รายงานผลการศึกษา

Effective interventions for the screening, brief intervention, referral and treatment of harmful alcohol use: an umbrella review

ธันวาคม 2564

คณะผู้วิจัย

Miss.Siobhan Botwright
รศ. ดร. พญ.ธัญญรัตน์ อโนทัยสินทวี
ดร. ภญ.ปฤษฐพร กิ่งแก้ว
ดร.รุ่งนภา คำผาง
รศ. ดร.วรรณฤดี อิสรานุวัฒน์ชัย
Miss.Saudamini Vishwanath Dabak
นางสาวจิราธร สุตะวงศ์
ภญ.โชติกา สุวรรณพานิช
นางสาวนิชาต์ มูลคำ
นางสาวณิชาภา พัดเจริญ
นางสาวเณอริลิณญ์ ประทุมสุวรรณ์

สสส สำนักงานกองทุนสนับสนุนการสร้างเสริมสุขภาพ
HITAP Health Intervention and Technology Assessment Program

รายงานผลการศึกษา

Effective interventions for the screening, brief intervention, referral and treatment of harmful alcohol use: an umbrella review

ภายใต้โครงการพัฒนาข้อเสนอแนะเพื่อเพิ่มการเข้าถึงบริการดูแลผู้มีปัญหาการดื่มสุรา
เลขที่สัญญา ๖๑-๐๐-๑๘๑๒

เสนอ

สำนักงานกองทุนสนับสนุนการสร้างเสริมสุขภาพ (สสส.)

จัดทำโดย

Miss. Siobhan Botwright
รศ.ดร.พญ.ธัญญรัตน์ อโนทัยสินทวี
ดร.ภญ.ปฤษฐพร กิ่งแก้ว
ดร.รุ่งนภา คำผาง
รศ.ดร.วรรณฤดี อิสรานุวัฒน์ชัย
Miss. Saudamini Vishwanath Dabak
นางสาวนิชาต์ มูลคำ
นางสาวณิชาภา พัดเจริญ
นางสาวเณอริลิณญ์ ประทุมสุวรรณ์
นางสาวจิราธร สุตะวงศ์

มูลนิธิเพื่อการประเมินเทคโนโลยีและนโยบายด้านสุขภาพ

ธันวาคม 2564

ABSTRACT

Background Alcohol addiction has been identified as one of the leading causes of disability adjusted life years in Thailand. This umbrella review aims to provide a comprehensive overview of the interventions that are effective in the prevention and treatment of harmful alcohol use, and to provide a comparison with existing interventions provided in Thailand.

Methods We searched the Cochrane Systematic Review Database, MEDLINE via PubMed, EMBASE, PsycINFO, and the International HTA Database, for published systematic reviews on screening interventions in any population; interventions to prevent harmful alcohol use in individuals identified as risky drinkers; interventions to treat individuals with alcohol dependency or alcohol use disorder; or interventions to prevent relapse in individuals already treated for alcohol dependency or alcohol use disorder (recovery management). We only included systematic reviews of RCTs that reported on behavioural or health outcomes related to alcohol use. Articles were screened independently and in duplicate, following which data was extracted using a standardised data extraction form. Quality of systematic reviews was assessed using AMSTAR 2.

Results The literature search yielded 9,566 studies, of which 86 were included for data extraction. Most systematic reviews were judged to be of low quality. For screening, brief interventions and referral to treatment, there was mixed evidence of effectiveness, which may be due to differences in how the interventions were delivered. Brief counselling interventions and brief advice based on biomarkers of liver disease showed evidence of a durable effect over 1 year. Digital brief interventions were not shown to be superior to face to face interventions. Similarly, there is mixed evidence for most psychosocial interventions, with most studies suggesting small effect sizes of short duration. Peer-based mentoring for adolescents had a large effect size lasting more than 1 year, although results come from a single systematic review. Among pharmacological interventions, there is good evidence to suggest that topiramate (anticonvulsant), nalmefene (opioid antagonist), and galantamine are effective. Valproic acid and flupenthixol decanoate were shown to be effective, but with low certainty in the evidence. Evidence to support the use of disulfiram, baclofen, acamprosate, naltrexone, and varenicline remains inconclusive; no other pharmacological interventions were found to be effective. There was scant evidence on the effect of combining a psychosocial and pharmacological intervention, often with wide confidence intervals from underpowered studies. Regarding alternative therapies, acupuncture may be effective, but there is no evidence to support transcranial magnetic stimulation.

Discussion Our study identified seven interventions with moderate-high certainty of effect, none of which are systematically implemented in Thailand: brief counselling intervention, brief advice based on biomarkers of liver injury or liver fibrosis, brief intervention delivered by lay health worker, mentoring for adolescents delivered by peers, topiramate, nalmefene, and galantamine. We recommend further review of brief interventions, to understand the important factors influencing effectiveness, and further research to identify which combinations of psychosocial and pharmacological interventions are most effective.

POLICY RECOMMENDATIONS

1. **Interventions for inclusion under UCBP and/or within clinical practice guidelines**

   1.1. Among adults identified to have high-risk drinking behaviour, systematically conduct diagnostic tests for alcohol-related liver disease and discuss biomarker results during brief advice sessions.

   1.2. Implement a peer-led mentoring programme among youth with risky drinking. This may be best introduced as a pilot project among youth in settings with higher rates of alcohol misuse, in order to evaluate effectiveness and optimise implementation (e.g. frequency of sessions, training of mentors) before wide-scale roll-out. Current evidence suggests that the mentoring programme should provide general support to youth, without a specific focus on alcohol use.

2. **Revisions to NLEM**

   2.1. Evaluate the following medications for inclusion in the NLEM for treatment of alcohol use disorder: nalmefene, topiramate and galantamine.

3. **Research priorities**

   3.1. Evaluate therapies combining a psychosocial intervention with a pharmacological intervention with good evidence of effectiveness, to identify whether addition of the psychosocial intervention can improve size or duration of effect.

   3.2. Review the effectiveness of interventions to prevent relapse of recovered individuals.

   3.3. Identify the main determinants affecting the outcomes of screening, brief intervention, and referral to treatment interventions.

Table of Contents

Table of table

Table of figure

Effective interventions for the screening, brief intervention, referral and treatment of harmful alcohol use: an umbrella review

BACKGROUND

Alcohol use places a considerable burden on health systems, economies and societies across the globe. The 2016 Global Burden of Disease study ranked alcohol use as the seventh leading risk factor for premature death and disability, and the leading risk factor for people aged 15-49 years (1). Alcohol consumption has been linked to 60 acute and chronic diseases, with the base of evidence suggesting that risk of alcohol-attributable disability and death increases with volume of alcohol consumption and frequency of heavy drinking occasions (1–4). Beyond immediate health impact, alcohol misuse can place significant societal and economic burden on countries: studies conducted across twelve countries suggest that the economic burden ranges from 0.45% and 5.44% of gross domestic product (5,6).

Harmful alcohol use has been defined as drinking that causes detrimental health and social consequences for the drinker, the people around the drinker and society at large, as well as patterns of drinking that are associated with increased risk of adverse health consequences (5). Screening, brief interventions and referral to treatment typically seek to identify and prevent harmful alcohol use within the general population (7). Alcohol use disorders represent a sub-set of harmful alcohol use, characterised by chronic relapsing brain disorder with an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences (8). Treatment for alcohol use disorders may be psychosocial or pharmacological, with evidence that a combination of both approaches may be most effective (7,9).

In Thailand, the 2014 Burden of Disease estimated that alcohol addiction was responsible for 3% of the total disease burden, and the leading cause of disability adjusted life years (10). Prevalence of alcohol use disorders has been estimated at 5.4% (11). Thailand has a long history in implementing a coordinated alcohol control policy, following the five areas of intervention recommended in the WHO SAFER technical package, namely strengthening restrictions on alcohol availability; advancing drink-driving countermeasures; facilitating access to screening, brief

interventions and treatment; enforcing restrictions on alcohol advertising, sponsorship and promotion; and raising alcohol prices (12,13).

Interventions in Thailand are split into three levels (14). The **first** level includes campaigns and interventions in the general population to prevent and manage drinking behaviour; the **second** covers screening and brief interventions for individuals with risky drinking behaviours; and the **third** is concerned with the treatment and rehabilitation of individuals with alcohol use disorder. This review will examine interventions that could be provided under the latter two levels, to identify whether any effective screening, brief interventions or treatment for harmful alcohol use are currently missing from the benefits package provided under the Thai Universal Coverage Scheme.

Prior systematic reviews and umbrella reviews for prevention and treatment of harmful alcohol use have either focused on specific interventions (e.g. brief interventions (15–18), pharmacotherapy for withdrawal (19), self-help groups (20)) or specific populations (e.g. pregnant women (21,22), youth (23–25)). Moreover, existing reviews include limited analysis of applicability across settings and contexts, especially with regards to health system structures and resourcing (16). This umbrella review aims to provide a comprehensive overview of the interventions that are effective in the prevention and treatment of harmful alcohol use, and to provide a comparison with existing interventions provided in Thailand.

METHODS

The protocol for this review was designed following the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) (26) guidelines and the Cochrane Handbook Chapter V: Overviews of Reviews (27).

Search strategy

We searched for published systematic reviews in the Cochrane Systematic Review Database, MEDLINE via PubMed, EMBASE and PsycINFO. We additionally searched the International HTA Database (26), to identify any unpublished systematic reviews of alcohol interventions conducted by national health technology assessment (HTA) agencies. We developed our search terms based on the following themes: (1) alcohol use; (2) screening, brief intervention, referral; (3) psychosocial

treatment; (4) pharmacological treatment; (5) systematic review. The search terms were iteratively revised to ensure that no systematic reviews identified by existing umbrella reviews on alcohol interventions were missed. All databases were searched from inception to September 3, 2021. No language restrictions were applied. The search strategy for each database is detailed in the annex.

Eligibility criteria

We included systematic reviews of the following interventions:

- screening interventions in any population;
- interventions to prevent harmful alcohol use in individuals identified as risky drinkers;
- interventions to treat individuals with alcohol dependency or alcohol use disorder; and
- interventions to prevent relapse in individuals already treated for alcohol dependency or alcohol use disorder (recovery management).

We excluded any reviews of population level interventions, such as laws, regulations and taxes; advertising and awareness campaigns; and education campaigns or curricula that are conducted without prior risk screening. All comparators and study settings were eligible for inclusion. Studies had to report outcomes related to alcohol consumption, binge drinking, alcohol abstinence, alcohol-related injuries, or alcohol-related morbidity/mortality for inclusion. Studies evaluating substance use or addiction were excluded if alcohol-specific outcomes were not reported separately.

We only included systematic reviews of randomised controlled trials (RCTs), using the definition of systematic review from Krnic Martinic et al (26). We did not include reviews of observational studies since findings are often context specific and subject to greater bias than for RCTs (28). If a systematic review included both RCTs and observational studies, it was excluded if outcomes from RCTs were not reported separately.

Study selection

Search results were first screened by title/abstract and then by full text. At both steps, two reviewers screened studies independently, with any conflicts resolved by a third reviewer. Next,

studies were categorised by intervention type (Table 1), following classifications adapted the World Health Organization (WHO)/United Nations Office on Drugs and Crime (UNODC) International Standards for the Treatment of Drug Use Disorders (7). If one or more systematic reviews with meta-analysis were identified for a specific sub-category, only systematic reviews with meta-analysis were included in the data extraction step, to facilitate presentation of effect size.

Table 1 Categorisation of studies included in this review.

Category	Sub-category	Definition
1. Screening, brief intervention and referral	1.1 Screening	A brief process to identify indicators for the presence of alcohol use disorder.
	1.2 Brief intervention	A structured therapy of short duration (typically 5-30 minutes) with the aim of helping an individual cease or reduce their alcohol consumption.
	1.3 Referral to treatment	Interventions to speed up or reduce drop-out during referral to treatment, in individuals assessed to have clinically significant harmful alcohol use.
2. Psychosocial interventions	2.1 Cognitive behavioural therapy	Patients are introduced to new coping skills and cognitive strategies to replace maladaptive behavioural and thinking patterns.
	2.2 Contingency management	Patients are given concrete rewards to reinforce positive behaviours, such as abstinence, treatment attendance, or compliance with medication.
	2.3 Community reinforcement approach	Patients seek to modify the way in which they interact with their community in order to gain positive reinforcement, for example through family interactions, healthy social activities, or employment.
	2.4 Motivational interviewing/ enhancement	Patients increase their motivation to change a behaviour, through collaborative sessions with a clinician that recognise autonomy of the patient.
	2.5 Family-oriented treatment approach	A collection of methods that utilise family relationships to positively influence the behaviour of an individual with alcohol use disorder. Families and caregivers may participate in and support the treatment process.

	2.6 Mutual help group	Patients participate in groups that provide information, structured activities and peer support in a non-judgemental environment.
3. Pharmacological interventions	Medications to manage alcohol withdrawal and/or dependence, encompassing: 3.1 Anticonvulsants 3.2 Antidepressants 3.3 Antipsychotics 3.4 Aversive agents (medications that produce, or cause, a negative feeling/sensation if alcohol is misused) 3.5 Baclofen 3.6 Benzodiazepines 3.7 Glutamate antagonist 3.8 Opioid antagonist 3.9 Other	
4. Combination therapies	Two or more interventions are delivered simultaneously. The interventions may be from the same or different classes.	
5. Other	May include alternative therapies, including acupuncture, yoga, or brain stimulation.	

Data extraction and quality assessment

A standardised extraction form was developed and piloted before use. Data was extracted by a single reviewer and checked by a second reviewer for consistency. Quality of systematic reviews was assessed using A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2, which comprises 16 domains (7 critical domains and 9 non-critical domains) and provides an overall confidence rating in results of the review from 'High' (i.e., no or one non-critical weakness) to 'Critically low' (i.e., more than one critical flaw with or without non-critical weaknesses) (29). During data analysis, certainty of findings was judged from ''High'' to ''Very low'', according to AMSTAR rating, methodological quality of RCTs, size of effect, sample size, and concordance between results.

