



Assessing the European impact of alcohol misuse and illicit drug dependence research: clinical practice guidelines and evidence-base policy

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ABSTRACT

Background Despite alcohol and illicit drug dependence being one of the most common diagnoses in Europe, there is heterogeneity of research evidence used in policy and practice.

Objective We sought to (1) evaluate European research outputs on alcohol misuse and drug addiction in 2002–2018 in the Web of Science, (2) compare these with their burden of disease and (3) determine their impact in several ways.

Methods A bibliometric research was undertaken including an assessment of the citation counts, the influence of research on members of national health advisory committees, and their contribution to the evidence base of clinical practice guidelines (CPGs).

Findings There were 3201 analysed references cited in 28 CPGs across 11 European Countries on alcohol misuse and illicit drug abuse. Research conducted in the USA dominated both sets of CPGs, while many European countries were overcited relative to their research presence. The illicit drug research appeared to be adequate relative to the evidence of harm in Europe. However, alcohol misuse research appeared grossly inadequate to the harm it causes by a factor of 20.

Conclusions The volume of research on illicit drug addiction is commensurate to the European burden, whereas alcohol misuse is far below what is needed to curb a significant source of harm.

Clinical implications The research asymmetries call for attention to the causes of the problem. Development of research-based solutions to a serious social harm is needed, including minimum pricing and collaborative work to harmonise efforts on disease management and treatment practices across European countries.

BACKGROUND

Alcohol and drugs are psychoactive substances altering brain function.¹ Alcohol consumption above 14 units a week has been associated with adverse health outcomes and repeated use is considered to lead to alcohol dependence.^{2,3} Similarly, drug use has been linked to a cluster of behavioural, cognitive and physiological symptoms with repeated use considered one of the most common diagnoses in Europe (>4%; known as dependence syndrome or drug addiction).⁴ It is the repeated use of the psychoactive substance, that is, alcohol and drugs, that is understood to cause physical and mental harm,⁵ and the strong desire to take the substance (medically prescribed or not), a key characteristic of dependence.⁵

Key messages

What is already known about this subject?

- Alcohol is the most harmful substance to individuals and society with harm ranging from mental and physical damage, addiction, crime and costs to the economy and communities.
- Illicit drugs have tough controls under the UN 1961 Single Convention on Narcotic Drugs and the 1971 Convention on Psychotropic Substances.

What are the new findings?

- The illicit drug research appears to be adequate relative to the evidence of harm in European countries, but alcohol misuse research is grossly inadequate to the harm it causes and in Europe the shortfall is by a factor of 20.
- Clinical practice guidelines relating to drug dependence are mostly influenced by research from France, Italy, Spain and Austria, while research from Germany and Sweden is more prominent in relation to guidelines for alcohol dependence.
- The cited references on clinical practice guidelines concerning both alcohol and illicit drug dependence peaked around 2006, as pharmacological agents can take as many as 12 years from laboratory or initial screening through to clinical trials and marketing approval.

How might it impact on clinical practice in the foreseeable future?

- To facilitate public health strategy on targeting harms from alcohol; however, more research is needed to close the current evidence-practice gap revealed by our study.
- Scandinavian countries are performing well relative to others in Europe, such as Germany and Italy, but even these countries are seriously under-researching the problem.
- Increase collaboration between countries to eliminate the potential overlap or duplicated efforts in the developed guidelines and establish a greater consensus in the clinical practice recommendations for people with addictions across European countries.

It has been reported that 139 million years of 'healthy' life are lost to alcohol consumption globally, with 3.3 million deaths accounting for 5.1% of



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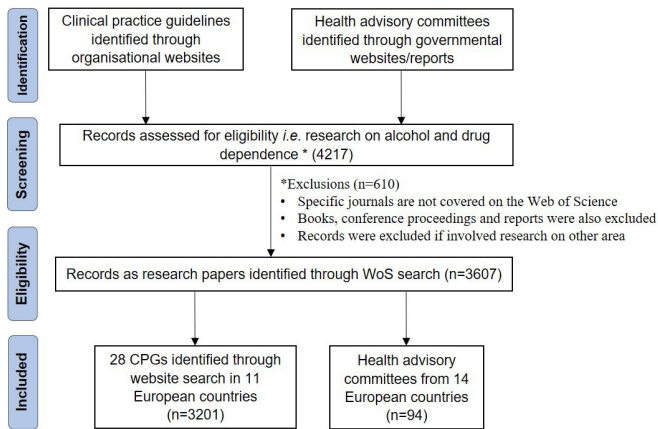


Figure 1 The PRISMA flowchart of the study (adapted from Moher *et al.*, 2010).¹⁹ CPG, clinical practice guideline; WoS, Web of Science.

the global burden of disease, a pattern that is markedly higher for European countries.⁶ The conventional measures of health burden are shorter life, pain and suffering; these are tabulated as disability-adjusted life years (DALYs) with the associated data available from the World Health Organization (WHO)⁷ for the years 2000–2015.⁶ The direct effect of alcohol on mental health in Europe, as measured using DALYs, is more than double to that reported globally (1.0% vs 0.49% of DALYs, respectively). Data also show substantially higher harm caused by alcohol misuse in contrast to the drugs that are made illicit such as amphetamine, crack cocaine, heroin, methamphetamine and benzodiazepines (4.0% vs 0.8% of DALYs, respectively).⁸ Despite these differences however, both alcohol and illicit drugs are regulated, but in very different ways: while alcohol is regulated by taxation, sales and restriction on age of purchase; aforementioned illicit drugs are prohibited by law/legislations.⁴

An often-overlooked element is alcohol's harm to others that undermines public safety. For instance, the burden from alcohol was estimated at 7.0% in South Africa with two-fifths due to interpersonal violence.⁹ It has been argued that DALYs estimates of 4.3% for alcohol misuse¹⁰ are skewed towards the harm caused to the person under the influence of alcohol,^{11 12} thus failing to take into account the deaths and serious injuries from road traffic accidents (RTAs) and interpersonal violence. Taken all the available evidence into account, including that the total percentage of DALYs is attributed more highly to alcohol (4.0%) than illicit drug (0.8%) misuse,⁸ one can safely postulate that the toll from alcohol misuse in the European countries will be at least five times that from addiction to illicit drugs, as it is for the whole world.¹³ Specifically, alcohol-attributable RTAs are of the order of 12% of total casualties,¹⁴ which is about 1.25 million deaths each year,¹⁵ adding a further 0.3% to the burden in the last decade. Interpersonal violence adds to this, with the average 1.08% of world DALYs where alcohol is involved in about 50% of perpetrators and possibly 40% of victims,¹⁶ thus adding a further 0.5% to the burden, making the total just over 5% globally and 5.5% in the EU.

