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Australian alcohol guidelines for low-risk drinking

Draft for public consultation

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Abbreviations

AAF	alcohol attributable fraction
AIHW	Australian Institute of Health and Welfare
ARBD	alcohol-related birth defects
ARND	alcohol-related neurodevelopmental disorders
AMD	age-related macular degeneration
AUD	alcohol use disorder
BAC	blood alcohol concentration
CHD	coronary heart disease
CI	confidence interval
CNS	central nervous system
CVD	cardiovascular disease
DoHA	Australian Government Department of Health and Ageing
ED	emergency department
FAS	fetal alcohol syndrome
FASD	fetal alcohol spectrum disorder
GABA	gamma-amino butyric acid
HCV	hepatitis C virus
ICAP	International Center for Alcohol Policies
IQ	intelligence quotient
MDMA	methylenedioxymethamphetamine (also known as ecstasy)
NDSHS	National Drug Strategy Household Survey
NHMRC	National Health and Medical Research Council
NRMMC	Natural Resource Management Ministerial Council
OECD	Organisation for Economic Co-operation and Development
OR	odds ratio
RR	relative risk
SGA	small for gestational age
STD	sexually transmitted disease
WHO	World Health Organization

Summary

This edition of the Australian Alcohol Guidelines *(Australian Guidelines for Low-Risk Drinking)* contains three distinct types of health advice:

- *A single, universal guideline* for Australian adults that provides a recommended low-risk drinking level to reduce both the immediate and long-term harm from alcohol consumption (**Guideline 1**).
- *Two guidelines with special precautions* for children and adolescents, and for pregnant and breastfeeding women (**Guidelines 2 and 3**).
- *Additional health advice and precautions* for specific groups of adults who have an increased risk (such as young adults, older people, people with a family history of alcohol dependence), for people with physical or mental conditions made worse by alcohol, and for specific situations (such as taking part in high-risk activities or using illicit drugs).

This edition of the Australian Alcohol Guidelines presents data that clearly show the level of risk associated with different patterns and levels of drinking. Increasing levels of alcohol intake are associated with increasing risk of alcohol-related accidents, injuries, disease and death.

Guideline 1 recommends a single, universal low-risk level of alcohol intake for both men and women. In setting the guideline, the NHMRC considered the risks of increasing levels of alcohol intake for two patterns of drinking and two types of harm:

- drinking on any single occasion with the attendant risk of accidents and injuries
- regular drinking over a period of time with the attendant risk of developing alcohol-related diseases.

In each case, 'low-risk' has been conservatively defined as the level of alcohol intake that, for healthy adults, will:

- keep the risk of accidents and injuries, or of developing alcohol-related diseases, at tolerably low levels (compared with not drinking)
- reduce the lifetime risk of death from an alcohol-related injury, or from an alcohol-related disease, to less than 1 in 100 (that is, one death for every 100 people who drink at that specified level and pattern).

To achieve these outcomes, the recommended alcohol intake for both men and women is the same: two standard drinks or less in any one day.

Importantly, **Guideline 1** does not represent a 'safe' or 'no-risk' drinking level; neither is it a proscriptive level of drinking that must be followed in all situations. Rather, it is an advisory drinking level that will enable healthy adults to maintain a low risk of alcohol-related accidents, injuries, diseases and death. Drinking at levels higher than this recommended level of alcohol intake is associated with a significantly increasing risk of these complications and the risk of death from alcohol-related disease escalates much more rapidly for women than for men.

How to use this document

This document is organised into the following sections:

- **Summary**
  The summary presents the *Guidelines* and the *Additional health advice and precautions* in a simple format for easy reference.
- **Part A (Background)**
  Part A provides important background information about the *Guidelines* and describes the principles used to derive them. It also includes an overview of the health effects of alcohol and drinking patterns in Australia.
- **Part B (Guidelines)**
  Part B presents each *Guideline* with a rationale and explanation of the underpinning scientific evidence. Further details of the scientific evidence are in Appendixes 4–8.
- **Part C (Additional health advice and precautions)**
  Part C presents a rationale and evidence for each section of the *Additional health advice and precautions*.
- **Appendixes**
  The appendixes contain additional information about the working committee, guideline development process and evidence underpinning the guidelines.

Readers are advised to read Part A before they read Parts B and C as it contains essential background information concerning levels and patterns of drinking, risks of drinking, and the approach used by the NHMRC to set the *Guidelines*.

Australian alcohol guidelines for low-risk drinking

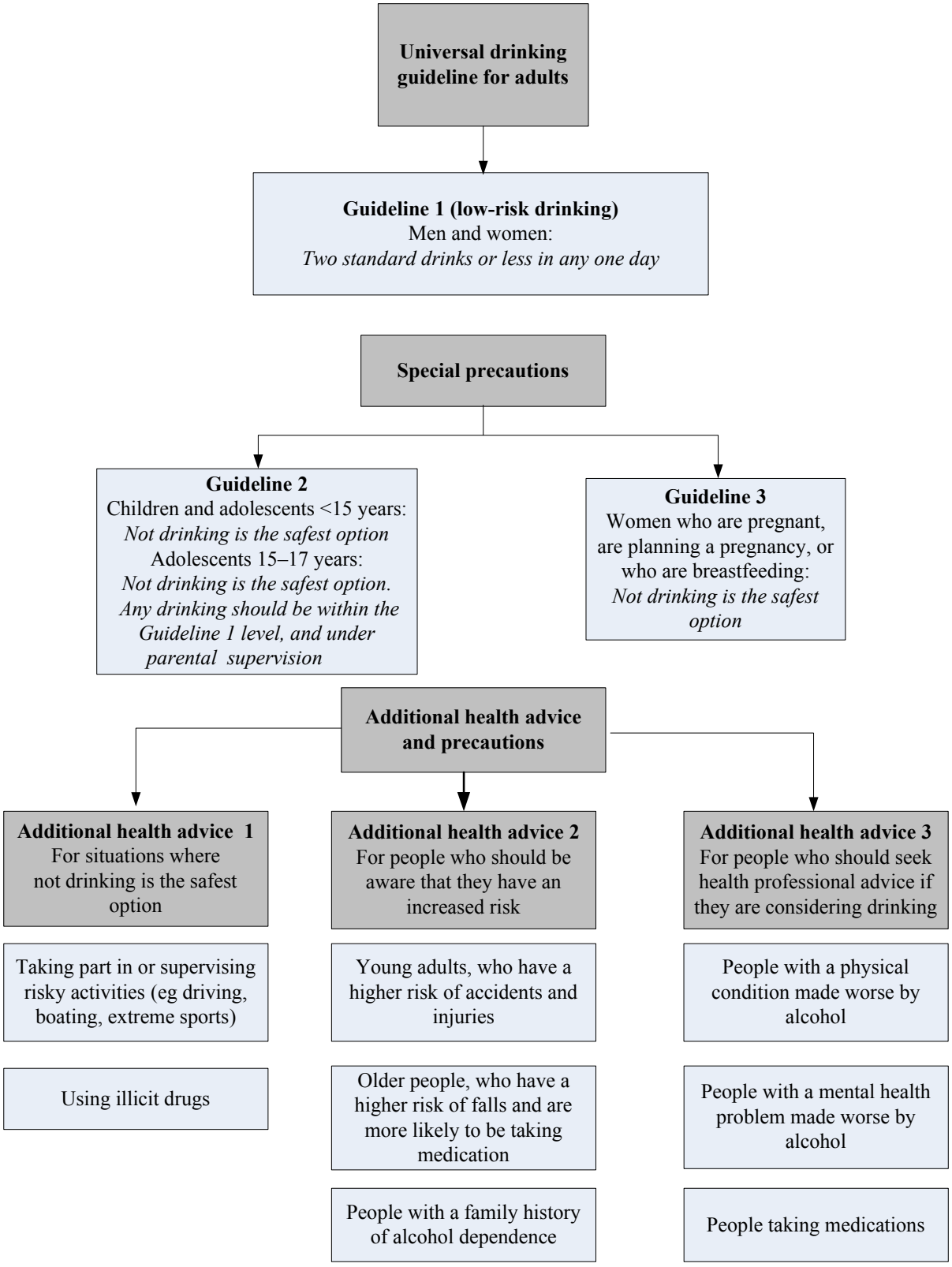
Guideline 1 **For low risk of both immediate and long-term harm from drinking:**
Men and women 1.1 Two standard drinks or less in any one day.

Guideline 2 **For children and young people under 18 years of age**
2.1 Parents and carers are advised that not drinking is the safest option for children and adolescents under 15 years of age.
2.2 Not drinking is the safest option for adolescents aged 15-17 years. If drinking does occur, it should be under parental supervision and within the adult Guideline for low-risk drinking (two standard drinks or less in any one day).

Guideline 3 **For women who are pregnant, are planning a pregnancy or are breastfeeding**
3.1 Not drinking is the safest option.

Additional health advice and precautions 1 **For situations where not drinking is the safest option:**
Taking part in, or supervising, risky activities
Using illicit drugs
Additional health advice and precautions 2 **For people who should be aware that they are at increased risk if they drink**:
Young adults
Older people
People with a family history of alcohol dependence
Additional health advice and precautions 3 **For people who should seek health professional advice if they are considering drinking:**
People with a physical condition made worse by alcohol
People with a mental health problem made worse by alcohol.
People taking medications

At a glance


Universal drinking guideline for adults
Guideline 1 (low-risk drinking)
Men and women:
Two standard drinks or less in any one day
Special precautions
Guideline 2
Children and adolescents <15 years:
Not drinking is the safest option
Adolescents 15–17 years:
Not drinking is the safest option. Any drinking should be within the Guideline 1 level, and under parental supervision
Guideline 3
Women who are pregnant, are planning a pregnancy, or who are breastfeeding:
Not drinking is the safest option
Additional health advice and precautions
Additional health advice 1
For situations where not drinking is the safest option
Taking part in or supervising risky activities (eg driving, boating, extreme sports)
Using illicit drugs
Additional health advice 2
For people who should be aware that they have an increased risk
Young adults, who have a higher risk of accidents and injuries
Older people, who have a higher risk of falls and are more likely to be taking medication
People with a family history of alcohol dependence
Additional health advice 3
For people who should seek health professional advice if they are considering drinking
People with a physical condition made worse by alcohol
People with a mental health problem made worse by alcohol
People taking medications

PART A

Background

1 Introduction

1.1 Why are guidelines needed?

In Australia, alcohol is the most commonly used recreational drug. People drink alcohol for a number of reasons, including the relaxing and socialising effects of small to moderate doses. However, alcohol has well-documented toxic effects on many organs and systems in the body including the brain, heart, cardiovascular system, liver, gut, pancreas, kidneys and reproductive system, and is also a recognised fetal teratogen (a substance that can cause birth defects). Alcohol also has profound effects on mental processing, which can, in turn, affect mood and judgment, leading to an increased risk of accidents, injuries and self harm. As with all toxins, the effect of alcohol increases with the amount consumed (dose). At high blood alcohol levels, acute alcohol poisoning can occur, resulting in acute organ failure, coma or death.

Burden of disease[1]

The World Health Organization (WHO) has estimated that in 2002, worldwide, alcohol caused 3.7% of all deaths (2.1 million) and 4.4% of the total burden of disease (WHO 2007). In Australia, alcohol is second only to tobacco as a preventable cause of drug-related death and hospitalisation; between 1992 and 2001, more than 31,000 deaths were attributed to risky or high risk alcohol consumption as defined by the 2001 NHMRC guideline limits, and over half a million (577 269) completed hospital episodes were caused in the eight years between 1993–94 and 2000–01 (Chikritzhs et al 2003). The number of emergency department presentations caused by alcohol across the country is unknown but is likely to account for a large proportion of all presentations (McLeod et al 2000, Poynton et al 2005, Watt et al 2004, 2006).

Alcohol accounts for 13% of all deaths among 14–17-year-old Australians. It has been estimated that one Australian teenager dies and more than 60 are hospitalised each week from alcohol-related causes (Chikritzhs et al 2004). Alcohol is also a significant contributor to premature death and hospitalisation among older Australians. Among 65–74-year-olds, almost 600 die every year from injury and disease caused by drinking above the 2001 NHMRC low-risk drinking levels, and a further 6500 are hospitalised (Chikritzhs and Pascal 2005). Alcohol-attributable injury and disease are particularly high among Indigenous Australians. The rate of alcohol-attributable death among Indigenous Australians is about twice that for the non-Indigenous population (Chikritzhs et al 2007).

Alcohol-related accidents and injuries

Drinking alcohol has been associated with higher risk of injury in many settings, including motor vehicle and bicycle accidents, incidents involving pedestrians, falls, fires, drowning, sports and recreational injuries, alcohol poisoning, overdose, suffocation, inhalation of vomit, assault, violence, and intentional self-harm (Chikritzhs et al 2000, Ridolfo and Stevenson 2001, Chikritzhs et al 2003). Overall, more people die from the acute effects of alcohol than

[1] 'Burden of disease' is the cumulative effect of a broad range of harmful health consequences on a community.

the long term or chronic effects. In fact, more people die from alcohol caused road injury alone than from all alcohol-related cancers, cardiovascular disease and alcohol dependence combined (Chikritzhs et al 2003). Any single occasion of heavy drinking increases the risk of injury and death for the drinker and may place others at risk. Adolescents and younger adults are particularly vulnerable and heavy drinking in this group can form part of a pattern of risk-taking behaviour (see Part B, Guideline 2 and Part C, Additional health advice and precautions 1). For Australian men, almost one-third (31%) of motor vehicle deaths and one-quarter (25%) of motor vehicle injuries have been attributed to alcohol consumption; for women the figures are 11% in each case. The figures are similar for pedestrian accidents, while about one-third of all self-inflicted injuries and suicides have been linked to alcohol consumption in men (32%) and women (29%) (Ridolfo and Stevenson 2001).

Alcohol-related diseases

In terms of the overall contribution of alcohol to deaths and ill-health in Australia, alcohol consumption accounted for 3.3% of the total burden of disease and injury in Australia in 2003: 4.9% in males and 1.6% in females (Begg et al 2007). This compared with a contribution of 7.8% for tobacco smoking, 7.5% for high body mass, 7.6% for hypertension and 6.6% for physical inactivity (Begg et al 2007). However, the choice of dataset for the estimation of alcohol consumption may have led to an underestimate of its contribution to the true burden of disease and injury. This is borne out by the higher published figures for New Zealand (10% and 4% for men and women, respectively; Connor et al 2005).

On the other hand, low levels of alcohol consumption have been reported to reduce the risk of ischaemic heart disease (particularly in middle-aged and older males) and ischaemic stroke (in older females) and to have some other beneficial health effects (see Appendix 5). However, the extent of these effects is disputed. Importantly, these potential benefits can be achieved with an intake of about one drink every second day. Any risk reduction needs to be balanced against the risks of contracting cancer or other chronic diseases at low levels of drinking (see Chapter 3 for further details).

Social and economic consequences

In addition to the health issues resulting from alcohol consumption, there are social consequences, both for the drinker and for others in the community. These consequences include harm to family members (including children) and to friends and workmates, as well as to bystanders and strangers. Alcohol-related disturbance and assault ranges from minor acts of vandalism or offensive behaviour to far more serious antisocial behaviour, which can result in affront, violence or injury to others. Among respondents to the 2004 National Household Drug Survey (AIHW 2005), 21.9% reported that they had been verbally abused in the past 12 months by a person affected by alcohol, 11.8% that they had been in a frightening situation, and 3.7% that they had been physically abused (AIHW 2005).

In terms of government responses to alcohol problems, treatment and care in the health system is only part of the story. For example, of total government expenditures on alcohol problems in Scotland in 2002–03, only 23% were estimated to be in health services, with 20% in welfare services and 57% in police and emergency services (Scottish Health Economics Unit 2004).

The costs accrue not only to government health and welfare systems, but also to industry through absenteeism, premature retirement, and impaired or lost productivity. It has been estimated, for example, that alcohol cost the Australian community about $15.3 billion in 2004–05, when factors, such as crime and violence, treatment costs, loss of productivity and premature death were taken into account (Collins and Lapsley in press). These figures are recognised to be conservative, as the cost of alcohol-related absenteeism alone has recently been estimated at $1.2 billion per year using the self-report data from the 2001 National Drug Strategy Household Survey (Pidd et al 2006).

Therefore, compliance with these low-risk drinking guidelines has the potential to achieve considerable savings to government health and welfare programs, and to the economy as a whole. The realisation of these potential savings requires implementation of a comprehensive range of policies to encourage low-risk drinking, over and above the publication of these guidelines.

1.2 Who will use this document?

The Australian Alcohol Guidelines are intended to give Australians clear guidelines on how to avoid or minimise the harmful consequences of drinking alcohol — from both the immediate (or short-term) effects of each drinking occasion and the longer-term effects of regular drinking.

These guidelines provide a resource for a wide range of groups and individuals, including health professionals, community groups, industry, professional organisations, schools and educational organisations. They will also inform policy makers, planners, decision makers, and those responsible for providing alcohol, who have a broader responsibility to the community and whose decisions may influence the health of communities.

Members of the general public wanting to make decisions about their own drinking may also be interested in these guidelines. However, as it is a technical document, it is not primarily aimed at the general public. Other plain-English booklets and factsheets will be produced to help individuals, families and community groups to understand and implement these guidelines.

Nevertheless, these guidelines and evidence summaries are presented, as far as possible, in language accessible to general readers and are intended to provide the clearest possible advice, as well as a framework for further decision making about alcohol use. Further details of the research that underpins these guidelines is presented in Appendixes 4–8 for those readers who wish to review the scientific evidence in more detail.

1.3 What has changed since the last guidelines?

These guidelines have changed significantly since the last edition (NHMRC 2001). In particular, the number of guidelines has been reduced and the text simplified to provide one overarching guideline for all adults, and two guidelines with special precautions for children and adolescents, and pregnant or breastfeeding women.

In the previous guidelines, two levels of drinking above guideline levels were designated as ‘risky’ and ‘high risk’, respectively. These terms are not used in this new edition of the

guidelines as risk increases progressively with the amount of alcohol consumed. Any drinking above the guideline levels therefore carries a higher risk than not drinking, as shown by both the risk of injury and disease compared to not drinking, and the lifetime risks of specific patterns and levels of drinking.

The approach for this edition of the guidelines has been to present data that clearly show the level of risk associated with the universal guideline level (see Chapter 2 for a detailed account of this approach). This is a significant change from the 2001 edition of these guidelines, in which the low-risk drinking level was based on scientific evidence of harms but without a quantified level of risk associated with the guideline levels.

This new approach has led to a simplified, universal guideline level for alcohol intake for both immediate and long-terms risks (Guideline 1), which is significantly lower than the 2001 guideline levels. However, the new guideline level is not intended to be a prescriptive level of drinking that must be followed in all situations. Rather, it is a guideline for low-risk drinking and drinkers are advised that drinking at higher levels is associated with significantly increased risks of alcohol-related accidents, injuries, disease and death.

The guidelines for children, and for women during pregnancy and breastfeeding, are both more conservative than the comparable 2001 guidelines, with advice to consider not drinking in these situations. The guideline for adolescents is to drink extremely cautiously, with parental supervision. These changes have been based on research data in animals and humans for the effect of alcohol on neurodevelopment, comparison with the regulation of the use of other toxic substances during pregnancy and breastfeeding, and modelling of harms (for adolescents).

Other health advice and precautions are presented separately in Part C, and were revised based on available research studies and other relevant considerations.

1.4 Drinking terminology[2]

Alcohol

The term ‘alcohol’ describes a series of organic chemical compounds, but only one type, *ethyl alcohol* or *ethanol*, is found in drinks intended for human consumption, and this is the type that is the subject of these guidelines. Other forms of alcohol, including methanol, are more toxic to humans than ethanol and are not suitable for human consumption.

Alcohol dependence

The terms ‘alcoholism’ or ‘alcoholics’ are avoided because they are ambiguous and stigmatising. Instead, the term ‘alcohol dependence’ is used (see Section 1.4).

[2] Definitions of other terms used in this document are included in the Glossary.

Intoxication

'Intoxication' is a widely used term with no consistent or formally agreed definition. It is usually taken to describe when a person's blood alcohol concentration is elevated to a level at which they cannot function within their normal range of physical and mental abilities. Levels above about 0.05–0.08% are sometimes taken as a proxy measure of intoxication (see Section 3.3). In lay terms, intoxication is a subjective feeling, the experience of a substantial effect of alcohol on mood, brain function, and psychomotor function. However, there are marked variations in the amount of alcohol different people need to consume in order to experience intoxication.

Binge-drinking

This term is avoided as far as possible in these guidelines because its meaning is ill-defined and unclear. It was formerly used to refer to an extended period (usually more than a day) devoted to drinking at levels leading to intoxication. However, more recently, it has been used to describe single-occasion drinking of a substantial amount, particularly by adolescents and young adults.

Drinking occasion

In these guidelines, a drinking occasion refers to a sequence of drinks taken without the blood alcohol concentration reaching zero in between. This might include a drink at home at the end of the day or over dinner, or at specific event, such as a party, night out, visit to the pub, a family or business event or other function. It may also include drinking spread across more than one context or venue, for instance on a 'Friday night out'.

Standard drink

These guidelines follow the previous edition of the Australian alcohol guidelines (NHMRC 2001), in defining a 'standard drink' as containing 10 grams of alcohol (equivalent to 12.5 mL of pure alcohol). Where possible, in discussing the evidence, amounts of alcohol are defined in grams and Australian standard drinks. The notion of a standard drink is used widely, but the definition varies from country to country (see Appendix 3).

The term 'standard drink' should not be confused with a *serving* of alcohol, which is often larger. For example for table wine, a standard drink corresponds to 100 mL of wine, whereas a typical serve is about 130 mL. In Australia, all bottles, cans and casks containing alcoholic beverages are required by law to state on the label the approximate number of standard drinks they contain. Table 1.1 provides a rough guide.

It can sometimes be difficult to translate standard drinks into real-life situations. There are no common glass sizes used across all public drinking environments, or in private homes, and people commonly underestimate what they drink. The problem is compounded where large containers (jugs, casks, flagons) are shared, where glasses are topped up by another person, where the composition of mixed drinks is not known (eg cocktails or punch at a party), and when pre-mixed spirit drinks contain a variable amount of alcohol per bottle or can. Hence, it may be challenging to calculate accurately the numbers of standard drinks consumed.

Drinking levels

Wherever possible, these guidelines define levels of drinking precisely using the Australian standard drink (10 grams alcohol). Where descriptive terms such as 'heavy', 'moderate' or 'light' are used, some quantitative descriptors are included, wherever possible.

Table 1.1 Numbers of Australian standard drinks in common containers of various alcoholic beverages

Alcoholic beverage		Standard drinks
Light beer (2.7% alcohol):		
1 can or stubbie	=	0.8 standard drink
Medium light beer (3.5% alcohol):		
1 can or stubbie	=	1 standard drink
Regular beer (4.9% alcohol):		
1 can or stubbie	=	1.5 standard drinks
1 jug	=	4 standard drinks
1 slab (cans or stubbies)	=	about 36 standard drinks
Wine (9.5%–13% alcohol):		
750-mL bottle	=	about 7 to 8 standard drinks
4-litre cask	=	about 30 to 40 standard drinks
Spirits:		
1 nip (30 mL)	=	1 standard drink
Pre-mixed spirits (around 5% alcohol):		
1 can (375 mL)	=	1.5–2.5 standard drinks (depending on strength)

2 Principles for setting low-risk drinking guidelines

2.1 Patterns of drinking

The previous edition of the Australian Alcohol Guidelines (*Australian Alcohol Guidelines: Health Risks and Benefits*; NHMRC 2001) introduced the concept that *patterns* of drinking, as well as *levels* of consumption are important.

'Levels of drinking' refer to how much people drink (the volume), while 'patterns of drinking' refer to how people drink and the circumstances in which they drink. Patterns of drinking may refer to several aspects of drinking behaviour, including variations in drinking over time and the number and characteristics of heavy drinking occasions. It also includes the settings where drinking takes place, the activities associated with drinking, the personal characteristics of the drinkers and their drinking companions, the types of beverage consumed, and the clusters of drinking norms and behaviours often referred to as 'drinking cultures' (Rehm et al 1996).

2.2 Risks of drinking

The introduction of the concept of patterns of drinking allowed both the risk of harm occurring during the short period of time after drinking, and the long-term risk associated with regular drinking to be considered for the previous edition of these guidelines. This edition builds further on this distinction by also considering the accumulation of risk over a lifetime for both the accidents and injuries that occur after a single drinking occasion and the ill-health that results from regular drinking (such as liver cirrhosis, cancer, heart disease and stroke, alcohol dependence, mental health and other associated drinking problems).

Risk scenarios

To take account of the levels and patterns of drinking, as well as accumulated lifetime risks of drinking, these guidelines are based on two main risk scenarios:

- *Risks of accidents, injuries and self harm through impaired function and cognition during and immediately after drinking alcohol.* These risks include the immediate increase in the risk of injury associated with drinking a defined amount of alcohol on a single drinking occasion (compared with not drinking); and the accumulated lifetime risk of death associated with many drinking occasions.
- *Risks of developing alcohol-related diseases as a result of regular drinking* (defined by the total amount of alcohol typically consumed per day and over time). These risks include the risk of developing alcohol-related diseases as a result of regular drinking at specific levels, compared with not drinking; as well as the accumulated lifetime risk of death that can be attributed to drinking at different levels.

Setting a low-risk drinking guideline

The risks associated with drinking alcohol increase with the amount consumed. There is no clear level of drinking below which alcohol-related accidents and injuries do not occur, or

below which there is no reduction in the length or quality of life due to alcohol-related diseases. The average risk of injury associated with a drinking occasion rises progressively with the number of drinks consumed (and the blood alcohol concentration), although the risk may be greater for inexperienced than for experienced drinkers. Similarly, the risk of developing an alcohol-related disease increases with the regular number of drinks consumed.

This poses a dilemma for those setting guidelines for low-risk alcohol consumption. What constitutes a low risk? To answer this question and determine a low-risk drinking level for Guideline 1, the NHMRC assessed the following risk scenarios:

1. The relative risk (compared with not drinking) of:
   (a) immediate nonfatal accidents and injuries after a single occasion of drinking a specific number of standard drinks (1, 2, 3 standard drinks, etc)
   (b) developing one or more of a range of alcohol-related diseases for people drinking on a regular basis at specific levels (eg number of standard drinks per day).
2. The accumulated absolute lifetime risk of:
   (a) death due to an accident or injury as a result of drinking at specific levels on many occasions.
   (b) death from an alcohol-related disease after regular drinking at specific levels.

The patterns of drinking and risk scenarios that form the basis of Guideline 1 are shown diagrammatically in Figure 2.1. The terms used to describe risk are further explained in Box 2.1.

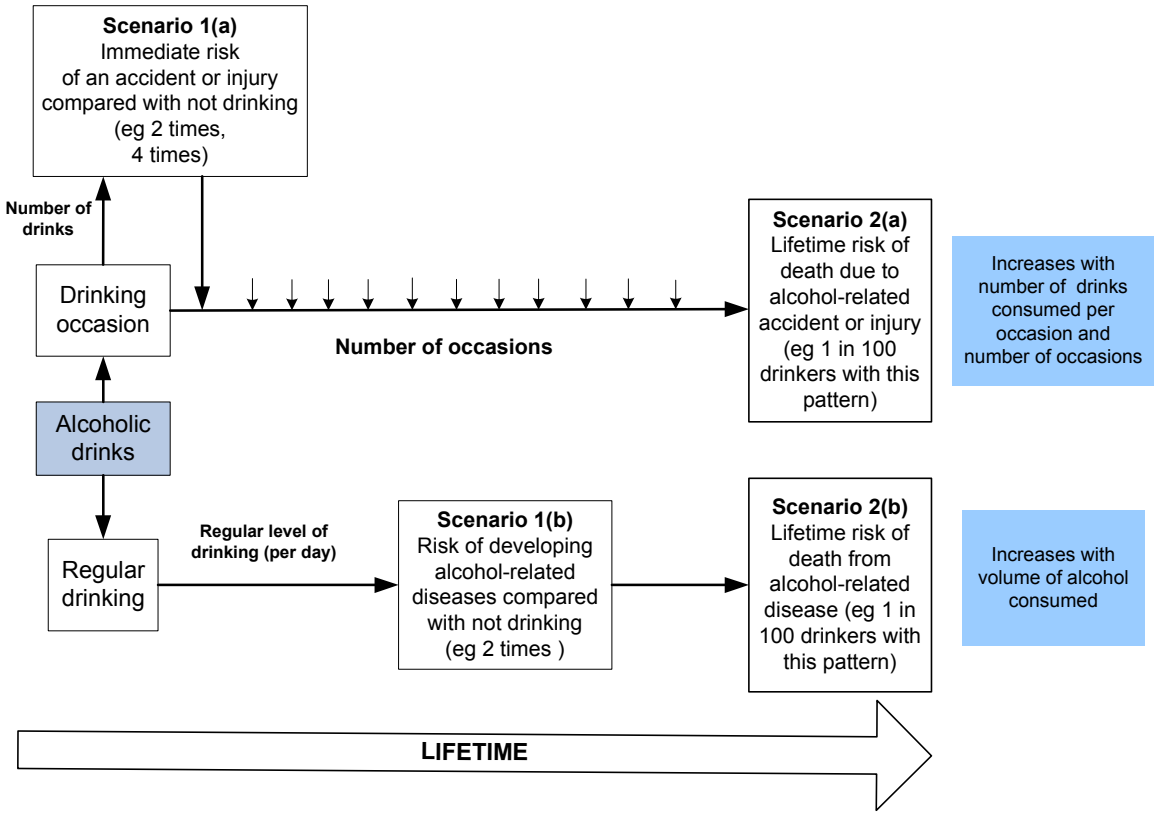


Figure 2.1 Relationship between patterns of drinking and risk scenarios for accidents and injuries, and alcohol-related diseases

Box 2.1 Risk terminology

Risk can be expressed in two different ways: relative risk and absolute risk.

Relative risk

Relative risk is the risk in an exposed group (drinkers) divided by (relative to) the risk in a non-exposed group (non-drinkers). For example if:

> 3 people in every 1000 who drink 2 alcoholic drinks per day are injured in a certain time period; and
>
> 1 person in every 1000 nondrinkers is injured in the same time period; then
>
> the relative risk of injury after drinking 2 drinks (compared with no drinks) = 3/1 = 3

That is, in this example, the risk of injury is 3-times higher after drinking 2 drinks, than it is after drinking no drinks.

In these guidelines, the risks of being injured or of developing an alcohol-related disease after drinking specific numbers of drinks at either a single occasion (for injuries) or on a regular basis (for alcohol-related diseases) are expressed as relative risks (eg '2-times', '3-times'), unless otherwise stated.

Absolute risk

In the above example, the actual (or 'absolute') risks of injury before and after drinking are 1 in 1000 and 3 in 1000. This is often expressed as a percentage (0.1% and 0.3%, respectively).
Note that the relative risk on its own does not give any information about the absolute risk.
For example, absolute risks of 1 in 10 versus 3 in 10, also gives a relative risk of 3.

Lifetime risk means the accumulated risk from drinking either at many drinking occasions, or on a regular daily basis over a lifetime. In these guidelines, lifetime risk of death from an injury or from an alcohol-related disease is expressed as an absolute risk amongst the people who drink at a specific level (eg 1 in 100 people who drink 2 drinks per day).

A lifetime risk of death of 1 in 100 — that is, one death for every 100 people drinking at the specified pattern and level —has been considered to be 'low-risk' by the NHMRC for the purpose of setting the universal guideline for adults (Guideline 1).

However, determining the lifetime risk of death is a very conservative measure as it does not take into account reduction in the quality of life associated with injuries or prolonged illnesses. Nevertheless, lifetime risk of death is a common outcome used for measuring risk from exposures to hazardous substances. For instance, in terms of exposure to carcinogenic compounds in drinking water, the *Australian Drinking Water Guidelines* are set at a concentration that 'could give rise to a risk of 1 additional cancer per 1,000,000 (million) people, if water containing the compound at that concentration were consumed over a lifetime' (NHMRC 2004). However, most people accept much higher risks than this for lifestyle issues where they have some personal control (eg the risk of car travel).

Taking account of potential risk reductions from drinking

As noted in Section 1.1, drinking may reduce the risk of some cardiovascular and cerebrovascular disorders, particularly for men over 45 years and women after menopause. Where appropriate, such risk reductions have been acknowledged in these guidelines, particularly with respect to cardiovascular disease for people from middle age onwards. However, in creating the risk curves used to underpin Guideline 1, there has been no need to

consider these risk reductions, since any reductions can be gained by lower levels of drinking than set by the guideline (approximately one drink every second day; see Appendix 5). The international clinical consensus is that people should not take up or maintain drinking for health benefits (see Section 1.1).

2.3 Variations in guideline levels for different groups

As with any population health guidelines, it is not possible to take account of the full range of individual variation, and this needs to be considered in applying the guidelines. There is wide variability in the way individuals react to alcohol, determined by factors such as gender, body size and composition, age, experience of drinking, genetics, nutrition and individual metabolism. To take account of some of these issues, the NHMRC has distinguished three distinct types of advice:

- *A single, universal guideline* for Australian adults that provides a recommended low-risk drinking level to reduce both immediate and long-term harm from alcohol consumption (**Guideline 1**).
- *Two guidelines with special precautions* for children and adolescents, and for pregnant and breastfeeding women (**Guidelines 2 and 3**).
- *Additional health advice and precautions* for specific groups of adults who have an increased risk (such as young adults, older people, people with a family history of alcohol dependence), for people with physical or mental conditions made worse by alcohol, and for specific situations (such as taking part in high-risk activities or using illicit drugs).

