Measuring the Health Risks and Benefits of Alcohol

Over the years, scientists have documented the effects of alcohol on many of the body's organ systems and its role in the development of a variety of medical problems, including cardiovascular diseases, liver cirrhosis, and fetal abnormalities. Alcohol use and abuse contribute to injuries, automobile collisions, and violence. Alcohol can markedly affect worker productivity and absenteeism, family interactions, and school performance, and it can kill, directly or indirectly. On the strength of this evidence, the United States and other countries have expended considerable effort throughout this century to develop and refine effective strategies to limit the negative impact of alcohol (Bruun et al. 1975; Edwards et al. 1994).

In the past two decades, however, a growing number of epidemiologic studies have documented an association between alcohol consumption and lower risk for coronary heart disease (CHD), the leading cause of death in many developed countries (Chadwick and Goode 1998; Criqui 1996*a*,*b*; Zakhari 1997). Much remains to be learned about this association, the extent to which it is due specifically to alcohol and not to other associated lifestyle factors, and what the biological mechanisms of such an effect might be.

This section reviews information gained from epidemiologic studies on the health effects of alcohol use, with emphasis on new evidence. These studies focus on the extent to which alcohol consumption is associated with an increase or decrease in the risk of disease or death (Rothman and Greenland 1998). Many of the studies considered in this section use the traditional epidemiologic approach of relating average alcohol consumption to health outcomes (Rehm 1998). In light of recent research focusing on the patterns of alcohol consumption, such as daily drinking versus binge drinking, this section also discusses the impact of these patterns on health-related consequences (Rehm et al. 1996).

Definitions Related to Drinking

Studies investigating the health effects of alcohol vary in their definitions of "low," "moderate," and "heavy" drinking. According to the *Dietary Guidelines for Americans*, issued jointly by the U.S. Department of Agriculture and the U.S. Department of Health and Human Services, moderate drinking is no more than two standard drinks per day for men and no more than one per day for women (U.S. Department of Agriculture 1995). The National Institute on Alcohol Abuse and Alcoholism further recommends that people aged 65 and older limit their consumption of alcohol to one drink per day. Information on drinking levels as they are defined in the individual studies cited in this report can be found in the original references.

Finally, this overview addresses some of the approaches with which scientists are attempting to draw a more revealing and informative picture of how alcohol affects health, for example, by looking at mortality in terms of number of years lost as well as number of lives, measuring disability as well as illness and mortality, and looking at populations as well as individuals. Alcohol consumption has health consequences beyond the individual who is consuming alcohol, such as damage suffered by others as a result of alcohol-related motor vehicle collisions. Specific consequences for society are covered in the subsequent section on violence and in the chapters on economics and on prevention.

Topics not considered here include skeletal health and osteoporosis, diabetes, and cholelithiasis (gallstones). Definitive evidence has thus far not emerged from epidemiologic studies as to whether low to moderate alcohol consumption protects against, increases, or has no effect on the risk for these conditions. (The chapter on medical consequences provides more detailed discussions of individual health consequences of alcohol and of research aimed at revealing biological mechanisms for the alcohol-health connections suggested by epidemiologic studies.)

The information gained in the studies described here will be important not only to policy makers but also to health professionals and the individuals they advise with regard to alcohol's potential impact on health.

Risks and Benefits of Alcohol Consumption: Physical Health

Cardiovascular Diseases

Cardiovascular diseases account for more deaths among Americans than any other group of diseases. Of all causes of death, CHD is first, and stroke is third after cancer (U.S. Department of Health and Human Services [USDHHS] 1995). The role of alcohol as both a risk factor and a potential protective factor for cardiovascular diseases and the mechanisms that underlie the impact of alcohol on the cardiovascular system have been reviewed extensively in previous reports to Congress (see, for example, National Institute on Alcohol Abuse and Alcoholism [NIAAA] 1997) and in a comprehensive research monograph (Zakhari and Wassef 1996), and are considered as well in the chapter on medical consequences. The discussion below highlights recent findings concerning the role of alcohol in CHD, stroke, hypertension, and peripheral vascular disease.

Coronary Heart Disease. Several large prospective studies have reported a reduced risk of death from CHD across a wide range of alcohol consumption levels. (See the boxes "The Study of Risk" and "Does Abstaining Increase Risk?") These include studies among men in the United Kingdom (Doll et al. 1994), Germany (Keil et al. 1997), Japan (Kitamura et al. 1998), and among more than 85,000 U.S. women enrolled in the Nurses' Health Study (Fuchs et al. 1995). In research studies, definitions of moderate drinking vary.

How Much Is a Drink?

In the United States, a drink is considered to be 0.5 ounces (oz) or 15 grams of alcohol, which is equivalent to 12 oz (355 milliliters [mL]) of beer, 5 oz (148 mL) of wine, or 1.5 oz (44 mL) of 80-proof distilled spirits.

However, in these studies, most, if not all, of the apparent protective effect against CHD was realized at low to moderate levels of alcohol consumption. (In the last study cited above, for example, "light to moderate" drinking ranging from one to three drinks *per week* to one to two drinks *per day* was associated with a reduced risk of death from cardiovascular diseases.)

Similarly, a meta-analysis that pooled data from 19 cohort studies and 6 case-control studies found that although the risk of death from CHD was reduced at all levels of alcohol consumption, the maximum reduction in risk occurred at low levels (English et al. 1995). Other studies also have shown that drinking more is not associated with any additional reduction in risk (Maclure 1993).

An analysis of data from a 9-year follow-up of 490,000 Americans in the Cancer Prevention Study II (Thun et al. 1997) showed that, compared with abstainers, both men and women who consumed alcohol had a 30 to 40 percent lower risk of death from all cardiovascular diseases, with little relationship to the amount consumed. The reduced risk of death from CHD was especially marked among people at particular risk for cardiovascular diseases.

In addition to a reduced risk of heart disease death, several large studies have found a decreased incidence (number of new cases) of CHD in people consuming alcohol at low to moderate levels. For example, an analysis of data from the 1988 National Health Interview Survey indicated that both men and women had a reduced risk of heart disease at lower levels of drinking (the risk increased at drinking levels above five drinks per day for men and two drinks per day for women) (Hanna et al. 1997).

