

**Submission to the National Health and Medical Research Council
on the**

Australian alcohol guidelines for low risk drinking

**Draft for public consultation
October 2007**

**Submitted by members of
the National Alcohol Beverage Industries Council Inc:**

**Australian Hotels Association
Australian Liquor Stores Association Inc
Australasian Associated Brewers Inc
Clubs Australia
Distilled Spirits Industry Council of Australia Inc
Liquor Merchants Association of Australia and
Winemakers' Federation of Australia Inc**

And:

Lion Nathan Limited

Prepared and written by Creina Stockley
Health and Regulatory Information Manager
The Australian Wine Research Institute
08 8303 6612
PO Box 197
Glen Osmond SA 5064

Contact details

Dominic Nolan

Director of Government and Community Affairs
Winemakers' Federation of Australia
0419 287 734
PO Box 3891
Manuka ACT 2603

11 December 2007

Table of contents

1. EXECUTIVE SUMMARY	3
2. INTRODUCTION–CONTRIBUTION OF THE AUSTRALIAN ALCOHOL INDUSTRY	6
3. GENERAL COMMENTS ON PART A. SECTIONS 1 – 4.....	8
3.1. CREDIBILITY OF THE DRAFT REVISED GUIDELINES	8
3.2 RELEVANCE OF SIMPLE GUIDELINES	15
3.3 AMBIGUOUS AIM AND JUDGEMENTAL TONE OF THE DRAFT REVISED GUIDELINES	16
3.4 OTHER ISSUES.....	18
4. SPECIFIC COMMENTS.....	21
4.1 ACTUAL GUIDELINES	21
4.1.1 GUIDELINE #1 LOW-RISK DRINKING FOR ADULTS (PAGE 39).....	21
4.1.2 GUIDELINE 2 SPECIAL PRECAUTIONS FOR CHILDREN AND YOUNG PEOPLE UNDER 18 YEARS OF AGE (PAGE 50).....	28
4.1.3 GUIDELINE 3 - SPECIAL PRECAUTIONS CONCERNING PREGNANCY AND BREAST FEEDING (PAGE 57).....	31
4.2 ADDITIONAL ADVICE AND PRECAUTIONS.....	35
4.2.1 ADDITIONAL HEALTH ADVICE AND PRECAUTIONS 1:.....	35
4.2.2 ADDITIONAL HEALTH ADVICE AND PRECAUTIONS 2:.....	36
4.2.3 ADDITIONAL HEALTH ADVICE AND PRECAUTIONS 3:.....	42
4.3 APPENDICES.....	45
4.3.1 APPENDIX 3 COMPARISON OF INTERNATIONAL GUIDELINES (PAGE 82).....	45
4.3.2 APPENDIX 4 <u>RISK OF ALCOHOL-RELATED ACCIDENTS, INJURIES AND OTHER SHORT- TERM HARMS: EVIDENCE DETAILS</u> (PAGE 90).....	47
4.3.3 APPENDIX 5 <u>RISK OF ALCOHOL-RELATED DISEASE: EVIDENCE DETAILS</u> (PAGE 99)..	48
4.3.4 APPENDIX 6 <u>LIFETIME RISK OF DEATH FROM ALCOHOL-RELATED ACCIDENTS AND INJURIES</u> (PAGE 110)	54
4.3.5 APPENDIX 7 <u>LIFETIME RISK OF DEATH FROM ALCOHOL-RELATED DISEASES</u> (PAGE 114).....	56
4.3.6 APPENDIX 8 <u>ALCOHOL USE IN PREGNANCY AND BREAST FEEDING: EVIDENCE DETAILS</u> (PAGE 118).....	57
APPENDIX 1 TABLE OF DIFFERENCES BETWEEN THE CURRENT AND REVISED DRAFT GUIDELINES	69
APPENDIX 2 REFERENCES.....	72

1. Executive summary

This submission is presented by all sectors of the production and sale of alcohol in Australia, including beer, wine and spirits producers, clubs, hotels and retail liquor stores.

The Australian alcohol beverage and hospitality sector consulted with a broad range of scientific, medical and demographic statistical modelling opinion in formulating this Submission.

The Australian alcohol beverage and hospitality sector is committed to the goal of reducing alcohol misuse and abuse as evidenced by extensive involvement in targeted programs including contribution to DrinkWise Australia, standard drinks labelling and a quasi-regulatory regime for alcohol advertising.

The sector strongly supported the development and release of the NHMRC *Australian Alcohol Guidelines: health risk and health benefits* (2001), and continues to support the responsible consumption of alcohol. It is appropriate that these Guidelines be reviewed periodically but it is critical that reviews be based on the most recent and credible scientific information available as well as considering community expectations.

This Submission is a comprehensive critique of the draft revised Guidelines released for public comment on Friday, 12 October 2007.

On the weight of empirical evidence, the draft revised Guidelines do not make an adequate case for replacing the current Guidelines. The draft revised Guidelines are ambiguous and confusing as to their intent and purpose. They also lack credibility as they contain fundamental flaws and lack sufficient scientific rigor. Most importantly, however, they lack relevance for the general Australian population and so will not have the desired purpose of minimising alcohol-related harm.

The draft revised guidelines do, however, provide improvement in certain areas over the existing Guidelines, which is outlined in the body of this Submission.

The Australian alcohol beverage and hospitality sector, therefore, recommends that the status quo should prevail and that the current Guidelines be maintained until there is sufficient and significant scientific evidence to justify change.

The sector also recommends that if the NHMRC does move from the status quo, extensive consultation should be undertaken on a substantially-revised draft revised Guidelines given the complexity and importance of the issues outlined in this Submission.

There are three main areas of concern with the draft revised Guidelines, which are detailed in this Submission as follows.

1.1 Mathematical modelling

- The empirical evidence is thin, predominantly unpublished and hence not peer reviewed. No primary public policy should be based on papers that have no scientific standing in the discipline.
- The mathematical modelling on which draft revised Guideline #1 is based excludes the health benefits of moderate alcohol consumption. This exclusion is also contradictory and inconsistent with the statement on page 16, paragraph 3 of the draft revised Guidelines stating that health

benefits ensue from an alcoholic drink every second day. Additionally, the White et al. 2002 paper used in the mathematical modelling actually acknowledges a J-shaped relationship between alcohol consumption and all-cause mortality. The exclusion appears to be based predominantly on two recently published papers (Fillmore et al. 2006 and Harriss et al. 2007) the methodology and conclusions of which have been, and continue to be, contested, and where all other biomedical and even epidemiological evidence has been disregarded. The issue then becomes what does the J-shaped curve for all-cause mortality look like? If the health benefit extends to three to four alcoholic drinks/day for men, then it should follow that men can drink up to that limit without affecting their mortality adversely. The optimum drinking level for improving mortality will be at the bottom of the J-shape, which will obviously be less. Klatsky and Udaltsova's (2007) recent re-analysis seems to take benefit out to at least three US standard drinks/day or 42 g/day. Mukamal's (2006) meta-analysis of 34 studies shows a similar effect, as does Doll's (2005) meta-analysis. If the draft revised Guidelines accept the reality of the J-shaped curve as is stated in the text, then its authors are being disingenuous by only considering death and various harms attributable (at least in part) to alcohol in their mathematical modelling. This exclusion of the healthy benefits also has important implications for the balance and hence credibility of the draft revised Guidelines' content.

- The mathematical modelling on which draft Guideline #1 is based, also does not consider age and weight/body mass differences (all calculations are on population 'averages'). It is also unclear whether the average weights used in the calculations are appropriate for an Australian population which currently has an average weight of approximately 82 kg for men and 66 kg for women for 25-34 year olds.
- The data used in the mathematical modelling and the resultant revised draft Guidelines may not necessarily be representative of the Australian general population. The use of emergency room data and the validity of combining emergency room and alcohol-related disease data is questioned.

1.2 The draft revised Guidelines and additional health advice and precautions

- The draft revised Guidelines and accompanying text predominantly emphasise and focus on a limited range of epidemiological evidence in isolation of the pharmacological and physiological scientific evidence.
- Guidelines themselves need to be culturally relevant. The science base for the health consequences of both alcohol abuse and moderate consumption is not the only criteria or factor that should be considered when producing guidelines. Indeed, the purpose of recommendations is not to facilitate debate and discourse about the science but to facilitate a change in behaviour. Thus, it is important to take into account the prevailing drinking culture of a population, because only in that way is it possible to produce a public health message that is likely to be respected and regarded. The draft revised Guidelines fail to acknowledge that the majority of Australians who consume alcohol, do so responsibly and sensibly on most, although not all, occasions. The level of risk of drinking above the level in draft revised Guideline #1 is not put in context with other life risks.
- The draft revised Guidelines do not give any guidance on how alcohol should be consumed and no discussion on patterns, merely an amount per day. Guidance is also required on low risk drinking patterns to enable individuals to make fully informed decisions on how to lower their risk of short and longer-term alcohol-related harms. It has been shown that specific occasions of heavy consumption, usually by people who generally consume a light-to-moderate amount in low

risk ways, result in most alcohol-related harms or problems. When episodes of heavy consumption and intoxication are analysed rather than just mean consumption levels (Stockwell et al. 1996), a greater reduction in alcohol-related harm within a community would be observed than if all alcohol consumers were targeted to consume less. Accordingly, the drinking pattern is often a better predictor of alcohol-related harm than simply the amount consumed (Rehm et al. 2001) and a greater reduction of risk in the general community may be achieved through focusing on patterns rather than on a low level consumption per se.

- The draft revised Guidelines do not provide any guidance or advice for Australian women who choose to consume alcohol during their pregnancy. Stating a level below which there appears to be little evidence of harm to the developing foetus as well as encouragement to discuss the issue with their health professional would be appropriate advice. In addition, advice should be included that alcohol consumption above this level during the first trimester of pregnancy presents the highest risk to the developing foetus.

1.3 Presentation

- The structure of the draft revised Guidelines—three basic guidelines and three additional health advice sections and precautions—makes it more difficult to determine and interpret the advice and any rationale. The sections which relate to the sub-categories and special groups are later in the document in contrast to the current Guidelines where the guideline, rationale and comments are all included together.
- It is unclear what the actual aim of the draft revised Guidelines is, that is, whether the draft revised Guidelines are for the general public as a guide, as a resource for a wide range of groups and individuals, including health professionals, community groups, industry, professional organizations, schools and educational organizations, or to inform policy makers and planners, decision makers and those responsible for providing alcohol. As currently presented it neither guides, nor provides a resource nor informs.
- The tone of the draft revised Guidelines is judgmental and negative rather than neutral.

In conclusion, it is recommended that the NHMRC retains the current *Australian Alcohol Guidelines: health risks and health benefits* until all the issues raised in this Submission have been satisfactorily addressed and there is significant and sufficient scientific evidence to support a change from the current Guidelines and recommendations to minimise risk and maximise benefits.

The following pages (8 to 68) critique and discuss the specific issues of concern.

2. Introduction–Contribution of the Australian alcohol industry

2.1 Economic contribution of the Australian alcohol industry

The following section regarding economic contribution of the alcohol industry in Australia is taken largely from the Distilled Spirits Industry Council of Australia (DISCA) Pre-Budget Submission 2007/08.

2.1.1 The Alcohol industry in Australia

The alcohol industry makes a significant economic and social contribution to Australia and Australians.

In economic terms, it is estimated that:

- the alcohol industry contributes \$18.31 billion annually to the Australian economy (MCDS 2006, p 4);
- the estimated total taxation revenue collected by the Australian governments from alcohol beverages in 2005-06 was \$5.61 billion (including \$1.37 billion of GST revenue); and
- the industry is estimated to directly employ 36,000 persons in total, and indirectly contributes to the employment of 205,000 (including individuals in pubs, taverns and bars) (MCDS 2006, p 4). Furthermore, additional employment and economic benefits flow to rural and regional areas through the production of grapes, barley, hops, sugar cane and other inputs to the production of alcoholic beverages. This is in addition to the packaging and promotion of alcoholic beverages and the transport of the raw material and finished products.

These numbers do not include the significant multiplier benefits of associated economic activity such as the more than \$650 million spent by more than 5.5 million domestic and international wine tourism visitors in 2006 (WFA 2007).

Alcohol is widely enjoyed throughout society and is accepted as a way of relaxing and socialising. Furthermore, evidence over the past decades has shown that, when consumed at appropriate levels, alcohol can provide tangible health benefits for consumers (NHMRC 2001, p 3).

The majority of Australians consume alcohol in a responsible manner without harm to themselves or to others. In 2004, it was estimated that 1.5 million Australians consumed alcohol daily, 6.8 million on a weekly basis and a further 5.5 million on a less than weekly basis (AIHW 2005a, p 19).

2.1.2 Alcohol revenue estimates

It is estimated that the Federal and State Governments in Australia will collect approximately \$5.93 billion in taxation revenue from the production and consumption of alcohol beverages in the 2007-08 financial year.

The sources of this revenue are:

- excise duty (on the local manufacture of beer and spirits);
- customs duty (on the importation of beer and spirits);
- Wine Equalisation Tax (WET) (on the wholesale, or equivalent, sale of locally produced and imported wine and cider); and
- Goods and Services Tax (GST) (on the local final consumption of all products).

For the 2007-08 year, it is estimated that the Federal and State Governments will receive the following taxation revenue from the alcohol beverage sector:

- \$1,204m in customs duty;
- \$2,663m in excise duty;
- \$682m in WET;
- Resulting in \$4,549 non-GST revenue;
- \$1,382m in GST revenue for the States and territories;
- Resulting in \$5,931m in total.

The 2007/08 DSICA Pre-Budget Submission estimates that the States and Territories will receive \$1,382 million in GST revenue from alcohol products in 2007-08. This is a conservative estimate, and does not include a component to reflect the GST on the service element where alcohol products are served on-premise.

The alcohol industry contributes significantly to Australia's economic well-being. The industry makes a multi-billion dollar contribution to the Australian economy annually, and provides direct and indirect employment opportunities for many Australians. Furthermore, the alcohol industry provides a valuable taxation source to both the Federal and State Governments.

2.2 Contribution to education, research and social programs

The Australian alcohol industry is mindful of its responsibility as a producer of products that may be irresponsibly consumed by some in the community. In recognition of this responsibility, alcohol producers are involved in a wide range of education and research initiatives independently, with community stakeholders and in conjunction with state and Federal Governments.

The alcohol industry supported the National Health and Medical Research Council (NHMRC) *Australian Alcohol Guidelines: health risk and health benefits* (2001) recommendations of a maximum of four and two standard drinks per day for men and women, respectively. These Guidelines were promoted through retail liquor outlets, industry newsletters and hotels, and supported through other initiatives such as the Alcohol Beverages Advertising Code (ABAC) Scheme.

Australian alcohol producers are voluntarily adopting responsible consumption messages on package labels such as "Enjoy wine in moderation" as well as implementing a voluntary standard drinks logo on package labels to clearly identify number of standard drinks for consumer information and support the current Guidelines.

The industry established the ABAC Scheme in 1992 that has continually been expanded and strengthened over the intervening years to ensure a strict regime that has resulted in the quasi-regulation of advertising in partnership with the Australian Federal Government.

The alcohol producers contribute more than \$5 million per annum to DrinkWise Australia, an evidence based organisation charged with promoting change towards a more responsible drinking culture in Australia. DrinkWise Australia is funded by, but independent of, the alcohol industry and is governed by a Board of Directors half from industry and half from the community with expertise in the law and order, health and social marketing fields.

3. General comments on Part A. Sections 1 – 4

It cannot be disputed that there are significant economic, medical and social consequences from irresponsible or high risk alcohol consumption. Any alcohol drinking guidelines, however, need to be credible and relevant in order to facilitate changes in the behaviour of those consuming alcohol irresponsibly and at high risk. Credibility is related to both balance and cultural relevance of content. Consequently, there are three general issues identified that are of considerable concern in the draft revised Guidelines which are discussed as follows. Specific issues relating to the actual guidelines and their methodology are discussed in separate sections.

3.1. Credibility of the draft revised Guidelines

3.1.1 Cultural relevance

Putting current Australian alcohol consumption into perspective, from the Australian Institute of Health and Welfare [AIHW] (2005, 2007), the pattern of alcohol consumption by the Australian population has remained relatively unchanged over the period 2001 to 2004, as has the amount of alcohol consumed over the period 1994 to 2004. In 1997, an external review was undertaken of the policy and progress of the *National Drug Strategy 1993–1997*. The review revealed that in the community the mean level of alcohol consumption had declined since 1987, when the first Guidelines were published, but the proportion of consumers who drank alcohol heavily at least once per week had only declined by approximately 4%, and consumers who habitually drank heavily were resistant to change (Single and Rohl 1997). Those consumers resistant to change included adolescent and young adult Australians and indigenous Australians.

In the 12 months preceding the 2004 National Drug Strategy Household Survey, **only 10% of the Australian population consumed alcohol in an amount and pattern considered risky or of high risk to health in the long-term** according to the definitions in the NHMRC *Australian Alcohol Guidelines health risk and health benefits* (2001) ; **7% drank at risky levels** (29–42 standard [10 g] drinks/week for men and 15–28 for women), while **3% drank at high risk levels** (43 or more standard drinks/week for men and 29 or more for women). Again, individuals aged 20-29 years were most likely to do this, and were also the group least likely to abstain from alcohol consumption. Seventy-four percent of Australians aged 14 years and over, however, consumed alcohol in amounts that were considered a low risk to health in the long-term while 16% were abstinent.

Concerning short-term alcohol-related harm, **35% of Australians aged 14 years and over, consumed alcohol in amounts that were considered risky or high risk for short-term harm at least on one occasion** during the 12 months preceding the survey (more than seven and five drinks on any one day for men and women, respectively). Again, individuals aged 14-19 years were most likely to do this weekly.

These statistics suggest that the Australians aged over 29 years generally consume alcohol both responsibly and sensibly, and generally at a low risk level for both short- and long-term harm. Compared with countries such as the UK, from the UK General Household Survey 2005, 35% and 20% of UK men and women, respectively, aged over 18 years drank more than the daily recommended maximum of respective four and three standard (8 g) drinks (<http://www.heartstats.org/temp/Tabsp7.6spweb06hs1hs.xls>).

Accordingly, there is concern that the credibility and relevance of the guidelines has been compromised. It is stated on page 18 that the guideline level has been simplified, but perhaps the guidelines have become simplistic and hence of less relevance to the majority of Australian

consumers who already (and generally) consume alcohol both responsibly and safely. Indeed, the new draft Guideline #1 substitutes the current recommendations “that the consumption of alcohol by men should not exceed four units or 40 g of absolute alcohol per day on a regular basis, or 28 units per week; and that the consumption of alcohol by women should not exceed two units or 20 g of absolute alcohol per day on a regular basis, or 14 units per week”, with a basic two standard drinks or less on any one day for both men and women.

This is without discussed scientific evidence for the replacement and reduction of four standard drinks to two for men, and without discussed evidence relating to the context or relevance of the lifetime risk in ‘real-life’ terms and compared to other lifetime risks, such as the risk of pedestrian, car and plane travel. In addition, the increased risk of harm to women’s body organs and tissues compared to men’s from consuming comparable amounts of alcohol is disregarded.

For example, on **page 25, paragraph 1** the draft revised Guidelines state “the intention is to enable people to assess their level of risk as objectively as possible based on the scientific evidence”, but guidance is also required to enable informed evaluation and management of the risk or else the level of risk becomes meaningless rather than meaningful to the individual.

Indeed, it is only stated but not discussed on **page 23 paragraph 2** that “...most people accept much higher risks than this for lifestyle issues where they have some personal control (e.g. the risk of car travel).” Thus it is unhelpful to include the figure (2.1) and box (2.1) of technical risk terminology on **pages 22 and 23**, as they do not adequately explain the risks and relate them to real-life.

Equally to state on **page 9, paragraph 11**, that “low risk has been conservatively defined as the level of alcohol intake...that will reduce lifetime risk of death to 1 in 100, that is, one death for every 100 people who drink at that specified level and pattern”, is also unhelpful as death is a fixed variable, only the context of which can change.

This lower level for men is also not culturally relevant for Australian men as evidenced from the 2004 National Drug Strategy Household Survey where 16% of Australian men aged 14 years and over drank greater than seven or more standard drinks per day at least yearly, 14.5% at least monthly and 10% at least weekly, and in particular for Australian men aged 14-19 years who drank at this risky levels at least weekly. This observation is despite the general decline in alcohol consumption since 1982. This is not merely an Australian observation but is also observed internationally (WHO 2001).

Research suggests that telling an individual that a behaviour is harmful or providing information about the risk associated with a behaviour is insufficient to affect an individual’s actions. In addition, increasing an individual’s knowledge about a health risk does not necessarily cause that individual to change or modify negative or risky behaviour (Eggs 1989).

To change the behaviour of an individual is complex, for example, an individual must:

- feel personally susceptible to the health risk;
- believe that the risk can cause a significant harm; and
- know what actions can be taken to avoid the harm, and also know the cost or benefit of the actions; if the costs outweigh the benefits, the action to avoid the harm is unlikely to be taken.

Personal susceptibility or relevance is affected by a range of social and psychological factors, which act to establish the context of the judgement regarding credibility and hence the eventual effectiveness of a guideline (Cvetkovich and Earle 1995). Indeed, for a guideline to be effective, it should involve the individual consumer, such that the individual will read the guideline and process

the information contained in the guideline. It should also be relevant to the individual, as well as believable or credible. Thus the proposed guideline, which is simplistic and culturally not relevant, is unlikely to influence any individual, of the general population or the identified ‘at risk’ groups, to change or modify their risky alcohol consumption.

It is considered that product warnings, for example, can not readily and reliably be targeted to ‘high risk’ groups and individuals, such as excessive consumers of alcohol, whether regular consumers or ‘binge drinkers’. The personal experiences affecting judgments of personal risk, motivations for high risk behaviour and the individual pharmacological and physiological properties of, and responses to, alcohol, all make it difficult to design warnings that are effective with these individuals.

Young people, for example, who are an ‘at risk’ group, may have difficulty in judging or perceiving risks associated with alcohol consumption. This is because if an event has not occurred to an individual, and he/she cannot associate it with a particular risk, then the individual may perceive that the risk may not occur in the future—that is, the risk is not related or relevant to them personally (Patterson *et al.* 1992). Also ‘at risk’ individuals apparently give greater weight to uneventful experiences with alcohol interpreted to indicate that it carries low risk (Cvetkovich and Earle 1994, 1995). Indeed, the possibility that there are different reasons and motivations for high-risk behaviour makes it difficult to effectively target messages to these individuals.

3.1.2 Balance – Exclusion of health benefits in the modelling studies

It has been demonstrated previously in Australia in the 1995 and 1998 editions of *The quantification of drug-caused mortality and morbidity in Australia* (English *et al.* 1995, Riddolfo and Stevenson 2001), and internationally (Rehm *et al.* 2003, 2007) that low risk alcohol consumption can confer economic, social and medical benefits such as a reduced risk of, and death from, cardiovascular diseases, and is acknowledged in the Australian Institute Health and Welfare’s *A guide to Australian alcohol data (2004)* and in the introduction to the *National Alcohol Strategy 2006–2009*.

Indeed from the 1998 edition:

“The effect of alcohol consumption on illness and injury is more complex. In 1998 an estimated 3,271 people died as a consequence of hazardous and harmful levels of alcohol consumption. In addition to the harmful effects, however, when consumed at moderate levels alcohol appears to be associated with a decrease in heart disease and stroke. The number of people in Australia who drink at moderate levels far outweighs the number who drink at hazardous or harmful levels, so this apparent protective effect is greater for the overall population than the harmful effect for deaths, though not for potential years of life lost. Thus the estimated net reduction in deaths associated with alcohol consumption in 1998 was 2,371 but the estimated net potential years of life lost due to alcohol consumption in 1998 was 21,147.

The reason that alcohol appears to be associated with a net decrease in deaths but a net increase in potential years of life lost is because the decrease applies to illnesses which occur at older ages while the harmful effects apply across all ages. Deaths at younger ages contribute more potential years of life lost than deaths at older ages. Thus in 1998 the net effect of alcohol consumption at ages below 65 years was to cause an estimated 2065 deaths, leading to 47,887 potential years of life lost, while the net effect at ages 65 years and over was associated with a decrease of 4,436 deaths or 26,739 potential years of life lost”

This second paragraph is particularly pertinent to the draft revised guidelines, as the two population groups that the guidelines should aim to influence most are the younger adults (with the highest rate of short-term alcohol-related harms) and the older adults (increased percentage of population and hence potential public health burden in Australia). Thus, the draft revised Guidelines have to be made more credible and relevant by inclusion of information on low risk patterns of consumption as well as on amounts.

Cardiovascular disease (CVD) is the leading cause of death in developed countries, accounting for 25–50% of all deaths, and its incidence is increasing in developing countries, associated with economic growth and development (Singh et al. 1996, WHO 2002, 2003). The main factors responsible for this incidence are represented by the high rates of patients with uncontrolled high blood pressure (hypertension) and a high cholesterol concentration (dyslipidaemia), and the epidemic of obesity and type 2 diabetes, which tend to appear together as metabolic syndrome (MS) (Dunstan et al, 2002 and Zimmit et al. 2005). In 2000, CVD accounted for nearly 40% of all deaths in Australia, over 50% of Australians were overweight (BMI>25 kg/m²), while 7.5% of Australians were diagnosed as diabetic. The incidence of type 2 diabetes is expected to approximately double by 2010, thus posing a significant health burden on the government.

