Alcohol consumption, drinking patterns, and ischaemic heart disease: a review of meta-analyses

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Abstract

Background: Much discussion has revolved around the diverse findings on the complex relationships between one of the leading risk factors globally, alcohol consumption, and the leading cause of death and burden of disease globally, ischaemic heart disease (IHD). While most research to date has focused on average alcohol consumption, there is accumulating evidence that drinking patterns might modify this relationship.

Methods: We used the many meta-analyses published in the last 10 years to summarize the evidence from observational and experimental studies. We also conducted a systematic search of the literature up to fourth week of March using PRISMA guidelines to identify observational studies examining the relationship between alcohol consumption drinking patterns and IHD in comparison to lifetime abstainers where possible.

Results: Using current abstainers as the reference group leads to systematic bias. With regard to average alcohol consumption in relation to lifetime abstainers, the relationship is clearly J-shaped. Women experience slightly stronger beneficial associations and also a quicker upturn to a detrimental effect at lower levels of average alcohol consumption compared to men. Drinkers with <30 g/day and no episodic heavy drinking had the lowest IHD risk (RR = 0.64, 95% CI 0.53-0.71). Drinkers with episodic heavy drinking occasions had a risk similar to lifetime abstainers (RR = 1.12, 95% CI 0.91-1.37). Chronic heavy drinkers also had a similar risk compared with lifetime abstainers (RR = 1.04, 95% CI 0.83-1.31). People with alcohol use disorder have an elevated risk of IHD (RR = 1.62, 95% CI 1.34-1.95 in men and RR = 2.09, 95% CI 1.28-3.41 in women) compared with the general population.
Conclusions: Epidemiological evidence for a beneficial effect of low alcohol consumption without heavy drinking episodes is strong and is supported by experimental evidence. There is systematic evidence that episodic and chronic heavy drinking do not provide any beneficial effect on IHD. Thus, average alcohol consumption is not sufficient to describe the risk relation between alcohol consumption and IHD. Alcohol policy should try to reduce heavy drinking patterns.

Keywords: Alcohol, binge drinking, heavy drinking, ischaemic heart disease, meta-analysis, systematic review.
**Introduction**

Ischaemic heart disease (IHD) is the leading cause of death and disease burden in the US [1], Europe [2], and globally [3, 4], and alcohol consumption is one of the leading risk factors for mortality and morbidity [5, 6]. Certainly, there are well-established risks from neuro- and hepato-toxical, and carcinogenic effects caused by alcohol consumption (for example the risk for cancers of the upper aerodigestive tract [7-9], injuries [6, 10], and liver cirrhosis [6, 10, 11]). On the other hand, there has been much debate about a beneficial effect of alcohol consumption on IHD [12-14]. High prevalence of both exposure and disease make this question a frequent topic among general practitioners, researchers, media, and the public alike. Aside from numerous individual studies, several meta-analyses published in the last decade have summarized the association between alcohol consumption and IHD risk. In this review, we will examine what systematic evidence is available to define the relationship between alcohol consumption and IHD.

