

## ORIGINAL ARTICLE

### The Economic Burden of Alcohol Dependence in Europe

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**Abstract** — **Aims:** To determine the economic burden pertaining to alcohol dependence in Europe. **Methods:** Database searching was combined with grey literature searching to identify costs and resource use in Europe relating to alcohol dependence as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) or the World Health Organisation's International Classification of Diseases (ICD-10). Searches combined MeSH headings for both economic terms and terms pertaining to alcohol dependence. Relevant outcomes included direct healthcare costs and indirect societal costs. Main resource use outcomes included hospitalization and drug costs. **Results:** Compared with the number of studies of the burden of alcohol use disorders in general, relatively few focussed specifically on alcohol dependence. Twenty-two studies of variable quality were eligible for inclusion. The direct costs of alcohol dependence in Europe were substantial, the treatment costs for a single alcohol-dependent patient lying within the range €1591–€7702 per hospitalization and the annual total direct costs accounting for 0.04–0.31% of an individual country's gross domestic product (GDP). These costs were driven primarily by hospitalization; in contrast, the annual drug costs for alcohol dependence were low. The indirect costs were more substantial than the direct costs, accounting for up to 0.64% of GDP per country annually. Alcohol dependence may be more costly in terms of health costs per patient than alcohol abuse. **Conclusions:** This review confirms that alcohol dependence represents a significant burden for European healthcare systems and society. Difficulties in comparing across cost-of-illness studies in this disease area, however, prevent specific estimation of the economic burden.

**Keywords** alcohol dependence; alcoholism; economic burden; Europe

#### INTRODUCTION

Several attempts have previously been made to estimate the burden of alcohol use and alcohol use disorders overall, both in Europe and globally (Andlin-Sobocki *et al.*, 2005; Anderson and Baumberg, 2006; Rehm *et al.*, 2009; Rehm *et al.*, 2010; Gustavsson, 2011; Olesen *et al.*, 2012). However, many of these studies do not report on the economic burden associated with alcohol dependence specifically. Although alcohol dependence is a clinical condition associated with substantial disability and loss of quality of life (Saarni *et al.*, 2007; Saatcioglu *et al.*, 2008; Samokhvalov *et al.*, 2010), the tangible and intangible costs associated with this particular sub-category of alcohol misuse in Europe are unclear. It has been suggested that a substantial 61% of the costs associated with alcohol use can be attributed to alcohol dependence or heavy drinking (Mohapatra *et al.*, 2010). However, no previous literature review to assess the cost-of-illness studies of alcohol dependence has been performed. While treatments exist for alcohol dependence, the scale of the economic benefits that could potentially be gained from its effective prevention and treatment, therefore, also remains uncertain.

The terminology surrounding alcohol dependence, alcohol abuse and alcohol misuse is often unclear. Alcohol misuse is generally considered an umbrella term for both 'alcohol dependence' and 'alcohol abuse'. Two main classification systems are commonly used to differentiate alcohol dependence from alcohol abuse: the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the World Health Organization's International Classification of Diseases (ICD-10). Concordance between the two classification systems is high (Saunders, 2006). Under both systems, a

diagnosis of alcohol dependence demands that three or more of a set of criteria were met within the previous year; these criteria include tolerance, withdrawal, persistent consumption despite harmful consequences and a loss of interest in alternative activities or former interests.

In 2010, the European Medicines Agency stated that the main goals of treatment for alcohol dependence are to achieve abstinence, reduce the frequency and severity of relapse and improve health and psychosocial functioning. In contrast to the zero-tolerance approach of preventing relapse, the alternative 'harm reduction approach' advocates a reduction in alcohol consumption, and is now also considered a valid treatment goal for many alcohol-dependent patients (European Medicines Agency, 2010). In addition to psychosocial therapy, a number of adjuvant therapeutic agents, such as disulfiram, acamprosate and naltrexone, have been developed over the past few decades to help patients avoid relapse. Despite the first of these agents being available since the 1950s, it is thought that the number of patients benefitting from them is small (European Medicines Agency, 2010) and the prevalence of alcohol dependence as defined by the DSM-IV and the ICD-10 remains high (European Medicines Agency, 2005; Wittchen and Jacobi, 2005; Anderson and Baumberg, 2006).

At global level, estimates of the prevalence of alcohol dependence in Europe are particularly high. A report ordered by the European Commission and conducted by the Institute of Alcohol Studies in 2006 found that Europe is the heaviest drinking region in the world, with an estimated 23 million Europeans being alcohol dependent every year (Anderson and Baumberg, 2006). A prevalence rate of 5.2% was reported for several European countries in 2004 (European Medicines Agency, 2005), while a range of 0.1–6.6% was

reported in a multi-method analysis of data from various European countries in 2005 (Wittchen and Jacobi, 2005).

