Chapter 12

Alcohol use

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Summary

Alcohol has long been known as a risk factor for disease. The 1990 Global Burden of Disease (GBD) study (Murray and Lopez 1996a, 1996b) identified alcohol as one of the major global risk factors, accounting for 1.5% of global deaths, 2.1% of years of healthy life lost owing to premature mortality, 6.0% of years of life lost owing to disability and 3.5% of disability-adjusted life years (DALYs).

Based on the epidemiological literature, and modelling the relationship between alcohol exposure and disease, two dimensions of alcohol consumption were defined as exposure variables:

- average volume of alcohol consumption; and
- pattern of drinking.

Average volume of consumption was estimated using both existing estimates of country-specific adult per capita consumption (based on production and sales data) and self-reported alcohol consumption from general population surveys. Country-specific patterns of drinking were defined using indicators of high-volume drinking occasions and types of drinking situation (e.g. drinking with meals). These indicators were drawn from key informant surveys and general population surveys, where available. Optimal scaling procedures were used to determine whether drinking patterns formed a single dimension and the relative impact of the underlying indicators on the pattern value.

The relationship between exposure and various disease categories was estimated by the following methods. Estimates of the relationship between categories of average volume of alcohol consumed and chronic disease were based on disease-specific meta-analyses. Estimates of the relationship between average volume of alcohol consumption and acute disease were based on alcohol-attributable fractions (AAFs) published in the literature. To estimate the impact of patterns of drinking on the risk

of ischaemic heart disease (IHD) and injuries, multilevel modelling with random intercept and random slope was used.

Effects of alcohol on someone other than the drinker were either included in the AAFs of the literature (e.g. alcohol-related injury) or were modelled indirectly (e.g. in the case of the effect of alcohol on the newborn).

Both average volume of alcohol consumption and patterns of drinking varied markedly across subregions.[1] Average volume of drinking was highest in EUR-A, EUR-C and AMR-A, and lowest in EMR-B, EMR-D and SEAR-D. Patterns were most detrimental in EUR-C, EUR-B, AMR-D and AFR-E. Patterns were least detrimental in EUR-A and WPR-A.

Existing research indicates causal relationships between average volume of consumption and more than 60 International Statistical Classification of Diseases and Related Health Problems (ICD) codes, including both chronic diseases (malignant neoplasms, neuro-psychiatric conditions, cardiovascular diseases, gastrointestinal conditions) and injuries (intentional and unintentional). Although most of these relationships involve a detrimental impact of alcohol, there are beneficial relationships between alcohol and IHD, cerebrovascular disease and type II diabetes for certain combinations of average volume of consumption and patterns of drinking. Patterns of drinking were also associated with the level of injury burden from alcohol, although no pattern of drinking had beneficial effects on injury.

The present analysis found that alcohol-related burden of disease is considerable: 3.2% of global mortality and 4.0% of the global burden of disease measured in DALYs. In terms of alcohol-related mortality, almost half of the global burden is related to acute causes, i.e. unintentional and intentional injuries, particularly unintentional injuries. The next most important category comprises malignant neoplasms with 20% of the overall alcohol-related mortality burden, followed by cardiovascular diseases (15% of all alcohol-attributable deaths) and other noncommunicable diseases, primarily liver cirrhosis (13%). However, although the overall proportion of cardiovascular deaths attributable to alcohol reflects a net result of 15%, this figure does not give a clear picture of the underlying structure of the relationship between alcohol consumption and cardiovascular disease. In particular, although alcohol was estimated to cause a total of almost 600 000 cardiovascular deaths in the year 2000, exceeding even the alcohol-related deaths of unintentional injuries, this figure was partly "offset" by the beneficial effects of alcohol on IHD and stroke. Across all diseases, more males than females die from the effects of alcohol, with a ratio of about 10 : 1.

In terms of DALYs, 4.0% of the overall global disease burden was attributable to alcohol. The biggest differential effect of alcohol on mortality vs morbidity was for neuro-psychiatric diseases. Neuro-psychiatric diseases are often disabling, but not fatal, and this is reflected in the markedly higher proportion of overall disease burden caused by

this category compared to alcohol-attributable mortality (38% of alcohol-attributable DALYs vs 6% of alcohol-attributable deaths). As with alcohol-related mortality, males have more than five times the alcohol-related disease burden in terms of DALYs than females.

Alcohol-attributable disease burden is expected to further increase in the future. This is due partly to increases in consumption in developing and emerging economies in south-east Asia and partly to shifting patterns of morbidity and mortality, in particular the increased significance of chronic diseases and injuries related to alcohol. This trend, however, could be reversed quickly, as much of the disease burden of alcohol is almost immediately preventable (40% of the overall alcohol-attributable burden is from acute conditions). While a total ban on alcohol is not realistic, there are other alcohol policy measures that could be implemented to reduce the resulting disease burden.

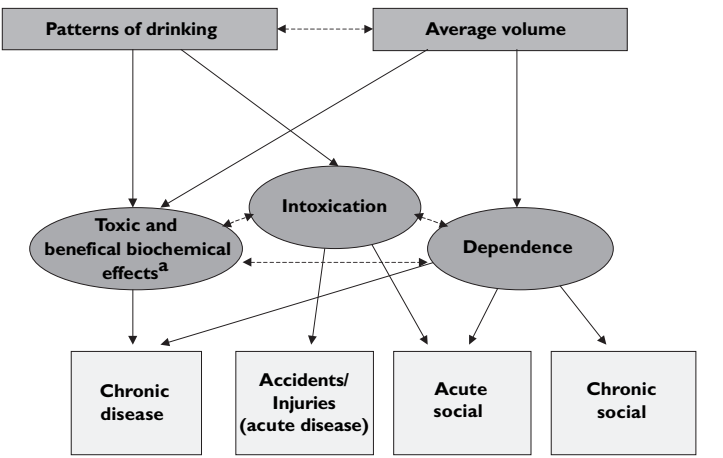
1. Introduction

1.1 Definition of alcohol as a risk factor

The relationship between alcohol consumption and health and social outcomes[2] is complex and multidimensional. Figure 12.1 gives an overview.

Alcohol consumption is linked to long-term biological and social consequences through three intermediate outcomes: intoxication,

Figure 12.1 Model of alcohol consumption, intermediate outcomes and long-term consequences



[a] Independent of intoxication or dependence.

dependence and direct biochemical effects. Examples of such biochemical effects are the promotion of blood clot dissolution and direct toxic effects on acinar cells triggering pancreatic damage.[3] Figure 12.1 shows only the main causal pathways. Intoxication may, for example, lead to chronic social consequences (e.g. when a drunken driver kills somebody and thereafter loses his or her job and social standing). Most of the consequences of intoxication are nonetheless covered by acute health and social consequences.

- *Direct biochemical effects* of alcohol consumption may influence chronic disease, either beneficially or in a harmful way. Beneficial effects include the influence of moderate drinking on IHD by reducing plaque deposits in arteries, protecting against blood clot formation and promoting blood clot dissolution (Zakhari 1997). Examples of harmful effects include increasing the risk of high blood pressure, direct toxic effects on acinar cells triggering pancreatic damage (Apte et al. 1997) and hormonal disturbances (Emanuele and Emanuele 1997). The term "direct toxic and beneficial effects" is used to summarize all the biochemical effects of alcohol on body functions other than intoxication and dependence.
- *Intoxication* is a powerful mediator, mainly for acute outcomes such as accidents, intentional injuries or deaths, domestic conflict and violence, although episodes of intoxication can also be implicated in chronic health and social problems. The effects of alcohol on the central nervous system mainly determine the subjective feeling of intoxication. These effects are felt and can be measured even at consumption levels that are light to moderate (Eckardt et al. 1998).
- *Alcohol dependence* is a disorder in itself, but is also a powerful mechanism sustaining alcohol consumption and mediating its impact on both chronic and acute physiological and social consequences (Drummond 1990).

Biological mechanisms have historically been the most important criteria in establishing the causal link between alcohol consumption and health outcomes (English et al. 1995; Hill 1965; Rothman and Greenland 1998a).

Total consumption or average volume of consumption has been the usual measure of exposure linking alcohol to disease (Bruun et al. 1975). Average volume was linked to more than 60 disease conditions in a series of recent meta-analyses (English et al. 1995; Gutjahr et al. 2001; Ridolfo and Stevenson 2001; Single et al. 1999a).

As shown in Figure 12.1, average volume of consumption as a risk factor works mainly through biochemical effects or through dependence to produce long-term consequences. Although average volume is somewhat correlated with intoxication, this correlation is not of sufficient strength to adequately predict acute effects of alcohol related to injury

and death. Such effects are much better predicted by patterns of drinking (Rehm et al. 1996). For example, the same overall average volume of alcohol can be consumed in small quantities regularly with meals (e.g. two drinks a day with meals) or in large quantities on few occasions (e.g. two bottles of wine on a single occasion every Friday). Data on the influence of patterns of drinking are less available than data on overall consumption, but evidence is accumulating that patterns of drinking affect the link between alcohol and disease (Bondy 1996; Puddey et al. 1999; Rehm et al. 1996, 2003) and between alcohol and mortality (Rehm et al. 2001d). In other words, the impact of an average volume of consumption on mortality or morbidity is partly moderated by the way alcohol is consumed by the individual, which in turn is influenced by the social context (Room and Mäkelä 2000). It should be noted that patterns of drinking have been linked not only to acute health outcomes such as injuries (Greenfield 2001; Rossow et al. 2001) but also to chronic diseases such as IHD and especially sudden cardiac death (Britton and McKee 2000; Chadwick and Goode 1998; Puddey et al. 1999; Trevisan et al. 2001a, 2001b).

1.2 Choice of exposure variable

To determine the impact of alcohol on burden of disease, both average volume of consumption and pattern of drinking have to be considered and included in the analysis. Unfortunately, average volume of consumption and pattern of drinking are not independent at the level of the individual drinker, because average volume is often determined by heavy drinking occasions (Rehm and Gmel 2000a). Consider someone who drinks eight drinks per day. This person has by definition both a high average volume of consumption and many heavy drinking occasions. On the aggregate level, however, the two dimensions can be statistically independent, as described below in section 2.3.

Average volume of drinking is a relatively simple concept, at least on a theoretical level. It is more difficult to conceptualize patterns of drinking on a worldwide scale. For the comparative risk assessment (CRA) project (see also WHO 2002), aspects of drinking patterns likely to contribute to consequences were identified as a first step in this process (see also Rehm et al. 2001a, 2001b). Table 12.1 provides an overview of the results of this exercise.

1.3 Choice of theoretical minimum

Because the relationship between alcohol and disease or injury stems from two potentially interrelated dimensions—average volume of alcohol consumption and drinking pattern—the theoretical minimum or other counterfactual scenarios that provide a reference for hypothetical risk reduction should take both dimensions into account. One obvious and important counterfactual would be total abstinence from alcohol. If all effects of alcohol on health were negative, this would obviously be

Table 12.1 Patterns of drinking relevant to CRA

Pattern indicators	*Link to disease*
Proportion of the adult population who abstain from alcohol	The same adult consumption per capita will have more detrimental effects in countries where drinking is concentrated among fewer people. *This variable was later dropped from the pattern analyses, as it has been incorporated into the average drinking categories*
Heavy drinking occasions[a] High usual quantity of alcohol per occasion Proportion of drinkers who drink daily or nearly daily Proportion of drinking occasions when drinkers get drunk Festive drinking common—at fiestas or community celebrations	The fewer occasions on which a given amount of alcohol is consumed, the more detrimental the consequences (Puddey et al. 1999; Room et al. 2002; Walsh and Rehm 1996). Heavy drinking occasions lead to an increase in injuries. Also, heavy drinking occasions have been shown to lead to detrimental cardiovascular outcomes
Drinking with meals—how common to drink with meals	Drinking with meals has been shown in epidemiological and biological research to be less detrimental than drinking at other times (Gentry 2000; Ramchandani et al. 2001; Trevisan et al. 2001a)
Drinking in public places—how common to drink in public places	Drinking in public often requires transportation, and thus has been linked to traffic accidents and injuries (Fahrenkrug and Rehm 1994)
Drinking linked to violence	Alcohol-related violence is an important cause of injuries. *This variable confounds exposure and a potential consequence and was thus dropped in subsequent analyses*

[a] This is often termed "binge drinking". However, the definition of binge drinking varies widely (e.g. from heavy festive drinking with intoxication lasting more than one day to having five or more drinks on one occasion). It was therefore decided not to use the term in this work.

the ideal theoretical minimum. However, it has been shown that alcohol, if consumed in a regular pattern of light to moderate doses, has protective effects against IHD and potentially other ischaemic diseases (Ashley et al. 2000; Puddey et al. 1999).

The cardioprotective effect has the most relevance to countries with established market economies, which tend to have the longest life expectancy and the highest proportion of deaths from ischaemic disease (Murray and Lopez 1996a). In addition, the pattern of light regular drinking associated with this protective effect, when it occurs, is found mainly in these countries. Drinking to intoxication, heavy drinking occasions and other more detrimental drinking patterns, on the other hand, are often the prevalent drinking style outside established market economies[4] (see Table 12.3 for an overview of country-by-country drinking patterns). Economic development and patterns of drinking are correlated to a higher degree than volume of alcohol consumption and economic development (Pearson correlation of 0.6 between patterns and per capita gross national product [GNP] on the 2001 data set of the CRA

with 89 countries, where the correlation between average volume of consumption and GNP is 0.2; see Rehm et al. 2001a, 2001b). Unfortunately, insufficient research has been carried out to identify the causal determinants of this relationship.

It is proposed to establish the following counterfactual scenarios for measuring the effects of alcohol consumption:

- total abstinence, which would mean an increase in the disease burden of some cardiovascular categories for established market economies and countries with a general pattern of light to moderate drinking;
- as a sensitivity analysis, the current status in patterns of drinking with different scenarios for volume of drinking;
- as a sensitivity analysis, the current status in average consumption with different values for patterns of drinking; and
- changing both average volume of consumption and drinking patterns towards light, regular drinking.

The overall attributable burden of disease should be calculated using abstainers as the comparison group, as this provides the *global* theoretical minimum. Owing to the large contribution of neuropsychological disease and injuries, neither of which benefits from alcohol consumption, it is also likely that at the population level in every subregion except AMR-A, EUR-A and WPR-A abstinence results in the lowest population risk. The cardioprotective effect will be included in established market economies with light to moderate drinking patterns by using relative risks smaller than 1, thus subtracting "prevented burden" from the burden of disease for these countries.

2. Estimating risk factor levels

2.1 Measuring average volume of alcohol consumption and patterns of drinking

To quantify the effects of alcohol on population health, it is necessary to measure the two key exposure variables, average volume of alcohol consumption and patterns of drinking, at the population level around the world.

Average volume of alcohol consumption

There have been a number of attempts to gather country-level data on average volume of alcohol consumption, most recently by the World Health Organization (WHO) in the *Global status report on alcohol* (1999). Most attempts have tried to arrive at an aggregate figure per country, i.e. per capita consumption or adult per capita consumption (i.e. per capita consumption for all inhabitants aged >15 years). For several reasons, however, this aggregate figure is insufficient for health impact

assessment. First, as a global figure, this approach does not allow disaggregation into different groups (e.g. as defined by sex and age), which is needed for valid estimates of burden of disease. Second, per capita consumption estimates are usually based on production figures or sales data, and thus do not include consumption of home-made or illegally imported alcohol (see discussion of unrecorded consumption in Giesbrecht et al. 2000; Leifman 2001; Summer 2000).

On the positive side, the production and trade or sales data required to calculate per capita consumption have traditionally been collected by various sources (including the alcoholic beverage industry and international agencies such as the Food and Agriculture Organization of the United Nations [FAO]) and are available for most countries of the world. FAO collects production and trade data for different alcoholic beverages, mainly from ministries of agriculture and customs departments. For some countries, estimates include data on alcoholic beverages outside the usual beer, wine and spirits categories (e.g. palm wine and sorghum beer) but they do not systematically include home production or illicit production.

To use per capita consumption data for detailed risk analysis, we combined this source with survey data from various countries. Survey data are especially important in determining the proportion of abstainers in a country, as well as in dividing the overall volume into drinking categories by sex and age groups. In addition, some surveys can be used to estimate unrecorded consumption (e.g. Kühlhorn et al. 1999; and the current WHO-supported efforts in Brazil, China, India and Nigeria).[5]

Although survey data are essential for refining per capita estimates, they also have problems that preclude them from being used as the single source of data. In particular, survey data from many established market economies considerably underestimate total volume (Midanik 1988; Midanik and Harford 1994; Rehm 1998a; de Vries et al. 1999).[6] In addition, survey data are less available than per capita consumption data on an international level (Rehm and Gmel 2000b; WHO 1999). Nevertheless, by combining both kinds of information one may arrive at disaggregated estimates. In this combination, the per capita estimates based on production and sales (combined with data on unrecorded consumption where available) are taken as the overall value. Surveys are then used to estimate the distribution of this overall volume among various groups, as defined by abstinence and different levels of drinking, and by sex and age.

Patterns of drinking

Existing general population surveys cover some of the patterns of drinking listed in Table 12.1, but rarely would one find all features in one representative survey in a particular country. Moreover, not all surveys on drinking patterns are recent. Therefore, to develop drinking pattern estimates for the 14 subregions used in the CRA, key informant question-

Table 12.2 Countries with returned key informant questionnaires

Subregion	*Countries that returned questionnaires in at least one phase*	*Total no. of countries in subregion*
AFR-D	Burkina Faso, Nigeria, Seychelles	26
AFR-E	Congo, Namibia, South Africa, Zambia	20
AMR-A	Canada, USA	3
AMR-B	Argentina, Brazil, Costa Rica, Mexico, Trinidad and Tobago	26
AMR-D	Peru	6
EMR-B	None	13
EMR-D	None	9
EUR-A	Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Malta, Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Switzerland, United Kingdom	26
EUR-B	Armenia, Bulgaria, Poland, Slovakia, The former Yugoslav Republic of Macedonia	16
EUR-C	Belarus, Estonia, Hungary, Latvia, Lithuania, Russian Federation	9
SEAR-B	Sri Lanka, Thailand	3
SEAR-D	India	7
WPR-A	Australia, Japan, New Zealand, Singapore	5
WPR-B	China, Fiji, Malaysia, Micronesia, Palau, Papua New Guinea, Philippines, Republic of Korea, Solomon Islands	22
Total		191

naire studies were undertaken in early 2000 (Rehm et al. 2001b; for the key informant questionnaire see Appendix 1 in European Addiction Research 2001) and repeated in 2001, using a slightly modified questionnaire.[7] In 2000, 61 questionnaires were sent out, 52 of which were returned, and in 2001 another 155 were sent out, 40 of which were returned. Table 12.2 lists, by subregion, the countries for which key informant surveys were received. Together with survey data, the responses from the survey on patterns provided sufficient data for a first estimate of patterns of drinking for all subregions.

SUMMARY OF DATA SOURCES USED

The following country level measures of alcohol consumption were used in the analysis:

- adult per capita consumption based on sales data or production and trade data;
- unrecorded consumption based on various estimates;
- survey data on abstinence, average volume consumed in different sex and age groups, and patterns of drinking; and

- key informant information on various aspects of patterns of drinking.

Data for all years after 1998 were considered. Data were checked for consistency across time and for internal consistency (e.g. survey vs per capita estimates of average volume of consumption).

2.2 Data sources for average volume of alcohol consumption

Data on adult per capita and unrecorded consumption were taken from the *Global status report on alcohol* (WHO 1999) and from the WHO Global Alcohol Database, created by the Marin Institute for the Prevention of Alcohol and Other Drug Problems and currently maintained by the Swiss Institute for the Prevention of Alcohol Problems. Surveys were also collected from this database, but additional surveys were accessed based on individual contacts (including several experts from each subregion) and by announcing this project on a specific WHO listserve and at the Annual Alcohol Epidemiology Symposia of the Kettil Bruun Society for Social and Epidemiological Research on Alcohol. Data on drinking patterns were collected from researchers and health officials known to WHO who had the knowledge to serve as key informants for their countries or regions. Key informant information was collected by surveys in early 2000 and in mid 2001.

Categorical levels for average volume of alcohol per day in relating consumption to chronic disease were selected to be consistent with previous meta-analyses (English et al. 1995; Gutjahr et al. 2001; Ridolfo and Stevenson 2001; Single et al. 1999a; for a discussion of the background to these categories see English et al. 1995; Holman et al. 1996) and were defined as follows:

- *abstainer*: a person not having had a drink containing alcohol within the last year;
- *average volume drinking category I*: for females 0–19.99 g pure alcohol daily; for males 0–39.99 g pure alcohol daily;
- *average volume drinking category II*: for females 20–39.99 g pure alcohol daily; for males 40–59.99 g pure alcohol daily; and
- *average volume drinking category III*: for females 40 g or more pure alcohol daily; for males 60 g or more pure alcohol daily.[8]

This categorization of average drinking, rather than using a continuous measure of consumption, makes it possible to derive different shapes of risk curve (linear, J-shape, threshold, etc.) while, at the same time, allowing inclusion of data from studies in which only categorical information on levels of alcohol consumption were collected. Using per capita consumption data derived from production and trade or sales data plus unrecorded consumption as the first estimate of overall alcohol con-

sumption, the following strategy was adopted to generate age- and sex-specific prevalence rates.

- For each subregion, the average adult per capita consumption, including unrecorded consumption for the population aged ≥15 years, was estimated as a population-weighted average of country-specific per capita consumption data. All entries per country after 1998 were taken and averaged to obtain a stable estimate for 2000. The weights were derived from the average population aged ≥15 years in each country for the years after 1998, on the basis of United Nations population data. Country-specific adult per capita data were estimated for 132 countries (see Table 12.3). Per capita consumption was known and adult per capita consumption could be calculated for more than 90% of the world's population. Survey information on abstinence was available for 69 countries, in particular from almost all countries with population larger than 100 million resulting in more than 80% of the world population with available survey data. This means that more than 50% of the countries for which data were available on per capita consumption also had survey data available.
- Country-specific survey data of the ratio of male to female consumption were used to allocate proportionally the overall adult per capita consumption to adult male and adult female per capita consumption.
- Based on surveys, the age-specific prevalence of drinking was calculated on the assumption that the average per capita consumption and the proportions of male and female abstainers were correct.

2.3 Data sources for patterns of drinking

Initial estimates of drinking patterns across a range of countries were based on two surveys of key informants selected by WHO staff, conducted in early 2000 and mid 2001. The surveys covered relevant drinking characteristics within different countries or regions. In most cases, respondents had access to national or regional survey data, although these data had not always been published in the international literature. In addition, the informants provided a confidence rating for their responses (i.e. whether based on surveys or just best guesses). This information was used for decisions about inclusion of data when conflicting information existed. As listed in Table 12.1, the survey considered five main areas of drinking patterns that might be expected to affect the impact of volume of drinking: proportion of abstainers, heavy drinking occasions, drinking with meals, drinking in public places and drinking linked to violence (later dropped from analyses because of its interference with outcome measures).

The key informant ratings were analysed using optimal scaling analysis (Bijleveld et al. 1998, chapter 2). This analysis is similar to factor analysis, but permits the simultaneous inclusion of ordinal and categor-

ical data. As with factor analysis, this statistical technique allows the analyst to determine the number of underlying dimensions and the relation of items to each dimension. In the analysis of patterns of drinking, one global dimension was identified and labelled as detrimental impact (for details see Rehm et al. 2001b).

The results of the optimal scaling analysis were very similar to a score derived simply by summing the ratings of the key informant survey (Pearson correlation: 0.93). To further simplify the pattern values into robust general categories based on these scale values, the countries were placed in four categories and assigned values from 1 to 4. By the time the final pattern values were constructed, additional survey data were available as well as the second wave of key informant data, allowing refinement and corrections of estimates. Also, the proportion of abstainers was no longer included as one of the parameters of pattern weights, because rates of abstinence were taken into account separately as one of the average volume of consumption categories. The underlying variables and the scoring pattern can be found in Appendix A.

To apply pattern values to estimate the burden of disease attributable to alcohol, countries with missing data on drinking pattern values were assigned the same category as that of neighbouring countries, taking into consideration geographical and cultural proximity. The pattern values for more than 130 countries worldwide can be seen in Table 12.3.[9]

Patterns of drinking thus defined were found to be unrelated to volume: the overall Pearson correlation between pattern values and per capita consumption for the countries included is –0.126 and the more appropriate Spearman correlation is –0.072. Both correlations do not achieve statistical significance; that is, they are not significantly different from zero (both correlations based on 132 countries with data on both variables). This suggests that drinking pattern may provide important unique information about the risks of drinking alcohol beyond that captured by per capita consumption.

Although this procedure allowed us to derive drinking pattern values from a combination of empirical data and expert judgement, these patterns still needed to be validated empirically to demonstrate that they were, in fact, related to outcomes. In other words, pattern values serve as a description of one aspect of exposure that is theoretically postulated to be related to harm, but such a relation still has to be empirically established. In addition, the degree of influence of patterns on harm (i.e. how much weight to assign to drinking pattern in calculating the burden of disease attributable to alcohol) had to be estimated. Moreover, the weight to be assigned to drinking pattern may vary by type of outcome, sex and age. A later section of this chapter describes how these weights were developed.

2.4 Methods for obtaining estimates where more than one data source exists

For estimating overall consumption, clear hierarchies were used for integrating per capita data into the WHO Global Alcohol Database and subsequently into this work.

- Scientifically derived and well documented local estimates (e.g. from the National Drug Research Institute in Australia, see Catalano et al. 2001) were given first priority.
- Production/sales data were used, such as the annual data on per capita consumption published by the alcohol industry (e.g. Productschap voor Gedistilleerde Dranken 1999, 2000).
- FAO production and trade data were used where other data were not available.

If more than one data point existed for the time after 1998 (e.g. per capita estimates for 1998 and 1999), data points were averaged. With respect to survey data, if more than one representative survey with more than 2000 persons existed, the most recent survey estimates were used. Survey data were always given priority over key informant estimates in estimating pattern values.

2.5 Methods for obtaining estimates where no data source exists

Most regions had sufficient data for estimating prevalence of average volume of drinking, based on per capita consumption (including unrecorded consumption) plus the sex-specific ratio of abstinence derived from surveys. Survey data on abstinence were available for 69 countries (52.3% of all 132 countries included), and were additionally estimated for 39 countries (29.5% of all the countries). Estimation was based on abstinence rates in adjoining countries. Survey data on abstinence were available for many of the countries with large populations: Brazil, China, India, Mexico, Nigeria, the Russian Federation, South Africa, the United States of America and the major (western) European countries. These surveys were taken as indicators for the respective subregions. Regional numbers are to a large degree influenced by a limited number of highly populated countries. Thus, it is important to get the numbers for these countries correct by investing limited resources in estimating alcohol consumption for these countries, rather than attempting to improve the data for all countries in the world.[10]

Data were scarcer with respect to patterns of drinking. Only 44 countries (33.3% of 132 countries) had sufficient information on patterns to compute a pattern score. For another 88 countries (66.6%), data on patterns had to be estimated. Clearly, it is a priority for future estimates that more data on drinking patterns be collected for use in these analyses (see

also Rehm and Gmel 2000b). As with per capita consumption, ratings on drinking patterns for countries for which no data were available were based on social and cultural factors (Muslim vs non-Muslim country, type of drinking culture, etc.) and on drinking patterns in surrounding countries.

2.6 Description of databases, including methodological qualities

A description of the WHO Global Alcohol Database can be found in the *Global status report on alcohol* (WHO 1999). The Swiss Institute for the Prevention of Alcohol Problems constantly updates and expands the Database, which includes both adult per capita and survey data. In addition, many surveys were directly sent to the first author of this work, especially from countries that also supplied key informant information. Additional surveys from developing countries can be found in a WHO collection (WHO 2001). The data in the WHO Database are selected and scrutinized according to set criteria. The data from established market economies are usually based on more reliable sales data and better-quality surveys than those from developing countries.

2.7 Characteristics of excluded studies/databases

Studies were excluded only if better survey information was available for the same country. Better survey information was defined in terms of how recently the survey had been conducted, the availability of a probability sample of at least 2000 respondents, or other quality criteria (e.g. a representative survey based on probabilistic sampling of the whole country vs a non-representative survey or regional survey; better alcohol measures, such as quantity–frequency measure vs frequency-only measure; or larger survey at the same time).

2.8 Estimates of country data and exposure dimensions by subregion, age and sex

Table 12.3 provides country-specific information on alcohol consumption, drinking patterns, percentage abstainers and validity ratings for estimates. Also shown are the relevant subregion and the population aged ≥15 years in 2000.

Table 12.4 gives estimates of the proportion of population in each of the four categories of average alcohol consumption described above by subregion, sex and age. The CRA required two age groups for people aged >70 years: 70–79 years and ≥80 years. With a lack of evidence to differentiate between these two age categories, both were assumed to have the same prevalence and risk relations.

