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Relation between Average Alcohol Consumption and Disease: An Overview

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Key Words
Alcohol · Acute consequences · Chronic disease · Overview · Volume of drinking · Patterns of drinking · Counterfactual scenario

Abstract
Objective: To conduct an overview of alcohol-related health consequences and to estimate relative risk for chronic consequences and attributable fractions for acute consequences. Methods: Identification of alcohol-related consequences was performed by means of reviewing and evaluating large-scale epidemiological studies and reviews on alcohol and health, including epidemiological contributions to major social cost studies. Relative risks and alcohol-attributable fractions were drawn from the international literature and risk estimates were updated, whenever possible, by means of meta-analytical techniques. Results: More than 60 health consequences were identified for which a causal link between alcohol consumption and outcome can be assumed. Conclusions: Future research on alcohol-related health consequences should focus on standardization of exposure measures and take into consideration both average volume of consumption and patterns of drinking.

Introduction

Over the last decade, research on alcohol-related health consequences has rapidly expanded. Generally, studies assessing such consequences distinguish between chronic (e.g. cancers) and acute (e.g. accidents) outcomes [1]. Such a categorization seems to be practical as these two categories could be grossly distinguished by E-codes versus all other codes in the ICD-9. In addition, chronic consequences mainly related to long-term alcohol use are, in most cases, associated with the volume of drinking and assumed to be cross-culturally stable. In contrast, acute consequences were seen to be more influenced by drinking pattern (such as heavy episodic drinking) and cultural factors [2]. As a consequence alcohol-attributable fractions of chronic consequences were often derived by indirect methods which combine cross-culturally pooled meta-analytic risk estimates with country-specific prevalence of volume-oriented consumption categories. On the other hand attributable fractions of acute consequences influenced by the cultural environment and drinking pattern were usually assessed by direct methods (e.g., case counts of police records of drinking and driving [3]). Such a gross classification, however, is overly simple. For example, there is increasing evidence that (a) some ‘chronic’ consequences are more or at least evenly related to heavy episodic drinking [4, 5]; (b) some ‘acute’ consequences such as suicides may be differently related to...
both chronic heavy drinking, and acute episodes of intoxication [6, 7] or the association may differ across cultures ranging from negative to positive association [8], and (c) some chronic consequences can be assessed by direct methods (e.g. alcoholic dependence syndrome).

To summarize the state-of-the-art in the field of alcohol-related consequences, we compiled and evaluated recent scientific evidence. First, comprehensive overviews of the relationship between consumption and morbidity/mortality, often undertaken as epidemiological input to social cost studies, were compared [9–16]. Completeness was also verified with other general overviews of health conditions related to alcohol consumption [17–20]. Since these studies differed greatly in their attribution of alcohol causality to health conditions, we set out to: (1) search for new evidence to clarify causality in relation to conditions on which existing mortality/morbidity studies were discordant; (2) suggest an up-to-date list of alcohol-related health conditions, and (3) offer pooled estimates of relative risks (RRs) or attributable fractions for those consequences, which were considered established.

**Methods**

Identification of Consequences

Identification of alcohol-related consequences was performed by means of reviewing and evaluating large-scale epidemiological studies on alcohol and health, including epidemiological input to major social cost and comprehensive reviews [9–21]. Scientific papers were collected primarily from the peer-reviewed, international literature. Following accepted guidelines established in the first major review [13], evidence was assessed according to methodological criteria such as quality of studies, relevance and strength of evidence, as well as biological plausibility. All conditions were included in the final list (tables 1–4), for which the evidence for a causal relationship with alcohol was conclusive [for more detailed information about the process of reviewing and evaluating the empirical evidence see, 22].

