Weiner, D. A., Abraham, M. E., & Lyons, J. S. (2001). Clinical characteristics of youth with substance use problems and implications for residential treatment. Psychiatric Services, 52: 793-799. Godley, M. D., Godley, S. H., Dennis, M. L., Funk, R., & Passetti, L. L. (2002). Preliminary outcomes from the assertive continuing care experiment for adolescents discharged from residential treatment. Journal of Substance Abuse Treatment, 23(1): 21-32	

Kapitel “3.7.2 Schwangere und erwachsene Frauen”

Guideline	Evidence level
1 (NICE CG115, 2011)	Currently not evidence- based.
Statement	
Experience of care: The studies focusing on women and alcohol problems emphasize that a non-judgemental atmosphere in primary care is necessary in order to foster openness and willingness to change with regard to their alcohol problems.	
Further references	
n/a	

Guideline	Evidence level
3 (NICE, PH 24, 2010)	Seven studies graded ++ [highest quality appraisal]
Statement	
Evidence statement 6.3 (p. 81): Brief interventions are effective in reducing alcohol consumption in both men and women.	
Further references	
Not further specified.	

Guideline	Evidence level
4 (Medical Specialty Society, 2010)	Currently not evidence- based.
Statement	
Brief interventions are effective and should be provided by health care providers for women with at-risk drinking. (II- 2B). If a woman continues to use alcohol during pregnancy, harm reduction/treatment strategies should be encouraged. (II-2B) Pregnant women should be given priority access to withdrawal management and treatment. (III-A)	
Further references	
Chang, G. (2004).Screening and brief interventions in prenatal care settings. Alcohol Research and Health 28(2), 80. Stade, B. C., Bailey, C., Dzendoletas, D., Sgro, M., Dowswell, T., & Bennett, D. (2009). Psychological and/or educational interventions for reducing alcohol consumption in pregnant women and women planning pregnancy. Cochrane Database of Systematic Reviews, 2. Reynolds, K. D., Coombs, W., Lowe, J. B., Peterson, P. L., & Gayoso, (1995). Evaluation of a self-help program to reduce alcohol consumption among pregnant women. Substance Use & Misuse, 30(4), 427- 443. Handmaker, N. S., Miller, W. R., & Manicke, M. (1999). Findings of a pilot study of motivational interviewing with pregnant drinkers. Journal of Studies on Alcohol and Drugs, 60(2), 285. Jones-Webb, R., McKiver, M., Pirie, P., & Miner, K. (1999). Relationships between physician advice and tobacco and alcohol use during pregnancy. American Journal of Preventive Medicine, 16(3), 244-247.	

Chang, G., McNamara, T. K., Orav, E. J., Koby, D., Lavigne, A., Ludman, B., & Wilkins-Haug, L. (2005). Brief intervention for prenatal alcohol use: a randomized trial. Obstetrics and Gynecology, 105(5 Pt 1), 991.
O'Connor, M. J., & Whaley, S. E. (2007). Brief intervention for alcohol use by pregnant women. American Journal of Public Health, 97(2).
Boyd, S. C., & Marcellus, L. (Eds.) (2007). With Child: Substance use during pregnancy. A woman- centred approach. Halifax, NS: Fernwood Publishing, pp 91–104.
British Columbia Ministry of Health (2005). Harm reduction: a British Columbia community action guide. Victoria, BC: Government of British Columbia.
National Institute on Alcohol Abuse and Alcoholism (NIAAA) (rev. 2008). Alcohol: A women's health issue. U.S. Department of Health and Social Services. Rockville, MD: NIAAA. Available at: http://pubs.niaaa.nih.gov/pu blications/brochurewomen/ Woman_English.pdf Accessed May 2014.

Guideline	**Evidence level**
6 (Veterans Health Administration, 2009)	Currently not evidence- based.
Statement	
Recommendation: Contraindications for any alcohol use include: Pregnancy or trying to conceive. Discussion/ Recommendation: "Assessing women, teenagers, older adults, and other vulnerable individuals for victimization by another member of the household also is important. Patients should be linked with prenatal and primary healthcare for domestic violence. Ideally, linkage to these programs includes more than a phone number; and should assist patients in scheduling initial appointments and arranging for transportation" (p.49).	
Further references	
n/a	

Guideline	**Evidence level**
8 (TIP 49; U.S. Department of Health und Human Services, SAMHSA, 2009)	Currently not evidence- based.
Statement	
Caution with medications when women are pregnant or plan to become pregnant or are breastfeeding. Certain conditions warrant advising a patient to abstain from rather than reduce drinking. As noted in the NIAAA (2006) clinician's guide, these conditions include when drinkers: Are or may become pregnant.	
Further references	
n/a	

Guideline	**Evidence level**
9 (New York State Department of Health, 2005, revised 2009)	Currently not evidence- based.
Statement	
Recommendations: Clinicians should recommend inpatient or outpatient treatment for alcohol dependent pregnant women. Pregnant women who are physically dependent on alcohol should undergo medically supervised detoxification prior to initiating longer-term abstinence-based treatment.	

Recommendation: Clinicians should screen all substance-using women for trauma and physical and/or sexual abuse, which may trigger or exacerbate substance use in female patients. Initial assessments of new female patients should include questions that document whether a woman has a history of past or current physical or sexual abuse.
Further references
Substance Abuse and Mental Health Services Administration (2004). Results from the 2003 National Survey on Drug Use and Health: National Findings. Rockville, MD: U.S. Department of Health and Human Services. Available at: http://oas.samhsa.gov/nhsd a/2k3nsduh/2k3ResultsW.pdf Najavits, L. M. (2002). Seeking safety: A treatment manual for PTSD and substance abuse. New York, NY: Guilford Press. Najavits, L. M., Weiss, R. D., & Shaw, S. R. (1997). The link between substance abuse and posttraumatic stress disorder in women. The American Journal on Addictions, 6(4), 273-283.

Guideline	**Evidence level**
13a (American Psychiatric Association, 2006)	Pregnancy: Qualititative review [F], other [G] (see near right)
Statement	
Pregnancy:Goals for treatment of pregnant, substance-using women include (1) providing appropriate treatment for substance-use disorder (2) treating co-occurring medical or psychiatric disorders, 3) monitoring the safety of patient behaviors during pregnancy as well as during the postpartum period, 4) facilitating competent parenting behaviors, and 5) motivating the patient to remain abstinent after childbirth. The optimal therapeutic approach is non-punitive and maintains patient confidentiality.	
Further references	
Pregnancy: Suchman, N., Mayes, L., Conti, J., Slade, A., & Rounsaville, B. (2004). Rethinking parenting interventions for drug- dependent mothers: from behavior management to fostering emotional bonds. Journal of Substance Abuse Treatment, 27(3), 179-185. [F] Finnegan, L. P., & Kendall, S. R. (1992). Maternal and neonatal effects of alcohol and drugs, in substance abuse: A comprehensive textbook (2nd ed.). Edited by Lowenstein, J. H., Ruiz, P., & Millman, R. B. Baltimore, MD: Williams & Wilkins, pp 628–656. [G]	

