Method for moderation: measuring lifetime risk of alcohol-attributable mortality as a basis for drinking guidelines

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Abstract

The objective of this paper was to determine separately the lifetime risk of drinking alcohol for chronic disease and acute injury outcomes as a basis for setting general population drinking guidelines for Australia. Relative risk data for different levels of average consumption of alcohol were combined with age, sex, and disease-specific risks of dying from an alcohol-attributable chronic disease. For injury, combinations of the number of drinks per occasion and frequency of drinking occasions were combined to model lifetime risk of death for different drinking pattern scenarios. A lifetime risk of injury death of 1 in 100 is reached for consumption levels of about three drinks daily per week for women, and three drinks five times a week for men. For chronic disease death, lifetime risk increases by about 10% with each 10-gram (one drink) increase in daily average alcohol consumption, although risks are higher for women than men, particularly at higher average consumption levels. Lifetime risks for injury and chronic disease combine to overall risk of alcohol-attributable mortality. In terms of guidelines, if a lifetime risk standard of 1 in 100 is set, then the implications of the analysis presented here are that both men and women should not exceed a volume of two drinks a day for chronic disease mortality, and for occasional drinking three or four drinks seem tolerable. Copyright © 2008 John Wiley & Sons, Ltd.

Key words: alcohol, average volume, patterns, mortality, risk assessment, chronic disease, injury

Introduction

In the last two decades, guidelines for “low-risk drinking” or “sensible drinking” have emerged in a number of countries (Hawks, 1994; ICAP, 2003; Harding and Stockley, 2007). This has been an activity that has arisen spontaneously in one place after another, often at subnational levels or by professional organizations such as cancer associations, and without any particular “top-down” encouragement, for instance, by the World Health Organization (WHO). Early manifestations include a citation of “Anstie’s limit” from the 1860s in

a 1974 official US report (NIAAA, 1974; Baldwin, 1977) and a book for lay readers entitled *How Much Is Too Much?* (Gross, 1984), which explored the diversity in research evidence on risk thresholds for different consequences of drinking, and also in professional opinions about limits. Many in public health circles have been sceptical about such guidelines (Casswell, 1996), in terms both of their questionable effect on behaviour, and of the possibility of perverse effects, with people “drinking up” to whatever was specified as a limit.

Typically, the guidelines have been set by a blue-ribbon committee of some sort, on the basis of a committee vote. The processes of setting such guidelines have often been quite opaque. Looking back 20 years at how the original British guidelines were set, Richard Smith recently remarked that they were “really plucked out of the air . . . It was sort of an intelligent guess by a committee” (Norfolk, 2007). In recent years, the basis for the guidelines adopted has become more explicit. Thus both the Ontario guidelines of 1996 and the Australian guidelines of 2001 were based on substantial literature reviews of the medical epidemiological literature which were separately published (Bondy et al., 1999; Single et al., 1999).

However, an element of mystery has remained in the setting of the guidelines. The task that is set for a committee asked to produce a set of guidelines on “low-risk” or “safe” drinking levels is not inherently a scientific task. Most often, the task is relatively arbitrarily limited to health risk, excluding alcohol-attributable social harm. But even then, the potential health harms from drinking are many, and for each of them there is a different risk curve relating amount and pattern of drinking to the chances of the harm occurring (Rehm et al., 2003b; Rehm et al., 2003a; Rehm et al., 2004). Almost all of these risk curves have no apparent threshold, and they may also vary with the circumstances of drinking and characteristics of the drinker. A further complication is the likelihood of protective effects of drinking, with their own risk curves, for some specific disorders.

The central audience for national guidelines has been defined as adults. Frequently, a differentiation in the specific guidelines has been made between men and women but not usually on other population differentiations such as adult age, although some problems from a given level or pattern of drinking may vary more by age than by gender (e.g. different forms of injuries; Rehm et al., 2004; Rehm et al., 2006). Starting in the mid-1990s, there has been a trend to define two sets of guidelines: one in terms of volume of drinking over time to lower risk of chronic illness, and another in terms of amount of drinking on an occasion or day to lower risk of injury or acute harm (e.g. Bondy et al., 1999; NHMRC, 2001).

