FOR DEBATE

Defining Substance Use Disorders: Do We Really Need More Than Heavy Use?

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Abstract — **Aims:** The aim of the study was to explore whether the concept of heavy substance use over time can be used as definition of substance use disorder. **Methods:** Narrative review. **Results:** Heavy use over time clearly underlies the neurobiological changes associated with current thinking of substance use disorders. In addition, there is evidence that heavy use over time can explain the majority of social problems and of burden of disease (morbidity and mortality). A definition of substance use disorders via heavy use over time would avoid some of the problems of current conceptualizations, for instance the cultural specificity of concepts such as loss of control. Finally, stressing the continuum of use may avoid the high level of stigmatization currently associated with substance use disorders. **Conclusion:** 'Heavy substance use over time' seems to be a definition of substance use disorders in line with results of basic research and epidemiology. Additionally, it reduces stigmatization. This approach should thus be further explored.

INTRODUCTION

In the last half century, a variety of definitions and concepts for what we now call 'substance use disorders' have been proposed in international classification systems (Room, 1998), starting with the now infamous split in the late 1950s by the WHO between drug addiction and drug habituation, with alcohol and tobacco in the latter category (World Health Organization, 1957; http://whqlibdoc.who.int/trs/WHO_TRS_116.pdf). At that time, in accordance with political orthodoxy, the WHO Expert Committee on Addiction-Producing Drugs distinguished between the addiction-producing illegal drugs with the characteristics of compulsion, tolerance, psychological and physical dependence and a detrimental effect on the individual and society, in contrast to the habit-forming drugs, including alcohol and tobacco, with the characteristics of a desire to take the drug for individual well-being, little or no tendency to increase the dose, some degree of psychological but no physical dependence, and little or no (if any, they would be primarily on the individual) detrimental effects (World Health Organization, 1957, pp. 9–10). As consequence, the Committee concluded that for illegal drugs, there should be strict national and international control, while warning labels and some national control measures should suffice for alcohol and tobacco; but 'any warning concerning habituation should not carry the stigma of addiction' (World Health Organization, 1957, p. 14).

Our view on alcohol and tobacco as dependence-producing drugs and their impact on the individual and society relative to illegal drugs has since changed dramatically (see for instance Nutt *et al.*, 2010). In both major classification systems currently used (World Health Organization, 1992; American Psychiatric Association, 2000) dependence has been defined as a syndrome of physiological, behavioural and cognitive phenomena, which lead to loss of control over use. Several criteria must be fulfilled for a diagnosis of dependence, and these criteria are the same for all psychoactive substances. The new revision of one of the systems, DSM-5, abandons the term 'dependence' in this established meaning (see below). Instead it substitutes 'use disorder', defined in terms of eleven criteria including physiological, behavioural and cognitive elements, as well as consequences of criteria, any two of which qualify for a diagnosis (American Psychiatric Association, 2013).Theories about habituation and compulsion and the underlying neural levels have also changed (Everitt and Robbins, 2005). However, there is still no binding international agreement on control of alcohol (Room *et al.*, 2008; Rehm and Room, 2009), and thus some of the ideas about distinguishing between drugs in terms of prohibition and control based on outmoded ideas of relative dependence-propensity and harmfulness continue to persist.

The example of the 1957 WHO definition is given as illustration of two points: (a) definitions of disease and disease categories change dramatically even over a short time and (b) they are subject to various social, economic and political influences (Neuman *et al.*, 2005; Frances, 2013), despite repeated calls for more evidence-based definitions of substance use disorders and policies (Wood *et al.*, 2010). These points are not only true for substance use, but also for definitions and policies in the wider field of mental health, as the recent debate on DSM-5 shows (Frances, 2013), or in medicine as a whole. Obviously, it is hard to define normal vs. diseased, and various interests push the definitions in different directions. However, there is a need for defining disease for a variety of reasons, not least because of its associated consequences such as individually experienced disability, loss of functioning and lack of well-being (Broome, 2004), as well as societal costs and lack of productivity (e.g. Rehm *et al.*, 2007a) and health care costs.

THE RELATIONSHIP BETWEEN HEAVY USE, SUBSTANCE USE DISORDERS AND CONSEQUENCES

Given the relatively rapid fluctuations in definitions and terminology (once characterized by Bruun, 1971, as moving 'compulsively from one model to another'), we feel free to propose to define all substance use disorders, i.e. alcohol, tobacco, illegal drugs and prescription opioid use disorders, completely differently: as heavy use over a period of time (see Li *et al*., 2007b; Saha *et al*., 2007, for earlier reflections on use patterns as part of the definition of use disorders). The main arguments can be characterized in the following five statements:

> (1) Heavy use over time is responsible for the changes in the brain and other physiological characteristics of substance use disorders

The use of psychoactive substances has short- and long-term impacts on the brain. Short-term effects can lead to intoxication or even death via overdose (for a more elaborate taxonomy of harm based on short- vs. long-term use see Fischer *et al*., 1997), and long-term heavy use leads to changes in the brain that are characteristic of what is currently covered by terms such as 'addiction', 'dependence' and 'substance use disorders' (conceptually: Leshner, 1997; Volkow and Li, 2005; for common classification systems: World Health Organization, 1992; American Psychiatric Association, 2000). In a recent overview where the authors were charged with summarizing the neurocognitive effects of addiction vs. heavy use for the Dutch Medical Research Council, they ended up concluding that any such distinction is impossible to make in the current literature, because there are no studies on neural effects of substance dependence without prolonged heavy use (Wiers *et al*., 2012). Thus, the effect of prolonged heavy use on the brain appears to be at least largely overlapping if not identical with what is called 'addiction' or 'substance use disorders'. In addition, heavy use over time leads to other physiological changes such as in skin conductance level (Kaplan *et al*., 1985).

