International Scientific Forum on Alcohol Research
Examining risks and benefits of alcohol consumption
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Comments on Proposed US Dietary Guidelines, 2010

Members of our International Scientific Forum on Alcohol Research have been pleased to review the draft, released on June 15, 2010, of proposed new United States Dietary Guidelines for 2010. Overall, our members found the draft to be interesting, balanced, and accurate. The new version does not appear to critically appraise the literature it has used – rather it has reported it. Some members commented that rather than just focusing on warnings against heavy drinking, the new Guidelines appear to take into account the large amount of recent epidemiologic and experimental data that support some potential beneficial health effects of moderate drinking.

Most Forum members agreed that the draft is remarkably balanced. One member stated that you can evaluate the "political acceptability" of two points: First, the Committee "largely agreed" on the NIAAA 2009 definition of moderation as "low-risk" drinking, as responses to alcohol may relate to medications, disease, being underage, driving, pregnancy, etc.. (The physiological intake of most foods and even physical activity could be similarly defined as "low-risk" behaviors.) Secondly, the Committee indicated a strong need for further investigations focused on moderate drinking and healthy lifestyle.

Given below are selected comments from Forum members relating to specific sections of the draft Guidelines report (Introduction, List of Questions, Needs for Future Research). Section 3 of our comments describes certain topics that our Forum members suggest the Guidelines Committee consider as additional topics of importance for the Guidelines. New references listed throughout our Comments are shown in bold, with detailed information on these references provided at the end of these comments.

1. Introduction

1.1 Cancer: Other than the known marked increase in risk of upper aero-digestive cancers from heavy alcohol use, a primary concern of physicians and the public relates to an increase in the risk of breast cancer among women. The increased risk of breast cancer in women who drink small to moderate amounts of alcohol is worrisome. This

means that young and middle-aged women may have no cardiovascular benefits to expect from alcohol consumption, but an increased risk from breast cancer. Such a finding should be put into perspective by including information on other effects of moderate drinking.

The Diet Cancer Report (http://www.dietandcancerreport.org) shows a very slight increase in breast cancer risk with alcohol intake (an increase that would not be considered clinically important in most experimental studies). Remarkably, the same amount of alcohol associated with breast cancer is "protective" for cardiovascular disease and total mortality, and the number of people who would be affected would be much higher. Thus, while the majority of prospective studies suggest a modest increase in breast cancer risk even at an average intake of only about 1 typical drink per day, it is important to have a balanced perspective, not only acting in fear facing adverse effects, but by also accounting for beneficial effects of moderate drinking on other conditions. Women should not be scared off from a daily drink in fear of breast cancer only to thereby lose the much greater health benefits accorded the cardiovascular system. Ideally, we would be able to accurately estimate individual risks; as of now, we can only guess at them.

1.2 Diabetes: As stated by the Guidelines Committee, many studies have shown lower risk of type 2 diabetes for moderate drinkers in comparison with abstainers. The previous meta-analyses listed in the Guidelines report have been supported by a recent meta-analysis by **Pietraszek et al (2010)** that concluded: "light to moderate alcohol consumption seems to reduce the risk of type 2 diabetes by 30%, while heavy drinkers have the same or higher risk than total abstainers." **Crandall et al (2009)** have also shown that pre-diabetics who consume alcohol are at lower risk of developing diabetes. The analysis was from the Diabetes Prevention Program, involving patients from 27 centers throughout the US.

Another recent paper by **Joosten et al 2010** showed that moderate drinking considerably lowered the risk of developing type 2 diabetes even among subjects who are otherwise following a healthy lifestyle (not obese, non-smokers, physically active, eating a healthy diet). The authors suggest that moderate drinking should be considered as a complement, and not as an alternative, to other healthy lifestyle habits that lower the risk of chronic diseases such as diabetes and coronary heart disease.

Cardiovascular disease remains as the leading cause of death among diabetics. Thus, it may also be important to comment on the very convincing and consistent data over many decades indicating a much lower risk of cardiovascular disease among diabetics who drink alcohol in comparison with abstainers.