Differences between the protocol and review

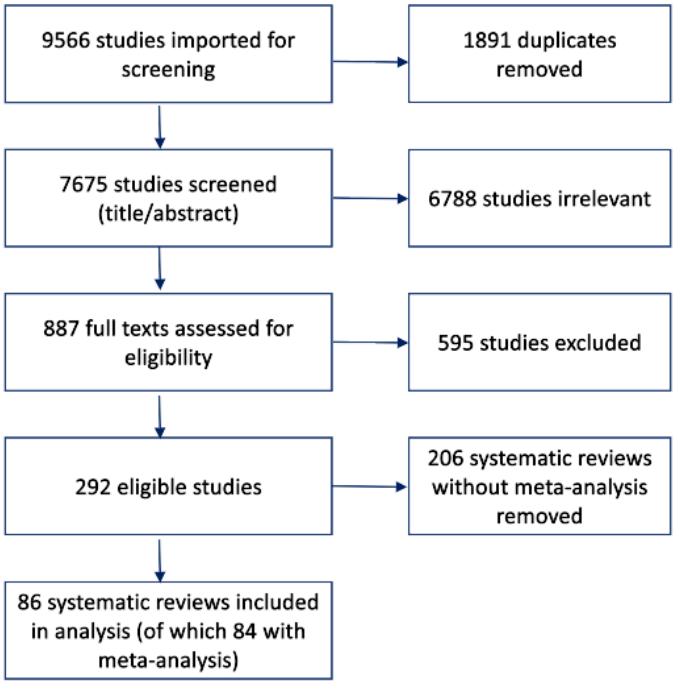
The protocol for this review is registered in PROSPERO, CRD42021275471. There are three main deviations from the original protocol. Firstly, to facilitate comparison of effect sizes, we restricted

our analysis to systematic reviews with meta-analysis, and only included systematic reviews without meta-analysis if no meta-analysis was identified for a given class of intervention. Secondly, in light of time constraints, we did not contact review authors for missing information. Finally, we did not use a citation matrix to exclude systematic reviews with overlapping RCTs, in order not to restrict the scope of interventions included in our review

RESULTS

The literature search yielded 9566 studies. After removal of duplicates and exclusion of studies based on the abstract or full text, 262 studies were identified as eligible for inclusion according to our criteria (Figure 1). Of these, 84 articles were systematic reviews with meta-analysis and were included for data extraction. The systematic reviews with meta-analysis encompassed all classes of intervention except referral to treatment. We therefore included the two systematic reviews without meta-analysis that had been identified for this category.

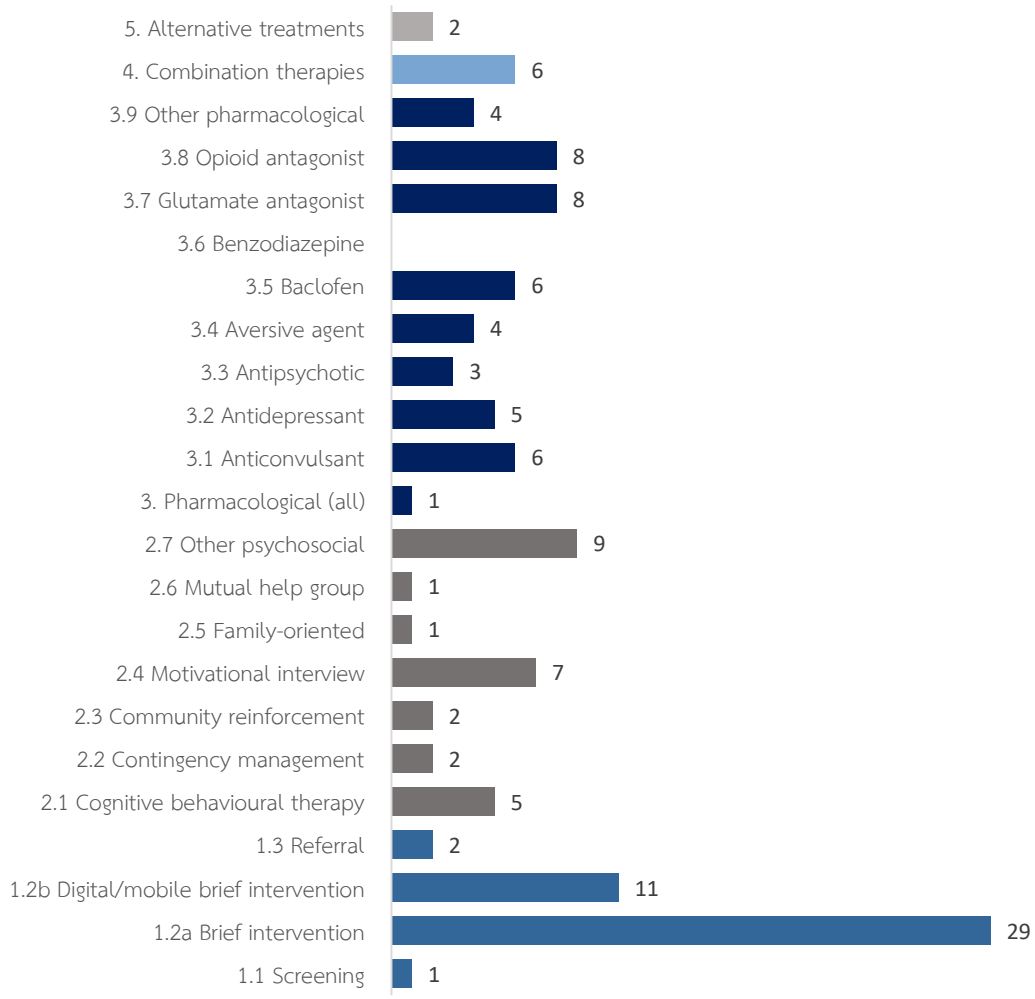
Figure 1 Flow diagram of study selection.



Of the included studies, there was 1 on screening (30), 29 on brief interventions (15,31–58), 11 on digital or mobile based brief interventions (33,41,46,48,55,59–64), 2 on referral to treatment

(65,66), 5 on cognitive behavioural therapy (52,56,67–69), 2 for contingency management (39,67), 2 for community reinforcement (70,71), 7 for motivational interviewing/enhancement (25,52,67,72–75), 1 for family-oriented treatment approach (25), 1 for mutual help groups (70), 9 for other psychosocial interventions (including counselling, mentoring, and controlled drinking) (23,52,74,76–82), 6 on anticonvulsants (67,83–87), 5 on antidepressants (67,88–91), 3 on antipsychotics (67,89,92), 4 on disulfiram (67,87,89,93), 6 on baclofen (67,86,89,94–96), 8 on acamprosate (67,86,87,89,97–100), 8 on opioid antagonists (67,86,87,89,97,101–103), 4 for other pharmacological interventions (67,89,104,105), 1 across all pharmacological interventions (91), 6 looking at combinations of interventions (39,67,89,98,106–108), 1 on acupuncture (109), and 1 on transcranial magnetic stimulation (110) (Figure 2). No reviews of benzodiazepines met our inclusion criteria, as only short-term craving or withdrawal outcomes were reported and not changes in behaviour or health outcomes. Only one study reported results for recovery management interventions (preventing relapse in treated individuals) (52).

Figure 2 Number of systematic reviews included for each type of intervention.



Many of the included reviews evaluated interventions in specific populations: 9 in youth, 6 in college/university students, 6 in patients with comorbid mental health or substance use disorders, 4 in hospital patients, 2 in patients seeking care for non-alcohol related problems in primary health facilities, 1 in cancer survivors, and 1 in pregnant women (Table 2). In most of the reviews, more than two-thirds of RCTs were conducted in Europe and North America, with the exception of two reviews that focused on low- and middle-income countries (LMICs) (52,54).

Overall, most of the systematic reviews received a low rating in the AMSTAR 2 quality assessment and only 10 of the 84 studies received a high rating (Table 2). The most common weaknesses

were not providing justification for excluded studies, not accounting for risk of bias in meta-analysis, and not reporting on the sources of funding for included studies.

Table 2 Characteristics of included studies.

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Palpacuer, 2010 (86)	DMA, NMA	alcohol dependence or AUD	3.1 anticonvulsants 3.5 baclofen 3.7 glutamate antagonist 3.8 opioid antagonist	NR	High
Cheng, 2020 (67)	NMA	alcohol dependency diagnosed	2.1 CBT, 2.2 CM, 2.4 MI 3.1 anticonvulsants 3.2 antidepressant 3.3 antipsychotic 3.4 aversive agent 3.5 baclofen 3.7 glutamate antagonist 3.8 opioid antagonist 3.9 other pharmacological 4. combinations	Primary care	Moderate
Minozzi, 2018 (94)	DMA	AUD	3.5 baclofen	Outpatient	High
Agabio, 2018 (105)	DMA	alcohol dependence	3.2 SSRI 3.2 5-HT2	Outpatient, inpatient	Low
Beyer, 2019 (31)	DMA, NMA	patients who	1.2 brief intervention	Primary care, including	Low

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
		presented to primary (including emergency) care for treatment not related to their alcohol consumption, but who screened positive for hazardous or harmful drinking		emergency departments and trauma centres were included if it was the patient's first contact	
Skinner, 2014 (93)	DMA	a diagnosis of alcohol abuse or dependence	3.4 aversive agent	NR	Critically low
Steele, 2021 (32)	DMA, NMA	Adolescents aged 12 to 20 years	1.2 brief intervention	Excluded college setting	Moderate
Rosner, 2010 (98)	DMA	Alcohol dependence	3.7 glutamate antagonist 4. combinations	NR	Low
Hennessy, 2019 (33)	NMA	Undergraduate college students, not older than 30 years of age	1.2 brief intervention	College, any country	Low
Riper, 2009 (34)	DMA	quantifiable levels of alcohol consumption that exceeded recommendations for low-risk drinking; students and pregnant women were excluded	1.2 brief intervention	Internet-based	Low

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Doherty, 2017 (35)	DMA	Hazardous or harmful alcohol use; military and veterans	1.2 brief intervention	NR	Critically low
Rose, 2018 (96)	DMA	Alcohol use disorder with anxiety or depression	3.5 baclofen	NR	Low
Huibers, 2007 (111)	DMA	No restrictions	2.1 CBT	Delivered by general practitioner or family physician	Low
McQueen, 2011 (36)	DMA	Heavy alcohol users admitted to general hospital inpatient units	1.2 brief intervention	hospital	Low
Pani, 2014 (83)	DMA	Alcohol dependence	3.1 anticonvulsant	NR	Low
Jarosz, 2013 (107)	DMA	Alcohol-dependent patients	4. combinations	NR	Moderate
Ipser, 2015 (88)	DMA	people diagnosed with alcohol dependence or abuse and an anxiety disorder	3.2 antidepressant	Outpatient or inpatient	Low
Ballesteros, 2004 (37)	DMA	hazardous drinkers	1.2 brief intervention	Primary care	Critically low
Rosner, 2010 (103)	DMA	alcohol dependence	3.8 opioid antagonist	NR	Low
Elzerbi, 2017 (38)	DMA	hazardous or harmful drinking	1.2 brief intervention	Emergency department	Critically low

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Gao, 2018 (39)	DMA, NMA	AUD	1.2 brief intervention 2.2 CM 4. combination	NR	Moderate
Bertholet, 2005 (40)	DMA	Risky drinker; individuals attending primary care facilities but not seeking help for alcohol-related problems	1.2 brief intervention	Primary care	Low
Donoghue, 2014 (59)	DMA	Hazardous/harmful alcohol consumption	1.2 brief intervention	health care settings, including primary care and the emergency department	Moderate
Carey, 2012 (41)	DMA	College or university students	1.2 brief intervention	College and university settings	Critically low
Simioni, 2015 (65)	SR	patients with excessive drinking, including those with AUDs, in somatic inpatient settings	1.3 referral to treatment	Somatic inpatient settings	Moderate
Jonas, 2012 (112)	DMA	adolescents with alcohol misuse identified by screening in primary care settings	1.2 brief intervention	Primary care settings	Moderate
Beich, 2003 (30)	DMA	NA	1.1 screening	General practice settings	Low

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Fachini, 2012 (43)	DMA	College students engaged in heavy episodic drinking	1.2 brief intervention	Public universities	Critically low
Egholm, 2018 (108)	DMA	risky drinking who were undergoing all types of surgical procedures	4. combination	NR	Low
Sayegh, 2017 (73)	DMA	Alcohol use disorder	2.4 MI	NR	Low
Donoghue, 2015 (97)	DMA	alcohol dependence or harmful alcohol use/alcohol abuse	3.7 glutamate antagonist 3.8 opioid antagonist	In/out-patient	Moderate
Mason, 2012 (99)	DMA	Alcohol dependence	3.7 glutamate antagonist	NR	Critically low
Carney, 2016 (44)	DMA	adolescents under the age of 19 in education who used alcohol or other drugs, or both, but did not meet the criteria for substance dependence, but had faced negative behavioural consequences due to their substance use	1.2 brief intervention	high school, secondary school, or a further education training college	High
Foxcroft, 2014 (72)	DMA	Aged up to 25 years old	2.4 MI	NR	High

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Palpacuer, 2015 (101)	DMA	non-abstinent alcohol dependence	3.8 opioid antagonist	NR	High
Prestwich, 2016 (71)	DMA	No specific population, the majority are college or university students	1.2 brief intervention	Educational settings, medical and community settings	Moderate
Sullivan, 2011 (45)	DMA	Unhealthy alcohol use	1.2 brief intervention	Primary care	Critically low
Foxcroft, 2015 (113)	DMA	University or college students	1.2 brief intervention	college or university settings	High
Lesouef, 2014 (95)	DMA	Alcohol-dependent	3.5 baclofen	NR	Moderate
Gilligan, 2019 (25)	DMA	young people who have not previously consumed alcohol, currently consume alcohol, or have heavy or problematic alcohol use	2.4 MI, 2.5 family-oriented approach	NR	High
Riper, 2018 (79)	Individual patient data meta-analysis (IPDMA)	Adults ≥ 18 years old with regular or problem drinking level (e.g. AUDIT ≥ 8 in male and ≥ 6 in female; FAST ≥ 3, etc.). Exclude: students and pregnant women	1.2 brief intervention (Digital-based interventions)	Individual patient data meta-analysis (IPDMA)	Low
Streeton, 2001 (102)	DMA	alcohol dependence or abuse	3.8 opioid antagonist	inpatient and outpatient	Critically low

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
MacArthur, 2018 (48)	DMA	Children and young people with binge drinking, heavy/hazardous drinking, or regular/problem drinking	1.2 brief intervention	School-based	Moderate
Simioni, 2015 (66)	SR	drinking above the lower risk limits	1.3 referral to treatment	Emergency departments	Critically low
Mellentin, 2017 (82)	DMA	Diagnosed with sub-clinical or clinical AUD	2.7 other	NR	Low
Kranzler, 2019 (84)	DMA	Alcohol dependence or alcohol use disorder	3.1 anticonvulsant	NR	Critically low
Oon-Arom, 2019 (104)	DMA	Patients people with problematic alcohol use	3.9 other	Trials conducted in in- or out-patient settings in any country were included	Moderate
Apodaca, 2003 (114)	DMA	Problem drinker	1.2 brief intervention	intervention provided by health professional	Low
Moreira, 2010 (47)	DMA	Alcohol misuse among university/college students	1.2 brief intervention	NR	High
Dinh-Zarr, 2009 (49)	DMA	People diagnosed with alcohol dependence, alcohol abuse, or hazardous use of alcohol	1.2 brief intervention	Clinical setting	Critically low