Guideline	**Evidence level**
13b (American Psychiatric Association, 2006)	Family therapies: Randomized trial [A–], qualititative review [F] (see near right)
Statement	
Family therapies: More recent studies have demonstrated the effectiveness of family involvement in substance use disorder treatment for both women and men. The support for behavioral couples treatment is particularly strong.	
Further references	
Family therapies: Winters, J., Fals-Stewart, W., O'Farrell, T. J., Birchler, G. R., & Kelley, M. L. (2002). Behavioral couples therapy for female substance-abusing patients: Effects on substance use and relationship adjustment. Journal of Consulting and Clinical Psychology, 70(2), 344. [A–]	

O'Farrell, T. J., & Fals- Stewart, W. (2002). Behavioral couples and family therapy for substance abusers. Current Psychiatry Reports, 4(5), 371-376. [F]

Guideline	**Evidence level**
13c (American Psychiatric Association, 2006)	PTSD: Randomized trial [A–], quantitative review [F], other [G] (see near right)
Statement	
PTSD: PTSD is common among individuals with a substance use disorder (about 20%), with women having about twice the rate of co-occurring PTSD as men. Specific integrated psychotherapies for PTSD co- occurring with a substance use disorder have been developed and evaluated. "One study of 107 women were randomly assigned [sic] to receive Seeking Safety treatment, a manual-guided relapse prevention therapy, or standard community treatment found that women receiving Seeking Safety or relapse prevention therapy had significant reductions in substance use, PTSD, and psychiatric symptoms over the 3-month treatment period, whereas the symptoms of women who received standard community treatment worsened; furthermore, the Seeking Safety and relapse prevention groups maintained the greater improvements in substance use and PTSD symptoms at the 6- and 9- month follow-ups. Outcomes did not differ between the Seeking Safety and the relapse prevention groups" (p.59).	
Further references	
PTSD: Hien, D. A., Cohen, L. R., Miele, G. M., Litt, L. C., & Capstick, C. (2004). Promising treatments for women with comorbid PTSD and substance use disorders. American Journal of Psychiatry, 161(8), 1426-1432. [A–] Najavits, L.M. (2002). Clinicians' views on treating posttraumatic stress disorder and substance use disorder. Journal of Substance Abuse Treatment, 22, 79–85. [G] Brady, K. T. (2001). Comorbid posttraumatic stress disorder and substance use disorders. Psychiatric Annuals, 31, 313–319. [G] Blume, S. B. (1991). Sexuality and stigma: The alcoholic woman. Alcohol Health & Research World, 15:139–146. [G] Winfield, I., George, L. K., Swartz, M., & Blazer, D. G. (1990). Sexual assault and psychiatric disorders among a community sample of women. American Journal of Psychiatry, 147(3), 335-341. [E] Ladwig, G. B., & Andersen, M. D. (1989). Substance Abuse in Women: Relationship Between Chemical Dependency of Women and Fast Reports of Physical and/or Sexual Abuse. Substance Use & Misuse, 24(8), 739-754. [G] Stevens, S., Arbiter, N., & Glider, P. (1989). Women residents: Expanding their role to increase treatment effectiveness in substance abuse programs. Substance Use & Misuse, 24(5), 425-434. [G]	

Kapitel “3.7.3 Ältere Menschen”

Guideline	Evidence level
1 (NICE CG115, 2011)	LoE V
Statement	
Lower threshold for admission in inpatient assisted withdrawal : As older people are more likely to have comorbid physical and mental health problems and be socially isolated, a lower threshold for admission for assisted alcohol withdrawal may be required (Dar, 2006) (page 38) As noted earlier, older people can have higher levels of physical comorbidity, cognitive impairment, a lower capacity to metabolise alcohol and medications, and be in receipt of a larger number of medications than younger people. In addition, older people can be more frail and prone to accidents and falls. Therefore it is prudent to have a lower threshold for admission for inpatient assisted alcohol withdrawal in older people who misuse alcohol.(page 202) *Age appropriate treatment:* No clinical evidence evaluating the efficacy of different settings for the treatment of alcohol misuse were identified for children, young people or older populations. (page 224)	
Further references	
Dar K. (2006) Alcohol use disorders in elderly people: fact or fiction? Advances in Psychiatric Treatment 12: 173-181	

Guideline	Evidence level
13 (American Psychiatric Association, 2006)	LoE V; LoE Ib
Statement	
Age appropriate treatment: There is a paucity of empirical data on the treatment of substance use disorders in the elderly population; it is generally accepted that empirically supported treatments of adult substance use disorders can be effectively applied to the treatment of elderly patients. Some modifications, such as slowing the pace of therapy, placing follow-up outreach calls, and providing patients with written information, improve the effectiveness of some therapies (page 67) *LoE V* Kofoed et al. reported that VA patients age 54 years or older who received specialized services for elderly patients as part of a treatment program were four times more likely to complete the program and remained in treatment longer than those who received conventional services, although posttreatment relapse rates were comparable in the two group (page 67) LoE V *interventions in Primary Care:*	

A large multisite study (PRISM-E) has also shown that primary care patients screening positive for a substance use disorder prefer to be treated within the medical system, with integrated psychiatric and substance abuse services, rather than to have facilitated referral to outside treatment (31(A-)). (page 67) *LoE 1b*
Further references
Kofoed LL, Tolson RL, Atkinson RM, Toth RL, Turner JA. (1987) Treatment Compliance of older Alcoholics: Elder- Specific Approach is Superior to „Mainstreaming“. Journal of Studies on Alcohol. 48(1): 47-51 Kirchner JE, Leykoff S (2006). PRISM-E: comparison of integrated care and enhanced speciality referral in managing at-risk alcohol use.. Psychiatric Services 57: 954-958

Guideline	**Evidence level**
14 (Substance Abuse and Mental Health Services Administration U.S., 2006)	LoE V
Statement	
Age appropriate treatment: Oslin and colleagues *(2002)* find that older adults had greater attendance and lower incidence of relapse than younger adults in treatment and conclude that older adults can be treated successfully in mixed-age groups, provided that they receive age-appropriate individual treatment. (chapter 10)	
Further references	
Oslin DW, Pettinati H, Volpicelli JR.(2002) Alcoholism treatment adherence: Older age predicts better adherence and drinking outcome. Am J Geriatr Psychiatry. 10 (6) 740-747	

Klinische Fragestellung

„Welche Bedeutung haben körperliche Erkrankungen (z.B. Des Magens, der Bauchspeicheldrüse, der Leber, Tumore, Polyneuropathie, epileptische Anfälle, Demenz) für das Management einer Alkoholkonsumstörung?“

Guidelines	Australien (2009)	NICE (2010)	VA DOD (2009)	BAP (2004)	WFSBP 2008
Recommendation	Comorbidity Abstinence	Delir, seizures, Liver			
Strength of recommendation / Evidence	Comorbidity: A I Abstinence indicated: D IV	Delir, seizures: 2++ Liver 1b			
Reference	Gossop et al 2007 *Addict Biol* 12(2): 190-196. Cargiulo, T 2007, Understanding the health impact of alcohol dependence. *American Health-Syst Pharmacy* 64: S5-S11.	Schuckit MA, Tipp JE, Reich T et al. The histories of withdrawal convulsions and delirium tremens in 1648 alcohol dependent subjects. *Addiction.* 1995; 90(10):1335-1347. Wetterling T, Driessen M, Kanitz RD et al. The severity of alcohol withdrawal is not age dependent. *Alcohol & Alcoholism.* 2001; 36(1):75-78. Elphick DA, Dube AK, McFarlane E et al. Spectrum of liver histology in presumed decompensated alcoholic liver disease. *American Journal of Gastroenterology.* 2007 102(4):780-788.			

