COMMENTARY
IS THERE A FUTURE FOR QUANTIFYING DRINKING IN THE DIAGNOSIS, TREATMENT, AND PREVENTION OF ALCOHOL USE DISORDERS?
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INTRODUCTION
This commentary is based on a Plenary Address at the 2006 Meeting of the International Society for Biomedical Research on Alcoholism (ISBRA) held in Sydney, Australia, which posed the simple question: Is There a Future for Quantifying Drinking in the Diagnosis, Treatment, and Prevention of Alcohol Use Disorders? The intention is to stimulate dialogue among the many disciplines represented in the alcohol field about where we should be going with respect to diagnostic criteria for alcohol use disorders (AUDs), now that the American Psychiatric Association (APA) and the World Health Organization (WHO) have launched initiatives for the construction of the fifth revision of the APA Diagnostic and Statistical Manual (DSM-V) and the 11th edition of the WHO International Classification of Diseases (ICD-11).

Our position is that quantifying drinking is very relevant to the diagnosis, treatment, and prevention of AUDs. Good examples are the diagnostic criteria developed over time for other complex diseases (e.g. hypertension and diabetes), in which diagnoses are a combination of quantifiable measures (e.g. blood pressure and blood glucose level) and risk factors for disease (e.g. age, weight, lifestyle, and co-morbid conditions). For each of these disorders, diagnostic criteria have developed from simple cutpoints (e.g. diastolic and systolic blood pressure cutpoints for diagnosing hypertension in relation to heart attack and stroke), but have been continually refined as data on other dimensions of risk became available. The data to develop multidimensional, scalable diagnostic criteria for AUDs similar to those for hypertension (National Heart, Lung, and Blood Institute, 2001a), diabetes (American Diabetes Association, 2006), and high blood cholesterol (National Heart, Lung, and Blood Institute, 2001b) are not yet sufficiently refined owing to the absence of quantifiable biomarkers. However, as described below, we do have enough data to begin developing diagnostic criteria for AUDs based on symptom severity and the quantification of drinking as a dimension in the diagnosis, treatment, and prevention of AUDs. An effort in this direction to guide future treatment-prevention strategies is both opportune and feasible.

ALCOHOL USE AND HARM IN ANTIQUITY
Alcohol is probably humanity’s most primitive intoxicant. Human societies from pre-history to modern times have discovered how to make and to use fermented beverages from sugar sources native to their environments (McGovern et al., 2004). Evidence of this use comes both from the pre-historic archaeological record, as well as later recorded histories. Many accord the honour of the oldest drink in the world to barley beer which was produced in pre-dynastic Egypt around 4200 B.C. (el-Guebaly and el-Guebaly, 1981). However, a mixed fermented beverage of rice, honey, and fruit has been found in pottery remains from the Neolithic village of Jiahu in Henan province in ancient China dating to 7000 B.C. There is also evidence of unique cereal beverages produced during the Shang and Western Zhou Dynasties of ancient China around 2000 BC (McGovern et al., 2004).

Ethanol’s properties as an analgesic and a disinfectant (McGovern et al., 2004), as well as its very important role as a source of ‘safe’ hydration given the uncertainty of early water sources (Keller, 1966), all likely contributed as much to the development of alcoholic beverages by ancient societies as its mind-altering effects. However, it is these effects and their association with harm in various ancient societies that led to warnings about immoderate alcohol use. For example, early Chinese literature makes reference to alcohol’s role in the fall of dynasties as a result of alcohol overindulgence by rulers (Hao et al., 2005). Excessive drinking was discouraged in ancient Greece. In Book II of the Laws of Plato, the 5th century B.C. Greek philosopher outlined appropriate behaviour with regard to alcohol; ‘...boys shall not taste wine at all until they are 18 years of age... as a precaution against the excitableness of youth.’ Moderate drinking was allowed between ages 18 and 30, with no restrictions on drinking after age 40 (Jowett, 1994–2000). Finally, during the Middle Ages physicians began to describe specific pathologies resulting from excessive alcohol consumption. In the 11th century A.D., Simeon Seth, a physician in Constantinople, wrote that drinking wine to excess caused inflammation of the liver, a condition he treated with pomegranate syrup (Sournia, 1990).