Many studies have reported an association between the level of drinking, or alcohol consumption in general, and economic burden (Anderson and Baumberg, 2006). These estimates include the healthcare costs of alcohol-related diseases, judicial costs and costs associated with the loss of productivity from unemployment, absenteeism and premature retirement or mortality. The Alcohol in Europe report estimated that the tangible costs of alcohol in 2003 amounted to €125 billion, equivalent to 1.3% of European gross domestic product (GDP) (Anderson and Baumberg, 2006). The intangible costs of alcohol (pertaining to the value placed on pain, suffering and loss of life) amounted to €270 billion. However, the burden relating specifically to the medical condition of alcohol dependence, which could be reduced with effective treatment, is considerably more unclear.

This literature review aimed primarily to ascertain the economic burden of alcohol dependence in Europe. The secondary aim, dependent on the availability of data, was to investigate the changing burden of alcohol dependence in Europe over time and to assess the difficulties of comparing cost-of-illness studies in this area.

## MATERIALS AND METHODS

### *Database review*

A database review was performed to identify publications reporting the economic burden of alcohol dependence. Alcohol dependence was defined according to the criteria specified by either the DSM-IV or the ICD-10. PubMed (including MEDLINE and MEDLINE In-Process), Journals@Ovid and the Cochrane Library were searched in October 2011. Searches combined MeSH headings for both economic terms and terms pertaining to alcohol dependence, as well as relevant text word searches. The economic terms included 'costs and cost analysis[MeSH]', 'cost[tw]', 'econom\*[tw]' and 'burden[tw]'.

Libraries from each database were merged and de-duplicated, abstracts were screened for inclusion by a single assessor and extracted results were confirmed by a second reviewer. To be included, articles had to present cost or resource use data for alcohol-dependent patients in the European Union. Alcohol dependence was considered to encompass terms such as alcoholism, alcohol withdrawal and alcohol addiction. There were no limits on the study type or length of study follow-up, and outcomes for alcohol-dependent populations could be compared with no population or any other population, including alcohol abusers. Finally, the articles had to be in English or any European language.

Full texts were obtained for articles deemed eligible based on information presented in their abstracts. Full texts were subjected to identical screening criteria, with an additional exclusion category for articles not presenting costs for alcohol dependence separately to costs for alcohol abuse or misuse.

### *Grey literature searching*

In addition to the database review, grey literature searching of publically available material from public health bodies

was performed. These searches were conducted in Google with search terms similar to those used in the literature review, comprising both an economic and an alcohol dependence component. The data sources identified were subjected to the same screening criteria as the articles identified in the literature review, with the same inclusion and exclusion criteria.

### *Extraction of results*

The relevant outcomes that were extracted included direct healthcare costs and indirect societal costs, including carer costs and those associated with the judicial system (legal and prison costs). Data on resource utilization in terms of healthcare resources, such as hospitalization, were also collected. The major summary measures were anticipated to be mean cost per alcohol-dependent patient and total cost of alcohol dependence on a national or international level.

To enable direct comparison of costs across years and currencies, all the costs were converted into Euros 2012. Costs from Eurozone countries that were published before the introduction of the Euro were inflated to 2002 using Eurostat and inflation.eu, converted into Euros using the average exchange rate in 2002 on OANDA and then inflated to 2012. Costs published in Euros were simply inflated to 2012 values. Costs in British pounds were inflated to 2012 and converted into Euros (using the exchange rate on 23 March 2012). All the costs were then adjusted for purchasing power parity (PPP) using the 2010 PPP rates from Eurostat (2012). These costs were also presented as a proportion of either total GDP (for costs on a national level) or GDP per inhabitant (for costs per patient), using data from Eurostat (2012). Costs on a national level presented as a proportion of total GDP were also presented as a proportion of GDP spent on healthcare, using data from the Organisation for Economic Co-operation and Development (OECD/European Union, 2010).

## RESULTS

The combined searches for the database review resulted in 4123 unique records for screening. A total of 4027 of these records were excluded (rationales are presented in Fig. 1) and 95 records included at the abstract review stage. Of the 95 abstracts eligible for inclusion, full texts for 25 were not obtainable and 59 records were excluded following full-text review. In total, 11 full texts (pertaining to ten different studies) were deemed eligible for extraction.

Of the 59 articles excluded following full-text review, 23 reported economic or resource utilization outcomes for alcohol-dependent patients combined with outcomes for alcohol abuse; nine did not report any outcomes pertaining to alcohol dependence; 18 presented outcomes pertaining to alcohol dependence that were not relevant to the scope of this review; and eight reported economic or resource utilization data pertaining to alcohol dependence, but in non-European patients. In addition, one article was found to be a duplicate.