Most meta-analyses of epidemiological data have shown a beneficial association from alcohol consumption on IHD, most often described as a curvilinear, so-called ‘J-shaped’ relationship [15, 16], but also sometimes as a flattened out inverse association [15, 17, 18]. The specific shape of the risk curve seems to depend at least on sex and IHD outcome (mortality versus morbidity). Findings of a beneficial effect are supported by a substantial number of short-term experimental studies on the effect of alcohol consumption on several surrogate biomarkers for IHD in a dose-dependent relationship [19, 20], including improved lipid profiles, inhibition of platelet activation, reduction of fibrinogen levels, and anti-inflammatory effects. In particular, high density lipoprotein (HDL) cholesterol levels have a clear dose-response relationship with alcohol consumption, with the highest levels observed in people with the highest alcohol consumption [21, 22]. Many criticisms have arisen over the last three decades questioning the relationship found in epidemiological studies because of limited quality of alcohol assessment, the influence of drinking pattern, adjustment for confounding, or the inability for
observational studies to determine causality [13, 23]. Although criteria for a causal relationship [24] seem to be fulfilled (see also [15, 18]), a direct link for alcohol consumption on IHD risk from long-term randomized trials is currently and for the foreseeable future missing. Thus, epidemiological studies, as is the case for many other IHD risk factors, play an important role in assessing the role of alcohol consumption on disease risk. The efforts made in recent systematic reviews and meta-analyses, and several detailed individual studies enable us to examine these issues here with a focus on i) the reference group (i.e. the use of lifetime abstainers and not current abstainers as the reference group because of the so-called ‘sick-quitter’ effect [25]), ii) the influence of drinking pattern (in particular episodic heavy drinking among on average moderate drinkers [26]), and iii) the influence of several other important risk factors for IHD, such as age, smoking status, physical activity, and body mass index (BMI), all of which might confound risk estimates for alcohol.

Methods

Using PRISMA guidelines [27], we conducted two systematic searches based on previous meta-analyses [15, 26, 28] using electronic databases from their inception (clinical samples) or 1980 (population samples) to fourth week of March 2014 for original articles, excluding letters, editorials, conference abstracts, reviews, and comments for variations of search terms for the exposure (alcohol consumption), outcome (IHD), and study design. Additionally, we hand searched references of identified papers and relevant reviews and meta-analyses. Details of the searches can be found in the online supplement in Text S1, Figures S1 and S2.

Data abstraction

From all relevant articles we extracted authors’ names, year of publication, country, calendar year(s) of baseline examination, follow-up period, setting, assessment of IHD and alcohol consumption or alcohol use disorder diagnosis, mean and range of age at baseline, sex, number of observed IHD cases or deaths
among participants by drinking group, number of total participants by drinking group, adjustment for potential confounders, and relative risk and its standard error. We used the most adjusted relative risk reported, and gave priority to estimates comparing drinking to lifetime abstainers. Information found in related papers from the same cohort was used where possible. The first author performed the literature search and abstracted the data. Full-text articles with uncertain eligibility were discussed by both authors until consensus was reached. To control for subjectivity, 10 papers were randomly selected and extracted by the second author. No changes in abstraction were recorded. Primary authors were not contacted in case there was not enough information presented in the article.

**Statistical analysis**

Standardized mortality ratios (i.e. comparisons of mortality risks of patients in alcohol use disorder treatment with the sex- and age-specific general population; see [29]), hazard ratios, odds ratios, and relative risks were treated as equivalent measures of risk. Analyses were stratified by sex where possible. If necessary, relative risks within studies were re-calculated based on the method described by Hamling *et al.* [30] and pooled across studies using inverse-variance weighted DerSimonian-Laird random-effect models to allow for between-study heterogeneity [31]. We quantified between-study heterogeneity using Cochran’s Q [32] and the $I^2$ statistic [33]. $I^2$ can be interpreted as the proportion of the total variation other than chance that is due to heterogeneity between studies. We tested for potential publication bias using Egger’s test [34]. We did not find evidence for such publication bias. Sensitivity analyses for the influence of single studies on the pooled relative risks were conducted omitting one study at a time and re-estimating the pooled relative risk. No change in conclusions was observed. All meta-analytical procedures were conducted on the natural log scale in Stata statistical software, version 12.1 (Stata Corp, College Station, Texas), and $p<0.05$ (two-sided) was considered statistically significant.
Results

In the following paragraphs, we describe the results of previous systematic reviews and meta-analyses on alcohol consumption and IHD risk. Furthermore, we systematically investigate the role of heavy drinking patterns using high-quality observational studies based on updated systematic searches and meta-analyses. We identified seven studies providing data on episodic heavy drinking at low to moderate average alcohol consumption (<30 g/day), and 12 studies with chronic heavy drinking (≥60 g/day) in comparison to lifetime abstainers (Tables S1 and S2, Figures S3, S4, S7, S8). In addition we investigate IHD risk in patients in AUD treatment (Table S1, Figures S5, S6).