<table>
<thead>
<tr>
<th>ICD-9</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>291</td>
<td>Alcoholic psychoses</td>
</tr>
<tr>
<td>303</td>
<td>Alcohol-dependence syndrome</td>
</tr>
<tr>
<td>305.0</td>
<td>Alcohol abuse</td>
</tr>
<tr>
<td>357.5</td>
<td>Alcoholic polyneuropathy</td>
</tr>
<tr>
<td>425.5</td>
<td>Alcoholic cardiomyopathy</td>
</tr>
<tr>
<td>535.3</td>
<td>Alcoholic gastritis</td>
</tr>
<tr>
<td>571.0–571.3</td>
<td>Alcoholic liver cirrhosis</td>
</tr>
<tr>
<td>790.3</td>
<td>Excess blood alcohol</td>
</tr>
<tr>
<td>980.0, 980.1</td>
<td>Ethanol and methanol toxicity</td>
</tr>
</tbody>
</table>

Relative Risks and Attributable Fractions

Some conditions such as alcoholic psychosis or alcohol dependence syndrome are, by definition, causally related and wholly attributable to alcohol (table 1). For most conditions, however, alcohol is a contributory rather than a sufficient cause [23]. Thus, a measure of the fraction of cases attributable to alcohol (alcohol-attributable fraction, AAF) is needed for each of these conditions. To determine attributable fractions a counterfactual scenario is required, that is a description of an alternative distribution of exposure, to which the actual distribution is contrasted [24]. The prevailing counterfactual scenario for alcohol as a risk factor is abstinence (e.g. no alcohol at all), although other scenarios such as moderate consumption have been applied as well [3, 13]. The AAF for chronic conditions are usually determined indirectly by combining RR and prevalence data at different levels of consumption [for a detailed description of the method see, 10]. For the purpose of the present study, only RR will be presented. RRs were drawn essentially from English et al. [13]. Risk estimates were updated whenever possible (e.g. for female breast cancer, diabetes, coronary heart disease) by inclusion of studies appearing since English et al. [13]. Pooling of several risk estimates was performed by means of precision-based weighting [13]. Methods and results of the pooling-procedure (meta-analysis) have been described in more detail elsewhere [22].

In contrast, the AAFs for acute consequences such as accidents and injuries are usually determined directly by assigning empirically given cases to alcohol whenever the responsible individual was under the influence of alcohol at the time of the event. To cite an example, road accidents are attributed to alcohol whenever the accident-responsible driver tested positive for alcohol (e.g. at a blood alcohol concentration, BAC, of >0.05%). As RR estimates are usually rare, for the purpose of the present study AAFs from the international literature [10, 13, 22, 25] were compared.

**Results**

To structure the presentation and discussion of results, we suggest that alcohol-related health consequences be categorized as follows: (1) chronic consequences, such as wholly alcohol-attributable consequences, cancer (neoplasm), cardiovascular disease, liver cirrhosis, effects of prenatal alcohol exposure and other chronic harms; (2) benefits of alcohol consumption, such as cardiovascular disease and other conditions, and (3) acute consequences, such as accidental injury and poisoning, suicide, interpersonal violence and assaults.

**Chronic Consequences of Drinking**

**Wholly Alcohol-Attributable Consequences**

With regard to the attribution of alcohol-relatedness, most unproblematic are those consequences that, by definition, are wholly alcohol-attributable (AAF = 1; table 1).
More complicated to assess are those consequences where alcohol plays a contributory role. These will be presented and discussed cause-specifically in the following sections.

Cancer

Oropharyngeal, Esophageal and Liver Cancer: Alcohol has consistently been related to the risk of cancer of the mouth (lip, tongue), pharynx, larynx, hypopharynx, esophagus and liver [1, 13, 17–19, 21]. The relationship between the average volume of alcohol consumption and cancer is usually characterized as being monotonically increasing but this may be partially an artifact of the methods [18]. Evidence for these cancers has accumulated from case-control and cohort studies. Recently, much emphasis has been put into the biochemical mechanisms to explain the carcinogenic behavior of alcohol in laboratory studies [19].