With respect to children and adolescents (Guideline 2), the literature does not allow a formal analysis in terms of lifetime risks. The NHMRC took note of analyses of self-reported harms ('harm scores') from the 2004 National Drug Strategy Household Survey (AIHW 2005). The NHMRC also took note of the most recent studies of the effects of alcohol on neurodevelopment throughout childhood, adolescence and early adulthood.

With respect to drinking by pregnant and breastfeeding women, as well as children and adolescents, the NHMRC has taken note of the most recent studies of the effects of alcohol on fetal development, and on neurodevelopment throughout childhood, adolescence and into the mid-20s. The basis for regulatory arrangements for the use of medications or other substances during pregnancy and childbirth were also considered.

Detailed recommendations in relation to specific health conditions are beyond the scope of these guidelines. Specialist professional organisations and societies are encouraged to develop additional guidelines, within the overall framework of these guidelines, to meet such needs.

2.4 Interpretation of guideline levels

If a person chooses to drink more than the guideline levels, they should understand that their risk of harm will, on average, be higher than that for a person who chooses not to drink. The increase in risk of harm depends on the extent to which intake exceeds the guideline level of consumption. Conversely, a drinker who wishes to reduce their level of risk can choose to drink less than the guideline level. This is consistent with public health messages in a range of other areas. The intention is to enable people to assess their level of risk as objectively as possible, based on the scientific evidence.

Importantly, these guidelines are concerned with risks to life and limb, and not with moral or normative standards about drinking. Various groups in Australian society differ about what they consider to be 'sensible' or 'responsible' drinking, and about when and whether they consider drinking is appropriate or acceptable. There is a need for continuing public debate about such standards of conduct. However, this discussion is beyond the scope of this document.

When making decisions about their drinking levels and patterns, drinkers should also take into account the fact that drinking can adversely affect others, and in some circumstances may be against the law. The most visible effects on others, including children, result from accidents and injury (including violence) during or after drinking occasions. While risk curves covering risks to others are not currently available, drinking at the guideline level for low risk is also likely to keep the risk to others low.

2.5 How has the evidence been assessed?

These guidelines are based on scientific evidence from the following sources:

- a recent literature review of epidemiological studies for a broad range of alcohol-related issues, including meta-analyses of prospective cohort and other epidemiological studies of alcohol's causative role in different health conditions
- specific research and modelling on lifetime risk commissioned by the Australian Government Department of Health and Ageing (DoHA) for these guidelines
- specific research and modelling on the harms of alcohol at different ages (harm scores).

These methods are described briefly below. A summary of the evidence in relation to each guideline is included in Part B. An overview of the guideline development process is presented in Appendix 2.

Literature review

In preparation for the update of the guidelines, the NHMRC commissioned a literature review on a range of topics to be covered by the guidelines. The reviewers searched EMBASE.com (a composite database including MEDLINE and EMBASE) and the Cochrane Library from 2000 to early 2007 for all papers relating to alcohol, alcohol use, alcohol consumption, drinking, intoxication, problem drinking and related terms. Only papers describing human studies were included. This provided a potential 223 153 articles from EMBASE.com,

74 Cochrane reviews, 208 other articles from the Cochrane Library and 6637 clinical trials from the Cochrane Central Register of clinical trials. These articles were then used as the basis for subject-specific searches.

Subject-specific searches were also carried out in the Project Cork database and some other databases relevant to specific topics. Additional references included references in the bibliographies of publications identified in the search and references supplied by the guideline development committee and based on their expertise in specific areas. The subject areas addressed by the reviewers were:

- Aboriginal and Torres Strait Islander people
- adolescents and young adults
- the elderly
- people with a family history of alcohol abuse
- differences between men and women
- occupational groups
- women who are pregnant or breastfeeding
- alcohol dependence
- abstinence

The literature review also looked at the health outcomes associated with alcohol consumption.

For each subject area, abstracts of all the identified articles were retrieved and reviewed for relevance. At this stage, reviewers excluded papers published before 2001, as well as off-topic papers, duplicates and papers that were not about human research or were not research studies (eg letters, editorials).

The remaining papers were grouped by study type (systematic reviews, randomised controlled trials, prospective cohort studies and other observational studies) and the relevant data were extracted by two reviewers and tabulated. A brief overview of each subject area was prepared. The guideline development committee and technical writer subsequently further analysed selected studies, as required.

Modelling studies

Lifetime risk

DoHA commissioned lifetime risk-modelling studies of injuries, and of alcohol-related diseases, for use in the update of these guidelines. The aim was to estimate the absolute risk of alcohol-attributable deaths for Australians during their lifetime based on:

- the number of drinks consumed at single (heavier) drinking occasions and the number of such occasions (for risk of injuries)
- regular (daily) drinking levels (for risk of alcohol-related diseases)

Details of these models are shown in Appendixes 6 and 7.

Harm scores

To help with differentiating recommendations for particular age groups, the NHMRC considered a further modelled assessment of the amount of harm caused by a given level of drinking, based on the National Drug Strategy Household Survey for 2004. The harm score was created from the series of questions on self-reported problems from drinking (see Guideline 2, Section G2 for further details).

3 Overview of alcohol effects

3.1 Immediate effects of alcohol

The most obvious and immediate effects of alcohol are on the brain. People drink alcohol for a variety of reasons, for example to experience the immediate feeling of relaxation, wellbeing and loss of inhibitions. The social and psychological benefits of alcohol may also include enhanced creativity and a therapeutic value in times of stress. However, as the intake of alcohol increases, these effects are counterbalanced by less pleasant adverse effects, such as drowsiness, loss of balance, nausea and vomiting, as well as the other harmful effects described below.

Alcohol dampens the brain's arousal, motor and sensory centres, dampening reactions to stimuli and affecting coordination, speech, cognition and the senses. The first potentially adverse effect of alcohol consumption is loss of fine motor skills and inhibitions. A blood alcohol concentration (BAC) of about 0.05 g/100 mL (or 0.05%), which is the legal limit for driving in Australia, was based on controlled studies testing driving skills (Transport and Road Research Laboratory 1987). Above this BAC, performance, behaviour and physical health deteriorate progressively (see Section 3.3 for further discussion of BACs).

If the BAC reaches a high enough level, it leads to unconsciousness and, eventually, inhibition of normal breathing. This may be fatal, particularly as the person may vomit and can inhale vomit and suffocate. Alcohol also affects the pituitary gland at the base of the brain, suppressing the production of a hormone that keeps the body's fluid reserves in balance. The kidneys fail to reabsorb an adequate amount of water, and the body excretes more water than it takes in, leaving the person dehydrated and with a headache.

As alcohol intake increases, both skills and inhibitions decrease and therefore risky behaviour, injuries and trauma increase. Also, without the cognitive or verbal capacity to resolve conflicts, physical violence becomes more likely.

The immediate effects of alcohol on the brain are often less apparent in people who drink regularly, as they acquire a degree of tolerance. Tolerance occurs because the liver becomes more efficient at breaking down alcohol. The person learns to cope with, and compensate for, the deficits induced by alcohol. Despite this tolerance, the long-term effects remain damaging, particularly as the drinkers who have greater tolerance for alcohol are those who subject themselves to higher blood alcohol levels more frequently.

3.2 Alcohol-related diseases

Table 3.1 lists some of the diseases and disorders associated with alcohol consumption. In particular, alcohol affects the following major systems and organs:

- **Liver** — alcohol consumption is one of the most common causes of cirrhosis of the liver, causing tissue destruction and scarring, and leading to an increased risk of infection, blood clotting problems, decreased quality of life, and death.

- **Gut and pancreas** — alcohol can alter normal gut secretions and irritate the gut lining, causing diarrhoea and inflammation. Alcohol can also inflame the pancreas, sometimes chronically, causing severe pain.
- **Heart and circulatory system** — the effect of alcohol on these systems is complex: low levels of alcohol raise high-density lipoprotein (good) cholesterol and reduce plaque accumulations in arteries. It also has a mild anti-coagulating effect, keeping platelets from clumping together to form clots, thus potentially reducing the risk of heart attack and ischaemic stroke; at higher levels of intake, however, alcohol raises blood pressure and may increase the risk of arrhythmias, shortness of breath, cardiac failure, haemorrhagic stroke and other circulatory problems.

Alcohol also has the following important chronic effects:

- **Cancer** — alcohol is associated with an increased risk of cancer overall, and is a cause of cancer of the mouth, throat and oesophagus. Alcohol is also a risk factor for other cancers, such as cancer of the stomach, breast, liver and pancreas, and has also been associated with bowel cancer.

- **Unborn and breastfeeding babies** — alcohol can enter the bloodstream of an unborn child when the mother drinks, and sufficient quantities, particularly in the first few weeks after conception, can cause fetal alcohol syndrome. Heavy drinking episodes and occasional peak blood alcohol levels can also increase the risk of miscarriage, low birth weight, cognitive defects and congenital malformations. Alcohol also enters breastmilk.

- **Mental health** — although a small amount of alcohol may bring short-term relief from stress, sustained drinking increases anxiety levels, and may lead to dependence when the stress is ongoing. Alcohol consumption increases the risk of mental illness (eg depression) in people who are already prone to these conditions.

- **Sleep** — although alcohol can help to induce sleep, it leads to poorer quality sleep, increased wakefulness and arousal several hours later, and worsens sleep disorders.

- **Sexual problems** — alcohol can also cause or exacerbate a range of sexual problems, particularly male impotency.

- **Eye disease** — alcohol consumption can increase the risk of eye problems, including cataracts, drusen (accumulations of extracellular material in the eye) and age-related macular degeneration.

- **Alcohol dependence** — alcohol is an addictive drug and regular use can result in alcohol dependence. Alcohol dependence is a complex phenomenon. In brief, it refers to situations where a person feels a strong need to drink so that drinking is given priority over other behaviours that the person had previously found much more important. Dependence ranges from mild to severe. People with severe dependence drink regularly above guideline levels, often find it hard to limit how much they drink, and generally have marked tolerance to the effects of alcohol. If they stop drinking for a few hours, they experience tremulousness and anxiety.

Table 3.1 Alcohol-related diseases and disorders associated with heavy alcohol consumption

Gastrointestinal disorders	**Cancer**
Gastritis Oesophagitis Duodenitis Pancreatitis	Mouth and pharynx Larynx Oesophagus Stomach Breast Liver Colon
Cardiovascular disorders	**Haematological disorders**
High blood pressure Ischaemic heart disease (including heart attack) Ischaemic stroke (blood clot) Intracranial haemorrhage (haemorrhagic stroke) Cardiomyopathy Arrhythmia	Bone marrow suppression Nutritional and blood-loss anaemia
Liver disease	**Immune system disorders**
Fatty liver Alcoholic hepatitis Cirrhosis Liver cell cancer (see above)	Impaired immune system More frequent infections and associated complications
Nervous system and mental health	**Psychiatric**
Dependence Withdrawal syndrome (delirium tremens) Seizures Alcohol-related brain damage Peripheral neuropathy	Psychiatric comorbidities are exacerbated Suicide
Musculoskeletal	**Metabolic conditions**
Alcoholic myopathy Osteoporosis	Hypoglycaemia Lactic acidosis Hyperuricaemia and gout Hypertriglyceridaemia Acetaldehyde reaction
Nutritional conditions	**Other**
Wernicke-Korsakoff syndrome Folate deficiency Vitamin A depletion Pellagra	Sexual dysfunction Eye disease Foetal alcohol syndrome Psoriasis Sleep disturbance

Source: NHMRC 1999, 2001, 2003, Standridge et al (2004)

Although the epidemiological data are not clear on the relationship between alcohol intake and being overweight or obese, alcohol intake certainly adds energy intake (kilojoules) to the normal diet and may also increase energy intake and fat storage further by increasing appetite and displacing fat and carbohydrate oxidation (NHMRC 2003)

Regular, light to moderate alcohol consumption has been associated with reduced risks of some conditions, including ischaemic heart disease and stroke (see above), gall stones, dementia and one type of diabetes. However, the extent of the risk reductions is uncertain and

recent research indicates that previous studies that claimed significant benefits of alcohol consumption have tended to overestimate the effects (see Guideline 1, Part B).

Further details and evidence for the health effects of alcohol are presented in Guideline 1 in Part B of these guidelines and in Appendix 5.

3.3 Metabolism of alcohol

After an alcoholic drink is consumed, the alcohol is absorbed rapidly from the stomach and small intestine into the bloodstream. The blood alcohol level after drinking a specific number of drinks depends on the rate at which the alcohol is consumed, and the rate at which it is broken down by biochemical processes in the liver (National Institute on Alcohol Abuse and Alcoholism 1997). The rate of absorption is affected by factors that slow down absorption, such as food in the gut, and by the temperature and alcohol concentration of the drink. However, alcohol usually starts to affect the brain within about five minutes of being swallowed.

After the consumption of one standard drink (10 grams of alcohol), the BAC reaches its peak about 30–45 minutes later. Rapid consumption of multiple drinks results in a higher BAC because the liver has a relatively fixed rate of metabolism regardless of how many drinks are consumed. In general, the following BACs can be expected about 0.5–1.5 hours after consumption of up to five standard drinks in succession (National Institute on Alcohol Abuse and Alcoholism 1997):

- 1 standard drink 0.01–0.02 g/100 mL
- 2–3 standard drinks 0.04–0.05 g/100 mL
- approximately 4 standard drinks 0.06–0.07 g/100 mL
- approximately 5 standard drinks 0.08–0.09 g/100 mL

When a person stops drinking, the blood alcohol level falls slowly over time, as the alcohol in the blood is gradually broken down by the liver. It generally takes about an hour to clear one standard drink, although this varies from person to person, and is faster in men than in women (see Section 2.3). The rate of this metabolism depends on several factors including liver size, body mass and composition, and alcohol tolerance (Edenberg 2007). Differences in the speed of alcohol metabolism between people are also related to inter-individual variation in the genes that control expression of alcohol-metabolising enzymes in the liver (Whitefield and Martin 1994, Li et al 1998, Edenberg 2007).

As the reduction in BAC depends on liver metabolism, which can only proceed at a specific rate, activities such as eating, drinking coffee, having a cold shower, vomiting or exercise do not reduce BAC. After a very heavy drinking occasion, it will take many hours for BAC to return to zero.

3.4 Factors that affect susceptibility to alcohol

- **Sex** — women tend to have a smaller body size and a higher proportion of body fat than men. As alcohol is not taken up by fatty tissues, for women, a given amount of alcohol is distributed over a smaller body volume with less absorption. In addition, the ability to break down alcohol is limited by the size of the liver, and women on average have smaller livers than men. On the other hand, the higher level of risk-taking behaviour among men means that, over a lifetime, male risks exceed female risks for a given pattern of drinking (See Guideline 1 evidence text).
- **Age** — in general, the younger and smaller a person is (eg children), the less tolerant they are to alcohol. Younger people also have less experience of drinking and its effects. In addition, puberty is often accompanied with risk-taking behaviours (such as an increased risk of drinking, sometimes in association with other dangerous physical activities or risky sexual behaviour). Finally, as people age, their tolerance for alcohol decreases and the risk of falls, driving accidents and adverse interactions with medications increases.
- **Mental health and sleeping patterns** — people who have, or are prone to, mental illness (eg anxiety and depression, schizophrenia) may have worse symptoms after drinking. Alcohol can also disrupt the later part of the sleep cycle, which may trigger a variety of mental health problems in people who are already prone to these conditions.
- **Medication and drug use** — alcohol can interact with a wide range of prescribed and over-the-counter medications, herbal preparations and illicit drugs. This can alter either the effect of the alcohol or the medication and has the potential to cause serious harm to both the drinker and others.
- **Specific health conditions that are made worse by alcohol** — people who already have health conditions caused or exacerbated by alcohol, such as alcohol dependence cirrhosis of the liver, alcoholic hepatitis or pancreatitis (see Table 2.1), are at risk of the condition becoming worse if they drink alcohol.
- **Family history of alcohol dependence** — people who have a family history of alcohol abuse and dependence (particularly among first-degree relatives) have an increased risk of developing dependence themselves.

4 Drinking in Australia

Unless otherwise indicated, the information in this chapter is based on the latest reports of the National Drug Strategy Household Survey (AIHW 2005), available through the Australian Institute of Health and Welfare[3], and the Australian Secondary School Students Use of Alcohol Survey (DoHA 2004).[4]

4.1 Drinking patterns in Australia

The majority of Australians have tried alcohol, and continue to drink throughout life. Australian household surveys show that over 90% of people aged 14 years or over have tried alcohol in their lifetime, and over 80% of people in this age group consumed an alcoholic drink in the past 12 months. About 9% of the population aged 14 years or over have never had a full serve of alcohol and about 16% have not consumed alcohol in the past year. Over the past 10 years, there has been a steady increase in the proportion of people consuming an alcoholic drink in the previous 12 months.

Risk of alcohol-related harm

As noted in Section 1.4, the previous edition of the *Australian Alcohol Guidelines* (NHMRC 2001) introduced the concept of *patterns* of drinking in addition to the overall *levels* of consumption. The risk of accidents and injuries occurring during the time period immediately after drinking was labelled as short-term risk, while the risk of developing alcohol-related diseases (such as liver cirrhosis, cardiovascular disease or cancer) from regular drinking over a lifetime was labelled as long-term risk. From 2001, data and information collection systems about alcohol consumption in Australia changed to accommodate this approach. Therefore, in this chapter, drinking levels are referred in terms of the NHMRC 2001 alcohol guideline levels for low risk of harm. That is, up to 6 standard drinks in any one day for men or up to 4 for women to reduce risk of accident or injury; and up to 4 standard drinks per day/28 per week for men, or up to 2 per day/14 per week for women to reduce alcohol-related disease risks.

Risk of alcohol-related accidents and injuries

Of all Australians aged 14 years or over, almost half (48%) reported drinking alcohol at or below 2001 guideline levels for short-term harm. However, about one-third (35%) of people drank at above 2001 guideline levels on at least one occasion in the 12 months before the 2004 survey.

[3] http://www.aihw.gov.au/drugs/index.cfm
[4] http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/publishing.nsf/Content/mono55

Risk of alcohol-related harm in the long term

Most Australians aged 14 years or over (74%) reported drinking at or below 2001 guideline levels to reduce the risk of alcohol-related diseases. However, about 10% of people reported drinking above 2001 guideline levels.

Age groups

Rates of drinking at above 2001 guideline levels among 14–19-year-olds are similar to the rates for the general population — about 10% for alcohol-related disease risk and 40% for accident and injury risk.

People in the 20–29-year age group show the riskiest drinking profile. About 60% drink at above 2001 guideline levels for accidents and injuries and about 15% drink at above 2001 guideline levels for alcohol-related diseases.

Surveys of school students show that over 80% of 12–15-year-olds have consumed at least part of an alcoholic drink in their lifetime, and about 60% consumed alcohol in the past year. The corresponding figures for 16–17-year-olds are 95% and 87%. There has been a small but steadily decreasing trend in these numbers since 1999. Population level surveys also show slight declining trends in drinking at above 2001 guideline levels by people under 20 years of age. However, among school students who report drinking in the past week, there have been increasing numbers drinking at above 2001 guideline levels for accidents and injuries, especially in the 12–15-year age group — particularly girls. This may be related to ready-to-drink products (especially premixed spirit drinks), which are becoming increasingly popular with teenagers.

Beer or spirits appear to be the adolescent beverages of choice; neat spirits or mixed drinks are the main causes of intoxication (Lintonen and Konu 2001, Marchi et al 2003, Miller and Plant 2003). Some studies have shown that teenagers who consume beer or spirits are more likely to drink to excess than wine drinkers (Lintonen and Konu 2001, Miller and Plant 2003).

Although older people tend to consume less alcohol at any one session than younger people, they are more likely to drink every day. About 11% of people aged 60 years or more drink at above 2001 guideline levels for accidents and injuries; about 6% drink at above 2001 guideline levels for alcohol-related disease risks.

Cultural and occupational groups

National household surveys show that less drinking at above 2001 guideline levels occurs in homes where English is not the first language spoken. People living in rural or remote areas are more likely to drink at higher levels compared with people in major cities and towns.

Most surveys show that Aboriginal and Torres Strait Islander people are less likely to drink alcohol than other Australians. However, when they do consume alcohol, they are more likely than other Australians to do so at above 2001 guideline levels. Thus, approximately 20% of Indigenous peoples drink at above 2001 guideline levels for alcohol-related disease risks (compared with about 10% of other Australians). Approximately 50% of Indigenous people

drink at above 2001 guideline levels for accidents and injuries (compared with about 34% of other Australians).

Drinking at above 2001 guideline levels has been identified across occupational categories and industry groups. Tradespeople and unskilled workers are more likely to drink at above 2001 guideline levels. The hospitality, agricultural, and mining industries have the largest proportion of workers drinking at above guideline levels.

4.2 Where do Australians drink?

Table 4.1 shows the responses to a national household survey of drinking venues (AIHW 2005). The table shows that people most often consume alcohol in their own or a friend's home. The 14–19-year age group is most likely to drink at private parties. As people age, they drink more often at home and less often at private parties.

The 40–49-year age group is most likely to drink in restaurants or cafes. The 20–29-year age group is most likely to drink in licensed premises (pubs, clubs) but also report a higher proportion of drinking at dance parties and in the workplace (including university or colleges) than other age groups.

Table 4.1 Percentage of people who reported recent drinking at different venues, 2004

Place	Age group						
	14–19	20–29	30–39	40–49	50–59	60+	14+
In my home	57.6	75.1	86.7	88.7	88.8	87.4	83.0
At a friend's house	58.4	65.1	61.8	56.9	52.2	43.3	56.1
At licensed premises	42.3	76.0	55.9	49.0	46.6	39.4	52.5
At restaurants or cafes	20.6	54.9	57.3	58.2	57.4	47.1	52.0
At private parties	70.5	59.7	49.4	47.0	41.7	31.9	48.0
At the workplace	2.4	10.5	9.7	6.2	4.5	1.0	6.1
At raves or dance parties	16.2	14.6	3.0	2.3	1.4	0.8	5.4
In public places	8.7	4.3	3.1	3.0	1.8	1.0	3.2
In a car	8.9	5.4	2.4	1.4	0.5	0.1	2.6
At school/TAFE/ university, etc	3.3	4.2	0.6	0.3	0.5	0.1	1.3
Other	8.3	3.2	2.1	1.4	1.5	0.9	2.4

Notes: Respondents could select more than one response
Source: National Drug Strategy Household Survey (AIHW 2005)

4.3 Attitudes to alcohol

Australians have mixed attitudes towards alcohol. Regular use of alcohol by adults is considered acceptable by more than three-quarters of Australians aged 14 years or over. However, about one-third (33%) of people consider alcohol to be the most serious concern for the general community, and 10% think alcohol is a drug most likely to be associated with a 'drug problem'.

Australians tend to overestimate the amount they think they can safely drink. In 2004, more than one-third of Australians thought an adult could drink in excess of the NHMRC 2001

low-risk guideline for accidents and injuries (6 standard drinks for men and 4 for women) without putting their health at risk. More than 10% of people thought the 2001 alcohol-related disease risk guideline (4 standard drinks per day for men and 2 per day for women) could be exceeded without health risks.

Most Australians support more severe penalties for drink driving, stricter laws for serving intoxicated people, and strict monitoring of late-night licensed premises. However, only 20% of people support increasing the price of alcohol.

Since 2001, there have been significant changes in the type of alcohol young people are drinking. Although overall consumption rates have not increased greatly, the percentage of school students drinking premixed spirits has doubled in 12–15-year-olds as well as 16–17-year-olds. About half of 12–17-year-old female school students drink premixed spirits. The change towards premixed spirit drinks has come at the expense of beer and unmixed spirits.

One example of the community's changing attitudes to alcohol is seen in the way local government has responded to alcohol misuse and related health and social problems. Although local government are not considered the lead agency responding to alcohol harm in the community, they have gained representation on national drug and alcohol committees.

PART B

Australian alcohol guidelines for low-risk drinking

Guideline 1 Low-risk drinking for adults

Guideline 1 **For low risk of both immediate and long-term harm from drinking:**
Men and women 1.1 Two standard drinks or less in any one day.

Rationale

This guideline applies to men and women aged 18 years or over and sets a standard drinking level that will reduce both the risk of injury, violence and self harm, and the risk of developing alcohol-related diseases.

The guideline limits are based on international epidemiological research that has quantified the risks of injuries and alcohol-related diseases after different levels of alcohol consumption (converted to Australian standard drinks) and with different patterns of drinking (see Section 2.1).

Importantly, this guideline does not represent a 'safe' or 'no-risk' drinking level; neither is it a prescribed intake level. Rather, it represents a drinking level that, for healthy adults, will:

- keep the risk of accidents and injuries, or of developing alcohol related diseases, at tolerably low levels (compared with not drinking)
- reduce the lifetime risk of death from an alcohol-related injury or disease to less than 1 in 100 people who drink at that level.

The guideline drinking level is based on an average bodyweight. People with lower bodyweights (below 60 kg for men and 50 kg for women), should consider drinking less than the guideline level.

Analysis of risks

The principles used to set Guideline 1 are described in Section 2.2. The results of the quantitative analysis of risk are shown in Box G1.1 and Figure G1.1. A summary of the studies that underpin these results is provided below; further details are shown in Appendixes 4–8.

Box G1.1 Risks of drinking at Guideline 1 level (men and women)

1. The relative risk (RR), compared with not drinking, of:

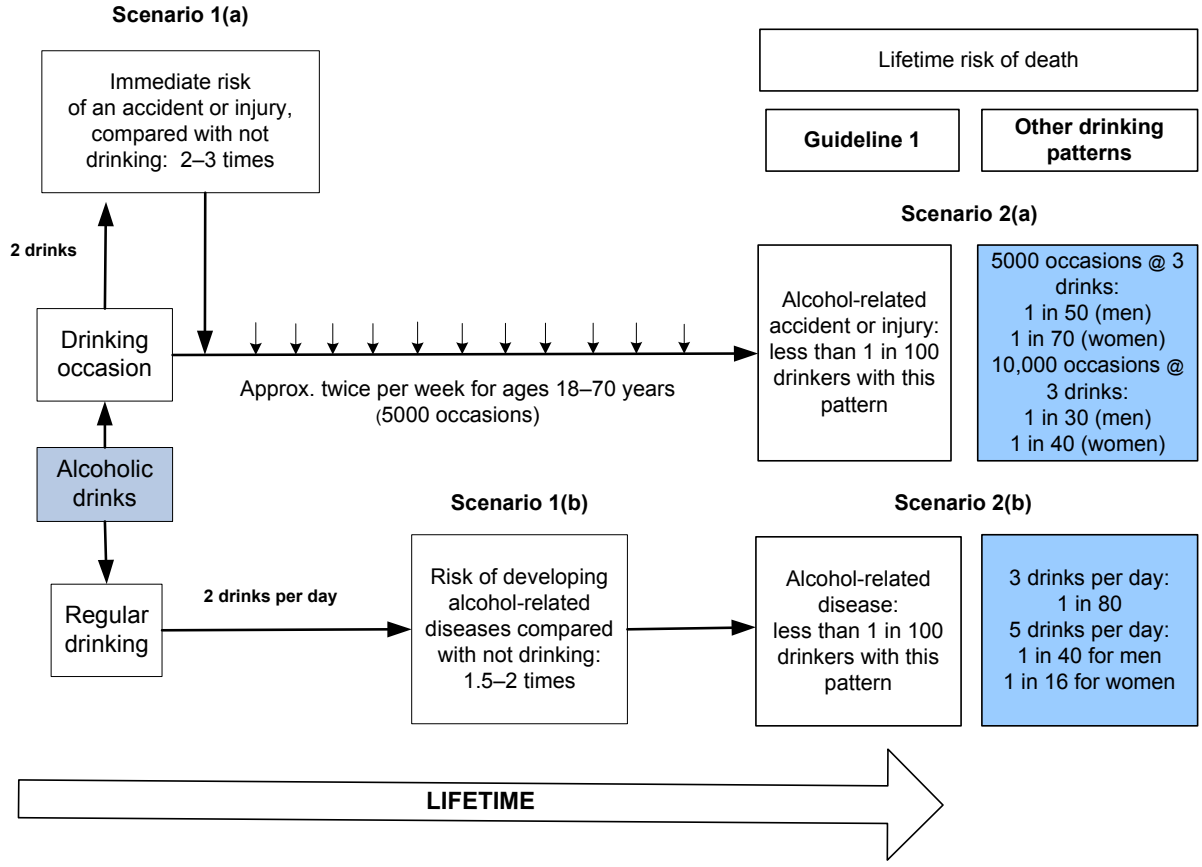
   (a) nonfatal accidents and injuries as a result of a single occasion of drinking at a specific level
   2 standard drinks (1 occasion): 2 to 3 times

   (b) developing one or more of a range of alcohol-related diseases for people drinking on a regular basis at specific levels (eg number of standard drinks per day)
   2 standard drinks per day (regular): 1.5 to 2 times higher

2. The accumulated absolute lifetime risk of:

   (a) death due to an accident or injury as a result of drinking at specific levels on many occasions
   2 standard drinks (twice per week): under 1 in 100

   (b) death from an alcohol-related disease after regular drinking at specific levels
   2 standard drinks per day (regular): under 1 in 100



Note: See Box G1.1 for explanation of scenario numbers

Figure G1.1 Risk scenarios relating to Guideline 1 (two drinks or less on any one day)

Evidence summary

Scenario 1
Risks of alcohol consumption compared with not drinking (relative risks)

1(a) Immediate risk of nonfatal accidents and injuries

Injuries are the leading cause of death for people under 44 years of age and about two-thirds of all injuries involve people under 30 years of age. People over 65 years of age have the next highest risk. Alcohol-related injuries account for between 10% and 20% of all injuries in people over 16–18 years of age (see Appendix 4).

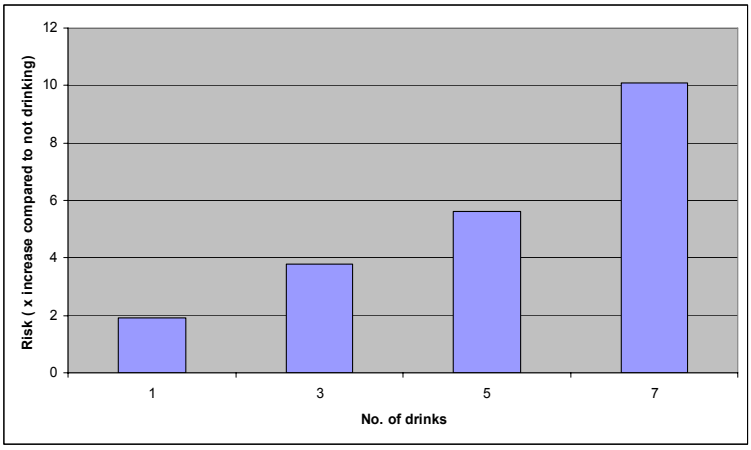
Unlike the long-term health effects of alcohol (such as heart disease, cancer or cirrhosis of the liver) where there have been many epidemiological studies (and, in recent years, several major meta-analyses), the acute effects of alcohol have been less well studied. This is because the large cultural differences in drinking patterns and exposure to potential risk factors make the results of studies from different countries difficult to compare and to combine in meta-analyses.

However, there have been a number of studies of the acute effects of alcohol in injury patients who present to emergency departments and these studies have shown a similar pattern of injury risk (Vinson et al 2003, Borges et al 2004a, Cherpitel et al 2004a, Spurling and Vinson 2005, Borges et al 2006, Gmel et al 2006). A summary of these studies is shown in Appendix 4.

Table G1.1 shows a summary of the relative risk of injury after drinking specific numbers of drinks compared with not drinking (relative risk is explained in Chapter 2, Box 2.1). The table shows that the risk of injury is increased by between about 2 and 10 times after drinking, depending on the amount of alcohol consumed. Borges et al (2006) showed that even after one standard drink, the risk of injury is almost doubled (see graph inset in Table G1.1). These studies also showed that the risk of injury increased more for people whose level of consumption varied significantly from time to time, and was particularly high for those who occasionally drank much more than their usual amount (see Appendix 4).

Table G1.1 also shows that, for any given level of drinking, women have a higher relative risk of injury. However, emergency department studies show that most injuries involve men rather than women, and approximately two-thirds of all patients with an alcohol-related injury are men (see Appendix 4). The majority of cross-sectional studies have also shown that men drink more alcohol than women and therefore suffer more hazardous and harmful effects (Bergman and Kallmen 2002, Seale et al 2002, Worrall et al 2002, Delva et al 2004, Geisner et al 2004, Parry et al 2005), although Flanagan et al (2004) reported no gender difference in lifetime prevalence of regular drinking. As for injuries overall, the emergency department studies show that most alcohol-related injuries involve young people under 30 years of age (see Appendix 4).