An additional 26 studies identified through grey literature searching were screened for inclusion, and 11 full texts were eligible for extraction. In total, therefore, 4148

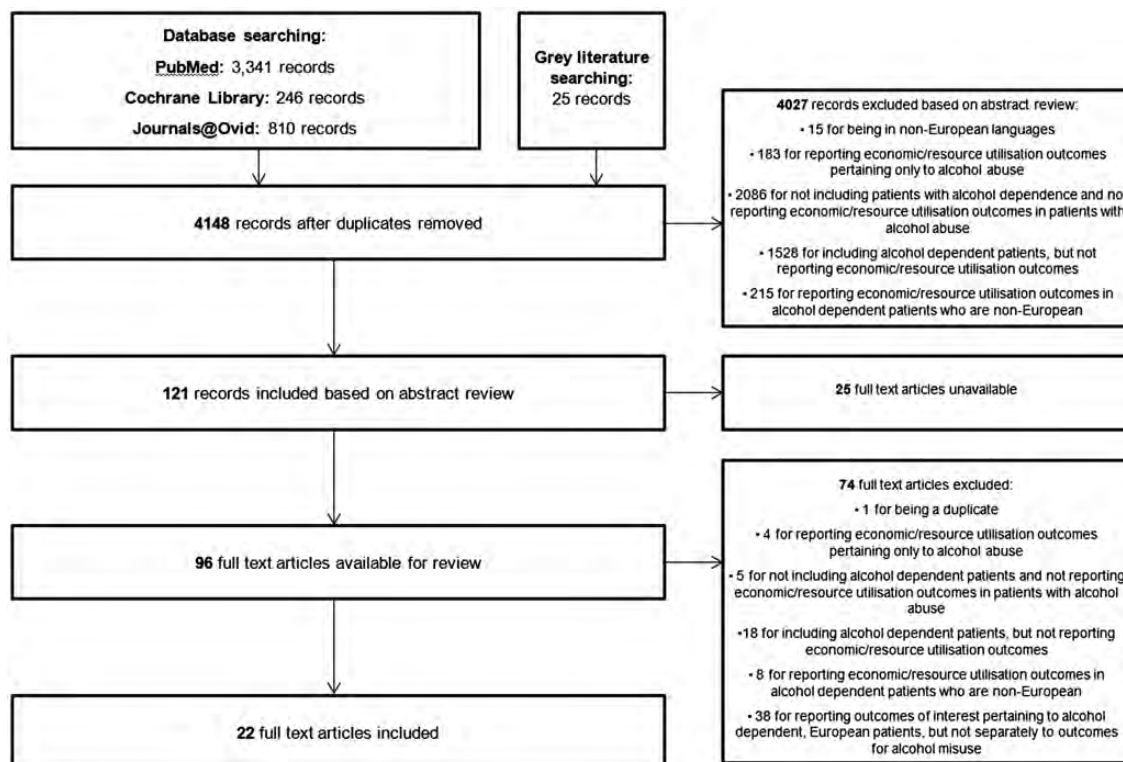


Fig. 1. Flow of papers through the literature review

records were captured through both the database searching and grey literature searching and ultimately 22 records were extracted (Fig. 1). Of these, 11 included records sourced from the database review and 11 from the grey literature searching.

The majority of articles identified presented one of two types of outcome: cost or resource use per alcohol-dependent patient or total economic burden/resource utilization at national level (Table 1). Three studies were prospective, one was a review, one was a factsheet, one presented a brief summary of symposium proceedings, one entailed a survey, four entailed retrospective medical chart reviews and 10 entailed the retrospective collation of national statistics. However, the relative quality of many of the studies was difficult to assess due to the poor reporting of the methodologies and cost sources used.

Table 2 presents extracted data on healthcare cost per patient from the seven studies reporting this outcome. The studies are varied, being conducted in France, Germany, Switzerland and the UK and presenting costs from 1964 to 2007. With the exception of the daily costs of treatment reported in a French study in 1964 (Lereboullet, 1968), all treatment costs for a single patient lie within the range of 5.3–15.0% of GDP per inhabitant (Niquille *et al.*, 1991; McKenna *et al.*, 1996; Nalpas *et al.*, 2003; Salize *et al.*, 2004; Parrott *et al.*, 2006; Stamm *et al.*, 2007). However, despite the cost conversion into Euros 2012 performed, the reported outcomes are different enough to restrict direct comparison of costs. For example, reported healthcare cost per patient may encompass hospitalization cost per day, total cost of a single hospitalization or total hospitalization costs over the course of a year.

Resource utilization by alcohol-dependent patients with regard to length of hospital stay is presented in Table 3. Five studies reported this outcome. While three studies present comparable measures, such as length of stay per hospitalization per patient in days (Lereboullet, 1968; Niquille *et al.*, 1991; Nalpas *et al.*, 2003), one study presents the total annual number of hospital days consumed by alcohol-dependent patients (Kopp and Fenoglio, 2000) and another presents only the proportion of alcohol-dependent patients in a 6-month period with length of hospital stay less than and >24 h (Baune *et al.*, 2005). Of the three studies presenting comparable outcomes, the oldest study is an outlier, reporting a mean length of stay per hospitalization per patient of 55 days (Lereboullet, 1968). The other two studies indicate a range of 11–28 days per hospitalization per patient (Niquille *et al.*, 1991; Nalpas *et al.*, 2003). One reason for the difference in length of stay estimations may be that one study considered length of stay in rehabilitation centres (Nalpas *et al.*, 2003), while another considered hospitalization in general hospital wards (Niquille *et al.*, 1991).