ACUTE AND CHRONIC CONSEQUENCES OF EXCESSIVE ALCOHOL USE
Although the ancients recognized that excessive alcohol use caused harm to the individual and to society, it is through modern epidemiological studies that the acute and chronic consequences of high-risk drinking have been documented.

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Acute consequences

Acute consequences of alcohol use arise from drinking too much too fast and the impaired brain function (intoxication) that results from this pattern of drinking. Usually termed ‘binge drinking,’ this harmful drinking pattern, which measures the number of drinks per occasion or in a row, is defined by the U.S. National Institute on Alcohol Abuse and Alcoholism (NIAAA) as a pattern of drinking alcohol that brings blood alcohol concentration to 0.08 g percent or above. For the typical adult, this pattern corresponds to consuming 5 or more drinks (male), or 4 or more drinks (female), in about 2 h (NIAAA, 2004). Although binge drinking occurs among all age groups, youth and young adults are especially likely to binge drink. In 2005, the rate of binge drinking (i.e., five or more drinks at the same time or within a couple of hours of each other) on at least 1 day in the past 30 days was 19.7% among 16 or 17 year olds and 41.9% for young adults aged 18 to 25 (SAMHSA, 2005a). This high-risk drinking pattern often leads to tragic consequences (Hingson et al., 2005) most notably alcohol-related traffic fatalities (Yi et al., 2004). Other acute consequences of excessive alcohol use include unintentional death and injury other than traffic accidents, homicide and violence, suicide attempts, sexual assault, risky sexual behaviour, and vandalism.

Chronic effects of alcohol use

Excessive drinking over a long period of time, drinking too much and too often, imposes a significant health liability on the body’s major organ systems including the brain. Drinking in this pattern is associated with a number of disease entities including cancer, cardiovascular diseases, digestive tract conditions, dementia, alcohol dependence and at least 50 other disease entities. For example, in a meta-analysis of alcohol consumption and the risk of a number of diseases, Corrao et al. (2004) found a dose–response relationship between the amount of alcohol consumed daily and relative risk for various diseases such as liver cirrhosis, chronic pancreatitis, and certain cancers (Figure 1). By comparison, data from the NIAAA National Epidemiological Survey on Alcohol and Related Conditions (NIAAA NESARC, 2001–2002) indicate that the relative risk for developing alcohol dependence (AD) as a function of daily average consumption is considerably greater than for any other condition shown in Figure 1. In most cases, including AD, the relationship between daily amount of alcohol consumed (g/day) is linear—the greater the quantity consumed the higher the relative risk. For coronary heart disease, Corrao et al. (2004) found a j-shaped dose response. Even in this instance, the relative risk increased over 100 g/day (about 6 U.S. standard drinks daily). Although chronic effects are generally associated with drinking large amounts of alcohol over a long period of time, frequently, episodic heavy drinking patterns (e.g. more than 5–6 drinks per occasion) are also harmful in the setting of existing organ damage.

Volume of consumption

The relationship between alcohol consumption and health and social outcomes is complex and multi-dimensional. As reviewed by Rehm et al. (2003), three intermediate mechanisms lead to both acute and chronic effects of alcohol. These are: intoxication (pharmacologic effects), dependence, and direct biological effects such as the long-term toxic effect of excessive drinking on the liver. An individual’s exposure
to alcohol—how much for how long—is the mediating factor in each of these mechanisms and risk for alcohol-related problems. How much for how long, or the volume of alcohol consumption, is measured by: drinks on a typical drinking day ($a$) and the number of drinking days per unit time ($b$). Accordingly, $a \times b =$ the average volume of pure ethanol or number of standard drinks per week or month. Average volume of consumption has been a standard in alcohol epidemiology for some time, and has been linked to more than 60 disease conditions (Rehm et al., 2003). For example, in a prospective population study, Becker et al. (1996) found that the risk of developing future liver disease could be predicted by self-reported daily alcohol intake. Risk is increased significantly for men who consume 28–41 drinks per week and for women who consume 14–27 drinks per week. Alcohol consumption is a risk for mortality, as well as morbidity. Chronic excessive drinking leads to increased relative risk for death by at least 50% for all-cause mortality at a volume of alcohol consumption between 50–100 g ethanol per day, i.e. 6 standard drinks (Gmel et al., 2003). The relative risk for the acute and chronic consequences of alcohol use based on average daily alcohol intake varies by gender, age, and other demographic factors.