The direct mental health burden from illicit drug addiction has been steadily increasing as a percentage of total world disease burden from 0.44% in 2000 to 0.66% in 2015. In Latin America, the death toll in 2016 varied between less than 3 per 100 000 in Chile to over 91 per 100 000 in El Salvador and the calculated total of homicides was 127 000. If half of these were drug-related, it would suggest a total of about 63 000 deaths each year, which although horrifying is only a fraction of those

from RTAs calculated above (about 0.12% of the total disease burden). So, the total burden from addiction to illicit drugs has risen from about 0.56% to 0.78% between 2000 and 2015: this is much less than that attributable to alcohol misuse. The situation in Europe is similar, because alcohol is widely consumed and often in large amounts. It appears safe to estimate that the toll from alcohol will be at least five times that from drug misuse, as it is for the whole world.

OBJECTIVE

Little is known about the level of evidence-base that underpins clinical practice guidelines (CPGs) for alcohol and illicit drug misuse used by healthcare professionals, policy makers and researchers. Yet, alcohol and illicit drug dependence cause measurable health burden through (1) direct impact on mental health, (2) indirect impact on physical health and (3) downstream/upstream effect on others. The current study therefore attempts to address the evidence-practice gap by gauging the level of scientific evidence underpinning the CPGs and policy for alcohol and illicit drug misuse across European countries over a period of 12 years (2002–2013); something that is addressed markedly in cancer¹⁷ and diabetes.¹⁸

We examined the research outputs (as a conventional indicator of quality), their citations on the associated CPGs and the influence on members of national health advisory committees' evidence-based recommendations. These measures combined give a comprehensive view of the utility of the European research portfolio, relative standing of the European countries, and the impact of research in different health conditions and domains (*eg*, genetics, epidemiology, drug treatment).

METHODS

We set out to understand how the research on alcohol and illicit drug dependence compares with each other, across the various European countries and on indicators such as (1) bibliometric analysis of research output, (2) CPGs and (3) health advisory committees' evidence-base. For an outline of the methodology, see the PRISMA flowchart¹⁹ represented in figure 1.

Specifically, we have:

1. *identified* and assessed the citation scores of the European research outputs on both geometric and arithmetic means;
2. *compared* the relative amount of attention given to alcohol and illicit drug misuse respectively in research underpinning CPGs by:
 - i. *examining* the research output compared with Gross Domestic Product (GDP) and DALYs;
 - ii. *identifying* which countries' research is most influential;
 - iii. *comparing* the research levels (RLs) (*eg*, basic, clinical or both) of scientific articles;
 - iv. *understanding* which research domains (*eg*, epidemiology, pharmacological treatments and other) were most influential on the three measures;
 - v. *identifying* how up to date is the evidence-base underpinning CPGs (*ie*, gap to citation);
 - vi. *calculating* the publication rate of the cited evidence-base by publication year;
 - vii. *classifying* the concerned research domain;
 - viii. *gauging* the influence of research on policy/funding by looking at trends over time;
 - ix. *examining* research outputs and citations on CPGs (over-citation ratio);
3. *gauged* the level of expertise of the health advisory committees.

The volumes of research output on alcohol misuse (excluding work on alcohol in chemistry) and on illicit drug addiction were determined by the application of special ‘filters’ to the Web of Science (WoS) Clarivate Analytics (proprietary of Evaluametrics Ltd.). Each filter consisted of three parts: (1) list of specialist journals with all articles deemed relevant; (2) list of selected title-words and (3) list of WoS subject categories where papers were excluded from the set of identified papers. We also excluded drug-related papers from journals whose titles covered both topics (eg, American Journal of Drug and Alcohol Abuse, Drug and Alcohol Dependence) and others concerned with illicit drug addiction (eg, Addictive Behaviours, Psychology of Addictive Behaviours). We included papers of drugs used specifically to treat alcohol misusers and drug addicts.

The two filters were calibrated²⁰ with reference to outputs of eponymous departments (where addresses contained the terms ADDICT* or ALCOHOL). The illicit drug addiction filter had the precision (or specificity), $p=0.98$, recall (sensitivity), $r=0.69$ and calibration factor of $p/r=1.42$. The alcohol misuse filter had the precision, $p=0.78$, and recall, $r=0.56$, and calibration factor of 1.39. This means that there would have been 42% more papers on illicit drug addiction and 39% more papers on alcohol misuse if the filters had been perfect in the identification of relevant papers.

Research output

Bibliographic details of the selected papers (articles and reviews from 2002 to 2013) were downloaded to a series of files, 500 at a time from the WoS. These were converted into an Excel spreadsheet by means of a specifically designed Visual Basic Application (VBA) programme (proprietary of Evaluametrics Ltd, see Acknowledgements). The two lists of ALCOHOL and ADDICT* papers were scanned to remove obviously irrelevant ones (eg, alcohols in chemistry). The citation scores (year by year) were similarly downloaded from the WoS, and the files brought together in the same format by another VBA programme. Five-year citation scores for papers from 2002 to 2012 were calculated as Actual Citation Impact (ACI) and copied to the original spreadsheet. The countries whose researchers were credited with each paper were calculated as fractional counts; for example, a paper with one French and two German addresses would be classified as $FR=0.33$, $DE=0.67$. These fractions were used to multiply citation scores for each paper to give fractional citation counts; these reflect more accurately the credit for each country than integer counts. The paper titles were parsed to show whether they should be classed as ‘clinical’, ‘basic’ or ‘both’ on the basis of two lists of title words²¹ with their mean RL as a continuous variable. Finally, the paper titles and journal names were analysed by another VBA programme to show if the papers described research of a specific domain, such as epidemiology or drug treatment.

Data analysis

Analysis of citation scores was based on arithmetic and geometric means (representing different measures of citation impact) and on the number of papers from European countries that had sufficient citations to put them into the top 5% of all European papers. To calculate geometric means, unity was added to each citation score and subtracted from the resulting geometric mean; this was conducted by the logarithms of individual citation scores that also determined the arithmetic means. A geometric mean was used to avoid bias from a few highly cited papers.²²

Clinical practice guidelines

Selection

King’s College London (KCL) graduate students were recruited and trained to identify clinical guidelines in the field of alcohol misuse and drug addiction in the 28 EU Member States and the three European Free Trade Association countries: Iceland, Switzerland and Norway (*ie*, together these countries are termed EUR31 and referred as such throughout this manuscript). These countries are listed in online supplementary table S1 with their International Standards Organization (ISO2) digraph codes, alongside other leading countries.

Students were instructed to visit the websites of the organisations publishing guidelines in their respective countries or by contacting the relevant development bodies to gain access to these documents. While the documents were in the respective languages (rarely in English), their bibliography was in English due to the research being cited mostly in English-language journals. For the full list of these organisations, see online supplementary table 2.

The CPGs were identified through the websites of each development body within each European country and their publication details were recorded in an Excel spreadsheet. While the search was restricted to 2002–2013, some of the cited references were published before 2002. Due to the high volume of CPGs published in the EUR31 countries during 2002–2013, the work was limited to an analysis of those that dealt with diseases and disorders causing 1% or more of the European disease burden, as measured by DALYs⁷.

Data processing

The details of the cited references within the clinical practice guidelines were recorded as a series of search statements in Excel, including keywords from the title, publication year and author and were then run against the WoS. Their full bibliographic details were downloaded as text files from the WoS and were then converted by means of a VBA programme into an Excel spreadsheet. An additional programme carried out analysis of the addresses for each paper. Fractional count of each country was tabulated as described under *research outputs*. These were then compared with their presence as a percentage of the world totals in research in the two areas. We also compared the RLs of the cited references with those of European research papers in ALCOHOL and ADDICT* and their partition into research domains.

