

REVIEW

Economic evaluations of interventions aimed at the prevention, treatment and/or rehabilitation of alcohol-related disorders: A systematic review

Evaluaciones económicas de intervenciones dirigidas a la prevención, tratamiento y/o rehabilitación de trastornos por consumo de alcohol: Una revisión sistemática

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Abstract

The aim of this systematic literature review is to identify economic evaluations of programmes or interventions aimed at the prevention, treatment and rehabilitation of alcohol use disorders, as well as to determine those types of programmes, treatments or interventions that are efficient. The systematic literature review was conducted by searching the following databases: National Health Service Economic Evaluation Database (NHS EED), Health Technology Assessment (HTA), MEDLINE Ovid and PubMed. The search terms used were in English. No time restriction was applied. A data extraction form was used to draw information. The systematic review follows the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) on reporting systematic reviews. The interventions were classified into three categories: "A" treatments for people with alcohol use disorders (tertiary prevention); "B" treatments for people at risk for alcohol-related problems (secondary prevention); "C" policy legislation and enforcement interventions (primary prevention). Furthermore, the "A" interventions were subclassified into psychological, pharmacological and combined interventions. The review included 63 papers. In terms of treatments for people with alcohol use disorders, any psychosocial intervention compared to no intervention appeared to be a dominant strategy. In terms of treatments for people at risk of alcohol-related problems, brief intervention appears to be dominant or cost-effective when compared to no intervention. Advertising controls, tax increases, licensing, legal drinking age, and mass media campaigns seem to be dominant or cost-effective strategies compared to no intervention or random breath testing. Previous reviews have been extended by depicting alcohol programmes according to their efficiency. Despite this, the available studies in this regard have heterogeneous approaches and most do not adequately define the costs included in their analyses. Therefore, it is necessary to encourage the evaluation of the efficiency of these types of interventions to aid decision-making in public health.

Keywords: alcohol, systematic review, efficiency, cost-effectiveness, intervention classification

Resumen

El objetivo de esta revisión sistemática de la literatura es identificar evaluaciones económicas de programas o intervenciones dirigidas a la prevención, tratamiento y rehabilitación de trastornos por consumo de alcohol, así como determinar aquellos tipos de programas, tratamientos o intervenciones que son eficientes. Se realizó una revisión sistemática de la literatura mediante la búsqueda en las siguientes bases de datos: National Health Service Economic Evaluation Database (NHS EED), Health Technology Assessment (HTA), MEDLINE Ovid and PubMed. Los términos de búsqueda utilizados fueron en inglés. No se aplicó ninguna restricción de tiempo. Se utilizó un formulario de extracción de datos para resumir la información. La revisión sistemática siguió las recomendaciones (PRISMA-P) sobre la presentación de informes de revisiones sistemáticas. Las intervenciones fueron clasificadas en tres categorías: «A» tratamientos para personas con trastornos por consumo de alcohol (prevención terciaria); «B» tratamientos para personas en riesgo de problemas relacionados con el alcohol (prevención secundaria); «C» legislación sobre políticas e intervenciones de aplicación (prevención primaria). Además, las intervenciones «A» fueron subclassificadas en intervenciones psicológicas, farmacológicas y combinadas. Se incluyeron 63 documentos. En términos de tratamientos para personas con trastornos por uso de alcohol, cualquier intervención psicosocial en comparación con ninguna intervención parece ser una estrategia dominante. En términos de tratamientos para personas en riesgo de problemas relacionados con el alcohol, la intervención breve parece ser dominante o rentable en comparación con no hacer nada. Los controles publicitarios, las subidas de impuestos, las licencias, la edad legal para consumir alcohol y las campañas en los medios de comunicación parecen ser una estrategia dominante o rentable en comparación con ninguna intervención o prueba aleatoria de alcoholemia. Se han ampliado las revisiones anteriores al mostrar los programas de alcohol según criterios de eficiencia. A pesar de ello, los estudios disponibles al respecto tienen enfoques heterogéneos y la mayoría no define adecuadamente los costes incluidos en su análisis. Por tanto, es necesario continuar evaluando en términos de eficiencia este tipo de intervenciones para informar mejor la toma de decisiones en salud pública.

Palabras clave: alcohol, revisión sistemática, eficiencia, coste-efectividad, clasificación intervenciones

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Alcohol consumption ranks as a leading risk factor for mortality and disability around the world, representing 5.3% of all deaths and 5.1% of all disability-adjusted life years (DALY) worldwide (World Health Organization, 2018). Smyth et al. (2015) confirmed that alcohol misuse was associated with increased risk of mortality, cancer and injury and an insignificantly reduced risk of myocardial infarction. The amount and pattern of alcohol consumption can have different associations with health outcomes and costs. Three decades ago, Burke (1988) already estimated the economic impact of alcohol use disorder (AUD) and alcoholism quantifying losses of billions of dollars per year because of lost productivity and employment. Rehm et al. (2009) stated that the costs associated with alcohol amount to more than 1% of the gross national product in high-income and middle-income countries, with the costs of social harm constituting a major proportion in addition to health costs, and actions to reduce burden and costs associated with alcohol should be urgently increased.

Economic Evaluation (EE) is the most relevant tool to health care decision-makers (Goeree & Diaby, 2013) to compare alternative courses of action both in terms of their costs and health outcomes. There are four different types of EEs with the main difference being the way outcomes are measured, valued and included in the analysis (Drummond, Sculpher, Claxton, Stoddard & Torrance, 2015). With Cost-Effectiveness Analysis (CEA) alternatives are compared in terms of costs and outcomes, and outcomes are measured and valued in natural units collected in clinical trials or observational studies. In a Cost-Utility Analysis (CUA), expected costs and outcomes for each intervention are calculated, with the outcome measure mainly expressed as quality adjusted life years (QALYs), which combines quality of length and length of life into a single measure (Drummond et al., 2015). The results of an EE are presented in terms of an incremental cost-effectiveness ratio (ICER), which is literally the differences in mean expected costs divided by the difference in mean expected outcomes (Drummond et al., 2015). The ICER provides a measure of the expected cost needed to gain a unit of effect. When a program or an intervention improves the outcomes and lower (saves) costs then it is said that exists dominance (Drummond et al., 2015). During the past few years, economic evaluations have become more important as a source of information for decision makers in the public health field (Drummond et al., 2007; Williams, McIver, Moore & Bryan, 2008). It has been proven that the market itself does not achieve efficient solutions, so decision makers play a key role because they can decide how to allocate scarce resources (Drummond et al., 2015; Gold, Siegel, Russell & Weinstein, 1996; Kernick, 2003; Sloan & Hsieh, 2012). Therefore, to reduce the disease and injury burden associated with alcohol consumption, it is important to identify the cost-effective interventions to support national health strategies and initiatives to reduce harmful alcohol use.

Donaldson, Mugford & Vale (2002) argued for the value of systematic reviews of economic evaluations as a tool to promote evidence-informed health care. They suggest that the value of systematic review of economic evaluation evidence is not to generate a single authoritative result or recommendation about relative cost effectiveness but, rather, to help decision makers understand the structure of the resource allocation problem and potential impacts.

Some systematic reviews have been published, evaluating different types of programs, strategies or interventions such as psychological therapies (Meads, Ting, Dretzke & Bayliss, 2007) and pharmacological treatments (Ndegwa & Cunningham, 2009) from an efficiency point of view, trying to identify which service provision the National Health Service (NHS) should be promoting to reduce alcohol consumption. In addition, other systematic reviews of effectiveness, such as on mass media campaigns to reduce alcohol-impaired driving and alcohol-related crashes (Yadav & Kobayashi, 2015), community pharmacy interventions or alcohol management interventions (Brown et al., 2016) have been published, highlighting the most effective in terms of health outcomes. In addition, Barbosa, Godfrey & Parrott (2010) carried out a review of the methodology that was adopted in previous economic evaluations of alcohol treatment, and they offered research recommendations with a view to enhancing the consistency and harmonization of economic evaluation in the alcohol usage field. The added value of this new review on alcohol-related economic evaluations is the inclusion of programs distinguishing between treatments for people with alcohol use disorders, treatments for people at risk of alcohol-related problems, and policy, legislation and enforcement interventions. This implies mapping the efficiency of all available interventions to deal with this public health problem.