> (2) Heavy use is responsible for intoxication and for the withdrawal and tolerance phenomena regarded as central to current definitions of addiction or dependence

During the deliberations on the new DSM-5, the website of the American Psychiatric Association featured the following explanation for changes in the new concept: (as it is no longer on the website, cited after Rehm *et al*., 2011a).

There was general agreement that 'dependence' as a label for compulsive, out-of-control drug use has been problematic. It has been confusing to physicians and has resulted in patients with normal tolerance and withdrawal being labelled as 'addicts.' This has also resulted in patients suffering from severe pain having adequate doses of opioids withheld because of fear of producing 'addiction'. Accordingly, the word 'dependence' is now limited to physiological dependence, which is a normal response to repeated doses of many medications including beta-blockers, antidepressants, opioids, anti-anxiety agents and other drugs. The presence of tolerance

and withdrawal symptoms is not counted as symptoms to be counted for the diagnosis of substance use disorder when occurring in the context of appropriate medical treatment with prescribed medications.

Tolerance and withdrawal, criteria for substance dependence in both major classification systems, are natural physiological reactions to prolonged use above a certain dose of psychoactive substances, and they occur whether the substance was prescribed by a doctor or not. Thus, it makes no sense to assign any diagnostic value to the origin of the substance. The point here is that continued heavy use of psychoactive substances produces physiological reactions that are key in our current concept of substance use disorders. Whether such states are reversible or not depends on a multitude of factors; it is possible to overcome substance use disorders (e.g. the experiences with heroin use disorders of Vietnam veterans, Robins, 1993), while on the other hand prescribing psychoactive substances may create long-term heavy use requiring treatment for opioid use disorders (see, for example, the high correlations between medical use and non-medical use or substance use disorders for prescription opioids, Fischer *et al*., 2012).

> (3) Heavy use over time is responsible for the main social consequences of substance use disorders, such as problems in fulfilling social roles

Heavy use over time is a primary driver of the social harms from use of psychoactive substances. Illustrating this from alcohol, an Australian study of harms to family members and friends from another's drinking found such harm to be widespread in the population, with 28.5% of adults reporting such harm in the last year. The person whose drinking had affected them most adversely was described on average as drinking 13 drinks on an occasion when drinking heavily, and drinking 5 or more drinks at least 3 times a week (Laslett *et al*., 2010, 2011).

It is also well recognized that heavy use of alcohol over time potentially adversely affects work performance (Gmel and Rehm, 2003). An analysis of self-reported problems from drinking in a US national sample of adult males found that work problems, family problems and criminal-law problems were all most strongly predicted by the regular drinking of five or more drinks on an occasion (Gmel *et al*., 2000).

> (4) Heavy use over time is responsible for the majority of the substance-attributable burden of disease and mortality

There are clear dose–response relationships to disease and most health harm for both alcohol and tobacco (Corrao *et al*., 2004; Doll and Bradford Hill, 2004; Rehm *et al*., 2010a). As a result, in recent analyses for alcohol, Rehm and colleagues, pooling the results of all EU countries, found that >77% of the net mortality burden (i.e. after subtracting the beneficial effects of alcohol consumption on ischaemic disease and diabetes from the overall alcohol-attributable burden—Rehm *et al*., 2010a) and 67% of the overall mortality burden attributable to alcohol were due to heavy drinking, defined as >60 g/day for men, and >40 g/day for women (Rehm *et al*., 2013). Using an independent analysis for alcohol dependence, about

71% of the net burden and 62% of all the harmful alcohol-attributable mortality burden were caused by alcohol dependence (Rehm *et al.*, 2013; Roerecke and Rehm, 2013). As alcohol dependence is clearly characterized by heavy drinking (Dawson *et al.*, 2008; Schuckit, 2009), one plausible potential explanation for these results would be that the pathway by which alcohol dependence causes mortality is via heavy drinking. Obviously, this pathway should be substantiated in further research using adequate statistical methodology such as structural equation modelling (Muthén, 1984).

For other psychoactive substances, similar associations can be made. For tobacco, there are clear dose–response relationships to disease and most harm (e.g. Khuder, 2001), and for illegal drugs, heavy use is often defined by high frequency of use, such as daily or almost daily use. For instance, for cannabis, daily use over time has been linked to a number of negative health and other outcomes, and has thus been highlighted as a public health concern (Fischer *et al.*, 2011; http://www.emcdda.europa.eu/publications/thematic-papers/daily-cannabis-use).

> (5) Heavy use over time as a definition better fits the empirical data and may diminish stigmatization and avoids pointing attention away from highest-risk categories

One possible advantage of characterizing substance use disorders in this way would be that such a definition is less stigmatizing than the label of addiction. The importance of stigmatization has already been highlighted in the citation from the WHO Expert Committee above (World Health Organization, 1957), and recently summarized empirical research found alcohol use disorders to be the most stigmatized mental disorders, closely followed by illegal drug use disorders (Schomerus *et al.*, 2011; see also Schomerus *et al.*, 2013). A comparative study in >10 countries, including low and mid-income countries, found drug use disorders more stigmatized than alcohol use disorders, but overall the high stigmatization of substance use disorders was corroborated in this study as well (Room *et al.*, 2001).