Follow-up of another large U.S. survey, the National Health and Nutrition Examination Survey I (Rehm et al. 1997*b*), found that, after an average of nearly 15 years of follow-up, the incidence of CHD in men who drank was lower across all levels of consumption than in nondrinkers. Incidence also was reduced among women, but only in those consuming low to

The Study of Risk

Epidemiologic research often uncovers evidence pointing to specific lifestyles, toxins, characteristics, or other factors that may make an individual or a population more or less likely to develop a given disease or to adopt a particular behavior. This likelihood is called risk, and the factors contributing to it are called risk factors. Factors that appear to reduce risk are called protective factors.

Researchers seek to identify, define, and study risk and risk factors for several reasons: to find out which individuals or groups are most likely to develop a disease; to gain an understanding of what may cause a disease; and, with that information, ultimately to be able to develop strategies to prevent or cure a disease.

Much of our understanding of how alcohol affects health and disease and society at large comes from epidemiologic studies, which compare various groups of persons who share common characteristics. Observations and data are collected at several levels: whole populations, groups representing a cross section of the general population, and special groups (for example, premenopausal women). Results of several different studies usually are compared to identify factors that contribute to health and disease and to evaluate the risk associated with those factors. However, estimates of risk arrived at from studying groups of people may not necessarily reflect the risk of a particular individual.

Defining Risk

Risk is the estimated likelihood of a certain outcome, such as the development of heart disease or colon cancer. Disease risk is related to certain characteristics, such as gender or age. For example, cancers of the breast and prostate are considered diseases of older age. Thus, the risk or likelihood of developing one of these cancers increases with age.

A multitude of factors can influence the risk of developing certain diseases. For example, smoking increases the risk for lung cancer, and high cholesterol is a risk factor for the development of heart disease. In contrast, regular physical activity or exercise lowers the risk for heart disease.

Types of Risk

Three types of risk are commonly used in studying health and disease: absolute risk, relative risk, and attributable risk. *Absolute risk* refers to the rate at which a disease (or mortality from that disease) occurs in the general population. Absolute risk is expressed as the number of cases in a specific group within a specific time period (for example, 50 cases of a given disease per 100,000 Americans occur annually) or as a cumulative risk up to a certain age. One well-known example of cumulative absolute risk is the often-cited statistic that breast cancer affects one in eight women in the United States. This number actually refers to the likelihood that a non-Hispanic white woman who lives to age 85 will develop breast cancer at some point during her lifetime.

A second type of risk, *relative risk*, is used to define the strength of a relationship between a risk factor, such as alcohol intake, and the occurrence of disease. A relative risk of 1.0 is the benchmark against which risk factors or protective effects are measured. A relative risk of 1.0 therefore reflects the rate of occurrence of disease in the absence of any risk factor (for example, the frequency of a disease among abstainers). (Another statistical term, *odds ratio*, is used to estimate relative risk under certain conditions.) Relative risks below 1.0 imply a protective effect in comparison with the reference category, often abstainers. A relative risk of, say, 0.5 for three alcoholic drinks per week and occurrence of a particular disease suggests that consuming that amount of alcohol halves the risk of developing that disease. In contrast, a relative risk of 2.0 suggests a doubling of risk. In general, the higher the relative risk, the stronger the evidence not only for increased risk but also for a causal relationship. Not all relative risks of equal value are equivalent in importance, however. For example, small relative risks may be of great importance to public health if large numbers of persons in the population are affected.

The third type of risk, *attributable risk*, considers the amount of disease in the population that could be prevented by changes in risk factors.

Epidemiologists also use other terms to describe the impact of alcohol on various aspects of society, such as health, disease, quality of life, mortality, and other factors. These measures are often very useful in developing health policy. Some of these terms include:

- **AAF—Alcohol-Attributable Factor:** AAF's are estimates of the fractions of deaths from disease and injuries that may be due to alcohol.
- **YPLL—Years of Potential Life Lost:** YPLL is an estimate of the extent to which alcohol contributes to premature death; the YPLL usually is calculated by subtracting from a standard age, such as the life expectancy in a particular region.
- **DALY—Disability-Adjusted Life Years:** DALY combines years of life lost and years lived with disability, in which each year lived with disability is adjusted according to the severity of the disability.

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- **GBD—Global Burden of Disease:** GBD can be used to estimate the extent to which alcohol may account for occurrence of disease worldwide or regionally, or the percentage thereof.

Studying Risk

Researchers use a variety of approaches to study how alcohol and other factors affect health and disease. Sometimes they use *correlation studies*, which investigate alcohol intake and disease occurrence at the population level. In these studies, rates of particular diseases (or mortality) are compared with rates of consumption of alcohol at one point in time or over a period of time. Such comparisons help to identify trends in intake and disease incidence.

Another type of study used to examine the relationship between alcohol and disease risk is the case-control study. In *case-control studies*, individuals with a specific disease (the cases) are compared with a similar group of persons without that disease (the controls). Information about all study participants is then collected, often through interviews. Researchers analyze this information in an effort to find differences between the two groups with respect to alcohol intake. Failure to find such a difference would suggest that alcohol was not a cause of the disease being studied. Case-control studies also are called *retrospective studies* because they examine study participants' past lifestyle, activities, or characteristics with respect to the presence or absence of a disease.

In *prospective cohort studies*, the drinking habits of a large group, or cohort, of initially healthy individuals are examined. The cohort is then followed over time, often for more than 10 years. The relationship between drinking patterns and disease development (or absence) during the follow-up period is then analyzed and compared. Information in cohort studies is often collected using self-administered questionnaires.

Controlled trials are characterized by randomization, in which participants are randomly assigned to an experimental group or a control group. In a *double-blind* controlled trial, neither the volunteers nor the researchers know who belongs to which group. Trials examining the effects of alcohol may not be able to be "blinded," because the odor and taste of many alcoholic beverages are readily identified. Furthermore, because many of alcohol's deleterious effects are well defined, for ethical reasons controlled trials of alcohol in humans are restricted to short-term studies of limited scope (for example, an examination of alcohol's effect on circulating hormone levels within a few hours after administration of alcohol).

More recently, researchers have begun to pool data from several studies and perform what is known as a meta-analysis. *Meta-analyses* often allow modest but potentially important relationships between alcohol (or other factors) and disease to surface. Such relationships may be overlooked because of the relatively small size and inadequate statistical power of an individual study. The power to detect an effect from alcohol and other risk factors generally increases with larger data sets. Meta-analyses ideally include all relevant studies, preferably prospective studies or other studies judged to be well designed and conducted.

moderate levels of alcohol. In fact, an increased risk was observed in women consuming more than 28 drinks per week.