Lifetime abstainers and former drinkers

The majority of studies on alcohol consumption and IHD used current abstainers (i.e. no current alcohol intake and no assessment of past alcohol intake) as the reference group and thus did not distinguish between lifetime abstainers and former drinkers. For almost 30 years this has been the most important question about the validity of epidemiological findings on the alcohol-IHD relationship. Shaper put forward the concept of a ‘sick-quitter’ to describe the elevated risk of many current abstainers and former drinkers for health outcomes [25]. A recent systematic investigation using evidence from 54 epidemiological studies has shown that indeed former drinkers were at higher risk for IHD mortality [35]. The pooled IHD mortality risk among former drinkers was 1.54 (95% confidence interval [CI] 1.17-2.03) in women, and 1.25 (1.15-1.36) in men in comparison to lifetime abstainers. The definition of lifetime abstainers (e.g. whether less than 12 drinks over the lifetime or very infrequent drinking over the lifetime with no more than 12 drinks in a single year) did not influence the conclusions about this effect.
Average alcohol consumption

Another recent meta-analysis [15] presented the risk of current drinkers by level of average alcohol intake in comparison to lifetime abstainers where those estimates were available and simultaneously adjusting studies using current abstainers (i.e. compensating for the elevated risk in former drinkers) based on the above mentioned meta-analysis. The results clearly showed evidence for a beneficial effect when all available studies were included regardless of sex and IHD outcome (incidence, mortality, or morbidity). In particular, all pooled IHD risk estimates were statistically significant for average alcohol consumption between 1-2 drinks/day (point estimates were between 0.69 and 0.81 in comparison to lifetime abstainers). The results also showed that the particular J-shape of the association differed by sex and IHD outcome in stratified analyses. Sex seems to be important in that women experience slightly stronger beneficial associations and also a quicker upturn to a detrimental effect at lower levels of average alcohol consumption compared to men [15], which might be related to sex-specific biological factors, such as of body fat distribution, body size, and alcohol solubility [36-38].

Although some meta-analyses [16, 18, 39] have reported a protective association even for chronic heavy alcohol consumers in population studies (total alcohol intake on average ≥60 g/day), these results need to be interpreted with caution because the reference group is of crucial importance, as shown above. The association seems beneficial among chronic heavy drinkers only when current abstainers (i.e., lifetime abstainers and former drinkers) are the reference group. For example Ronksley et al. [18] reported a pooled RR of 0.76 (95% CI 0.52-1.09) for IHD incidence and 0.75 (0.63-0.89) for IHD mortality among chronic drinkers consuming ≥60 g/day. In order to examine the risk of episodic and chronic heavy drinking in comparison to lifetime abstainers, we conducted novel meta-analyses of IHD risk among several groups of alcohol intake using updated systematic searches based on prior systematic reviews and meta-analyses [15, 26, 40] (please see Text S1, Figures S1 and S2 for technical details). IHD mortality risk among male chronic heavy drinkers (≥60 g/day) was similar to lifetime abstainers with no indication
for a protective association (RR = 1.00, 95% CI 0.74-1.36, Figure 1, Figure S3, Table S1). Similarly, IHD incidence (i.e. using both mortality and morbidity outcomes) showed no indication of a protective effect (RR = 1.04, 95% CI 0.83-1.31, Figure S4, Table S1). Such chronic heavy drinking is rarely observed in women in population studies and there are not enough studies to systematically investigate chronic heavy drinking compared to lifetime abstention in women. The above mentioned IHD mortality risks among men by average alcohol consumption in comparison to lifetime abstainers are displayed in Figure 1.