Table G1.1 Risk of injury and emergency department visit after drinking, compared with not drinking

Study	Subjects	Number of drinks	Risk (relative risk or odds ratios)		
			Males	Females	All
Vinson et al 2003[a]	2517	Any (case–control)	3.0	3.3	–
	1856			4.2	–
		Any (case-crossover)	3.7		
				1.9	–
		1–2 drinks[b]	1.7		
				6.3	–
		3–4 drinks[b]	6.0		
Cherpitel et al 2004a	938	Any (all injuries)	4.0	5.8	4.3
Borges et al 2004a	961	Any	–	–	4.3
Watt et al 2004[a]	488	Any	–	–	2.1
		Up to 4 drinks (females) Up to 6 drinks (males)	–	–	1.7
		More than 4 drinks (females) More than 6 drinks (males)	–	–	2.4
Watt et al 2006[a]	593	Up to 4 drinks (females) Up to 6 drinks (males)	–	–	1.1
		More than 4 drinks (females) More than 6 drinks (males)	–	–	3.3
Borges et al 2006[ac]	4230	Any	–	–	5.7
				–	
		1	–		1.9
				–	
		3	–		3.8
				–	
		5	–		5.6
				–	
		7+	–		10.1
Borges et al 2006 (contd)					

a These authors reported odds ratios. However, as the risk of injury is low overall, these two measures are very similar
b Drink size not specified
c The original data of Borges et al (2006) has been converted to Australian standard drinks

There have been few studies of the association between alcohol intake and injury type: Watt et al (2005) found no association, while Johnston and McGovern (2004) found an association between alcohol-related falls and craniofacial injury. Several studies have shown a higher proportion of violence-related injuries among those drinking before the incident than for non-alcohol-related injuries (Cherpitel et al 2004a, Borges et al 2004a, Borges et al 2006).

Several studies have investigated the relationship between blood alcohol concentration (BAC) and injury severity, however the results are mixed. Li et al (1997) and Johnston and McGovern (2004) both reported that injury severity increased proportionate to BAC. In a case-control study, Watt et al (2006) found that patients who drank alcohol above low-risk levels or who drank beer in the six hours before being injured were significantly more likely to sustain serious rather than minor injuries. In contrast, Porter (2000) found no significant association between BAC and fatal injuries, and a trend towards decreased injury severity with the presence of alcohol.

Substantial impairment in cognitive function, attention span, and reaction time can also remain well after alcohol has been metabolised and passed from the body as a result of a 'hangover' effect.

Details about the relationship between alcohol consumption and cognitive functioning (including hangover), aggressive behaviour, violence, suicide and self-harm, risk-taking behaviour, mental health, sexual function and sleep are given in Appendix 4.

1(b) Risk of developing alcohol-related diseases

Alcohol consumption has been associated with a range of long-term (chronic) diseases that can reduce quantity and quality of life. These are listed in Chapter 3 and include various forms of cancer, hypertension, haemorrhagic stroke, ischaemic stroke, heart disease, cirrhosis of the liver, alcohol dependence, alcohol-related brain damage and a range of other problems. However, at low levels of consumption, alcohol may also reduce the risks of some diseases: reductions in heart disease, ischaemic stroke, diabetes, gallstones and dementia have all been recorded.

There is a very large literature dating back several decades that has used the best epidemiological data to describe the risks and benefits of alcohol for a range of alcohol-related diseases and disorders. However, alcohol intake was not measured consistently in these studies, making it difficult to compare results. Until the mid-1990s, there was little systematic work done to describe the overall dose–response relationship between alcohol consumption and the risk of disease. In the past 10 years, however, there have been a number of major studies that have combined the data from the major epidemiological studies worldwide to derive the overall impact of alcohol on developing, or dying from, individual diseases and conditions. This approach was first used by English et al (1995) but there have been a number of subsequent studies that have updated this work. Table G1.2 shows the relative risks at different levels of drinking for developing major alcohol-related diseases, based on more recent data from Corrao et al 1999. Further details are given in Appendix 5.

Table G1.2 Relative risks for developing disease conditions by level of drinking (ages 15–60)

Disease	Baseline risk, without drinking[b] (M/F)	Relative risk (by standard drinks per day)[a]						
		1	2	3	4	6	8	10
Lip, oral and pharyngeal cancer	0.65 0.28	1.31 1.33	1.67 1.72	2.08 2.18	2.53 2.69	3.53 3.88	4.58 5.19	5.57 6.51
Oesophageal cancer	0.58 0.14	1.17	1.37	1.61	1.88	2.55	3.42	4.52
Liver cancer	0.45 0.19	1.08	1.15	1.23	1.31	1.48	1.65	1.810
Breast cancer	0.05 6.45	1.08	1.17	1.26	1.36	1.58	1.85	2.15
Hypertensive diseases	0.18 0.16	1.15	1.33	1.53	1.77	2.35	3.12	4.15
Ischaemic heart disease	14.76 3.92	0.82	0.81	0.82	0.84	0.93	1.01	1.13
Ischaemic stroke	0.93 0.88	0.85	0.84	0.94	1.12	1.73	2.21	1.72
Haemorrhagic stroke	1.14 1.07	1.16	1.35	1.57	1.82	2.46	3.32	4.48
Cirrhosis of liver	0.51 0.24	1.21 1.32	1.45 1.73	1.72 2.25	2.02 2.89	2.71 4.64	3.51 7.17	4.38 10.69

a Figures are for men (top) and women (bottom), respectively. If only one relative risk is given, the risk did not vary significantly by sex

b The baseline risk is the overall absolute risk (unrelated to alcohol) of developing the disease per 1000 people aged 15–60 years (eg 0.65 means 0.65 people in every 1000)

Source: Based on data from Corrao et al (1999)

The meta-analysis approach has also been used to assess the risks of death from all the major causes combined. English et al (1995) reported that the relationship between alcohol intake and risk of death from alcohol-related diseases for both men and women drops at low alcohol intake because the risk is reduced compared with not drinking, but then rises sharply as the risk increases (a J-shaped curve). In this study, the lowest observed relative risk for death (approximately 0.8–0.9 times that of nondrinkers; or 10–20% less risk) from all causes was associated with an intake of 1–2 Australian standard drinks per day for men and 0–1 drinks for women (English et al 1995, Holman et al 1996).

Burger et al (2004) reviewed the epidemiological literature up to 1999 to derive 'tolerable upper alcohol levels' for the German population. Based on this review, the levels were set at 10–12 g/day for healthy women and 20–24 g/day for healthy men.

Most recent studies of deaths from all causes have also shown a reduction in the risk of harm with increased alcohol consumption to a maximum of about 17–18% at about 0.5 (half) a standard drink per day for both men and women (for example, Di Castelnuovo et al 2006). This reduction in deaths from all causes is due to the specific reduction of ischaemic heart disease and stroke events; the risk of cancer, cirrhosis of the liver and alcohol dependence all rise linearly with increasing daily alcohol intake. This is reflected at higher alcohol doses, as the risk of harm increases steeply following a J-curve (Corrao et al 1999, Corrao et al 2000,

Gmel et al 2003, Corrao et al 2004, Standridge et al 2004, White et al 2004, Di Castelnuovo et al 2006, White et al 2007).

Some recent analyses have questioned the J-shaped relationship between alcohol and health benefits. Fillmore et al (2006) suggested that studies that classify people who have recently stopped or reduced their drinking as 'abstainers' overestimate the health benefits of alcohol consumption, since those who have recently reduced or stopped alcohol use may have done so because of alcohol-related ill health. When they did meta-analyses only on studies free from misclassification biases, Fillmore et al (2006, 2007) found no significant cardioprotective or all-cause associations. Importantly, Fillmore and colleagues identified the initial study by English et al (1995) as among the studies that introduced systematic misclassification bias.

However, Harris et al 2007 investigated the relationship between usual daily alcohol intake, beverage type and drinking frequency on cardiovascular (CVD) and coronary heart disease (CHD) mortality in a prospective cohort study (11.4 years) that accounted for systematic misclassification of intake. The Melbourne study had a total of 38,200 volunteers (23,044 women) aged 40–69 years at baseline (1990–94) and measured self-reported alcohol intake using beverage-specific quantity–frequency questions (usual intake) and a drinking diary for the previous week. Usual daily alcohol intake was associated with reduced CVD and CHD mortality for women but not men. This benefit appeared to be mainly from wine, although comparison of beverages was not possible. Drinking frequency was associated inversely with CVD and CHD death for men but not women. However, the international clinical consensus is that people should not take up or maintain drinking for health benefits (see Section 1.1).

White et al (2007) also assessed how the relationship between alcohol consumption and risk of death varied with age and sex (see Appendix 8, Table A8.1). They found that, for young people under 35 years, there was no risk reduction from drinking alcohol at any level and that the level of alcohol consumption corresponding to the lowest mortality rates gradually increases with age after that time. The analysis also showed that the relative risk of alcohol consumption, compared to not drinking, decreased most markedly with age for men: for about 16 standard drinks per week, the relative risk dropped from about 1.2 at 16–24 years, to 1.0 at 45–54 years (see Appendix 8, Table A8.1).

Scenario 2
Absolute lifetime risk

2(a) Lifetime risk of death due to an alcohol-related accident or injury

As described in Section 2.5 the Australian Government Department of Health and Ageing (DoHA) commissioned a modelled approach to determine the accumulated lifetime risk of death from alcohol-related road traffic accidents, poisoning, fall, fire, drowning, suicide, violence (homicide), and other unintentional or intentional injuries.[5] Lifetime risk was calculated for an increasing number of drinks per occasion and for various numbers of occasions over a lifetime. Details of the modelling are shown in Appendix 6.

[5] Rehm J, Taylor B, Patra J and Room R. Determination of injury mortality risk by volume and number of drinking occasions, Unpublished paper, Centre for Addiction and Mental Health, Toronto, Canada, July 2007.

Table G1.3 Examples of lifetime drinking patterns

Drinking occasions	Lifetime drinking scenarios (examples only)
100	One or two times per year for ages 18–70 Approximately once per month for ages 18–25
500	Approximately once per month for ages 18–25 then decreasing to 3–4 times a year to age 70
1000	Approximately once per week for ages 18–25 years decreasing to once per month to age 70
5000	Approximately twice per week for ages 18–70 years
10 000	Every other day for ages 18–70 years
20 000	Most days for ages 18–70 years

Table G1.3 shows the relationship between numbers of drinking occasions and some possible lifetime drinking scenarios. Figure G1.2 shows the lifetime risks for men and women drinking at specified levels on 5000 occasions. For this number of occasions, for both men and women, the risk of alcohol-attributable injury death is below 1 in 100 if they drink more than two drinks per occasion. Figure G1.2 shows the increasing risks at 10 000 and 20 000 occasions.

These estimates are conservative in the sense that they are based on studies of nonfatal injuries. The relevant literature indicates that injuries tend to be more severe when alcohol is involved, and thus the relative risks and proportion of alcohol-related injuries are larger for fatal compared with nonfatal injuries (Rehm et al 2004). On the other hand, basing these estimates on emergency room studies may have led to an overestimate of the effects, because people who attend emergency rooms with injuries do not represent the general population. They may be characterised as more risk taking, and thus the risk for alcohol in this population may be higher than in the general population. Unfortunately, data are not available to assess this potential effect.

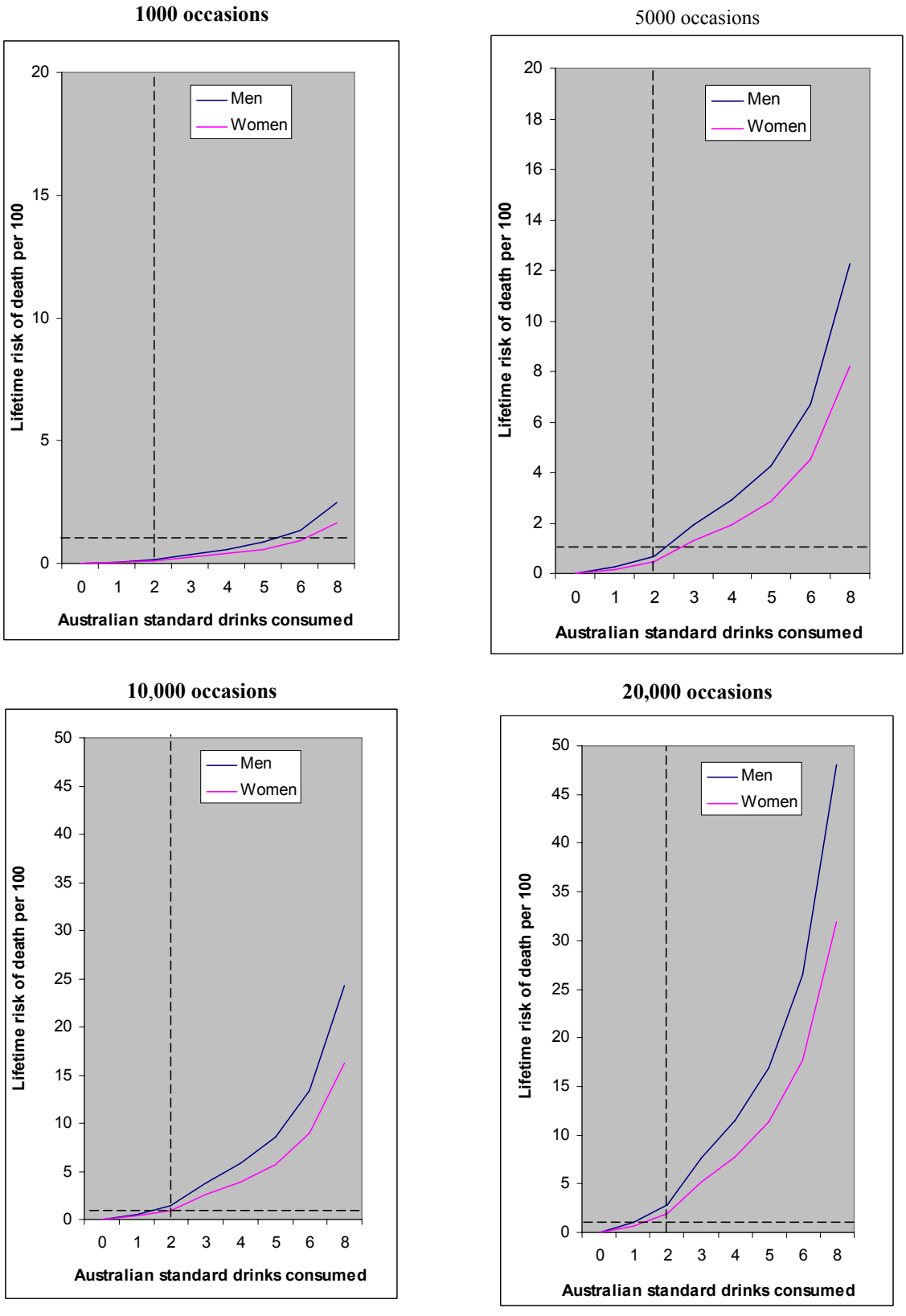


Figure G1.2 **Lifetime risk of death from an accident or injury for drinking at different levels (standard drinks) for 1000, 5000, 10,000 and 20,000 drinking occasions, per 100 drinkers with that drinking pattern**

2(b) Lifetime risk of death due to an alcohol-related disease

As for the accident and injury data above, DoHA commissioned modelling of the accumulated lifetime risk of death from a range of alcohol-related diseases.[6] The diseases included in the study were those where accepted causal and detrimental effect of alcohol consumption has been shown: lip, oral and pharyngeal cancer, oesophageal cancer, liver cancer, breast cancer, hypertensive diseases, ischaemic heart disease, ischaemic stroke, haemorrhagic stroke, cirrhosis of the liver, alcohol use disorders (Rehm et al 2003, Baan et al 2007). The modelling used the relative risks of developing each disease at different levels of drinking, compared to not drinking, to derive the proportion of deaths attributable to alcohol for each disease. These figures were then applied to age-specific death rates for each disease in Australia to determine the lifetime risks. Details of the relative risks, alcohol attributable fractions and calculations are shown in Appendix 7.

The results are shown in Figure G1.3 as the lifetime absolute risks of alcohol-related disease deaths per 100 people who drink at each level (in terms of the number of standard drinks consumed per day). As the average volume of alcohol consumption increases, the lifetime risk of death from alcohol-related disease increases for both men and women. A lifetime risk of 1 in 100 people drinking at that level is achieved at between 2 and 3 drinks per day for men and women. Above 2 drinks per day, the lifetime risk increases sharply for both men and women, and the lifetime risk for women increases to about 20–30% above that for men at 3–4 standard drinks to an almost two-thirds (66%) higher risk than men at 10 standard drinks per day. Overall, the risk for women increases by approximately 10% per standard drink per day consumed.

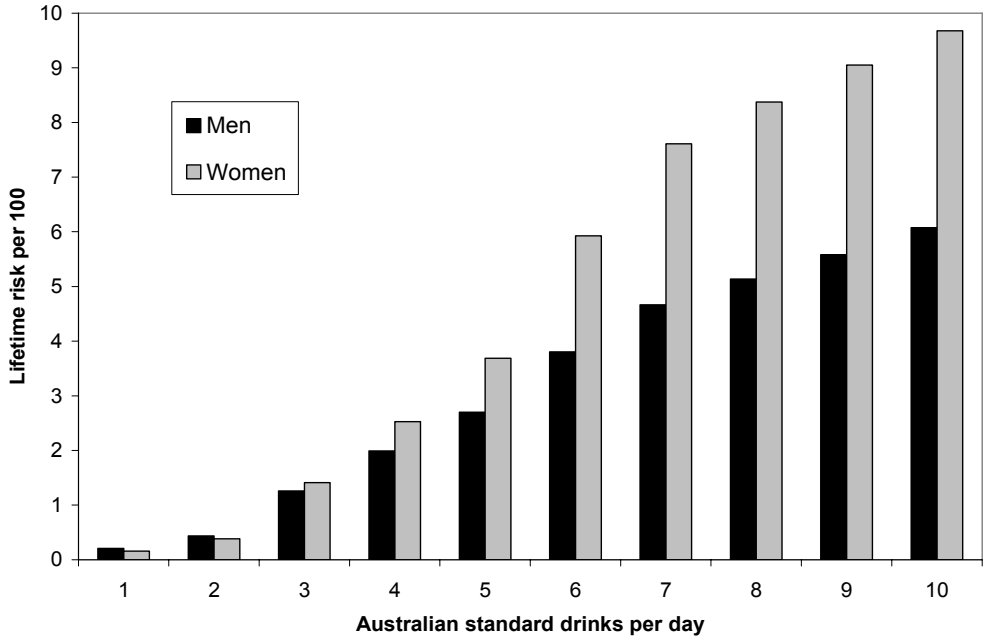


Figure G1.3 Lifetime risk of death from an alcohol-related disease, by number of standard drinks per day, per 100 people with that drinking pattern, Australia 2002

[6] Taylor B, Rehm J, Patra J and Room R. Determination of alcohol-attributable lifetime risk for chronic conditions for different levels of average consumption, Unpublished paper, Centre for Addiction and Mental Health, Toronto, Canada, July 2007.

This approach has some limitations. First, life expectancy and the absolute risk of mortality from diseases are both based on one year of Australian data (2002) and may therefore change over time. However, as these parameters do not change much in the short term, this should not bias the outcome. Second, the results also assume that the relative risks are the same in Australia as in the countries where the studies included in the meta-analyses have been done (predominantly the United States and the United Kingdom). However, the effects of alcohol on alcohol-related diseases are mainly based on biological mechanisms, and there is no reason to believe that this will be different in different countries that have a similar genetic make-up. However, the relative risks from the meta-analyses are clearly estimates, and the real risks may fluctuate to a certain degree, although applying different relative risk estimates from different authors to the data did not change the results noticeably (Rehm et al 2007).

Guideline 2 Special precautions for children and young people under 18 years of age

Guideline 2 **For children and young people under 18 years of age**	
2.1	Parents and carers are advised that not drinking is the safest option for children and adolescents under 15 years of age.
2.2	Not drinking is the safest option for adolescents aged 15-17 years. If drinking does occur, it should be under parental supervision and within the adult Guideline for low-risk drinking (two standard drinks or less in any one day).

Rationale

This guideline applies to children and adolescents up to 18 years of age and provides guidance for parents and carers, as well as for the young people themselves, about the safest option to prevent alcohol-related harms during these years.

The NHMRC was aware that there is a range of views about the optimal age to start drinking, and that a number of cultural groups in Australia introduce children to small amounts of alcohol at an early age. However, Guideline 2 is based on an assessment of the potential harms of alcohol for this age group, as well as a range of epidemiological research that, although not conclusive, indicates that alcohol may adversely affect brain development and be linked to alcohol-related problems later in life.

As for adult drinking, based in the epidemiological data, it was not possible to set a 'safe' or 'no-risk' drinking level for children and adolescents. However, it is clear that the safest option for children and younger teenagers is to not drink at all and the safest option for older teenagers (15–17-year-olds) is to delay the initiation of drinking for as long as possible.

Serving drinks to young people under the age of 18 years by parents, carers or other adults is the subject of legislation in each state and territory. Supervision of drinking by young people therefore needs to take account of these local restrictions.

Analysis of risks

The principles used to set Guideline 2 are described in Section 2.3. The key points from the analysis are shown in Box G2.1. A summary of the evidence that underpins these findings is provided below.

Box G2.1 Analysis of the risks of drinking by children and adolescents

- Risks of accidents, injuries, violence and self harm are high among underage drinkers.
- Risk-taking behaviour, unsafe sex choices, sexual coercion and alcohol overdose increase when adolescents drink alcohol.
- Initiation of alcohol use at a young age may increase the likelihood of negative physical and mental health problems, social problems and alcohol dependence.
- Childhood and adolescence are critical times for brain development and the brain is more sensitive to alcohol-induced damage during these times, while being less sensitive to cues that moderate alcohol intake.
- Self-reported harm scores show that 12–14-year-olds report the highest levels of harm per litre of alcohol consumed of any age group (4–5 times that of 40–44-year olds), with 15–17-year-olds reporting more than twice as much harm as 40–44-year-olds.

Evidence summary

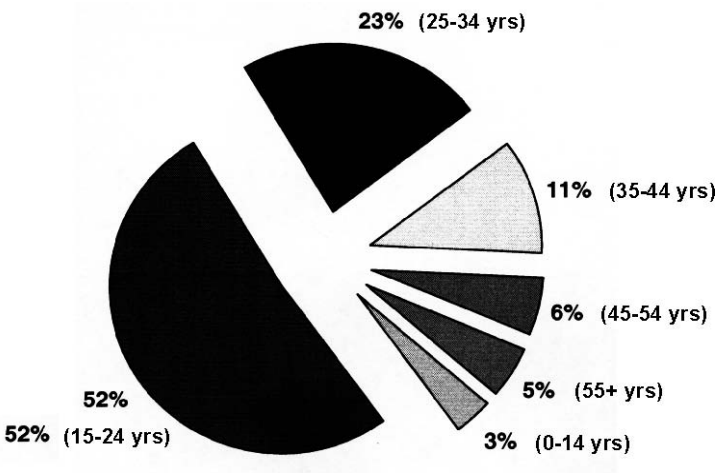
Risk of injury and self-harm

Underage drinking contributes to the three leading causes of death among adolescents — unintentional injuries, homicide and suicide (Stephens 2006, Miller et al 2007). Between 1993 and 2001, 28% of all alcohol-related injury deaths and more than one-third (36%) of alcohol-related injury hospitalisations were sustained by young people aged 15–29 years (Chikritzhs et al 2003) and about half (54%) of all serious road injuries involve young people (see Figure G2.1).

Alcohol consumption as an adolescent or young adult is also associated with physical injury, risky sexual behaviour, adverse behavioural patterns and academic failure (Bonomo et al 2001, Zhang et al 2002, Abbey et al 2003ab, Barnett et al 2003, Howard et al 2003, Vinson et al 2003, Johnson and Stahl 2004, Swahn et al 2004, Coleman and Carter 2005, Kebede et al 2005, Mora-Rios et al 2005, Boyd et al 2006, Davis et al 2006, Dye and Upchurch 2006, Fallu et al 2006, French and Maclean 2006, Kaysen et al 2006, Shepherd et al 2006).

A nationwide survey of teenagers in Finland found that 13% of 14-year-olds, 41% of 16-year-olds and 62% of 18-year-olds reported being under the influence of alcohol during a violent incident (Mattila et al 2005). Similarly, an American cohort study found 11% of youths reported being influenced by alcohol during a fight. These individuals were significantly more likely than their sober counterparts to injure others or sustain an injury during the fight (Kodjo et al 2004). A register-based retrospective cohort study of 334 000 adolescents in Sweden showed that alcohol was significantly associated with the severity of motorcycle-related injury (Zambon and Hasselberg 2006).

The prevalence of risk-taking behaviours increases in adolescence and the likelihood of injury increases further still when alcohol is also involved. A recent study of high-school students found a strong dose–response relationship between binge-drinking and risky behaviours, including riding in a car with an intoxicated driver and using illicit drugs (Miller et al 2007). The United States National Youth Survey (Swahn and Bossarte 2007) showed that alcohol use in adolescents, and particularly in pre-teenagers, is a strong predictor of both suicidal ideation and completed suicide for both males and females.



Source: National Alcohol Indicators Bulletin 2, May 2000 (Chikritzhs et al 2000)

Figure G2.1 Overall age distribution among alcohol-related serious road injuries occurring on Australian roads (excluding Victoria), 1990–1997

A particular concern is the increase in adolescent risky sexual behaviour when alcohol is involved (Coleman and Cater 2005). Results from a prospective cohort study in America have shown that use of alcohol decreases the likelihood that adolescents will use a condom, especially at their first sexual experience (Dye and Upchurch 2006). However, a diary study of young adults showed that when young people expect to get drunk, they plan for sexual activity that may occur (Leigh et al 2007).

Adolescents who drink alcohol are at risk of sexual coercion (Davis et al 2006). A controlled trial in which 180 youths were given either an alcoholic beverage or a placebo and asked to give their opinion about a hypothetical sexual situation showed that intoxicated participants viewed the woman in the vignette as more aroused, and the man as more justified in his attempts to force the woman to have intercourse with him (Abbey et al 2003a).

Death by alcohol overdose in adolescents is also a risk, due to their generally smaller physique, preference for drinking spirits and lower alcohol tolerance. A recent emergency-department surveillance study found that 56% of poisonings admissions were due to acute alcohol intoxication (Cheng et al 2006). Although alcohol is often used by depressed and suicidal adolescents as a means of self harm or an attempt on their life, unintentional alcohol poisoning is also common (Cheng et al 2006).

Age of first drinking

Several studies have indicated that initiating alcohol use at an early age increases the likelihood of later adverse physical and mental health problems (Hemmingsson and Lundberg 2001, Hingson et al 2003, Guilamo-Ramos et al 2004, Toumbourou et al 2004, Wells et al 2004, Jefferis et al 2005). Hingson et al (2003) showed that those who first became drunk by 19 years were more likely to be alcohol dependent and heavy drinkers in later life; while Wells et al (2004) reported that drinking status at 16 years is a predictor of negative alcohol outcomes as a young adult. Both Hingson et al (2006) and Toumbourou et al (2004) demonstrated that teens who were drinking by 14 years were more likely to experience alcohol dependence than their peers who did not drink until they were over 21 years old. A recent study by Warner et al (2007) found that both age of drinking onset and

feeling drunk during first alcohol experience increased the odds of problem drinking into adulthood. Furthermore, this level of risk was higher in men than women (Pitkanen et al 2005).

However, the way in which adolescents are introduced to alcohol may affect future drinking patterns. A national cross–sectional survey of adolescents (Foley et al 2004) found that provision of alcohol to adolescents by their parents or adult relatives at home reduced the level of underage drinking. However, providing alcohol to adolescents at a party was associated with a two-fold risk of binge-drinking (Foley et al 2004).

Many authors have suggested that strategies to minimise risk for young people are of crucial importance, and learning about drinking and its effects is central in fostering drinking behaviour that minimises or contains risk (Bailey et al 2004, Barnow et al 2004, Weinberg and Wyatt 2006).

Effect on brain development

Although the prevalence of alcohol use disorders in adolescents is high, human studies that show the effects of alcohol consumption on brain development during this period are scarce. Much of the information about the effect of alcohol on brain development is drawn from studies of animal models. Animal research has shown that young animals are more sensitive to ethanol-induced disruptions in brain plasticity and are also less sensitive to cues that serve to moderate alcohol intake (Spear 2004).

In a study of adolescent and adult rats, Crews et al (2000) found that the effects of a four-day alcohol binge were worse for adolescent rats. Although brain damage was found in both age groups, substantial frontal lobe deterioration was observed only in adolescent rats.

Human studies are largely limited to adolescents with alcohol use disorders, who display significant and detrimental changes in brain development compared with their non alcohol-using peers. Studies of these young people have shown that significant changes in brain structure accompany heavy drinking. Alcohol-abusing adolescents tend to have smaller pre-frontal cortices and white matter volumes — an effect more pronounced for males than females (De Bellis et al 2005). White matter structural irregularities and reduced hippocampal volumes have also been observed (Brown and Tapert 2004). It has been shown that hippocampal function is uniquely responsive to alcohol during adolescent development and may be more sensitive to neurotoxicity during this period (White and Swartzwelder 2004).

Adolescent drinking is associated with diminished retrieval of verbal and nonverbal material, and poorer performance on attention-based testing (Brown and Tapert 2004). Brown and Tapert (2004) suggest that physiological effects of alcohol withdrawal over the teen years contribute to deterioration in cognitive functioning in visuospatial tasks. Cognitive impairment is also common in young adults with alcohol dependence (Kelly and Witkiewicz 2003).

Mental health

Alcohol use, especially when initiated early, elevates the risk for a multitude of mental health and social problems (Brown and Tapert 2004). The existence of psychiatric comorbidities in adolescents who abuse substances is common, especially for conditions such as depression, anxiety, bipolar disorder, conduct disorder and attention-deficit/hyperactivity disorder (Turner and Gil 2002, Brown and Tapert 2004, Chen et al 2006, Deas and Brown 2006, Cargiulo 2007).

The nature of the relationship between alcohol use and mental health in adolescence is somewhat reciprocal. Youths with certain mental health disorders are more likely to initiate alcohol use and accelerate their use throughout adolescence (Brown and Tapert 2004). In turn, alcohol use may contribute to poor mental health.

In a random sample of more than 27 400 college students from across America, Weitzman (2004) found that students with poor mental health were likely to report frequent, heavy and heavy episodic drinking and were also more likely to drink with the intent of getting drunk. In a similar study, Geisner et al (2004) found that the association between psychological distress and negative drinking consequences was greater for male college students than females.

One of the major complications of adolescent alcohol use is self-harm, having suicidal thoughts and suicide (Miller et al 2007). Alcohol use disorders, in conjunction with major depression, represent an especially high risk profile for adolescent suicidal behaviour and completed suicide (Sher 2006). In addition, those adolescents with alcohol use disorders tend to complete suicide at a greater rate than those without alcohol problems (Sher 2006). It has been suggested that those adolescents who use drinking as a method of coping are more likely to suffer from depression, which precipitates binge-drinking. Binge-drinking is predictive of suicidal behaviour (Windle 2004).

Self-reported harm scores

The guideline development committee considered the level of harm caused by a given level of drinking for different age groups using data from the National Drug Strategy Household Survey (NDSHS) for 2004 (AIHW 2005).

These data were used to derive harm scores from the series of questions on self-reported problems from drinking, with one point assigned for each positive response concerning the past 12 months.[7] The harm items used for NDSHS were as follows:

- In the past 12 months, did you undertake the following activities while under the influence of alcohol?
  - Went to work
  - Went swimming
  - Operated a boat
  - Operated hazardous machinery

[7] Room R and Livingston M. Variation by age in the harm per drinking volume and heavier drinking occasion. AER Centre for Alcohol Policy Research, Turning Point Alcohol and Drug Centre, Fitzroy, Vic; revised September 2007.

- Created a public nuisance or disturbance
- Caused damage to property
- Stole money, goods or property
- Verbally abused someone
- Physically abused someone.

Figure G2.2 shows results for a harm index (the score divided by the volume of drinking), presented as a ratio with the score at 40–44 years set as 1.0. The index is much higher for 12–14-year-olds than for any other age group, and at 15–17 years is still more than twice as high in both sexes as for 40–44-year-olds. After this there is a long and steady decline in the index with increasing age. Generally, the harm index is similar for males and females at a given age, although slightly higher for females at ages 12–14 and for males at ages 18–19, compared with the same sex at 40–44 years.

The NHMRC also considered the pattern of harm scores per volume of drinking among the minority of drinkers at each age who reported drinking no more than one or two drinks on any occasion. The proportion limiting their drinking in this way was 22% among 12–14-year-olds, fell as low as 7% among 18-19-year-olds, and then gradually rose to 39% among 75–79 year olds. In this minority of drinkers keeping their drinking within Guideline 1, the drinking-related harm scores were of course low. But the patterning of the harm index by age again showed a much higher value among 12–14-year-olds, and a somewhat higher value among 15–17-year olds, than among older respondents (Figure G2.3).

Taken together, the analyses suggest that drinkers under the age of 15 years are much more likely than older drinkers to experience risky or antisocial behaviour connected with their drinking, providing the basis for Guideline 2.1. The rates are also somewhat elevated among drinkers aged 15–17 years, warranting the recommendation for caution (Guideline 2.2). The analyses further show that to a lesser extent drinkers in their late teens and their 20s are also showing a propensity to get into more trouble per unit of alcohol than their elders.