An association between moderate drinking and lower risk for CHD does not necessarily mean that alcohol itself is the cause of the lower risk. For example, a review of population studies indicates that the higher mortality risk among abstainers may be attributable to shared traits—socioeconomic and employment status, mental health, overall health, and health habits such as smoking—rather than participants' nonuse of alcohol (Fillmore 1998*a*).

It is also important to note that, as will be discussed later in this section, the apparent benefits of moderate drinking on CHD mortality are offset at higher drinking levels by increased risk of death from other types of heart disease, cancer, liver cirrhosis, and trauma (USDHHS 1999). The U.S. Department of Agriculture (USDA) and the USDHHS, in the *Dietary Guidelines for Americans*, have defined moderate drinking as one drink per day or less for women and two or fewer drinks per day for men (USDA 1995). In addition, the NIAAA further recommends that people aged 65 and older limit their consumption of alcohol to one drink per day.

Role of Type of Alcoholic Beverage. Some researchers have argued that wine confers special protection against CHD (Goldberg et al. 1995). Others have concluded that any benefit of

alcoholic beverages in protecting against CHD is derived mostly or wholly from alcohol itself rather than from components of particular beverages (Doll 1997; Rimm et al. 1996).

Laboratory studies as well as studies in humans have produced mixed results concerning the effects of wines in reducing the concentration of lipids, or fats, in the blood (for reviews, see Chadwick and Goode 1998; Goldberg et al. 1995) or in raising the blood levels of antioxidants—compounds that counter the effect of destructive by-products of metabolism (Puddey and Croft 1997). A study of Chinese men found no additional reduction in overall mortality associated with drinking rice-fermented wine (Yuan et al. 1997).

Role of Drinking Patterns. The pattern of drinking, rather than the type of alcohol consumed, may help explain how drinking wine might protect against CHD. Researchers have suggested that in some studies the pattern of drinking for wine drinkers differed from the pattern for those consuming other alcoholic beverages (Doll 1997) and that this difference in pattern could explain differences in associated CHD risk (Grønbœk et al. 1995; Klatsky and Armstrong 1993). For example, people usually consume wine in small amounts on almost every day rather than in large amounts on only one or two days a week.

In a review, one researcher concluded that a pattern of frequent drinking may confer some protection against CHD and that large amounts are not needed to achieve a beneficial effect (Bondy 1996). Alcohol consumed with meals was found to reduce the high levels of blood lipids that occur after eating (Criqui and Ringel 1994; Veenstra et al. 1990). One study demonstrated that the positive effect on blood lipids conferred by moderate alcohol use was present only while alcohol was being consumed (Rubin and Rand 1994).

Other studies have reported a reduced risk of coronary death or acute myocardial infarction with moderate, regular drinking and an increased risk associated with binge drinking (McElduff and Dobson 1997; Kauhanen et al. 1997*a*,*b*).

In summary, current evidence suggests that drinking small to moderate amounts of alcohol is associated with reduced risk of CHD. Little, if any, additional benefit is derived from drinking larger amounts. Lowered CHD risk is most closely associated with a consistent pattern of drinking small amounts of alcohol. The apparent CHD benefit is largely, if not wholly, attributable to alcohol itself and not to specific beverages or to other constituents of particular beverages. The question of potential additional benefits of certain alcoholic beverages such as red wine is not fully settled; future research should help clarify this issue (Klatsky et al. 1997; Rimm et al. 1996).

Finally, because many of the epidemiologic studies from which much of the evidence is derived have involved middle-aged or older persons in stable social situations, the findings may not necessarily apply to younger drinkers (whose risk of CHD is low to begin with) or to other social groups.

Stroke and Hypertension. Cerebrovascular disease, in which arteries in the brain are blocked or narrowed, can lead to a sudden, severe disruption of blood supply to the brain, called a stroke. Ischemic stroke, which is by far the predominant type of stroke, results from a blockage of a blood vessel; hemorrhagic stroke is due to rupture of a blood vessel. Alcohol-related hypertension, or high blood pressure, may increase the risk of both forms of stroke. Yet, in people with normal blood pressure, the risk of ischemic stroke may be decreased due to the apparent ability of alcohol to lessen damage to blood vessels due to lipid deposits and to reduce blood clotting. Alcohol's anticlotting effects, while perhaps decreasing the risk of ischemic stroke, may increase the risk of hemorrhagic stroke (Hillbom and Juvela 1996). These studies are coming closer to providing a clear picture of the relationship between alcohol and risk of stroke.

Effects of Alcohol on Stroke Risk. The relationship between alcohol consumption and stroke risk has been examined in two recent overviews. In a meta-analysis, researchers compared the relationship between alcohol consumption and the risk of ischemic and hemorrhagic strokes

(English et al. 1995). They detected no differences in the risk patterns for the two types of stroke, but found clear evidence that heavy drinking was associated with increased stroke risk, particularly in women. At low levels of alcohol consumption, they found the evidence to be inconsistent regarding a protective effect against stroke. In the second overview, the author drew a similar conclusion from 12 case-control and 14 cohort studies, finding that although moderate drinking (defined in this review as usual consumption of fewer than two drinks daily for men and less than one drink daily for women) does not appear to increase the risk of ischemic stroke, it is not clear whether moderate drinking protects against this type of stroke (Camargo 1996). On the other hand, moderate drinking may increase the risk of hemorrhagic stroke, although the evidence is inconsistent. Other recent studies also fail to offer clear evidence that moderate drinking protects against stroke (Knuiman and Vu 1996; Yuan et al. 1997).

In contrast, the Cancer Prevention Study II found that, in men, all levels of drinking were associated with a significant decrease in the risk of stroke death, but in women, the decreased risk was significant only among those consuming one drink or less daily (Thun et al. 1997). A recent study reported that among male physicians in the Physicians' Health Study, those who consumed more than one drink a week had a reduced overall risk of stroke compared with participants who had less than one drink per week (Berger et al. 1999). The authors concluded that the benefit was apparent with as little as one drink per week.

Among young people, long-term heavy alcohol consumption has been identified as an important risk factor for stroke (You et al. 1997). Very recent alcohol drinking, particularly drinking to intoxication, has been found to be associated with a significant increase in the risk of ischemic stroke in both men and women aged 16 through 40 years (Hillbom et al. 1995). In another study, researchers reported that recent drinking of alcohol was associated with the onset of stroke in young people during weekends and holidays, possibly reflecting an association with heavy drinking (Haapaniemi et al. 1996).