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Rooke, 2010 (60)	DMA	No specific population, the majority are young adults	1.2 brief intervention (Digital-based interventions)	Home and research setting	Critically low
Elzerbi, 2015 (50)	DMA	participants were non-treatment-seeking and met a minimum criterion of hazardous or harmful drinking	1.2 brief intervention	Primary healthcare or emergency department	Critically low
Wilk, 1997 (51)	DMA	Alcohol abuse, dependence,or heavy drinking	1.2 brief intervention	Primary care and hospital	Critically low
Hunt, 2019 (74)	DMA	diagnosed with a severe mental illness	2.4 MI 2.6 mutual help group 2.7 other	NR	High
Van Ginneken, 2021 (52)	DMA	children (aged < 18 years) and adults with mental disorders [includes AUD] or distress seeking first-level care/primary care or detected in the community in LMICs	1.2 brief intervention 2.1 CBT 2.4 MI 2.7 other	LMICs, intervention delivered by primary-level workers	High
O'Connor, 2018 (53)	DMA	adolescents or adults age 12 years or older who nondependent alcohol users	1.2 brief intervention	primary care, other outpatient health care settings	Moderate
Thomas, 2011 (115)	DMA	adolescents	2.7 other	Community-based	Moderate

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Ghosh, 2021 (54)	DMA	non-dependent, harmful or hazardous alcohol use	1.2 brief intervention	LMICs	Critically low
Vanderkam, 2020 (116)	DMA	adult patients with alcohol or tobacco use disorder	3.9 other	NR	Moderate
Henssler, 2020 (77)	DMA, NMA	Alcohol dependence or alcohol abuse/harmful use	2.7 other	community-based, out-patient, in-patient	Moderate
Maiti, 2017 (110)	DMA	diagnosis of substance use disorder	5. alternative therapy	NR	Moderate
Ujhelyi-Gomez, 2021 (76)	DMA	Alcohol use (casual or dependent)	2.7 other	NR	Low
Murphy, 2021 (106)	DMA	AUD	4. combination	Alcohol clinic	Moderate
Davis, 2017 (68)	DMA	Emerging adults ages 18–25, not college students	2.1 CBT	Not for profit and Hospital	Moderate
Stokes, 2020 (91)	DMA	Substance abuse/dependence and diagnosis of bipolar or major depressive disorder	3. pharmacological (all) 3.2 antidepressants	NR	Moderate
Southern, 2016 (109)	DMA	Alcohol dependence, inpatients of at least 14 days, have been drinking within 10 days of enrolment	5. alternative therapy	outpatient alcoholism treatment programme	Moderate

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Bendtsen, 2021 (61)	DMA	Risky drinker (harmful and hazardous)	1.2 brief intervention	Any setting	Moderate
Saxton, 2021 (55)	DMA	hazardous alcohol use, 16 years and older	1.2 brief intervention	NR	Low
Dedert, 2014 (62)	DMA	Alcohol misuse, high-risk AUD, AUD diagnosis	1.2 brief intervention (digital)	Outpatients in any setting (general medical, emergency room, and community) or participants not engaged in clinical care who are enrolled through self-assessments	High
Hunter, 2019 (70)	DMA	Alcohol dependents	2.3 community re-enforcement	community-based	Low
Li, 2021 (117)	DMA, NMA	adults with alcohol use disorders and comorbid depression or depressive symptoms	3.2 antidepressant 3.3 antipsychotic 3.4 aversive agent 3.5 baclofen 3.7 glutamate antagonist 3.8 opioid antagonist 3.9 other 4. combination	NR	Moderate
Dranitsaris, 2009 (100)	DMA	Patients with alcohol dependence	3.7 glutamate antagonist	NR	Moderate
Cheng, 2020 (85)	DMA	alcohol dependence or AUD	3.1 anticonvulsant	NR	Critically low

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Mujcic, 2020 (78)	DMA	Cancer survivors who have drunk alcohol in the past week	2.7 other	Distance-based	High
Hai, 2019 (81)	DMA	Women of childbearing age (18-45 years) with any level of drinking behaviour	2.7 other	Internet, prenatal clinic, hospitals	Low
Klimas, 2018 (56)	DMA	Problem alcohol use	1.2 brief intervention 2.1 CBT 2.4 MI	NR	High
Kaner, 2018 (15)	DMA	people with hazardous or harmful alcohol consumption as identified by a screening tool	1.2 brief intervention	Primary care	Low
Kaner, 2017 (63)	DMA	People living in the community whose alcohol consumption had been screened as hazardous or harmful	1.2 brief intervention (digital)	NR	Critically low
Kishi, 2013 (92)	DMA	primary diagnosis of alcohol dependence	3.3 antipsychotics	NR	Critically low
Riper, 2011 (80)	DMA	AUD, excluding students	2.7 other	Workplace, community, hospital	Low
Jonas, 2014 (87)	DMA	Adults with AUD	3.1 anticonvulsant 3.4 aversive agent 3.7 glutamate antagonist 3.8 opioid antagonist	Outpatient settings	Moderate

Author/year	Study type	Population	Interventions	Context/setting	AMSTAR rating
Bastola, 2020 (64)	DMA	Occasional drinker and/or binge drinking college students and younger adults (up to 39 years)	1.2 brief intervention	Mobile-based provision	Critically low
Yuvaraj, 2019 (57)	DMA	adults aged more than 18 years, in employment and who were found to be current alcohol drinkers	1.2 brief intervention	face-to-face counselling or web-based intervention	Moderate
Subhani, 2021 (58)	DMA	High-risk drinking behaviour	1.2 brief intervention	NR	High

AUD – alcohol use disorder; CBT – cognitive behavioural therapy; CM – contingency management; DMA – systematic review with direct meta-analysis; LMIC – low- and middle-income country; MI – motivational interview/enhancement; NA – not applicable; NMA- systematic review with network meta-analysis; NR – not reported; SR – systematic review

1. Screening, brief intervention and referral to treatment

Only one low-quality review was identified for screening interventions. For universal screening in general practice settings, the review suggests that for every 1,000 people screened, around 25 will qualify for brief intervention, following which two or three patients will reduce their alcohol consumption to below recommended maximum levels after 12 months (30). Overall methodological quality was low, suggesting potential overestimation of effect (30). The review concluded that the intensive effort from general practitioners was not justified given the small effect size. It should be noted that all RCTs were conducted in either the USA, UK, or Australia.

For brief interventions, there was mixed evidence across the 40 reviews identified, which may be due to differences in how the interventions were delivered. In general, brief interventions were normally defined as a 10–15-minute session, which may or may not be followed up with follow-up sessions less than 5 minutes. While brief interventions appear to be effective in reducing alcohol consumption in the short-term, the effect does not appear to extend beyond one year. However, it should be noted that a review of brief advice based on biomarkers of liver injury

found a significant effect lasting 3 years post-intervention (58). Brief motivational interviewing has shown a small effect in reducing alcohol consumption, mostly in studies in adolescents, but it ceases to be effective for outcomes to reduce drinking by 50% or more (32,51,75). There is moderate quality evidence that brief counselling interventions may be effective in the longer term, especially in risky drinkers (53,57,112), and one review from LMICs suggests that it is possible to deliver effective brief interventions through lay health workers (52). Minimal interventions (less than 5 minutes) did not show any effect (37), although there is no evidence to suggest that extended brief interventions, which entail 10-15 minute follow-up sessions, provide any additional benefit (15,37). Personalized normative feedback combined with self-directed interventions does not appear to be effective (55).

Most digital brief interventions (including screening and brief intervention) aiming to reduce alcohol consumption had a short-term effect among hazardous or harmful alcohol users in community and health-care settings. Electronic screening and brief interventions were effective in reducing alcohol consumption among hazardous alcohol users (up to 12 months follow-up) (59). Personalised advice for hazardous or harmful alcohol users using computers or mobile devices may reduce heavy drinking better than no intervention or providing only general health information, but there was little or no difference when compared with face to face conversation (63).

School-based digital intervention for young adults was effective among college students only for short term follow-up and there was no effect in terms of reduction in binge drinking behaviour. Computer-delivered interventions for alcohol use have a significant effect for reducing alcohol consumption (standardised drinking behaviour), among young adults (60). Some brief intervention programs for college student delivered through online platforms were effective in reducing drinking frequency (e-CHUG) and quantity (AlcEDU, THRIVE, and e-CHUG) compared to control group (assessment only), measured 0–3 months post-intervention (33). Similar findings on short-term (≤ 13 weeks) effectiveness of computer-delivered interventions (CDIs) were found in another systematic review; and there are no statistically significant differences for longer follow-up (41). Another systematic review study also suggested that no significant different for alcohol consumption in long term outcomes (6 to 12 months), either among college student or adult group (62).

There were only two reviews looking at alcohol treatment utilisation as an outcome. There were no meta-analysis results available. There was no evidence of efficacy for inpatient brief

intervention alone for increasing subsequent alcohol treatment utilisation among AUDs patients from somatic inpatient settings; however, interventions with post-discharge booster sessions might be beneficial (65,66).

2. Psychosocial interventions

There is mixed evidence for the effectiveness of cognitive behavioural therapy (CBT). Whilst one review found no evidence of effect for abstinence in alcohol dependent individuals after 1 year (67), another found CBT to be effective for treatment, but not prevention, in young adults (68). One review examining the relative effect of delivering CBT through general practitioners instead of nurses found no significant difference in outcomes after 1 year (111). Another review considering delivery of CBT by lay health workers found mixed evidence of effectiveness compared to enhanced usual care: whilst there does not appear to be a durable effect, the evidence is based on low quality evidence from two studies (52).

For contingency management, one review found no evidence of effectiveness in maintaining abstinence after 1 year (67). Another review found that contingency management found no abstinence benefit when compared with control or any other comparator, but there was a significant effect of contingency management combined with another psychosocial intervention (defined in the paper as cognitive behavioural therapy, motivational interviewing, or twelve step facilitation) during treatment, although the effect was not shown to last after treatment end (39). In both reviews, insignificant effects were driven by very large confidence intervals, indicating the need for better data.

For the community reinforcement approach, reviews provide support for the effect of social network interventions on promoting abstinence in alcohol dependent populations and reducing consumption in college students (70,71). However, one review had high risk of bias, and the other suggested that even large changes in social influence only yield very minor changes in alcohol use, and the meta-analysis showed high heterogeneity. There is therefore limited evidence to support the implementation of social network interventions.

For motivational interviewing, 1 review found no significant effect, 1 found a significant effect, and 4 studies had mixed evidence across outcomes and timeframes (25,52,67,72,73,118). Both studies reporting abstinence at 12 months found no significant effect (67,118). The only meta-analysis including a sample size of more than 1,000, which was judged to be high quality, found a

significant effect in favour of motivational interviewing for young adults across all outcomes up to 4 months, but for longer time periods effect sizes were either not significant or very small (72). All reviews concluded that there is either no or minimal benefit from motivational interviewing. It appears that any effect is probably not durable beyond 3-6 months, and there is no evidence to suggest that intensive motivational interviewing provides any additional benefit over conventional motivational interviewing (75). This contrasts with a review on mentoring for adolescents, which found a long-term significant effect beyond 1 year (115). Two mentoring interventions were covered by the meta-analysis: a programme to match youth with a Big Brother or Big Sister, who met with the youth around once a week for 3-4 hours to provide general support (rather than explicitly aiming to change behaviour); and a peer-mentoring programme conducted around once a week by mentors who themselves had often participated in the programme, targeted at youth from deprived backgrounds. In both programmes, the mentor received supervision and support from a case manager, and the relationship between mentor and youth lasted on average around 1 year (115).

The only review identified for family-oriented treatment approaches found no evidence that family-based prevention programmes targeted at the parents of young people reduce alcohol consumption (25). Similarly, only one review was identified for mutual help groups, suggesting limited effectiveness of twelve step facilitation (118), although the review only included individuals with comorbid mental illness.

One review evaluating the effectiveness of psychosocial interventions during pregnancy and motherhood (encompassing brief interventions, cognitive behavioural therapy, and motivational interviewing) found a very large significant effect for interventions during pregnancy, and a small effect for interventions during motherhood (76), suggesting that interventions may be more effective in populations with a strong rationale for reducing alcohol consumption. However, this evidence was based on RCTs with high risk of bias and the review did not report on duration of effect.

Two reviews with different target populations and comparators found no evidence to support the use of controlled drinking, either for dependent individuals or casual drinkers (77,78). A review of cue exposure therapy similarly found no evidence of effect (82).

In terms of the delivery of psychosocial interventions, 1 review examined the effectiveness of interventions delivered by primary workers in LMICs (52). Although no evidence of effect was

found for counselling by lay counsellors or for comprehensive psychosocial rehabilitation at the community level, in both cases the evidence for the intervention comes from a single underpowered study with wide confidence intervals. Another review identified a single study suggesting that reducing caseload of community workers has no effect, although the study was also underpowered (118).

Internet-based alcohol interventions in community and healthcare settings are effective in reducing mean weekly alcohol consumption and in achieving adherence to low-risk drinking limits among adults (79). However, there is no significant effective in reducing alcohol consumption in workplace settings (79), and other population group (women of childbearing age (81) and students (64).

3. Pharmacological interventions

A pooled analysis of all pharmacological interventions for the treatment of comorbid alcohol use and mood disorders found no significant effect, except for abstinence from alcohol in patients with comorbid major depressive disorder (91). Among all patients with alcohol use disorder, there is no evidence that adding brief intervention to pharmacotherapy has any effect on abstinence after treatment ends (39). Both these results should be interpreted with caution, as they pool across many pharmacological interventions.

A review of anticonvulsants suggests they may be effective in treating alcohol dependence, although the result for abstinence was not significant (83). Reviews evaluating individual anticonvulsants indicate that carbamazepine and oxcarbazepine are not effective (67). Although there is mixed evidence for gabapentin, the effect for most outcomes is not significant and the others have only a very small effect (84,85). There is weak evidence from one study that valproic acid may be effective (87). Topiramate is the only anticonvulsant with good evidence of effectiveness against both placebo and other pharmacological interventions (67,86).

None of the antidepressants show a significant effect (67,88,89,91,105). One low quality review found a significant improvement in abstinence with SSRI compared to placebo (105), but two other reviews found no significant effect (89,91).

Two reviews aggregating across antipsychotics found no significant effect (89,92). Considering individual antipsychotics, none were shown to be effective (67,89,92), with the exception of

flupentixol decanoate, which had a significant improvement on abstinence rates at 1 year and AUDIT scores after 3 months (67,92).

Disulfiram was the only aversive agent identified in the review. Two moderate quality reviews found no effect on abstinence after 1 year; the mean difference was not significant and close to zero (67,92). Another moderate quality study in patients with comorbid depression found a large odds ratio for remission rate, but the standard mean difference was not significant and the timeline was not specified (89). A fourth review found a significant effect looking across multiple measures of alcohol use, with significantly higher efficacy in open label trials and those with nurse supervision, suggesting that real world effectiveness of disulfiram may be higher than would be expected from the results of blinded RCTs (93), although the review was judged to be critically low quality.