Female Breast Cancer. Much research has been conducted over the last decade on female breast cancer. In overviews prior to 1995, it was most often concluded that evidence of a causal relationship with alcohol was insufficient [26, 27]. However, recent studies and reviews have shown that not only hazardous or harmful but even moderate alcohol consumption can cause female breast cancer [9]. A meta-analysis by Smith-Warner et al. [28] found a clear linear relationship over the whole continuum of consumption. Other original studies supported this finding [21, 29–34]. In contrast to the weight of evidence, Zhang et al. [35] concluded from their investigation that moderate intake did not increase the risk of breast cancer, and that low drinking was associated with a protective effect. This finding, however, appears to be a notable outlier [36] and, so far, has not been corroborated by any further study. Recent studies focus on plausible biological mechanisms including alcohol’s effect on hormones and tissue, alcohol’s contribution to the initiation and progression/promotion of breast cancer, but also alcohol’s interaction with nutritional factors [19, 37].

Stomach, Pancreas, Colon, Rectum and Prostate Cancers. Furthermore, many recent research projects have investigated whether cancers of the stomach, pancreas, colon, rectum and prostate are alcohol-related. Overall, evidence for a causal relationship between alcohol and cancer of these sites, if any, was weak and inconclusive [37–50]. On prostate cancer, again most studies did not report observing an increased risk [51–54], whereas two cohort studies [55, 56] and one case-control study [57] reported a small increased risk in men who consume even moderate amounts of alcohol. Overall, evidence for a causal relationship between alcohol and cancer of the stomach, pancreas, colon, rectum and prostate is so far not conclusive.

Major Salivary Glands, Ovarium, Endometrium and Bladder. Moreover, it has been hypothesized that alcohol might constitute a risk factor for cancer of the major salivary glands [58, 59], ovariurn, endometrium [43, 60–62], and the bladder [43, 63–65]. For each of these sites, results were either scarce or heterogeneous, or the effects, if any, were found not to be statistically significant.

Cardiovascular Disease

The role of alcohol, as both a risk and protective factor for cardiovascular disease has been studied extensively in the past decade. As far as coronary heart disease (CHD) is concerned, the effect of moderate alcohol consumption clearly is a beneficial one. Furthermore, most studies suggest that low-level consumption equally offers some protection against stroke, particularly ischemic stroke. The benefits of alcohol consumption on both stroke and CHD are therefore discussed in the following section. In contrast, hypertension and other cardiovascular disorders such as cardiac arrhythmias and heart failure as well as ill-defined descriptions and complications of heart disease are adversely affected by alcohol [4, 66–69]. The weight of evidence suggests that hazardous and harmful levels of consumption cause hypertension in both men and women [13, 70–74]. Low-level intake, however, was not associated with hypertension in men, while it conferred a small protective effect in women [13, 72].

Liver Cirrhosis

Alcohol is regarded as the leading cause of cirrhosis in established market economies [13, 75–77]. Whereas the association with alcoholic liver cirrhosis is clear with all cases being attributable to alcohol, debate remains whether this equally applies to unspecified liver cirrhosis. Several authors contend that, empirically, it is extremely difficult to separate alcoholic from unspecified liver cirrhosis and that the term ‘unspecified liver cirrhosis’ is applied when no specific etiological factor is reported or identified [13]. Research in the USA indicated that an appreciable proportion of cirrhosis deaths without mention of alcohol was in fact attributable to alcohol [78]. On the other hand, to apply AAFs of liver cirrhosis to other countries can be extremely misleading. In many countries (e.g., China or India) liver cirrhoses are caused by other factors such as viral infections. The corresponding AAFs have been shown to vary between less than 10% (China) and 90% (Finland) [1].
Table 2. Chronic alcohol-related health effects with relative risks