Effects of Alcohol on Blood Pressure. The relationship between alcohol consumption and blood pressure is noteworthy because hypertension is a major risk factor for stroke as well as for CHD. A national consensus panel in Canada recently conducted an extensive review of the evidence concerning this relationship (Campbell et al. 1999), concluding that studies have consistently observed an association between heavy alcohol consumption and increased blood pressure in both men and women. Researchers analyzing data from middle-aged British men found an association between heavy drinking and an overall increased risk of stroke that was largely related to alcohol's effect on blood pressure (Wannamethee and Shaper 1996). However, in many studies comparing lower levels of alcohol use with abstention, findings are mixed. Some studies have found low alcohol consumption to have no effect on blood pressure or to result in a small reduction, while in other studies blood pressure levels increased as alcohol consumption increased.

Randomized controlled trials to determine the effect of reductions in alcohol consumption on blood pressure in people with both normal and high blood pressure have consistently found that reductions in alcohol consumption were associated with declining blood pressure levels, although not all of these reductions were statistically significant (Cushman et al. 1998). Drinking pattern—how often drinking occurs—may have as important an effect on blood pressure as how much a person drinks (Russell et al. 1991).

In summary, heavy drinking appears to increase the risk of hypertension and, although the evidence is not entirely consistent, also may increase the risk of stroke. It remains uncertain whether lower levels of alcohol can help prevent ischemic stroke. In addition to examining how much alcohol is consumed, it may be important to consider drinking pattern in determining stroke risk.

Peripheral Vascular Disease. The possibility that alcohol may protect against CHD has led researchers to hypothesize that alcohol may protect against peripheral vascular disease, a condition in which blood flow to the extremities is impaired due to narrowing of the blood vessels. In a 1985 analysis of data from the Framingham Heart Study, alcohol was not found to have a significant relationship, either harmful or protective, with peripheral vascular disease (Kannel and McGee 1985). Other studies also have failed to find a significant relationship between alcohol consumption and peripheral vascular disease, although a few have noted weak and inconsistent evidence of a protective association (Camargo et al. 1997).

However, an important recent study produced different results. In an analysis of the 11-year follow-up data from more than 22,000 men enrolled in the Physicians' Health Study, researchers found that daily drinkers who consumed seven or more drinks per week had a 26-percent reduction in risk of peripheral vascular disease (Camargo et al. 1997). This study took into account the effects of smoking, exercise, diabetes, and parental history of myocardial infarction.

Two other studies found inconsistent results with regard to gender. One study of middle-aged and older men and women in Scotland showed that as alcohol consumption increased, the prevalence of peripheral vascular disease declined in men but not in women (Jepson et al. 1995). In contrast, among people with non-insulin-dependent diabetes, alcohol was associated with a lower prevalence of peripheral vascular disease in women but not in men (Mingardi et al. 1997). Clearly, the relationship of alcohol consumption to peripheral vascular disease requires further study.

Liver Cirrhosis

There is no question that alcohol abuse contributes significantly to liver-related morbidity (illness) and mortality in the United States. The effects of alcohol on the liver include inflammation (alcoholic hepatitis) and cirrhosis (progressive liver scarring). As many as 900,000 people in the United States suffer from cirrhosis, and some 26,000 of these die each year. From 40 to 90 percent of people with cirrhosis are estimated to have a history of alcohol abuse (Dufour et al. 1993).

The risk for liver disease is related to how much a person drinks: the risk is low at low levels of alcohol consumption but increases steeply with higher levels of consumption (Edwards et al. 1994). This relationship has been confirmed in middle-aged and elderly adults enrolled in the Cancer Prevention Study II (Thun et al. 1997), in the 12-year follow-up study of more than 87,000 middle-aged women enrolled in the Nurses' Health Study (Fuchs et al. 1995), and among blacks and whites included in an analysis of the 1986 National Mortality Followback Survey (Parrish et al. 1993).

Gender also may play a role in the development of alcohol-induced liver damage. Some evidence indicates that women are more susceptible than men to the cumulative effects of alcohol on the liver (Becker et al. 1996; Gavaler and Arria 1995; Hisatomi et al. 1997; Naveau et al. 1997; NIAAA 1997).

Cancer

Alcohol has been linked to a number of cancers, including cancers of the head and neck (mouth, pharynx, larynx, and esophagus), digestive tract (stomach, colon, and rectum) and breast (World Cancer Research Fund/American Institute for Cancer Research [WCRF/AICR] 1997; Doll et al. 1993; International Agency for Research on Cancer [IARC] 1988).

Cancers of the Head and Neck. Alcohol is clearly established as a cause of cancer of various tissues in the airway and digestive tract, including the mouth, pharynx, larynx, and esophagus (Doll et al. 1993; IARC 1988; La Vecchia and Negri 1989; Seitz and Pöschl 1997; WCRF/AICR 1997). Research suggests that the risk of cancers of the upper digestive tract is associated with both the concentration of alcohol in beverages and the number of drinks consumed (Doll et al. 1993). Even users of mouthwash containing a high

alcohol concentration are at increased risk for cancers of the oral cavity and pharynx (Doll et al. 1993; Kato and Nomura 1994).

Alcohol acts synergistically with tobacco to dramatically increase the risk of cancers of the oral cavity, pharynx, larynx, and esophagus (Doll et al. 1993; Longnecker 1995), that is, above that for alcohol or tobacco use alone.

Stomach and Pancreatic Cancers. An increased risk of gastric or stomach cancer among alcohol drinkers has been identified in several, but not the majority, of case-control or cohort studies. In 1988, the IARC concluded that there was insufficient evidence of causation. There exist plausible mechanisms by which alcohol consumption might play a role in gastric cancer, particularly in cancers of gastric cardia, the uppermost portion of the stomach adjoining the esophagus. The link between alcohol use and chronic gastritis (stomach inflammation) is clear, although progression from chronic gastritis to neoplasia is less well understood and probably involves other factors in addition to alcohol (Bode and Bode 1992, 1997). A detailed review of the evidence concluded that a role for alcohol in stomach cancer cannot be ruled out completely, but there is insufficient evidence to demonstrate that alcohol plays a direct role (Doll et al. 1993).