Therefore, the goal of this paper is to conduct a systematic literature review of economic evaluations of treatments for people with alcohol use disorders or at risk of alcohol-related problems and of policy legislation and enforcement interventions, considering the findings from previous literature reviews (Angus, Latimer, Preston, Li & Purshouse, 2014; Barbosa et al., 2010; Chisholm, Doran, Shibuya & Rehm, 2006; Hill, Vale, Hunter, Henderson & Oluboyede, 2017; Hoang et al., 2016; Kaner et al., 2017; Kelly, Abry, Ferri & Humphreys, 2020; Kruse et al., 2020; Ludbrook, 2004; Ludbrook et al., 2002; Mujoomdar & Spry, 2009; Poldrugo, Haeger, Comte, Walburg & Palmer, 2005; Rehm & Barbosa, 2018; Slattery et al., 2002; White, Skirrow, George & Memon, 2018). The specific objectives of this review are (a) to conduct a qualitative review of the methodological aspects of each of the identified studies; (b) to identify the most studied and efficient programs and strategies to treat people with alcohol use disorders or people at risk of alcohol-related problems; and (c) to group all existing interventions into the three categories stated before ("A": treatments for people

with alcohol use disorders; “B”: treatments for people at risk of alcohol-related problems; “C”: policy legislation and enforcement interventions).

Method

Search strategy

The systematic literature review was conducted by searching three databases: National Health Service Economic Evaluation Database (NHS EED), Health Technology Assessment (HTA), MEDLINE Ovid and PubMed. All databases were searched from their inception to 24th July 2020, using keywords: (alcohol*:ti or drink*:ti or detoxificat*:ti) crossed with (cost benefit* or cost effect* or cost utilit* or cost minim* or unit* adj cost or cost*) for the NHS EED and Health Technology Assessment (HTA) searches; and (alcohol\$[Title] or drink\$[Title] or detoxificat\$[Title]) and (cost\$ benefit\$ or cost\$ effect\$ or cost\$ utilit\$ or cost\$ minim\$ or unit\$ adj cost\$) for the MEDLINE and PubMed searches. The search terms used were in English.

Inclusion criteria

The inclusion criteria consisted of considering papers about economic evaluations related to humans, with no time restriction (search conducted till 24th July 2020), who undertake programmes for treating people with alcohol use disorders (classified as “A” in the data extraction tables), people at risk of alcohol-related problems (classified as “B” in the data extraction tables), and policy legislation and enforcement interventions (classified as “C” in the data extraction tables). Papers were excluded if they were review articles, were not full economic evaluations (comparative analysis of alternative courses of action in terms of both costs (resource use) and consequences (outcomes, effects) that aims to produce measures of incremental resource use, costs and/ or cost-effectiveness) (Drummond et al., 2015) providing an Incremental Cost-Effectiveness Ratio (ICER) as a result, did not use the term ‘alcohol’ as a drink, or did not focus on programmes associated with reducing or preventing alcohol consumption. Review papers were kept to check that identified papers by previous economic evaluation review were included. Papers included were those identified by the search strategy and some others obtained from citation tracking of identified key articles.

Data extraction and synthesis method

Data from included papers was extracted using the same structure as the standardised data extraction tool for economic evaluations in Joanna Briggs Institute for Evidence Based Practice (JBI-ACTUARI) (The Joanna Briggs Institute, 2014). The quality and validity of the included studies were subjected to double review by two independent reviewers using the standardised critical appraisal tools from the Joanna Briggs Institute from JBI-ACTUARI for economic

evaluations (The Joanna Briggs Institute, 2014). Whenever there was a discrepancy, papers were reviewed a second time by both reviewers to reach a consensus. No additional data was extracted. The systematic review follows the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) on reporting systematic reviews (Moher et al., 2015)¹.

The data extracted will cover descriptive data about the (i) study population/participants, alcohol dependence level, intervention, comparator(s) and outcomes; (ii) study methods, including evaluation design type, analytic viewpoint(s); source of effectiveness data, prices and currency used for costing, time period of analysis; sensitivity testing; measures of resource use; cost and health effect/clinical and cost effectiveness; and, (iii) study context (geographical, year of publication, health care and broader service delivery setting and culture). Regarding the alcohol dependence, the Tenth Revision of the International Classification of Diseases and Health Problems (ICD-10) defines the dependence syndrome as being a cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviours that once had greater value (World Health Organization, 1992). This concept is of much importance in the alcohol context in order to describe the importance and level of this abusive behaviour and the potential consequences that they could have. Data on definition of alcohol dependence and people at risk of alcohol dependence was summarised. All existing interventions were classified according to treatment for people with alcohol use disorders; treatments for people at risk of alcohol related problems; and, policy, legislation and enforcement interventions. To do so, were considere some advices from policy makers, definitions developed by published reviews (Barbosa et al., 2010; Chisholm et al., 2006; Ludbrook, 2004; Ludbrook et al., 2002; Slattery et al., 2002) and results obtained from this systematic literature review.

Results

Description of included studies

Figure 1 documents the flowchart of articles through the study and the reasons for exclusion. Finally, a total of 65 economic evaluations specifying 192 estimates for the ICER that met the initial inclusion criteria were included in the analysis. Fifteen literature reviews (Angus et al., 2014; Barbosa et al., 2010; Chisholm et al., 2006; Hill et al., 2017; Hoang et al., 2016; Kaner et al., 2017; Kelly et al., 2020; Kruse et al. 2020; Ludbrook, 2004; Ludbrook et al., 2002; Mujoomdar & Spry, 2009; Poldrugo et al., 2005; Rehm & Barbosa, 2018; Slattery et al., 2002; White et al., 2018) were examined to check that all papers included in them were also included in our review. No additional stu-

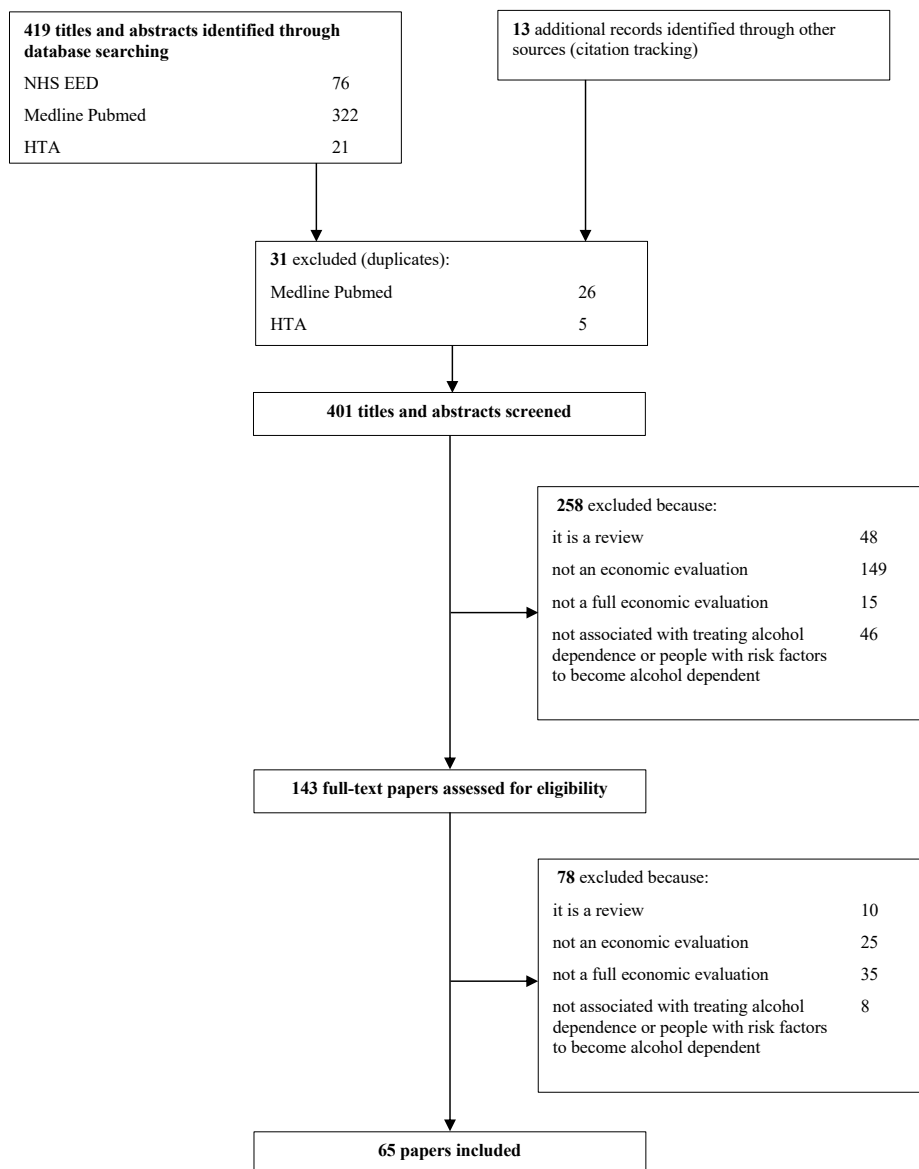
dies were included because they were not economic evaluations or not full economic evaluations (they did not calculate the incremental cost-effectiveness ratio).