These results support the findings of White et al (2007), who showed that the overall relative risk of drinking, compared to not drinking, was highest for 16–24-year olds and decreased progressively in older age groups (see Guideline 1, Evidence summary and Appendix 8, Table A8.1)

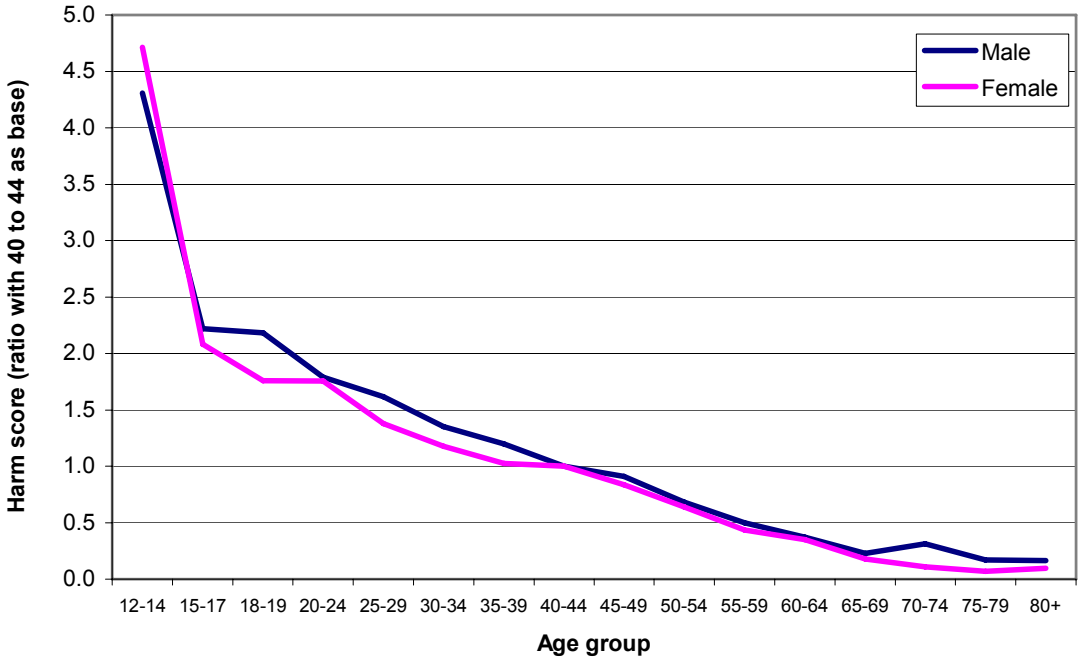


Figure G2.2 Harms index by volume of drinking, by age for males and females

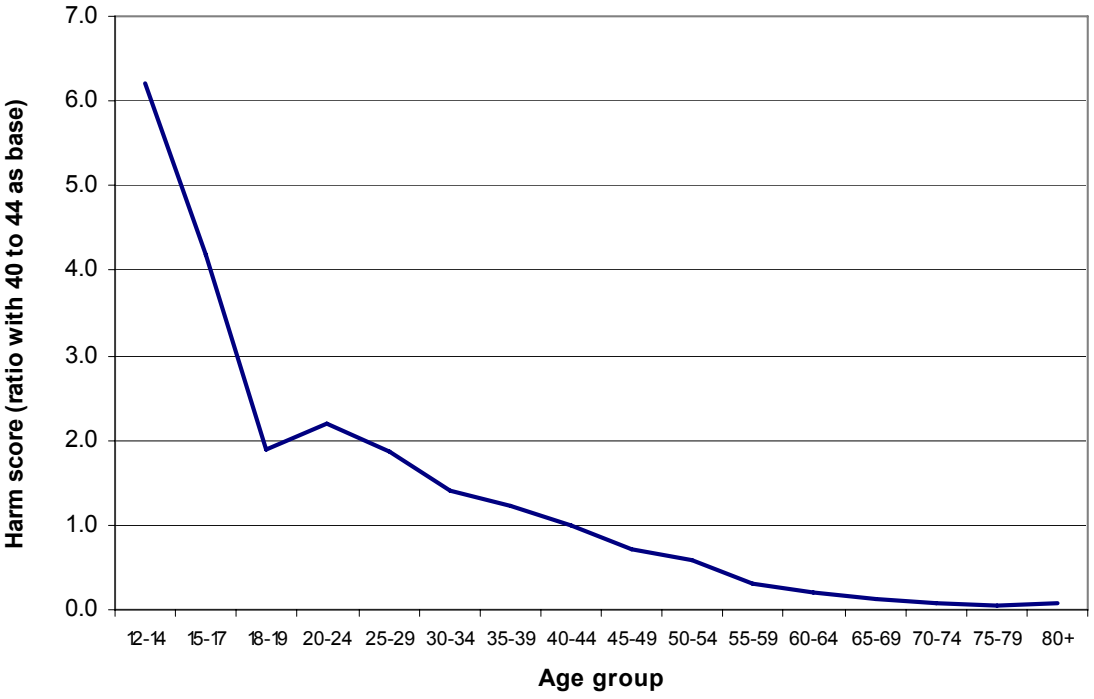


Figure G2.3 Harms index by drinking occasions of less than three drinks, by age (males and females combined)

Guideline 3 Special precautions concerning pregnancy and breastfeeding

Guideline 3 **For women who are pregnant, are planning a pregnancy or are breastfeeding**
3.1 Not drinking is the safest option.

Rationale

This guideline applies to women who are pregnant, planning a pregnancy, or who are breastfeeding. It is based on an assessment of the potential harms of alcohol for the developing fetus and for young babies during the breastfeeding period.

Alcohol readily crosses the placenta. It is a well-known teratogen (ie it can cause birth defects), is toxic to the fetus and can damage the developing brain. In humans, exposure of the fetus to alcohol may result in a spectrum of adverse effects, referred to collectively as fetal alcohol spectrum disorder (FASD). In addition, high-level and/or frequent intake of alcohol in pregnancy increases the risk of miscarriage, stillbirth and premature birth, and may reduce the growth rate of the developing fetus. These conditions can be prevented by avoiding alcohol during pregnancy.

As with alcohol exposure at other ages, the harm caused to a developing fetus or newborn baby increases with the dose of alcohol. The most serious of the adverse pregnancy outcomes occur when pregnant women consume high levels of alcohol frequently, particularly during the first trimester (including the time before the pregnancy is confirmed). The effect of low-to-moderate alcohol consumption, on the other hand, is the subject of current debate and research. It has been suggested that low-to-moderate intakes may result in adverse neurodevelopmental and behavioural outcomes. However, interpretation of the existing literature is hampered by methodological problems, including accurate documentation of alcohol intake during pregnancy and breastfeeding, and failure to adjust for other confounding factors. Furthermore, predicting risk for an individual is difficult because of confounding factors such as maternal age, nutrition, previous alcohol use, polydrug use and maternal and fetal genetics, which can modify the effect of alcohol on the unborn child.

Hence, although the risks from low-level drinking (such as one or two drinks per week) during pregnancy and breastfeeding are likely to be low, a ‘no-effect’ level has not been established, and it is therefore impossible to set a ‘safe’ or ‘no-risk’ drinking level for pregnant and breastfeeding women to avoid harm to their unborn fetus or young baby. This uncertainty is reflected in policy regarding alcohol use in pregnancy within Australia and overseas (O’Leary et al 2007). Most policies stress that heavy drinking or intoxication pose the greatest risk and several stress that a safe level has not been established and that not drinking is the safest option. This is in line with the regulation of medications, where any evidence of reproductive toxicity (ie during gestation or breastfeeding) results in a warning to avoid these substances at these times.

Analysis of risks

The principles used to set Guideline 3 are described in Section 2.3. The key points from the analysis are shown in Box G3.1. The evidence summary focuses on the recent literature with an emphasis on adverse outcomes relating to low-to-moderate levels of alcohol intake. The analysis is based on systematic reviews and prospective cohort studies, which provide the highest level of evidence for the risks of alcohol consumption during pregnancy. Further details are shown in Appendix 8.

Box G3.1 Analysis of the risks of drinking during pregnancy and breastfeeding

- Alcohol is a teratogen and toxic to the developing fetus. High levels may cause miscarriage, stillbirth, growth retardation, fetal alcohol syndrome, birth defects, and neurological, cognitive and behavioural problems.
- Heavy drinking or intoxication pose the greatest risk but some recent studies suggest that even low levels of alcohol consumption may adversely affect neurodevelopmental and behavioural outcomes.
- Alcohol enters the breastmilk and may adversely affect lactation, infant behaviour (eg feeding, arousal) and psychomotor development of the breastfed baby.
- The relative risk of drinking during pregnancy or breastfeeding (compared to not drinking) has not been determined across a range of drinking levels. Hence, a safe ('no-effect') level has not been established on a population basis. Furthermore, individual factors mean that actual risks vary considerably from one person to another.
- Pharmaceutical products or other chemical agents that show any toxicity to developing fetuses or infants, even at very low levels of exposure, are not permitted to be used during pregnancy or breastfeeding.

Evidence summary

Drinking during pregnancy and breastfeeding

Rates of drinking, and of drinking at levels likely to cause harm, are increasing in Australian women. Rates of drinking during pregnancy are high. In a 2004 national survey, 47% of women reported drinking during pregnancy and breastfeeding. In a Western Australian survey, 59% reported drinking during pregnancy, of whom 14% had a heavy drinking session in the three months before pregnancy and 15% had drunk at above the level recommended in the NHMRC guidelines during the first trimester (Colvin 2007). In the same survey, 47% of pregnancies were unplanned, indicating that many fetuses may inadvertently be exposed to alcohol before pregnancy is confirmed.

Fetal alcohol spectrum disorders in Australia

A recognisable pattern of malformations called fetal alcohol syndrome (FAS) has been described in children exposed to high levels of alcohol in utero (Lemoine et al 1968, Jones et al 1973, Hoyme et al 2005, Astley and Clare 2000). These children have characteristic facial abnormalities, impaired growth and abnormal function or structure of the central nervous system. They experience lifelong problems, including learning difficulties and disrupted

education, increased rates of mental illness, drug and alcohol problems and trouble with the law (Streissguth et al 2004). A number of other alcohol-related birth defects (ARBD) and alcohol-related neurodevelopmental disorders (ARND) have also been described following exposure to alcohol during pregnancy (Lemoine et al 1968, Jones et al 1973, Hoyme et al 2005, Astley and Clare 2000). Collectively these conditions constitute fetal alcohol spectrum disorders (FASD).

Damage to the fetus depends on the quantity, frequency and timing of alcohol consumption and is influenced by maternal factors. For example, FAS and ARNB usually occur after high levels of alcohol consumption early in pregnancy (during early embryogenesis). It is therefore particularly important for women who are pregnant or planning to become pregnant to avoid drinking alcohol at levels sufficient to cause intoxication. Later exposure to alcohol, in the third trimester of pregnancy, may be related to damage to the cerebellum, hippocampus and prefrontal cortex (Riley and McGee -2005).

FAS continues to occur in Australia (Bower et al 2000, Harris and Bucens 2003, Elliott et al 2006). However, rates are likely to be an underestimate due to lack of clinician knowledge about the condition and how to manage it and fear of stigmatising the family and child (Payne et al 2005, Elliott et al 2006). In Australia FAS rates are higher in Indigenous than in non-Indigenous communities. Many affected children are in foster care; many others have an affected sibling suggesting missed opportunities for prevention (Elliott et al 2006). Rates of ARBD and ARND in Australia and rates of miscarriage, stillbirth, prematurity and intrauterine growth retardation attributable to alcohol are not known.

Pregnancy outcomes (miscarriage, stillbirth, prematurity, intrauterine growth retardation, post-natal growth)

Research in both humans and animals has shown that alcohol is toxic to the developing fetus and that maternal drinking at high levels results in miscarriage, stillbirth, growth retardation, fetal alcohol syndrome, alcohol related birth defects and neurological, cognitive and behavioural effects (NHMRC 1999, 2001). The effects of exposure to lower levels of alcohol are a subject of current debate. Some recent studies suggest that even low levels of alcohol consumption may adversely affect pregnancy outcomes, particularly neurodevelopmental and behavioural outcomes.

A systematic review of case-control and cohort studies (Polygenis 1998) found no increase in fetal malformations with moderate alcohol consumption (between 28 grams of alcohol [about 3 drinks] per week and about 3 drinks per day) in the first trimester compared to an intake below this level (OR 1.01; 95% CI 0.94 to 1.08). However, the authors acknowledged the difficulty faced by researchers in accurately estimating alcohol intake from self-reports (due to underreporting and recall bias). Of 24 studies identified as potentially relevant for the review, they excluded 16 because of problems with data quality, including failure to quantify alcohol intake, use of different definitions of malformation, and inability to identify controls and to adjust for confounders. The authors also cautioned against causing unnecessary anxiety in pregnant women who have consumed alcohol during pregnancy but also stated that although the risk of major malformations was not found to be associated with 'moderate' alcohol intake 'the results are not intended to justify drinking in pregnancy' (Polygenis 1998).

A systematic review by Henderson et al (2007) identified a number of good-quality studies that evaluated adverse pregnancy outcomes, including miscarriage, stillbirth, premature birth,

intrauterine growth retardation (small for gestational age) and birth defects including FAS, where the level of alcohol consumed during pregnancy was well enough defined to make dose comparisons. The studies showed no increase in the above adverse pregnancy events at low-to-moderate prenatal alcohol exposure (defined as up to about 80 g alcohol, or 8 standard drinks, per week). However, the studies were not robust enough to conclude that this level of alcohol intake during pregnancy is safe. This review did not address developmental, cognitive or behavioural outcomes.

In a prospective cohort study of over 18,000 women, Kesmodel et al (2001) found a J-shaped relationship between prenatal alcohol intake and preterm delivery. After adjusting for confounders, the risk of preterm delivery was significantly increased with an intake of 5 or more drinks per week at 16 weeks gestation and 1–2 drinks per week at 30 weeks gestation. In over 40,000 pregnancies Albertsen (2004) found no association with prematurity at intakes below 4 drinks per week.

A prospective cohort study by Kesmodel et al (2002a) reported a five-fold increase in risk of spontaneous abortion when five or more drinks per week were consumed in the first trimester. However, this group included all the women who reported drinking at a level of 5–40 drinks per week, so it is difficult to draw any conclusions about the effect of the lower doses. Lower levels of alcohol consumption in the first trimester, or drinking at any level in the second trimester, were not associated with increased risk of spontaneous abortion.

Covington et al (2002), in a large prospective cohort study, found that after controlling for potential confounders, alcohol exposure independently predicted low birth weight and length. Furthermore, children of women aged 30 years or more and exposed to moderate-to-high levels of alcohol were five-times more likely to fall below the tenth percentile for weight at age seven.

In a prospective cohort study of adolescents aged 14 years who had been exposed to an average of three or more drinks per week in the first trimester, Day et al (2002) found a significant decrease in weight, height, head circumference and skin-fold thickness compared with controls (who consumed less than three drinks per week). There was a dose-response relationship between growth deficit and prenatal alcohol exposure; effects on growth were detectable at average intakes of below one drink per day; and effects were most marked with exposure in the first trimester.

Facial malformation

Prenatal exposure to high levels of alcohol is known to cause facial dysmorphology. Van der Leeden et al (2001) confirmed previous findings, showing significant differences in facial features in alcohol-exposed and unexposed children at three months, but not seven months of age.

Neurodevelopment

Wass et al (2001) found using ultrasound in utero that prenatal exposure to alcohol independently reduced the size of the frontal cortex but not of other brain structures This finding was dose-dependent; was observed at intakes of 2–6 drinks per day, and was most

marked in mothers aged 30 years or more. This finding is consistent with impairment of executive function, working memory and attention observed in children with FASD.

Carter et al (2005) found a dose relationship between prenatal alcohol exposure and decreased visual acuity in infants. An effect was observed at an intake of one or more drinks per day and was more evident in mothers aged 30 years or more. De los Angeles Avaria et al (2004) found that prenatal alcohol exposure damaged the developing peripheral nervous system, indicated by a significant reduction in nerve-conduction velocity and amplitude that persisted at one year of age. Hepper et al (2005) found delayed maturation of spontaneous startle behaviour in fetuses exposed to alcohol than in non-exposed fetuses and a persistent effect on startle behaviour at term. It is suggested that alcohol affects the neurological pathways controlling startle behaviour. Women were included in the study group if they consumed at least 10 g of alcohol (1 drink) for the duration of their pregnancy (the mean intake was 40 g per week).

Neurobehaviour and cognition

Testa et al (2003) published a systematic review of mental development in infants following different levels of prenatal alcohol exposure (less than one drink per day, 1–1.99 drinks per day and two or more drinks per day). After adjusting for confounding, drinking during pregnancy had a significant, negative, linear (dose-dependent) impact on mental development in children aged 12–13 months. Although trends were similar in children aged 6–8 months and 18–36 months the decrease in mental development index was not significant in these age groups. This may reflect different methods of assessment for different ages and difficulty in accurately documenting alcohol intake. The authors concluded that 'because the literature is neither large nor conclusive, and because of heterogeneity in measurement, analysis and samples, caution is urged in interpreting results.'

In addition to this systematic review, the effect of prenatal alcohol exposure on neurobehaviour and cognition has been investigated in a number of prospective studies. In a small study, Van der Leeden et al (2001) identified neurological abnormalities in 7-month-old infants exposed prenatally to alcohol. However, infants whose mothers consumed from 20 g to more than 110 g alcohol per week were pooled in the analysis, making an assessment of response at lower doses impossible. Burden et al (2005b) showed that, compared with controls, children exposed prenatally to alcohol (as more than 14 g absolute alcohol per day) had deficits in working memory and executive function but not impulsivity or sustained attention at 7.5 years of age. The effect increased with increasing alcohol consumption, with a loss of 3 points (from a mean of 100) for every 28 g alcohol/day consumed. The effect was also most marked for numeracy tasks, persisted after controlling for IQ and was more evident when mothers were aged 30 years or more. In another study, Burden et al (2005a) found that working memory (slower processing speed and efficiency) was the dimension of attention most affected by prenatal exposure to more than 14 g absolute alcohol per day. This adverse effect was more pronounced in children born to mothers aged 30 years or more.

Richardson et al (2002) found that prenatal exposure to three or more drinks per week had a significant deleterious effect on children's verbal and nonverbal learning and memory score at 10 years of age. Willford et al (2004) found that prenatal alcohol exposure was associated with deficits in learning and short and long term memory, but only in the verbal domain, in the same cohort at 14 years of age. Binge-drinking in the first trimester predicted significant deficits in performance. However, in both age groups an effect was seen in light drinkers

(average of less than three drinks per week; or less than 42 g alcohol per week, assuming US drink size) and moderate drinkers (3 to 6 drinks per week; or 42 to 84 g alcohol per week, assuming US drink sizes). None of the children studied had FAS. In both studies, first and second trimester exposure affected verbal learning and second and third trimester exposure affected memory. Furthermore, the problems with learning and memory become more obvious with age. Thus light to moderate alcohol exposure may permanently impair learning and memory.

In an Australian birth cohort study by O'Callaghan et al (2007), no association was found between alcohol consumption of less than one glass (0.5oz absolute alcohol) per day in early pregnancy and intellectual ability, learning and attention at 14 years of age. Drinking of more than five drinks on one or more occasion was associated with decreased cognitive ability (measured by Raven's Standard Progressive Matrices Test) with a linear relationship between outcome and frequency of 'binge-drinking'.

Connor et al (2006) found that abnormalities of motor coordination demonstrated in children exposed to alcohol prenatally persisted into adulthood only in children with other features of FASD. It is possible that measures used to assess motor coordination were insufficiently sensitive or that motor problems seen in childhood represent developmental delay which normalises with increasing age.

Goldschmidt et al (2004) found that in a group of women with low socioeconomic status, light-to-moderate prenatal alcohol use (less than one drink per day) in the first and second trimesters independently predicted poor overall school performance at 10 years of age as rated by the child's teacher. Deficits in reading recognition and comprehension and teachers' rating of poor school performance were significantly associated with second-trimester binge-drinking.

Howell et al (2006) found that prenatal alcohol exposure (average of 6 oz absolute alcohol per week) independently predicted lower intelligence scores and specific academic deficits, especially in mathematics, in adolescents with a low socioeconomic status who did not have dysmorphic features associated with alcohol exposure. In a large longitudinal study, Bailey et al (2004) found that seven-year old children exposed to binge-drinking prenatally had significantly lower verbal IQ scores, regardless of the amount of overall pregnancy exposure and after controlling for other prenatal exposures and postnatal environment factors.

Studies were also identified that investigated the effect of prenatal alcohol exposure on child behaviour. Sood et al (2001) found that children aged 6–7 years with any prenatal alcohol exposure scored higher for externalising (aggression, delinquency) and internalising (anxiety, depression, withdrawal) behaviours after adjusting for confounders. The odds ratio for delinquent behaviour was 3.2-times in children who had been exposed to any level of alcohol compared with non-exposed controls. The adverse effects on behaviour were dose-related and were evident at low levels of exposure (average 0.3oz absolute alcohol/day) and the authors concluded that 'no alcohol in pregnancy remains the best medical advice.' Nulman et al (2004) investigated a small cohort of children exposed to binge-drinking (5–6 drinks per occasion) in the first trimester. Most mothers stopped binging between four and eight weeks gestation. There was no difference in any of the global indexes of intellectual function or in language development in alcohol exposed children compared with controls. However, exposed children displayed greater social disinhibition than controls.

Prenatal alcohol exposure and alcohol disorders

In two studies, prenatal alcohol exposure predicted alcohol-problems in adolescence. In a prospective cohort study, Baer et al (2003) found that prenatal alcohol exposure was a risk factor for alcohol problems at 21 years of age after adjusting for sex, other demographic factors, family history of alcohol problems, prenatal exposure to nicotine and other drugs, and other aspects of the family environment. Exposure to heavy maternal episodic drinking triples the odds of mild alcohol dependence at age 21 years, however the mechanism for this is not known. Adolescents exposed prenatally are also more likely to experience adverse consequences from heavy episodic drinking. Alati et al (2006) examined the effect of maternal alcohol use on the onset of alcohol disorders in offspring. In this large Australian study the odds-ratio for developing early-onset alcohol disorders (at between 13 and 17 years) was 2.95 for exposure to alcohol (three or more drinks a few times each month) in early pregnancy and 1.35 for exposure in late pregnancy after adjusting for confounders and excluding those with a family history of alcohol problems., The odds ratio for developing late-onset disorder (between ages 18 and 21 years) was 3.29 for those exposed to alcohol in early pregnancy. This paper suggests that prenatal alcohol exposure has an independent role in the causation of alcohol disorders in adulthood. The loss to follow-up in this study was considerable, but after analysis of the group lost to follow-up the authors concluded that attrition did not substantially bias the results.

Breastfeeding

Breastfeeding is the safest and best method for nurturing and optimising infant growth and health. In 2001, the WHO recommended exclusive breastfeeding for six months, with continued breastfeeding until two years of age, together with complementary foods (NHMRC 2003).

Alcohol consumed by breastfeeding mothers rapidly enters the mother's milk and is consumed by the baby. Mothers therefore need advice on its use during breastfeeding. The effect of alcohol consumption by breastfeeding mothers on milk production (lactogenesis), breastmilk and infant blood alcohol concentration, and on the breastfeeding infant have been described in a well-conducted systematic review of research from 1990–2005 by Giglia and Binns (2006). The review found limited research on the effect of alcohol on breastfed infants, with most research being conducted on animal models. Results from both animal and human studies have consistently shown a decrease in lactational performance with alcohol consumption (both in terms of milk production by the mother and consumption by the baby). Alcohol intake by breastfeeding mothers at levels similar to the NHMRC 2001 guideline levels for women may also have a negative effect on infant development and behaviour (Giglia and Bins 2006).

A randomised controlled trial by Schuetze et al (2002) investigated the short-term impact of infant exposure to alcohol in breastmilk on mother–infant interactions and infant arousal. Exposure to even small amounts of alcohol through breastmilk affects infant arousal. After consuming breast milk containing alcohol, infants spent proportionately less time in quiet sleep and more time in quiet alert and crying states, indicating that exposure to alcohol in breast milk may not be sedating.

Little et al (2002) investigated the effect of alcohol and breastfeeding. The results of this study however, did not support previous reports of an adverse effect on infant motor

development by infant exposure to alcohol in the breastmilk. The authors suggest that a reason for this discrepancy may be that the dose of alcohol reaching the lactating infant is small, and tests of infants and toddlers have limited ability to pick up small effects.

Ho et al (2001) used pharmacokinetic modelling to determine the time it would take for alcohol to be completely eliminated from breastmilk in a women of a given bodyweight, after consuming a given number of drinks. Table G3.1 shows the length of time an average woman of a given bodyweight should delay breastfeeding their infant, after consuming a given number of drinks, before assuming a zero level of alcohol in her milk (Ho et al 2001). The study is limited by the fact that the authors chose to use the typical average decay for blood alcohol concentration of 15 mg/mL/hour, although this value may be faster or slower in some women. Therefore, the figures in Table G3.1 are only an estimate.

Table G3.1 Time taken for alcohol to be cleared from breastmilk (hours: minutes)

Maternal weight (kg)	Australian standard drinks						
	1	2	3	4	5	6	7
50	1.51	3.43	5.35	7.27	9.18	11.11	13:03
59	1.42	3.26	5.09	6.52	8.36	10.19	12.02
66	1.37	3.15	4.53	6.31	8.10	9.48	111.26
70	1.33	3:07	4.41	6.15	7.50	9.24	10.57

Notes:
Time is calculated from the beginning of drinking.
Assumptions made: alcohol metabolism is constant at 15 mg/dL; height of the women is 162.56 centimetres. One drink is roughly equivalent to 1.7 standard Australian drinks (more specifically: 340 g of 5% beer, 141.75 g of 11% wine, or 42.53 g of 40% liquor).

Example 1: for a 40.8 kg woman who consumed 3 drinks in 1 hour, it would take 8 hours 30 minutes for there to be no alcohol in her breast milk, but for a 95.3 kg woman drinking the same amount, it would take 5 hours 33 minutes.

Example 2: for a 63.5 kg woman drinking 4 beers starting at 8:00 PM, there would be a zero level of alcohol in her breast milk 9 hours 17 minutes later (ie, at 5:17 AM)

Source: Giglia and Binns 2006 (adapted from Ho et al 2001)

Genetic protection

Some research has also shown that there is a genetic component to the effects of alcohol on the individual and that this extends to the effect of alcohol on the developing fetus, with some genotypes conferring increased adverse effects of alcohol and others providing protection (Jacobson et al 2006). This makes it difficult to estimate absolute risk in an individual unless this genetic component is known. Metabolic rates, risk of reacting to alcohol related metabolites and the degree of reaction at a biochemical and inflammatory level are all affected by genetic factors.

PART C

Additional health advice and precautions

Additional health advice and precautions 1:
For situations where not drinking is the safest option

Taking part in, or supervising, risky activities

Alcohol consumption increases the risk of harm to drinkers and to others. Alcohol therefore should not be consumed before or during risky activities, such as driving, flying an aircraft, water sports or snow sports.

Occupational activities, such as aircraft piloting or heavy vehicle operation, and recreational activities, such as skiing, snowboarding or water sports, require a high level of attention, psychomotor skills and concentration. Consumption of alcohol can affect each of these aspects of performance. Supervising other people taking part in risky activities, including young children, also requires a high level of attention and concentration.

Attention, psychomotor skills and concentration are all reduced after consuming alcohol. Australian state and territory laws allow a blood alcohol concentration (BAC) of up to 0.05% while driving for full licence holders, zero for learner drivers, and 0–0.02% for provisional drivers (depending on state). Those who operate commercial aircraft, public or heavy vehicles, commercial vessels, machinery, and mobile plant or farm equipment must observe blood alcohol levels required by their employer's company policy as well as those required by law.

Blood alcohol typically remains below 0.05% if an average-sized male drinks no more than two drinks in the first hour, and one drink per hour thereafter, and if females of average size drink no more than one standard drink per hour. Learner and provisional drivers need to avoid drinking alcohol for at least six hours before driving.

Most laboratory-based studies of the relationship between blood alcohol concentration to cognitive and psychomotor impairment show a positive dose-response curve above 0.04 for reaction time, tracking and divided attention (Howland et al 2006). The results of studies that have examined impairment at low BACs (in the range of 0.01 to 0.05) are mixed, depending on how impairment and performance are measured (Howland et al 2000, Fell and Voas 2006, Howland et al 2006, Ritz-Timme et al 2006, Breitmeier et al 2007).

A recent double-blind, placebo-controlled trial found that a BAC of 0.03 reduced cognitive functions that relied on perception and processing of visual information, especially in complex and urgent tasks (Breitmeier et al 2007). Fell and Voas (2006) performed a meta-analysis that found that the relative risk of being involved in a fatal crash as a driver is 4–10 times greater for drivers with BACs between 0.05 and 0.07, compared with drivers with a BAC of zero. Maritime cadets showed significant decreases in their ability to concentrate and plan, diminished concentration and accuracy, and an increased risk disposition at a blood alcohol concentration of 0.02 (Ritz-Timme et al 2006). An American study found that in 44% of all watercraft-related drownings, the deceased had a positive blood alcohol reading (Browne et al 2003).

There are good data to show that impairment persists even after BAC has returned to normal (Wiese and Shlipak 2000, Kim et al 2003, Prat et al 2007,Barrett et al 2004). A recent study

on maritime academy cadets found that residual effects were found on some complex performance tasks (Rosenhow et al 2006), and a further study found that off-the-job drinking was associated with workers' injury compensation claims (Ragland et al 2002).

Using illicit drugs

Alcohol may interact with illicit drugs, which can have dangerous or lethal consequences.

There are a range of documented adverse outcomes from using illicit drugs. Further, combining illicit drugs with alcohol can increase the risk of adverse outcomes. Drugs such as cannabis, amphetamines, lysergic acid diethylamide (LSD), ecstasy, cocaine and heroin are increasingly used with alcohol, placing users at risk of overdose and death (NHMRC 2001). Many studies have reported that any level of alcohol consumption is a significant predictor of nonfatal and fatal drug overdose (Kaye and Darke 2004, Coffin et al 2007, Kerr et al 2007). There have been several studies documenting that illicit drug users are typically unaware of the potentiating effects of alcohol and illicit drugs (Dietze et al 2005, Neira-Leon et al 2006).

The combined used of alcohol and cannabis is dangerous when driving or engaging in other activities requiring motor skill and judgment. Like alcohol, cannabis has been shown to impair psychomotor performance and perception. Several studies have shown that the combined use of alcohol and cannabis is associated with higher risk of motor vehicle crashes (O'Kane et al 2002, Ramaekers et al 2006, Appenzeller et al 2005). The National Highway Traffic Safety Administration conducted a driving simulation study that found that the effects of 0.04 g/dL of alcohol and moderate doses of marijuana (tetrahydrocannabinol concentration 200 μ/kg bodyweight) are greater in combination than for either drug alone (National Highway Traffic Safety Administration 2000). This study found that aspects of driving performance, especially reaction time, visual search frequency and ability to perceive or respond to changes in relative velocity of other vehicles were negatively affected by the combination of alcohol and cannabis.

The combination of methylenedioxymethamphetamine (MDMA or ecstasy) and alcohol is common, especially in young adults. Several studies have shown that the combined effects of the drug are dangerous, especially when driving or taking part in other risky activities (Kuypers et al 2006, Ramaekers and Kuypers 2006, Ramaekers et al 2006). In a driving simulation, Kuypers et al (2006) showed that MDMA moderated the impairing effects of low-dose alcohol (equivalent to BAC 0.06 mg/mL) on road-tracking performance, but could not overcome alcohol-related impairment on other aspects of driving. Another driving simulator study found similar results — the stimulant effects of MDMA were never sufficient to overcome alcohol-induced impairment of impulse control or risk-taking behaviour (Ramaeker and Kuypers 2006).

Concomitant use of alcohol and cocaine poses health risks to the user. A recent systematic literature review found that combining any dose of alcohol and cocaine induces greater-than-additive effects on heart rate and 30% greater blood cocaine concentrations (Pennings et al 2002). The systematic review included studies that used retrospective data to suggest that combining alcohol and cocaine leads to formation of cocaethylene, a compound that may potentiate cardiotoxic effects greater than the use of either drug alone (Pennings et al 2002). An Australian study found that the combination of alcohol and cocaine is more common in

users who are socially integrated, rather than those users at societal margins (Shearer et al 2007).

The synergistic effects of alcohol and heroin also increase the risk of non-fatal and fatal overdose. Heroin and alcohol are central nervous system (CNS) depressants that, at high doses, suppress breathing. Breathing is regulated by the neurotransmitters glutamate and gamma-amino butyric acid (GABA). Alcohol decreases the excitatory effect of glutamate, while heroin increases the inhibitory effect of GABA, resulting in a reduced respiration rate. For these reasons, the concomitant presence of alcohol and heroin has been described in many forensic examinations of heroin overdose victims (Coffin et al 2007, Darke et al 2007).

Additional health advice and precautions 2:

For people who should be aware that they have an increased risk

Young adults

Young adults up to the age of 25 are at particular risk of harm from alcohol consumption.

The issues for young adults are similar to those for adolescents (see Guideline 2), in particular:

- like adolescents, young adults continue to be greater risk takers than older adults, but still have poorly developed decision-making skills — factors that are reflected in the high levels of injuries sustained by this age group.
- alcohol affects brain development in young people; thus, drinking, particularly binge-drinking, at any time before brain development is complete (which is not until 25 years of age) may adversely affect later brain function.

In addition, young adults are also the adult age group most likely to take mood-altering drugs (see 'Additional advice and precautions 1' in Part C).

Risk taking and injuries

As discussed under Guideline 1, between one-third and one-half of injuries involve young people under the age of 30 years.

Alcohol increases the likelihood of injuries caused by violence, self harm, suicide and homicide, and from accidental injuries, especially motor vehicle accidents and falls (Vinson et al 2003, Borges et al 2004ab, Cherpitel et al 2004a, Spurling and Vinson 2005, Borges et al 2006, Stephens 2006, Miller et al 2007). Several studies from emergency departments show that approximately 35% of all injuries are alcohol-related (Humphrey et al 2003), and that two-thirds of those injuries are sustained by males under 30 years of age (Borges et al 2004, Cherpitel et al 2004a, Gmel et al 2006). Approximately one-third of alcohol-related injuries involve violence, and females aged less than 30 years are the group most likely to be the victims of alcohol-related violence (Cherpitel et al 2004a). For further information, see Guideline 1 and Appendix 4.

