EDITORIAL

Why Less Is Always More in the Treatment of Alcohol Use Disorders

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Alcohol is a major risk factor for mortality and burden of disease[1] and causally affects more than 200 *International Statistical Classification of Diseases and Related Health Problems (ICD)* 3-digit disease categories.[2] Reducing the health harms of alcohol is therefore one of the most important medical goals in the world today. For most major causes of alcohol-attributable death, the risk associations between lifetime drinking and mortality are exponential.[3] For all-cause mortality in high-income countries, depending on the distribution of causes of death in these countries, this means that the resulting risk association between the level of alcohol consumption and all-cause mortality is also exponential after 100 g of alcohol consumption per week.[4] The consequence of this is that reducing the level of drinking will reduce harm, and given the exponential association between the level of alcohol use and most outcomes, it is most important to cut down the highest levels.[5] Thus, a reduction from 10 drinks to 6 drinks is more important for mortality risk than the same absolute reduction from 4 drinks to 0 drinks.

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But what about the psychiatric consequences of alcohol use, such as dependence and misuse? How does the level of alcohol consumption associate with alcohol use disorders?

First, by definition, alcohol use disorders would not exist without alcohol use, which explains the traditional focus over many generations on abstinence-based treatment. Second, it has been shown that heavy alcohol use over time leads to changes in brain function, which is a defining characteristic for alcohol use disorders. This association is quite strong. For example, in a large representative survey in the United States, the correlation was 0.94 for men and 0.95 for women between the numbers of symptoms for alcohol dependence present (per the *DSM-IV*) and the mean level of drinking (in grams per day).[6] In other words, heavy drinking over time can be used to define alcohol use disorders. This conclusion was strongly endorsed by the recently finished European Union–funded Addiction and Lifestyles in Contemporary Europe Reframing Addictions Project, which brought together approximately 200 scientists from more than 25 countries.[7] This view is not new: in 1986, a report of the Royal College of General Practitioners in the United Kingdom had already pointed out the central importance of level of drinking for disease, including but not limited to what are currently called alcohol use disorders.[8]

In this volume of *JAMA Psychiatry*, Falk et al[9] introduced into treatment outcome estimates the European Medicines Agency drinking risk levels concept,[10] which is based on an older World Health Organization publication on monitoring acute risks of alcohol consumption. These authors tested the feasibility of these estimates as outcome measures using 3 US-based, multisite, placebo-controlled randomized clinical trials of medications (naltrexone, varenicline, and topiramate) for treating alcohol dependence. According to these guidelines, there are 4 sex-specific drinking levels in addition to abstinence, including up to 20 g of pure alcohol per day for women and up to 40 g per day for men (labeled low risk), between 21 g and 40 g per day for women and 41 g to 60 g per day for men (medium risk), between 41 g and 60 g per day for women and 61 g to 100 g per day for men (high risk), and 61 g or more per day for women and 101 g or more per day for men (very high risk). Falk et al[9] compared risk reductions by 1 or 2 levels with the 2 standard criteria used by the US Food and Drug Administration (total abstinence or no heavy drinking days) and found similar outcomes, as determined via effect sizes. In addition, the authors also found that these outcomes were aligned with the drinking reduction goals of many patients and captured clinically meaningful improvements experienced by more patients than either abstinence or no heavy drinking days. These features they deemed to be attractive to both patients and clinicians.

Overall, the results of Falk et al[9] are not very surprising. The standard criteria and the new criteria suggested by the European Medicines Agency are correlated by definition and can be seen as part of 1 continuum of drinking from being abstinent to the maximum amount that humans can possibly imbibe per day. This means they will always correlate to a certain degree, and even a categorization originally intended to measure risks for acute outcomes, such as traffic injury, will produce similar effect sizes as other measures.

For current dichotomous or categorical measures based strictly on consumption, the determination whether such measures are clinically relevant is a different question. The answer must be determined via linking these data with data on additional long-term clinical outcomes, such as hospitalizations or mortality. The problem common to most such treatment trials is that the time of follow-up is short, and usual trial sizes are inadequate to determine clinical significance, because end points such as hospitalizations or mortality are too rare. However, given the associations between the level of alcohol use and mortality and other clinically relevant

outcomes, it is clear that marked reductions of heavy drinking will be clinically relevant.

In sum, we conclude that levels of alcohol use can be used as a defining characteristic of alcohol use disorders. Reducing these levels is important and thus should be the major goal of all treatment interventions. While reducing consumption to zero (total abstinence) will be ideal in terms of mortality and other disease outcomes, clinically meaningful results can be achieved with reductions to lower levels of drinking. With alcohol treatment strategies, less is always more.

ARTICLE INFORMATION

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