Further to the data collated on length of hospital stay, a fact sheet from the Institute of Alcohol Studies (2009) presented the number of UK NHS admissions with a primary diagnosis of disease specifically related to alcohol for every year between 1995/1996 and 2006/2007. Summing the number of admissions specifically for 'dependence syndrome', 'withdrawal state' and 'withdrawal state with delirium', the number of admissions increased from 16,894 in 1995/1996 to 20,886 in 2006/2007.

Table 4 presents the cost of drugs for alcohol dependency. Three studies report cost per patient, ranging from €86.61 to €557.89, and 0.3 to 1.8% of GDP per inhabitant



Table 2. Mean cost of healthcare per alcohol-dependent patient. Studies are listed chronologically by year of cost

References	Country	Year of cost	Cost components	Original cost in source	Up-rated and PPP-adjusted cost in Euros 2012 (€)	Up-rated and PPP-adjusted cost as a proportion of GDP per inhabitant (%)
Lereboullet (1968)	France	1964/1965	Hospital cost for treating chronic alcoholics per patient per day	78.82 French francs	93	0.31
Niquille <i>et al.</i> (1991)	Switzerland	1988/1989	Total hospital charges per patient per hospitalization	11,900 Swiss francs	7702.36	15.04
McKenna <i>et al.</i> (1996)	UK	1992/1993	Total health service cost per patient over a 6-month period	£1222.06	1907.83	6.96
Salize <i>et al.</i> (2004)	Germany	1998	Average hospital cost per alcoholic AOK enrollee per year	€3008	2890.40	9.54
Nalpas <i>et al.</i> (2003)	France	2000	Total cost of hospitalization for alcohol withdrawal per patient	€1397.50	1591.22	5.34
Stamm <i>et al.</i> (2007)	Germany	2000	Total hospital costs per alcoholic patient per year	€1577.55	1610.44	5.32
Parrott <i>et al.</i> (2006)	UK	2003/2004	Total cost of treatment per treatment episode per patient at two alcohol detoxification services	Centre 1: £1113 Centre 2: £1054	Centre 1: 1857.10 Centre 2: 1758.66	Centre 1: 6.78 Centre 2: 6.42

Table 3. Length of hospital stay for alcohol dependence. Studies are listed chronologically by the year the data originated from

References	Country	Year data originated from	Estimate components	Length of stay (days)
Lereboullet (1968)	France	1964/1965	Mean length of stay per hospitalization per patient with chronic alcoholism	55.26
Niquille <i>et al.</i> (1991)	Switzerland	1988/1989	Mean length of stay per hospitalization per alcoholic patient	16
Kopp and Fenoglio (2000)	France	2000	Total national number of hospital stays in 1993 and average duration of hospital stay for alcohol-dependent men and women with psychological symptoms of alcohol dependence	Men: 68,077 hospital stays in 1993 with an average length of stay of 9.6 days Women: 21,841 hospital stays in 1993 with an average length of stay of 9.5 days
Nalpas <i>et al.</i> (2003)	France	2000	Mean length of stay per hospitalization per patient with alcohol withdrawal	Centre 1: 11 Centre 2: 28 Centre 3: 19 Centre 4: 19
Baune <i>et al.</i> (2005)	Germany	2000/2001	Proportion of alcohol-dependent and alcohol withdrawal patients in a 6-month period with hospital stays $\geq 24$ h	Alcohol dependence: 68.3% Alcohol withdrawal: 82.2%

(McKenna *et al.*, 1996; Nalpas *et al.*, 2003; Stamm *et al.*, 2007). However, as with hospital stay, the outcomes are not directly comparable between studies, one study presenting drug costs per hospitalization (Nalpas *et al.*, 2003), another drug cost per 6 months (McKenna *et al.*, 1996) and another drug costs per year (Stamm *et al.*, 2007). Several studies were also identified that reported the total annual economic burden of prescription drugs for alcohol dependency; these costs ranged from 0.000005% of total GDP for one city in the UK (Jones *et al.*, 2010) to 0.0002% for England as a whole (Scottish Government Social Research, 2010). These costs ranged from 0.00006 to 0.002% of the total annual GDP spent on healthcare.

The total annual direct national costs of alcohol dependence are presented in Table 5. These costs are expected to be the most comparable outcome across studies, although in some cases the methodological quality of the studies is difficult to assess as the methodology is not reported in detail. The estimates ranged from 0.041% of GDP in 1996 (Brecht *et al.*, 1996) to 0.314% in 2002 (Bergmann and Horch, 2002), both estimates being from Germany. In terms of annual GDP spent on healthcare, these costs amounted to 0.39% (Brecht *et al.*, 1996) and 2.99% (Bergmann and

Horch, 2002), respectively. Table 6 reports the indirect, social costs of alcohol dependence in Europe, with estimates ranging from 0.0009% of annual GDP (a Scottish estimate of the annual cost of unemployment due to alcohol dependency; Scottish Government Social Research, 2010) to 0.640% (a European-wide estimate of the intangible cost of alcohol dependence on family members; Anderson and Baumberg, 2006). The highest estimate (Anderson and Baumberg, 2006) amounted to 7.72% of annual GDP spent on healthcare for the European Union as a whole. Indirect costs on a national level are not directly comparable, as the studies investigate different social costs and measure them in different ways.