The credibility and relevance of the draft revised guidelines is also questioned due to:

- the ever-increasing evidence that the light to moderate consumption of alcohol does have beneficial health effects for the general population; and
- and lack of inclusion of this evidence in any risk calculations apart from a relative risk of 1, which implies no harms to health yet no benefits.

This is a significant flaw in the mathematical modelling. The primary health benefit is a reduction in risk of, and death from, cardiovascular disease, which is observed in healthy individuals and in those with hypertension, diabetes and existing cardiovascular disease (Mukamal et al. 2001, Tanasecu et al. 2001, Malinski et al. 2004, Koppes et al. 2006).

For example, the draft revised Guidelines on **page 23, paragraph 3**, states that “As noted in Section 1.1, drinking may reduce the risk of some cardiovascular diseases and cerebrovascular disorders...where appropriate such risks have been acknowledged...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...”. This statement is contrary to the bulk of the biomedical evidence, and based on only two studies and three recent contentious publications – Fillmore et al. 2006, 2007 and Harriss et al. 2007, and was not explained in Appendix 5 as cited in the text or in any of the Appendices, except on **pages 44 and 45**.

White et al. (2002) still observed a J-shaped (albeit shallow) relationship between alcohol consumption and all-cause mortality for men aged 35 years and over and women aged 55 years and over when the risk factors for cardiovascular disease increase, and thus highlights the importance of age-related guidance. This statement was also made **on page 16, paragraph 3**, while on **page 30, paragraph 2**, it was stated that “regular, light to moderate alcohol consumption has been associated with reduced risks of some conditions ...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 over-estimate the effects”.

The conclusions of Fillmore’s publication can be questioned in that there have been, especially in recent years, a number of prospective epidemiologic studies that have avoided the errors used by Fillmore et al. to exclude studies from their analyses. For example, these prospective epidemiologic studies have used ‘lifetime abstainers’ as the referent group, and have included occasional drinkers within specific ‘low-intake’ categories, and not mixed them into categories of abstainers or regular consumers of small amounts. One could use such studies to test the hypotheses the authors present and avoid the two types of errors that the authors have sought to evaluate. The first type of error is the

former drinker misclassification error (“failure to separate former drinkers...from complete abstainers”), and the second is the occasional drinker misclassification error (“failure to separate occasional drinkers...from complete abstainers”).

A review of all recent studies that have avoided the two errors described above, and accounted for the pattern of drinking as well, is needed to fully test the hypotheses proposed by Fillmore et al. Only two studies for cardiovascular mortality and seven studies for total mortality were used as a basis for the final conclusions of Fillmore et al. in this paper, and these can not be considered as ‘representative’ of the general population. The analysis also inappropriately used significance testing for inference, and has ignored quantification for possible biases, for example, from misclassification or residual confounding.

Klatsky and Udaltsova (2007) reworked previously published data (Klatsky et al. 1992, Klatsky et al. 2003) to address the purported confounding and potential over-estimation of a health benefit from moderate alcohol consumption claimed by Fillmore et al (2006, 2007), and showed a shallower but still significant J-shaped relationship between alcohol consumption and all-cause mortality risk that is not discussed in the draft revised Guideline. The data was of 21,535 deaths through to 2002, where the follow-up included 2,618,523 person-years of observation with a mean follow-up of 20.6 years. Their re-analysis reconfirmed the relationship previously published with an increased risk for individuals consuming more than three (14 g) drinks per day and a reduced risk at three or less drinks per day, almost always due to a reduced risk of death from cardiovascular disease. Former consumers were observed to be at increased risk of death from non-cardiovascular disease and occasional consumers were observed to have a risk similar to lifelong abstainers.

There are also other relatively recent studies where neither type of ‘error’ studied by Fillmore et al. (2006) was present. For example, a study by Mukamal et al. (2006) on a large group of older adults which separated lifetime abstainers from former drinkers, and occasional drinkers from regular light drinkers, demonstrated reductions in the risk of a variety of cardiovascular outcomes from moderate consumption. In another study on older people by Tolvanen et al. (2005) where ex-drinkers were separated from lifetime abstainers, total mortality was highest in the ex-drinkers and lifetime abstainers, and 30–40% lower in current consumers. In addition, another study by Klatsky et al. (2005) which identified lifetime abstainers and separated occasional drinkers from regular light drinkers showed that consumption of one to two drinks/day was associated with 40% less heart failure associated with coronary artery disease.

One of the salient points to come out of eight commentaries, which were published in the February 2007 edition of the journal *Addiction Research and Theory*, on the Fillmore et al. 2006 paper, as well as from commentaries in the May 2007 edition of *The Annals of Epidemiology*, is that there is evidence for plausible biological mechanisms for protection against coronary heart disease by moderate alcohol consumption which adds credence to a causal hypothesis. As previously mentioned, these mechanisms include effects via high density lipoprotein, improved haemostatic factors, improved endothelial function, and a lower risk of diabetes mellitus.

An earlier meta-analysis of 42 experimental studies, which examined the effects of alcohol consumption on cardiovascular biomarkers, attributed the cardioprotective effect of light-to-moderate alcohol consumption 60% to effects on high density lipoprotein, 20-30% to fibrinogen, 5-10% to insulin and 0-5% to other haemostatic factors (Rimm et al. 1999). The meta-analysis also estimated that 30 g of alcohol per day would increase the plasma concentration of high density lipoprotein by approximately 4 mg/dL which would be associated with a 17% reduction in risk of coronary heart disease. It would also decrease the plasma concentration of fibrinogen by approximately 0.075 g/L, which would be associated with a 12.5% reduction in risk of coronary heart disease (Hines and Rimm

2001). This translated into an overall 24.7% reduction in the risk of coronary heart disease from the consumption of 30 g of alcohol per day. Klatsky et al. (2007) further translated this into a 10% reduction in risk of all-cause mortality.

Interestingly, in their reply to the eight commentaries on this point, Fillmore et al. (2007) do not dispute the evidence for plausible biological mechanisms and merely suggest that “the lot falls to epidemiology to establish whether human populations will benefit greatly from the use of alcohol and if they should be advised to use the substance for medicinal purposes”.

From the commentary by Rehm (2007), “All scientific knowledge is subject to revision, and there may be new evidence leading to changes in decision-making, but given the current level of knowledge, the convergence of experimental and observational knowledge supports the cardioprotective effects [of light to moderate alcohol consumption].”

Biomedical and epidemiological evidence generally suggest that a reduced risk of death from cardiovascular disease is associated with one to two standard drinks of alcohol per day for both men and women (Maclure 1993, Corrao et al. 2000, Rehm et al. 2001, Klatsky et al. 1992, Gmel et al. 2003, Klatsky 2003, Corrao et al. 2004, Di Castelnuovo et al. 2006, Klatsky and Udeltsova 2007, Rehm et al. 2007) and some of these studies have even been cited in the draft Guideline but dismissed without discussion. For example, in a meta-analysis by Rehm et al. (2007) it was observed that when heavy consumption (greater than 39 g alcohol/day for men and 19 g for women) was excluded from estimations of benefits and risks from alcohol consumption, the net effect was beneficial, where consistent with other observations, the net burden was higher for younger ages and the net benefit for older ages.

In addition, concerning the pattern or regularity of consumption necessary to confer cardiovascular benefits, the literature is consistent in that the pattern of alcohol consumption required for cardioprotection is regular consumption, which can be determined as daily consumption (McElduff and Dobson 1997). This regularity is related to short-term or acute effects on the dissolution of blood clots and on platelet aggregation, which are readily reversible (Renaud *et al.* 1984, Renaud *et al.* 1992, Hendriks *et al.* 1994), and to longer-term effects on plasma antioxidant capacity, on low density lipoprotein oxidation and on systolic blood pressure (Klatsky *et al.* 1977, Gillman *et al.* 1995, Klatsky 1995). Furthermore, any lowering effect of alcohol on systolic blood pressure is readily reversible, within seven to 14 days (Puddey *et al.* 1985), such that regular consumption is necessary to maintain this particular cardioprotective effect (Klatsky *et al.* 1990, Gillman *et al.* 1995, Klatsky 1995).

Conversely, binge drinking is seen to significantly increase systolic blood pressure, which significantly increases the risk of a heart attack or stroke (Hillbom and Kaste 1981, Hillbom *et al.* 1984, Donahue *et al.* 1986, Suhonen *et al.* 1987, Kozarevic *et al.* 1988, Renaud and Ruf 1996).

Indeed, essentially all epidemiological studies that have considered patterns of consumption have shown that regular moderate consumption is allied to lower risk of diseases rather than occasional consumption, while episodic heavy consumption, considered as binge drinking, negates any beneficial health effect.

For example, from a 2003 study by Mukamal et al., men who consumed alcohol three to four or five to seven days per week had decreased risks of myocardial infarction compared with men who consumed alcohol less than once per week, where the risk was similar among men who consumed less than 10 g of alcohol per drinking day and those who consumed 30 g or more. This is a similar observation to that of Tolstrup et al. 2004, where for the same average consumption of alcohol, an infrequent intake implied a higher risk of mortality than a frequent one, and also to that of Baglietto et

al. 2006, who investigated associations between average volume of alcohol consumption, beverage type and consumption pattern, and all-cause mortality. After adjustment for total amount of alcohol consumed, the number of drinking days was inversely associated with the risk of dying in men, confirming previous observations about the effect of average volume of alcohol and beverage type and suggest that consumption pattern is an independent risk factor for all-cause mortality. The beneficial health effects of alcohol may thus be limited or linked to certain patterns of consumption (Puddey et al. 1999, Rehm et al. 2003) as are the harmful effects.

These observations therefore suggest that the draft Australian alcohol guidelines for low risk drinking should include advice about drinking patterns as well as the amount of alcohol necessary to achieve and maintain a low risk of alcohol-related harm and any potential benefits.

3.2 Relevance of simple guidelines

Indeed, while the draft revised Guidelines build on the 1987, 1992 and 2001 recommendations regarding responsible drinking behaviour, and attempt to address when, where and under what circumstances hazardous consumption and associated high risk is likely to occur, as there are various alcohol consumption patterns, the reduction of this variety and complexity to a single measure of mean daily intake is also likely to hide patterns of consumption that are particularly harmful, such as episodic heavy consumption considered as 'binge drinking'.

At least 33 countries have definitions for moderate or low risk alcohol consumption that differ significantly (Stockley 2007). Only 26 of the 33 countries that have been reviewed have precise general definitions, but the others either have definitions for specific population groups such as pregnant women or recommend abstinence. Fifteen percent of countries now have a maximum level only for weekly consumption and 58% have a level for daily consumption; 27% have a level for both weekly and daily consumption.

The definition for moderate daily consumption ranges from 20 g of alcohol/day for men and 10 g for women (Poland, Slovenia and Germany) to 60 g of alcohol/day for men (France) and 40 g of alcohol/day for women (Italy). For weekly consumption the definition ranges from 42 g of alcohol/week for men and 28 g for women (Portugal) to 252 grams of alcohol/week for men and 168 g for women (Denmark and South Africa). There appears to be no relationship between a country's definition and its current per capita consumption, but there may be a relationship with the typical amount of alcohol consumed per occasion and the alcohol-related harm experienced (Bobak et al. 2006).

Rehm et al. (2007) also observed that the injury burden was generally linked to single occasion heavy drinking, such that the net impact of on-average moderate alcohol consumption depends on patterns of consumption, which confirms that specific occasions of heavy consumption, usually by people who generally consume moderate amounts of alcohol in low-risk ways, result in most alcohol-related harm (Single and Rohl 1997).

For example, in 1997, acute conditions such as alcohol-related road injuries related to occasional high-risk consumption accounted for 28% of all Australian alcohol-related deaths, while chronic conditions such as cirrhosis of the liver related to sustained high-risk consumption accounted for 42% (Chikritzhs et al. 2001). Thus individuals with stable patterns of moderate alcohol consumption have the lowest all-cause mortality where individual changes in alcohol consumption are followed by corresponding changes in mortality (Gronbaek et al. 2004). Accordingly, drinking pattern is often a better predictor of alcohol-related harm than simply the amount consumed (Rehm et al. 2001).

In conclusion, guidance is also required on low risk drinking patterns to enable individuals to make fully informed decisions on how to lower their risk of short and longer-term alcohol-related harms.

3.3 Ambiguous aim and judgemental tone of the draft revised Guidelines

The aim of the current Guidelines is three-fold: to enable Australians to make informed choices about their drinking and health; to enable health professionals to provide evidence-based advice on drinking and health; and to promote individual and population health, and minimise harm from alcohol.

It is unclear, however, what the actual aim of the draft revised Guidelines is:

- on page 17, paragraph 3 they state “are intended to **give Australians** clear guidelines on how to avoid or minimize the harmful consequences of drinking alcohol...”;
- on page 17, paragraph 3 they state “**provide a resource for** a wide range of groups and individuals, including **health professionals, community groups, industry, professional organizations, schools and educational organizations**. They will also **inform policy makers and 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”;
- on page 17, paragraph 4 they state “members of the **general public** wanting to make decisions about their own drinking may also be interested in these guidelines”, but also go on to state “**as it is a technical document it is not aimed at the general public**”; and
- on page 25, paragraph 1 they state “the intention is to **enable people** to assess their level of risk as objectively as possible based on the scientific evidence”.

These four citations are contradictory. Furthermore, the aim of the draft revised Guidelines appears to be as broad and complex as the aim of the current Guidelines, which was one of the criticisms levelled at it at *The Australian Alcohol Guidelines: Is it time for a new direction? A community consultation forum hosted by the Premier’s Drug Prevention Council* on 1 February 2007.

Surely, the purpose of alcohol guidelines is not to facilitate debate and discourse about the scientific evidence but to facilitate a change in behaviour, and specifically enable individuals to make informed decisions about their alcohol consumption.

While the specific population groups being targeted by recommendations may differ, generally most governments are principally concerned with reducing the economic, health and social consequences of alcohol misuse *per se*. Guidelines should be aimed at the population groups that are misusing alcohol or drinking cultures that are likely to lead to misuse, which is also the approach advocated by the World Health Organization (World Health Organization 1999; World Health Organization 2005).

Furthermore, on page 18 the draft revised Guidelines go on to state “the new guideline is not intended to be a prescriptive level of drinking that must be followed in all situations” and “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.”

This statement is also confusing, contradictory and at odds with statements from the previous pages. It cannot be a guideline and not be potentially prescriptive. Indeed, from the Merriam-Webster online dictionary, a guideline is defined as “an indication or outline of policy or conduct” and from the Free Dictionary by Farlex “a statement or other indication of policy or procedure by which to determine a

course of action” and a “rule or principle that guidance to appropriate action” or “a rule or principle that provides guidance to appropriate behaviour”.

If not prescriptive, then why do the guidelines state on **page 18, paragraph 3** that “any drinking above the guideline levels therefore carries a higher **risk than non 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”. Please note that this highlighted text should also be “**than drinking at the prescribed levels and non-drinking**”.

The draft revised Guidelines could certainly be considered prescriptive if, as stated on **page 17, paragraph 1**, “...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...”, where “...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”.

In addition, on **page 25, paragraph 2**, while it is stated that “these guidelines are concerned with risks to life and limb, and not with moral...standards about drinking”, it goes on to state “there is a need for continuing public debate about such standards of conduct”. These statements are examples of a judgemental tone and hence inappropriate in advisory and general government guidelines.

3.4 Other issues

On page 17, paragraph 1, the Collins and Lapsley reference (in press) has not been published nor released for peer review by the Department of Health, and as such it and the accompanying text should be deleted until it has been released for peer review.

On page 18, section 1.3 it is also stated that “there 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 qualified level of risk associated with the guideline levels.”

We would like to highlight that **while the safe, harmful and hazardous drinking levels in the 1987 and 1992 editions of the guidelines were based on a variety of scientific and social opinions rather than on a detailed review of the epidemiological research, the risk levels within 2001 edition were based on a meta-analysis undertaken in 1996 of 16 cohort studies which examined the relationship between the level of consumption and all-cause mortality, and a further 132 epidemiological studies were examined for 10 specific alcohol-associated causes of death, such as cardiovascular disease. The meta-analysis determined that the relative risks of mortality as defined in the recommendations were consistent with available epidemiological evidence (Holman et al. 1995, 1996).**

The meta-analysis also determined that a pattern of usual alcohol consumption consistent with the recommendations for ‘safe’ drinking levels would confer a mortality risk similar to or less than that observed in abstainers for people aged 35 years or older. Above ‘safe’ drinking levels, the mortality risk increases – this J-shaped relationship between the amount of alcohol consumed and risk of cardiovascular disease and mortality from all-causes was first described by Klatsky et al. in 1974.

The current Guidelines define a general level of alcohol consumption at which there is minimal risk of harm in the longer-term, such as liver cirrhosis, but where there might also be some longer-term health benefits, such as a reduced risk of cardiovascular disease, for a proportion of the population. They also define a daily level of alcohol above which the short-term risk of harm, such as accidents, significantly increases.

Page 18, paragraph 4, the current Guidelines are equally conservative as the draft revised Guidelines for pregnant women as they state “may consider not drinking at all”, but breastfeeding women are not considered in the current Guidelines.

Page 28, Section 3, the draft revised Guidelines **have shortened, over-simplified and not referenced the text of an important section of the guidelines on which the risk of alcohol-related harm is derived, which dilutes the usefulness of this section for the general public, health professionals and policymakers.** Terminology such as blood alcohol concentration, dampening, tolerance are not explained, and a table of alcohol-related harms (and benefits) could accompany the text.

Page 29, paragraph 3, there is also evidence to suggest that minimal increased risk of certain cancers, in particular those of the aerodigestive tract, breast and colon (Hamajima et al. 2002, Corrao et al. 2004, Morch et al. 2007, Thygesen et al. 2007, Tjonneland et al. 2007) and liver cirrhosis, occurs below 20-25 g of alcohol per day (WHO 2007). Above 50 g of alcohol per day there is, however, a dose dependent increase in relative risk for these chronic diseases (Corrao et al. 2004, WHO 2007).

Page 30, paragraph 1, the scientific data also show that the effect of alcohol on body weight and the development of obesity is complex. One standard drink (10 g alcohol) of a wine and sparkling wine contains between 220 and 285 kJ, which increases to approximately 345 kJ for fortified wine. Alcoholic beverages may contribute up to 6% of the total foodstuff energy in the Australian diet for light to moderate consumers of alcohol, as from epidemiological data, light to moderate consumers of alcohol generally add alcohol to their normal diet.

This figure is dependent, however, on factors, such as amount and pattern of alcohol consumption, concomitant food intake, diet (carbohydrate, fat and protein, which are the other major energy substrates), exercise and gender; this means that at least 94% of calories are derived from other sources. In contrast, for excessive consumers, such as those alcohol dependent or alcoholics, the contribution of alcohol to total foodstuff energy may increase to 50% as alcohol is often consumed instead of, or in preference to, other foodstuffs. Approximately one third of epidemiological studies on alcohol and body weight suggest that there is a positive correlation between alcohol consumption and body weight, one third found a negative correlation and one third found no association at all (McDonald *et al.* 1993, Westerterp 1995).

The discrepancies in data may result from methodological differences between the studies. Statistical analysis of the relationship between alcohol intake and body weight (body mass index), however, should not be used to determine whether the calories or energy from alcohol 'count' or 'do not count' towards body weight due to the limited contribution of alcohol to total energy intake. Also, epidemiological studies, which suggest that alcohol-derived energy 'does not count' are not supported by the measurement of alcohol-induced thermogenesis, which indicates that the thermic effect of alcohol is intermediate between that of carbohydrate and fat (>5–10%), and that of protein (20–30%). The magnitude of the thermogenic effect is dependent, however, on the amount of alcohol consumed, where approximately 80–85% of the alcohol-derived energy is utilised by the body for healthy non-alcoholic consumers.

In addition, when alcohol is consumed, in conjunction with a meal, it becomes the priority substrate and temporarily displaces carbohydrate and fat from oxidative metabolism in the liver. Since there is a maximum oxidation rate for alcohol of approximately 0.1 g/kg (0.7 kcal/g) fat-free mass per hour, only approximately 50% of the resting energy expenditure can be covered by alcohol oxidation and substantially less if this is related to total energy expenditure, which includes physical activity. This implies that, potentially, alcohol can temporarily and transiently spare the oxidation of other substrates up to a maximum level of 50% of the resting value. **This contrasts with the effect of carbohydrate consumption on carbohydrate utilisation which can be highly modulated and which can contribute, even post-absorptive, approximately 100% of the energy expenditure following supra levels of glycogen stores consecutive to massive carbohydrate loading.**

Alcohol consumed in addition to a normal diet is expected to lead to fat storage since it spares fat from oxidation, but this will be associated with a lower weight gain in bodyweight than when carbohydrate is stored as glycogen, such as excessive carbohydrate consumption, due to the significant difference in energy density of fat (9 kcal/g) versus the glycogen–water pool (1 kcal/g).

In conclusion, alcohol does contribute to the total calorific intake of moderate consumers of alcohol and enhances the development of a positive energy balance. The significance of the contribution, however, does significantly depend on, for example, the composition of the diet of the consumer, the amount and pattern of alcohol consumed, and the level of physical activity or exercise of the consumer.

Page 31, Section 3.3, is factually flawed in some small sections, for example, the text should read as follows:

- Paragraph 3, line 4: broken down by biochemical processes in **the stomach and** liver
- Paragraph 3, line 5: Insert: There is a 3–4-fold variation in the rate of alcohol metabolism between individuals.
- Paragraph 3, line 6: food (**and the type of food**) in the **stomach** (not gut)...concentration of the drink, **speed of consumption and concomitant consumption of other drugs**
- Paragraph 3, line 4, reference to Section 2.3 should be removed as there is no discussion of this issue in that section and should be replaced with Section 3.4, which does discuss this issue.

Page 32, Section 3.4, is factually flawed in some sections, for example, the text should read as follows:

- Paragraph 1, lines 2 and 3 (Sex): Insert: As alcohol is **only taken up slowly by fatty tissue...distributed into a smaller volume of body water** and delete **...with less absorption.**
- Paragraph 2, (Age): Insert: A younger and smaller a person has less body water into which the alcohol can distribute and will thus have a higher BAC for a given amount of alcohol, than an older and bigger person. In addition, an older person will also have less body water.
- Prior to Paragraph 1: Insert: There is also a 2–3-fold variation in the pharmacodynamics of alcohol because of individual differences, which influences the extent to which individuals are affected by a given dose of alcohol. These individual differences affect alcohol-induced toxic and behavioural effects, drinking behaviour, the potential for the development of alcohol dependence and the risk of alcohol-induced organ and tissue damage

Page 33, Section 4, this section is predominantly statistical data without accompanying discussion to put it into context or relevance with the new draft revised Guidelines.

4. Specific comments

4.1 Actual guidelines

4.1.1 Guideline #1 Low-risk drinking for adults (page 39)

Current Guideline 1 To minimise risks in the short and longer term, and gain any longer-term benefits For men 1.1 an <i>average</i> of no more than 4 standard drinks a day, and no more than 28 standard drinks over a week; 1.2 not more than 6 standard drinks in any one day; 1.3 one or two alcohol-free days per week. For women 1.4 an <i>average</i> of no more than 2 standard drinks a day, and no more than 14 standard drinks over a week; 1.5 not more than 4 standard drinks in any one day; 1.6 one or two alcohol-free days per week.	Draft Guideline 1 For low risk of both immediate and long-term harm from drinking: <i>Men and women</i> 1.1 Two standard drinks or less in any one day.
--	---

The differences between the current Guideline #1 and draft Guideline #1 can be summarised as follows:

- No gender differentiation;
- No maximum amount per week;
- No maximum amount per occasional higher drinking days (binge drinking pattern);
- No maximum amount per hour (low risk drinking pattern); and
- No alcohol-free days per week.

There are six specific issues of concern with this draft guideline and two general issues.

4.1.1.1 No gender differentiation

It is noted that the draft revised Guidelines are based almost entirely on epidemiological evidence rather than pharmacological and physiological science, where risk has been calculated with a mathematical model to significantly increase after two standard drinks per day uniformly for both men and women. Above this level, for women the risk for cancer predominantly increases while for men the risk for accidents significantly increases. It is acknowledged and stated (on page 32, paragraph 1) that although detoxication is faster in men than in women where men can consume more alcohol before the risk of harm to their body's organs and tissues increases (as shown in Figure G1.3), men generally exhibit more risk-taking behaviour over a lifetime than women and hence sustain more immediate injuries (as shown in G1.2).

While gender differences in alcohol pharmacokinetics are cited in Section A, it should also be stated in the text to draft Guideline #1 that there are also physiological gender differences in body size and the distribution of fat and water, as well as in alcohol metabolism that determine that for a given amount of alcohol, the resultant BAC is greater in women than in men (Marshall et al. 1983, Tanaka 1999, Li et al. 2000, Baraona et al. 2001, Ramchandani et al. 2001). The maximal BAC may be approximately 10-16% greater in women compared to men. This is clearly shown in the tables and text of Taylor et al. 2007 (as alcohol consumption increases) and White et al. 2007.

