AIM Alcohol in Moderation

For more information please email Helena.Conibear@aim-digest.com or Alison.Rees@aim-digest.com

Alcohol consumption and the elderly, do adult responsible drinking guidelines apply?

by Dr Erik Skovenborg, The Scandinavian Medical Alcohol Board

The Royal College of Psychiatrists in London published a report in June relating primarily to problems of unrecognized alcohol misuse among the elderly. The report provides guidelines for psychiatrists and family physicians on how to find and how to treat elderly people who misuse alcohol and drugs[1]. A few pages of the lengthy report, however, concern the evidence base for a proposed reduction of sensible limits of alcohol intake for older people and state: "Current recommended 'safe limits' for alcohol consumption are based on work in younger adults. Because of physiological and metabolic changes associated with ageing, these 'safe limits' are too high for older people; recent evidence suggests that the upper 'safe limit' for older people is 1.5 units per day or 11 units per week. In older people, binge drinking should be defined as >4.5 units in a single session for men and >3 units for women."

A UK unit is 10 ml or 8 grams of pure alcohol and The Royal College of Psychiatrists' suggestions for sensible limits for older people are in accordance with the recommendations from the American Geriatrics Society[2] and the National Institute on Alcohol Abuse and Alcoholism[3]. The American organisations recommend that older adults who have no contraindications to alcohol use limit their intake to no more than one drink per day. One American Standard Unit of Alcohol is 18 ml or 14 grams of pure alcohol.

Is there an evidence base to justify these reduced daily guidelines for healthy elderly consumers?

Coronary heart disease is the leading cause of death in older people, and the obvious coronary health benefits of a moderate alcohol consumption found in several large population studies highlight the considerable difficulty in balancing the apparent risks and benefits of alcohol use. Even though very little is known about the potential for a social movement backlash if a guideline is perceived as overly restrictive, the repeatedly demonstrated benefits of a light to moderate alcohol intake call for an updated and realistic evaluation of the potential risks and benefits of alcohol consumption beyond one drink per day in the elderly population.

Alcohol metabolism and tolerance in older people

The National Institute on Alcohol Abuse and Alcoholism and The Royal College of Psychiatrists classifies greater intake than 14 grams of pure alcohol per day as at-risk drinking for older people, partly because of the greater sensitivity of older adults to the physiological effects of alcohol. Among the physiological and metabolic changes associated with ageing and decreasing alcohol tolerance, dwindling body water is the most important problem according to NIAAA. "Between the ages of 25 and 60, the proportion of total body weight represented by fat almost doubles in men and increases by 50% in women. As lean body mass diminishes and adipose tissue increases, the volume of total body water decreases. Because of the dramatic changes in body fat and lean body mass among men as they age, for older men no more than one drink a day is a more prudent definition of moderate"[4].

The issue of dwindling body water through the years

Mary Dufour et al quote a Canadian monograph "Drugs and Aging" for the problem of dwindling body water through the years[5]. The issue of body water is discussed in the chapter "Age-Related Changes" with a reference on page 9 to an old investigation from Rochester, USA, where the volume of lean body mass was estimated from repeated assays of 40K isotope counting. [6] Longitudinal observations on body weight and estimated lean body mass for six male subjects from Rochester showed a decline in lean body mass in four, an increase in one subject and the

observations for the last one was difficult to interpret. In thirteen additional subjects studied with two assays of 40K over an interval of time the average loss of lean body mass was 0.24 kg per year. In the 42 years following age 25 lean body mass declined from 59 to 47 kg in males and from 40 to 35 kg in females.

Recent data on Total Body Water

More recent data on aging, lean body mass and total body water (TBW) have told another story. For clinical purposes TBW has been estimated by anthropometric equations (formulae based on age, sex, weight, and height) developed by Watson et al[7].

- **TBW (litres) for males**: 2.447 – (0.09516 x years of age) + (0.1074 x height in cm) + (0.3362 x weight in kg).
- **TBW (litres) for females:** - 2.097 + (0.1069 x height in cm) + (0.2466 x weight in kg).

Watson et al's anthropometric equations indicate that age is not a significant variable in the prediction equation for females. The equation for males includes age as a variable, but supposing no change of height and weight during the years a 25-year-old male (height 175 cm, weight 75 kg) would loose only 4 litres of body water (44 litres to 40 litres) en route to his sixty-seventh birthday.

Data for the Watson formula were selected from 458 men and 265 women from 30 different studies including data from numerous individuals born before the occurrence of the secular trend towards increasing body size and fatness during most of the 20th century. Chumlea et al has presented total body water reference values and new prediction equations for adults based on four data sets containing a total of 604 white men, 128 black men, 772 white women, and 191 black women who were 18 to 90 years old[8]. TBW in these healthy adults is relatively stable through a large portion of adulthood, and according to the most recent equation a 25-year-old male is going to loose only 1.3 litres of body water en route to his sixty-seventh birthday.

Cross-sectional data versus longitudinal studies

The reported age and sex trends in TBW were derived from analyses of cross-sectional data. Such analyses cannot demonstrate a valid effect of age because the independence of each subject and potential cohort effects. The prerequisite to demonstrate a real change of TBW with age requires the validity that comes from a longitudinal study of individuals followed over time. The sample size of Forbes & Reina was indeed very small, and the findings could be considered possibly anecdotal. Chumlea et al presents data from a study sample of 274 men and 292 women between 18 and 64 years of age observed at regularly scheduled visits in The Fels Longitudinal Study[9]. The mean ratio of TBW to weight of participants in the study declined with age as a function of a decrease of fat-free mass (FFM) and an increase in body fatness. In men, the mean TBW/weight declined from approximately 58% at age 18 years to approximately 46% at age 64 years. In the women TBW/weight decreased from 48% at age 18 years to 43% at age 64 years. A study of eleven men and 14 women aged 23-46 years and 10 men and 11 women aged 63-81 years confirmed the decrease of fat-free mass in older subjects: FFM in young men: 59.9 ± 8.9 kg; in old men 56.0 ± 6.5 kg; FFM in young women: 44.6 ± 2.5 kg, in old women 38.6 ± 5.8 kg[10]. Even so the TBW volume was not significantly different in the young and old subjects (TBW in young men: 41.1 ± 5.9 L; in old men 40.8 ± 5.8 L; TBW in young women: 30.2 ± 2.3 L, in old women 28.1 ± 3.2 L) due to a significantly higher hydration of fat-free mass in older subjects: TBW:FFM (%) in young men: 68.7 ± 4.0, in old men 73.3 ± 11.4; TBW:FFM (%) in young women 67.5 ± 3.1, in old women 72.5 ± 6.9.

Aging and ethanol metabolism

The Royal College of Psychiatrists' report "Our invisible addicts" refers to altered metabolism as another example of the physiological and metabolic changes associated with ageing and decreasing alcohol tolerance, stating: "As people age, there is a fall in the ratio of body water to fat, decreased hepatic blood flow and inefficiency of liver enzymes". However, the only two relevant references in the psychiatrists' report reach the opposite conclusion that studies in humans have not shown changes related to age in ethanol metabolism[11,12]. In alcohol drinking experiments (wine and pear-schnapps, 0.65 grams of alcohol per kg bodyweight) carried out in 20 men over 60 years old the peak alcohol concentration and the course of the alcohol curve were compared with the results of drinking experiments with young persons published in the literature. No appreciable differences between the two age groups could be detected[13].Vestal et al studied the effect of aging on the distribution and elimination of ethanol in a group of 50 healthy

men ranging in age from 21 to 81 years. Ethanol was administered in a continuous 1-hr infusion at a mean dose of 0.57 gm/kg body weight. At the end of the infusion period peak ethanol concentration in blood water was correlated with age and increased 33% over the adult life span (20 to 90 years of age). The mean peak ethanol concentration in the 25 older men (177 mg/dl) was around 15% higher than the peak ethanol in the 25 younger men (153 mg/dl). However, rates of ethanol elimination were not affected by age[14]. Lucey et al studied the influence of age and gender on blood ethanol concentrations in 14 men and 14 women 21–40 years old and 14 men and 15 women ≥ 60 years old. All subjects were given ethanol (0.3 g/kg) on three occasions: orally after an overnight fast; orally after a standard meal; and by intravenous infusion after a standard meal. Blood ethanol average areas under the curve were significantly greater for ethanol given orally when fasted and IV ethanol when fed but not after ethanol orally in the fed state[15].