<table>
<thead>
<tr>
<th>Disease</th>
<th>ICD-9 intake</th>
<th>RR</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>females</td>
<td>males</td>
<td>females</td>
<td>males</td>
<td>females</td>
<td>males</td>
</tr>
<tr>
<td>Lip and oropharyngeal cancer</td>
<td>140, 141, 143–146, 148, 149, 230.0</td>
<td>1.45</td>
<td>1.45</td>
<td>1.85</td>
<td>1.85</td>
<td>5.39</td>
<td>5.39</td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>150, 230.1</td>
<td>1.80</td>
<td>1.80</td>
<td>2.38</td>
<td>2.38</td>
<td>4.36</td>
<td>4.36</td>
</tr>
<tr>
<td>Liver cancer</td>
<td>155, 230.8</td>
<td>1.83</td>
<td>1.83</td>
<td>3.90</td>
<td>3.90</td>
<td>4.93</td>
<td>4.93</td>
</tr>
<tr>
<td>Laryngeal cancer</td>
<td>161, 231.0</td>
<td>1.08</td>
<td>–</td>
<td>1.30</td>
<td>–</td>
<td>1.66</td>
<td>–</td>
</tr>
<tr>
<td>Female breast cancer</td>
<td>174, 233.0</td>
<td>1.34</td>
<td>1.23</td>
<td>7.22</td>
<td>7.52</td>
<td>7.52</td>
<td>6.83</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>401–405</td>
<td>0.85</td>
<td>1.02</td>
<td>1.27</td>
<td>1.43</td>
<td>1.79</td>
<td>2.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>427.0, 427.2, 427.3</td>
<td>1.51</td>
<td>1.51</td>
<td>2.23</td>
<td>2.23</td>
<td>2.23</td>
<td>2.23</td>
</tr>
<tr>
<td>Heart failure</td>
<td>428–429</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Esophageal varices</td>
<td>456.0–456.2</td>
<td>1.26</td>
<td>1.26</td>
<td>9.54</td>
<td>9.54</td>
<td>9.54</td>
<td>9.54</td>
</tr>
<tr>
<td>Gastroesophageal hemorrhage</td>
<td>530.7</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Unspecified liver cirrhosis</td>
<td>571.5–571.9</td>
<td>1.26</td>
<td>1.26</td>
<td>9.54</td>
<td>9.54</td>
<td>9.54</td>
<td>9.54</td>
</tr>
<tr>
<td>Acute and chronic pancreatitis</td>
<td>577.0, 577.1</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>634</td>
<td>1.20</td>
<td>–</td>
<td>1.76</td>
<td>–</td>
<td>1.76</td>
<td>–</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>656.5</td>
<td>0.89</td>
<td>0.89</td>
<td>1.62</td>
<td>1.62</td>
<td>1.62</td>
<td>1.62</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>696.1</td>
<td>1.58</td>
<td>1.58</td>
<td>1.60</td>
<td>1.60</td>
<td>2.20</td>
<td>2.20</td>
</tr>
<tr>
<td>Prematurity</td>
<td>764</td>
<td>0.93</td>
<td>0.93</td>
<td>1.36</td>
<td>1.36</td>
<td>1.36</td>
<td>1.36</td>
</tr>
<tr>
<td>Intrauterine growth retardation</td>
<td>765</td>
<td>0.99</td>
<td>0.99</td>
<td>1.68</td>
<td>1.68</td>
<td>1.68</td>
<td>1.68</td>
</tr>
</tbody>
</table>

n.a. = Relative risks not applicable because the attributable fraction was obtained by a direct method: 530.7 = 0.47; 577.0 = 1.00; 577.1 = 0.84.

* Heart failure-attributable fraction determined indirectly from other circulatory diseases.