A similar situation may exist for pancreatic cancer. Alcohol is a cause of chronic inflammation of the pancreas; thus, a link between alcohol and pancreatic cancer is conceivable, though unproven (Doll et al. 1993). Recently, researchers found alcohol use to be associated with one type of cancer of the esophagus—esophageal squamous cell carcinomas—but not adenocarcinomas of the esophagus or gastric carcinomas (Gammon et al. 1997).

Colorectal Cancer. Comprehensive reviews have found evidence of a weak, positive association between alcohol and colon and rectal cancers (Doll et al. 1993; Longnecker 1992; Longnecker et al. 1990; Seitz and Pöschl 1997). More recent studies indicating a weak association between alcohol and colon cancer suggest that smoking may serve as a trigger, or initiator, of this cancer (Yamada et al. 1997). In some cases of rectal cancer, the metabolite acetaldehyde may act in conjunction with alcohol, playing a role as a cocarcinogen (Seitz and Pöschl 1997).

Breast Cancer. An association between alcohol and breast cancer has been suspected for two decades, but a number of overviews have concluded that the evidence is not sufficiently compelling to report a causal relationship (English et al. 1995; IARC 1988; McPherson et al. 1993).

Recent meta-analyses have defined a modest, direct relationship between alcohol intake and risk of breast cancer (Longnecker 1992, 1994; Longnecker et al. 1988; Smith-Warner et al. 1998; WCRF/AICR 1997). At least one such study, however, found a stronger association with heavy drinking (Howe et al. 1991).

Epidemiologic evidence indicates that alcohol consumption may increase breast cancer risk in women using hormone replacement therapy following menopause (Zumoff 1997). The Women's Health Study indicated such an association (Colditz 1990), as did the Iowa Women's Health Study (Gapstur et al. 1992), but a third study did not (Friedenreich 1994). Whether alcohol is more strongly associated with pre- or postmenopausal breast cancers remains uncertain (Schatzkin and Longnecker 1994).

For a more detailed discussion of the role of alcohol in breast cancer, see the chapter on medical consequences.

Prostate and Endometrial Cancers. In general, studies examining whether alcohol use influences the development of prostate cancer have so far failed to find any consistent significant relationships, particularly at low and moderate levels of alcohol intake (Breslow and Weed 1998; Longnecker 1994; WCRF/AICR 1997). Similarly, no consistent relationship between alcohol consumption and risk for endometrial cancer has been observed (Newcomb et al. 1997).

Psychosocial Consequences and Cognitive Effects

Stress Reduction

Alcohol use plays a role in many social activities, from the "business lunch" to the parties to the special occasions, such as gift giving. The benefits to those who drink during social occasions are greatly influenced by culture, the setting in which drinking occurs, and people's expectations about alcohol's effects (Goldman et al. 1987; Heath 1987; Leigh 1989; Leigh and Stacy 1991).

In the few studies available of people who reported receiving psychological benefits from alcohol use, the number of benefits reported correlated with how much alcohol they drank as well as with how often they drank heavily (Hauge and Irgens-Jensen 1990; Mäkelä and Mustonen 1988). Stress reduction, mood elevation, increased sociability, and relaxation are the most commonly reported psychosocial benefits of drinking alcohol (Baum-Baicker 1985; Hauge and Irgens-Jensen 1990; Leigh and Stacy 1991; Mäkelä and Mustonen 1988). Alleviating psychological stress may be the most significant of these potential benefits, since stress reduction is reported to contribute to a lowered risk of cardiovascular disease and other health problems (Klatsky 1996; Pohorecky 1990; Poikolainen 1994; Zeichner et al. 1983). However, studies have not measured the effectiveness of alcohol use relative to other means for reducing stress-related diseases.

There is extensive evidence indicating that people who suffer psychological distress and rely on alcohol to relieve their stress are more likely to develop alcohol abuse and dependence (Castaneda and Cushman 1989; Kessler et al. 1996, 1997). Even moderate amounts of alcohol can be harmful to people with mood and anxiety disorders because their symptoms are likely to worsen, and they may experience adverse drug interactions if they are taking medication (Castaneda et al. 1996).

Alcohol Dependence and Abuse

One known risk of alcohol use is alcohol dependence and abuse. The National Longitudinal Alcohol Epidemiologic Survey (Grant et al. 1994), a U.S. household survey of more than 42,000 people, found that 7 percent of adults met the criteria for alcohol dependence, abuse, or both. Alcohol dependence means that a person continues to drink despite experiencing significant alcohol-related problems and cognitive, behavioral, and physiologic symptoms, such as physical withdrawal or the need to drink increasingly large amounts. Alcohol abuse is characterized by continued drinking despite adverse effects on family or work, trauma, or negative health consequences (American Psychiatric Association 1994; World Health Organization [WHO] 1992).

Because vulnerability to alcohol dependence varies greatly among individuals, it is difficult to assess the risk of dependence in relation to how much a person drinks. Two persons exposed to alcohol in exactly the same way may or may not have the same outcome for many reasons, including genetic differences, personality, behavioral features, and environment. Any of these differences may alter a person's level of risk in relation to any of the outcomes discussed in this overview (trauma, cancer, and cardiovascular disease for example), but individual variation is particularly important for alcohol dependence. It is unclear whether researchers can adequately quantify the risk of dependence arising from moderate drinking, in the absence of progression to heavy drinking or binge drinking, without taking individual differences into account.

Psychiatric Comorbidity. Most mental disorders occur much more often than expected by chance among people who are abusing alcohol or are alcohol dependent (Kessler et al. 1996). Of these individuals, those who are alcohol dependent are more likely than alcohol abusers to have mental disorders. In fact, alcohol dependence elevates the risk for all types of affective and anxiety disorders (Kessler et al. 1996).

One recent study found that alcohol consumption is related to the lifetime prevalence of mental disorders (Ross et al. 1997). In this study, current at-risk drinkers, defined as individuals who had consumed at least 29 alcoholic drinks in the

previous week, had approximately twice the risk of mental disorder as lifetime abstainers (Ross et al. 1997). The likelihood of having an antisocial personality disorder was very high for current at-risk drinkers compared with lifetime abstainers. In addition, current at-risk drinkers were two to three times as likely as lifetime abstainers to have mood disorders and between one-and-a-half and two times as likely to have anxiety disorders. Unlike in previous studies (Leifman et al. 1995; Lipton 1994; Vaillant 1995), Ross and colleagues found no protective effect for any kind of drinking pattern (Ross et al. 1997).