A definition based on heavy use over time may constitute an improvement with respect to stigmatization, as it is *de facto* just one end of a continuum of use, and as most people in Europe use alcohol, they could place themselves on the continuum (World Health Organization, 2011; Shield *et al.*, 2012); such a definition might lead substance use problems to be perceived similarly as hypertension, hyperuricemia or elevated blood sugar; i.e. as a sign to change lifestyle or to start using medication (Nutt and Rehm, Unpublished manuscript). Thus, conceptualizing the disorder in terms of heavy use over time on a continuum of use implicitly points to reduction of use, including but not limited to abstinence, as a solution. Such solutions are not that clear from current definitions of substance use disorders. It should be noted that while reduction of use and abstinence are linked to clear benefits in terms of morbidity and mortality (Rehm and Roerecke, 2013; Rehm *et al.*, 2013, for alcohol; Popova *et al.*, 2009, for tobacco; Hser *et al.*, 2001 for illegal drugs), some of the health consequences may be irreversible.

We believe that redefining substance use disorders in terms of heavy use over time will also avoid pointing attention away from those most at risk of harm from their substance use.

Consider tobacco dependence as an example. First, there seems to be no added value in using a term like tobacco dependence instead of smoking a pack of cigarettes for the past year except that we stigmatize these smokers further. Second, as surveys show, the prevalence of dependence as defined by DSM-IV is often similar to the prevalence of smokers smoking 20 cigarettes or more (Lessov *et al.*, 2004; Loukola *et al.*, 2008; John *et al.*, 2009); however, the correlation between dependence and number of cigarettes smoked is commonly low, i.e. <0.5, indicating that heavy smokers and dependent smokers only overlap to a limited extent (Kawakami *et al.*, 1999; Strong *et al.*, 2003; DiFranza *et al.*, 2010). To give an example, Loukola *et al.*, (2008) found that 48% in their sample of Finnish twins were dependent by DSM-IV criteria and 50% smoked heavily (≥20 during heaviest smoking period or ≥40 on a single day), but the correlation between DSM-IV nicotine dependence and prevalence of heavy smoking was only $r = 0.44$. Thus, many heavy smokers were not dependent. To give another example from our ALICE RAP calculations: in the German Epidemiological Surveys of Substance Abuse (ESA) from 2009 (Kraus and Pabst, 2010), 51% of those smoking 20 or more cigarettes were not dependent by DSM-IV criteria. In other words, those heavy smokers did not endorse at least three of the seven criteria, for whatever reason.

However, what does this mean for health risks? Are heavy smokers who are not classified as dependent less at risk for disability or dying from lung cancer (Lim *et al.*, 2012)? Do they have a higher chance to quit smoking? We have no evidence for this, and some evidence to the contrary, i.e. heavy use predicting later abstinence better than dependence according to DSM-IV criteria (Hendricks *et al.*, 2008). Thus Occam's razor, i.e. the principle of parsimony stating that among competing explanations the explanation with the fewest assumptions should be selected, as well as the stigmatization argument would suggest simply using the criterion of heavy use, which has proven strong links to tobacco-related health harm. Regarding the stigmatization argument, it seems that the tobacco field is a prime example of how public health-relevant 'addictive' behaviour can be changed without labelling people as mentally ill (Frances, 2013).

For other substances, we have similar phenomena. Each survey conducted without any pre-screening of respondents shows a number of people who qualify for alcohol dependence in any given year with low average consumption of one drink or less and/or few or even no heavy drinking occasions (Caetano *et al.*, 1997; Caetano and Cunradi, 2002; Rehm *et al.*, 2008; in a different age group: Holly and Wittchen, 1998), or people who qualify for cannabis dependence having smoked cannabis <10 times in the last year, and never more than one joint per occasion (see also the examples of Room, 1998). People with such a profile of use clearly are not of much concern to public health, and neither are they in need of medical interventions.

Another example from alcohol use disorders may also help to justify the term heavy use over time as conceptually more adequate. Consider the following example: the two most recent surveys for alcohol use disorders revealed a 12.5% prevalence of alcohol dependence in Latvia (Snikere *et al.*, 2011) and <0.5% in Italy (de Girolamo *et al.*, 2006, using standard survey methodology—Composite International Diagnostic Interview CIDI; see Rehm *et al.*, 2005, 2012, for background on methodology and a European overview of

prevalence rates). Even if we allow for methodological problems with the Italian estimate, as it was based on the World Mental Health survey (Grant *et al*., 2007), which at the time asked dependence questions only if the respondent had previously answered affirmatively to the abuse criteria, other evidence from Italy would suggest prevalence of alcohol dependence at most 1/5 to 1/10 that of Latvia (Scafato *et al*., 2005). If we look at the per capita consumption of the two countries for 2010, we find a recorded consumption of 6.1 for Italy and 9.8 for Latvia, with unrecorded consumption being estimated at an additional 1.4 for Italy and 1.8 for Latvia (http://www.who.int/substance_abuse/activities/gisah/en/). Thus, the overall drinking level is quite similar and nothing would suggest a 5- to 10-fold difference in alcohol dependence prevalence. However, the drinking patterns are different, with Latvia showing a more harmful drinking style characterized by irregular heavy drinking occasions (Popova *et al*., 2007; World Health Organization, 2011), which has been shown to lead to a higher disease burden (Rehm *et al*., 2007c).