These figures assume no alcohol consumption leading to harm for young people under the age of 15 years. This is certainly not true for young people in established market economies, where drinking starts early and where alcohol-related harm can be found (though not with a

Table 12.3 Per capita alcohol consumption, patterns of drinking and abstinence in selected countries after 1998

Country	*Subregion*	*Adult per capita alcohol consumption*[a]	*Unrecorded consumption*[b]	*Pattern value*[c]	*Validity pattern value*[d]	*Percentage male abstainers*[e]	*Percentage female abstainers*[f]	*Validity of abstinence*[g]	*Population aged ≥15 years (000s)*
Albania	EUR-B	4.77	3.00	3	0	12.0	36.0	0	2195.8
Algeria	AFR-D	0.47	0.16	3	0	80.0	98.0	0	19 939.8
Argentina	AMR-B	16.30	1.00	2	1	7.0	21.0	1	26766.9
Armenia	EUR-B	2.88	1.44	2	1	9.9	60.0	1	2656.9
Australia	WPR-A	9.19	0.00	2	1	15.8	24.0	1	14988.4
Austria	EUR-A	13.90	1.00	1	0	13.0	33.0	1	6814.9
Azerbaijan	EUR-B	2.86	1.43	3	0	12.0	36.0	0	5520.9
Barbados	AMR-B	7.43	–0.50	2	0	29.0	70.4	0	213.6
Belarus	EUR-C	12.22	4.90	4	0	2.0	4.0	1	8322.3
Belgium	EUR-A	11.45	0.50	1	0	9.6	20.5	1	8420.4
Belize	AMR-B	6.35	2.00	4	0	24.0	44.0	0.5	145.0
Bolivia	AMR-D	5.74	3.00	3	0	23.8	44.6	1	5028.6
Bosnia and Herzegovina	EUR-B	7.65	3.00	3	0	12.0	36.0	0	3223.8
Botswana	AFR-E	5.33	3.00	3	0	37.0	70.0	0	938.4
Brazil	AMR-B	8.59	3.00	3	1	36.4	57.0	1	121038.8
Bulgaria	EUR-B	13.08	5.00	2	1	8.0	16.0	1	6890.0
Burkina Faso	AFR-D	3.81	3.32	3	0	—	—	—	6287.6
Burundi	AFR-E	7.42	4.75	3	0	—	—	—	3591.1
Cambodia	WPR-B	0.36	0.12	3	0	74.4	96.0	0	6603.7
Cameroon	AFR-D	4.35	2.62	3	0	—	—	—	8524.9

continued

Table 12.3 Per capita alcohol consumption, patterns of drinking and abstinence in selected countries after 1998 (*continued*)

Country	*Subregion*	*Adult per capita alcohol consumption*[a]	*Unrecorded consumption*[b]	*Pattern value*[c]	*Validity pattern value*[d]	*Percentage male abstainers*[e]	*Percentage female abstainers*[f]	*Validity of abstinence*[g]	*Population aged ≥15 years (000s)*
Canada	AMR-A	9.43	1.00	2	1	17.3	28.0	1	25248.1
Central African Republic	AFR-E	3.01	1.00	3	0	—	—	—	2078.4
Chile	AMR-B	8.34	1.00	3	0	31.4	46.5	1	10883.1
China	WPR-B	4.83	1.00	2	1	15.9	70.7	1	960300.9
Colombia	AMR-B	8.30	2.00	3	0	31.4	46.5	0.5	28470.8
Costa Rica	AMR-B	6.70	2.00	3	0	45.0	75.0	1	2721.4
Croatia	EUR-A	18.39	4.50	3	0	12.0	36.0	0	3709.2
Cuba	AMR-A	5.66	2.00	2	0	29.0	70.4	0	8823.4
Cyprus	EMR-B	9.29	1.00	1	0	1.2	15.4	0	603.0
Czech Republic	EUR-A	15.02	1.00	2	1	3.1	8.1	1	8547.7
Democratic People's Republic of Korea	SEAR-D	5.14	1.00	3	0	—	—	—	17399.1
Denmark	EUR-A	14.32	2.00	1	1	2.0	4.0	1	4341.6
Djibouti	EMR-D	.66	0.22	3	0	—	—	—	373.4
Dominican Republic	AMR-B	5.71	1.00	2	0	29.0	70.4	0	5687.8
Ecuador	AMR-D	5.49	3.66	3	0	20.0	40.0	0.5	8368.2
Egypt	EMR-D	0.92	0.46	2	0	70.0	98.0	0.5	44274.2
El Salvador	AMR-B	4.64	2.00	4	0	8.7	37.7	0	4041.9
Eritrea	AFR-E	2.55	0.85	3	0	—	—	—	2151.5
Estonia	EUR-C	11.70	5.00	3	0	5.0	10.0	1	1152.4

Ethiopia	AFR-E	1.68	0.84	3	0	—	—	—	33690.1
Fiji	WPR-B	2.95	1.00	3	0	74.3	97.5	1	561.3
Finland	EUR-A	11.69	2.00	3	1	8.0	10.0	1	4239.6
France	EUR-A	15.62	1.00	1	1	7.3	11.3	1	48032.9
Gabon	AFR-D	7.34	4.00	3	0	—	—	—	733.5
Georgia	EUR-B	7.36	2.00	2	0	12.0	36.0	0	3868.9
Germany	EUR-A	14.40	1.00	1	1	4.2	5.4	1	69469.4
Ghana	AFR-D	3.64	1.82	3	0	—	—	—	11489.3
Greece	EUR-A	11.39	2.00	2	1	1.2	15.4	1	9051.8
Guatemala	AMR-D	3.71	2.00	4	0	45.0	62.0	0.5	6420.1
Guyana	AMR-B	12.07	2.00	3	0	20.0	40.0	0	604.3
Haiti	AMR-D	5.38	0.00	2	0	58.0	62.0	0.5	4874.7
Honduras	AMR-B	4.22	2.00	4	0	8.7	37.7	0	3784.3
Hungary	EUR-C	17.35	4.00	3	0	6.6	21.4	1	8329.4
Iceland	EUR-A	6.41	1.00	3	0	9.1	13.3	0	215.4
India	SEAR-D	2.00	1.65	3	1	75.0	96.0	1	676054.8
Indonesia	SEAR-B	0.58	0.50	3	0	74.4	96.0	0	147181.7
Iraq	EMR-D	0.48	0.00	2	0	80.0	98.0	0	13558.9
Ireland	EUR-A	15.21	1.00	3	1	9.0	16.0	1	2938.4
Israel	EUR-A	2.91	1.00	2	1	21.0	48.7	1	4492.5
Italy	EUR-A	10.34	1.50	1	1	14.7	30.2	1	49133.0
Jamaica	AMR-B	4.28	1.00	2	0	29.0	70.4	0	1780.9
Japan	WPR-A	8.47	2.00	1	1	12.0	23.0	1	107949.3

continued

Table 12.3 Per capita alcohol consumption, patterns of drinking and abstinence in selected countries after 1998 (*continued*)

Country	*Subregion*	*Adult per capita alcohol consumption*[a]	*Unrecorded consumption*[b]	*Pattern value*[c]	*Validity pattern value*[d]	*Percentage male abstainers*[e]	*Percentage female abstainers*[f]	*Validity of abstinence*[g]	*Population aged ≥15 years (000s)*
Jordan	EMR-B	0.28	0.14	2	0	74.0	98.0	0	3871.8
Kazakhstan	EUR-C	10.11	6.90	4	0	10.0	27.0	0	11751.4
Kenya	AFR-E	6.83	5.00	3	0	45.0	65.0	0	17137.1
Kyrgyzstan	EUR-B	5.89	4.00	3	0	60.0	80.0	0	3054.5
Lao People's Democratic Republic	WPR-B	5.82	2.00	3	0	—	—	—	3044.4
Latvia	EUR-C	16.48	7.00	3	0	15.0	46.2	1	1940.2
Lebanon	EMR-B	5.60	2.00	3	0	—	—	—	2208.6
Lesotho	AFR-E	3.16	1.58	3	0	—	—	—	1294.2
Liberia	AFR-D	4.54	2.00	3	0	—	—	—	1824.6
Lithuania	EUR-C	11.41	4.90	3	0	15.0	46.2	0	2964.8
Luxembourg	EUR-A	17.32	–2.00	1	0	1.0	4.0	0.5	352.9
Malaysia	WPR-B	4.26	3.40	3	0	35.1	63.5	1	14678.4
Mauritius	AFR-D	15.62	11.00	3	0	22.0	53.0	1	865.2
Mexico	AMR-B	8.15	4.00	4	1	15.8	46.5	1	66105.2
Mongolia	WPR-B	4.45	2.00	3	0	20.2	62.7	0	1740.8
Morocco	EMR-D	1.16	0.58	3	0	—	—	—	19121.7
Myanmar	SEAR-D	0.62	0.42	2	0	45.0	93.5	0	32887.4
Namibia	AFR-E	5.40	1.80	3	1	60.9	47.1	1	1008.5
Netherlands	EUR-A	10.39	0.50	1	1	14.0	26.5	1	12926.5

New Zealand	WPR-A	11.32	0.50	2	1	10.0	14.0	1	2986.5
Nicaragua	AMR-D	3.71	1.00	4	0	8.7	37.7	0	2905.3
Nigeria	AFR-D	6.94	3.50	2	1	46.2	54.9	1	63465.7
Norway	EUR-A	7.50	2.00	3	1	8.0	17.0	1	3588.2
Pakistan	EMR-D	0.23	0.20	3	0	90.0	99.0	0	91048.8
Papua New Guinea	WPR-B	0.88	0.50	3	1	22.0	86.5	1	2948.4
Paraguay	AMR-B	9.55	1.50	3	0	18.0	38.0	0.5	3323.7
Peru	AMR-D	5.43	1.00	3	1	16.6	23.6	1	17094.4
Philippines	WPR-B	6.40	3.00	3	1	10.0	70.0	1	48096.9
Poland	EUR-B	12.64	5.00	3	1	11.6	25.7	1	31240.1
Portugal	EUR-A	15.06	1.00	1	0	14.8	48.8	1	8261.3
Republic of Korea	WPR-B	14.20	7.00	3	1	7.1	14.2	1	36775.6
Republic of Moldova	EUR-C	29.36	12.00	4	0	9.0	18.0	0	3360.7
Romania	EUR-B	16.27	4.00	3	0	23.0	53.0	0	18364.0
Russian Federation	EUR-C	16.39	5.85	4	1	9.0	8.0	1	120255.0
Rwanda	AFR-E	6.36	4.32	3	0	—	—	—	4224.2
Saudi Arabia	EMR-B	0.21	0.14	2	0	95.0	99.0	0	12848.8
Senegal	AFR-D	1.26	0.84	3	0	—	—	—	5244.9
Seychelles	AFR-D	11.00	5.16	3	1	10.0	45.0	1	69.0
Sierra Leone	AFR-D	4.22	2.41	3	0	—	—	—	2716.7
Singapore	WPR-A	3.14	1.00	2	0	74.4	96.0	0	2778.7
Slovakia	EUR-B	19.30	7.00	3	1	5.1	21.6	1	4326.7

continued

Table 12.3 Per capita alcohol consumption, patterns of drinking and abstinence in selected countries after 1998 (*continued*)

Country	*Subregion*	*Adult per capita alcohol consumption*[a]	*Unrecorded consumption*[b]	*Pattern value*[c]	*Validity pattern value*[d]	*Percentage male abstainers*[e]	*Percentage female abstainers*[f]	*Validity of abstinence*[g]	*Population aged ≥15 years (000s)*
Slovenia	EUR-A	13.42	5.20	3	1	31.2	55.4	1	1669.0
South Africa	AFR-E	12.41	2.20	3	1	55.3	83.1	1	26236.4
Spain	EUR-A	13.28	1.00	1	1	7.0	24.0	1	33863.3
Sri Lanka	SEAR-B	0.57	0.38	3	0	74.4	96.0	1	13912.4
Sudan	EMR-D	0.69	0.46	3	0	—	—	—	17863.6
Suriname	AMR-B	5.96	0.00	3	0	30.0	55.0	0.5	290.0
Swaziland	AFR-E	7.89	4.05	3	0	—	—	—	574.6
Sweden	EUR-A	9.07	2.00	3	1	7.0	12.0	1	7288.2
Switzerland	EUR-A	12.49	0.50	1	1	11.0	27.0	1	6097.3
Syrian Arab Republic	EMR-B	0.70	0.36	2	0	—	—	—	9546.7
Tajikistan	EUR-B	5.23	3.95	3	0	60.0	80.0	0	3692.5
Thailand	SEAR-B	11.70	2.00	3	1	30.5	71.7	1	45909.9
The former Yugoslav Republic of Macedonia	EUR-B	8.56	3.20	3	1	20.0	40.0	1	1559.4
Trinidad and Tobago	AMR-B	2.36	0.00	2	1	29.0	70.4	1	970.9
Tunisia	EMR-B	1.80	0.50	2	0	70.0	95.0	0	6677.8
Turkey	EUR-B	4.30	2.70	3	0	35.0	55.0	0	47742.9
Turkmenistan	EUR-B	2.85	1.00	3	0	35.0	55.0	0	2780.1

Uganda	AFR-E	13.30	10.71	3	0	45.0	67.0	0.5	10877.2
Ukraine	EUR-C	8.00	4.00	3	1	12.0	36.0	0	41487.6
United Arab Emirates	EMR-B	3.68	1.00	2	0	—	—	—	1757.7
United Kingdom	EUR-A	11.88	2.00	2	1	8.0	14.0	1	47761.2
United Republic of Tanzania	AFR-E	6.47	2.00	3	0	—	—	—	18291.2
United States	AMR-A	9.47	1.00	2	1	28.1	42.6	1	218586.3
Uruguay	AMR-B	9.54	2.00	3	0	7.0	21.0	0	2509.7
Uzbekistan	EUR-B	2.92	1.90	3	0	60.0	80.0	0	15211.3
Venezuela	EUR-C	9.59	2.00	3	0	30.0	55.0	0.5	15942.8
Viet Nam	WPR-B	2.26	1.00	3	0	—	—	—	53320.3
Zambia	AFR-E	3.96	1.00	4	1	35.0	70.0	1	4837.4
Zimbabwe	AFR-E	12.65	9.00	4	0	7.0	36.0	0.5	6847.3

— No data.

[a] Average annual per capita consumption by adults (≥15 years) after 1998 in litres of pure alcohol, including estimates of unrecorded consumption (average of available years).

[b] Estimated annual per capita unrecorded consumption by adults (≥15 years) after 1998 in litres of pure alcohol (based in part on the *Global status report on alcohol*). Negative values reflect where estimated cross-border shopping by non-residents and drinking by tourists exceeds any estimated unrecorded consumption by residents.

[c] 1 denotes the least detrimental pattern value and 4 denotes the most detrimental. Pattern values are assumed to be relatively stable and were derived for the 1990s.

[d] 0 = imputed based on regional and cultural similarities, or based on data from the *Global status report on alcohol*; 1 = questionnaire available with sufficient non-missing values to allow optimal scaling.

[e] Proportion of adult males who were abstainers for the year before the survey.

[f] Proportion of adult females who were abstainers for the year before the survey.

[g] 0 = imputed based on regional and cultural similarities; 0.5 = based on survey but only for subsections of the country or not differentiated for sex; 1 = survey data, differentiated for sex.

high prevalence) before the age of 15 years (Hibell et al. 2000). However, as data for this age group are scarce and as the prevalence rates for drinking and harm are low, the conservative approach of estimating no alcohol-related harm for this age group was adopted. The decision to model alcohol-related harm at zero for people's own drinking does not mean that there will be no alcohol-related harm estimated in this age group altogether. Rather, owing to the nature of effects, we must deviate from the standard epidemiological model and include effects of drinking on other externalities. To give just one example of this type of harm, a drunken driver may kill innocent bystanders or passengers driving in his car who are younger than 15 years, and this would be a fatality caused by alcohol.

The following distribution data were based on survey-based information on abstainers for 69 countries. For distributional information on drinkers, the following sources were considered:

- AFR-D, Nigeria (Mustonen et al. 2001 and newer survey data reported in the key informant questionnaire from I. Obot/O. Gureje);
- AFR-E, South Africa (Department of Health 1998, South African Demographic and Health Survey);
- AMR-A, Canada and the United States (surveys provided by E. Adlaf for Canada and T. Greenfield for the United States);
- AMR-B, Brazil (São Paulo) (Galduróz et al. 2000) and Mexico (surveys provided by the Mexican Institute of Psychiatry); see also WHO (2001) for country reports on Costa Rica and Mexico, and Jutkowitz and Hongsook (1994);
- AMR-D (survey data for Peru and Jutkowitz and Hongsook 1994);
- EMR-B and EMR-D (only per capita information and general distribution information as approximately log-normal[11] with some data on abstinence);
- EUR-A (based on the average of many country surveys);
- EUR-B, Poland (based on survey information provided by key informants);
- EUR-C, the Russian Federation (published national and regional survey data from Bobak et al. 1999; Malyutina et al. 2001);
- SEAR-B, Sri Lanka and Thailand (survey estimates provided by key informants);
- SEAR-D, India (regional survey data provided by key informants);
- WPR-A, Australia and New Zealand (survey data, see English et al. 1995; Ridolfo and Stevenson for Australia and http://www.aphru.ac.nz/projects/Larger for New Zealand); and

- WPR-B, China (Wei et al. 1999 and additional information by the first author).

The numbers in Table 12.4 are given as a proportion of the age–sex-specific population. Thus, for females aged 15–29 years in WPR-B, 67.4% are estimated to abstain, 32.6% are estimated to drink the equivalent of between 0 g and 20 g pure alcohol per day, 0.1% are estimated to drink between 20 g and 40 g, and less than 0.05% are estimated to drink more than 40 g. In the oldest age group, 89.8% of females are estimated to abstain, 10.2% to drink the equivalent of up to 20 g pure alcohol per day, and less than 0.05% to drink more.

Currently, pattern values assigned to each country and then computed as a population-weighted average for each subregion are not specific by sex and age (see Table 12.5). This may change in the future when survey data on patterns become more available.

2.9 Quantitative and qualitative sources of uncertainty

Uncertainty analysis

As described, alcohol consumption as a risk factor has two dimensions: average volume and patterns. It is thus proposed to base the uncertainty analysis on the weighted average of the available information for both dimensions for each subregion. Uncertainty analysis is undertaken to give an indication on uncertainty, based on different characteristics such as the source or variability of the estimated data. It will also be used to calculate the confidence intervals (CIs) of the alcohol-related burden. Classically, CIs for prevalence are determined by sample size, assuming that the underlying individual data are representative of the subregion. For some subregions, however, we do not have probabilistic samples. As alcohol consumption is a social activity and can vary markedly from one country to another within a region, one cannot automatically assume that the countries without surveys would have the same alcohol distribution as the countries with surveys. Thus, the procedure based on sample size cannot be used here. Moreover, prevalence was derived from both aggregate- (per capita consumption) and individual-level data in a triangulation of information, for which there is no statistical theory for readily deriving CIs.

The algorithms specified below were developed after extensive discussions with experts in the field. They are intended to reflect the quantity and quality of the underlying data sources. Aggregate-level data exist for all countries. To estimate average volume of alcohol consumption, we propose to base uncertainty analysis on the amount of survey information available in a subregion. The procedure allowed the estimation of lower or upper limits, even if no survey information existed. In Pakistan, for example, per capita alcohol consumption set clear upper boundaries for the highest drinking categories, since some values would

Table 12.4 Estimated proportions of population in average volume of consumption categories by sex, age and subregion, in 2000[a]

Subregion	Sex	Average volume of consumption category[b]	Age group (years)					
			15–29	30–44	45–59	60–69	70–79	≥80
AFR-D	Male	Abstinence	0.510	0.462	0.514	0.565	0.616	0.616
		D I	0.420	0.447	0.396	0.354	0.323	0.323
		D II	0.063	0.073	0.072	0.063	0.044	0.044
		D III	0.007	0.018	0.018	0.018	0.016	0.016
	Female	Abstinence	0.746	0.697	0.697	0.746	0.796	0.796
		D I	0.234	0.267	0.265	0.237	0.191	0.191
		D II	0.019	0.030	0.029	0.010	0.010	0.010
		D III	0.001	0.007	0.010	0.007	0.003	0.003
AFR-E	Male	Abstinence	0.432	0.375	0.428	0.482	0.536	0.536
		D I	0.431	0.430	0.403	0.368	0.354	0.354
		D II	0.125	0.161	0.135	0.116	0.082	0.082
		D III	0.012	0.034	0.034	0.033	0.029	0.029
	Female	Abstinence	0.715	0.664	0.664	0.715	0.766	0.766
		D I	0.243	0.277	0.271	0.237	0.203	0.203
		D II	0.036	0.046	0.046	0.036	0.025	0.025
		D III	0.006	0.012	0.018	0.012	0.006	0.006
AMR-A	Male	Abstinence	0.240	0.221	0.268	0.374	0.431	0.431
		D I	0.522	0.583	0.577	0.525	0.498	0.498
		D II	0.164	0.146	0.105	0.095	0.064	0.064
		D III	0.074	0.050	0.050	0.006	0.006	0.006
	Female	Abstinence	0.360	0.331	0.409	0.584	0.633	0.633
		D I	0.563	0.620	0.548	0.382	0.337	0.337
		D II	0.050	0.033	0.027	0.025	0.023	0.023
		D III	0.027	0.016	0.016	0.008	0.007	0.007
AMR-B	Male	Abstinence	0.220	0.203	0.172	0.199	0.358	0.358
		D I	0.671	0.674	0.711	0.714	0.605	0.605
		D II	0.035	0.045	0.045	0.031	0.025	0.025
		D III	0.074	0.078	0.072	0.056	0.012	0.012
	Female	Abstinence	0.463	0.444	0.444	0.488	0.538	0.538
		D I	0.464	0.475	0.486	0.450	0.429	0.429
		D II	0.028	0.028	0.026	0.030	0.020	0.020
		D III	0.046	0.053	0.044	0.032	0.013	0.013
AMR-D	Male	Abstinence	0.298	0.264	0.304	0.398	0.498	0.498
		D I	0.677	0.712	0.672	0.585	0.494	0.494
		D II	0.017	0.016	0.016	0.013	0.008	0.008
		D III	0.008	0.008	0.008	0.004	0.001	0.001
	Female	Abstinence	0.431	0.393	0.487	0.548	0.628	0.628
		D I	0.536	0.572	0.483	0.428	0.356	0.356
		D II	0.024	0.025	0.021	0.019	0.012	0.012
		D III	0.009	0.009	0.008	0.005	0.004	0.004
EMR-B	Male	Abstinence	0.789	0.838	0.838	0.887	0.976	0.976
		D I	0.191	0.149	0.149	0.107	0.024	0.024
		D II	0.013	0.010	0.010	0.004	0.000	0.000
		D III	0.006	0.003	0.003	0.001	0.000	0.000

Table 12.4 Estimated proportions of population in average volume of consumption categories by sex, age and subregion, in 2000[a] (*continued*)

Subregion	Sex	Average volume of consumption category[b]	Age group (years)					
			15–29	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
	Female	Abstinence	0.937	0.968	0.968	0.998	1.000	1.000
		D I	0.052	0.027	0.027	0.002	0.000	0.000
		D II	0.008	0.005	0.005	0.000	0.000	0.000
		D III	0.003	0.000	0.000	0.000	0.000	0.000
EMR-D	Male	Abstinence	0.898	0.898	0.898	0.947	0.987	0.987
		D I	0.101	0.102	0.102	0.052	0.013	0.013
		D II	0.001	0.000	0.000	0.000	0.000	0.000
		D III	0.000	0.000	0.000	0.000	0.000	0.000
	Female	Abstinence	0.975	0.990	0.990	1.000	1.000	1.000
		D I	0.024	0.010	0.010	0.000	0.000	0.000
		D II	0.001	0.000	0.000	0.000	0.000	0.000
		D III	0.001	0.000	0.000	0.000	0.000	0.000
EUR-A	Male	Abstinence	0.074	0.074	0.093	0.139	0.186	0.186
		D I	0.748	0.721	0.701	0.723	0.717	0.717
		D II	0.087	0.102	0.096	0.069	0.042	0.042
		D III	0.091	0.102	0.110	0.069	0.055	0.055
	Female	Abstinence	0.138	0.138	0.173	0.259	0.346	0.346
		D I	0.698	0.726	0.662	0.635	0.571	0.571
		D II	0.123	0.103	0.124	0.085	0.065	0.065
		D III	0.041	0.033	0.041	0.021	0.017	0.017
EUR-B	Male	Abstinence	0.237	0.284	0.284	0.331	0.379	0.379
		D I	0.653	0.606	0.625	0.598	0.582	0.582
		D II	0.054	0.054	0.049	0.038	0.016	0.016
		D III	0.056	0.056	0.042	0.033	0.024	0.024
	Female	Abstinence	0.410	0.461	0.512	0.614	0.614	0.614
		D I	0.507	0.449	0.414	0.328	0.339	0.339
		D II	0.068	0.069	0.053	0.047	0.037	0.037
		D III	0.016	0.021	0.021	0.010	0.010	0.010
EUR-C	Male	Abstinence	0.088	0.088	0.110	0.164	0.219	0.219
		D I	0.602	0.662	0.584	0.629	0.669	0.669
		D II	0.188	0.159	0.185	0.132	0.067	0.067
		D III	0.123	0.091	0.121	0.075	0.045	0.045
	Female	Abstinence	0.140	0.140	0.175	0.263	0.351	0.351
		D I	0.719	0.743	0.683	0.645	0.588	0.588
		D II	0.115	0.096	0.116	0.079	0.051	0.051
		D III	0.026	0.020	0.026	0.013	0.011	0.011
SEAR-B	Male	Abstinence	0.631	0.561	0.701	0.841	0.981	0.981
		D I	0.359	0.410	0.295	0.156	0.018	0.018
		D II	0.007	0.024	0.003	0.002	0.000	0.000
		D III	0.002	0.006	0.001	0.001	0.000	0.000
	Female	Abstinence	0.885	0.914	0.914	0.943	0.953	0.953
		D I	0.103	0.078	0.078	0.052	0.047	0.047
		D II	0.009	0.008	0.008	0.005	0.000	0.000
		D III	0.002	0.000	0.000	0.000	0.000	0.000

continued

Table 12.4 Estimated proportions of population in average volume of consumption categories by sex, age and subregion, in 2000[a] (*continued*)

Subregion	Sex	Average volume of consumption category[b]	Age group (years)					
			15–29	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
SEAR-D	Male	Abstinence	0.717	0.637	0.796	0.956	1.000	1.000
		D I	0.276	0.338	0.201	0.044	0.000	0.000
		D II	0.006	0.020	0.002	0.001	0.000	0.000
		D III	0.002	0.005	0.001	0.000	0.000	0.000
	Female	Abstinence	0.937	0.968	0.968	0.998	1.000	1.000
		D I	0.051	0.028	0.028	0.002	0.000	0.000
		D II	0.007	0.004	0.004	0.000	0.000	0.000
		D III	0.005	0.000	0.000	0.000	0.000	0.000
WPR-A	Male	Abstinence	0.095	0.095	0.119	0.179	0.238	0.238
		D I	0.834	0.849	0.812	0.776	0.730	0.730
		D II	0.033	0.028	0.032	0.023	0.013	0.013
		D III	0.037	0.028	0.037	0.023	0.018	0.018
	Female	Abstinence	0.163	0.163	0.204	0.306	0.408	0.408
		D I	0.806	0.812	0.766	0.675	0.578	0.578
		D II	0.023	0.019	0.023	0.015	0.011	0.011
		D III	0.008	0.006	0.008	0.004	0.003	0.003
WPR-B	Male	Abstinence	0.153	0.153	0.153	0.204	0.256	0.256
		D I	0.769	0.761	0.761	0.719	0.684	0.684
		D II	0.055	0.053	0.053	0.051	0.040	0.040
		D III	0.022	0.032	0.032	0.026	0.020	0.020
	Female	Abstinence	0.674	0.674	0.674	0.786	0.898	0.898
		D I	0.326	0.326	0.326	0.214	0.102	0.102
		D II	0.001	0.000	0.000	0.000	0.000	0.000
		D III	0.000	0.000	0.000	0.000	0.000	0.000

[a] Prevalences are rounded to full percentages. Thus, a value of zero does not necessarily indicate that there are no people in a certain category, but may indicate a prevalence of less than 0.005 or 0.5%.

[b] **Drinking categories are defined as follows:**

Risk factor: alcohol—first dimension: average volume of consumption.

Units: grams of pure alcohol per day.

Definitions of categories of risk factor levels

Level 1:	Abstinence	abstainer
Level 2:	D I	drinking category I: women >0–<20 g; men >0–<40 g
Level 3:	D II	drinking category II: women 20–<40 g; men 40–<60 g
Level 4:	D III	drinking category III: women >40 g; men >60 g

not be physically possible within the overall volume consumed in this country.

In operationalizing these principles, the validity of the abstainer category was selected (for values in individual countries see Table 12.3). This variable was aggregated using the population aged ≥15 years as a

Table 12.5 Patterns of drinking by subregion

Subregion	*Pattern value*[a]	*Validity of pattern value*
AFR-D	2.48	0.52
AFR-E	3.09	0.24
AMR-A	2.00	0.97
AMR-B	3.14	0.77
AMR-D	3.10	0.38
EMR-B	2.01	0.00
EMR-D	2.35	0.00
EUR-A	1.34	0.92
EUR-B	2.93	0.31
EUR-C	3.62	0.75
SEAR-B	2.50	0.22
SEAR-D	2.95	0.93
WPR-A	1.16	0.98
WPR-B	2.15	0.93

[a] Pattern values were defined as follows:

Risk factor: alcohol—second dimension: patterns of drinking.

Units: range between 1 and 4; originally derived from optimal scaling and then based on addition of values of each pattern component (see Appendix A for details); subregional averages are population-weighted country averages.

Definitions of categories of risk factor levels

Level 1: based on score of initial pattern components, with values in the lowest quartile reflecting least detrimental patterns of drinking such as least heavy drinking occasions, drinking with meals, no fiesta drinking and least drinking in public places.

Level 2: based on score of initial pattern components, with values in the second lowest quartile.

Level 3: based on score of initial pattern components, with values in the second highest quartile.

Level 4: based on score of initial pattern components, with values in the highest quartile reflecting detrimental patterns such as many heavy drinking occasions, drinking outside meals, high level of fiesta drinking and drinking in public places.

weight. The resulting values were treated in the uncertainty analysis as follows:

For aggregated validity values of 0	Base prevalence estimate on full range from 0 to twice the point estimate (i.e. point estimate plus 100% of the point estimate).
For aggregated validity values >0 and <0.5	Point estimate ±50% of point estimate of prevalence.
For aggregated validity values ≥0.5 and <0.75	Point estimate ±25% of point estimate of prevalence.

For aggregated validity values ≥0.75	Point estimate ±10% of point estimate of prevalence.

This applies to both sexes, as most surveys include both males and females. Further corrections were made based on per capita consumption for subregions where certain distributions were not plausible because the known per capita consumption could not be derived with less than a certain proportion of abstainers (for EMR-B: maximum CI for abstainers ±15%, minimum: ±1%; for EMR-D: maximum ±10%, minimum: ±1%; for SEAR-B: maximum ±10%, minimum: ±1%; for SEAR-D and WPR-B: minimum: ±0.2%). The results can be seen in Table 12.6.

Similarly, for constructing CIs around patterns of drinking (see Table 12.7), the validity of the underlying pattern values was used. Again, using the weighted average on the validity ratings of the pattern value (see Table 12.3 for the underlying country data), the following uncertainty ranges were proposed:

For validity of pattern value of 0	Uncertainty analysis on full range of pattern values (i.e. using pattern values 1 and 4 as bounds).
For validity of pattern value ranging from >0 and <0.5	Point estimate ± 1.
For validity of pattern value ranging from ≥0.5 and <0.75	Point estimate ± 0.5.
For validity of pattern value ranging from ≥0.75	Point estimate ± 0.25.

The validity of pattern value ranged from 0 (e.g. only expert judgements for pattern in EMR-B and EMR-D with no underlying data) to values above 0.95 for several subregions (theoretically 1 if all the pattern values of constituent countries were derived from survey estimates).

The suggested procedure clearly reflects our range of knowledge. For example, we have no knowledge about patterns in EMR-B and EMR-D, where the uncertainty estimates consequently varied between 1 (best possible pattern) and 4 (most detrimental pattern), whereas we have good data for many other subregions (e.g. all the A mortality strata subregions), where the uncertainty estimates vary by only ± 0.25 (e.g. EUR-A, between 1.09 and 1.59).