Use of alcohol by young adults compounds the likelihood of high-risk behaviours that are common to this age group (Watt et al 2004, Miller et al 2007). Observational studies have shown that alcohol increases the prevalence of unsafe sex behaviours (Coleman and Cater 2005, Lin et al 2005, Abbey et al 2006, Dye and Upchurch 2006). A number of randomised controlled trials have shown that drinking increased participants' likelihood of making risky choices about sexual activity (Maisto et al 2002, Maisto et al 2004, Testa et al 2006). Conversely, Leigh et al (2007) showed that young people prepare for safe sex when they know that they will be drinking. Young people who drink alcohol are also at risk of sexual coercion (Abbey et al 2003ab, Davis et al 2006, Farris et al 2007).

Cognitive effects (brain damage)

During adolescence and young adulthood, the human brain is sensitised to injury from alcohol and is less able to respond to physiological cues to stop drinking (Spear 2004). Studies have shown significant and detrimental effects in brain structure when alcohol is abused during this period. Young adults who misuse alcohol tend to have smaller prefrontal cortices and white matter, structural abnormalities of white matter and reduced hippocampal volumes (White and Swartzwelder 2004, De Bellis et al 2005). These structural changes lead to a diminished ability to retrieve verbal and nonverbal material and poorer performance in attention-based tests (Brown and Tapert 2004). Cognitive impairment is also common in young adults with alcohol dependence (Kelly and Witkiewicz 2003).

Young people have a significantly lower tolerance to alcohol and relative inexperience at performing certain tasks that require attention and psychomotor coordination, placing them at increased risk of alcohol-related harm. For example, although the risk of motor-vehicle accidents increase proportionate to blood alcohol concentration, younger drivers at a given BAC are at greater risk than older drivers at the same blood alcohol level, due to their relative inexperience and lower alcohol tolerance (Mayhew et al 1986, Zador et al 1991, Harrison and Fillmore 2005).

Mental health

Alcohol use elevates the risk for a number of mental health and social problems in young adults (Brown and Tapert 2004). The existence of psychiatric comorbidities in young people who abuse alcohol is common, especially for conditions such as depression, anxiety, bipolar disorder, conduct disorder and attention-deficit/hyperactivity disorder (Turner and Gil 2002, Brown and Tapert 2004, Chen and Storr 2006, Deas and Brown 2006, Cargiulo 2007).

Young people who use alcohol to cope with their mental health or social problems are more likely to drink dangerously. Large American cross–sectional studies have shown that college students suffering from social anxiety disorders report frequent heavy and heavy episodic drinking, and drinking with the intention of getting drunk (Geisner et al 2004, Weitzman 2004). Binge-drinking, in combination with depression, is a significant predictor of suicidal ideation, self harm and suicide in young people (Windle 2004, Miller et al 2007, Sher 2006).

Heart disease

Alcohol has no immediate benefit for young people and young adults in protecting against heart disease, as very few people show clinical signs of atherosclerosis (hardening of the arteries) below 40 years of age. The one exception to this is a small number of people with a strong family history of atherosclerotic heart disease in young adulthood (Femia et al 2006). It is not yet known whether a regular pattern of drinking is an advantage for young adults in reducing their risk of heart disease in later life. Any potential benefit needs to be weighed against the significant risk of death or injury from other alcohol-related causes in young adulthood.

Older people

Although light to moderate alcohol consumption in older adults may lower the risk of several chronic conditions, including age-related bone loss, heart failure, stroke, atherosclerosis, cognitive impairment and dementia, for some older adults, drinking alcohol increases the risk of falls and injuries, as well as some chronic conditions.

Although drinking volume declines with age, drinking alcohol remains an enjoyable aspect of a healthy lifestyle for many older adults. Population-based studies estimate that approximately 40% of males and 30% of females aged over 60 years drink at a moderate level (Ganry et al 2001, Breslow et al 2003, Breslow and Smothers 2004, Aira et al 2005). The decline in alcohol consumption in the older population is primarily associated with the onset of health problems (Moos et al 2005).

There are a number of studies that suggest that light to moderate alcohol consumption (one to two drinks per day) may convey some health benefits to older adults, including reduced bone loss in males and females (Baron et al 2001, Bakhireva et al 2004, Mukamal et al 2007), and reduced risk of cardiovascular conditions such as heart failure (Bryson et al 2006), stroke (Mukamal et al 2005) and atherosclerosis (Mukamal et al 2003, Hougaku et al 2005, Mattace-Raso et al 2005). Data from prospective cohort studies and cross–sectional surveys also suggest that light to moderate alcohol consumption may protect against cognitive impairment and dementia in older adults (Bond et al 2001, Huang et al 2002, Mukamal et al 2003, Bond et al 2004, Cassidy et al 2004, den Heijer et al 2004, Hajat et al 2004, Ganguli et al 2005, Deng et al 2006, Reid et al 2006, McDougall et al 2006, McGuire et al 2007).

However, for some elderly people, drinking poses a risk (Fink et al 2002). Elderly people are more vulnerable to the effects of alcohol due to changes in their body composition, decreased metabolic capacity, the presence of comorbid conditions and the medications that regulate these conditions (Aira et al 2005). A population-based study of adults aged over 75 years found that among those that used alcohol at any level, almost 87% also regularly used medications that had potentially adverse interactions with alcohol (Aira et al 2005).

Alcohol can increase the risk of falls, motor vehicle accidents and suicide in elderly people (Margolis et al 2002, Akechi et al 2006, Sorock et al 2006). Alcohol and medication, either alone or in combination, can increase the falls-related injury risk (Fletcher and Hirdes 2005). A prospective cohort study showed that the risk of falls and fall-related injuries was increased for older adults who drank more than 18 standard drinks per week (Pluijm et al 2006). Another longitudinal study found that consumption of 14 or more drinks per week was associated with an increase in falls risk, although the study collected data once per year, which may not be sufficient (Mukamal et al 2004).

Older drivers are also at greater risk of motor vehicle crashes, particularly at intersections (Grabowski et al 2004, Mayhew et al 2006). A large prospective cohort study of older women found that crash risk was significantly increased for those participants who had fallen in the previous year, while vision status and medical diagnoses were not significantly associated with crash risk (Margolis et al 2002).

Older people are advised to consult with their health professionals about the most appropriate level of drinking for their health.

People with a family history of alcohol dependence

People with a family history of alcohol-related problems, including alcohol dependence, are more at risk than the general population of being unable to control their level of drinking. Anyone with first or second-degree relatives with alcohol dependence should consider reducing their drinking below Guideline 1 and discuss their alcohol intake with their health professional.

Family history is a strong predictor of developing an alcohol abuse disorder. The children of alcoholic parents are at significantly greater risk of dependence (Haber et al 2005). Social and environmental factors, such as being exposed to a family culture that accepts heavy drinking, may contribute to development of dependence in the children of heavy drinkers (Hingson et al 2003). Social environments and routines, such as tobacco smoking, can contribute to increased drinking frequency and hence lead to dependence (Barrett et al 2006, Grucza et al 2006).

Some individuals inherit variations of the genes that regulate alcohol metabolism, which may influence their susceptibility to alcoholism (Ilveskoski et al 2001, Hasin et al 2002, Petrakis et al 2004). The liver enzyme systems involved in alcohol metabolism are alcohol dehydrogenase (ADH), aldehyde dehydrogenase (ALDH) and microsomal P4502E1 (CYP2E1) (Gemma et al 2006). All these enzymes have been shown to vary between individuals. Since these variations can either accelerate or slow alcohol metabolism, recent studies have looked for a correlation between metabolic variability and differences in alcohol abuse (Quertemont 2004, Gemma et al 2006).

Other individuals inherit variations in the genes that encode the hormones of the hypothalamic–pituitary axis. These hormones are involved in regulating reward systems, which are heavily implicated in alcoholism (Dai et al 2002ab, Dai et al 2005).

Additional health advice and precautions 3:

For people who should seek professional advice about drinking

People with physical health problems that are made worse by alcohol

Drinking leads to poorer outcomes for many diseases and conditions, including alcohol-related diseases such as cirrhosis of the liver, alcoholic pancreatitis, alcohol-related brain damage and alcohol dependence. Anyone under treatment for any of these conditions, or any other problem that might be made worse by alcohol, should discuss their alcohol intake with their health professional. In many instances, temporary or permanent abstinence may be necessary.

Table 3.1 in Chapter 3 showed the scope of health problems that have been associated with alcohol intake. For people who have serious diseases, directly related to alcohol consumption, including alcohol dependence, any further drinking may aggravate the condition causing immediate problems or worsening of the prognosis for the longer term. For some people, however, a planned drinking program under the supervision of a health professional may be an appropriate option.

Alcohol consumption may also impair the immune system, leading to poorer outcomes for infectious and other diseases related to immune function. In addition, alcohol may reduce the efficacy of medications, which can also lead to poorer outcomes.

People with mental health problems

Drinking leads to poorer outcomes for people who have a mental health problem. Anyone under treatment for a mental health problem should discuss their alcohol intake with their health professional. In many instances, temporary or permanent abstinence may be necessary. Carers can encourage people with a mental health problem to stay within guideline levels, or to abstain if necessary.

Alcohol abuse is associated with a high prevalence of several mental health conditions, including social phobias and anxiety disorders, uni- and bipolar depression, and schizophrenia. There is a high degree of comorbidity between individuals with anxiety, depressive and schizophrenic diagnoses (Cosci et al 2005).

The literature surrounding alcohol use and anxiety disorders is large and complex; however, it has been shown repeatedly that individuals with social phobias are much more comfortable in social situations if they have used alcohol (Abrams et al 2002, Lehman et al 2002, Lewis and Vogeltanz-Holm 2002, Thomas et al 2003). These individuals are at high risk of dependence if they continue to drink to manage their condition (Abrams et al 2001).

Although the majority of epidemiological literature suggests an association between alcohol use and depression, the exact nature of the relationship is unclear. This may in part be due to

the manner in which both consumption and depression are measured (Graham et al 2007). Some studies have described a J-shaped relationship between alcohol and depression (Alati et al 2005), while others have found a U-shaped relationship (Graham et al 2007). In a longitudinal study, Haynes et al (2005) found that excessive alcohol consumption was not associated with the onset of anxiety and depression, but that abstinence was associated with lower depressive risks. A meta-analysis found that a higher proportion of people diagnosed with alcohol dependence also suffer comorbid mental health disorder than people who suffer with a mental health disorder who are also alcohol-dependent (Jane-Lopis and Matytsina 2006). In a population-based survey, Graham et al (2007) found no data to support the notion that light to moderate drinking (defined by low frequency or low volume) protects against major depression.

A meta-analysis of 35 epidemiological studies showed that alcohol problems are more common in people who are depressed than in the general population (Sullivan et al 2005). The meta-analysis reported a median prevalence of current or lifetime alcohol problems in depressed patients of 16% and 30%, respectively, compared with 7% and 16–24% current or lifetime alcohol problems in the general population (Sullivan et al 2005). Furthermore, the study found that alcohol abuse was associated with worse outcomes in terms of depression course, self harm and suicide risk, social functioning and health care use.

Alcohol use is also high in manic–depressive patients (Goldstein et al 2006a). Patients who suffer from bipolar disorder and alcohol dependence have significantly reduced quality of life compared with patients with bipolar disorder only (Singh et al 2005). A study in a psychiatric population by Goldstein et al (2006a) found that even if alcohol consumption volume was low (measured using definitions of the Canadian Alcohol Guidelines and Khavari Alcohol Test), it remained associated with measures of illness severity in both male and female patients. It is thought that the adverse effects of alcohol on bipolar disorder may occur over a range of consumptions, rather than being confined to alcoholics or heavy drinkers (Goldstein et al 2006a).

There is a well-established comorbidity between schizophrenia and alcohol abuse, although the certainty of the association between alcohol abuse as an independent risk factor for schizophrenia is not clearly defined. Studies of schizophrenic patients have reported a wide range of prevalences for alcohol abuse, with younger, male schizophrenics more likely to suffer from alcohol dependence (Cantor-Graae et al 2001). A recent Swedish study found that alcohol abuse was the most common type of substance abuse among schizophrenics (Cantor-Graae et al 2001). It is thought that alcohol abuse, especially early in the illness, determines the earlier onset of schizophrenia and may increase the severity of common psychotic symptoms, such as hallucination and unusual content of thought (Mohamed et al 2006 Mauri et al 2006).

In the short term, when consumed at nationally defined levels of moderate consumption, alcohol typically induces positive feelings and happiness (Eckardt et al 1998). However, as blood alcohol concentration decreases, anxiety and depression are common (Kushner et al 2000). Those who use alcohol to cope with their mental health problems have a tendency to become dependent (Kushner et al 2000, Carrigan and Randall 2003, Thomas et al 2003). Numerous studies have shown that when people with significant alcohol dependence stop drinking entirely, their mood usually worsens over the first few hours and days, but after two to three weeks it is greatly improved (Lynskey 1998, Kushner et al 2000).

Alcohol also causes interruptions to normal sleep patterns, in particular the later, heavier part of the sleep cycle (Castaneda et al 1998). While alcohol may induce sleep in the short term, it leads to increased arousal and wakefulness several hours after consumption (Castaneda et al 1998, Peppard et al 2007). Sleep disruption and chronic sleep deprivation can increase the risk of injury, disrupt cognitive processes and trigger a variety of mental health problems (Castaneda et al 1998, Williamson and Feyer 2000, Drummond et al 2006).

In addition to all these effects, alcohol — even at low levels (one or two drinks) — can interact adversely with most of the medications commonly prescribed for treating mental health problems, including antidepressants, benzodiazepines and muscle relaxants (Castaneda et al 1998, Weathermon and Crabb 1999, Koski et al 2005) (see 'Additional health advice and precautions 3, in Part C).

People taking medications

Alcohol may interact with prescribed and over-the-counter medications and increase or reduce their effectiveness.

Alcohol is a central nervous system depressant that may interact with other drugs, including prescription and over-the-counter medications, herbal preparations and illicit drugs (Weathermon and Crabb 1999, Izzo and Ernst 2001, Koski et al 2005, Pringle et al 2005). Alcohol can exert direct effects on the absorption of medications, change the way medications are metabolised, or interfere with the effect of the medication at its site of action (Weathermon and Crabb 1999).

The effects of combining alcohol and medication depend on the type and dosage of medication, the volume of alcohol consumed, and also on personal factors, such as genetics, sex and comorbid health conditions (Weathermon and Crabb 1999). Commonly prescribed classes of medications, such as benzodiazepines, barbiturates, opiates, analgesics, antidepressants, antibiotics, antihistamines and anti-inflammatories have known interactions with alcohol. Some interactions between alcohol and medications have serious implications for driving a motor vehicle or operating heavy machinery.

People taking medications (including herbal preparations) should check with their doctor or pharmacist about harmful interactions of their medications and alcohol. In many instances, either temporary or permanent abstinence may be necessary, particularly for people taking multiple medications.

APPENDIXES

Appendix 1 Committee membership and terms of reference

Membership, NHMRC Review of the Australian Alcohol Guidelines Working Committee

Professor Jon Currie (Chair)	St Vincent's, Melbourne Department of Addiction Medicine NHMRC National Health Committee member
Professor Steve Allsop	Director, National Drug Research Institute Curtin University of Technology, WA
Professor Robert Batey	Clinical Advisor Centre for Drug and Alcohol NSW Health Department
Dr Ngaire Brown	Menzies School of Medical Research Charles Darwin University, NT (until August 2007)
Mr Bruce Clark	Representing consumers
Professor Charlotte de Crespigny	Professor of Nursing (Alcohol and Other Drugs) Flinders University, SA
Professor Elizabeth Elliott	Professor of Paediatrics & Child Health Children's Hospital Westmead, NSW
Professor Ann Roche	National Centre for Education on Training and Addiction Flinders University, SA National Centre for Education on Training and Addiction Flinders University, SA
Professor Robin Room	School of Population Health, University of Melbourne Director, AER Centre for Alcohol Policy Research, Turning Point Alcohol and Drug Centre , VIC
Corresponding members:	
Professor Margaret Hamilton	Multiple and Complex Needs Panel (until August 2007)
Dr Michael Bolton	Medical Advisor Damascus Health Service, Queensland.
Observer:	
Ms Kellie Fixter	Australian Government Department of Health and Ageing
NHMRC secretariat:	
Ms Heather Bishop	
Technical writer:	
Dr Janet Salisbury	Biotext Pty Ltd, Canberra

Terms of reference

1. The working committee will oversee and provide expertise in the review of the Australian Alcohol Guidelines. The review should take into account, but not be limited to, the following:
   - the *Australian Alcohol Guidelines: Health Risks and Benefits* (2001);
   - the best available current scientific evidence;
   - comments provided by the broader community through public consultation;
   - the needs of health service providers; and
   - any other relevant matter.
2. The working committee will provide regular reports on the progress of guideline development.
3. The working committee will provide the NHMRC CEO with a draft report for the CEO to seek advice from Council.
4. The NHMRC will engage a consultant to assist the working committee in this task.

Appendix 2 Process report

In October 2001, the NHMRC issued the *Australian Alcohol Guidelines: Health Risks and Benefits,* 2001. The guidelines were developed by the NHMRC in collaboration with the Population Health Division of the Australian Government Department of Health and Ageing (DoHA), with funding from DoHA.

During 2005 there was increased media interest in the alcohol guidelines, with particular focus on the effects of drinking during pregnancy and foetal alcohol syndrome (FAS).

Following consultation with DoHA, the former NHMRC Health Advisory Committee (HAC) agreed to start an update of the guidelines in 2006–07. The revised version of the guidelines is intended to form the evidence base for developing future policies and community materials on the effects of alcohol consumption. The NHMRC is developing the revised guidelines in collaboration with the Population Health Division of DoHA, under the auspices of the National Health Committee (NHC), which is a principal committee of the NHMRC.

The aim of the updated Australian Alcohol Guidelines is to provide a resource for a wide range of groups and individuals, including health professionals, community groups, industry, professional organisations, schools and educational organisations. It will also inform policy makers, planners, decision makers, and those responsible for the provision of alcohol, who have a broader responsibility to the community and whose decisions may influence the health of communities.

Literature review

A systematic literature review, which analysed and synthesised the best available current evidence in regard to alcohol consumption, was conducted to inform the updating of the guidelines. The methods used for this review are described in Section 2.5.

Working committee

An expert working committee was appointed to guide the redevelopment of the revised Australian Alcohol Guidelines. The committee is chaired by Professor Jon Currie, and the members have expertise in alcohol related matters (see Appendix 1). A DoHA representative attended committee meetings as an observer.

Public consultation

The NHMRC Council has delegated to the NHC the authority to review the draft of the revised Australian Alcohol Guidelines and, when satisfied, release it for public consultation. Under this arrangement, the draft guidelines have been released for 60 days public consultation period, to provide the public with ample opportunity to have input into the development of the guidelines. This process will assist the working committee to ensure the quality, usefulness and uptake of the final guidelines.

It is anticipated that a final draft of the revised Australian Alcohol guidelines will be presented to the NHMRC Council for approval and recommendation to the Chief Executive Officer for issuing in March 2008.

Appendix 3 Comparison of international alcohol guidelines

This appendix summarises some of the differences between alcohol guidelines used in different countries. Most information is from the International Center for Alcohol Policies table on international guidelines (ICAP 2007) and the World Health Organization's 2004 report on alcohol policy (WHO 2004), both available online[8]. Primary sources are provided where possible, but many of the guidelines are not available in English. A list of the sources used is included at the end of this appendix.

Standard drinks

So far, there is no international standard drink size. Standard drinks vary considerably between countries — in the Organization for Economic Cooperation and Development (OECD) countries, the smallest standard drink is 8 grams of alcohol, and the largest is 19.75 grams (WHO 2004). Standard drink sizes (in grams of alcohol) for various countries are shown in Figure A3.1.

General recommendations

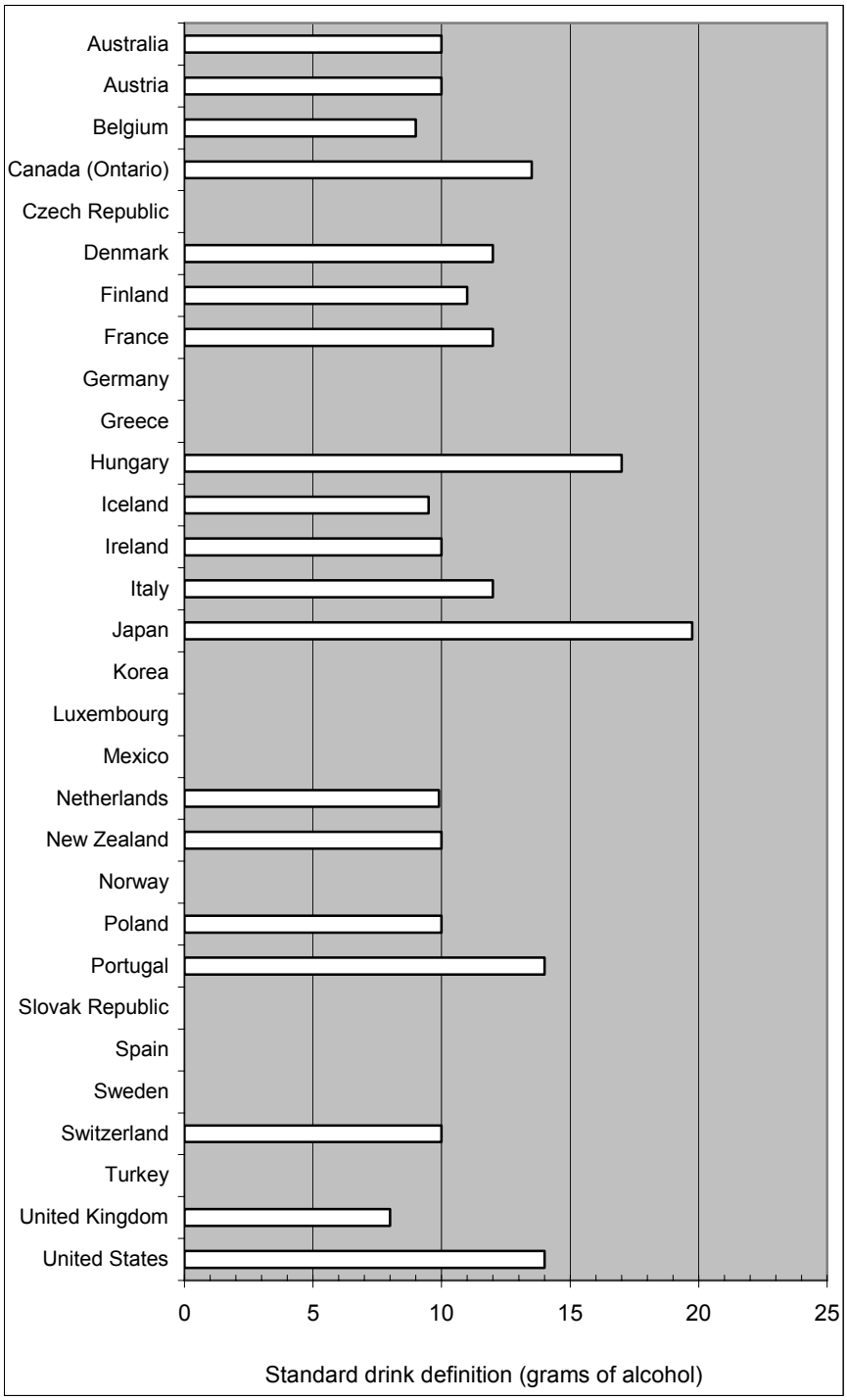
Alcohol consumption

Most of the overseas guidelines make specific recommendations about the maximum amount of alcohol that should be consumed on a regular basis by fit, healthy people. The levels recommended by different countries are given in Figure A3.2. Where a range was provided, the maximum value was used (so 'no more than 20–24 g per day' becomes '24 g').

Two countries supply a recommended maximum for a single drinking session. New Zealand recommends no more than 60 g for men and 40 g for women on a single occasion (ALAC 2004). Switzerland's drinking guidelines recommend a maximum of 48 g per event, at a maximum rate of 24 g per hour (ICAP 2007).

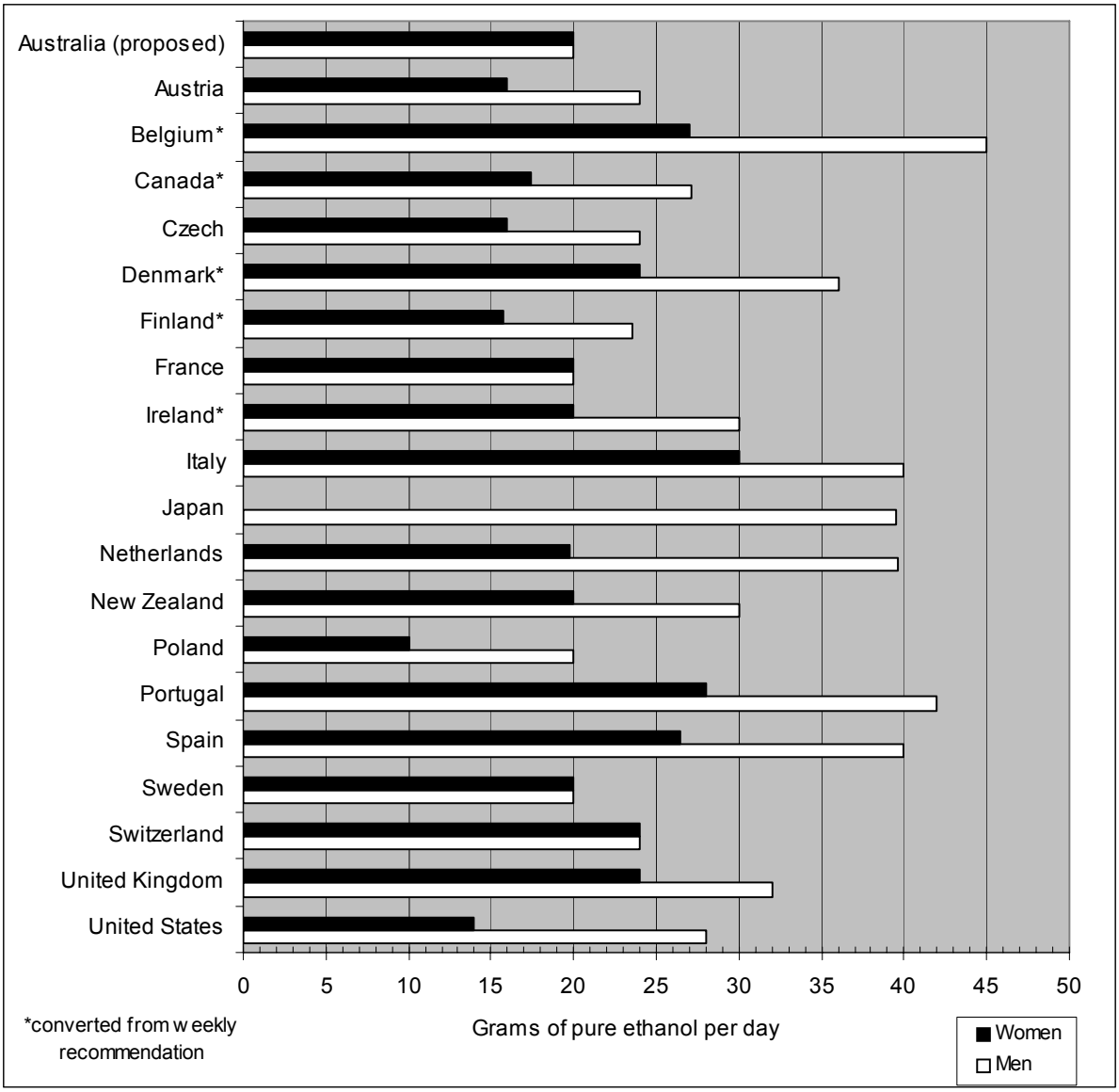
Two other countries set maximum drinking levels for exceptional circumstances. In Italy, the daily limit not to be exceeded is 1.0 g per kilo of body weight, compared to 0.6g as a recommended maximum (ICAP 2007). In Austria, the hazardous limit for a day is given as 60g for men and 40g for women, compared to the recommended maximum of 24g for men and 16g for women (ICAP 2007).

[8] ICAP table: http://www.icap.org/PolicyIssues/DrinkingGuidelines/GuidelinesTable/tabid/204/Default.aspx
WHO report: http://www.who.int/substance_abuse/publications/en/Alcohol%20Policy%20Report.pdf



Source: ICAP 2007

Figure A3.1 Standard drink definitions in different countries (grams of alcohol)



Source: ICAP 2007

Figure A3.2 Recommendations of safe level of alcohol consumption in OECD countries

While these figures provide a good idea of the diversity of guidelines in use, they should not be taken out of context — many of the guidelines set a maximum weekly amount of alcohol (which precludes drinking the maximum level each day), and some guidelines recommend alcohol-free days. Also, many of the guidelines specifically exclude certain groups from drinking the full amount shown above – for example, pregnant women or people who are on medication.

Restrictions

Purchasing alcohol

In the OECD countries, there are a range of age restrictions on the purchase and use of alcohol (WHO 2004). In some countries, the purchasing age restrictions vary depending on whether the alcohol is sold on or off the premises. Some countries also have different age restrictions for different types of alcoholic beverage (beer, wine or spirits). Tables A3.1 and A3.2 summarise the age restrictions in the countries studied (on premises and off premises, respectively).

Table A3.1 Age restrictions for the purchase of alcohol on premises

Age (years)					
16	**17**	**18**	**19**	**20**	**21**
Austria (B,W) Belgium (B,W) France Germany (B,W) Italy Luxembourg Netherlands (B,W) Portugal Spain Switzerland (B,W)	Greece	Australia Austria (S) Belgium (S) Czech Republic Denmark Finland Germany (S) Hungary Ireland Mexico Netherlands (S) New Zealand Norway (B,W) Poland Sweden Switzerland (S) Turkey United Kingdom	Canada Korea	Iceland Japan Norway (S)	United States

Source: WHO 2004
B = Beer; W = Wine; S = Spirits

Table A3.2 Age restrictions for the purchase of alcohol off premises

Age (years)						
15	**16**	**17**	**18**	**19**	**20**	**21**
Denmark	Austria (B,W) France Germany (B,W) Italy Netherlands (B,W) Portugal Spain Switzerland (B,W)	–	Australia Austria (S) Czech Republic Finland (B,W) Germany (S) Hungary Ireland Mexico Netherlands (S) New Zealand Norway (B,W) Poland Switzerland (S) Turkey United Kingdom	Canada Korea	Finland (S) Iceland Japan Norway (S) Sweden	United States

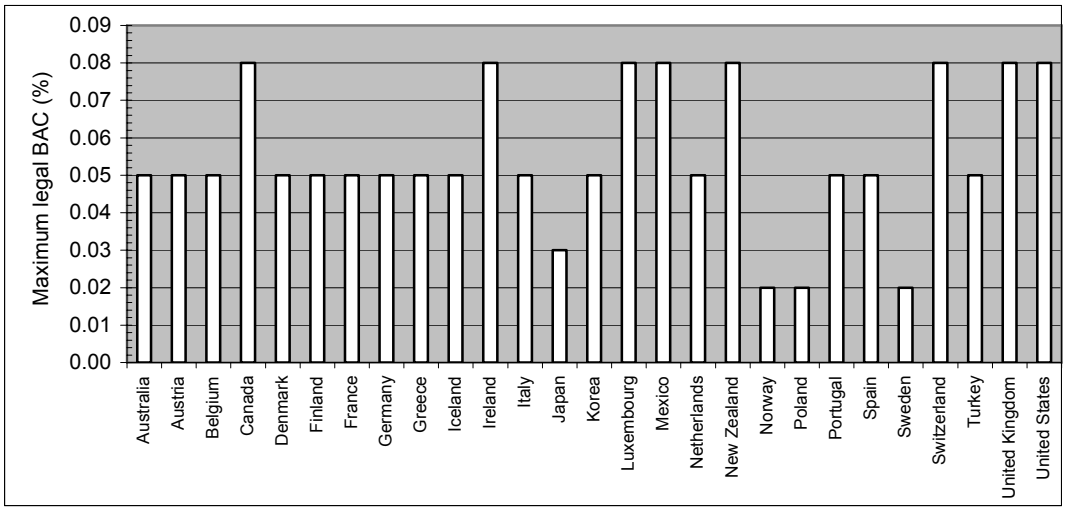
Source: WHO 2004
B = Beer; W = Wine; S = Spirits
Greece and Luxembourg are reported to not sell alcohol off-premises

Driving under the influence of alcohol

Many countries set a maximum blood alcohol concentration (BAC) that people may have while driving. It is also possible to use random breath testing to check for people above the legal BAC.

As the WHO 2004 report shows, the legal BAC for driving varies in the OECD countries (see Figure A3.3). The maximum BAC is based on the type of licence a person holds, so it may be lower for people with certain licences.

Ten of the countries reported using random breath testing often, eleven sometimes, one rarely, and six never (WHO 2004). Hungary and the Czech Republic did not use random breath testing but still had a maximum BAC (WHO 2004).



Source: WHO 2004
No information was available for the Slovak Republic
Hungary and the Czech Republic have a zero tolerance policy, so the maximum BAC for these countries is 0 (not shown)

Figure A3.3 Maximum legal blood alcohol concentration (BAC) while driving, by country

Advice to specific groups and for specific situations

Many countries provided additional guidelines for higher risk situations and groups of people.

Age

The Italian guidelines recommend reduced consumption for the elderly, and these guidelines provide specific quantities for elderly male and female drinkers: these were, respectively, 75% and 83% of the figures provided in the general guidelines (ICAP 2007).

