Is the evidence base really shifting for low risk drinking guidelines?

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Introduction

There is no single international standard for safe or unsafe alcohol drinking levels. Worldwide, approximately two billion people consume alcoholic beverages such as wine, beer and spirits. Its use is associated with celebrations, business and social functions, and it is consumed in religious and cultural ceremonies. While the highest per capita alcohol consumption is observed in developed countries, it has, however, decreased in most developed countries over the past 25 years. It has correspondingly increased in developing countries and the countries of central and eastern Europe (WHO 1999, 2000, Bloomfield et al. 2003, WHO 2004, WHO 2014).

The mean adult global per capita consumption of 'pure' alcohol is 6.2 L per year, which has not appreciably changed in the past 25 years. This translates into 13.5 g of 'pure' alcohol per day, of which 50% is in the form of spirits, 35% as beer and 8% as wine (WHO 2014). The mainly beer-drinking regions are European, North American and South American countries, while the mainly wine-drinking regions are primarily the wine-producing European and South American countries. Spirits are mainly consumed by the South East Asian and Western Pacific countries.

The pharmacological textbooks list alcohol as a drug that has dose-dependent effects. When the dose is low to moderate, the effect can be considered as a benefit to health but when the dose is high or abusive, the effect is considered as a harm to health, with 200 or more different types of alcohol-related harms having been documented (WHO 2014). Indeed, of those 2 billion people that consume alcoholic beverages worldwide, approximately 76.3 million or 3.9 % have alcohol-related problems due to alcohol abuse (WHO 2011). In addition, approximately 3.3 million people will die from alcohol-related harms, such that harmful alcohol consumption accounts for 5.9 % of all deaths worldwide (WHO 2014).

The burden is not equally distributed among countries, as alcohol consumption is the highest risk factor for disease in low mortality developing countries but only the third highest risk factor in developed countries (WHO 2002). Furthermore, while high-income countries generally have the highest alcohol consumption, it does not follow that high income and high consumption always translate into high alcohol-related problems and high-risk drinking (WHO 2014). Western European countries have some of the highest consumption rates but their net alcohol-attributable mortality rates are relatively low, though their alcohol-related disease burden may be high. Many eastern European countries have the highest consumption, risky patterns of drinking and, accordingly, high levels of alcohol-related deaths and disabilities (WHO 2014).

Key findings from the 2015 Organisation for Economic Co-operation and Development (OECD) report entitled Tackling harmful alcohol use which listed alcohol health policy recommendations (Sassi 2015), included the following:

- Average annual consumption in the 35 OECD countries has reduced in the past 20 years by approximately 2.5%;

- Rates of hazardous drinking (a weekly amount of pure alcohol of 140 grams or more for women, and 210 grams or more for men) and heavy episodic drinking ('binge drinking', defined as five to eight drinks in one session depending on the country) in young people, especially women, have, however, increased in many OECD countries; and

- Approximately four in five drinkers would reduce their risk of death from any cause if they cut their alcohol consumption by one unit per week.

Role of guidelines

Recommendations on drinking levels considered 'minimum risk' for men and women exist in many countries globally. Official guidelines on alcohol consumption are usually produced by a government, public health body, medical association or non-governmental organization, such as the World Health Organization (WHO) to advise on levels of alcohol consumption considered 'safe, 'responsible', or 'low risk'.

The WHO's low risk responsible drinking guidelines of 2010 are:

- Women should not drink more than two 10 g drinks a day on average;

- For men, not more than three 10 g drinks a day on average;

- Try not to exceed four 10 g drinks on any one occasion; and

- Don't drink alcohol in some situations, such as when driving, if pregnant or in certain work situations and abstain from drinking at least once a week. Men or women who consistently drink more than these recommended levels may increase risks to their health.

While the definition for moderate consumption is relatively consistent in the medical literature based on a level above which the risk of all-cause mortality increases (approximately 20 g alcohol/day for both men and women) there are some significant differences between countries' definitions.

Based on this scientific evidence, a consistent message could be expected worldwide. Such differences are less surprising, however, when one also considers other factors. There are numerous possible reasons why government guidelines and recommendations for safe alcohol consumption differ, and why there is not a single international recommendation that is satisfactory for all.

How alcohol drinking guidelines are positioned varies across countries and often reflects prevailing views on the culture and role of alcohol in society, the prevailing government, and broader health promotion efforts (Stockley and Harding 2007). For example, recommendations about alcohol drinking may be part of broader nutritional or dietary guidelines, as is the case in Argentina, China, Denmark, the Netherlands and the USA, for example. There can be stand-alone recommendations that focus exclusively on alcohol such as in Australia, Canada and the United Kingdom (UK), or alcohol consumption can be addressed under the umbrella of a national drugs or addiction strategy such as in India, Poland and Switzerland. In other countries, such as Namibia, Mauritius and Uganda, alcohol drinking guidelines are part of the national strategy to address non-communicable diseases.