In conclusion elderly men will present around 9-15% higher blood ethanol concentrations than younger persons when ethanol is taken without food, however, the effective peak blood ethanol concentration may be significantly higher for elderly women. The age and gender difference seems to be eliminated when ethanol is ingested with a meal.

A list of alleged medical conditions for which alcohol intake is contraindicated

"Old age per se is not a contraindication to moderate alcohol consumption. In older individuals who have no medical conditions for which alcohol is contraindicated (the list is a long one including hypertension, cardiac arrhythmias, ulcers, a history of alcohol abuse or dependence, liver disease, and cognitive impairment to name a few) and who take no drugs (prescription or over-the-counter) that adversely interact with alcohol, the physician may feel comfortable affirming the acceptability of moderate consumption." [16] The prevalence of at-risk drinking in the United States between 1971 and 1974 in older adults (NHANES I and NHANES Epidemiologic Follow-up survey 1992) was 10% (18% of men, 5% of women). The majority of at-risk drinkers (69%) were identified as such because their use of alcohol was deemed risky in the presence of relevant co-morbidities - e.g. drinking 2-3 drinks per day and having gout or anxiety or taking medication for pain. [17]

To support recommendations for abstinence in special medical conditions, an understanding of how health status of low-to-moderate drinkers compares with non-drinkers in each separate case is needed so patients can understand the potential benefits of altering their drinking behaviour. The listing of medical conditions for which alcohol is contraindicated was compiled by the National Institute of Alcohol Abuse and Alcoholism almost 20 years ago, so let us cross-check the current medical evidence base for the long record of alleged contraindications to enjoyment of alcoholic beverages in the autumnal years.

Hypertension

Hypertension is associated with a doubled risk for cardiovascular disease and may account for 30% of events associated with cardiovascular disease[18]. The risk relationship between alcohol consumption and hypertension may best be described as a "threshold effect": little increase in risk is found up to about 20-30 ml of alcohol per day, beyond which blood pressure increases markedly. At a drinking level ≥ 3 drinks/day net harm is usually seen in epidemiological studies. A biological mechanism for this link remains unclear, however, assuming a causal link heavy drinking may be the commonest reversible cause of hypertension[19].

The results of several studies indicate that moderate alcohol consumption is not contraindicated in patients with hypertension. An Italian study of 13 middle-aged, hypertensive, centrally obese individuals (8 women, 5 men) received, in an open randomized crossover experiment, 250 ml red wine (23 g of ethanol) and a placebo equivalent, together with a standardized lunch. Wine with the meal produced a mean reduction of 5.3 mmHg in postprandial blood pressure which persisted for most of the day[20]. Moderate drinking does not appear to pose a cardiovascular risk in men with hypertension, according to an observational study of 11,711 hypertensive men (40 to 75 years of age at baseline) who self-reported alcohol consumption every four years for 16 years. After adjustment for diet and other potential confounders, subjects consuming about 1 to 4 drinks per day (10-49 g alcohol/day) had an 32% lower risk for myocardial infarction than did abstainers. Alcohol consumption did not affect subjects' risk for stroke, cardiovascular-related

mortality, or all-cause mortality[21]. Results from the Physicians' Health Study even suggest that light to moderate alcohol consumption is associated with a reduction in risk of total and cardiovascular mortality in hypertensive men; the reduction in risk was of similar magnitude for men younger than 60 years and for men 60 years and older[22] .

Cardiac arrhytmias

The development of cardiac arrhythmias, particularly atrial fibrillation, after bouts of heavy alcohol consumption, often at weekends or holidays, was first described by Ettinger, who coined the memorable term "Holiday Heart"[23]. Cardiac arrhythmias presenting during weekend or holiday drinking episodes were associated with conduction delays and depressed cardiac performance in a group of patients, who all gave stories of consuming at least 6-10 drinks daily at least ten years. Most studies suggest that a modest and regular intake of alcohol is not contraindicated in people with cardiac arrhytmias.

Atrial Fibrillation: The prevalence of Atrial Fibrillation (AF) goes from 1.1 per 1000 patients at age 40 to 105 at age 90. Evidence for an association between alcohol consumption and risk of AF is conflicting. Cohort studies such as the Framingham Heart Study did not find any association between alcohol consumption and risk of AF[24]. A nested case-control study in the UK General Practice Research Database reported an adjusted relative risk of 2.4 among subjects that consumed more than 42 units (>420 g) of alcohol per week[25]. However, the prospective Cardiovascular Health Study reported that alcohol consumption reduced the risk of AF in older adults, in which the levels of alcohol use were low and in which binge drinking was uncommon[26]. A similar association was found in men but not women in a cohort of people aged over 60 years in Busselton[27]. In the Danish Diet, Cancer, and Health Study the mean consumption of alcohol per day was 28.2 g in men and 13.9 g in women. When using the lowest quintile of alcohol consumption in men (4.1 g alcohol/d) as a reference, the adjusted hazard rate ratio of AF in men in the top quintile (68.7 g/d) was 1.46. In women moderate alcohol consumption did not seem to be associated with risk of AF[28].

Ventricular arrhythmias: Binge drinking has been shown to increase ventricular ectopic activity and to promote the onset of ventricular tachyarrhythmias[29]. These ventricular arrhythmias are potentially life threatening and could be responsible for the finding that binge drinking accounts for a proportion of patients with sudden unexpected death. In a cohort study of survivors of acute myocardial infarction, who have a 4- to 6-fold increased baseline risk of sudden cardiac death, binge drinkers had a 2-fold higher risk of mortality than drinkers who did not binge[30]. When compared with abstainers rather than other drinkers, binge drinking (3 drinks = 40-45 g of ethanol in 1-2 hours) was associated with a hazard ratio of 1.4 (CI 0.9-2.2.). Alcohol intake was inversely associated with mortality among patients who did not report binge drinking with hazard ratios of 0.75 (CI 0.57-1.00) among light drinkers and of 0.59 (CI 0.33-1.04) among heavier drinkers. In Finland the traditional way of drinking infrequently but heavily has remained quite common. In the Kuopio Ischaemic Heart Disease Risk Factor Study the risk of fatal myocardial infarction was substantially increased (relative risk 6.50 (CI 2.05-20.61)) in men whose usual dose of beer was 6 or more bottles per session compared with men who usually consumed less than 3 bottles after adjustment for age and total alcohol consumption[31].

Heart Failure

Heart Failure (HF) is one of the leading causes of hospitalization of the elderly. In the New Haven EPESE cohort study of 2235 elderly persons (mean age 73.7 years) consumption of about 1.5 to 4 drinks per day was associated with a significantly reduced risk of HF: relative risk 0.53 (CI 0.32-0.88) compared with nondrinkers[32]. A meta-analysis of data from 6 studies suggest that infrequent and light-to-moderate drinking is associated with a lower risk of heart failure[33]. However, long-term heavy alcohol consumption has been associated with worsening cardiac function, and chronic alcoholism is one of the most important causes of dilated cardiomyopathy[34], and current HF guidelines discourage alcohol use in HF patients[35]. However, among patients with ischemic left ventricular systolic dysfunction light-to-moderate alcohol intake (1-14 drinks per week) was associated with a reduced risk of all-cause mortality: relative risk 0.78 (CI 0.69-0.89) and trends toward reductions in the risk of arrhythmic death[36]. In a group of 420 HF outpatients no adverse relationship between moderate alcohol consumption (2 or fewer drinks per day) and mortality, hospitalization, or health status (1-year

outcomes) were identified[37]. These data do not support the need for complete alcohol abstinence for all HF patients among those who drink in moderation.

Gastric ulcer

In residents of Olmsted County aged 20 to 64 years, alcohol intake was not associated with dyspepsia[38]. However, in the presence of acute inflammation, irritation or ulceration in the mouth, throat, oesophagus or stomach, strong alcoholic beverages should usually not be used, because the local irritation produced by these beverages will probably cause undue pain and discomfort[39]. Alcoholic drinks are also contraindicated in conditions marked by suspected gastric haemorrhage. Compared with drinkers of <1 drink/week, the relative risks of upper gastrointestinal bleeding among current drinkers ranged from 0.8 for 1-6 drinks/week to 6.3 for ≥ 35 drinks/week[40]. The risk of major upper gastrointestinal bleeding is highest among persons who are both heavy drinkers (≥21 drinks per week) and users of aspirin and other nonsteroidal anti-inflammatory drugs[41].