In addition it should also be stated that women's organs and tissues are more susceptible to the toxic effects of alcohol and its metabolite, acetaldehyde (Saunders et al. 1981, The Gut Foundation 1984,

Gavaler 1982, Corti 1988, Mumenthaler et al. 1999) such that harmful effects of regular heavy drinking are observed earlier in women than in men and with increased severity than in men (Piazza et al. 1989, Randall et al. 1999, King et al. 2003, Hernandez-Avila et al. 2004). Women are, therefore, at greater risk than men for certain acute and chronic conditions (Fuchs et al. 1995, Bradley et al. 1998, Kamper-Jorgensen et al. 2004, Flensburg-Madsen et al. 2007), and hence women have greater mortality at lower levels of consumption than men (Holman et al. 1996, Rehm et al. 1998).

In addition, although several epidemiological studies also suggest that there is an increased risk of breast cancer for women with increasing alcohol consumption as stated on page 29, paragraph 3 (Tjonneland et al. 2007), the risk of breast cancer from alcohol consumption is additive with other risks such as: lifestyle; family history; medical history; nulliparity; endogenous/exogenous hormones (such as hormone replacement therapy); body mass index; and environmental exposure to carcinogens (Gapstur et al. 1992). It should also not be considered in isolation from the risk of other factors for mortality, such as cardiovascular disease, which is the primary cause of mortality in Australia. Thus, it may be advisable for women to enumerate and evaluate their risk factors for cardiovascular disease and for breast cancer before considering any abstinence from alcohol.

The results of the relatively recent Australian Longitudinal Study of Women's Health from 1996–2004 suggest, however, that the majority of Australian women consume alcohol at harmful levels sporadically during their life (50 g on one occasion or 140 g/week) and only a small percentage maintain this level of alcohol consumption over their life (Clemens et al. 2007). Less than 6% of any of the three cohorts was consuming alcohol at levels associated with long-term harm. Indeed, only 0.6% of the younger cohort, 0.9% of the mid-aged and 0.4% of the older-aged currently consumed alcohol at a level associated with long-term harm using the current Guidelines, while 2.5% of the younger cohort, 1.6% of the mid-aged and 0.6% of the older-aged currently consumed alcohol at a level associated with short-term harm using the current Guidelines.

4.1.1.2 No maximum amount per hour or per week

As discussed on page 13 of this Submission, in contrast to the current Guideline #1, the lack of advice on a maximum amount per week or maximum amount per hour provides no guidance as to appropriate drinking patterns to reduce risk of alcohol-related harm in the short or longer-term. Indeed, it is stated, however, on **page 9, paragraph 5** that “this edition...presents data that clearly show the level of risk associated with different patterns and levels of drinking”. **While the draft revised Guideline #1 does show the level of risk associated with a level of drinking, it does not show the level of risk associated with different drinking patterns.**

Gronbaek et al. (2004) observed that individuals with stable patterns of light and moderate alcohol intake had the lowest all-cause mortality, where individual changes in alcohol intake were followed by corresponding changes in mortality. It needs to be clearly stated in the draft revised Guidelines that regular moderate consumption has been observed to prolong any acute and short-term beneficial effects of alcohol and phenolic components on haemostasis (Renaud, Beswick et al. 1992; Hendriks, Veenstra et al. 1994) and also maintain or promote any long-term beneficial effects, including on blood pressure (Puddey, Beilin et al. 1985; Klatsky 1995), while regular **heavy alcohol** consumption is associated with long-term or chronic harms such as hepatic cirrhosis, haemorrhagic stroke, hypertension, pancreatitis and certain cancers (Becker et al. 1996, Gronbaek et al. 2004), while irregular or occasional risky consumption is associated with acute or short-term harms such as accidents and accompanying injuries.

4.1.1.3 No maximum amount per occasional higher drinking days

As discussed on page 9 of this Submission, the revised draft Guideline #1 does not consider a maximal amount per occasional drinking day, does not take into account the Australian drinking

culture, and hence does not provide a maximum limit to reduce or minimise harm on an “occasional heavy drinking day”.

4.1.1.4 Exclusion of health benefits from the mathematical modelling

As previously discussed on page 10 of this Submission, (cardiovascular) health benefits are assigned a relative risk value of 1 (on page 115 in Table A7.2), that is, no benefit or harm for drinking between 0 and three to four standard drinks/day. Indeed, the draft revised Guidelines actually accept benefits on page 44 and in Table G1.2, where the J-shaped curve goes to six standard drinks/day for ischaemic heart disease (Corrao et al. 1999). The exclusion is also contradictory and inconsistent with the statement on page 16, paragraph 3 of the draft revised Guidelines of benefits ensuing from a drink every second day.

The justification for this exclusion only relates to two recent studies and three recent papers — Fillmore et al. 2006 and 2007 and Harriss et al. 2007. It is beyond all reasonable doubt that there are cardiovascular and other health benefits as there is good biological evidence for these benefits. There is only doubt concerning the extent and depth of the J-shaped curve, again as previously discussed on page 11 of this Submission.

What is also not considered on pages 44 and 45 of the revised draft Guidelines are the other health benefits from moderate alcohol consumption which are also supported with sound biological evidence, for example, a reduced risk of non-coronary cardiovascular diseases (Mukamal 2007), diabetes mellitus (Perry et al. 1995, Rimm et al. 1995, Djousse et al. 2007), gallstones (Leitzman et al. 1998, Kono et al. 1992, 2002), age-related visual impairment (Obisesan et al. 1998, Hiratsuka and Li 2001), incident dementia and Alzheimer’s disease (Mukamal et al. 2003, Simons et al. 2006). Cognitive function has also been observed to improve (Zuccala et al. 2001, Stampfer et al. 2005). These benefits are briefly discussed and effectively disregarded on pages 99–103, although primarily in the context of the harms ensuing from heavy alcohol consumption. A reduced risk of hip fracture (Nelson et al. 1994, May et al. 1995, Nguyen et al. 1996, Mukamal et al. 2007) and rheumatoid arthritis (Voigt et al. 1994) may also be conferred at a moderate level of alcohol consumption.

Interestingly, the incidence of these diseases is greatest in aging populations. For example, cognitive dysfunction or impairment is associated with increased disability and an increased need for institutionalised care, especially in an ageing population. While cardiovascular disease accounted for 40% of all Australian deaths in 2000 and cancer accounted for 25–30%, 6% of the Australian population aged 65 years and over were diagnosed with dementia. Dementia is a form of cognitive dysfunction whereby an individual loses the ability to think, remember and reason due to physical changes in the brain. Given the anticipated ageing of the Australian population over the next 50 years, for example, the median age of Australia’s population is projected to increase from 35.4 years in 2000 to 46.5 years in 2050 (ABS 2003), research on risk factors for these diseases is a national priority. Thus it would be pertinent that their reduced relative risk would be included in any mathematical modelling.

On **page 45, paragraph 3**, the draft revised Guidelines cite the Harriss et al. 2007 prospective cohort study as a reason, in addition to the Fillmore et al. 2006 and 2007 papers which were discussed on pages 11-12 of this Submission, for discounting and excluding health benefits in the mathematical modelling.

Harriss et al. 2007 state that the present study was carried out to investigate the relationship between usual daily alcohol intake, beverage type and drinking frequency on cardiovascular (CVD) and coronary heart disease (CHD) mortality, accounting for systematic misclassification of intake. The source was The Melbourne Collaborative Cohort Study, with mean follow up of 11.4 years. There

were a total of 38,200 volunteers (23,044 women) aged 40–69 years at baseline in 1990–1994. Exposure was self-reported alcohol intake using beverage-specific quantity–frequency questions (usual intake) and drinking diary for previous week. The results showed that compared with life-time abstinence, usual daily alcohol intake was associated with lower CVD and CHD mortality risk for women but not men. For women, the hazard ratio [HR (95% CI)] for CVD for those drinking > 20 g/day alcohol was 0.43 (0.19–0.95; *P* trend = 0.18), and for CHD, 0.19 (0.05–0.82; *P* trend = 0.24). Male former drinkers had over twice the mortality risk for CVD [HR = 2.58 (1.51–4.41)] and CHD [HR = 2.91 (1.59–5.33)]. Wine was the only beverage associated inversely with mortality for women. Compared with drinkers who consumed no alcohol in the week before baseline, drinking frequency was associated inversely with CVD and CHD mortality risk for men but not women. HR for men drinking 6–7 days/week was 0.49 (0.29–0.81; *P* trend = 0.02) for CVD, and 0.49 (0.26–0.92; *P* trend = 0.23) for CHD.

Harriss et al. conclude that 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. In summary, the study showed an inverse (‘protective’) association between larger amounts of alcohol and cardiovascular and coronary mortality among women but not among men, while more frequent drinking was protective against such deaths only for men.

There are some particular problems with this study that may limit any policy implications of the reported results, for example, the number of women consuming larger amounts of alcohol is inadequate for demonstrating differences between men and women in the association between alcohol and mortality. This study supports, however, many other studies that have shown that more frequent alcohol intake tends to be associated with lower CVD and CHD, but that such putative protection is negated by binge drinking. The lack of an inverse association between the amount of alcohol and CVD and CHD among men in this study could be because, unlike in women, there is no protection from alcohol in men (as suggested by the authors). It is, however, more likely related to an unhealthy pattern of drinking among men, that is, large amounts on few days per week or ‘binge drinking’. Thus this study adds little information on misclassification of alcohol intake and while Harriss et al. refer to a recent paper stating that ex-drinkers have often been included in the referent group, most recent prospective studies have, appropriately, used life-time abstainers as the referent group.

Detailed concerns are as follows:

- (1) Small numbers of CVD and CHD events among women. While the total number of female subjects is large, the numbers of fatal events from CVD and CHD in some categories of alcohol consumption were very small. For example, the authors state that women consuming >20 g/day of alcohol had about 60% fewer CVD deaths and about 80% fewer CHD deaths, but the numbers of events in these categories were only 7 and 2, respectively. Certainly, these are too few to be able to state that women have a different association than men between alcohol and mortality.
- (2) Small numbers of former drinkers. The statements about markedly increased risk among men who were former drinkers (while probably true) are also based on small numbers: among men who were “former drinkers,” there were 25 CVD deaths and 21 CHD deaths. For women, there were only 7 CVD deaths and 5 CHD deaths in this exposure category.
- (3) Lack of a clear trend for an association between alcohol and mortality. Among both men and women, there was no apparent pattern of effect (either a more favourable or a more adverse effect) with increasing amounts of alcohol, so their reporting of *p* for trend is not meaningful.

(4) Lack of data on “misclassification of intake.” While the title suggests that this paper accounts for misclassification of intake, the analyses on quantity are based on a single baseline assessment of intake, and do not take into account changes in alcohol intake over the 11 years of follow up. Hence, the ability to study one important aspect of misclassification of intake (i.e., that due to changes in drinking habits) is not possible. The authors state that they have evaluated misclassification of intake by separating ex-drinkers from never drinkers. However, while ex-drinkers and never drinkers were sometimes combined in older studies, most recent studies have separated these two groups as well.

(5) Frequency of drinking and mortality. For men, there was no reduction in CVD or CHD from the *amount* of alcohol consumed, but a clear and rather striking decrease in risk for more *frequent* drinking. (For frequency, in comparison with subjects reporting none during the previous week, subjects reporting consumption on 3-5 and 6-7 days per week had about 50% fewer deaths from both CVD and CHD.) This points out the importance of drinking *pattern*, with frequent intake of small amounts being associated with lower mortality. Unfortunately, while the authors adjusted for total intake in their presentation of drinking frequency, they do not provide a table of average total intake in each frequency category, which might have helped explain the differences according to amount and frequency, and the authors do not present data on “binge drinking” among their subjects.

4.1.1.5 Weights used for mathematical modelling

The average weights of 50 kg for women and 60 kg for men used in the mathematical modelling and calculations are not appropriate for the Australian population.

There is concern, from page 39, paragraph 6 of the draft revised Guidelines that the average body weight used in the mathematical calculations may be lower than that actually observed in Australia. For example, the draft revised Guidelines go on to state that “people with lower bodyweights, below 60 kg for men and 50 kg for women, should consider drinking less than the guideline level.”, that is, that the risk is less than 1 in 100 of an alcohol related event in a life-time based on an average weight of 50 kg for women and 60 kg per men. From data supplied in the 19th Australian Total Dietary Survey, the average body weight of an adult Australian male aged 25-34 years in 1995 was 82 kg and that of a female was 66 kg (NNS 1995) for ages 25–34 years. Given that the proportion of males with a BMI>25 has increased from 52% in 1995 to 62% in 2005, it is likely that the average weight has also increased (ABS 2004/05).

It is noted that the Australian Drinking Water Guidelines use an average adult weight of 70 kg consistent with developed countries such as Canada, but that the WHO figure is 60 kg to cater for lighter body weights in developing countries.

In principle, using greater average body weights for men and women in the calculations would revise the harm levels. If the relationship between body mass and alcohol is linear then it would be a simple calculation to make a revised level, but if the relationship is non-linear we would need to know what the exact relationship is. If the relationship between body mass and alcohol is linear, for example, then the calculated risk levels in this draft revised Guidelines are in error by approximately 17% (10/60), which is potentially statistically significant.

Furthermore, body mass index is a better indicator of BAC than body weight.

The mathematical modelling and calculations also did not consider age differences in alcohol pharmacokinetics. For example, for comparable amount of alcohol consumed, older people (aged 65 years and over) will have a higher maximum BAC than younger people as they have less body water into which the alcohol distributes (approximately 51:61% for men and 52:46% for women).

4.1.1.6 Bias of emergency room data

The immediate risk of non-fatal accidents and injuries (page 41, 1(a)) used in the mathematical modelling is based on accident and emergency data. Accident and emergency data is from a non-representative population, generally of lower socio-economic status, younger-aged (Roche et al. 2001, Nordqvist et al. 2006, Nielsen et al 2007), associated with different drinking patterns such as heavy episodic or binge with prior alcohol-related problems (Roche et al. 2001, WHO 2007) and polydrug use, and aggregated around different events such as violent and even criminal events (Cheripitel 1996, D'Onofrio and Degutis 2004, Cheripitel 2007). For example, the likelihood of injury has been found to increase dramatically for individuals pursuing heavy episodic drinking patterns at least three times a year compared to those who never pursue this pattern (Cheripitel et al., 1995).

This non-representative population is highlighted in an 8-year longitudinal cohort study of emergency department patients conducted in the USA, over half (58%) of all injured patients had a documented arrest history, and arrests were significantly more common in those who came back to the emergency department for repeat trauma versus those who did not revisit the emergency department (70.4% vs. 55.9%, respectively; $p < 0.05$). In this sample, 21% (34/161) had been convicted of 97 property-related crimes, 26% (42/161) of 109 violence-related crimes, 23% (37/161) of 98 drug-related offenses, and 17.4% (28/161) of 89 other non-traffic-related crimes. Emergency department recidivism for trauma care was thus associated with multiple substance abuse behaviours and drug-related arrests.

Also D'Onofrio and Degutis (2004) observed that attendance in emergency departments was inversely associated with age, such that these young adult patients have the highest prevalence of binges in the USA (SAMHSA 2003), which can easily escalate to drinking patterns that require intervention. This statistic is mirrored in Australia (AIHW 2004). In addition, particularly in young adults, these drinking patterns often occur in conjunction with driving, where according to the 2001 National Household Survey on Drug Abuse (2003), 3 million people aged 16–20 years had driven under the influence of alcohol at least once in the past year. Motor vehicle crashes are the number one cause of death in people aged one–35 years, and the eighth leading cause of death overall (CDC 2004). Again this statistic is mirrored in Australia (personal communication 2007, Motor Vehicle Commission).

A Swedish study of 2782 patients aged 18–70 years registered for an injury at a Swedish emergency department during an 18-month period, also showed that the proportion of risky drinkers was higher in the study population compared with the general population in the same area, and were disproportionately represented by young men episodically consuming heavy amounts of alcohol; there were few significant associations between drinking pattern and injury remained when age and sex were controlled for (Nordqvist et al. 2006).

Furthermore, this non-representative population presenting at Australian emergency departments is highlighted by a pilot study by Roche et al. 2001. Of the 402 injury presentations in the study period, a total of 236 injury cases were interviewed, of whom 45% and 29% of male and females, respectively, had consumed alcohol 6 and 24 hours prior to injury. The mean age for all injury presentations was 35.1 years, and 32.6 years, respectively, for alcohol injury cases. For both injury groups, males were significantly younger than females. Recent alcohol ingestion was three times more common among male than female injury presentations, and with females drinking at significantly lower levels. Of males who had consumed alcohol 6 hours prior to injury, nearly 70% were drinking at NHMRC harmful levels and 61% had drunk more than eight standard drinks.

Overall, alcohol-involved injury cases commonly occurred among low-income, single males around 30 years of age who were regular heavy drinkers who were drinking heavily in licensed

premises prior to their injury, and who sustained injury through intentional harm. In addition, one in five of the alcohol-involved injury cases were aged 15-18 years, that is, below the legal age of purchase. Among those who had consumed alcohol within the last 6 hours, and the injury sample overall, there were a high proportion of hazardous and harmful drinkers.

Young Australians 12-24 years currently account for only 18% of the Australia population (23% of these were aged between 12 and 14 years, 38% were aged 15–19 years and 39% were aged 20-24 years) (AIHW 2007), where illicit drugs (12%) and alcohol (11%) were the largest contributors to their disease burden.

While the draft revised Guidelines acknowledge this on page 46, paragraph 2 by stating that “basing these estimates on emergency room studies may have led to an over-estimate 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...”, the mathematical modelling undertaken does not take this non-representation into account and this simple caveat is not satisfactory.

Furthermore, it is questioned as to whether it is methodologically valid to integrate and model immediate risk accident and emergency data (as shown in Figure G1.2), together with long-term or chronic alcohol-related diseases such as cancer and liver cirrhosis (as shown in Figure G1.3), which is a mixture of consumption pathology and risk-taking behaviour, with different aetiology. As Rehm et al. (2007) recognised, there are systematic differences in assessment between alcohol and medical epidemiological studies (King et al., 1994).

4.1.1.7 General issues with drafting

- On page 45 paragraphs 1 and 4, the White et al. 2007 reference cited should actually be White et al. 2002. This reference is also incorrectly cited on page 109 in Table A4.2 and on page 55.
- On page 45 paragraph 4 refers to Appendix 8, Table A8.1 – there is no Appendix 8 in the draft revised Guidelines and does correlate with tables in any other appendices. This reference is also incorrectly cited on page 55.

4.1.1.8 Critique of publication White et al. 2002

The White et al 2002 paper cited on pages 45 and 55, matches aggregate mortality data with aggregate data on alcohol consumption, by gender and age, but we can only infer any causal link since the data are aggregate, not individual.

This paper has some age specific findings, which are not translated into the risk guidelines. The logic of these findings is that there should be different risk levels not just by gender but by age group as well. Logically, as this paper shows, risks vary significantly by age and not just by gender. If risk levels are broken down by gender, then why not age as well in the risk guidelines?

One issue, of course, in how these findings, which are based on data from England and Wales in 1997, translate to Australia in 2007. That is especially the case given the large non-English speaking (and therefore non-Anglo) minority within the population.

The authors of this paper also point to the ‘averages’ problem in such an analysis, that is, the risks are based on average probabilities.

Furthermore, this paper does not take into account a reduced risk of cardiovascular disease from moderate consumption.

4.1.2 Guideline 2 Special precautions for children and young people under 18 years of age (page 50)

<p>Current Guideline 9 Young adults (aged about 18–25 years)* 9.1 are especially urged not to drink beyond the levels set in Guideline 1; 9.2 should not drink at all for at least several hours before undertaking potentially risky activities (eg driving, swimming, boating); 9.3 should not mix alcohol with other mood altering drugs. * While this guideline applies to people aged about 18–25 years, the issues and concerns overlap with those covered under Guideline 10, ‘Young People’.</p>	<p>Draft 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 - 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).</p>
<p>Current Guideline 10 Young people (up to about 18 years)* 10.1 should follow the recommendations under Guideline 9; AND 10.2 if they choose not to drink, should be supported in this decision; 10.3 in settings where alcohol is available to them, should be supervised by adults at all times; 10.4 should keep any drinking to a minimum; 10.5 most importantly, should not drink to become intoxicated; 10.6 to become responsible adult drinkers, a gradual, supervised introduction to alcohol is recommended. * While this guideline applies young people up to about 18 years of age, the issues and concerns overlap with those covered under Guideline 9, ‘Young Adults’.</p>	<p>Draft 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).</p>

The differences between the current Guidelines 9 and 10 and draft Guideline #2 and Additional health advice #2 can be summarised as follows:

- drinking should be kept to a minimum versus not drinking is considered to be the safest option
- urged not to drink beyond the levels set in Guideline #1 versus if drinking occurs it should be kept to within the levels set in Guideline #1

There are two general concerns with drafting and a reference of the rationale.

The risk of mortality and morbidity from accidents, including motor vehicle accidents, drowning and suicide, increases with any amount of consumption. The available data suggest that this risk is greatest for young adults aged 18–24 years who regularly consume alcohol above moderate amounts (Britton et al. 2003; Klatsky and Armstrong 1993; Wells and MacDonald 1999). Binge drinking (more than five to six drinks on an occasion) is a common and hazardous pattern of drinking in this age group, irrespective of ethnicity. In 1995, while approximately two-thirds of Australian consumers drank alcohol at a harmful level on one occasion in the past year, generally their consumption could

be classified as low risk (McAllister 1995; Single and Rohl 1997), but the converse was observed for young adults. In 1998, alcohol consumption that was risky for either acute or chronic harm was found to comprise 93% of all alcohol consumption for young men aged 18–24 years compared to 67% for men per se (Stockwell et al. 2002). Cardioprotection is not considered relevant for young adults, as the risk of mortality and morbidity from accidents predominates (Single et al. 1999). This is succinctly stated in the *Dietary Guidelines for Americans* and the *Canadian Low-Risk Drinking Guidelines*¹²

Although the World Health Organization has not defined what moderation is for young adults in its *Global Status Report: Alcohol and Young People* (2001), certain countries have definitions. The New Zealand guidelines recommend that young adults should simply drink alcohol in amounts “less than moderation,” while the Australian guidelines recommend that young adults should not drink more than the recommended 40 and 20 g of ethanol/day for men and women, respectively, nor should alcohol be mixed with other mood-altering drugs. The latter guidelines also recommend that young adults should not drink immediately prior to undertaking risky activities such as boating, driving or swimming. Interestingly, the Israeli guidelines recommend that “students” should not drink more than one standard drink per drinking occasion.

Australia is the only country to include recommendations for consumption of alcohol by adolescents aged under 15 years. This inclusion in the current Guidelines was in response to the 2001 National Drug Strategy Household Survey which showed that Australian children as young as 14 years of age consumed alcohol on a daily and weekly basis (AIHW 2002). Indeed, in 2004, 25% of Australian 14- to 19-year-olds reported drinking alcohol on either a daily or weekly basis during the past 12 months, compared with 50% of the general population 14 years and over (Australian Bureau of Statistics 2006). In the Australian Secondary Students’ Alcohol and Drug Survey in 2005, 47% of 16- to 17-year-olds described themselves as current drinkers, that is, they had consumed alcohol in the week prior to the survey, and 22% of 12- to 15-year-olds described themselves as current drinkers (White and Hayman 2006).

The Australian Temperament Project, which analysed adolescent and young adult alcohol consumption to identify early predictors and later consequences of different drinking patterns, observed that moderate alcohol consumption in adolescence does not protect young adults from harmful alcohol consumption patterns in the future, while abstinence from alcohol during adolescence may protect against future harmful alcohol consumption (Waters 2005).

The underage consumption of alcohol is increasing in developed and developing countries (Swedish Council for Information on Alcohol and Other Drugs 2000). There may be a correlation between the age of commencing alcohol consumption and the risk of alcohol-related problems (Grant and Dawson 1997; Grant et al. 2001; Hibell et al. 2004).

Most countries, however, shy away from discussing childhood or underage consumption and do not include recommendations for underage drinking in their guidelines. Indeed, it is often stated that their guidelines apply only to people of legal drinking age who can publicly purchase, possess and consume alcohol, such as in the U.S.A., where the legal age is 21 years. The Danish, Italian, Norwegian, Swiss and U.S. guidelines simply state that adolescents or children under the age of 15

¹ <http://www.health.gov/dietaryguidelines/dga2005/document/pdf/DGA2005.pdf>

² http://www.camh.net/About_Addiction_Mental_Health/Drug_and_Addiction_Information/low_risk_drinking_guidelines.html

years should not drink alcohol, while the Swedish guidelines state that children should grow up in an alcohol-free environment (Ministry of Health and Social Affairs 2002).