Following a rule that guidelines in its charge should be reviewed every five years, the Australian National Health and Medical Research Council (NHMRC) organized a review of the Australian alcohol guidelines in 2007 (NHMRC, 2007). It was in this context that

the present analyses were undertaken, with the aim of moving forward the basis for drinking guidelines by measuring and specifying the level of risk attached to particular levels or patterns of drinking. On the basis of the analysis, a review committee could decide on one or more levels of risk as the cutoff-points for the guidelines. The level of risk associated with the guidelines would then be specified, as would levels of risk at other levels or patterns of drinking.

The analysis is oriented to a widely-used metric for risks: the lifetime risk of death associated with a given level of a particular risk factor. In regulating environmental poisons or food additives, for instance, there is usually a careful quantification, on the basis of the best available evidence, of what the risk of exposure is. Typically, these risks are expressed in terms of the risk from lifetime exposure to the substance at a given level. The arbitrary limit often used for environmental toxins has been 1 : 1 000 000: that the chance of death attributable to a given level of exposure over a lifetime should be no more than one in a million. This standard is used in Australia for contaminants of drinking water, for instance; the WHO guidelines on these suggest a more lenient risk threshold of 1 : 100 000 (NHMRC, 2004). It is clear that lesser limits have also been used in particular instances. A study of regulation of risky substances in the US and Canada mentions risk thresholds set at 1 : 22 000 and 1 : 10 000. There is even one instance, concerning the risk from naturally-occurring radon seeping out through a house's foundations, where the risk was set at 1 : 100, though this case was clearly an outlier in terms of normal practices (Harrison and Hoberg, 1994).

The lifetime level of risk of death from chronic disease from a given level of alcohol consumption is conceptually analogous to the lifetime risk from continuing exposure to a given level of a contaminant or additive in the food supply. For mortality risks from particular drinking events – primarily, but not solely, from injury – a different conceptual analogy must be used. Analyses of the risks of injury or other harm from drinking events have usually expressed the risk in terms of the relative risk for each particular event. A drinker who survives a drinking event with a high relative risk without incident then lives to run the same risk another day. But clearly a more relevant consideration, in terms of the individual's overall drinking pattern and survival, is the cumulative risk from a succession of such events. This problem is similar, for instance, to the

problem of calculating the risk of HIV infection from unprotected sex. While the per-act risk may be relatively low, cumulatively the risk becomes substantial. Thus it has been noted that a risk of 1 in 10 000 for HIV transmission for one sexual act translates into a 7% infection rate after 10 years of daily sex (Varghese et al., 2002).

The main objective of this paper, using these conceptual frames, was to determine separately the lifetime risk of drinking alcohol for chronic disease and acute injury outcomes. As a risk analysis, the paper considers only the adverse health effects of alcohol. While there is a substantial literature on protective effects of light drinking for ischemic heart disease and some other conditions (Rehm et al., 2003b; Rehm et al., 2004; Ashley et al., 2000), the extent of the effects is contested (e.g. Fillmore et al., 2006). More importantly, a protective effect is based on a different conceptual framework from an adverse effect, since the same effect could potentially be gained by other means incurring lesser risk. Furthermore, it appears that most of any beneficial effect can be gained at a low level of drinking, for instance a drink every second day (Criqui,

1994) – well below the level of any likely low-risk drinking guideline.

Methods

Modelling lifetime injury mortality risk required estimation of risk based on the volume of alcohol consumed per drinking occasion (drinking pattern), and then combining this information with assumptions on the number of such occasions and with age, sex, and disease-specific injury mortality data. Chronic disease mortality risk, however, was based on average daily volume to generate lifetime chronic disease mortality risk for each age group, sex, and disease category. The specific steps that were taken for injury and disease are outlined.

Step 1: Identify causal conditions

Step 1 was common to both injury and chronic disease mortality risk. We consulted the literature for all relevant meta-analyses to identify which injury/chronic disease categories were causally related to alcohol, using the approach of the WHO Comparative Risk Analysis (Ezzati et al., 2004; Rehm et al., 2004). The results of this are shown in Table 1.