Switzerland recommends that children abstain from drinking alcohol (ICAP 2007). Denmark and Luxembourg recommend that children under 15 and 16 years old, respectively, do not drink (ICAP 2007).

Pregnancy

Many of the OECD countries recommend total abstinence for women who are pregnant (ICAP 2007). Some also offer advice and guidelines for mothers who intend to drink.

The following countries recommend abstinence from alcohol during pregnancy: Canada (CAMH 2006), Denmark, France, Iceland, Israel, the Netherlands, New Zealand, Norway, Poland, Sweden and the United States (ICAP 2007).

Switzerland and the United Kingdom also recommend abstinence, but provide additional recommendations – maximum daily and weekly limits for those who chose to drink, advice never to become intoxicated, and a reminder that the risks are highest in the earlier stages of pregnancy, starting at conception (ICAP 2007).

Breastfeeding

Guidelines in Canada (CAMH 2006), Iceland and the United States recommend abstinence while breastfeeding (ICAP 2007). In New Zealand, the Ministry of Health's food and nutrition guidelines for pregnant and breastfeeding women recommend that women avoid drinking alcohol at all during pregnancy unless prescribed during pregnancy and breastfeeding (MoH 2006).

Medication

The Czech Republic guidelines mention that their standard recommendations do not apply to people taking medication (ICAP 2007). The Ireland guidelines mention that alcohol is contra-indicated by many medications, and provides some information on types of medication and problems that can occur (HPU 2003). The Italian guidelines recommend reducing alcohol consumption, as do the Canadian Low Risk Drinking Guidelines (CAMH 2006, ICAP 2007).

Health or social problems

According to the ICAP international guidelines table, Italy singled out type II diabetes with obesity as a condition in which alcohol should be limited. France's recommendations suggested abstinence for some conditions, including viral hepatitis and epilepsy. The guidelines in Spain and Canada gave similar advice (CAMH 2006, ICAP 2007).

Driving or other intensive activity

France, Italy, Luxembourg, Switzerland, Canada and the United States specifically identify the risks associated with driving in their alcohol guidelines (CAMH 2006, ICAP 2007). New Zealand (ALAC 2004), Italy and Switzerland also identify operating heavy machinery as a specific risk (ICAP 2007).

Health benefits

As shown in the ICAP international guidelines table, Sweden, the United Kingdom and the United States acknowledge that research may show some health benefits for specific groups in using alcohol. The United Kingdom guidelines mention that the health benefits can occur at low levels, needing no more than one standard unit of alcohol per day (about eight grams). The United Kingdom and Canada guidelines both advise that nondrinkers should not begin drinking alcohol for the health benefits (CAMH 2006, ICAP 2007).

Sources[9]

ALAC (Alcohol Liquor Advisory Council) (2004). *Low Risk Drinking*, online text. http://www.alcohol.org.nz/LowRiskDrinking.aspx

CAMH (Centre for Addiction and Mental Health) (2006). *Low-Risk Drinking Guidelines,* online text. http://www.camh.net/About_Addiction_Mental_Health/Drug_and_Addiction_Information/low_risk_drinking_guidelines.html

HPU (Health Promotion Unit) (2003). *The Facts about Alcohol*, online text. http://www.healthpromotion.ie/topics/alcohol/alcofacts/facts_about_alcohol/

ICAP (International Center for Alcohol Policy) (2007). *International Drinking Guidelines,* online text. http://www.icap.org/PolicyIssues/DrinkingGuidelines/GuidelinesTable/tabid/204/Default.aspx

MoH (New Zealand Ministry of Health) (2006). *Food and Nutrition Guidelines for Healthy Pregnant and Breastfeeding Women*: *A Background Paper*, MoH, Wellington. http://www.moh.govt.nz/moh.nsf/by+unid/F4F10903136588EFCC25716200123030?Open

WHO (World Health Organization) (2004). *Global Status Report: Alcohol Policy,* WHO, Geneva. http://www.who.int/substance_abuse/publications/en/Alcohol%20Policy%20Report.pdf

[9] All sites viewed on 25 September 2007

Appendix 4 Risk of alcohol-related accidents, injuries and other short-term harms: evidence details

Risk of injuries

There have been a number of studies of the acute effects of alcohol in injury patients who present to emergency departments and these studies have shown a similar pattern of injury risk (Vinson et al 2003, Borges et al 2004a, Cherpitel et al 2004b, Watt et al 2004, Spurling and Vinson 2005, Watt et al 2005, Borges et al 2006, Gmel et al 2006). A summary of these studies is shown in Table G1.1 in Part B of these guidelines. Further details are in Table A4.1, below.

Other short-term effects of alcohol consumption

Cognitive performance

Some studies have demonstrated that very low levels of alcohol consumption may slightly improve cognitive and psychomotor performance and reduce the risk of significant cognitive decline (Dufouil et al 1997, Espeland et al 2005).

As blood alcohol concentration increases however, cognitive function and psychomotor performance decrease rapidly (Easdon et al 2005). Less than two standard drinks may result in cognitive and psychomotor effects that increase risk of injury, such as effects on reaction time, cognitive processing, coordination and vigilance (Tagawa et al 2000, Howland et al 2001, Marinkovic et al 2001, Marinkovic et al 2004, Moulton et al 2005, Breitmeier et al 2007). Blood alcohol concentrations of about 0.05% impair driving ability (Tagawa et al 2000).

It is not only the peak of BAC that is relevant for injury; alcohol can have significant effects on psychomotor abilities with BAC levels as low as 0.03% (Eckardt et al 1998). A recent study tested 16 male subjects and found that at a BAC of 0.03%, verbal intelligence, general performance, vigilance towards acoustic and optical stimuli and general response time to these stimuli were not significantly impaired. However, cognitive functions that depend on processing of visual information and perception were significantly impaired (Breitmeier et al 2007).

Experience at performing certain tasks and tolerance of alcohol both influence the blood alcohol concentration at which a person may display cognitive and motor impairment (Preusser et al 1978). For example, although the risk of motor-vehicle accidents increase proportionate to blood alcohol concentration, younger drivers at a given blood alcohol concentration are at greater risk than older drivers, due to their relative inexperience and lower alcohol tolerance (Mayhew et al 1986, Zador et al 1991, Harrison and Fillmore 2005). Several studies have demonstrated that whilst blood alcohol concentrations up to 0.05% may not significantly impair psychomotor performance, they invoke a level of drowsiness sufficient to impair performance and increase motor vehicle crash risk (Banks et al 2004,

Barrett et al 2004, Barrett et al 2005). In combination with other drugs, such as marijuana, the effects of alcohol on crash risk are compounded (Lamers et al 2001, Kuypers et al 2006).

In addition to the increased risks while blood alcohol levels are raised, recent studies have indicated that, in areas such as cognitive function, attention span, and reaction time, substantial impairment can exist well after alcohol has been metabolised and passed from the body (Schweizer et al 2004, Schweizer et al 2006). Such temporary impairment, and its attendant risk, is the result of a 'hangover' effect (Verster et al 2003).

Aggressive behaviour and violence

Alcohol consumption increases the likelihood and extent of aggressive behaviours, increasing the chance that a conflict or dispute will not be resolved peacefully by verbal means. Injury risk from violence, both physical and sexual, is therefore increased (Hingson et al 2001, Giancola 2002, Jewkes et al 2002, Moraes and Reichenheim 2002, Howard et al 2003, Borges et al 2004ab, Cherpitel et al 2004a, Ogle and Miller 2004, Haggard-Grann et al 2006, Mousavi and Eshagian 2005, Borges et el 2006).

Some studies have shown that sexual aggression and violence increases when alcohol is consumed (Howard et al 2003). Gross et al (2001) included 160 male undergraduates in a randomised controlled trial to study the effect of alcohol consumption on aggressive behaviour. Students were assigned to two pairs of groups to consume alcohol or not (one pair of groups were blinded to their group; the others were not blinded) and were shown an audiotape of a sexual assault. Groups that consumed alcohol (or expected to do so) took longer to identify the inappropriate male sexual behaviour in the audiotape; and groups that consumed alcohol over-estimated the woman's sexual arousal in the scenario. Another small randomised controlled trial demonstrated that among men who have exposure to violent pornography, alcohol can have direct and indirect effects on sexual aggression (Norris et al 2002).

Alcohol consumption does not always increase aggressive behaviour, probably due to its interaction with personality. Several laboratory studies have used various measures of aggressiveness to demonstrate that alcohol interacts with personality characteristics and other factors related to a personal tendency towards violence (Cheong et al 2001, Giancola 2002abc, Parrott and Giancola 2004, Giancola 2006, Parrot and Giancola 2006).

Some studies have indicated that the role of alcohol in aggression may be different between the sexes. Gussler-Burkhardt and Giancola (2005) randomised males and females to alcohol and placebo groups. Participants competed in an interpersonal task where electric shocks are received from and administered to a fictitious opponent. In this study, alcohol increased aggression for males, but not females.

Alcohol is a significant contributor to between-partner violence (Moraes and Reichenheim 2002, Mousavi and Eshagian 2005, Ramisetty-Mikler et al 2007). Male drinking during a domestic violence incident increases the risk of injury and its severity to female partners (Testa et al 2003). The likelihood of female-initiated domestic violence is positively associated with heavy male drinking (Caetano et al 2005). In about 50% of cases of domestic, physical and sexual violence, the perpetrator has been drinking before the violence occurs, although the direct role of alcohol in precipitating or exacerbating the violence is not always clear (Room and Rossow 2001).

English et al (1995) estimated that alcohol is associated with about 16% of child abuse cases. Mothers who suffer from alcohol abuse disorders have also been shown to be significantly more punitive towards their children (Miller et al 1999). Alcohol is also an important factor in homicide: more than half of homicides and assaults are committed under the influence of alcohol (Martin 2001). A case-control study found that perpetrator problem drinking was associated with an eight-times increased risk of partner abuse and a two-times increased risk of femicide or attempted femicide (Sharps et al 2001).

Risk-taking behaviour

The relationship between alcohol consumption and risk-taking is well-established, but complex (Watt et al 2004). Alcohol consumption is associated with risk taking, impulsivity and sensation-seeking behaviours. People who exhibit these characteristics are more likely to engage in activities that may increase their injury risk (Cherpitel et al 1999).

A small study under laboratory conditions showed an increase in risk-taking using an impulsiveness questionnaire (Lane et al 2004). Laboratory-based observational studies have also shown that individuals are more likely to make risky choices after drinking alcohol than groups of individuals (Abrams et al 2006).

Other than injury, alcohol consumption is associated with risky behaviours such as sexual promiscuity. Observational studies have shown that alcohol intoxication increases the likelihood that people will engage in unprotected sex (Lin et al 2005, Abbey et al 2006). Abbey et al (2006) also found that intoxicated individuals are less likely to discriminate between low-risk and high-risk partners when choosing to have unprotected sex. By contrast, when perceived levels of intoxication are higher than actual intoxication, the likelihood of engaging in unsafe sex is lower (Maisto et al 2002, Maisto et al 2004). A recent study of high-school students found a strong dose-response relationship between binge-drinking and risky behaviours including riding in a car with an intoxicated driver and using illicit drugs (Miller et al 2007).

Laboratory-based studies also support the association between alcohol consumption and risk-taking behaviour. A number of randomised controlled trials have shown that drinking increased participants' likelihood of making risky choices about sexual activity (Maisto et al 2002, Maisto et al 2004, Testa et al 2006). Conversely, Leigh et al (2007) showed that young people prepare for safe sex when they know that they will be drinking.

Self-harm and suicide

Alcohol use is significantly associated with episodes of deliberate self harm (McCloskey and Berman 2003). A recent multi-centre study found that alcohol was involved in more than half of all self-harm cases presenting at emergency departments in the United Kingdom (Hawton et al 2007). Longitudinal data shows that the prevalence of alcohol use around the time of a deliberate self-harm episode has increased for both males and females over the past two decades (Haw et al 2005, O'Loughlin and Sherwood 2005).

Heavy drinking is a major risk factor for suicide and suicidal behaviour in both males and females across the lifespan (Cherpitel et al 2004b, Kaminer et al 2006, Kolves et al 2006, Sher 2006). Alcohol consumption is associated with increased suicide risk in the general population, but is more strongly associated with enhanced risk in the psychiatric population (McCloud et al 2004). A recent review of studies on completed (37 studies) and attempted

suicides (16 studies) found that between 10% and 69% of attempted suicides involve alcohol, and that between 10% and 73% of attempted suicides are alcohol-related (Cherpitel 2004b).

In middle age, there appears to be a 'u-shaped' relationship between alcohol use and suicide, with non-drinkers and regular heavy drinkers at the greatest risk of suicide, and occasional drinkers at the lowest risk of death from suicide (Akechi et al 2006). Waern (2003) found that a history of alcohol misuse or dependence was common in males and females aged over 65 years who completed a suicide attempt. Alcohol misuse and dependence was more prevalent in male suicide cases (35%) than female suicide cases (18%). Not all alcohol-dependent patients attempt suicide, however and there are some studies which point to the difference being low serum cholesterol levels in those who do attempt suicide (Pektas et al 2004, Deisenhammer et al 2006).

While the available data are poor, there appears to be a particularly strong association between suicide and alcohol use among some Aboriginal and Torres Strait Islander peoples (Hunter 1999, Tatz 1999). A recent study found that Indigenous suicide rates increased by 800% in the Northern Territory between 1981 and 2002, with 72% of cases involving alcohol misuse (Measey et al 2006).

Mental health

Alcohol accompanies and, to some extent, encourages good times, sociability, shared experiences, and personal enjoyment and well-being (Peele 1997). The social and psychological benefits may also include enhanced creativity and a therapeutic value in times of acute stress. Whilst a small amount of alcohol may induce short-term stress relief, it does not address the cause of stress. There is considerable evidence that repeated use of alcohol to dampen stress may increase anxiety levels and lead to a degree of dependence on alcohol, especially in vulnerable individuals (Kushner et al 2000, Carrigan and Randall 2003, Thomas et al 2003).

Studies in human populations show that moderate consumption of alcohol typically induces positive feelings and happiness whilst blood alcohol concentration rises (Eckardt et al 1998). Alcohol is, however, a central nervous system depressant, and in the hours following alcohol consumption, increased anxiety and depression are common (Kushner et al 2000). People who depend upon or misuse alcohol tend to have higher prevalences of mood and anxiety disorders, and vice versa, and for these people the depressive effects of alcohol are of particular consequence (Hakko et al 2005, Goldstein et al 2006a). For these reasons, alcohol is frequently associated with deliberate self-harm and suicide (see further details about these issues, above).

Further details about the effects of alcohol on people with mental health problems are given in Part C ('Additional precautions and advice').

Sleep and sexual function

Moderate consumption of alcohol is commonly viewed as a sleep aid. While alcohol may induce sleep in the short-term, it leads to increased arousal and wakefulness several hours after consumption and is implicated in aggravating sleep disorders (Castaneda et al 1998, Peppard et al 2007). Even at moderate levels, alcohol has been shown to disrupt the latter, heavier, part of the sleep cycle (Castaneda et al 1998). Sleep disruption and chronic sleep deprivation can increase the risk of injury, disrupt cognitive processes and trigger a variety of

mental health problems (Castaneda et al 1998, Williamson and Freyer 2000, Drummond et al 2006).

Alcohol use can cause or exacerbate a range of sexual problems in males and females. At low levels, alcohol can reduce inhibition and increase sexual desire (Cheng et al 2007), however beyond the level of the guidelines, the depressive effects of alcohol are apparent. For males, excessive alcohol consumption or long-term alcohol abuse may result in the inability to achieve and maintain an erection (Bacon et al 2003, Arackal and Benegal 2007). Females may find achieving orgasm more difficult due to depressed nervous system responses. In females who consume alcohol heavily, the likelihood of heavy or irregular menstrual periods, spontaneous abortion and infertility is greater when alcohol is consumed above the guideline levels (Bradley 1998).

Table A4.1 Studies of injury patients in emergency departments (EDs)

Study	Population	N	Study details	Results (general)	Relative risks/odds ratio
Humphrey et al 2003	Random sample of injured patients in New Zealand ED	166	Interviews and breath testing Case-crossover study with data collected on: • Injury • Drinking in 6 hours before injury • Drinking on same day of week one week before injury	35% of all injuries were alcohol-related; >60% of injured were males aged <30 years Median pre-injury alcohol intake 103 mL 29% of alcohol-related injuries occurred at home, 25% in licensed premises, 21% in public places,16% in private vehicles The victims and perpetrators of most violence-related injuries (17% of cases) had consumed alcohol Alcohol-related injuries were more severe (by triage code) than non alcohol-related injuries (*P*=0.047)	Case-crossover results: RR (drinking cf no drinking) 2.8 (95%CI 1.99 to 3.96) Cumulative risk of 1.14 for every 30 mL alcohol consumed
Vinson et al 2003	Injured patients >18 years in 3 EDs in Missouri, United States Age, sex, injury time-matched controls	2517 (1432 men) 1856 (948 men)	(i) Case–control study (ii) Case-crossover study (injured patients) with data collected on: • Injury • Drinking in 6 hours before injury • Drinking in same 6-hour period the day before • Past month hazardous drinking (> 60 drinks in past 28 days)/alcohol dependence; alcohol consumption measured as US standard drinks (14 g ethanol: 12 oz beer, 5 oz wine or liquor)	Both analyses found exponential dose-response relationships between injury risk and quantity of alcohol consumed 6 hours before the injury Effect of alcohol on injury risk is more strongly related to acute exposures than long-term alcohol exposure	(i) Case-control results: Male: OR 3.0 (95%CI 2.1 to 4.3)] Female: OR 3.3 (95%CI 1.9-5.8) (ii) Case-crossover results: (drinking in 6 hours before cf drinking same hours previous day) Male: OR 3.7 (95%CI 2.2 to 6.1) Female: OR 4.2 (95%CI 3.0 to 5.8) 1-2 drinks: OR 1.7 (male); 1.9 (female) 3-4 drinks: OR 6.0 (male); 6.3 (female)
Borges et al 2004a	Injured patients >18 years in 3 EDs in California and Mexico	961 (630 men)	Case-crossover study with data collected on: Injury Positive blood alcohol content (BAC) >0.01 mg/ mL or higher Drinking in 6 hours before injury Usual alcohol consumption over past 12	Two-thirds of injured were male; 45% were <30 years of age 15% of injured people consumed alcohol in the 6 hours before the injury Injury risk highest in the first hour after alcohol consumption; drinking from 2-6 hours prior to injury did not further increase the risk	RR (hour after drinking cf no drinking) 4.33 (95%CI 3.55 to 5.27) Patients <30 years: RR 6.04(95% CI 4.51 to 8.10; *P*=0.006) High school only: RR 10.48 (95%CI 6.67 to 16.46) *P*<0.001 No dependence history: RR 10.18 (95%

Study	Population	N	Study details	Results (general)	Relative risks/odds ratio
			months	BAC and self-reported alcohol consumption at ED admission showed similar results Risk of injury higher for those who have no history of drunkenness or alcohol dependence	CI 7.51 to 13.80) *P*<0.001 No drunkenness history: RR11.99 (95% 7.86 to 18.24) *P*<0.001
Cherpitel et al 2004a	Injured patients >18 years in EDs in Warsaw (W) and Sosnowiec (S), Poland	938 (506 [W], 432 [S])	Case-crossover study with data collected on: • Injury • Quantity and frequency of usual drinking • Alcohol, abuse, harmful drinking in past year • Drinking during 6 hours before injury • Quantity/type of drink in 6 hours before injury	All injuries: Two-thirds of injured were male; one-third were <30 years of age Four-fold injury risk increase for those drinking in 6 hours before injury Injury risk higher for those with alcohol use disorders (AUD) Violence-related injuries: 17-fold increased risk if drinking in 6 hours before injury Injury risk significantly greater for females, those <30 years and those without an AUD.	All injuries (drinking 6 hours before cf usual drinking) RR total: 4.3 (95%CI 3.4 to 5.3) RR male: 4.0 (95%CI 3.2 to 5.1) RR female: 5.8 (95%CI 3.6 to 9.3) RR <30 years: 4.5 (95% CI 3.1 to 6.4) RR AUD: 5.8 (95%CI 4.1 to 8.4) Violence-related injuries RR total: 17.5 (95%CI 11.3 to 27.1) RR male: 14.9 (95%CI 9.4 to 23.7) RR female: 323.5 (95%CI 16.8 to 6234.3)
Watt et al 2004	Injured patients aged ≥15 years in ED at Gold Coast Hospital	488 cases	Case control study with data collected on: Injury Usual drinking patterns Self-reported quantity of alcohol consumed in 24 hours before injury Drinking setting Beverage preference Alcohol consumption measured according to NHMRC guidelines for low, medium and high risk drinking	Consuming any alcohol in 6 hours before injury significantly increased injury risk Adjusting for usual alcohol consumption increased alcohol-injury odds ratios Adjusting for risk-taking and substance use, changes in injury risk observed for all measures of alcohol consumption Confounding exists in alcohol-injury relationship due to usual drinking, risk taking and substance abuse	All injuries (any drinking cf no drinking) OR drinking 6hrs before: 2.96 (95%CI 1.5 to 5.8) OR drinking 6-24 hours before: 1.34 (95% CI 0.8 to 2.4) Above low risk OR: 2.41 (95% CI 1.1 to 5.2) Beer drinking OR: 1.86 (95%CI 0.9 to 3.9) Spirits drinking OR: 3.05 (95%CI 1.1 to 8.2) Beverage combination OR: 3.16 (95%CI 1.1 to 8.8)
Watt et al 2005	Injured patients ≥15 years at Gold Coast Hospital ED	593	Cross-sectional study Self-reported quantity of alcohol consumption in 24 hours before injury Beverage preference	No significant association between any of three measures of alcohol consumption and injury type Effects of acute alcohol consumption are not	None reported

Study	Population	N	Study details	Results (general)	Relative risks/odds ratio
			Drinking setting Substance use Risk-taking behaviour Nature of injury/body part injured	specific to injury type	
Spurling and Vinson 2005	As for Vinson et al 2003		As for Vinson et al 2003	Population attributable fraction (PAF) for acute injury risk 8.6% (95% CI 5.7 to 11.5) (case-control), 10.6% (95% CI 7.8 to 13.5) (case-crossover) PAF of injury after non-hazardous consumption (<5 drinks for males, <4 drinks for females) 4.5% (case-crossover) and 3.1% (case-control) PAF of injury due to alcohol dependence 3.1%	Case control Low risk: OR 2.0 (95% CI 1.4 to 2.8) High risk: OR 10.8 (95%CI 5.6 to 21) Total male PAF: 10.8% Total female PAF: 5.9% Case-cross over (drinking in 6 hours before cf drinking same hours previous day) Low risk: OR 2.7 (95% CI 2.0 to 3.8) High risk: OR 9.5 (95% CI 5.2 to17.0) Total male PAF: 13.7% Total female PAF: 6.6%
Borges 2006	Injured patients (≥ 18 years) in 10 EDs worldwide	4230	Case-crossover study with data collected on: • Injury • Drinking in 6 hours before injury • Drinking during the same time on the same day of the previous week	18% of injured had drunk alcohol in 6 hours before injury Of these, 85% were males, 48% were <30 years, and 32% had violence-related injuries (assault or self harm) Borges et al (2004a) and Borges et al (2006) found lower risk for people with alcohol dependence and higher frequency of drunkenness. Injury risk was highest for those who occasionally drink more than usual	OR (drinking before injury): 5.7 (95%CI 4.5 to 7.3). OR increased with the consumption of a single drink: OR (1 drink) 3.3 (95%CI 1.9 to 5.7) OR (≥ 6 drinks) 10.1 (95%CI 7.0 to 14.6) Each additional drink increased the risk of injury by 25% (OR 1.25 (95% CI 1.20 to 1.30)
Gmel et al 2006	Patients (≥16 years) admitted to the surgical ward of ED (Lausanne, Switzerland) between January	5077 (I) 3659 (NI)	ED data collected on: • Injury • Drinking in 24 hours before ED attendance • Frequency of having drunk ≥ 4 (female) or≥ 5 (male) drinks in past month	Males <45 years more likely to be injured than females of same age (two-thirds, versus one-third Females > 65 years more likely to be injured than males of the same age For all risk groups, those who had not drunk in 6 hours before, ORs ≤2 (results not	Alcohol <4 (female) or <5 (male)drinks: Low risk OR: 2.35 (female) 2.11(male) Chronic high OR: 2.44 (female) 2.85 (male) RSOD OR: 3.8 (female) 3.18 (male) Risk accumulators OR: 1.61 (female) 2.50 (male)

Study	Population	N	Study details	Results (general)	Relative risks/odds ratio
	2003 – June 2004 (I = injured; NI = not injured)		5 groups constructed to calculate alcohol attributable fraction: • Abstainers • Low-risk drinkers: no more than 7 (female) or 14 (male) drinks/week; and no heavy drinking episodes (HED)* in past month • Chronic high-volume drinkers: >7 or 14 drinks/week as usual volume; no HED in past month • Risky single occasion drinkers (RSODs): no more than 7 or 14 drinks/week; some HED in past month • Risk accumulators: >7 or 14 drinks/week, plus HED in past month *Heavy episodic drinking volume not defined but likened to binge-drinking	presented) Risk of injury increased with volume of drinking, HED, and pre-attendance drinking People who usually drink little but drink heavily on occasion appear to be at greatest risk	Alcohol ≥4 (female) or ≥5 (male) drinks: RSOD OR: 7.38 (female) 6.38 (male) Risk accumulators OR: 4.43 (female) 3.32 (male) Alcohol attributable injuries: RSODs + ≥4 (female) or ≥5 (male) drinks before the injury: 46.9% (male); 23.2% (female) Low-risk drinkers + <4 (female) or <5 (male) drinks before the injury: 20.4% (male); 47.5% (female)
Watt et al 2006	As for Watt et al 2005	593	Cross-sectional study Self-reported quantity of alcohol consumption in 6 and 24 hours before Usual alcohol consumption patterns Drinking setting Risk-taking behaviour Injury severity	Drinking setting and usual drinking patterns were not significantly associated with injury severity in either crude or adjusted analyses Acute alcohol consumption not associated with minor or moderate injury Some suggestion that acute alcohol consumption associated with serious injury	Risk of injury (drinking cf no drinking in 6 hours before) Above low risk OR: 3.35 (95%CI 1.2 to 9.6) Drinking beer OR: 3.54 (95%CI 1.1 to 11.1)

Appendix 5 Risk of alcohol-related diseases: evidence details

Alcohol consumption has been associated with a range of long-term (chronic) diseases. These are listed in Section 2.4 of Part A of these guidelines. Adverse effects that may cause premature death include various forms of cancer, hypertension, haemorrhagic stroke, ischaemic stroke, heart disease, cirrhosis of the liver and alcohol dependence. In addition, other adverse effects of alcohol, such as cognitive impairment, mental health problems, pancreatitis, eye disease and sexual health issues can reduce quality of life. At low levels of consumption, alcohol may also have some benefits; reductions in heart disease, ischaemic stroke, diabetes, gallstones and dementia have all been recorded.

There is a very large literature, dating back several decades, which has used the best epidemiological data to describe the risks and benefits of alcohol for a range of chronic diseases and disorders. However, the way in which alcohol was measured in most of these studies was different, making it difficult to compare results. Until the mid-1990s, there was little systematic work undertaken to describe the overall dose-response relationship between alcohol consumption and the risk of disease. In the past 10 years, however, there have been a number of studies that have combined the data from the major epidemiological studies worldwide to derive the overall impact of alcohol on developing or dying from alcohol-related diseases and conditions (see below).

These findings are summarised in Guideline 1, in Part B of these guidelines. Further details of the major studies are provided in Tables A5.1 and A5.2.

Other long-term health effects of alcohol consumption

Diabetes

The relationship between alcohol consumption, insulin sensitivity, type 2 diabetes mellitus and the metabolic syndrome that clinically precedes it, is not clear (Hulthe and Fagerberg 2005). Whilst J- or U-shaped relationships have been seen in these populations and nondiabetic adult male and female populations (Ashley et al 2000, Dixon et al 2002, Moriya et al 2003), linear associations with no clear upper limit have also been observed in nondiabetic subjects of all ages (Kato et al 2003).

In a recent randomised controlled trial, middle-aged women who consumed 30 g alcohol/day (2 standard drinks) received beneficial effects on insulin, triglyceride concentrations and insulin sensitivity (Davies et al 2002). A similar finding was observed in a cohort of female moderate drinkers (Beulens et al 2005). By contrast, a recent population-based cross-sectional study found that lifetime drinking patterns were significantly associated with the prevalence of decreased insulin sensitivity and the diabetes-related metabolic syndrome (Fan et al 2006). Some studies have reported an increased incidence of type 2 diabetes with heavy alcohol consumption (Wei et al 2000).

Consumption of alcohol can be a risk for hypoglycaemia in patients suffering from type 1 diabetes. Alcohol and hypoglycaemia have independent, but additive effects on cognitive

function. It is recommended that type 1 diabetics who plan to drive, abstain from alcohol (Cheyne et al 2004).

Appetite

Although alcohol acts as a short-term appetite enhancer (Caton et al 2004, Gee 2006), chronic alcoholics often suffer from malnutrition (Halsted 2004). Heavy drinkers are characterised by deficiencies of folate, thiamine, pyridoxine and other vitamins, which increases the likelihood of anaemia, compromised cognition and night blindness. The causes of alcoholic malnutrition are multi-faced and include, loss of appetite (anorexia), abnormal digestion of macronutrients and micronutrient malabsorption, increased skeletal and protein breakdown and abnormal interaction between ethanol and lipid metabolism (Halsted 2004).

Obesity

Alcohol is an energy-dense food source, containing 7.1 kcal/g (Suter 2005). Therefore individuals who consume large amounts of alcohol may not compensate for the additional energy increase, resulting in weight gain and potential problems with obesity (Foster and Marriot 2006). However, there is some conjecture as to whether alcohol consumption represents an increase in risk for overweight and obesity. Some studies have suggested that weight gain is inevitable, due to the high caloric content of alcohol and its appetite stimulating effects (Suter 2005, Foster and Marriott 2006). Other studies have suggested that heavy drinkers are at risk, whereas those who drink moderately are at no greater risk of the conditions (Arif et al 2005). Koppes et al (2005) found a moderate inverse association between alcohol consumption and waist circumference.

Wannamethee et al (2005) found that men who consumed more than 21 units/week had higher levels of central and general adiposity than lighter drinkers, irrespective of the type of alcohol they consumed, although the association was most clearly seen in beer and spirit drinkers. There is general agreement between authors that the absolute amount of alcohol consumed, drinking frequency and genetic factors all influence an individual's tendency to gain weight (Suter 2005).

Gallstones

Recent studies have confirmed that moderate alcohol consumption may protect against gallstones because alcohol lowers bile cholesterol saturation, reducing the rate of cholesterol gallstone formation (Holman et al 1996, English et al 1995, Ashley et al 2000, Cuevas et al 2004). One study suggested that men who drank 45 g (4.5 standard drinks) or more of alcohol on five to seven days per week halved their risk of gallstones (Leitzmann et al 1998).

Sexual function

Chronic alcohol consumption has been shown to negatively affect sexual function, especially in males (Frias et al 2002, Sarkola et al 2003). The likelihood that males will suffer from retarded ejaculation increases with heavy drinking (Richardson et al 2006), and the prevalence of impotence and infertility is also common in men who are dependent on alcohol. Several studies have shown an association between heavy alcohol consumption and increased prevalence of sperm defects (Auger et al 2001, Marinelli et al 2004), which can contribute to male infertility. In a systematic review, Marinelli et al (2004) found three studies that showed a dose-dependent impact of alcohol on sperm morphology and volume.

Drinking alcohol has been shown to alter the levels of circulating sex hormones in women (Onland-Moret et al 2005). Women who consume more than 25 g of alcohol/day have higher levels of oestrogenic precursor hormones compared to women who do not drink. Levels of male sex hormones in these women, including testosterone and its precursors, did not differ between the drinking groups. The results support the hypothesis that drinking alcohol increases the risk of breast cancer by increasing female sex steroid levels.

Vision

Alcohol has been associated with two important conditions of the eyes: cataracts and age-related macular degeneration (AMD). The Blue Mountains Eye Study reported that heavy drinking (defined as 9 standard drinks per week or more) increases the risk of nuclear, cortical and posterior subcapsular cataracts (Hiratsuka and Li 2001).

The relationship between alcohol and AMD is more difficult to evaluate due to the number of variables, including the different types and symptoms of AMD, definitions of alcohol intake and types of alcohol. However, the majority of studies have shown that drinking more than 6 beers per week increases the risk of developing drusen and drinking more than about 3 drinks per day, particularly of wine or spirits, is associated with development of AMD (Cho et al 2000, Klein et al 2002, Buch et al 2005, Arnarsson et al 2006).

The relationship between alcohol consumption and glaucoma is not clear, with some researchers reporting a protective effect of moderate drinking (about 3-4 standard drinks per day) (Fan et al 2004). However, others have shown that alcohol consumption increases intraocular pressure, which is a risk factor for glaucoma (Yoshida et al 2003).

Sexually transmitted diseases

There are recent studies that alcohol consumption may increase the prevalence of some sexually transmitted diseases (STDs), including hepatitis C (HCV) (Safdar and Schiff 2004, Anand and Thornby 2005, Kulig and Beresford 2005). In a recent systematic review, Cook et al (2005) found 11 studies that measured the association between problem drinking and sexually transmitted diseases. Eight of the included studies found statistically significant increases in the risk of STDs, including gonorrhoea, syphilis, trichomonas, chlamydia or herpes simplex type 2. However, the authors suggested that the relationship between alcohol misuse and greater STD prevalence might be confounded by factors such as risk-taking behaviour.