Data analysis

Our analysis focused on evaluating the evidence-base of CPGs. This was based on fractional counts for the cited research papers for alcohol use and illicit drug dependence for each of the two sets of CPGs. The analysis was on (1) the country contribution to the cited research papers, (2) the RL of the papers and their respective journals, (3) the research domains of each country’s clinical guideline, (4) gap to citation years, (5) publication year and (6) citation trend over time. For the analysis of country contribution and RL of papers, see *data analysis* section under *research output*.

Research domain

Cited papers were grouped according to the type of research they relate to (eg, epidemiology and pharmacological treatments) on a comparative basis between alcohol misuse and illicit drug CPGs.

Gap to citation years

The gap between the papers' citation on the CPGs was plotted on a cumulative basis and contrasted between alcohol and illicit drug dependence.

Publication year

The publication year of the cited research papers in relation to the CPGs was plotted and a comparison was made between alcohol and illicit drug dependence.

Citation trend over time

Five-year citation scores for research papers between 2002 and 2012 were calculated as ACI. The analysis of citation scores was based on both the arithmetic and geometric means and on the numbers of papers from selected European countries with enough citations to put them into the top 5% of all EUR31 papers. For further details, see *data analysis* section under *research output*.

Health Advisory committees

Various health advisory committees on alcohol and illicit drug dependence were identified across European countries. The members were identified from governmental websites, or official White or strategic papers issued by the European Departments or Ministries of Health. Their names were entered in WoS as 'experts' on the subject for access to their publication portfolio. Research papers for each country were identified and mapped against alcohol or illicit drug dependence research and only relevant research was kept for analysis. Online supplementary table 2 shows further details on the health advisory committees.

FINDINGS

Research output

We analysed gross outputs of ALCOHOL and ADDICT* papers in comparison to all biomedical research, defined by means of an address filter with 138 terms indicative of a wide range of subject areas (see Methods) and of prominent research performers (figure 2). There is an increasing gap (since the mid-1990s) between the outputs of illicit drug addiction research and alcohol misuse research, with the latter now being barely half of the former.

The rate of output expansion varied across countries: for some, the absolute number of papers in alcohol misuse was declining. Scatter is evident when output is plotted against time; hence, the annual average percentage growth is somewhat artificial. The illicit drug addiction research grew at 5.3% per year worldwide, while in Europe, this was exceeded by Denmark (18.5%), Portugal (17%, but from a very low base), Norway (15.6%) and Ireland (13.5%). A somewhat smaller growth of 2% per year was shown by Austria, France, UK and Switzerland. In contrast, alcohol misuse research grew much more slowly at 2.7% per year worldwide, while in Europe, the fastest growing countries were Ireland (26% but from a low base), Norway (14.5%), Portugal and the Netherlands (10.4%). However, a decline over a 12-year period was evident for Germany (-4.7%), Finland (-3.2%), Greece (-1.3%), Sweden (-0.9%) and France (-0.5%).

Within the EUR31 countries, the amount of research on both alcohol misuse and illicit drug addiction correlates moderately well with the GDP (figure 3). In alcohol misuse research (left graph), Denmark, Finland and Sweden perform well above expectations, while Denmark, Switzerland, Netherlands and Belgium publish about twice the expected amount. In contrast, Romania and the Czech Republic publish less than half the amount expected from their GDP. For research on illicit drug dependence, Iceland, Finland, Norway, Sweden, Denmark, Estonia and Switzerland publish twice as much as the correlation line would suggest. However, Greece, Slovakia, Germany and France are publishing only half the expected numbers of papers, while Romania's output is less than one-fifth of the amount expected.

Clinical practice guidelines

We analysed 3201 references cited within 28 CPGs used from 11 European countries. The number of guidelines for alcohol and illicit drug dependence, including the cited references, are presented in online supplementary table 3. There were 13 CPGs with a total of 1484 references concerned with alcohol misuse and 15 CPGs with 1717 references concerned with illicit drug addiction. The UK's CPGs had the most numerous references (and not surprising, since authors tend to overcite work from their respective country). However in terms of country contribution per paper the USA is the biggest contributor to the CPG

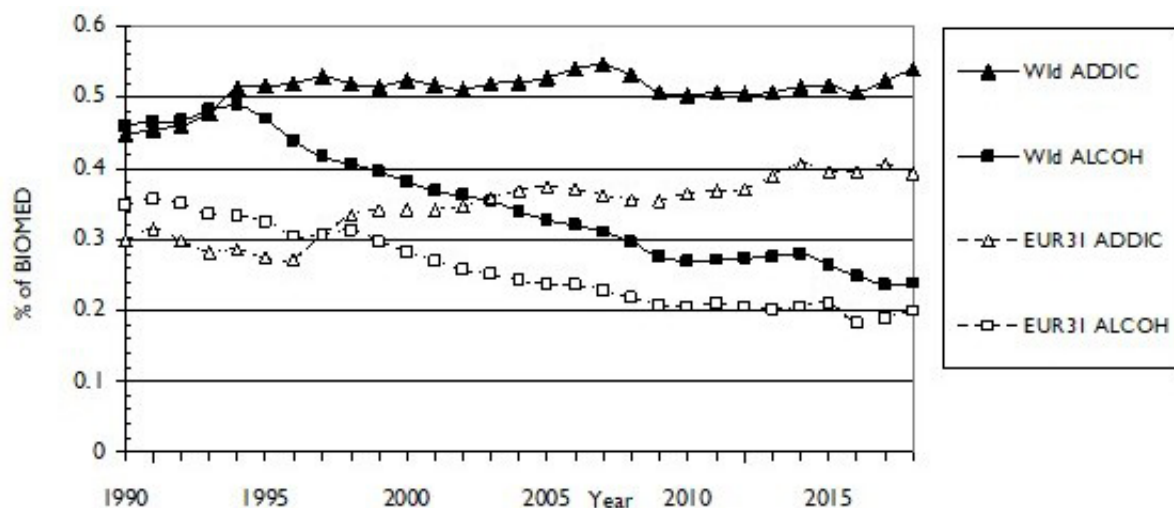


Figure 2 Alcohol misuse (ALCOH) and illicit drug addiction (ADDIC) research outputs as percentages of all biomedical research in 1990–2018, worldwide and in the EUR31 countries (3-year running means).