**INDIVIDUAL VARIATIONS IN RESPONSE TO ALCOHOL**

Individuals differ in how fast they metabolize alcohol (pharmacokinetics) and in the extent to which they are affected by a given dose of alcohol (pharmacodynamics). These individual differences affect drinking behaviour, the potential for the development of AD, and the risk for developing alcohol-induced organ damage. Individual variation in the absorption, distribution, and metabolism of alcohol are estimated to be 3–4 fold (Li et al., 2001). The between-individual variation in alcohol metabolic rates is due, in part, to allelic variants of the genes encoding the alcohol metabolizing enzymes, alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH). The pharmacokinetics of alcohol determines the time course of alcohol concentration in the blood after drinking an alcoholic beverage and the degree of exposure of organs to alcohol’s effects. Individual variations in sensitivity and adaptive responses to alcohol’s action (e.g. sensitivity, tolerance, dependence) are at least 2–3 fold. About one-half of the pharmacokinetic and pharmacodynamic effects of alcohol is genetic (Hurley et al., 2002).

**Alcohol use disorders: a developmental trajectory**

In the United States, 65% of the population age 18 and older are drinkers. Of those who drink, 72% drink at levels that do not increase risk for AUDs (NIAAA NESARC, 2001–2002). With respect to DSM-IV alcohol abuse (AA) and AD, 28% of the adult population evidence a high-risk drinking pattern, such as binge drinking, that places them at increased risk for developing DSM-IV AA and/or AD and other acute and potentially chronic consequences of high-risk drinking (NIAAA NESARC, 2001–2002). As noted above, most at risk for alcohol use problems are youth and young adults who consume alcohol in patterns quite different from older adults. For example, 12–20-year olds drink less frequently than older adults age 26 and older, but consume more per occasion—about 5 drinks per occasion six days/month versus three drinks per occasion but nine drinking days/month (SAMHSA, 2005b). Binge drinking is not limited to youth and young adults in the United States. The high rates of binge drinking reported by youth in several European countries (Hibell, et al., 2004) are also at great risk for the acute consequences of alcohol use due to harmful drinking patterns. Two additional facets of youthful drinking should be stressed. One is that individuals who begin drinking at age 15 raise their risk of developing AD at some point in their lifetimes by 4-fold (Grant and Dawson, 1998; Li et al., 2004; Hingson et al., 2006). As shown in Figure 2, the current prevalence of AD in the United States for persons age 18 and older is estimated at 3.8% (Grant et al., 2004); for youth aged 12–17, the prevalence of AD is 2% (SAMHSA, 2003). New cases of DSM-IV AD peak sharply at age 18, while occurrence of new cases drops dramatically after age 25. No subsequent age group experiences an occurrence of new cases of AD that even remotely approaches the surge in the 18- to 25-year-old group. As in almost all cases of alcohol use problems, more males are affected than females (Grant et al., 2004) in line with the sex differences in high-risk drinking (Dawson et al., 2004) and are at higher risk for developing AD over the course of their lifetimes (Knopik et al., 2004). Obviously, looking at high-risk drinking during adolescence and early adulthood is a priority. Although many in this population will ‘age-out’ (Dawson et al., 2006), they are at significant risk of dying or suffering lifetime disability as a result of their high-risk drinking, necessitating a shift in thinking from categorical problems that many will not experience to measures of quantity, frequency, and pattern of drinking that put youth and young adults at risk for harm.