Effects of Prenatal Alcohol Exposure

Today, there is ample evidence that alcohol consumption during pregnancy is related to various risks to the fetus which include gross congenital anomalies and fetal alcohol syndrome [79–92]. Fetal alcohol syndrome has been characterized as a continuum, with minor physical malformations at one end and serious neurobiological dysfunctions including mental retardation on the other end [93]. The prenatal teratogenic effects of alcohol also include lethal consequences such as spontaneous abortion, low birth weight, fetal damage and premature/intrauterine growth-retardation [62, 94, 95] even at low levels of average consumption during the first trimester of pregnancy.

Other Chronic Conditions

Other risks of alcohol consumption currently discussed in the literature are epilepsy [96–98], acute and chronic pancreatitis and psoriasis. Whereas for pancreatitis the causal role of alcohol seems to be clear, Skinazi et al. [99] and Amman et al. [100] contend that the discrimination between acute and chronic pancreatitis is not justifiable since the overwhelming majority of patients presenting with acute pancreatitis have at the same time an underlying chronic pancreatitis [101, 102]. On psoriasis, our search did not yield any recent studies. English et al. [13] found that the results of the pooled estimates were consistent with a moderately strong and statistically significant effect.

Given that the chronic consequences discussed above are caused not only by alcohol but by other factors as well, it is necessary to estimate the likelihood of alcohol causation (by means of RRs). Table 2 summarizes the evidence on alcohol-related chronic consequences and presents the respective RRs at different levels of consumption.

Benefits of Alcohol Consumption

Cardiovascular Disease

CHD is one of the leading causes of death in established market economies and developing countries [103]. At the same time, the most important health benefits of alcohol have been found in the area of CHD at low to moderate levels of consumption [18, 72, 104–111]. Only a few studies have failed to substantiate this association in men [112] or women [113, 114]. Some studies found that alcohol may offer protection against CHD not only at low to moderate intake but across the continuum of alcohol consumption [71, 115–119]; they nevertheless show that most of the protective effect is gained at low levels of consumption such as one drink every other day. Furthermore, the relationship appears to be associated with par-
ticular patterns of drinking [4, 120, 121]. The biological mechanisms explaining the protective effect of alcohol are, for example, increased high-density cholesterol levels and antithrombotic effects [1, 122–125]. To date, the crucial point in assessing the effect of alcohol on CHD remains hazardous consumption [118].

**Other Conditions**

Cerebrovascular disease (stroke) comprises two essential subtypes which are differently affected by alcohol. As far as ischemic stroke is concerned, the predominant type of stroke, the weight of evidence including biological mechanisms suggests similar effects as for CHD, namely that low to moderate consumption may offer some protection [71, 74, 105, 116, 126–130]. Concerning hemorrhagic stroke, the weight of evidence suggests an increase in risk even at low levels of consumption [126, 131–133].

Furthermore, alcohol may offer some protection against diabetes and cholelithiasis (gallstones). The Australian meta-analysis by English et al. [13] concluded that there was some evidence that alcohol may protect against the onset of diabetes. Since then, the findings from a cohort of more than 40,000 male health professionals showed that moderate alcohol consumption may decrease the risk of diabetes, perhaps through the effects of alcohol on insulin sensitivity [71, 74, 105, 116, 126–130]. Concerning hemorrhagic stroke, the weight of evidence suggests an increase in risk even at low levels of consumption [126, 131–133].

Table 3 gives an overview of diseases on which alcohol has potentially beneficial effects.

<table>
<thead>
<tr>
<th>Disease</th>
<th>ICD-9 intake</th>
<th>RR</th>
<th>RR</th>
<th>RR</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>low females</td>
<td>low males</td>
<td>hazardous females</td>
<td>hazardous males</td>
</tr>
<tr>
<td>Diabetes</td>
<td>250</td>
<td>0.92</td>
<td>0.99</td>
<td>0.87</td>
<td>0.57</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>410–414</td>
<td>0.82</td>
<td>0.82</td>
<td>0.83</td>
<td>0.83</td>
</tr>
<tr>
<td>Stroke</td>
<td>430–438</td>
<td>0.59</td>
<td>0.69</td>
<td>0.51</td>
<td>0.95</td>
</tr>
<tr>
<td>Cholelithiasis</td>
<td>574</td>
<td>0.82</td>
<td>0.82</td>
<td>0.68</td>
<td>0.68</td>
</tr>
</tbody>
</table>