Table 1. Injury and chronic disease categories causally related to alcohol and alcohol-attributable fraction/relative risk source

Cause of death	Source
<i>Injury</i>	
Road traffic accidents	(Ridolfo & Stevenson, 2001)
Poisoning	(WHO, 2002)
Falls	(Ridolfo & Stevenson, 2001)
Fire	(Ridolfo & Stevenson, 2001)
Drowning	(Ridolfo & Stevenson, 2001)
Other unintentional injuries	(WHO, 2002)
Suicide	(Ridolfo & Stevenson, 2001)
Violence (homicide)	(WHO, 2002)
Other intentional injuries	(WHO, 2002)
<i>Chronic diseases</i>	
Lip, oral and pharyngeal cancer	(Corrao et al., 1999)
Esophageal cancer	(Corrao et al., 1999)
Liver cancer	(Corrao et al., 1999)
Breast cancer	(Corrao et al., 1999)
Alcohol use disorders	Own calculations based on National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (http://niaaa.census.gov/)
Hypertensive diseases	(Corrao et al., 1999)
Ischemic heart disease	(Corrao et al., 1999)
Ischemic stroke	(Corrao et al., 1999)
Haemorrhagic stroke	(Corrao et al., 1999)
Cirrhosis of liver	(Corrao et al., 1999)

Injury

Step 2: Dividing the risk into baseline and alcohol-attributable risk

To estimate the absolute lifetime risk of alcohol-attributable injury death, we first had to estimate the risk of injury mortality that was not alcohol-attributable i.e. the baseline risk. We did this using Australian injury mortality data obtained from the WHO Global Burden of Disease project for the year 2002. By dividing the number of deaths from each injury category by the total population at risk (in each age and sex group), the total risk of injury death for one year in each age and sex group was calculated. To get the baseline risk (not including the risk due to alcohol), we multiplied the overall risk by the age/sex/disease-specific alcohol-attributable fraction (AAF) and subtracted the resulting number (alcohol-attributable risk) from the total risk. The AAF was Australia-specific and obtained from Ridolfo and Stevenson (2001) or the WHO Comparative Risk Analysis (Western Pacific A Region) (Rehm et al., 2004; WHO, 2002) (see Table 2).

Example: there were 286 deaths from motor vehicle accidents in men 30–44 years old out of a total population of 2 204 725 men in that age group; thus the total risk was $(286/2204725) \times 1000 = 0.130$ deaths per 1000 men in this age group. This is the total risk. Multiplying this by the AAF [0.305 from Ridolfo and Stevenson (2001)] and subtracting this from the total risk gives us the baseline risk: $0.130 - (0.130 \times 0.305) = 0.090$ deaths from motor vehicle accidents per 1000 population of men 30–44 not attributable to alcohol.

Step 3: Risk function

The next step required estimating the impact of different patterns of alcohol consumption on the baseline risk (by volume per occasion and number of drinking occasions). To get an estimate of the risk of different levels of alcohol, data from a 10-country emergency room study were used ($N = 4320$, 91% response rate) (Borges et al., 2006), in which patients presenting with an injury were asked about their alcohol consumption prior to the injury. This study reported relative risks (RRs) corresponding to the consumption of numbers of a standard drink which was defined as 16 millilitres of pure alcohol. Since an Australian standard drink is defined at 10 grams of alcohol (NHMRC, 2007), we modelled the emergency room data and converted the RR to Australian standard drinks for up to five drinks based on the model, and used Borges et al. (2006) for over this amount (see Table 3 for a comparison of the

Table 3. Conversion of alcohol intake volumes from emergency room studies (Borges et al., 2006)

Before conversion ("Drinks" in international settings, approximately 12.5 grams)		After conversion (Australian 10.0 gram standard drinks)	
Number of drinks	RR	Number of drinks	RR
0	1	0	1
1	3.3	1	1.9
2.5	3.9	3	3.8
4.5	6.5	5	5.6
>6	10.1	7+	10.1