In the case of healing gastric or duodenal ulcer no rigid rule can be set. Since alcohol stimulates gastric acid secretion, a relation to peptic ulcer disease has long been suspected[42]. Beer, wine and sherry significantly increase gastric acid output (by 57% to 95% of maximal acid output) and release of gastrin up to 5-fold compared with control[43]. However, several large cohort studies did not provide any evidence for a relation between alcohol consumption and peptic ulcer disease[44,45]. A recent Danish prospective cohort study assessing the impact of multiple risk factors, including Helicobacter pylori infection, on the incidence of peptic ulcer disease found a U-shaped relation between alcohol consumption and peptic ulcer disease. The nadir of the distribution was 6-12 drinks weekly due to a low number of ulcers among people who drank moderate amounts of wine.

Ulcer and Helicobacter pylori

Bland diets with no alcoholic beverages have been prescribed for generations in patients with peptic ulcer disease. The diets didn't work, however, and that is no wonder; a recent meta-analysis suggested that 95% of all hospitalised ulcer cases in the USA were attributable to Helicobacter pylori infection, use of nonsteroidal anti-inflammatory drugs and tobacco smoking[46]. The in vitro bactericidal activity of red wine against Helicobacter pylori is very high[47]. In a German population sample the inverse graded relation between alcohol consumption and active infection with Helicobacter pylori was particularly strong for alcohol consumed in the form of wine[48].

Heartburn

Patients with gastro-esophageal reflux disease (GERD) complaining to their doctor of heartburn are met with a list of changes to make in their life-style: avoid alcohol, carbonated beverages, citrus fruit and juices, quit smoking, no coffee, do not eat spicy or fatty foods, be careful with chocolate and don't snack before bed. No published evidence of the efficacy of dietary measures exists, and neither tobacco nor alcohol cessation has been associated with improvement in symptoms[49].

A history of alcohol abuse or dependence

Alcohol dependence is a leading cause of morbidity and premature death, accordingly the best advice for patients with a history of alcohol abuse or dependence is total abstinence.

Alcoholism and mood and anxiety disorders have strong associations when considered on a lifetime basis. The National Epidemiological Survey on Alcohol and Related Conditions (NESARC) covers the comorbidity of DSM-IV substance use disorders and nine independent mood and anxiety disorders in a nationally representative US sample of 43,093 respondents. The prevalence of any current mood disorder was 9.21 percent, representing 19.2 million adult Americans 20 percent of which had a co-morbid substance disorder that was more likely to be alcohol. The prevalence of any current anxiety disorder was 11.08 percent, representing 23 million adult Americans, 15 percent of which had a co-morbid substance use disorder[50]. Individuals with co-occurring mental health and substance use disorders (CMSD) have worse clinical courses and outcomes and are at increased risk of suicide and social and occupational impairment and disability. For these patients total abstinence is mandatory.

Liver disease

The adverse effects of heavy drinking on the liver (hepatotoxicity and impairment of hepatic regeneration) are associated with the

development of liver cirrhosis, a severe disease often leading to death. Some patients develop cirrhosis soon after having undertaken heavy abuse, whereas others remain unaffected for years; the average time is between 10 and 20 years. The Copenhagen City Heart Study (one drink = 12 g alcohol) observed a steep dose dependent increase in the relative risk of alcohol induced liver disease above a "threshold" of 7-13 drinks/week in women and 14-27 drinks/week in men. Women had a significantly higher relative risk of developing alcohol-related liver disease than men at any given level of alcohol intake; at an alcohol intake of 28-41 drinks/week, the relative risk for developing alcohol-induced cirrhosis in was 7.0 (CI 3.8-12.8) for men and 17.0 (CI 6,8-40.8) for women. Of those individuals consuming ≥ 70 drinks/week, only 7% were cirrhotic and only 19% had any evidence of alcohol induced liver disease at all. The study found a rate of development of alcohol induced liver cirrhosis of 1.1% in 60- to 69-year old men with an alcohol intake ≥ 70 drinks/week[51]. The Dionysos Study found that 30 g alcohol/day is the minimal quantity of alcohol compatible with a measurable risk of developing cirrhosis. Only 4% of individuals consuming more than 6 drinks daily had cirrhosis and only 10% had any evidence of liver disease at all. Drinking alcohol outside mealtimes increased the risk of developing alcohol induced liver damage[52]. A new meta-analysis supports the theory that there is a threshold of drinking above which the risk is increased suggesting that the risk increases only with intake of more than 24 grams/day of alcohol for women and 36 grams/day of alcohol for men[53].

Cognitive impairment

In most situations the cognitive potential for performing many tasks generally exceeds what is required, but the gap between level of performance and potential may diminish as people get older. A dose of alcohol may be considered to impose a kind of stress test of task performance and, if older persons are performing closer to their maximum potential, they may be less able to compensate for the alcohol-induced disturbances of their behaviour. If this is the case, then the amount of behavioural impairment induced at a given blood alcohol concentration (BAC) should be greater for older persons. A group of 14 younger pilots (mean age = 27, range 21-34) and older pilots (mean age = 60, range 51-69) flew a Frasca 141 simulator in a flight task that they had previously learned but not practiced for several months. After completing a baseline flight, pilots were tested during either an alcohol (BAC = 0.1%) or a placebo condition. Detrimental effects of alcohol on the main outcome measure was found at both the acute and the 8-hour post-drink (hangover) testing, however, there was no significant difference between the older and the younger pilots' performance of the flight task or in susceptibility to alcohol either while intoxicated or during hangover[54]. Older drivers (>55 years) have consistently the lowest rate of alcohol-impaired driving of any age group[55].

In a study of 57 subjects – 28 in the young (21-40 years) and 29 in the old (> 60 years) group – with a low dose of alcohol (0.3 g alcohol/kg given IV after a standard breakfast) age rather than alcohol accounted for most of the differences in the kind of neural functions that come into play in activities such as walking, driving and writing[56]. Tupler et al examined the effects of aging on alcohol pharmacodynamics over progressive dosing schedules (0.4, 0.6, 0.8, 1.0 g/kg) in groups of young (25.0 ± 2.9 years), middle-aged (41.1 ± 6.6 years), and young-elderly adults (60.9 ± 2.6 years) using three computerized cognitive-neuromotor tasks. Results reflected differences in the patterns but not the magnitude of impairment for elderly subjects. Results failed to confirm that impairment would be either more severe, or more sustained, as a function of aging[57]. The modest effects of aging in responses to alcohol should be viewed in the light of as much as 3- to 4-fold differences in the metabolism of alcohol and 2- to 3-fold differences in behavioural responses to alcohol between different individuals[58].

Alcohol and dementia

Heavy alcohol use have a significant and negative effect on everyday cognitive performance, and the presence of cognitive and neuropsychological deficits have been observed in heavy drinkers[59]. Long-term abuse of alcohol is associated with alcohol dementia. (Wernicke-Korsakoff's Syndrome). Alcoholic beverage consumption may exacerbate cognitive impairment and dementias due to other causes, and recognition of heavy alcohol consumption in cognitively impaired patients is important, as chronic alcohol toxicity represents one cause of potentially reversible dementia[60]. In a study of occurrence

and risk factors of delirium in the Sub-Intensive Care Unit for the elderly, heavy alcohol use was independently associated with delirium[61].

Gout

Patients with gout may be able to enjoy wine in moderation with their meal because the increase in serum uric acid per serving per day is very different for beer: 0,46 mg/dl, liquor: 0.29 mg/dl and wine: 0.04 mg/dl. The study was performed in moderately drinking men and women; the possibility that wine drinking may have an effect on uric acid level at a higher consumption cannot be ruled out[62]. Compared with men who did not drink alcohol the risk of gout was trebled in men drinking more than 5 beers per day. The increase in risk per drink per day was 17%. The increase in risk of gout varied among the individual alcoholic beverages:

Beer: increase in risk per serving per day: 49%;
Spirits: increase in risk per serving per day: 15%;
Wine: no increase in risk with increasing levels of wine consumption.

Beer is the only alcoholic beverage acknowledged to have a large purine content[63].