Liver cirrhosis rates, often used as indirect indicator for dependence, differ between the two countries, with age-standardized rates for 2008, the last year available in the WHO data bank (http://www.who.int/healthinfo/global_burden_disease/estimates_country/en/), being 6.8 per 100,000 for Italy and 15.3 per 100,000 for Latvia. If we look into average heavy drinking rates, the following picture emerges: at a cut-off of 60 g pure alcohol per day, we would have a prevalence of 3.5% in Italy, and 8.5% in Latvia, and with a cut-off at 80 g 1.5 and 4.6% for Italy and Latvia, respectively (prevalence of heavy drinking calculated by triangulating survey and per capita information: Rehm *et al*., 2007b, 2010b; Kehoe *et al*., 2012; assuming that 80% of the sold alcohol is consumed). Even though the average drinking rate may not be the most meaningful alcohol consumption statistic for Latvia, as it is composed of fewer drinking occasions with much higher drinking per occasion (see below), all the resulting ratios between both countries are much closer to each other and the liver cirrhosis mortality ratio than to the dependence figures. We believe that a better explanation of the divergent dependence rates are cultural differences and norms, which would prescribe that in Italy one would not traditionally admit to losing control over one's drinking, whereas losing control may be the very reason why many Latvians drink heavily (Room, 2006, 2007). As a result questions about control and other psychological criteria in DSM-IV or ICD 10 tend to be answered differently, even with the same underlying behaviour (Room *et al*., 1996; Room, 2006; Rehm *et al*., 2012). Differences in criteria endorsement could also be shown with respect to age (Miller *et al*., 1991; Saha *et al*., 2006; Pabst *et al*., 2012).

ATTEMPTS AT INTEGRATING USE INTO THE SUBSTANCE USE DISORDER CONCEPT

Several nicotine dependence screening instruments, of which the Fagerström Test for Nicotine Dependence (FTND, just re-named Fagerström Test for Cigarette Dependence; Heatherton *et al*., 1991) is the most often used, already include smoking quantity as a central item, and are therefore highly correlated with use measures (Park *et al*., 2012). Similarly, one of the most widely used screening instruments in the alcohol field, the Alcohol Use Disorder Identification Test (AUDIT) has three questions on use (sometimes used on their own as a screening measure, the AUDIT-C: Bush *et al*., 1998), which determine to a large extent whether people are scored positively or not (Babor *et al*., 2001; Gmel *et al*., 2001). Thus in a Swedish population study (Hradilova Selin, 2006), 71% of the positive scores of those scoring 8+ (the usual cut-off) on the AUDIT as a whole were derived from the AUDIT-C. Though it was initially not intended as such, the AUDIT has commonly come to be 'viewed as screening for alcohol dependence' (Hradilova Selin, 2006). Frequency of use as indicator of heavy use is part of the WHO Alcohol, Smoking and Substance Involvement Screening Test (ASSIST, WHO ASSIST Working Group, 2002).

Also, in the instructions of several versions of the CIDI, there are filter variables for only asking questions on substance use disorders above a certain threshold of use (e.g. M-CIDI: Wittchen *et al*., 1998). Finally, there have been numerous attempts to integrate heavy use indicators into the criteria for substance use disorders statistically, e.g. via item-response theory driven analyses, usually with the result that such indicators fit similarly to the current criteria (for alcohol Li *et al*., 2007a,b; Borges *et al*., 2010; Saha *et al*., 2010; for cannabis: Piontek *et al*., 2011).

HOW TO DETERMINE THRESHOLDS?

The population distribution of psychoactive substance use is a continuum (for example Rehm *et al*., 2010b), with most people abstaining for their lifetime from any given substance (for alcohol, see Shield *et al*., 2013; for a general overview of global exposures, see Lim *et al*., 2012). In this sense it will be somewhat arbitrary to define thresholds and cut-points for heavy use. Is somebody who drinks 60 g of pure alcohol on average a day a non-heavy user, while somebody who drinks 70 g a heavy user? Applying an exact threshold to a continuum is arbitrary, but we need such thresholds as many systems in our society are built on them (such as treatment decision-making and disorder codes for reimbursement of interventions).

For all psychoactive substances we suggest two thresholds: one for so-called brief interventions, which consist of advice to cut down with motivational support (Agerwala and McCance-Katz, 2012), and one for formal therapy, either psychosocial or pharmaceutical or both. While we will not give a list of such thresholds for all substances in this piece, we illustrate their construction with two examples: tobacco and alcohol.

Table 1 illustrates the relationships between numbers of cigarettes smoked (current) and dependence diagnosis in the past 12 months, based on four different surveys from Germany, the UK and Switzerland (part of the ALICE RAP Project). Again we see the phenomenon that dependence is prevalent already at low levels of cigarettes per day, but that there is also a clear dose–response relationship.

There is consensus that brief interventions should be given to all smokers, irrespective of status of dependence or smoking use disorders (http://www.nice.org.uk/nicemedia/live/11375/31864/31864.pdf). For formal therapy associated with heavy smoking, we suggest a cut-off of 10 cigarettes/day and more, as virtually all randomized clinical studies and thus our knowledge regarding effectiveness of interventions are restricted to this group. However, if a smoker wants to quit, therapy should be offered.

Table 1. Proportion of nicotine dependent persons by current quantity of cigarettes used per day

Cigarettes per day	Germany ESA, DSM 2009 (%)	Germany ESA, DSM 2006 (%)	ESA, FTND 2006 (%)	Switzerland AMIS, FTND 2011 (%)	UK APSM, FTND 2007 (%)
0–4	9.8	10.2	2.0	2.9	2.1
5–9	18.4	22.9	3.3	10.4	13.5
10–14	18.5	22.2	17.1	18.2	33.8
15–19	30.8	32.3	40.8	54.4	51.4
20–24	44.4	41.6	54.6	67.0	72.7
25–29	37.6	50.0	90.6	93.3	85.7
30+	51.5	50.9	95.4	93.2	96.4

Remarks: ESA 2006: Epidemiological Survey of Substance Abuse 2006 (Kraus and Baumeister, 2008). ESA 2009: Epidemiological Survey of Substance Abuse 2009 (Kraus and Pabst, 2010). AMIS 2011: Addiction Monitoring in Switzerland (Gmel *et al.*, 2012). APSM 2007: Adult Psychiatric Morbidity Survey (National Centre for Social Research and University of Leicester, 2011).