Table 2. AAFs for injury mortality by age and sex and injury type

Injury categories	15–29 years		30–44 years		45–59 years		60–69 years		70–79 years		80+ years	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Road traffic accidents	30.5	10.7	30.5	10.7	30.5	10.7	30.5	10.7	30.5	10.7	30.5	10.7
Poisoning	29.0	23.0	16.0	15.0	16.0	15.0	16.0	15.0	8.0	7.0	8.0	7.0
Falls	22.0	14.0	22.0	14.0	22.0	14.0	12.0	4.0	12.0	4.0	12.0	4.0
Fire	44.0	44.0	44.0	44.0	44.0	44.0	44.0	44.0	44.0	44.0	44.0	44.0
Drowning	34.0	34.0	34.0	34.0	34.0	34.0	34.0	34.0	34.0	34.0	34.0	34.0
Other unintentional injuries	29.0	23.0	29.0	23.0	24.0	19.0	24.0	19.0	24.0	19.0	24.0	19.0
Suicide	32.3	28.5	32.3	28.5	32.3	28.5	32.3	28.5	32.3	28.5	32.3	28.5
Violence (homicide)	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0
Other intentional injuries	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	10.0	10.0	10.0	10.0

original and converted data). Next, we had to combine the alcohol RR with the baseline risk to get an estimate of alcohol-attributable risks for different consumption patterns and apply it to a lifetime.

Step 4: Combination of baseline risk and alcohol-based RR

For this last step, we had to combine the baseline risk from Step 2 with the consumption-based risks of Step 3 to estimate the absolute risk of injury death after consuming a specific number of drinks in a way that reflected real-time and cumulative risk based on lifetime drinking habits, i.e. the probability of dying given the baseline risk and having had a certain, specified number of drinks in a pattern of such drinking over a lifetime. This was done using a probability scenario that incorporated Steps 1 and 2 in the following way, using the same approach we applied to Canadian data (see Taylor et al., 2008):

$$\Pr(\text{death} \mid N) = 1 - (1 - (\Pr(\text{death})_d/i_d))^N$$

where N is the number of drinking occasions per year (1, 12, 24, 52, 156, 260, 365). These equate to once per year, once per month, twice per month, once per week, three times per week, five times per week, and every day, respectively), d represents the number of drinks consumed per occasion, $\Pr(\text{death} \mid N)$ is the risk of injury death (per 1000) given N lifetime drinking occasions, $\Pr(\text{death})_d$ is the risk of injury death for one drinking occasion per year, depending on the number of drinks per occasion. This is the baseline risk (from Step 2) multiplied by the standard drink-specific RRs (from Step 3). The value of i_d is the "risk period". This is the time period in which the person is at risk of an alcohol-attributable injury death. When a person drinks one drink, for example, he or she is not at risk for an entire day (24 hours). Rather, risk should be based on the average time it takes for the liver to metabolize a certain number of drinks and thus was modelled based on work from the National Institute for Alcohol Abuse and Alcoholism (NIAAA, 1997). Generally, for one, three, five, and seven drinks per occasion, the per-occasion risk equates to periods of 30 minutes, two hours, three hours and 4.8 hours were used. Thus, to give an example: for three drinks per occasion we assumed a risk period of two hours during the 24-hour period of that day. So, i_d becomes $365 \times (24/2)$, as it is based on the probability of one year.

Again, coming back to our example of motor vehicle accident mortality in men 30–44 years old, let us do a sample calculation in those men who drink daily three drinks per occasion and a Related Risk of 3.77. Using the formula outlined earlier for a man who drinks daily and who consumes three drinks per occasion and a risk period of two hours, the resulting alcohol-attributable risk for injuries is about 0.06 per 1000 for this lifetime period. For overall lifetime risk of injury, the risks of different periods have to be combined.

Probabilities were computed for each age, sex, disease, and consumption group and added up across disease categories and ages to get final estimates by consumption group and gender.

Chronic disease

Step 2: Calculation of total risk

As for injury categories, absolute one-year age-, sex-, and disease-specific overall risks were generated. Next, AAFs had to be applied to the total risk to generate alcohol-attributable risks, but AAFs first had to be computed based on average daily alcohol consumption levels.