For baclofen, two studies showed no significant effect against any outcome or comparator (89,96), one study found a significant increase in abstinence at 1 year, although with a wide confidence interval (67), and 3 studies found mixed evidence across outcomes (but with no consistency across reviews for the outcomes that were significant) (86,94,95). There remains inconclusive evidence on the benefit of baclofen.

There is mixed evidence for the effectiveness of acamprosate. Although many reviews have shown a significant increase in abstinence compares to placebo over the short and long term (67,97,99,100,103), one review found mixed results across outcomes (87), and two reviews found no significant effect compared with placebo (86,89). When compared against other pharmacological interventions, there is either no significant effect or acamprosate is inferior to the comparator (86,87,89,95,98). Similarly, there is discordance among reviews considering a combined regimen of acamprosate and naltrexone, with one study finding a significant effect for abstinence after 1 year and another finding no effect on abstinence, although the latter may be due insufficient power to detect an effect (67,98).

For opioid antagonists, nalmefene showed a small but significant effect across all outcomes when compared to placebo, with the exception for mortality which had too great a confidence interval to show any significant effect (86,87,101). However, there was no significant effect compared to any other pharmacological treatment, except one study which showed superiority of topiramate (86). By contrast, the evidence for naltrexone is less conclusive. Two reviews rated as critically low or low quality found naltrexone to be effective compared to placebo across all assessed

outcomes (102,103), 1 moderate quality review found no significant effect compared to placebo for AUD remission rate in individuals with comorbid mental health disorders (89), and 3 reviews had mixed evidence across outcomes (86,87,97). For the reviews with mixed evidence, one moderate quality review found that the effect for 50mg oral naltrexone was no longer significant when only RCTs with low risk of bias were included; for 100mg oral naltrexone there is a significant effect for heavy drinking but not for return to drinking or alcohol consumption; and for injectable naltrexone there is an effect for reduced consumption but not return to drinking (87). Another high quality review with mixed evidence only found a significant effect for 1 of 5 outcomes when naltrexone was compared with placebo, and provides some evidence that naltrexone may be inferior to baclofen or topiramate (86). There is also evidence that naltrexone may potentially be inferior to disulfiram (89), although a critically low quality review found no significant benefit of disulfiram compared with naltrexone (93). Naltrexone was not found to be effective when delivered in combination with disulfiram, GHB, or escitalopram (67,89), although one review suggests that naltrexone, escitalopram and GHB delivered in combination may be effective for improving abstinence (67), and another review found improvements in AUD remission rate compared with placebo when naltrexone was delivered in combination with an SSRI (89). There was a very large effect size for preventing relapse and heavy drinking days when naltrexone was delivered with psychosocial interventions, although results come from a single RCT so should be interpreted with caution, and it is worth noting that no significant effect was found for abstinence at longer periods of follow-up (106,107).

One review including antiepileptics found a significant reduction in remission rate among patients with comorbid depression, although no superiority was shown when compared against other pharmacological interventions with evidence of effectiveness (89). Other reviews found evidence that galantamine (commonly used in the treatment of Alzheimers) may improve abstinence after 1 year (67), and mixed evidence for varenicline (commonly used for smoking cessation) to treat problematic alcohol use, as there was a significant effect for reducing consumption but not heavy drinking days (104). No evidence was found to suggest effectiveness of atenolol (67), bromocriptine (89), buspirone (89), GHB (67), levetiracetam (67), lisuride (67), lithium (89), memantine (89), modafinil (67), or pregabalin (67).

4. Combining interventions

One review looking at the combination of psychosocial and pharmacological interventions found a significant improvement in abstinence outcomes during treatment, but the confidence intervals were too wide to identify a significant effect after treatment end (39). As discussed in the section above, there is some evidence to support the combination of the following combinations: naltrexone + psychosocial, naltrexone + GHB + escitalopram, acamprosate + naltrexone. Conversely, there is currently no evidence to support the following combinations: disulfiram + naltrexone, GHB + naltrexone, escitalopram + naltrexone.

5. Alternative treatments

A review of transcranial magnetic stimulation studies found no significant effect in alcohol dependent individuals (110). However, a review of acupuncture did find an effect in reducing craving and withdrawal (109).

DISCUSSION

Our review provides an overview of interventions that have been evaluated for identifying, preventing, and treating harmful alcohol use. In total we identified seven interventions with moderate to high certainty of effectiveness (Table 3), none of which are systematically implemented in Thailand.

Although our review questioned the effectiveness of screening interventions, this finding come from a single review on universal screening in general practice settings, and it is possible that community-based screening, or screening for certain high-risk groups, may be more effective. Furthermore, the effectiveness of screening is likely to be very context-specific, as it depends on access and utilisation of services, as well as the incidence of harmful drinking in a given setting. We therefore recommend further review of screening interventions, in particular to identify best practice to effectively identify individuals requiring brief intervention and/or referral to treatment.

Brief interventions are covered generally under the universal healthcare benefit package in Thailand. Our review suggests that the majority of brief interventions are of short duration without long-term effect. Since there is moderate evidence of the effectiveness of brief interventions delivered by lay health workers, regular delivery of brief interventions by this cadre of health

workers may improve accessibility and help to address the short duration of effect. In terms of the content of brief interventions, providing feedback to hazardous drinkers based on biomarkers of liver damage has been shown to have a strong, long-lasting effect at three years. Similarly, brief counselling interventions appear to have longer duration of effect than other brief interventions. It may be beneficial to conduct a more in-depth review to identify the key features of brief interventions that have greater effect, in order to develop a guideline for implementation of brief interventions in Thailand.

Though digital technology could potentially support screening, brief interventions, and referral to treatment for alcohol dependence, moderate-to-low quality evidence suggests there may only be short-term effects. Personalised advice through computers or mobile devices may make little or no difference to reduce drinking compared to face-to-face conversation. Surprisingly, mobile phone text messaging for preventing young people on binge drinking behaviour may have no impact or making problem drinking worse. Theory-based approaches for designing and developing behavioural change intervention had been promoted by the Medical Research Council (MRC) (119). Only a few systematic reviews had extracted theory constructs including normative beliefs, social norms, social support, social cognitive theory, transtheoretical model of behavioural change and health belief model. However, it is still unclear whether these theory constructs are associated with greater effect due to aggregation bias in meta-analysis. Individual patient data meta-analysis (IPDMA) could be used to identify moderators at the participant, intervention, or study design levels that are associated with treatment outcomes. Future research could explore which components are associated with increasing effectiveness and could potential inform future behavioural change complex interventions.

The only psychosocial intervention with moderate/high certainty of effect in our review was mentoring provided to adolescents. Mentoring was conducted by peers on a weekly basis, with supervision and support from a case manager. It appears that mentoring sessions do not need to explicitly focus on harmful behaviours, but rather provide general support and advice. It would be beneficial to review evidence from other types of mentoring programmes for adolescents, to identify whether they are as effective as peer-led programmes. Although further evidence is required beyond the single meta-analysis included in our review, mentoring for adolescents appears to be a promising strategy to prevent progression of risky drinking in adolescents and young adults.

With regards to pharmacological interventions, our review suggests that it may be worth conducting further evaluation of nalmefene, topiramate and galantamine for inclusion in the National List of Essential Medicines for the treatment of alcohol use disorder. Finally, our review seems to suggest that combination of psychosocial and pharmacological interventions may be the best strategy to address alcohol use disorder, which is in line with existing WHO guidance (5). Our review identified a limited number of combinations, and it may be worth conducting further research to identify optimal combination of regimens, especially between psychosocial and pharmacological interventions that are effective when administered individually.

Table 3 Summary of effective interventions identified in the review. See text for further details and discussion of interventions with mixed evidence. Status in Thailand was determined through consultation with two experts.

Intervention	Effect size (95% CI)	Certainty of benefit	Status in Thailand
Screening, brief interventions, referral to treatment			
Brief counselling intervention (53,57,112)	• MD % heavy use episodes -1.59 (-2.15 to -1.03) • OR heavy drinking 0.67 (0.58 to 0.77) • MD alcohol consumption at 12 months -3.573 (-4.758 to -2.389)	**Moderate –** studies rated moderate in AMSTAR, effect sizes are medium but there are only behavioural outcomes	In self-opening rehab facilities there may be counselling; brief interventions are provided
Brief intervention, brief motivational interview, and/or counselling by lay health worker (52)	• SMD drinks per drinking day -0.37 (-0.52, -0.22) • SMD Amount of alcohol consumed -0.23 [-0.56, 0.09] • SMD ASSIST/AUDIT score -0.22 [-0.32 , -0.11]	**Moderate –** high AMSTAR rating but effect sizes are relatively small and only measure behavioural outcomes	May occur in places
Brief advice based on biomarkers of liver injury or liver fibrosis	• WMD weekly alcohol intake −74.4 g/week (-126.1, -22.6)	**High –** single meta-analysis of moderate quality, but covers long-term outcomes and	Not regularly conducted

Intervention	Effect size (95% CI)	Certainty of benefit	Status in Thailand
(58)	• WMD GGT levels −19.7 IU/l (−33.0, −6.4). • RR alcohol-related death 1.9 (1.0–3.8) • Fewer days in hospital (ratio 2.2) • 47% reduction in new injuries and less traffic violation and police arrests	behavioural as well as health outcomes	
2. Psychosocial interventions			
Mentoring for adolescents (115)	RR alcohol use 0.71 (0.57, 0.90)	**Moderate –** only one meta-analysis of moderate quality identified (including 3 RCTs), but effect size is after 12 to 18 months and for standard care or counselling comparator	Not implemented
3. Pharmacological interventions			
Topiramate (anticonvulsant) (67,86)	OR abstinence0.45 (0.24, 0.83) SMD alcohol consumption -0.77 (-1.12, -0.42) SMD heavy drinking day -0.59 (-0.96, -0.22)	**Moderate –** AMSTAR rating is moderate/high, small number of studies for abstinence outcome, some discordance between results	Not for the treatment of alcohol use disorder
Valproic acid (anticonvulsant) (87)	MD return to any drinking -0.32 (-0.52, -0.11)	**Low –** moderate AMSTAR rating, but based on small sample	Not for the treatment of alcohol use disorder
Flupenthixol decanoate (antipsychotic) (67,92)	OR AUDIT score 0.44 (0.2-0.98) SMD abstinence 0.34 (0.11,0.58)	**Low –** moderate and critically low AMSTAR rating, effect at 12 weeks and 12 months, 66 RCTs included	Not for the treatment of alcohol use disorder

Intervention	Effect size (95% CI)	Certainty of benefit	Status in Thailand
Nalmefene (opioid antagonist) (86,87,101)	MD heavy drinking days -1.65 (-2.41, -0.89) SMD alcohol consumption -0.2 (-0.3, -0.1)	**Moderate –** high AMSTAR rating but small treatment effect size	Not available in Thailand
Galantamine (67)	OR relapse 0.31 (0.11, 0.87)	**Moderate –** large effect size but wide confidence interval, low risk of bias in RCTs, moderate AMSTAR rating, evidence from single review only	Not for the treatment of alcohol use disorder
4. Combination of interventions			
Intensive perioperative cessation programme (disulfiram, chlordiazepoxide, motivational counselling, brief interview, B vitamins) (108)	RR abstinence 8.22 (1.67, 40.44)	**Very low –** although there is a very large effect size, it comes from one low quality review of 3 RCTs conducted in Denmark, and the effect was only measured up to 3 months	Not officially, but individual hospitals may provide counselling and/or drugs before surgery.
Naltrexone + psychosocial interventions (106,107)	MD % heavy drinking days -11.00 (-18.18, -3.82) MD % drinking days -10.50 (-18.1, -2.9) RR relapse 0.74 (0.55, 0.98) RR remission 1.73 (1.05, 2.94)	**Low –** AMSTAR rating of reviews is moderate and there is a large effect size, but results are taken from a single RCT	Naltrexone is not available in Thailand
5. Alternative therapies			
Acupuncture (109)	SMD alcohol withdrawal -0.50 (-0.83, -0.17)	**Low** – moderate AMSTAR rating, but only two RCTs with small sample size and risk of bias in blinding	Alternative medicine is available, but not specifically listed for alcohol use.

CBT – cognitive behavioural therapy; MD – mean difference; MI – motivational interview; OR – odds ratio; RR – risk ratio; SMD – standard mean difference; TSF – twelve step facilitation; WMD – weighted mean difference

As noted in table 4, our review highlighted two interventions with limited evidence of effect that are being implemented in Thailand: twelve-step facilitation (implemented in some rehabilitation clinics), and transcranial magnetic stimulation (implemented in certain hospitals and rehabilitation clinics). Further research is needed to provide a more comprehensive view of the evidence for these interventions, to rationalise whether they should continue to be implemented.

Table 4 Interventions with no or limited evidence of effectiveness.

Intervention	Status in Thailand	Summary of available evidence
1. Screening, brief intervention, referral to treatment		
Minimal intervention (general advice on alcohol consumption lasting 3-5 minutes)	Conducted in certain places	1 review found no evidence of effectiveness across a range of outcomes (37).
Primary and secondary prevention measures targeting alcohol use and at least one other risk behaviour	Not implemented	1 review found no evidence of effectiveness (48).
Tailored text message	Not implemented	No evidence of a difference in reducing **binge drinking** with both short-term and long-term interventions, or in reducing average drinks per occasion and standard drinks per occasion in short-term interventions was found in any population (e.g. students, general population and primary care patients) (61,64).
2. Psychosocial interventions		
Family-based prevention programmes targeted at the parents of young people	Not implemented	1 review found no significant effect for prevalence, frequency, or volume of alcohol use (25).

Intervention	Status in Thailand	Summary of available evidence
Twelve step facilitation (TSF)	Conducted in some rehab clinics	1 review in patients with co-occurring mental illness found a very small significant effect at 6 months, but no significant effect at 3, 9, or 12 months (118).
Controlled drinking	Not implemented	2 reviews found no benefit of controlled drinking – one review compared controlled drinking with abstinence-based strategies in dependent patients, while the other was distance-based for cancer survivors with any level of alcohol consumption and compared with no intervention (77,78).
3. Pharmacological interventions		
Carbamazepine (anticonvulsant)	Not for the treatment of alcohol use disorder	1 review found no significant effect for abstinence (67).
Gabapentin (anticonvulsant)	Not for the treatment of alcohol use disorder	2 reviews found a small but significant effect for reduction in % heavy drinking days, but no significant effect for all other measures of alcohol consumption or abstinence (84,85).
Oxcarbamazepine (anticonvulsant)	Available in Thailand but not listed on NLEM	1 review found no significant effect for abstinence (67).
Antidepressants	Not for the treatment of alcohol use disorder	No evidence for significant effect compared to placebo for citalopram, escitalopram, fluoxetine, fluvoxamine, tianeptine, paroxetine, NRI, SARI, SSRI, nefazodone, mirtazapine, trazodone, or tricyclic antidepressants (67,88,89,91,105).
Antipsychotics (except flupenthixol decanoate)	Not for the treatment of alcohol use disorder	No evidence for significant effect in pooled analysis across antipsychotics, or for amisulpride, aripiprazole, olanzapine, quetiapine, or tiapride (67,89,92).
Atenolol	Not for the treatment of alcohol use disorder	1 review found no significant effect for abstinence (67).
Bromocriptine	Not for the treatment of alcohol use disorder	1 review found no significant effect for remission in patients with comorbid depression (89).
Buspirone	Available in Thailand but not listed on NLEM	1 review found no significant effect for remission in patients with comorbid depression (89).