Overall evaluation of quality for exposure data

Data on production and trade or sales required for estimating adult per capita consumption have been collected systematically for decades in most countries. In this sense, alcohol as a risk factor for global health is privileged compared to some other risk factors, where exposure data are

Table 12.6 Estimated uncertainty range (±%) around point estimate for prevalence of average volume of consumption categories

Subregion	Sex	Average volume of consumption category	Age group (years)					
			15–29	30–44	45–59	60–69	70–79	≥80
AFR-D	Male	Abstinence	5.10	4.62	5.14	5.65	6.16	6.16
		D I	4.20	4.47	3.96	3.54	3.23	3.23
		D II	0.63	0.73	0.72	0.63	0.44	0.44
		D III	0.07	0.18	0.18	0.18	0.16	0.16
	Female	Abstinence	7.46	6.97	6.97	7.46	7.96	7.96
		D I	2.34	2.67	2.65	2.37	1.91	1.91
		D II	0.19	0.30	0.29	0.10	0.10	0.10
		D III	0.01	0.07	0.10	0.07	0.03	0.03
AFR-E	Male	Abstinence	10.80	9.37	10.71	12.05	13.39	13.39
		D I	10.77	10.75	10.08	9.21	8.84	8.84
		D II	3.12	4.03	3.36	2.91	2.05	2.05
		D III	0.31	0.85	0.84	0.83	0.72	0.72
	Female	Abstinence	17.88	16.61	16.61	17.88	19.16	19.16
		D I	6.07	6.93	6.78	5.92	5.07	5.07
		D II	0.90	1.16	1.16	0.90	0.63	0.63
		D III	0.15	0.30	0.45	0.30	0.15	0.15
AMR-A	Male	Abstinence	2.40	2.21	2.68	3.74	4.31	4.31
		D I	5.22	5.83	5.77	5.25	4.98	4.98
		D II	1.64	1.46	1.05	0.95	0.64	0.64
		D III	0.74	0.50	0.50	0.06	0.06	0.06
	Female	Abstinence	3.60	3.31	4.09	5.84	6.33	6.33
		D I	5.63	6.20	5.48	3.82	3.37	3.37
		D II	0.50	0.33	0.27	0.25	0.23	0.23
		D III	0.27	0.16	0.16	0.08	0.07	0.07
AMR-B	Male	Abstinence	2.20	2.03	1.72	1.99	3.58	3.58
		D I	6.71	6.74	7.11	7.14	6.05	6.05
		D II	0.35	0.45	0.45	0.31	0.25	0.25
		D III	0.74	0.78	0.72	0.56	0.12	0.12
	Female	Abstinence	4.63	4.44	4.44	4.88	5.38	5.38
		D I	4.64	4.75	4.86	4.50	4.29	4.29
		D II	0.28	0.28	0.26	0.30	0.20	0.20
		D III	0.46	0.53	0.44	0.32	0.13	0.13
AMR-D	Male	Abstinence	7.46	6.60	7.60	9.96	12.45	12.45
		D I	16.93	17.80	16.80	14.62	12.34	12.34
		D II	0.41	0.39	0.39	0.31	0.19	0.19
		D III	0.20	0.20	0.20	0.10	0.02	0.02
	Female	Abstinence	10.79	9.83	12.17	13.70	15.70	15.70
		D I	13.40	14.31	12.09	10.70	8.90	8.90
		D II	0.60	0.63	0.53	0.48	0.31	0.31
		D III	0.22	0.23	0.21	0.12	0.09	0.09
EMR-B	Male	Abstinence	15.00	15.00	15.00	15.00	15.00	15.00
		D I	19.55	15.25	15.25	11.00	2.65	2.65
		D II	1.21	1.00	1.00	1.00	1.00	1.00
		D III	1.00	1.00	1.00	1.00	1.00	1.00

continued

Table 12.6 Estimated uncertainty range (±%) around point estimate for prevalence of average volume of consumption categories (*continued*)

Subregion	Sex	Average volume of consumption category	Age group (years)					
			15–29	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
	Female	Abstinence	15.00	15.00	15.00	15.00	15.00	15.00
		D I	5.40	2.87	2.87	1.00	1.00	1.00
		D II	1.00	1.00	1.00	1.00	1.00	1.00
		D III	1.00	1.00	1.00	1.00	1.00	1.00
EMR-D	Male	Abstinence	10.00	10.00	10.00	10.00	10.00	10.00
		D I	5.07	5.09	5.09	2.61	1.00	1.00
		D II	1.00	1.00	1.00	1.00	1.00	1.00
		D III	1.00	1.00	1.00	1.00	1.00	1.00
	Female	Abstinence	10.00	10.00	10.00	10.00	10.00	10.00
		D I	1.18	1.00	1.00	1.00	1.00	1.00
		D II	1.00	1.00	1.00	1.00	1.00	1.00
		D III	1.00	1.00	1.00	1.00	1.00	1.00
EUR-A	Male	Abstinence	0.74	0.74	0.93	1.39	1.86	1.86
		D I	7.48	7.21	7.01	7.23	7.17	7.17
		D II	0.87	1.02	0.96	0.69	0.42	0.42
		D III	0.91	1.02	1.10	0.69	0.55	0.55
	Female	Abstinence	1.38	1.38	1.73	2.59	3.46	3.46
		D I	6.98	7.26	6.62	6.35	5.71	5.71
		D II	1.23	1.03	1.24	0.85	0.65	0.65
		D III	0.41	0.33	0.41	0.21	0.17	0.17
EUR-B	Male	Abstinence	5.92	7.10	7.10	8.28	9.47	9.47
		D I	16.34	15.14	15.63	14.94	14.55	14.55
		D II	1.35	1.36	1.23	0.96	0.39	0.39
		D III	1.39	1.40	1.05	0.82	0.59	0.59
	Female	Abstinence	10.24	11.52	12.80	15.36	15.36	15.36
		D I	12.66	11.22	10.35	8.20	8.47	8.47
		D II	1.70	1.73	1.32	1.18	0.91	0.91
		D III	0.39	0.53	0.53	0.26	0.26	0.26
EUR-C	Male	Abstinence	2.19	2.19	2.74	4.11	5.48	5.48
		D I	15.05	16.55	14.60	15.72	16.72	16.72
		D II	4.69	3.98	4.63	3.29	1.68	1.68
		D III	3.07	2.27	3.03	1.88	1.12	1.12
	Female	Abstinence	3.51	3.51	4.39	6.58	8.77	8.77
		D I	17.97	18.58	17.07	16.12	14.69	14.69
		D II	2.88	2.40	2.90	1.97	1.27	1.27
		D III	0.64	0.51	0.64	0.33	0.27	0.27
SEAR-B	Male	Abstinence	10.00	10.00	10.00	10.00	10.00	10.00
		D I	17.96	20.48	14.73	7.80	1.00	1.00
		D II	0.37	1.18	1.00	1.00	1.00	1.00
		D III	1.00	1.00	1.00	1.00	1.00	1.00
	Female	Abstinence	10.00	10.00	10.00	10.00	10.00	10.00
		D I	5.16	3.88	3.88	2.62	2.36	2.36
		D II	0.46	0.41	0.41	1.00	1.00	1.00
		D III	1.00	1.00	1.00	1.00	1.00	1.00
SEAR-D	Male	Abstinence	7.17	6.37	7.96	9.56	10.00	10.00
		D I	2.76	3.38	2.01	0.44	0.20	0.20
		D II	0.20	0.20	0.20	0.20	0.20	0.20
		D III	0.20	0.20	0.20	0.20	0.20	0.20

Table 12.6 Estimated uncertainty range (±%) around point estimate for prevalence of average volume of consumption categories (*continued*)

Subregion	Sex	Average volume of consumption category	Age group (years)					
			15–29	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
	Female	Abstinence	9.37	9.68	9.68	9.98	10.00	10.00
		D I	0.51	0.28	0.28	0.20	0.20	0.20
		D II	0.20	0.20	0.20	0.20	0.20	0.20
		D III	0.20	0.20	0.20	0.20	0.20	0.20
WPR-A	Male	Abstinence	0.95	0.95	1.19	1.79	2.38	2.38
		D I	8.34	8.49	8.12	7.76	7.30	7.30
		D II	0.33	0.28	0.32	0.23	0.13	0.13
		D III	0.37	0.28	0.37	0.23	0.18	0.18
	Female	Abstinence	1.63	1.63	2.04	3.06	4.08	4.08
		D I	8.06	8.12	7.66	6.75	5.78	5.78
		D II	0.23	0.19	0.23	0.15	0.11	0.11
		D III	0.08	0.06	0.08	0.04	0.03	0.03
WPR-B	Male	Abstinence	1.53	1.53	1.53	2.04	2.56	2.56
		D I	7.69	7.61	7.61	7.19	6.84	6.84
		D II	0.55	0.53	0.53	0.51	0.40	0.40
		D III	0.22	0.32	0.32	0.26	0.20	0.20
	Female	Abstinence	6.74	6.74	6.74	7.86	8.98	8.98
		D I	3.26	3.26	3.26	2.14	1.02	1.02
		D II	0.20	0.20	0.20	0.20	0.20	0.20
		D III	0.20	0.20	0.20	0.20	0.20	0.20

Table 12.7 Uncertainty analysis for patterns of drinking, by subregion

Subregion	Pattern value	Validity of pattern value	Lower boundary for uncertainty	Upper boundary for uncertainty
AFR-D	2.48	0.52	1.98	2.98
AFR-E	3.09	0.24	2.09	4.00
AMR-A	2.00	0.97	1.75	2.25
AMR-B	3.14	0.77	2.89	3.39
AMR-D	3.10	0.38	2.10	4.00
EMR-B	2.01	0.00	1.00	4.00
EMR-D	2.35	0.00	1.00	4.00
EUR-A	1.34	0.92	1.09	1.59
EUR-B	2.93	0.31	1.93	3.93
EUR-C	3.62	0.75	3.37	3.87
SEAR-B	2.50	0.22	1.50	3.50
SEAR-D	2.95	0.93	2.70	3.20
WPR-A	1.16	0.98	1.00	1.66
WPR-B	2.15	0.93	1.90	2.40

available only in established market economies, if at all. Unfortunately, adult per capita consumption figures *per se,* as described above, cannot be used as exposure data for global burden of disease because these figures do not give any specification about who consumed alcohol, when and in what quantities. This can only be specified by using representative surveys of the general population. Thus, for the current exercise, adult per capita figures had to be supplemented by survey data and, where such data were not available, by expert judgements. This procedure may have introduced errors at different points.

- *Errors in adult per capita consumption estimates.* Because per capita estimates are derived mainly from production and trade or sale, other sources (home brewing, cross-border smuggling, illegal production, etc.) are often ignored. There is a long tradition of trying to estimate this *unrecorded* consumption, but mainly in established market economies where the proportion of unrecorded to recorded is low relative to other parts of the world. For example, see the recent European Comparative Alcohol Study (ECAS) estimates for Europe (http://www.fhi.se/pdf/ECAS_2.pdf; Leifman 2001) compared to the estimates of unrecorded consumption for sub-Saharan Africa given below. In addition, estimation of unrecorded consumption is particularly difficult in regions where alcohol is prohibited for religious reasons. In summary, although these sources of error exist, the global aggregate estimates on adult per capita consumption are among the best and most reliable sources for global risk factors.

Adult per capita consumption figures then were used to derive prevalence rates for specific drinking categories for different age–sex groups. This derivation was based on survey data with the following potential sources of error.

- *Survey measurement error.* Alcohol surveys are subject to measurement errors that apply generally to surveys (for an overview see Groves 1989). However, the most important sources of error relating to estimating alcohol consumption include non-probabilistic sampling, sampling schemes that exclude groups with a high alcohol consumption, and measurement bias. The major problem with survey estimates of alcohol consumption is that surveys generally account for 66% or less of alcohol produced or sold (Midanik 1988; Midanik and Harford 1994; Rehm 1998a; de Vries et al. 1999). However, combining survey and aggregate (i.e. per capita) estimates may ameliorate the problem of underreporting that is characteristic of survey estimates.
- *Errors in combining adult per capita and survey data.* Although combining survey and aggregate data can rectify the underreporting of survey data, other sources of error may be created by this procedure. This is especially true if the difference in overall adult consumption between aggregate and survey estimates is large. There are theoreti-

cally several ways in which the survey estimates could be used to arrive at the per capita figures. For example, the prevalence of all drinking categories could be proportionally increased to cover the difference between survey and per capita estimates. This is not possible, however, as the rate of abstainers would automatically change as well. Thus, a procedure must be selected to keep the proportion of abstainers from the survey fixed and proportionally increase the higher consumption categories at the expense of the middle category. Even if this procedure is plausible it may introduce error, such as when survey underreporting differs for different age–sex groups. Nevertheless, the overall benefits of combining surveys and adult per capita data seem to outweigh this disadvantage.

There are other potential sources of error in the exposure estimates.

- *Errors in estimating missing survey data.* Survey data are available for only some countries, so that regional figures had to be estimated from selected countries where surveys were available. This introduces error, and overall the lack of data for some countries is probably the most important source of error for exposure estimates. The more survey data are lacking, the more severe is this problem. Thus it is least severe for those who abstain from alcohol, because even when survey data on the amount of alcohol consumed were not available, many countries had survey data in which respondents were asked whether or not they consumed alcohol. The problem of error in estimating missing survey data was most severe for estimates of drinking patterns, where expert judgements had to be used to supplement survey results, and where no production and trade or sale estimates were available for triangulation.

Overall, this listing of sources for potential errors and biases clearly indicates that the results of CRA, while based on the best available sources, are accompanied by large uncertainties, only some of which could be quantified.

3. Estimating risk factor–disease relationships

3.1 Outcomes to be assessed, evidence of causality and exclusions

Average volume of alcohol consumption has been related to more than 60 categories of the ninth revision of the ICD (ICD-9). This review restricts itself to categories that have already been identified in systematic meta-analyses, together with depression, which we describe in more detail below. Specifically, the following meta-analytical reviews were used: Gutjahr et al. 2001; English et al. 1995; Ridolfo and Stevenson 2001; Single et al. 1996, 1999a.

The categories that have been selected in modelling the impact of patterns of drinking are based on our own literature reviews. The analyses involving drinking patterns include the two main ICD categories for which sufficient evidence of a causal link to drinking patterns has been established: IHD and injuries. In addition, we restricted modelling of the protective effects of moderate regular drinking on type II diabetes and stroke to established market economies with the best drinking patterns (AMR-A, EUR-A and WPR-A), as there is evidence that patterns influence these diseases as well (for detailed reasoning, see below).

Assessment of causality

Following the procedure described by English et al. (1995), the evidence of causality between alcohol consumption and disease outcomes (including both harmful and protective effects for particular diseases) is assessed in accordance with the Australian National Health and Medical Research Council's (NHMRC) *Guidelines for the development, implementation and evaluation of clinical practice guidelines*, which are the most used in the alcohol field and close to the criteria of Hill (1965). Sufficient evidence of causality includes outcomes for which the evidence indicates that an association (positive or negative) exists between alcohol consumption and the disease or injury and that chance, confounding variables and other bias can with reasonable confidence be ruled out as factors in this association. This judgement was made using the usual criteria for establishing causality in epidemiology (Hill 1965; Rothman and Greenland 1998a), with the most weight placed on the following four criteria:

- consistency across several studies;
- established experimental biochemical evidence of mediating processes, or at least physiological plausibility;
- strength of the association (effect size); and
- temporality (i.e. cause before effect).

Two examples of judgements regarding somewhat controversial outcomes may illustrate this process. For lung cancer, meta-analysis showed a consistent effect with a relatively large effect size (English et al. 1995; but see the meta-analysis of Bagnardi et al. 2001, which came to a different conclusion), after adjusting for smoking in at least some studies. However, evidence for the possible biological mechanisms is not conclusive at present (Bandera et al. 2001) and residual confounding from smoking cannot be excluded as an alternative explanation. Thus, consistent with a recent review of the epidemiological evidence, the evidence for alcohol causing lung cancer was not judged sufficient to establish causality according to the criteria listed above (Bandera et al. 2001), and thus lung cancer was excluded as an alcohol-related disease outcome in this work.

On the other hand, although English et al. (1995) concluded that there was not sufficient evidence linking alcohol consumption and breast cancer, recent advances both in biological and epidemiological research have changed this evaluation (especially Smith-Warner et al. 1998; Singletary and Gapstur 2001; see below for detailed reasoning), so that breast cancer now is included in the list of alcohol-related outcomes.

It was concluded that there was limited evidence of causality when an association (positive or negative) was observed between alcohol consumption and the disease or injury for which a causal interpretation was considered to be credible, although chance, confounding variables or other bias cannot be ruled out with reasonable confidence. These diseases were not included in determining either alcohol-related mortality or burden of disease.

It was concluded that there was inadequate evidence of causality when the available studies were of insufficient quantity, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal connection.

It was concluded that there was evidence suggesting lack of causality when several adequate studies, covering the full range of levels of alcohol consumption in the population, indicated a lack of a relationship (positive or negative) between alcohol consumption and the disease or injury. This conclusion is inevitably limited to diseases and injuries, levels of consumption and lengths of observations covered by the available studies, and the possibility of very small risks at the levels of exposure studied can never be excluded.

Excluded outcomes and reasons for exclusion

A list of outcomes considered and excluded can be found in English et al. (1995). Some of these outcomes had been reconsidered in subsequent reviews (Gutjahr et al. 2001; Ridolfo and Stevenson 2001; Single et al. 1999a) and we followed Gutjahr et al. (2001) for the final selection of outcomes. Otherwise, the only restriction was one of age. Outcomes for people under 15 years of age *who had been drinking themselves* and subsequent alcohol-related consequences were excluded for two reasons:

- there are not enough global data on drinking in these age groups; and
- the epidemiological basis linking drinking to health outcomes is scarce.

Based on these considerations, the conservative choice was made not to include these outcomes.

As stated above, this does not mean that no alcohol-related outcomes are calculated for the age group under 15 years. On the contrary, so-called second-hand effects of alcohol (somebody else's drinking causing alcohol-related harm to a person) are included in the estimation.

3.2 Overview of methods

Meta-analyses on average volume of drinking and disease

Meta-analyses were the bases for estimating the risk relationships between average volume of alcohol consumption and chronic disease. In alcohol epidemiology, there is a tradition of conducting such meta-analyses as part of social cost studies (English et al. 1995; Gutjahr et al. 2001; Ridolfo and Stevenson 2001; Single et al. 1999a). We used the results of the most recent existing meta-analyses (Gutjahr et al. 2001) for most outcomes, and Ridolfo and Stevenson (2001) for breast cancer and the subtypes of stroke. Details such as inclusion and exclusion of studies are described below.

Multilevel modelling to determine pattern weights

For estimating the contribution of patterns of drinking applied to IHD and injuries, a new methodology had to be developed. Details of this method are described and discussed in Rehm and Gmel (2000b) and Gmel et al. (2001). It consists of combining multilevel[12] models with pooled cross-sectional time series models, and aims at maximizing methodological rigour and practical feasibility for the data available to undertake such an analysis. The principal variables for the present study are time series of adult per capita alcohol consumption and mortality for different countries, and one value measuring drinking patterns in a country. One could imagine conducting time series analyses separately for each country and then relating the patterns measured with the different estimates obtained for the relationship between alcohol consumption and mortality. However, time series data on both mortality and alcohol consumption for any single country are commonly too short (Rehm and Gmel 2001a) to perform reliable estimation and hypothesis testing, and there are no time-specific data on patterns of drinking within a country to determine pattern weights in this manner. Even for established market economies, there are at most 40 consecutive years of data from the same source (see e.g. Table 12.12 for the length of time series on IHD mortality and adult per capita consumption). In many developing and emerging economies, however, if data are available at all, they cover less than 10 consecutive years. Similarly, for many countries, owing to social and political changes (e.g. the countries of the former Soviet Union), longer time series inherently do not exist.

A common strategy to overcome such data shortcomings for parameter estimation is pooling of data across countries[13] to increase overall sample size, and to set constraints for several parameters (Greene 2000). Examples of such constraints could be to assume similar (i.e. differences statistically not significant) error variances (homoscedasticity) across countries, or to estimate the same regression parameters across all countries, or to assume a distribution for varying parameters (e.g. fixed vs random).

The approach adopted for the present study consists of pooling time series of differing lengths across countries and conducting multilevel analysis. For this approach, statistical problems arise from three major sources.

1. Pooling of data may violate the independence assumption in regression analysis. This concerns at least two aspects. First, the variability of measurements made in different countries is usually much greater than the variability of measurements within one country. Thus, data points are not independent of each other. In addition, within-country variability itself may differ among countries (heteroscedastic variances). Second, as countries provide different numbers of disease and consumption data points, countries with more data points (mainly established market economies) would have a higher impact on an overall estimate of the association between alcohol consumption and mortality than countries for which fewer data points exist (mainly developing and emerging economies). Such a disproportionate contribution to an overall regression estimate would be aggravated by the fact that the population sizes of countries would be often inversely related to the number of data points contributed to the regression analysis by such countries. For IHD mortality, for example, Switzerland (31 data points) and Norway (33 data points) would far outweigh the more populous South Africa (3 data points) and the Russian Federation (8 data points), even though they do not contribute substantially to the global burden of disease.
2. The estimation of time series needs further attention as regards to stationarity (stochastic or deterministic trends in the data) and the correlation of residuals within a country over time (autocorrelation).
3. The use of pooled cross-sectional time series analysis complicates estimation compared to a single time series alone, as errors (or residuals, both are used synonymously in this chapter) may co-vary across sections, and the degree of stationarity or autocorrelation may vary across sections (see below).

It should be noted that it was not possible to estimate all potential effects simultaneously. Either estimation of parameters failed to converge (potential explanations will be discussed below), the available standard software did not include the estimation of more complex models, or estimation of models was not applicable in the present context. To give an example of the latter, the estimation of cross-sectional correlation of errors would need time series that are equal in length (so-called balanced panels), at least with the available software used for estimation (Shazam: Whistler et al. 2001; STATA: StataCorp 1999; HLM: Bryk et al. 1996; MLWin: Yang et al. 1999). It was not possible to test models that include

cross-sectional autocorrelation in the present context, since balanced panel data are not available.

As not all potential shortcomings and drawbacks of multilevel and pooled cross-sectional time series models could be considered in one single model, sensitivity analysis was performed in two phases.

In phase 1, to determine pattern weights, multilevel analyses were conducted using a pilot sample of 29 European countries[14] for which data were available for at least three consecutive years in the 1990s on each of the following variables: adult per capita alcohol consumption, standardized mortality and per capita GNP (level-1 variables) and an estimate of patterns of drinking (level-2 variable assumed to be time-invariant). Calendar year was used to control for omitted variable bias and the time structure (Gmel et al. 2001);[15] per capita GNP was included to control for economic strength as a potential confounder. The analyses to elucidate pattern weights for IHD and injuries have, for the present work, used the same methodology (for details see Gmel et al. 2001). For the sensitivity analysis and for the final pattern weights to calculate burden of disease in this chapter, data were taken from the following sources.

- Mortality data (either all-cause mortality in the sensitivity analysis or IHD/injury) were obtained from the WHO Mortality Database and age-standardized using United Nations population estimates. Direct standardization of mortality rates was performed using the latest WHO world standard population (Ahmad et al. 2000). The reference population is quite "young" with regard to the age distributions of populations in established market economies, but better reflects developing and emerging economies. On the other hand, the new WHO standard takes into account the reduced mortality rates in the older age groups nowadays, which have made the distribution a little "older" than the formerly widely used SEGI standard (Segi 1960).
- Adult per capita alcohol consumption data were again taken from WHO Global Alcohol Database described above.
- Per capita GNP data were taken from World Bank statistics, which used the Atlas method to arrive at standardized, de-inflated values in US dollars for the year 2000.

For all countries in this phase, time series data were collected from 1962 onwards on the four level-1 variables—standardized mortality (either all-cause mortality in the sensitivity analyses or IHD and injury in the final estimates), calendar year, adult per capita alcohol consumption and per capita GNP.

In phase 2, different models were run to especially take into account the cross-sectional time series structure, i.e. to assess the impact of eventually violating statistical assumption in hierarchical multilevel models.

For this exercise, data on countries where a long time series exists were used to try to estimate effects such as heteroscedasticity and error structure (autocorrelation) with some precision. Per capita consumption and data on all-cause mortality for 15 countries were obtained from ECAS, and are extensively described in the February 2001 supplement to *Addiction* (e.g. Norström 2001). Briefly, per capita alcohol consumption, measured in litres of pure alcohol per inhabitant aged ≥15 years, was obtained from the Brewers Association of Canada (1997). Age-specific data on all-cause mortality were obtained from the WHO Mortality Database and standardized to the WHO 1998 standard population (Ahmad et al. 2000). For all countries, time series were available for a time span of at least 40 years. Worldwide, few if any countries exist that would be able to provide longer time series (say 60 or more years) of annual data.

Sensitivity analysis, phase 1: multilevel models

The main difference between multilevel models and simple regression models is that the association between the outcome (mortality) and the independent variables (adult per capita consumption; calendar year as a control variable) is not fixed but varies across cross-sections (i.e. countries). Therefore, multilevel modelling analytically takes into account the lack of independence stemming from a potentially lower variability of data within a country compared to the variability between countries.

Essentially, this problem is the same as in cluster sampling, where variation between clusters is usually also higher than variation within clusters. Two approaches to account for cluster sampling have been suggested (see Lehtonen and Pahkinen 1994). One, the design-based approach, treats cluster sampling and the effect of it on parameter estimates as a nuisance. The information on variation across different clusters and variation within clusters is not included in the model. The estimation of CIs for relevant parameters (e.g. slopes and intercepts in regression analysis) without considering cluster sampling, however, is usually biased. Commonly, standard errors of parameters are underestimated, i.e. CIs are estimated to be narrower than they really are. The design-based approach accounts for these effects by adjusting the standard errors for the impact of the design, e.g. the cluster sampling, but does not model the effects explicitly. The other approach, the model-based approach, treats the different variability across clusters as one parameter of interest in the study and explicitly models this variability. For this approach, multilevel (random coefficient) models are used. Comparison of the two approaches has shown that they yield similar results, but that the model-based (random coefficient) approach yields additional information as it is partly able to model the variability of estimates, and therefore to explain it (Skinner et al. 1989).

Our modelling is one variant of the model-based random coefficient approach. The rationale of multilevel models in the present context is described in detail by Rehm and Gmel (2000b); see also Bryk and Raudenbush (1992); Hox (1995); Kreft and de Leeuw (1998). Briefly, intercept and slopes are assumed to vary randomly[16] across sections. In a two-level analysis this variation can be predicted by variables at the level of the cross-sections (e.g. per subregion). In the present study the variation in the slopes of adult per capita consumption to predict mortality will be explained by drinking patterns per country. Thus, it is assumed that drinking patterns moderate the association between adult per capita consumption and mortality. The corresponding model (without control variables) can be described as follows:

$$\text{mortality\_rate}_{tc} = \beta_{0c} + \beta_{1c} \times \text{alcohol}_{tc} + \varepsilon_{tc} \quad (1)$$

where t = index of time
c = index of countries

The coefficients β_{0c} and β_{1c} symbolize random variables, which vary across countries. Therefore, the simplest way to model this random variation is given by the following equation:

$$\beta_{00} = \gamma_{0c} + \mu_{0c} \quad (2)$$

where γ_{00} = global intercept of mortality rate
μ_{0c} = country-specific variation of intercepts of mortality rates

similarly $\beta_{1c} = \gamma_{10} + \mu_{1c}$

where γ_{10} = global slope of impact of alcohol (level-2 intercept of alcohol)
μ_{1c} = country specific variation of alcohol impact

Influences of country-specific drinking patterns on the slopes of per capita consumption can then be modelled as:

$$\text{pattern\_weight} = \beta_{1c} = \gamma_{10} + \gamma_{11} \times \text{pattern\_value}_{c} + \mu_{1c} \quad (3)$$

The impact of one unit of per capita consumption on mortality is thus assumed constant in time but specific for each country, and is denoted by β_{1c}. This impact itself (throughout this chapter called "pattern weight") is regarded both as a dependent variable and as a predictor variable, for which the value not only varies across countries but also systematically depends on drinking pattern (i.e. pattern value) observed in the respective country.

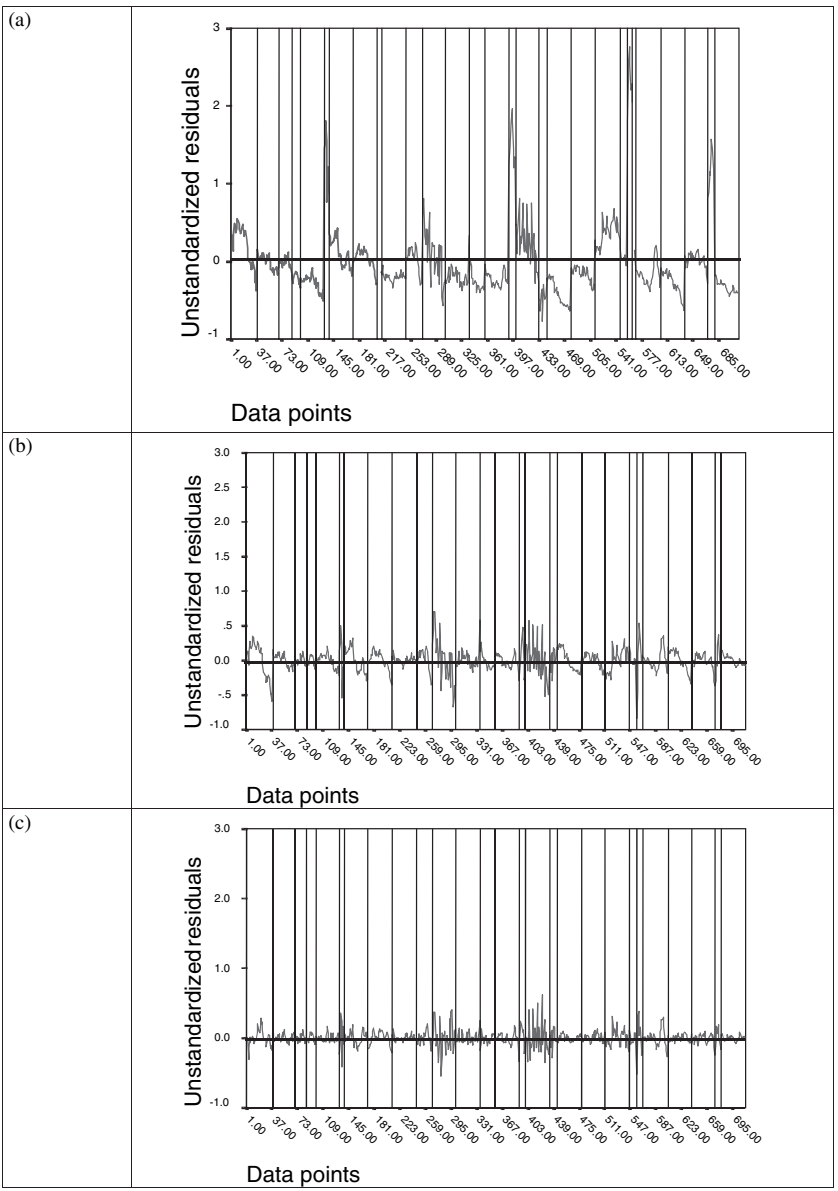
The coefficient γ_{10} can be regarded as a baseline measure for the impact of per capita consumption on mortality.[17] The country-specific deviations

are introduced by the patterns of drinking in the country and a country specific error term μ_{1c}.

Note that if we estimated, in a simple one-level analysis, a global coefficient β_1 (not varying across countries), this measure would not necessarily be the same as γ_{10} in a random coefficients model including level-2 variables. The coefficient γ_{11} can be regarded as the contribution of drinking patterns to modifying the detrimental effects of per capita consumption on mortality. This modifying effect per unit of drinking patterns is treated as being the same for all countries. But clearly drinking patterns vary between countries, and therefore the impact on mortality β_{1c} is specific to each country. There may remain unexplained variation in these country-specific impact coefficients. This is expressed by the level-2 error term μ_{1c}.

Figure 12.2 shows the modifications in residuals for different models. Figure 12.2(a) reflects a simple regression model in which all countries were simply pooled into one data set and analysis was performed without any multilevel modelling (i.e. standard multiple regression; in terms of multilevel modelling this would be a model with constant intercepts and constant slopes). Vertical lines in Figure 12.2 separate residuals within a country from those in other countries. It can be seen that residuals (ε_{tc}) are clearly not independent, as for some countries all residuals were greater than zero whereas for other countries all residuals were below zero. In addition, residuals within a country clearly exhibit trends over time, which also violates the independence assumption. In Figure 12.2(b), a random intercept model was used. This means that for each country a separate intercept was estimated but the association between alcohol consumption and mortality was constant (i.e. it was estimated that the global level of mortality differed across countries, but the association between alcohol consumption and mortality was assumed to be the same across all countries). In this model residuals were more clustered around zero (owing to the random intercept), although there were still trends in the residuals. In the final model also, slopes were allowed to vary across countries (i.e. the association between alcohol consumption and mortality could vary across countries). In addition, control for confounding (GNP as constant slope term) and for omitted variable bias and potential deterministic trend stationarity (calendar year as a random slope term) was included in the multilevel model. The residuals of such a model (Figure 12.2[c]) look very much as they should, as they exhibit neither visible trends nor autocorrelation. Thus, such a model not only turned out to be feasible but it also seemed to account for most of the undesirable aspects of residuals in time series analysis, such as nonstationarity and autocorrelated residuals. Nevertheless, the variability of errors still seems to be different across countries (heteroscedasticity).

Figure 12.2 Level-1 residuals of multilevel models: a) constant intercept and constant alcohol slope; b) random intercept and constant alcohol slope; c) random intercept and random slope (including control for confounding, i.e. constant slope for GNP and random slope for calendar year)



Unstandardized residuals are the raw residuals as indicated by formula 1 above.

Sensitivity analysis, phase 2: pooled cross-sectional time series models

The models discussed above could also be seen as pooled cross-sectional time series models in so far as data used consisted of time series. The models discussed here, however, include special features to deal with the structure of residuals, namely correlations in time. For the models discussed above, the order of data points in time within a country is not taken into account and could be randomly rearranged within each country. In time series analysis, however, it is often assumed that (within each country) values that are closer in time may be more correlated than values that are more separated in time. Thus, the time span between two values must be taken into account. This could not be done by the multilevel modelling, only indirectly by including calendar year into the models.

The sensitivity analyses of different pooled cross-sectional time series models used data on 15 countries from the ECAS project. As a starting point we analysed the data with multilevel models as outlined for Figure 12.2(c), using three different estimation techniques with three different statistical software packages (2-stage OLS with STATA; iterative GLS with MLWin; restricted ML with HLM). Parameter estimates across the three models were comparable and differed less than those from models discussed below (for details of findings see Gmel et al. 2001; for details of differences in estimators see Kreft and de Leeuw 1998).

The simplest model of a pooled time series design, called the "constant coefficient model" (Sayrs 1989) or "population-averaged model with independent errors" (StataCorp 1999), would stack all observations across time points and cross-sections into one data file and analyse the combined data by standard regression techniques (e.g. OLS regression for an interval-scaled dependent variable). Such a model would assume that observations across time and cross-sections are completely independent of each other. This model equals a "multilevel" model with a single fixed intercept and a single fixed slope. This means that neither the ordering in time nor the grouping within cross-sections (countries) must be obeyed and, hence, that there is no association between the time points within a cross-section or between time points over cross-sections, and that there is no relationship between the cross-sections within a time point or between time points. The constant coefficient model often serves as a reference model only. It could be written as follows.

1. Zero expectation of errors for all cross-sections:

   $E(\varepsilon_{ct}) = 0$ for all c, t

2. Constant error variance for all cross-sections:

   $V(\varepsilon_{ct}) = \sigma^2$ for all c, t

3. Uncorrelatedness of errors within and across cross-sections:

   $COV(\varepsilon_{it}, \varepsilon_{jt}) = 0$ for any i, j, t

where t = index of time
c, i, j = index of countries, where it ≠ jt

Assumptions 1 and 2 would be violated when, for example, mortality in a country is always higher than the overall prediction across all countries and all time points. For such a country all errors would be positive. Similarly, the error variances may vary across countries (heteroscedasticity) owing to the fact that, for example, mortality is measured with different reliability in different countries. Typical for time series data, errors may be correlated within a country (autocorrelation within cross-section) but also at the same time point across countries, which would violate assumption 3. An example of such a pattern may be seen in the Nordic countries, where there are similar alcohol policies.

Related to the corresponding procedures in STATA (StataCorp 1999) two sets of models were run. The first set uses GEE estimation (Liang and Zeger 1986) and allows different descriptions of the correlation matrix within cross-sections, subject to the constraint that the same correlation matrix applies to all cross-sections. The following models were used, with $R_{t,s}$ being the t,s element of the correlation matrix, where t and s describe time points (here, years).