**WHAT IS THE RELATIONSHIP OF ALCOHOL CONSUMPTION VOLUME, FREQUENCY AND PATTERN TO AA AND AD?**

The clinical standards used for diagnosing AUDs are the American Psychiatric Association’s Diagnostic and Statistical Manual, Fourth Edition, DSM-IV (APA, 1994) and the World Health Organization International Classification of Diseases, Tenth Revision, ICD-10 (WHO, 1992). DSM-IV distinguishes between alcohol abuse and alcohol dependence, while ICD-10 distinguishes between harmful use of alcohol and the alcohol dependence syndrome. Both sets of criteria define alcohol use problems as maladaptive patterns of use leading to clinically significant impairment and distress. Diagnostic criteria fall into three major categories: pharmacologic effects, maladaptive behavioural changes, and the severity of addiction including the consequences of compulsive use of alcohol (Figure 3). Neither classification system addresses the quantity, frequency, or the pattern of alcohol use. Clinically, abuse and harmful use have traditionally been considered milder forms of AUDs than alcohol dependence (Saha et al., 2006).
The history of why these two major classification systems are both alike and different makes for an interesting read and is instructive as to the politics in the international psychiatric problems community (See Caetano, 1986 and Hasin et al., 2006). However, both systems are categorical, each is used clinically to distinguish between two forms of alcohol use problems, yet neither addresses an individual’s exposure to alcohol (how much, how often) as a part of its diagnostic criteria or levels of severity of individual criteria. Although there are many problems with having two somewhat, but not
Despite its name, NLAES was a cross-sectional survey for its fifth revision.

NIAAA NATIONAL SURVEYS

Among the issues discussed by Edwards and Gross (1976) in their seminal paper outlining a ‘provisional alcohol dependence syndrome’ was a lack of data to validate the syndrome. Their hope was that the paper would stimulate the necessary discussion, research, and data to prove, improve, or disprove (with alternatives) what they had proposed. We, indeed, now have data, and it appears that Edwards and Gross were right in the main.

The NIAAA National Longitudinal Alcohol Epidemiologic Survey

In 1992, NIAAA conducted the National Longitudinal* Alcohol Epidemiologic Survey (NLAES), a general population survey with 42,862 respondents age 18 and older and a 91% response rate. The NLAES included extensive questions concerning alcohol consumption, as well as items designed to provide psychiatric classification of alcohol use disorders according to DSM-IV criteria. In addition, there were a variety of other questions concerning family history of alcoholism, alcohol treatment, health conditions, major depressive disorder, and basic demographic information. As a part of this survey, NIAAA developed the alcohol use and associated disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV), to measure diagnostic definitions of AUDs in common use in the alcohol, drug, and mental health problems fields.

The NIAAA National Epidemiological Survey on Alcohol and Related Conditions

In 2001–2002, NIAAA conducted the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), a representative sample of the United States population age 18 and older. NESARC also was designed to be a longitudinal survey with its first Wave of interviews fielded in 2001–2002 and the second Wave in 2004–2005. The sample size for Wave I was 43,093 with an 81% response rate. Wave II was designed to re-interview all persons in the original Wave I sample.

As with its predecessor survey, NESARC assesses the prevalence of AUDs and co-morbid psychiatric illnesses. It also addresses a wide-range of AUD indicators such as the quantity and frequency of alcohol consumed, drinking patterns such as binge drinking, as well as detailed demographic and socioeconomic data. Finally, both surveys used the same AUDADIS instrument, providing an opportunity to, among other things, analyses trends over time.

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DO ALCOHOL USE DISORDERS FALL ALONG A CONTINUUM OF SEVERITY?

As one would expect with a database as rich as that of both NLAES and NESARC, there has been a large number of papers produced by both the study authors and a growing number of secondary analyses looking at many different facets of AUDs and co-morbid psychiatric conditions. Among these are analyses using NESARC data to look at DSM-IV alcohol abuse and dependence categories. These analyses and other studies (e.g. Krueger et al., 2004; Langenbucher et al., 2004; Kahler and Strong, 2006; Proudfoot et al., 2006; Saha et al., 2006) suggest that AUDs are not bi-axial (abuse and dependence), but fall along a continuum of severity. In addition, current criteria for alcohol abuse are not associated only with a milder form of AUD; three of the four criteria actually tap into the more severe end of an alcohol problems continuum, and, current criteria for abuse and dependence contain redundancies, i.e. carry essentially the same information on case severity (Saha et al., 2006).