## DISCUSSION

Evidence from this review indicates that the economic burden of alcohol dependence in Europe is large, the annual total direct costs at national level ranging from €1 billion to €7.8 billion in Euros 2012, accounting for 0.04–0.31% of a country's annual GDP (Table 5; Banz *et al.*, 1993; Brecht *et al.*, 1996; Bergmann and Horch, 2002; Salize *et al.*, 2004).

Table 4. Drug costs for alcohol dependence

Type of cost	References	Country	Year of cost	Cost components	Original cost in source	Up-rated and PPP-adjusted cost in Euros 2012 (€)	Up-rated and PPP-adjusted cost as a proportion of GDP per country (%)	Up-rated and PPP-adjusted cost as a proportion of GDP spent on healthcare per country (%)	Up-rated and PPP-adjusted cost as a proportion of GDP per inhabitant (%)
Per patient	McKenna <i>et al.</i> (1996)	UK	1992/1993	Mean drug costs per patient over a 6-month period	£84.72	168.67	–	–	0.62
	Stamm <i>et al.</i> (2007)	Germany	1999/2000	Total drug costs per alcoholic patient per year	€546.50	557.89	–	–	1.84
	Nalpas <i>et al.</i> (2003)	France	2000	Total drug costs per patient per hospitalization	€76.07	86.61	–	–	0.29
Total economic burden	Scottish Government Social Research (2010)	England	2006/2007	Total annual and national burden to the NHS of alcohol dependency-prescribed drugs	£2.1 million	3,279,313	0.0002	0.0022	–
		Scotland	2007	Total annual and national burden. Included drugs are acamprosate and disulfiram. Separate costs provided for benzodiazepines under different assumptions of prevalence for prescriptions of benzodiazepines for alcohol withdrawal (5%, 10% and 25%)	Acamprosate and disulfiram: £866,125 Benzodiazepines: 5% £388,313 10% £766,626 25% £1,941,566	1,352,518 606,381 1,197,143 3,031,911	0.0001 0.00004 0.0001 0.0002	0.0009 0.00041 0.0008 0.002	– – – –
		England	2000/2001	Total annual and national economic burden of alcohol dependency-prescribed drugs. Drugs included were acamprosate and disulfiram	£1.6 million	2,997,911	0.0002	0.0020	–
	Jones <i>et al.</i> (2010)	England	2008/2009	Total annual burden of alcohol dependency-prescribed drugs in Leeds. Drugs included were acamprosate and disulfiram	£56,234	82,937.68	0.000005	0.000056	–
	Department of Health, Social Services and Public Safety (2010)	Northern Ireland	2008/2009	Total annual burden of alcohol dependency-prescribed drugs in Northern Ireland. Drugs included were acamprosate and disulfiram	£0.3 million	442,459.82	0.00003	0.0003	–

Within cost type, studies are listed chronologically by year of cost.

Table 5. Total direct national costs of alcohol dependence. Studies are listed chronologically by year of cost

References	Country/ region	Secondary references	Year of cost	Cost components	Original cost in source	Up-rated and PPP-adjusted cost in Euros 2012 (€)	Up-rated and PPP-adjusted cost as a proportion of GDP per country (%)	Up-rated and PPP-adjusted cost as a proportion of GDP spent on healthcare per country (%)
Brecht <i>et al.</i> (1996)	Germany	N.A.	1990	Total annual economic cost (including cost of treatment in acute hospitals, ambulatory care and rehabilitation units)	DM 1553 million (subdivided into acute hospitals: DM 869 million; ambulatory care: DM 311 million; and rehabilitation units: DM 373 million)	1,014,047,666 Acute hospitals: 567,422,680 Ambulatory care: 203,070,717 Rehabilitation units: 243,554,269	0.041 Acute hospitals: 0.023 Ambulatory care: 0.008 Rehabilitation units: 0.010	0.390 Acute hospitals: 0.218 Ambulatory care: 0.078 Rehabilitation units: 0.094
Reynaud <i>et al.</i> (1999)	France	N.A.	1996	Total annual economic cost of alcoholism based on two different methods	Method 1: 14 billion francs (lower estimate) or 16 billion francs (higher estimate) Method 2: 20 billion francs	Method 1: 2,312,169,347 to 2,900,459,447 Method 2: 3,625,574,308	Method 1: 0.131–0.150 Method 2: 0.188	Method 1: 1.17–1.34 Method 2: 1.68
Reynaud <i>et al.</i> (2001)	France	N.A.	1996	Total annual economic cost of alcoholism based on two different methods	Method 1: \$2.3 billion (lower estimate) or \$2.7 billion (higher estimate) Method 2: \$3.3 billion	Method 1: 2,364,978,101 to 2,776,278,640 Method 2: 3,393,229,449	Method 1: 0.122–0.144 Method 2: 0.176	Method 1: 1.09–1.28 Method 2: 1.57
Salize <i>et al.</i> (2004)	Germany	Banz <i>et al.</i> (1993) Bergmann and Horch (2002)	1989 2002	Total annual societal cost Total annual direct costs of care	€2.7 billion €8.1 billion	2,594,445,587 7,783,336,760	0.105 0.314	0.998 2.99