Intervention	Status in Thailand	Summary of available evidence
GHB	Not available in Thailand	1 review found no significant effect for abstinence (67).
Levetiracetam	Not for the treatment of alcohol use disorder	1 review found no significant effect for abstinence (67).
Lisuride	Not available in Thailand	1 review found no significant effect for abstinence (67).
Lithium	Not for the treatment of alcohol use disorder	1 review found no significant effect for remission in patients with comorbid depression (89).
Memantine	Not for the treatment of alcohol use disorder	1 review found no significant effect for remission in patients with comorbid depression (89).
Modafinil	Not available in Thailand	1 review found no significant effect for abstinence (67).
Pregabalin	Available in Thailand but not listed on NLEM	1 review found no significant effect for abstinence (67).
4. Combinations of interventions		
Naltrexone + disulfiram	Naltrexone is not available in Thailand	1 review found no evidence of effect for AUD remission rate in patients with comorbid depression (89).
Naltrexone + GHB	Naltrexone is not available in Thailand	1 review found no significant effect in improving abstinence at 1 year follow-up (67).
Naltrexone + escitalopram	Naltrexone is not available in Thailand	1 review found no significant effect in improving abstinence at 1 year follow-up (67).
5. Alternative therapies		
Transcranial magnetic stimulation	Used in some hospitals, rehab, neurological departments	1 study found no evidence of effect (110).

NLEM – national list of essential medicines

Our review has a number of limitations. Firstly, we had a very broad research question encompassing many different intervention types. We were therefore unable to conduct an in-depth review of each intervention type. Our decision to conduct an umbrella review means that we may have missed interventions, although this is unlikely given that all categories of intervention were included in our review. Secondly, while we used a strict definition of systematic

reviews and only included reviews of RCTs to ensure high quality evidence and comparability across studies, this approach also meant we excluded many reviews. As a result, we only included one systematic review for many of the classes of interventions listed in Table 1, limiting the certainty of our findings. Thirdly, we did not include search terms for recovery management or health outcomes. For outcomes search terms, we did run a test search with health outcomes included, but this strategy yielded too many papers for review (around 20,000 articles), and our decision to only include behavioural outcomes in the search terms is consistent with other reviews of alcohol prevention and treatment. However, we cannot be sure whether the reason that we identified so few reviews looking at recovery management is due to lack of reviews or weaknesses in our search strategy. Fourthly, for many of the outcomes reported in our review, the confidence intervals are very large, which means that some effective interventions may have been missed. Finally, most of the reviews included in our analysis were judged to be of low quality, interventions were often poorly described, and there was notable discordance between outcomes across studies, which limits confidence in our results.

Nonetheless, a major strength of our review is that it fills a gap in the literature to provide a comprehensive overview of interventions to address harmful alcohol use. We believe that our review has succeeded in identifying interventions that are most effective for implementation, as well as interventions that require further review of their effectiveness, to support the prevention and treatment of harmful alcohol use in Thailand.

POLICY RECOMMENDATIONS

1. **Interventions for inclusion under UCBP and/or within clinical practice guidelines**

    1.1. Among adults identified to have high-risk drinking behaviour, systematically conduct diagnostic tests for alcohol-related liver disease and discuss biomarker results during brief advice sessions.

    1.2. Implement a peer-led mentoring programme among youth with risky drinking. This may be best introduced as a pilot project among youth in settings with higher rates of alcohol misuse, in order to evaluate effectiveness and optimise implementation (e.g. frequency of sessions, training of mentors) before wide-scale roll-out. Current evidence suggests that

the mentoring programme should provide general support to youth, without a specific focus on alcohol use.

2. Revisions to NLEM

2.1. Evaluate the following medications for inclusion in the NLEM for treatment of alcohol use disorder: nalmefene, topiramate and galantamine.

3. Research priorities

3.1. Evaluate therapies combining a psychosocial intervention with a pharmacological intervention with good evidence of effectiveness, to identify whether addition of the psychosocial intervention can improve size or duration of effect.

3.2. Review the effectiveness of interventions to prevent relapse of recovered individuals.

3.3. Identify the main determinants affecting the outcomes of screening, brief intervention, and referral to treatment interventions.

REFERENCES

1. GBD 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet (London, England) [Internet]. 2018 Sep 22 [cited 2021 Aug 24];392(10152):1015–35. Available from: https://pubmed.ncbi.nlm.nih.gov/30146330/

2. Charlet K, Heinz A. Harm reduction-a systematic review on effects of alcohol reduction on physical and mental symptoms. Addiction biology [Internet]. 2017 Sep 1 [cited 2021 Aug 24];22(5):1119–59. Available from: https://pubmed.ncbi.nlm.nih.gov/27353220/

3. Rehm J, Gmel GE, Gmel G, Hasan OSM, Imtiaz S, Popova S, et al. The relationship between different dimensions of alcohol use and the burden of disease—an update. Addiction (Abingdon, England) [Internet]. 2017 Jun 1 [cited 2021 Aug 24];112(6):968. Available from: /pmc/articles/PMC5434904/

4. Laramée P, Leonard S, Buchanan-Hughes A, Warnakula S, Daeppen J, Rehm J. Risk of All-Cause Mortality in Alcohol-Dependent Individuals: A Systematic Literature Review and Meta-Analysis. EBioMedicine [Internet]. 2015 Oct 1 [cited 2021 Aug 24];2(10):1394–404. Available from: https://pubmed.ncbi.nlm.nih.gov/26629534/

5. World Health Organization. Global strategy to reduce the harmful use of alcohol [Internet]. Switzerland: World Health .... Geneva; 2010 [cited 2021 Aug 24]. Available from: https://www.who.int/substance_abuse/msbalcstragegy.pdf%0Ahttp://scholar.google.ca/scholar?q=Global+strategy+to+reduce+the+harmful+use+of+alcohol.+&btnG=&hl=en&as_sdt=1%2C5&as_ylo=2008#4

6. Thavorncharoensap M, Teerawattananon Y, Yothasamut J, Lertpitakpong C, Chaikledkaew U. The economic impact of alcohol consumption: a systematic review. Substance abuse treatment, prevention, and policy [Internet]. 2009 Nov 25 [cited 2021 Aug 24];4. Available from: https://pubmed.ncbi.nlm.nih.gov/19939238/

7. World Health Organization. International Standards for the Treatment of Drug Use Disorders [Internet]. Geneva; 2020 [cited 2021 Aug 24]. Available from: https://www.who.int/publications/i/item/international-standards-for-the-treatment-of-drug-use-disorders

8. National Institute on Alcohol Abuse and Alcoholism (NIAAA). Understanding Alcohol Use Disorder [Internet]. [cited 2021 Aug 24]. Available from: https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/understanding-alcohol-use-disorder

9. Gao J, Cao J, Guo T, Xiao Y. Association between alcoholic interventions and abstinence rates for alcohol use disorders: A meta-analysis. Medicine [Internet]. 2018 Dec 1 [cited 2021 Aug 24];97(50). Available from: https://pubmed.ncbi.nlm.nih.gov/30558020/

10. International Health Policy Program. Thailand burden of disease attributable to risk factors 2014. 2018.

11. World Health Organization, OMS, World Health Organization. Global status report on alcohol and health 2018. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO. Poznyak V, Rekve D, editors. 2018 [cited 2021 Aug 24];478. Available from: https://apps.who.int/iris/bitstream/handle/10665/274603/9789241565639-eng.pdf?ua=1

12. World Health Organization. The SAFER technical package: five areas of intervention at national and subnational levels. [Internet]. Geneva; 2019 [cited 2021 Aug 24]. Available from: https://www.who.int/publications/i/item/the-safer-technical-package

13. Treerutkuarkul A. Moving Thailand's mountain of alcohol-related harm. Bulletin of the World Health Organization [Internet]. 2017 Jul 1 [cited 2021 Aug 24];95(7):487. Available from: /pmc/articles/PMC5487977/

14. Alcohol Addiction Treatment and Rehabilitation Subcommittee. Guidelines for screening and rehabilitation of people with alcohol use problems. Nonthaburi; 2018.

15. Kaner E, Beyer F, Muirhead C, Campbell F, Pienaar E, Bertholet N, et al. Effectiveness of brief alcohol interventions in primary care populations. The Cochrane database of systematic reviews [Internet]. 2018 Feb 24 [cited 2021 Aug 24];2(2). Available from: https://pubmed.ncbi.nlm.nih.gov/29476653/

16. Elzerbi C, Donoghue K, Drummond C. A comparison of the efficacy of brief interventions to reduce hazardous and harmful alcohol consumption between European and non-European countries: A systematic review and meta-analysis of randomized controlled trials. Addiction. 2015 Jul 1;110(7):1082–91.

17. Shorter GW, Bray JW, Giles EL, O'donnell AJ, Berman AH, Holloway A, et al. The variability of outcomes used in efficacy and effectiveness trials of alcohol brief interventions: A systematic review. Journal of Studies on Alcohol and Drugs. 2019;80(3):286–98.

18. O'Donnell A, Anderson P, Newbury-Birch D, Schulte B, Schmidt C, Reimer J, et al. The impact of brief alcohol interventions in primary healthcare: a systematic review of reviews. Alcohol and alcoholism (Oxford, Oxfordshire) [Internet]. 2014 Jan [cited 2021 Aug 24];49(1):66–78. Available from: https://pubmed.ncbi.nlm.nih.gov/24232177/

19. Amato L, Minozzi S, Davoli M. Efficacy and safety of pharmacological interventions for the treatment of the Alcohol Withdrawal Syndrome. Cochrane Database of Systematic Reviews [Internet]. 2011 Jun 15 [cited 2021 Aug 26];(6). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008537.pub2/full

20. Kelly JF, Humphreys K, Ferri M. Alcoholics Anonymous and other 12-step programs for alcohol use disorder. Cochrane Database of Systematic Reviews [Internet]. 2020 Mar 11 [cited 2021 Aug 26];2020(3). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012880.pub2/full

21. Lui S, Terplan M, Smith EJ. Psychosocial interventions for women enrolled in alcohol treatment during pregnancy. Cochrane Database of Systematic Reviews. 2008;(3).

22. Smith EJ, Lui S, Terplan M. Pharmacologic Interventions for Pregnant Women Enrolled in Alcohol Treatment. Cochrane Database of Systematic Reviews [Internet]. 2009 [cited 2021 Aug 26];(3). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD007361.pub2/full

23. Thomas RE, Lorenzetti D, Spragins W. Mentoring adolescents to prevent drug and alcohol use. Cochrane Database of Systematic Reviews [Internet]. 2011 Nov 9 [cited 2021 Aug 26];(11). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD007381.pub2/full

24. Foxcroft DR, Coombes L, Wood S, Allen D, Almeida Santimano NML. Motivational interviewing for alcohol misuse in young adults. Cochrane Database of Systematic Reviews. 2015 Sep 1;2015(9).

25. Gilligan C, Wolfenden L, Foxcroft DR, Williams AJ, Kingsland M, Hodder RK, et al. Family-based prevention programmes for alcohol use in young people. Cochrane Database of Systematic Reviews [Internet]. 2019 Mar 19 [cited 2021 Aug 26];2019(3). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012287.pub2/full

26. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic Reviews 2015 4:1 [Internet]. 2015 Jan 1 [cited 2021 Aug 24];4(1):1–9. Available from: https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/2046-4053-4-1

27. Pollock M, Fernandes RM, Becker LA, Pieper D, Hartling L. Chapter V: Overviews of Reviews. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). [Internet]. 2021 [cited 2021 Aug 24]. Available from: https://training.cochrane.org/handbook/current

28. Blonde L, Khunti K, Harris SB, Meizinger C, Skolnik NS. Interpretation and Impact of Real-World Clinical Data for the Practicing Clinician. Advances in Therapy 2018 35:11 [Internet]. 2018 Oct 24 [cited 2021 Nov 4];35(11):1763–74. Available from: https://link.springer.com/article/10.1007/s12325-018-0805-y

29. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ [Internet]. 2017 Sep 21 [cited 2021 Aug 24];358. Available from: https://www.bmj.com/content/358/bmj.j4008

30. Beich A, Thorsen T, Rollnick S. Screening in brief intervention trials targeting excessive drinkers in general practice: systematic review and meta-analysis. BMJ (Clinical research ed) [Internet]. 2003 Sep 6 [cited 2022 Jan 10];327(7414):536–40. Available from: https://pubmed.ncbi.nlm.nih.gov/12958114/

31. Beyer FR, Campbell F, Bertholet N, Daeppen JB, Saunders JB, Pienaar ED, et al. The Cochrane 2018 Review on Brief Interventions in Primary Care for Hazardous and Harmful Alcohol Consumption: A Distillation for Clinicians and Policy Makers. Alcohol and Alcoholism [Internet]. 2019 Jul 1 [cited 2022 Jan 10];54(4):417–27. Available from: https://academic.oup.com/alcalc/article/54/4/417/5486343

32. Steele DW, Becker SJ, Danko KJ, Balk EM, Adam GP, Saldanha IJ, et al. Brief Behavioral Interventions for Substance Use in Adolescents: A Meta-analysis. Pediatrics [Internet]. 2020 Oct 1;146(4):e20200351. Available from: https://doi.org/10.1542/peds.2020-0351

33. Hennessy EA, Tanner-Smith EE, Mavridis D, Grant SP. Comparative Effectiveness of Brief Alcohol Interventions for College Students: Results from a Network Meta-Analysis. Prevention science : the official journal of the Society for Prevention Research [Internet]. 2019 Jul 15 [cited 2022 Jan 10];20(5):715–40. Available from: https://pubmed.ncbi.nlm.nih.gov/30604290/

34. Riper H, van Straten A, Keuken M, Smit F, Schippers G, Cuijpers P. Curbing problem drinking with personalized-feedback interventions: a meta-analysis. American journal of preventive medicine [Internet]. 2009 Mar [cited 2022 Jan 10];36(3):247–55. Available from: https://pubmed.ncbi.nlm.nih.gov/19215850/

35. Doherty AM, Mason C, Fear NT, Rona R, Greenberg N, Goodwin L. Are brief alcohol interventions targeting alcohol use efficacious in military and veteran populations? A meta-analysis. Drug and alcohol dependence [Internet]. 2017 Sep 1 [cited 2022 Jan 10];178:571–8. Available from: https://pubmed.ncbi.nlm.nih.gov/28750345/