NESARC findings

NESARC data were examined using item response theory (IRT) to determine whether DSM-IV alcohol abuse, alcohol dependence and consumption criteria were arrayed along a single continuum of severity. Findings from this analysis challenge current DSM-IV abuse and dependence categories (Saha et al., 2006):

- DSM-IV diagnostic criteria are arrayed along a continuum of severity with some dependence criteria among the least severe criteria, and some abuse criteria among the most severe. For example, drinking in larger amounts or over a longer period than intended (larger/longer) and persistent desire or one or more unsuccessful efforts to cut down or control drinking (quit/control), both criteria for alcohol dependence, not only appear earliest along a continuum of symptom severity, but cluster with the hazardous use criterion for alcohol dependence. The AA criteria legal problems and neglect of roles not only appear last along a continuum of severity, but are clustered with the AD criterion important activities given up or reduced because of drinking:
  - Alcohol abuse and alcohol dependence are not distinct entities, nor is alcohol abuse prodromal to dependence;
  - Physical dependence and addiction are defining elements of the AUD continuum.

In a subsequent paper, Saha et al. (2007), examined the role of the quantity and frequency of drinking in relationship to the AUD continuum of severity. They found that the frequency of drinking in a high-risk drinking pattern (5+ drinks for men or 4+ drinks for women) at least once a week is an early quantifiable marker and risk factor for AUDs.

Relationship of quantity/frequency and drinking pattern to prevention and treatment

The findings from NESARC and other studies have major implications for screening, diagnosis, and treatment of alcoholism. For one, the general population consists of individuals...
who run the gamut from those who are not (at the time of the survey) at risk for AUDs to those who are at risk drinkers, to individuals whose use of alcohol is causing mental and/or physical harm, to those who exhibit early dependence, and finally to those who have developed chronic dependence. Proposed interventions would range from preventive measures to behavioural and medication therapies.

The development of quantitative criteria will lead to better assessment of the stage of the disease for any given individual, and inform development of improved treatment approaches for the differing severity levels of alcohol dependence. They also lay the groundwork for research examining the dimensional properties of AUDs, including the quantity, frequency and pattern of consumption, and for the development of multidimensional, scalable, and quantitative criteria that more accurately reflect risk, (e.g. family history, comorbidity, variation in individual responsiveness to alcohol’s rewarding and aversive actions), severity, and treatment actions.

CONCLUSION

The current diagnosis for alcohol dependence or alcoholism is categorical (3 out of 7 cut point). Recent publications are convincing that existing criteria can be scaled across a continuum representing severity of dependence. At best, only one of the four DSM-IV alcohol abuse criteria map to mild dependence and three to severe dependence. They do not measure the level of severity; neither do they consider the many dimensions that are involved in the initiation of alcohol use, the development of compulsive alcohol-seeking behaviour, genetics, and a host of other factors that could affect the type and course of treatment. Criteria based on the quantity and frequency of alcohol use can improve diagnosis when used in combination with existing diagnostic criteria. Risk factors for AUDs that could help improve prevention and treatment include host susceptibility (personality/temperament) and responses to alcohol; developmental factors such as risky behaviours and internalizing/externalizing comorbidities. As we refine our understanding of the development of AUD, sub-typing risk by etiological factors and co-occurring disorders might be other dimensions to consider. An example that considers a severity scale for AD together with scalable or potentially scalable dimensions of risk, including alcohol consumption, is shown in Figure 4.

Is there a future for quantifying drinking in the diagnosis, treatment, and prevention of AUD? The answer is decidedly yes, and the opportunity is here and now. It will take both clinicians and researchers from all disciplines to understand the complexities of AUDs and to translate them into research and clinical diagnostic criteria that will improve how we all go about our business.

REFERENCES