While the aforementioned investigations were conducted using data from population studies, evidence from clinical samples involving patients with alcohol use disorder (AUD) in alcohol treatment showed a detrimental association with IHD mortality in both men and women (RR = 1.62, 95% CI 1.34-1.95 in men and RR = 2.09, 95% CI 1.28-3.41 in women compared to the general population, Figures S5 and S6, Table S1, see also [28]). Patients with AUD are typically missed or underrepresented in population studies [41]. Among those reporting the strongest elevated risk for IHD are studies from Russia [42, 43]. These studies consistently report substantially elevated RRs in heavy drinkers; however, alcohol consumption seems so prevalent in Russia that there have not been enough lifetime abstainers to define the risk relationship in comparison to zero alcohol intake over the life course. Nevertheless, the risk among heavy alcohol drinkers in comparison to low level drinkers [42, 43] was substantial (Figure 1).

Although no reliable comparisons exist because lifetime abstention is rare in Russia, one can speculate whether the estimates for heavy drinking are over- or underestimates compared to life time abstainers. Assuming the reference group (0.2 half litre bottles of vodka per week or 4.6 g/day on average) has a similar risk compared to low level drinkers elsewhere (RR = 0.81), the adjusted risk would be 1.58 (95% CI 1.48-1.69), only slightly less than assuming the risk among on average low level drinkers in Russia is indeed equal to that of lifetime abstainers elsewhere (RR = 1.00, Figure 1). However, given the heavy
episodic drinking pattern common in Russia, one would not necessarily expect to find any beneficial effect from any alcohol consumption on IHD risk on a population level as we argue below. Similarly, if one assumes a beneficial effect from average moderate alcohol consumption for 25% of the population, the risk in male patients with AUD would be slightly less (RR = 1.36, 95% CI 1.13-1.64). In summary, the relationship between average alcohol consumption and IHD risk is clearly J-shaped with an increased IHD risk at high levels of alcohol consumption when compared to lifetime abstainers or low level drinkers.

**Drinking pattern**

Alcohol can be consumed in many different ways, leading to the concern that an episodic heavy drinking pattern may confound or modify the relationship seen for average volume of alcohol intake and IHD risk [44, 45]. McElduff and Dobson were the first to present a stratified risk matrix by amount of alcohol consumption on drinking days and frequency of such drinking days on myocardial infarction (MI) risk in the Australian part of the MONICA project [46]. Since then, several other studies have examined the alcohol-IHD relationship with similar detail making it possible to investigate the influence of drinking patterns more systematically. Excluding the potential problem of lifetime abstainers and former drinkers, a recent meta-analysis examined drinking patterns among current drinkers who were not chronic heavy drinkers (i.e. excluding those with average total alcohol intake of ≥60 g/day) [26]. This meta-analysis found a significant difference when comparing episodic heavy drinkers with moderate regular drinkers with a pooled RR = 1.45 (95% CI 1.24-1.70). Other studies published since then have shown similar findings [35, 47].

Paying special attention to the effects of alcohol consumption patterns, we systematically examined IHD risk among two distinct drinking groups with the same average alcohol intake (Figure 2). Compared to lifetime abstainers, the pooled RR for IHD incidence was 0.64 (95% CI 0.53-0.71) for moderate drinkers without heavy drinking occasions, and 1.12 (95% CI 0.91-1.37) for drinkers with the same average
amount who engaged in heavy episodic drinking (Figure 2, Table S2, Figures S7 and S8). The corresponding risk between these two drinking groups was RR=1.75 (95% CI 1.36-2.25), higher than the estimate from the previous meta-analysis [26]. In other words, the impact of episodic heavy drinking seems to be greatest at low levels of average alcohol consumption in studies that have separated lifetime abstainers from former drinkers and were well adjusted for potential confounders (Table S2). Furthermore, the risk estimate for non-heavy low level drinking was lower (i.e. stronger in magnitude for a beneficial effect) than previous investigations of average alcohol consumption without taking into account episodic heavy drinking occasions [15, 18].