Klinische Fragestellung:

„Soll gleichzeitig oder in einer bestimmten Reihenfolge behandelt werden?“

Guideline	Australien (2009)	NICE UK 2010)	VA DOD (2009)	BAP (2004)	WFSBP (2008)
Recommendation			Gleichzeitige Behandlung som. Störungen		
Strength of recommendation / Evidence			A I		

Reference			Willenbring ML, Olson DH. A randomized trial of integrated outpatient treatment for medically ill alcoholic men. Arch Intern Med 1999 Sep;159(16):1946-52. Willenbring ML, Olson DH, Bielinski J B. Integrated outpatient treatment for medically ill alcoholic men: results from a quasi-experimental study. J Stud Alcohol 1995 May;56(3):337-43.		

Klinische Fragestellung

„Welche Bedeutung haben psychische Störungen (z.B. Schizophrenie, Depression, bipolare affektive Störung, Angststörung, Posttraumatische Belastungsstörung, Persönlichkeitsstörungen, Essstörungen, Nikotinabhängigkeit, andere Substanzstörungen oder substanzunabhängige Verhaltenssüchte wie Pathologisches Glücksspiel oder Onlinesucht, ADHS) für das Management einer Alkoholkonsumstörung?“

Guideline	Australien (2009)	NICE (2010)	VA DOD (2009)	BAP (2004)	WFSBP (2008)	NICE (2011)
Recommendation	Diagnosis, Interventions		Intervention for persons at risk, Med. Supervised			There is some evidence to suggest that active treatment of comorbid mental health problems may improve drug and alcohol substance misuses outcomes
Strength of recommendation / evidence	Diagnosis: A, 1b; More interventions: B, 1		Intervention or persons at risk: III I Med. Supervised wd: III C	B		

Reference	Schneider, U, Altmann A, Baumann M et al. 2001, Comorbid anxiety and affective disorder in alcohol- dependent patients seeking treatment: the first Multicentre Study in Germany. *Alcohol Alcohol* 36(3): 219-223. Project MATCH Research Group 1997, Matching alcoholism treatments to client heterogeneity: Project MATCH posttreatment drinking outcomes.*J Stud Alcohol* 58: 7- 29.		Hirschfeld RM, Russell JM. Assessment and treatment of suicidal patients. N Engl J Med 1997 Sep 25; 337(13):910-5.	Lingford-Hughes AR, Welch S, Nutt DJ; British Association for Psychopharmacolo gy Evidence-based guidelines for the pharmacological management of substance misuse, addiction and comorbidity: recommendations from the British Association for Psychopharmacolo gy. J Psychopharmacol. 2004 Sep;18(3):293-335.	Sullivan et al. 2004	Charney, A. A., Paraherakis, A. M. & Gill, K. J. (2001) Integrated treatment of comorbid depression and substance use disorders. *Journal of Clinical Psychiatry, 62,* 672–677. Hesse, M. (2004) Achieving abstinence by treating depression in the presence of substance- use disorders. *Addictive Behaviors, 29,* 1137– 1141. Watkins, K. E., Paddock, S. M., Zhang, L., *et al.* (2006) Improving care for depression in patients with comorbid substance misuse. *American Journal of Psychiatry, 163,* 125– 132.

Klinische Fragestellung

„Bei welchen komorbiden Störungen soll in welcher Reihenfolge und Intensität behandelt werden?“

Guideline	Australien (2009)	NICE (2010)	VA DOD (2009)	BAP (2004)	WFSBP (2008)	NICE (2011)
Recommendation			1. Prioritize and address other medical and psychiatric co-occurring conditions. 2. Recommend and offer cessation treatment to patients with nicotine dependence. 3. Treat concurrent psychiatric disorders consistent with VA/DoD clinical practice guidelines (e.g., Major Depressive Disorder, Bipolar Disorder, Post Traumatic Stress, Psychoses) including concurrent pharmacotherapy. 4. Provide or arrange treatment via referral for medical conditions (e.g. management of diabetes, chronic heart failure, management of unexplained medical symptoms). (See other VA/DoD Clinical Practice Guidelines at: www.healthquality.va.gov 5. Provide multiple services in the most accessible setting to promote engagement and coordination of care. 6. Monitor and address deferred problems and emerging needs through ongoing treatment plan updates. 7. Coordinate care with other providers	Erst Alkohol, dann komorbide Störung		Depression or anxiety disorder, treat alcohol misuse first. Assess after 3-4 weeks of abstinence. PTSD Treatment for individual PTSD can improve substance misuse. Treat dependence before trauma- focused treatment. (NCCMH 2005) PTSD-treatment may be important to optimize Outcomes for PTSD + alcohol dependence (Back et.al.2006). Sertraline for pat. with PTSD (Brady et.al. 2002+200) ADHD Alcohol Use disorder+ ADHD =>improved ADHD symptoms from Atomoxetine vs. placebo reduced cum. number of heavy drinking days but not increased time to relapse of heavy drinking. (Wilens et.al. 2008) Alcohol+Opioids => actively treat both Alcohol+Stimula nts, Cannabis or Benzodiazepine s=> actively treat both
Strength of recommenddation / evidence			Alle I B; sonst III I	Depression= B Angst = S Psychose = D		

Reference			Friedmann PD, Hendrickson JC, Gerstein DR, Zhang Z. The effect of matching comprehensive services to patient's needs on drug use improvements in addiction treatment. Addiction 2004 Aug;99(8):962-72. McLellan AT, Grissom GR, Zanis D, Randall M, Brill P, O'Brien CP. Problem- service 'Matching' in addiction treatment. Arch Gen Psychiatry 1997 Aug;54(8):730-5.	Lingford- Hughes AR, Welch S, Nutt DJ; British Association for Psychophar macology Evidence-based guidelines for the pharmacolog ical management of substance misuse, addiction and comorbidity: recommenda tions from the British Association for Psychophar macology. J Psychophar macol. 2004 Sep;18(3):29 3-335.		