1.3 Hypertension and stroke: A recent meta-analysis by **Patra et al (2010)** supported earlier reports on the relation of alcohol drinking to stoke. These investigators found a dose-response relationship for hemorrhagic stroke with a monotonically increasing risk for increasing consumption, whereas ischemic stroke showed a curvilinear relationship, with a protective effect of alcohol for low to moderate consumption and an increased risk

for higher exposure. For more than 3 drinks on average/day, in general women had higher risks than men, and the risks for mortality were higher compared to the risks for morbidity. These authors conclude that their results indicate that heavy alcohol consumption increases the relative risk of any stroke while light or moderate alcohol consumption may be protective.

1.4 Total mortality: Certain Forum members believed that the "26,000 fewer deaths averted by moderate drinking" is a gross underestimate. A large number of recent papers relate alcohol consumption to mortality, and the findings are very consistent in showing that moderate drinkers are at lower risk of both incidence and mortality from many of the disease of ageing, as well as for total mortality risk. As stated in the Guidelines, a recent meta-analysis (Di Castelnuovo, 2006) indicated that moderate drinkers had approximately 20% lower mortality risk than abstainers.

It may be useful for the Guidelines Committee to comment on definitions of "moderate drinking." **Rehm et al (2007)**, in a report on the net effects on mortality of alcohol consumption in Canada, found that when binge drinkers were included in the moderate category (based on weekly average number of drinks), the net number of deaths associated with alcohol was increased (due mainly to excess drinking outcomes in the young). When, however, binge drinkers were excluded, the net effect was considerably fewer deaths because there were very few alcohol-related deaths in the young and many fewer deaths in the elderly. Emphasizing the differing health effects of binge drinking versus regular moderate consumption is an important message for the public.

McCaul et al (2010) recently reported on alcohol and mortality risk from two prospective cohorts of community-dwelling men aged 65–79 years at baseline in 1996 (n = 11,727) and women aged 70–75 years in 1996 (n = 12,432). These investgators reported that in people over the age of 65 years, alcohol intake of four standard drinks per day for men and two standard drinks per day for women was associated with lower mortality risk. The authors stated that, for men, their data suggested that the risk was reduced further if accompanied with 1 or 2 alcohol-free days per week.

1.5 Hepatic effects: Excessive alcohol intake is a key factor in the development of hepatic cirrhosis. On the other hand, the relation of light-to-moderate drinking to liver disease is more tenuous. The USDA Guidelines should present reliable data backing the statement that "alcohol consumption may modulate pharmaceutical catabolism by liver enzymes and may potentiate the carcinogenic potency of hepatotoxins." In a recent paper, **Rehm et al (2010)** describe a "j-" or "u-" shaped relation of alcohol to risk of cirrhosis. For light drinking, these authors state that for "women in morbidity studies, one to two drinks daily had virtually the identical risk as lifetime abstention." They also state that "relative to lifetime abstainers, men who consumed one to two drinks per day had lower risk of liver cirrhosis (RR = 0.3, 95% CI 0.2, 0.4)."

The draft Guidelines fail to discuss nonalcoholic fatty liver disease (NAFLD), the most common cause of hepatic dysfunction in the US population. It has been shown from NHANES III data that NAFLD suspected from abnormal liver function tests was

much lower in moderate drinkers of wine than in non-drinkers: the adjusted odds ratio was 0.15 (95% confidence interval, 0.05-0.49)(**Dunn et al, 2008**). The authors of that paper concluded that wine consumption is associated with reduced prevalence of suspected NAFLD. A recommendation that all patients suspected of having any type of liver disease abstain from alcohol consumption could have a significant negative impact on a population that is otherwise at high risk for cardiovascular disease.

2. Comments on Questions 1-6 included in Guidelines report

2.1 Question 1. Alcohol and weight gain: In addition to many studies in recent years showing that moderate drinking is not associated with excess weight gain was a recent report by **Wang et al (2010)**. In a well-done analysis of normal-weight (BMI < 25) women health professionals in an observational study, over a 12.9 year follow-up period 41.3% became overweight (BMI ≥ 25) and 3.8% became obese (BMI ≥ 30). Throughout the follow up, women who consumed between 5 and 30 grams of alcohol per day (up to about 2 _ typical US drinks) had a much lower risk of becoming overweight or obese, with the risk about 30% lower for those averaging 15 grams of alcohol per day or more than it was for non-drinkers. Moderate drinkers showed an even greater reduction in the risk of becoming obese.