1. The independence structure (i.e. $R_{t,s} = 1$ for t = s and 0 otherwise) is equivalent to a model for which all observations are pooled into one file and analysed as if all data come from the same underlying population.

2. The autoregressive (AR) structure (i.e. for an autoregressive structure of order 1, $R_{t,s} = 1$ for t = s and $\rho^{|t-s|}$ otherwise) models an exponentially decaying correlation in time within a cross-section, hence assuming that the less observations are correlated the more they are separated in time.

3. The stationary structure (i.e. for stationarity of order 1, $R_{t,s} = 1$ for t = s, ρ for |t−s| = 1, and 0 otherwise) permits a correlation only between two consecutive time points.

4. The nonstationary structure (i.e. for nonstationarity of order g, $R_{t,s} = 1$ for t = s, ρ_{ts} for g ≥|t−s| >0) permits correlations for all observations separated by up to g time points. The correlation may differ with the number of time points between two observations, and with the location in time (i.e. a different correlation between 1950 and 1951 and between 1974 and 1975). A completely unconstrained correlation matrix would be a nonstationary structure with g = n – 1 (number of time points).

The second set of models uses GLS estimation. Compared with the GEE models, this method relaxes the restrictions of sameness within cross-section correlation matrices. Hence, it permits the estimation of heteroscedastic variances across sections, and the estimation of cross-

sectional specific autoregression (i.e. each country is allowed to have its own error variance and its own magnitude of autocorrelation). The models are restricted to autoregressive models of order 1.

Thus, the GEE models in STATA permit a greater flexibility in estimating error structures, but assume that these structures are constant for all countries. On the other hand, the GLS models in STATA allow the coefficients of autocorrelated residuals and the error variance to vary across countries, but are restricted to an autocorrelation of order 1 only. None of these models allows for testing of random coefficient models. Thus, the association between alcohol consumption and mortality is assumed to be constant across all countries. The same is true of variables to adjust for confounding, omitted variable bias and time trends (GNP and calendar time). Models were used with and without inclusion of calendar time.

The findings can be summarized as follows.

- Measurements within countries are highly correlated in such a way that accounting for correlations only at lags 1 or 2 were not sufficient (e.g. models with stationary or nonstationary structure up to order 2). Thus, the correlations of higher order remained significant. Better fits were obtained, for example, under the assumption of an autoregressive structure, i.e. exponentially decaying correlations with increasing time span between measurements. In general, point estimates of coefficients for the alcohol–mortality association increased with better control of this autoregressive structure, indicating that insufficient control would bias estimates of this association downwards.

- The inclusion of calendar time as a constant coefficient control variable acted in the same direction as controlling for autoregression and clearly performed better than controlling for nonstationarity alone; controlling for nonstationarity did not further improve the estimation of the alcohol coefficient when used in addition to calendar time. As a conclusion, the use of calendar time as a continuous variable is at least as good as other methods (e.g. differencing) to account for nonstationarity in the present context. However, inclusion of autoregression further improved estimation even when calendar time was included.

- Whether the autoregressive structure was estimated to be constant across countries or to be country-specific resulted in smaller differences than those between an autoregressive structure and a structure restricted to low-order lag correlations (nonstationary or stationary). It should be noted, however, that the estimation of higher order (>2) nonstationary structures (which allow more flexibility of the correlation matrix) did not converge to a solution. This was probably because of the number of parameters that needed estimation. For a

model with an autoregressive structure (e.g. of order 1), although correlations for higher lags can be significant, only 1 parameter must be estimated as it is assumed that correlations of time points with higher lag orders follow an exponentially decaying function of the correlation at lag 1. In nonstationary models, correlations with a higher lag order can vary freely and must be estimated separately.

- The inclusion of heteroscedasticity (unequal variances) did not improve models, or did so only marginally.

As already mentioned, it appeared that the better the error structure of time series was captured, the higher were the point estimates for the relationship between alcohol consumption and mortality. In none of these models, however, could varying coefficients for this relationship across countries be modelled. The underlying assumption of these pooled cross-sectional models is that there is a constant relationship and that pooling is used to increase sample size for efficient estimation, while adjusting for a more complex error structure than independence. However, tests for constant coefficients showed that there is significant variation across countries for both the coefficient of alcohol consumption and for calendar year, pointing to geographically differing and not altogether changing associations. Although the autocorrelated error structure could not be accounted for, random coefficient models yielded the highest association for alcohol consumption, pointing to the possibility that the use of random coefficient models better captured the data and the error structure than constant coefficient models accounting for autocorrelated residuals, by estimating a constant effect of alcohol consumption and a constant effect of calendar time. Clearly, random coefficient models including the autoregressive error structure may further improve estimation.

There is software that can in principle handle autocorrelation and heteroscedasticity in multilevel models (Bryk et al. 1996; Yang et al. 1999). It should be noted, however, that in the present study the inclusion of autocorrelated disturbances failed to converge. The possible reason for the nonconvergence might be that the model was already well specified with the inclusion of random coefficient time trends, and the additional inclusion of further parameters might therefore have resulted in colinearity problems. This seems to be a general problem in analysis of aggregate data in the alcohol field, where relatively low variability within series is coupled with relatively short series. It is, however, not likely that the omission of autocorrelated disturbances in random coefficient models may have greatly distorted the findings. Although including autocorrelation of errors resulted in further improvement, this improvement was relatively minor in pooled cross-sectional time series models with constant alcohol coefficients that adjusted for a constant coefficient of calendar time, compared to the improvement from random coefficients models. In addition, in random coefficient models without including autocorrelation

the impact of calendar year was not estimated as being constant across all countries, and might therefore further account for autocorrelation, as it separately adjusted in each country and therefore better captured the country-specific confounding than a country-averaged model.

The advantage of random coefficient models was that not only could the association between consumption and mortality vary across countries, but so could the associations with the control variable time. Thus, the adjustment of time could be analysed in a country-specific manner. Finally, none of the pooled cross-sectional time series models could analyse variations in the relationship between alcohol consumption and mortality as being moderated by patterns.

In conclusion, all sensitivity analysis performed indicated that multilevel modelling outperformed pooled cross-sectional time series models, although the autocorrelated error structure could not be taken into account directly. As estimation of such a structure was not feasible even for the longer time series in the field, there was no hope that this could be done when more countries with relatively short series (fewer than 10 data points) were added. On the contrary, adding other countries would increase the cross-country variability and reduce the impact of autocorrelation within country, especially as this may have little impact given the few data points.

3.3 Criteria for identifying relevant studies

The criteria listed in Table 12.8 apply to all meta-analyses used to estimate the relationship between per capita consumption and specific diseases (English et al. 1995).

Alcohol-related consequences were thus identified by reviewing and evaluating large-scale epidemiological studies on alcohol and health, including epidemiological input into major reviews (Collins and Lapsley 1991; Corrao et al. 1999; Devlin et al. 1997; English et al. 1995; Gurr 1996; Harwood et al. 1998; Klingeman and Gmel 2001; Rice et al. 1991; Ridolfo and Stevenson 2001; Single et al. 1996, 1999a, 1999b; Stinson et al. 1993; U.S. Department of Health and Human Services 2000). Papers were collected primarily from the peer-reviewed international literature. As indicated above under the discussion on causality, we followed the accepted guidelines established in the first major review (English et al. 1995). All conditions for which evidence of a causal relationship was conclusive were included in the final list. Discussion of disease conditions where causality was not judged to be sufficient can be found in section 3.5.

3.4 Description of studies, including methodological qualities

More than 6000 studies were included in the different analyses on which the estimates for this chapter were based. For further descriptions we refer to the original publications of the meta-analyses (English et al.

Table 12.8 Exclusion criteria for studies used in determining the relationship between average volume of consumption and mortality/morbidity in CRA

Reason for exclusion	*Explanation and/or examples*
Restricted study population	The study was carried out in a sample that was difficult to generalize for the entire population (for example, a cohort of persons suffering from a particular disorder)
Inappropriate comparison group	The control group was contaminated by a high exposure to the risk factor under consideration or other factors related to the condition
No quantitative exposure measure	Exposure was alcohol dependence rather than alcohol consumption, or alcohol consumption was undefined or had poorly defined nominal categories (for example, "regular" vs "non-regular" drinkers) or was limited to frequency of consumption (without considering quantity) or was measured in a manner not representative of general exposure (for example, with meals or in the last 24 hours)
Duplication of study	A study was reported in more than one paper, and was already included in the review. A second important way in which a study may be duplicated is when it has already been included in the earlier review conducted by members of the project team. These studies are included in the review but not re-examined in detail
Sample size too small	There was an insufficient number of cases (n <20 deaths or outcomes)
Inadequate control for confounding variables	An important confounding variable was not controlled for in the study (for example, smoking not controlled for when examining impact on heart disease, or only bivariate relationships and relative risks presented)
Results not usable	Data were presented in a manner that precludes their use (for example, data only presented in graphs that are difficult to read)
No age- or sex-specific data presented	This was done where unacceptable (i.e. where the condition under review is strongly related to age or sex)

1995; Gutjahr et al. 2001; Ridolfo and Stevenson 2001; Single et al. 1999a). Nevertheless, we provide here a general methodological description of the studies used and their assumptions.

Most studies reviewed used either a cohort or case–control design (Rothman and Greenland 1998b). For epidemiological studies on alcohol consumption using these designs, the following limitations generally apply.

- Alcohol use is mostly measured by only a few questions, either separating frequency of drinking and quantity per occasion or combining them into one modified frequency question in the tradition of nutritional epidemiology (e.g. Rehm 1998a, 1998b for further descriptions and a critique). Research has shown that such questions may lead to underestimates of true consumption. Also, data on the relationship

between patterns of drinking and health outcomes are limited, as typical questions in epidemiological surveys cannot be used to measure drinking patterns (Rehm 2000). Studies with more complete alcohol assessment are mostly cross-sectional, or the baseline assessment was carried out very recently so that no longitudinal results can yet be reported.

- The relationships between alcohol consumption and chronic disease outcomes are often based on outcomes assessed at follow-up, regressed on several variables from the baseline assessment. These procedures assume that the baseline variables are stable over time, or that they are somehow good indicators of the postulated theoretical relationship (e.g. Rehm et al. 1996). For example, in assessing the relationship between volume of consumption and liver cirrhosis, it must be assumed that heavy consumption persists after baseline and is a good indicator for overall tissue exposure, which is the theoretical determinant (Lelbach 1975, 1976). Work on the regression dilution bias has shown that the size of the real effect is often underestimated by using only the baseline assessment (Clarke et al. 1999) if the exposure is somewhat constant or preserves rank order over time. Moreover, there is evidence from longitudinal studies that individual drinking patterns are not stable over time (Fillmore 1988; Vaillant and Hiller-Sturmhofel 1996), which may obscure the apparent relationship even further.
- The relationship between alcohol consumption and outcomes must be assumed to be fairly constant across settings, in that results of epidemiological studies from a few countries are applied to others. While this may be justified with biologically based relationships (e.g. alcohol and breast cancer),[18] such an assumption is more problematic with casualties and injuries as outcomes, since these are much more context-dependent.

All of these points indicate that the results of the meta-analyses on which our estimates are based will have limits with regard to precision. These limits are not captured by the CI for combined relative risks.

3.5 Relative risks and attributable fractions

Some conditions, such as alcoholic psychosis or alcohol dependence syndrome, are by definition causally related and wholly attributable to alcohol (i.e. they would not exist in the absence of alcohol consumption) (Table 12.9). For most conditions, however, alcohol is a contributory rather than a sufficient cause (Rothman and Greenland 1998a). Pooling of risk estimates for these diseases from individual studies was performed by means of precision-based weighting (English et al. 1995). Methods and results of the pooling procedure (meta-analysis) have been described in more detail elsewhere (Gutjahr and Gmel 2001).

In contrast, the alcohol-attributable fractions (AAFs) for acute consequences such as injuries are usually directly determined from the blood alcohol concentration (BAC) at the time of the injury. For example, road accidents are attributed to alcohol according to whether the driver responsible for the accident tested positive for alcohol and to what degree (e.g. BAC ≥0.05%).[19] In the case of traffic accidents we have relative risk estimates, based on case–control studies, for different levels of BAC (Ridolfo and Stevenson 2001; see also McLeod et al. 1999). But relative risk estimates are usually rare for acute consequences other than traffic injuries. Thus, for the purpose of the present study, AAFs from the international literature were used (English et al. 1995; Gutjahr and Gmel 2001; Ridolfo and Stevenson 2001; Single et al. 1996; Stinson et al. 1993).

To structure the presentation and discussion of results, alcohol-related health consequences will be categorized as follows.

1. Chronic harmful effects of alcohol consumption, excluding depression and IHD:
   - wholly alcohol-attributable outcomes;
   - cancers (neoplasms);
   - cardiovascular diseases;
   - liver cirrhosis;
   - effects of prenatal alcohol exposure;
   - neuropsychological conditions; and
   - other chronic diseases.
2. Chronic beneficial effects of alcohol consumption, excluding IHD:
   - ischaemic stroke; and
   - other conditions (type II diabetes, gallstones).
3. IHD as a chronic condition where alcohol has harmful and beneficial consequences:
   - depression; and
   - acute adverse effects:
     — unintentional injuries (motor vehicle accidents, poisonings, falls, drownings, other unintentional injuries)
     — intentional injuries (self-inflicted injuries, homicide, other intentional injuries).

Table 12.9 Disease conditions that are by definition fully alcohol-attributable (AAF = 1)

ICD-9 code	*Disease*
291	Alcoholic psychoses
303	Alcohol dependence
305.0	Alcohol abuse
357.5	Alcoholic polyneuropathy
425.5	Alcoholic cardiomyopathy
535.3	Alcoholic gastritis
571.0–571.3	Alcoholic fatty liver, acute alcoholic hepatitis, alcoholic cirrhosis of liver, unspecified alcoholic liver damage
790.3	Elevated blood alcohol level
980.0, 980.1	Toxic effect of ethyl alcohol, toxic effect of methyl alcohol

3.6 Chronic harmful effects of alcohol consumption, excluding depression and IHD

Wholly alcohol-attributable diseases

A number of diseases are by definition fully attributable to alcohol (AAF = 1). These are listed in Table 12.9.

Diseases with a contributory role

Cancer

Oropharyngeal, oesophageal and liver cancers. Alcohol has consistently been related to the risk of cancer of the mouth (lip, tongue), pharynx, larynx, hypopharynx, oesophagus and liver (Corrao et al. 1999; English et al. 1995; Gurr 1996; Single et al. 1999; U.S. Department of Health and Human Services 2000; WHO 2000). The relationship between average volume of alcohol consumed and cancer incidence is usually characterized as increasing almost monotonically (Bagnardi et al. 2001), but this may partially be an artefact of the methods used (Single et al. 1999). Evidence for the role of alcohol in these cancers has accumulated from case–control and cohort studies. Recently, much emphasis has been placed on investigating biochemical mechanisms in laboratory studies to explain the carcinogenic behaviour of alcohol (U.S. Department of Health and Human Services 2000).[20]

Female breast cancer. Much research has been conducted over the last decade on breast cancer. Prior to 1995, it was usually concluded that evidence of a causal relationship with alcohol was insufficient (English et al. 1995; Rosenberg et al. 1993; Schatzkin and Longnecker 1994). Recent studies and reviews have shown, however, that not only haz-

ardous or harmful drinking but also even moderate alcohol consumption can cause female breast cancer (Single et al. 1999a). A meta-analysis by Smith-Warner et al. (1998) found a clear linear relationship over the whole continuum of consumption. Other original studies supported this finding (Bowlin et al. 1997; Corrao et al. 1999; Nasca et al. 1994; Royo-Bordonada et al. 1997; Swanson et al. 1997; Van den Brandt et al. 1995; Wingo et al. 1997). In contrast to the weight of evidence, Zhang et al. (1999) concluded from their investigation that moderate intake did not increase the risk of breast cancer, and that a low level of drinking was associated with a protective effect. This finding, however, appears to be a notable outlier (Longnecker 1999) and, so far, has not been corroborated. Recent studies have focused on plausible biological mechanisms, including alcohol's effect on hormones and tissue, its contribution to the initiation, progression and promotion of breast cancer, and its interaction with nutritional factors (for an overview see Singletary and Gapstur 2001; Soler et al. 1998; U.S. Department of Health and Human Services 2000).

Cancers of the stomach, pancreas, colon, rectum and prostate. Many recent research projects have investigated whether these cancers are alcohol-related. Overall, evidence for a causal relationship between alcohol and cancer of these sites, if any was found, was weak and inconclusive (Bode and Bode 1997; Boutron et al. 1995; De Stefani et al. 1998; Gapstur et al. 1994; Harnack et al. 1997; Ji et al. 1996; Longnecker and Enger 1996; Lundberg and Passik 1997; Piette et al. 1998; Sarles et al. 1996; Seitz et al. 1998a, 1998b; Singborg 1998; Soler et al. 1998). On prostate cancer, again most studies did not report observing an increased risk (Breslow and Weed 1998; Ellison et al. 1998; Hiatt et al. 1994; Tavani et al. 1994), whereas two cohort studies (Ajani et al. 1998; Putnam et al. 1998) and one case–control study (Hayes et al. 1996) reported a small increased risk in men who consume even moderate amounts of alcohol. In conclusion, evidence for a causal relationship between alcohol and cancer of the stomach, pancreas, colon, rectum and prostate has not so far produced consistent results, especially with regard to physiological pathways. Thus, we did not include these cancers, even though some of them showed significantly elevated risks in a recent meta-analysis (Bagnardi et al. 2001).

Cancer of salivary glands, ovary, endometrium, bladder. It has been hypothesized that alcohol might constitute a risk factor for cancer of the major salivary glands (Horn-Ross et al. 1997; Muscat and Wynder 1998), ovary, endometrium (Bradley et al. 1998; Longnecker and Enger 1996; Newcomb et al. 1997; Parazzini et al. 1995) and bladder (Bruemmer et al. 1997; Donato et al. 1997; Longnecker and Enger 1996; Yu et al. 1997). For each of these sites, results were scarce or conflicting, and

the effects, if any, were not statistically significant. Moreover, there is no knowledge of physiological pathways for these sites.

There is an almost linear dose–response relationship between volume of drinking and the relative risk of alcohol-related cancers. Although there have been speculations about the impact of patterns of drinking, especially for breast cancer (Kohlmeier and Mendez 1997), the current state of knowledge does not suggest that these play an important role in the etiology of cancer.[21] Thus, the alcohol-attributable burden for cancer will be modelled exclusively on average volume.

Cardiovascular disease

The role of alcohol, as both a risk and protective factor for cardiovascular disease, has been studied extensively in the past decade. IHD has been the focus of most research and is discussed separately below. Most studies suggest that low-level consumption also offers some protection against ischaemic stroke, and this condition is therefore also discussed in the section below on the beneficial effects of alcohol.

In contrast, hypertension and other cardiovascular disorders such as cardiac arrhythmias, heart failure and ill-defined descriptions and complications of heart disease are adversely affected by alcohol (see e.g. Friedman 1998; Klatsky 1995; Puddey et al. 1999; Rosenqvist 1998; U.S. Department of Health and Human Services 1997; Wood et al. 1998). The weight of evidence suggests that daily consumption of more than 30 g pure alcohol for men (and presumably lower levels for women) causes hypertension (Beilin et al. 1996; Curtis et al. 1997; English et al. 1995; Grobbee et al. 1999; Keil et al. 1997; Klatsky 1996). Low-level intake, however, was not associated with hypertension in men, and may even confer a small protective effect in women (English et al. 1995). There are some indications that hypertension may be related to the pattern of heavy drinking occasions (Murray et al. 2002; Puddey et al. 1999; Wannamethee and Shaper 1991).

For haemorrhagic stroke, the weight of evidence suggests an increase in risk for males even at low levels of consumption (Berger et al. 1999; Jackson 1994; Sacco et al. 1999; You et al. 1997). For females, the most recent meta-analyses of Ridolfo and Stevenson (2001) suggested a protective effect for drinking categories I and II but an 8-fold increased risk for drinking the equivalent of more than 40 g pure alcohol daily (see Table 12.10). Patterns of drinking not only play a role in any protective effects of alcohol on IHD but are also relevant for risk of stroke (Hillbom et al. 1998) and sudden cardiovascular death or cardiovascular death in general (Kauhanen et al. 1997a, 1997b; Kosarevic et al. 1982; Poikolainen et al. 1983; Wannamethee and Shaper 1992), with heavy drinking occasions and intoxication resulting in increased risk. Patterns of drinking should therefore be included in future estimates of harmful cardiovascular outcomes.

Liver cirrhosis

Alcohol consumption has been identified as the leading cause of liver cirrhosis in established market economies (Corrao et al. 1997, 1998; English et al. 1995). Whereas the association with alcoholic liver cirrhosis is clear, with all cases being attributable to alcohol, debate remains as to whether this equally applies to unspecified liver cirrhosis. Several authors contend that, empirically, it is extremely difficult to separate alcoholic from unspecified liver cirrhosis, and that the term "unspecified liver cirrhosis" is applied when no specific etiological factor is reported or identified (English et al. 1995). Research in the United States and in Central and South American countries has indicated that an appreciable proportion of deaths from cirrhosis without mention of alcohol was in fact attributable to alcohol (Haberman and Weinbaum 1990; Puffer and Griffith 1967; Room 1972).[22]

On the other hand, applying AAFs of liver cirrhosis to other countries can be extremely misleading. In many countries (e.g. China and India), liver cirrhosis is mainly caused by other factors such as viral infections. The corresponding AAFs have been shown to vary between less than 10% (China) and 90% (Finland) (WHO 2000).

The relationship between alcohol consumption and liver cirrhosis seems to depend mainly on volume of drinking and is independent of pattern of drinking (Lelbach 1975, 1976). However, some research also indicates a potential effect of occasions of heavy drinking (Rhodés et al. 1993). Moreover, there is some indication that spirits are especially harmful in causing liver cirrhosis (Gruenewald and Ponicki 1995; Kerr et al. 2000; Longnecker et al. 1981; Schmidt 1991). The problem with this research is that it is almost entirely based on ecological studies and thus describes only correlations, which may have other causes (Morgenstern 1998; Rehm and Gmel 2001a).

Effects of prenatal alcohol exposure

Today, there is ample evidence that alcohol consumption during pregnancy is related to various risks to the fetus, which include gross congenital anomalies and fetal alcohol syndrome (FAS) (Alvear et al. 1998; Church et al. 1997; Faden et al. 1997; Habbick and Snyder 1997; Larkby and Day 1997; Larroque and Kaminski 1996; Mattson et al. 1997; Passaro and Little 1997; Passaro et al. 1996; Polygenis et al. 1998; Roebuck et al. 1998; Shu et al. 1995; Windham et al. 1995). FAS has been characterized as a continuum, with minor physical malformations at one end and serious neurobiological dysfunctions, including mental retardation, at the other (Connor and Streissguth 1996). The prenatal teratogenic effects of alcohol also include lethal outcomes comprising spontaneous abortion, low birth weight, fetal damage, prematurity and intrauterine growth retardation (Abel 1997; Bradley et al. 1998; Windham et al. 1997). These can occur even at low average

volumes of consumption, particularly during the first trimester of pregnancy.

Mental conditions

The co-morbidity of alcohol dependence with other mental conditions is high, both in clinical and in general population samples (e.g. Grant and Harford 1995; Merikangas et al. 1998). The crucial question in this respect is about causation. We have included depression in this review only where we believe the evidence to be sufficient to conclude a causal role for alcohol. Since this relationship is controversial, it is discussed below in a separate section.

Other chronic conditions

Other risks of alcohol consumption currently discussed in the literature include epilepsy (see e.g. Jallon et al. 1998; Leone et al. 1997; Martin et al. 1995), acute and chronic pancreatitis and psoriasis. Whereas for pancreatitis the causal role of alcohol seems to be clear, Amman et al. (1996) and Skinazi et al. (1995) contend that the discrimination between acute and chronic pancreatitis is not justifiable, since the overwhelming majority of patients presenting with acute pancreatitis at the same time have an underlying chronic pancreatitis (Robles-Diaz and Gorelick 1997; Thakker 1998). On psoriasis, our search did not yield any recent studies. English et al. (1995) found that the results of the pooled estimates were consistent with a moderately strong and statistically significant effect of average volume of consumption.

Table 12.10 summarizes the relative risks at different levels of consumption for alcohol-related chronic consequences.

3.7 Beneficial health effects of alcohol consumption on disease

Ischaemic stroke

Cerebrovascular disease (stroke) consists of several subtypes, the most common being ischaemic stroke and haemorrhagic stroke, which are affected differently by alcohol. For ischaemic stroke (the predominant type) the weight of evidence, including biological mechanisms, suggests effects similar to those for IHD, namely that low to moderate consumption may offer some protection (Beilin et al. 1996; Hillbom 1998; Keil et al. 1997; Kitamura et al. 1998; Knuiman and Vu 1996; Sacco et al. 1999; Thun et al. 1997; Yuan et al. 1997; Wannamethee and Shaper 1996). It seems that this protective effect is more pronounced in females (Table 12.11).

Other beneficial health effects

Alcohol consumption may offer some protection against type II diabetes and cholelithiasis (gallstones) (see also Ashley et al. 2000 for a recent

Table 12.10 Relative risks for chronic harmful alcohol-related disease for different drinking categories (relative to abstainers)

		Relative risk					
		Drinking category I		*Drinking category II*		*Drinking category III*	
Disease or condition	*ICD-9 codes*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*
Lip and oropharyngeal cancer	140, 141, 143–146, 148, 149, 230.0	1.45	1.45	1.85	1.85	5.39	5.39
Oesophageal cancer	150, 230.1	1.80	1.80	2.38	2.38	4.36	4.36
Liver cancer	155, 230.8	1.45	1.45	3.03	3.03	3.60	3.60
Laryngeal cancer	161, 231.0	1.83	1.83	3.90	3.90	4.93	4.93
Female breast cancer, <45 years	174, 233.0	NA	1.15	NA	1.41	NA	1.46
Female breast cancer, ≥45 years		NA	1.14	NA	1.38	NA	1.62
Epilepsy	345	1.23	1.34	7.52	7.22	6.83	7.52
Hypertension[a]	401–405	1.40	1.40	2.00	2.00	4.10	2.00
Cardiac arrhythmias	427.0, 427.2, 427.3	1.51	1.51	2.23	2.23	2.23	2.23
Heart failure and ill-defined complications of heart disease[b]	428, 429						
Haemorrhagic stroke	430–432	1.27	0.59	2.19	0.65	2.38	7.98
Oesophageal varices	456.0–456.2	1.26	1.26	9.54	9.54	9.54	9.54
Gastro-oesophageal haemorrhage[c]	530.7	NA	NA	NA	NA	NA	NA
Unspecified liver cirrhosis	571.5–571.9	1.26	1.26	9.54	9.54	13.00	13.00
Acute and chronic pancreatitis[a]	577.0, 577.1	1.30	1.30	1.80	1.80	3.20	1.80
Spontaneous abortion	634	NA	1.20	NA	1.76	NA	1.76
Low birth weight	656.5	1.00	1.00	1.40	1.40	1.40	1.40
Psoriasis	696.1	1.58	1.58	1.60	1.60	2.20	2.20
Prematurity	764	0.93	0.93	1.36	1.36	1.36	1.36
Intrauterine growth retardation	765	0.99	0.99	1.68	1.68	1.68	1.68

NA Not applicable.

[a] Relative risk estimates taken from Corrao et al. (1999); most major cost studies derived AAFs for acute and chronic pancreatitis directly (e.g. Australia, for 577.0: 0.24; for 577.1: 0.84 [English et al. 1995]).

[b] Heart failure AAF determined indirectly from other circulatory diseases.

[c] Relative risks not applicable because AAFs were usually obtained directly (e.g. Switzerland, for 530.7: 0.47).

Sources: unless otherwise indicated Gutjahr et al. (2001); Ridolfo and Stevenson (2001).

overview on beneficial effects of alcohol). The Australian meta-analysis by English et al. (1995) concluded that there was some evidence that alcohol may protect against the onset of type II diabetes. Since then, the findings from a cohort of more than 40 000 male health professionals showed that moderate alcohol consumption may reduce the risk of type II diabetes, perhaps through the effects of alcohol on insulin sensitivity (Rimm et al. 1995). In addition, findings from the British Regional Heart Study indicated a protective effect (Perry et al. 1995). Further, a follow-up of men enrolled in the United States Physicians Study revealed a marked negative association of incident type II diabetes with alcohol consumption (Ajani et al. 1999). In a recent prospective study, a U-shaped association was found between alcohol and type II diabetes (Wei et al. 2000).

On the other hand, Kao et al. (1998) found evidence (based on small numbers) of an inverse relationship between alcohol consumption and the risk of type II diabetes for women. This relationship was not found in men; indeed, men consuming more than 21 units of alcohol per week were at increased risk of type II diabetes. A protective effect of moderate alcohol consumption against type II diabetes may be mediated through the effects of alcohol on glucose tolerance and insulin resistance. Moderate alcohol drinking has been shown to increase insulin sensitivity (Facchini et al. 1994; Kiechl et al. 1996) and lower insulin resistance (Lazarus et al. 1997), even in young adult drinkers (Flanagan et al. 2000). Finally, there is some evidence that inflammatory processes may mediate alcohol-induced diabetes (Imhof et al. 2001; Pradhan et al. 2001). In summary, there is growing evidence from cohort studies that moderate alcohol consumption reduces the risk of diabetes and a plausible underlying biological mechanism has been identified. This was the reason for including this effect as a beneficial effect in subregions with beneficial drinking patterns (established market economies with best mortality pattern: AMR-A, EUR-A, WPR-A). For all other subregions, no effect was modelled for these drinking categories. However, evidence for the relationship between alcohol consumption and diabetes is far from conclusive at present.

There is evidence that alcohol consumption may offer some protection against gallstones (English et al. 1995; Holman et al. 1996). These findings have been substantiated by recent large-scale cohort and case–control studies, which reported an inverse relationship (Attili et al. 1998; Caroli-Bosc et al. 1998; Chen et al. 1999; Leitzmann et al. 1998). Table 12.11 gives an overview of diseases for which alcohol potentially has beneficial effects.

Table 12.11 Relative risks for chronic beneficial alcohol-related health effects for different drinking categories (compared to abstainers)

		Relative risk					
		Drinking category I		*Drinking category II*		*Drinking category III*	
Disease or condition	*ICD-9 code*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*
Type II diabetes	250	0.99	0.92	0.57	0.87	0.73	1.13
Ischaemic stroke	433–435	0.94	0.52	1.33	0.64	1.65	1.06
Cholelithiasis	574	0.82	0.82	0.68	0.68	0.50	0.50

Source: Gutjahr et al. 2001; Ridolfo and Stevenson 2001.

3.8 IHD as a chronic condition for which alcohol has harmful and beneficial consequences

Epidemiology—average volume of consumption

IHD[23] is one of the leading causes of death in the world (Murray and Lopez 1996a). The most important health benefits of alcohol in terms of IHD have been found at low to moderate levels of average volume of consumption (Beaglehole and Jackson 1992; Doll 1998; Edwards et al. 1994; Fuchs et al. 1995; Goldberg et al. 1995; Hillbom 1998; Holman et al. 1996; Jackson 1994; Rehm et al. 1997; Single et al. 1999a; Svärdsudd 1998). Only a few individual-level studies have failed to substantiate this association in men (Hart et al. 1999) or women (Fillmore et al. 1998; Maskarinec et al. 1998).

While some studies have suggested that alcohol may offer protection against IHD across the entire continuum of consumption (Camargo et al. 1997; Doll et al. 1994; Keil et al. 1997; Rehm et al. 1997 [males only]; Kitamura et al. 1998; Thun et al. 1997), they nevertheless show that most of the protective effect is gained at low levels of consumption, such as one drink every other day.

Overall, average volume of drinking and IHD show a J-shape relationship in the usual medical epidemiological cohort studies in established market economies (Corrao et al. 2000). Compared to abstinence, low to moderate average consumption of alcohol has been found to confer a lower risk of IHD incidence and mortality. For higher levels of average volume of consumption, the risk relationship is reversed (e.g. Corrao et al. 2000; Friedman and Kimball 1986; Rehm et al. 1997), with heavy average consumption being associated with a risk larger than that for abstainers. In the most recent meta-analysis Corrao et al. (2000) demonstrated the described J-shape, and also demonstrated several other characteristics from the literature on average volume of consumption and IHD.