Table 6. Total indirect national costs of alcohol dependence. Studies are listed chronologically by year of cost

References	Country/ region	Secondary references	Year of cost	Cost components	Original cost in source	Up-rated and PPP-adjusted cost in Euros 2012 (€)	Up-rated and PPP-adjusted cost as a proportion of GDP per country (%)	Up-rated and PPP-adjusted cost as a proportion of GDP spent on healthcare per country (%)	Up-rated and PPP-adjusted cost as a proportion of GDP per inhabitant (%)
Brecht <i>et al.</i> (1996)	Western Germany	N.A.	1990	Total annual indirect costs of alcoholism (including the costs attributed to inability to work, early retirement and premature mortality)	DM 4422 million (subdivided into inability to work: DM 1150 million; early retirement: DM 988 million; and premature mortality: DM 2284 million)	2,887,391,358 (subdivided into inability to work: 750,904,582; early retirement: 645,124,980; and premature mortality: 1,491,361,796)	0.117 Inability to work: 0.030 Early retirement: 0.026 Premature mortality: 0.060	1.110 Inability to work: 0.289 Early retirement: 0.248 Premature mortality: 5.461	–
Salize <i>et al.</i> (2004)	Germany	Bergmann and Horch, 2002	2002	Total annual social costs of alcoholism	€11.8 billion	11,338,688,119	0.458	4.360	–
Anderson and Baumberg (2006)	Europe	N.A.	2003	Total intangible cost of alcohol dependence on family members across 1 year	€68 billion	78,490,934,637	0.640	7.716	–
Cabinet Office Strategy Unit (2003)	UK	N.A.	2001	Total annual cost of absenteeism among alcohol-dependent employees	£1.2 billion	2,083,428,571	0.122	1.404	–
Scottish Government Social Research (2010)	Scotland	Study by Catalyst/ Scottish Executive	2001	Total annual cost of unemployment due to alcohol dependency for men and women	£84 million	145,840,179	0.009	0.098	–
		Scottish Government (application of method used by the Cabinet Office Strategy Unit)	2001	Total annual cost of unemployment due to alcohol dependency for both men and women	£146 million	253,483,929	0.015	0.171	–
		Update of Catalyst/ Scottish Executive report	2007	Total annual cost of unemployment due to alcohol dependency for men only	£150.9 million	235,641,964.29	0.014	0.159	–
		Update of Scottish Government's 2001 analysis	2007	Total annual cost of unemployment due to alcohol dependency for both men and women	£191.5 million	299,041,964	0.018	0.201	–
Jeanrenaud and Pellegrini (2007)	Switzerland	N.A.	2007	National annual intangible cost of alcohol dependence on household members	CHF 1.6 billion	1,119,758,219.89	0.281	2.648	–
				Annual intangible cost of alcohol dependence per individual household member	CHF 5400	3779.18	–	–	7.381



This translates into a range of 0.39–2.99% of annual GDP spent on healthcare per country. The main cost driver for direct costs appears to be hospitalization for alcohol-dependent patients, which can consume as much as 15% of annual GDP per inhabitant for a single patient (Niquille *et al.*, 1991), and is in turn likely to be affected by the length of hospital stay. In contrast, drug costs for alcohol dependency at national level account for a very small proportion of an individual country's annual GDP, ranging from 0.000005% (Jones *et al.*, 2010) to 0.0002% annually (Cabinet Office Strategy Unit, 2003; Scottish Government Social Research, 2010). As a proportion of GDP spent on healthcare, these costs remain small, ranging from 0.00006 to 0.002% annually. Estimates for length of stay per hospitalization per patient vary widely, with a range of 11–28 days recorded in four specialized French alcoholism treatment centres in 2000 (Nalpas *et al.*, 2003). Similar to the findings in the 2003 Alcohol in Europe report on the cost of alcohol consumption overall (Anderson and Baumberg, 2006), indirect costs of alcohol dependence also appear to be substantial, accounting for up to 0.64% of annual European GDP as a whole (€68 billion; Table 6; Brecht *et al.*, 1996; Cabinet Office Strategy Unit, 2003; Anderson and Baumberg, 2006; Scottish Government Social Research, 2010). These indirect costs amount to 7.7% of annual GDP spent on healthcare in the EU. Evidence also suggests that alcohol dependence is more costly per patient in terms of health costs than alcohol abuse (€1908 versus €986, respectively, for a 6-month period after conversion into Euros 2012; McKenna *et al.*, 1996).