A protective effect of moderate alcohol consumption against diabetes may be mediated through the effects of alcohol on glucose tolerance and insulin resistance. Moderate alcohol drinking has been shown to increase insulin sensitivity [139–141] and lower insulin resistance [142], even in young adult drinkers [143]. In summary, there is growing evidence from cohort studies that moderate alcohol consumption reduces the risk of diabetes and a plausible underlying biological mechanism has been identified.

With regard to cholelithiasis (gallstones) there is some evidence that alcohol may offer some protection against gallstones [13, 72]. These findings have been substantiated by recent large-scale cohort and case-control studies which reported an inverse relationship [144–147].

**Acute Consequences**

**Accidental Injury and Poisoning, Suicide, Interpersonal Violence and Assaults**

Alcohol use has been associated with increased risk of traumatic injury in a variety of settings such as traffic accidents, accidents in professional and recreational contexts, falls, arson, but also self-inflicted injury (including suicide) and injuries resulting from interpersonal violence [68, 148, 149]. The assessment of causality is often difficult and needs triangulation by different sources, such as time series analyses, natural experiments, case-control studies, emergency-room studies, general population surveys, and experimental designs [150]. The context of drinking, social and cultural environment, and drinking patterns, however, is probably as important as the amount of alcohol consumed. To give an example, studies on violent incidents have repeatedly shown that alcohol consumption precedes violent events and the amount of

*Alcohol-Related Health Consequences*
Table 4. Acute alcohol-related health effects with attributable fractions from international comparisons

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>females</td>
<td>males</td>
<td>females</td>
<td>males</td>
<td>females</td>
</tr>
<tr>
<td>Traffic accident injuries</td>
<td>E810–E819</td>
<td>0.42</td>
<td>0.42</td>
<td>0.00–0.34</td>
<td>0.18–0.43</td>
</tr>
<tr>
<td>Non-traffic accident injuries</td>
<td>E820–E825</td>
<td>0.42</td>
<td>0.42</td>
<td>0.00–0.34</td>
<td>0.18–0.43</td>
</tr>
<tr>
<td>Bicycle accident injuries</td>
<td>E826</td>
<td>0.20</td>
<td>0.20</td>
<td>0.00–0.34</td>
<td>0.18–0.43</td>
</tr>
<tr>
<td>Other road vehicle accident injuries</td>
<td>E829</td>
<td>0.20</td>
<td>0.20</td>
<td>0.00–0.34</td>
<td>0.18–0.43</td>
</tr>
<tr>
<td>Water transport accident injuries</td>
<td>E830–E839</td>
<td>0.20</td>
<td>0.20</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Air-space transport accident injuries</td>
<td>E840–E845</td>
<td>0.16</td>
<td>0.16</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Accidental ethanol and methanol poisoning</td>
<td>E860.0–E860.2</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Accidental fall injuries</td>
<td>E880–E888</td>
<td>0.35</td>
<td>0.35</td>
<td>0.34</td>
<td>0.34</td>
</tr>
<tr>
<td>Arson injuries</td>
<td>E890–E899</td>
<td>0.45</td>
<td>0.45</td>
<td>0.44</td>
<td>0.44</td>
</tr>
<tr>
<td>Accidental excessive cold</td>
<td>E901</td>
<td>0.25</td>
<td>0.25</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Accidental drowning</td>
<td>E910</td>
<td>0.38</td>
<td>0.38</td>
<td>0.03–0.50</td>
<td>0.03–0.50</td>
</tr>
<tr>
<td>Accidental aspiration</td>
<td>E911</td>
<td>0.25</td>
<td>0.25</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Striking against/struck by objects</td>
<td>E917</td>
<td>0.25</td>
<td>0.25</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Caught in/between objects</td>
<td>E918</td>
<td>0.25</td>
<td>0.25</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Occupational and machine injuries</td>
<td>E919–E920</td>
<td>0.25</td>
<td>0.25</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Accidental firearm missile injuries</td>
<td>E922</td>
<td>0.25</td>
<td>0.25</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Suicide, self-inflicted injuries</td>
<td>E950–E959</td>
<td>0.28</td>
<td>0.28</td>
<td>0.02–0.10</td>
<td>0.02–0.15</td>
</tr>
<tr>
<td>Victim, fight, brawl, rape</td>
<td>E960</td>
<td>0.46</td>
<td>0.46</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>Victim assault firearms</td>
<td>E965</td>
<td>0.46</td>
<td>0.46</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>Victim assault cutting instrument</td>
<td>E966</td>
<td>0.46</td>
<td>0.46</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>Victim child battering</td>
<td>E967</td>
<td>0.46</td>
<td>0.46</td>
<td>0.16</td>
<td>0.16</td>
</tr>
<tr>
<td>Victim assault other</td>
<td>E968</td>
<td>0.46</td>
<td>0.46</td>
<td>0.47</td>
<td>0.47</td>
</tr>
<tr>
<td>Late effects of injuries by another</td>
<td>E969</td>
<td>0.46</td>
<td>0.46</td>
<td>0.47</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Ranges refer to age-specific attributable fractions whereby minimum and maximum estimates are shown.