The UK guidelines state that if alcohol is consumed underage then it should be in an appropriate amount for the age group with reference to their physical development, as body size and stage of physical development determine blood alcohol concentration. Culture, however, influences the acceptable age for alcohol consumption within a country or cultural group; certain Mediterranean countries introduce children to alcohol, albeit diluted, in early childhood (Engels and Knibbe 2000). For example, the Luxembourg guidelines advocate that children and adolescents younger than 16 years of age should drink only moderately, without specifying daily or weekly amounts.

4.1.2.1 General issues with drafting

- On page 55 paragraph 4, the White et al. 2007 reference cited should actually be White et al. 2002.
- On page 55 paragraph 4 refers to Appendix 8, Table A8.1 – there is no Appendix 8 in the draft revised Guidelines and does correlate with tables in any other appendices.

4.1.2.2 Critique of unpublished and hence non-peer reviewed publication Room and Livingston 2007

This paper, which is cited on page 54 of the draft revised Guideline, is not a scholarly paper. It is a short note to accompany the draft revised Guidelines for the working committee, and as such should not be used to derive any scientific evidence. The paper is based on the 2004 NDSHS and the 2003-04 Victorian surveys. It relates consumption to self-reported harm, measured as the number of problems mentioned as a result of alcohol use. The main disadvantages of these surveys also apply to the analyses such as sampling, reliability and validity of the questions, and self-reports.

The paper does not calculate standard errors in the estimates, and this is a problem because the sample sizes in some of the categories (especially those aged under 18 years) are small. When the estimates are restricted to drinkers only, they are likely to be very small. The paper does not report on this, beyond the numbers in Table 1, which do not reflect the numbers in the particular age and risk categories.

4.1.3 Guideline 3 - Special precautions concerning pregnancy and breast feeding (page 57)

<p>Current Guideline 11 Women who are pregnant or might soon become pregnant 11.1 may consider not drinking at all; 11.2 most importantly, should never become intoxicated; 11.3 if they choose to drink, over a week, should have less than 7 standard drinks, AND, on any one day, no more than 2 standard drinks (spread over at least two hours); 11.4 should note that the risk is highest in the earlier stages of pregnancy, including the time from conception to the first missed period.</p>	<p>Draft Guideline 3 For women who are pregnant, are planning a pregnancy or are breastfeeding 3.1 Not drinking is the safest option.</p>
---	---

The differences between the current Guideline #1 and draft Guideline #3 can be summarised as follows:

- No information regarding intoxication
- No information regarding maximum limits if pregnant women chose to drink
- No information about the trimesters of pregnancy and potential risk of harm to the developing fetus from alcohol consumption

It is considered that the draft Guideline #3 is too simple and non-specific to be effective and useful guidance for pregnant women, to enable them to make informed decisions concerning their alcohol consumption during pregnancy and during lactation to at least reduce their consumption if not to abstain completely.

4.1.3.1 Alcohol consumption in Australian women during pregnancy

A recent study of alcohol consumption during pregnancy in non-indigenous West Australian women, suggests that while 79.8% of women reported consuming alcohol in the three months before pregnancy, 58.7% drank alcohol in at least one trimester of pregnancy (Colvin et al. 2007). This was despite receiving advice to abstain. Interestingly, the proportion of women consuming one to two drinks on a typical occasion did not change significantly during pregnancy, but the number of occasions declined. Although the proportion of women consuming more than two standard drinks on a typical occasion declined after the first trimester, 19.0% of women consumed this amount in at least one trimester of pregnancy and 4.3% of women consumed five or more standard drinks on a typical occasion in at least one trimester of pregnancy. In the first trimester of pregnancy, however, 14.8% of women drank outside the current Australian guideline for alcohol consumption in pregnancy, although this percentage decreased to 10% in the second and third trimesters. It is the first trimester of pregnancy in particular, where there is highest risk of alcohol-related harm to the developing foetus, which is stated in the current Guidelines. The West Australian population of women can be considered to be representative of the population of women in the other Australian States and Territories.

Another similar study undertaken in Perth women suggests while 67.3% of women reported consuming alcohol before pregnancy, 32% of these women ceased consuming alcohol during

pregnancy, although the remaining 48% of these women consumed alcohol during pregnancy, with 82.2% of these women consuming up to two standard drinks per week. At 4, 6 and 12 months postpartum, 46.7%, 47.4% and 42.3% of breastfeeding women were consuming alcohol, respectively, up to two standard drinks per week (Giglia and Binns 2007).

Another Australian study by Giglia and Binns (2007) also showed that there is a variable level of knowledge regarding consuming alcohol and breastfeeding among Australian mothers. While the majority of participants in the study were aware of the recommendations regarding alcohol during pregnancy they felt that a similar level of information was required to provide direction and support during lactation. The participants in the study were largely unaware of the effects of alcohol on breastfeeding performance and the development of the infant. The majority of the women in the focus groups also expressed concern at the lack of guidance available regarding 'safe' or 'low risk' alcohol consumption practices during lactation.

In summary, irrespective of advice to guidance to the contrary, approximately one half to two thirds of Australian women consume alcohol during their pregnancy. A low risk level should thus also be included in Guideline #3, to inform pregnant women that if they do chose to consume alcohol, they should ensure that they consume below this level, as at above this level there is a significantly increased risk of alcohol-related harm to the developing foetus. In addition, advice should be included that alcohol consumption above this level during the first trimester of pregnancy presents the highest risk to the developing foetus. Encouragement to discuss the issue with their health professional should also be included.

4.1.3.2 Incidence of alcohol-related foetal abnormalities in Australia

The risk and incidence of alcohol-related foetal abnormalities needs to be put into perspective for the Australian population.

Although data on the birth prevalence of FAS in Australia are limited, they suggest that population rates are substantially lower than in North America, France and Sweden (Sampson et al. 1997, Chambers et al. 20005) However, the prevalence of FAS in Indigenous Australian children is much higher than for non-indigenous children (Bower et al. 2000, Harris and Bucens 2003, Elliott et al. 2005) in keeping with findings from other Indigenous populations (May et al. 1991, Burd and Moffatt 1994, Stratton et al. 1996, Sampson et al. 1997, Chambers et al. 2005).

Concerning the West Australian data on the incidence of FAS, approximately three quarters of these diagnoses occurred in Aboriginal children; the birth prevalence was 1.1/1000 live births compared with 0.02/1000 live births for non-Aboriginal children (Bower et al. 1994). Indeed, in 1994, it was postulated that the incidence of FAS in Australia was 1 to 2/1000 live births (Lipson 1994); this estimate was from unpublished obstetric hospital data. In 1995, from data collected for the National Drug Strategy, there were no hospital admissions assigned to FAS and thus an incidence could not be determined (English et al. 1995); this was also observed in other epidemiological studies (Gibson et al. 1983, Lumley et al. 1985, Bell and Lumley 1989, Walpole 1990).

Furthermore, these data estimate that the incidence of low birth weight resulting from excessive and heavy consumption of alcohol was extremely small, 0.4/1,000. In 2000, the incidence of FAS from the Births Defects Registry in WA with additional data from the Rural Pediatric Service (RPS) database was still 0.02/1,000 for non-Aboriginal children but had increased to 2.76/1,000 for Aboriginal children in WA (Bower et al. 2000). These figures reflect the low prevalence of excessive or heavy consumption of alcohol by non-indigenous women during pregnancy in Australia. For example, as previously stated, a recent study of alcohol consumption during pregnancy in non-indigenous West Australian women, suggests that while 79.8% of women reported consuming

alcohol in the three months before pregnancy, 58.7% drank alcohol in at least one trimester of pregnancy (Colvin et al. 2007) and only 4.3% of women consumed five or more standard drinks on a typical occasion in at least one trimester of pregnancy. The West Australian population of women can be considered to be representative of the population of women in the other Australian States and Territories.

4.1.3.3 Amount of alcohol and alcohol-related foetal abnormalities including FAS

Alcohol consumption by pregnant women is controversial and the available evidence continues to be conflicting as to whether any amount of alcohol harms the foetus (Maier and West 2001; O’Leary 2004), as alcohol readily crosses the placental barrier.

The consumption of heavy amounts of alcohol by pregnant women has unequivocally been associated with adverse effects on the developing foetus, although “a high level of alcohol intake alone generally does not result in a diagnosis of FAS (Day 1992)”. Indeed, the nutritional status of the mother, her ingestion of drugs including caffeine and nicotine, and her educational, ethnicity, genetic, marital, parity and socio-economic status contribute to the development of FAS (Aase 1981, Sokol et al. 1986, Michaelis and Michaelis 1994, Abel and Hannigan 1995, Jacobson et al. 1996).

Twelve countries have a guideline for alcohol consumption during pregnancy. Ten of these 12 are unanimous in stating that pregnant women or those planning pregnancy should abstain from alcohol. Abstinence is also recommended during breastfeeding, as alcohol readily crosses into breast milk. The U.K. guidelines of 1995, however, recommended that pregnant women or those planning pregnancy should reduce their alcohol consumption to no more than 8–16 grams of alcohol per week, based on a review and report by the Department of Health’s Expert Committee on Toxicology (1995) which concluded that consumption of 16 g of alcohol per day and above was associated with reduced birthweight, but there was no convincing evidence that 8–16 g of alcohol per week has any adverse effects on the developing foetus. A subsequent meta-analysis of approximately 20,000 exposed fetuses, determined there was no evidence that moderate consumption, as distinct from light consumption, does increase the risk of foetal abnormalities, where moderate consumption was defined as greater than two standard drinks of alcohol per week but less than two standard drinks per day in the first trimester (Polygenis et al. 1998).

While a recent review on the effects of low to moderate prenatal alcohol consumption (up to 83 g/week) on foetal and early infant development also concluded that there was no convincing evidence of adverse effects, methodological weaknesses in the reviewed research precluded the conclusion that alcohol consumption at any level is safe during pregnancy (Henderson et al. 2007).

The UK National Institute of Clinical Excellence, however, state that pregnant women can safely consume up to one and a half standard drinks per day after the first trimester. The recent UK guidelines of 2007³ consequently now recommend abstinence during pregnancy and advise against intoxication, but importantly also recommend that women who do choose to consume alcohol before and during pregnancy, should consume no more than 8–16 g of alcohol once or twice a week.

4.1.3.4 Relationship between alcohol consumption and other pregnancy outcomes

The relationship between alcohol consumption and other pregnancy outcomes apart from FAS appears controversial and uncertain, so it is difficult to draw any conclusion and give absolute advice, although a maximum daily amount and pattern to minimise risk should be advised. This must be

³ http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_074920

made clear in the text to Guideline #3 as the issue is complex. Accordingly, the text for each pregnancy outcome section should be summarised to clarify this.

For every paper that claims that any alcohol negatively influences a birth outcome, another paper refutes it, as exemplified in the draft Guideline in page 60, paragraph 2, where Kesmodel et al. (2001) observed an increased risk of preterm delivery with consumption of five or more alcoholic drinks per week at 16 weeks gestation and with consumption of more than one to two drinks per week at 30 weeks gestation but Albertsen (2004) did not with four drinks per week over the gestation period. An increased risk of preterm birth was also not observed by Parazzini et al. 2003, however, until more than three drinks on average per day were consumed.

Concerning low birth rate, while Covington et al. (2002) on page 60, paragraph 4, observed that more than 14 alcoholic drinks/week decreased birth weight and length, and lower weight at age seven years, O'Callaghan et al. (2003) did not observe this. Furthermore, Mariscal et al. (2005) observed that alcohol consumption of less than 6 g/day, actually decreased the risk for low birth weight but the risk was increased when more than 12 g/day of alcohol was consumed. The risk was decreased again when the 12 g/day was confined to weekends for non-cigarette smoking women. This also shows the confounding of cigarette smoking and the importance of influence of patterns of alcohol consumption.

Concerning spontaneous abortion, while Kesmodel et al. (2002) on page 60 paragraph 3, observed an increased in risk of spontaneous abortion when five or more alcoholic drinks/week were consumed in the first trimester, which was corroborated by Henrikse et al. (2005) but at 10 or more alcoholic drinks/week, but not by Maconochie et al. (2006).

Concerning neurobehaviour and cognition on page 61, O'Callaghan et al. (2007) did not observe any adverse attention, learning or cognition outcomes when less than one alcoholic drink/day was consumed but drinking more than this in late pregnancy and indeed binge drinking, was associated with an increased risk of overall learning difficulties. D'Onofrio et al. (2007), however, that polydrug use during pregnancy was a better indicator of behavioural and learning difficulties.

4.2 Additional advice and precautions

4.2.1 Additional health advice and precautions 1:

- **For situations where not drinking is the safest option (page 67)**

Current Guideline 2 When undertaking activities that involve risk or a degree of skill 2.1 to avoid the risk of harm to the drinker and others, do not drink alcohol before or during such activities.	Draft 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) - 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.
--	---

The differences between the current Guideline #2 and draft Additional health advice #1 can be summarised as follows:

- advice not to drink alcohol before or during such activities versus alcohol therefore should not be consumed before or during risky activities

There is one specific concern with the drafting. The draft revised Guideline provides specific examples of situations where drinking is not the safest option, such as taking part in or supervising risky activities and lists driving, flying, water and snow sports. It is recommended that specific examples are not listed. For example, the draft Additional health advice #1 is in conflict with the Federal and State Government's drink driving legislation because, as stated on page 28 paragraph 2, the blood alcohol limit for driving in Australia is 0.05% based on controlled studies of driving skills. The blood alcohol limit is not 'no alcohol'. Such a short list of 'risky activities' also does not capture all the potential risky activities.

Concerning page 67, paragraph 4, the definition of an average sized adult is important. In 1998, the average sized Australian adult male weighed 82 kg and the average sized Australian female 66 kg (NNS 1995). Given that in 2004/05 62% of Australian males and 45% of Australian females had a BMI greater than 25 (ABS 2006), whereas in 1995 the figures were 52% and 37%, respectively, it is anticipated that the average weight figures have correspondingly increased.

4.2.2 Additional health advice and precautions 2:

- For people who should be aware that they have an increased risk (page 70)

Young adults (page 70)

<p>Current Guideline 9 Young adults (aged about 18–25 years)* 9.1 are especially urged not to drink beyond the levels set in Guideline 1; 9.2 should not drink at all for at least several hours before undertaking potentially risky activities (eg driving, swimming, boating); 9.3 should not mix alcohol with other mood altering drugs. * While this guideline applies to people aged about 18–25 years, the issues and concerns overlap with those covered under Guideline 10, ‘Young People’.</p>	<p>Draft 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 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).</p>
--	--

The differences between the current Guideline #9 and draft Additional health advice #2 can be summarised as follows:

- Advice not to drink beyond the levels set in Guideline 1 versus should be aware that they have an increased risk

It should be noted that the text in this section is repetitive to Guideline #2 pages 50–55. Also, on page 71, paragraph 5, moderate consumption may confer a modicum of cardioprotection for younger adults (Power et al. 1998; Thadhani et al. 2002), but is not generally considered relevant for young adults, as the risk of mortality and morbidity from accidents predominates (Single et al. 1999).

Older people (page 72)

Current Guideline 8 Older people 8.1 are advised, if they drink, to consider drinking less than the levels set in Guideline 1.	Draft Additional health advice 2 For people who should be aware that they have an increased risk - Older people, who have a higher risk of falls and are more likely to be taking medication - 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.
--	--

The differences between the current Guideline #8 and draft Additional health advice #2 can be summarised as follows:

- advice to drink less than the levels set in Guideline 1 versus advice to be aware that drinking alcohol increases the risk of falls and injuries, as well as some chronic conditions.

It should be noted that concerning elderly populations, the relationship between alcohol consumption and mortality has been less well documented. Older adults are generally defined as persons aged 65 years or older. In 2000 they represented approximately 12% of the Australian populations (Kinsella and Velkoff 2001). Globally this population group is projected to nearly triple by 2050. Significant factors in life expectancy include gender, genetics, hygiene, diet, exercise and lifestyle. Older adults have an increased absolute risk of cardiovascular disease, and consequently the beneficial effects of moderate alcohol consumption may outweigh any harmful effects in this population group, in particular when coupled with a Mediterranean-style diet (Knoops et al. 2004; Trichopoulou and Critselis 2004), although it has also been postulated that any cardioprotective effect for cardiovascular disease may be negated by increased morbidity and mortality from other causes (Van de Water and Boshuizen 1995).

Two US cohort studies have shown that light to moderate alcohol consumption in men and women aged over 65 years may be associated with a reduced risk of all-cause mortality by 30–40%, a third study has shown no such association (Scherr *et al.* 1992, Brandt *et al.* 1993, Holbrook and Barrett-Connor 1993). The two former studies observed, however, significant differences in cognitive function or mental performance and greater bone density (which is major cause of disability), in addition to a reduced risk of mortality from cardiovascular disease. Moderate alcohol consumption has consequently also been shown to significantly lengthen survival, on average by 7.6 months for men aged 60–74 years of age and 2.7 months for women over 64 years of age when consuming 10–70 g of alcohol per week, although the risk of all-cause mortality did not increase with heavier consumption (Simons et al. 2000). Moderate alcohol consumption was also observed in the *Dubbo Study of the Elderly* which commenced in 1998/89, to decrease the risk of other ageing conditions such as loss of cognitive function and osteoporosis, although heavier consumption was observed to increase their risk (Simons et al. 1991, Simons *et al.* 1996, Simons et al. 2006).

There are certain caveats concerning a definition of moderate consumption for older adults, however. Because of a decrease in the body's total water content with ageing, a higher blood alcohol concentration is observed for a given amount of alcohol; simultaneously, neurological tolerances to

alcohol decrease. In addition, with increasing age comes increasing use of medications that may interact with alcohol and hence influence blood alcohol concentration and ensuing adverse effects. Furthermore, any alcohol consumption can exacerbate certain cardiovascular diseases such as hypertension and cardiac arrhythmias (National Institute on Alcohol Abuse and Alcoholism 1995; 1998). While 11 of the 33 reviewed guidelines include recommendations for adolescents and/or young adults, only the current Australian, German and Italian guidelines recommend that older adults should reduce their alcohol consumption to below the definition for moderate, but they do not necessarily advocate abstinence. Coincidentally, these guidelines are from countries that have relatively large ageing populations.

People with a history of alcohol dependence (Page 73)

Current Guideline 5 People with a relative* who has, or has had, a problem with alcohol 5.1 are advised to be careful about how much they drink; 5.2 should take particular care to have regular alcohol-free days (one or two days per week); 5.3 might consider not drinking at all. * first-degree relatives (parents, siblings) or second-degree relatives (grandparents, uncles, aunts, cousins).	Draft Additional health advice 2 For people who should be aware that they have an increased risk - 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.
---	---

The differences between the current Guideline #5 and draft Additional health advice #2 can be summarised as follows:

- No advice to have regular alcohol-free days versus should consider reducing their drinking below Guideline 1
- No advice to consider not drinking at all versus should consider reducing their drinking below Guideline 1

The accompanying text to the Additional health advice #2 has been over-simplified with no clear conclusions provided.

Until recently, medical science has attempted to apply linear models of cause and effect to diseases whose origins are polygenic or a consequence of complex gene-environment interactions. For example, separate models of alcohol dependence have been developed for the social, psychological, behavioural, genetic and biological aspects of dependence where the variance in predicting who will become an alcoholic has been attributed 50% to behavioural and social factors, and 50% to genetic and biological factors. Indeed, the risk of alcohol dependence varies by gender and culture, where genetics can determine the specific risk and protection factors for an ethnic group and an individual, which are based on variation in alcohol and acetaldehyde dehydrogenase alleles or variants, and the heritable and non-heritable co-morbid psychopathological factors, such as depression, risk-taking and stress.

Heredity studies have been undertaken to determine the genetic ‘liability’ for alcoholism, including studies of identical and non-identical twins, and adoption studies. From these studies there appear to be two types of alcoholics: primarily male with a 9-fold genetic risk; and both male and female with a lesser genetic risk, but a greater significant environmental influence leading to an earlier onset of alcoholism. It has been proposed that the difference between the two types is related to the inherited personalities, such that easily stressed individuals are more susceptible to alcoholism, in particular in a heavy drinking culture. It has also been proposed that alcoholism is a polygenetic disorder, that is, there are different genes affecting or influencing the frequency and quantity of alcohol consumed by an individual as well as the development of neuroadaptation or tolerance by an individual. From animal studies, the influence of the environment is apparent where adopted mice drink as do their adopted parents rather than their biological parents.

Indeed, studies in animal models and humans have identified both genetic and environmental factors contributing to alcohol consumption, such that this complex behavioural trait is influenced by multiple factors as follows:

1. Genetic factors specifically related to the pharmacology of alcohol;
2. Psychological factors; and
3. Socio-cultural factors

There are two primary biological or genetic factors that influence alcohol consumption behaviour and the development of alcoholism: alcohol metabolism and neuroadaptation. In the US population, for example, there is a three-fold variation in the rate of alcohol metabolism and hence elimination of alcohol from the body, which determines the level and hence duration of exposure of the body organs and tissues to alcohol. Of this variation, approximately 40–60% is directly attributable to genetics and the remainder to environmental influences, such as the concurrent consumption of food and/or other drugs.

An increased rate of alcohol metabolism confers a lower blood alcohol and/or acetaldehyde concentration and less toxicity to tissues and organs, while a decreased rate confers a higher blood alcohol and/or acetaldehyde concentration that can infer systemic cardiovascular and gastrointestinal adverse reactions, such as nausea, vomiting, headache, tachycardia, low blood pressure and facial flushing. Alcohol is metabolised primarily by the enzyme alcohol dehydrogenase (ADH) to acetaldehyde. Acetaldehyde is further metabolised by the enzyme acetaldehyde dehydrogenase (AIDH) to acetate. There are genetic variants of ADH and AIDH, which are more or less active at metabolising; less active genetic variants result in an inability to metabolise alcohol or acetaldehyde and hence a high blood alcohol or acetaldehyde concentration results and remains until the secondary metabolic pathway is induced. Asian populations, such as the Chinese and Japanese, inherit primarily the active ADH2 variant whereby alcohol is rapidly converted to acetaldehyde, but they also primarily inherit the inactive AIDH2₂ gene whereby the toxic acetaldehyde is not further converted to acetate, and accumulates in the blood and tissues. A systemic adverse reaction ensues that generally discourages excessive consumption and effectively protects these individuals against the development of alcoholism. The protection is relative rather than absolute, however, as the adverse effects can be overcome with a significantly slowed drinking pattern.

Neuroadaptation or tolerance to the aversive behaviourally-impairing effects of ethanol on the central nervous system and on motor function develops with chronic or repeated drinking and enables heavier and excessive consumption; the aversive effects generally discourage excessive consumption. Continued excessive consumption is, however, encouraged by a relative insensitivity, also genetically predisposed, to the aversive systemic cardiovascular and gastrointestinal effects of a high blood concentration of alcohol and acetaldehyde, and to those of the central nervous system and motor function.

The psychological factors contributing to consumption behaviour include an expectancy of pleasurable effects such as social stimulation and dis-inhibition, that is, positive reinforcing effects which occur at a low to moderate level of alcohol consumption. Conversely, expectancy of aversive effects such as loss of central nervous system and motor skills, that is, negative reinforcing effects which occur at higher levels of alcohol consumption, generally discourages excessive consumption and potentially promotes abstinence.

The socio-cultural factors contributing to consumption behaviour include ethnicity, family, peers and religion.

Thus some people drink alcohol but others do not, some people drink more alcohol than others and some people drink alcohol despite negative consequences. These differences in alcohol consumption behaviour reflect both different kinds of environmental conditions and different genetic profiles.

Continued excessive alcohol consumption leads to alcoholism, or a physical dependence on alcohol. The rate of alcoholism is approximately five-times higher in families of alcoholics than in the general population, which is currently the best predictor of the development of alcoholism for an individual. If the influence of family environment is removed, however, the rate of alcoholism is approximately three-times higher in the adopted-out sons and daughters of alcoholics than those of non-alcoholics, whereby a low level of response to alcohol at age 20 years was associated with a four-fold greater likelihood of developing alcoholism.

4.2.3 Additional health advice and precautions 3:

- For people who should seek professional advice about drinking (page 74)

People with physical health problems that are made worse by alcohol (page 74)

<p>Current Guideline 4 People with a health or social problem that is related to alcohol, or made worse by alcohol (including alcohol dependence)</p> <p>4.1 should consider not drinking at all; 4.2 are strongly advised to stop drinking for at least several weeks or months; 4.3 might then try drinking at low levels (substantially below Guideline 1)* under professional supervision; 4.4 should not drink if they have developed severe alcohol dependence; 4.5 should never drink if they have a severe health problem made worse by alcohol (eg cirrhosis, pancreatitis); 4.6 if they have hepatitis C or other forms of chronic viral hepatitis, should consider drinking only infrequently and well below the levels recommended in Guideline 1. * The appropriate level will vary from person to person.</p>	<p>Draft Additional health advice 3 For people who should seek health professional advice if they are considering drinking</p> <p>- People with a physical condition 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.</p>
---	---

The differences between the current Guideline #4 and draft Additional health advice #3 can be summarised as follows:

- advice to consider not drinking at all versus should seek health professional advice if they are considering drinking, where in many instances, temporary or permanent abstinence may be necessary
- advice to stop drinking for at least several weeks or months versus should seek health professional advice if they are considering drinking, where in many instances, temporary or permanent abstinence may be necessary
- advice to subsequently try drinking at low levels below Guidelines #1 versus should seek health professional advice if they are considering drinking, where in many instances, temporary or permanent abstinence may be necessary

The advice provided in the draft Additional health advice #3 has been simplified and the onus placed on the patient and health professional.