It is difficult to draw conclusions on whether the burden of alcohol dependence has altered over time. Estimates from two German studies may be suggestive of an increasing burden, with direct national costs increasing from 0.04% of GDP in 1990 to 0.31% of GDP in 2002 (Brecht *et al.*, 1996; Bergmann and Horch, 2002). However, we have insufficient information to ascertain how similar the cost components and methodologies used to derive the estimates were in these two studies. Updates of figures in government reports may provide a more reliable insight into the changing economic burden of alcohol dependence over time; it can be seen in the Scottish Government Social Research, (2010) that the annual cost of unemployment due to alcohol dependency increased from €253.5 million in 2001 to €299 million in 2007 (after conversion into Euros 2012). In this report, attempts were made to use the same methodology in 2007 as in 2001, making these two cost estimates comparable.

The increasing number of hospital admissions in the UK NHS for 'dependence syndrome', 'withdrawal state' and 'withdrawal state with delirium' between 1995/1996 and 2006/2007 may also indicate an increasing burden of alcohol dependence, with all of these diagnoses pertaining to alcohol dependence as defined by the World Health Organization's ICD-10 criteria (Institute of Alcohol Studies, 2009). The possible increasing burden of alcohol dependence in the UK may be correlated with an increase in per capita alcohol consumption since the 1960s, in contrast to a declining trend in many southern European countries such as Italy and Spain (World Health Organization, 2011).

While the cost and resource utilization estimates captured in Tables 2–6 confirm that alcohol dependence is associated with a considerable economic burden, it is clear from the relatively small number of studies identified that there is a

lack of data specifically available for the alcohol-dependent population. This is highlighted by the large number of records excluded from the literature search for the reason that they reported the economic burden of alcohol abuse, or outcomes on alcohol-dependent patients combined inseparably with outcomes for alcohol abuse. Government reports and other reports at national level generally fail to present costs for alcohol dependence separately to costs for alcohol abuse, instead presenting aggregate results for the number of emergency room attendances, inpatient hospitalization and criminal justice system resource use. This means that only certain costs directly relevant to alcohol-dependent individuals, such as the cost of prescription drugs for alcohol dependency, can be extracted. According to one report by the UK Cabinet Office, analysing data separately for dependent drinkers would be valuable only if policy were to be formulated specifically for alcohol-dependent subgroups (Cabinet Office Strategy Unit, 2003). It seems that the costs of alcohol dependence are regularly overshadowed by the costs of alcohol abuse overall and are often neglected in research. As the burden of alcohol dependence is still substantial, however, and dependence is a manageable condition, there is an unmet clinical need, which could be alleviated by the targeting of valid treatment goals other than relapse prevention, such as harm reduction.

Comparing cost estimates from different cost-of-illness studies is notoriously difficult (World Health Organization, 2009). The challenges presented by such cross-study comparisons were acknowledged in a summary of symposium proceedings, which presented annual societal cost of alcohol dependence estimates in Germany ranging from €2.7 billion to €11.9 billion (Salize *et al.*, 2004). Possible reasons cited for the wide variation in estimates included the use of different definitions, data sources, cost categories and calculation methods. Similar problems were identified during this review and are discussed in further detail below.

Only a limited number of studies considered in this review defined the alcohol-dependent population in terms of standardized, internationally recognized instruments such as the ICD-10, DSM-IV or the Michigan Alcoholism Screening Test (Niquille *et al.*, 1991; Nalpas *et al.*, 2003). It is, therefore, unlikely that the populations included in each study were fully comparable. While efforts were made to include only those studies pertaining specifically to alcohol dependence, it is possible that differential and potentially misleading use of the word 'alcoholic' or 'alcoholism' in some studies may have led to the inadvertent inclusion of costs for patients with alcohol abuse. Also with regard to older studies, such as Lereboullet (1968), it is known that the definition of alcohol dependence has evolved in recent decades (Saunders, 2006).

Government reports account for many of the cost sources identified in the grey literature searching (Kopp and Fenoglio, 2000; Bergmann and Horch, 2002; Cabinet Office Strategy Unit, 2003; Institute of Alcohol Studies, 2009; Department of Health Social Services and Public Safety, 2010; Jones *et al.*, 2010; Scottish Government Social Research, 2010). These reports tend to use national data sets, and where costs pertaining to alcohol dependency are presented, they can be assumed to be relatively robust. However, when comparing across studies, it was often unclear whether the cost components were identical and

whether the costing sources were of equivalent reliability and accuracy. Some costs were found to be inherently more comparable as the number of possible cost components was necessarily limited; for example, all government estimates for the cost of prescription drugs for alcohol dependency included costs for acamprosate and disulfiram only (Cabinet Office Strategy Unit, 2003; Department of Health Social Services and Public Safety, 2010; Jones *et al.*, 2010; Scottish Government Social Research, 2010).