Adverse alcohol-medication interactions

Many prescription and over-the-counter medications can interact with alcohol, leading to increased risk of illness, injury, or death. Prescription medications are used by 60-78% of older adults[64]. Among the elderly receiving prescriptions, the mean number of drugs prescribed is two to three per patient, and a small minority of the elderly are prescribed a large number of drugs, and these patients deserve special consideration. Presence of chronic disease not only increases the number of prescription drugs, but also increases risk and severity of potential drug-alcohol interactions[65]. Concurrent alcohol and prescription medication use is common in older populations. Older drinkers who take one or more drugs, which place them at potential risk for negative drug-alcohol interaction, represent one-quarter of a random sample of elderly community dwellers[66].Thirty-eight percent of a sample of residents (mean age 83 ± 6 years) of retirement communities in Milwaukee reported using both alcohol and a high risk medication. The alleged high risk drugs commonly used were antihypertensives in 50%, aspirin in 27%, nonsteroidal anti-inflammatory drugs (NSAIDs) in 20%, medication for congestive heart failure in 18%, H2 blockers in 16%, sedatives in 5%, and warfarin in 5%[67].

To exert its desired effect, a drug generally must travel through the bloodstream to its site of action, where it produces some change in an organ or tissue. The drug's effect then diminish as it is metabolized by enzymes and eliminated from the body. The extent to which a dose of a drug reaches its site of action is termed availability. Alcohol can influence the effectiveness of a drug by altering its availability. First, an acute dose of alcohol (single drink) may inhibit a drug's metabolism by competing with the drug for a similar family of drug metabolizing enzymes. This interaction prolongs and enhances the drug's availability, potentially increasing the risk of adverse side effects. Second, in contrast, long-term ingestion of alcohol may activate hepatic drug-metabolizing enzymes, thus decreasing the drug's availability leading to diminished drug efficacy. Third, enzymes activated by long-term alcohol consumption may transform some drugs into toxic chemicals that can damage the liver or other organs. Fourth, alcohol can magnify the inhibitory effects of sedative and narcotic drugs at their site of action in the brain. And finally, some drugs affect the metabolism of alcohol, thus altering its availability and its potential for intoxication and adverse effects[68].

Even if the number of theoretically possible adverse alcohol-drug interactions is high, most of the interactions discussed below have been found in heavy drinkers or alcoholics. Robust data on the actual risk of adverse drug events associated with moderate drinking are extremely limited; e.g. the review below of current literature on alcohol-medication interactions found no evidence for high risk status for antihypertensive and congestive heart failure medication, H2 blockers, statins, and warfarin. These drugs accounted for 89 percent of the alleged adverse drug-alcohol interactions reported in Milwaukee residents.

Acetaminophen: Paracetamol is a safe drug when used in therapeutic doses: up to 1 g every 4 hours and not more than 4 g/24 hours. Some 5-8% of a therapeutic dose of paracetamol is converted to a toxic metabolite; the theoretical single hepatotoxic dose in an adult is normally about 15 g. When a single dose of alcohol is given at or about the same time as paracetamol, it protects against liver damage by competing with the drug for the same family (CYP2E1) of drug

metabolizing enzymes. Long-term heavy use of alcohol causes a modest (a factor of two) and short-lived (about 5 days) induction of CYP2E1 enzymes potentially increasing the hepatotoxicity of paracetamol in alcoholics. Fasting may increase the risk of liver damage by decreasing the major detoxification pathway (glucuronide conjugation) of the toxic paracetamol metabolite in the liver. Chronic alcoholics thus may be at increased risk of paracetamol hepatotoxicity during the first few days of alcohol abstinence, especially if the alcoholic stops drinking due to acute illness including gastrointestinal symptoms and fasting. However, the available evidence does not support claims for a major toxic interaction between alcohol and paracetamol and acute liver damage has never been produced by therapeutic doses of paracetamol[69].

Antibiotics: In combination with acute alcohol consumption some antibiotics may cause disulfiram-like reactions (i.e. flushing, nausea, vomiting, sweating and headache): cephalosporins, chloramphenicol, furazolidone, griseofulvin, metronidazole, nitrofurantoine, quinacrine. The availability of isoniazid and rifampicin, drugs used to treat tuberculosis, is decreased by long-term alcohol use[70].

Anticoagulants: Warfarin is prescribed to retard the blood's ability to clot. In a clinical experiment with seven normal subjects, daily ingestion of 296 ml/day of fortified wine during fasting had no effect on therapeutic anticoagulant blood levels of warfarin[71]. Moderate drinking did not adversely influence the safety of low-dose warfarin in a randomized trial of men enrolled in the CABG Trial[72].

Antidepressants: Alcohol increases the sedative effect of tricyclic antidepressants impairing driving ability[73]. Use of depressant medications is related to consuming alcohol for personal effects reason and having concerns about one's own drinking suggesting that users of antidepressants may be more likely to be at risk for alcohol problems[74]. In patients taking tricyclic antidepressants, alcohol consumption increases the risk of orthostatic hypertension, a sudden drop in blood pressure when a person stands up, especially among the elderly. SSRI's (e.g. fluoxetine, paroxetine, sertraline) have the best safety profile of all antidepressants, even when combined in large quantities with alcohol.

Antidiabetic medications: Alcohol may interact with antidiabetic medications like chlorpropamide, glyburide, and tolbutamide to produce disulfiram-like reactions (i.e. flushing, nausea, vomiting, sweating and headache) in 10-20% of patients receiving these drugs[75].

Antihistamines: Alcohol may intensify the sedation caused by some antihistamines and may cause drowsiness, decreased motor skills and impaired driving ability[76]. The newer antihistamines (cetirizine, desloratadine, mizolastine, fexofenadine) have less interaction with alcohol and may not impair driving task performance[77].

Antihypertensives: In a population of men with hypertension, moderate intake of alcohol was associated with a decreased risk for myocardial infarction but not with risks for total death or death due to cardiovascular disease. Inclusion of the number of antihypertensive medications that patients reported taking in the analyses did not alter the observed associations with alcohol[78].

Antipsychotic medications: Alcohol increases the sedative effect of antipsychotic drugs like chlorpromazine resulting in impaired motor skills and coordination[79].

Antiseizure medication: Acute alcohol intake increases the availability and possible toxicity of phenytoin, while long-term intake may decrease availability, reducing the protection against epileptic seizures[80].

Antiulcer medication: H2-receptor antagonists like cimetidine and ranitidine may increase the availability of alcohol and may produce an increase in blood alcohol concentration, however, the interaction between H2 antagonists and alcohol is clinically insignificant[81].

Aspirin: Alcohol inhibits thromboxane A2 formation and therefore may have a synergistic effect with aspirin as exemplified by an excessive bleeding time. Alcohol enhances the aspirin-induced prolongation of the bleeding time when given simultaneously or up to 36 hours after aspirin ingestion[82]. Older people mixing alcoholic beverages with aspirin to treat pain are in high risk of stomach bleeding.

Immune modulators: Medications like methotrexate that affect immune cell function are associated with risk of liver damage. This risk is increased with alcohol consumption. In case of rheumatoid arthritis a light intake of alcohol well within the recommended limits is allowed. In case of psoriasis it is recommended to avoid alcohol

altogether[83].

Narcotic pain relievers: The combined use of opiates and alcohol enhances the effect of these narcotics on the central nervous system producing drowsiness, sedation, decreased motor skills, decreased cough reflex, increased choking risk, and increased risk of death from overdose[84].

Nonsteroidal anti-inflammatory drugs like ibuprofen and naproxen are known to increase the risk of gastrointestinal complications. The presence of either NSAID use or a history of alcohol abuse led to an odds ratio of 2.9 for severe gastrointestinal events, whereas the presence of both risk factors simultaneously led to an odds ratio of 10.2[85]. An increase in risk of gastrointestinal bleeding has been found if NSAID use was concomitant with three or more alcoholic drinks per day[86].

Sedatives and hypnotics: Benzodiazepines such as diazepam are generally prescribed to treat anxiety and insomnia. The additive effect of benzodiazepines and moderate doses of alcohol may cause drowsiness increasing the risk of accidents and impairing driving ability[87]. Older adults who use psychoactive medications like sleeping pills and tranquilizers are more likely to drink to forget and to relieve tension and anxiety[88].