Klinische Fragestellung

„Welches sind wirkungsvolle Verfahren für die Therapie der einzelnen Komorbiditäten? Depression, Angst, Bipolar, Schizophrenie?“

Guideline	**Australien (2009)**	**NICE (2010)**	**VA DOD (2009)**	**BAP (2004)**	**WFSBP (2008)**	**NICE** **CG87 2009 Borderline personality disorder** **CG120 2011: Psychosis with coexisting substance misuse.** **CG 90 2009: Depression** **CG 38 2006: Bipolar disorder** **CG 26 2005: PTSD** **CG 82 2009 Schizophrenia** **CG 77 2009: Antisocial personality disorder** **CG 133 2011: Self-harm: long-term treatment** **CG 113 2011: Anxiety**
Recommendation						
Strength of recommenddation / evidence	Psychosocial Depression Anxiety: Concurrent CBT, B II CBT, BT, IPT B, I „mood disorders, Psychosis“: Integrated psychosocial treatment D IV Pharmakotherapie Depression/Angst, BZD nicht empfohlen für Angstbehandlung S SSRI nicht empfohlen für AD Behandlung B II					Depression SSRI B, TCA > SSRI B; Bipolar, Valproat D Angst: Paroxetin D Buspiron B Schizo, 2nd generation antispychotics D FGA vs. SGA: Level C
Reference	Psychotherapie, psychosoz. Behandlung Horsefall et al 2009; Tiet and Mausbach 2007, Hesse 2009 Personality: Nielsen et al 2007 Schizophrenia Graeber et al 2003, Pharmakotherapie SSRI Nunes and Levin 2004 Torrens et al 2005					Depression SSRI/TCA: Nunes and Levin 2004 ALC + Bipolar, Valproat, Salloum et al 2005 Angst: Randall et al. 2001, Malec et al. 1996 Schizophrenie Soyka et al 2008; Potvin et al 2006

Kapitel „3.8 Medizinische Rehabilitation und andere Formen der Postakutbehandlung“

Klinische Fragestellung

1. Welche Wirksamkeit (positive, fehlende, unerwünschte) weisen postakute Interventionsformen im kontrollierten Vergleich bei der Behandlung des Alkoholabhängigkeitssyndroms auf?

Guideline	**NICE (CG115), UK, National Institute for Health and Clinical Excellende (NICE), 2011.**	**NICE (CG 100), UK, National Institute for Health and Clinical Excellence (NICE), 2010.**	**VA/DoD USA, Department of Defense, 2009.**	**Incorporating alcohol pharmacotherapies into medical practice. USA, Department of Health and Human Services, 2009.**	**Treatment of Patients with Substance Use Disorders. USA, American Psychiatric Association, 2006.**
Aussage ja/nein	ja	nein	nein	ja	ja
Evidenz (levels of evidence)	a) / b) Ia			a) / b) Ia	a) / b) Ia
Empfehlungsgrad (A, B, 0, KKP)	a) KKP b) A			a) KKP b) A	a) / b) A

Aussage inhaltlich	a) Psychologische, psychosoziale und pharmakologische Interventionen sind wirksam bei AUD: Positive Effekte mit guter Evidenzbasis für: CBT, VT allg., Paartherapie; psychodynamische Kurzzeittherapie (nur 1 Studie); Moderate Evidenz für: Motivierungsansätze und Kurzinterventionen, Counselling (integriert in and. Formen); moderate Evidenz, aber ohne spez. Wirkung: 12 Schritte Therapieziele: - „In the initial assessment in specialist alcohol services of all people who misuse alcohol, agree the goal of treatment with the service user. Abstinence is the appropriate goal for most people with alcohol dependence, and people who misuse alcohol and have significant psychiatric or physical comorbidity (for example, depression or alcohol-related liver disease).” (p. 173)			a) Pharmakologische Intervention bei AUD mit Acamprosat, Disulfiram und Naltrexon ist wirksam. b) Therapieziele: “If a patient with an AUD is unwilling to be completely abstinent, he or she may be willing to cut down on alcohol use.” (p. 56)	a) Medikamentöse und psychosoziale Behandlungsformen sind für sich wirksam. Allerdings keine Aussagen zu Kombination und Dominanz von Pharmakotherapie. (Ist literaturbasiert bis Febr. 2005 genannt (Die APA bezeichnet die Leitlinie selbst nicht mehr als aktuell gültig, da entgegen der eigenen Qualitätsstandards älter als 2 Jahre).) b) Erstes Ziel ist Abstinenz, jedoch auch harm-reduction bei reduziertem Trinkverhalten wird als erreichbares Ziel angegeben. The ideal outcome for most individuals with substance use disorders is total cessation of substance use. S. 17. For example, reductions in the amount or frequency of substance use, substitution of a less risky substance, and reduction of high-risk behaviors associated with substance use may be achievable goals when abstinence is initially unobtainable (12, 13). S. 17. For optimal outcome, the treatment of a substance use disorder may also include strategies that target repair of damages or losses that resulted from the individual’s substance use; aid in developing effective interpersonal, vocational, and proactive coping skills; and enhance familial and interpersonal relations that will

	„For harmful drinking or mild dependence, without significant comorbidity, and if there is adequate social support, consider a moderate level of drinking as the goal of treatment unless the service user prefers abstinence or there are other reasons for advising abstinence.” (p. 174)				support an abstinent life- style. It is particularly important to provide comprehensive treatments when individuals have co-occurring psychiatric or general medical conditions that significantly influence relapse risk (e.g., chronic pain, depression, anxiety, impaired cognition, and impulse control disorders) (22–24). S. 17. The long-term goals of treatment for patients with an alcohol use disorder are identical to those for patients with any type of substance use disorder and include abstinence (or reduction in use and effects), relapse prevention, and rehabilitation. S. 89. However, abstinence is the optimal goal that achieves the best long-term overall functioning (9). S. 89.
Relevante Literatur aus Leitlinie					

Klinische Fragestellung

Von welchen der folgenden Bedingungen ist die Wirksamkeit abhängig?

Patientengruppen (z.B. Co- und Multimorbidität, Geschlecht, Alter, sozioökonomischer Status, Migrationshintergrund)

	NICE (CG115), UK, National Institute for Health and Clinical Excellende (NICE), 2011.	**NICE (CG 100), UK, National Institute for Health and Clinical Excellence (NICE), 2010.**	**VA/DoD USA, Department of Defense, 2009.**	**Incorporating alcohol pharmacotherapies into medical practice. USA, Department of Health and Human Services, 2009**	**Treatment of Patients with Substance Use Disorders. USA, American Psychiatric Association, 2006.**
Aussage ja/nein	ja	nein	ja	ja	ja
Evidenz (levels of evidence)	/		/	/	/
Empfehlungsgrad (A, B, 0, KKP)	KKP		KKP	KKP	KKP