Step 3: Calculating the consumption-specific AAF

This step had two parts – the first was to compute the RR for different average daily consumption levels. For this analysis, we calculated the RR in 10-gram increments, using lifetime abstainers as the reference category, modelling most diseases using data from Corrao et al. (1999), except for ischemic heart disease, which was based on another publication by Corrao et al. (2004). For age groups over 60, the RR for chronic disease mortality tends to decrease with age, so this was accounted for based on the work of Klatsky and Udaltsova (2007). The second part of this step was to generate an AAF for each age, sex, and disease category based on the RR and prevalence (Walter, 1976, 1980) for all chronic disease categories except for alcohol use disorder (AUD), based on the following formula (see Table 4):

$$\text{AAF}_i = P \times (\text{RR}_i - 1) / [P \times (\text{RR}_i - 1) + 1]$$

where i represents 10–100 grams per day in 10-gram increments (i.e. 10 grams of pure alcohol per day to 100 grams of pure alcohol per day) and P is the prevalence of alcohol consumption. For this, since we were only

Table 4. AAFs (%) for chronic disease mortality by age and disease category (male/female combined)

Disease conditions	Alcohol-attributable fractions (male/female, %) ¹			
	10 grams	20 grams	30 grams	40 grams
Lip, oral and pharyngeal cancer	23.5/24.7	40.0/41.9	51.9/54	60.5/62.9
Esophageal cancer	14.6	27.1	37.7	46.7
Laryngeal cancer	7.0	13.3	18.9	23.9
Breast cancer	7.4	14.2	20.6	26.4
Hypertensive diseases	13.3	24.8	34.8	43.4
Ischaemic heart disease	0.0	0.0	0.0	0.0
Ischemic stroke	0.0	0.0	0.0	10.9
Haemorrhagic stroke	13.9	25.9	36.2	45.1
Cirrhosis of liver	17.3/24.4	31.0/42.2	41.8/55.5	50.5/65.4

¹If only one AAF is given, attributable risk did not vary significantly by sex.

dealing with drinkers at a defined level of drinking (10 grams/day, 20 grams/day, etc.), we used 100% prevalence, assuming all drinkers drink in the same quantity at 10 grams, 20 grams, 30 grams to 100 grams per day. The component RR_i is the relative risk for drinking level i .

Alcohol use disorder is, by definition, 100% attributable to alcohol, i.e. it would disappear completely if alcohol was not present. Therefore, the issue here was not determining the portion of risk that was alcohol attributable, but rather to estimate the risk of developing AUD at a given level of drinking. For this, survey data were used. The US-based National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) data were used (sample size = 43 093 persons 18 years and older, response rate = 81%) (for more information, please see the NESARC website at: <http://niaaa.census.gov/>). The risk of AUD by age and sex based on average daily drinking that year (from Rehm et al., 2007a) was derived and modelled for daily consumption categories corresponding to Australian standard drinks (10 grams per day to 100 grams per day) (see Figure 1; a similar diagram is found for women but is not shown), and AAFs of all AUD deaths for different levels of drinking were based on these risk estimates.

Step 4: Combination of total risk and AAF

The last step required combining the total risk and the computed AAF for each age, sex, and disease category to get the one-year, alcohol-attributable risk for each category. To get the lifetime risk, age-sex-disease one-year risks were multiplied by the time spent in each age

category; e.g. for women 30–44, their one-year alcohol-attributable risk of death would be multiplied by 15, since they would have spent 15 years in this “risk-block”. For those 20–29, it would have been multiplied by 10 years. For those in the oldest age category, their risks were multiplied by the residual life expectancy [obtained from WHO (2004)]. So, for women 80+, their one-year was multiplied by three (83 year average life expectancy for Australian women – 80 years). Finally, the risks were added up across age groups and disease categories.

Results

Figures 2 and 3 show the results of the injury analysis for Australian men and women, respectively. For both men and women, the absolute lifetime risk of injury

Figure 1. Risk for AUD (men) by average level of alcohol consumption (own calculations based on NESARC data using quadratic regression).