Statins (lipid-lowering drugs): Patients with coronary heart disease who need to be treated with lipid-lowering drugs could benefit from the effect of alcohol on cardiovascular risk[89]. A moderate consumption of alcohol, in combination with simvastatin, has been shown to increase the beneficial effect upon HDL cholesterol[90]. Alcohol ingestion of 20 g per day for 6 weeks together with fluvastatin 40 mg per day had no effect on the efficacy and safety of fluvastatin treatment in patients with primary hypercholesterolemia[91]. An important issue is the safety of the combination of life-long statin treatment and alcohol consumption. These drugs have the potential to affect liver function, however, co-administration of simvastatin and alcohol in Wistar rats has been proved to be safe[92]. Moderate drinking did not adversely influence the safety of even high-dose lovastatin among men in the CABG Trial[93].

Alcohol – a bane for some elderly

"Ferdinand C. Helwig had a relative who occasionally dined with him. Before and after a full dinner, this relative would have a drink which he enjoyed. His conversation sparkled, and he was full of life. When he later went home to bed, he would have a pleasant, relaxed night of sleep. When he did not dine out, he was neither sparkling, nor vivacious; and he customarily slept badly. His difficulty lay in the fact that his daughter, with whom he lived, would not permit him to drink, because she feared that he might be addicted to alcohol. He was then eighty-three years old," [94]. Alcoholism certainly turns the use of alcohol into a dangerous bane for some of the elderly. Alcohol intake may also be a risk factor for fall injury and fracture especially among shaky old men or women who are unsteady on their feet. A final cause of worry is the association of alcohol consumption and the risk of certain types of cancer.

Late-onset alcoholism

The National Longitudinal Alcohol Epidemiological Survey reported a prevalence of alcohol abuse or dependence for 1.2% for men and 0.3% for women > 65 years old[95]. Most older alcoholics have had alcoholism for many years. In contrast, the concept of late-onset alcoholism characterize those who develop problem drinking later in life. In a sample of 268 alcoholics about 17% reported that they started harmful drinking after the age of 60. Compared with early-onset alcoholics late-onset problem drinkers drank lower amounts of alcohol, underwent fewer detoxifications, suffered from psychiatric comorbidity less often, showed less alcohol-related physical and psychosocial complications, and they had a higher rate of abstinence after 12 months[96]. Contrary to expectation life stressors did not predict drinking problem onset in a prospective study of late-onset problem drinking. Compared with stable non-problem drinkers, late-onset problem drinkers were more likely to report heavier alcohol consumption, greater friend approval of drinking, more reliance of avoidance coping strategies, were more likely to smoke, and were less likely to have acute medical conditions that could potentially be complicated by alcohol consumption. Late-onset problem drinkers reported mild to moderate drinking problems (e.g. confusion, inebriation and family conflict or problems), and spontaneous recovery rates were high[97]. Late-onset alcohol consumption may indicate a different underlying disorder. Before getting demented, patients with Alzheimer's disease are affected by slight cognitive changes in

a pre-clinical phase of 5-8 years. The awareness of this impairment might lead to feelings of help- or hopelessness and self-treatment with alcohol[98].

Alcohol intake as a risk factor for fall injury and fracture

"In an isolated, unsupervised, unobserved environment, one drink in combination with another drug, a slight visual or muscular impairment or other small disability might be just the impetus required to shatter the fragile balance and cause a catastrophe such as a fall resulting in a hip fracture, which leads to a greater loss of movement and perhaps ultimately of the precious freedom to live and function independently – truly a great price to pay," [99].

A review of 26 published studies that assessed the effects of alcohol consumption on falls or fall injuries concluded that four studies found an increased risk for falls or fall injuries associated with exposures ranging from daily use to an average weekly consumption of ≥21 drinks when compared with non-drinkers or individuals consuming ≤11 drink per week. Twenty-one studies found no association between increased alcohol use and falls or fall injuries. In contrast one study found that participants who reported daily use of alcohol had decreased risk for falls compared with non-drinkers[100].

Alcohol use and risk of cancer

The Second Expert Report on Food, Nutrition, Physical Activity, and the Prevention of Cancer was published 2007 by the American Institute for Cancer Research[101]. A chapter dedicated to alcohol and cancer finds the evidence that alcoholic drinks are a cause of cancers of the mouth, pharynx, and larynx, oesophagus, colorectal (men), and breast is convincing. They are probably a cause of colorectal cancer in women, and of liver cancer. The evidence does not show a clear level of consumption of alcoholic drinks below which there is no increase in risk of the cancers it causes. The evidence shows that all alcoholic drinks have the same effect whether beers, wines, spirits, or other alcoholic drinks. The important factor is the amount of ethanol consumed.

However, thresholds were identified in that document (and in many others), such as an increased risk of colorectal cancer is apparent above a threshold of 30 g/day of ethanol for both sexes, and cirrhosis (associated with heavy drinking) is an essential precursor of liver cancer caused by alcohol. The importance of associated smoking in the risk of upper aero-digestive cancers must also be mentioned. In the absence of tobacco smoking there seems to be little or no effect of moderate alcohol consumption on the risk of such cancers. In the Million Women Study increasing alcohol intake was strongly associated with an increased risk of cancers of the upper aero-digestive tract among current smokers, but was not associated with an increased risk in never smokers or past smokers[102].

The Danish Nurse Cohort Study (17 647 nurses followed from 1993 until the end of 2001) analysed the impact of alcohol intake and drinking pattern on the risk of breast cancer[103]. The relative risk of breast cancer was 2.30 (CI: 1.56–3.39) for alcohol intake of 22-27 drinks per week, compared to 1-3 drinks per week. Among alcohol consumers, weekly alcohol intake increased the risk of breast cancer with 2% for each additional drink consumed. Weekend consumption increased the risk with 4% for each additional drink consumed Friday through Sunday. Binge drinking of 4–5 drinks the latest weekday increased risk with 55%, compared with consumption of one drink.

Several analyses mention interference with the metabolism of folates as a mechanism leading to alcohol-related cancer. Like several other studies first prospective study based on a European population showed that the association between alcohol intake and risk of breast cancer was present mainly among women with low folate intake, and there was no association among women with a folate intake higher than 350micrograms per day[104].

Alcohol – a boon for many of the elderly

Health status is closely related to the ageing process. The biological process of ageing reflects the interactions between our genetic inheritance and environmental influences. The ageing process includes progressive and irreversible biological changes, resulting in a growing risk of chronic diseases, cognitive impairments and an impairment of functions[105]. In the Alameda County Study long-term predictors of healthy ageing and high levels of physical functioning were: higher family income level, absence of hypertension, absence of arthritis, absence of back pain, being a non-smoker, having normal weight, and consuming moderate amounts of

alcohol[106].

Alcohol use and psychological benefits

A person's self-rating of health status is an independent predictor of mortality[107]. A cross-sectional analysis of the associations between alcohol intake and subjective health in a random sample drawn from the general population aged 25-64 years in Finland concluded that moderate alcohol intake is related to a self-perception of good health[108]. Satisfaction with quality of life and happiness are key indices of successful ageing. Alcohol use can be associated with psychological and social well-being, which can be considered important health outcomes in their own right. The psychological benefits associated with alcohol consumption include stress reduction, mood enhancement, and cognitive performance[109]. Primary care patients who drank in a frequent, low-quantity pattern generally had better overall Health-Related Quality of Life than patients from other consumption groups[110]. Regular alcohol consumption is associated with increasing quality of life and mood in older Californian men and women[111].

Alcohol use and successful aging

Among 13,894 women in the Nurses' Health Study, investigators prospectively examined alcohol use assessed at midlife in relation to "successful ageing," which was defined as survival to age 70 years, not having a major chronic disease (such as coronary disease, cancer, stroke, diabetes), and having no major cognitive impairment, physical impairment, or mental health problems. Only 11% of the women met these criteria. The results indicate that moderate drinkers, especially those consuming wine and drinking regularly, were more likely to exhibit successful ageing. For average amount consumed, the largest benefit (an increase of 28%) was among women who reported 15.1 – 30 g of alcohol per day (an average of just over 1 to 2 .5 drinks per day), when compared with non-drinkers. The frequency of drinking was especially important: in comparison with non-drinkers, women who drank only on 1 to 2 days per week had little increase in their risk of successful ageing, but those drinking on at least 5 days per week had almost a 50% greater chance of successful ageing[112].