It has been shown that patients with chronic HCV infection who consume large amounts of alcohol have more severe liver disease than those HCV patients who abstain, and are less receptive to anti-retroviral therapy (Safdar and Schiff 2004, Kulig and Beresford 2005). A recent meta-analysis found no evidence to suggest that alcohol increases replication of the HCV virus and that the damage caused by alcohol abuse and HCV are additive (Anand and Thornby 2005).

Some studies indicate that the increased prevalence of STDs may be due to alcohol-induced reductions in immune system function. Bayramgurler et al (2005) described the case of a chronic alcoholic who suffered from a rare form of secondary syphilis, usually seen in severely malnourished or immunocompromised HIV positive patients, and offered the hypothesis that the patient was susceptible to this infection only as a result of severe alcohol-related immunosuppression.

Overall, alcohol consumption may increase the prevalence of some STDs including HCV, gonorrhoea, syphilis, trichomonas, chlamydia and herpes simplex virus type 2. Increased prevalence may be due to immunosuppression or increases in risk-taking behaviour under the influence of alcohol.

Brain structure and function

The relationship between chronic heavy alcohol consumption and cognitive impairment is well established (Friend et al 2005, Liappas et al 2005, Rosenbloom et al 2005, Glass et al 2006). Heavy drinkers exhibit negative structural and metabolic brain changes, and have an increased risk of dementia (Gilchrist et al 2005, Gazdzinski et al 2005). Some studies suggest that people drinking 70–84 grams of alcohol (7–8.5 Australian standard drinks) per day over an extended period of time show some degree of cognitive inefficiency. People drinking 98 to 126 grams alcohol (10–12.5 Australian standard drinks) per day show mild cognitive deficits, and 140 grams (14 Australian standard drinks) or more per day results in moderate cognitive deficits similar to those found in people with diagnosed alcohol dependence (Parsons and Nixon 1998).

People who regularly drink heavily may develop a thiamine deficiency. Prolonged deficiency of this B vitamin causes a reduction in energy supply to the brain, causing the neurological disorder, Wernicke-Korsakoff syndrome (Day et al 2004, Thomson and Marshall 2006).

Heavy alcohol consumption is also associated with negative changes in brain structure, including atrophy and severe frontal lobe dysfunction (Moselhy et al 2001). Many studies have found significant reductions in white matter, grey matter, cerebrospinal fluid volume (Cardenas et al 2005, De Bruin et al 2005, Rohlfing et al 2006). In females, the detrimental effects occur at lower levels of alcohol consumption (Anstey et al 2006). These changes may be responsible for the cognitive impairment seen in people with chronic alcohol dependence (Mochizuki et al 2005).

Whilst excessive drinking is associated with higher rates of dementia, some studies suggest that moderate alcohol consumption may protect against neural degeneration and therefore moderate drinkers may have improved cognitive function and lower rates of dementia as they age (Ashley et al 2000, Ruitenberg et al 2002, Zuccala et al 2001, Huang et al 2002, Pihl et al 2003, Deng et al 2006). Several studies point to a ‘J-shaped’ relationship between alcohol consumption and dementia, where the greatest risk of dementia is for abstainers and heavier drinkers (Anttila et al 2004). A recent study found that drinkers (compared to non-drinkers) had significantly lower rates of depression, higher cognitive performance, cognitive flexibility, verbal memory and greater knowledge of memory processes (McDougall et al 2006). The maintenance of cognition in moderate drinkers is persistent between the sexes (Barnes et al 2007) and remains across a variety of ethnic groups (Bond et al 2004, Britton et al 2004, Lindeman et al 2005).

Excessive alcohol consumption leads to brain atrophy and reduced cerebrospinal fluid volumes, both of which contribute to cognitive decline (Cardenas et al 2005, De Bruin et al 2005, Rohlfing et al 2006). In turn, cognitive impairment increases the person’s inability to function socially or professionally.

Mental health

Heavy alcohol consumption is associated with several mental health conditions, including social phobias and anxiety disorders, uni- and bipolar depression and schizophrenia. Further details are included in Part C ('Additional precautions and advice').

Table A5.1 Meta-analyses of risks of specific alcohol-related conditions

69 years	Condition	Study details	Results (general) [a]	Relative risks/odds ratio
Corrao et al 1999	12 alcohol-related neoplasm and non-neoplastic diseases/injuries	• Literature searched 1996-1998 • Meta-regression models used to evaluate linear and non-linear effects of alcohol intake on relative risk • Evaluated risk at 25 g/day, 50 g/day, 100 g/day	• 200 studies selected, 123 studies with higher quality scores used for meta-analysis • Ischaemic stroke, gastric and duodenal ulcer risk appear independent of alcohol • Low alcohol intake (25 g/day) showed significant risk for all other conditions	Essential hypertension:[a] 0–25 g/day: RR 1.4 (95% CI 1.3 to 1.5) 50 g/day: RR 2.0 (95% CI 1.8 to 2.3) ≥100 g/day: RR 4.1 (95% CI 3.1 to 5.9 Breast cancer: 0–25 g/day: RR 1.2 (95% CI 1.0 to 1.4) 50 g/day: RR 1.5 (95% CI 1.1 to 2.0) ≥100 g/day: RR 2.2 (95% CI 1 to 4.0)
Corrao et al 2000	Coronary heart disease	• Literature searched 1966-1998 • Meta-regression models used to evaluate non-linear effects of alcohol intake on relative risk	• 51 studies selected, 28 cohort studies used for meta-analysis • Lower protective and harmful effects for females, males living outside Mediterranean and studies where outcome measure was fatal event	0–20 g/day: RR 0.80 (95% CI 0.78 to 0.83) Up to 72 g/day: RR 0.96 (95% CI 0.92 to 1.00) ≥89 g/day: RR 1.05 (95% CI 1.00 to 1.10)
Di Castelnuovo et al 2002	Vascular risk	• Published studies to September 2001 • General variance-based methods used to evaluate effects of beer and wine consumption on vascular risk	• 13 studies involving 209,418 people examined effect of wine • 10 studies supported J-shaped relationship of wine and vascular risk • Inverse relationship between mortality and vascular risk up to 150 mL of wine, maximum risk reduction up to 750 mL/day (not statistically significant) • Risk with moderate beer consumption measured in 15 studies involving 208,036 people [b] • 7 studies involving 136,382 people found no relationship between varying amounts of beer and vascular risk • Evidence of significant inverse relationship between light-moderate wine consumption and vascular risk • Smaller, significant inverse relationship between light-moderate beer consumption and vascular risk	Up to 150 mL wine/day: RR 0.68 (95%CI 0.59 to 0.77) Light-to-moderate beer intake:[b] RR 0.78 95% CI 0.70 to 0.86)

69 years	Condition	Study details	Results (general) [a]	Relative risks/odds ratio
Reynolds et al 2003	Stroke	• Literature search 1966-April 2002 • 35 observational studies of total stroke, ischaemic stroke or haemorrhagic stroke	• Meta-analysis revealed a J-shaped relationship between alcohol consumption and total and ischaemic stroke and a linear relationship between alcohol consumption and haemorrhagic stroke	The lowest risk for total stroke was among those consuming < 12 g/day The lowest risk for ischaemic stroke was among those consuming < 12–24 g/day Risks were similar for men and women (slightly lower in women at < 12 g/day)
Corrao et al 2004	15 major alcohol-related neoplasms and non-neoplastic diseases	• Literature search 1966-1998 • Fixed and random effects models used to evaluate linear and non-linear effect of alcohol intake Alcohol intake of 25, 50 and 100 g/day considered	• 156 studies selected, pooled *N* =116,702 subjects • Strong risk trends for cancers of oral cavity, oesophagus and larynx, hypertension, liver cirrhosis, chronic pancreatitis, injuries and violence • Weaker trends for colon, rectal and breast cancer • Significant increased risk for ≥25 g/day across most diseases (except CHD, ischaemic stroke, ulcer, colon and rectal cancer) • Threshold values for ischaemic and haemorrhagic stroke • J-shaped relationship for CHD • No clear relationship for gastroduodenal ulcer	Coronary heart disease (males and females)[a] 0–25 g/day: RR 0,80 (95%CI 0.79 to 0.83) 50 g/day: RR 0.87 (95% CI 0.84 to 0.90) ≥100 g/day: RR 1.13 (95% CI 1.06 to 1.21)

Standridge et al 2004	Vascular risk, dementia, diabetes, osteoporosis	General review of large cohort and cross-sectional studies (including Physicians, Health Professionals, Nurses Health, Framingham, SOLVD trials, Rotterdam, and Copenhagen City Heart)	• Moderate, non-abusive consumption [c]
			  • lowers vascular risk (CHD, myocardial infarct, heart failure, stroke)
			  • lowers dementia, diabetes, osteoporosis risk (results not presented here)
			• Maximum benefit of alcohol occurs after ½ standard drink
			• Benefits lost, risk increases at lower volumes for women than men
			• Risk of abuse may prohibit clinical encouragement of drinking solely for health benefits
			• No compelling reason to recommend cessation in individuals who have demonstrated pattern of moderate, non-abusive consumption [c]
				Coronary heart disease[a]
				Monthly drinkers (male): RR 1.02
				Weekly drinkers (male): 0.82
				Daily drinkers (male): 0.61
				
				Myocardial infarct
				Alcohol 3–4 days/week (male): RR 0.68
				Alcohol 5–7 days/week (male): RR 0.63

69 years	Condition	Study details	Results (general) [a]	Relative risks/odds ratio
White et al 2004	15 major alcohol-related neoplasms and non-neoplastic diseases	• Alcohol consumption in units/week (1 unit = 9 g alcohol) • Measured risk for any drinking, drinking above nadir (above lowest risk alcohol consumption), more than British Guidelines (males; 21 units/week; females 14 units/week)	• Ischaemic heart disease deaths prevented by alcohol consumption approximately equal to other deaths attributable to alcohol • Drinking above recommended limits remains responsible for many deaths and a large loss of person-years of life	Deaths prevented by alcohol: Male: 0.8% (95% CI 0.2 to 1.3%) Deaths attributable to any alcohol: Female: 0.1% (95% CI –0.3 to 0.4%) Deaths attributable to alcohol above nadir: Female: 1.2% Male: 2.8% Deaths attributable to alcohol above guidelines: Female: 0.8% (95% CI 0.6 to 1.0%) Male: 2.1% (95% CI 1.9 to 2.3%) Person years of life lost to 65 years: Any drinking: 5.6 (female), 10.3% (male) Above nadir: 6.0% (female), 12.6% (male) Above guidelines: 4.0% (female), 8.5% (male)
Fillmore et al 2006	Coronary heart disease mortality	• Prospective mortality studies • Literature search 1950s-mid 2004 • Modelling to accommodate for misclassification bias for abstainer category (i.e. distinction made between never-drinkers and former drinkers)	• 54 all-cause mortality studies, 35 CHD mortality studies • No significant all-cause or cardiac protection associated with alcohol consumption at any level • Estimates of mortality from heavier drinking may be higher than previous estimates (because of previous misclassification bias)	Various OR calculations presented with and without misclassification errors. Without misclassification errors showed ORs for all-cause mortality of close to 1.0 (approx. 0.95) for drinking up to 24 grams per day, 1.0 for drinking 25-44 g/day and 1.2 for >45 g/day)

69 years	Condition	Study details	Results (general) [a]	Relative risks/odds ratio
McPherson 2007	6 types of cancer	• Summary of cancer mortality relative risks from Corrao et al 2004	• Moderate consumption (2-3 drinks/day for men, 1-2 drinks/day for women) cancer risk does not increase above two-fold • Association between alcohol and breast cancer is not strong and not necessarily causative	For 25 g/day alcohol: Oral cavity/pharynx cancer: RR 1.9 Oesophageal/larynx cancer: RR 1.4 Colorectal cancer: RR 1.1 Liver cancer: RR 1.2
Harris et al 2007	Cardiovascular (CVD and coronary heart disease (CHD) mortality	• Prospective cohort study with mean follow up of 11.4 years (Melbourne Collaborative Cohort Study) • 38,200 volunteers (23,044 women) aged 40–69 years at baseline • Self-reported alcohol intake compared to lifetime abstention (ie no misclassification error; see Fillimore et al 20006, above)	• Usual daily alcohol intake was associated with lower CVD and CHD mortality risk for women but not for men. • Male former drinkers had over twice the mortality risk for CVD and CHD. • Benefit for women appeared to be mostly from wine (as wine was the only beverage associated inversely with mortality for women) but comparison of beverages was not possible. • Drinking frequency was associated inversely with CVD and CHD mortality risk for men but not for women	Women drinking >20 g/day: HR for CVD: 0.43 (95%CI 0.19 to 0.95; Ptrend = 0.18) HR for CVD: 0.19 (95%CI 0.05 to 0.82; Ptrend = 0.24)

a Selected results presented. Refer to publication for complete list of results.

b 'Light-to-moderate' and 'moderate' drinkers defined by authors based on meta-analysed data, no explicit statement detailing what alcohol volume/time period constitutes these categories.

c 'Moderate, non-abusive' drinking defined by authors based on literature review data, no explicit statement of alcohol volume/time period that constitutes this category

Table A4.2 Meta-analyses of risks of death (all causes)

Study	Condition	Study details	Results (general)	Relative risk/odds ratios
Gmel et al 2003	All-cause mortality	• Literature searched until 2000 • Precision-weighted pooling of relative risks; precision-weighted hierarchical analysis	• 79 included studies • Male ex-drinkers had higher mortality risk than lifetime abstainers • The higher and more diverse alcohol consumption, the wider the dip of the J-shaped curve • Protective effect greater for persons older at baseline • Longer follow up time showed less protective benefit • Overall benefit of light-moderate (males: 9 to 15 g/day; females: 3 to 13 g/day) drinking remained under all conditions indicating high validity of J-shaped relationship between alcohol consumption and all-cause mortality risk	Male exdrinkers: RR 1.21 (95%CI 1.10 to 1.32) Female exdrinkers: RR 1.44 (95%CI 1.28 to 1.61)
Di Castelnuovo et al 2006	All-cause mortality	• Literature search to end 2005 • Weighted regression analysis of polynomials	• 34 studies on males and females; 1,015,835 subjects and 94,533 deaths • J-shaped relationship between alcohol and total mortality was confirmed in both males and females • Protection apparent at up to 30 g/day for males and 20 g/day for females • Doses of above 45 g/day for males and 30 g/day for females associated with increased mortality • Degree of association in males was lower in United States than Europe	Max protection (females): 18% (99% CI 13 to 22%) at 5 g/day Max protection (males): 17% (99% CI 15 to 19%) at 5 g/day
Klatsky and Udaltsova 2007	All-cause mortality	• Cox proportional hazard models used to evaluate 21,535 deaths • Models adjusted for age, sex, ethnicity, body mass index, marital status, education, smoking	• The relationship of alcohol to total mortality is J-shaped • Relationship is similar for men and women • Decreased mortality risk for <3drinks/day, increased risk for >3 drinks/day • Occasional drinkers and abstainers have similar risk profile • Former drinkers at increased risk • Benefit of light-moderate drinking (<3 drinks/day) not apparent until middle life	

White et al 2007	All-cause mortality	• Analysis of published systematic reviews (Corrao et al 1999, 2000) and mortality data for England and Wales 1997	• A direct dose-response relation found between alcohol consumption and risk of death in women aged 16–54 years and men aged 16–34 years. At older ages the relationship becomes J-(or U) shaped. • The level at which the risk is lowest increases with age, ranging from 0 in men and women under 35 years to 3 units per week (24 g) in women > 65 years, and 8 units (64 g) per week in men > 65 years. • The decrease in relative risk of drinking (compared to no drinking) with age is more marked in men than in women. • The level of alcohol consumption that carries a 5% increase in mortality increases in age from 8 to 20 units (64–160 g) per week for women and 5 to 34 units (40–272 g) per week for men.	

Appendix 6 Lifetime risk of death from alcohol-related accidents and injuries

Lifetime risk

A modelled analysis of absolute lifetime risk of death from alcohol-related accidents and injuries was commissioned by the Australian Government Department of Health and Ageing to inform the development of these guidelines.[10] The analysis focused on injury categories for which alcohol has an accepted causal effect (based on established epidemiological data: English et al 1995, Rothman and Greenland 1998). These injury categories are listed in Table A6.1. Alcohol-attributable injury deaths per drinking occasion, and lifetime risk, were calculated using four main steps.

Table A6.1 Conditions caused by alcohol consumption with source for information on alcohol attributable fraction

Cause of death	Source
Road traffic accidents	Ridolfo and Stevenson (2001)
Poisoning	World Health Organization (2002)
Falls	Ridolfo and Stevenson (2001)
Fire	Ridolfo and Stevenson (2001)
Drowning	Ridolfo and Stevenson (2001)
Other unintentional injuries	World Health Organization (2002)
Suicide	Ridolfo and Stevenson (2001)
Violence (homicide)	World Health Organization (2002)
Other intentional injuries	World Health Organization (2002)

Step 1 — fatal injury risk on any specific day

The overall sex- and age-specific risk of fatal injury per day was determined for each category of injury without the impact of alcohol. This was calculated by dividing the sex- and age-specific number of injury deaths (by injury category) by the total population at-risk in each age and sex category for males and females, respectively, for Australia in 2002. Mortality data was obtained from the WHO Global Burden of Disease Project 2002 (WHO 2002) for age categories 15–29, 30–44, 45–59, 60–69, 70–79, and 80+.

Step 2 — fatal injury risk without the impact of alcohol (residual risk)

The proportions of injury deaths that could be linked to alcohol consumption for men and women — called the 'alcohol attributable fraction' (AAF) — were obtained from the sources shown in Table A6.1. Each age- and sex-specific AAF was multiplied by the overall risk of injury from step 1 to obtain the portion of the overall risk for each injury category that is linked to alcohol consumption. This rate was then subtracted from the corresponding overall age- and sex-specific risk to estimate the 'residual risk' that is, the injury mortality risk that would have occurred in Australia without any involvement of alcohol in the year 2002 (ie due

[10] Rehm J, Taylor B, Patra J and Room R. Determination of injury mortality risk by volume and number of drinking occasions, Unpublished paper, Centre for Addiction and Mental Health, Toronto, Canada, July 2007.

to other environmental or personal factors). This residual injury mortality risk was used for all subsequent calculations.

Step 3 — injury risk from alcohol consumption on a single occasion

The injury risks corresponding to consumption of specific numbers of standard drinks were identified from a recent World Health Organization (WHO)-sponsored study of hospital emergency rooms in 10 countries (Borges et al 2006). In this study, emergency room patients who were injured were given a questionnaire that asked about what they had been drinking before the accident, as well as at the same time one week before (N = 4320, 91% response rate). These yielded drinking level-specific odds ratios corresponding to specific numbers of standard drinks. In accordance with standard epidemiological practice for rare events, the odds ratios were used as estimates of the increased risk of injury after drinking a specific number of drinks compared to not drinking; that is, the relative risk of drinking compared with not drinking (see Box 2.1 in Section 2.2). However, since the standard drink size used in this study (12.6 grams of pure alcohol) did not equal the standard drink size of Australia (10 grams), the Borges et al (2006) data were converted and modelled by a linear regression model for up to 5 drinks. Beyond 5 standard drinks, the original study data were used. Table A6.2 shows the raw data in 12.6-gram standard drinks and the corresponding data after conversion to Australian standard drinks.

Table A6.2 Relative risk data for Australian standard drinks

Before conversion (12.6-gram standard drinks)		**After conversion** (Australian 10-gram standard drinks)	
Number of drinks	**OR**	**Number of drinks**	**OR**
0	1	0	1
1	3.3	1	1.9
2.5	3.9	3	3.8
4.5	6.5	5	5.6
>6	10.1	7+	10.1

OR = odds ratio (used as an estimate of relative risk)
Source: Borges et al (2006)

The residual injury risk from step 2 was multiplied by the relative risk of injury associated with alcohol consumption before the event (for 1–7+ Australian standard drinks). This gave the absolute risk of having a fatal injury after consuming a specific number of drinks. For instance, if the risk of one person dying in a road traffic accident is 1 in 1000, and the relative risk of injury after drinking 5 drinks is 5.6 (see Table A6.2), then the resulting risk is 0.001 × 5.6 = 0.0056, or approximately 6 in 1000).

Step 4 — risk from alcohol consumption on multiple occasions

Steps 1–3 only account for one lifetime drinking occasion, whereas in fact, the probability of injury mortality increases with the frequency with which a person drinks in addition to how much he/she consumes. This relationship is shown in Equation 1:

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

Where

N = the number of drinking occasions (e.g., 50, 100, 500, 1,000, 5,000, 10,000, or 20,000):

Pr(Death | N) = the risk of injury death (per 1000) given N lifetime drinking occasions

$Pr(death)_d$ = the risk of injury death for one drinking occasion per year, depending on the number of drinks per occasion

i_d = adjustment to the yearly risk to reflect the actual risk period, which is the measured time period over which alcohol exerts its effects. i_d varies also with numbers of drinks consumed in the drinking occasion. For example, for 3 drinks per occasion we assumed a risk period of 3 hours during the 24-hour period of that day. So, i_d becomes $365 \times (24/3)$, as it is based on the probability of one year.

This risk scenario (ie the relative risks associated with each drinking event) obviously changes as the amount of consumption increases for each drinking occasion. After the consumption of one standard drink, the blood alcohol concentration reaches its peak roughly 30–45 minutes after ingestion. Rapid consumption of multiple drinks results in higher blood alcohol in the period following ingestion because the liver has a relatively fixed rate of metabolism. The approximate BACs after consumption of specific numbers of Australian standard drinks are shown in Section 3.3. The exact levels obviously differ among individuals and with the context of drinking (with or without food etc), but the following risk periods (the time following consumption where risk is significantly higher) can be assumed: for 1 drink, 30 minutes; for 3 drinks, 2 hours; for 5 drinks, 3 hours; for 7+ drinks (assuming about 8 drinks), 4.8 hours. These were the time periods modelled with the above formula.

Results

Figure G1.2 in Part B of these guidelines shows the results for lifetime risk of death from an alcohol-related accident or injury, by the number of lifetime drinking occasions and number of Australian standard drinks consumed before the injury. The risk is expressed per 100 drinkers with that drinking pattern. Comparing the graphs for men and women, for all numbers of drinking occasions and numbers of standard drinks, men are at a higher risk per day than women. This is due to the fact that injury mortality per se is higher among men than among women, based on higher rates of risk behaviour at a given level of drinking by men (see discussion below). However, both men and women show similar patterns of increasing risk of injury mortality as both the lifetime drinking occasions and the number of drinks consumed increase.

These estimates are conservative in the sense that they are based on studies of nonfatal injuries. The relevant literature indicates that injuries tend to be more severe when alcohol is involved, and thus the relative risk (RR) and AAF are larger for fatal compared to nonfatal injuries (Rehm et al 2004). On the other hand, basing these estimates on emergency room studies may have led to an overestimate of the effects. Clearly, those who attend emergency rooms with injuries are not representative of the general population. They may be characterised as more risk-taking, and thus the RR for alcohol in this population may be higher than in the general population. Unfortunately, we do not have data to quantify this potential effect.

Finally, the lifetime risk curves are in apparent contradiction with the fact that for single occasions of alcohol intake the RR for women after drinking is higher than for men (see Table A4.1 in Appendix 4), which occurs because, on average, women get more intoxicated for the same amount alcohol. However, men have a higher lifetime risk of injury in all

cultures, presumably related to a higher propensity for risk taking and this accounts for the higher lifetime risk for men compared to women for the same number of drinking occasions.

Appendix 7 Lifetime risk of death from alcohol-related diseases

Lifetime absolute risk of death from chronic diseases

A modelled analysis of absolute lifetime risk of death from alcohol-related accidents and injuries was commissioned by the Australian Government Department of Health and Aging to inform the development of these guidelines. [11]

The analysis included a range of chronic conditions where accepted epidemiological criteria have shown a causal and detrimental effect of alcohol consumption (Rehm et al 2003, Baan et al 2007). These conditions are listed in Table A7.1 with the source of the information used to derive the risks associated with alcohol consumption.

Table A7.1 Conditions caused by alcohol consumption and included in the analyses

Cause of death	Source
Lip, oral and pharyngeal cancer	Corrao et al 1999
Oesophageal cancer	Corrao et al 1999
Liver cancer	Corrao et al 1999
Breast cancer	Corrao et al 1999
Hypertensive diseases	Corrao et al 1999
Ischemic heart disease	Corrao et al 2004
Ischemic stroke	Corrao et al 1999
Haemorrhagic stroke	Corrao et al 1999
Cirrhosis of liver	Corrao et al 1999
Alcohol use disorders	Calculated from NESARC data (Grant et al 2003)

Using data from the studies shown in Table A7.1, the risks of developing each condition was calculated for drinking one Australian standard drink (10 grams alcohol) to 10 standard drinks per day (in one standard drink intervals compared to people who do not drink alcohol (ie the relative risk). The results of these calculations are shown in Table A7.2 for people aged 15–60 years. As the relative risks tend to decrease with age, the figures for people above 60, were calculated obtained using the method described by Klatsky and Udaltsova (2007).

[11] Taylor B, Rehm J, Patra J and Room R. Determination of alcohol-attributable lifetime risk for chronic conditions for different levels of average consumption, Unpublished paper, Centre for Addiction and Mental Health, Toronto, Canada, July 2007.

Table A7.2 Relative risks for disease conditions by categories of drinking (ages 15-60)

Disease conditions	Relative risks (by standard drinks per day)[a]									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Lip, oral and pharyngeal cancer	1.31 1.33	1.67 1.72	2.08 2.18	2.53 2.69	3.02 3.26	3.53 3.88	4.06 4.52	4.58 5.19	5.09 5.85	5.57 6.51
Oesophageal cancer	1.17	1.37	1.61	1.88	2.19	2.55	2.95	3.42	3.94	4.52
Liver cancer	1.08	1.15	1.23	1.31	1.40	1.48	1.56	1.65	1.73	1.81
Breast cancer	1.08	1.17	1.26	1.36	1.47	1.58	1.71	1.85	1.99	2.15
Hypertensive diseases	1.15	1.33	1.53	1.77	2.04	2.35	2.71	3.12	3.6	4.15
Ischaemic heart disease[b]	1	1	1	1	1	1	1	1.01	1.03	1.13
Ischemic stroke[b]	1	1	1	1.12	1.4	1.73	2.04	2.21	2.12	1.72
Haemorrhagic stroke	1.16	1.35	1.57	1.82	2.12	2.46	2.86	3.32	3.86	4.48
Cirrhosis of liver	1.21 1.32	1.45 1.73	1.72 2.25	2.02 2.89	2.35 3.68	2.71 4.64	3.1 5.8	3.51 7.17	3.94 8.80	4.38 10.69

[a] Figures are for men (top figure) and women (bottom figure); if only one RR is given, the risk did not vary significantly by sex.
[b] 1= no detrimental effect compared to abstainers (ie beneficial effects are not taken into account in this calculation); see Table G1.2 in Part B of these guidelines for actual RRs.

As the objective of this calculation was to estimate the risks of consuming alcohol, the cardioprotective and other beneficial effects were not included in the calculations; that is, where there was no detrimental effect, or a beneficial effect, the RR was recorded as 1.0.

The RR estimates in Table A7.2 were used to calculate the AAFs for men and women using the following formula (adapted from Walter 1976, Walter 1980):

$$AAF_i = P \times (RR_i-1) / [P \times (RR_i-1) + 1]$$

Where

i = level of drinking (ie 10, 20, 30 … up to 100 g pure alcohol per day)

P = 100% prevalence, assuming all drinkers drink in same quantity

RR_i = relative risks for level i

The AAFs calculated in this way are shown in Table A7.3.

Table A7.3 Alcohol attributable fractions (AAFs) for disease conditions by standard drinks per day (ages 15–60)

Disease conditions	AAFs (%), by standard drinks per day[a]									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Lip, oral and pharyngeal cancer	23.5 24.7	40.0 41.9	51.9 54	60.5 62.9	66.9 69.4	71.7 74.2	75.4 77.9	78.2 80.7	80.4 82.9	82.1 84.6
Oesophageal cancer	14.6	27.1	37.7	46.7	54.3	60.7	66.1	70.7	74.6	77.9
Laryngeal cancer	7.0	13.3	18.9	23.9	28.4	32.4	36.0	39.2	42.1	44.7
Breast cancer	7.4	14.2	20.6	26.4	31.9	36.9	41.5	45.9	49.9	53.6
Hypertensive diseases	13.3	24.8	34.8	43.4	50.9	57.4	63.1	68.0	72.2	75.9
Ischaemic heart disease	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	2.9	11.5
Ischemic stroke	0.0	0.0	0.0	10.9	28.3	42.0	51.0	54.8	52.8	41.8
Haemorrhagic stroke	13.9	25.9	36.2	45.1	52.8	59.3	65.0	69.9	74.1	77.7
Cirrhosis of liver	17.3 24.4	31.0 42.2	41.8 55.5	50.5 65.4	57.5 72.8	63.2 78.4	67.8 82.7	71.5 86.1	74.6 88.6	77.1 90.6

[a] Figures are for men (top figure) and women (bottom figure); if only one figure is given, the AAF did not vary significantly by sex

For alcohol dependence or alcohol use disorders (AUD), which are, by definition, 100% determined by alcohol consumption, the risk of acquiring the disorder was determined for different drinking levels using the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) database.[12]

The year 2002 was selected as the reference year for the determination of absolute risk for chronic disease. For each chronic disease category on the list, the age-specific death rates were calculated separately for men and women. The following age categories were used: 15–29, 30–44, 45–59, 60–69, 70–79 and 80 and older.

The AAFs from Table A7.3 were applied, yielding the absolute risk of dying from alcohol-attributable disease categories within one year. In the special case of AUD, the mortality risk for AUD in 2002 was based on the average drinking in that year (derived from per capita consumption and survey information).

The absolute age-specific one-year risks for all chronic diseases were derived by adding up the specific disease risks separately for men and women. The lifetime absolute risk was then calculated by adding up all the age-specific risks, based on the life expectancy for Australians in 2002 of 77.9 for men or 83.0 for women (WHO 2004). For example, the absolute risk between the ages 30 and 44 was calculated by multiplying the one-year age-specific absolute risk for that category by 15 (as each individual would live for 15 years between ages 30 and 44). Adding up the age-specific absolute risks gave the absolute lifetime risk to die of a chronic disease as a result of drinking alcohol.

[12] The NESARC survey is a large representative survey from the United States conducted in 2001–02 with a sample size of 43,093 respondents aged 18 years and older and an overall response rate of 81% (Grant et al 2003). http://niaaa.census.gov/

This approach reflects the higher absolute risk of chronic disease mortality for men compared to women in general, in the absence of any alcohol involvement, which may result in some counterintuitive findings (eg when the absolute risk for a given disease is higher for men than for women, outweighing a higher alcohol attributable fraction for women).

The results for lifetime risk of death from an alcohol-related disease, by the number of Australian standard drinks regularly consumed per day, are shown in Figure G1.3 in Part B of these guidelines. The risk is expressed per 100 drinkers with that drinking pattern. The results show that, as the average volume of alcohol consumption increases, the lifetime absolute risk of death from chronic disease increases for both men and women. A lifetime risk of 1 in 100 people is achieved for people drinking at between 2 and 3 drinks per day for both men and women.

While it uses the best available information, this approach has some limitations. First, the absolute risk of mortality is based on one year of Australian mortality; in this case, 2002. Obviously, absolute risks for different disease categories change over time, and thus the transfer into guidelines is only legitimate as long as similar mortality patterns apply. The same problem occurs with life expectancy, which is based on the patterns of deaths in a single year, and may misestimate the real life-expectancy of the people born in any one year. However, as the patterns of deaths for chronic diseases do not change much in the short term, the chosen approach will not cause any major bias in the results.

Second, the results also assume that the relative risks are the same in Australia as in the other countries where the research for the meta-analyses on risk relations have been conducted (usually predominantly the US and UK). However, the effects of alcohol on chronic disease are mainly based on biological mechanisms, and there is no reason to believe that the effect of alcohol on different diseases is different in different countries with similar genetic make-up. However, the RRs from the meta-analyses are clearly estimates, and the real RRs may fluctuate to a certain degree. Unfortunately, there is no better way to estimate RRs for Australia alone. Furthermore, applying different RR estimates from different authors to the alcohol-attributable fractions did not change the results noticeably (Rehm et al 2007).

Appendix 8 Alcohol use in pregnancy and breastfeeding: evidence details

To inform a guideline on drinking by pregnant and breastfeeding women, the literature review commissioned for this update of the Australian Alcohol Guidelines included a review of research on the effects of alcohol on the developing fetus in utero and on breastfed babies. Details of how the literature review was conducted are included in Section 2.5.

For the effect of alcohol on the developing fetus in utero, the literature review included 264 articles from 2001 to early 2007. Among these included papers were 2 systematic reviews, 34 prospective cohort studies, 48 lower level observational studies and 7 case studies on the effects of prenatal alcohol exposure.

The working committee reviewed the systematic reviews (plus one additional review from 1998), and the prospective cohort studies (as this type of study provides the highest level of evidence for an aetiology, or risk of harm, question). After an initial review of the studies, 26 of the prospective cohort studies were selected for further analysis as they included information about alcohol dose and pregnancy/fetal outcomes that were most relevant to the development of a guideline drinking level for pregnant women. The results of this further analysis for the 26 prospective cohort studies are shown in Table A8.1.