Alcohol-attributable fractions (male/female, %) ¹					
50 grams	60 grams	70 grams	80 grams	90 grams	100 grams
66.9/69.4	71.7/74.2	75.4/77.9	78.2/80.7	80.4/82.9	82.1/84.6
54.3	60.7	66.1	70.7	74.6	77.9
28.4	32.4	36.0	39.2	42.1	44.7
31.9	36.9	41.5	45.9	49.9	53.6
50.9	57.4	63.1	68.0	72.2	75.9
0.0	0.0	0.0	1.0	2.9	11.5
28.3	42.0	51.0	54.8	52.8	41.8
52.8	59.3	65.0	69.9	74.1	77.7
57.5/72.8	63.2/78.4	67.8/82.7	71.5/86.1	74.6/88.6	77.1/90.6

Figure 2. Lifetime risk per 1000 of overall injury mortality by number of standard drinks consumed and lifetime drinking occasions among men in Australia, 2002.

increased as the number of drinks per occasion and the number of drinking occasions increases, although men suffer about 30% higher risks than women at all levels of drinking except for over five occasions per week, where men suffer about double the risk of injury death. Additionally, for both men and women, a significant jump in risk was seen at three drinking occasions per week, at which point the risk substantially increases for each corresponding increase in the number of drinking occasions thereafter. A lifetime risk of injury death of

1 in 100 is reached for consumption levels of three drinks consumed about five times per week for men and daily for women. Among men, the risk rises to a maximum of 75 per 1000 population for daily drinking occasions of seven or more drinks, and the risk for women reaches 42 per 1000 at the same level. At levels at or below once per week, risks are much closer together. Interestingly, the data is best modelled by a quadratic function through the origin, showing the non-linear effect of alcohol on risk of injury death,

Figure 3. Lifetime risk per 1000 of overall injury mortality by number of standard drinks consumed and lifetime drinking occasions among women in Australia, 2002.

Figure 4. Lifetime risk per 1000 of overall chronic disease mortality by average daily alcohol consumption in grams per day of pure alcohol among men and women in Australia, 2002.

indicating that risk increases at a rate that is more than proportional to the number of drinks consumed.

Lifetime risk of chronic disease mortality shows a different relationship with alcohol. This relationship graphically looks much more linear than the lifetime risk of injury death. Figure 4 shows that the lifetime risk of chronic disease death increases as average daily volume increases. What is most striking in this graph is the higher risk among women compared to men at higher daily volume levels. The risk for women also

increases faster with increased consumption than for men. At 10 grams per day, lifetime risk for women is actually lower than that for men, but increases to over 50% higher (96 versus 60 per 1000) at 100 grams. Overall, risk increases by about 10% with each 10-gram (one drink) increase in alcohol consumption. The risks for men and women are quite similar at average daily volume levels below 40 grams per day, while at higher levels of drinking large differences by sex are seen.

Discussion

The paper introduces a new methodology to model lifetime risk of different patterns of drinking alcohol. Before going into the interpretation we would like to point out some limitations of this approach. First, the approach is limited to death from medical risks as defined by the International Classification of Disease, i.e. chronic disease and injury. Social harm, sometimes estimated to incur higher costs than health harm, was not included (Babor et al., 2003). Neither alcohol-attributable illness nor disability was included directly. Second, we assumed that RRs for chronic disease, which were derived from meta-analyses based mainly on other countries (for an overview see Rehm et al., 2003b), would apply for Australia. This seemed to be a reasonable assumption, as these risks are mainly biological, and previous meta-analysis showed no significant heterogeneity of risks in Caucasian samples (see Rehm et al., 2003b). With respect to injury, while we recognize that mortality risks are partly shaped by risk-taking behaviour, this behaviour is not independent of alcohol consumption. (e.g. Deery and Love, 1996; Bazargan-Hejazi et al., 2007). Perceived risk which, in part, governs behaviour, actually decreases with increasing alcohol consumption, even for well-accepted high risk activities such as drinking and driving (Holubowycz and McLean, 1995). The main point here is that decisions to engage or not engage in risky behaviour are influenced in a major way by alcohol. Third, the AAFs used to generate the non-alcohol-attributable risk and the RR data modelled for number of drinks came from different sources (WHO/Corrao/Ridolfo and Stevenson and Borges et al., respectively). Data did not allow verification of the assumption that the RRs computed using the Borges et al. data were the same as those used for AAF development, but we would assume that the RR for the number of drinks would underestimate the AAF, since Borges et al. is based on morbidity data, not mortality as for Ridolfo and Stevenson/WHO. Fourth, as noted, the analysis is of adverse risks; thus we decided to omit modelling the beneficial consequences of light to moderate drinking. As indicated earlier, most of these benefits can be achieved without incurring substantial risk, e.g. by drinking one drink every other day (Criqui, 1994). Fifth, the risks for injury were based on emergency room studies, which may misestimate the risk for death. On the one hand, as noted earlier, data from non-fatal injuries is likely to underestimate the relative