Characteristics of included studies

All these results refer to the 65 papers included in the systematic literature review. From these studies, there was one that evaluated a drug (Baclofen) as an intervention in uncomplicated alcohol-withdrawal syndrome. This study was also included in this systematic literature review because these people still have alcohol use disorders or being people at risk of alcohol-related problems. Of these 65 articles, 4 studies included interventions classified exclusively

as primary prevention, 23 as secondary prevention (aimed at people with risky alcohol consumption), 24 as tertiary prevention (aimed at alcohol-dependent people) and 14 as secondary and tertiary prevention (aimed at people with risky alcohol consumption and dependent people). Almost seventy percent of papers ($n = 44$) were published in the last ten years (between 2010 and 2020). Only 9,2% of papers ($n = 6$) first appeared between 1991 and 2002. The last year of the search up to the date indicated produced five published studies. Appendix 1 contains a list of the 65 papers included in the present systematic literature review. See Table 1 for further details on the main characteristics of included Table 1 studies.

Figure 1
Flowchart of study identification and selection



Of the 65 articles included, 23.1% (n = 15) were from Europe (one of those was from Spain), 21.5% (n = 14) from the United States, 12.3% (n = 8) from Australia, 26.2% (n = 17) from the United Kingdom, 6.2% (n = 4) from India, and the remaining from Brazil, Estonia, and Italy. Four papers studied more than one country. The average age of populations, weighted by sample, included in the study was approximately 38 years, though only 46% of studies reported age. Most of the studies (73.8%; n = 48) reported the sample size; eighteen of those comprised a sample higher than 10,000; however, three comprised a sample lower than 100 people. The gender of the people was specified in 58.7% of the studies included in the economic evaluation; from those, 35.1% were men only. Only one study specified the socioeconomic status of the participants. Only two studies (3.2%) offered monetary

compensation for participating in the study. Thirty-two (50.8%) studies were trial based, all randomised with the exception of two studies.

More than half of the studies (56.9%; n = 37) stated that the participants had alcohol dependence. However, only seventeen (47.2%) of those defined this condition, whose definition was based on in grams per day or week, or consumed units, drinks, per day/week, or based on AUDIT score, WHO criteria, the ICD-10, or based on the Diagnostic Interview Schedule for Psychoactive Substance Dependence (DSM). A high number of studies (n = 25; 39.7%) stated that their participants attributed health conditions to alcohol, among them, cardiovascular- (n = 19) and liver- (n = 14) related diseases and cancer (n = 14) the most frequent ones, followed by car accidents (n = 11). See Table 1 for further details.

Table 1

Main characteristics of included studies and definitions of alcohol dependence and people at risk of alcohol dependence

Authors	Sample size	Alcohol dependence*	Definition of alcohol dependence	Definition of people at risk of alcohol dependence	Type of EE (according to reviewers)	Perspective**
Agus A et al., 2019	8226	No dependence	No definition included	Heavy episodic drinking (HED) ^a	CEA	Funder
Angus C et al., 2014	ns	-	No definition included	No definition included	CUA	Funder
Barbosa C et al., 2010	608	Dependence	No definition included	Hazardous drinking: ≤54.99 g/day (women); ≤79.99 g/day (men); Harmful drinking: ≥55 g/day (women); ≥80 g/day (men)	CUA	Funder
Barbosa C et al., 2015	9835	ns	No definition included	No definition included	CEA; CUA	Provider; Social
Barbosa C et al., 2017	976	ns	No definition included	No definition included	CEA	Provider
Barrett B et al., 2006	290	Dependence	No definition included	Any man drinking more than 8 units of alcohol in any one session at least once a week; any woman drinking more than 6 units in any one session at least once a week	CEA	Social
Blankers M et al., 2012	136	Dependence	AUDIT Score >8 and a weekly consumption of more than 14 standard (10 g ethanol) drinking units	No definition included	CEA; CUA	Social
Brodtkorb T-H et al., 2016	100,000	Dependence	No definition included	Males/Females: Very high risk (>101 / >60 g per day) High risk (61-100 / 41-60 g per day) Medium risk (41-60 / 21-40 g per day) Low risk (1-40 / 1-20 g per day)	CUA	Funder; Social
Byrnes JM et al., 2010	ns	No dependence	No definition included	No definition included	CUA	Funder
Chisholm D et al., 2004	ns	Dependence	No definition included	Hazardous and harmful alcohol consumption was defined as consuming on average more than 20 and 40 g of pure alcohol per day for females and males, respectively.	CUA	Social
Chisholm D et al., 2018	529	ns	No definition included.	Hazardous and harmful alcohol consumption was defined as consuming on average more than 20 and 40 g of pure alcohol per day for females and males, respectively.	CUA	ns
Cobiac L et al., 2009	ns	Dependence	No definition included	No definition included	CUA	Funder
Cordovilla-Guardia S et al., 2020	294	No dependence	No definition included	No definition included	CBA	Funder
Corry J et al., 2004	20463; 30999	Dependence	No definition included	No definition included	CEA	Funder
Coulton S et al., 2017	529	No dependence	No definition included	AUDIT Score >8 is indicative of hazardous alcohol use	CUA	Funder; Social
Cowell AJ et al., 2012	656	Dependence	No definition included	At least one heavy drinking episode ^b	CEA	Provider
Crawford MJ et al., 2015	797	ns	No definition included	Men who drink more than eight standard drinks on one occasion one a month or more, and women who drink more than six standard drinks on one occasion once a month or more (Modified-Single Alcohol Screening Questionnaire [M-SASQ])	CUA	Funder
Deluca P et al., 2020	3326	No dependence	No definition included	>6= 3 on the AUDIT-C → high-risk drinkers <3 on the AUDIT-C → low-risk drinkers or abstainers	CUA	Funder
Drost RM et al., 2016	690	No dependence	No definition included	No definition included	CEA	Funder; Social

Table 1 (cont.)

Authors	Sample size	Alcohol dependence*	Definition of alcohol dependence	Definition of people at risk of alcohol dependence	Type of EE (according to reviewers)	Perspective**
Drummond C et al., 2009	112	No dependence	No definition included	AUDIT score > or = 8	CUA	ns
Dunlap LJ et al., 2010	1379	Dependence	No definition included	No definition included	CEA	Patient
Dunlap LJ et al., 2020	101	Dependence	No definition included	No definition included	CEA	Patient
Gentilello LM et al., 2005	ns	Dependence	No definition included	Either a blood alcohol level ≥ 100 mg/dL or a positive result on a standard brief alcohol disorder screening questionnaire	CBA	Funder
Giles EL et al., 2019	443	Dependence	AUDIT score ≥ 8	AUDIT score ≥ 4 OR Scored positive on the A-SAQ (Adolescent Single Alcohol Questionnaire); ≥ 3 was considered for possible hazardous or harmful drinking.	CUA; CCA	Funder
Havard A et al., 2012	244	Dependence	No definition included	People who had alcohol consumption in the 6 hours prior to the onset of their condition or who perceived alcohol to be a contributing factor in the condition with which they presented in the emergency department.	CEA	Provider
Holm AL et al., 2014a	ns	No dependence	No definition included	Excess alcohol consumption ^f .	CUA	Funder
Holm AL et al., 2014b	ns	No dependence	No definition included	Excess alcohol consumption ^f	CUA	Funder
Hunter R et al., 2017	763	No dependence	No definition included	AUDIT-C ≥ 5 for men or AUDIT-C ≥ 4 for women	CUA	Funder
Ingels JB et al., 2013	473	No dependence	No definition included.	No definition included.	CEA	
Kruger J et al., 2014	1445	No dependence	No definition included.	No definition included.	CUA	Funder
Kunz FM et al., 2004	194	Dependence	AUDIT score >8	People who have used alcohol in the past 12 months with a CAGE score ≥ 1	CEA	ns
Lai T et al., 2007	ns	Dependence	No definition included	No definition included	CUA	Funder
Laramée P et al., 2014	ns	Dependence	Alcohol-dependent people with high/very high drinking risk levels (defined based on the WHO criteria for risk consumption on a single drinking day) ^d	No definition included	CEA; CUA	Funder
Laramée P et al., 2016	ns	Dependence	Alcohol-dependent people with high/very high drinking risk levels ^d	No definition included	CUA	Funder
Li T et al., 2017	33560	No dependence	No definition included	No definition included	CEA; CBA	Funder
Millier A et al., 2017	824	Dependence	No definition included	No definition included	CUA	Social; Third-party payer
Moore SC et al., 2020	832	No dependence	No definition included	No definition included	CEA	Funder; Social
Moraes E et al., 2010	89	Dependence	No definition included	No definition included	CEA	Social
Mortimer D & Segal L 2005	ns	Dependence	No definition included	No definition included	CUA	Social
Nadkarni A et al., 2017a	316	No dependence	No definition included	Harmful drinking. AUDIT Score 12-19	CEA; CUA	Funder; Social
Nadkarni A et al., 2017b	278	No dependence	No definition included	AUDIT Score 12-19	CEA; CUA	Funder; Social
Nadkarni A et al., 2019	135	Dependence	AUDIT Score ≥ 20	No definition included	CEA	Funder; Social
Navarro HJ et al., 2011	17030	Dependence and no dependence	AUDIT Score ≥ 20	Risky drinkers (AUDIT Score 8–19, representing WHO categories of hazardous and harmful drinking)	CEA	ns
Neighbors CJ et al., 2010	84	Dependence	No definition included	No definition included	CEA; CUA	Provider; social
Olmstead TA et al., 2019	138	Dependence and/or current alcohol abuse	DSM-IV TR (APA, 2000) ^e	No definition included	CEA	Provider
Palmer AJ et al., 2000	ns	No dependence	-	-	CEA	Funder
Purshouse RC et al., 2013	ns	Dependence	AUDIT Score >8	No definition included	CUA	Funder
Robinson E et al., 2020	ns	No dependence	No definition included	No definition included	CEA	Social
Reddy VK et al., 2014	60	Dependence	No definition included	No definition included	CEA	Funder; patient
Rychlik R et al., 2003	814	Dependence	No definition included	No definition included	CEA	ns

Table 1 (cont.)