* No AAFs provided by the authors.

drinking is related to the severity of subsequent violence, pointing to causality in standard epidemiological terms [151]. The bar atmosphere, expectancies of alcohol effects, and the social and cultural environment ‘permitting’ alcohol to disinhibit norms are highly important [6, 19] to alcohol becoming a ‘cause’ of violent events. Overall, in the literature on alcohol-related mortality and morbidity, there is a broad consensus that alcohol plays a causal role in the events summarized in table 4.

Although some causal role of alcohol for acute consequences can be assumed, some very important methodological issues need to be clarified when it comes to quantifying the fractions of consequences attributed to alcohol [152]. For example, accidents are often attributed to alcohol whenever the responsible individual tested BAC-positive. However, from a strict epidemiological point of view, blood or breath tests can give only an indication of an association; since it cannot be determined how many such accidents would have happened even without drinking, it is virtually impossible to determine precisely the role of alcohol in these events [21, 153]. Clearly, in reviews of experimental studies [154, 155] psychophysical functions showed deficits already at BAC levels of about 0.03–0.05 g/100 ml and deficits increased with increasing levels which explained the mechanism of alcohol contribution for accidents. However, an elevated BAC level alone is not a sufficient indicator for alcohol being the cause of an accident, and hence AAFs determined by BAC thresholds are usually biased.

**Discussion**

The present paper is aimed at summarizing and updating the available evidence on alcohol-related consequences and the quantification of the alcohol attribution of established consequences. Of course, the list of established conditions presented here is not a definitive list of alcohol-related consequences. Rather, it should be regularly updated in the light of ongoing research and the appearance of new evidence. Biological evidence plays a key role here, as some of the consistent associations between alcohol and disease are currently refused because of the lack of biological plausibility (e.g. alcohol and lung cancer).
Besides establishing causality, the quantification of the AAF is at least of equal importance for the estimation of alcohol-related burden. For consequences, which are assumed to be stable across cultures and related mainly to total volume of consumption, the pooling of studies primarily needs comparable exposure levels (besides quality of research design and publishing of relevant statistics) [115]. Studies, however, often differ greatly with respect to assessment of exposure. For example, levels depicted as a moderate intake often are not comparable. Standardization of exposure levels, e.g. those used by English et al. [13], would further help meta-analytical reviews and more stable estimation of RRs.