- There was a pronounced sex effect, showing that women were less protected for a given level of consumption, with an earlier upturn of the curve.
- The beneficial effect of alcohol was less pronounced for fatal outcomes.
- The study results were inconsistent, especially with respect to relative risk for higher intake, indicating additional influencing factors not controlled for.
- The better quality studies placed the maximum beneficial effect at lower levels of average alcohol intake. The maximum protective effect was measured at 20 g pure alcohol per day; the relative risk = 1 line, equivalent to abstainers' risk, was crossed at 72 g per day; and there was a significant detrimental effect over 89 g per day.
- More specifically, cohort studies, wholly adjusted studies, studies that compared drinkers with lifetime abstainers and those that excluded sick subjects at baseline showed less beneficial effects than case–control studies, unadjusted or partially adjusted studies, studies that compared drinkers with current abstainers and those that included sick subjects.
- Mediterranean countries showed more protective effects for the same levels of average consumption.

The epidemiological evidence that light to moderate average alcohol consumption protects against IHD is strengthened by substantial evidence concerning the biological mechanisms by which a protective effect could be mediated (Rankin 1994; Renaud et al. 1993; Single et al. 1999b; Svärdsudd 1998). First, moderate alcohol intake has been linked to favourable lipid profiles, especially an increase in high-density lipoproteins (HDL) (Baraona and Lieber 1998). It has been estimated that as much as 40–50% of the protective effect may be attributable to this mechanism (Criqui et al. 1987; Criqui and Ringel 1994; Suh et al. 1992). Second, moderate alcohol intake favourably affects coagulation profiles, particularly through its effects on platelet aggregation (McKenzie and Eisenberg 1996; Rubin 1999) and fibrinolysis (Reeder et al. 1996). Third, low to moderate consumption of alcohol has been shown to favourably affect insulin resistance (Kiechl et al. 1996; Lazarus et al. 1997; Rankin 1994). Fourth, it has been postulated that alcohol could protect against IHD through its effect on hormonal profiles, particularly its estrogen effects (Svärdsudd 1998). Fifth, the alcohol metabolite acetate has been postulated to protect against IHD by promoting vasodilation (U.S. Department of Health and Human Services 1997). Sixth, alcohol affects inflammation and, through this pathway, can influence IHD (Imhof et al. 2001; Jacques et al. 2001; Morrow and Ridker 2000; Ridker 2001). Finally, it is possible that some of the effect is mediated through the anti-

oxidative constituents of alcohol beverages, especially wine (Reinke and McCay 1996). Nevertheless, most of the protective effect appears to be linked to ethanol *per se*.

The protective effect of light to moderate consumption has been questioned on several grounds. The role of the comparison group has been questioned (Shaper 1990a, 1990b; Shaper et al. 1988), it being suggested that the abstainer group includes people who have stopped drinking because of health reasons and these are responsible for the elevated disease risk compared to light and moderate drinkers. Many subsequent studies controlled for this effect by taking lifetime abstainers as the comparison group (Rehm and Sempos 1995). Nevertheless, in most established market economies, where most of the research on alcohol and IHD has taken place, abstainers constitute only a minority of the general population and the possibility that they have other behavioural characteristics responsible for the elevated IHD risk cannot be excluded. No alternative explanation has ever been empirically demonstrated, however. For instance, social isolation has been theoretically claimed to confound the alcohol–mortality relationship (Skog 1996), but empirical research has not been able to substantiate this effect (Murray et al. 1999).

In conclusion, the relationship between average volume of drinking and IHD seems to be J-shaped. Light to moderate drinking is associated with a lower IHD risk than abstinence or heavy drinking. However, the results are inconsistent, indicating that factors other than those included in the study may also determine the relationship. One of the main factors may be pattern of drinking (i.e. the way in which the same average amount of alcohol is consumed). In this respect two patterns deserve mentioning: irregular heavy drinking and drinking with meals.

Epidemiology—patterns of drinking

Heavy drinking occasions

Heavy drinking occasions have been linked to adverse cardiovascular events for some time (Poikolainen 1983). However, many studies had used wider endpoints than IHD (Kauhanen et al. 1997b) or samples of problem drinkers or persons with alcohol-use disorders (Dyer et al. 1977; Rosengren et al. 1987; Rossow and Amundsen 1997), where heavy drinking patterns are confounded with volume.

Some of the more recent studies have controlled for (average) volume of drinking. A case–control study in Australia (McElduff and Dobson 1997) compared 11 511 cases of acute myocardial infarction or coronary death with 6077 randomly selected controls. If people drank in binges (usually five or more drinks on an occasion for women, nine or more drinks on an occasion for men), there were no protective effects for coronary events and relative risks were mainly larger than 1 compared to abstainers (indicating higher risks for major coronary events). This

elevated risk was present even in groups with low overall volume of drinking. As expected, the authors also found a protective effect of daily drinking, which was most pronounced for regular light to moderate drinkers.

Similarly, Murray et al. (2002) evaluated the cardiovascular consequences of binge drinking (eight or more drinks at a sitting) and usual (non-binge) drinking of alcohol in a longitudinal, population-based study. Interview data from 1154 men and women aged 18 to 65 years in Winnipeg, Canada were linked to health care utilization and mortality records in an eight-year follow-up period. Cox proportional hazards regressions were estimated separately for men and women. The outcomes included first event for physician visits, and hospitalizations and deaths due to IHD, hypertension, or other cardiovascular disease. Binge drinking increased the risk of IHD in men (hazard ratio [HR] of 2.3, 95% CI 1.2–4.2) and women (HR of 1.1, 95% CI 1.02–1.2) and increased the risk of hypertension in men (HR of 1.6, 95% CI 1.04–2.4) but not women. Binge drinking had no effect on the risk of other cardiovascular disease. All of these results were controlled for average volume of drinking. Again, the expected cardioprotective effects were confirmed in both men and women. The harmful effects of heavy drinking occasions on IHD morbidity and mortality could thus be disaggregated from the effect of average volume of drinking. Finally, Trevisan et al. (2001a) found in a case–control design that, after adjustment for average volume of consumption, weekend drinking by men was significantly related to risk of myocardial infarction compared to men drinking less than once a week (logistic regression: OR 1.9, 95% CI 1.2–3.2).

In addition to the effect on IHD, there appears to be a relationship between irregular heavy drinking occasions and other forms of cardiovascular death, especially sudden cardiac death (Kauhanen et al. 1997b; Wannamethee and Shaper 1992; Wood et al. 1998). This is consistent with the physiological mechanisms of increased clotting and reducing the threshold for ventricular fibrillation after heavy drinking occasions, which have been reviewed by McKee and Britton (1998). Specifically, heavy drinking occasions have been shown to increase the blood level of low-density lipoproteins (LDL), which in turn have been linked to negative cardiovascular outcomes. Contrary to low or moderate steady drinking, heavy irregular drinking occasions are not associated with an increase in levels of HDL, which have been linked to favourable cardiovascular outcomes. In addition, irregular drinking is associated with increased risk of thrombosis after cessation of drinking (Renaud and Ruf 1996). Finally, irregular heavy drinking seems to predispose to histological changes in the myocardium and conducting systems, as well as to a reduction in the threshold for ventricular fibrillation. In conclusion, irregular heavy drinking occasions are mainly associated with physiological mechanisms that increase the risk of sudden cardiac death and other cardiovascular outcomes, in contrast to the physiological

mechanisms triggered by regular low to moderate consumption that are linked to favourable cardiac outcomes. Nevertheless, individual-level studies are still scarce and some studies show no effects (Murray et al. 1998).

Drinking with meals

Trevisan et al. (2001b) reported on drinking with meals and IHD mortality based on the Risk Factor and Life Expectancy Study, a pooled series of epidemiological studies conducted in Italy with 8647 males and 6521 females aged 30–59 years at baseline and free of cardiovascular disease. Subjects were followed up for an average of seven years. Alcohol consumption showed a protective effect on IHD, and drinking wine with meals was linked to more positive outcomes than drinking wine outside meals. Compared to drinking with meals, drinking wine outside meals had a relative risk of 1.8, 95% CI 0.97–3.5 for IHD in males, adjusted for average volume of drinking and other potential confounders. There were not enough IHD cases to conduct a similar analysis for females, but the effects for all-cause mortality for females showed a five-fold risk for wine outside meals compared to wine with meals (relative risk of 5.0, 95% CI 1.5–10.9).

Another study (Trevisan et al. 2001a), using a case–control design, examined 443 male myocardial infarction survivors and 922 healthy controls aged 35–69 years. Compared to non-drinkers the age, education and smoking-adjusted odds ratios for former drinkers and current drinkers were 0.67, 95% CI 0.32–1.38 and 0.47, 95% CI 0.24–0.95, respectively, confirming the overall cardioprotective effect of alcohol consumption (see above). Men who reported drinking without food at least 75% of the time had an odds ratio of 1.5, 95% CI 0.96–2.3 compared to those who drank mainly with meals and snacks, after adjustment for age, education and volume of alcohol consumed.

The potential mechanisms linking consumption of alcoholic beverages with meals to a lower IHD risk, compared to consumption between meals, remain to be fully clarified. However a few mechanisms have been hypothesized. A study by Trevisan et al. (1987) in a large sample of Italian men and women found a significant association between drinking between meals and higher prevalence of hypertension, compared to drinking with meals, even after adjustment for differences in alcohol consumption between these drinking pattern categories. These findings were recently confirmed in another study using a population-based sample in the United States (Wu and Trevisan 2001). Finally, Foppa et al. (1999) found in a controlled randomized trial that moderate consumption of wine with a meal reduced postprandial blood pressure. Drinking with meals has also been shown to positively affect fibrinolysis (Hendriks et al. 1994) and lipid levels (Veenstra et al. 1990).

Other potential physiological links between drinking with meals and these IHD risk factors include a reduced absorption of alcohol owing to

the presence of food in the gastrointestinal tract (Gentry 2000). Another physiological link may be that food increases the alcohol elimination rate (Ramchandani et al. 2001).

Aggregate-level studies on patterns and average consumption

Given the described relative scarcity of individual-level studies, it is not surprising that much of the argumentation is based on aggregate-level studies, especially on Russian experience with the natural experiment of the Gorbachev anti-alcohol campaign. The Russian Federation is generally considered to be one of the countries with the highest rates of irregular heavy drinking (Bobak et al. 1999; Malyutina et al. 2001). Thus, if a heavy drinking style has an adverse impact on cardiovascular disease in general and on IHD in particular, such effects should have become evident at the population level in the experience of the anti-alcohol campaign during the last years of the Soviet Union. In the period 1984–1987, when estimated total alcohol consumption in the Russian Federation fell by about 25% (Shkolnikov and Nemtsov 1997), age-adjusted male deaths from circulatory disease fell by 9% (Leon et al. 1997). After the end of the campaign, the death rate rose again quite dramatically. The role of alcohol in the recent drastic increases in mortality in the Russian Federation, however, remains controversial, as many other changes occurred in the late 1980s and early 1990s (Bobak and Marmot 1999; Britton and McKee 2000; Leon et al. 1997; McKee et al. 2001; Notzon et al. 1998; Shkolnikow et al. 2001). There seems to be general agreement, however, that alcohol has played an important role in increasing mortality rates, although the level of impact is unclear.

There is another indirect line of research on the effect of heavy drinking on IHD. Countries with a tradition of heavier or binge drinking on weekends show proportionately high IHD or cardiovascular disease mortality on or immediately after the weekend (Germany, IHD: Willich et al. 1994; Moscow, cardiovascular disease events: Chenet et al. 1998; Lithuania, IHD events: Chenet et al. 2001; Scotland, IHD events: cf. Evans et al. 2000). Other aggregate-level research on per capita alcohol consumption and IHD have failed to find effects, even for countries with the best drinking pattern (i.e. drinking pattern = 1) in a time series analysis with differenced data, controlling for tobacco (Hemström 2001). Finally, Skog (1983) also found no significant effects in a time series analysis on differenced data for Norway.

Summary of the epidemiological evidence

In conclusion, the relationship between drinking and IHD is complex, and the epidemiological literature on it is evolving. There seems to be a clear beneficial effect, supported by biochemical evidence, of regular light to moderate drinking, but it is unclear how many people actually drink in a manner that will provide them with these benefits. Also, there are

indications that irregular bouts of heavy drinking are linked to physiological mechanisms, which are in turn linked to negative IHD outcomes, as well as to other negative cardiovascular disease outcomes. Better surveys are needed, including the measurement of biomarkers indicative of the relationships specified above. In these surveys, the relevant variables such as irregular heavy drinking or drinking with meals should also be included.

Many of the individual-level cohort studies on the relationship between average volume of drinking and IHD have been carried out on special populations such as nurses, doctors or other health professionals, mostly in established market economies, who have relatively regular and potentially beneficial drinking patterns. As a result, the effect of average volume of alcohol consumption may be overstated in the usual meta-analysis. Thus, the results of these analyses cannot be applied worldwide, since more detrimental patterns of drinking prevail in the majority of countries. Moreover, the impact of pattern of drinking has to be included, in addition to the effects of average volume of drinking.

Unfortunately, as described above, patterns of drinking cannot be modelled by meta-analysis owing to the scarcity of data on the relationship between exposure and outcome. Thus, we used the multilevel modelling approach described earlier to incorporate patterns of drinking into the estimates.

Measuring the effect of average volume of consumption and drinking pattern on IHD mortality

The details of determining the impact of average volume and pattern of drinking on IHD are described earlier. The characteristics of the data set are given in Table 12.12.

Table 12.13 gives an overview of the most important results with respect to the differential impact of alcohol consumption on IHD mortality. As predicted, in countries with consumption pattern 1, alcohol had beneficial effects on the incidence of IHD. For countries with pattern 2, the impact on IHD varied around zero (i.e. no marked impact of alcohol). In countries with pattern 3, alcohol showed a detrimental impact on IHD for males only. For countries with pattern 4, the detrimental impact of alcohol was pronounced for both males and females. Assuming interval scales between the categories of the pattern variable, the models were estimated as in Table 12.14.

Again, in countries with pattern 1, beneficial effects appeared for both males (–0.0214) and females (–0.0376). These consumption models indicate that the overall effect of IHD at an average pattern level (2.51 in the sample used) is detrimental for males and not significantly different from zero for females. In other words, the results from individual-level studies could be replicated in this aggregate-level study. This means that for countries such as France and Italy we expect a beneficial effect of alcohol on IHD mortality; for countries such as Slovenia and the United

Table 12.12 Characteristics of the data set for calculating the relationship between per capita consumption, patterns of drinking and IHD mortality (per 1000 population per year)

Country	*IHD mortality males*	*IHD mortality females*	*Average per capita alcohol consumption*	*Pattern of drinking*	*Per capita GNP*	*Year of first data*	*Year of latest data*	*Number of years*
Albania	0.99	0.40	2.20	3	585.71	1992	1998	7
Argentina	1.37	0.70	27.48	2	3 472.00	1966	1996	25
Armenia	3.34	2.30	2.53	2	507.14	1992	1998	7
Australia	2.75	1.36	11.19	2	10 341.76	1964	1997	34
Austria	1.92	1.00	14.16	1	11 136.05	1962	1999	38
Azerbaijan	4.10	2.40	2.10	3	746.67	1990	1999	9
Bahamas	0.95	0.46	14.33	2	7 067.69	1969	1995	13
Bahrain	2.04	1.72	5.33	2	7 423.33	1985	1988	3
Barbados	0.93	0.56	7.88	2	3 357.42	1964	1995	31
Belarus	4.03	2.20	9.68	4	2 651.11	1989	1998	9
Belgium	1.44	0.63	12.35	1	9 487.10	1964	1994	31
Belize	0.53	0.38	6.01	4	1 127.86	1964	1995	28
Bulgaria	2.14	1.28	11.97	2	1 898.24	1982	1998	17
Canada	2.45	1.22	9.74	2	11 367.65	1964	1997	34
Chile	1.16	0.74	11.58	3	1 562.26	1964	1994	31
Colombia	1.09	0.70	5.49	3	993.68	1967	1994	19
Costa Rica	1.30	0.84	4.48	4	1 268.13	1964	1995	32

continued

Table 12.12 Characteristics of the data set for calculating the relationship between per capita consumption, patterns of drinking and IHD mortality (per 1000 population per year) (*continued*)

Country	*IHD mortality males*	*IHD mortality females*	*Average per capita alcohol consumption*	*Pattern of drinking*	*Per capita GNP*	*Year of first data*	*Year of latest data*	*Number of years*
Croatia	1.78	1.03	13.24	3	3 638.33	1993	1998	6
Czech Republic	2.76	1.43	15.42	2	3 915.71	1986	1999	14
Denmark	2.59	1.32	10.91	2	13 139.70	1964	1996	33
Dominican Republic	0.46	0.31	2.91	2	729.52	1965	1985	21
Ecuador	0.37	0.24	2.30	3	882.90	1964	1995	31
El Salvador	0.38	0.25	1.95	4	564.74	1964	1993	19
Estonia	4.16	2.18	13.43	3	3 107.50	1992	1999	8
Finland	3.25	1.37	7.42	3	10 642.42	1964	1996	33
France	0.82	0.35	23.15	1	11 120.29	1964	1997	34
Germany	1.59	0.80	13.63	1	26 661.67	1993	1998	6
Greece	0.94	0.44	9.69	2	5 027.14	1964	1998	35
Guatemala	0.26	0.21	2.42	4	644.71	1964	1984	17
Guyana	1.17	0.69	8.42	3	540.00	1977	1994	5
Honduras	0.20	0.13	2.27	4	418.67	1966	1981	15
Hungary	2.54	1.30	15.85	3	2 837.83	1977	1999	23
Iceland	2.30	1.06	5.42	3	12 691.82	1964	1996	33
Ireland	2.80	1.39	10.86	3	5 865.76	1964	1996	33
Israel	1.89	1.19	3.04	2	8 236.36	1975	1996	22

Italy	1.35	0.74	18.48	1	8418.18	1964	1996	33
Jamaica	0.64	0.48	3.12	2	927.14	1964	1985	7
Japan	0.53	0.32	5.78	1	13654.41	1964	1997	34
Kazakhstan	3.79	2.10	7.24	4	1691.00	1989	1998	10
Kyrgyzstan	2.98	1.76	1.88	3	488.00	1995	1999	5
Latvia	4.27	2.06	8.53	3	3149.00	1989	1998	10
Lithuania	3.73	2.24	5.76	3	2380.00	1989	1998	5
Luxembourg	1.54	0.65	17.37	1	19366.77	1967	1997	31
Malta	2.05	1.23	5.27	1	4004.85	1965	1998	33
Mauritius	2.10	1.01	3.30	3	1473.71	1964	1998	35
Mexico	0.60	0.38	3.94	4	1877.94	1962	1995	34
Netherlands	1.86	0.83	9.39	1	10900.29	1964	1997	34
New Zealand	2.80	1.33	11.36	2	7426.29	1964	1998	35
Nicaragua	0.41	0.29	3.29	4	448.24	1964	1994	17
Norway	2.27	0.98	5.11	3	14216.06	1964	1996	33
Peru	0.42	0.32	6.10	3	828.89	1966	1989	18
Philippines	0.74	0.44	2.73	3	454.76	1964	1996	21
Portugal	1.06	0.59	18.85	1	3844.86	1964	1998	35
Republic of Korea	0.18	0.09	8.90	3	6664.62	1985	1997	13
Romania	2.16	1.37	10.78	3	1432.00	1989	1998	10
Russian Federation	3.87	1.92	8.88	4	2683.75	1991	1998	8

continued

Table 12.12 Characteristics of the data set for calculating the relationship between per capita consumption, patterns of drinking and IHD mortality (per 1000 population per year) (*continued*)

Country	*IHD mortality males*	*IHD mortality females*	*Average per capita alcohol consumption*	*Pattern of drinking*	*Per capita GNP*	*Year of first data*	*Year of latest data*	*Number of years*
Singapore	1.44	0.79	2.30	2	9 106.86	1964	1998	35
Slovakia	2.85	1.57	12.54	3	2 437.50	1992	1995	4
Slovenia	1.27	0.66	14.80	2	8 912.00	1994	1998	5
South Africa	1.01	0.46	10.30	3	3 606.67	1993	1995	3
Spain	0.83	0.40	17.20	1	5 554.17	1962	1997	36
Sri Lanka	0.45	0.22	.27	3	268.46	1964	1986	13
Suriname	0.92	0.54	6.43	3	1 749.05	1964	1992	21
Sweden	2.54	1.27	7.57	3	13 042.42	1964	1996	33
Switzerland	1.43	0.68	14.99	1	15 815.16	1964	1994	31
Thailand	0.02	0.01	3.58	3	541.20	1964	1994	25
The former Yugoslav Republic of Macedonia	1.22	0.58	5.76	3	1 350.00	1994	1997	4
Trinidad and Tobago	2.05	1.28	4.76	2	3 254.33	1962	1994	30
Ukraine	4.19	2.48	4.64	3	1 276.00	1990	1999	10
United Kingdom	2.67	1.23	9.49	2	9 210.00	1964	1998	35
United States	2.68	1.39	9.46	2	14 028.53	1964	1997	34
Uruguay	1.77	0.96	8.08	3	1 680.00	1966	1990	24
Uzbekistan	3.72	2.67	1.07	3	733.33	1996	1998	3
Venezuela	1.38	0.94	8.31	3	2 992.50	1969	1994	24

Table 12.13 Average effect of consumption of 1 litre of pure alcohol per capita[a] for different drinking patterns

Pattern of drinking	*Males*	*Females*
1	–0.016227	–0.038174
2	0.004050	–0.014323
3	0.053951	0.001908
4	0.084529	0.035584

[a] This corresponds to coefficient β_3 in the model shown in the footnote.

Level-1 model

$$\text{Mortality rate} = \beta_0 + \beta_1^{a}\,(\text{YEAR}) + \beta_2^{a}\,(\text{GNP\_PC}) + \beta_3^{a}(\text{PC\_ALCOHOL}) + \varepsilon$$

Level-2 model

$$\beta_0 = \gamma_{00} + \mu_0$$

$$\beta_1 = \gamma_{10} + \mu_1$$

$$\beta_2 = \gamma_{20}$$

$$\beta_3 = \gamma_{30} + \gamma_{31}^{a}\,(\text{PATB}) + \gamma_{32}^{a}\,(\text{PATC}) + \gamma_{33}^{a}\,(\text{PATD}) + \mu_3$$

where

mortality = age-standardized IHD mortality

YEAR = year of observation

GNP_PC = GNP per capita

PC_ALCOHOL = per capita adult (≥15 years) alcohol consumption

PATB = dummy variable for pattern 2

PATC = dummy variable for pattern 3

PATD = dummy variable for pattern 4.

Table 12.14 Effect of per capita consumption and drinking patterns on standardized IHD rates, assuming equal intervals between pattern values

	Coefficient	*SE*	*t-value*	*df*	*P*
Males					
Effect of per capita consumption at average pattern[a]	0.033503	0.013417	2.497	72	0.013
Deviations from average patterns	0.036353	0.011622	3.128	72	0.002
Females					
Effect of per capita consumption at average pattern[a]	–0.004433	0.008263	–0.537	72	0.591
Deviations from average patterns	0.021969	0.006806	3.228	72	0.002

[a] Patterns of drinking were entered grand-mean-centred into the equation. Thus, the effect of per capita consumption displayed here is the effect at the grand mean of pattern, which is 2.51 in this sample.

States there will be no overall effect; for countries such as the Republic of Korea and Ukraine we expect an overall detrimental effect of alcohol for males; and for countries such as the Russian Federation we expect a detrimental effect for both males and females. The results from this model are consistent with the finding that the anti-alcohol campaign in the Gorbachev era had such an impact on IHD mortality in the Russian Federation.

The model has limitations, however. Most notably, each country has been assigned one pattern value that is assumed to be stable over time. Whereas patterns have been found to be stable in the past (Room 1992; Simpura 2001), clearly this assumption is an oversimplification. Moreover, it is clear that in most countries there are people with different drinking patterns. Thus, future research should be based on distributions of patterns by sex and age, rather than on one pattern value per country.

The results of this model are not consistent with a recent ecological analysis by Hemström (2001), using a time series approach with differenced data. Hemström (2001) found a random distribution of insignificant negative (beneficial) and positive (detrimental) alcohol effect estimates. He used only per capita data without any control for drinking pattern. However, based on individual-level studies and the results of the present analysis, beneficial effects would have been expected for countries with a consumption pattern of 1, such as France, Italy, Portugal and Spain. We can only speculate on the difference in results between the two analyses. Hemström's time series were relatively short (45 years per country), not allowing some of the tests for correct model specification (Rehm and Gmel 2001a). There also may have been some overdifferencing problems with co-integration or the joint use of differencing and taking the logarithm, which may have obscured the effect (Greene 2000; Hatanaka 1996; Yaffee 2000).

On the other hand, the present analysis draws on relatively limited time series in a wide range of drinking cultures, which increases the ability to generalize but which also has limitations. Our findings for the pattern-1 subgroup have the strong advantage of convergent data from individual-level studies, supported by biological plausibility. We have therefore used our finding of a protective effect at the population level for the countries with beneficial patterns (pattern 1) as a current best estimate of effects (for comparison with results using coefficients from meta-analysis).

Given the limits of ecological analysis, individual-level data should always be given priority in judgements of causality, although not necessarily in terms of estimates of the overall effect of changes in a risk factor at the population level (Skog 1996). This applies to our analysis as well.

Determining AAFs for IHD, including patterns of drinking

To arrive at the AAFs, the results of the dummy regression were taken and only effects larger than ±0.015 were modelled. However, since the

multilevel analysis could only control for per capita GNP as a confounder, and since there are general limits in controlling for confounding in such analyses (Morgenstern 1998), the effects of alcohol indicators were halved in order to be conservative and to adjust for any other confounding. This approach, though arbitrary in the choice of halving, is consistent with that taken in risk analysis for other risk factors (e.g. tobacco) to avoid residual confounding.

Taking into consideration the distribution of patterns in all countries within the 14 subregions, and standardized mortality rates after 1994, the AAFs can be derived (Table 12.15).

Table 12.15 shows the effects of alcohol-attributable IHD mortality based on aggregate-level analysis, halving the effects to adjust for potential confounding. This can easily be done by using the respective values in the formulas above.

Alternatively, one may use the relative risks from the individual-level studies as a basis and apply them to the subregions AMR-A, EUR-A and WPR-A, as almost all of the studies come from these subregions. Such an approach leads to higher cardioprotective effects (see Table 12.16) and may well contain overestimates based on the usual cohort composition, where people with more regular drinking styles are overrepresented. However, individual-level studies are usually preferred to ecological studies both for establishing causality and for making estimates of impact (e.g. Morgenstern 1998). Further, with respect to overall disease burden attributable to alcohol, this provides a more conservative approach to estimating.

The resulting AAFs, using individual-level estimates of relative risk for AMR-A, EUR-A and WPR-A, would be –0.11, –0.15 and –0.15, respectively. The cardioprotective effect estimated in this way is larger than that given above (see Table 12.15). We used these estimates for the final calculations. The numbers for EUR-B are given only for sensitivity analysis. Overall, the average patterns for this subregion (2.9) are much closer to the average pattern for EUR-C (3.6) than that for EUR-A (1.3). Thus, we did not feel justified in using the estimates based on studies almost exclusively from countries with beneficial patterns (A subregions).

3.9 Depression

Background and epidemiology

Alcohol is implicated in a variety of mental disorders that are not alcohol-specific. However, no major overview on alcohol-attributable burden of disease has yet included these disorders (English et al. 1995; Gutjahr et al. 2001; Rehm et al. 2001a, 2001b; Ridolfo and Stevenson 2001; Single et al. 1999). While the causality of the relation is hard to define, sufficient evidence now exists for us to include an estimate of the causal role of alcohol in depression, a major mental disorder.

Table 12.15 AAFs predicted by the multilevel analysis

	Age group (years)					
Subregion	*All*	*15–29*	*30–44*	*45–59*	*60–69*	*≥70*
Males						
AFR-D	0.02	0.03	0.03	0.03	0.03	0.02
AFR-E	0.07	0.07	0.08	0.08	0.07	0.07
AMR-A[a]	0.00	0.00	0.00	0.00	0.00	0.00
AMR-B	0.16	0.15	0.15	0.16	0.17	0.15
AMR-D	0.08	0.09	0.10	0.11	0.10	0.08
EMR-B	0.00	0.00	0.00	0.00	0.00	0.00
EMR-D	0.01	0.01	0.01	0.02	0.01	0.00
EUR-A[a]	–0.04	–0.04	–0.04	–0.04	–0.04	–0.04
EUR-B	0.11	0.12	0.12	0.12	0.12	0.11
EUR-C	0.15	0.14	0.15	0.14	0.14	0.15
SEAR-B	0.01	0.02	0.03	0.04	0.02	0.00
SEAR-D	0.04	0.06	0.12	0.14	0.04	0.00
WPR-A[a]	–0.07	–0.07	–0.07	–0.08	–0.07	–0.07
WPR-B	0.01	0.01	0.01	0.01	0.01	0.01
Females						
AFR-D	0.00	0.00	0.00	0.00	0.00	0.00
AFR-E	0.00	0.00	0.00	0.00	0.00	0.00
AMR-A[a]	0.00	0.00	0.00	0.00	0.00	0.00
AMR-B	0.02	0.02	0.02	0.02	0.02	0.02
AMR-D	0.03	0.03	0.03	0.04	0.03	0.03
EMR-B	0.00	0.00	0.00	0.00	0.00	0.00
EMR-D	0.00	0.00	0.00	0.00	0.00	0.00
EUR-A[a]	–0.10	–0.10	–0.10	–0.10	–0.10	–0.10
EUR-B	0.00	0.00	0.00	0.00	0.00	0.00
EUR-C	0.03	0.03	0.03	0.03	0.03	0.03
SEAR-B	0.00	0.00	0.00	0.00	0.00	0.00
SEAR-D	0.00	0.00	0.00	0.00	0.00	0.00
WPR-A[a]	–0.10	–0.10	–0.11	–0.11	–0.10	–0.10
WPR-B	0.00	0.00	0.00	0.00	0.00	0.00

[a] The estimates for AMR-A, EUR-A and WPR-A serve only as sensitivity analysis as the AAFs for these subregions will be based on individual-level studies (see Table 12.16 below).

In the general population, alcohol dependence and major depression co-occur over-proportionally, on both a 12-month and a lifetime basis (Kessler et al. 1996, 1997; Lynskey 1998). Among alcohol consumers in the general population, higher volume of consumption is associated with more symptoms of depression (Graham and Schmid 1999; Mehrabian 2001; Rodgers et al. 2000). Compared to moderate drinkers, both higher

Table 12.16 Ischaemic heart disease AAFs for selected subregions, applying relative risk estimates[a]

	Age group (years)														
	15–29		*30–44*		*45–59*		*60–69*		*70–79*		*≥80*		*Total*		
Subregion	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	*All*
AMR-A	–0.14	–0.12	–0.15	–0.13	–0.14	–0.11	–0.12	–0.08	–0.11	–0.07	–0.11	–0.07	–0.13	–0.08	–0.11
EUR-A	–0.18	–0.16	–0.17	–0.17	–0.17	–0.16	–0.17	–0.14	–0.16	–0.13	–0.16	–0.13	–0.16	–0.13	–0.15
EUR-B[b]	–0.15	–0.11	–0.13	–0.10	–0.14	–0.09	–0.13	–0.07	–0.12	–0.07	–0.12	–0.07	–0.13	–0.08	–0.11
WPR-A	–0.18	–0.17	–0.19	–0.17	–0.18	–0.16	–0.17	–0.14	–0.15	–0.12	–0.15	–0.12	–0.17	–0.13	–0.15

[a] Relative risks are 0.82, 0.83 and 1.12 for drinking categories I, II and III for men and 0.82, 0.83 and 1.00 for women.

[b] EUR-B estimates are only given for reasons of sensitivity analysis (see section 3.6).

(Bjork et al. 1999) and lower (Rodgers et al. 2000) levels of depressive symptoms have been found among abstainers. Among patients under treatment for alcohol abuse and dependence, the prevalence of major depression is higher than in the general population (Lynskey 1998; Schuckit et al. 1997a). Similarly the prevalence of alcohol abuse and dependence is higher for patients under treatment for depression (Alpert et al. 1999; Blixen et al. 1997).

This suggests that alcohol abuse is linked to depressive symptoms, and that alcohol dependence and depressive disorders co-occur to a larger degree than expected by chance. However, it is not clear in the individual case whether depression caused alcohol problems, whether alcohol consumption or alcohol problems caused depression, or whether both could be attributed to a third cause (Vaillant 1993). The pathway from depression to problematic alcohol use and alcohol dependence has long been discussed under the heading of self-medication (i.e. the use of alcohol to alleviate depressive symptoms). In addition, a shared third cause could be certain neurobiological mechanisms (see Markou et al. 1998) or genetic predisposition. Moreover, all three pathways of causation may co-exist at the same time, with different proportions of the co-occurring morbidities being attributable to each, and of course some co-occurrence being simply due to chance.