Guidelines are usually intended to form the evidence base for developing future policies and community materials on the health effects of alcohol consumption. They also aim to establish clear advice for the general population on how to avoid or minimise the harmful health consequences of drinking too much alcohol. Acting as a resource for a range of groups including health professionals, community groups, industry, professional organisations, schools and educational organisations, they will also inform policy-makers, planners, decision-makers, and those responsible for providing alcohol, who have a broader responsibility to the community.

Changing guidelines

In the past two years, two countries have reviewed and considerably changed their alcohol drinking guidelines, namely, The Netherlands in 2015 and the UK in 2016. The USA also recently reviewed its alcohol drinking guidelines but did not appreciably change them. The primary changes to the Dutch and UK alcohol drinking guidelines are as follows:

New Dutch guidelines

It is now recommended that men and women not drink alcohol, or at least drink no more than one 10 g standard drink per day (70 g/week). The previous guidelines from 2006 recommended limiting alcohol consumption to one standard drink per day for women and two standard drinks for men.

New UK guidelines

It is now recommended that men and women drink up to fourteen 8 g standard drinks per week (112 g/week), and to keep health risks to a low level, spread consumption evenly over three or more days. The previous guidelines from 1995 recommended not regularly drinking more than two to three 8 g units/day for women and three to four 8 g units/day for men; this equates to up to 168 g/week for women and up to 224 g/week for men.

The UK Chief Medical Officers' advice for men and women who wish to keep their short-term health risks from a single drinking occasion to a low level is to limit the total amount of alcohol drunk on any single occasion, to drink more slowly, drink with food, and alternate alcoholic drinks with water, for example.

New US guidelines

The US alcohol drinking guidelines are a part of its Dietary Guidelines for Americans (2015-2020). It currently states that if alcohol is consumed, it should be in moderation—up to one 12 g drink per day for women and up to two 12 g drinks per day for men—and only by adults of legal drinking age; this equates to up to 84 g/week for women and up to 168 g/week for men.

These differences between recommendations suggests that as the scientific evidence is not different in different countries, it may be differently interpreted.

Has the evidence base for guidelines changed?

The scientific evidence relating to both abusive and moderate alcohol consumption is itself not sufficiently consistent to produce precise recommendations for safe drinking for every alcohol consumer. There is no clear scientific evidence that uniformly applies to all population groups. Indeed, the many factors influencing a definition of low risk alcohol consumption for a specific population group include age, body mass index, ethnicity, family history, mental and physical health, and the use of medications.

Rather than the scientific evidence base for alcohol drinking guidelines having changed recently, perhaps it is the focus that has changed. This change could be three-fold as follows:

1. There has been a change in focus away from individual consumer factors and influences on blood alcohol concentration (BAC), such as age, body mass index, gender and associated effects, good and bad, on human health;

2. There has also been change in focus away from pattern of consumption compared to amount; and

3. There has been a change in focus towards risk of death over a lifetime, adding the risk of death from short-term harms together with that from longer-term harms, and the focus of long-term harms has also changed away from cardiovascular diseases towards cancers (Cao and Giovannucci 2016).

The WHO (2016) suggests that the four main non-communicable disease are cardiovascular diseases, cancers, diabetes and chronic lung diseases, and these were responsible for 68% of all deaths globally in 2012. This information is not particularly new. Although cardiovascular diseases are the leading causes of adult deaths worldwide, where there is a clear j-shaped relationship between alcohol consumption and the risk of death from cardiovascular diseases (Bergmann et al. 2013, Dai et al. 2015, Klatsky 2015), cancer is now the second leading cause of death, for example, generally occurring later in life. The gap has also narrowed between the two leading causes of death and the role of alcohol in cancer causation is much less clear.

The overall relationship between alcohol consumption and cancer is complex, and there may be threshold effects in the relationship between alcohol consumption and the risk of cancer (Breslow et al. 2011, Cao and Giovannucci 2016). In a study of cancers of the upper aero-digestive tract (UADT), liver and colorectum, the risk only increased when more than 25 g alcohol/day was consumed (Bagnardi et al. 2015). It has also been suggested that the risk of developing a cancer of the aero-digestive tract is less when alcohol is consumed with food (Dal Maso et al. 2002). A comprehensive review of more than 7,000 peer-reviewed papers on the association of lifestyle factors and cancer undertaken by the World Cancer Research Fund, in cooperation with the American Institute for Cancer Research (2007), reports that an increased risk for colorectal cancer is only apparent above a threshold of 30 g alcohol/day for both men and women (Bagnardi et al. 2013, Klarich et al. 2015).

It is also known that the cumulative effect of other lifestyle choices associated with drinking contributes to the occurrence of cancer. Of all lifestyle factors related to cancer, the attributable risk for tobacco was 20.1%, physical inactivity 5.6%, body mass 3.9%, and alcohol 3.1% (Begg et al. 2007, Begg et al. 2008).