People with mental health problems (page 74)

<p>Current Guideline 6 People with a mental health problem (including anxiety or depression) and/or sleep disturbance</p> <p>6.1 if they do drink, should take particular care to stay within the levels set in Guideline 1, and should consult with their doctor or pharmacist about possible side-effects;</p> <p>6.2 may need to consider not drinking at all, if they find it difficult to keep their drinking within these guideline levels;</p> <p>6.3 may need to stop drinking entirely if symptoms persist.</p>	<p>Draft Additional health advice 3 For people who should seek health professional advice if they are considering drinking</p> <p>- People with a mental health problem made worse by alcohol</p> <p>- 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.</p>
--	---

The differences between the current Guideline #6 and draft additional health advice #3 can be summarised as follows:

- should take particular care to stay within the levels set in Guideline 1, and should consult with their doctor or pharmacist about possible side-effects versus should discuss their alcohol intake with their health professional versus in many instances, temporary or permanent abstinence may be necessary, where carers can encourage people with a mental health problem to stay within guideline levels, or to abstain if necessary
- may need to consider not drinking at all, if they find it difficult to keep their drinking within these guideline levels versus in many instances, temporary or permanent abstinence may be necessary
- may need to stop drinking entirely if symptoms persist versus in many instances, temporary or permanent abstinence may be necessary

The advice provided in the draft Additional health advice #3 has been simplified and the onus placed on the patient and health professional.

People taking medications (page 76)

<p>Current Guideline 7 People taking medications or other drugs 7.1 should carefully read the labels and pamphlets with their medications (including herbal preparations), to check for harmful interactions with alcohol. Some people may need to reduce their drinking or stop drinking alcohol altogether; 7.2 are advised to be very cautious if drinking alcohol while using benzodiazepines, heroin, methadone or other central nervous system depressants; 7.3 if they are taking a number of medications, are at greater risk of increasing the effects of alcohol and/ or decreasing the effectiveness of their medication. These people may need to reduce or stop drinking alcohol; 7.4 should consult their doctor or a pharmacist to discuss any aspect of their medication, including possible interactions with alcohol.</p>	<p>Draft Additional health advice 3 For people who should seek health professional advice if they are considering drinking - People taking medications - Alcohol may interact with prescribed and over-the-counter medications and increase or reduce their effectiveness. - Alcohol may interact with illicit drugs, which can have dangerous or lethal consequences.</p>
---	--

The differences between the current Guideline #7 and draft Additional health advice #3 can be summarised as follows:

- people taking medications or other drugs should carefully read the labels and pamphlets with their medications (including herbal preparations), to check for harmful interactions with alcohol. Some people may need to reduce their drinking or stop drinking alcohol altogether versus people taking medications should seek health professional advice if they are considering drinking
- advice to be very cautious if drinking alcohol while using benzodiazepines, heroin, methadone or other central nervous system depressants versus alcohol may interact with prescribed and over-the-counter medications and increase or reduce their effectiveness, and alcohol may interact with illicit drugs, which can have dangerous or lethal consequences
- advice if they are taking a number of medications, are at greater risk of increasing the effects of alcohol and/ or decreasing the effectiveness of their medication. These people may need to reduce or stop drinking alcohol versus alcohol may interact with prescribed and over-the-counter medications and increase or reduce their effectiveness
- advice consult their doctor or a pharmacist to discuss any aspect of their medication, including possible interactions with alcohol versus advice to seek health professional advice if they are considering drinking

The advice provided in the draft Additional health advice #3 has been simplified and the onus placed on the patient and health professional. The text of the Additional health advice #3 has, however, been oversimplified, and advice should also be included on reducing or ceasing any alcohol consumption while on medication. The term “dangerous or lethal consequences” is meaningless and needs to be spelt out in simple terms such as “may lead to temporary or permanent disability or death”.

4.3 Appendices

4.3.1 Appendix 3 Comparison of international guidelines (page 82)

The appropriateness or relevance of the inclusion of other countries data in the Australian Alcohol Guidelines as a comparison is questioned. There is no discussion as to the appropriateness or relevance of this comparison and what it might mean for Australia and the Australian Alcohol Guidelines.

A comparison of world-wide standard drink definitions and guidelines on alcohol consumption reveals wide disparity among countries and widely differing views of what are regarded as appropriate or ‘safe’ maximum levels of alcohol consumption and associated consumption patterns. In some countries, and even within regions of a country, it is considered safe to consume more alcohol than in other countries and regions, sometimes two or three times as much. Some governments make recommendations for daily intakes, some weekly, and some both daily and weekly. For example, safe consumption for men lies between 27 and 50 g alcohol per day, and between 47 and 280 g per week (Harding and Stockley 2007). Most, but not all, governments make different recommendations for men and women, where a safe level of consumption for women approximates half of that considered to be safe for men. Only some governments, however, also take an individual’s age and body weight into account, or specify levels for individuals with certain medical conditions, as well as for pregnancy. In addition there is no consistency on the size of the standard drink between countries, which generally reflects differences in cultures and customs.

As the science is the same wherever alcohol is consumed, a more consistent guideline could be expected world-wide. There are five factors, however, that are taken into account by governments when setting guidelines such that there is no satisfactory single international guideline.

4.3.1.1 Science

The scientific evidence relating to both abusive and moderate alcohol consumption is itself not sufficiently consistent to produce precise recommendations for safe alcohol consumption. There is no clear scientific evidence that uniformly applies to all population groups. Indeed, the many factors influencing the definition of safe alcohol consumption for a specific population group include age, body mass index, ethnicity, family history, mental and physical health, and concomitant medications. Consequently, the definition will vary between population groups, between and within countries. Thus, governments will usually use simple messages and recommendations that apply to the majority general population rather than use complex ones for minority specific population groups. The recommendations of the Australian, Canadian and UK governments have evolved, however, to include definitions of safe alcohol consumption for specific population groups in addition to a basic generalised recommendation.

4.3.1.2 Culture

The science base for the health consequences of both alcohol abuse and moderate consumption is not the only criteria or factor that is considered by governments when producing such guidelines. Indeed, the purpose of recommendations is not to facilitate debate and discourse about the science but to facilitate a change in behaviour. Thus, it is important to take into account the prevailing drinking culture of a population, because only in that way is it possible to produce a public health message that is likely to be respected and regarded. Interestingly, from Tables included in the text those countries with a more Mediterranean-style diet, lifestyle and consumption pattern such as drinking wine with daily meals, appear to have higher recommended maximum levels for alcohol consumption than do other countries, especially those with a culture of binge beer and spirits drinking (Bloomfield et al. 2003). Distinctions between countries’ consumption patterns are declining, however, as beverage

preferences have begun to homogenise globally (Bloomfield et al.2003) as seen in a trend towards binge drinking and intoxication among young adults irrespective of country (Britton et al. 2003).

4.3.1.3 Economics and terms of reference

While the specific population group being targeted by recommendations may differ, generally most governments are principally concerned with reducing the economic, health and social consequences of alcohol misuse *per se*, and their recommendations are aimed at the population groups who are misusing alcohol or who have a drinking culture that is likely to lead to misuse.

4.3.1.4 Target audience

An additional layer of complexity is the intended audience of the guidelines, for example, in Australia they were written for general population in addition to health professionals and policymakers while the Canadian guidelines were written primarily for health promotion in the general population and are specifically intended to assist physicians in providing appropriate advice to patients. Furthermore, the UK guidelines have acted as a review of medical evidence on alcohol consumption in order to develop policies on alcohol consumption that foster responsible non-abusive behaviour. In contrast, the US guidelines serve as authoritative advice for the general population about how good dietary habits can promote health and reduce risk for major chronic diseases, and also serve as the basis for Federal food and nutrition education programs.

4.3.1.5 Ministerial approval

Finally, government guidelines may have to be approved or endorsed by groups of government ministers before they can be implemented and this adds a further source of variability, as inevitably political judgement is involved.

In the light of these five factors, therefore, it is likely, if not inevitable, that governments will produce guidelines that are first, not the same, and second, differ markedly in their nature.

4.3.2 Appendix 4 Risk of alcohol-related accidents, injuries and other short-term harms: evidence details (page 90)

The text on page 90 under the heading Cognitive performance, is similar to the text of Additional health advice and precautions #1: For situations where not drinking is the safest option: Taking part in, or supervising, risky activities on pages 67 and 68 of the draft revised Guideline. Please see previous comments on page 35 of this Submission. Thus the text on page 90 on should either be expanded or summarised.

4.3.3 Appendix 5 Risk of alcohol-related disease: evidence details (page 99)

There is concern with the quality and hence relevance of the information included in this Appendix. Specific concerns are as follows for each section presented in the Appendix.

4.3.3.1 Diabetes and obesity

The relevance of discussion in the draft revised Guidelines regarding alcohol consumption, diabetes and obesity is poorly written, unclear and there is no real conclusion drawn.

Page 99, paragraph 4 of the draft revised Guidelines states “the relationship between alcohol consumption, insulin sensitivity, type 2 diabetes mellitus and the metabolic syndrome that clinically preceded it, is not clear” (Hulthre and Fagerberg 2005).

This is disputed.

The draft revised Guidelines go on to state “Whilst J- and U-shaped relationships have been seen in these populations and nondiabetic adult male and female populations (Ashley et al. 2000, Dixon et al. 20002, Moirya et al. 2003), linear associations with no clear upper limit have also been observed in non-diabetic subjects of all ages” (Kato et al. 2003).

Risk factors for cardiovascular disease include a high body mass index (BMI; being overweight or obese), a poor diet (including an excessive dietary intake of animal fats and salt) and lack of exercise, cigarette smoking, excessive alcohol consumption, a high and unbalanced blood cholesterol concentration and a high blood pressure, as well as genetic predisposition and certain diseases and disorders, such as diabetes mellitus (Hunter et al. 1995, Norrish et al. 1995, Wieslisbach et al. 1997). Another recently recognized risk factor is a high concentration of the amino acid, homocysteine, in plasma (Welsh et al. 1998).

In Australia, over 50% of men and women are overweight and 20% are actually obese, having a BMI greater than 30 kg/m². Blood fat disturbance in combination with high blood pressure and type 2 diabetes often occur together in susceptible individuals, and is referred to as the ‘metabolic syndrome’ (Reaven 1993). The blood fat disturbance relates to being overweight or obese, especially in individuals who store their fat in the abdominal area. An excess of toxic free fatty acids in the blood stream may cause or contribute to the insulin sensitivity and impaired insulin function observed with this syndrome, which generally eventually develops into type 2 diabetes.

Another potential beneficial health effect of alcohol is the improvement of insulin sensitivity, possibly by reducing the concentration of free fatty acids in blood (Avogaro et al. 2002). In turn, the improved insulin sensitivity lowers the concentration of insulin, glucose and triglycerides in the blood, and increases that of HDL. Additionally, LDL particles become less dense, less adherent and less easily oxidized. Altogether, this reduces the risk of developing type 2 diabetes, as well as improving control of blood glucose and reducing the risk of cardiovascular disease in type 2 diabetics, who have a greater risk of cardiovascular disease compared with healthy individuals (Ajani et al. 2000a, Solomon et al. 2000). Indeed, epidemiological studies suggest that regular and moderate alcohol consumption significantly reduces the risk of developing type 2 diabetes (Ajani et al. 2000b, Hu et al. 2001). The American Diabetes Association now advises that moderate alcohol consumption by type 2 diabetics should not be routinely discouraged (Solomon et al. 2000).

The American Heart Association recommends that the concentration of homocysteine in plasma should be maintained below 10 µmol/L. Homocysteine is closely linked to the metabolism of the essential

amino acid, methionine. It has a direct toxic effect on the lining of blood vessels that alters their function (Bellamy et al. 1998) and leads to key early steps in the atherogenic process. Three micronutrients are important cofactors in homocysteine metabolism. Folate and vitamin B12 are cofactors for the methylation of homocysteine to methionine, and vitamin B6 is involved in its breakdown. Deficiency of any of these micronutrients leads to a higher concentration of homocysteine and increased risk. It has recently been proposed that the presence of folate and vitamin B6 in beer may lead to a beverage-specific advantage through lowering of homocysteine concentration (van der Gaag et al. 2000). While high or abusive alcohol consumption is associated with an increased plasma concentration of homocysteine (Cravo et al. 1996, Bleich et al. 2001), the effect of low to moderate consumption on the concentration of homocysteine has been inconsistent (Ayaori et al. 2000, Cuevas et al. 2000).

The severely obese (BMI >35 kg/m²) are at increased risk of type 2 diabetes, cardiovascular morbidity and mortality. In a study of 486 severely obese subjects, their pattern of alcohol consumption was monitored and their risk of cardiovascular disease determined. Alcohol consumers showed a marked reduction in the prevalence of type 2 diabetes compared with non-consumers. A U-shaped relationship was observed between both the amount and frequency of alcohol consumption and the plasma concentration of fasting triglyceride, fasting glucose, glycosylated haemoglobin A1c and insulin measurements. In this group, comprising predominantly women consumers of less than 100 g/week had more favorable insulin measures, with insulin sensitivity best in those consuming 20 to 100 g of alcohol/week, that is, two to 10 standard drinks/week, which is considered to be light alcohol consumption. Of the alcohol consumers, 165 nominated wine and 111 spirits or beer as the alcoholic beverage most frequently drunk. Wine consumers had a significantly lower fasting insulin level and improved insulin sensitivity.

These patients went on to have a laparoscopic adjustable gastric band placed to help them lose weight. Those patients consuming more than 100 g/week of alcohol, especially wine, had significantly better weight loss than those with nil or negligible consumption. Those consuming 20 to 100 g/week had an intermediate outcome. These results demonstrate that light to moderate alcohol consumption, especially wine consumption, is associated with a lower prevalence of type 2 diabetes, improved insulin sensitivity and more favorable cardiovascular risk profile in the severely obese (Dixon et al. 2002).

The same 416 severely obese patients were also studied for any relationship between both the amount and type of alcohol consumption and concentration of fasting plasma homocysteine. A U-shaped relationship was observed whereby light to moderate alcohol consumption was associated with a lower and more favorable plasma concentration of homocysteine. Those patients consuming up to 100 g/week of alcohol had a significantly lower homocysteine concentration compared with non-consumers. The lower concentration of homocysteine in regular alcohol consumers was associated with a higher concentration of folate. Red wine consumers had a significantly lower mean fasting concentration of homocysteine compared with non-consumers, beer and spirit consumers and white wine consumers. Red wine consumption was an independent predictor for a lower plasma concentration of homocysteine after controlling for sex, age, and weight, and plasma concentration of folate and vitamin B12.

The mechanisms for the beneficial effect of red wine are unclear. The concentration of micronutrients are unlikely to provide the answer as it has been observed that the effect of red wine is independent of the plasma concentration of folate and vitamin B12, and red wine contains negligible quantities of vitamin B6 (van der Gaag et al 2000). An alteration in the relationship between the concentration of homocysteine concentration, and that of folate and vitamin B12 has been observed as people lose weight (Dixon et al. 2001). A higher plasma concentration of folate and vitamin B12 is needed to maintain the concentration of homocysteine as weight is lost. It may be postulated that the phenolic

compounds alter the dose-response curve in the other direction with a lower plasma concentration of homocysteine achieved with an equivalent micronutrient concentration.

In conclusion, these studies of obese patients show that those consuming alcohol regularly are far less likely to be diabetic, have significantly better insulin sensitivity and a healthier blood lipid profile, with a lower plasma concentration of triglyceride and a higher plasma concentration of HDL. In addition, red wine consumers have a significantly lower plasma concentration of homocysteine.

4.3.3.2 Vision

The draft revised Guidelines regarding alcohol consumption and vision is poorly written, unclear and there is no real conclusion drawn.

Concerning age-related visual impairment, errors in interpretation of the studies cited, and selected citations from these studies have been observed, for example:

Page 101, paragraph 2, the draft Guideline states “Alcohol has been associated with two important conditions of the eyes...The Blue Mountains eye Study reported that heavy drinking increases the risk of nuclear, cortical and posterior subcapsular cataracts (Hiratsuka and Li 2001).

Hiratsuka and Li (2001) also state “Moderate alcohol use, however, has been reported to be possibly protective against age-related macular degeneration, cataract and diabetic retinopathy.” As well as that “chronic alcoholism is associated with a significantly increased risk of cataract, keratitis, colour vision deficiencies and corneal arcus”.

Page 101, paragraph 2, the Blue Mountain Eye Study of 1997 paper is said to support the statement “heavy drinking increases the risk of nuclear, cortical and posterior sub capsular cataracts”. It does not. It actually states that “Alcohol consumption was associated with a reduced prevalence of cortical cataract: compared with people who did not drink, the adjusted OR for cortical cataract among people who drank at least one drink a day was 0.7 (95%CI, 0.6-0.9). Heavy alcohol consumption was associated with nuclear cataract in current smokers but not in never smokers”.

Page 101, paragraph 3, the cited Anarsson et al. (2006) study actually states that “We found current alcohol consumption to decrease the risk of drusen formation and to increase the risk of pigmentary abnormalities”.

Furthermore, other studies such as Smith and Mitchell (1996) found no evidence that alcohol is casually associated with age-related maculopathy, Ajani et al. (1999) found that alcohol intake was not appreciably associated with the risk of incident age-related maculopathy as did Knudtson et al. 2007, who found that alcohol consumption was unlikely to strongly increase or decrease the risk of age-related maculopathy as did Douglas et al. 2007. DeAngelis et al. (2004) only saw a nonsignificant association between mean lifetime alcohol consumption of alcohol and risk of age-related maculopathy while Fraser-Bell et al. (2006) found that heavy consumption of greater than five drinks per session was associated with a greater risk of age-related maculopathy, and Buch et al. (2005) (which was also cited and incorrectly interpreted in the draft revised Guidelines) found that excess alcohol consumption (>250 g per week or 25 standard drinks per week) to increase the risk of early age-related macular degeneration, where Klein et al. (2002) (which was also cited in the draft revised Guidelines) found that people who reported being heavy drinkers at baseline were more likely to develop late age-related macular degeneration (RR = 6.94, 95% CI: 1.85, 26.1) than people who reported never having been heavy drinkers.

Only Obisean et al. (1998) found that there was a statistically significant but negative association between age-related macular degeneration and alcohol consumption, where moderate wine consumption was actually associated with a decreased odds of developing the disease. In addition, Cho et al. (2000) (which was also cited in the draft revised Guidelines) actually states that “the pooled relative risks (RRs) and 95% confidence intervals (CIs) for age-related macular degeneration compared with nondrinkers were 1.0 (0.7-1.2) for drinkers who consumed 0.1 to 4.9 g/d of alcohol; 0.9 (0.6-1.4) for 5 to 14.9 g/d; 1.1 (0.7-1.7) for 15 to 29.9 g/d; and 1.3 (0.9-1.8) for 30 g/d or more. Among women, however, there was a suggestion of a modest increased risk of the disease in drinkers who consumed 30 g/d or more (RR, 1.5; 95% CI, 1.0-2.4); this was limited to an increased risk of the early and dry form (RR, 2.0; 95% CI, 1.2-3.4). No specific type of alcohol provided protection against age-related macular degeneration”.

4.3.3.3 The brain and cognitive function

Five paragraphs on **page 102** are devoted to brain structure and function, and of these, two are either completely or partially concerned with cognitive function, although the focus is on heavy alcohol consumption. The relevance of the discussion in the draft revised Guidelines regarding alcohol consumption and cognitive function is, however, unclear and there is no real conclusion drawn.

It has been suggested that there is also a J-shaped relationship between alcohol consumption and cognitive function. Cognitive dysfunction or impairment is associated with increased disability and an increased need for institutionalised care, especially in an ageing population. While cardiovascular disease accounted for 40% of all Australian deaths in 2000 and cancer accounted for 25–30%, 6% of the Australian population aged 65 years and over were diagnosed with dementia. Dementia is a form of cognitive dysfunction whereby an individual loses the ability to think, remember and reason due to physical changes in the brain. Given the anticipated ageing of the Australian population over the next 50 years, for example, the median age of Australia’s population is projected to increase from 35.4 years in 2000 to 46.5 years in 2050 (ABS 2003), research on risk factors for these diseases is a national priority.

Prior to a study by Zuccala et al. (2001), there was conflicting evidence on the relationship between alcohol consumption and cognitive function (Cervilla et al., 2000; Dent et al., 1997; Dufouil et al., 1997; Elias et al., 1999; Harwood et al., 1999; Hendrie et al., 1996; Leibovici et al., 1999; Teri et al., 1990). Zuccala et al. (2001) analyzed the association between alcohol consumption and cognitive impairment in 15,807 hospitalized older patients who were enrolled in an Italian multicentre pharmacoepidemiology survey. The probability of cognitive impairment was reduced among male patients who reported an average daily alcohol consumption of 1 L or less of wine, as compared with abstainers, but the probability increased among heavier drinkers. Among women, only the lightest-drinking category (<0.5 L) showed a decreased probability of cognitive dysfunction when compared with abstainers, whereas heavier drinking was associated with an increased probability of cognitive impairment. The prevalence of alcohol abuse was similar among participants with cognitive impairment (0.9%) and those with normal cognitive functioning (1%). The results of this study indicated that moderate alcohol consumption, that is, <40 g per day for women and <80 g for men, is associated with reduced probability of cognitive impairment as compared with abstinence, after adjusting for potential confounders. This nonlinear association persisted when cerebrovascular and Alzheimer’s disease were considered separately. Such a nonlinear association might explain the conflicting results of previous studies regarding the relationship between alcohol consumption and cognitive functioning.

The observed gender difference in amount of alcohol consumption necessary for improved cognitive function, confirms that observed by Elias et al. in 1999 who showed that ‘superior’ cognitive performance was found with in the range of four to eight drinks/day for men and two to four drinks/ day for women, compared to abstainers.

Subsequent studies have also independently assessed the association between alcohol consumption and cognitive function and have affirmed the observations of Zuccala et al. (2001) but have also provided more detailed data (Ganguli, et al. 2005, Stampfer et al. 2005, McDougall et al. 2006, Reid et al. 2006, Wright et al. 2006). For example, Reid et al. (2006) in a study of 760 US men aged 65 years or older showed that current light to moderate alcohol consumption considered as up to seven drinks per week, compared to abstinence, had better cognitive function. In particular, processing speed, which is the ability to perform tasks requiring rapid visual scanning and mental processing of information, was better even after adjusting for potential confounders such as education and occupation. In addition, the study assessed the effects of cumulative lifetime alcohol consumption on cognitive function and showed that the number of years of light to moderate alcohol consumption was strongly associated with better cognitive function. Results from a small survey study by McDougall et al. (2006) also suggested that men aged 65 years or older who drank moderately had significantly less depression, higher self-reported general health and higher cognitive function, flexibility and verbal memory.

Several studies had shown that the association between alcohol consumption and cognitive function is stronger for women than for men, which may simply reflect a gender difference in cognitive function or perhaps a misclassification of moderate alcohol consumers. Such a gender difference was not, however, observed by in a longitudinal study of 1624 Japanese American men and women aged over 65 years (Bond et al. 2005). Other studies which assessed women specifically, such as the US Nurses' Health Study, suggested that for women aged 71 to 80 years, up to 15 g alcohol per day did not impair cognitive function and actually improved it compared to abstinence (Stampfer et al. 2005); the women also had a decreased risk of cognitive impairment of approximately 20%. No significant differences were observed in cognitive performance or risk between beer and wine consumers. Furthermore, a study of women aged 65–80 years, showed that women consuming any alcohol performed better on tests of verbal knowledge, fluency and memory, and figural memory, attention and working memory and motor speed compared to abstainers ($P < 0.05$) (Espeland et al. 2006). After covariate adjustment, mean scores were higher among women reporting ≥ 1 drink/day by 5.7% for verbal knowledge ($p < 0.001$) and by 5.7% for phonemic fluency ($p = 0.004$), compared to abstainers.

The beneficial effects of alcohol on the risk of cardiovascular and cerebrovascular diseases, such as heart attacks and strokes, have been partly attributed to changes in lipid and haemostatic or blood flow factors (Rimm et al., 1999). These changes include alcohol-induced increases in the concentration of high density lipoprotein-cholesterol and the thrombolytic proteins tissue type plasminogen activator activity and tissue type plasminogen activator antigen, and alcohol-induced reductions in fibrinogen, and clotting cofactors factor VII and von Willebrand factor. These changes are also associated with atherosclerosis which is the accumulation of atheromatous plaques containing cholesterol and lipids on the innermost layer of the walls of large and medium-sized arteries.

