

Critique 119: A consensus statement on the association of moderate alcohol consumption and health — 13 August 2013

Poli A, Marangoni F, Avogaro A . . . de Gaetano G . . . et al (total of 36 authors). Moderate alcohol use and health: A consensus document. Nutrition, Metabolism, & Cardiovascular Disease 2013;23:487-504. <http://dx.doi.org/10.1016/j.numecd.2013.02.007>

Authors' Abstract

Aims: The aim of this consensus paper is to review the available evidence on the association between moderate alcohol use, health and disease and to provide a working document to the scientific and health professional communities.

Data synthesis: In healthy adults and in the elderly, spontaneous consumption of alcoholic beverages within 30 g ethanol/d for men and 15 g/d for women is to be considered acceptable and do not deserve intervention by the primary care physician or the health professional in charge. Patients with increased risk for specific diseases, for example, women with familiar history of breast cancer, or subjects with familiar history of early cardiovascular disease, or cardiovascular patients should discuss with their physician their drinking habits. No abstainer should be advised to drink for health reasons. Alcohol use must be discouraged in specific physiological or personal situations or in selected age classes (children and adolescents, pregnant and lactating women and recovering alcoholics). Moreover, the possible interactions between alcohol and acute or chronic drug use must be discussed with the primary care physician.

Conclusions: The choice to consume alcohol should be based on individual considerations, taking into account the influence on health and diet, the risk of alcoholism and abuse, the effect on behaviour and other factors that may vary with age and lifestyle. Moderation in drinking and development of an associated lifestyle culture should be fostered.

Forum Comments

Note: *One of the 36 authors of the consensus statement, G. de Gaetano, is a member of this Forum; he has not provided any comments on this Forum critique.*

Background: As is clear from this consensus statement, there are a huge amount of research data available on the relation of alcohol consumption to health and disease. The present paper is an attempt by a large number of Italian scientists to reach a consensus on the relation of moderate alcohol consumption to health. It results from discussions among 36 prominent scientists, and has been approved by 19 separate societies or federations in Italy, including societies in nutrition, cardiology, and general medicine, as well as organizations of scientists dealing with diabetes, hypertension, and obesity.

Our International Scientific Forum on Alcohol Research (the Forum) was established in 2010 with a goal of carrying out unbiased, scientifically sound appraisals of emerging research relating alcohol consumption and health. We consider the present publication to be an important contribution to this field, and that it provides key data that can be of use to physicians and other health-care providers, as well as to individuals setting health policy.

The overall impression of Forum members is that light-to-moderate drinking by middle-aged and older adults who have no contraindications to alcohol (e.g., prior abuse, uncontrolled epilepsy, and a few other medical conditions) is associated almost exclusively with beneficial health benefits. Such healthy outcomes are generally not seen among the young, due mainly to the rarity of the occurrence of the “diseases of ageing” among the young. It is also related to their frequent abuse of alcohol, from binge drinking, including heavy drinking games, and purposely drinking just for intoxication.

The Forum recognizes the importance of messages to the public (including to practicing physicians) regarding alcohol and health, and think that the present consensus has great merit. Members of the Forum agree with the authors of this report that changes in one’s drinking habits should be discussed with the person’s physician, as age, sex, underlying medical conditions, religion, and other factors should be taken into account. On the other hand, the Forum believes that any advice related to drinking should be evidence-based; guidelines should not be based on outmoded or paternalistic views that are not supported by current research.

Specific comments on the present consensus report: Forum members have carefully reviewed the consensus report, and here give comments on the conclusions for different outcomes. This Forum critique also provides data on some recent important publications related to alcohol and health that were not available when the consensus statement was developed.

While giving a very good overall assessment of the current knowledge on alcohol and health, the report contains a number of statements that appear to reflect “political” rather than “scientific” beliefs. As stated by Forum member Waterhouse, “This document is a refreshing review; however, it appears to be primarily a political document with a number of key compromises. In particular, two of the four conclusions were issues that were not addressed in the review. First there is conclusion #3, that pregnant women should be discouraged from drinking, but the authors present zero data on this question, i.e. they do not cite data demonstrating the effect of moderate alcohol consumption on pregnancy outcomes. The authors also specifically conclude that abstainers should not be encouraged to drink when, again, they present no data or discussion of the problems associated with such a recommendation. Instead, the data they do present shows again and again that abstinence, compared to moderate consumption, is a major risk factor for heart disease, obesity, metabolic syndrome, and other diseases. Thus, while the review of the scientific data is sound, and generally well done and conclusions 1 and 2 are derived from the data presented, it seems that conclusions 3 and 4 were added to appease political agendas of the 19 societies.” Reviewer Finkel stated: “This is an excellent, tempered overview of current understanding. However, I feel it implies more guilt to modest drinking vis-à-vis carcinogenesis than is deserved.”