Authors	Sample size	Alcohol dependence*	Definition of alcohol dependence	Definition of people at risk of alcohol dependence	Type of EE (according to reviewers)	Perspective**
Schädlich PK & Brecht JG, 1998	2000	Dependence	People who meet at least 5 DSM criteria for alcohol dependence and are alcohol-dependent according to the Munich Alcoholism Test.	No definition included	CEA	Funder
Schulz DN et al., 2014	1733	No dependence	No definition included	No definition included	CEA; CUA	Funder; Social
Slattery J et al., 2002	1000	Dependence	Definition of alcohol dependence based on the International Classification of Disease (ICD-10) diagnostic categories ^f	No definition included	CEA	Funder
Sluiter RL et al., 2018	ns	Dependence	No definition included	No definition included	CEA	Social
Smit F et al., 2011	1254000	Dependence	Alcohol dependence based on the WHO criteria ^g	No definition included	CBA; CUA	Funder
Solberg LI et al., 2008	4000000	No dependence	-	-	CUA	Funder; social
Sumnall H et al., 2017	12738	No dependence	No definition included	Heavy episodic drinking (HED) ^h	CEA	Social
Tariq L et al., 2009	1110000	Dependence	Alcohol dependence based on DSM-IV criteria ^a	"High risk groups are defined as women who drink 2 or more standard alcohol drinks (i.e., 20 grams ethanol) per day; and men who drink 4 or more standard alcohol drinks (i.e. .40 grams ethanol) per day; without meeting the DSM-IV criteria for alcohol dependency"	CEA; CUA	Funder
Torfs K & De Graeve D, 1991	65909	Dependence	Physical dependence on alcohol and drinking >200 g/day	No definition included	CEA	Funder
UKATT Research Team, 2005	608	Dependence	No definition included	No definition included	CUA	ns
van den Berg M et al., 2008	ns	No dependence	No definition included	Alcohol consumption risk levels based on the Environment Chronic Disease Model ^h	CEA; CUA	Funder
Watson J et al., 2013	422	Dependence	AUDIT score ≥20	AUDIT score ≥8	CUA	Funder
Weisner C et al., 2000	541	Dependence	Alcohol dependence based on the DSM-IV criteria ^a	No definition included	CEA	ns
Wutzke SE et al., 2001	ns	No dependence	No definition included	Alcohol consumption is classified according to the Australian National Health and Medical Research Council criteria ⁱ	CEA	Funder
Zarkin GA et al., 2008	1383	Dependence	Alcohol dependence is determined by DSM-IV criteria ^a	No definition included	CEA	Provider

Note: ns: information not specified; CEA: cost-effectiveness analysis; CUA: cost-utility analysis; DSM: Diagnostic and Statistical Manual of Mental Disorders.

* The definition of dependence is cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviours that once had greater value (World Health Organisation, 1992).

**Funder perspective: taking into account the outcomes and costs of interest for the organisation funding the intervention; Social perspective: capturing all relevant outcomes and costs borne by providers and potential beneficiaries (society as a whole); Provider perspective: taking into account the outcomes and costs of interest for the organisation implementing the intervention (i.e., National Health System, University, etc.); Patient perspective: taking into account the outcomes and costs of interest for the patient.

^a Heavy episodic drinking (HED): defined as the consumption of 6 or more units in a single episode for male students and 4.5 or more units for female students. ^b Heavy drinking episode: any man drinking 5 or more drinks on an occasion or any woman drinking 4 or more drinks on an occasion. ^c Excess alcohol consumption: Hazardous drinking → 12-23.9 g/day for women and 24-35.9 d/day for men. Harmful drinking → >24 g/day for women and >36 g/day for men. ^d Alcohol-dependent people with high/very high drinking risk levels are defined based on the WHO criteria for risk consumption on a single drinking day: ≥41 g/day for women; ≥61 g/day for men.

^e Definition of alcohol dependence according to DSM-IV TR (APA, 2000). Reference: American Psychiatric Association (APA). (2000). DSM-IV-TR. Barcelona: Masson. ^f Definition of alcohol dependence based on the ICD-10. Reference: World Health Organization. ICD-10: International statistical classification of diseases and related health problems (10th revised ed Vol. 1) Geneva, Switzerland: Author; 1992. ^g Alcohol dependence is defined, based on the WHO criteria, as meeting "at least 3 of the following criteria: tolerance; withdrawal symptoms; impaired control; preoccupation with acquisition and/or use; persistent desire or unsuccessful efforts to quit; sustains social, occupational, or recreational disability; and use continues despite adverse consequences." ^h Definitions of alcohol consumption categories: moderate: fewer than two standard drinks (< 20 g) per day for women, and fewer than four standard drinks (< 40 g) per day for men; excessive: 2-4 standard drinks (20-40 g) per day for women, and 4-6 standard drinks (40-60 g) per day for men; dangerous: more than four standard drinks (> 40 g) per day for women, and more than six standard drinks (> 60 g) per day for men. ⁱ Alcohol consumption classification according to the Australian National Health and Medical Research Council (NHMRC) criteria (NHMRC, 1992). These criteria define safe drinking as less than 40 g (four standard drinks) for men and less than 20 g (two standard drinks) for women with two alcohol-free days per week. Drinking above these levels is defined as 'hazardous' and above 60 g and 40 g per day, respectively as 'harmful'.

Assessment of methodological quality of the included studies

The JBI ACTUARI was used to assess the quality of the included studies. All studies reached an acceptable level of quality to be included in the systematic review. Commonly, these results refer to the 192 ICERs produced by the systematic literature review. In relation to items measured through the JBI ACTUARI related to well-defined question/objective, comprehensive description of alternatives, identification of relevant costs and outcomes for each alternative and their adjustment for differential timing, clinical effectiveness, incremental analysis of costs and consequences, and sensitivity analysis, the assessment of the included studies is presented below. In general, all papers defined the research question and the programmes or interventions appropriately that were compared in the analysis. The description of alternatives was comprehensive, although on many occasions (49.2%), papers did not report the sample size of each arm and the duration of intervention. Fifty percent of papers took the funder perspective, mostly the National Health System, and only 18.8% adopted a social perspective. The lifetime horizon was used in 57.1% of studies, with a time horizon lower than one year not frequent. Costs and outcomes have been adjusted for differential timing in more than fifty percent of papers, presenting outcomes and costs not appropriately adjusted in 39.68% of papers. Clinical effectiveness was established, using mainly a quality-of-life measure (47.6%) followed by a clinical measure (39.7%) or both at the same time (12.7%). It is clear in all papers how they have derived the effectiveness estimate. Forty-six percent of papers did not specify which types of costs were included in their analysis. Of those that specified types of costs, 79.4% of papers included the direct health care-related costs as well as different types of costs such as direct non-health-related costs, patient costs or intervention costs. Only ten papers (26.5%) included productivity losses. Informal care costs were included at three papers. From all papers specifying the use of the social perspective, 81.8% of those included costs related to loss of productivity. Costs and outcomes have been measured accurately, though in costs, in many instances, the use of resources has not been reported separately. It is important to report use of resources separately from costs/prices for transparency, comparability and transferability reasons. In order to understand and evaluate if the cost data used in the economic evaluation was sensible it is always easier if the resources are reported separately from the costs/prices. Almost 60% of studies ($n = 35$) were conducting a cost-utility analysis. Forty-nine per cent of papers used a decision analysis to estimate costs and outcomes, 48.4% of them being models different from a decision tree and a Markov model. Fully 88.9% of papers conducted a sensitivity analysis, mostly a deterministic (57.1%) rather than a probabilistic (42.9%) one. Of those doing a probabilistic sensitivity analysis, the

vast majority (79.2%) represented a cost-effectiveness acceptability curve.