As atherosclerosis has been associated with both Alzheimer's disease and vascular dementia, it had been suggested that any beneficial effect of alcohol on atherosclerosis could be expected to benefit these major subtypes of dementia by preserving brain vasculature, consequently resulting in better cognitive function. Wright et al. (2006), however, showed that the appearance of plaque on the carotid artery which carries blood to the brain was not associated with alcohol consumption and alcohol-associated improvements in cognitive function. This suggests then that alcohol may impact cognition through a separate vascular or degenerative pathway. Among older persons without cerebrovascular disease, those who moderately consume alcohol have been shown to have fewer white-matter abnormalities and infarcts on magnetic resonance imaging than abstainers (Mukamal et al. 2001), where pronounced reductions in the risk of both vascular dementia and Alzheimer's disease have been shown among persons consuming one to six standard drinks per week (Mukamal et al. 2003).

Indeed, there is also evidence which suggests that a light to moderate amount of alcohol may stimulate the release of acetylcholine in the hippocampus leading to improved cognitive function such that a light amount of alcohol in normal subjects appears to improve memory for events experienced before consumption where the impairment of memory performance by chronic and heavy alcohol consumption parallels the reduction of acetylcholine neurotransmission (Fadda and Rossetti 1998).

In conclusion, the protective effect of light to moderate alcohol consumption against cognitive dysfunction, including dementia (Simons et al. 2006), has been consistently observed over the past five years. Thus, while excessive alcohol consumption should be avoided, it would appear safe and reasonable to recommend the continuation of light to moderate alcohol consumption in those already imbibing.

4.3.4 Appendix 6 Lifetime risk of death from alcohol-related accidents and injuries (page 110)

There are concerns regarding the methodology in this Appendix as follows.

4.3.4.1.1 Comments on Rehm et al. 2007 unpublished, non-peer-reviewed paper

The Rehm et al. 2007 paper cited on pages 45 and 110, is a fairly straightforward analysis relating risk and injury to alcohol consumption using an alcohol attributable fraction (AAF), here injury is not a health-related risk per se. The only point of contention is the AAF, which is derived from an AIHW publication and a WHO publication.

4.3.4.1.2 Scientific basis and credibility of references used in Appendices 6 and 7

The conclusions drawn in Appendixes 6 and 7 are primarily based on mathematical modelling from three unpublished papers that have not been subjected to peer review previously, that are not readily accessible to the general public, as well as not cited in the reference list. In addition, as the White et al. 2002 paper shows, risks vary significantly by age and not just by gender, such that if risk levels are broken down by gender they should also be broken down by age. None of the papers also take into account health benefits from moderate alcohol consumption. Thus the scientific basis for revising the maximum limits of alcohol per day is poor.

Furthermore, the Borges et al. 2006 paper cited on page 111, was used to identify the injury risks corresponding to consumption of specific numbers of standard drinks from a WHO-sponsored study of hospital emergency rooms in 10 countries. These 10 countries are: Argentina, Belarus, Brazil, Canada, China, the Czech Republic, India, Mexico, Mozambique, New Zealand, South Africa and Sweden. These countries have considerably different population demographics and hence patterns of alcohol consumption and different risks of alcohol-related harm. For example, Rehm, Monteiro and colleagues (2001) ascribed to Argentina, Australia, Canada, the Czech Republic, New Zealand, Sweden and even South China (level 2), which implies that all these countries have a similar cultural consumption pattern for alcohol as might be anticipated from their similar population demographic, but a higher score was ascribed to South Africa (3), India and Mexico (4), which suggests that South Africa, India and Mexico would experience more alcohol-related harms compared to Australia and the other six countries at the same level of per capita consumption, due to its different cultural consumption pattern.

The study undertaken by Borges et al. (2006) compared heavy drinkers and chronic alcoholics from a single emergency room in each country, such that patients may not be representative of other facilities in each country and indeed, the population groups compared are not representative of the general population. Indeed, in a related paper by Cherpitel 2007 on the WHO-sponsored study of hospital emergency rooms in 10 countries, most countries in an effort to maximize identification of potential participants sampled patients only at times during which a high prevalence of drinking and/or injury among emergency room admissions was expected and hence was not even representative of general emergency room patients.

There were five other study limitations listed in the Borges et al. (2006) paper on page 457, including that all analyses were based on patients' reported alcohol consumption on two occasions one week apart. Over or under-estimation may result such that, as concluded in the paper, more research is required on the validity of methods for eliciting alcohol use in case-crossover analyses. Furthermore, Cherpitel (2007) states on page 211 that at least two of these countries found that significant proportions of those reporting alcohol use during the six hours prior to the injury also reported other illicit drug use using the same time period (Argentina and Mexico), which underscores the importance

of considering other substance use with alcohol and the risk of injury. Other important limitations cited include not taking into account the age of the patient and the severity of the injury.

Thus, apart from the issue of bias in emergency room data as discussed in page 26 of this Submission, **the validity of using the data from this disparate multi-country emergency room study as an indication of injury risk from alcohol consumption on a single occasion, with potential confounding from other illicit drug use, is also questioned.** The cultural and socio-economic differences between these countries and the Australian population raise significant questions on the validity of comparisons of emergency room data, which in itself is a questionable indicator of broader community trends.

4.3.5 Appendix 7 Lifetime risk of death from alcohol-related diseases (page 114)

There are concerns regarding the methodology in this Appendix as follows.

4.3.5.1 Comments on Taylor et al. 2007 unpublished, non-peer-reviewed paper

The Taylor et al. 2007 paper which is cited on page 48 and again on page 114, appears to be a draft appendix or chapter from either a book or a research paper, which has not been peer reviewed.

The limitations of the study are listed on pages 9 and 10 of the Taylor et al. 2007 paper, and the second limitation is the most pertinent limitation, namely, “the chosen approach clearly reflects the higher absolute risk of chronic disease mortality for men compared to women in general **without regard to alcohol involvement**” which has resulted in certain counter-intuitive findings. The concluding statement does not lend confidence in the results: “these assumptions seem to be reasonable and not associated with too large a potential bias”.

4.3.5.2 Scientific credibility of references used in Appendices 6 and 7

For discussion please see page 54 of this Submission.

4.3.5.3 General comments

As discussed in the draft revised Guidelines on page 117, paragraph 3, when comparing or using international alcohol data, it is important to use data from similar cultures (Bloomfield et al. 2003). Overall, studies reviewed by Bloomfield suggest that relatively consistent patterns appear to exist across the reported studies with respect to abstinence and frequency of drinking (e.g., relatively high abstinence rates in the Mediterranean countries and highest frequency of consumption in the wine-producing countries of Europe). Measures of binge drinking and mean consumption levels, however, exhibited less consistency. It is difficult to determine whether these inconsistencies stem from methodological problems or from real changes in drinking behaviours, which no longer fit the traditional typologies of drinking cultures (e.g., the wet/dry dichotomy). Indeed, some of the methodological problems involved in measuring drinking rates across countries, such as differences in drinking cultures, drink sizes, and measurement. For example, traditionally, the wet/dry distinction has been described as follows:

- In wet cultures, alcohol is integrated into daily life and activities (e.g., is consumed with meals) and is widely available and accessible. In these cultures, abstinence rates are low, and wine is largely the beverage of preference. European countries bordering the Mediterranean have traditionally exemplified wet cultures; and
- In dry cultures, alcohol consumption is not as common during everyday activities (e.g., it is less frequently a part of meals) and access to alcohol is more restricted. Abstinence is more common, but when drinking occurs it is more likely to result in intoxication; moreover, wine consumption is less common. Examples of traditionally dry cultures include the Scandinavian countries, the USA, and Canada.

Australia is generally considered to be a wet culture. Thus it is important to compare Australian data with data from similar countries where access is less restricted, abstinence less common and when drinking occurs it is at low risk levels.

4.3.6 Appendix 8 Alcohol use in pregnancy and breast feeding: evidence details (page 118)

The following table includes additional references from 2001 onwards, as well as recent reviews, not cited in the draft revised Guidelines.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Harris and Bucens 2003		Cases identified through review of medical records and outpatient letters of children seen by Royal Darwin Hospital paediatric staff, and also by tracing potentially affected siblings, or incidentally during clinical work.	All children from the Top End born from 1990 – 2000 were potentially included.	FAS	Establish the prevalence of FAS in the Top End in the Northern Territory in indigenous and non indigenous populations.		17 identified with FAS 26 identified with partial FAS or alcohol-related neurodevelopment disorder. Prevalence of FAS v calculated as 0.68 per 1000 live births, but could be as high as 1.7 if partial cases were assumed to be full cases, due to insufficient records. The prevalence was 1.87 and 4.7 per 1000 live births for indigenous and non indigenous children. The difference between indigenous and non indigenous was significant.
Khaole et al 2004		10 women who had given birth to FAS children (FAS mothers) and 20 Controls were studied to determine how they metabolize alcohol in a single limited-access quasi-experimental session of voluntary consumption of alcohol.	30	Mothers had free choice in the consumption of any amount of their favourite beverage for ~ 2.5 h, but their drinking was terminated if the breath alcohol concentrations (BrAC) exceeded 150 mg%. BrACs was measured during ethanol consumption and for several hours after, for estimation of alcohol exposure and pharmacokinetics.	Alcohol exposure and pharmacokinetics of alcohol in a group of women who had given birth to children with FAS, compared with women who had not given birth to FAS children.		FAS mothers consumed significantly larger amount of alcohol, and achieved significantly higher peak BrAC levels than Controls. The rate of decline of alcohol from the circulation (β -60) showed a 2-fold variation across subjects but there was no significant difference between the two groups.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
May et al 2004		Women of childbearing age. One sample of women is from prenatal clinics serving Plains Indian women. The second sample is of women from the Plains whose children were referred to special diagnostic developmental clinics, as their children were believed to have developmental issues consistent with prenatal alcohol consumption. The third sample is of women from South Africa, each of whom has given birth to a child diagnosed with full fetal alcohol syndrome (FAS).			FAS		Data across samples conform to expected trends on many variables. For example, the maternal age at onset of pregnancy, a major risk factor for FAS, ranged from a mean of 23.5 years for the prenatal clinic sample, to 23.8 years for the developmental clinic sample, to 27.6 for the sample of women who had delivered children with FAS. Other variables of maternal risk for FAS expected from the extant literature, such as high gravidity and parity, binge drinking, heavy intergenerational drinking in the mother's extended family and immediate social network, and length of drinking career, were compared across the three samples with variable results. However, normative measures of drinking problems are unreliable when reported across cultures. An unexpected finding from this three-sample comparison was the differential risk found when comparing U.S. women to South African women. Women in the U.S. Plains Indian samples report high consumption of alcohol in a binge pattern of drinking, yet there is less detectable damage to the fetus than among the South African women. Body mass index (BMI) and lifelong and current nutrition may have a substantial impact, along with the above factors, in relative risk for an FAS birth. The level of risk for producing a child with FAS is influenced by environmental and behavioural conditions that vary between populations and among individual women. Also, because many syndromes are genetically based, there is a need for full behavioural and genetic histories of the mother, family, and child being studied. Collecting extensive behavioural information as well as genetic histories will provide the required information for making an accurate diagnosis of

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Gemma et al 2007	Review				Fetal alcohol syndrome		Alcohol-related damages on newborns and infants include a wide variety of complications from facial anomalies to neurodevelopmental delay, known as fetal alcohol syndrome (FAS). However, only less than 10% of women drinking alcohol during pregnancy have children with FAS. Understanding risk factors increasing the probability for newborns exposed in utero to alcohol to develop FAS is therefore a key issue. The involvement of genetics as one risk factor in FAS has been suggested by animal models and by molecular epidemiological studies in different populations, bearing allelic variants for enzymes, such as ADH and CYP2E1, involved in ethanol metabolism. Indeed, one of the major factors determining the peak blood alcohol exposure to the fetus is the metabolic activity of the mother, in addition to placental and fetal metabolism, explaining at least partially, the risk of FAS. The different rates of ethanol metabolism may be the result of genetic polymorphisms, the most relevant of which have been described in the paper.
D'Onofrio et al 2007		Women recruited from the community	4912	Mothers rated their 4-11 year old children on the Behavior Problem Index (BPI) at each wave of assessment. The BPI included 13 items from the Child Behavior Checklist that had the strongest associations with Child Behavior Checklist factor scores.	Maternal report of conduct problems (CPs) and attention/impulsivity problems (AIPs) during childhood (ages 4-11 years) using standardized assessments related to psychiatric diagnoses.	Participants assessed annually between 1979 and 1994, then biennially since then. Retention rates >90% or better during the first 16 waves of data collection.	There was an association between PAE and offspring CPs that was independent of confounded genetic and fixed environmental effects and the measured covariates. The CPs in children of mothers who drank daily during pregnancy were 0.35 SD greater than those in children whose mothers never drank during pregnancy. Although AIPs were associated with PAE when comparing unrelated offspring, children whose mothers drank more frequently during pregnancy did not have more AIPs than siblings who were less exposed to alcohol in utero. Additional subsample analyses suggested that maternal polysubstance use during pregnancy may account for the association between PAE and AIPs.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Sayal et al 2007		85% of pregnant women in Avon (SW England) with expected delivery date between April 1991 and December 1992	14541	Alcohol consumption before and during the 1 st trimester was assessed by postal questionnaire using the following categories: <1 glass/week ≥1 glass/week 1-2 glasses/day 3-9 glasses/day ≥10 glasses/day (1 glass = 8g alcohol)	Child mental health outcomes were measured using the Strengths and Difficulties Questionnaire, which has 4 symptom scales relating to hyperactivity/inattention, conduct problems, emotional symptoms, and peer relationships.	Information on alcohol consumption collected via postal questionnaire at 18 weeks gestation.	Consumption of <1 drink per week during the 1 st trimester was independently associated with clinically significant mental health problems in girls at 47 months. This gender-specific association persisted to 81 months and was confirmed by later teacher ratings. No dose-response relationship was observed, and no gender effect was unexpected.
O'Callaghan et al 2007		Mothers enrolled at the first antenatal visit to Mater Misericordiae Mothers' Hospital in Brisbane.	8556	Alcohol consumption assessed at first antenatal visit with the following options: daily, a few times a week, a few times a month, a few times a year, rarely, and never. Several days after delivery alcohol consumption during the last trimester was assessed with the following options: daily, a few times a week, a few times a month, and not at all. Quantity was assessed with the following options: ≥7 glasses, 5-6 glasses, 3-4 glasses, 1-2 glasses, less than one glass, and never drink.	The Wide Range Achievement Test-Revised (WRAT-R) and Raven's Standard Progressive Matrices Test (Raven's) were administered to adolescents. Mothers completed the Child Behaviour Checklist (CBCL) and adolescents completed the Youth Self Report (YSR). Learning was assessed by mother and adolescent questionnaires. Maternal measures included the quantity and frequency of alcohol consumption and the extent of binge drinking.		For consumption of <1 glass/day in early or late pregnancy, there was no association with any attention, learning or cognitive outcomes. The strongest estimates of effect were found among those for consuming ≥1 glasses/day. Exposure in late pregnancy was associated with increased prevalence of overall learning difficulty in the unadjusted, although not the adjusted analysis. Binge drinking was associated with a higher prevalence of Raven's scores <85 (1 standard deviation).

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Maier and West 2001					Cognitive and behavioral deficits.		The consequences of maternal alcohol use during pregnancy on the outcome of offspring depend, among other factors, on the amount and pattern of alcohol consumption. Animal studies found that binge-like drinking patterns, in which the fetus is exposed to high blood alcohol concentrations (BACs) over relatively short periods of time, are particularly harmful, even if the overall alcohol amount consumed is less than that of those of more continuous drinking patterns. Long-term studies in humans have confirmed that children of binge-drinking mothers exhibited especially severe cognitive and behavioral deficits. Binge drinking may be particularly harmful because it results in high BACs, may occur during critical periods of brain development, and may be associated with repeated withdrawal episodes.
Juhl et al 2002		Women recruited to the Danish National Birth Cohort within the first 24 weeks of pregnancy from 1997-2000.	39612		Odds ratio for a prolonged waiting time to pregnancy according to alcohol intake.		In nulliparous women neither moderate nor high alcohol intake was related to longer waiting time to pregnancy compared with a low intake. In parous women, a modest association was seen only in those with an intake of >14 drinks/week (subfecundity OR 1.3; 95% confidence interval 1.0-1.7). Women who reported no alcohol intake had a slightly longer waiting time (subfecundity OR 1.2; 95% confidence interval 1.1-1.3) than women with a moderate intake of alcohol.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Henriksen et al 2004		Recruited from 50000 members of 4 trade unions in Denmark from 1992-1994	430	Women collected morning urine for 10 days from day 1 of vaginal bleed each cycle. hCG was measured to detect pregnancies. Alcohol intake (number of drinks in the week before the questionnaire) and potential confounding factors were reported in monthly questionnaires.	Spontaneous abortion related to both male and female alcohol intake.	Alcohol consumption at time of conception. Couples without previous pregnancy attempts were enrolled when birth control was discontinued were followed until clinically recognised pregnancy or for 6 menstrual cycles. BMI, reproductive illness, smoking and caffeine intake were included as confounding factors.	186 pregnancies were detected with 131 resulting in spontaneous abortion and 55 resulting in spontaneous abortion. Female alcohol intake was associated with 2-3 times the adjusted risk of spontaneous abortion compared with no intake, and male alcohol intake was associated with 2-5 times the adjusted risk. Only the adjusted relative risks for 10 or more drinks/week compared with no intake were statistically significant. Both male and female alcohol intakes during the week of conception increased the risk of early pregnancy
Maconochie et al 2006		Women samples from the electoral roll in England. 603 women aged 18-55 whose most recent pregnancy had ended in 1 st trimester miscarriage and 6116 women aged 18-55 whose most recent pregnancy had progressed beyond 12 weeks (control).	6719		First trimester miscarriage.		After adjustment for confounding, the following factors were independently associated with increased risk: high maternal age; previous miscarriage, termination or infertility; assisted conception; low pre-pregnancy body mass index; regular or high alcohol consumption; feeling stressed (including trend with number of stressful or traumatic events); high parity, age and changing partner. Previous live birth, nausea, vitamin supplementation and eating fresh fruits and vegetables daily were associated with reduced risk. Women who were feeling well enough to fly or to have sex. After adjustment for nausea, we did not confirm an association with caffeine consumption, smoking moderate or occasional alcohol consumption; nor did we find an association with educational level, socioeconomic circumstances or working during pregnancy.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Parazzini et al 2003		502 women who delivered pre-term babies in 2 hospitals in Italy, and 1966 women who gave birth at term to healthy infants of normal weight.	2468		Preterm birth relating to alcohol consumption.	Confounding factors included maternal education, marital status, parity, smoking, caffeine consumption, previous preterm births, maternal BMI at conception and hypertension in pregnancy.	No increased risk of preterm birth was observed in women drinking one or two drinks/day in pregnancy but three or more drinks/day increased the risk (multivariate odds ratios (OR) 2.0 for ≥ 3 drinks during the first trimester, 1.8 during the second and 1.9 during the third). When the analysis was conducted separately for preterm births with normal weight or SGA, the increased risk was observed for preterm SGA only (multivariate OR for ≥ 3 drinks during the first trimester=3.6, 95% confidence interval (CI) 1.3–11.1); the estimated multivariate OR for ≥ 3 drinks/day during the first trimester of preterm babies with normal weight for gestational age was only slightly above unity and not statistically significant (multivariate OR 1.4, 95% CI 0.5–3.7).
Chiapparino et al 2006		555 women who delivered SGA babies in 2 hospitals in Italy, and 1966 women who gave birth at term to healthy infants of normal weight.	2521		Small at gestational age related to alcohol drinking.	Confounding factors included maternal education, marital status, parity, smoking, caffeine consumption in the 3 rd trimester, previous SGA births, maternal BMI at conception, nausea during the 1 st trimester and hypertension in pregnancy.	No increase in the risk of SGA birth was observed in women drinking one or two drinks/day in pregnancy but three or more per day increased the risk: odds ratios (OR) were 3.2 (1.7–6.2) for ≥ 3 drinks during the first trimester, 2.7 (1.4–5.3) during the second and 2.9 (1.5–5.7) during the third.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Mariscal et al 2005		552 women delivering single newborn weighing less than 2500g, and 1451 control women selected from a random sample of all delivering women from the University of Cantabria Hospital, Spain.	2003	Data collected from personal interviews (carried out within 3 days of delivery), clinical charts and prenatal care records. Alcohol consumption of: less than 6 g/day less than 12 g/day more than 12 g/day Consumption on weekdays or weekends only	Low birth weight		Alcohol consumption of less than 6 g/day decreased the risk for low birth weight (adjusted OR = 0.64; 95% CI, 0.46–0.88). A similar result was obtained for moderate drinkers (<12 g/day) on weekends only. An opposite relationship was observed between alcohol consumption on weekdays of 12 g/day or greater (adjusted OR = 2.67; 95% CI, 1.39–5.12), not observed in those drinking on weekends only. The interaction between alcohol consumption and tobacco smoking was analyzed. Weekday drinkers of 12 g/day or greater showed an increased risk in smokers. Alcohol consumption on weekends only in nonsmokers was inversely related. The influence of alcohol was greater for small-for-gestational-age (SGA) than non-SGA babies.
O'Callaghan et al 2003	Prospective cohort	Mothers enrolled at the first antenatal visit to Mater Misericordiae Mothers' Hospital in Brisbane	8556	The quantity and frequency of alcohol consumption in early and late pregnancy and a measure of binge drinking in early pregnancy were recorded.	Weight or head circumference (HC) at birth or 5 years	Level of cigarette use in early pregnancy and maternal age and level of education and family income were also measured.	Light and moderate alcohol consumption in early pregnancy had no independent effects on weight or HC at birth or 5 years. Binge drinking in early pregnancy was not associated with restricted HC. There was no effect modification by concurrent cigarette use in early pregnancy. An apparent effect of alcohol in late pregnancy on birth weight was due to confounding by cigarette use, with social risk being an independent predictor.
Colvin et al 2007		10% random sample of nonindigenous women giving birth in Western Australia.	4839	Alcohol consumption in 4 periods - 3 months before pregnancy and each trimester of pregnancy. Questions were framed to measure volume, frequency and type of alcoholic beverage.	Alcohol consumption during pregnancy was assessed.	From 1995 to 1997, women were surveyed once at 12 weeks after delivery.	46.7% of the women had not planned the pregnancy. 79.8% reported drinking alcohol in the 3 months before pregnancy. 58.7% reported drinking in at least 1 trimester. The proportion of women drinking 1-2 drinks on an occasion did not change much during pregnancy, although the number of occasions decreased. 19% consumed at least 2 drinks in at least 1 trimester, and 4.3% consumed 5 or more drinks on a typical occasion in 1 at least trimester. 14.8% drank more than the Australian guidelines recommends in the 1 st trimester, dropping to 10% in the 2 nd and 3 rd trimesters.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Tsai et al 2007		A sample of 188,290 women aged 18–44 years participated in the Centers for Disease Controls and Prevention (CDC)'s Behavioral Risk Factor Surveillance System (BRFSS) survey during the period of 2001–2003.	188290	Reported alcohol use patterns and average volume were examined for pregnant and nonpregnant women. Efforts were made to evaluate and characterize women who practiced various levels of binge drinking.			The results showed that approximately 2% of pregnant women and 13% of nonpregnant women in the United States engaged in binge drinking during the period 2001–2003. Among the estimated average of 6.7 million women of childbearing age overall who engaged in binge drinking during the period, approximately 28.5% women also reported consuming an average of 5 drinks or more on typical drinking days, or about 21.4% women consumed at least 4 drinks on average in a month. Larger proportions of binge drinkers with high usual quantity of consumption were found among women of younger ages (18–24 years) or current smokers.
Henderson, Kesmodel and Grey 2007	Review	Pregnant women or women who are trying to become pregnant	14 studies		Adverse outcomes considered included miscarriage, stillbirth, intrauterine growth restriction, prematurity, birth-weight, small for gestational age at birth, and birth defects including FAS and neurodevelopment.	observational studies	There were no consistently significant effects of alcohol on any of the outcomes considered. There was a possible effect on neurodevelopment. Many of the reported studies had methodological weaknesses, despite being assessed as having reasonable quality.
Henderson Grey and Brocklehurst 2007	Review	Pregnant women or women who are trying to become pregnant	46 studies		Outcomes considered were miscarriage, stillbirth, intrauterine growth restriction, prematurity, birthweight, small for gestational age at birth and birth defects including FAS.		The search resulted in 3630 titles and abstracts, which were narrowed down to 46 relevant articles. At low to moderate levels of consumption, there were no consistently significant effects of alcohol on any of the outcomes considered. Many of the reported studies had methodological weaknesses.
O'Leary 2004	Review			Maternal age, Race, genetic factors and socio-economic status, tobacco, cannabis, and cocaine	FAS		The current data do not demonstrate an association between a low level of alcohol consumption and FAS or FAE, but clearly identify an association between pattern and quantity of alcohol consumption, the timing of intake and a range of component causes.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
Guerrini et al 2007	Review				Alcohol misuse, malnutrition and genetic susceptibility on brain growth and plasticity		The “dyad: alcoholic mother and foetus” is a very complex entity in which several elements such as genes, metabolism, diet, drugs and social habits play a role at different stages in the development of the brain. The literature on the effects of alcohol consumption on the developing brain is extensive. However, very few evidences have been reported regarding the combined neurotoxic effects of poor nutrition and alcohol consumption. The consequences of ethanol intake alone or combined with poor maternal nutrition appear to be severe and life-long. Alcohol exerts neurotoxic effects on the developing brain directly acting on fetal brain tissues, and indirectly either interfering with placental physiology or by impairing the mother's physiology. Alcohol misuse in pregnancy is also frequently associated with other conditions that can potentially increase the brain damage such as malnutrition and smoking. This article reviews the effects of poor nutrition and alcohol misuse during pregnancy on the development of the fetal brain and discusses the cumulative effects of these two environmental factors and their interaction with maternal and fetal genetic make-ups.