For the negative consequences of alcohol consumption, for example alcohol-related cancers, there is no level of consumption that is risk free. Australian guidelines to reduce the health risks from drinking alcohol reported a lifetime risk of an alcohol-related death as nearly 1 in 100 for both men and women at a consumption of 20 g/day, increasing to about 4 in 100 at 40 g/day (National Health Medical Research Council, 2009). At a population level, and accounting for potential reductions in the risk of ischaemic events, any alcohol consumption above 10 g pure alcohol on average per day is associated with higher overall mortality (Rehm *et al.*, 2011b). So, from a public health point of view, recommendations for brief interventions for more than one drink daily on average could be justified. In addition, for alcohol, there are clear indications that patterns of drinking are important, most importantly the frequency of heavy drinking occasions. Thus, drinking 10 drinks 3 days a week is more harmful than drinking 5 drinks 6 days a week (Rehm *et al.*, 2006).

There have been attempts to define thresholds based on the AUDIT (see above), with different thresholds being proposed for brief interventions and for referral to formal treatment (Babor *et al.*, 2001). Analogous thresholds can be justified for the already mentioned consumption items of the AUDIT, the AUDIT-C (Dawson *et al.*, 2012): average frequency, average quantity and frequency of heavy drinking occasions. Future research will have to determine the best exact models incorporating both average consumption and heavy drinking occasions. Guidelines of the European Medicines Agency might imply a threshold for brief interventions of >40 g pure alcohol on average per day for men and 20 g for women; or alternatively at two 60 g (men)/48 g (women) drinking occasions per week. Also a threshold of 80 g of average daily consumption for at least 6 months for men, and 50 g for women, could serve as a basis for formal therapy (European Medicines Agency, 2010).

The point here is that establishing meaningful consumption criteria for brief intervention or formal therapy is possible. More research and a formal process for integrating the evidence are necessary, as it has been done for hypertension in several countries such as the US (http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.pdf).

CONCLUSIONS

We have given evidence to redefine the concept of substance use disorders in terms of heavy use over time. Such a concept would incorporate all the necessary elements for decisions on prevention and treatment, and it would avoid culturally relative arbitrary definitions in terms of loss of control or of failure to fulfil social roles. It seems we do not need any other construct to describe the phenomenon of heavy use over time, such as the term addiction. Establishing heavy use over time as the relevant entity may also contribute to a de-stigmatization of people who use psychoactive substances heavily. It would also help to initiate lifestyle changes and treatment and other interventions for heavy use earlier in time, e.g. with brief interventions in primary health care (e.g. Kaner *et al.*, 2007, for alcohol; Humeniuk *et al.*, 2012, for illicit drugs; Doran *et al.*, 2006, for tobacco). It may also help to close the treatment gap for substance use disorders by lowering stigmatization, especially for alcohol (Rehm *et al.*, 2013).

REFERENCES

Agerwala SM, McCance-Katz EF. (2012) Integrating screening, brief intervention, and referral to treatment (SBIRT) into clinical practice settings: a brief review. *J Psychoactive Drugs* **44**:307–17.

American Psychiatric Association. (2000) *Diagnostic and Statistical Manual of Mental Disorders (4th edition, text revision)*. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (2013) *Substance Use and Addiction-Related Disorders*. Philadelphia: American Psychiatric Association.

Babor T, Higgins-Biddle J, Saunders J *et al.* (2001) *AUDIT—The Alcohol Use Disorders Identification Test: Guidelines for use in primary care*. Geneva: World Health Organization.

Borges G, Ye Y, Bond J *et al.* (2010) The dimensionality of alcohol use disorders and alcohol consumption in a cross-national perspective. *Addiction* **105**:240–54.

Broome J. (2004) *Weighing Lives*. Oxford: Oxford University Press.

Bruun K. (1971) Finland: the non-medical approach. In Kiloh LG, Bell DS (eds). *Alcoholism and Drug Dependence*. 29th International Congress on Alcoholism and Drug Dependence. Australia: Butterworths, 545–59.

Bush K, Kivlahan DR, McDonell MB *et al*. (1998) The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. *Arch Intern Med* **158**:1789–95.

Caetano R, Cunradi C. (2002) Alcohol dependence: a public health perspective. *Addiction* **97**:633–45.

Caetano R, Tam T, Greenfield T *et al*. (1997) DSM-IV alcohol dependence and drinking in the U.S. population: a risk analysis. *Ann Epidemiol* **7**:542–9.

Corrao G, Bagnardi V, Zambon A *et al*. (2004) A meta-analysis of alcohol consumption and the risk of 15 diseases. *Prev Med* **38**:613–9.

Dawson DA, Li TK, Grant BF. (2008) A prospective study of risk drinking: at risk for what? *Drug Alcohol Depend* **95**:62–72.

Dawson DA, Smith SM, Saha TD *et al*. (2012) Comparative performance of the AUDIT-C in screening for DSM-IV and DSM-5 alcohol use disorders. *Drug Alcohol Depend* **126**:384–8.

de Girolamo G, Polidori G, Morosini P *et al*. (2006) Prevalence of common mental disorders in Italy: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD). *Soc Psychiatry Psychiatr Epidemiol* **41**:853–61.

DiFranza J, Ursprung WW, Lauzon B *et al*. (2010) A systematic review of the Diagnostic and Statistical Manual diagnostic criteria for nicotine dependence. *Addict Behav* **35**:373–82.