Table A8.1 Prospective cohort studies of alcohol consumption in pregnancy

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
2001							
Kesmodel et al 2001	Prospecti ve cohort	Women attending ante-natal classes (single pregnancy) 1989–91 and 1992–96	18,228	Alcohol intake at 16 and 30 weeks gestation classified into five categories: 1-2 drinks/week 3-4 drinks/week 5-9 drinks/week >10 drinks/week 10-14 drinks/week	Main outcome: Pre-term deliveries (gestational age at delivery) Dependent variables: maternal lifestyle/obstetric risk factors (self-reported)	Article in German, only abstract available Analyses adjusted for smoking, caffeine intake, maternal age/height/ pre-pregnant weight/marital status/ occupational status/educated/parity/chronic diseases/ previous pre-term delivery/ mode of labour initiation	Risk of pre-term delivery at 16 weeks (cf ≤1 drink/week): 1-2 drinks/week: RR 0.91 (95%CI 0.76 to 1.08) 3-4 drinks/week: RR 0.86 (95%CI 0.64 to 1.15) 5-9 drinks/week RR 0.89 (95% CI 0.52 to 1.52) ≥10 drinks/week: RR 2.93 (95% CI 1.52 to 5.63) 10-14 drinks/week: RR 3.41 (95% CI 1.76 to 6.81) Risk of pre-term delivery at 30 weeks (cf ≤ 1 drink/week) 1-2 drinks/week: RR 0.69 (95% CI 0.56 to 0.86) 3-4 drinks/week: 0.82 (95%CI 0.60 to 1.13) 5-9 drinks/week: RR 0.97 (95% CI 0.58 to 1.64) ≥10 drinks/week: RR 3.56 (95% CI 1.78 to 7.13) 10-14 drinks/week: RR 3.47 (95%CI 1.64 to 7.35)

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
							J-shaped curve between alcohol consumption and risk of pre-term delivery
Van der Leeden (2001)	Prospective (7 months follow-up)	Mothers attending immunisation clinic	79 infants (Exposed *N*=29; control *N* =50)	Self-reported maternal alcohol consumption during pregnancy classified into four categories: No alcohol (≤25 mL/week; ≤20 g /week) Moderate (25-140 mL/week; 20-110 g/week) Severe >140 mL/week (> 20 g /week) "Begin" (Alcohol consumed during first trimester only) excluded from analysis	Main outcomes: Neurological development (interviewer-administered examination) Facial features (anthropometry, observation) Behavioural questionnaire (7 months only) (mother's self-report)	Follow up at 3 and 7 months of age Pre-term infants (delivered at ≤37 weeks gestation) excluded from analyses [n=22]	Significant differences in facial features of exposed vs. non-exposed children at 3 months Significant difference in neurological performance of exposed vs. non-exposed at 7 months More behavioural difficulties in exposed infants at 7 months It is possible to recognise alcohol-related defects within the first year of life thus allowing early intervention.
Wass et al 2001	Prospective (30 weeks follow-up)	Women 12 to 42 weeks gestation attending either high or low risk pre-natal clinics, reporting >0 alcohol use during pregnancy	167 women (Abstainer/low *N*=70; heavy *N*=97)	Self-reported maternal alcohol consumption around time of conception classified into groups: Abstainer/low: ≤1 oz/day Moderate: 1.0 to 2.99 oz/day Heavy: >2.99 oz/day	Main outcome: Ultra-sonographic assessments of fetal brain features: trans-cerebellar diameter; frontal lobe; thalamus to calvarium; biparietal diameter Dependent variables: maternal cigarette/ marijuana/	Followed up between 1 and 6 times (depending on gestational age at recruitment) Adjustment for other licit/illicit drug use	Frontal lobe below 10th percentile (cf abstainer/low) Moderate: OR 3.04 Heavy: 6.15 Frontal lobe below 25th percentile (cf abstainer/low) Moderate: OR 1.18 Heavy: 3.48

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
					cocaine/other drug use (self-reported)		Non –exposed foetuses: 4% below 10th percentile Heavily exposed foetuses: 23% below 10th percentile Alcohol exposure associated with reduction in frontal cortex, but not other brain structures
Sood et al (2001)	Prospective cohort study (6-7 years follow-up)	Black women attending maternity clinic drinking at least 0.5fl oz/day; 5% random sample of abstainers	501 child-parent dyads	Average maternal self-reported (two-week recall) alcohol exposure (average absolute alcohol [fl oz]/day over duration of pregnancy) classified into 3 groups: Abstainer: 0 fl oz/day Low: 0 to <0.3 fl oz/day (63.8% of subjects) Moderate/heavy: ≥0.3 fl oz/day (13% of subjects)	Main outcome: Adverse child behaviour Child behaviour checklist (Achenbach); Child IQ (Wechsler) (Interviewer-administered) Dependent variables: maternal age/education/psychopathologies/family structure/socioeconomic status/exposure to violence (self-reported) Child's whole blood lead level	Initial screen at antenatal clinic, follow up 6-7 years later	Delinquency (alcohol exposure [dichotomous variable] cf not) OR 1.8 (95% CI 1.0 to 3.0) Delinquency (alcohol exposure [ordinal variable] cf not) Low alcohol: OR 3.0 (95% 1.3 to 7.3) Moderate/heavy: OR 3.3 (95% CI 1.3 to 8.7) Even low levels (one drink/week) of maternal alcohol consumption adversely related to child behaviour (dose-response relationship) No alcohol during pregnancy remains the best medical advice.
2002							
Covington et al (2002)	Historical prospective cohort	African-American, HIV negative, singleton	540 families (1100 eligible;	Self-reported (two-week recall) maternal alcohol consumption (Absolute alcohol [fl.oz]/day)	Main outcome: Offspring anthropometry (weight; height; head	Followed up approx 7 years after birth Substantial component of	Children born to mothers ≥30 years and prenatally exposed to moderate/high alcohol up to 14 lb lighter, OR 5.0 likely below 10th

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
	study (7 years follow-up)	pregnancies	665 contacted, 540 participated)	averaged throughout pregnancy Maternal urine alcohol/meconium (complete for 20% subjects) Cut-points of low and moderate alcohol consumption not defined	circumference; skinfold, pubertal stage; illness/hospitalisation frequency (self-reported) Dependent variables: Maternal age/ pre-pregnancy weight/height (self-reported)	analysis was directed at illicit drugs	percentile for weight at 7 years Prenatal exposure to alcohol was significantly related to low weight and length at birth and at age 7, suggesting that long-term height and weight deficits are evident among children born to alcohol-using women
Day et al (2002)	Prospective (MHPCD study) (14 years of follow-up)	Women in 4th prenatal month averaging ≥3 drinks/week in first trimester, plus 33% random sample of non-drinkers selected	565 (85% participation rate)	Self-reported maternal alcohol consumption at each trimester (3-month recall) classified into four categories: Abstainers Light: >0 to <0.2 drinks/day Moderate: >0.2 to <0.89 drinks/day Heavy: >0.89 drinks/day	Main outcome: offspring size Dependent variables: maternal: depression (CESD scale); anxiety (Spielberger); stress (Dohrenwend); support (Berkman); maternal age/education/employment/income (maternal self-report) Current child environment (Baker)	Follow up at 4 and 7 months prenatally; 8, 18 months, 3, 6, 10 and 14 years after birth	First trimester alcohol exposure used to predict 14-year-old offspring weight: Abstainers: Child weight 152 lbs Light: Child weight 149 lbs Moderate: Child weight 143 lbs Heavy: Child weight 136 lbs Prenatal alcohol exposure continues to affect size at age 14 years in this cohort of children followed since their fourth month of gestation
Kesmodel et al (2002)	Prospective cohort study	Women with singleton pregnancies attending antenatal clinic 1986-1996	24,768 (95% participation rate)	Self-reported maternal alcohol consumption during pregnancy (measured as drinks/week [drink equivalent to one bottle beer/glass wine/schnapps or 12g	Main outcome: Still birth (hospital files/birth registry) and infant death (death registry) Dependent variables: maternal caffeine	Pregnancies ending in spontaneous abortion and pregnancies for which no alcohol consumption recorded were excluded from analyses	Still births (cf no alcohol) 1-2drinks/week: RR 1.27 (95% CI 0.81 to 1.98) 3-4 drinks/week: RR 1.25 (95% CI 0.63- to 2.47) ≥5 drinks/week: RR 2.65 (95%CI

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
				alcohol]) classified into four categories: <1drink/week 1-2 drinks/week 3-4 drinks/week ≥5 drinks/week	intake/smoking/age/ height, pre-pregnancy weight/ parity/marital status/occupation/education (self-reported)		1.18 to 5.97) Infant death (cf no alcohol) 1-2 drinks/week: RR 0.85 (95% CI 0.53 to 1.36) 3-4 drinks/week: RR 0.90 (95% CI 0.43 to 1.89) ≥5 drinks/week: RR 1.38 (95% CI 0.50 to 3.86) Women who drink moderately during pregnancy have increased risk of still birth, however there is little to no relationship between alcohol intake during pregnancy and infant death
Richardson et al (2002)	Prospective cohort study (MHPCD study) (10 years of follow-up)	Women (50% African-American, 50% Caucasian) at medical assistance pre-natal clinic	593 (83% of birth cohort, 170 lost to follow up since baseline)	Usual, minimum, maximum quantity and frequency of beer, wine, liquor, beer cooler, wine cooler use during pregnancy, classified into several measures: Average drinks/day(log transformed) Binge-drinking (≥4 drinks/day) in each trimester (yes/no) Binge-drinking frequency (binges/trimester)	Child neuropsychological outcomes: Wisconsin Card-Sorting Test; Wide Range Assessment of Memory and Learning Test; Trail Making (Adult Version); Colour/Word Inference Test; Grooved Pegboard Test; Continuous Performance Test (interviewer-administered) Maternal and child	Interviews at end of each trimester, 8 and 18 months of age, 3, 6, 10, 14 and 16 years of age Children with confounding conditions (cerebral palsy, mental retardation, visual impairment, deafness) excluded from analyses	First and second trimester alcohol use significant predictor of negative learning and memory scores

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
					environment factors as for Day et al 2002 (self-reported)		
2003							
Baer et al (2003)	Prospective cohort study (21 years follow-up)	Women presenting at antenatal clinics in Washington or Seattle	433 (500 of original cohort (1529) all heavy drinkers, continuum of other drinkers)	Alcohol consumption during pregnancy, measured as: Average absolute ounces/day Drinking occasions/month Heavy episodic drinking: average drinks/occasion, maximum drinks/occasion, ≥drinks on an occasion, 5-point quantity-frequency-variability scale	Main outcome measure: young adult drinking rates/problems (self-reported) Dependent variables: prenatal exposures (nicotine, aspirin, caffeine, antibiotics);family history of alcoholism (interviewer-administered questionnaire)	Prenatal alcohol and other exposures measured at 5 months gestation; family history of alcoholism assessed at 14 and 21 years (interviewer administered); parental alcohol/drug use assessed every 3 years from child's birth (interviewer-administered); child drinking at 21 years (self-report)	Prenatal alcohol exposure is a risk factor for the development of drinking problems in humans. Potential mechanisms for the role of fetal exposure and the development of alcohol problems deserve study
2004							
Albertsen et al (2004)	Prospective cohort study (followed from 6-10 weeks gestation until birth)	Women in Danish National Birth Cohort who delivered pre-term	40892 women in cohort, 1880 pre-term deliveries	Self-reported maternal average weekly consumption of beer/wine/spirits during pregnancy (assume alcohol ≈between beverage types, 12g), classified into categories: Non-drinkers 0.5 drinks/week 1-1.5 drinks/week	Main outcome: Gestational age at delivery Preterm (before 37 weeks) Moderate preterm (32-37 weeks) Very pre-term (before 32 weeks)	Confounders included obstetric factors (maternal diabetes, hypertension, bleeding episodes during pregnancy), household occupational status, maternal age, height, weight, coffee consumption, smoking, infant gender	Risk of preterm delivery (alcohol cf abstinence) 4 to <7 drinks/week: RR 1.15 (95% CI 0.84 to 1.57) ≥7 drinks/week: RR 1.77 (95% CI 0.94 to 3.31) Risk of very pre-term delivery (alcohol cf abstinence) ≥7 drinks/week: 3.26 (95%CI 0.80 to 13.24) Alcohol consumption below 4

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
				2-3.5 drinks/week 4-6.5 drinks/week ≥7 drinks/week Alcohol preference (beverage consumed ≥50% occasions): beer, wine, spirits, mixed			drinks/week does not increase the risk of preterm delivery Daily alcohol intake during pregnancy increases risk of preterm delivery, independent of type of alcohol consumed.
De Los Angeles Avaria et al (2004)	Prospective cohort study (18 months follow-up)	Women presenting for antenatal screening, suspected of consuming at least 2 oz absolute alcohol/day	30 (Exposed *N*=17, control *N*=13)	Self-reported maternal alcohol consumption of ≥ 2 oz absolute alcohol/day prenatally, as confirmed by home visit Non-drinkers, as confirmed by home visit	Main outcome: nerve conduction velocity of medial, ulnar, peroneal and tibial nerves (interviewer-administered examination)	Assessment performed during newborn period, and at 12-14 months	Alcohol-exposed subjects had slower ulnar motor nerve velocity (*P*=0.007), smaller proximal (*P*=0.018) and distal (*P*=0.051) amplitude, reduced tibial nerve velocity (*P*=0.06) and decreased distal amplitude Prenatal alcohol exposure results in significantly reduced nerve conduction velocity and amplitude in children up to one year old
Goldschmidt et al 2004	Prospective cohort study (MHPCD study) (10 years follow-up)	All women presenting to prenatal clinic who reported drinking ≥3drinks/week during pregnancy and next woman who drank less	606 (selected from 10 year follow up cohort of 636)	Assessed at each month during first trimester, once each for second and third trimesters; current alcohol use at 10 year follow-up Usual, minimum, maximum quantity and frequency of beer, wine, liquor, beer cooler, wine cooler use Average drinks/day(log transformed) Binge-drinking (≥4	Main outcome: child academic achievement at age 10 (WRAT-R) Dependent variables: child's depression/anxiety (Children's Depression Inventory) Other maternal and environmental measures as for Day et al 2002	Follow up at 4 and 7 months gestation, and 3,6, 10,14 and 16 years of age post-natal	Exposure to alcohol during first and second trimester predicted poorer teachers' ratings of overall school performance Second trimester binge-drinking predicted lower reading scores.

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
				drinks/day) in each trimester (yes/no)			
Nulman et al (2004)	Prospective cohort study	Women who telephoned information service 1987-1997 seeking advice on appropriate alcohol consumption during pregnancy; controls sought advice on non-harmful medications	102 parent-child dyads (exposed *N*=51, control *N*=51)	Self-reported maternal alcohol consumption variables were: Number of binge-drinking sessions Number of drinks/binge Alcohol index: product of number of drinks and number of sessions, divided by 100	Main outcome: child intellectual function (Infant Development [Bayley]/Scale of Children's Abilities [McCarthy]/Intelligence Scale for Children [Wechsler]); Language (Reynell Scale); temperament (Carey) (interviewer-administered) Dependent variables: maternal factors, age, height, weight, smoking, education, IQ (self-reported)	Children's age varied depending on when they were recruited to study; intellectual tests applied that were suitable to child's chronological age	Binge-drinking during first trimester appears not to affect intelligence or cognitive/language development Children exposed in utero to binge-drinking exhibited more dis-inhibited behaviours
Willford et al (2004)	Prospective cohort study (MHPCD study) (14 years follow-up)	Women (50% African-American, 50% Caucasian) at medical assistance pre-natal clinic	569 (of 580 eligible for analysis)	Assessed at each month during first trimester, once each for second and third trimesters; current alcohol use at 10 year follow-up Usual, minimum, maximum quantity and frequency of beer, wine, liquor, beer cooler, wine cooler use Average drinks/day(log	Main outcome: Child learning and memory (Children's Memory Scale) Dependent variables: child depression (Kovacs); anxiety (Reynolds); health behaviours (Jessor) (self-reported) Maternal and environmental	Follow up at 4 and 7 months gestation , and 3,6, 10,14 and 16 years of age post-natal	Prenatal alcohol exposure leads to deficits in verbal learning. Initial deficits in acquisition responsible for deficits in immediate and delayed recall of verbal information in alcohol-exposed (but non fetal alcohol syndrome-diagnosed) children

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
				transformed) Binge-drinking (≥4 drinks/day) in each trimester (yes/no) Light drinking: < 3 US drinks per week (<42 g alcohol/week) Moderate: 3–6 US drinks per week (42–84 g alcohol/ week) Heavy: 1 or more US drinks per day (≥14 g alcohol per day)	characteristics as per Day et al 2002 (self-reported)		
2005							
Beblo et al (2005)	Prospective cohort study	Pregnant black women presenting to antenatal clinic	208 women (abstainers *N*=49, moderate *N*=127, heavy *N*=32)	Self-reported maternal absolute alcohol intake/day (AAD) around conception: Abstainers: AAD=0 g/day Moderate: AAD=<60 g/day Heavy: AAD=≥60 g/day Self-reported maternal absolute alcohol intake/drinking day (AADD) around conception: Abstainers (AADD = 0) Moderate: AADD <130 g)	Main outcome: levels of doco-sahexenoic acid (DHA) and arachidonic acid (AA) in umbilical cord vessels (from maternal plasma) Dependent variables: maternal smoking, drug/alcohol history (interviewer-administered)	Plasma sample taken immediately prior to delivery Umbilical arteries and veins dissected from cords immediately after delivery	Arterial umbilical wall DHA levels (drinking cf abstainers) Moderate and heavy: 14% higher Arterial umbilical wall AA levels (drinking cf abstainers) Moderate and heavy: 10% higher Alcohol intake during pregnancy is associated with altered DHA and AA status in foetal tissues; differences most likely a result of a direct influence of alcohol on foetal metabolism.

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
				Heavy: AADD ≥130 g			
Burden et al (2005a)	Prospective cohort study (7.5 years follow-up)	Black women recruited 1986-1989 during first prenatal visit; moderate and heavy drinkers over-represented by including all women reporting >0.5 oz AA/day, 5% random sample of lower level drinkers	337 parent-child dyads	Self-reported maternal absolute alcohol consumption for each day of week of conception for beer, wine, spirits (first antennal visit only) Self-reported maternal absolute alcohol consumption (2 week recall) for beer, wine, spirits at subsequent follow ups	Main outcome: child attention and working memory (Mirsky) (Interviewer-administered); intelligence (Wechsler); language (McCarthy); working memory (WISC-II) Morphology/anthropometry (interviewer-assessed) (7.5 years) Dependent variables: post-partum demographic and socio-environmental data, parental drug/alcohol use, CESD (Radloff), IQ (Dunn), depression (maternal self-report) Maternal timeline follow-back interview	Follow up at 6.5, 12, 13 months and 7.5years Children with low birthweight, preterm (<32 weeks), chromosomal abnormalities, neural tube defects or multiple births excluded	Adverse effects of drinking in pregnancy (at least 14 g alcohol per day) primarily for working memory Effects on working memory exacerbated when mothers aged ≥30 years at time of child's birth Working memory may be the most important aspect of attention that is adversely affected by prenatal alcohol exposure.
Burden et al (2005b)	Prospective cohort study (7.5 years	Black women recruited 1986-1989 during first prenatal visit; moderate and	337 parent-child dyads	Self-reported maternal absolute alcohol consumption for each day of week of conception for beer,	Main outcome: cognitive processing speed and efficiency: memory-scanning (Sternberg	Follow up at 6.5, 12, 13 months and 7.5years Children with low-birth weight, pre-term (<32 weeks), chromosomal	Prenatal alcohol exposure (at least 14 g alcohol per day) associated with slower processing speed on several Sternberg tasks and number comparison efficiency

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
	follow-up)	heavy drinkers over-represented by including all women reporting >0.5 oz AA/day, 5% random sample of lower level drinkers		wine, spirits (first antennal visit only) Self-reported maternal absolute alcohol consumption (2 week recall) for beer, wine, spirits at subsequent follow ups	paradigm), mental rotation (Kail), number comparison (Kail and Park), arrow discrimination, colour naming (Stroop) Dependent variables as for Burden et al 2005a	abnormalities, neural tube defects or multiple births excluded	No significant performance differences on reaction time Prenatal alcohol exposure linked to slower processing speed. RT deficit for complex cognition but not automatic processing is involved, partially accounting for previously-reported effects on working memory
Carter et al (2005)	Prospective cohort study (6.5 months of follow-up)	Data from a prospective cohort study of women from a Cape Coloured community in Cape Town, South Africa, on the effects of heavy prenatal alcohol exposure on neurobehavioral development. The women were recruited between 1999 and 2002 at an antenatal clinic. Any woman averaging at least 1.0 oz absolute alcohol per day (AA/day) during	131 (61 born to heavy drinkers, 70 to low level drinkers or abstainers)	Using a timeline follow-back approach, each mother was interviewed regarding her pregnancy alcohol and drug use at recruitment, at a follow-up antenatal visit, and when the infant was 1 month old. Volume was recorded for each type of alcohol beverage consumed each day and converted to oz of absolute alcohol (AA) (liquor—0.4, beer—0.04, wine—0.2). The alcohol module of the Diagnostic Interview Schedule was also administered to each mother to determine	Infant visual acuity assessed with Teller Acuity Cards	Data were obtained on a broad range of control variables, including maternal age, years of education, marital status, parity, maternal depression, and infant sex. Prenatal control variables also included maternal smoking and illicit drug use during pregnancy. A complete eye examination was not conducted, so it is not possible to know the source of the alcohol-related lower acuity scores.	Poorer acuity at 6.5 months was associated with higher average daily alcohol consumption at conception and during pregnancy. Although the amount of alcohol consumed on a given occasion was not related to acuity, infants born to mothers who binge drank were more likely to have acuity values below the 5th percentile than infants born to mothers who did not binge drink ($P<.005$). The relation of pregnancy drinking to acuity was dose-dependent, with effects clearly evident in those women whose drinking averaged at least 0.5 oz AA/day ($P<.05$). The effect of alcohol exposure on acuity was seen primarily in infants whose mothers were 30 years or older at delivery, even though the older mothers did not drink larger quantities of alcohol.

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
		the first trimester of pregnancy or reporting a history of at least 2 incidents of binge-drinking (≥5 drinks/occasion) per month during the first trimester was invited to participate in the study. The next woman initiating antenatal care at this clinic who drank <0.5 oz AA/day, did not binge drink during the first trimester, and whose gestational week of pregnancy was within 2 weeks of that of the previously recruited heavy-drinking participant was also recruited.		whether she met Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition (DSM-IV) criteria for alcohol abuse or dependence.			
Gauthier et al (2005)	Case control (analysis	The study was designed as a case control	872 (565	Interviews were conducted with mothers after delivery to estimate	Maternal questionnaire (modification of that	Multiple births, infants with gestational ages less than 36 weeks or more	Infants whose mothers reported alcohol use, excessive drinking or smoking in pregnancy were more

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
	of a subset from a case control study)	study of small for gestational age (SGA) infants, with all SGA deliveries and a random sample of appropriate for gestational age sex and race (AGA) infants from two hospitals included in the original sample. 872 newborns (≥36 weeks gestation) were included for this study of maternal alcohol consumption and infection.	SGA/307 AGA)	the average number of drinks consumed each week during pregnancy, and whether or not a woman had binged (defined as consuming at least five drinks in a single day). No definition was provided for a standard drink.	used by the Centers for Disease Control) and interview. Newborn infection was defined in this analysis as the documentation of Group B Streptococcus (GBS), other sepsis, or the diagnosis of clinical sepsis by the attending physician. Maternal sexually transmitted diseases were excluded from the analysis.	than 42 weeks, and infants with races other than African-American or Caucasian were excluded from the sample due to the original study design. A significantly higher number of mothers were interviewed at the public hospital compared to the private hospital. However the participation rate did not differ between mothers of SGA and AGA infants at either hospital. Other possible confounding factors such as prolonged rupture of membranes, chorioamnionitis, maternal antibiotic use were not controlled.	likely to have a newborn diagnosed with an infection than were mothers who reported abstaining from alcohol or cigarettes (P<0.05). When controlling for race and smoking, SGA infants whose mothers used any alcohol had a 2.5-fold increase risk of infection, while excessive alcohol use (defined as ≥7 drinks/week) increased the risk 3–4-fold (depending on the trimester). In a multivariable logistic regression analysis controlling for low maternal income, smoking, and SGA, excessive alcohol use during the 2nd trimester increased the risk of newborn infection (OR 3.7, 95%CI 1.1-12.8)
Hepper et al 2005	Prospecti ve cohort study (15 weeks follow-up)	Healthy, non-smoking women with singleton pregnancies	56 (drinkers N=23, abstainers N=33)	Participants divided into two categories on basis of alcohol consumption: Drinkers (≥1 unit (10g) alcohol each week for duration of pregnancy	No. of fetal spontaneous startles during 45 minute ultrasound Interviewer-administered assessment of: maternal demographics (age, parity, marital status, employment status, obstetric history,	45 min interview at 20, 25, 30, 35 weeks gestation	Alcohol-exposed foetuses exhibited higher startle frequency than non-exposed foetuses (P=<0.001), but this moderated by gestational age Exposure to alcohol delays natural maturation of spontaneous startle behaviour, but has only a small permanent effect

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
					problems during pregnancy, anxiety levels (Spielberger), delivery method, infant gender, Apgar score (1 and 5 minutes after birth)		
2006							
Alati et al (2006)	Prospecti ve cohort study	Follow-up of mothers and children from the University of Queensland Study of Pregnancy and Its Outcomes (MUSP), originally recruited from women attending antenatal clinics at the Mater hospital between 1981 and 1984	2138	Mothers were interviewed about their frequency and quantity of alcohol consumption during pregnancy, at birth and at follow-ups. Amounts were reported per glass, with the assumption of 10g alcohol/glass. Analysis focussed on the quantity of alcohol consumed at any drinking occasion, with responses were divided into 'no alcohol/up to 2 glasses' and '3 or more glasses'	Outcome was onset of alcohol disorder from adolescence to 21 years of age, assessed using the lifetime version of the Composite International Diagnostic Interview– computerized version.	Follow-up interviews were conducted at birth, 6 months, and 5, 14, and 21 years. The 21 year follow-up represents 35.4% of the original birth cohort. There were no differences between those lost to follow-up and those still in the study according to maternal alcohol consumption in pregnancy. Confounders measured at the first antenatal visit included mother's age, education, marital status and smoking. The potential confounder of genetic susceptibility could not be controlled for, but analysis was repeated excluding results from those whose fathers or siblings developed alcohol disorders, and the final conclusions were unaffected.	In utero alcohol exposure of 3 or more glasses was associated with alcohol disorders. Compared to adults whose mothers drank less than 3 glasses, the risk of developing early-onset alcohol disorders at age 21 years were higher for those exposed to maternal drinking in early pregnancy (OR 2.95, 95%CI 1.62-5.36) and for those exposed in late pregnancy (OR 1.35, 95%CI 0.69-2.63). There was also a strong association between alcohol exposure in early pregnancy and late-onset alcohol disorders (OR 3.29, 95%CI 1.74-6.24]). The authors conclude that a biological origin of adult alcohol disorders is supported and suggests that the association is not explained solely by maternal drinking or smoking during childhood and adolescence or other intervening factors.

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
Connor et al (2006)	Prospective cohort study with a case control component (25 years of follow-up)	The longitudinal cohort from the Seattle Prospective Longitudinal Study consisted of 402 adults who had been exposed to varying levels of alcohol as foetuses. The clinical component consisted of 30 adults with FAE, 30 with FAS and 30 controls.	402 90 (30 FAE/30FAS/30 control)	The cohort selected for follow-up reflected the entire range of prenatal alcohol exposure from complete abstinence to binge-drinking patterns throughout pregnancy.	Motor effects including balance and unilateral, bilateral, finger, hand and foot coordination.	In the 25 year follow-up, 402 of the original 500 selected were followed-up.	The dose-dependent motor coordination effects of alcohol previously found in children do not appear to persist into adulthood, except in those highly exposed children who also have other accompanying neuropsychological effects in childhood.
Hepper et al 2005	Prospective cohort	All participants were non-smokers with healthy pregnancies	56 total (23 who drank alcohol during pregnancy, 33 who did not)	Details of alcohol consumption were obtained during a semi-structured interview. The mothers in the drinking group reported drinking at least 10 g of alcohol each week for the duration of their pregnancy. The mean number of alcohol units consumed weekly by mothers who drank during their pregnancy was 4.2 (SD 1.9).	The number of spontaneous startles exhibited by foetuses was recorded at 20, 25, 30 and 35 weeks gestation during a 45-minute ultrasound observation.	All babies were born healthy and none had signs of FAS or FAE.	Foetuses exposed to maternal alcohol consumption exhibited a significantly higher frequency of spontaneous startles (P = 0.001) compared to foetuses of non-drinking mothers. This difference reduced across gestation but did not fully disappear by 35 weeks. The authors conclude that prenatal exposure to alcohol results in a delayed maturation of spontaneous startles in the foetus and a smaller but significant permanent effect on startle behaviour
Howell et al	Prospective cohort	Cases were recruited from a	265	Mean alcohol consumption during	Wechsler Intelligence Scale for	The special education contrast group was not	Alcohol-affected youth had significantly lower IQs than those in

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
(2006)	(nest case-control)	longitudinal study cohort. Original recruitment was between 1980 and 1985 from a prenatal clinic in Atlanta, Georgia. Women were recruited if they reported drinking at least two drinks per week during pregnancy. In addition, 84 students were recruited from special education programs as a contrast group.	(181 from longitudinal cohort, 84 from special education programs)	pregnancy was 12 oz/AA/week (SD 8.59) for the dysmorphic group, 0 oz/AA/week (SD 11.49) for the control group and 10.9 oz/AA/week for the exposed but non-dysmorphic group (SD not reported). AA = absolute alcohol	Children; Wechsler Individual Achievement Test; Vineland Adaptive Behaviour Scales School attendance, conduct and achievement assessed from school records.	followed longitudinally. There may be limitations to the generalisation of this study to other groups, as the study population was selected from a low socioeconomic, predominantly African-American area	the other three groups. Academic achievement was most impaired in the special education group who showed lower performance over all, but alcohol-affected youth showed significant deficits on mathematics subtests. There was no increased incidence of conduct problems in school records related to alcohol exposure. The authors suggest behaviour problems may be due to environmental effects over life span, rather than prenatal exposure to alcohol.
Jacobson et al 2006	Prospective cohort	African American mothers attending their first prenatal visit between 1986 and 1989 were recruited. All women reporting alcohol consumption averaging at least 0.5 oz absolute alcohol/day were recruited.	263 mother/child pairs	To reduce the risk that alcohol might be confounded with cocaine exposure, 53 heavy cocaine (>2 days/week) light alcohol (<7 drinks/week) users were also included. Alcohol consumption was assessed at prenatal interviews and the Michigan Alcoholism Screening Test was given. Although the frequency of drinking during pregnancy among the non-abstaining	Tests during infancy included the Mental Development Index, the Fagan Test of Infant Intelligence and the Visual Expectancy Paradigm. At 7.5 years the children were tested for memory, category fluency and sustained attention. Their teachers were also asked to complete a report and ADHD	The children were assessed during infancy and at 7.5 years. An assessment of a wide range of confounders was included.	The results of this study were consistent with the hypothesis that the maternal ADH1B*3 allele provides some protection to the foetus from prenatal alcohol exposure. Women without the ADH1B*3 allele drank twice as much alcohol at conception than those with at least one allele. With the exception of infant birth weight and processing (as measured by the Fagan Test of Infant Intelligence), negative effects from alcohol consumption were only seen in infants whose mothers lacked the ADH1B*3 allele. There was no consistent pattern of protection for

Study	Study type	Population	N	Indicators	Outcomes	Quality information	Results
		A random sample of approximately 5% of lower level drinkers and abstainers was also invited to participate.		women decreased by more than 50% (from 1.9 to 0.9 days per week) the number of drinks consumed per occasion declined by only 20% (from 4.5 to 3.6 on average). Therefore many of the women in the study were drinking at levels considered risky to the foetus.	assessment.		children with the ADH1B*3 allele.
O'Callaghan et al 2007	Prospective cohort study (14 year follow-up)	Participants in the Mater-University of Queensland Study of Pregnancy (MUSP) Women attending antenatal clinics at the hospital from 1981 to 1984 were invited to participate.	7223 (On follow-up, 5139 completed questionnaires and 3731 completed testing)	Frequency and quantity of maternal alcohol consumption was determined by asking 'In the last three months, how often did you drink alcohol' and 'How much did you drink at those times?' The extent of binge-drinking was measured by asking how frequently consumption exceeded 5 glasses. One glass was estimated to equal 0.5 oz alcohol.	Adolescents completed the Wide Range Achievement Test — Revised and Raven's Standard Progressive Matrices Test as well as the Youth Self Report. Mothers completed the Child Behaviour Checklist (CBCL). Learning was assessed by a series of questions in the mother and adolescent questionnaires.	Analysis suggests that mothers not included in the study were likely to be younger, less educated, financially disadvantaged and more likely to consume alcohol. There was a low prevalence of heavy drinkers, and they were more likely to be lost to follow-up.	The authors suggest that consumption of <1 drink/day does not lead to adverse outcomes in relation to attention, learning and cognitive abilities. Binge-drinking was associated with a Raven's score <85 (a test of non-verbal intelligence with a mean of 100). No other associations were statistically significant.

Abbreviations: TAC, Teller Acuity Cards; LC-PUFA, long-chain polyunsaturated fatty acids; DHA, doco-sahexaenoic acid; AA, arachidonic acid; NR, not reported

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