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The Comparative Risk Assessment for alcohol as part of the Global Burden of Disease 2010 Study: What changed from the last study?

Editorial

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In December 2012, the new results of the Comparative Risk Assessment (CRA) for alcohol within the Global Burden of Disease and Injury (GBD) Study 2010 were presented at a joint meeting of the GBD Group and the journal *Lancet* at the Royal Society in London (Lim et al., 2012). At first glance, there do not appear to be many changes to alcohol consumption as a risk factor for death and disability: it is identified as the third most important risk factor, as it was in the last CRA (World Health Organization, 2009). The burden of disease attributable to alcohol had increased, compared to the 2004 estimate (Rehm, Mathers et al., 2009), but this could be due to an increase in global population, or to variations in the methodologies behind the 2004 and 2010 estimates.

On further reflection, however, it is apparent that a great deal has changed, in terms of both the overall ordering of risk factors and the alcohol findings. Between 2004 and 2010, the most important risk factors changed from childhood underweight and unsafe sex to high blood pressure and tobacco smoking (including passive smoking), reflecting the increasing importance of non-communicable disease in the global picture (Lim et al; World Health Organization, 2011). And if 1990 is compared with 2010 using the same methodology, the impact of alcohol consumption did increase, in terms of both absolute and relative figures for burden of disease (Lim et al., 2012).

What explains the change in the contribution of alcohol consumption to the burden of disease over the past 20 years, and how have the methodologies used to measure this burden changed over the last 10 years? Let us start with the methodological changes which may explain the increase from the 2000Rehm et al., 2003; Rehm et al., 2004) to the 2010 CRA (Lim et al., 2012). These changes are quite substantial. First, new disease categories have been identified since 2000 as causally attributable to alcohol. For instance, the International Agency for Research on Cancer conducted a comprehensive review meeting on alcohol consumption in 2007, and added breast cancer and colorectal cancers to the list of cancers causally related to alcohol (Baan et al., 2007; International Agency for Research on Cancer, 2010, 2012). While the 2000 CRA[1] had already included breast cancer, based on substantial scientific evidence already documented by that point (Rehm et al., 2004), much of the research on colorectal cancer is more recent, including a large-scale epidemiological study in eight European countries with more than 350,000 participants (International Agency for Research on Cancer, 2012; Schütze et al., 2011). In addition, it had become clearer that ethanol is the main carcinogenic ingredient in alcoholic beverages (Lachenmeier, Przybylski, & Rehm, 2012). Meanwhile, a "residual" category of cancer (Other neoplasms GBD category: IIB) was removed from the list, because there is currently no way to quantify the impact of alcohol in this category (Rehm, Baliunas et al., 2010).

Then there were changes resulting from the inclusion of additional disease categories only recently added by the GBD group, such as pancreatitis and atrial fibrillation. For both of these categories, the causal relation to alcohol consumption had been recognized for some time, but the quantification of risk relations was missing and had to be established (Irving, Samokhvalov, & Rehm, 2009; Samokhvalov, Irving, & Rehm, 2010a). However, the biggest change in alcohol-attributable disease categories was the addition of infectious disease. While the link between alcohol consumption, especially heavy consumption, and infectious diseases has long been known (Rush, 1785), there were questions about causality and quantification of risk relations (Parry, Rehm, Poznyak, & Room, 2009). These questions were relatively easy to address for tuberculosis (Lönnroth, Williams, Stadlin, Jaramillo, & Dye, 2008; Rehm, Samokhvalov et al., 2009) and pneumonia (Samokhvalov, Irving, & Rehm, 2010b); the resulting attributable fractions are presented in this issue (Shield, Samokhvalov, & Rehm, 2013). However, establishing causality was more problematic for HIV/AIDS and sexually transmitted infections, where active behavior plays a necessary role in transmission pathways (Shuper et al., 2010). The main counter-argument against causality was that a third factor—for instance a tendency towards risk taking, as a personality trait—could influence both alcohol consumption and unsafe sex as the main transmission pathway. While experimental research could establish that there is a causal impact of alcohol on intention for unsafe sex (Rehm, Shield, Joharchi, & Shuper, 2012), the quantification of risk relations could not be undertaken within the temporal frame of the CRA. Clearly it is not the case that alcohol caused HIV transmission, or caused progression of the disease,

in *every* case of HIV/AIDS associated with alcohol consumption (Baliunas, Rehm, Irving & Shuper, 2010); therefore, future research must strive to find a methodology to quantify the causal proportion. As a consequence, at this time, only a part of the disease burden associated with HIV/AIDS can be calculated as attributable to alcohol consumption—namely, the part due to drinking-related lack of adherence to antiretroviral medication. These results, not yet included in the CRA for 2010 (Lim et al., 2012), are presented in this issue (Shield, Shuper, Gmel and Rehm, 2013). A more detailed explanation and discussion of the assumptions and methodology of these estimates can be found in a contribution by Gmel and colleagues (Gmel, Shield & Rehm, 2011).