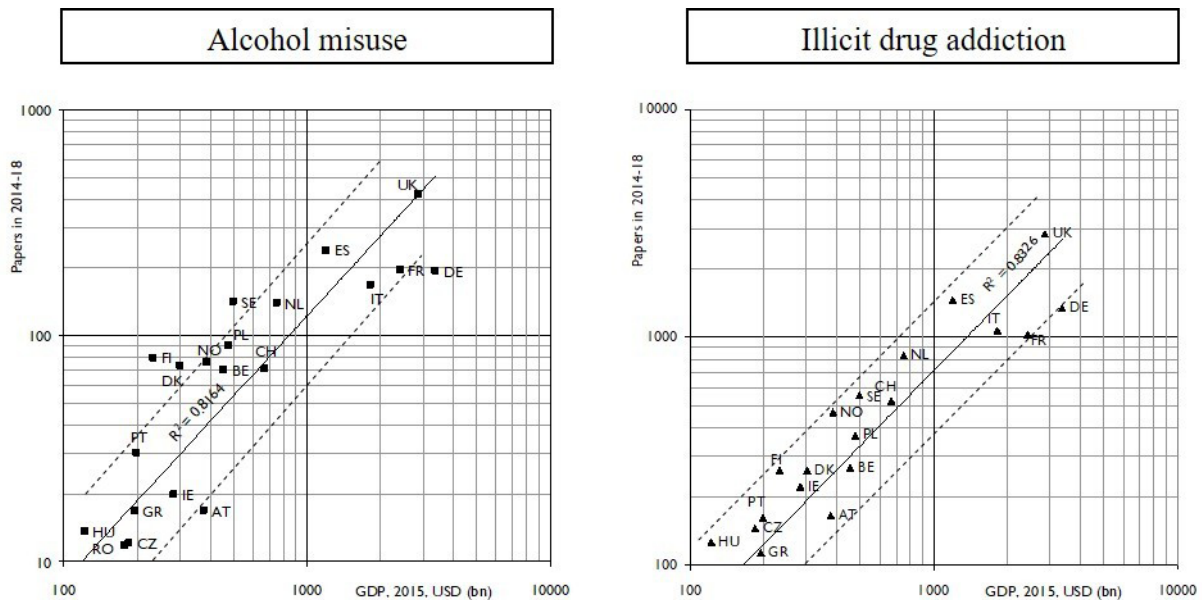


Figure 3 Outputs on alcohol misuse (left graph) and illicit drug addiction (right graph) from EUR31 countries in 2014–2018 (see online supplementary table S1 for codes) against the GDP in 2015 on PPS. Dashed lines show values twice and a half of those expected from the regression line (which is based on values for 29 of 31 European countries). GDP, gross domestic product; PPS, purchasing power standard.

references, thus making the UK second (online supplementary table S4, online supplementary file). Nonetheless, it is evident that the UK population suffers twice as much from illicit drugs than from alcohol, while the opposite applies for Finland and Lithuania. Based on the data from DALYs, provided by WHO⁷, the pattern of illicit drug and alcohol dependence for each country is schematically presented in online supplementary figure S1.

Further, figure 4 shows ACI per paper for world and EUR31 papers in both alcohol and illicit drug dependence, year by year, between 2002 and 2013. The ACI data for 2013 papers were extrapolated from the 4-year citation scores; the factor relating them is 1.37. While the data are scattered and time trends difficult to discern, the citation scores for alcohol misuse papers appeared to be increasing steadily with a decline evident in recent

years and the EUR31 papers overtaking the world average after 2009. This may in part reflect the increasing output of papers from east Asian countries that tend to be less cited. Regarding papers on illicit drugs, the reverse is true, with citation scores being relatively constant until 2011 when an increase becomes apparent. Again, the EUR31 papers overtook the world average in the last 3 years of the study period.

However, the gross contribution of a country to the references underpinning the guidelines is not a fair reflection of the value of the country's research to clinical practice if the following is considered: (1) CPGs contain unequal number of references, (2) there are no references from some European countries and (3) there is a noticeable tendency to overcite one's own country's research.²³ A better indication is the overcitation ratio (OCR) of a country's papers by CPGs from other countries (online supplementary

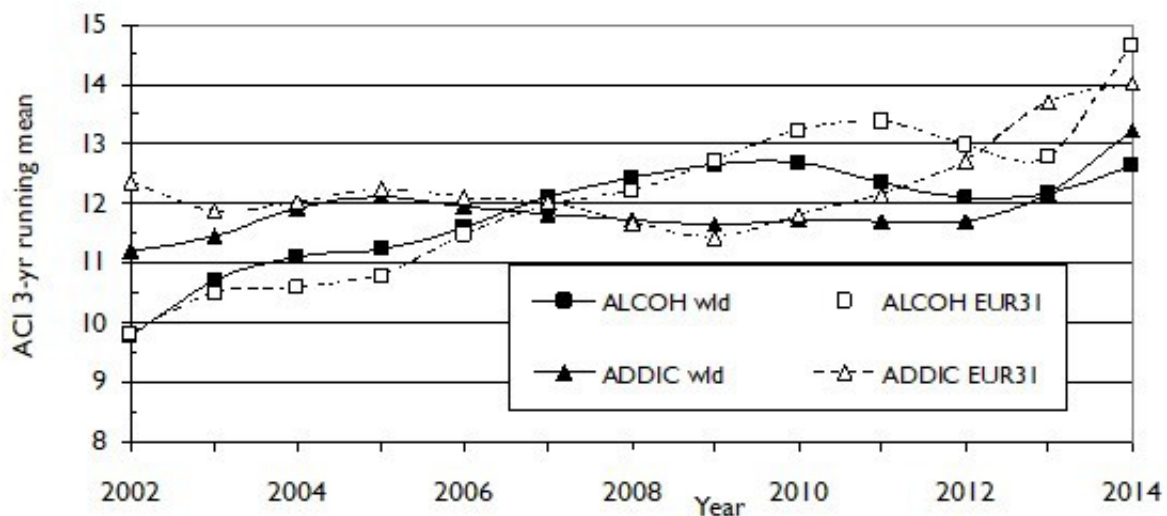


Figure 4 Arithmetic mean 5-year citation counts for world and EUR31 papers on alcohol misuse (ALCOH) and drug addiction (ADDIC) from 2002 to 2014 (3-year running means).

table 6). This means that the counts of CPG citations must be reduced by the number received from own country CPGs before dividing them by the total number of references (again, reduced by the number of own country CPGs). For example, the presence of the Netherlands in references on alcohol misuse CPGs was 19.1 papers, but 6.2 of these were from the Dutch CPGs, which had 257 references out of the grand total of 1484. Hence, its true citation presence was not $19.1/1484=1.29\%$ but lower: $12.9/1227=1.05\%$. The latter percentage can then be compared with the Dutch presence in alcohol misuse research, which was 1.77%, indicating that Dutch papers were undercited by a factor of $1.05/1.77=0.59$. We show the OCR for countries citing their own-country papers on their CPGs with the values calculated from the earlier results with diabetes and cancer research for the year 2010 where the expected $OCR=14.7 \times (\% \text{ presence})^{-0.75}$. This comparison was only made for those countries with $>1\%$ of world research (Online supplementary table 5, online supplementary file).

The results for the individual European countries are shown for the whole 12-year period in the online supplementary tables S6 and S7 (online supplementary file). The countries are ordered by their mean ranking on the three indicators: arithmetic mean, geometric mean and World-Scale (WS), and the ratio of the numbers of papers in the top 5% and receiving 38 cites or more, to the mean of 100. In both subject areas, Netherlands was ranked first, but the next ranked countries differed between the two subjects. Some of the WS values for countries with small outputs are not statistically significant, for example, those of Ireland and Malta in illicit drug addiction research.