The importance of drinking patterns becomes particularly important when looking at Russian studies [42, 48-50]. A relatively frequent consumption pattern in Russia is episodic heavy to very heavy consumption with sometimes prolonged binges (‘zapoi’, an episode of continuous drunkenness lasting two or more days in combination with withdrawal from normal social life [51]). This drinking pattern is so extreme that it is heavy with regard to both average and episodic consumption (for example Malyutina et al. [48] in the Russian component of the MONICA project, reported that only 7% of their sample drank 40 g pure alcohol or less per typical occasion). Moreover, 12% of this Russian sample were current abstainers. On the other hand, 55% of the sample reported drinking 80 g or more per typical occasion and only 8% a drinking frequency of more than 2 days per week. In contrast, the National Health Interview Survey cohort from the US had 16% lifetime abstainers, 15% former drinkers, 42% infrequent or moderate drinkers, and only 27% of the participants drank 3 or more drinks (≥36 g pure alcohol) per drinking day [52].

There is substantial epidemiological evidence showing no protective effect on IHD risk from episodic heavy drinking, whereas the evidence for a beneficial effect is substantial and strongest among non-heavy low level drinkers. In summary, there are modifying effects from such drinking patterns on the relationship between average alcohol consumption and IHD risk.
Confounding from other risk factors for IHD

Residual confounding is an issue for all risk factors for IHD in observational studies. Many risk factors for IHD have been identified [1]. Inclusion of potential confounders had little influence on the pooled risk estimates from meta-analyses examining drinking versus non-drinking status [18]; this finding was similar within categories of average alcohol consumption in a pooled individual-data analysis of eight cohort studies (confounders included: age, year of baseline, smoking, BMI, education, physical activity, energy intake, polyunsaturated fat, monounsaturated fat, saturated fat, fiber, cholesterol intake, study design) [53]. Aside from adjustment for confounding, many studies have reported stratified analyses by important risk factors for IHD, which we describe in detail below.

Age

Hvidtfeldt et al., in a pooled individual-level analysis, showed an inverse relationship for each sex and each of three age groups based on eight cohort studies with 250,000 participants [53]. An inverse relationship based on 64,000 participants stratified into below 60 years of age and 60 years or above has been shown in Chinese men [54]. An analysis of the male British Doctors cohort found an inverse relationship both among participants younger than 75 years and those 75 years and above [55]. In a case-control study from Japan, Miyake et al. found an inverse relationship both among participants younger than 65 years and those 65 years and above [56]. A case-control study from Portugal showed a U-shape in those under 45 years of age and an elevated risk only in study participants with more than 60 g/day among participants 45 years or older [57]. The Honolulu Heart Program cohort showed an inverse relationship both among participants aged between 51-65 years and those 65-75 years old [58].

Smoking

Although numerous modifiable risk factors for IHD have been identified, their influence on the alcohol-IHD relationship seems to be small, except for smoking. Smoking is, aside from age, the most important
risk factor for IHD, and several studies have provided evidence on its influence on the alcohol-IHD relationship. It should be noted that alcohol is one of the most investigated risk factors for IHD [59]. Inoue et al., in a pooled individual analysis by smoking status, showed a J-shape in never smokers and a U shape in current smokers, with the highest category of average alcohol consumption being 92 g/day or more in 300,000 Japanese subjects [60]. A Chinese cohort study showed a similar inverse relationship in both current smokers and current non-smokers [54]. An inverse relationship among never smokers, a U-shape in former smokers, and an exponential relationship in current smokers was reported in a male Scottish sample of factory workers between 35-64 years old and with 30 years of follow-up [61]. Ebbert et al. showed an inverse relationship among never smokers and former smokers, and no relationship among current smokers in a low consumption cohort, the Iowa Women’s Health study [62]. An analysis of the Framingham study with 24 years of follow-up showed an inverse relationship among non-smokers, no relationship among light smokers (≤ 1 pack/day), and an inverse relationship among heavy smokers (>1 pack/day) in men. In women, a U-shape was found among non-smokers and smokers [63]. An analysis of the British Regional Heart Study showed an inverse relationship among former smokers, no relationship among current smokers, and an unclear relationship among never smokers. However, there were too few IHD deaths among never drinkers to reach a firm conclusion [64]. In an investigation of the National Health and Nutrition Examination Survey (NHANES I) in women 45-74 years old, an inverse in both smokers and non-smokers was reported [65].