Findings of the review

These results refer to the 192 ICERs produced by the systematic literature review. In summary, for both people with alcohol dependence and people with high risk factors to become alcohol dependent, psychological interventions were the most evaluated in terms of efficiency, which were shown to be cost-effective or dominant when compared to doing nothing. In relation to pharmacological interventions, which were aimed to people with alcohol dependence, the drugs most used and evaluated were nalmefene and acamprosate, followed by other opioids and opioid antagonists and other drugs such as baclofen and disulfiram. The policy, legislation and enforcement interventions were mainly based on tax increases observing a tendency for dominance or cost-effectiveness when compared to no intervention.

The different economic evaluations found cover a range of interventions such as psychosocial interventions; pharmacological treatments; brief interventions; and policy and legislation or enforcement interventions. Other interventions have been also included such as residential treatment, random breath testing, GP telemarketing, etc. See Table 2 for definitions of the various programmes and interventions informed by this systematic literature review and four other previous published reviews (Barbosa et al., 2010; Chisholm et al., 2006; Ludbrook et al., 2002; Slattery et al., 2002) that already did tasks in terms of homogenisation of the taxonomy for treating people with alcohol use disorders or people at risk of alcohol-related problems.

All these different interventions have been classified according to the availability of efficiency evidence according to the objectives of the programmes. The classification used was also based on those previous published reviews (Barbosa et al., 2010; Chisholm et al., 2006; Ludbrook et al., 2002; Slattery et al., 2002) and this systematic review. You can consult the definition of these interventions in the supplemental material (Table S1), and the classification of the types of alcohol programs in Table 2.

Treatments for people with alcohol dependence (32.8%; $n=63$) have been the most evaluated compared to treatments for people at risk of alcohol-related problems (28.6%; $n=55$) and policy, legislation and enforcement interventions (22.9%; $n = 44$). These percentages have been calculated according to the total number of comparisons in terms of efficiency found ($n=192$). In addition, the remaining 15.3% of comparisons studied a combination of different types of interventions ($n=29$). For further details, see Table 3.

Regarding treatments for people with alcohol dependence ($n=63$), 29.5% were focused in psychosocial interventions; 9.8% in pharmacological interventions; 1.6% evaluated other interventions such as residential treat-

ment; and, the remaining 59.0% evaluated a combination of these types of interventions. In terms of psychosocial interventions, despite the low number of estimates in this case ($n = 18$), it seemed that when any of these types of interventions (i.e., motivational interviewing; behavioural self-control training; coping/social skills training; etc.) were compared to 'no intervention' then the intervention was dominant, which means that the intervention was more effective and less costlier than the comparison. In this line, it could be highlighted the study carried out by Slattery et al. (2002) who found that different psychosocial interventions for people with alcohol dependence were dominant resulting in savings between £923 and £1,643 per additional abstinent patient compared with standard treatment. However, no particular intervention showed a clear tendency in terms of efficiency when compared to another. The low number of economic evaluations on pharmacological interventions ($n=7$) and the heterogeneity of evidence found lead to the impossibility of establishing conclusions

in terms of the efficiency for this type of programmes. Although the number of comparisons of exclusively pharmacological interventions was low, there were some economic evaluations of combined interventions that include drugs. So, these studies have been added to the pharmacological interventions. So, a total of 34 comparisons based mainly on treatment with acamprosate, an N-methyl-D-aspartate (NMDA) receptor modulator, and opioids or opioid antagonists such as nalmefene have been added. Despite the greater number of existing comparisons when including the combined interventions that included drugs, no conclusive results could be found related to acamprosate. The use of acamprosate exclusively for the treatment of alcohol dependence has been shown to be dominant or cost-effective in the 3 comparisons made with placebo. When used in combination with a psychological intervention and medical management, it was dominated by medical management and placebo, as well as by the combination of medical management, opioids or opioid antagonists,

Table 2

Types of alcohol programs for alcohol dependence (Source: own; and Barbosa et al., 2010; Chisholm et al., 2004; Ludbrook et al., 2002; Slattery et al., 2002)

A. Treatments for people with alcohol dependence	
Psychosocial interventions	Pharmacological interventions
Motivational Interviewing	Acamprosate
Motivational Enhancement Therapy	Opioids and opioid antagonists (i.e., Naltrexone, Nalmefene, etc.)
Social Behaviour and Network Therapy	Disulfiram
Behavioural Self Control Training	Lithium
Coping/Social Skills Training	Selective serotonin reuptake inhibitors
Marital, Couples or Family Therapy	Benzodiazepines
Moderation-oriented cue exposure	Baclofen
Relapse prevention	Beta-blockers
Longer intervention	Alpha and beta receptor agonists adrenergic
Cognitive Behavioural Therapy	Other interventions (i.e., residential treatment)
12-Step Facilitation Therapy	Combined interventions
Group Therapy	
Community Reinforcement Approach	
B. Treatments for people at risk of alcohol-related problems	
Brief interventions	
School-based interventions	
Family skills interventions program	
Other interventions (i.e., GP telemarketing, eHealth)	
Combined interventions	
SBIRT (Screening, Brief Intervention and Referral to Treatment)	
Stepped care	
AMPP (Alcohol Misconduct Prevention Program)	
AIMS (Alcohol intoxication management service)	
Community prevention initiatives	
C. Policy, legislation and enforcement interventions	
Drunk-driving legislation/enforcement (random breath testing)	
Advertising controls/bans	
Tax increases	
Licensing	
Legal drinking age	
Mass-media campaigns	
Combined interventions	
Server training	

Note. *Highlighted areas mean that authors have found evidence on efficiency of these interventions.

Table 3

Types of interventions compared (65 papers; 192 comparisons in terms of efficiency)

Intervention	Comparator (check general definitions of these interventions in Table 2)	Efficiency results*	References
A: Treatments for people with alcohol dependence (n=63)			
Psychosocial interventions (n=18)			
Motivational Interviewing (n=3)	Motivational Interviewing (+3 months) (n=1)	Dominated	Cowell AJ et al., 2012
	No intervention (n=1)	Dominant	Slattery J et al., 2002
	Brief intervention (n=1)	Cost-effective	Neighbors CJ et al., 2010
Motivational Enhancement Therapy (n=1)	Brief interventions (n=1)	Cost-effective	Mortimer D & Segal L, 2005
Social Behaviour and Network Therapy (n=2)	Motivational Enhancement Therapy (n=2)	Indifferent (both cost-effective) (n=1) Cost-effective (n=1)	Barbosa C et al., 2005; UKATT Research Team, 2005
Behavioural Self Control Training (n=1)	No intervention (n=1)	Dominant	Slattery J et al., 2002
Coping/Social Skills Training (n=1)	No intervention (n=1)	Dominant	Slattery J et al., 2002
Marital, Couples or Family Therapy (n=1)	No intervention (n=1)	Dominant	Slattery J et al., 2002
Moderation-Oriented Cue Exposure (n=1)	Behavioural Self Control Training (n=1)	Cost-effective	Mortimer D, Segal L, 2005
Relapse Prevention (n=1)	No intervention (n=1)	ns	Slattery J et al., 2002
Longer intervention (trained staff consultations) (n=1)	Brief interventions (n=1)	Not cost-effective	Holm AL et al., 2014a
eHealth intervention (n=1)	Current practice (a) (n=1)	Cost-effective	Smit F et al., 2011
Combined behavioural intervention (n=2)	Medical Management + placebo (n=2)	Dominated	Dunlap LJ et al., 2010; Zarkin GA et al., 2008
Provision of brief psychosocial interventions (3 visits) for persons with hazardous and harmful alcohol use (50% coverage). (n=2)	No intervention or Current situation (n=2)	Cost-effective	Chisholm D et al., 2018
Enhanced usual care (EUC) + Counselling for Alcohol Problems (CAP) (n=1)	EUC alone (n=1)	Cost-effective	Nadkarni et al., 2019
Pharmacological interventions (n=7)			
Acamprosate (n=4)	Placebo (n=3)	Dominant (n=1) ns (n=2) Cost-effective (n=1)	Rychlik R et al., 2003; Schädlich PK & Brecht JG, 1998; Slattery J et al., 2002; Torfs K & De Graeve D, 1991
	Standard care (n=1)		
Baclofen (n=1)	Benzodiazepines (<i>Chlordiazepoxide</i>) (n=1)	Dominated	Reddy VK et al., 2014
Opioid or opiate antagonists (n=1)	Placebo (n=1)	ns	Slattery J et al., 2002
Disulfiram (n=1)	Placebo (n=1)	ns	Slattery J et al., 2002
Other interventions (n=1)			
Residential treatment (n=1)	Drunk-driving legislation (n=1)	Not cost-effective	Cobiac L et al., 2009
Combined interventions (n=37)			
Motivational Interviewing + Home visits (beginning and end of treatment) (n=1)	Motivational Interviewing + Relapse prevention (n=1)	Cost-effective	Moraes E et al., 2010
Motivational Interviewing + Cognitive Behavioural Therapy + Therapist support (n=1)	Motivational Interviewing + Cognitive Behavioural Therapy (n=1)	Cost-effective	Blankers M et al., 2012
Psychosocial support + Opioid or opiate antagonists (Nalmefene) (n=2)	Psychosocial support (n=2)	Cost-effective; Dominant	Laramée P et al., 2014, 2016
Medical Management + combined behavioural intervention + Acamprosate (n=2)	Medical Management + placebo (n=1)	Dominated	Dunlap LJ et al., 2010
	Medical Management + Opioid or opiate antagonists + Acamprosate (n=1)	Dominated	Zarkin GA et al., 2008
Medical Management + combined behavioural intervention + placebo (n=2)	Medical Management + Opioid or opiate antagonists (n=1)	Dominated	Zarkin GA et al., 2008
	Medical Management + placebo (n=1)	Dominated	Dunlap LJ et al., 2010
Medical Management + combined behavioural intervention + Opioid or opiate antagonists (n=2)	Medical Management + Opioid or opiate antagonists + Acamprosate (n=1)	Dominated	Zarkin GA et al., 2008
	Medical Management + placebo (n=1)	Dominated	Dunlap LJ et al., 2010
Medical Management + combined behavioural intervention + Opioid or opiate antagonists + Acamprosate (n=2)	Medical Management + Opioid or opiate antagonists + Acamprosate (n=1)	Dominated	Zarkin GA et al., 2008
	Medical Management + placebo (n=1)	Dominated	Dunlap LJ et al., 2010
Medical Management + Opioid or opiate antagonists + Acamprosate (n=2)	Medical Management + placebo (n=1)	Cost-effective	Dunlap LJ et al., 2010
	Medical Management + Opioid or opiate antagonists (n=1)	Cost-effective	Zarkin GA et al., 2008