Although there are very few data points and some anomalous results (eg, Netherlands in addiction research), the main pattern shown by the UK, Finland and the Netherlands in alcohol, and Sweden in illicit drug addiction research, is that the observed values of OCR are several times greater than the values expected based on the WoS papers and citations. However, the reverse is true for Spain where the papers are slightly more cited by Spanish researchers than by its guideline authors.

Country contribution

The country contribution to guidelines for alcohol and illicit drug dependence is shown in the online supplementary figure

S2 (online supplementary file). The UK and Netherlands are almost equally contributing to both conditions. However, guidelines relating to illicit drug dependence are mostly influenced by research from France, Italy, Spain and Austria. In contrast, research from Germany and Sweden is more prominent in relation to guidelines for alcohol dependence.

Research level

The RL of all the references cited in the mental health CPGs from the 11 European countries was 1.1, while that of the journal was 1.4. Regarding alcohol dependence, the average RL was 1.1 for the research papers and 1.5 for their respective journals (online supplementary figure S3, online supplementary file). The cited research papers of each European country related to the CPGs are more clinical than the journal in which the papers are published in; this is more the case for the illicit drug dependence guidelines.

Research domain

There were six main research domains concerning both alcohol misuse and illicit drug dependence (figure 5), demonstrating heterogeneity within each disease area. Namely, higher emphasis is evident on pharmacological interventions for illicit drug addictions and epidemiological research for alcohol misuse, as well as across the different countries (eg, diagnostic research in Belgian CPGs for alcohol misuse compared with prognosis for illicit drug addiction in Hungarian CPGs).

Gap to citation years

The research papers underpinning CPGs for illicit drug addiction reflect a shorter time period from publication to citation than the alcohol ones, as shown in figure 6.

Publication year

The publication year is parametrically distributed from 1990 to 2013, showing a similar pattern between references underpinning CPGs on alcohol and illicit drug addictions. The peak year of 2006 features 8% of citations in illicit drugs and 7% in alcohol dependence within the guidelines (online supplementary figure S4, online supplementary file).

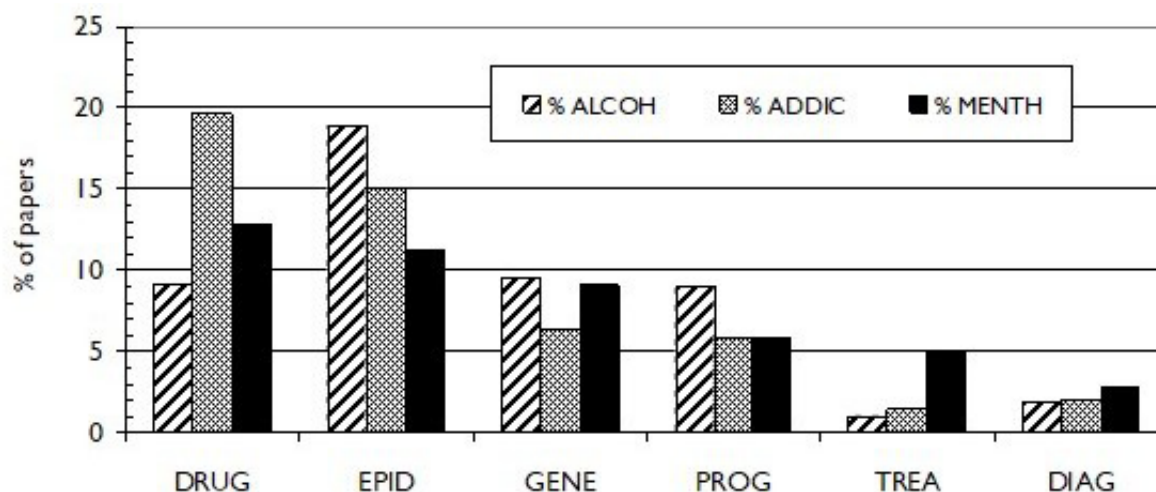


Figure 5 The research domains of the cited papers for clinical practice guidelines related to alcohol and drug dependence, and of MENTH papers in 2002–2013, between six research types. DIAG=diagnosis; DRUG=drug treatment; EPID=epidemiology; GENE=genetics; MENTH=mental health; PROG=prognosis; TREA=other (non-drug) treatments.

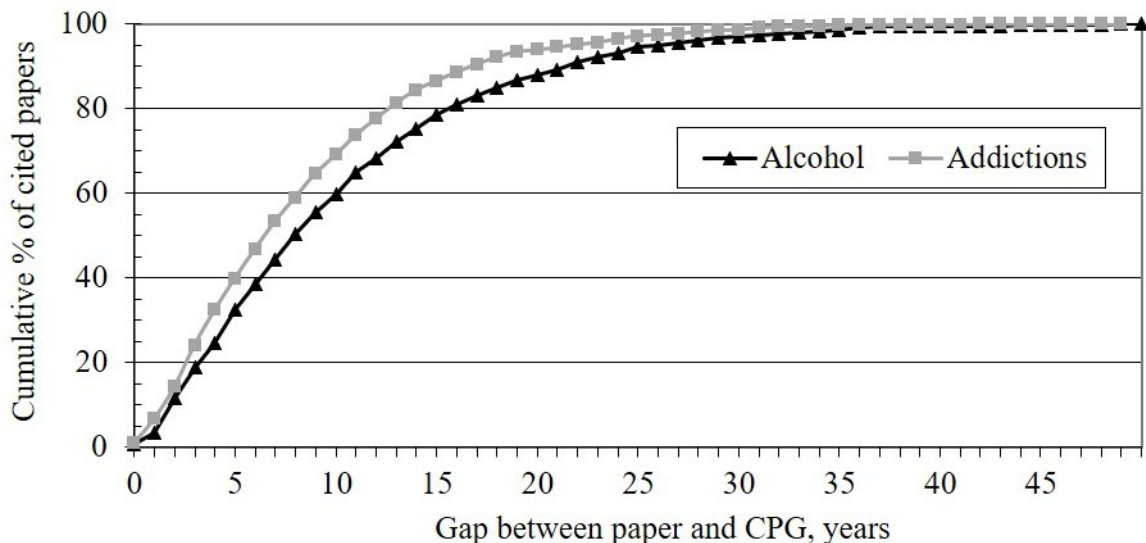


Figure 6 The publication gap in years for the cumulative per cent of cited research for guidelines in alcohol (ALC) and drug (ADD) addictions with the difference between the two showing statistical significance, $p < 0.05$. CPG, clinical practice guideline.

Citation trend over time and across the clinical guidelines

The citation rate over time (online supplementary table S8) demonstrates that research on alcohol dependence has seen a decrease, whereas there is an increase on illicit drug addictions research. The collective evidence-base (ie, number of papers) has a linear relationship with the citation across the CPGs, an almost perfect fit ($R=0.989$ for alcohol and $R=0.977$ for illicit drug dependence; online supplementary figure S5, online supplementary file). The majority of papers are cited only once, while less than 10 papers are cited on a maximum of 4 out of 13 CPGs for illicit drugs and 2 papers are cited in 6 out of 15 clinical guidelines.