Doll R, Bradford Hill A. (2004) The mortality of doctors in relation to their smoking habits: a preliminary report. *Br Med J* **328**:1529–33.

Doran CM, Duszynski KM, Beilby JJ *et al*. (2006) Use of pharmacotherapies for the management of addictive behaviours in Australian clinical practice. *Addict Behav* **31**:1947–58.

European Medicines Agency. (2010) *Guideline on the Development of Medicinal Products for the Treatment of Alcohol Dependence*. London, UK: European Medicines Agency.

Everitt BJ, Robbins TW. (2005) Neural systems of reinforcement for drug addiction: from actions to habits to compulsion. *Nat Neurosci* **8**:1481–9.

Fischer B, Kendall P, Rehm J *et al*. (1997) Charting WHO—goals for licit and illicit drugs for the year 2000: are we 'on track'? *Public Health* **111**:217–75.

Fischer B, Jeffries V, Hall W *et al*. (2011) Lower risk cannabis use guidelines for Canada (LRCUG): a narrative review of evidence and recommendations. *Can J Public Health* **102**:324–7.

Fischer B, Nakamura N, Urbanoski K *et al*. (2012) Correlations between population levels of prescription opioid use and prescription-opioid-related substance use treatment admissions in the USA and Canada since 2001. *Public Health* **126**:749–51.

Frances A. (2013) *Saving Normal: An Insider's Revolt Against Out-Of-Control Psychiatric Diagnosis, DSM-5, Big Pharma, and the Medicalization of Ordinary Life*. New York, USA: William Morrow.

Gmel G, Rehm J. (2003) Harmful alcohol use. *Alcohol Res Health* **27**:52–62.

Gmel G, Rehm J, Room R *et al*. (2000) Dimensions of alcohol-related social harm in survey research. *J Subst Abuse* **12**:113–38.

Gmel G, Heeb J, Rehm J. (2001) Is the frequency of drinking an indicator of problem drinking? A psychometric analysis of a modified version of the alcohol use disorders identification test in Switzerland. *Drug Alcohol Depend* **64**:151–63.

Gmel G, Kuendig H, Maffli E *et al*. (2012) *Suchtmonitoring Schweiz/Jahresbericht – Daten 2011 [Addiction monitoring in Switzerland: Annual data for 2011]*. Bern, Switzerland: Bundesamt für Gesundheit.

Grant BF, Compton WM, Crowley TJ *et al*. (2007) Errors in assessing DSM-IV substance use disorders. *Arch Gen Psychiatry* **64**:379–80.

Heatherton TF, Kozlowski LT, Frecker RC *et al*. (1991) The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict* **86**:1119–27.

Hendricks PS, Prochaska JJ, Humfleet GL *et al*. (2008) Evaluating the validities of different DSM-IV based conceptual constructs of tobacco dependence. *Addiction* **103**:1215–23.

Holly A, Wittchen H-U. (1998) Patterns of use and their relationship to DSM-IV abuse and dependence of alcohol among adolescents and young adults. *Eur Addict Res* **4**:50–7.

Hradilova Selin K. (2006) Alcohol Use Disorder Identification Test (AUDIT): What does it screen? Performance of the AUDIT against four different criteria in a Swedish population sample. *Subst Use Misuse* **41**:1881–99.

Hser Y, Hoffman V, Grella C *et al*. (2001) A 33-year follow-up of narcotics addicts. *Arch Gen Psychiatry* **58**:503–8.

Humeniuk R, Ali R, Babor T *et al*. (2012) A randomized controlled trial of a brief intervention for illicit drugs linked to the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) in clients recruited from primary health-care settings in four countries. *Addiction* **107**:957–66.

John U, Meyer C, Rumpf HJ *et al*. (2009) Nicotine dependence criteria and nicotine withdrawal symptoms in relation to pain among an adult general population sample. *Eur J Pain* **13**:82–8.

Kaner EF, Beyer F, Dickinson HO *et al*. (2007) Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database Syst Rev* **18**:CD004148.

Kaplan RF, Cooney NL, Baker LH *et al*. (1985) Reactivity to alcohol-related cues: physiological and subjective responses in alcoholics and nonproblem drinkers. *J Stud Alcohol* **46**:034–272.

Kawakami N, Takatsuka N, Inaba S *et al*. (1999) Development of a screening questionnaire for tobacco/nicotine dependence according to ICD-10, DSM-III-r, and DSM-IV. *Addict Behav* **24**:155–66.

Kehoe T, Gmel G, Jr, Shield K *et al*. (2012) Determining the best population-level alcohol consumption model and its impact on estimates of alcohol-attributable harms. *Popul Health Metr* **10**:6.

Khuder SA. (2001) Effect of cigarette smoking on major histological types of lung cancer: a meta-analysis. *Lung Cancer* **31**:139–48.

Kraus L, Baumeister SE. (2008) Studiendesign und Methodik des Epidemiologischen Suchtsurveys 2006 [Study design and methodology of the 2006 Epidemiological Survey of Substance Abuse]. *Sucht* **54**:S6–S15.

Kraus L, Pabst A. (2010) Studiendesign und Methodik des Epidemiologischen Suchtsurveys 2009. *SUCHT-Zeitschrift für Wissenschaft und Praxis/Journal of Addiction Research and Practice [Study design and methodology of the 2009 Epidemiological Survey of Substance Abuse]* **56**:315–26.

Laslett AM, Catalano P, Chikritzhs T *et al*. (2010) *The Range and Magnitude of Alcohol's Harm to Others*. Fitzroy, VIC: Turning Point Alcohol & Drug Centre.