Table 3 (cont.)

Intervention	Comparator (check general definitions of these interventions in Table 2)	Efficiency results*	References
Medical Management + Opioid or opiate antagonists (n=2)	Medical Management + placebo (n=2)	Cost-effective	Dunlap LJ et al., 2010; Zarkin GA et al., 2008
	Medical Management + placebo (n=1)	Dominated	Dunlap LJ et al., 2010
Medical Management + Acamprosate (n=2)	Medical Management + Opioid or opiate antagonists (n=1)	Dominated	Zarkin GA et al., 2008
Opioid or opiate antagonists + Residential treatment (n=1)	Random breath testing (n=1)	Not cost-effective	Cobiac L et al., 2009
Group behavioral couples' therapy + individual-based treatment (n=8)	Standard behavioral couples' therapy + individual-based treatment (n=8)	Dominant or cost-effective	Dunlap LJ et al., 2020
Nalmefene + Psychosocial support (n=10)	Psychosocial support alone (n=2)	Cost-effective or dominant	Brodtkorb T-H et al., 2016; Millier A et al., 2017
	No treatment (n=4)	Cost-effective or dominant	
OPRM1 Screening: OPRM1 genotype-guided treatment allocation of naltrexone to G-allele carrying AUD patients (n=1)	No OPRM1 Screening: Random (non-genotype guided) treatment allocation to pharmacological treatment with naltrexone or acamprosate (n=1)	Cost-effective	Sluiter et al., 2018
B: Treatments for people at risk of alcohol-related problems (n=55)			
Brief interventions (n=26)			
	Brief intervention (+ 3 months) (n=1)	Dominated	Cowell AJ et al., 2012
	Random breath testing (n=1)	Cost-effective	Cobiac L et al., 2009
Brief interventions (face-to-face) (n=19)	No intervention (n=15)	Dominant (n=2) Dominant or cost-effective (n=3) Cost-effective (n=10)	Angus C et al., 2014; Chisholm D et al., 2004 (n=3); Gentilello LM et al., 2005; Lai T et al., 2007; Mortimer D & Segal L, 2005 (n=2); Purshouse RC et al., 2013; Solberg LI et al., 2008 (n=2); Tariq L et al., 2009; Wutzke SE et al., 2001 (n=2); Havard et al., 2012
	Control (b) (n=1)	Cost-effective	Wutzke SE et al., 2001
	Current situation (c) (n=1)	Cost-benefit	Cordovilla-Guardia S et al., 2020
Brief interventions (by phone) (n=1)	Brief interventions (face-to-face) (n=1)	Dominant	Holm AL et al., 2014b
Strong African American Families-Teen program (SAAF-T) (n=1)	Attention-control intervention (ACI) (n=1)	Cost-effective	Ingels JB et al., 2013
Personal feedback and Brief Advice (PFBA) (face-to-face) (n=2)	Control group (screening alone) (n=2)	Not cost-effective (n=2) (in the low-risk and high-risk trials)	Deluca P et al., 2020
Personal feedback + smartphone- or web-based brief intervention (eBI) (n=2)		Dominated (n=2) (in the low-risk and high-risk trials)	
Brief advice (face-to-face) + an offer of an appointment with an Alcohol Health Worker (AHW) (n=1)	Control treatment: general health information leaflet (n=1)	Not cost-effective	Crawford MJ et al., 2015
Other interventions (n=22)			
E-mail with a feedback report on personal drinking patterns (n=1)	E-mail with a feedback report on personal drinking patterns (+3 months) (n=1)	ns	Cowell AJ et al., 2012
eHealth intervention (n=1)	No intervention (n=1)	Cost-effective	Smit F et al., 2011
Non-Directive Reflective Listening (n=1)	Brief intervention (Assessment and feedback) (n=1)	Not cost-effective	Mortimer D & Segal L, 2005
A sequential web-based computer-tailored multisession program (n=1)	A simultaneous web-based computer-tailored multisession program (n=1)	Dominated (CUA)	
A sequential web-based computer-tailored multisession program (n=1)	Control (n=1)	Cost-effective (CEA) Dominated (CUA)	Schulz DN et al., 2014
A simultaneous web-based computer-tailored multisession program (n=1)		Cost-effective (CEA) Dominated (CUA)	
A theory-based online health behaviour intervention (U@Uni) (n=1)	Control (n=1)	Cost-effective	Kruger J et al., 2014
Brief Treatment (BT) (SBIRT service) (n=1)	Brief Intervention (BI) (SBIRT service) (n=1)	Cost-effective	Barbosa C et al., 2017
Alcohol intoxication management services (AIMSs) model (n=6)	Usual care (n=6)	Dominant or cost-effective	Moore SC et al., 2020
Facilitated access to an interactive website (n=1)	Face-to-face brief intervention delivered by a general practice (n=1)	Cost-effective	Hunter R et al., 2017
Alcohol Misconduct Prevention Program (AMPP) (n=3)	Historical control group (n=1)	Cost-effective and cost-benefit	Li T et al., 2017
Stepped care (n=2)	Control group minimal intervention (n=2)	Dominant or Cost-effective	Coulton S et al., 2017; Drummond C et al., 2009

Table 3 (cont.)