A detailed review of the literature in this research area can be found elsewhere (National Institute on Alcohol Abuse and Alcoholism).

Cognitive Performance

Although the relationship between heavy alcohol consumption and cognitive impairment is well established, the effects of moderate drinking on the ability to perform cognitive tasks, including remembering, reasoning, and thinking, are largely unexplored.

Most studies of the relationship between alcohol consumption and dementia, notably Alzheimer's disease (Tyas 1996), have failed to find statistically significant associations. However, several recent studies suggest that moderate alcohol consumption may have a positive effect on cognitive function. In an analysis of baseline data (data collected at the beginning of a study) for persons aged 59 through 71 who were enrolled in the Epidemiology of Vascular Aging Study in France, moderate alcohol consumption was associated with higher cognitive functioning among women but not men after a number of possible confounding variables were controlled for (Dufouil et al. 1997).

Another study, which followed 3,777 community residents in France who drank primarily wine, found a markedly reduced risk of the incidence of dementia among moderate drinkers relative to abstainers (Orgogozo et al. 1997). This analysis controlled for age, gender, education, occupation, and baseline cognitive functioning. Observations from at least one study showed that the relationship between higher cognitive functioning and moderate drinking was confined to men with cardiovascular disease or diabetes, both of which are associated with impaired circulation (Launer et al. 1996). An understanding of the mechanisms by which alcohol may affect the brain will enable researchers to clarify the relationship between alcohol consumption and cognitive performance.

Effects on Society of Alcohol Use: Injuries and Violence

Researchers have identified and classified a wide variety of adverse consequences for people who drink and their families, friends, co-workers, and others they encounter (Edwards et al. 1994; Harford et al. 1991; Hilton 1991*b*,*c*). Alcohol-related problems include economic losses resulting from time off work owing to alcohol-related illness and injury, disruption of family and social relationships, emotional problems, impact on perceived health, violence and aggression, and legal problems.

The risk of such consequences for the individual varies widely and depends on the situation. However, researchers have found a general trend toward an increased risk of adverse effects on society as the average alcohol intake among individuals increases (Mäkelä and Mustonen 1988; Mäkelä and Simpura 1985). The pattern of drinking also is important in determining the risk of alcohol-related problems. Variables such as the frequency of heavier drinking occasions (Midanik 1995; Midanik et al. 1996; Room et al. 1995) and the frequency of drinking to intoxication (Harford et al. 1991; Hilton 1991*a*; Knupfer 1984; Midanik 1995) help to predict potential problems related to alcohol, even after average volume of intake is controlled for.

Injuries

Alcohol use is associated with increased risk of injury in a wide variety of circumstances, including automobile crashes, falls, and fires (Cherpitel 1992; Freedland et al. 1993; Hingson and Howland 1993; Hurst et al. 1994). The

increased risk of injury stems primarily from reduced cognitive function, impaired physical coordination and performance, and increased risk-taking behavior (Koelega 1995). In addition, alcohol increases the likelihood of more serious injury and lowers the probability of survival because of its effects on the heart and circulatory system (Fuller 1995; Li et al. 1997). Culture and drinking environment also influence the relationship between alcohol and various types of injury (Cherpitel 1997*a,b*).

Research shows that as people drink increasing quantities of alcohol, their risk of injury increases steadily and the risk begins to rise at relatively low levels of consumption (Cherpitel et al. 1995). An analysis of risk in relation to alcohol use in the hours leading up to an injury has suggested that the amount of alcohol consumed during the 6 hours prior to injury is related directly to the likelihood of injury occurrence (Vinson et al. 1995). The evidence showed a dose-response relationship between intake and injury risk—the more a person drank, the greater the risk—and found no level of drinking to be without risk.

In contrast, two studies of injury among older adults reported a U-shaped relationship between alcohol use and occupational injury (Zwerling et al. 1996) and between alcohol use and traumatic deaths (Ross et al. 1990). In these studies, abstaining was associated with a higher risk of injury than were low to moderate levels of alcohol intake. However, abstinence among the elderly may be related to existing health or cognitive problems, which, in turn, are related to risk of injury (Zwerling et al. 1996).

The pattern of drinking, such as binge drinking, clearly relates to the relative risk of injury, with risk increasing markedly as blood alcohol concentration rises (Hurst et al. 1994). Tolerance to the effects of alcohol may mediate the risk and severity of injury (Li et al. 1997), but the degree of protection is limited. Both frequent heavy drinking and frequent drunkenness are associated with injury, particularly that resulting from violence (Cherpitel 1996). Variation in the amount a person drinks on different occasions appears to have the strongest relationship with a high risk of injury; in contrast, consistently drinking small amounts of alcohol across occasions is associated with a lower risk of injury (Gruenewald et al. 1996*a,b*; Treno et al. 1996).

Violence

Patterns of alcohol consumption also increase the risk of violence and the likelihood that aggressive behavior will escalate (Cherpitel 1994; Martin 1992; Martin and Bachman 1997; Norton and Morgan 1989; Zhang et al. 1997). Alcohol appears to interact with personality characteristics, such as impulsiveness and other factors related to a personal propensity for violence (Lang 1993; Zhang et al. 1997). Violence-related trauma also appears to be more closely linked to alcohol dependence symptoms than to other types of alcohol-related injury (Cherpitel 1997*b*). See the section "Alcohol and Violence" later in this chapter for a more detailed discussion.

Assessing Risks and Benefits: Mortality, Morbidity, and Disability

The relationships and studies described in this section reflect the current state of knowledge and take into account concerns about the methodological rigor of epidemiologic studies in the field of alcohol and health. Many of these relationships have proven to be stable across studies, settings, and research designs. Research on the biological underpinnings of the most important relationships, such as between alcohol and CHD or alcohol and some cancers, has identified possible mechanisms through which alcohol can have an impact on these diseases.

Research findings continue to confirm an association between moderate drinking and lower CHD risk. Research is now in progress to clarify the extent to which alcohol itself, or other factors or surrogates such as lifestyle, diet, exercise, or additives to alcoholic beverages, may be responsible for the lower risk. Broader means of quantifying the relationships between relative risks and specific consumption levels and patterns are needed to more clearly and simply describe epidemiologic findings and translate them into improved public health strategies.

Overall Mortality

The overall impact of alcohol consumption on mortality can be assessed in two ways (Rehm and Bondy 1998): (1) by conducting meta-analyses using epidemiologic studies that examine all factors contributing to mortality, or (2) by combining risk for various alcohol-caused diseases with a weighted prevalence or incidence of each respective disease.