For many of the alcohol-related consequences, substantial evidence has been accumulated that patterns of drinking are equally important as predictors of both chronic and acute health outcomes [4, 5, 121, 156]. For example, cardiovascular disease as a chronic outcome is also influenced by the pattern of drinking [4, 157]. Thus, an investigation by McElduff and Dobson [120] showed that a pattern of moderate regular drinking was associated with a reduction in risk of CHD when compared to abstainers, whereas binge drinkers displayed an increased risk. Similarly Walsh and Rehm [158] showed for a range of consequences that the same amount of alcohol was more detrimental when drank in a more irregular manner.

The impact of drinking patterns on the risk of consequences, as well as the protective effect for some consequences at lower levels, raises the question of the counterfactual scenario to calculate AAFs. Commonly, abstinence is used as counterfactual. Hence, the alcohol-attributable burden estimated by means of AAF and calculated under this scenario estimates the burden that could be avoided if everybody in a population switched to no consumption at all. Such a scenario widely avoids arguments about whether drinking patterns should be included in determining the RRs as all drinking would disappear. The avoidable burden from patterns of drinking would be attributed to the respective categories of volume of drinking [see the recent literature about refining the preventive paradox, e.g. 159, 160].

The usefulness of abstinence as the counterfactual (or the theoretical minimum) [3], on the other hand, can be questioned on several grounds. First, total abstinence of a population is an unrealistic scenario for most countries in the world (maybe with the exception of some countries where abstinence and prohibition are religiously motivated). Hence, from a public health point of view abstinence may be difficult to communicate in most countries, especially as the preventive message of moderate consumption for the heart has reached a wide audience [161]. Second, abstinence as a counterfactual would also underestimate the avoidable burden at least in established market economies, as the ‘prevented’ burden would partly counterbalance the ‘caused’ burden. In countries in which the prevention of CHD plays a minor role, however, probably more burden would be avoided with abstinence as the counterfactual compared with, e.g., moderate consumption as the counterfactual [103].

On the other hand, the use of a moderate volume of drinking as a counterfactual scenario [13] is also questionable. First, as drinking patterns modify the association between the volume of drinking and health consequences [3], a counterfactual scenario defined by volume only would underestimate the avoidable burden. Second, some acute consequences (e.g. accidents) have higher risks even at moderate levels of consumption and the question is not whether an individual should be abstinent or a moderate consumer, but whether he or she should abstain in certain risky situations. Other acute consequences are more closely related to heavy occasional drinking than volume of drinking as well as to environmental and socio-cultural factors [20].

To summarize, a single counterfactual scenario may not be equally well applicable to all consequences and in all cultures. In addition to modeling the attributable burden as deviation from abstinence, different scenarios should be integrated and sensitivity analyses should be performed.

However, without sufficient data such discussions are mainly theoretical and do not lead to any solutions. The use of patterns of drinking in epidemiological research is still scarce, and focus is often placed on the (average) volume of drinking only [162]. To integrate patterns of drinking in a comparative risk assessment, worldwide standardized measures of exposure, including volume and patterns of drinking, are urgently needed. Moreover, the proportion of mortality and morbidity stemming from acute consequences is at least as important as that from chronic consequences, not only in young people [9]. With the exception of some countries (mainly the Scandinavian countries, Canada, USA, Australia), for which the share of the global burden of disease is small in comparison to countries such as China, India, or Brazil, data and estimates on AAFs for acute problems are rare. Therefore AAFs from other countries are often applied to those countries for which data are lacking, despite the knowledge that the cultural environment is of particular importance for such consequences.
In conclusion, research on alcohol-related health outcomes at present not only needs to take into consideration both the average (volume) consumption and patterns of drinking and to standardize the assessment of exposure, it also needs to conduct studies on those outcomes which are culturally co-determined to a large extent, especially in developing and emerging countries.

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