36. Mcqueen J, Howe TE, Allan L, Mains D, Hardy V. Brief interventions for heavy alcohol users admitted to general hospital wards. The Cochrane database of systematic reviews [Internet]. 2011 Aug 10 [cited 2022 Jan 10];2011(8). Available from: https://pubmed.ncbi.nlm.nih.gov/21833953/

37. Ballesteros J, Duffy JC, Querejeta I, Ariño J, González-Pinto A. Efficacy of brief interventions for hazardous drinkers in primary care: systematic review and meta-analyses. Alcoholism, clinical and experimental research [Internet]. 2004 Apr [cited 2022 Jan 10];28(4):608–18. Available from: https://pubmed.ncbi.nlm.nih.gov/15100612/

38. Elzerbi C, Donoghue K, Boniface S, Drummond C. 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. Annals of emergency medicine [Internet]. 2017 Nov 1 [cited 2022 Jan 10];70(5):714-723.e13. Available from: https://pubmed.ncbi.nlm.nih.gov/28669555/

39. Gao J, Cao J, Guo T, Xiao Y. Association between alcoholic interventions and abstinence rates for alcohol use disorders A meta-analysis. Medicine (United States) [Internet]. 2018 Dec 1 [cited 2022 Jan 10];97(50). Available from: https://journals.lww.com/md-journal/Fulltext/2018/12140/Association_between_alcoholic_interventions_and.59.aspx

40. Bertholet N, Daeppen JB, Wietlisbach V, Fleming M, Burnand B. Reduction of alcohol consumption by brief alcohol intervention in primary care: systematic review and meta-analysis. Archives of internal medicine [Internet]. 2005 May 9 [cited 2022 Jan 10];165(9):986–95. Available from: https://pubmed.ncbi.nlm.nih.gov/15883236/

41. Carey KB, Scott-Sheldon LAJ, Elliott JC, Garey L, Carey MP. Face-to-Face Versus Computer-Delivered Alcohol Interventions for College Drinkers: A Meta-Analytic Review, 1998 to 2010. Clinical psychology review [Internet]. 2012 Dec [cited 2022 Jan 10];32(8):690. Available from: /pmc/articles/PMC3511828/

42. Jonas DE, Garbutt JC, Amick HR, Brown JM, Brownley KA, Council CL, et al. Behavioral counseling after screening for alcohol misuse in primary care: A systematic review and meta-analysis for the U.S. preventive services task force. Annals of Internal Medicine. 2012 Nov 6;157(9):645–54.

43. Fachini A, Aliane PP, Martinez EZ, Furtado EF. Efficacy of brief alcohol screening intervention for college students (BASICS): a meta-analysis of randomized controlled trials. Substance Abuse Treatment, Prevention, and Policy [Internet]. 2012 Sep 12 [cited 2022 Jan 10];7:40. Available from: /pmc/articles/PMC3499225/

44. Carney T, Myers BJ, Louw J, Okwundu CI. Brief school-based interventions and behavioural outcomes for substance-using adolescents. The Cochrane database of systematic reviews [Internet]. 2016 Jan 20 [cited 2022 Jan 10];2016(1). Available from: https://pubmed.ncbi.nlm.nih.gov/26787125/

45. Sullivan LE, Tetrault JM, Braithwaite RS, Turner BJ, Fiellin DA. A meta-analysis of the efficacy of nonphysician brief interventions for unhealthy alcohol use: implications for the patient-centered medical home. The American journal on addictions [Internet]. 2011 Jul [cited 2022 Jan 10];20(4):343–56. Available from: https://pubmed.ncbi.nlm.nih.gov/21679266/

46. Foxcroft DR, Moreira MT, Almeida Santimano NM l., Smith LA. Social norms information for alcohol misuse in university and college students. The Cochrane database of systematic reviews [Internet]. 2015 Jan 26 [cited 2022 Jan 10];1(1). Available from: https://pubmed.ncbi.nlm.nih.gov/25622306/

47. Moreira MT, Smith LA, Foxcroft D. Social norms interventions to reduce alcohol misuse in university or college students. The Cochrane database of systematic reviews [Internet]. 2009 [cited 2022 Jan 10];(3). Available from: https://pubmed.ncbi.nlm.nih.gov/19588402/

48. Macarthur G, Caldwell DM, Redmore J, Watkins SH, Kipping R, White J, et al. Individual-, family-, and school-level interventions targeting multiple risk behaviours in young people. The Cochrane database

of systematic reviews [Internet]. 2018 Oct 5 [cited 2022 Jan 10];10(10). Available from: https://pubmed.ncbi.nlm.nih.gov/30288738/

49. Dinh-Zarr TB, Goss CW, Heitman E, Roberts IG, DiGuiseppi C. Interventions for preventing injuries in problem drinkers. Cochrane Database of Systematic Reviews [Internet]. 2004 Jul 19 [cited 2022 Jan 10];(3). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD001857.pub2/full

50. Elzerbi C, Donoghue K, Drummond C. A comparison of the efficacy of brief interventions to reduce hazardous and harmful alcohol consumption between European and non-European countries: a systematic review and meta-analysis of randomized controlled trials. Addiction (Abingdon, England) [Internet]. 2015 Jul 1 [cited 2022 Jan 10];110(7):1082–91. Available from: https://pubmed.ncbi.nlm.nih.gov/25916993/

51. Wilk AI, Jensen NM, Havighurst TC. Meta-analysis of Randomized Control Trials Addressing Brief Interventions in Heavy Alcohol Drinkers. Journal of General Internal Medicine [Internet]. 1997 [cited 2022 Jan 10];12(5):274. Available from: /pmc/articles/PMC1497107/

52. van Ginneken N, Chin WY, Lim YC, Ussif A, Singh R, Shahmalak U, et al. Primary-level worker interventions for the care of people living with mental disorders and distress in low- and middle-income countries. Cochrane Database of Systematic Reviews [Internet]. 2021 Aug 5 [cited 2022 Jan 10];2021(8). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD009149.pub3/full

53. O'Connor EA, Perdue LA, Senger CA, Rushkin M, Patnode CD, Bean SI, et al. 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. JAMA [Internet]. 2018 Nov 13 [cited 2022 Jan 10];320(18):1910–28. Available from: https://jamanetwork.com/journals/jama/fullarticle/2714536

54. Ghosh A, Singh P, Das N, Pandit PM, Das S, Sarkar S. Efficacy of brief intervention for harmful and hazardous alcohol use: a systematic review and meta-analysis of studies from low middle-income countries. Addiction (Abingdon, England) [Internet]. 2021 [cited 2022 Jan 10]; Available from: https://pubmed.ncbi.nlm.nih.gov/34159673/

55. Saxton J, Rodda SN, Booth N, Merkouris SS, Dowling NA. The efficacy of Personalized Normative Feedback interventions across addictions: A systematic review and meta-analysis. PLOS ONE [Internet]. 2021 Apr 1 [cited 2022 Jan 10];16(4):e0248262. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0248262

56. Klimas J, Fairgrieve C, Tobin H, Field CA, O'Gorman CSM, Glynn LG, et al. Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users. The Cochrane

database of systematic reviews [Internet]. 2018 Dec 5 [cited 2022 Jan 10];12(12). Available from: https://pubmed.ncbi.nlm.nih.gov/30521696/

57. Yuvaraj K, Eliyas SK, Gokul S, Manikandanesan S. Effectiveness of Workplace Intervention for Reducing Alcohol Consumption: a Systematic Review and Meta-Analysis. Alcohol and alcoholism (Oxford, Oxfordshire) [Internet]. 2019 May 1 [cited 2022 Jan 10];54(3):264–71. Available from: https://pubmed.ncbi.nlm.nih.gov/30957142/

58. Subhani M, Knight H, Ryder S, Morling JR. Does Advice Based on Biomarkers of Liver Injury or Non-Invasive Tests of Liver Fibrosis Impact High-Risk Drinking Behaviour: A Systematic Review With Meta-analysis. Alcohol and Alcoholism [Internet]. 2021 Feb 24 [cited 2022 Jan 11];56(2):185–200. Available from: https://academic.oup.com/alcalc/article/56/2/185/6105939

59. Donoghue K, Patton R, Phillips T, Deluca P, Drummond C. The Effectiveness of Electronic Screening and Brief Intervention for Reducing Levels of Alcohol Consumption: A Systematic Review and Meta-Analysis. Journal of Medical Internet Research [Internet]. 2014 [cited 2022 Jan 10];16(6). Available from: /pmc/articles/PMC4060043/

60. Rooke S, Thorsteinsson E, Karpin A, Copeland J, Allsop D. Computer-delivered interventions for alcohol and tobacco use: a meta-analysis. Addiction (Abingdon, England) [Internet]. 2010 Aug [cited 2022 Jan 10];105(8):1381–90. Available from: https://pubmed.ncbi.nlm.nih.gov/20528806/

61. Bendtsen M, McCambridge J, Åsberg K, Bendtsen P. Text messaging interventions for reducing alcohol consumption among risky drinkers: systematic review and meta-analysis. Addiction (Abingdon, England) [Internet]. 2021 May 1 [cited 2022 Jan 10];116(5):1021–33. Available from: https://pubmed.ncbi.nlm.nih.gov/33047865/

62. Dedert EA, McDuffie JR, Stein R, McNiel JM, Kosinski AS, Freiermuth CE, et al. Electronic Interventions for Alcohol Misuse and Alcohol Use Disorders: A Systematic Review. Annals of internal medicine [Internet]. 2015 Aug 4 [cited 2022 Jan 10];163(3):205–14. Available from: https://pubmed.ncbi.nlm.nih.gov/26237752/

63. Kaner EFS, Beyer FR, Garnett C, Crane D, Brown J, Muirhead C, et al. Personalised digital interventions for reducing hazardous and harmful alcohol consumption in community-dwelling populations. The Cochrane database of systematic reviews [Internet]. 2017 Sep 25 [cited 2022 Jan 10];9(9). Available from: https://pubmed.ncbi.nlm.nih.gov/28944453/

64. Bastola MM, Locatis C, Maisiak R, Fontelo P. The Effectiveness of Mobile Phone-Based Text Messaging to Intervene with Problem Drinking in Youth and Younger Adult Population: A Meta-Analysis. Telemedicine Journal and e-Health [Internet]. 2020 Mar 1 [cited 2022 Jan 10];26(3):270. Available from: /pmc/articles/PMC7071024/

65. Simioni N, Cottencin O, Rolland B. Interventions for Increasing Subsequent Alcohol Treatment Utilisation Among Patients with Alcohol Use Disorders from Somatic Inpatient Settings: A Systematic Review. Alcohol and alcoholism (Oxford, Oxfordshire) [Internet]. 2015 Jul 1 [cited 2022 Jan 10];50(4):420–9. Available from: https://pubmed.ncbi.nlm.nih.gov/25780027/

66. Simioni N, Rolland B, Cottencin O. Interventions for Increasing Alcohol Treatment Utilization Among Patients with Alcohol Use Disorders from Emergency Departments: A Systematic Review. Journal of substance abuse treatment [Internet]. 2015 Nov 1 [cited 2022 Jan 10];58:6–15. Available from: https://pubmed.ncbi.nlm.nih.gov/26206477/

67. Cheng HY, McGuinness LA, Elbers RG, MacArthur GJ, Taylor A, McAleenan A, et al. Treatment interventions to maintain abstinence from alcohol in primary care: systematic review and network meta-analysis. BMJ [Internet]. 2020 Nov 25 [cited 2022 Jan 10];371. Available from: https://www.bmj.com/content/371/bmj.m3934

68. Davis JP, Smith DC, Briley DA. Substance use prevention and treatment outcomes for emerging adults in non-college settings: A meta-analysis. Psychology of Addictive Behaviors : Journal of the Society of Psychologists in Addictive Behaviors [Internet]. 2017 Mar 20 [cited 2022 Jan 10];31(3):242–54. Available from: https://europepmc.org/article/MED/28318279

69. Huibers MJH, Beurskens AJHM, Bleijenberg G, van Schayck CP. Psychosocial interventions by general practitioners. The Cochrane database of systematic reviews [Internet]. 2007 [cited 2022 Jan 10];2007(3). Available from: https://pubmed.ncbi.nlm.nih.gov/17636726/

70. Hunter RF, de La Haye K, Murray JM, Badham J, Valente TW, Clarke M, et al. Social network interventions for health behaviours and outcomes: A systematic review and meta-analysis. PLOS Medicine [Internet]. 2019 [cited 2022 Jan 10];16(9):e1002890. Available from: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002890

71. Prestwich A, Kellar I, Conner M, Lawton R, Gardner P, Turgut L. Does changing social influence engender changes in alcohol intake? A meta-analysis. Journal of Consulting and Clinical Psychology [Internet]. 2016 Oct 1 [cited 2022 Jan 10];84(10):845–60. Available from: /doiLanding?doi=10.1037%2Fccp0000112

72. Foxcroft DR, Coombes L, Wood S, Allen D, Almeida Santimano NML. Motivational interviewing for alcohol misuse in young adults. The Cochrane database of systematic reviews [Internet]. 2014 Aug 21 [cited 2022 Jan 10];2014(8). Available from: https://pubmed.ncbi.nlm.nih.gov/25140980/

73. Sayegh CS, Huey SJ, Zara EJ, Jhaveri K. Follow-up treatment effects of contingency management and motivational interviewing on substance use: A meta-analysis. Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors [Internet]. 2017 Jun 1 [cited 2022 Jan 10];31(4):403–14. Available from: https://pubmed.ncbi.nlm.nih.gov/28437121/

74. Hunt GE, Siegfried N, Morley K, Brooke-Sumner C, Cleary M. Psychosocial interventions for people with both severe mental illness and substance misuse. Cochrane Database of Systematic Reviews [Internet]. 2019 Dec 12 [cited 2022 Jan 10];2019(12). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD001088.pub4/full

75. Klimas J, Tobin H, Field CA, O'Gorman CSM, Glynn LG, Keenan E, et al. Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users. Cochrane Database of Systematic Reviews. 2014 Dec 3;2014(12).