Different cost calculation methods were also used in different studies. While some studies were bottom-up analyses (Lereboullet, 1968; Niquille *et al.*, 1991; McKenna *et al.*, 1996; Nalpas *et al.*, 2003; Baune *et al.*, 2005; Parrott *et al.*, 2006), others used varying top-down approaches (Brecht *et al.*, 1996; Reynaud *et al.*, 1999; Kopp and Fenoglio, 2000; Reynaud *et al.*, 2001; Bergmann and Horch, 2002; Cabinet Office Strategy Unit, 2003; Stamm *et al.*, 2007; Department of Health Social Services and Public Safety, 2010; Jones *et al.*, 2010; Scottish Government Social Research, 2010). The consequences of using alternative top-down approaches are highlighted by Reynaud *et al.* (1999, 2001), who used two different methods for estimating healthcare costs linked to alcoholism in France, obtaining estimates ranging from \$2.3 billion to \$3.3 billion annually.

Finally, the large diversity of study types included meant that developing standardized quality assessment criteria with which to appraise each one was impractical. Even within studies of the same type, assessing quality was difficult due to differences in primary objectives between studies. Many studies were not designed to capture the economic burden of alcohol-dependent patients, and in many cases data relevant to the alcohol-dependent population was presented only incidentally (Kopp and Fenoglio, 2000; Bergmann and Horch, 2002; Cabinet Office Strategy Unit, 2003; Baune *et al.*, 2005; Anderson and Baumberg, 2006; Department of Health Social Services and Public Safety, 2010; Scottish Government Social Research, 2010). While the methodology of many studies or reports may have been satisfactory to address their primary objectives, for the purposes of this study, the methodology pertaining to estimating the burden of alcohol dependence was often under-reported or poor. In addition, some reports captured by the literature searching were not primary studies but poorly referenced reviews, many of the original papers from which were either untraceable or unobtainable (Trillat, 1980).

In this review, standardization of cost estimates in terms of converting costs into Euros 2012 and presenting them as a proportion of GDP per country was performed to make costs more comparable between studies and across years. Despite the differences in methodology and uncertainty in cost estimates, it is reassuring to note that after conversion, all annual direct cost estimates fell within the relatively small range of 0.04–0.31% of GDP (Table 5). However, the range obtained for annual indirect costs of 0.001–0.6% of GDP (Table 6) is significantly larger. This is likely to be due to greater variation in the indirect cost components included in each study and differences in methodology.

It was not possible to perform data adjustment to account for differences in resource utilization as a result of, for example, changes in standard care procedures for treating alcohol-dependent patients. Variation in length of stay per

hospitalization per patient in two examples from France (55 days in 1964 versus 11 days in one specialist centre in 2000; Lereboullet, 1968 and Nalpas *et al.*, 2003) could improbably be interpreted as meaning that the healthcare resource burden of alcoholism in France has declined over time. More likely, the difference is due to a combination of different included populations and study designs and the fact that for many years now relapse prevention treatment has been preferentially conducted in an outpatient setting (European Medicines Agency, 2010).

A number of problems associated with the use of hospital or patient records in prevalence-based and top-down approaches to cost estimation mean that the economic burden of alcohol dependence in Europe has almost certainly been underestimated in this review. For example, many studies reporting the direct national costs of alcohol dependence (Table 5) are likely to have only included costs for health conditions wholly attributable to alcoholism (such as alcoholic liver cirrhosis). Health care costs for conditions where alcoholism is only one of a number of component causes, such as cancer and cardiovascular disease, may not have been captured at all. In addition, it has previously been proposed that there may be some stigma associated with disease category codes with 'alcoholic' in the name, which may lead to under-reporting of these categories in hospital records (Rehm *et al.*, 2010). Finally, it is the case that only a minority of patients suffering from alcohol use disorders receive treatment for their condition in Europe, with one estimate as low as 8.3% (Alonso *et al.*, 2004).

The relative paucity of studies in the literature addressing the economic burden of alcohol dependence presents an opportunity for new studies to be performed on this potentially manageable population of individuals. Based on our review of the available literature, it is clear that some degree of standardization in methodology and approach would benefit this important therapeutic area. Prospective studies should clearly define the alcohol-dependent population they are investigating in terms of ICD-10 or DSM-IV criteria. Furthermore, a detailed breakdown of cost components within broader categories such as 'drug costs' and 'hospitalization' should be provided, as well as greater clarification of terms such as, 'alcohol-related health disorders' and 'withdrawal syndrome'. Assumptions and data adjustments should be highlighted in a transparent and reproducible manner.

In conclusion, despite the shortcomings of the data discussed above, the economic burden associated with alcohol dependence is significant and represents a significant proportion of the costs associated with alcohol misuse overall. In addition, these shortcomings may have led to an underestimation of the impact, and further cost-of-illness studies in this therapeutic area are urgently needed. The value of such studies lies in their potential to define the extent of the adverse economic consequences associated with alcohol dependence, and the projected gains to be made from effective prevention and treatment. The variable quality of many studies means that they cannot be used with confidence in this respect. The development of a reliable evidence base for understanding the large economic burden associated with alcohol dependence may have important policy implications for healthcare systems and society overall.

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