Forum member Skovenborg also considered this to be a useful paper, but agreed that “several of the conclusions are written with a political correctness agenda with no scientific evidence base or discussion.” He added, “To their credit the authors confront the problem of underreporting of alcohol consumption — especially among heavy drinkers — and the problems of defining the limit of moderate and the start of harmful consumption. The authors also speak clearly in favour of the importance of total mortality as the most objective way to evaluate the role of alcohol and health. The authors conclude that ‘a window of healthy consumption’ exists, and indicate a reversion point where the mortality of drinkers equals or exceeds the mortality of abstainers. The conclusion of the quoted paper: ‘Low levels of alcohol intake (1-2 drinks per day for women and 2-4 drinks per day for men) are inversely associated with total mortality in both men and women’ is changed in the consensus document to ‘1-1.5 drinks/d in women and about 3 drinks/d in men.’” Reviewer Ursini added: “Too often solid science is tainted by biases of ‘political correctness,’ trying to minimize the disappointment of some people who had hoped for a different outcome.”

Forum member Van Velden commented: I agree that this consensus paper is well balanced, although it does not mention current reports on the molecular and genetic influence that may play a significant role in the response to alcohol consumption. People react differently to alcohol ingestion due to nutrigenetic effects. Future research should concentrate on the effect of the genetic blueprint on alcohol consumption. Most epidemiological reports are based on the assumption that 'one size fits all,' whereas environmental influences on health outcomes depend on specific genetic profiles."

Alcohol and cardiovascular disease: Reviewer Zhang pointed out that while the authors state: "Less evidence is presently available to describe the effects of alcohol in patients with pre-existing CHD [coronary heart disease]," they then go on to describe a number of studies that refute that argument. For example, Zhang states that "they mention a recent meta-analysis of eight studies involving a total of 16,531 subjects with cardiovascular events which reported that low-to-moderate (5-25 g/d) alcohol consumption is associated with a significantly lower incidence of cardiovascular and all-cause mortality." These data confirm in CHD patients what has been observed in healthy subjects. They also state that "A positive effect of moderate alcohol consumption was also apparent in patients who underwent angioplasty procedures, in whom both atherosclerosis progression and clinical relapses appeared to be positively influenced by alcohol intake." The authors cited Mukamal et al (2006) and Niroomand et al (2004) to support these statements.

Mukamal (2003) has also stated in another paper: "Over a median follow-up of nearly 4 years, we found mortality rates of 6.4 deaths per 100 patient-years among abstainers, 3.4 among light drinkers, and 2.4 among moderate drinkers ($p < 0.001$). Thus, light and moderate drinkers appear to have a more favorable prognosis than abstainers following acute MI."

In a more recent, and very well-done, analysis based on the follow up of more than 50,000 subjects from The Health Professionals Follow-up Study (HPFS), 1,818 men were confirmed with incident non-fatal myocardial infarction (MI); among MI survivors, 468 deaths were documented during up to 20 years of follow up (Pai et al, 2012). In that study, in comparison with no alcohol consumption, the pre-MI and the post-MI intakes of light (0.1-9.9 g/day) and moderate (10.0-29.9 g/d) amounts of alcohol were both associated with lower risk of all-cause mortality and cardiovascular mortality. The significant reductions in all-cause mortality risk (22% lower for 0.1-9.9 g/day and 34% lower for 10.0 – 29.9 g/day, in comparison with non-drinkers) were not seen for consumers of ≥ 30 g/day; for this highest consumer group, the adjusted hazard ratio was 0.87 with 95% CI of 0.61-1.25.

Forum member Zhang also comments on potential difficulties in interpreting data of certain outcomes (e.g., myocardial infarction) and the subsequent course of subjects when alcohol may affect both the initial occurrence of the disease and events during follow up. "There are two potential problems with this kind of study: (1) the study can only assess the direct but not total effect of alcohol on mortality; and (2) potential collider stratification bias will further dilute the direct effect." Whenever the course following a MI is related to alcohol consumption after the MI, earlier drinking must also be taken into account.