Alcohol use and cognitive vitality

The unimpaired ability to reason is crucial to optimal ageing and survival in older persons. The lifetime risk for a 55-year-old man of becoming demented is 16%, and the lifetime risk for a woman of a woman of the same age is as high as 33%. The results of several studies support the idea that moderate alcohol consumption is associated with better cognitive performance[113]. Of participants in the Whitehall II Study who reported drinking alcohol in the past year, those who consumed at least one drink in the past week, compared with those who did not, were significantly less likely to have poor cognitive function. The beneficial effect extended to those drinking more than 240 g of alcohol per week[114]. Alcohol consumption was beneficial to cognitive function in men and women aged 55-88 years from the Framingham Heart Study. Women who drank moderately (2-4 drinks/day) showed superior performance in many cognitive domains relative to abstainers. For men, superior performance was found within the range of 4-8 drinks/day[115]. In a representative American older cohort over an average of 7 years follow-up period, a pattern of mild-to-moderate drinking, compared to not drinking, was associated with lesser average decline in cognitive domains[116].

The observed relation between alcohol and cognition persists after adjusting the analyses for a number of social and health characteristics, however, older persons who are in good cognitive and physical health may be more likely than less healthy peers to indulge in low-moderate alcohol consumption as part of their social activities[117]. In a community-based sample of subjects aged 70 years and older, drinking was most commonly associated with social activities and few took alcohol to cope with personal situations[118].

Alcohol use and risk of dementia

A reduced risk of cognitive impairment and dementia associated with light to moderate alcohol consumption (1-28 drinks per week) has been observed among older black Americans[119], men with diabetes or cardiovascular disease in the Zutphen Elderly Study[120], older people from the Bordeaux area[121], Framingham residents aged 55-89 years[122], participants if the Treatment Trial of Hypertension in Older Adults[123], elderly French non-ApoE epsilon4 carriers[124], residents of Rotterdam aged 55 and older[125], participants aged 65 years and older of the Canadian Study of Health and Aging[126], very old Swedes from Stockholm[127], Baltimore residents in the Epidemiologic Catchment Area

Study[128], Copenhagen men and women aged 65 years or more[129], subjects aged 45-70 years from the Netherlands[130], elderly American men and women[131,] men and women from Finland aged 65-79 years[132] elderly persons from New York City without the ApoE epsilon-4 allele[133], middle-aged Whitehall civil servants[134], postmenopausal women in the Women´s Health Initiative Memory Study[135], men and women from the British 1946 birth cohort[136], a representative elderly community sample from Pennsylvania[137], retired American nurses[138], men and women aged 60 years and older living in Dubbo, Australia[139], and a sample of oldest-old American women[140].

The benefit of moderate alcohol for cognition has been shown in both men and women, although the amount and pattern of drinking is very different between the two sexes. In a cohort study of Finnish twins occasional excessive alcohol consumption in light to moderate drinkers (binge drinking at least monthly or passing out as a result of excessive alcohol use at least twice during the previous year) was associated with an increased risk of dementia[141]. A recent meta-analysis of 143 papers describing the relative drinking of alcohol and cognition found that moderate drinking seems to reduce the risk of dementia and cognitive decline in older subjects[142].

Alcohol use and physical vitality

Older age is a significant predictor associated with increased rate of functional decline, however, in an American cohort study of 2,581 people aged 65 and older exercise as well as moderate alcohol consumption were associated with decreased rates of functional decline[143]. In a survey of 9704 women 65 years or older non-drinkers had significantly poorer function on all of the 12 performance measures (muscle strength, agility, coordination, gait and balance) except tandem walk compared with current moderate drinkers[144]. An inverted J-shaped curve characterized the association between estimates of alcohol consumption and leisure-time physical activity in the 1990 National Health Interview Survey. The likelihood of displaying a physically active lifestyle (odds ratios) increased from abstinence (1.00) to moderate drinking (1.84), and then declined at heavier consumption (1.61). Stratified analyses yielded similar results with peaks at light or moderate consumption for persons aged 55 and over[145].

Alcohol use and activities of daily living

In a health survey of older adults the low-risk drinkers (< 9 drinks/week for women, < 12 drinks/week for men) scored significantly better than abstainers on all measures of health functioning: General Health, Physical Functioning, Physical Role Functioning, Bodily Pain, Vitality, Mental Health, Emotional Role Functioning, and Social Functioning. Also at-risk drinkers (drinking ≥9 drinks/week for women and ≥12 drinks/week for men) scored significantly better than abstainers on all measures but Mental Health[146]. Heavy alcohol use, however, may contribute to functional decline in older populations. In older women an intake of >14 drinks per week was associated with an impaired function (i.e. difficulty with three or more activities of daily living) compared to non-drinkers[147]. In a prospective study older men who consumed more than 24 g alcohol each day were 20% more likely to sustain a loss of mobility at 4-year follow-up compared to non-drinkers[148]. In an American cohort study the following health behaviours were significantly associated with losing mobility in late life: current smoking, low physical activity, high body mass index, and not consuming small-to-moderate amounts of alcohol[149].

Alcohol use and bone strength

Abuse of alcohol is considered to be an important risk factor for fractures and osteoporosis[150], however, mounting epidemiological evidence indicates a positive association between moderate intake of alcoholic beverages and higher bone mineral density[151]. More limited findings provide some evidence for translation of this association into reduced fracture risk. In a large case-control study in Sweden those women who reported drinking alcohol had a decreased risk of hip fracture (OR 0.80; CI, 0.69-0.93)[152]. In older American men light to moderate alcohol intake is associated with stronger bones; as alcohol intake increased, so did hip and spine bone mineral density. Men with light intake of alcohol (<14 drinks per week) had a lower risk of two or more incident falls than abstainers[153]. In a British study of postmenopausal women (including 1232 twin pairs) wine intake was associated with a positive association with spine bone mineral density[154].

Alcohol use and weight maintenance

Among the 8,236 respondents who participated

in the Third National Health and Nutrition Survey, those who reported drinking one or two drinks per day had about half the risk of obesity as compared to non-drinkers. The odds of obesity were significantly greater among binge drinkers and those consuming four or more drinks/day[155]. In the Diet, Cancer and Health Study, a cross-sectional population study including 25,325 men and 24,552 women from Denmark, the most frequent drinkers had the lowest odds ratios for being obese. The results indicate that frequent drinking of small amounts of alcohol is the optimal drinking pattern regarding weight maintenance[156].

Alcohol use as part of a healthy diet

Several cohort studies have shown that Mediterranean type diet increase longevity. The Mediterranean diet is characterised by a high intake of vegetables, legumes, fruits, and cereals; a moderate to high intake of fish; a low intake of saturated lipids but high intake of unsaturated lipids, particularly olive oil; a low to moderate intake of dairy products, mostly cheese and yogurt; a low intake of meat; and a modest intake of ethanol (men consuming 10 g to 50 g of ethanol per day and women consuming from 5 g to 25 g), mostly as wine. In a multicentre, prospective cohort study of 74,607 men and women, aged 60 or more from nine European countries adherence to a Mediterranean diet was associated with lower overall mortality[157]. In the HALE population adhering to a Mediterranean diet (hazard ratio [HR], 0.77; CI 0.68-0.88), moderate alcohol use (HR, 0.78; CI, 0.67-0.91), physical activity (HR, 0.63; CI, 0.55-0.72), and nonsmoking (HR, 0.65; CI, 0.57-0.75) were associated with a lower risk of all-cause mortality[158].

Alcohol use and risk of diabetes

In a population of middle-aged Dutch women alcohol consumption was associated with a decreased risk of diabetes: odds ratio per 12.5 g/day increment in alcohol use 0.58 (CI 0.49-0.69). Adiponectin appeared to be mediator of this association[159]. In a prospective study of 4655 participants of the Cardiovascular Health Study light to moderate alcohol consumption was associated with a lower incidence of DM among elderly people, irrespective of the type of beverage consumed[160].

In men and women 65 years or older from The Cardiovascular Health Study 9 of 10 new cases of diabetes appeared to be attributable to 5 lifestyle factors including light to moderate alcohol consumption[161].