Aussage inhaltlich	Bei Comorb.: i.d.R. Erst Beh. Alk, dann zeitlich versetzte Mitbehandlung; keine Evidenz für Geschlecht; jung/alt		Die Effizienz bei integrierter Behandlung von psychisch-comorbiden Patienten ist noch unklar. Disease-specific treatment has been shown to efficacious for patients diagnosed with SUD or other psychiatric disorders alone. While there have been a number of theories about how to treat COD among patients with SUD, there has been little data to support the best approach. In the simplest sense, existing efficacious treatment that successfully reduces psychiatric symptoms in patients with such symptoms alone should also reduce psychiatric symptoms in patients with both psychiatric CODs and SUD. A review of 59 studies (36 RCTs evaluating treatment of dual diagnosis) concluded that although no treatment was identified as efficacious for both psychiatric disorders and substance- related disorder, the author found: 1) existing efficacious treatments for reducing psychiatric symptoms also tend to work in dual-diagnosis patients,	Bei einzelnen Interventionen existieren sec. Analysen hierzu.	Bei einzelnen Interventionen existieren Analysen hierzu. Auf dieser Basis substanzübergreifend Aussagen zu Komorbidität. Insgesamt dominieren leichte Fälle ohne Komorbidität bzw. homogene Stichproben. Other evidence suggests that the association between treatment setting and outcome may be a complex one that is influenced by the characteristics and treatment needs of the individual patient. Magura et al. (965) studied a cohort of 248 patients who were newly admitted to inpatient rehabilitation or intensive or regular outpatient care and determined whether they were naturalistically matched or mismatched to care according to ASAM patient placement criteria. At 3 months after intake, individuals who received regular outpatient care when intensive outpatient care would have been recommended as more appropriate had poorer drinking out- comes. In individuals who received residential as compared with intensive outpatient treatment, there also was a trend for a better outcome.

			2) existing efficacious treatments for reducing substance-use also decrease substance use in dually diagnosed patients, 3) the efficacy of integrated treatment is still unclear (Tiet & Mausbach, 2007).		Rychtarik et al. (966) also examined individual factors that might determine the appropriateness of a given treatment setting for an individual patient. They found that individuals with a high level of involvement with alcohol and lower cognitive abilities had better outcomes when treated in inpatient settings, whereas those with lower levels of alcohol involvement did better in outpatient settings. S. 147 Anmerkung zu ASAM: To appropriately match patients and treatment settings, many clinicians, health insurers, hospitals, and treatment agencies use the American Society of Addiction Medicine (ASAM) patient placement criteria (39). S. 22 There is consensus (e.g., ASAM patient placement criteria) that individuals in one or more of the following categories may require hospital-level care: 1. Individuals with drug overdoses who cannot be safely treated in an outpatient or emergency department setting (e.g., individuals with severe respiratory depression, individuals in a coma) Individuals in withdrawal who are at risk for a severe or complicated withdrawalsyndrome (e.g., individuals dependent on multiple substances, individuals with a history of delirium tremens) or cannot receive the necessary medical assessment, monitoring, and treatment in a less intensive setting 3. Individuals with acute or chronic general medical conditions that make detoxification in a residential or ambulatory setting unsafe (e.g., individuals with severe cardiac disease)

					4. Individuals with marked psychiatric comorbidity who are an acute danger to themselves or others (e.g., individuals who have depression with suicidal thoughts, acute psychosis) 5. Individuals manifesting substance use or other behaviors who are an acute danger to themselves or others 6. Individuals who have not responded to less intensive treatment efforts and whose substance use disorder(s) poses an ongoing threat to their physical and mental health
Relevante Literatur aus Leitlinie					22. Mee-Lee D, Shulman GD, Fishman M, Gastfriend DR, Griffith JH (eds): ASAM Patient Placement Criteria for the Treatment of Substance-Related Disorders, 2nd ed., revised. Chevy Chase, Md, American Society of Addiction Medicine, 2001 [G]; 965. Magura S, Staines G, Kosanke N, Rosenblum A, Foote J, DeLuca A, Bali P: Predictive validity of the ASAM Patient Placement Criteria for naturalistically matched vs mis- matched alcoholism patients. Am J Addict 2003; 12:386–397 [C]; 966. Rychtarik RG, Connors GJ, Whitney RB, McGillicuddy NB, Fitterling JM, Wirtz PW: Treatment settings for persons with alcoholism: evidence for matching clients to inpatient versus outpatient care. J Consult Clin Psychol 2000; 68:277–289

Klinische Fragestellung

Von welchen der folgenden Bedingungen ist die Wirksamkeit abhängig?

Setting (ambulant, ganztägig ambulant, stationär)

Guideline	**NICE (CG115), UK, National Institute for Health and Clinical Excellende (NICE), 2011.**	**NICE (CG 100), UK, National Institute for Health and Clinical Excellence (NICE), 2010.**	**VA/DoD USA, Department of Defense, 2009.**	**Incorporating alcohol pharmacotherapies into medical practice. USA, Department of Health and Human Services, 2009.**	**Treatment of Patients with Substance Use Disorders. USA, American Psychiatric Association, 2006.**
Aussage ja/nein	ja	ja	ja	ja	ja
Evidenz (levels of evidence)	/	/	/	/	/
Empfehlungsgrad (A, B, 0, KKP)	KKP	KKP	KKP	KKP	KKP
Aussage inhaltlich	Ansatz stepped care ++, gemeinde-orientierte Ansätze bei sehr starker Abh. und bei schädl. Konsum sind wirksam.	Komplikationsrisiko bei häufigeren früheren Entzugsbehandlungen.	recommendations for specific levels of care. In that regard, there is now a fair amount of research that indicates patients with greater substance use severity and co-occurring problems such as psychiatric disorders and housing problems will do better in more intensive forms of treatment. Conversely, those with lower severity levels will do as well of better in less intensive forms of treatment. However, there is little controlled evidence to support the validity of the ASAM criteria. When both the patient and provider agree on what is to be accomplished and how this is to be done, the chances of achieving a good outcome are enhanced (Putnam et al., 1994; Sanchez-Craig & Lei, 1986).	Initial tw. Stationär, Verlaufsbehandlung immer ambulant	Dominanz ambulanter Behandlung. Bessere Ergebnisse postakuter Interventionen bei vorangegangener Entzugsbehandlung. Nur wenige Vergleichsstudien. Daher keine evidenzbasierte Aussagen. In addition, the optimal treatment setting and subsequent treatment outcome are likely to vary depending on the characteristics of the individual patient (965, 966). S. 90

Klinische Fragestellung

Von welchen der folgenden Bedingungen ist die Wirksamkeit abhängig?