Most cited research papers

The most cited research paper (appeared six times) on alcohol was Sullivan *et al* (1989),²⁴ a Canadian study cited in the clinical guidelines of Lithuania, Spain (three times), Netherlands and UK. The second cited paper (appeared six times) was from the USA appearing in the Spanish and Lithuanian CPGs. One of the most cited research papers (appeared four times) in the CPGs on illicit drug dependence was a USA study by Woody *et al*,²⁵ cited most prominently by Lithuania, Netherlands, Sweden and UK.

Disease burden

Regarding alcohol misuse, the amount of research currently undertaken and reported is grossly inadequate to the disease burden. In the last few years, the amount of alcohol-related research worldwide has declined to only about 0.27% of biomedicine, which when corrected for the filter's calibration factor (1.39) gives a true value of 0.38%. However, this is still only about 1/13th of the burden's percentage of DALYs, estimated earlier at 5.0% worldwide. In Europe, where the amount of research (even when corrected) is only at 0.27% and the disease burden is at 5.5%, the lack of research is far greater, that is, 1/20th the amount that would correspond to the problems associated with alcohol dependency. The amount of research is clearly grossly inadequate to the problems it can cause and in Europe the shortfall is by a factor of 20. This pattern does not seem to be improving, rather the reverse: it is getting progressively worse (figure 1). Scandinavian countries are performing

better relative to the rest of Europe, particularly Germany and Italy, but even they are seriously under-researching the problem (online supplementary table S9). In contrast, the amount of research on illicit drug addiction seems to be appropriate for the disease burden, at least in Europe, although deaths of (mainly) young men in the supply chain in Central and South America should be taken into account²⁶ (online supplementary table S10).

Health Advisory committees

We found the names and affiliations of members of national health advisory committees in 21 European countries. We identified 12804 papers authored by the members of which a relatively small number concerned alcohol or illicit drug addiction. The issue of concern was the relative numbers of each, which might be expected to influence the advice that the members would proffer their governments. The papers by the members, many of whom were medical researchers, were matched against the five files of non-communicable disease papers for 2009–2013, created during the EU mapping project.²⁷ A total of 35 papers on alcohol and 59 on illicit drug misuse were found, but only 14 of 21 countries had any such papers. This suggests that Member State governments were getting more advice and advocacy for the control of illicit drugs than they were on the problems of alcohol misuse. For countries with most research on these subjects, see table 1. It can be seen that the sum of papers on both disorders was much less than 1% of the total. This suggests that these topics were not likely to receive much attention even by the Member States with high research activity by their committee members. For almost all, except Germany, alcohol dependence received much less attention than illicit drug addiction.

Clinical implications

Our findings lend support to the growing literature with obvious and important implications on current debates surrounding illicit drugs and alcohol dependence policy-making and clinical practice. This bibliometrics study revealed obvious asymmetries in the research coverage on these topics. While the *illicit drug research* appears to be adequate relative to the evidence of harm in Europe, *alcohol misuse research* is grossly inadequate to the

Table 1 Numbers of research papers on alcohol and illicit drug dependence published by members of national health advisory committees in 2009–2013

Country (ISO2 code)	Total papers	Alcohol dependence	Illicit drug dependence	Both areas	%
Ireland (IE)	10	0	1	1	10.0
Finland (FI)	100	2	0	2	2.0
Austria (AT)	1384	3	23	26	1.9
Estonia (EE)	347	1	4	5	1.4
Lithuania (LT)	145	1	1	2	1.4
Hungary (HU)	1311	2	8	10	0.8
Spain (ES)	1179	2	6	8	0.7
Germany (DE)	2010	11	2	13	0.6
Netherlands (NL)	2554	8	7	15	0.6
Poland (PL)	794	2	2	4	0.5
France (FR)	294	1	0	1	0.3
Italy (IT)	965	1	2	3	0.3
Czech Republic (CZ)	969	0	3	3	0.3
United Kingdom (UK)	403	1	0	1	0.2

ISO2, International Standards Organization.

harm it causes, and in Europe the shortfall is by a factor of 20. The research on alcohol dependency (as a percentage of biomedical research), in particular, has been steadily declining both worldwide and in Europe, while research on illicit drug addiction has been static worldwide and increasing in Europe. The absolute volumes of this research have not declined however; the increase may be partly an artefact because journal coverage of the WoS is now much greater than previously reported. It is important to highlight at this point that increasing the amount of research does not equate to improving clinical practice and the lives of patients. High-quality research should be undertaken, and not just an increase in the number of studies/trials conducted.

Our findings also indicate that European governments may receive more advice and advocacy for the control of illicit drugs than on the problems of alcohol misuse, thus inadvertently hampering the public health strategy on targeting alcohol harms.^{28–30} Our research further contributes to the complex drug policy issues and status quo debates in terms of regulatory regimes, making integrated judgement in terms of an optimal policy in reducing the harms difficult to reach.³¹ On the one hand, *illicit drugs* have tough controls under the UN 1961 Single Convention on Narcotic Drugs and the 1971 Convention on Psychotropic Substances (2010), and in the UK domestic legislation by the 1971 Misuse of Drugs Act. In contrast, *drugs such as alcohol* are regulated by taxation, sales and age restrictions on purchase. The distinction in the regulatory regimes between the two does not correspond to the evidence of physical, psychological and social harm of these substances,^{4 31–34} yet it is understood that the harms are exacerbated by their availability and legal status.^{4 35} In fact, greater harm is caused by alcohol misuse, both worldwide and in Europe.^{10 13 36–38} The European rating of drug harms revealed that alcohol is the most harmful drug to individuals and society with harm ranging from mental and physical damage, addiction, crime and costs to the economy and communities.³² The discrepancies in the regulatory regimes also contradict previous expert reports postulating that aggressively targeting harms from alcohol is a valid and necessary public health strategy.^{28–30}

To provide guidance to policy makers in health, policing and social care, the harms that illicit drugs and alcohol cause

and how to reduce them need to be assessed and substantiated with evidence – something that is considered a complex task due to a range of ways in which drugs can cause harm.^{4 31 39}

The complexity of the policy problem is further exacerbated by the regional and stakeholder differences in the outcomes they consider and value in terms of harm caused to the individual and society and how to best reduce it.^{4 31 39–41} Our findings reflect this variation showing skewed regional coverage on the topic across the countries. While CPGs relating to *drug dependence* are mostly influenced by research from France, Italy, Spain and Austria, the research from Germany and Sweden is more prominent in relation to guidelines for *alcohol dependence*.