Establishing the causal link between alcohol and depression

Causal relations in epidemiology are usually based on several criteria (Hill 1965; Rothman and Greenland 1998a). Using these criteria, we will review the evidence that part of the burden of depression is caused by alcohol. As indicated above, this does not preclude the possibility that part of the burden of alcohol dependence is also caused by depression, or that part of the co-occurrence is causally related to some third factor. Following the majority of the literature, we base our argumentation mainly on alcohol dependence rather than alcohol consumption *per se*. This is done mostly for reasons of data availability: depression and alcohol dependence are usually part of the same mental health surveys, and almost all estimates of co-occurrence stem from this kind of survey. It is not usual to include questions on alcohol consumption *per se* in this type of survey, nor is it usual to include a diagnosis of depression in alcohol surveys.

Prevalences of alcohol dependence or alcohol use disorders (i.e. alcohol dependence and harmful use of alcohol) were thus used as indicator of alcohol consumption drinking categories, assuming a constant relationship between the two variables. This indicator relationship was also made possible by the fact that alcohol use disorders by definition have an AAF of 1.0—that is, under the counterfactual scenario (Murray and Lopez 1999) of no alcohol available at all, there would be no burden due to alcohol dependence. Moreover, in different regions of the world,

average volume of drinking and prevalence of alcohol dependence are correlated to a high degree ($r = 0.86$) (Rehm and Eschmann 2002).

Temporal order

Causal factors must precede consequences. Logically, therefore, only that fraction of depression in which the onset of alcohol problems preceded the onset of depression can be caused by alcohol problems. The fraction in which alcohol problems came first is an upper bound for the proportion of depressive disorders caused by alcohol dependence. This upper bound is summarized in Table 12.17 for different forms of depression in several countries, based on the International Consortium in Psychiatric Epidemiology (ICPE) (Merikangas et al. 1998).

Clearly, in all areas (i.e. countries, provinces and cities) mentioned in Table 12.17, the proportion of depressive disorders preceded by alcohol dependence is higher for males than for females. This corresponds to the higher prevalence of alcohol dependence in these areas. In fact, the proportion of rates of depressive disorders and alcohol problems correlate to 0.80 (major depression) and 0.82 (other depressions) for these areas (Pearson correlations; alcohol dependence rates from *World health report 2001* and Rehm and Eschmann 2002). This means that at least 64% of the variation in the proportion of depressive disorders in the various subregions can be statistically "explained" by the variation in alcohol dependence. Of course, the remarks made above on possible forms of causal pathway still apply. This relationship provides a basis for predicting such rates for other subregions where data are lacking (see below).

Another indicator of the role of alcohol dependence in causing some depressive disorders is the comparison between onsets for different mental disorders co-occurring with alcohol disorders. In the US National Comorbidity Survey (Kessler et al. 1996) the proportion of disorders preceded by alcohol dependence was higher for depression than for any other disorder.

Consistency

Epidemiological studies are very consistent, both in the general population and in clinical samples, in showing that alcohol dependence and depressive disorders co-occur to a higher degree than might be expected by chance. This has been observed in several countries and regions (e.g. Merikangas et al. 1998; Swendson et al. 1998). In fact, we do not know of any study where alcohol dependence and depressive disorders did not co-vary to a larger degree than that expected by chance.

The co-variation between the proportion of people with depressive disorders with a preceding alcohol dependence and the prevalence of alcohol dependence is also consistent across countries (see above).

Table 12.17 Percentages of the population in which the onset of alcohol problems[a] occurred prior to diagnosis of depression, by country, age and sex

		Major depression[b]					*Other depressions*[c]				
	Age group	*Males*		*Females*		*Total*	*Males*		*Females*		*Total*
Country/Area	*(years)*	*n*	*%*	*n*	*%*	*%*	*n*	*%*	*n*	*%*	*%*
USA (NCS)	15–29	119	31.1	241	15.6	20.7	39	28.6	67	11.6	17.8
	30–44	168	47.0	286	21.1	30.6	68	51.7	121	22.4	33.0
	45–59	59	30.8	117	10.5	17.3	35	32.8	65	13.9	20.6
	60–69	—	—	—	—	—	—	—	—	—	—
	≥70	—	—	—	—	—	—	—	—	—	—
	Total	345	38.7	644	17.1	24.7	142	40.7	253	17.4	25.8
USA	15–29	46	20.8	78	13.7	16.3	25	34.8	32	17.0	24.8
CA	30–44	37	20.9	63	7.5	12.5	40	32.8	23	12.5	25.3
Fresno	45–59	11	1.8	24	21.4	15.1	9	14.3	10	0.0	6.7
	60–69	—	—	—	—	—	—	—	—	—	—
	≥70	—	—	—	—	—	—	—	—	—	—
	Total	94	18.5	165	12.5	14.7	74	31.3	65	12.9	22.7
Mexico	15–29	23	8.2	36	2.9	5.0	14	18.6	7	0.0	12.1
Mexico	30–44	12	30.1	50	2.0	7.3	4	40.4	11	0.0	11.7
City	45–59	6	31.8	14	0.0	9.8	4	20.4	8	0.0	6.3
	60–69	—	—	—	—	—	—	—	—	—	—
	≥70	—	—	—	—	—	—	—	—	—	—
	Total	41	17.9	99	2.0	6.7	22	23.4	26	0.0	10.6
Canada	15–29	56	20.6	123	20.3	20.4	43	26.8	54	19.7	22.8
Ontario	30–44	98	47.0	177	6.1	20.7	47	46.7	62	11.9	26.9
	45–59	29	33.6	85	3.0	10.8	9	22.4	36	2.8	6.7
	60–69	—	—	—	—	—	—	—	—	—	—
	≥70	—	—	—	—	—	—	—	—	—	—
	Total	183	36.8	386	10.0	18.6	98	35.8	152	12.5	21.7
Netherlands	15–29	70	26.9	177	10.1	14.9	46	17.4	76	6.4	10.6
	30–44	180	35.9	317	13.6	21.7	72	15.8	146	7.8	10.5
	45–59	129	31.9	180	7.2	17.5	58	32.2	118	3.7	13.2
	60–69	18	33.7	33	4.0	14.4	11	0.0	26	0.0	0.0
	≥70	—	—	—	—	—	—	—	—	—	—
	Total	397	32.9	707	10.7	18.7	187	20.4	366	5.7	10.6
Brazil	15–29	10	61.0	23	2.5	20.2	4	0.0	6	37.8	23.4
	30–44	21	10.0	53	17.0	15.1	7	28.6	22	22.2	23.8
	45–59	14	17.6	36	6.5	9.5	15	21.1	15	4.0	12.8
	60–69	2	66.7	10	0.0	12.8	2	100.0	6	22.2	38.5
	≥70	2	50.0	5	0.0	12.7	1	0.0	5	0.0	0.0
	Total	48	26.7	126	9.4	14.2	29	23.9	54	16.9	19.4
Germany	15–29	126	14.6	213	4.8	8.4	39	17.7	84	2.4	7.3
	30–44	—	—	—	—	—	—	—	—	—	—
	45–59	—	—	—	—	—	—	—	—	—	—
	60–69	—	—	—	—	—	—	—	—	—	—
	≥70	—	—	—	—	—	—	—	—	—	—
	Total	126	14.6	213	4.8	8.4	39	17.7	84	2.4	7.3

Table 12.17 Percentages of the population in which the onset of alcohol problems[a] occurred prior to diagnosis of depression, by country, age and sex (*continued*)

		Major depression[b]					*Other depressions*[c]				
	Age group	*Males*		*Females*		*Total*	*Males*		*Females*		*Total*
Country/Area	*(years)*	*n*	%	*n*	%	%	*n*	%	*n*	%	%
Japan	15–29	2	100.0	7	0.0	20.1	0	NA	5	0.0	0.0
	30–44	5	23.7	3	0.0	15.1	4	32.2	2	0.0	21.0
	45–59	4	0.0	5	0.0	0.0	2	0.0	6	0.0	0.0
	60–69	3	0.0	2	0.0	0.0	1	0.0	3	0.0	0.0
	≥70	1	100.0	1	0.0	49.8	1	100.0	1	0.0	49.8
	Total	14	24.9	17	0.0	11.4	7	27.4	16	0.0	8.3
Chile	15–29	37	28.6	67	11.3	17.4	11	0.0	47	11.4	9.3
	30–44	30	27.2	53	2.0	11.1	11	2.2	70	5.7	5.2
	45–59	13	44.0	42	6.7	15.4	18	39.3	50	1.7	11.6
	60–69	8	21.6	6	0.0	12.0	8	69.1	11	1.0	29.3
	≥70	2	7.2	6	0.0	1.9	1	20.4	5	0.0	2.8
	Total	89	29.2	173	6.6	14.3	48	26.5	182	5.6	10.0

NCS National Comorbidity Survey.

— No data.

[a] For NCS, Brazil, Chile and the Netherlands, defined as having an alcohol problem, alcohol dependence or alcohol abuse. In all other countries/areas, defined as either having alcohol dependence or alcohol abuse.

[b] In all countries, major depression is defined with exclusion and without hierarchy.

[c] In all countries, other depression is defined as having dysthymia or bipolar disorder with exclusions and without hierarchy.

Source: Table numbers were calculated using the International Consortium for Psychiatric Epidemiology data (see also Merikangas et al. 1998).

Strength of association

It has been consistently found that alcohol-dependent individuals demonstrate a two- to three-fold increase in risk of depressive disorders (e.g. Hilarski and Wodarki 2001; Schuckit 1996; Swendson et al. 1998). This is an effect comparable in size with many other causal effects (Gutjahr et al. 2001) (Table 12.19).

Reversibility (remission during abstinence)

Key evidence for a causal effect of alcohol dependence on depressive disorders comes from studies that analyse what happens to rates of depressive disorders when patients with clinical symptoms abstain from drinking. Most of these studies come to the conclusion that many depressive syndromes markedly improve within days or weeks of abstinence (Brown and Schuckit 1988; Dackis et al. 1986; Davidson 1995; Gibson and Becker 1973, Penick et al. 1988; Pettinati et al. 1982; Willenbring 1986). Of course, other things change within therapy, so not all of the

effect is necessarily due to the pharmacological effect of drinking. In addition, experimental studies have found that more symptoms of depression are reported during heavy drinking episodes (Isbell et al. 1955; Schuckit et al. 1997b; Tamarin et al. 1970; Weiner et al. 1971). In conclusion, there is sufficient evidence that abstinence substantially removes symptoms of depression in alcohol-dependent persons within a short time.

Family patterns

Several studies have tried to separate alcohol-dependent persons with primary (sometimes called "independent") depressive disorders from those with secondary (sometimes called "induced") depressive disorders by examining different family patterns of both alcohol dependence and depressive disorders. For instance, Hesselbrock et al. (1983) and Schuckit et al. (1997b) found higher rates of depressive disorders, rather than alcoholism, in close relatives of alcohol-dependent patients with primary depression than in patients with secondary depression. Other studies, both in clinical samples and in the general population, did not find different rates of alcohol dependence or affective disorders based on the primary–secondary distinction (Grant and Pickering 1997; Hasegawa et al. 1991). Thus, the studies on genetic vulnerability suggest differences between primary and secondary transmission, but are not conclusive.

Biological mechanisms

There are several plausible mechanisms by which alcohol dependence may cause depressive disorders (Markou et al. 1998), but research is not yet conclusive. It should be noted that there is a biological link via intoxication or heavy use rather than via dependence alone.

Dose–response relationship

Merikangas et al. (1998) found that there is a continuum in the magnitude of co-morbidity as a function of position on the spectrum of substance use (use, problems, dependence). While there are relationships at the level of symptoms in the general population, the relationships are strongest between alcohol dependence and depressive disorders (see above).

Potential alternative explanations

There may be other explanations for the co-occurrence of alcohol dependence and depressive disorders, either from genetic disposition or the environment. For example, Grant and Pickering (1997) suggested that alcoholism and major depression might be alternative manifestations of the same underlying disorder. Nevertheless, there is no explanation for the finding that depressive symptoms increase markedly during bouts of heavy drinking and disappear during periods of abstinence, even if no antidepressant medication is given. This is the strongest indication of a causal effect.

Summary of evidence on causality

Overall, we find sufficient evidence of causality for the influence of alcohol dependence on depressive disorders. The evidence indicates that a clear and consistent association exists between alcohol dependence and depressive disorders and that chance, confounding variables and other bias can be ruled out with reasonable confidence as factors in this association. Consistent with the assessments for other disease and injury categories, most weight was placed on consistency across several studies, strength of the association, reversibility, temporal order and the fact that the effect was at least physiologically plausible.

Estimating AAFs of depressive disorders

Quantitative estimates of the proportion of depressive disorders attributable to alcohol can be derived from the high correlation between alcohol dependence and the proportion of depressive disorders with preceding alcohol-use disorders (see above), using alcohol dependence rates in different subregions of the world (Table 12.18, columns 3 and 4).

The empirical data on proportion of depressive disorders with preceding alcohol-use disorders were regressed on survey results of alcohol dependence for the same subregions without a constant. The omission of the constant was due to the fact that in a situation without any alcohol dependence, the proportion of alcohol-attributable depressive disorders should also be zero. Thus, the regression line must pass through the origin. Since the relationship is quite close, the respective regression coefficients became highly significant even with few data points.

Clearly, the proportions in columns 3 and 4 of Table 12.18 are the upper limit of depressive disorders attributable to alcohol. In order to derive a realistic proportion of alcohol-attributable depressive disorders, we need to subtract the proportion of co-occurrences due to chance. In a situation of chance, the occurrence of alcohol-use disorders in depressed persons should be exactly equal to the occurrence of alcohol-use disorders in non-depressed persons (i.e. the general population). Thus, the prevalence of alcohol-use disorders was first subtracted from the upper limit to derive AAFs. The prevalence of alcohol dependence was taken from *The world health report 2001*, which itself was based on a pooled analysis of survey results. The relationship between alcohol dependence and alcohol abuse (i.e. harmful use in ICD-10) was derived from the US National Comorbidity Survey (Kessler 1998) and was assumed to be constant across subregions. This assumption was necessary as there were fewer data on alcohol abuse than on alcohol dependence, and as the diagnostic systems used vary considerably for this diagnosis.

To control for possible confounding, the effects were halved as has been done elsewhere (e.g. IHD analysis above) as well as for other risk factors (Peto et al. 1992 for smoking; see also chapter 11). The resulting estimates for AAFs of depressive disorders can be found in Table 12.18, columns 5 and 6.

Table 12.18 Prevalence of alcohol dependence by subregion and sex, and AAFs (percentage of depressive disorders) in people aged ≥15 years

Subregion	*Prevalence of alcohol dependence (%)*[a]	*Upper limit for AAF, major depression*	*Upper limit for AAF, other depression*	*AAF, major depression*	*AAF, other depression*
Males					
AFR-D	1.37	5.17	5.31	1.68	1.76
AFR-E	2.89	10.93	11.24	3.56	3.71
AMR-A	8.04	30.37	31.22	9.89	10.31
AMR-B	5.72	21.60	22.20	7.04	7.34
AMR-D	5.13	19.39	19.93	6.32	6.59
EMR-B	0.07	0.25	0.26	0.09	0.09
EMR-D	0.07	0.26	0.26	0.09	0.09
EUR-A	5.61	21.21	21.80	6.91	7.20
EUR-B	1.16	4.39	4.52	1.43	1.49
EUR-C	8.22	31.05	31.91	10.11	10.54
SEAR-B	0.77	2.91	2.99	0.95	0.99
SEAR-D	1.58	5.96	6.13	1.94	2.03
WPR-A	3.12	11.77	12.10	3.84	4.00
WPR-B	1.78	6.73	6.91	2.19	2.29
Females					
AFR-D	0.10	0.37	0.38	0.12	0.12
AFR-E	0.31	1.17	1.20	0.37	0.38
AMR-A	2.14	8.10	8.33	2.52	2.63
AMR-B	1.18	4.46	4.59	1.39	1.45
AMR-D	1.19	4.50	4.63	1.40	1.46
EMR-B	0.00	0.02	0.02	0.01	0.01
EMR-D	0.01	0.02	0.02	0.01	0.01
EUR-A	1.18	4.46	4.58	1.39	1.45
EUR-B	0.23	0.88	0.91	0.28	0.29
EUR-C	1.39	5.24	5.39	1.63	1.70
SEAR-B	0.07	0.26	0.26	0.08	0.09
SEAR-D	0.05	0.20	0.21	0.07	0.07
WPR-A	1.12	4.22	4.34	1.31	1.37
WPR-B	0.05	0.19	0.19	0.06	0.06

[a] From *World health report 2001*, based on survey results (Rehm and Eschmann 2002) and then estimated consistently with DisMod,[24] taking into account case fatality, duration and/or incidence.

These results show that AAFs of depressive disorders vary substantially in different subregions of the world. They reflect differences in rates of heavy alcohol consumption and alcohol dependence. Thus, AAFs are considerably larger for males than for females. They are highest in the

Russian Federation and its surrounding countries (EUR-C) and in North America (AMR-A), and almost nonexistent in Muslim-dominated areas (EMR-B and EMR-D).

Conclusions on alcohol and depression

Based on standard criteria of causality, we conclude that there is sufficient evidence for a causal relation between alcohol-use disorders and depressive disorders. We suspect that careful examination would also reveal a relationship between heavy drinking and depressive disorders, although heavy drinking unfortunately is not usually measured as an endpoint in epidemiological cohort studies.

The status of alcohol abuse as a causal agent in depression is not as clear. There are co-occurrences between alcohol abuse and depressive disorders that are larger than chance (Kessler et al. 1996, 1997), but the relationship is weaker compared to the relationship with alcohol dependence. This may have to do with the less clear conceptual status of alcohol abuse, which is defined in the current version of the *Diagnostic and statistical manual of mental disorders* (DSM) (American Psychiatric Association 1994) nosology to include social and legal responses to the patient's drinking, and which is not a category of disorder in ICD. On the other hand, many studies found only one factor when analysing criteria of alcohol dependence and alcohol abuse, or a division of factors that did not correspond to the division between the diagnoses in DSM. Thus, the relationship between alcohol abuse and depressive disorders should be clarified in future research. It may have relevance, beyond burden of disease research, in helping to clarify the status of alcohol abuse in general.

3.10 Summary of relative risk for chronic diseases, using CRA disease categories

Relative risk estimates are summarized in Table 12.19.

3.11 Acute adverse health consequences

Alcohol use has been associated with increased risk of injury in a wide variety of settings, including road traffic accidents (involving vehicles, bicycles and pedestrians), falls, fires, injuries related to sports and recreational activities, self-inflicted injuries and injuries resulting from interpersonal violence (Cherpitel 1992; Freedland et al. 1993; Hingson and Howland 1987, 1993; Hurst et al. 1994; Martin 1992; Martin and Bachman 1997; U.S. Department of Health and Human Services 1997, 2000). There is also some evidence that the presence of alcohol in the body at the time of injury may be associated with a greater severity of injury and a less positive outcome (Fuller 1995; Li et al. 1997).

Table 12.19 Relative risk for major chronic disease categories by sex and average drinking category

			Males			*Females*		
Disease	*ICD-9 (4-digit)*	*ICD-10 (4-digit)*	*Drinking category I*	*Drinking category II*	*Drinking category III*	*Drinking category I*	*Drinking category II*	*Drinking category III*
Conditions arising during the perinatal period	760–779 except 771.3	P00–P96						
Low birth weight	764–765	P05–P07	1.00	1.40	1.40	1.00	1.40	1.40
Malignant neoplasms	140–208	C00–C97						
Mouth and oropharynx cancers	140–149	C00–C14	1.45	1.85	5.39	1.45	1.85	5.39
Oesophagus cancer	150	C15	1.80	2.38	4.36	1.80	2.38	4.36
Liver cancer	155	C22	1.45	3.03	3.60	1.45	3.03	3.60
Female breast cancer*	174	C50	NA	NA	NA	1.14	1.41	1.59
>45 years of age*			NA	NA	NA	1.15	1.41	1.46
≥45 years of age*			NA	NA	NA	1.14	1.38	1.62
Other neoplasms	210–239	D00–D48	1.10	1.30	1.70	1.10	1.30	1.70
Type II diabetes	250	E10–E14	1.00	0.57	0.73	0.92	0.87	1.13

Neuro-psychiatric conditions	290–319, 324–359	F01–F99, G06–G98						
Unipolar major depression	300.4	F32–F33	AAFs were estimated indirectly based on prevalence of alcohol dependence					
Epilepsy	345	G40–G41	1.23	7.52	6.83	1.34	7.22	7.52
Alcohol-use disorders	291, 303, 305.0	F10	AAF 100%	AAF 100%	AAF 100%	AAF 100%	AAF 100%	AAF 100%
Cardiovascular diseases	390–459	I00–I99						
Hypertensive disease	401–405	I10–I13	1.40 0.82	2.00 0.83	4.10 1.00	1.40 0.82	2.00 0.83	2.00 1.12
Ischaemic heart disease	410–414	I20–I25	AAFs were modelled including patterns of drinking (see text above for details)					
Cerebrovascular disease	430–438	I60–I69						
Ischaemic stroke*	433–435		0.94	1.33	1.65	0.52	0.64	1.06
Haemorrhagic stroke*	430–432		1.27	2.19	2.38	0.59	0.65	7.98
Digestive diseases	530–579	K20–K92						
Cirrhosis of the liver	571	K70, K74	1.30	9.50	13.00	1.30	9.50	13.00

NA Not applicable.

Sources: Gutjahr et al. 2001; Ridolfo and Stevenson 2001; if indicated by * the category III estimates for IHD were based on Corrao et al. 2000.

Unintentional injuries

Alcohol consumption produces effects that are often perceived as positive, as evidenced by the widespread popularity of drinking. But it also leads to actions that result in unintentional injury and death. This section highlights research findings on causality of alcohol involvement and findings relevant to establishing dose–response relationships and drinking patterns. It focuses on traffic injuries, as most of the research has been conducted in this area, and traffic accidents are the most important component of unintentional injuries (Rehm et al. 2003b).

Studies relating average volume of drinking to risk of injury have found the risk of injury to be positively related to increasing average intake levels of alcohol, with the risk increasing at relatively low volumes of intake (Cherpitel et al. 1995). Two studies of injury among older adults reported a U-shaped relationship between alcohol use and occupational injury (Zwerling et al. 1996) and traumatic deaths (Ross et al. 1990). However, abstinence could be related to existing health problems or cognitive deficits that are, in turn, related to accident risk (Zwerling et al. 1996). Hence the higher risk among abstainers is likely to be purely spurious.

Several patterns of drinking have been related to risk of injury. Frequent heavy drinking and frequent subjective drunkenness are both associated with injury, particularly injury resulting from violence (Cherpitel 1996a). Frequency of heavy drinking has also been associated with a greater likelihood of death due to injury, relative to other causes (Li et al. 1994). One important line of research in this area has empirically defined a parameter of usual drinking pattern that is most closely associated with the risk of injury and drunk driving behaviour, after adjusting for other drinking pattern variables and characteristics of the drinker (Gruenewald and Nephew 1994; Gruenewald et al. 1996a, 1996b; Treno and Holder 1997; Treno et al. 1997). The greatest risk was found in individuals who consume relatively large amounts on some occasions, and whose highest amounts are markedly greater than their average amount per occasion.

Several retrospective studies have compared BAC in individuals who have experienced a collision or trauma, compared with selected individuals not involved in trauma, using a case–control design (Cherpitel 1992; Freedland et al. 1993; Fuller 1995; Hurst et al. 1994; Stoduto et al. 1993; U.S. Department of Health and Human Services 1997). One of the most influential case–control series was the Grand Rapids Study of 5985 collisions (Borkenstein et al. 1964; Hurst et al. 1994). Statistically adequate re-analysis of the Grand Rapids Study indicates that all levels of BAC are associated with an increased risk of crashes, relative to a BAC of zero, with an accelerating slope in which the risk of injury increases markedly with high BACs (Hurst et al. 1994).

There are clear reasons why alcohol is related to injury. Moderate doses of alcohol have been demonstrated in controlled experimental studies to have cognitive and psychomotor effects that are relevant to the risk of injury, such as reaction time, cognitive processing, coordination and vigilance (Eckardt et al. 1998; Kruger et al. 1993; Moskowitz and Robinson 1988; U.S. Department of Health and Human Services 1997). The comprehensive recent review by Eckardt et al. (1998) concluded that the threshold dose for negative effects on psychomotor tasks is generally found at around 40–50 mg% (equivalent to 0.04–0.05%). The authors also stated, "injury can occur as a result of alcohol's disruption of psychomotor function in individuals at BACs of approximately 10 mM", which is equal to a BAC of little less than 50 mg%.

Dose–response curves observed in experimental data are not always monotonic. For example, a recent experimental study (Lloyd and Rogers 1997) assessed the effects of low doses of alcohol given with a meal, and found that 8 g of absolute alcohol (about 0.25 litre of beer) resulted in improved performance of complex cognitive tasks relative to no alcohol, but that 24 g of absolute alcohol produced impaired performance. Such J-shaped or U-shaped effects of low ethanol doses on task-specific performance are explicable pharmacologically (Eckardt et al. 1998). The Grand Rapids Study also found that dose–response curves varied somewhat between novices and frequent, experienced drinkers.

In summary, the evidence indicates that the amount consumed per occasion, and more specifically the blood alcohol content, is the critical feature in determining risk of injury. Blood alcohol concentrations as low as 40–50 mg% may cause psychomotor impairment, leading to increased risk of injury in circumstances such as driving or operating machinery.

Thus, despite methodological problems, there is evidence of causality for the most researched injury category (traffic accidents). Table 12.20 gives the AAFs for different kinds of injuries in four recent reviews. The reviews based their estimates on meta-analyses or other summaries of the relations found in published studies. It should be recognized that, while there are many such studies, they are mostly from a relatively small range of countries. Most of the AAFs were directly derived, for example from police statistics, although there are case–control studies as well (McLeod et al. 1999).

Causality, at least for traffic accidents, can be established since:

- alcohol is clearly associated with the outcome;
- there is a dose–response relationship: the higher the BAC, the higher the chance of injury;
- there is a biochemical explanation for the relationship; and
- with suitable interventions to reduce alcohol consumption, the outcome is reduced as well. Thus, in a meta-analysis, Shults et al.

Table 12.20 AAFs of acute alcohol-related health effects in the adult general population

		Review							
		Stinson et al. 1993; USA		*English et al. 1995; Australia*		*Single et al. 1996; Canada*		*Ridolfo and Stevenson 2001; Australia*	
Injury	*ICD-9 code*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*
Motor vehicle traffic accidents	E810–E819	0.42	0.42	0.37	0.18	0.43	0.43	0.33 (d);[a] 024 (h);[a] pedestrians 0.40 (d); 0.37 (h)	0.11 (d) and (h); pedestrians 0.17 (d); 0.06 (h)
Motor vehicle nontraffic accidents	E820–E825	0.42	0.42	0.37	0.18	0.43	0.43		
Bicycle accident injuries	E826	0.20	0.20	0.37	0.18	0.20	0.20		
Other road vehicle accident injuries	E829	0.20	0.20	0.37	0.18	0.20	0.2		
Water transport accident injuries	E830–E839	0.20	0.20	—	—	0.20	0.20	—	—
Air-space transport accident injuries	E840–E845	0.16	0.16	—	—	0.16	0.16	—	—
Accidental ethanol and methanol poisoning	E860.0–E860.2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Accidental fall injuries	E880–E888	0.35	0.35	0.34	0.34	0.20–0.34[b]	0.13–0.34[b]	0.22 for age <65; 0.12 for age ≥65	0.14 for age <65; 0.04 for age ≥65

Arson injuries	E890–E899	0.45	0.45	0.44	0.44	0.38	0.38	0.44	0.44
Accidental excessive cold	E901	0.25	0.25	—	—	0.25	0.25	—	—
Accidental drowning	E910	0.38	0.38	0.34	0.34	0.31–0.50[b]	0.31–0.50[b]	0.34	0.34
Accidental aspiration	E911	0.25	0.25	1.00	1.0	0.25	0.25	1.00	1.00
Striking against/struck by objects	E917	0.25	0.25	—	—	0.07	0.07	—	—
Caught in/between objects	E918	0.25	0.25	—	—	0.07	0.07	—	—
Occupational and machine injuries	E919–E920	0.25	0.25	0.07	0.07	0.07	0.07	0.07	0.07
Accidental firearm missile injuries	E922	0.25	0.25	—	—	0.25	0.25	—	—
Suicide, self-inflicted injuries	E950–E959	0.28	0.28	0.12	0.08	0.23–0.31[b]	0.11–0.19[b]	0.32	0.29
Victim fight, brawl, rape	E960	0.46	0.46	0.47	0.47	0.27	0.27	0.47	0.47
Victim assault, firearms	E965	0.46	0.46	0.47	0.47	0.27	0.27	0.47	0.47
Victim assault, cutting instrument	E966	0.46	0.46	0.47	0.47	0.27	0.27	0.47	0.47
Victim child battering	E967	0.46	0.46	0.16	0.16	0.16	0.16	0.16	0.16
Victim assault, other	E968	0.46	0.46	0.47	0.47	0.27	0.27	0.47	0.47
Late effects of injuries by another	E969	0.46	0.46	0.47	0.47	0.27	0.27	0.47	0.47

— No data.

[a] (d), deaths; (h), hospitalizations.

[b] Ranges refer to age-specific AAFs; minimum (>0) and maximum estimates are shown.

(2001) found random breath-testing programmes or selective breath-testing checkpoints to be effective in reducing mortality from traffic accidents by 18% and 20%, respectively.

Intentional injuries

Alcohol is strongly associated with violent crime (Graham and West 2001), although this association varies considerably across settings (Murdoch et al 1990; Room and Rossow 2001). Studies on violence have repeatedly shown that alcohol consumption precedes violent events, and that the amount of drinking is related to the severity of the subsequent violence. In addition, the experimental literature suggests that alcohol plays a causally contributing role[25] in aggression. Meta-analyses of experimental studies suggest a small to moderate effect size of about 0.22 (Bushman 1997) in the overall relationship between alcohol consumption and aggression. Some effort has been made to separate pharmacological effects from expectations,[26] but the general conclusion is that expectations form part of the "psycho-pharmacological" effects of alcohol (Bushman 1997; Graham et al. 1998), and neither can nor should be separated in attempting to understand the effects of alcohol. Alcohol bathes the brain in chemicals and it is likely that a number of different effects of alcohol contribute to the increased likelihood of aggressive behaviour. First, alcohol seems to have an effect on the serotonin (5HT) and GABA brain receptors, similar to that produced by some benzodiazepines (Pihl et al. 1993). The subjective experience of this effect may be a reduced level of fear and anxiety about social, physical or legal consequences of one's actions. This reduced fear or anxiety may result in increased risk-taking by some drinkers. This particular causal pathway has received support from animal research linking alcohol, GABA receptors and aggression (Miczek et al. 1993) and from experimental and observational research showing higher risk taking associated with alcohol intoxication (Graham et al. 2000; Pihl and Peterson 1993). Alcohol also affects cognitive functioning (Peterson et al. 1990), leading to impaired problem solving in conflict situations (Sayette et al. 1993) and overly emotional responses or emotional lability (Pihl et al. 1993). Other behavioural and attitudinal effects of alcohol related to aggression have been identified, although at this point not necessarily linked to particular pharmacological effects on the brain. These include a narrow and tenacious focus on the present (Graham et al. 2000; Washburne 1956), also described as "alcohol myopia" (Steele and Josephs 1990) and increased concerns with demonstrating personal power, at least for men (Graham et al. 2000; McClelland et al. 1972; Tomsen 1997).

Alcohol-related violence involves more complex issues of social interaction than would be relevant to drink–driving and other alcohol-related accidental injuries. In particular, the effects of alcohol are moderated by both the environment and the characteristics of the drinker (Chermack and Giancola 1997; Lipsey et al. 1997; Rossow et al. 2001; U.S. Depart-

ment of Health and Human Services 2000). For example, meta-analysis of experimental research on alcohol and aggression found that the effects of environmental manipulation to increase aggression were stronger for intoxicated than for sober participants. In another meta-analysis, Ito et al. (1996) found that the effects of alcohol were greater in situations characterized by greater anxiety, inhibition conflict and frustration, while differences between sober and intoxicated persons were smaller in situations involving high provocation or self-focused attention. Further, given sufficient disincentives for aggression the effects of alcohol on aggression can be reduced or even eliminated altogether (Hoaken et al. 1998; Jeavons and Taylor 1985).