Intervention	Comparator (check general definitions of these interventions in Table 2)	Efficiency results*	References
Screening, Brief Intervention, and Referral to Treatment (SBIRT) in Emergency Departments (Trauma Centers included) (n=1)	SBIRT in Outpatient Medical Settings (Federally Qualified Health Centers or hospital outpatient clinics) (n=1)	Cost-effective	Barbosa C et al., 2015
Web-based computer-tailored school intervention based on I-Change model (n=1)	Care as usual (CAU) (n=1) (waiting list control condition)	Cost-effective for population subgroups	Drost RM et al., 2016
Combined interventions (n=7)			
Brief intervention + referral to alcohol treatment services (n=1)	Opportunistic identification and an information only control (n=1)	Cost-effective	Barrett B et al., 2006
Brief intervention + health information packet (n=1)	Health information packet (n=1)	Cost-effective	Kunz FM et al., 2004
Brief interventions + GP Telemarketing + GP Support (n=1)	Random breath testing (n=1)	Cost-effective	Cobiac L et al., 2009
Enhanced usual care (EUC) + Counselling for Alcohol Problems (CAP) (n=2)	EUC alone (n=2)	Dominant or Cost-effective	Nadkarni et al., 2017a, 2017b
A combined universal school and parental alcohol intervention called the Steps Towards Alcohol Misuse Prevention Programme (STAMPP) (n=1)	Control group: Education as normal (EAN) (n=1)	Cost-effective	Sumnall H et al., 2017
School-based universal alcohol harm reduction curriculum + brief parental intervention (n=1)	Education as normal (EAN) (n=1)	Cost-effective	Agus A et al., 2019
C: Policy, legislation and enforcement interventions (n=44)			
Advertising controls/bans (n=6)	Brief intervention (n=1)	Dominant	Holm AL et al., 2014b
	Random breath testing (n=1)	Dominant	Cobiac L et al., 2009
	No intervention or Current situation (c) (n=4)	Dominant or cost-effective (n=3) Dominated (n=1)	Chisholm D et al., 2004 (n=3); Lai T et al., 2007
Random breath testing (n=4)	Current situation (c) (n=1)	Dominated	Lai T et al., 2007
	No intervention (n=3)	Dominant or cost-effective	Chisholm D et al., 2004 (n=3)
A rate that maintains the current deadweight loss of taxation (n=1)		Dominant	
A rate that maintains existing taxation Revenue (n=1)	Existing taxation system (n=3)	Dominant	Byrnes JM et al., 2010
A rate equal to the existing rate applied to spirits (n=1)		Dominant	
Tax increases (n=11)	Brief intervention (n=1)	Dominant	Holm AL et al., 2014b
	Random breath testing (n=1)	Dominant	Cobiac L et al., 2009
	No intervention or Current situation (c) (n=8)	Dominant (n=1) dominant or cost-effective (n=4) cost-effective (n=2)	Chisholm D et al., 2004 (n=3); Holm AL et al., 2014a; Lai T et al., 2007; van den Berg M et al., 2008; Chisholm D et al., 2018
	Minimum unit floor price applied to all types of alcoholic drinks (n=1)	Dominant	Robinson E et al., 2020
Licensing (n=6)	Brief intervention (n=1)	Dominant	Holm AL et al., 2014b
	Random breath testing (n=1)	Cost-effective	Cobiac L et al., 2009
	No intervention or Current situation (c) (n=4)	Dominant (n=3) Dominated (n=1)	Chisholm D et al., 2004 (n=3); Lai T et al., 2007
Legal drinking age (n=2)	Brief intervention (n=1)	Cost-effective	Holm AL et al., 2014b
	Random breath testing (n=1)	Dominant	Cobiac L et al., 2009
Mass-media campaigns (n=3)	Random breath testing (n=3)	Cost-effective	Cobiac L et al., 2009; Chisholm D et al., 2018
Enactment and enforcement of drunk driving laws and blood alcohol concentration limits (via sobriety checkpoints) (n=2)	No intervention or Current situation (n=2)	Cost-effective	Chisholm D et al., 2018
Enactment and enforcement of restrictions on the physical availability of retailed alcohol (via reduced hours of sale) (n=2)	No intervention or Current situation (n=2)	Cost-effective	Chisholm D et al., 2018
Combined interventions (n=5)			
Tax increases + Advertising controls (n=4)	No intervention or Current situation (c) (n=4)	Cost-effective	Chisholm D et al., 2004 (n=3); Lai T et al., 2007
Tax increases + Random breath testing (n=1)	Current situation (c) (n=1)	Dominated	Lai T et al., 2007

Table 3 (cont.)

Intervention	Comparator (check general definitions of these interventions in Table 2)	Efficiency results*	References
A & B (n=22)			
Motivational Interviewing + Feedback report (n=1)	Motivational Interviewing + Feedback report (+ 3 months) (n=1)	Cost-effective	Cowell AJ et al., 2012
Group female-specific cognitive behavioral therapy (G-FS-CBT) (n=1)	Individual female-specific cognitive behavioral therapy (I-FS-CBT) (n=1)	Cost-effective	Olmstead TA et al., 2019
Motivational Enhancement Therapy + Brief interventions + Referral to local specialist alcohol services (n=1)	Brief intervention + Informative leaflet (n=1)	Dominant or cost-effective	Watson J et al., 2013
Brief interventions + 12-Step Facilitation Therapy + Marital, Couples or Family Therapy + Group Therapy + Pharmacological interventions (not specified the type) + Relapse prevention + Physician appointments (four times the intensity of interventions than the control group) (n=1)	Brief interventions + 12-Step Facilitation Therapy + Marital, Couples or Family Therapy + Group Therapy + Pharmacological interventions (not specified the type) + Relapse prevention + Physician appointments (n=1)	ns	Weisner C et al., 2000
Brief interventions + Cognitive Behavioural Therapy + Marital, Couples or Family Therapy + Acamprosate (n=2)	No intervention (n=2)	Cost-effective	Corry J et al., 2004 (n=2)
Self-reported contact for mental health problem + Cognitive Behavioural Therapy + Brief intervention + Acamprosate (n=2)	No intervention (n=2)	Cost-effective	Corry J et al., 2004 (n=2)
Acamprosate + Brief intervention (n=1)	Brief intervention (n=1)	Dominant	Palmer AJ et al., 2000
Brief intervention (weekly therapy) + Opioid or opiate antagonists (n=1)	Brief intervention + Placebo (n=1)	ns	Mortimer D & Segal L, 2005
Screening + Brief Intervention (BI) by a GP (n=11)	Screening alone (n=11)	Cost-effective	Navarro HJ et al., 2011
Brief intervention for alcohol problems (n=1)	Usual practice (n=1)	Cost-effective	Giles EL et al., 2019
B & C (n=7)			
Brief intervention + Tax increases (n=1)	Current situation (c) (n=1)	Dominated	Lai T et al., 2007
Tax increases + Advertising controls + Brief intervention (n=4)	No intervention or Current situation (c) (n=4)	Dominated (n=1) ns (n=3)	Chisholm D et al., 2004 (n=3); Lai T et al., 2007
Tax increases + Advertising controls + Random breath testing + Licensing + Brief intervention (n=1)	Current situation (c) (n=1)	Cost-effective	Lai T et al., 2007
Tax increases + Advertising controls + Licensing + Brief intervention (n=1)	Current situation (c) (n=1)	Dominated	Lai T et al., 2007

Note. (a) "Current practice" is defined as usual care in the Netherlands. Authors do not specify in what usual care consists of.

(b) "Control" is defined as a strategy in which there is no initial training and no ongoing support on programme implementation.

(c) "Current situation" is defined as a "do nothing counterfactual", a situation where no interventions exist.

ns: information not specified.

*Dominant: the new intervention or treatment is found to be less costly and more effective, so it will be getting more health for less cost. This means the new intervention or treatment dominates the comparator. Dominated: the new intervention or treatment is found to be less effective and more costly, so it means the new intervention or treatment is dominated by the comparator.

and acamprosate. Therefore, when used in combination with an opioid or opioid antagonist, it was cost-effective or dominant. Likewise, when the combination of medical management with acamprosate was compared with medical management and placebo, as well as with medical management and opioids or opioid antagonists, it turned out to be dominated by the latter combinations. However, in relation to use of nalmefene combined with psychological therapy, it demonstrated its cost-effectiveness or dominance compared with psychological therapy alone or placebo in the 12 comparisons found in this review (Brodtkorb, Bell, Irving & Laramée, 2016; Laramée, Bell, Irving, & Brodtkorb, 2016; Laramée et al., 2014; and Millier et al., 2017). The same applies to the economic evaluation of combined interventions in this case (see Table 3).

In terms of treatments for people with high risk factors to become alcohol dependent brief intervention has been the largest evaluated (47.8%). When comparing this intervention to no intervention, in spite of the low amount of evidence, it seemed that brief intervention (mainly focused in brief advice in this case) could be a dominant or cost-effective strategy. Similarly, when this type of intervention was applied in different settings, for instance, according to the study carried out by Barbosa, Cowell, Bray & Aldridge (2015), the combined intervention known as SBIRT which includes brief intervention results in costs savings and improvements in health in both emergency departments and outpatient settings, being more cost-effective, which means that it provides better effectiveness at a lower cost, in emergency departments than in outpatient settings. No other conclusions could be withdrawn from other interventions

or combined interventions (e.g. brief intervention + referral to alcohol treatment services) in terms of efficiency due to the inconsistency of evidence found (see Table 3).

In the case of policy, legislation and enforcement interventions, and acknowledging there could be a tendency for interventions such as advertising controls, random breath testing, Tax increases, and licensing, for dominance or cost-effectiveness when compared to no intervention. For instance, in the study carried out by Chisholm et al. (2018), a 50% increase in consumption tax rates resulted in a low cost of implementation (less than I \$ 0.10 per capita), a level of impact in health translated into more than 500 years of healthy life gained by one million inhabitants and a very favorable level in terms of the cost-effectiveness ratio, which is less than I \$ 100 per year of healthy life gained, this being the strategy of most profitable intervention among those evaluated (see Table 3).