Moreover, the cited references on clinical practice guidelines concerning both alcohol and illicit drug dependence peaked around 2006, which is currently over a decade ago. Such lack of more recent evidence may be an indicator of preference by guideline developers for older and what might be perceived as more established research, since pharmacological agents on average can take as many as 12 years from laboratory or initial screening through to clinical trials and marketing approval. This linear relationship of the evidence-base, as cited across the CPGs, both for alcohol and illicit drug addictions guidelines, with the research domains indicates the degree of heterogeneity that exists between the underlying clinical recommendations made by each Member State. Furthermore, the fact that the members of national health advisory committees produce a small number of alcohol and/or illicit drug dependence research outputs (the issue of concern was the relative numbers of each, which might be expected to influence the advice that these researchers would proffer their governments) may add to this issue. Hence, the opportunities for increased collaboration between countries could eliminate the potential overlap or duplicated efforts in the developed guidelines and lead to a greater consensus in the clinical practice recommendations for people with addictions across Europe.⁴²

It has been argued that a regulatory regime with legal but regulated access would offer the best approach to reduce the overall net harms from alcohol in European countries – as proposed by an international panel of experts using a novel evidence-based approach to formulating and revising drug policy.³¹ For example, applied to the UK, this would mean stricter regulation of alcohol, with stronger emphasis on regulatory controls such as those supported by the WHO, *ie.* higher taxes, limited marketing and state owned or regulated sales outlets.^{3 31} Dealing with the problems of alcohol misuse is likely to be mainly a sociological and political challenge, rather than a scientific one. Higher pricing seems to be a good policy for reducing consumption, as it has been for cigarettes in the European Union, particularly in poorer Member States.⁴³

Some countries have already adopted such regimes, in particular those countries that produce more research on alcohol misuse, with evidence showing its impact on alcohol consumption, related health harms and costs.^{44–47} For example, higher taxes on alcohol were introduced in *Iceland* and in *Norway*, where following prohibition from 1919 to 1922, a state monopoly *Vinmonopolet* was created to help curb and encourage responsible alcohol consumption. State liquor monopolies also exist in Finland, Iceland, the Faroe Islands and Sweden, but not Denmark where policy relies on individual control rather than on public regulation.⁴⁸ In Sweden, *Systembolaget*, a government owned chain of liquor stores, confines its advertising to the need to drink responsibly and to remind minors that they must not buy alcohol. In Scotland, the setting of a minimum price for a unit of alcohol on health grounds has now been approved by the

UK Supreme Court, despite a challenge by the Scotch Whisky Association, and has operated since the beginning of May 2018.

To facilitate public health strategy on targeting harms from alcohol more research is needed to close the current evidence-practice gap revealed by our study. Dealing with the problems of alcohol misuse is arguably a sociological and political challenge, further compounded by influences from commercial and other competing interests.^{49 50} Perhaps the biggest challenge is to devise acceptable and sustainable methods to reduce harm (*ie*, discourage dangerous levels of drinking by the few without antagonising the goodwill of the many) by following the aforementioned recommendations proposed by WHO and various international expert groups and test some of the implementation strategies used by the Scandinavian countries across other EU member states.⁵¹

What is more, while guidelines on treating alcohol and drug dependence were available in 11 EU member states, there is a lack of such guidelines in other Member States. It is also important to recognise that we have evaluated small countries on level terms with the large ones. To illustrate this, if we score the countries with 8 points for first place on one indicator, 7 for second place and so on, then in *illicit drug* addiction research the UK is in overall first place with 21 points, followed by Germany (18), Norway (15), Netherlands and Sweden (14), France and Switzerland (13) and Finland and Italy (12). In contrast, in *alcohol misuse research*, Norway is in first place with 22 points and a place on all five indicators, followed by Denmark (19), Netherlands, Switzerland and the UK (18), Italy and Sweden (12) and Belgium (11). However, it appears that different countries show advantage on different indicators. Scandinavian countries in particular are performing well relative to others in Europe, such as Germany and Italy, but even they are seriously under-researching the problem. This dire situation with a lack of steady linear increase in research has been noted before.^{52 53}

Strengths and limitations

Several limitations exist. First, the recall of the two filters is not as high as expected; hence, the subjects are under-represented, although the shortfall was corrected. Second, some country outputs were so small that citation data may be unrepresentative. Third, not all the countries had CPGs on both of these research areas; hence, presence of individual countries among cited references may be skewed although we allowed for the overcitation of own country research. The representation of the amount of research by bibliometric means is always challenging, and the two filters that were employed, significantly underestimated the volumes of papers. This means that the apparent worldwide shortfall in research into the addictions (0.52% of biomedicine compared with a burden of 0.78% in recent years) is an artefact, and the true research output would have been $0.52 \times 1.43 = 0.74\%$, which is almost equal to the disease burden. However, this is the first study to our knowledge that has systematically assessed research evidence through multiple indicators of impact: research outputs, CPGs and health advisory committees.

CONCLUSION

The aim of the current study was to examine the degree of scientific evidence underpinning the clinical practice guidelines, research outputs and recommendations across European countries on illicit drug addictions and alcohol misuse. Our study highlighted higher disease burden related to alcohol misuse and less on illicit drug dependence across Europe. That is, the research on alcohol misuse is weak relative to its health and

social harms, while that on illicit drug addiction is more proportionate. Discrepancies across European countries exist, especially in terms of their research impact with certain countries being overcited relative to their research presence.

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REFERENCES

- Hanson D. Historical evolution of alcohol consumption in society. *alcohol: science, policy and public health* 2013;4–14.
- Department of Health D. *UK Chief Medical Officers' Alcohol Guidelines Review. Summary of the Proposed New Guidelines*: Department of Health and Social Care London, 2016. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/489795/summary.pdf
- World Health Organization (WHO). *Global strategy to reduce the harmful use of alcohol*, 2010.
- Nutt DJ, King LA, Phillips LD. Drug harms in the UK: a multicriteria decision analysis. *The Lancet* 2010;376:1558–65.
- World Health Organization (WHO). *The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines*. Geneva: World Health Organization, 1992.
- World Health Organization (WHO). *Global status report on alcohol and health 2018*. World Health Organization, 2019.
- World Health Organization (WHO). *Health statistics and information systems: estimates for 2000–2012: causespecific mortality*. Geneva: WHO, 2015.
- Rehm J, Taylor B, Room R. Global burden of disease from alcohol, illicit drugs and tobacco. *Drug Alcohol Rev* 2006;25:503–13.
- Schneider M, Norman R, Parry C, et al. Estimating the burden of disease attributable to alcohol use in South Africa in 2000. *S Afr Med J* 2007;97:664–72.
- Rehm J, Imtiaz S. A narrative review of alcohol consumption as a risk factor for global burden of disease. *Subst Abuse Treat Prev Policy* 2016;11:37.
- Jones A, McMillan MR, Jones RW, et al. Habitual alcohol consumption is associated with lower cardiovascular stress responses – a novel explanation for the known cardiovascular benefits of alcohol? *Stress* 2013;16:369–76.
- Sayed BA, French MT. To your health!: re-examining the health benefits of moderate alcohol use. *Soc Sci Med* 2016;167:20–8.
- Rehm J, Shield KD, Gmel G, et al. Modeling the impact of alcohol dependence on mortality burden and the effect of available treatment interventions in the European Union. *Eur Neuropsychopharmacol* 2013;23:89–97.
- WECoPRTA C, Organization WH. *Who expert Committee on problems related to alcohol consumption: second report*. World Health Organization, 2007.