In sum, regarding average alcohol consumption, in all but one population study, an inverse or J-shaped curve has been observed in never- or non-smokers. Evidence in smokers is mixed. Some studies reported an inverse relationship, some a threshold relationship, and some no clear relationship. Regarding clinical samples (Figures S7 and S8), there is the possibility that the detrimental association from alcohol consumption is overestimated because of uncontrolled confounding from smoking in these
samples. On the other hand, the prospective Russian study by Zaridze et al. [43] clearly showed a substantially increasing risk with increasing alcohol consumption among male smokers.

**Other confounding factors**

Some evidence exists for the alcohol-IHD relationship stratified by physical activity and BMI. Pedersen et al. investigated fatal IHD in the Copenhagen City Heart Study [66]. They found an inverse relationship for both physical activity level and average alcohol consumption in a low consumption cohort. The risk for non-drinkers and drinkers with less than 1 drink per week was consistently higher compared to drinkers of 1-14 drinks per week and 15 or more drinks. They concluded that both physical activity and alcohol consumption were factors for lower IHD risk. Bazzano et al. found an inverse relationship for participants with a BMI ≥25 and <25, with stronger evidence among those with a BMI <25 [54].

In sum, the epidemiological evidence shows that only in smokers there is some evidence that there is no beneficial association with alcohol consumption, and possibly a threshold effect, pointing to possible effect modification with alcohol consumption. Evidence for a beneficial association was consistent across age groups and in non-smokers. Available evidence for the influence of physical activity and BMI is sparse; although this evidence points to a beneficial association, as well. Furthermore, a beneficial association has been observed in hypertensive, diabetic, and patients with cardiovascular diseases, and survivors of myocardial infarction [67-73]. An inverse relationship has been observed in healthy individuals in a US cohort [74], and no association in a UK cohort [75].

**Experimental evidence**

Long-term randomized studies on alcohol exposure and IHD mortality or morbidity in the general population are unavailable. Regular alcohol intake has been found to have beneficial, dose-dependent effects on surrogate biomarkers for IHD risk in short-term experimental studies, mainly by increasing HDL cholesterol levels, inhibiting platelet activation, reducing fibrinogen levels, and producing anti-
inflammatory effects [19, 76]. The increase in HDL cholesterol was also evident in experimental studies
with regular heavy drinking (i.e. ≥60 g/day every day) [77-82], and the highest levels of HDL cholesterol
are found in people with alcohol use disorders [21]. Despite elevated levels of HDL cholesterol even in
regular heavy alcohol consumers [83], an increase in low-density lipoprotein (LDL) and other detrimental
effects of episodic and chronic heavy alcohol consumption on heart disease risk seem to negate those
beneficial effects, resulting in an overall neutral or detrimental association. The detrimental effect on
blood pressure and arrhythmias [44, 84-90] and atrial fibrillation [44, 89, 91-93], in particular from
episodic and chronic heavy drinking might play a role here, in combination with anti-atherosclerotic and
anti-thrombotic processes. Although systematic experimental evidence for the effect of episodic heavy
drinking is limited, the biochemical effects might involve HDL and LDL cholesterol levels, arrhythmias,
and thrombosis [45]. It seems that episodic heavy drinking increases LDL cholesterol levels without a
favourable effect on HDL [45], and possibly a transient detrimental effect on thrombosis, hypertension,
and arrhythmias [44, 45]. Prolonged chronic heavy drinking can result in the most extreme form of
cardiac tissue damage, cardiomyopathy [94]. There is substantial experimental evidence for a beneficial
effect of low to moderate regular alcohol consumption on IHD, but not for episodic heavy drinking.
Further work should focus on the specific effects of drinking patterns on the heart in both observational
and experimental studies.