Study	Study type	Population	N	Indicators	Outcomes	Quality Information	Results
O'Leary et al 2006	Review				Alcohol use during pregnancy in Australia and other English-speaking countries		<p>It is well accepted that heavy alcohol consumption during pregnancy is a risk factor for fetal alcohol spectrum disorder, but research findings for exposure to low to moderate alcohol levels during pregnancy are equivocal, allowing a range of interpretations. The 2001 guideline from the National Health and Medical Research Council (NHMRC) for low-risk drinking "women who are pregnant or might soon become pregnant" recommends fewer than seven standard drinks per week, and no more than two standard drinks on any one day. This position has polarised health professional and consumer opinion in Australia. The NHMRC guidelines on alcohol are scheduled for review in 2007. We surveyed the alcohol and pregnancy policies and clinical practice guidelines in Australia and six other English-speaking countries to identify current policy. Documents were obtained through Internet searches and direct contact with relevant organisations. The policies and guidelines varied both across and within countries, and the NHMRC guideline, while not universally supported in Australia, is in step with the policies of the United Kingdom and Canada. Research is needed to elucidate the true association between low to moderate alcohol consumption and fetal harm, the impact of different policies on rates of maternal alcohol consumption during pregnancy, and any untoward outcomes of an abstinence message, to inform and underpin future policy development in Australia.</p>

Appendix 1. Table of differences between the current and draft revised Guidelines

<u>Current</u>	<u>Draft</u>
<p>Guideline 1 To minimise risks in the short and longer term, and gain any longer-term benefits For men 1.1 an <i>average</i> of no more than 4 standard drinks a day, and no more than 28 standard drinks over a week; 1.2 not more than 6 standard drinks in any one day; 1.3 one or two alcohol-free days per week. For women 1.4 an <i>average</i> of no more than 2 standard drinks a day, and no more than 14 standard drinks over a week; 1.5 not more than 4 standard drinks in any one day; 1.6 one or two alcohol-free days per week.</p>	<p>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.</p>
<p>Guideline 2 When undertaking activities that involve risk or a degree of skill 2.1 to avoid the risk of harm to the drinker and others, do not drink alcohol before or during such activities.</p>	<p>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) - 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.</p>
<p>Guideline 3 When responsible for private and public drinking environments 3.1 actively promote responsible drinking; 3.2 strive to make sure that those being served alcohol do not become intoxicated, and suggest alternatives to alcohol; 3.3 refuse to serve alcohol to people who are intoxicated; 3.4 minimise the potential for harm in the setting; 3.5 closely supervise or monitor young people.</p>	<p>[No replacement]</p>
<p>Guideline 4 People with a health or social problem that is related to alcohol, or made worse by alcohol (including alcohol dependence) 4.1 should consider not drinking at all; 4.2 are strongly advised to stop drinking for at least several weeks or months; 4.3 might then try drinking at low levels (substantially below Guideline 1)* under professional supervision; 4.4 should not drink if they have developed severe alcohol dependence; 4.5 should never drink if they have a severe health problem made worse by alcohol (eg cirrhosis, pancreatitis); 4.6 if they have hepatitis C or other forms of chronic viral hepatitis, should consider drinking only infrequently and well below the levels recommended in Guideline 1. * The appropriate level will vary from person to person.</p>	<p>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 - 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.</p>

<p>Guideline 5 People with a relative* who has, or has had, a problem with alcohol 5.1 are advised to be careful about how much they drink; 5.2 should take particular care to have regular alcohol-free days (one or two days per week); 5.3 might consider not drinking at all. * first-degree relatives (parents, siblings) or second-degree relatives (grandparents, uncles, aunts, cousins).</p>	<p>Additional health advice 2 For people who should be aware that they have an increased risk - 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.</p>
<p>Guideline 6 People with a mental health problem (including anxiety or depression) and/or sleep disturbance 6.1 if they do drink, should take particular care to stay within the levels set in Guideline 1, and should consult with their doctor or pharmacist about possible side-effects; 6.2 may need to consider not drinking at all, if they find it difficult to keep their drinking within these guideline levels; 6.3 may need to stop drinking entirely if symptoms persist.</p>	<p>Additional health advice 3 For people who should seek health professional advice if they are considering drinking - People with a mental health problem made worse by alcohol - 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.</p>
<p>Guideline 7 People taking medications or other drugs 7.1 should carefully read the labels and pamphlets with their medications (including herbal preparations), to check for harmful interactions with alcohol. Some people may need to reduce their drinking or stop drinking alcohol altogether; 7.2 are advised to be very cautious if drinking alcohol while using benzodiazepines, heroin, methadone or other central nervous system depressants; 7.3 if they are taking a number of medications, are at greater risk of increasing the effects of alcohol and/ or decreasing the effectiveness of their medication. These people may need to reduce or stop drinking alcohol; 7.4 should consult their doctor or a pharmacist to discuss any aspect of their medication, including possible interactions with alcohol.</p>	<p>Additional health advice 3 For people who should seek health professional advice if they are considering drinking - People taking medications - Alcohol may interact with prescribed and over-the-counter medications and increase or reduce their effectiveness. - Alcohol may interact with illicit drugs, which can have dangerous or lethal consequences.</p>
<p>Guideline 8 Older people 8.1 are advised, if they drink, to consider drinking less than the levels set in Guideline 1.</p>	<p>Additional health advice 2 For people who should be aware that they have an increased risk - Older people, who have a higher risk of falls and are more likely to be taking medication - 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.</p>
<p>Guideline 9 Young adults (aged about 18–25 years)* 9.1 are especially urged not to drink beyond the levels set in Guideline 1; 9.2 should not drink at all for at least several hours before undertaking potentially risky activities (eg</p>	<p>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 - Young adults up to the age of 25 are at particular risk of</p>

<p>driving, swimming, boating); 9.3 should not mix alcohol with other mood altering drugs. * While this guideline applies to people aged about 18–25 years, the issues and concerns overlap with those covered under Guideline 10, ‘Young People’.</p>	<p>harm from alcohol consumption. The issues for young adults are similar to those for adolescents (see Guideline 2).</p>
<p>Guideline 10 Young people (up to about 18 years)* 10.1 should follow the recommendations under Guideline 9; AND 10.2 if they choose not to drink, should be supported in this decision; 10.3 in settings where alcohol is available to them, should be supervised by adults at all times; 10.4 should keep any drinking to a minimum; 10.5 most importantly, should not drink to become intoxicated; 10.6 to become responsible adult drinkers, a gradual, supervised introduction to alcohol is recommended. * While this guideline applies young people up to about 18 years of age, the issues and concerns overlap with those covered under Guideline 9, ‘Young Adults’.</p>	<p>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).</p>
<p>Guideline 11 Women who are pregnant or might soon become pregnant 11.1 may consider not drinking at all; 11.2 most importantly, should never become intoxicated; 11.3 if they choose to drink, over a week, should have less than 7 standard drinks, AND, on any one day, no more than 2 standard drinks (spread over at least two hours); 11.4 should note that the risk is highest in the earlier stages of pregnancy, including the time from conception to the first missed period.</p>	<p>Guideline 3 For women who are pregnant, are planning a pregnancy or are breastfeeding 3.1 Not drinking is the safest option.</p>
<p>Guideline 12 People who choose not to drink alcohol 12.1 should not be urged to drink to gain any potential health benefit, and should be supported in their decision not to drink.</p>	<p>[No replacement]</p>

Appendix 2 References

- AIHW (2002). National Drug Strategy Household Survey, Australian Institute of Health and Welfare.
- AIHW (2004). A guide to Australian alcohol data, Australian Institute of Health and Welfare.
- AIHW (2004). National Drug Strategy Household Survey, Australian Institute of Health and Welfare.
- AIHW (2007). Young Australians: their health and wellbeing, Australian Institute of Health and Welfare.
- Ajani, U. A., W. G. Christen, J. E. Manson, R. J. Glynn, D. Schaumberg, J. E. Buring and C. H. Hennekens (1999). "A Prospective Study of Alcohol Consumption and the Risk of Age-Related Macular Degeneration." *Annals of Epidemiology* **9**(3): 172-177.
- Ajani, U. A., J. M. Gaziano, P. A. Lotufo, S. Liu, C. H. Hennekens, J. E. Buring and J. E. Manson (2000). "Alcohol Consumption and Risk of Coronary Heart Disease by Diabetes Status." *Circulation* **102**(5): 500-505.
- Ajani, U. A., C. H. Hennekens, A. Spelsberg and J. E. Manson (2000). "Alcohol Consumption and Risk of Type 2 Diabetes Mellitus Among US Male Physicians." *Archives of internal medicine* **160**(7): 1025-1030.
- Andréasson, S., H. D. Holder, A. L. Klatsky, K. Mukamal, J. Rehm, A. Romelsjö, A. G. Shaper, B. Rodgers, T. D. Windsor, T. M. Caldwell, et al. (2007). "Commentaries on Fillmore, Kerr, Stockwell, Chikritzhs, Bostrom." *Addiction Research & Theory* **15**(1): 3-33.
- Arnarsson, A., T. Sverrisson, E. Stefánsson, H. Sigurdsson, H. Sasaki, K. Sasaki and F. Jonasson (2006). "Risk Factors for Five-Year Incident Age-related Macular Degeneration: The Reykjavik Eye Study." *American Journal of Ophthalmology* **142**(3): 419-428.e1.
- Ashley, M. J., J. Rehm, S. Bondy, E. Single and J. Rankin (2000). "Beyond ischemic heart disease: are there other health benefits from drinking alcohol?" *Contemporary Drug Problems* **27**(4): 735.
- Australia New Zealand Food Authority (2001). The 19th Australian Total Diet Survey, FSANZ.
- Australian Bureau of Statistics (1995). National Nutrition Survey, ABS.
- Australian Bureau of Statistics (2006). 2004-2005 National Health Survey: Summary of Results, ABS.
- Australian Bureau of Statistics. (2006, 8 December 2006). "Alcohol consumption in Australia: A snapshot 2004-05." from <http://www.abs.gov.au/AUSSTATS/abs@.nsf/ProductsbyReleaseDate/0B973AF7706E8B15CA2571D4001C8654?OpenDocument#>.

- Avogaro, A., R. M. Watanabe, L. Gottardo, S. de Kreutzenberg, A. Tiengo and G. Pacini (2002). "Glucose Tolerance during Moderate Alcohol Intake: Insights on Insulin Action from Glucose/Lactate Dynamics." *J Clin Endocrinol Metab* **87**(3): 1233-1238.
- Ayaori, M., T. Hisada, H. Yoshira, H. Shige, T. Ito, K. Nakajima, Higashi K., Yonemura. A., T. Ishikawa, F. Ohsuzu, et al. (2000). "Effect of alcohol intake on the levels of plasma homocysteine in healthy males." *J. Nutr. Sci. Vitaminol.* **46**(4): 171-174.
- Baglietto, L., D. R. English, J. L. Hopper, J. Powles and G. G. Giles (2006). "Average volume of alcohol consumed, type of beverage, drinking pattern and the risk of death from all causes." *Alcohol and Alcoholism* **41**(6): 664-671.
- Baraona, E., C. S. Abittan, K. Dohmen, M. Moretti, G. Pozzato, Z. W. Chayes, C. Schaefer and C. S. Lieber (2001). "Gender Differences in Pharmacokinetics of Alcohol." *Alcoholism: Clinical and Experimental Research* **25**(4): 502-507.
- Becker, U., A. Deis, T. I. Sorensen, M. Grønbaek, K. Borch-Johnsen, C. F. Müller, P. Schnohr and G. Jensen (1996). "Prediction of risk of liver disease by alcohol intake, sex, and age: A prospective population study." *Hepatology* **23**(5): 1025-1029.
- Bellamy, M. F., I. F. W. McDowell, M. W. Ramsey, M. Brownlee, C. Bones, R. G. Newcombe and M. J. Lewis (1998). "Hyperhomocysteinemia After an Oral Methionine Load Acutely Impairs Endothelial Function in Healthy Adults." *Circulation* **98**(18): 1848-1852.
- Bleich, S., K. Bleich, S. Kropp, H. J. Bittermann, D. Degner, W. Sperling, E. Ruther and J. Kornhuber (2001). "Moderate alcohol consumption in social drinkers raises plasma homocysteine levels: a contradiction to the 'French Paradox'?" *Alcohol and Alcoholism* **36**(3): 189-192.
- Bloomfield, K., T. Stockwell, G. Gmel and N. Rehn (2003). "International Comparisons of Alcohol Consumption." *Alcohol Research & Health* **27**(1): 95-109.
- Bobak, M., H. Pikhart, A. Pajak, R. Kubinova, S. Malyutina, H. Sebakova, R. Topor-Madry, Y. Nikitin and M. Marmot (2006). "Depressive symptoms in urban population samples in Russia, Poland and the Czech Republic." *British Journal of Psychiatry* **188**(4): 359-365.
- Bond, G. E., R. L. Burr, S. M. McCurry, M. M. Rice, A. R. Borenstein and E. B. Larson (2005). "Alcohol and cognitive performance: a longitudinal study of older Japanese Americans. The Kame Project." *International psychogeriatrics / IPA* **17**(4): 653-668.
- Bradley, K., K. Bush, M. McDonell, T. Malone, S. Fihn and A. C. Q. I. P. (ACQUIP) (1998). "Screening for problem drinking." *Journal of General Internal Medicine* **13**(6): 379-388.
- Brandt, J., K. A. Welsh, J. C. Breitner, M. F. Folstein, M. Helms and J. C. Christian (1993). "Hereditary influences on cognitive functioning in older men. A study of 4000 twin pairs." *Archives of Neurology* **50**(6): 599-603.

- Breitmeier, D., I. Seeland-Schulze, H. Hecker and U. Schneider (2007). "The influence of blood alcohol concentrations of around 0.03% on neuropsychological functions—a double-blind, placebo-controlled investigation." *Addiction Biology* **12**(2): 183-189.
- British Heart Foundation. (2005). "Alcohol consumption by sex, country of Great Britain and Government Office Region in England, adults aged 16 and over, 2005, Great Britain." from <http://www.heartstats.org/temp/Tabsp7.6spweb06hs1hs.xls>.
- Britton, A., E. Nolte, I. R. White, M. Grønbaek, J. Powles, F. Cavallo and K. McPherson (2003). "A comparison of the alcohol-attributable mortality in four European countries." *European Journal of Epidemiology* **18**(7): 643-652.
- Buch, H., T. Vinding, M. la Cour, G. B. Jensen, J. U. Prause and N. V. Nielsen (2005). "Risk factors for age-related maculopathy in a 14-year follow-up study: the Copenhagen City Eye Study." *Acta Ophthalmologica Scandinavica* **83**(4): 409-418.
- Casbon, T. S., J. J. Curtin, A. R. Lang and C. J. Patrick (2003). "Deleterious effects of alcohol intoxication: Diminished cognitive control and its behavioral consequences." *Journal of Abnormal Psychology* **112**(3): 476-487.
- Centre for Addiction and Mental Health (2007). Low - Risk Drinking Guidelines, CAMH.
- Cervilla, J. A., M. Prince and A. Mann (2000). "Smoking, drinking, and incident cognitive impairment: a cohort community based study included in the Gospel Oak project." *J Neurol Neurosurg Psychiatry* **68**(5): 622-626.
- Cherpitel, C. J. (1996). "Drinking Patterns and Problems and Drinking in the Event: An Analysis of Injury by Cause Among Casualty Patients." *Alcoholism: Clinical and Experimental Research* **20**(6): 1130-1137.
- Cherpitel, C. J. (2007). "Alcohol and injuries: a review of international emergency room studies since 1995." *Drug and Alcohol Review* **26**(2): 201-14.
- Cherpitel, C. J., T. Tam, L. Midanik, R. Caetano and T. Greenfield (1995). "Alcohol and non-fatal injury in the U.S. general population: A risk function analysis." *Accident Analysis & Prevention* **27**(5): 651-661.
- Chikritzhs, T. N., H. A. Jonas, T. R. Stockwell, P. F. Heale and P. M. Dietze (2001). "Mortality and life-years lost due to alcohol: a comparison of acute and chronic causes." *The Medical journal of Australia* **174**(6): 281-284.
- Cho, E., S. E. Hankinson, W. C. Willett, M. J. Stampfer, D. Spiegelman, F. E. Speizer, E. B. Rimm and J. M. Seddon (2000). "Prospective Study of Alcohol Consumption and the Risk of Age-Related Macular Degeneration." *Archives of Ophthalmology* **118**(5): 681-688.
- Clemens, S. L., S. L. Matthews, A. F. Young and J. R. Powers (2007). "Alcohol consumption of Australian women: results from the Australian Longitudinal Study on Women's Health." *Drug & Alcohol Review* **26**(5): 525-535.

- Colvin, L., J. Payne, D. Parsons, J. J. Kurinczuk and C. Bower (2007). "Alcohol Consumption During Pregnancy in Nonindigenous West Australian Women." *Alcoholism: Clinical and Experimental Research* **31**(2): 276-284.
- Corrao, G., V. Bagnardi, A. Zambon and S. Arico (1999). "Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol-related conditions: a meta-analysis." *Addiction* **94**(10): 1551-1573.
- Corrao, G., V. Bagnardi, A. Zambon and C. La Vecchia (2004). "A meta-analysis of alcohol consumption and the risk of 15 diseases." *Preventive Medicine* **38**(5): 613-619.
- Corrao, G., L. Rubbiati, V. Bagnardi, A. Zambon and K. Poikolainen (2000). "Alcohol and coronary heart disease: a meta-analysis." *Addiction* **95**(10): 1505-1523.
- Corti, B. (1988). Recent research on the effects of alcohol on women. Perth, National Centre for Research into the Prevention of Drug Abuse.
- Cravo, M. L., L. M. Gloria, J. Selhub, M. R. Nadeau, M. E. Camilo, M. P. Resende, J. N. Cardoso, C. N. Leitao and F. C. Mira (1996). "Hyperhomocysteinemia in chronic alcoholism: correlation with folate, vitamin B-12, and vitamin B-6 status." *American Journal of Clinical Nutrition* **63**(2): 220-224.
- Cuevas, A., V. Guasch, O. Castillo, V. Irribarra, C. Mizon, A. Martin, P. Strobel, D. Perez, A. Germain and F. Leighton (2000). "A high-fat diet induces and red wine counteracts endothelial dysfunction in human volunteers." *Lipids* **35**(2): 143-148.
- Doll, R., Peto, R., Boreham, J. and Sutherland, J. (2005) Mortality in relation to alcohol consumption: a prospective study among male British doctors. *International Journal of Epidemiology* **43**(1): 199-204.
- D'Onofrio, G. and L. C. Degutis (2004). "Screening and brief intervention in the emergency department." *Alcohol Research & Health* **28**(2): 63-72.
- DeAngelis, M. M., A. M. Lane, C. P. Shah, J. Ott, T. P. Dryja and J. W. Miller (2004). "Extremely Discordant Sib-Pair Study Design to Determine Risk Factors for Neovascular Age-Related Macular Degeneration." *Archives of Ophthalmology* **122**(4): 575-580.
- Dent, O. F., M. R. Sulway, G. A. Broe, H. Creasey, S. C. Kos, A. F. Jorm, C. Tennant and M. J. Fairley (1997). "Alcohol consumption and cognitive performance in a random sample of Australian soldiers who served in the second world war." *BMJ : British Medical Journal* **314**(7095): 1655-.
- Department of Health. (2007). "The Pregnancy Book 2007." from http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_074920.
- Department of Health and Ageing (2006). National Alcohol Strategy 2006 - 2009 Department of Health and Ageing.

- Di Castelnuovo, A., Costanzo, S., Bagnardi, V., Donati, M.B., Iacoviello, L., de Gaetano, G. (2006) Alcohol dosing and total mortality in men and women: an updated meta-analysis of 34 prospective studies. *Archives of Internal Medicine* **166**(22):2437-45
- Dixon, J. B., M. E. Dixon and P. E. O'Brien (2001). "Elevated homocysteine levels with weight loss after Lap-Band® surgery: higher folate and vitamin B₁₂ levels required to maintain homocysteine level." *International Journal of Obesity & Related Metabolic Disorders* **25**(2): 219.
- Dixon, J. B., M. E. Dixon and P. E. O'Brien (2002). "Alcohol Consumption in the Severely Obese: Relationship with the Metabolic Syndrome." *Obesity Research* **10**(4): 245-252.
- Dixon, J. B., M. E. Dixon and P. E. O'Brien (2002). "Reduced plasma homocysteine in obese red wine consumers: a potential contributor to reduced cardiovascular risk status." *European Journal of Clinical Nutrition* **56**(7): 608.
- Djousse, L., M. L. Biggs, K. J. Mukamal and D. S. Siscovick (2007). "Alcohol Consumption and Type 2 Diabetes Among Older Adults: The Cardiovascular Health Study." *Obesity* **15**(7): 1758-1765.
- Donahue, R. P., R. D. Abbott, D. M. Reed and K. Yano (1986). "Alcohol and hemorrhagic stroke. The Honolulu Heart Program." *JAMA* **255**(17): 2311-2314.
- Douglas, I. J., C. Cook, U. Chakravarthy, R. Hubbard, A. E. Fletcher and L. Smeeth (2007). "A Case-Control Study of Drug Risk Factors for Age-Related Macular Degeneration." *Ophthalmology* **114**(6): 1164-1169.
- Dufouil, C., P. Ducimetière, P. Ducimetière, A. Alperovitch and E. V. A. S. G. for the (1997). "Sex Differences in the Association between Alcohol Consumption and Cognitive Performance." *American Journal of Epidemiology* **146**(5): 405-412.
- Earle, T. and G. Cvetkovich (1994). *Risk Communication: The Social Construction of Meaning and Trust. Future Risks and Risk Management*. B. Brehmer and N.-E. Sahlin. Dordrecht, Kluwer Academic: 141-181.
- Earle, T. and G. Cvetkovich (1995). *Social Trust: Toward a Cosmopolitan Society*. Westport, CT, Praeger.
- Easdon, C. M. and M. Vogel-Sprott (2000). "Alcohol and behavioral control: Impaired response inhibition and flexibility in social drinkers." *Experimental and Clinical Psychopharmacology* **8**(3): 387-394.
- Elias, P. K., M. F. Elias, R. B. D'Agostino, H. Silbershatz and P. A. Wolf (1999). "Alcohol Consumption and Cognitive Performance in the Framingham Heart Study." *American Journal of Epidemiology* **150**(6): 580-589.
- Engels, R. C. M. E. and R. A. Knibbe (2000). "Young people's alcohol consumption from a European perspective: risks and benefits." *European Journal of Clinical Nutrition* **54**(3): S52.

- English, D., D. A. Holman and E. Milne (1995). The Quantification of Drug Caused Morbidity and Mortality in Australia. Canberra, AGPS.
- Engs, R. C. (1989). "Do warning labels on alcoholic beverages deter alcohol abuse?" *The Journal of School Health* **59**(3): 116.
- Espeland, M. A., L. H. Coker, R. Wallace, S. R. Rapp, S. M. Resnick, M. Limacher, L. H. Powell and C. R. Messina (2006). "Association between Alcohol Intake and Domain-Specific Cognitive Function in Older Women." *Neuroepidemiology* **27**(1): 1-12.
- Fadda, F. and Z. L. Rossetti (1998). "Chronic ethanol consumption:from neuroadaptation to neurodegeneration." *Progress in Neurobiology* **56**(4): 385-431.
- Farlex (2007). *The Free Dictionary*.
- Fillmore, K. M., W. C. Kerr, T. Stockwell, T. Chikritzhs and B. A. (2006). "Moderate alcohol use and reduced mortality risk: Systematic error in prospective studies." *Addiction Research and Theory* **14**(2): 101-112.
- Fillmore, K. M., T. Stockwell, T. Chikritzhs, A. Bostrom and W. Kerr (2007). "Moderate Alcohol Use and Reduced Mortality Risk: Systematic Error in Prospective Studies and New Hypotheses." *Annals of Epidemiology* **17**(5, Supplement 1): S16-S23.
- Flensburg-Madsen, T., J. Knop, E. L. Mortensen, U. Becker and M. Grønbaek (2007). "Amount of alcohol consumption and risk of developing alcoholism in men and women." *Alcohol and Alcoholism* **42**(5): 442-447.
- Fogarty, J. N. and M. Vogel-Sprott (2002). "Cognitive Processes and Motor Skills Differ in Sensitivity to Alcohol Impairment." *Journal of Studies on Alcohol* **63**(4): 404-411.
- Fraser-Bell, S., J. Wu, R. Klein, S. P. Azen and R. Varma (2006). "Smoking, Alcohol Intake, Estrogen Use, and Age-related Macular Degeneration in Latinos: The Los Angeles Latino Eye Study." *American Journal of Ophthalmology* **141**(1): 79-87.
- Fuchs, C. S., M. J. Stampfer, G. A. Colditz, E. L. Giovannucci, J. E. Manson, I. Kawachi, D. J. Hunter, S. E. Hankinson, C. H. Hennekens, B. Rosner, et al. (1995). "Alcohol consumption and mortality among women." *The New England journal of medicine* **332**(19): 1245-1250.
- Ganguli, M., J. Vander Bilt, J. A. Saxton, C. Shen and H. H. Dodge (2005). "Alcohol consumption and cognitive function in late life: a longitudinal community study." *Neurology* **65**(8): 1210-1217.
- Gapstur, S. M., J. D. Potter, T. A. Sellers and A. R. Folsom (1992). "Increased Risk of Breast Cancer with Alcohol Consumption in Postmenopausal Women." *American Journal of Epidemiology* **136**(10): 1221-1231.
- Gavaler, J. S. (1982). "Sex-related differences in ethanol-induced liver disease: artifactual or real?" *Alcoholism: Clinical and Experimental Research* **6**(2): 186-196.