Problems with quantification of alcohol-attributable disease burden continue to exist for mental disorders. Consider alcohol consumption and depression as an example. Clearly, alcohol consumption and alcohol use disorders can make a causal contribution to depression (Rehm et al.,2004). There is even a separate category in the Diagnostic and Statistical Manual of Mental Disorders for substance-induced depression, in both DSM-IV (American Psychiatric Association, 2000) and the proposed DSM-V (http://www.dsm5.org/pages/default.aspx). But the reverse causality is also true, and there may be additional factors—such as genetic vulnerability—for both depression and heavy alcohol consumption or alcohol use disorders. Similar arguments could be made for anxiety and other mental disorders. Thus, the results of the CRA clearly underestimate the indirect effect of alcohol through mental disorders, because these estimates exclude all mental disorders due to alcohol consumption except for alcohol use disorders. In 2000, the impact of consumption on depression was estimated (Rehm et al., 2004), but it was decided that the algorithm used was not sufficiently validated to re-use it in this round of the GBD.

Other differences concern the calculation of injury and the determination of disability weights. For injuries, the determination of attributable fractions was previously linked to a seminal study in 2000/2004 and adjusted based on exposure dimensions (English et al., 1995; Rehm et al.,2004). In the new CRA, a formula was developed that was based directly on average drinking and episodic heavy drinking and their relative risks (Shield, Gmel, Patra, & Rehm, 2012), drawing on analyses by Taylor, Rehm and colleagues (Taylor et al., 2010; Taylor, Shield, & Rehm, 2011). The new disability weights (for a general overview, see Rehm & Frick, 2010) were established based on an empirical study.

In addition to the methodological differences between the GBD 2000/2004 and the GBD 2010 in calculating the alcohol-attributable burden, there were other differences concerning the estimation of exposure and its uncertainty (for details see Rehm, Klotsche, & Patra, 2007 for the earlier GBDs; and Rehm, Kehoe et al., 2010, as well as Gmel, Shield, Frick et al., 2011for the GBD 2010). Most importantly, the triangulation between survey results and *per capita* consumption changed as a result of recent research (Kehoe, Gmel, Shield, Gmel, & Rehm, 2012).

The changes between GBD 2000/2004 and GBD 2010 make these efforts difficult to compare in a meaningful way. This was one of the reasons why the current GBD study group undertook the task of making new estimates for 1990 which were comparable to those from 2010. The results show that alcohol consumption has increased in impact as a risk factor (Lim et al., 2012) from rank 6 in1990 to rank 3 in 2010. What are the reasons for this change? First, more alcohol was consumed in 2010 than in1990. Second, the distribution of disease changed, and the disease categories more highly attributable to alcohol increased in relative weight. This is true for non-communicable chronic diseases (cancer, cardiovascular disease, liver cirrhosis; see (Parry, Patra, & Rehm, 2011) and (Room, Rehm, & Parry, 2011)), and for injuries, almost all of which have a strong link to alcohol consumption (Rehm, Popova, & Patra, 2009; Shield et al., 2012). It is also true for mental disorders, although the contribution of alcohol use to these is underestimated, for the reasons described above.

The difference between 1990 and 2010 will thus persist, even when the numbers from Lim et al. (2012) will be corrected in one of the next issues of Lancet, because the relationship with ischaemic heart disease had been overestimated (see Roerecke & Rehm, 2010; 2011; 2012; for the correct relationships).

Both of these trends towards an increase in alcohol's contribution to the burden of disease are also expected to continue, unless there are interventions. The World Health Organization has thus started to

implement a global strategy to reduce the harmful use of alcohol, with taxation and pricing policies figuring prominently (World Health Organization, 2010). The third original contribution to this special section, from Bundit Sornpaisarn and colleagues (Sornpaisarn, Shield, Cohen, Schwartz, & Rehm, 2012), is thus particularly pertinent, as it gives information on the effects of taxation in low- and middle-income countries, where the effects of alcohol consumption are the largest, both in absolute numbers (Lim et al., 2012), and relative to high income countries (Rehm, Anderson et al., 2009).

Footnote

1. The 2004 CRA used the alcohol-attributable fractions of the 2000 CRA, and thus cannot be considered an independent CRA.

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