Behandlungsdauer

Guideline	**NICE (CG115), UK, National Institute for Health and Clinical Excellende (NICE), 2011.**	**NICE (CG 100), UK, National Institute for Health and Clinical Excellence (NICE), 2010.**	**VA/DoD USA, Department of Defense, 2009.**	**Incorporating alcohol pharmacotherapies into medical practice. USA, Department of Health and Human Services, 2009.**	**Treatment of Patients with Substance Use Disorders. USA, American Psychiatric Association, 2006.**
Aussage ja/nein	ja	nein	ja	ja	ja
Evidenz (levels of evidence)	/		/	/	/
Empfehlungsgrad (A, B, 0, KKP)	KKP		KKP	KKP	KKP
Aussage inhaltlich	1-12 Wochen		Längere Behandlungszeiten für schwer erkrankte Suchtpatienten führen zu besserem Outcome. Leichtere Fälle sollten von der Grundversorgung behandelt werden.	3-12 Monate Behandlungszeitraum	Keine Empfehlung da unklare Ergebnislage da keine systematischen Vergleichsstudien. 28 Tage als Untergrenze. Residential treatment of ≥ 3 months is associated with better long-term outcome in such patients (II=Recommended with moderate clinical confidence). S. 11 Some evidence suggests that longer treatment stays and treatment completion may be associated with better outcomes (959, 1304) S. 147
Relevante Literatur aus Leitlinie					959. Moos RH, Finney JW, Cronkite RC: Alcoholism Treatment: Context, Process, and Outcome. New York, F]; 1304. McKay JR, Alterman AI, McLellan AT, Snider EC: Treatment goals, continuity of care, and outcome in a day hospital substance abuse rehabilitation program. Am J Psychiatry 1994; 151:254–259 [B];Oxford University Press, 1990

Klinische Fragestellung

Von welchen der folgenden Bedingungen ist die Wirksamkeit abhängig?“

Interventionskompenenten

Guideline	**NICE (CG115), UK, National Institute for Health and Clinical Excellende (NICE), 2011.**	**NICE (CG 100), UK, National Institute for Health and Clinical Excellence (NICE), 2010.**	**VA/DoD USA, Department of Defense, 2009.**	**Incorporating alcohol pharmacotherapies into medical practice. USA, Department of Health and Human Services, 2009.**	**Treatment of Patients with Substance Use Disorders. USA, American Psychiatric Association, 2006.**
Aussage ja/nein	ja	nein	nein	ja	ja
Evidenz (levels of evidence)	Ia, Ib, IIb			Ia, Ib	Ia, Ib
Empfehlungsgrad (A, B, 0, KKP)	A, B			B, 0	B, 0

Aussage inhaltlich	**Motivationale Techniken:** - "One computerised session of MET (drinker's check up) was significantly better than control in reducing average drinks per day at 1-month follow-up (moderate effect size)." (p. 243) Effekt: -0.67, CI: 95% - "MET (with relapse prevention) (ROSENBLUM2005b) was significantly more effective than control at reducing heavy alcohol use when assessed at 5-month followup (moderate effect size)." (p. 243) Effekt: -0.70, CI: 95% "[…] favoured MET over control in the number of people who drank excessively and frequently (ten or more drinks, six or more times) at 6-month follow-up (large effect size)." (p. 243) Effekt: 0.66, CI: 95% "The clinical evidence showed that no significant difference could be found between motivational techniques and other active interventions in maintaining abstinence at up to 15-month follow-up. Furthermore, no difference between groups was observed in reducing the number of participants who had lapsed or reducing heavy drinking at all follow- up points." (p. 243)			"Acamprosate significantly more effective than placebo in reducing drinking days, increasing complete abstinence, and lengthening time to relapse." (p.10) "Compared with using placebo, short- term treatment (less than or equal to 12 weeks) with naltrexone significantly improved relapse rates during active treatment and a medication-free followup period." (p. 28) "Studies concluding that disulfiram is effective in treating AUDs frequently emphasize the circumstances in which it is administered to patients. In particular, the level and quality of supervision a patient receives while taking disulfiram are believed to be important elements in its success" (p. 18)	"For promoting abstinence and preventing relapse in patients with substance use disorders, certain medications may be useful. Examples of such medications are disulfiram, naltrexone, and acamprosate for alcohol use disorders and bupropion for nicotine dependence." (p. 35)

	Kognitive Verhaltenstherapie: - "[…] resulting in a moderate effect size, cognitive behavioural therapies were significantly better than treatment as usual in reducing the number of participants who lapsed and relapsed when assessed at 6-month follow- up." (p. 262); Effekt: 0.75, CI: 95% "[…] cognitive behavioural therapies were found to be more effective at maintaining abstinence/light days when assessed up to 18-month follow-up […]." (p. 262) Effekt: -0.74, CI: 95% "For maintaining abstinence, an individual assessment treatment programme was significantly more effective than a packaged CBT program when assessed post-treatment (moderate effect size, based on a single study)." (p. 263) Effekt: 0.39, CI: 95% - "More intensive coping skills was significantly better than standard coping skills at maintaining abstinent/light drinking at 12-month follow- up - (moderate effect size) […]." (p. 267); Effekt: -0.65, CI: 95% - "Individual CBT was significantly more effective than group CBT in reducing the number of heavy drinkers at 15-month follow- up." (p. 267); Effekte: 0.37, CI: 95% - **Verhaltenstherapie:** - "[…] behavioural therapies were more effective than control in reducing the amount of alcohol consumed (SMD = - 0.97, large effect size) and maintaining controlled				

	drinking (SMD = - 0.60, medium effect size) when assessed post-treatment." (CI: 95%), (p. 273) - "[…]one study (SITHARTHAN1997) showed a medium effect size favouring cue exposure over CBT in reducing drinks per occasion at 6-month follow- up." (p. 274); Effekt: -0.66, CI: 95% - "The clinical evidence indicates that there was no significant difference between cue exposure and BSCT in maintaining abstinence post-treatment or at 6-month followup." (p. 275) - **Kontingenzmanagement:** - "The review evidence indicated that contingency management (with network support) was more effective at maintaining abstinence than control post-treatment (large effect size) and up to 15-month follow-up (medium effect size). […]Contingency management (with network support) was more effective than control (low to medium effect size) at reducing drinking quantity when assessed at 6-, 9- and 21- month follow-up." (p. 281) PDA post-treatment: Effekt: - 0.80, CI: 95%; 15-month follow-up: Effekt: -0.50, CI: 95%; Drinking quantity: 6- month follow-up: Effekt: - 0.66, CI: 95%, 9-month follow-up: Effekt: -0.38, CI: 95%, 21-month follow-up: Effekt: -0.53, CI: 95% "[…] the addition of contingency management to standard care was beneficial in reducing the number of participants who relapsed to heavy drinking. Furthermore, the addition of contingency management to standard care was beneficial in reducing attrition rates." (p. 281-283); Number relapsed to heavy drinking: Effekt: 0.43, CI: 95%; Attrition (dropout): Effekt: 0.19, CI: 95%				

	- "The addition of contingency management to network support was not beneficial in maintaining abstinence both post- treatment and up to 9-month follow-up." (p. 284) **Angehörigenarbeit:** - "The clinical evidence showed that social network and environment-based therapies were significantly better than control at maintaining abstinence (moderate effect size) when assessed post-treatment and at 6-, 9-, 12-, 15- and 24- month follow-up." (p. 288); PDA post-treatment: Effekt: -0.76, CI: 95%; 6-month follow-up: Effekt: -0.75, CI: 95%; 9-month follow-up: Effekt: - 0.70, CI: 95%; 12-month follow-up: Effekt: -0.59, CI: 95%; 15-month follow-up: Effekt: -0.68, CI: 95%; 24-month follow-up: Effekt: - 0.49, CI: 95% "The clinical evidence did not reveal any significant difference between social network and environment- based therapies and other active interventions in maintaining abstinence, reducing the quantity of alcohol consumed, reducing the number of drinking days and attrition." (p. 290) **Paartherapie:** "[…] over longer periods, couples therapy was significantly more effective than other therapies in maintaining abstinence and/or light drinking (moderate effect size) when assessed up to 12-month follow-up. […]Couples therapy was significantly more effective than other active interventions in reducing heavy drinking episodes when assessed up to 12-month follow-up." (p. 296); PDA/light (no alcohol or one to three drinks) at 12- month follow-up: Effekt: - 0.54, CI: 95%;				