These findings support limited previous research suggesting that women gain less weight if they consume alcohol than if they are non-drinkers, although the mechanisms for such an effect remain unclear. For unknown reasons, men may not show the same inverse association between alcohol intake and body size. Overall, most observational studies provide no evidence that light-to-moderate drinking leads to increases in weight for women who are initially of normal body size.

While cross-sectional in nature, an earlier report by **Breslow et al (2005)**, not referenced in the Guidelines, was particularly enlightening. Among 46,000 never smoking subjects, drinking more per occasion increased weight, while drinking smaller amounts of alcohol more frequently was associated with lower body mass. For most conditions, small amounts of alcohol on a frequent basis seems to the drinking pattern associated with the healthiest outcomes.

2.2 Question 2. Alcohol and cognitive decline: Many previous studies have suggested that moderate drinking delays the decline in cognitive functioning associated with ageing. In a recent case-control study from Spain on the effects of smoking and alcohol use on the risk of Alzheimer's Disease (AD), **Garcia et al (2010)** found that the risk of AD was unaffected by any measure of tobacco consumption. On the other hand, alcohol consumers showed a 47% lower risk of AD than never consumers, with effects mainly among women and among never smokers. No differences were noted by type of alcoholic beverage consumed. The authors conclude that mean daily total consumption of alcohol showed increasingly protective dose-response relationships in women.

2.3 Question 3. Alcohol and coronary heart disease (CHD): Statin therapy has changed the natural history of CHD by reversing, stabilizing, and/or inhibiting plaque burden in the coronary arteries and elsewhere. **Mukamal et al (2006)** studied 1,244 men with CHD in a post-CABG trial, and found that moderate drinking did not adversely influence the safety of low dose warfarin or (even) high dose lovastatin. Epidemiologic studies suggest that moderate alcohol drinking has a substantial beneficial effect, possibly second only to statin therapy, in persons at risk. Disqualification of patients from responsible, moderate alcohol drinking because they use statins or are on anti-coagulants has wide implications with respect to cardiovascular disease.

2.4 Question 4. Alcohol and bone health: A number of recent prospective studies have confirmed that moderate alcohol consumption is positively associated with bone mineral density (BMD). While studies in the young indicate an increase in the risk of falls above a certain level of intake, most studies in the elderly actually show a lower risk of falls and fractures among moderate drinkers in comparison with non-drinkers (e.g., **Felson et al 1995, Macdonald et al 2004, Mukamal et al 2007, Berg et al 2008, Tucker et al 2009**).

The special properties of beer might deserve a mention (**Sripanyakorn et al 2004**). Silicon is an essential element in the diet of birds and mammals; in human bone cells silicon stimulates the secretion of collagen - the steel framework that together with calcium crystals make bone as solid as reinforced concrete. The effect on BMD by silicon is about twice the effect seen with other dietary elements such as calcium. Beer appears to be a major contributor to Si intake. Beer contains about 19 mg Si/l, and serum and urinary Si levels significantly increase following the ingestion of beer, confirming this as a readily bioavailable source of Si. Diets that are high in Si may contribute to beneficial effects on bone which, for moderate beer intake, may be in addition to, or separate from, the effect of ethanol.