76. Ujhelyi Gomez K, Goodwin L, Jackson L, Jones A, Chisholm A, Rose AK. Are psychosocial interventions effective in reducing alcohol consumption during pregnancy and motherhood? A systematic review and meta-analysis. Addiction [Internet]. 2021 Jul 1 [cited 2022 Jan 10];116(7):1638–63. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/add.15296

77. Henssler J, Müller M, Carreira H, Bschor T, Heinz A, Baethge C. Controlled drinking-non-abstinent versus abstinent treatment goals in alcohol use disorder: a systematic review, meta-analysis and meta-regression. Addiction (Abingdon, England) [Internet]. 2021 Aug 1 [cited 2022 Jan 10];116(8):1973–87. Available from: https://pubmed.ncbi.nlm.nih.gov/33188563/

78. Mujcic A, Blankers M, Bommelé J, Boon B, Berman AH, Verdonck-de Leeuw IM, et al. The effectiveness of distance-based interventions for smoking cessation and alcohol moderation among cancer survivors: A meta-analysis. Psycho-oncology [Internet]. 2020 Jan 1 [cited 2022 Jan 10];29(1):49–60. Available from: https://pubmed.ncbi.nlm.nih.gov/31663182/

79. Riper H, Hoogendoorn A, Cuijpers P, Karyotaki E, Boumparis N, Mira A, et al. Effectiveness and treatment moderators of internet interventions for adult problem drinking: An individual patient data meta-analysis of 19 randomised controlled trials. PLOS Medicine [Internet]. 2018 [cited 2022 Jan 10];15(12):e1002714. Available from: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002714

80. Riper H, Spek V, Boon B, Conijn B, Kramer J, Martin-Abello K, et al. Effectiveness of E-self-help interventions for curbing adult problem drinking: a meta-analysis. Journal of medical Internet research [Internet]. 2011 [cited 2022 Jan 10];13(2). Available from: https://pubmed.ncbi.nlm.nih.gov/21719411/

81. Hai AH, Hammock K, Velasquez MM. The Efficacy of Technology-Based Interventions for Alcohol and Illicit Drug Use Among Women of Childbearing Age: A Systematic Review and Meta-Analysis. Alcoholism, clinical and experimental research [Internet]. 2019 Dec 1 [cited 2022 Jan 10];43(12):2464–79. Available from: https://pubmed.ncbi.nlm.nih.gov/31557336/

82. Mellentin AI, Skøt L, Nielsen B, Schippers GM, Nielsen AS, Stenager E, et al. Cue exposure therapy for the treatment of alcohol use disorders: A meta-analytic review. Clinical psychology review [Internet].

2017 Nov 1 [cited 2022 Jan 10];57:195–207. Available from: https://pubmed.ncbi.nlm.nih.gov/28781153/

83. Pani PP, Trogu E, Pacini M, Maremmani I. Anticonvulsants for alcohol dependence. The Cochrane database of systematic reviews [Internet]. 2014 Feb 13 [cited 2022 Jan 10];2014(2). Available from: https://pubmed.ncbi.nlm.nih.gov/24523233/

84. Kranzler HR, Feinn R, Morris P, Hartwell EE. A meta-analysis of the efficacy of gabapentin for treating alcohol use disorder. Addiction (Abingdon, England) [Internet]. 2019 [cited 2022 Jan 10];114(9):1547–55. Available from: https://pubmed.ncbi.nlm.nih.gov/31077485/

85. Cheng YC, Huang YC, Huang WL. Gabapentinoids for treatment of alcohol use disorder: A systematic review and meta-analysis. Human psychopharmacology [Internet]. 2020 Nov 1 [cited 2022 Jan 10];35(6):1–11. Available from: https://pubmed.ncbi.nlm.nih.gov/32667088/

86. Palpacuer C, Duprez R, Huneau A, Locher C, Boussageon R, Laviolle B, et al. 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 [Internet]. 2018 Feb 1 [cited 2022 Jan 10];113(2):220–37. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/add.13974

87. Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. JAMA [Internet]. 2014 May 14 [cited 2022 Jan 10];311(18):1889–900. Available from: https://pubmed.ncbi.nlm.nih.gov/24825644/

88. Ipser JC, Wilson D, Akindipe TO, Sager C, Stein DJ. Pharmacotherapy for anxiety and comorbid alcohol use disorders. Cochrane Database of Systematic Reviews [Internet]. 2015 Jan 20 [cited 2022 Jan 10];2017(6). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD007505.pub2/full

89. Li J, Wang H, Li M, Shen Q, Li X, Rong X, et al. Efficacy of pharmacotherapeutics for patients comorbid with alcohol use disorders and depressive symptoms—A bayesian network meta‐analysis. CNS Neuroscience & Therapeutics [Internet]. 2020 Nov 1 [cited 2022 Jan 10];26(11):1185. Available from: /pmc/articles/PMC7564195/

90. Agabio R, Trogu E, Pani PP. Antidepressants for the treatment of people with co-occurring depression and alcohol dependence. Cochrane Database of Systematic Reviews. 2018 Apr 24;2018(4).

91. Stokes PRA, Jokinen T, Amawi S, Qureshi M, Husain MI, Yatham LN, et al. Pharmacological Treatment of Mood Disorders and Comorbid Addictions: A Systematic Review and Meta-Analysis: Traitement Pharmacologique des Troubles de L'humeur et des Dépendances Comorbides: Une Revue

Systématique et une Méta-Analyse. Canadian Journal of Psychiatry [Internet]. 2020 Nov 1 [cited 2022 Jan 10];65(11):749–69. Available from: https://journals.sagepub.com/doi/10.1177/0706743720915420?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed

92. Kishi T, Sevy S, Chekuri R, Correll CU. Antipsychotics for primary alcohol dependence: a systematic review and meta-analysis of placebo-controlled trials. The Journal of clinical psychiatry [Internet]. 2013 [cited 2022 Jan 10];74(7). Available from: https://pubmed.ncbi.nlm.nih.gov/23945459/

93. Skinner MD, Lahmek P, Pham H, Aubin HJ. Disulfiram efficacy in the treatment of alcohol dependence: a meta-analysis. PloS one [Internet]. 2014 Feb 10 [cited 2022 Jan 10];9(2). Available from: https://pubmed.ncbi.nlm.nih.gov/24520330/

94. Minozzi S, Saulle R, Rösner S. Baclofen for alcohol use disorder. Cochrane Database of Systematic Reviews [Internet]. 2018 Nov 26 [cited 2022 Jan 10];2018(11). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012557.pub2/full

95. Lesouef N, Bellet F, Mounier G, Beyens MN. Efficacy of baclofen on abstinence and craving in alcohol-dependent patients: a meta-analysis of randomized controlled trials. Therapie [Internet]. 2014 Sep 1 [cited 2022 Jan 10];69(5):427–35. Available from: https://pubmed.ncbi.nlm.nih.gov/25230278/

96. Rose AK, Jones A. Baclofen: its effectiveness in reducing harmful drinking, craving, and negative mood. A meta-analysis. Addiction (Abingdon, England) [Internet]. 2018 Aug 1 [cited 2022 Jan 10];113(8):1396–406. Available from: https://pubmed.ncbi.nlm.nih.gov/29479827/

97. Donoghue K, Elzerbi C, Saunders R, Whittington C, Pilling S, Drummond C. The efficacy of acamprosate and naltrexone in the treatment of alcohol dependence, Europe versus the rest of the world: a meta-analysis. Addiction [Internet]. 2015 Jun 1 [cited 2022 Jan 10];110(6):920–30. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/add.12875

98. Rösner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. The Cochrane database of systematic reviews [Internet]. 2010 Sep 7 [cited 2022 Jan 10];(9). Available from: https://pubmed.ncbi.nlm.nih.gov/20824837/

99. Mason BJ, Lehert P. Acamprosate for alcohol dependence: a sex-specific meta-analysis based on individual patient data. Alcoholism, clinical and experimental research [Internet]. 2012 Mar [cited 2022 Jan 10];36(3):497–508. Available from: https://pubmed.ncbi.nlm.nih.gov/21895717/

100. Dranitsaris G, Selby P, Negrete JC. Meta-analyses of placebo-controlled trials of acamprosate for the treatment of alcohol dependence: impact of the combined pharmacotherapies and behavior interventions study. Journal of addiction medicine [Internet]. 2009 Jun [cited 2022 Jan 10];3(2):74–82. Available from: https://pubmed.ncbi.nlm.nih.gov/21769002/

101. Palpacuer C, Laviolle B, Boussageon R, Reymann JM, Bellissant E, Naudet F. Risks and Benefits of Nalmefene in the Treatment of Adult Alcohol Dependence: A Systematic Literature Review and Meta-Analysis of Published and Unpublished Double-Blind Randomized Controlled Trials. PLoS medicine [Internet]. 2015 [cited 2022 Jan 10];12(12). Available from: https://pubmed.ncbi.nlm.nih.gov/26694529/

102. Streeton C, Whelan G. Naltrexone, a relapse prevention maintenance treatment of alcohol dependence: a meta-analysis of randomized controlled trials. Alcohol and alcoholism (Oxford, Oxfordshire) [Internet]. 2001 [cited 2022 Jan 10];36(6):544–52. Available from: https://pubmed.ncbi.nlm.nih.gov/11704620/

103. Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. The Cochrane database of systematic reviews [Internet]. 2010 Dec 8 [cited 2022 Jan 10];(12):CD001867. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21154349

104. Oon-arom A, Likhitsathain S, Srisurapanont M. Efficacy and acceptability of varenicline for alcoholism: A systematic review and meta-analysis of randomized-controlled trials. Drug and alcohol dependence [Internet]. 2019 Dec 1 [cited 2022 Jan 10];205. Available from: https://pubmed.ncbi.nlm.nih.gov/31678838/

105. Agabio R, Trogu E, Pani PP. Antidepressants for the treatment of people with co-occurring depression and alcohol dependence. The Cochrane Database of Systematic Reviews [Internet]. 2018 Apr 24 [cited 2022 Jan 10];2018(4). Available from: /pmc/articles/PMC6494437/

106. Murphy CE, Wang RC, Montoy JC, Whittaker E, Raven M. Effect of extended-release naltrexone on alcohol consumption: a systematic review and meta-analysis. Addiction (Abingdon, England) [Internet]. 2021 Jun 28 [cited 2022 Jan 10]; Available from: https://pubmed.ncbi.nlm.nih.gov/34033183/

107. Jarosz J, Miernik K, Wąchal M, Walczak J, Krumpl G. Naltrexone (50 mg) plus psychotherapy in alcohol-dependent patients: a meta-analysis of randomized controlled trials. The American journal of drug and alcohol abuse [Internet]. 2013 May [cited 2022 Jan 10];39(3):144–60. Available from: https://pubmed.ncbi.nlm.nih.gov/23721530/

108. Egholm JWM, Pedersen B, Møller AM, Adami J, Juhl CB, Tønnesen H. Perioperative alcohol cessation intervention for postoperative complications. Cochrane Database of Systematic Reviews [Internet]. 2018 Nov 8 [cited 2022 Jan 10];2018(11). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008343.pub3/full

109. Southern C, Lloyd C, Liu J, Wang C, Zhang T, Bland M, et al. Acupuncture as an intervention to reduce alcohol dependency: a systematic review and meta-analysis. Chinese Medicine [Internet]. 2016 Dec 15 [cited 2022 Jan 10];11(1):49. Available from: /pmc/articles/PMC5160025/

110. Maiti R, Mishra BR, Hota D. Effect of high-frequency transcranial magnetic stimulation on craving in substance use disorder: A meta-analysis. Journal of Neuropsychiatry and Clinical Neurosciences [Internet]. 2017 Mar 1 [cited 2022 Jan 10];29(2):160–71. Available from: https://neuro.psychiatryonline.org/doi/abs/10.1176/appi.neuropsych.16040065

111. Huibers M, Beurskens A, Bleijenberg G, Schayck CP van. Psychosocial interventions delivered by general practitioners. Cochrane Database of Systematic Reviews. 2003 Apr 22;

112. Jonas DE, Garbutt JC, Amick HR, Brown JM, Brownley KA, Council CL, et al. Behavioral counseling after screening for alcohol misuse in primary care: a systematic review and meta-analysis for the U.S. Preventive Services Task Force. Annals of internal medicine [Internet]. 2012 Nov 6 [cited 2022 Jan 10];157(9):645–54. Available from: https://pubmed.ncbi.nlm.nih.gov/23007881/

113. Foxcroft DR, Moreira MT, Almeida Santimano NML, Smith LA. Social norms information for alcohol misuse in university and college students. Cochrane Database of Systematic Reviews. 2015 Dec 29;2015(12).

114. Apodaca TR, Miller WR. A meta-analysis of the effectiveness of bibliotherapy for alcohol problems. Journal of clinical psychology [Internet]. 2003 Mar 1 [cited 2022 Jan 10];59(3):289–304. Available from: https://pubmed.ncbi.nlm.nih.gov/12579546/

115. Thomas RE, Lorenzetti D, Spragins W. Mentoring adolescents to prevent drug and alcohol use. The Cochrane database of systematic reviews [Internet]. 2011 Nov 9 [cited 2022 Jan 10];(11). Available from: https://pubmed.ncbi.nlm.nih.gov/22071836/

116. Vanderkam P, Solinas M, Ingrand I, Doux N, Ebrahimighavam S, Jaafari N, et al. Effectiveness of drugs acting on adrenergic receptors in the treatment for tobacco or alcohol use disorders: systematic review and meta-analysis. Addiction [Internet]. 2021 May 1 [cited 2022 Jan 10];116(5):1011–20. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/add.15265

117. Zeng J, Yu S, Cao H, Su Y, Dong Z, Yang X. Neurobiological correlates of cue-reactivity in alcohol-use disorders: A voxel-wise meta-analysis of fMRI studies. Neuroscience and Biobehavioral Reviews. 2021 Sep 1;128:294–310.

118. Hunt GE, Siegfried N, Morley K, Sitharthan T, Cleary M. Psychosocial interventions for people with both severe mental illness and substance misuse. Cochrane Database of Systematic Reviews. 2013 Oct 3;2013(10).

119. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ [Internet]. 2021 Sep 30 [cited 2022 Jan 17];374. Available from: https://www.bmj.com/content/374/bmj.n2061

ANNEX: Search strategy

MEDLINE via PubMed

Concept 1: harmful alcohol use

#1 alcohol-related disorders[MeSH Terms]

#2 drinking behavior[MeSH Terms]

#3 "alcohol use"[Title/Abstract]

#4 alcoholic*[Title/Abstract]

#5 alcoholism[Title/Abstract]

#6 alcohol[Title/Abstract] AND (drink*[Title/Abstract] OR intoxicat*[Title/Abstract] OR abus*[Title/Abstract] OR misus*[Title/Abstract] OR addict*[Title/Abstract] OR depend*[Title/Abstract] OR disorder*[Title/Abstract] OR risk*[Title/Abstract] OR consum*[Title/Abstract] OR withdraw*[Title/Abstract] OR detox*[Title/Abstract] OR treat*[Title/Abstract] OR therap*[Title/Abstract] OR excess*[Title/Abstract] OR reduc*[Title/Abstract] OR cessation[Title/Abstract] OR intervention*[Title/Abstract] OR abstain[Title/Abstract] OR abstinence[Title/Abstract] OR sober[Title/Abstract] OR problem*[Title/Abstract])

#7 drink*[Title/Abstract] AND (excess*[Title/Abstract] OR heavy[Title/Abstract] OR heavily[Title/Abstract] OR hazard*[Title/Abstract] OR binge[Title/Abstract] OR harm[Title/Abstract] OR harmful[Title/Abstract] OR problem*[Title/Abstract])

#8 [#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7]

Concept 2: screening, brief intervention, referral

#9 mass screening[MeSH Terms]

#10 diagnostic screening programs[MeSH Terms]

#11 counseling[MeSH Terms]

#12 interview, psychological[MeSH Terms]

#13 referral and consultation[MeSH Terms]

#14 screening[Title/Abstract]

#15 advice[Title/Abstract]

#16 referral[Title/Abstract]

#17 brief[Title/Abstract] AND (intervention*[Title/Abstract] OR therap*[Title/Abstract] OR interview*[Title/Abstract])

#18 minimal[Title/Abstract] AND (intervention*[Title/Abstract] OR therap*[Title/Abstract] OR interview*[Title/Abstract])

#19 early[Title/Abstract] AND (intervention*[Title/Abstract] OR therap*[Title/Abstract] OR interview*[Title/Abstract])

#20 motivat*[Title/Abstract] AND (intervention*[Title/Abstract] OR therap*[Title/Abstract] OR interview*[Title/Abstract])

#21 [#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20]

Concept 3: psychosocial interventions

#22 psychotherapy[MeSH Terms]

#23 motivation[MeSH Terms]

#24 self-help groups[MeSH Terms]

#25 counsel*[Title/Abstract]

#26 "contingency management"[Title/Abstract]

#27 "community reinforcement"[Title/Abstract]

#28 psychotherap*[Title/Abstract] OR psychosocial[Title/Abstract]

#29 behavio*[Title/Abstract] AND (therap*[Title/Abstract] OR intervention*[Title/Abstract])

#30 cognitive therap*[Title/Abstract]

#31 famil* therap*[Title/Abstract]

#32 "mutual help"[Title/Abstract]

#33 alcohol rehab*[Title/Abstract]

#34 alcohol program*[Title/Abstract]

#35 mentor*[Title/Abstract]

#36 [#22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35]

Concept 4: pharmacological interventions

#37 pharmacology[MeSH Terms]

#38 psychopharmacology[MeSH Terms]

#39 drug therapy[MeSH Terms]

#40 alcohol deterrents[MeSH Terms]

#41 anticonvulsants[MeSH Terms]

#42 narcotic antagonists[MeSH Terms]

#43 pharmacolog*[Title/Abstract]

#44 pharmacotherap*[Title/Abstract]

#45 "opioid antagonist"[Title/Abstract] OR "opioid antagonists"[Title/Abstract]

#46 anticonvulsant*[Title/Abstract]

#47 [#37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46]

#48 [#21 OR #36 OR #47]

Concept 5: systematic review

#49 meta-analysis as topic[MeSH Terms]

#50 meta-analysis[MeSH Terms]

#51 (meta analy*[Title/Abstract]) OR (metanaly*[Title/Abstract]) OR (metaanaly*[Title/Abstract]) OR (met analy*[Title/Abstract])

#52 (integrative research[Title/Abstract]) OR (integrative review*[Title/Abstract]) OR (integrative overview*[Title/Abstract]) OR (research integration*[Title/Abstract]) OR (research overview*[Title/Abstract]) OR (collaborative review*[Title/Abstract]) OR (collaborative overview*[Title/Abstract])

#53 (systematic review*[Title/Abstract]) OR (systematic overview*[Title/Abstract])

#54 (comparative efficacy[Title/Abstract]) OR (comparative effectiveness[Title/Abstract])

#55 (methodological overview*[Title/Abstract]) OR (methodologic* review*[Title/Abstract]) OR (quantitative review*[Title/Abstract]) OR (quantitative overview*[Title/Abstract]) OR (quantitative synthes*[Title/Abstract]) OR (pooled analy*[Title/Abstract])

#56 Embase*[Title/Abstract] OR Cinahl*[Title/Abstract] OR Cochrane[Title/Abstract] OR Medline[Title/Abstract] OR Pubmed[Title/Abstract]

#57 meta-regression[Title/Abstract] OR metaregression[Title/Abstract]

#58 meta-analysis[Publication Type]

#59 systematic[sb]

#60 (data synthes*[Title/Abstract]) OR (data extraction[Title/Abstract]) OR (data abstraction[Title/Abstract])

#61 [#49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60]

Combining concepts

#62 [#8 AND #48 AND #61]

Cochrane Database of Systematic Reviews

Concept 1: harmful alcohol use

#1 alcohol-related disorders[MeSH Terms] explode all trees

#2 drinking behavior[MeSH Terms] explode all trees

#3 ("alcohol use"):ti,ab,kw

#4 (alcoholic*):ti,ab,kw

#5 (alcoholism):ti,ab,kw

#6 (alcohol AND (drink* OR intoxicat* OR abus* OR misus* OR addict* OR depend* OR disorder* OR risk* OR consum* OR withdraw* OR detox* OR treat* OR therap* OR excess* OR reduc* OR cessation OR intervention* OR abstain OR abstinence OR sober OR problem*)):ti,ab,kw

#7 (drink* AND (excess* OR heavy OR heavily OR hazard* OR binge OR harm OR harmful OR problem*)):ti,ab,kw

#8 [#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7]

Concept 2: screening, brief intervention, referral

#9 mass screening[MeSH Terms] explode all trees

#10 diagnostic screening programs[MeSH Terms] explode all trees

#11 counseling[MeSH Terms] explode all trees

#12 interview, psychological[MeSH Terms] explode all trees

#13 referral and consultation[MeSH Terms] explode all trees

#14 screening:ti,ab,kw

#15 advice:ti,ab,kw

#16 referral:ti,ab,kw

#17 (brief AND (intervention* OR therap* OR interview*)):ti,ab,kw

#18 (minimal AND (intervention* OR therap* OR interview*)):ti,ab,kw

#19 (early AND (intervention* OR therap* OR interview*)):ti,ab,kw

#20 (motivat* AND (intervention* OR therap* OR interview*)):ti,ab,kw

#21 [#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20]

Concept 3: psychosocial interventions

#22 psychotherapy[MeSH Terms] explode all trees

#23 motivation[MeSH Terms] explode all trees

#24 self-help groups[MeSH Terms] explode all trees

#25 counsel*:ti,ab,kw

#26 "contingency management":ti,ab,kw

#27 "community reinforcement":ti,ab,kw

#28 (psychotherap* OR psychosocial):ti,ab,kw

#29 (behavio* AND (therap* OR intervention*)):ti,ab,kw

#30 (cognitive therap*):ti,ab,kw

#31 (famil* therap*):ti,ab,kw

#32 "mutual help":ti,ab,kw

#33 (alcohol rehab*):ti,ab,kw

#34 (alcohol program*):ti,ab,kw

#35 mentor*:ti,ab,kw

#36 [#22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35]

Concept 4: pharmacological interventions

#37 pharmacology[MeSH Terms] explode all trees

#38 psychopharmacology[MeSH Terms] explode all trees

#39 drug therapy[MeSH Terms] explode all trees

#40 alcohol deterrents[MeSH Terms] explode all trees

#41 anticonvulsants[MeSH Terms] explode all trees

#42 narcotic antagonists[MeSH Terms] explode all trees

#43 pharmacolog*:ti,ab,kw

#44 pharmacotherap*:ti,ab,kw

#45 ("opioid antagonist" OR "opioid antagonists"):ti,ab,kw

#46 anticonvulsant*:ti,ab,kw

#47 [#37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46]

Combining concepts & Concept 5: systematic review

#48 [#21 OR #36 OR #47]

#49 [#8 AND #48]

#50 [systematic review filter applied to #49]

Embase

Concept 1: harmful alcohol use

1. 'alcoholism'/exp

2. 'alcohol abuse'/exp

3. 'drinking behavior'/exp

4. 'alcohol withdrawal'/exp

5. (alcohol NEAR/3 (drink$ or intoxicat$ or abus$ or misus$ or addict$ or depend$ or disorder$ or risk$ or consum$ or withdraw$ or detox$ or treat$ or therap$ or excess$ or reduc$ or cessation or intervention$ or abstain or abstinence or sober)):ti,ab,kw

6. (drink$ NEAR/3 (excess$ or heavy or heavily or hazard$ or binge or harm or harmful or problem$)):ti,ab,kw

7. (alcohol NEAR/1 use):ti,ab,kw

8. (alcoholic$ or alcoholism):ti,ab,kw

9. or/1-8

Concept 2: screening, brief intervention, referral

10. 'screening'/exp

11. 'counseling'/exp

12. 'psychologic test'/exp

13. 'referral and consultation'/exp

14. (screening or advice or referral):ti,ab,kw

15. ((brief or minimal or early or motivat$) NEAR/3 (intervention$ OR therap$ OR interview$)):ti,ab,kw

16. or/10-15

Concept 3: psychosocial interventions

17. ‘psychosocial’
18. ‘psychotherapy’/exp
19. 'behavior therapy'
20. 'cognitive therapy'
21. motivation
22. 'self help'
23. (counseling or counselling):ti,ab,kw
24. (contingency NEAR/1 management):ti,ab,kw
25. (community NEAR/1 reinforcement):ti,ab,kw
26. (psychotherap$ or psychosocial):ti,ab,kw
27. (behavio$ NEAR/3 (therap$ or intervention$)):ti,ab,kw
28. (cognitive NEAR/1 therap$):ti,ab,kw
29. (famil$ NEAR/1 therap$):ti,ab,kw
30. (mutual NEAR/1 help):ti,ab,kw
31. (alcohol NEAR/3 rehab$):ti,ab,kw
32. (alcohol NEAR/3 program$):ti,ab,kw
33. (mentor$):ti,ab,kw
34. or/17-33

Concept 4: pharmacological interventions

35. ‘alcoholism therapy’
36. ‘anticonvulsive agent’/exp
37. ‘narcotic antagonists’/exp
38. psychopharmacology:ti,ab,kw
39. (pharmacolog$):ti,ab,kw
40. (pharmacotherap$):ti,ab,kw

41. (opioid NEAR/2 antagonist):ti,ab,kw

42. (anticonvulsant$):ti,ab,kw

43. or/35-42

44. 16 or 34 or 43

Concept 5: systematic review

45. ('meta-analysis' OR 'systematic review' OR 'meta-analysis as topic' OR 'meta analysis (topic)' OR 'systematic review (topic)') AND ('technology assessment' OR 'biomedical')

46. 'meta analysis'

47. ((systematic* NEAR/3 (review* OR overview*)):ti,ab,kw) OR ((methodologic* NEAR/3 (review* OR overview*)):ti,ab,kw)

48. ((quantitative NEAR/3 (review* OR overview* OR synthes*)):ti,ab,kw) OR ((research NEAR/3 (integrati* OR overview*)):ti,ab,kw)

49. ((integrative NEAR/3 (review* OR overview*)):ti,ab,kw) OR ((collaborative NEAR/3 (review* OR overview*)):ti,ab,kw) OR ((pool* NEAR/3 analy*):ti,ab,kw)

50. 'data synthes*':ti,ab,kw OR 'data extraction*':ti,ab,kw OR 'data abstraction*':ti,ab,kw51. (met analy* or metanaly*):ti,ab,kw,kf

51. 'meta regression*':ti,ab,kw OR 'metaregression*':ti,ab,kw

52. (comparative NEAR/3 (efficacy or effectiveness)):ti,ab,kw

53. 'meta-analy*' OR 'metaanaly*' OR 'systematic review*':ti,ab,kw

54. 'medline':ti,ab OR 'cochrane library':ti,ab OR pubmed:ti,ab OR 'embase':ti,ab OR 'cinahl':ti,ab

55. or/45-54

Combining concepts

58. 9 and 44 and 55

PsycINFO

Concept 1: harmful alcohol use

1. exp alcohol use disorder/

2. exp alcohol drinking patterns/

3. sobriety/

4. (alcohol NEAR/3 (drink$ or intoxicat$ or abus$ or misus$ or addict$ or depend$ or disorder$ or risk$ or consum$ or withdraw$ or detox$ or treat$ or therap$ or excess$ or reduc$ or cessation or intervention$ or abstain or abstinence or sober)).tw

5. (drink$ NEAR/3 (excess$ or heavy or heavily or hazard$ or binge or harm or harmful or problem$)).tw

6. ("alcohol use" or alcoholic$ or alcoholism).tw

7. or/1-6

Concept 2: screening, brief intervention, referral

8. exp health screening/

9. psychodiagnosis/

10. exp brief psychotherapy/

11. exp counseling/

12. professional referral/

13. (screening or advice or referral).tw

14. ((brief or minimal or early or motivat$) NEAR/3 (intervention$ OR therap$ OR interview$)).tw

15. or/8-14

Concept 3: psychosocial interventions

16. support groups/

17. self-help techniques/

18. group psychotherapy/

19. cognitive behavior therapy/ or behavior therapy/

20. motivational interviewing/

21. (community NEAR/1 reinforcement).tw

22. (psychotherap$ or psychosocial).tw

23. (behavio$ NEAR/3 (therap$ or intervention$)).tw

24. (cognitive NEAR/1 therap$).tw

25. (famil$ NEAR/1 therap$).tw

26. (mutual NEAR/1 help).tw

27. (alcohol NEAR/3 rehab$).tw

28. (alcohol NEAR/3 program$).tw

29. (mentor$).tw

30. (counseling or counselling).tw

31. (contingency NEAR/1 management).tw

32. or/16-31

Concept 4: pharmacological interventions

33. exp alcohol treatment/

34. pharmacotherap$.tw

35. psychopharmacolog$.tw

36. (drug NEAR/3 therap$).tw

37. (alcohol NEAR/3 deterrent).tw

38. Opioid?antagonist.tw

40. Anticonvulsant$.tw

41. (narcotic?antagonist or narcotic?agonist or narcotic?drug?).tw

42. pharmacolog$.tw

43. or/33-42

44. 15 or 33 or 43

Concept 5: systematic review

45. meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/

46. (meta-analysis).pt

47. ((systematic* NEAR/3 (review* or overview*)) or (methodologic* NEAR/3 (review* or overview*))).ti,ab,kw,kf

48. ((quantitative NEAR/3 (review* or overview* or synthes*)) or (research NEAR/3 (integrati* or overview*))).ti,ab,kw,kf

49. ((integrative NEAR/3 (review* or overview*)) or (collaborative NEAR/3 (review* or overview*)) or (pool* NEAR/3 analy*)).ti,ab,kw,kf

50. (data synthes* or data extraction* or data abstraction*).ti,ab,kw,kf

51. (met analy* or metanaly*).ti,ab,kw,kf

52. (meta regression* or metaregression*).ti,ab,kw,kf

53. (comparative NEAR/3 (efficacy or effectiveness)).ti,ab,kw,kf

54. (meta-analy* or metaanaly* or systematic review*).mp

55. (medline or cochrane or pubmed or embase or cinahl).ti,ab,hw

56. (meta-analysis or systematic review).md

57. or/45-56

Combining concepts

58. 7 and 44 and 57