	- Percentage of days heavy drinking (more than drinks per day) at 12- month follow-up: Effekt: - 0.71, CI: 95% “No significant difference was observed between BCT and other forms of couples therapy in maintaining abstinence when assessed post-treatment and up to 24- month follow-up. Similarly, no difference between these groups was observed in reducing heavy drinking and attrition rates post-treatment, and up to 12-month follow-up.“ (p. 296) - „[…] no significant benefit of more intensive couples therapy over brief couples therapy in reducing heavy drinking was observed up to 18-month follow-up.” (p. 300) - „The addition of parental skills training to BCT did not significant improve abstinence rates both post-treatment and up to 12-month follow- up.” (p. 300) - **Psychodynamische Kurzzeittherapie:** - “At 15-month follow-up, short-term psychodynamic therapy was significantly more effective than other therapies (in this case, cognitive behavioural relapse prevention) in maintaining abstinence, although the effect size was moderate.” (p. 312); Effekt: - 0.64, CI: 95% **Patientengruppen:** - “Guided self-help was significantly more effective than non-guided self-help in reducing the quantity of drinks consumed per week when assessed at 9-month follow- up.” (p. 318); Effekt: -0.54, CI: 95				

Relevante Literatur aus Leitlinie	MI: Hester (2005),Rosenblum (2005b), Sellman (2001), Davidson (2007), Match (1997), Shakeshaft (2002), Sobell (2002), UKATT (2005) CBT: Burtscheidt (2001), Monti (1993), Rosenblum (2005b), Connors (2001), Davidson (2007), Easton (2007), Eriksen (1986b), Lam (2009), Litt (2003), Match (1997), Morgenstern (2007), Sandahl (1998), Shakeshaft (2002), Sitharthan (1997), Vedel (2008), Walitzer (2009), Marques (2001), Monti (1990), Rosenblum (2005a), kog. VT mit Kontingenz-management: Litt (2007), Alessi (2007), Petry (2000) kog. VT ohne Kontingenzmanagement: Alden (1988), Monti (1993), Kavanagh (2006), Sitharthani (1997), Walitzer (2004), Heather (2000) Angehörigenarbeit: Litt (2007), Leigh (2009), UKATT (2005) Paartherapie: Falsstewart (2005, 2006), Lam (2009), Ofarrel (1992), Sobell (2000), Vedel (2008), Walitzer (2004), Zweben (1988) Psychodynamische Kurzzeittherapie: Sandahl (1998); Patientengruppen: Andreasson (2002)			Bouza, Magro, Muñoz, & Amate (2004), Brewer, Meyers, & Johnsen (2000), Kristenson (1995)	

Klinische Fragestellung

Welche Ergebnismaße (z.B. Abstinenz, Konsumreduktion, Rückfallraten, Mortalität, berufliche (Re-)Integration, Lebenszufriedenheit) sollen berücksichtigt werden?

Guideline	**NICE (CG115), UK, National Institute for Health and Clinical Excellende (NICE), 2011.**	**NICE (CG 100), UK, National Institute for Health and Clinical Excellence (NICE),**	**VA/DoD USA, Department of Defense, 2009.**	**Incorporating alcohol pharmacotherapies into medical practice. USA, Department of Health and Human Services, 2009.**	**Treatment of Patients with Substance Use Disorders. USA, American Psychiatric Association, 2006.**
Aussage ja/nein	ja	nein	nein	ja	nein
Evidenz (levels of evidence)	/			/	
Empfehlungsgrad (A, B, 0, KKP)	KKP			KKP	
Aussage inhaltlich	Abstinenz, Konsumreduktion, Ergebnis- und Prozessevaluation, Katamnesen 1 Monat bis 5 Jahre			Standardisierte Outcomemaße: time to relapse, time to first drink, drinks/day, Cumulative abstinence duration, Craving (OCDS, VAS)	
Relevante Literatur aus Leitlinie					

Klinische Fragestellung

Welche Wirksamkeit (positive, fehlende, unerwünschte) weisen postakute Interventionsformen im kontrollierten Vergleich bei der Behandlung des Alkoholabhängigkeitssyndroms auf?

Guideline	**Reha-Therapiestandards Alkoholabhängigkeit - Leitlinie für die medizinische Rehabilitation der Rentenversicherung (Deutsche Rentenversicherung, 2011)**	**Leitlinie zur sozialmedizinischen Beurteilung bei Abhängigkeits-erkrankungen (Deutsche Rentenversicherung, 2010)**	**AWMF S2-Leitlinie: Postakutbehandlung alkoholbezogener Störungen (Geyer et al., 2003)**
Aussage ja/nein	ja	nein	ja
Evidenz (levels of evidence)	/		/
Empfehlungsgrad (A, B, 0, KKP)	KKP		KKP

Aussage inhaltlich	Wirksamkeit von KVT eingebettet in multimodales Therapieprogramm; Vermeidung von Rückfällen durch SKT, Gemeindeprogramme, Verhaltensverträge, Motivationsförderung, Familien-/Paartherapie (S. 25)		a) Behandlung alkoholbezogener Störungen effektiver als Nicht- Behandlung und soll empfohlen werden. (S. 4) b) Effektivität der stationären Postakut-behandlung auch im internat. Vergleich (S. 5)
Relevante Literatur aus Leitlinie			

Klinische Fragestellung

Von welchen der folgenden Bedingungen ist die Wirksamkeit abhängig?

Patientengruppen (z.B. Co- und Multimorbidität, Geschlecht, Alter, sozioökonomischer Status, Migrationshintergrund)

	Reha-Therapiestandards Alkoholabhängigkeit - Leitlinie für die medizinische Rehabilitation der Rentenversicherung (Deutsche Rentenversicherung, 2011)	**Leitlinie zur sozialmedizinischen Beurteilung bei Abhängigkeitserkrankungen (Deutsche Rentenversicherung, 2010)**	**AWMF S2-Leitlinie: Postakutbehandlung alkoholbezogener Störungen (Geyer et al., 2003)**
Aussage ja/nein	ja	nein	ja
Evidenz (levels of evidence)	/		/ /
Empfehlungsgrad (A, B, 0, KKP)	KKP		KKP KKP
Aussage inhaltlich	Bislang gibt es keine eindeutigen Hinweise, welche Patienten mit welchen Merkmalen von welcher Therapiemethode am besten profitieren (Ia). Alkoholabhängige Patienten, die obdachlos bzw. arbeitslos sind oder an einer komorbiden psychiatrischen Störung leiden, bedürfen gleichermaßen der Unterstützung und Behandlung dieser zusätzlichen Problembereiche (Ia). (S. 29)		a) höhere Erfolgschancen bei Erwerbstätigkeit (S. 5) b) Komorbide Störungen mitbehandeln (S. 9)
Relevante Literatur aus Leitlinie			