Alcohol use and risk of coronary heart disease

In middle-aged and elderly men and women from Copenhagen light to moderate alcohol consumption (1-27 drinks per week) was associated with lower mortality[162]. In elderly men and women from Dubbo, Australia, moderate alcohol intake (1-28 drinks per week) appeared to be independently associated with a significant increase in life expectancy[163]. In The Cardiovascular Health Study of 5.888 men and women aged 65 and older, consumption of ≥14 drinks per week was associated with the lowest risk of coronary heart disease: Hazard Ratio's of 0.55 (CI, 0.34–0.91) for consumers of 14 to 20 drinks per week and 0.61 (CI, 0.34–1.11) for consumers of 21 or more drinks per week[164]. In a pooled analysis of 8 prospective studies including 192,067 women and 74,919 men an inverse association between alcohol and risk of coronary heart disease was observed in all age groups; hazard ratios among moderately drinking men (5.0 to 29.9 g/d) 39 to 50, 50 to 59, and ≥60 years of age were 0.58 (CI 0.36 to 0.93), 0.72 (CI 0.60 to 0.86), and 0.85 (CI, 0.75 to 0.97) compared with abstainers. The analyses indicated a smaller incidence rate difference between abstainers and moderate consumers in younger adults (incidence rate difference, 45 per 100,000; CI 8-84) than in middle-aged (incidence rate difference, 64 per 100 000; CI 24-102) and older adults (incidence rate difference, 89 per 100,000; CI 44-140)[165].

Alcohol use and stroke

In a prospective cohort study of 22,071 male physicians, 40 to 84 years old, light-to-moderate alcohol consumption reduces the overall risk of stroke and the risk of ischemic stroke[166]. In a prospective cohort study among 43,685 men from the Health Professionals Follow-up Study and 71,243 women from the Nurses' Health Study the small percentage of subjects who met criteria for 5 healthy lifestyle habits had a dramatic reduction in risk of stroke. The lifestyle factors associated with the largest decrease in risk for stroke were not smoking and consuming alcohol in moderation (men 5 to 30 g/d; women, 5 to 15 g/d)[167]. In the European EPIC Norfolk Study 4 health behaviours (including moderate alcohol

intake 1-14 units a week) combined predicted more than a twofold difference in incidence of stroke in men and women[168]. The weight of the available evidence indicates that light to moderate drinking is associated with a protective effect, whereas heavy consumption is associated with an increased risk of stroke.

Alcohol use and total mortality

The net protective or adverse association between alcohol and mortality from all causes in a particular population is a balance of increased risk of death from alcohol-related causes (such as cirrhosis, cancers of certain sites, accidents) and decreased risk of others (mainly coronary heart disease). Cohort studies using all-cause mortality as an outcome strike this balance implicitly, and these studies can be used to provide estimates of the net effect of alcohol on mortality in a population. However, no guidelines on safe drinking limits should be based on results of mortality studies alone. Prevention of alcohol problems must be based on the full spectrum of epidemiological and clinical research, including results on mortality, morbidity, social consequences and quality of life in general.

In the middle-aged and elderly participants of the American "Cancer Prevention Study II" light to moderate drinking (1-2 drinks per day) slightly reduced overall mortality[169]. In men and women over the age of 65 years from Western Australia alcohol intake of 4 standard drinks per day for men and 2 standard drinks per day for women was associated with lower mortality risk[170]. In a sample of 1,824 individuals between the ages of 55 and 65 during a 20-year follow-up period controlling only for age and gender, compared to moderate drinkers, abstainers had a more than 2 times increased mortality risk, heavy drinkers had 70% increased risk, and light drinkers had 23% increased risk. A model controlling for former problem drinking status, existing health problems, and key socio-demographic and social-behavioral factors, as well as for age and gender, substantially reduced the mortality effect for abstainers compared to moderate drinkers. However, even after adjusting for all covariates, abstainers and heavy drinkers continued to show increased mortality risks of 51 and 45%, respectively, compared to moderate drinkers[171]. In The Health and Retirement Study of US adults aged 55 and older moderate drinkers had a markedly more favorable risk factor profile. After adjusting for demographic factors, moderate drinking (vs no drinking) was strongly associated with less mortality (odds ratio = 0.50, CI 0.40–0.62). When traditional risk factors (smoking, obesity, and comorbidities) were also adjusted for, the protective effect was slightly attenuated (OR = 0.57, CI 0.46–0.72). When all risk factors were adjusted for, the protective effect was markedly attenuated but still statistically significant (OR = 0.72, CI 0.57–0.91)[172].

Drinking habits and drinking advice in old age

Findings from cross-sectional studies measuring quantity of alcohol use indicate that overall consumption declines with age, abstention rate increase, and men drink more than women across all age categories[173]. After adjustment of data from the first National Health and Nutrition Examination Survey (1971-71) for birth year and per capita alcohol consumption, alcohol intake fell by 11% with every decade of ageing[174]. In NHANES I heavy drinkers (men, smokers) tended to reduce their drinking faster than did light to moderate drinkers. A pronounced reduction in numbers reporting risky drinking with increasing age was also found in the UK based GENESiS Study[175]. The Behavioral Risk Factor Surveillance System (sample size 212,510 US adults) found by far the lowest rates of binge-drinking episodes per person per year in older adults ≥ 55 years[176]. A cross-sectional study of alcohol use in 270 healthy older persons showed a decline in percent drinkers with increasing age (slope = -2.7% per year); and the decline in the percent of subjects consuming any alcohol over time was confirmed in a longitudinal analysis of the use of alcohol over a seven-year period[177]. In the Honolulu Heart Program cohort of 1,604 older men current alcohol intake was compared with that found 25 years earlier when the same men were between ages 45-64 and free of cardiovascular disease: only 4% started to drink alcohol, while 30% were reclassified from drinkers to non-drinkers[178].

Some guidelines for low-risk drinking

In "Physician's Guide to Helping Patients with Alcohol Problems" (NIAAA 1995) the National Institute on Alcohol Abuse and Alcoholism offers recommendations for low-risk drinking. For individuals over the age of 65, NIAAA recommends "no more than one drink per day". A standard drink is one can (12 oz.) of beer; a

single shot (1.5 oz.) of hard liquor; a glass (5 oz.) of wine, all of which contain approximately 0.5 ounces of alcohol (14.8 ml = 12 grams of alcohol). In contrast to in the United States, current UK recommendations for older people are the same as for younger adults; men drinking three to four "standard units" of alcohol per day (an average of 1.7–2.25 American size drinks/d) and women drinking two to three standard units (1.1–1.7 American size drinks/d) "will not accrue significant health risk". Most other countries make no specific recommendations for older people; exceptions are Italy, where guidelines for older people are approximately 25% lower than for younger adults, and New Zealand and Australia, where guideline levels are the same for all adults, but older people are advised to consider drinking less.

Balancing the harms and benefits of alcohol consumption

Over the years moderate use of alcohol has been considered beneficial to older individuals, but what constitutes "moderate" depends on age, sex, genetic characteristics, and other factors. The balance of harm (alcoholism, liver disease, accidents, hypertension, hemorrhagic stroke, and some cancers) and benefit (a reduced risk of coronary heart disease, ischemic stroke, diabetes, and dementia) determines the weekly number of drinks associated with the lowest mortality and the highest quality of life in the older. Even moderate consumption of alcohol may carry harms and benefits. In two linked national cohorts (the US Health and Retirement Study and the English Longitudinal Study of Ageing), alcohol consumption in the disputed intake range of more than one to two drinks per day was not associated with greater risks of disability or mortality than the current US recommended level of more than none to one drink per day for older people[179]. An updated review is needed of the evidence base for the lower hazardous drinking definitions for older adults without specific contraindications because over-restrictive limits of consumption are in risk of encouraging nihilistic responses from the public.

Most guidelines on low-risk drinking suggest at least one day per week with no alcohol consumption. The ARF-CCSA joint policy statement states explicitly: "To minimise any risk of dependence, there should be at least one day per week when no alcohol is consumed."[180] The only reason given is that "many studies have shown a relationship between daily drinking and high volume consumption." In their paper "Daily drinking and harm" Walsh & Rehm conclude that there is not sufficient empirical evidence to recommend drink-free days[181].