Two of the most common cancers associated with alcohol consumption are those of the UADT and the female breast. Recent case-control analyses by Anantharaman et al. (2011) and Szymańska et al. (2011) of alcohol and the risk of cancers of the UADT also suggest that tobacco use is the most important factor in the risk of these cancers, and that the risk is enhanced among those who also consume two or more alcoholic drinks per day. Alcohol consumption alone among non-smokers had little effect on the risk, except for oesophageal cancer. Anantharaman et al. (2011) demonstrated that tobacco and alcohol use together accounted for 73% of total UADT cancer burden in the European Union, of which tobacco use alone accounted for 28.7%, alcohol use alone accounted for only 0.4%, but the combination of smoking and drinking accounted for 43.9%, of the population attributable risk. Similar results were reported by Hashibe et al. (2009), where the population attributable risk (PAR) for UADT from tobacco or alcohol was 72% (95% confidence interval 61-79%) for head and neck cancer, of which 4% was due to alcohol alone, 33% was due to tobacco alone, and 35% was due to tobacco and alcohol combined. Indeed, the most

recently published study by Dal Maso et al. (2016) concludes: "Compared to abstainers from both tobacco and alcohol consumption, the combined exposure to ethanol and/or cigarettes led to a steep increase of cancer risk up to a 35-fold higher risk (95% confidence interval 27.30-43.61%) among people consuming 84 g/day of ethanol and 10 cigarettes/day. The highest risk was observed at the highest levels of alcohol and tobacco consumption."

Concerning the relationship between alcohol and breast cancer, it has been suggested that consumption patterns may modify risk (Morch et al. 2007), such that the consumption of four to five drinks consumed per session may increase/double risk by 50% compared to only one drink consumed per session. Paradoxically, alcohol dependence does not increase the risk of breast cancer (Kuper et al. 2000). Dietary folate may play a protective role in carcinogenesis (Lin et al. 2013, Chen et al. 2014, Tio et al. 2014). The concurrent consumption of alcohol and folate (at least 300 mg/day of folate) has been observed to reduce the relative risk (RR) of alcohol-induced breast cancer from 1.24 to 1.05 for women consuming greater than 15 g alcohol/day (equivalent to approximately 1 to 2 standard drinks in different countries), and was reduced to 0.55 for women consuming greater than 600 mg/day of folate. Indeed, in the study by Zhang et al. (1999) the concurrent consumption of folate-containing vitamin supplements reduces the relative risk to 0.74 for women consuming greater than 15 g alcohol/day compared to those not using vitamins.

Boffetta and Hashibe (2006) in a review of alcohol and cancer stated that drinking, especially heavy drinking, increases cancer risk. They concluded, however, that: "Total avoidance of alcohol, although optimum for cancer control, cannot be recommended in terms of a broad perspective of public health, in particular in countries with high incidence of cardiovascular disease."

The association between lifetime alcohol consumption and death from cardiovascular diseases appears to be different from the association observed for alcohol-related cancers, digestive, respiratory, external and other causes (Bergmann et al. 2013). When all-cause mortality is considered, however, the data strongly suggested that light to moderate alcohol consumption reduces the risk of death from all causes (Di Castelnuovo et al. 2006, Howie et al. 2011, Chiva-Blanch et al. 2013, Ferrari et al. 2014). The pattern of alcohol consumption, such as binge drinking, may modify this relationship (Graff-Iversen et al. 2013, Bobak et al. 2016).

Conclusions

It appears that the role of light to moderate alcohol consumption in preventing cardiovascular disease, the leading cause of death throughout the developed world, is currently being down-played in government guidelines. Statements from scientists are carefully selected and many are thus being ignored. This includes that from Roerecke and Rehm (2014) who recently stated that: "For drinkers having one to two drinks per drinking day without episodic heavy drinking, there is substantial and consistent evidence from epidemiological and short-term experimental studies for a beneficial association with IHD [ischaemic heart disease] risk when compared to lifetime abstainers. The alcohol-IHD relationship fulfils all criteria for a causal association proposed by Hill."

The definitive experiment to determine association is a double-blind placebo-controlled clinical study but no long-term experimental study of alcohol consumption on risk of any chronic disease has ever been performed. In September 2016, however, the US National Institute on Alcohol Abuse and Alcoholism received funding to conduct such a study, focussing on cardiovascular diseases and diabetes. Its aim is to better determine the strengths of relationships observed to date in epidemiological studies, the results of which will undoubtedly shape subsequent alcohol drinking guidelines.

What is important regarding any risk to human health is BAC, which has been neglected in many countries' recent recommendations to its alcohol consumers. A return to guidelines that enable alcohol consumers to understand what amounts and patterns of alcohol consumption affect and influence their BAC and its associated short- and longer-term benefits and risks to their health, will serve governments and consumers alike well.

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