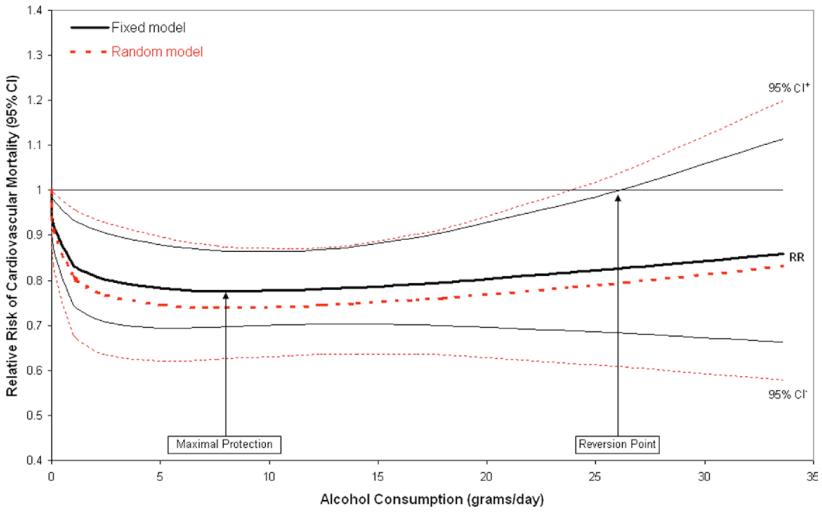
2.5 Question 5. Alcohol and unintentional injury: No comments

2.6 Question 6. Alcohol and lactation: The pregnancy and lactation sections deserve special attention. While heavy or binge drinking is never encouraged for pregnant women, prospective studies have not clearly established a link between low-moderate alcohol consumption in pregnancy and birth defects. This is not mentioned in the pregnancy section. As far as lactation is concerned, the section states that alcohol consumption has not been associated with higher rates of the neonate/offspring breast milk consumption, but that has been refuted in beer-consuming populations where the polysaccharide content of the beverage consumed has been linked to higher rates of newborn breast milk consumption. Beer contains a polysaccharide from barley which can stimulate prolactin secretion and may enhance the production of milk. The polysaccharide is also found in non-alcoholic beer, and the effect on prolactin can also be induced by non-alcoholic beer **(Mennella & Beauchamp, 1993; Koletzko & Lehner, 2000).**

3. Additional topics for potential emphasis in the Guidelines

It is appreciated that all topics related to alcohol cannot be covered in the new Dietary Guidelines. Nevertheless, there are a number of issues not included that our Forum members considered important to address. They relate to questions commonly being asked both by physicians and members of the general public. These topics are presented below.

3.1 Alcohol in patients with clinical cardiovascular disease: The role of alcohol in patients who have already been diagnosed with cardiovascular disease should be mentioned and discussed; guidelines in this area are scarce. Although some have reservations about advising an abstainer who has had a myocardial infarction to start to drink solely to reduce his subsequent health, there is little doubt that alcohol in moderation is protective against both cardiovascular and total mortality in patients who had suffered a vascular event. Of note are a number of papers on the effects of alcohol consumption among patients after they are diagnosed with cardiovascular disease. In a recent meta-analysis by **Costanzo et al (2010 a)**, the lowest relative risk of cardiovascular death ("maximal protection") was seen among subjects reporting as little as 5 grams of alcohol per day, the equivalent of only about 2 _ to 3 drinks/week. However, the relative risk (RR) of cardiovascular death remained lower than that of non-drinkers at all levels of alcohol intake; the 95% percentile estimate crosses that of non-drinkers at about 26 grams of alcohol/day (just over 2 typical drinks by US standards), as shown in the figure below from the paper.



Pooled curves of relative risk of cardiovascular mortality and alcohol intake, extracted from 7 independent relationships using fixed (solid lines) and random (dotted lines) models. RR = relative risk; 95% CI^- = lower value of confidence interval; 95% CI^+ = upper value of confidence interval.

Estimates of the association between alcohol and total mortality were very similar, with "maximal protection" of 18-20% at between 5-10 grams/day; the estimated relative risk remained lower than that of non-drinkers throughout the range of alcohol

intake, with the upper 95% percentile reaching the risk of non-drinkers at about 24 grams/day. A further paper by **Costanzo et al (2010 b)** supported these findings. (Further, in the list of references for the Guidelines the authors may want to add important reports by **Rotondo et al, 2001** and **Di Castelnuovo et al, 2006**.)

Carter et al (2010) recently reported better health and mental health functioning for moderately drinking subjects who continued to consume alcohol following a myocardial infarction (MI). A key problem with their analysis, and with all observational epidemiologic studies on this topic, is that the *reason* that some subjects stopped drinking after having an acute MI, while others continued to drink, is not known. Even though adjustments were made for many known related factors, there is always the possibility that subjects who stopped drinking were "sicker" in many ways than those who persisted in their alcohol consumption.