Laslett AM, Room R, Ferris J *et al*. (2011) Surveying the range and magnitude of alcohol's harm to others in Australia. *Addiction* **106**:1603–11.

Leshner AI. (1997) Addiction is a brain disease, and it matters. *Science* **278**:45–7.

Lessov CN, Martin NG, Statham DJ *et al*. (2004) Defining nicotine dependence for genetic research: evidence from Australian twins. *Psychol Med* **34**:865–79.

Li TK, Hewitt BG, Grant BF. (2007a) The alcohol dependence syndrome, 30 years later: a commentary. The 2006 H. David Archibald lecture. *Addiction* **102**:1522–30.

Li TK, Hewitt BG, Grant BF. (2007b) Is there a future for quantifying drinking in the diagnosis, treatment, and prevention of alcohol use disorders? *Alcohol Alcohol* **41**:57–63.

Lim SS, Vos T, Flaxman AD *et al*. (2012) A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **380**:2224–60.

Loukola A, Broms U, Maunu H *et al*. (2008) Linkage of nicotine dependence and smoking behavior on 10q, 7q and 11p in twins with homogeneous genetic background. *Pharmacogenetics J* **8**:209–19.

Miller NS, Belkin BM, Gold MS. (1991) Alcohol and drug dependence among the elderly: epidemiology, diagnosis, and treatment. *Compr Psychiatry* **32**:153–65.

Muthén B. (1984) A general structural equation model with dichotomous, ordered categorical, and continuous latent variable indicators. *Psychometrika* **49**:115–32.

National Centre for Social Research and University of Leicester. (2011) *Adult Psychiatric Morbidity Survey, 2007 [computer file]*, 3rd edn. Colchester, Essex: UK Data Archive.

National Health Medical Research Council. (2009) *Australian Guidelines to Reduce Health Risks from Drinking Alcohol*. Australia: Commonwealth of Australia.

Neuman MD, Bitton A, Glantz SA. (2005) Tobacco industry influence on the definition of tobacco related disorders by the American Psychiatric Association. *Tob Control* **14**:328–37.

Nutt DJ, King LA, Phillips LD. Drugs. FtISCo. (2010) Drug harms in the UK: a multicriteria decision analysis. *Lancet* **376**:1558–65.

Pabst A, Kraus L, Piontek D *et al*. (2012) Age differences in diagnostic criteria of DSM-IV alcohol dependence among adults with similar drinking behaviour. *Addiction* **107**:331–8.

Park S, Lee JY, Song TM *et al*. (2012) Age-associated changes in nicotine dependence. *Public Health* **126**:482–9.

Piontek D, Kraus L, Legleye S *et al*. (2011) The validity of DSM-IV cannabis abuse and dependence criteria in adolescents and the value of additional cannabis use indicators. *Addiction* **106**:1137–45.

Popova S, Rehm J, Patra J *et al*. (2007) Comparing alcohol consumption in central and eastern Europe to other European countries. *Alcohol Alcohol* **42**:465–73.

Popova S, Patra J, Rehm J. (2009) Avoidable portion of tobacco-attributable acute care hospital days and its cost due to implementation of different intervention strategies in Canada. *Int J Environ Res Public Health* **6**:2179–92.

Rehm J, Roerecke M. (2013) Reduction of drinking in problem drinkers and all-cause mortality. *Alcohol Alcohol* **48**:509–13.

Rehm J, Room R. (2009) Why do we need international regulations for alcohol control? *Nordic Stud Alcohol Drugs* **24**:447–50.

Rehm J, Room R, Van den Brink W *et al*. (2005) Alcohol use disorders in EU countries and Norway: an overview of the epidemiology. *Eur Neuropsychopharmacol* **15**:377–88.

Rehm J, Greenfield T, Kerr W. (2006) Patterns of drinking and mortality from different diseases—an overview. *Contemp Drug Probl* **33**:205–35.

Rehm J, Gnam W, Popova S *et al*. (2007a) The costs of alcohol, illegal drugs, and tobacco in Canada, 2002. *J Stud Alcohol Drugs* **68**:886–95.

Rehm J, Klotsche J, Patra J. (2007b) Comparative quantification of alcohol exposure as risk factor for global burden of disease. *Int J Methods Psychiatr Res* **16**:66–76.

Rehm J, Sulkowska U, Manczuk M *et al*. (2007c) Alcohol accounts for a high proportion of premature mortality in central and eastern Europe. *Int J Epidemiol* **36**:458–67.

Rehm J, Room R, Taylor B. (2008) Method for moderation: measuring lifetime risk of alcohol-attributable mortality as a basis for drinking guidelines. *Int J Methods Psychiatr Res* **17**:141–51.

Rehm J, Baliunas D, Borges GLG *et al*. (2010a) The relation between different dimensions of alcohol consumption and burden of disease—an overview. *Addiction* **105**:817–43.

Rehm J, Kehoe T, Gmel G *et al*. (2010b) Statistical modeling of volume of alcohol exposure for epidemiological studies of population health: the example of the US. *Popul Health Metr* **8**:3.

Rehm J, Frick U, Fischer B. (2011a) Substanzgebrauchsstörungen—ein neuer Ansatz im DSM 5? [Substance-use disorders—a new approach in DSM 5?]. *Sucht* **57**:54–5.

Rehm J, Zatonski W, Taylor B *et al*. (2011b) Epidemiology and alcohol policy in Europe. *Addiction* **106**:11–9.

Rehm J, Shield KD, Rehm MX *et al*. (2012) *Alcohol Consumption, Alcohol Dependence, and Attributable Burden of Disease in Europe: Potential Gains from Effective Interventions for Alcohol Dependence*. Toronto, Canada: Centre for Addiction and Mental Health.