Klinische Fragestellung
Von welchen der folgenden Bedingungen ist die Wirksamkeit abhängig?
Setting (ambulant, ganztägig ambulant, stationär)

Guideline	**Reha-Therapiestandards Alkoholabhängigkeit - Leitlinie für die medizinische Rehabilitation der Rentenversicherung (Deutsche**	**Leitlinie zur sozialmedizinischen Beurteilung bei Abhängigkeitserkrankungen (Deutsche Rentenversicherung, 2010)**	**AWMF S2-Leitlinie: Postakutbehandlung alkoholbezogener Störungen (Geyer et al., 2003)**
Aussage ja/nein	nein	ja	ja
Evidenz (levels of evidence)		/	/
Empfehlungsgrad (A, B, 0, KKP)		KKP	KKP
Aussage inhaltlich		keine detaillierte Aussage, welches Setting wirksamer ist, aber Kriterien, die bei der differenzierten Zuweisung berücksichtigt werden sollen (Ausmaß der bio-psycho-sozialen Störungen, Beschaffenheit des sozialen Umfelds des Abhängigkeitskranken hinsichtlich einer unterstützenden Funktion, berufliche Integration des Abhängigkeitskranken, Existenz einer stabilen Wohnsituation, Fähigkeit des Rehabilitanden zur aktiven Mitarbeit, zur regelmäßigen Teilnahme und zur Einhaltung des Therapieplans, Fähigkeit zur Einhaltung der Abstinenz, Dauer und Intensität der Abhängigkeitserkrankung, Einschätzung des Rehabilitanden und der betreuenden Suchtberatungsstelle).	Kriterien für die Zuweisung in ein bestimmtes Setting, Wirksamkeit des Community Reinforcement Approach (S. 5)
Relevante Literatur aus Leitlinie			

Klinische Fragestellung
Von welchen der folgenden Bedingungen ist die Wirksamkeit abhängig?
Behandlungsdauer

Guideline	**Reha-Therapiestandards Alkoholabhängigkeit - Leitlinie für die medizinische Rehabilitation der Rentenversicherung (Deutsche Rentenversicherung, 2011)**	**Leitlinie zur sozialmedizinischen Beurteilung bei Abhängigkeitserkrankungen (Deutsche Rentenversicherung, 2010)**	**AWMF S2-Leitlinie: Postakutbehandlung alkoholbezogener Störungen (Geyer et al., 2003)**

Aussage ja/nein	ja	ja	a
Evidenz (levels of evidence)	/	/	/
Empfehlungsgrad (A, B, 0, KKP)	KKP	KKP	KKP
Aussage inhaltlich	Die Behandlungsmethode sollte sich am Schweregrad der Alkoholabhängigkeit orientieren (je schwerer desto intensiver) (Ia). Bezüglich optimaler Dauer der Behandlung konnten keine allgemeingültigen Schlussfolgerungen gezogen werden (Ia).Für Patienten mit weniger stark ausgeprägter Symptomatik sind das Ausmaß und die Dauer anscheinend von geringer Bedeutung. Für diese Patientengruppe scheinen Selbsthilfe-Manuale oder wenige Therapiesitzungen den gleichen oder sogar besseren Effekt zu haben als intensivere Maßnahmen (Ia). (S. 21/22)	keine detaillierte Aussage, welche Behandlungsdauer wirksamer ist, aber Empfehlungen zur Dauer (Langzeittherapie stationär 10-16 Wochen, Kurzzeittherapie stationär 8 Wochen, ganztägig ambulante Rehabilitation 12 Wochen, niedrigfrequente ambulante Rehabilitation bis zu 18 Monaten mit maximal 120 Einzel- und Gruppengesprächen und 12 Angehörigengesprächen)	prognostisch ungünstig eingestufte Alkoholabhängige sollten länger als 8 Wochen behandelt werden (S. 5)
Relevante Literatur aus Leitlinie			

Klinische Fragestellung

Von welchen der folgenden Bedingungen ist die Wirksamkeit abhängig?

Interventionskomponenten

Guideline	**Reha-Therapiestandards Alkoholabhängigkeit - Leitlinie für die medizinische Rehabilitation der Rentenversicherung (Deutsche Rentenversicherung, 2011)**	**Leitlinie zur sozialmedizinischen Beurteilung bei Abhängigkeitserkrankungen (Deutsche Rentenversicherung, 2010)**	**AWMF S2-Leitlinie: Postakutbehandlung alkoholbezogener Störungen (Geyer et al., 2003)**
Aussage ja/nein	ja	ja	ja
Evidenz (levels of evidence)	/	/	/
Empfehlungsgrad (A, B, 0, KKP)	KKP	KKP	KKP
Aussage inhaltlich	Behandlungsmethoden, die Klienten aktiv in den Behandlungsprozess miteinbeziehen, scheinen günstigere Ergebnisse zu liefern. Techniken und Hilfen, die zu einer Stärkung der Ich-Fähigkeiten führen, können als generell wirksam angesehen werden. (S. 29)	Die Einbeziehung von arbeitsbezogenen Maßnah-men wird empfohlen, ohne dass Aussagen über die Wirksamkeit einer Rehabilitation mit oder ohne diese Interventionen genannt werden.	a) integrierte Behandlung empfohlen, da wirksamer als Einzelmethoden. b) Selbstmanagement wirksam c) 12-Schritte-Programm wirksam d) motivierende Gesprächsführung wirksam e) klassische VT wirksam f) CBT wirksam g) soziales Kompetenztraining wirksam h) Kontingenzmanagement wirksam i) klientenzentr. Gesprächspsychoth. wirksam j) Paar-/ u. Familienth. wirksam k) Ergo-/Arbeitsth. wirksam l)Sozialtherapie wirksam m) Körpertherapie wirksam (S. 4, 6-8)
Relevante Literatur aus Leitlinie			

Klinische Fragestellung

Welche Ergebnismaße (z.B. Abstinenz, Konsumreduktion, Rückfallraten, Mortalität, berufliche (Re-)Integration, Lebenszufriedenheit) sollen berücksichtigt werden?

Guideline	Reha-Therapiestandards Alkoholabhängigkeit - Leitlinie für die medizinische Rehabilitation der Rentenversicherung (Deutsche Rentenversicherung, 2011)	Leitlinie zur sozialmedizinischen Beurteilung bei Abhängigkeitserkrankungen (Deutsche Rentenversicherung, 2010)	AWMF S2-Leitlinie: Postakut-behandlung alkoholbezogener Störungen (Geyer et al., 2003)
Aussage ja/nein	nein	ja	nein
Evidenz (levels of evidence)		/	
Empfehlungsgrad (A, B, 0, KKP)		KKP	
Aussage inhaltlich		unterschiedliche Aspekte von Teilhabe als wesentliches Ziel der	
Relevante Literatur aus Leitlinie			

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