Beulens et al (2010) recently reported on effects of drinking alcohol among patients with clinically manifest vascular disease or diabetes (n = 5,447) from the SMART study. They found that moderate alcohol consumption (1–2 drinks/day) was not only associated with a reduced risk of vascular and all-cause death in these high-risk patients with clinical manifestations of vascular disease, but also with reduced risks of non-fatal events like CHD, stroke and possibly amputations.

3.2 Importance of pattern of drinking: It is quite clear that irregular, heavy drinking has adverse effects on health; most studies show that week-end binge drinking negates any potential health benefits of alcohol intake among patients who already have evidence of cardiovascular disease **(Mukamal et al, 2005)**. As previously discussed in Section 1.4, **Rehm et al (2007)** found that when binge drinkers were included in the moderate category (based on weekly average number of drinks), the net number of deaths associated with alcohol were increased (due mainly to excess drinking outcomes in the young). The net effect when binge drinkers were excluded from the moderate category was fewer deaths. The striking differences between binge drinking and regular moderate consumption (even when the total weekly alcohol intake is the same) need to be emphasized.

3.3 Drinking with meals: It may be important to discuss the timing of consumption of alcohol in relation to the ingestion of food. In the discussion of relevant contextual issues the draft of the Guidelines report has the following advice: "For those who choose to drink an alcoholic beverage, it is advisable to consume it with food to slow alcohol absorption. Data suggest that the presence of food in the stomach can slow the absorption of alcohol and thereby mitigate the associated rise in blood alcohol concentration." (The reference is not given for this statement, but may be **Jones, 1997.**)

The importance of first pass metabolism of alcohol is of critical importance to most drinkers and the conclusion of the Guidelines committee is very cautious indeed, considering the solid evidence reported by **Jones and Jönsson, 1994.** In their study, peak BAC was 67 mg/dl after ethanol with food compared with 104 mg/dl when drinking occurred after an overnight fast. Further, the mean area under the alcohol concentration-

time profile (0-6 hr) was 398 mg/dl x hr in the fasting state compared with 241 mg/dl x hr when ethanol was taken after food. The time required to metabolize the dose of ethanol was approximately 2 hr shorter when subjects had eaten breakfast before drinking alcohol.

Drinking ethanol with or after eating a meal, regardless of the nutritional composition, decreases the systemic availability of ethanol (**Jones 1993, Fraser et al 1995, Jones et al 1997, Jones 2000**). Because gastric emptying is slow and more prolonged with food in the stomach, the delivery of ethanol to the duodenum and the liver will be highly variable as will the hepatic clearance of ethanol. Provided that portal venous BAC remains fairly low and ethanol metabolizing enzymes are not fully saturated, part of the dose of ethanol can be cleared by hepatic first-pass metabolism, as one consequence of Michaelis-Menten elimination kinetics. The notion that food in some way boosts the rate of ethanol metabolism was confirmed in an experiment when a meal was eaten 5 hr after drinking ended, that is, when the post-absorptive phase of ethanol metabolism was well established. The mean rate of ethanol disappearance from blood was increased by 36-50% **(Fraser et al, 1995)**.

There is considerable inter- and intra-individual variability in ethanol bioavailability when ethanol 0.3 g /kg is given either before or after an evening meal. The overall mean Cmax when ethanol was given before a meal was significantly greater than the mean Cmax when ethanol was given 1 h after the meal (39.9 mg/dl vs 21.3 mg/dl respectively, $P < 0.0001$). The overall mean AUC when ethanol was given before a meal was also significantly greater than the mean AUC when ethanol was given after the meal (54.8 mg/dl h vs 33.6 mg/dl h respectively, $P < 0.0001$).