- 15 World Health Organization (WHO). *Global status report on road safety 2015*. World Health Organization, 2015.
- 16 Shield KD, Gmel G, Patra J, et al. Global burden of injuries attributable to alcohol consumption in 2004: a novel way of calculating the burden of injuries attributable to alcohol consumption. *Popul Health Metr* 2012;10:9.
- 17 Pallari E, Fox AW, Lewison G. Differential research impact in cancer practice guidelines' evidence base: lessons from ESMO, NICE and SIGN. *ESMO Open* 2018;3:e000258.
- 18 Pallari E, Lewison G, Ciani O, et al. The impacts of diabetes research from 31 European countries in 2002 to 2013. *Res Eval* 2018;27:270–82.
- 19 Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg* 2010;8:336–41.
- 20 Lewison G. The definition of biomedical research subfields with title keywords and application to the analysis of research outputs. *Res Eval* 1996;6:25–36.
- 21 Lewison G, Paraje G. The classification of biomedical journals by research level. *Scientometrics* 2004;60:145–57.
- 22 Thelwall M. The precision of the arithmetic mean, geometric mean and Percentiles for citation data: an experimental simulation modelling approach. *J Informetr* 2016;10:110–23.
- 23 Bakare V, Lewison G. Country over-citation ratios. *Scientometrics* 2017;113:1199–207.
- 24 Sullivan John T, John T, Kathy S, et al. Assessment of alcohol withdrawal: the revised clinical Institute withdrawal assessment for alcohol scale (CIWA-Ar). *Addiction* 1989;84:1353–7.
- 25 Woody GE, Luborsky L, McLellan AT, et al. Psychotherapy for opiate addicts. does it help? *Arch Gen Psychiatry* 1983;40:639–45.
- 26 National center for health statistics C. drug poisoning mortality in the United States, 1999–2017, 2019. Available: <https://www.cdc.gov/nchs/data-visualization/drug-poisoning-mortality/index.htm>
- 27 Pallari E, Lewison G. The research publications of members of European national noncommunicable disease health Advisory committees. *Journal of Scientometric Research* 2015;4:124.
- 28 Commons Ho. Alcohol. *Report number: HC 151-I House of Commons Health Committee*. London, 2010.
- 29 NICE. Alcohol-use disorders: preventing the development of hazardous and harmful drinking: NICE London 2010.
- 30 Giesbrecht N, österberg E. Who's global strategy to reduce the harmful use of alcohol: an assessment of recent policies and interventions in Finland and Ontario, Canada. *Nordic Studies on Alcohol and Drugs* 2013;30:297–316.
- 31 Rogeberg O, Bergsvik D, Phillips LD, et al. A new approach to formulating and appraising drug policy: a multi-criterion decision analysis applied to alcohol and cannabis regulation. *Int J Drug Policy* 2018;56:144–52.
- 32 van Amsterdam J, Nutt D, Phillips L, et al. European rating of drug harms. *J Psychopharmacol* 2015;29:655–60.
- 33 Haydock W. The rise and fall of the 'nudge' of minimum unit pricing: The continuity of neoliberalism in alcohol policy in England. *Crit Soc Policy* 2014;34:260–79.
- 34 Onyeka IN, Uosukainen H, Korhonen MJ, et al. Sociodemographic characteristics and drug abuse patterns of treatment-seeking illicit drug abusers in Finland, 1997–2008: the HUUTI study. *J Addict Dis* 2012;31:350–62.
- 35 Lloyd C, McKeganey N. Drugs research: an overview of evidence and questions for policy: Joseph Rowntree Foundation 2010.
- 36 Rehm J, Mathers C, Popova S, et al. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. *The Lancet* 2009;373:2223–33.
- 37 Nichols M, Scarborough P, Allender S, et al. What is the optimal level of population alcohol consumption for chronic disease prevention in England? modelling the impact of changes in average consumption levels. *BMJ Open* 2012;2:e000957.
- 38 Shield KD, Gmel G, Gmel G, et al. Life-Time risk of mortality due to different levels of alcohol consumption in seven European countries: implications for low-risk drinking guidelines. *Addiction* 2017;112:1535–44.
- 39 Nutt D, King LA, Saulsbury W, et al. Development of a rational scale to assess the harm of drugs of potential misuse. *The Lancet* 2007;369:1047–53.
- 40 Murphy PN. Assessing drug-related harm. *The Lancet* 2007;369:1856.
- 41 Voller F, Maccari F, Pepe P, et al. Changing trends in European alcoholic beverage drinking: selected social, demographic, economic factors, drinking's related harms, and prevention control policies between the 1960s and 2000s. *Subst Use Misuse* 2014;49:1515–30.
- 42 Ilse J, Prinzleve M, Zurhold H, et al. Cocaine and crack use and dependence in Europe – experts view on an increasing public health problem. *Addict Res Theory* 2006;14:437–52.
- 43 Yeh C-Y, Schafferer C, Lee J-M, et al. The effects of a rise in cigarette price on cigarette consumption, tobacco taxation revenues, and of smoking-related deaths in 28 EU countries-- applying threshold regression modelling. *BMC Public Health* 2017;17:676.
- 44 Purshouse RC, Meier PS, Brennan A, et al. Estimated effect of alcohol pricing policies on health and health economic outcomes in England: an epidemiological model. *The Lancet* 2010;375:1355–64.
- 45 Baccini M, Carreras G. Analyzing and comparing the association between control policy measures and alcohol consumption in Europe. *Subst Use Misuse* 2014;49:1684–91.
- 46 Jónsson RM, Kristjánsson S. Alcohol policy and public opinion in Iceland, 1989–2012. *Nordic Studies on Alcohol and Drugs* 2013;30:539–49.
- 47 Rossow I, Karlsson T, Raitasalo K. Old enough for a beer? compliance with minimum legal age for alcohol purchases in monopoly and other off-premise outlets in Finland and Norway. *Addiction* 2008;103:1468–73.
- 48 Elmeland K, Kolind T. 'Why Don't They Just Do What We Tell Them?' Different Alcohol Prevention Discourses in Denmark. *YOUNG* 2012;20:177–97.
- 49 Babor TF. How should we define, document, and prevent conflicts of interest in alcohol research? *Int J Alcohol Drug Res* 2016;5:5–7.
- 50 Baumberg B, Anderson P, Health AP. Health, alcohol and Eu law: understanding the impact of European single market law on alcohol policies. *Eur J Public Health* 2008;18:392–8.
- 51 Merz F. United nations office on drugs and crime: world drug report 2017. 2017. *SIRIUS-Zeitschrift für Strategische Analysen* 2018;2:85–6.
- 52 Rajendram R, Lewison G, Preedy VR. Worldwide alcohol-related research and the disease burden. *Alcohol Alcohol* 2006;41:99–106.
- 53 Delany PJ, Shields JJ, Willenbring ML, et al. Expanding the role of health services research as a tool to reduce the public health burden of alcohol use disorders. *Subst Use Misuse* 2008;43:1729–46.