Forum member Djoussé was surprised that the consensus report did not comment on the effects of alcohol on congestive heart failure, a disorder that is rapidly increasing in prevalence due to the ageing population; it is the leading cause of hospitalization in older adults in the US. "Although the literature on the topic is still limited, there are reasonable data in support of a reduced risk of heart failure with moderate drinking, including a meta-analysis (Padilla et al, 2010). With so many new cases each year, it is critical to provide the readership with complete and

balanced information on major endpoints that drive current medical expenditure.” Further, Djoussé agrees with other reviewers: “The third conclusion bullet is a blank statement at the end of the paper without any substantiation.”

Alcohol and diabetes: The authors of the consensus report appear to be especially cautious in their appraisal of moderate drinking and diabetes. Almost all prospective studies have confirmed early reports of a 30% or greater reduction in the risk of diabetes mellitus among moderate drinkers than among abstainers (e.g., Koppes et al 2005). In a recent population-based study from Norway (Rasouli et al, 2013), that was not available to the authors of the consensus report, the results support most previous work showing a rather large (approximately 30% or more) reduction in the risk of Type II diabetes mellitus to be associated with moderate drinking. Further, several clinical trials in humans have provided experimental data that support the epidemiologic evidence of a protective effect of wine/alcohol against diabetes (e.g., Shai et al 2007; Joosten et al, 2008).

Despite such evidence, the authors of the present paper state: “Current guidelines addressed to diabetic patients are rather cautious because of the calories and body-weight issues, in addition to some untoward metabolic and vascular effects of alcohol,” even though their own comments reflect the opposite effects of moderate drinking. Further, they do not point out the marked reduction in the risk of cardiovascular disease among diabetics who consume alcohol moderately. The latter has recently been well described by Nakamura et al (2009), who stated: “With the never-drinking category serving as a reference, the Cox multivariate-adjusted hazard ratios for non-daily and daily drinkers for cardiovascular mortality were 0.43 (95% confidence intervals: 0.19-0.95) and 0.45 (0.25-0.80), respectively, and 0.33 (0.12-0.91) and 0.31 (0.15-0.67) for all-heart disease mortality in the combined impaired glucose tolerance and diabetic Japanese men. Alcohol drinking in men with glucose intolerance was associated with a significant reduction in cardiovascular and all-heart disease mortality as seen in the general population in Japan.”

Another recent study from the European Prospective Investigation into Cancer and Nutrition (EPIC) was based on a cohort of 4,797 participants with a confirmed diagnosis of diabetes mellitus (Sluik et al, 2012). This study reported that, “using light alcohol consumption (>0-6 g/d) as the reference category, there was no relationship between greater consumption and total mortality [HR for >6-12 g/d was 0.89 (95 % CI 0.61, 1.30) in men and 0.86 (95 % CI 0.46-1.60) in women]. However, in individuals who at baseline reported abstaining from alcohol, mortality rates were increased relative to light consumers: HR was 1.52 (95 % CI 0.99, 2.35) in men and 1.81 (95 % CI 1.04, 3.17) in women.” The strong effects of moderate alcohol intake in lowering the risk of cardiovascular disease among diabetics should not be overlooked.

Alcohol and dementia: The consensus report describes a number of studies on alcohol and dementia, most of which show lower risk of dementia or cognitive decline among moderate drinkers than among non-drinkers. A recent extensive summary of data on alcohol and dementia (Panza et al, 2012) points out difficulties in judging the effects of alcohol, but concludes “Light-to-moderate alcohol use may be associated with a reduced risk of incident overall dementia and Alzheimer’s disease, whereas for vascular dementia and cognitive decline, and predementia syndromes, the current evidence is only suggestive of a protective effect.” A detailed critique of this paper is available at our Forum web-site (www.bu.edu/alcohol-forum/critique-100).