The meta-analysis approach to assessing overall mortality was used by researchers to examine the results of 16 studies, 10 of which were conducted in the United States (English et al. 1995). In this overview, researchers found the relationship between alcohol intake and mortality for both men and women to be J-shaped curves: the lowest observed risk for overall mortality was associated with an average of 10 grams of alcohol (less than one drink) per day for men and less for women. An average intake of 20 grams (between one and two drinks) per day for women was associated with a significantly increased risk of death compared with abstainers. The risk for women continued to rise with increased consumption and was 50 percent higher among those consuming an average of 40 grams of alcohol (between three and four drinks) per day than among abstainers. Men who averaged 30 grams of alcohol (two drinks) per day had the same mortality as abstainers, whereas a significant increase in mortality was found for those consuming at least 40 grams of alcohol per day.

The effect found in this evaluation—that, in industrialized countries, low to moderate drinking is associated with reduced overall mortality—holds true in more recent research in which epidemiologists adjusted statistically for the "unhealthy abstainer" effect. Including former drinkers in abstainer groups also can influence, and confound, the shape of the curve used to describe the relationship between alcohol intake and mortality (Fillmore et al. 1998*a*,*b*; Leino et al. 1998). (See the box "Does Abstaining Increase Risk?" For a discussion of the unhealthy abstainer effect, see Shaper 1990*a*,*b*; Shaper et al. 1988; Fillmore et al. 1998*a*,*b*; Leino et al. 1998. For examples of statistical control of this effect, see Fuchs et al. 1995; Rehm and Sempos 1995*b*.)

The proposed J-shaped relationship between alcohol intake and mortality does not apply in all cases, however. For example, because most of the physiologic benefit of moderate drinking is confined to ischemic cardiovascular conditions, such as CHD, in areas of the world where there is little mortality from cardiovascular diseases, alcohol provides little or no reduction in overall mortality. Rather, the relationship between intake and all-cause mortality assumes more of a direct, linear shape (Murray and Lopez 1996*c*), with increasing consumption associated with higher overall mortality. The same holds true for people under age 45, who have little ischemic cardiovascular mortality (Andréasson et al. 1988, 1991; Rehm and Sempos 1995*a*).

The impact of alcohol on all-cause mortality also changes with the measure used. For example, although studies have found that more deaths are prevented than are caused by alcohol in some countries, such as Australia (English et al. 1995) and Canada (Single et al. 1996, 1999), this relationship is reversed if years of life lost are considered. In other words, alcohol consumption causes more years of life lost than gained in these and other industrialized countries (Murray and Lopez 1996, 1997*a*) because even with the assumption that alcohol protects against ischemic heart disease, CHD tends to occur later in life, whereas harm resulting from injuries or other diseases tends to occur more often at younger ages. This is likely to be the case for the United States as well. (When interpreting these findings, it is important to keep in mind that the evaluations are based on the hypothesis that any level of alcohol consumption is beneficial with respect to CHD [English et al. 1995; Murray and Lopez 1996*c*; Single et al. 1996]. At least one recent study found an upturn in risk for CHD among women who were heavier drinkers [Rehm et al. 1997*a*], but these data have not yet been replicated.)

Researchers have examined the overall relationship between alcohol consumption and mortality

Does Abstaining Increase Risk?

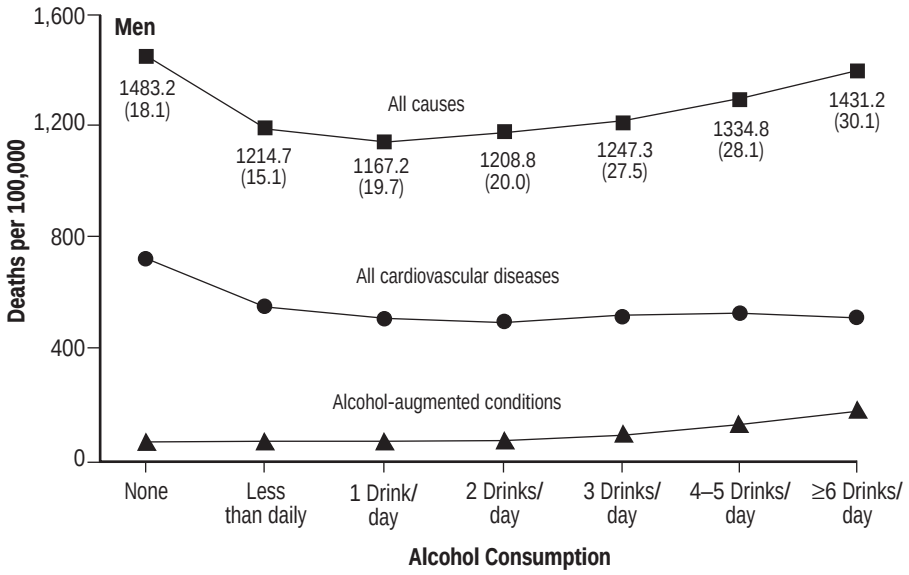
Epidemiologic evidence has shown that people who drink alcohol heavily are at increased risk for a number of health problems. But some studies described in this section suggest that individuals who abstain from using alcohol also may be at greater risk for a variety of conditions or outcomes, particularly coronary heart disease, than persons who consume small to moderate amounts of alcohol.

This type of relationship may be expressed as a *J-shaped* or *U-shaped curve*, which means that the risk of a disease outcome from low to moderate drinking is less than the risk for either abstinence or heavier drinking, producing a curve in the shape of the letter J or U (figure 1).

By examining the lifestyle characteristics of people who consume either no alcohol or varying amounts of alcohol, researchers may uncover other factors that might account for different health outcomes. For example, gender, age, education, diet, and social involvement are among the factors that may be taken into account in determining relative risk of disease.

Similarly, people may quit drinking because of health problems, or even if that is not the case, former drinkers may have characteristics that contribute to their higher mortality risk, such as smoking, drug use, and lower socioeconomic status. If former drinkers are included in the abstainers group, they may make alcohol appear to be more beneficial than it is. Therefore the best research studies will distinguish between former drinkers and those who have never used alcohol.