Rehm J, Shield KD, Rehm MX *et al*. (2013) Modelling the impact of alcohol dependence on mortality burden and the effect of available treatment interventions in the European Union. *Eur Neuropsychopharmacol* **23**:89–97.

Robins LN. (1993) The sixth Thomas James Okey Memorial Lecture. Vietnam veterans' rapid recovery from heroin addiction: a fluke or normal expectation? *Addiction* **88**:1041–54.

Roerecke M, Rehm J. (2013) Alcohol use disorders and mortality—a systematic review and meta-analysis. *Addiction* (epub ahead of print).

Room R. (1998) Alcohol and drug disorders in the International Classification of Diseases: a shifting kaleidoscope. *Drug Alcohol Rev* **17**:305–17.

Room R. (2006) Taking account of cultural and societal influences on substance use diagnoses and criteria. *Addiction* **101**:31–9.

Room R. (2007) Understanding cultural differences in young people's drinking. In Järvinen M, Room R (eds). *Youth Drinking Cultures: European Experiences*. Vermont: Ashgate Publishing, 17–40.

Room R, Janca A, Bennett LA *et al*. (1996) WHO cross-cultural applicability research on diagnosis and assessment of substance use disorders: an overview of methods and selected results. *Addiction* **91**:199–220.

Room R, Rehm J, Trotter RTI, (2001) Cross-cultural views on stigma, valuation, parity, and societal values towards disability. In Üstün TB, Chatterji S, Bickenbach JE *et al*. (eds). *Disability and Culture: Universalism and Diversity*. Seattle: Higrefe and Huber, 247–91.

Room R, Schmidt L, Rehm J *et al*. (2008) International regulation of alcohol. A framework convention is needed, as for tobacco control. *Br Med J* **337**:a2364.

Saha TD, Chou SP, Grant BF. (2006) Toward an alcohol use disorder continuum using item response theory: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychol Med* **36**:931–41.

Saha TD, Stinson FS, Grant BF. (2007) The role of alcohol consumption in future classifications of alcohol use disorders. *Drug Alcohol Depend* **89**:82–92.

Saha TD, Compton WM, Pulay AJ *et al*. (2010) Dimensionality of DSM-IV nicotine dependence in a national sample: an item response theory application. *Drug Alcohol Depend* **108**:21–8.

Scafato E, Allamani A, Patussi V *et al*. (2005) Italy. In Heather N. (ed). *WHO Collaborative project on Identification and Management of Alcohol-Related Problems in Primary Health Care—Report on Phase IV*. Geneva, Switzerland: World Health Organization, 131–44.

Schomerus G, Lucht M, Holzinger A *et al*. (2011) The stigma of alcohol dependence compared with other mental disorders: a review of population studies. *Alcohol Alcohol* **46**:105–12.

Schomerus G, Matschinger H, Angermeyer MC. (2013) Continuum beliefs and stigmatizing attitudes towards persons with schizophrenia, depression and alcohol dependence. *Psychiatry Res* (epub ahead of print).

Schuckit MA. (2009) Alcohol-use disorders. *Lancet* **373**:492–501.

Shield KD, Kehoe T, Gmel G *et al*. (2012) Societal burden of alcohol. In Anderson P, Møller L, Galea G (eds). *Alcohol in the European Union. Consumption, Harm and Policy Approaches*. Copenhagen, Denmark: World Health Organization Regional Office for Europe, 10–28.

Shield K, Rylett M, Gmel Gs *et al*. (2013) Global alcohol exposure estimates by country, territory and region for 2005—a contribution to the Comparative Risk Assessment for the 2010 Global Burden of Disease Study. *Addiction* **108**:912–22.

Snikere S, Trapencieris M, Koroleva I *et al*. (2011) *Atkari bu izraisoso vielu lietosana iedzi vota ju vidu 2011. Analitisks parskats. [Substance use among the population in 2011. Analytic report]*. Riga: Slimibu profilakses un kontroles centrs.

Strong DR, Kahler CW, Ramsey SE *et al*. (2003) Finding order in the DSM-IV nicotine dependence syndrome: a Rasch analysis. *Drug Alcohol Depend* **72**:151–62.

Volkow ND, Li TK. (2005) Drugs and alcohol: treating and preventing abuse, addiction and their medical consequences. *Pharmacol Ther* **108**:3–17.

WHO ASSIST Working Group. (2002) The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST): development, reliability and feasibility. *Addiction* **97**:1183–94.

Wiers RW, Cousijn J, Ter Mors-Schulte M *et al*. (2012) *State of the art: neurocognitieve effecten van verslaving [Neurocognitive effects of addiction]*. Den Haag, The Netherlands: ZonMw – Programma Risicogedrag en Afhankelijkheid.

Wittchen HU, Lachner G, Wunderlich U *et al*. (1998) Test-retest reliability of the computerized DSM-IV version of the Munich-Composite International Diagnostic Interview (M-CIDI). *Soc Psychiatry Psychiatr Epidemiol* **33**:568–78.

Wood E, Werb D, Kazatchkine M *et al*. (2010) Vienna Declaration: a call for evidence-based drug policies. *Lancet* **376**:310–2.

World Health Organization. (1957) *WHO Expert Committee on Addiction-Producing Drugs, Seventh Report*. Geneva, Switzerland: World Health Organization.

World Health Organization. (1992) *ICD-10 Classification of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines*. Geneva, Switzerland: World Health Organization.

World Health Organization. (2011) *Global Status Report on Alcohol and Health*. Geneva, Switzerland: World Health Organization.