As with alcohol-related accidents, some proportion of violence that occurs after people have been drinking might have occurred anyway, without the involvement of alcohol. Alcohol-related violence involves an interaction of the effects of alcohol on one or more people, the environment and the personality of the drinker (Graham et al. 1998). However, the environment for alcohol-related aggression is not independent of drinking.[27] For example, in environments devoted to drinking (e.g. bars, pubs), it does not make sense to try to determine the proportion of violence that would have occurred even if the person had not been drinking, because this particular environment does not exist without drinking. Although a few incidents that occur in bars involve interpersonal conflict between friends or couples that might have occurred in another setting, almost all incidents of aggression that occur in bars are unplanned, emerge from the social interaction in the bar (Graham and Wells 2001) and often involve strangers. Therefore, it seems reasonable to assume that close to 100% of incidents of violence occurring in bars and other environments where drinking is the main activity should be considered attributable to alcohol, either directly through the pharmacological effects of alcohol or indirectly through the social norms related to drinking.

Estimating the proportion of violence in other settings that should be attributed to alcohol is more problematic. There are pharmacological effects of alcohol, as described above, that make aggressive interactions more likely. This is more likely to be the case if all those involved have been drinking, owing to the interaction of the effects of alcohol on each person (Leonard 1984). In addition, alcohol is known to increase the likelihood of the escalation of conflict (Martin and Bachman 1997; Sharps et al. 2001). On the other hand, marital violence, for example, often occurs when neither party has been drinking. Therefore, the assessment of the exact proportion of alcohol-related violent injuries and death that should be attributable to alcohol is often difficult, and needs to be assessed from different sources, such as time series analyses, natural experiments, case–control studies, emergency-room studies, general population surveys and experimental designs (Pernanen 2001).

Deriving the AAFs for different subregions for injuries (both intentional and unintentional)

Injuries are also influenced by average volume of alcohol consumption and by patterns of drinking, especially by acute levels of BAC or intoxication. To model this relationship, a multilevel analysis identical to the one on IHD was used (for statistical derivation and specification of the model see section 3.2; for formulas see notes below Table 12.13). Table 12.21 gives an overview of the underlying data. Table 12.22 gives the main results of the analysis.

The effect of alcohol on injury at pattern 1 is 0.013 for males and 0.010 for females. The effect for pattern 2 populations is the same, as the coefficients did not significantly differ. For pattern 3, the effect is 0.056 for males and 0.014 for females. For pattern 4, the respective effects are 0.196 for males and 0.027 for females.

The results can be summarized as follows.

- Average volume of drinking has a significant detrimental effect on risk of injury even at consumption pattern 1, independent of sex. The impact is larger in males.
- The impact of per capita consumption on injury is different between different countries, as shown by the significant variance component.
- No significant difference in the effect of drinking on injury risk was found between patterns 1 and 2.
- Pattern 3 has a significantly higher injury risk for both sexes, but the impact is much stronger in males (about 10 times).
- Pattern 4 has the highest injury risk for both sexes, and again the impact is much stronger for males.

To estimate AAFs for injuries we used the Australian AAFs, since these reflected the most up-to-date information (Ridolfo and Stevenson 2001). These were converted into odds ratios,[28] which were applied to estimated exposure prevalence for all subregions, as with other diseases, multiplicatively adjusted by pattern weights from Table 12.22 and average volume of alcohol consumption. This procedure must be regarded as a crude approximation, yet the best attainable at present. Given the potential variation in the role of alcohol in casualties across settings, there is an urgent need for empirical studies of the relationship in different world regions, using a variety of methods. The WHO Collaborative Study on Alcohol and Injuries (www.who.int/substance_abuse/topic_alcohol_injuries.htm) constitutes a step forward on this.

Appendix B gives an overview of the derived AAFs for mortality for major categories of accidental and intentional injuries, as defined for the CRA project.

Table 12.21 Characteristics of data set to calculate the relationship between per capita consumption, patterns of drinking and injury mortality

Country	*Injury mortality, males per 1000*	*Injury mortality, females per 1000*	*Average per capita alcohol consumption*	*Pattern of drinking*	*Year of first data*	*Year of last data*	*Number of years*
Albania	0.74	0.21	2.20	3	1992	1998	7
Argentina	0.87	0.28	27.48	2	1966	1996	25
Armenia	0.37	0.10	2.53	2	1992	1998	7
Australia	0.78	0.31	11.19	2	1964	1997	34
Austria	1.07	0.39	14.16	1	1962	1999	38
Azerbaijan	0.68	0.14	2.10	3	1990	1999	9
Bahamas	0.97	0.30	14.30	2	1969	1995	13
Bahrain	0.33	0.09	5.33	2	1985	1988	3
Barbados	0.63	0.17	7.88	2	1964	1995	31
Belarus	1.55	0.35	9.68	4	1989	1998	9
Belgium	0.87	0.41	12.35	1	1964	1994	31
Belize	0.59	0.17	6.01	4	1964	1995	28
Bulgaria	0.89	0.26	11.97	2	1982	1998	17
Canada	0.81	0.31	9.74	2	1964	1997	34
Chile	1.44	0.33	11.58	3	1964	1994	31
Colombia	1.72	0.32	5.49	3	1967	1994	19
Costa Rica	0.94	0.25	4.48	4	1964	1995	32
Croatia	0.93	0.31	13.24	3	1993	1998	6
Czech Republic	0.92	0.40	15.42	2	1986	1999	14
Denmark	0.77	0.40	10.91	2	1964	1996	33
Dominican Republic	0.63	0.20	2.91	2	1965	1985	21
Ecuador	1.23	0.33	2.30	3	1964	1995	31
El Salvador	1.99	0.36	1.95	4	1964	1993	19
Estonia	2.50	0.58	13.43	3	1992	1999	8
Fiji	0.50	0.26	2.98	3	1978	1978	1
Finland	1.21	0.35	7.42	3	1964	1996	33
France	1.02	0.43	23.15	1	1964	1997	34
Germany	0.54	0.21	13.63	1	1993	1998	6
Greece	0.58	0.23	9.69	2	1964	1998	35
Guatemala	1.49	0.26	2.33	4	1964	1984	14
Guyana	0.90	0.24	9.50	3	1979	1994	4
Honduras	0.62	0.10	2.62	4	1976	1979	4
Hungary	1.39	0.54	15.85	3	1977	1999	23
Iceland	0.85	0.29	5.42	3	1964	1996	33
Ireland	0.60	0.24	10.86	3	1964	1996	33
Israel	0.56	0.29	3.04	2	1975	1996	22
Italy	0.64	0.24	18.48	1	1964	1996	33
Jamaica	0.41	0.10	3.12	2	1964	1985	7
Japan	0.68	0.27	5.78	1	1964	1997	34

continued

Table 12.21 Characteristics of data set to calculate the relationship between per capita consumption, patterns of drinking and injury mortality (*continued*)

Country	Injury mortality, males per 1000	Injury mortality, females per 1000	Average per capita alcohol consumption	Pattern of drinking	Year of first data	Year of last data	Number of years
Kazakhstan	1.65	0.44	7.24	4	1989	1998	10
Kyrgyzstan	0.91	0.25	1.88	3	1995	1999	5
Latvia	2.09	0.52	8.53	3	1989	1998	10
Lithuania	2.26	0.51	5.76	3	1989	1998	5
Luxembourg	0.97	0.37	17.37	1	1967	1997	31
Malta	0.35	0.14	5.27	1	1965	1998	33
Mauritius	0.80	0.26	3.30	3	1964	1998	35
Mexico	1.60	0.33	3.94	4	1962	1995	34
Netherlands	0.51	0.27	9.39	1	1964	1997	34
New Zealand	0.81	0.35	11.36	2	1964	1998	35
Nicaragua	1.25	0.28	3.29	4	1964	1994	17
Norway	0.69	0.27	5.11	3	1964	1996	33
Peru	0.67	0.21	6.13	3	1966	1989	16
Philippines	0.67	0.16	2.59	3	1964	1993	18
Portugal	0.98	0.28	18.85	1	1964	1998	35
Qatar	0.47	0.17	.84	2	1995	1995	1
Republic of Korea	1.09	0.38	8.90	3	1985	1997	13
Romania	1.11	0.33	10.78	3	1989	1998	10
Russian Federation	2.05	0.50	8.88	4	1991	1998	8
Singapore	0.64	0.23	2.30	2	1964	1998	35
Slovakia	1.04	0.31	12.54	3	1992	1995	4
Slovenia	1.15	0.38	14.80	2	1994	1998	5
Spain	0.60	0.19	17.20	1	1962	1997	36
Sri Lanka	1.01	0.40	.27	3	1964	1986	13
Suriname	1.05	0.37	6.43	3	1964	1992	21
Sweden	0.72	0.30	7.57	3	1964	1996	33
Switzerland	0.93	0.38	14.99	1	1964	1994	31
Tajikistan	0.58	0.16	2.52	3	1992	1992	1
Thailand	0.92	0.26	3.58	3	1964	1994	25
The former Yugoslav Republic of Macedonia	0.47	0.15	5.76	3	1994	1997	4
Trinidad and Tobago	0.95	0.27	4.79	2	1962	1994	29
Turkmenistan	0.43	0.18	2.13	3	1995	1995	1
Ukraine	1.41	0.32	4.64	3	1990	1999	10
United Kingdom	0.47	0.23	9.49	2	1964	1998	35
United States	0.92	0.32	9.46	2	1964	1997	34
Uruguay	0.84	0.28	8.08	3	1966	1990	24
Uzbekistan	0.46	0.15	1.07	3	1996	1998	3
Venezuela	1.29	0.33	8.31	3	1969	1994	24

Table 12.22 Effects of per capita consumption and patterns of drinking on risk of injury mortality

	Coefficient	*SE*	*t-value*	*df*	*P*	*Variance component*	*df*	χ^2	*P*
Males									
Average volume = per capita consumption									
Not adjusted	0.045	0.013	3.46	79	0.001	0.0106	72	584.1	0.000
Adjusted by GNP, year	0.047	0.012	3.90	79	0.000	0.0097	72	620.6	0.000
After inclusion of pattern dummy variables on second level	0.013	0.006	2.05	76	0.040	0.0080	69	532.1	0.000
Patterns of drinking[a]									
Pattern 2	–0.009	0.011	<1	76	0.391				
Pattern 3	0.043	0.014	3.13	76	0.002				
Pattern 4	0.173	0.062	2.77	76	0.006				
Females									
Average volume = per capita consumption									
Not adjusted	0.0097	0.0023	4.19	79	0.000	0.00028	72	398.7	0.000
Adjusted by GNP, year	0.0121	0.0021	5.91	79	0.000	0.00021	72	496.2	0.000
After inclusion of pattern dummy variables on second level	0.0096	0.0021	4.46	76	0.000	0.00020	69	412.8	0.000
Patterns of drinking[a]									
Pattern 2	–0.0024	0.0031	<1	76	0.440				
Pattern 3	0.0041	0.0030	1.40	76	0.163				
Pattern 4	0.0171	0.0077	2.24	76	0.025				

[a] Patterns 2, 3 and 4 are compared to pattern 1.

Another point concerns the relation of alcohol with type of outcome—morbidity vs mortality. In general, more severe outcomes are more related to alcohol than less severe outcomes (Rehm et al. 2003b; Single et al. 1999b). Consequently, the AAFs for mortality should be higher than the AAFs for morbidity. Unfortunately, most research to determine AAFs for injury did not explicitly separate mortality and morbidity (see, e.g. Table 12.20). Ridolfo and Stevenson (2001) explicitly separated the AAFs for motor vehicle accidents, and for males found 0.328 for deaths and 0.247 for hospitalizations; they lacked sufficient data for females. Based on their work and that of Cherpitel (1994, 1996b), we determined the ratio of AAF for morbidity as two thirds of the AAF for mortality. The ratio for other kinds of injury is lower (Cherpitel 1994, 1996b). To

be conservative, these ratios were set at 0.44 (or two thirds of the ratio for motor vehicle accidents) (Cherpitel 1994, 1996b).

3.12 Quantitative and qualitative sources of uncertainty

Since most of the chronic disease relationships with alcohol depend on biochemical processes linked to average volume of consumption over time, their hazards have been fairly stable across countries (Corrao et al. 2000). On the other hand, injuries are context-dependent to a much larger degree. A good example is the difference between liver cancer and traffic accidents. Based on biochemical evidence, there are reasons to believe that the relationship between average volume of alcohol consumption and liver cancer is relatively stable across different countries and societies, even though epidemiological work tends to be concentrated in established market economies. The most notable exception for chronic disease has been IHD, where patterns of drinking play a decisive role in determining the impact of average volume of drinking. On the other hand, the number of accidents (and alcohol-related traffic accidents in particular) depends on many background variables, as illustrated above. Thus, the risk relations between injuries and alcohol are much less stable and their transferability is more questionable. Where it has to be done, it should carry wider CIs.

Based on the above considerations, the following pertain.

- For chronic diseases, estimates of relative risk are usually based on meta-analyses of more than 20 studies with relatively small CIs. The uncertainty introduced by cross-population transfer of data is not that large, as the relationships depend on biochemical mechanisms. It is therefore suggested that ± 15% of the point estimate be used as the standard in an uncertainty analysis. This applies to all chronic disease categories where AAFs are directly derived from prevalence and relative risk.
- In all cases where AAFs are derived in other ways (e.g. injury), these fractions are more influenced by contextual differences from one region to another and should thus be modelled with more uncertainty. We suggest ± 30% of the point estimate to account for additional assumptions.
- IHD is the notable exception. In this case, estimates differ considerably (see the heterogeneity in the meta-analysis of Corrao et al. 2000), with respect not only to the magnitude but also to the direction of the relation. To account for this uncertainty and the difference of estimates in different models, we suggest the values set out in Table 12.23.

Table 12.23 is based on the following assumptions.

- For AMR-A, EUR-A and WPR-A, the results from the individual-level meta-analysis (Corrao et al. 2000) were taken as best estimates. For

Table 12.23 AAF estimates and uncertainty intervals for IHD by subregion

	Best estimates	
Subregion	*Males*	*Females*
AFR-D	0.02 (–0.05, 0.05)	0.00 (–0.03, 0.03)
AFR-E	0.07 (0.00, 0.09)	0.00 (–0.03, 0.03)
AMR-A[a]	–0.13 (–0.17, 0.00)	–0.08 (–0.12, 0.00)
AMR-B	0.16 (0.00, 0.21)	0.02 (–0.05, 0.05)
AMR-D	0.08 (0.00, 0.12)	0.03 (–0.05, 0.05)
EMR-B	0.00 (–0.03, 0.03)	0.00 (–0.03, 0.03)
EMR-D	0.01 (–0.03, 0.03)	0.00 (0.03, 0.03)
EUR-A[a]	–0.16 (–0.21, 0.10)	–0.13 (–0.17, 0.04)
EUR-B	0.11 (–0.13, 0.15)	0.00 (–0.08, 0.05)
EUR-C	0.15 (0.10, 0.20)	0.03 (0.02, 0.04)
SEAR-B	0.01 (–0.03, 0.03)	0.00 (–0.03, 0.03)
SEAR-D	0.04 (–0.03, 0.03)	0.00 (–0.03, 0.03)
WPR-A[a]	–0.17 (–0.23, –0.10)	–0.13 (–0.17, –0.07)
WPR-B	0.01 (–0.05, 0.05)	0.00 (–0.03, –0.03)

[a] Best estimates derived from relative risk and not from multilevel estimates.

these subregions the results from the aggregate multilevel analysis were taken as upper limits, and 30% lower than the best estimate as lower limits.

- For EUR-B, the aggregate multilevel results were taken as best estimates, and the results from the individual-level analysis was taken as lower limit, and 30% higher than the best estimate as upper limit.
- For all other subregions, the aggregate multilevel analysis results were taken as best estimates and, based on pattern and volume of the subregion, uncertainty intervals were chosen as follows:
  - ±0.03 in the case of low-volume drinking (average <3 g/day) and average pattern values lower than 3.5;
  - ±0.05 in the case of females for volumes >3 g/day and average pattern values lower than 3.5 (this restriction for females was intended to account for the higher uncertainty of pattern values for females); and
  - for all other estimates zero was taken as the lower bound, and the best estimate plus 30% as the upper bound (except for EUR-C, the only subregion with an average pattern value greater than 3.5).

A number of points need to be emphasized when interpreting these results. The underlying research for chronic disease is quite heterogeneous with respect to quality. In particular, measurement of alcohol provides limited information on patterns of drinking and for characteristics of abstainers. Most studies have just one time measurement of exposure. Often cohorts were selected with respect to minimizing loss to follow-up, and thus samples with more regular, low-to-moderate drinking styles were used. This constitutes a problem for estimating the effects of patterns of drinking, as well as for estimating the effects of continuous heavy drinking.

There is also a problem of measuring exposure with respect to acute consequences, although slightly different because often the BAC is given as the only indicator. Such a measure does not allow one to differentiate between the effects of pattern of drinking and average volume of alcohol consumption, as a heavy drinking occasion may be the exception or the norm. But for the population level, we need both types of information, as numbers of injuries will depend on both (see above). In addition, the BAC alone does not allow one to determine if alcohol was a contributing causal factor or not, only in combination with other information on control conditions, i.e. series of BACs in accident and non-accident conditions (Borkenstein et al. 1964). Unfortunately, such control conditions are lacking in most research (Gmel and Rehm 2003). Thus, with the exception of traffic accidents, the overall quality of the underlying research for most alcohol-related acute outcomes is of poor quality and derived AAFs may be subject to considerable error. This is reflected in the wide uncertainty margins suggested above.

3.13 Estimates of risk reversibility

Part of the risk from alcohol is immediately reversible: all acute risks can be completely reversed if alcohol is removed. Chronic diseases often depend on lifetime exposure, and thus risk is often reduced but not completely eliminated by removal of alcohol.

On the other hand, there are indications that a reduction of alcohol consumption in populations is associated with a fairly rapid decrease in chronic diseases such as liver cirrhosis. For example, time series analyses showed that decreases in per capita consumption were associated with considerable concurrent reductions in liver cirrhosis (e.g. Ramstedt 2001; Skog 1980; and especially Cook and Tauchen 1982).

Another example of a chronic condition with rapid, sometimes almost immediate remission is depression. In fact, most studies come to the conclusion that many depressive syndromes markedly improve within days to weeks of abstinence (Brown and Schuckit 1988; Dackis et al. 1986; Davidson 1995; Gibson and Becker 1973, Penick et al. 1988; Pettinati et al. 1982; Willenbring 1986).

It is not clear what effect alcohol removal would have on alcohol use disorders. Clearly, some criteria of both alcohol dependence and harmful

use of alcohol would no longer apply (e.g. continued use despite harmful consequences).

4. Discussion of estimates of alcohol-attributable burden

4.1 Mortality

Alcohol-related burden of disease is considerable: 3.2% of global mortality and 4.0% of global burden of disease as measured in DALYs. In terms of alcohol-related mortality, almost half of the global burden (46%) is related in acute causes, i.e. unintentional and intentional injuries (see Table 12.24; details in Appendix C). Within this mortality burden, for acute causes, unintentional injuries are by far the most important. The next important category is malignant neoplasms with 20% of the overall alcohol-related mortality burden, followed by cardiovascular diseases (15% of all alcohol-attributable deaths) and other noncommunicable diseases, a category almost entirely made up of liver cirrhosis (13%). Cardiovascular deaths are a special case in that different patterns of drinking lead to beneficial and detrimental outcomes. Thus, the net result of 15% does not give a clear picture of the underlying structure. Going beyond the net result, alcohol was estimated to cause a total of almost 600 000 cardiovascular deaths in the year 2000, exceeding even the alcohol-related burden of unintentional injuries. This figure was partly "offset" by the beneficial effects of alcohol on IHD and stroke. More males than females die of the effects of alcohol, with a ratio of about 10:1.

Table 12.24 Global deaths (000s) attributable to alcohol by major disease and injury categories, 2000

Disease or injury	*Males*	*Females*	*Total*	*Percentage of all alcohol-attributable deaths*
Conditions arising during the perinatal period	2	1	3	0
Malignant neoplasms	269	86	355	20
Neuro-psychiatric conditions	91	19	111	6
Cardiovascular diseases	392	−124	268	15
Other noncommunicable diseases (type II diabetes, liver cirrhosis)	193	49	242	13
Unintentional injuries	484	92	577	32
Intentional injuries	206	42	248	14
Alcohol-related mortality (all causes)	1638	166	1804	100
All deaths	29232	26629	55861	In comparison, estimated
Percentage of all deaths that can be attributable to alcohol	5.6	0.6	3.2	total for 1990: 1.5

The overall relationship between average volume of alcohol consumption and all-cause mortality is thus J-shaped in established market economies for age groups under 45 years, where benefits of light to moderate consumption on IHD apply (Holman et al. 1996; Rehm et al. 2001c). In countries with a predominant pattern of irregular heavy drinking, no J-shape can be expected and the shape between alcohol and all-cause mortality is expected to increase monotonically.

The estimated percentage of alcohol-attributable mortality (3.2%) is more than double that estimated in the 1990 GBD study (3.2% vs 1.5%). There are several reasons for this increase. First, alcohol consumption has increased overall, especially in the very populous SEAR-B, SEAR-D and WPR-B subregions, including China and India. In addition, in these subregions we do not expect benefits of drinking, unless the current patterns of drinking change to the positive. Second, the relative impact of injuries and chronic disease on overall mortality, both of which are related to alcohol, has increased over the past 10 years. Third, the methodologies are not comparable between the two estimates. The 2000 estimate differs in the following three major respects.

- It is much more disaggregated, with respect both to burden categories and to regional data. Thus, the present work has included adult per capita data for almost all countries, and much more survey-related data than available for the 1990 estimates.
- The present exercise explicitly includes quantifiable patterns of drinking for both IHD and injuries, whereas the 1990 estimates were almost entirely based on volume of consumption. This difference is most striking with regard to IHD, where the 1990 study considered only beneficial effects. The current exercise estimates both beneficial and detrimental effects, depending on patterns of drinking.
- The meta-analyses on average volume of consumption and different disease outcomes have become much more refined in terms of methodology (compare, e.g. Corrao et al. 1999, 2000 with the methodology of English et al. 1995).

Finally, the estimates in this work are restricted to GBD disease categories. Several diseases related to alcohol could not be accounted for, most notably cardiac arrhythmias and heart failure. In the GBD disease categories, cardiac arrhythmias and heart failure would be part of "other cardiac conditions". We had neither epidemiological studies on the hazards for various diseases in this broad category nor any data on the relative proportion of cardiac arrhythmias and heart failure among other cardiac conditions by subregion and sex, in order to separate these diseases. In addition, oesophageal varices, acute and chronic pancreatitis and several conditions occurring during the perinatal period could not be included for similar reasons. However, their alcohol-attributable mor-

tality burden would be likely to be minor compared to the "other cardiac conditions" mentioned above.

4.2 DALYs

Alcohol-attributable DALYs are summarized in Table 12.25. See Appendix D for details by subregion.

The biggest shift in the relative impact of disease categories compared to the pattern for alcohol-caused mortality is seen for neuropsychiatric diseases. Neuropsychiatric diseases are often disabling, but rarely fatal, and this is reflected in the markedly higher proportion of overall disease burden due to alcohol (38%) in this category compared to alcohol-attributable mortality (6%). Males have far more (>5-fold) alcohol-related disease burden than females. The mortality and burden of disease figures presented here are net figures, where the alcohol-related beneficial effects on disease have been subtracted from its harmful effects. Therefore, the detrimental effects of alcohol on mortality, and disease burden in general, far outweigh the beneficial effects.

What are the most striking differences between subregions? Clearly alcohol-related burden is most detrimental in the developed world. Here 9.2% of the entire disease burden is attributable to alcohol, only exceeded by the burden attributable to tobacco and blood pressure (see Table 12.26 and WHO 2002). Here also, the ratio of males to females is lowest. However, as Table 12.26 indicates, alcohol also places a toll on health in the developed world, with relatively low mortality

Table 12.25 Global burden of disease in 2000 attributable to alcohol according to major disease categories (DALYs in 000s)

Disease or injury	*Males*	*Females*	*Total*	*Percentage of all alcohol-attributable DALYs*
Conditions arising during the perinatal period	68	55	123	0
Malignant neoplasm	3180	1021	4201	7
Neuro-psychiatric conditions	18090	3814	21904	38
Cardiovascular diseases	4411	–428	3983	7
Other non-communicable diseases (type II diabetes, liver cirrhosis)	3695	860	4555	8
Unintentional injuries	14008	2487	16495	28
Intentional injuries	5945	1117	7062	12
Alcohol-related disease burden all causes (DALYs)	49397	8926	58323	100
All DALYs	761562	693911	1455473	In comparison, estimated total for 1990: 3.5
Percentage of all DALYs that can be attributable to alcohol	6.5	1.3	4.0	

Table 12.26 Burden of disease in 2000 attributable to tobacco, alcohol and drugs, by development status and sex

	High-mortality developing subregions (AFR-D, AFR-E, AMR-D, EMR-D, SEAR-D)			*Low-mortality developing subregions (AMR-B, EMR-B, SEAR-B, WPR-B)*			*Developed subregions (AMR-A, EUR-A, EUR-B, EUR-C, WPR-A)*		
	Males	*Females*	*Total*	*Males*	*Females*	*Total*	*Males*	*Females*	*Total*
Total DALYs (000s)	420711	412052	832763	223181	185316	408497	117670	96543	214213
Smoking and oral tobacco	3.4%	0.6%	2.0%	6.2%	1.3%	4.0%	17.1%	6.2%	12.2%
Alcohol	2.6%	0.5%	1.6%	9.8%	2.0%	6.2%	14.0%	3.3%	9.2%
Illicit drugs	0.8%	0.2%	0.5%	1.2%	0.4%	0.8%	2.4%	1.2%	1.8%

patterns. Here the disease burden attributable to alcohol is the highest of all 26 risk factors examined in the CRA of the GBD study in 2000 (Ezzati et al. 2002). In high-mortality developing subregions, in Africa and parts of south-east Asia, alcohol is not yet one of the major risk factors. Here, the most important risk factors are underweight, unsafe sex, unsafe water, sanitation and hygiene, and other environmental factors. However, if past developments can help predict the future, we can expect that the alcohol-attributable burden will increase in these subregions along with economic development (see also section 5).

4.3 Conclusions

Alcohol causes a considerable burden of disease, in terms both of mortality and disability. While the total elimination of alcohol is not realistic, there are evidence-based policy measures that could substantially reduce the burden of alcohol. The recent review by Ludbrook et al. (2001) on measures to reduce alcohol misuse assessed the quality of evidence for four types of intervention aimed at reducing alcohol use and its consequences. Their findings coincide with a number of earlier reviews (e.g. Bruun et al. 1975; Edwards et al. 1994) and with the overview of Babor et al. (2003). In sum, the following measures were found quite effective:

- policy and legislative interventions, including taxation on alcohol sales, drink-driving laws, restricted licensing of outlets and advertising controls;
- law enforcement, for example random breath-testing of drivers;
- community interventions; and
- brief interventions.

On the other hand, mass media and awareness campaigns were not found to be very effective, although they seemed to be somewhat more popular with politicians and policy-makers.

Since these interventions exist and have been empirically shown to reduce the burden of both chronic and acute disease caused by alcohol, and also alcohol-attributable social harm, there is no justification for alcohol-related disease to remain at such a high level in many parts of the world.

5. Projections of the future

Quantitative projections regarding future exposure to alcohol are feasible only for average volume of drinking, since it is extremely difficult if not impossible to judge how drinking patterns will alter over time (see Figures 12.3–12.5).

Adult per capita consumption in EUR-A and EUR-B seems to be driven by long-term trends (Mäkelä et al. 1981; Simpura 1998). There

Figure 12.3 Adult per capita consumption in litres of absolute alcohol for the AFR, EMR and EUR subregions

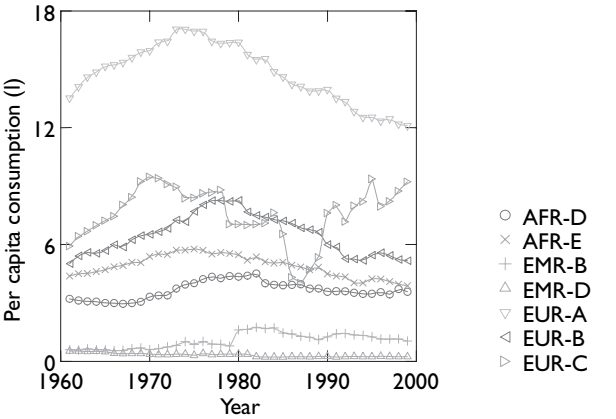
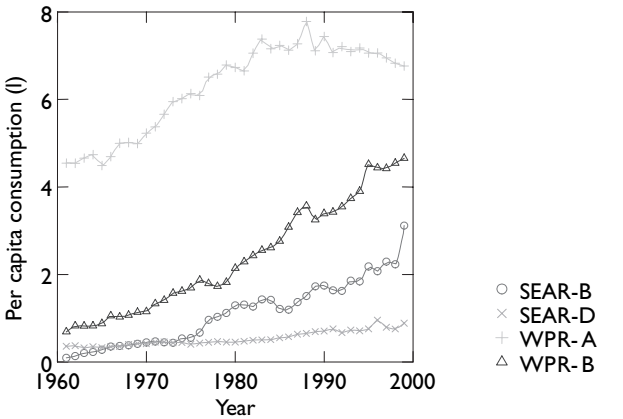
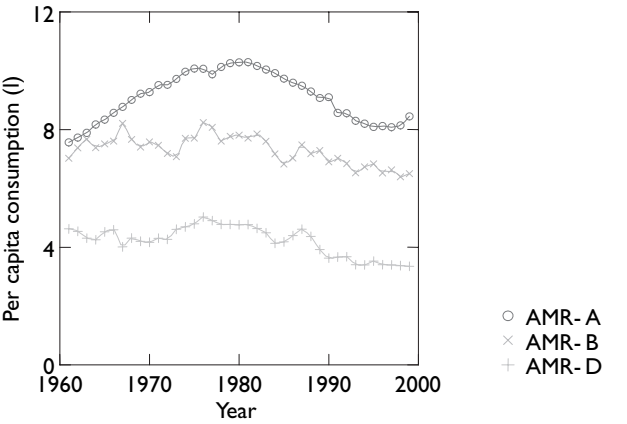


Figure 12.4 Adult per capita consumption in litres of absolute alcohol for the SEAR and WPR subregions



are indications that the current downward trend is levelling off. However, it is very hard to determine the period of long-term waves with short-term time series since 1960 or so. Thus, we predict a stable exposure for EUR-A and EUR-B at about the average level of consumption of the past 10 years. For EUR-C, the curve shows the most change. The dip at the end of the 1980s is due to the anti-alcohol campaign of the Gorbachev period in the former Soviet Union (White 1996). At the end

Figure 12.5 Adult per capita consumption in litres of absolute alcohol for the AMR subregions



of the campaign, alcohol consumption rose again to former levels. Again, since there is no clear trend after the campaign, we predict about the same level of consumption as the average of the years after the end of the Gorbachev campaign. No trends are apparent for EMR-B, EMR-D and AFR-D. Therefore, the most reasonable projection of future alcohol consumption would be the level of current consumption. To obtain more stable estimates, the average of the 1990s has been used.

For the South-East Asia and Western Pacific subregions, the following predictions appear justified based on the trend data shown in Figure 12.4. For WPR-A, there was an upward trend that seems to have stopped at the end of the 1980s; thus, the average volume of the 1990s was used as the best projection. For WPR-B and SEAR-B, consumption clearly increased and we modelled future consumption by a linear upward trend. The upward trend in SEAR-D was less pronounced, but nonetheless present, and we therefore again used the linear upward trend.

In the Americas, there has been a long wave of increasing and then decreasing consumption for North America (AMR-A), almost parallel to the European consumption. For AMR-B and AMR-D there are slight downward trends. Since the long-term wave seems to turn upwards again, and since the downward trends did not reach significance, it seems prudent to model the future for all three subregions at about the same as the average of the 1990s, as a stable estimate of the status quo.

Trends in drinking patterns have been studied in very special subsets of populations, such as youth in Europe (Hibell et al. 2000). But at the global level, for pattern of drinking, there is not even enough reliable data concerning the current situation, and thus quantitative predictions

are not possible. Therefore we assumed constant drinking patterns under a "business-as-usual" scenario. Projections of future adult per capita alcohol consumption are given in Table 12.27.

In three subregions (SEAR-B, SEAR-D and WPR-B) unrecorded consumption has to be added in order to predict burden, and these data need to be converted into drinking categories as above, based on surveys. Since we have neither survey data on the future nor any predictions for survey or unrecorded consumption, we suggest modelling future consumption as follows.

- For all subregions except SEAR-B, SEAR-D and WPR-B, predictions are based on 2000 data on proportions of drinking categories.
- Proportions of drinking categories II and III are increased by 2.1% over those for 2000 for SEAR-B and WPR-B, and by 0.7% for SEAR-D (Table 12.28). Of course, there are limits of linear increase, and we considered the current levels of consumption in the A subregions as upper limits.