Figure 1: Rates of death from all causes, all cardiovascular diseases, and alcohol-augmented conditions from 1982 to 1991, according to base-line alcohol consumption



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through conducting studies called time-series analyses, in which changes in overall mortality are related to changes in alcohol consumption. A recent study of 1982–90 data from 25 European countries estimated that increases or decreases of 1 liter in per capita consumption of pure alcohol were associated with corresponding increases or decreases of about 1 percent in all-cause mortality rates (Her and Rehm 1998). A recent analysis of European data from the turn

of the century (Norström 1996) indicated similar findings. Results from this type of analysis on the aggregate level contrast with results based on individual-level studies. Since aggregate-level analyses are quite scarce, more such studies would help to determine if these types of results can be replicated in different regions and time periods.

Morbidity and Disability

Quantifying the level of disability and morbidity related to alcohol can be difficult, in large part because few standardized measures exist. Both nationally and internationally, there is less information available on morbidity and disability than on mortality. In addition, the morbidity data are less reliable (Murray and Lopez 1996*a*), and existing measures for health-related disabilities are not standardized, often varying from country to country (Goerdt at al. 1996) because the current international classification, the *International Classification of Impairments, Disabilities and Handicaps* (ICIDH) (WHO 1980), is not used routinely in health service delivery in most countries, including the United States. This lack of standardization may change with the use of the new revision of the ICIDH, which will include a standardized assessment instrument (WHO 1997).

The most stable indicator of morbidity in industrialized countries appears to be hospitalizations. The risks of alcohol consumption clearly outweighed the benefits with regard to hospitalizations in Australia (English et al. 1995) and Canada (Single et al. 1999).

On the basis of measures of well-being or symptoms of depression or stress, several studies have found that both abstainers and heavily drinking persons report poorer subjective health than low to moderate drinkers (Fillmore et al. 1998*a,b*; Lipton 1994; Neff and Husaini 1982; Poikolainen et al. 1996). Moderate drinkers also may be more likely to have attributes that contribute to good mental and physical health (Kunz, 1997; Lipton 1994; Poikolainen et al. 1996). In one study, however, the J- or U-shaped association between alcohol use and poor subjective health was observed even after a number of such attributes were controlled for (Poikolainen et al. 1996). As with estimates of morbidity, measures that accurately and reliably capture the relationship between alcohol and disability are clearly needed.

Disability-Adjusted Life Years

One way to quantify the relationship between alcohol and health-related consequences is to use a measure called the disability-adjusted life year (DALY), which may prove useful in summarizing the effects of alcohol on the full spectrum of health outcomes (Murray and Lopez 1996*b*; see also the discussion of the Global Burden of Disease Study below). In addition to serving as a descriptive measure, the DALY provides a potentially useful tool for health policy purposes. Use of the DALY may assist policy makers in allocating resources for health care (WHO Ad Hoc Committee on Health Research Relating to Future Intervention Options 1996) and may allow for better measurement of specific policies or interventions designed to reduce harm or improve health. This measure does have its shortcomings, however, and must be considered together with other, more conventional approaches to balancing the risks and benefits of alcohol consumption on health and social well-being.

In the Global Burden of Disease Study (Murray and Lopez, 1996, 1997*b*), the researchers combined years of life lost and years lived with disability into a single indicator, DALY, in which each year lived with a disability was adjusted according to the severity of the disability (Murray and Lopez 1997*b,c*). Within this framework, the researchers identified three effects of alcohol: harmful effects in relation to injuries, harmful effects in relation to disease, and the protective effect in relation to ischemic heart disease (Murray and Lopez 1996*c*). Overall, the research team found that alcohol accounted for 3.5 percent of the global burden of disease (that is, mortality and disability together), 1.5 percent of all deaths, 2.1 percent of all life years lost, and 6 percent of all the years lived with disability (Murray and Lopez 1997*c*). In other words, the relative effect of alcohol on disability was considerably larger than its effect on mortality.

The Global Burden of Disease Study found tremendous differences in alcohol's impact on disability across different regions of the world. The most pronounced overall effect was observed in established market economies (mainly high-income as opposed to developing regions—10.3 percent of all DALY's in these regions were attributable to alcohol), Latin America and the Caribbean (9.7 percent), and the former socialist economies of Europe (8.3 percent). The researchers found the smallest effect of alcohol in the middle eastern crescent, which is not surprising given the region's high proportion of abstinent Islamic populations (Murray and Lopez 1997*a*).

Of course, these calculations can be only as precise as the underlying data. As mentioned above, there is a lack of data sources for alcohol-related morbidity and disability in all regions of the world, including the United States. Since the findings of the Global Burden of Disease Study indicate that alcohol may have a greater effect on nonfatal than fatal health consequences (for example, researchers have estimated 15.6 percent of all life years lost to disability in established market economies were due to alcohol, compared with 5.1 percent of all life years lost due to mortality) (Murray and Lopez 1996*b*, 1997*b*), more intense research efforts in this area will be important because of the high public health relevance.

In Closing

Epidemiologic studies have long provided evidence of the harm alcohol can cause to individual health and to society as a whole. Newer studies have identified an association between low to moderate alcohol consumption and reduced CHD risk and overall mortality. The most significant association with lower CHD risk is largely confined to middle-aged and older individuals in industrialized countries with high rates of cardiovascular diseases. Elucidation of the mechanisms by which alcohol affects CHD risk will clarify the relationship and may enable scientists to develop pharmacologic agents that could mimic or facilitate the positive effect of alcohol on health (Hennekens 1996), perhaps by augmenting the effects of other health-improving behaviors such as engaging in physical activity, eating a low-fat diet, and not smoking.

Guidelines to low-risk drinking exist in many countries (Bondy et al. in press; Hawks 1994; UK Inter-Departmental Working Group 1995; USDA 1995). At this point, research clearly indicates that no pattern of drinking is without risks. However, for individuals who continue to consume alcohol, certain drinking patterns may help reduce these risks considerably.

Among teenagers and young adults in particular, the risks of alcohol use outweigh any benefits that may accrue later in life, since alcohol abuse and dependence and alcohol-related violent behavior and injuries are all too common in young people and are not easily predicted. To determine the likely net outcome of alcohol consumption, the probable risks and benefits for each drinker must be weighed. These assessments are based on the individual drinker's consumption levels, his or her personal characteristics (such as age or preexisting risk factors for CHD), and subjective values, as well as on social considerations (Dufour 1996). Overall, within the entire picture of costs and consequences, the benefits of limited alcohol use will need to be weighed carefully against its significant costs to individuals and to society.

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