Conclusions

Alcohol’s effect on the human body and mind is quite strong, even at low doses [95]. Its neuro- and
hepato-toxical, and carcinogenic properties make it a potent risk factor for disease burden. However, its
effect on IHD risk also makes it an intriguing and sometimes controversial topic in disease epidemiology
and public policy. The quality of epidemiological studies has substantially improved over the last three
decades. Clearly, using current abstainers as the reference group leads to systematic bias and erroneous
conclusions. Using high-quality epidemiological evidence, a clear picture supported by short-term
experimental evidence emerges. When examining average alcohol consumption in comparison to lifetime abstainers, the relationship with IHD risk follows a J-curve. The curve turns into a detrimental association for much lower average alcohol levels in women compared with men. However, average alcohol consumption alone is not sufficient to describe the alcohol-IHD relationship. Drinking patterns play an important role and both episodic and chronic heavy drinking negate any beneficial association with IHD risk, or elevate the risk substantially. Nevertheless, for drinkers with 1-2 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 risk when compared to lifetime abstainers. The alcohol-IHD relationship fulfills all criteria for a causal association proposed by Hill [24]. Whether one is able to detect an inverse, U-shaped, or J-shaped relationship depends on the distribution of drinking pattern in a given population. Prevalence of heavy drinking patterns has been on the rise in many countries, such as Canada, the US, UK, and many Eastern European and Asian countries.[96-99] In the US, episodic heavy drinking is more common than chronic heavy drinking [99]. Aside from any effect on IHD, caution must be used when judging the overall risk-benefit relationship of any form of alcohol consumption on an individual level because of well-known detrimental effects on other disease outcomes, such as injuries and cancer [6, 7, 100]. Recommendations for clinical practitioners (aside from clear contra-indications because of other illnesses or medication intake) remain challenging because of the apparent simultaneous beneficial and detrimental effects from on average low alcohol consumption, and the fact that evidence from randomized controlled trials on long-term effects of alcohol consumption is and will be unavailable. Furthermore, there is no control mechanism for alcohol purchase as there is for prescription drugs as alcohol is freely available for self-and over-medication. Therefore, uptake of alcohol consumption should not be considered as a treatment option in prevention of IHD. In terms of public alcohol policy, the picture is clear: alcohol
consumption should be as low as possible, no amount of consumption is safe, and any type of episodic and chronic heavy drinking should be strongly discouraged [101, 102].

Abbreviations: AUD, alcohol use disorder; CI, confidence interval; HDL, high density lipoprotein; IHD, ischaemic heart disease; RR, relative risk.
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Declaration of interests
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Contributors
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REFERENCES


Figure legends

Figure 1 Ischaemic heart disease mortality in men by average alcohol consumption in comparison to lifetime abstention

Data points taken from Roerecke & Rehm [15, 35]. The risk for chronic heavy drinkers (≥60 g/day) was 1.00 (95% CI 0.74-1.36, see text and Table S1 and Figure S5). The Russian estimates were pooled from Zaridze et al. [42, 43].

Figure 2 Ischaemic heart disease incidence by drinking pattern among drinkers with average consumption of <30 g/day in comparison to lifetime abstention

Please see Table S2, Figures S3 and S4 for details.
†Taken from Roerecke & Rehm [26].
Figure 1. Ischaemic heart disease mortality in men by average alcohol consumption in comparison to lifetime abstention.
Figure 2. Ischaemic heart disease incidence by drinking pattern among drinkers with average consumption of <30 g/day in comparison to lifetime abstention.
Additional files provided with this submission:

Additional file 1: BMC_review_appendix_final.pdf, 268K
Additional file 2: PRISMA Checklist MR2.doc, 63K
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