3.4 Potential additional effects from polyphenols and other non-alcoholic substances: The Guidelines report does not provide information to deal with a persisting question from the public: "Must it be red wine?" Are there differences in effects of beverages according to whether or not they contain polyphenols and other active substances that are present predominantly in wine and some beers? This was possibly due to unconvincing evidence to date of meaningful differences in some epidemiologic studies, especially those in the US, where moderate amounts of wine or beer or spirits appear to be equivalent in terms of health. This would suggest that ethanol is the common denominator. If this is the view of the Guidelines Committee, it should be clearly mentioned, because the hypothesis that red wine is superior to other beverages is quite diffuse.

On the other hand, studies are increasingly demonstrating mechanisms by which non-alcoholic components of some beverages can lower cardiovascular risk (e.g., **Chalopin et al 2010**). There have been many hundreds of experimental studies demonstrating beneficial effects of resveratrol and other polyphenols on endothelial function, including recent publications by **Huang et al (2010)**, **Ungvari et al (2010),** and **Je et al (2010)**. Further, **Corder et al (2006)** and **Caton et al (2010)** have demonstrated protective effects against cardiovascular dysfunction from procyanidins.

Some of the confusion about whether beer and red wine are similar or different in terms of ability to reduce CVD risk is certainly due to the variable level of phytochemicals (irrespective of the amount of alcohol consumed). Red wines can be rich sources of flavonoids, but this is often not the case with modern-style fruity red wines described as having soft tannins. Studies of cocoa and other sources of polyphenols are fairly consistent in showing improvement in endothelial function from these substances. Wine that has not had a traditional long maceration to extract all the flavonoids will have lower amounts of such substances.

Beer can also be a fairly good source of flavonoids, but only if there is a good proportion of hops used in the brew, and PVPP filtration is not used as part of the "manufacturing" process; unfortunately use of PVPP is standard practice for most large breweries because it gives a clear, beer-tasting, solution virtually free of polyphenols, so there is no haze on storage, and hence long shelf-life. Consequently, it is difficult to distinguish the benefit of drinking red wine over beer without knowing more about individual drinking habits, or having some idea of the characteristic of products consumed in the population under study. Future research should address the contribution that phytochemicals can make to the protective effects of alcoholic drinks, so that evidence-based guidelines can take this contribution into account.

Guidelines should take into account experimental evidence achieved in test tubes or cell culture and processed by a rigorous rationale. Experimental studies almost always indicate that wine or wine constituents provide additional protection than just alcohol. From a non-epidemiological point of view, the alcoholic beverages have both a hormetic component (due to alcohol) and a nutraceutical effect (due to phytochemicals) that is not hormetic. It is difficult in epidemiologic studies to take account of both types of effect at the same time. Recommendations cannot arise from only one kind of information, even if considered to be "evidence based." We need to learn more about combining data from multiple sources and distilling the information to get an educated consensus. Integrating epidemiological evidence with a rigorous intellectual process of the information about the mechanisms involved would make stronger and possibly more educated recommendations.

A number of clinical trials in humans are now being done. For example, in a recent trial **Hamed et al (2010)** investigated the underlying molecular mechanism of endothelial progenitor cells (EPC) migration in young, healthy individuals who drank red wine. They found that red wine exerts its effect through the up-regulation of CXCR4 expression and activation of the SDF1a/CXCR4/Pi3K/Akt/eNOS signaling pathway, which results in increased EPC migration and proliferation and decreased extent of apoptosis. They conclude that their findings suggest that these effects could be linked to the mechanism of cardiovascular protection that is associated with the regular consumption of red wine.

4. Need for Future Research

4.1 Research on risks and benefits of moderate drinking: While there continues to be a huge amount of research related to alcohol abuse, until recently there has been limited research, in animals or in humans, of the net effects of moderate consumption. The French Haut Conseil de la Santé Publique emphasized in 2009 the need for additional research on the health risks and benefits associated with low intake of alcohol.

4.2 Mendelian randomization studies: We believe that alcohol dehydrogenase polymorphisms, with fast, intermediate and slow oxidizers, and other genes related to alcohol metabolism, should be studied more intensively in epidemiologic studies. In a field where large-scale clinical trials are not feasible, so called Mendelian randomization may be the best choice to find out about the real risks and benefits of alcohol.