In summary, the best estimates predict global increases in average consumption of alcohol, triggered by increases in developing and emerging economies in the South-East Asia and Western Pacific regions.

Table 12.27 Projections of adult per capita consumption by subregion, in litres of pure alcohol, excluding SEAR-B, SEAR-D and WPR-B

	Subregion					
	AFR-D	*AFR-E*	*AMR-A*	*AMR-B*	*AMR-D*	
Mean	3.543	4.127	8.276	6.669	3.462	
95% CI upper	3.608	4.258	8.428	6.826	3.558	
95% CI lower	3.478	3.996	8.125	6.512	3.366	
SD	0.085	0.171	0.197	0.204	0.125	
Trend	No trend	No trend	Long waves	No trend	No trend	
	EMR-B	*EMR-D*	*EUR-A*	*EUR-B*	*EUR-C*	*WPR-A*
Mean	1.248	0.238	12.632	5.372	8.316	7.012
95% CI upper	1.355	0.245	13.008	5.552	8.845	7.127
95% CI lower	1.142	0.231	12.255	5.192	7.787	6.897
SD	0.139	0.009	0.490	0.234	0.688	0.149
Trend	No trend	No trend	Long waves	No trend	No trend	Long waves

Table 12.28 Projections of adult per capita consumption by subregion, in litres of pure alcohol, for SEAR-B, SEAR-D and WPR-B

	Subregion		
	SEAR-B	*SEAR-D*	*WPR-B*
Increase per year in litres of pure alcohol after 2000	0.063	0.014	0.108
95% CI upper	0.068	0.016	0.115
95% CI lower	0.057	0.012	0.102
Increase in adult per capita consumption 2000 (%)	2.1	0.7	2.1
Trend	Linear upward	Linear upward	Linear upward
Shared variation: year and 1960–1999[a] consumption	88.0%	93.2%	96.8%

[a] The shared variation or "explained variance" denotes a measure of strength of the relationship, i.e. how much of the variation of adult per capita consumption is explained by the linear trend.

Acknowledgements

Parts of an earlier version of the contributions were made available on the WHO listserve for discussion, and we should like to thank all who responded. In addition, the authors would like to thank the following participants in the WHO expert meetings on alcohol as a risk factor for the burden of disease, held in Geneva on 29–30 January and 7–8 May 2001, for their valuable comments when revising prior versions: Mary Jane Ashley, Mary Assunta, Vivek Benegal, Susan Bondy, Ruth Bonita, Maximilian de Courten, Majid Ezzati, Oye Gureje, Wei Hao, Jennifer Hillebrand, Claudio Jeronimo da Silva, Håkan Leifman, Alan Lopez, Maria-Elena Medina-Mora, Zofia Mielecka-Kubien, Alexander Nemtsov, Ian B. Puddey, Margret Rihs-Middel, Leanne Riley, Kari J. Rummukainen, Shekhar Saxena, Raquel Shaw Moxam, Jussi Simpura, Bedirhan Üstün and Justin Willis.

Many people, too numerous to be listed here, contributed with data, and we wish to thank all of them for their help. Special thanks go to Ed Adlaf, Tom Greenfield, Wei Hao, Håkan Leifman, Maria-Elena Medina-Mora and Tim Stockwell for conducting data analyses or data searches specifically for this exercise. Special thanks also go to Ron Kessler and his team, who provided specific estimates for the point on alcohol and depression, without which it would have been impossible to estimate alcohol-attributable burden on depression.

WHO, the Swiss Federal Office of Public Health (contract no. 00.001588), the Swiss National Science Foundation, the Addiction Research Institute in Zurich, Switzerland, the Swiss Institute for the Prevention of Alcohol and Other Drug Problems in Lausanne, and the

Centre for Addiction and Mental Health in Toronto, provided financial and/or technical support for this study.

Parts of the assessment of relations between alcohol and disease were undertaken for the report *The social costs of alcohol consumption in Switzerland* and received financial support from the Swiss Federal Office of Public Health (grant no. 98-000794/8120).

Several anonymous reviewers, as well as the members of the editorial committee (Majid Ezzati, Alan Lopez, Anthony Rodgers), deserve special thanks for their help in finalizing the text, as does Steve Vander Hoorn for the repeated burden calculations.

Finally, the authors would like to thank the staff at the Swiss Institute for the Prevention of Alcohol and Other Drug Problems in Lausanne and the Addiction Research Institute in Zurich, especially Irene Bosshard and Elisabeth Grisel, for technical assistance.

Notes

1 See preface for an explanation of this term.

2 Social outcomes of alcohol consumption are defined as changes that affect the social behaviour of individuals, or their interaction with partners and other family members, or their circumstances (Rehm 2001). Social outcomes would include family problems, public disorder, or workplace problems (for overviews see Gmel and Rehm 2003; Klingeman and Gmel 2001). Social outcomes or consequences are not addressed in this chapter unless they are included in ICD-10. The majority of these problems are not covered by ICD-10, even though health is broadly defined by WHO to include well-being.

3 Intoxication and dependence are of course also influenced by biochemistry. However, since these two intermediate outcomes are central in shaping the effect of alcohol on many health and social outcomes, they are discussed separately. The other effects (e.g. on promotion of blood clot dissolution) are often specific for one disease or a limited group of diseases. Both intoxication and dependence are defined as health outcomes in ICD-10.

4 This is not to imply that there is no drinking to intoxication or occasions of heavy drinking in countries with established market economies; it is simply to say that this pattern of drinking is more common in countries with developing or emerging economies.

5 There are other ways of estimating unrecorded consumption, such as those based on available raw materials (see the estimates for the Russian Federation by Nemtsov 1998, 2000, 2002).

6 Surveys do not necessarily underestimate the recorded per capita consumption, even though the literature sometimes appears to imply it. For some countries, e.g. Mexico, adding up the figures from the survey may lead to higher estimates than the recorded per capita consumption.

7 This questionnaire can be obtained from the first author on request. It was finalized at a WHO expert meeting in Geneva, May 2001.

8 For comparison, a 75-cl bottle of wine contains about 70 g of pure alcohol.

9 As part of the process of developing these ratings, an earlier list of derived and assigned pattern values as shown in Table 12.3 was made available on a WHO listserve to a large number of key informants for critical assessment. This process resulted in the identification of local surveys, which helped improve the estimates.

10 This reasoning was also behind the list of those invited to a WHO workshop on unrecorded consumption in May 2001, where experts from Brazil, China, India, Nigeria and the Russian Federation met with other experts on the methodology of estimating unrecorded consumption to discuss current estimates and develop a methodology to improve data gathering.

11 Ledermann had been the first to claim that the distribution of alcohol consumption among drinkers is log-normal. Subsequent research found the exact shape to be different but still approximately log-normally distributed (e.g. Duffy 1986 and rejoinders).

12 These analyses are sometimes also called hierarchical linear analyses (Bryk and Raudenbush 1992). Since the term "hierarchical" is ambivalent (in sociology it has also been used to describe stepwise regression), we exclusively use the term "multilevel" in this chapter.

13 In the statistical literature units are called sections, hence the method used is called cross-sectional time series analysis. In our case, countries are sections.

14 Europe was taken as a pilot as data are most available there. The current analysis included data from 81 countries for injuries and 74 countries for IHD, most of them outside Europe.

15 Year is only controlling for the linear part of the time structure. However, sensitivity analyses were carried out to estimate the performance of the method used.

16 "Random" does not mean that the underlying relationships are completely random. Effects may be partly deterministic owing, for example, to different policies. The term "random" here means that effects across sections or countries cannot be estimated without error, and the errors are assumed to have a random distribution.

17 If the patterns were estimated as deviations from mean patterns, then the value of γ_{10} would reflect the average impact of adult per capita consumption.

18 Even for biologically based relationships, the relationship could be moderated by other factors such as diet (e.g. alcohol may be related to breast cancer through hormonal effects, but diet also affects hormonal levels and this may have an influence on the alcohol–breast cancer relationship). However, except for IHD, meta-analyses on alcohol and chronic disease have yielded fairly similar effects for different populations, so the assumption of applying the same effect for average volume of drinking is probably justified.

19 Such "categorical" attribution is quite different from the statistical estimation used in other epidemiological studies. For the usual derivation of alcohol-attributable fractions see Rothman and Greenland (1998b).

20 Type of beverage has been excluded so far from our consideration of patterns of drinking. While the evidence is not conclusive on the effect of beverage on all-cause mortality or on cardiovascular disease (e.g. Gruenewald et al. 2000; Kerr et al. 2000; Rimm et al. 1996), there are some indications that cancers of the gastrointestinal tract are differentially influenced by alcohol in higher concentration.

21 Part of this lack of an influence on patterns of cancer risk may be due to methodological reasons. Most epidemiological studies measure only volume of consumption and model only monotonically increasing trends, and thus could not detect any influence of patterns of drinking even if they were present.

22 In the Inter-American Investigation of Mortality, which studied 4000 deaths in each of 12 cities in 1962–1964, the final assignment of all deaths from cirrhosis "with mention of alcoholism" was 80.4% of all cirrhosis deaths. About half of these had been "without mention" on the death certificate. Only in Santiago and Mexico City was the final assignment for "with mention" less than twice the initial number. The study used searches of medical records and interviews with decedents' families and attending physicians to reassign deaths from the initial classification (Room 1972, based on Puffer and Griffith 1967).

23 IHD is used here for denoting all diseases with ICD-9 rubrics 410–414 (ICD-10: I20–I25). The same categories have also been labelled coronary heart disease (CHD).

24 DisMod is a software tool that may be used to check the internal consistency of epidemiological estimates of incidence, prevalence, duration and case fatality for diseases. The latest version (DisMod II) is distributed by WHO:

http://www3.who.int/whosis/burden/burden_dismod/burden_dismod_dismod2.cfm?path=whosis,burden,burden_dismod,burden_dismod_dismod2&language=english.

25 The notion of a causal contributing role is at the heart of the epidemiological concept of causality (Rothman and Greenland 1998). According to such standards, as explained in the text, the causal role of alcohol in intentional injuries is established. According to criteria used in criminology, this may not be the case.

26 Part of the effect of alcohol on aggression or on other more social outcomes is due to psychological variables. The term "expectations" denotes the individual predictions and expectancies of what will happen after consumption of alcohol. Experimental research has demonstrated that such psychological variables play a role in determining outcome.

27 Often traffic accidents are described as if the environment's effects are totally independent of the person's behaviour. However, tired drunk-drivers on the road at 03:00 might well not have been there if they had not been drinking. Intentionality (and alcohol's effects on it) forms part of what are called "accidents".

28 Odds = $p/(1 - p)$.

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Appendix A: "Pattern of drinking" variables and their relative weights

Heavy drinking occasions

(Maximum of 11 points for this component)

Daily drinking
Less than 20% daily drinking for males: 1 point
Less than 10% daily drinking for females: 1 point

Frequency of getting drunk
Most male drinkers usually get drunk when they are drinking: 2 points
Most males drinkers often get drunk: 1 point
Most female drinkers usually or often get drunk: 1 point

Usual quantity per drinking session
Males: more than 60% typically consume four or more drinks per session: 2 points
Males: between 40% and 60% consume four or more drinks per session: 1 point
Females: more than 50% consume four or more drinks per session: 2 points
Females: between 35% and 50% consume four or more drinks per session: 1 point

Fiesta binge drinking
Males: fiesta drinking commonly occurs: 1 point
Females: fiesta drinking commonly occurs: 1 point

Drinking with meals

(Maximum of 4 points for this component)

Males: rarely or never with meals: 2 points
Males: sometimes with meals: 1 point

Females: rarely or never with meals: 2 points
Females: sometimes with meals: 1 point

Drinking in public places

(Maximum of 2 points for this component)
Males: common and everyday: 1 point
Females: common and everyday: 1 point

Scoring (possible range: 0–17 points)

Scoring by summation of individual questions: range 0–17
10–17 points: assign a pattern value of 4
7–9 points: assign a pattern value of 3
4–6 points: assign a pattern value of 2
0–3 points: assign a pattern value of 1

Appendix B: Alcohol-attributable fractions (AAFs) for mortality from injuries

Note: AAFs for morbidity from injuries were derived by multiplying the mortality AAFs by two thirds for motor vehicle accidents and by four ninths for all other types of injury.

AFR-D			*Age group (years)*											
U148	*III.*	*Injuries*	*0–15*		*15–29*		*30–44*		*45–59*		*60–69*		*≥70*	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.10	0.07	0.25	0.08	0.28	0.12	0.12	0.09	0.10	0.07	0.10	0.07
U151		Poisonings	0.00	0.00	0.19	0.15	0.10	0.09	0.10	0.09	0.10	0.09	0.05	0.04
U152		Falls	0.00	0.00	0.14	0.09	0.14	0.09	0.14	0.09	0.11	0.05	0.07	0.02
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.17	0.16	0.21	0.20	0.21	0.20	0.16	0.16	0.16	0.16
U155		Other unintentional injuries	0.10	0.03	0.19	0.15	0.19	0.15	0.16	0.12	0.16	0.12	0.16	0.12
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.09	0.06	0.09	0.06	0.07	0.05	0.07	0.05	0.03	0.03
U158		Homicide	0.08	0.08	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.06	0.06

continued

Appendix B: Alcohol-attributable fractions (AAFs) for mortality from injuries (*continued*)

AFR-E			*Age group (years)*											
U148	*III.*	*Injuries*	*0–15*		*15–29*		*30–44*		*45–59*		*60–69*		*≥70*	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.15	0.10	0.50	0.12	0.54	0.17	0.31	0.13	0.26	0.10	0.26	0.10
U151		Poisonings	0.00	0.00	0.42	0.21	0.25	0.14	0.25	0.14	0.25	0.14	0.13	0.06
U152		Falls	0.00	0.00	0.34	0.13	0.34	0.13	0.34	0.13	0.27	0.08	0.20	0.04
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.39	0.23	0.45	0.28	0.45	0.28	0.37	0.22	0.37	0.22
U155		Other unintentional injuries	0.15	0.04	0.42	0.21	0.42	0.21	0.36	0.17	0.36	0.17	0.36	0.17
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.24	0.09	0.24	0.09	0.18	0.07	0.18	0.07	0.09	0.04
U158		Homicide	0.12	0.12	0.40	0.25	0.40	0.25	0.40	0.25	0.40	0.25	0.40	0.25
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.31	0.18	0.31	0.18	0.31	0.18	0.31	0.18	0.17	0.09

AMR-A			Age group (years)											
U148	III.	Injuries	0–15		15–29		30–44		45–59		60–69		≥70	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.18	0.12	0.38	0.14	0.42	0.20	0.21	0.16	0.17	0.12	0.17	0.12
U151		Poisonings	0.00	0.00	0.31	0.25	0.17	0.16	0.17	0.16	0.17	0.16	0.09	0.08
U152		Falls	0.00	0.00	0.24	0.15	0.24	0.15	0.24	0.15	0.18	0.10	0.13	0.04
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.28	0.27	0.33	0.32	0.33	0.32	0.27	0.26	0.27	0.26
U155		Other unintentional injuries	0.18	0.05	0.31	0.25	0.31	0.25	0.26	0.20	0.26	0.20	0.26	0.20
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.16	0.11	0.16	0.11	0.12	0.09	0.12	0.09	0.05	0.05
U158		Homicide	0.15	0.15	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.11	0.11

continued

Appendix B: Alcohol-attributable fractions (AAFs) for mortality from injuries (*continued*)

AMR-B			*Age group (years)*											
U148	*III.*	*Injuries*	*0–15*		*15–29*		*30–44*		*45–59*		*60–69*		*≥70*	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.18	0.12	0.56	0.14	0.60	0.20	0.36	0.16	0.30	0.12	0.30	0.12
U151		Poisonings	0.00	0.00	0.48	0.25	0.30	0.16	0.30	0.16	0.30	0.16	0.16	0.08
U152		Falls	0.00	0.00	0.39	0.15	0.39	0.15	0.39	0.15	0.32	0.10	0.24	0.04
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.44	0.27	0.50	0.32	0.50	0.32	0.43	0.26	0.43	0.26
U155		Other unintentional injuries	0.18	0.06	0.48	0.25	0.48	0.25	0.42	0.21	0.42	0.21	0.42	0.21
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.28	0.11	0.28	0.11	0.22	0.09	0.22	0.09	0.11	0.06
U158		Homicide	0.15	0.15	0.45	0.29	0.45	0.29	0.45	0.29	0.45	0.29	0.45	0.29
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.36	0.22	0.36	0.22	0.36	0.22	0.36	0.22	0.20	0.11

AMR-D		Age group (years)											
U148	III. Injuries	0–15		15–29		30–44		45–59		60–69		≥70	
		Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A. Unintentional injuries												
U150	Motor vehicle accidents	0.11	0.07	0.42	0.09	0.46	0.13	0.24	0.10	0.20	0.07	0.20	0.07
U151	Poisonings	0.00	0.00	0.34	0.16	0.20	0.10	0.20	0.10	0.20	0.10	0.10	0.05
U152	Falls	0.00	0.00	0.27	0.09	0.27	0.09	0.27	0.09	0.21	0.06	0.15	0.03
U153	Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154	Drownings	0.00	0.00	0.31	0.18	0.37	0.21	0.37	0.21	0.30	0.17	0.30	0.17
U155	Other unintentional injuries	0.11	0.03	0.34	0.16	0.34	0.16	0.29	0.13	0.29	0.13	0.29	0.13
U156	B. Intentional injuries												
U157	Self-inflicted injuries	0.00	0.00	0.18	0.07	0.18	0.07	0.14	0.05	0.14	0.05	0.06	0.03
U158	Homicide	0.09	0.09	0.32	0.19	0.32	0.19	0.32	0.19	0.32	0.19	0.32	0.19
U159	War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160	Other intentional injuries	0.00	0.00	0.24	0.14	0.24	0.14	0.24	0.14	0.24	0.14	0.12	0.07

continued

Appendix B: Alcohol-attributable fractions (AAFs) for mortality from injuries (*continued*)

EMR-B			*Age group (years)*											
U148	*III.*	*Injuries*	*0–15*		*15–29*		*30–44*		*45–59*		*60–69*		*≥70*	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.03	0.02	0.08	0.02	0.09	0.03	0.03	0.02	0.03	0.02	0.03	0.02
U151		Poisonings	0.00	0.00	0.06	0.04	0.03	0.03	0.03	0.03	0.03	0.03	0.01	0.01
U152		Falls	0.00	0.00	0.04	0.02	0.04	0.02	0.04	0.02	0.03	0.01	0.02	0.01
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.05	0.05	0.06	0.06	0.06	0.06	0.05	0.04	0.05	0.04
U155		Other unintentional injuries	0.03	0.01	0.06	0.04	0.06	0.04	0.04	0.03	0.04	0.03	0.04	0.03
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.03	0.02	0.03	0.02	0.02	0.01	0.02	0.01	0.01	0.01
U158		Homicide	0.02	0.02	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.02	0.02

EMR-D		Age group (years)											
U148	III. Injuries	0–15		15–29		30–44		45–59		60–69		≥70	
		Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A. Unintentional injuries												
U150	Motor vehicle accidents	0.01	0.01	0.04	0.01	0.04	0.01	0.02	0.01	0.01	0.01	0.01	0.01
U151	Poisonings	0.00	0.00	0.03	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00
U152	Falls	0.00	0.00	0.02	0.01	0.02	0.01	0.02	0.01	0.01	0.01	0.01	0.00
U153	Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154	Drownings	0.00	0.00	0.02	0.02	0.03	0.03	0.03	0.03	0.02	0.02	0.02	0.02
U155	Other unintentional injuries	0.01	0.00	0.03	0.02	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02
U156	B. Intentional injuries												
U157	Self-inflicted injuries	0.00	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00	0.00
U158	Homicide	0.01	0.01	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
U159	War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160	Other intentional injuries	0.00	0.00	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.01	0.01

continued

Appendix B: Alcohol-attributable fractions (AAFs) for mortality from injuries (*continued*)

EUR-A			*Age group (years)*											
U148	*III.*	*Injuries*	*0–15*		*15–29*		*30–44*		*45–59*		*60–69*		*≥70*	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.23	0.15	0.46	0.18	0.50	0.25	0.27	0.21	0.22	0.15	0.22	0.15
U151		Poisonings	0.00	0.00	0.38	0.31	0.22	0.21	0.22	0.21	0.22	0.21	0.12	0.10
U152		Falls	0.00	0.00	0.30	0.20	0.30	0.20	0.30	0.20	0.24	0.13	0.17	0.06
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.35	0.33	0.40	0.39	0.40	0.39	0.33	0.32	0.33	0.32
U155		Other unintentional injuries	0.23	0.07	0.38	0.31	0.38	0.31	0.32	0.26	0.32	0.26	0.32	0.26
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.21	0.14	0.21	0.14	0.16	0.12	0.16	0.12	0.07	0.07
U158		Homicide	0.19	0.19	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.14	0.14

EUR-B			Age group (years)											
U148	III.	Injuries	0–15		15–29		30–44		45–59		60–69		≥70	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.17	0.11	0.54	0.13	0.58	0.19	0.34	0.15	0.29	0.11	0.29	0.11
U151		Poisonings	0.00	0.00	0.46	0.24	0.28	0.15	0.28	0.15	0.28	0.15	0.15	0.07
U152		Falls	0.00	0.00	0.37	0.14	0.37	0.14	0.37	0.14	0.30	0.09	0.22	0.04
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.42	0.26	0.48	0.31	0.48	0.31	0.41	0.25	0.41	0.25
U155		Other unintentional injuries	0.17	0.05	0.46	0.24	0.46	0.24	0.40	0.20	0.40	0.20	0.40	0.20
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.27	0.10	0.27	0.10	0.20	0.08	0.20	0.08	0.10	0.05
U158		Homicide	0.14	0.14	0.44	0.28	0.44	0.28	0.44	0.28	0.44	0.28	0.44	0.28
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.34	0.21	0.34	0.21	0.34	0.21	0.34	0.21	0.19	0.10

continued

Appendix B: Alcohol-attributable fractions (AAFs) for mortality from injuries (*continued*)

EUR-C			*Age group (years)*											
U148	*III.*	*Injuries*	*0–15*		*15–29*		*30–44*		*45–59*		*60–69*		*≥70*	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.32	0.23	0.71	0.27	0.74	0.36	0.52	0.29	0.46	0.23	0.46	0.23
U151		Poisonings	0.00	0.00	0.64	0.42	0.45	0.30	0.45	0.30	0.45	0.30	0.27	0.16
U152		Falls	0.00	0.00	0.55	0.28	0.55	0.28	0.55	0.28	0.47	0.19	0.37	0.09
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.61	0.45	0.66	0.51	0.66	0.51	0.59	0.44	0.59	0.44
U155		Other unintentional injuries	0.32	0.11	0.64	0.42	0.64	0.42	0.58	0.36	0.58	0.36	0.58	0.36
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.43	0.21	0.43	0.21	0.35	0.18	0.35	0.18	0.19	0.11
U158		Homicide	0.28	0.28	0.62	0.47	0.62	0.47	0.62	0.47	0.62	0.47	0.62	0.47
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.52	0.38	0.52	0.38	0.52	0.38	0.52	0.38	0.33	0.21

SEAR-B			Age group (years)											
U148	III.	Injuries	0–15		15–29		30–44		45–59		60–69		≥70	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.07	0.04	0.30	0.05	0.34	0.08	0.16	0.06	0.13	0.04	0.13	0.04
U151		Poisonings	0.00	0.00	0.24	0.10	0.13	0.06	0.13	0.06	0.13	0.06	0.06	0.03
U152		Falls	0.00	0.00	0.18	0.06	0.18	0.06	0.18	0.06	0.14	0.04	0.09	0.02
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.21	0.11	0.26	0.14	0.26	0.14	0.20	0.11	0.20	0.11
U155		Other unintentional injuries	0.07	0.02	0.24	0.10	0.24	0.10	0.19	0.08	0.19	0.08	0.19	0.08
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.12	0.04	0.12	0.04	0.09	0.03	0.09	0.03	0.04	0.02
U158		Homicide	0.06	0.06	0.22	0.12	0.22	0.12	0.22	0.12	0.22	0.12	0.22	0.12
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.16	0.09	0.16	0.09	0.16	0.09	0.16	0.09	0.08	0.04

continued

Appendix B: Alcohol-attributable fractions (AAFs) for mortality from injuries (*continued*)

SEAR-D			*Age group (years)*											
U148	*III.*	*Injuries*	*0–15*		*15–29*		*30–44*		*45–59*		*60–69*		*≥70*	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.05	0.03	0.22	0.04	0.25	0.05	0.11	0.04	0.09	0.03	0.09	0.03
U151		Poisonings	0.00	0.00	0.17	0.07	0.09	0.04	0.09	0.04	0.09	0.04	0.04	0.02
U152		Falls	0.00	0.00	0.12	0.04	0.12	0.04	0.12	0.04	0.09	0.02	0.06	0.01
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.15	0.08	0.19	0.10	0.19	0.10	0.14	0.07	0.14	0.07
U155		Other unintentional injuries	0.05	0.01	0.17	0.07	0.17	0.07	0.14	0.06	0.14	0.06	0.14	0.06
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.08	0.03	0.08	0.03	0.06	0.02	0.06	0.02	0.03	0.01
U158		Homicide	0.04	0.04	0.16	0.08	0.16	0.08	0.16	0.08	0.16	0.08	0.16	0.08
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.11	0.06	0.11	0.06	0.11	0.06	0.11	0.06	0.05	0.03

WPR-A			Age group (years)											
U148	III.	Injuries	0–15		15–29		30–44		45–59		60–69		≥70	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.33	0.11	0.36	0.13	0.40	0.18	0.20	0.15	0.16	0.11	0.16	0.11
U151		Poisonings	0.00	0.00	0.29	0.23	0.16	0.15	0.16	0.15	0.16	0.15	0.08	0.07
U152		Falls	0.00	0.00	0.22	0.14	0.22	0.14	0.22	0.14	0.17	0.09	0.12	0.04
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.26	0.25	0.31	0.30	0.31	0.30	0.25	0.24	0.25	0.24
U155		Other unintentional injuries	0.16	0.05	0.29	0.23	0.29	0.23	0.24	0.19	0.24	0.19	0.24	0.19
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.15	0.10	0.15	0.10	0.11	0.08	0.11	0.08	0.05	0.05
U158		Homicide	0.14	0.14	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.10	0.10

continued

Appendix B: Alcohol-attributable fractions (AAFs) for mortality from injuries (*continued*)

WPR-B			*Age group (years)*											
U148	*III.*	*Injuries*	*0–15*		*15–29*		*30–44*		*45–59*		*60–69*		*≥70*	
			Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
U149	A.	Unintentional injuries												
U150		Motor vehicle accidents	0.10	0.07	0.25	0.08	0.28	0.12	0.13	0.09	0.10	0.07	0.10	0.07
U151		Poisonings	0.00	0.00	0.19	0.15	0.10	0.09	0.10	0.09	0.10	0.09	0.05	0.04
U152		Falls	0.00	0.00	0.14	0.09	0.14	0.09	0.14	0.09	0.11	0.06	0.07	0.02
U153		Fires	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U154		Drownings	0.00	0.00	0.17	0.16	0.21	0.20	0.21	0.20	0.16	0.16	0.16	0.16
U155		Other unintentional injuries	0.10	0.03	0.19	0.15	0.19	0.15	0.16	0.12	0.16	0.12	0.16	0.12
U156	B.	Intentional injuries												
U157		Self-inflicted injuries	0.00	0.00	0.09	0.06	0.09	0.06	0.07	0.05	0.07	0.05	0.03	0.03
U158		Homicide	0.08	0.08	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
U159		War	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
U160		Other intentional injuries	0.00	0.00	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.06	0.06

Appendix C: Alcohol-attributable deaths (000s) in 2000 by disease category, sex and subregion

		Subregions														*World*	
Disease category	*Sex*	*AFR-D*	*AFR-E*	*AMR-A*	*AMR-B*	*AMR-D*	*EMR-B*	*EMR-D*	*EUR-A*	*EUR-B*	*EUR-C*	*SEAR-B*	*SEAR-D*	*WPR-A*	*WPR-B*	*World*	*Total*
Maternal and perinatal conditions	Males	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	3
	Females	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	
Cancer	Males	7	18	10	10	1	0	1	30	6	15	4	7	13	147	269	355
	Females	3	6	7	7	1	0	0	21	4	9	1	1	5	23	86	
Neuro-psychiatric diseases	Males	5	12	7	14	2	1	1	13	4	8	4	9	1	13	91	111
	Females	1	3	2	2	0	0	0	4	1	3	0	1	0	2	19	
Cardiovascular diseases	Males	8	16	–27	48	4	1	3	–38	49	120	6	51	–6	157	392	268
	Females	3	5	–40	16	2	0	0	–129	11	37	1	0	–37	8	–124	
Other noncommunicable diseases	Males	9	14	10	24	3	0	1	27	12	26	4	6	4	54	193	242
	Females	3	4	2	5	1	0	0	9	6	12	1	2	1	3	49	
Unintentional injury	Males	17	45	19	56	9	3	2	26	22	112	31	60	7	75	484	577
	Females	4	7	6	5	1	0	1	8	3	18	5	12	3	20	92	
Intentional injury	Males	6	21	8	55	3	0	0	7	7	58	4	14	3	19	206	248
	Females	2	5	2	3	0	0	0	2	1	10	1	4	1	10	42	
All alcohol-attributable deaths	Males	53	125	27	207	22	6	8	65	100	338	51	148	23	465	1 638	1 804
	Females	15	30	–22	39	6	1	1	–85	25	88	9	21	–28	66	166	
All deaths	Males	2 206	3 154	1 342	1 459	290	409	1 750	2 020	1 034	1 878	6 358	616	5 483	55 862	26 629	55 861
	Females	6	3 001	1 392	1 120	237	287	1 602	2 054	916	1 721	1 022	5 764	519	4 944	29 232	
Deaths attributable to alcohol as a percentage of all deaths	Males	2.4	4.0	2.0	14.2	7.6	1.5	0.4	3.2	9.6	18.0	0.8	24.1	0.4	0.8	6.2	3.2
	Females	0.8	1.0	–1.6	3.5	2.3	0.3	0.1	–4.1	2.8	5.1	0.9	0.4	–5.3	1.3	0.6	

Appendix D: Alcohol-related disease burden in DALYs (000s) in 2000 by disease category, sex and subregion

		Subregion													World	
Disease category	*Sex*	*AFR-D*	*AFR-E*	*AMR-A*	*AMR-B*	*AMR-D*	*EMR-B*	*EMR-D*	*EUR-A*	*EUR-B*	*EUR-C*	*SEAR-B*	*SEAR-D*	*WPR-A*	*WPR-B*	*World*	*Total*
Maternal and perinatal conditions	Males	9	17	1	15	1	0	1	2	4	2	1	15	0	0	68	123
	Females	7	13	1	12	1	0	0	2	3	2	1	13	0	0	55	
Cancer	Males	107	260	99	116	12	6	11	282	72	175	58	125	117	1740	3180	4201
	Females	38	72	79	81	13	1	1	202	45	103	14	17	49	305	1021	
Neuro-psychiatric diseases	Males	305	828	2113	2979	305	20	170	1867	575	1509	524	1500	361	5033	18090	21904
	Females	31	141	682	792	82	3	9	514	109	398	74	101	160	717	3814	
Cardiovascular diseases	Males	98	207	–174	480	38	14	42	–233	449	1161	86	851	–39	1432	4411	3983
	Females	30	53	–256	162	16	1	1	–627	87	234	9	5	–219	76	–428	
Other noncommunicable diseases	Males	149	252	165	531	55	8	12	380	232	486	94	220	67	1045	3695	4555
	Females	44	74	25	101	20	2	2	147	96	196	17	69	3	66	860	
Unintentional injury	Males	576	1425	498	1815	268	100	80	643	675	2771	912	1837	141	2268	14008	16495
	Females	162	280	119	177	29	11	17	136	81	402	133	359	34	545	2487	
Intentional injury	Males	198	632	222	1919	110	14	12	162	176	1439	118	379	62	502	5945	7062
	Females	81	153	53	118	9	3	5	42	25	234	35	110	17	231	1117	
All alcohol-attributable DALYs	Males	1441	3621	2925	7854	789	162	328	3103	2183	7543	1793	4927	708	12020	49397	58323
	Females	393	785	702	1443	170	22	36	416	446	1570	284	675	43	1941	8926	
DALYs attributable to alcohol as a percentage of all DALYs	Males	2.0	3.5	11.9	17.3	8.6	1.3	0.6	11.1	10.2	21.5	5.3	2.8	8.1	29.1	6.5	4.0
	Females	0.6	0.8	3.2	4.1	2.2	0.2	0.1	1.6	2.5	6.5	1.0	0.4	0.6	1.8	1.3	