Discussion

Some previous literature reviews on the measures to reduce alcohol misuse have been published before (Angus et al., 2014; Barbosa et al., 2010; Chisholm et al., 2006; Hill et al., 2017; Hoang et al., 2016; Kaner et al., 2017; Kelly et al., 2020; Kruse et al., 2020; Ludbrook, 2004; Ludbrook et al., 2002; Meads et al., 2007; Mujoomdar & Spry, 2009; Ndegwa & Cunningham, 2009; Poldrugo et al., 2005; Rehm & Barbosa, 2018; Slatery et al., 2002; White et al., 2018; Yadav & Kobayashi, 2015); however, no one has addressed the question of identifying which programme or intervention was more efficient in terms of treatments for people with AUD, although Ludbrook (2004) looked at all possible alcohol-related approaches, spanning from treatment to prevention, and individual-level interventions to population approaches. In addition, Rehm and Barbosa (2018) concluded that the economic research to date is relatively scarce and not always rigorous. Thus, there is a need for this information, to inform the policy debate when determining the level of resource input necessary to tackle alcohol problems. Combining treatment/early intervention and policy interventions offers readers an overview of the range of choices for impacting AUD, and their potential for cost-effectiveness. This paper defines a starting point for decision makers by allowing them to prioritise classes of interventions that have a greater potential for being efficient. This analysis also points to areas (medication-assisted treatment) where additional economic evaluations are needed.

Although, in this systematic review of economic evaluations of interventions for people with alcohol use disorders or people at risk of alcohol-related problems, not much evidence has been found in terms of efficiency, some careful conclusions might be drawn. Unfortunately, the wide variety of outcome measures and costs does not allow decision mak-

ers to choose the intervention that is most efficient. It is impossible to determine whether differences in the cost per unit (e.g., QoL) gained are truly due to differences in efficiency of the interventions rather than to differences in the methods used for the comparisons, thus, most of the conclusions that can be drawn are limited to the interventions included in each separate study. However, this information could be helpful to clinical practice in terms of raising the importance of the need for evaluating all interventions in terms of efficiency. It also shows which interventions have been more commonly evaluated and which are the most important variables for taking in account in order to conduct economic evaluations on alcohol-related programs. In relation to the studies evaluating the efficiency of pharmacological interventions related to alcohol dependence, conclusions could be established regarding the use of nalmefene but not in relation to acamprosate due to the controversial and different results obtained in the studies found. Recently, Avanceña, Miller, Uttal, Hutton & Mellinger (2020) have carried out an economic evaluation based on the existing literature finding that the use of Acamprosate and naltrexone, as well as the use of Baclofen, gabapentin, and topiramate, compared to doing nothing, are cost-saving interventions in patients with alcohol-related cirrhosis.

Regarding conclusions referring to brief intervention, this recommendation was already established for Scotland (Ludbrook, 2004) some time ago. This result held in our review. Despite this, several authors (Falcón et al., 2018) describe barriers to implementing screening and brief intervention for alcohol consumption in some settings such as hospital emergency departments. Something to highlight was that not many drug-related studies to quit alcohol or help reduce alcohol intake have been evaluated from an efficiency point of view. Therefore, there is a need for the pharmaceutical industry, which produces drugs that reduce alcohol intake, to invest in measuring and evaluating the efficiency of their products to reduce alcohol intake and decrease relapse to heavy drinking. Additionally, no study aimed at improving cognitive functioning in patients with cognitive deterioration associated with alcohol use who are undergoing treatment for alcohol dependency has been identified in this systematic review. Nevertheless, authors such as Frías-Torres et al. (2018) suggest how cognitive rehabilitation therapy could improve this condition.

Other reviews of economic evaluations focused on pharmacological interventions, such as the use of Naltrexone (Mujoomdar & Spry, 2009), policy instruments (Chisholm et al., 2006), screening and brief interventions (Angus et al., 2014) and assessment of methods for economic evaluations of treatments for AUD (Barbosa et al., 2010) exist. However, they did not really assess the efficiency of those programs. This review still online presents the conclusions from Brown et al. (2016) who showed that there was a dearth of evaluations that assessed the effectiveness of

pharmacy-based interventions for alcohol management. The present study included all references these reviews provided, with the exception of some that were not full economic evaluations and thus did not provide an ICER (Alwyn, John, Hodgson & Phillips, 2004; Babor et al., 2006; Bischof et al., 2008; Humphreys & Moos, 1996; Lock et al., 2006; Long, Williams & Hollin, 1998; Nalpas et al., 2003; Pettinati et al., 1999; Shakeshaft, Bowman, Burrows, Doran & Sanson-Fisher, 2002; Sobell et al., 2002). In addition, it encourages the idea of thinking, in all these interventions, in terms of treating people with alcohol dependence; treating people at risk of alcohol-related problems, and policy, legislation and enforcement interventions. Therefore, if decision makers were thinking of implementing a potential programme in a particular country, the recommendable interventions according to the efficiency criteria would be any psychosocial intervention, brief interventions for people at risk of alcohol-related problems, and advertising controls, tax increases, licensing, legal drinking age, and mass media campaigns. Thus, the information generated by this systematic review would help in order to decide in which interventions invest public health resources to address rehabilitation of alcohol-related disorders.

In line with policy, legislation and enforcement interventions, given the favourable findings in terms of the incremental cost-effectiveness ratio, it seems to be recommendable for countries to promote these types of interventions in order to improve the efficiency of this public health problem. It is surprising the lack of economic evaluations of the preventive intervention based on a “minimum price per unit” or “minimum unit price” (MUP). On the one hand, Lonsdale, Hardcastle & Hagger (2012) concluded through focus groups that a series of objections were raised by the participants related to scepticism about whether the MUP is an effective means to reduce alcohol consumption, the perception that the policy “punishes” the moderate drinker and related to the concern that this measure may exacerbate existing social problems. On the other hand, the study participants expressed that this measure could work if it would be part of a broader campaign that included other educational activities. Additionally, Purshouse, Meier, Brennan, Taylor & Rafia (2010) concluded that The Sheffield alcohol policy model (Holmes et al., 2014) predicts that the establishment of an MUP would reduce alcohol-related harms to a greater extent than overall increases in taxes, with nearly twice the number of deaths prevented.

In addition, there was an interest to compare the efficiency of different interventions according to the level of alcohol dependence (i.e. efficiency of interventions targeted at those with moderate-to-severe alcohol dependence as compared to interventions targeted at less severe alcohol problems). However, the definitions used across studies for grading the alcohol dependence has been different (i.e. people with an AUDIT score >8; people drinking >200

g/day). Therefore, without a homogeneous definition it is not possible to study the impact on results according to different grades of alcohol dependence. In relation to the observed trend in the use and efficiency of interventions such as advertising controls, random breath testing, Tax increases, and licensing, it seems to be recommendable for countries to promote these types of interventions in order to improve the efficiency of this public health problem. There is a need for further research in order to characterise cost-effectiveness thresholds in the substance use field. In order to do so, more evidence in terms of cost-effectiveness needs to be provided of all these different interventions to tackle the alcohol dependence. However, there is a need to evaluate how much society is willing to pay for these types of interventions and the improvement on health outcomes generated. Thus, willingness to pay studies or discrete choice experiments could be used in order to explore this question.

One of the limitations of this review is the limited number of studies found from which to draw conclusions. Ideally, these conclusions should have been drawn according to the study country to ensure the applicability of the results to each particular context. Therefore, this review continues to suggest that further research needs to be conducted to evaluate the efficiency of interventions and programmes to reduce alcohol misuse around the world. Barbosa et al. (2010) pointed out some years ago that this type of literature was still rather sparse, and further research is required to fill the gaps. There is still a need to use common methodology in future economic evaluations of alcohol treatment, to produce more stable cost-effectiveness estimates and to inform decisions for resource allocation to efficient alcohol treatment. Another issue raised by this systematic literature review is that very few studies considered direct costs for the patient, productivity losses, and other costs, mainly referring to external effects such as criminal justice, fire services or accident fatality in studies for treating alcohol use disorders or people at risk of alcohol-related problems.

Not only is there a need for further research in efficiency but also in the effectiveness of different programmes or interventions. According to Yadav & Kobayashi (2015), despite the additional decade of evidence, available studies were heterogeneous in their approaches, so no conclusions about the effectiveness of mass media campaigns could be made. More studies in terms of effectiveness and cost-effectiveness are needed to evaluate programmes related to alcohol intake. In addition, there was also a need to report the cost methodology of the different studies better (Bray, Zarkin, Hinde & Mills, 2012). Costs related to the evaluation of programmes such as alcohol screening and brief intervention in medical settings might present large differences because the cost methodology was not commonly established.

In fact, there is a need to foster an evaluation culture among those responsible for delivering services and to design some guidelines in promoting this evaluation culture along this public health programme (Ludbrook, 2004). Careful attention needs to be paid in terms of evaluating efficiency of alcohol-related programs.

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Conflict of interests

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Appendices

Appendix 1 Papers included in the systematic review (n=65)

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