A recent paper by Neafsey and Collins (2011) also presents an excellent summary of the relation of alcohol intake to cognitive function. These authors reviewed a total of 143 previous publications on the topic, finding 74 studies, based on a total of more than 250,000 subjects, that provided risk estimates for varying levels of alcohol consumption which allowed the investigators to include them in a comprehensive meta-analysis. As stated by the authors, “These studies overwhelmingly found that moderate drinking either reduced or had no effect on the risk of dementia or

cognitive impairment.” In their new meta-analysis, the odds ratio for cognitive risk associated with moderate drinking of alcohol was 0.77, with nondrinkers as the reference group. This estimate is close to the estimates of reduction in the risk of cognitive dysfunction (RR of 0.73 and 0.74) seen in other recent selective meta-analyses. This study found that both light and moderate drinking provided a similar benefit, but heavy drinking was associated with non-significantly higher cognitive risk for dementia and cognitive impairment. Further, their results included finding no appreciable differences whether or not “sick quitters” were included in the reference group, little effect from adjustments for other lifestyle factors, and no significant differences between alcohol’s effects on dementia, Alzheimer’s dementia, or vascular dementia.

Alcohol and osteoporosis: To expand the description in the consensus report on alcohol and osteoporosis, a recent intervention trial evaluated the association of alcohol intake with indices of bone metabolism, and showed beneficial effects of moderate alcohol intake on factors that relate to osteoporosis in post-menopausal women (Marrone et al, 2012). The authors of this paper carried out an intervention study among 40 healthy post-menopausal women, given an average of 19 grams/day of alcohol, approximately 1½ typical drinks. Measurements were carried out while the women were consuming alcohol, after they had stopped drinking as part of the trial, and following resumption of alcohol. The study showed that abstinence from alcohol resulted in increased markers of bone turnover (hence, higher risk of developing osteoporosis), whereas resumption of alcohol reduced bone turnover markers.

Alcohol and cancer: Forum reviewers thought that the consensus report presented a very balanced discussion regarding alcohol and cancer. It has been shown consistently that heavy alcohol intake markedly increases the risk of upper-aero-digestive cancers, as described well by the authors.

The association of alcohol intake and cancer risk has been extensively explored in a recent paper from the National Institutes of Health in the United States (Breslow et al, 2011). The paper is based on repeated administrations of the National Health Interview Survey in the United States, with a total of more than 300,000 subjects and over 8,000 deaths from cancer. For total alcohol consumption (frequency x quantity), the data indicate a significant *reduction* in the risk of all-site cancers (RR=0.87, CI 0.80-0.94) for light drinkers (≤ 3 drinks per week). Moderate drinking (for women, $>3-7$ and for men, $>3-14$ drinks per week) consistently shows no effect, and only heavier drinking is associated with an increase in all-site cancer risk. For site-specific cancers, an increase in risk of lung cancer was seen only for heavier drinkers, with a tendency for less cancer among light drinkers. There was no evidence of an effect of total alcohol consumption on colorectal, prostate, or breast cancer.

The overall message of this analysis is that light to moderate alcohol intake does not appear to increase the risk of all-site cancer (and light drinking was shown in this study to be associated with a significant decrease in risk). Similarly, light to moderate consumption was not associated with site-specific cancers of the lung, colorectum, breast, or prostate. Heavier drinking is known to be associated with a large number of adverse health effects, including certain cancers, as was shown in this study.

As described in the consensus report, in most observational studies the risk of breast cancer is slightly higher among women who reportedly average only about one typical drink/day, in comparison with no alcohol consumption. This increase in risk appears to be ameliorated for women who do not binge drink, have adequate folate levels, and do not take hormone replacement therapy (HT). The interaction of HT and alcohol on breast cancer risk was shown recently among 40,000 women teachers in California (Horn-Ross et al, 2012). These authors found no increase in breast cancer risk for women consuming up to 20 g/day of alcohol who had not used HT. They conclude: “Following the cessation of HT use, alcohol consumption is not significantly associated with breast cancer risk . . . Our findings

confirm that concurrent exposure to HT and alcohol has a substantial adverse impact on breast cancer risk. However, after HT cessation, this risk is reduced.”

Forum reviewers noted that in the consensus report, no reference was given supporting the statement that women with a family history of breast cancer should avoid alcohol; in fact, Dennis et al (2011) reported that “Consumption of wine may protect against BRCA1-associated tumors, while women with BRCA2 mutations may be at greater risk of alcohol-induced breast cancer.”

Further, supporting the consensus comments on the effects of moderate drinking on total mortality, a new paper by Newcomb et al (2013) assessed alcohol intake in a cohort of 22,890 women with incident invasive breast cancer (BrCa); during a median follow-up period of 11.3 years after diagnosis of BrCa, 7,780 deaths occurred, including 3,484 attributed to breast cancer. They found that “moderate alcohol consumption before diagnosis showed a tendency towards lower risk of death from BrCa, and a significantly greater reduction in the risk of cardiovascular disease mortality and total mortality. Alcohol consumption after diagnosis was not associated with disease-specific survival, but was associated with a lower risk of total mortality. For women consuming alcohol prior to the diagnosis of BrCa, those who decreased their intake showed little effect on mortality, while those who increased their intake showed further lowering of their risk of cardiovascular and total mortality.”