A unit is a unit is a unit…

One problem in framing guidelines for alcohol use in older people is that standard drinks are defined quite differently in different countries. Three standard drinks in the United Kingdom would correspond to 24 g of pure alcohol, whereas two standard units in Canada contain 27.2 g of pure alcohol. Thus, the use of standard drinks in an international context is highly problematic. Another problem is that the results of most population studies are built on self-report of alcohol intake. Self-report of alcohol consumption may be called into question because of the discrepancy between alcoholic beverage sales data and survey reports of alcohol consumption. In general, comparison studies in the alcohol literature have shown that self-reported alcohol consumption accounts for only 40-60% of alcoholic beverages sold as measured by sales and tax data[182]. Some groups of drinkers defined either by demographics or drinking level, may bias their reports differently. Under reporting of alcohol intake may be explained by response errors, e.g. difficulties in recall of drinking practices and culturally determined socially desirable answers. To advise the public on "sensible" limits of alcohol methods for a correct assessment of intake are needed that both properly rank individuals according to alcohol intake and that also assess correctly the absolute level of intake[183].

Sensible limits of alcohol intake for older people

The ALSWH study provides 6-year longitudinal data on alcohol consumption, survival, and health-related quality of life for 12,432 Australian women (aged 70 to 75 at baseline) who mostly maintained stable levels of alcohol consumption during the study period. Women who did not consume alcohol and who drank rarely were more likely to die. If they survived, they had lower health related quality of life after adjustment for smoking, comorbidity, education, BMI, and area of residence. The health over time of women who drank alcohol at low levels of intake did not differ significantly according to how much alcohol they consumed, providing evidence that applying current alcohol-consumption recommendations

of up to 14 units a week for women to women in these older age ranges is appropriate[184]. In a Danish cohort study the effect of alcohol on mortality did not differ between middle-aged (50-64 years, mean = 56.6 years) and older subjects (>64 years old, mean = 69.9 years). There was a U-shaped risk function in both age groups, and light to moderate drinking (7-27 drinks of 12 g alcohol per week) was associated with the lowest mortality in both elderly men and women[185] .

Ian R. White and fellow statisticians from the London School of Hygiene and Tropical Medicine used data from non-Mediterranean cohort studies to estimate the relation between alcohol consumption and risk of death to find the level of alcohol consumption at which risk is least. Evidence based guidelines for sensible drinking (one unit = 9 g of alcohol) can be derived from the level at which risk is lowest if no more than a 5% increase in risk of mortality is considered acceptable. Women would be advised to limit their drinking to 1 unit a day up to age 44, 2 units a day up to age 74, and 3 units a day over age 75. Men would be advised to limit their drinking to 1 unit a day up to age 34, 2 units a day up to age 44, 3 units a day up to age 54, 4 units a day up to age 84, and 5 units a day over age 85[186].

Pattern of drinking

Emerging literature is showing that patterns of drinking play an important role in determining health outcomes and death in addition to or irrespective of alcohol volume. The usual assessment methods would not differentiate between a drink every day and seven drinks every Saturday, however, some health outcomes of these two drinking patterns differ dramatically. In a Dutch population survey those drinking 6 glasses per occasion 1-2 days per week were significantly more likely to report >3 health problems than those drinking 1-2 glasses per occasion 6-7 days per week[187]. A Danish cohort study of 28,448 women and 25,052 men aged 50-65 years found a different effect of drinking patterns in men and women. For men an inverse association was found between drinking frequency and risk of coronary heart disease across the entire range of drinking frequencies. The lowest risk was observed among men who drank daily: 0.59 (CI 0.48-0.71) compared with men who drank alcohol on less than one day a week. Among women alcohol intake was the primary determinant of the inverse association between drinking alcohol and risk of coronary heart disease; little difference was found between drinking frequency[188]. Participants of an Italian population-based case-control study who drank mainly without food had an adjusted odds ratio of myocardial infarction of 1.49 (CI 0.96-2.31) compared to those who drank mainly with food[189]. In Moscow City there is a significant increase in deaths from alcohol poisoning, accidents, and violence and cardiovascular diseases (especially sudden death) on Saturdays, Sundays and Mondays. This pattern is consistent with the known pattern of binge-drinking in Russia[190].

Most elderly have healthy drinking habits

Data from the 1988 National Health Interview Survey revealed striking age-related differences in drinking patterns. Usual quantity and heavy-drinking rates associated with problems decreased with age, whereas drinking frequency increased[191]. The fact that drinking frequency increases with age among non-problem drinkers, even as quantity and heavy-drinking rates decrease, suggests that it is normative for individuals who continue current regular drinking as they age, and it may reflect greater accessibility to alcohol and its integration into more aspects of their daily lives. The Tampere Longitudinal Study of ageing (a prospective cohort study of 365 men and 402 women aged 60-99 years) found the lowest relative risk of mortality for frequent drinkers (RR 0.6, CI 0.4-0.8) compared with abstainers. The mortality risk for wine drinkers was 0.5 (CI 0.3-0.9) for those 60-79 years old (n=278) and 0.7 (CI 0.5-1.2) for those 80-99 years old (n=46)[192]. In a prospective, longitudinal study in Wisconsin, USA drinking habits of the subjects changed from age 53 to 64. The older men and women consumed fewer drinks per occasion, heavy drinking decreased and the number of drinking days per week increased. Given that regular moderate drinking is the pattern associated in observational epidemiologic studies with decreases in the risk of many chronic diseases, the described change in drinking pattern can be considered a "healthy" change[193].

The elderly: marathon runners or nursing home residents?

There is a tremendous heterogeneity within the group considered "elderly", and generalizations are most often misleading. The age range of

the group spans at least 40 years and includes people in their late sixties, who are still actively employed and in excellent health, as well as people over 100 years of age, who are more likely to be cognitively and physically disabled. Moreover, the aging process is characterized by marked individual variations. Physiologic ageing does not parallel chronologic aging, and it is physiologic ageing – such as the modest 10-15% reduction of total body water as humans' age - that underlies age-related differences in the fate and action of alcohol[194]. In scientific terms the greatest risk is that what official health authorities like the National Institute on Alcohol Abuse and Alcoholism really mean by "elderly" is a well meaning but misguided attempt to envelop the major clinical issue of frailty into a term that applies to all older people. Frailty is an important factor in functional decline, morbidity, and mortality for some older people and much progress has been made in defining the phenotype, risk factors, manifestations, and outcomes of frailty as a clinical syndrome. However, most elderly people are not frail, and the proportion of older people who are disabled is dropping[195].

A better approach would be to promote clinical skills that selectively identify frail older people in the community, as well as skills and pathways to improve care of and sound advice for this vulnerable group. A related problem is the large number of comorbidities often exhibited by older people. Existing recommendations about alcohol use in frail elderly with special comorbidities has been based on expert opinion rather than data from prospective randomized clinical studies[196]. Older people often cut down on their alcohol use when they experience a decline in health. On the other hand, people who have depressive symptoms or chronic pain may increase their alcohol use in an attempt to treat these symptoms[197]. In the absence of pertinent evidence, a common sense case-by-case approach for older people with particular medical conditions and medications should be applied.

To your health!

With any medical advice there is risk and benefit. Caution should be exercised in framing guidelines for alcohol and they should be kept in the larger context of other favourable lifestyle factors, such as exercise and diet. No evidence has been found to suggest that non-drinkers should take up drinking. The importance of evidence based advice on alcohol use to the older is obvious. With sound advise to hand, each individual must decide whether or not to consume alcohol and, if alcohol is consumed, what level and pattern is appropriate. The relation between levels of drinking and all-cause mortality will vary depending on a person's underlying risk of various causes of death. The groups most likely to benefit from drinking small amounts of alcohol are older people at high absolute risk of coronary heart disease and ischemic stroke and at low absolute risk of injury, cirrhosis and other alcohol-related disease[198]. This hypothesis was confirmed by the results of a recent meta-analysis of the risk curve between alcohol and all-cause mortality: The older the persons at baseline, the more pronounced the protective effect[199].

Most protection of health seems to be conveyed by a pattern of very regular and light drinking, however, health is only one aspect in this decision. Most people do not drink for health reasons but for psychological and social benefits, since alcohol serves as a mood modifier, a relaxant, and a social lubricant[200]. No one should be choosing to drink for medical benefits rather than enjoyment and pleasure. In conclusion older people should not be advised to drink for health, but rather to drink – moderately – to their health!

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