risk for death, as alcohol has been shown to be more involved in more severe outcomes (Rehm et al., 2003a; Rootman et al., 2007). On the other hand, emergency-room treatment for injury may reflect general tendencies for risk-taking as well as the consequences of alcohol consumption, so that those coming for treatment are more injury-prone than the general population. A general tendency for risk-taking may also impact on consumption of alcohol. In the other direction, alcohol influences risk-taking, even in moderate doses, and especially when consumed in higher doses (Eckardt et al., 1998). At this point, it is not clear how the different potential biases impact our estimates for lifetime risk of injury. Clearly, more research is needed on these topics.

While limitations have to be acknowledged, the present analyses give valuable insight into the extent of the contribution of different patterns and levels of drinking to lifetime mortality risk. The most important finding is that the risks of dying from an alcohol-related condition, both for chronic illness and for injury, rise quickly above the ranges of risk deemed acceptable for environmental contaminants and food additives. Additionally, we examined these risks separately, while use of alcohol over time incurs both risks simultaneously. In this regard, our analyses are quite conservative.

Of course, alcohol consumption differs from a contaminant in drinking water, for instance, in that its consumption is voluntary. However, the risk from alcohol consumption potentially affects others, whereas the drinking water affects only the drinker. Regularly drinking a substantial amount of alcohol is clearly high-risk even among voluntarily-assumed risks. For instance, at the higher end of the range of common risks reported in the literature, the lifetime risk in the US of dying in a car accident for somebody that drives 10 000 miles per year has been estimated to be about 1 in 60 (Walsh, 1996), and of injury death for a cyclist riding his or her bicycle 3000 miles a year about 1 in 256 (Kifer, 2000).

If a lifetime risk standard of 1 in 100 is set for death from chronic illness, then the implications of the analysis presented here are that both men and women should not exceed a volume of between two drinks a day on a regular basis. In terms of amount per occasion for a pattern with some regularity, to keep the risk of death from alcohol-related injury below approximately 1 in 100, again both men and women should keep their consumption to three to four drinks or less.

In considering acceptable levels of risk for drinking, three other factors should be considered besides its status as a presumptively voluntary behaviour. First, as noted, alcohol incurs risks not only to oneself but to others as well (e.g. drinking by a mother imposes risk to the newborn; the effects of drinking driving on bystanders; e.g. Tai et al., 1998). Second, even if the risk is to oneself, alcohol incurs considerable costs to the society as whole (e.g. Rehm et al., 2007b). And third, as already mentioned, alcohol impacts decision-making itself (Eckardt et al., 1998).

Against usual presumptions in the literature, an analysis in terms of lifetime risks does not support different guidelines for men and women if the tolerable risk level is set at levels given earlier. Above these levels, however, there is a clear differentiation in risks by gender. For death from chronic illness, as has been well recognized, women are at greater risk than men at a given level of drinking and the gender differential increases at higher amounts of drinking. For death from injury, the results are different from usual expectations. Despite the greater blood-alcohol level resulting on average for women than for men from a given number of drinks (Dubowski, 1976; Cole-Harding and Wilson, 1987), men are at greater risk than women of alcohol-related injury death for a given number of drinks consumed the same number of times in a lifetime. The effects of the blood-alcohol difference are overwhelmed by the greater general propensity of men to die of injury, and probably also to some extent by gender differences in behaviour after drinking (e.g. Gussler-Burkhardt and Giancolo, 2005). A drinking guideline concerning drinking in the event and the risk of fatal injury should actually specify lower levels of drinking for men than for women to equalize the lifetime risk by gender.

Declaration of Interests

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