The conclusions of the authors of the Newcomb et al paper were supported in an accompanying editorial (Demark-Wahnefried, 2013) which stated: “Based on the best available evidence, including [the present report], it appears that modest alcohol consumption after breast cancer diagnosis, up to approximately one drink per day on average, may be associated with optimal overall survival, without compromising breast cancer-specific survival.”

The evaluation of alcohol consumption and breast cancer continues to present many difficulties to scientists. This was well described in a recent paper by Brooks and Zakhari (2013). The authors of this paper point out the necessity to consider the pattern of drinking (regular moderate versus binge-drinking, as the latter leads to much higher blood alcohol levels). Further, epidemiologic studies usually provide data for only a short period of time, while the development of cancer may relate to exposures over many decades. The authors also comment upon the effect that under-reporting of alcohol by study participants could exaggerate effects on cancer risk from light drinking. They conclude by emphasizing the overall net effects of moderate drinking, including reductions in the risk of cardiovascular disease and total mortality.

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Forum Summary

A group of Italian scientists has prepared a consensus paper to review the available evidence on the association between moderate alcohol use and health and disease. The report resulted from extensive discussions among 36 prominent Italian scientists, and provides a working document for the scientific and health professional communities. The report has been signed by 19 separate societies or federations in Italy, including societies in nutrition, cardiology, and general medicine, as well as organizations of scientists dealing with diabetes, hypertension, and obesity.

The consensus report ends with four conclusions:

“(1) In healthy adults and in the elderly, spontaneous consumption of alcoholic beverages within 30 g ethanol/d for men and 15 g/d for women is to be considered acceptable and do not deserve intervention by the primary care physician or the health professional in charge. In fact, there is no evidence to suggest complete abstention from alcohol drinking by moderate users.

(2) Patients with increased risk for specific diseases, for example women with familiar history of breast cancer, or subjects with familiar history of early CVD or cardiovascular patients should discuss their drinking habits with their physician.

(3) No abstainer should be advised to drink for health reasons.

(4) Alcohol use must be discouraged in specific physiological or personal situations or in selected age classes (children and adolescents, pregnant and lactating women and recovering alcoholics). Moreover, the possible interactions between alcohol and acute or chronic drug use must be discussed with the primary care physician.”

Forum reviewers considered this to be a well-done and generally well-balanced appraisal of the current literature on alcohol and health; it could help inform physicians and the general public about our current knowledge on this topic. However, Forum reviewers were concerned by several aspects of the report where it appeared that the conclusions were more “political” than “scientific” (perhaps necessary to gain the support of all of the societies endorsing the report).

The authors of the report provided good data to support their first two conclusions, and recent publications that were not available to the authors at the time they prepared their report strongly support these conclusions. However, Forum members found little data provided in the paper to support the third statement in their summary; in fact, the information the authors presented in the text would tend to support the opposite conclusion. Further, while it may be correct, their fourth conclusion was not supported by scientific data in the paper.

Forum members agreed that the importance of the effects of alcohol consumption on total mortality must always be considered, and agreed with the statement of the authors that “Low levels of alcohol intake (1-2 drinks per day for women and 2-4 drinks per day for men) are inversely associated with total mortality in both men and women.”

Key areas that the Forum believed could have been given more emphasis related to the association between alcohol and diabetes mellitus, where data strongly support an approximately 30% lower risk for moderate drinkers, in comparison with non-drinkers. And the risk of cardiovascular disease is considerably reduced among diabetics who consume alcohol moderately. And the potential effects of moderate drinking on reducing the risk of congestive heart failure, a rapidly increasing health problem related to ageing of the population, were not discussed. Forum members also wished that more emphasis had been given in the consensus report to the pattern of drinking: current data indicate that regular moderate drinking, rather than binge drinking, is the pattern associated with the most favorable health outcomes.

Overall, this consensus report is an important and useful addition to the scientific literature on the relation of moderate alcohol consumption to a variety of health outcomes. It could be of great values to physicians and policy makers when providing advice to the public regarding the effects of alcohol on health.

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