4.3 Differences among beverages in net health risks and benefits: In the proposed Guidelines, little was said about differences in effect by type of alcoholic beverage. As discussed in section 3.4, above, a large number of experimental studies confirm hypotheses of health benefits from many of the polyphenols and other substances in wines and some other beverages. Epidemiologic evidence of a greater effect of wine has frequently been reported, especially from European studies. Clarification of the possible contribution of polyphenols or other non-alcohol related substances to health protection is of importance and should be included in the *Needs for Future Research* section.

4.4 Evaluating genetic influences on alcohol effects: A plethora of genes are up and down regulated every day following the intake of different foods. In some cases a metabolic response is activated, in some cases an inflammatory response. Basic science recognizes that several phytochemicals are competent for damping excessive inflammatory responses (in terms of gene expression and enzyme regulation). Further research on this topic is sorely needed, especially since "personalized medicine" appears to be in our future.

4.5 Targeting recommendations regarding drinking according to gender, age, etc.: A number of medical conditions are variably related to alcohol, but what is fundamental, at least from a public health point of view, is that alcohol in moderation reduces total mortality, a hard, objective end-point. Thus, the balance between detrimental and beneficial effects of moderate drinking is definitely in favor of benefits.

Nonetheless, tailored suggestions are opportune: e.g., a young woman with very low cardiovascular risk but a strong family history of breast cancer may have nothing to gain in preventing cardiovascular accidents by drinking alcohol in moderation, while increasing (even if slightly) her risk of breast cancer. In contrast, a post-menopausal woman might gain much from moderate drinking as her chance to develop cardiovascular disease is much greater than her risk of developing breast cancer. A discussion with a health care provider is strongly advised for all people considering a change in their drinking habits; but, physicians should have up-to-date and balanced scientific data before giving patients advice. It is apparent that the protective effect of alcohol is more

pronounced among middle-aged and elderly people. On the other hand, alcohol consumption is a lifestyle habit, and most people continue into later life the habits (either healthy or unhealthy) that they acquired when young.

Considerable differences of opinion were found among Forum members regarding advice regarding alcohol consumption before middle age. One member argued that we cannot prevent a risk which is not present. In other words, the preventive effect of light to moderate alcohol consumption on the cardiovascular system can only work if there is risk. The increase in risk for disease starts at about 55 years in men and at about 65 years in women. For adolescents, young adults and young middle-aged people, there may be no health benefit from alcohol drinking.

Other Forum members disagreed, stating that the risk of cardiovascular disease becomes actual at 55, but it has been generated by a series of events in previous decades. One Forum member added: "On the subject of targeted recommendations regarding drinking, I believe it is a fallacy to ignore the fact that progression of atherosclerotic lesions leading to cardiovascular disease endpoints spans over generations and that earlier signs of atherosclerosis in form of fatty streaks can be observed already during adolescence. In the absence of solid data on light-to-moderate consumption in younger adults and overall health outcome, not just traffic accidents, it would be premature to suggest that only older adults can benefit from light-to-moderate drinking. The concept that a good diet starting from a young age can mitigate this process and reduce the risk of atheroma-related events in later life has to be a fundamental principle of dietary guidelines."

While myocardial infarction is uncommon in the young, in a pooled analysis by **Hvidtfeldt et al (2010)** covering a very large number of subjects, moderate alcohol intake was associated with considerably lower risk of coronary disease at all ages, including people who developed coronary artery disease before the age of 50. In comparison with non-drinkers, a lower risk of heart disease was seen over a wide range of alcohol intake, up to 60 grams/day in women and 90 grams/day in men. However, data on death due to heart disease or to other causes were not presented in this paper, and only the development of coronary artery disease was assessed.

In any case, the protective effect of light to moderate drinking in patients who have survived a myocardial infarction, and in diabetics, should be emphasized more; this is again in line with the fact that preventive (and curative) measures work even better in people with increased risk. On the other hand, there is a need for pertinent data on light-to-moderate in younger adults, as they are drinking anyway without recommendations. The idea of focusing advice regarding alcohol consumption only on the elderly or those with disease does not take into account our attempts to promote a healthy lifestyle throughout life for all for the prevention of many chronic diseases.

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