- Giglia, R. C. and C. W. Binns (2007). "Alcohol and breastfeeding: what do Australian mothers know?" *Asia Pacific Journal of Clinical Nutrition* **16**(S 1): 473-477.
- Giglia, R. C. and C. W. Binns (2007). "Patterns of alcohol intake of pregnant and lactating women in Perth, Australia." *Drug & Alcohol Review* **26**(5): 493-500.
- Gillman, M. W., N. R. Cook, D. A. Evans, B. Rosner and C. H. Hennekens (1995). "Relationship of Alcohol Intake With Blood Pressure in Young Adults." *Hypertension* **25**(5): 1106-1110.
- Gmel, G., E. Gutjahr and J. Rehm (2003). "How stable is the risk curve between alcohol and all-cause mortality and what factors influence the shape? A precision-weighted hierarchical meta-analysis." *European Journal of Epidemiology* **18**(7): 631-642.
- Grant, B. F. and D. A. Dawson (1997). "Age at onset of alcohol use and its association with DSM-IV alcohol abuse and dependence: results from the national longitudinal alcohol epidemiologic survey." *Journal of Substance Abuse* **9**: 103-110.
- Grant, B. F., F. S. Stinson and T. C. Harford (2001). "Age at onset of alcohol use and DSM-IV alcohol abuse and dependence: A 12-year follow-up." *Journal of Substance Abuse* **13**(4): 493-504.
- Grønbaek, M., D. Johansen, U. Becker, H. O. Hein, P. Schnohr, G. Jensen, J. Vestbo and T. Sørensen (2004). "Changes in Alcohol Intake and Mortality: A Longitudinal Population-based Study." *Epidemiology* **15**(2): 222-228.
- Hamajima, N., K. Hirose, K. Tajima, T. Rohan, E. E. Calle, C. W. H. Jr, R. J. Coates, J. M. Liff, R. Talamini, N. Chantarakul, et al. (2002). "Alcohol, tobacco and breast cancer - collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease." *British Journal of Cancer* **87**: 1234-1245.
- Harding, R. and C. S. Stockley (2007). "Communicating Through Government Agencies." *Annals of Epidemiology* **17**(5): S98-S102.
- Harriss, L. R., D. R. English, J. L. Hopper, J. Powles, J. A. Simpson, K. O'Dea, G. G. Giles and A. M. Tonkin (2007). "Alcohol consumption and cardiovascular mortality accounting for possible misclassification of intake: 11-year follow-up of the Melbourne Collaborative Cohort Study." *Addiction* **102**(10): 1574-1585.
- Harwood, D. G., W. W. Barker, D. A. Loewenstein, R. L. Ownby, P. St George-Hyslop, M. Mullan and R. Duara (1999). "A cross-ethnic analysis of risk factors for AD in white Hispanics and white non-Hispanics." *Neurology* **52**(3): 551-556.
- Henderson, J., R. Gray and P. Brocklehurst (2007). "Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome." *BJOG: An International Journal of Obstetrics and Gynaecology* **114**(3): 243-252.

- Hendrie, H. C., S. Gao, K. S. Hall, S. L. Hui and F. W. Unverzagt (1996). "The relationship between alcohol consumption, cognitive performance, and daily functioning in an urban sample of older black Americans." *Journal of the American Geriatrics Society* **44**(10): 1158-1165.
- Hendriks, H. F. J., J. Veenstra, E. J. M. V.-T. Wierik, G. Shaafsma and C. Kluit (1994). "Effect of moderate dose of alcohol with evening meal on fibrinolytic factors." *BMJ : British Medical Journal* **308**(6935): 1003-1006.
- Hernandez-Avila, C. A., B. J. Rounsaville and H. R. Kranzler (2004). "Opioid-, cannabis- and alcohol-dependent women show more rapid progression to substance abuse treatment." *Drug and Alcohol Dependence* **74**(3): 265-272.
- Hernández, O., M. Vogel-Sprott, T. Huchín-Ramirez and F. Aké-Estrada (2006). "Acute dose of alcohol affects cognitive components of reaction time to an omitted stimulus: differences among sensory systems." *Psychopharmacology* **184**(1): 75-81.
- Hibell, B., B. Andersson, T. Bjarnason, S. Ahlström, O. Balakireva, A. Kokkevi and M. Morgan (2000). *The ESPAD Report 1999. Alcohol and other drug use among students in 35 European countries*. Stockholm, Sweden, The Swedish Council for Information on Alcohol and Other Drugs (CAN) and the Pompidou Group at the Council of Europe.
- Hibell, B., B. Andersson, T. Bjarnason, S. Ahlström, O. Balakireva, A. Kokkevi and M. Morgan (2004). *The ESPAD Report 2003. Alcohol and other drug use among students in 35 European countries*. Stockholm, Sweden, The Swedish Council for Information on Alcohol and Other Drugs (CAN) and the Pompidou Group at the Council of Europe.
- Hillbom, M. and M. Kaste (1981). "Ethanol intoxication: a risk factor for ischemic brain infarction in adolescents and young adults." *Stroke* **12**(4): 422-425.
- Hillbom, M. E., M. Kangasaho and M. Hjelmjager (1984). "Platelet-aggregation and thromboxane-B2 formation after ethanol abuse - is there a relationship to stroke?" *Acta Neurologica Scandinavica* **70**(6): 432-437.
- Hines, L. M. and E. B. Rimm (2001). "Moderate alcohol consumption and coronary heart disease: a review." *Postgraduate Medical Journal* **77**(914): 747-752.
- Hiratsuka, Y. and G. Li (2001). "Alcohol and Eye Diseases: A Review of Epidemiologic Studies." *Journal of Studies on Alcohol* **62**: 397-402.
- Holbrook, T. L. and E. Barrett-Connor (1993). "A prospective study of alcohol consumption and bone mineral density." *British Medical Journal* **v306**(n6891): p1506(4).
- Hollman, P. C. H., M. V. D. Gaag, M. J. B. Mengelers, J. M. P. Van Trijp, J. H. M. De Vries and M. B. Katan (1996). "Absorption and disposition kinetics of the dietary antioxidant quercetin in man." *Free Radical Biology and Medicine* **21**(5): 703-707.
- Hollman, P. C. H., J. M. P. van Trijp, M. N. C. P. Buysman, M. S. v.d. Gaag, M. J. B. Mengelers, J. H. M. de Vries and M. B. Katan (1997). "Relative bioavailability of the antioxidant flavonoid quercetin from various foods in man." *FEBS Letters* **418**(1-2): 152-156.

- Holman, C. D. J., D. R. English, E. Milne and M. G. Winter (1996). "Meta-analysis of alcohol and all-cause mortality: a validation of NHMRC recommendations." *Medical Journal of Australia* **164**: 141-145.
- Hu, F. B., J. E. Manson, M. J. Stampfer, G. Colditz, S. Liu, C. G. Solomon and W. C. Willett (2001). "Diet, Lifestyle, and the Risk of Type 2 Diabetes Mellitus in Women." *N Engl J Med* **345**(11): 790-797.
- Huckenbeck, W. and W. Bonte (2003). *Alkohologie. Handbuch gerichtliche Medizin*. Berlin, Heidelberg, New York, Springer: 379-636.
- Hulthe, J. and B. Fagerberg (2005). "Alcohol Consumption and Insulin Sensitivity: A Review." *Metabolic Syndrome and Related Disorders* **3**(1): 45-50.
- Hunter, S. M., W. Bao and G. S. Berenson (1995). "Understanding the development of behaviour risk factors for cardiovascular disease in youth: the Bogalusa Heart Study." *American Journal of the Medical Sciences* **310**((suppl 1)): S114-S118.
- Kamper-Jørgensen, M., M. Grønbaek, J. Tolstrup and U. Becker (2004). "Alcohol and cirrhosis: dose-response or threshold effect?" *Journal of Hepatology* **41**(1): 25-30.
- Kato, I., Y. Kiyohara, M. Kubo, Y. Tanizaki, H. Arima, H. Iwamoto, N. Shinohara, K. Nakayama and M. Fujishima (2003). "Insulin-mediated effects of alcohol intake on serum lipid levels in a general population: The Hisayama Study." *Journal of Clinical Epidemiology* **56**(2): 196-204.
- Kennedy, R. S., J. J. Turnage, R. L. Wilkes and W. P. Dunlap (1993). "Effects of graded dosages of alcohol on nine computerized repeated-measures tests." *Ergonomics* **36**(10): 1195 - 1222.
- King, A. C., N. C. Bernardy and K. Hauner (2003). "Stressful events, personality, and mood disturbance:: Gender differences in alcoholics and problem drinkers." *Addictive Behaviors* **28**(1): 171-187.
- Kinsella, K. and V. A. Velkoff (2001). *An Aging World. Series P95/01-1*. U. S. C. Bureau. Washington, DC, U.S. Census Bureau U.S. Government Printing Office.
- Klatsky, A. L. (1995). Blood pressure and alcohol intake. Hypertension: pathophysiology, diagnosis and management. J. H. Laragh and B. M. Brenner. New York, Raven Press: 2649-2667.
- Klatsky, A. L. (2003). "Drink to Your Health?" *Scientific American* **288**(2): 75.
- Klatsky, A. L. and M. A. Armstrong (1993). "Alcoholic beverage choice and risk of coronary artery disease mortality: Do red wine drinkers fare best?" *American Journal of Cardiology* **71**(5): 467-469.
- Klatsky, A. L., M. A. Armstrong and G. D. Friedman (1992). "Alcohol and Mortality." *Annals of Internal Medicine* **117**(8): 646.
- Klatsky, A. L., M. A. Armstrong and H. Kipp (1990). "Correlates of alcoholic beverage preference: traits of persons who choose wine, liquor or beer." *Addiction* **85**(10): 1279-1289.

- Klatsky, A. L., D. Chartier, N. Udaltsova, S. Gronningen, S. Brar, G. D. Friedman and R. J. Lundstrom (2005). "Alcohol Drinking and Risk of Hospitalization for Heart Failure With and Without Associated Coronary Artery Disease." *American Journal of Cardiology* **96**(3): 346-351.
- Klatsky, A. L., G. D. Friedman and A. B. Siegelau (1974). "Alcohol Consumption Before Myocardial Infarction." *Annals of Internal Medicine* **81**(3): 294.
- Klatsky, A. L., G. D. Friedman, A. B. Siegelau and M. J. Gerard (1977). "Alcohol consumption and blood pressure Kaiser-Permanente Multiphasic Health Examination data." *N Engl J Med* **296**(21): 1194-1200.
- Klatsky, A. L. and N. Udaltsova (2007). "Alcohol Drinking and Total Mortality Risk." *Annals of Epidemiology* **17**(5, Supplement 1): S63-S67.
- Klein, R., B. E. K. Klein, S. C. Tomany and S. E. Moss (2002). "Ten-Year Incidence of Age-related Maculopathy and Smoking and Drinking: The Beaver Dam Eye Study." *American Journal of Epidemiology* **156**(7): 589-598.
- Knoops, K. T. B., L. C. P. G. M. de Groot, D. Kromhout, A.-E. Perrin, O. Moreiras-Varela, A. Menotti and W. A. van Staveren (2004). "Mediterranean Diet, Lifestyle Factors, and 10-Year Mortality in Elderly European Men and Women: The HALE Project." *JAMA* **292**(12): 1433-1439.
- Knudtson, M. D., R. Klein and B. E. K. Klein (2007). "Alcohol Consumption and the 15-year Cumulative Incidence of Age-related Macular Degeneration." *American Journal of Ophthalmology* **143**(6): 1026-1029.
- Kono, S., H. Eguchi, S. Honjo, I. Todoroki, T. Oda, K. Shinchi, S. Ogawa and K. Nakagawa (2002). "Cigarette Smoking, Alcohol Use, and Gallstone Risk in Japanese Men." *Digestion* **65**(3): 177-183.
- Kono, S., K. Shinichi, N. Ikeda, F. Yanai and K. Imanishi (1992). "Prevalence of Gallstone Disease in Relation to Smoking, Alcohol Use, Obesity, and Glucose Tolerance: A Study of Self-Defense Officials in Japan." *American Journal of Epidemiology* **136**(7): 787-794.
- Koppes, L., J. Dekker, H. Hendriks, L. Bouter and R. Heine (2006). "Meta-analysis of the relationship between alcohol consumption and coronary heart disease and mortality in type 2 diabetic patients." *Diabetologia* **49**(4): 648-652.
- Leibovici, D., K. Ritchie, B. Ledesert and J. Touchon (1999). "The effects of wine and tobacco consumption on cognitive performance in the elderly: a longitudinal study of relative risk." *Int. J. Epidemiol.* **28**(1): 77-81.
- Leitzmann, M. F., E. L. Giovannucci, E. B. Rimm, M. J. Stampfer, D. Spiegelman, A. L. Wing and W. C. Willett (1998). "The Relation of Physical Activity to Risk for Symptomatic Gallstone Disease in Men." *Annals of Internal Medicine* **128**(6): 417-425.

- Levine, J. M., G. G. Kramer and E. N. Levine (1975). "Effects of alcohol on human performance: An integration of research findings based on an abilities classification." *Journal of Applied Psychology* **60**(3): 285-293.
- Li, T.-K., J. D. Beard, W. E. Orr, P. Y. Kwo, V. A. Ramchandani and H. R. Thomasson (2000). "Variation in Ethanol Pharmacokinetics and Perceived Gender and Ethnic Differences in Alcohol Elimination." *Alcoholism: Clinical and Experimental Research* **24**(4): 415-416.
- MacDonald, I., G. Debtry and K. Westerterp (1993). Alcohol and overweight. Health issues related to alcohol consumption. P. M. Verschuren. Washington DC, ILSI Press: 264-279.
- Maclure, M. (1993). "Demonstration of Deductive Meta-Analysis: Ethanol Intake and Risk of Myocardial Infarction." *Epidemiol Rev* **15**(2): 328-351.
- Maier, S. E. and J. R. West (2001). "Drinking Patterns and Alcohol-Related Birth Defects." *Alcohol Research & Health* **25**(3): 168.
- Malinow, M. R., A. G. Bostom and R. M. Krauss (1999). "Homocyst(e)ine, diet and cardiovascular diseases: a statement for healthcare professionals from the nutrition committee, American Heart Association." *Circulation* **99**: 178-182.
- Malinski, M.K., Sesso, H.D., Lopez-Jimenez, F., Buring, J.E. and Gaziano, M. (2004) "Alcohol consumption and cardiovascular disease mortality in hypertensive men." *Archives of Internal Medicine* **164**: 623-628.
- Marshall, A. W., D. Kingstone, M. Boss and M. Y. Morgan (1983). "Ethanol elimination in males and females: relationship to menstrual cycle and body composition." *Hepatology* **3**(5): 701-707.
- May, H., S. Murphy and K. T. Khaw (1995). "Alcohol consumption and bone mineral density in older men." *Gerontology* **41**(3): 152-158.
- McAllister, I. (1995). "Health beliefs relating to alcohol and other drug use in the Australian population." *Drug and Alcohol Review* **14**: 187-199.
- McDougall, G. J., H. Becker and K. L. Areheart (2006). "Older males, cognitive function, and alcohol consumption." *Issues in Mental Health Nursing* **27**(4): 337-353.
- McElduff, P. and A. J. Dobson (1997). "How much alcohol and how often? Population based case-control study of alcohol consumption and risk of a major coronary event." *British medical journal (Clinical research ed.)* **314**(7088): 1159.
- Merriam-Webster (2007). Merriam-Webster online dictionary.
- Ministry of Health and Social Affairs (2002). Preventing alcohol-related harm. A comprehensive policy for public health in Sweden. Stockholm, Division for Public Health.
- Mitchell, M. C. (1985). "Alcohol-induced impairment of central nervous system function: Behavioral skills involved in driving." *Journal of Studies on Alcohol* **10**: 109-116.

- Mørch, L. S., D. Johansen, L. C. Thygesen, A. Tjønneland, E. Løkkegaard, C. Stahlberg and M. Grønbaek (2007). "Alcohol drinking, consumption patterns and breast cancer among Danish nurses: a cohort study." *Eur J Public Health*: ckm036.
- Mukamal, K. (2007). "Alcohol Intake and Noncoronary Cardiovascular Diseases." *Annals of Epidemiology* **17**(5, Supplement 1): S8-S12.
- Mukamal, K. J., H. Chung, N. S. Jenny, L. H. Kuller, W. T. Longstreth, M. A. Mittleman, G. L. Burke, M. Cushman, B. M. Psaty and D. S. Siscovick (2006). "Alcohol Consumption and Risk of Coronary Heart Disease in Older Adults: The Cardiovascular Health Study." *Journal of the American Geriatrics Society* **54**(1): 30-37.
- Mukamal, K. J., L. H. Kuller, A. L. Fitzpatrick, W. T. Longstreth, Jr., M. A. Mittleman and D. S. Siscovick (2003). "Prospective Study of Alcohol Consumption and Risk of Dementia in Older Adults." *JAMA* **289**(11): 1405-1413.
- Mukamal, K. J., W. T. Longstreth, Jr., M. A. Mittleman, R. M. Crum, D. S. Siscovick and D. Berezki (2001). "Alcohol Consumption and Subclinical Findings on Magnetic Resonance Imaging of the Brain in Older Adults: The Cardiovascular Health Study Editorial Comment: The Cardiovascular Health Study." *Stroke* **32**(9): 1939-1946.
- Mumenthaler, M.S., Taylor, J.L., O'Hara, R., Yesavage, J.A. (1999) Gender differences in moderate drinking effects. *Alcohol Research on Health* **23**(1): 55-64.
- Mumenthaler, M. S., J. L. Taylor, R. O'Hara, H.-U. Fisch and J. A. Yesavage (1999). "Effects of Menstrual Cycle and Female Sex Steroids on Ethanol Pharmacokinetics." *Alcoholism: Clinical and Experimental Research* **23**(2): 250-255.
- National Health and Medical Research Council (2004). Australian Drinking Water Guidelines, NHMRC.
- Nelson, H. D., M. C. Nevitt, J. C. Scott, K. L. Stone and S. R. Cummings (1994). "Smoking, alcohol, and neuromuscular and physical function of older women. Study of Osteoporotic Fractures Research Group." *Journal of the American Medical Association* **272**(23): 1825-1831.
- Nelson, L. R., A. N. Taylor, J. W. Lewis, R. E. Poland, E. Redei and B. J. Branch (1986). "Pituitary-Adrenal Responses to Morphine and Footshock Stress Are Enhanced following Prenatal Alcohol Exposure." *Alcoholism: Clinical and Experimental Research* **10**(4): 397-402.
- Nguyen, T. V., J. A. Eisman, P. J. Kelly and P. N. Sambrook (1996). "Risk Factors for Osteoporotic Fractures in Elderly Men." *American Journal of Epidemiology* **144**(3): 255-263.
- NHMRC (2001). Australian Alcohol Guidelines: Health Risks and Benefits, National Health and Medical Research Council.
- Nilsen, P., M. Holmqvist, C. Nordqvist and P. Bendtsen (2007). "Frequency of heavy episodic drinking among nonfatal injury patients attending an emergency room." *Accident Analysis & Prevention* **39**(4): 757-766.

- Nilsson, L. G., L. Backman and T. Karlsson (1989). "Priming and cued recall in elderly, alcohol intoxicated and sleep deprived subjects: a case of functionally similar memory deficits." *Psychological Medicine* **19**(423-433).
- Nordqvist, C., M. Holmqvist, P. Nilsen, P. Bendtsen and K. Lindqvist (2006). "Usual drinking patterns and non-fatal injury among patients seeking emergency care." *Public Health* **120**(11): 1064-1073.
- Norrish, A., D. North, R. O. Y. Lay Yee and R. Jackson (1995). "Do Cardiovascular Disease Risk Factors Predict All-Cause Mortality?" *Int. J. Epidemiol.* **24**(5): 908-914.
- O'Leary, C. M. (2004). "Fetal alcohol syndrome: Diagnosis, epidemiology, and developmental outcomes." *Journal of Paediatrics and Child Health* **40**(1-2): 2-7.
- Obisesan, T. O., R. Hirsch, O. Kosoko, L. Carlson and M. Parrott (1998). "Moderate wine consumption is associated with decreased odds of developing age-related macular degeneration in NHANES-1." *Journal of the American Geriatrics Society* **46**(1): 1-7.
- ONS (2005). UK General Household Survey, Office for National Statistics.
- Patterson, L.T., Hunnicutt, G.G., Stutts, M.A. (1992) Young adult's perceptions of warnings and risk associated with alcohol consumption. *J. Public Policy Market.* **11**(1): 96–103.
- Perry, I. J., S. G. Wannamethee, M. K. Walker, A. G. Thomson, P. H. Whincup and A. G. Shaper (1995). "Prospective study of risk factors for development of non-insulin dependent diabetes in middle aged British men." *British Medical Journal* **310**(6979): 560-564.
- Piazza, N. J., J. L. Vrbka and R. D. Yeager (1989). "Telescoping of alcoholism in women alcoholics." *International Journal of Addiction* **24**(1): 19-28.
- Power, C., B. Rodgers and S. Hope (1998). "U-shaped relation for alcohol consumption and health in early adulthood and implications for mortality." *The Lancet* **352**(9131): 877.
- Premier's Drug Prevention Council (2007). Community Consultation Forum: The Australian Alcohol Guidelines - Is It Time For A New Direction?
- Puddey, I. B., L. J. Beilin, R. Vandongen, I. L. Rouse and P. Rogers (1985). "Evidence for a direct effect of alcohol consumption on blood pressure in normotensive men. A randomized controlled trial." *Hypertension* **7**(5): 707-713.
- Puddey, I. B. and K. D. Croft (1999). "Alcohol, stroke and coronary heart disease. Are there anti-oxidants and pro-oxidants in alcoholic beverages that might influence the development of atherosclerotic cardiovascular disease?" *Neuroepidemiology* **18**(6): 292-302.
- Ramchandani, V. A., W. F. Bosron and T. K. Li (2001). "Research advances in ethanol metabolism." *Pathologie Biologie* **49**(9): 676-682.

- Randall, C. L., J. S. Roberts, F. K. del Boca, K. M. Carroll, G. J. Connors and M. E. Mattson (1999). "Telescoping of Landmark Events Associated with Drinking: A Gender Comparison." *Journal of Studies on Alcohol* **60**: 252-260.
- Reaven, G. M. (1993). "Role of Insulin Resistance in Human Disease (Syndrome X): An Expanded Definition." *Annual Review of Medicine* **44**(1): 121-131.
- Rehm, J., T. K. Greenfield and J. D. Rogers (2001). "Average Volume of Alcohol Consumption, Patterns of Drinking, and All-Cause Mortality: Results from the US National Alcohol Survey." *American Journal of Epidemiology* **153**(1): 64-71.
- Rehm, J., J. Klotsche and J. Patra (2007). "Comparative quantification of alcohol exposure as risk factor for global burden of disease." *International Journal of Methods in Psychiatric Research* **16**(2): 66-76.
- Rehm, J., Bondy, S. (1998) "Alcohol and all-cause mortality: an overview." *Novartis Foundation Symposium*. **216**:223-32; discussion 232-6.
- Rehm, J., M. Monteiro, R. Room, G. Gmel, D. Jernigan, U. Frick and K. Graham (2001). "Steps towards Constructing a Global Comparative Risk Analysis for Alcohol Consumption: Determining Indicators and Empirical Weights for Patterns of Drinking, Deciding about Theoretical Minimum, and Dealing with Different Consequences." *European Addiction Research* **7**(3): 138-147.
- Rehm, J., N. Rehn, R. Room, M. Monteiro, G. Gmel, D. Jernigan and U. Frick (2003). "The global distribution of average volume of alcohol consumption and patterns of drinking." *European Addiction Research* **9**(4): 147-156.
- Reid, M. C., P. H. Van Ness, K. A. Hawkins, V. Towle, J. Concato and Z. Guo (2006). "Light to Moderate Alcohol Consumption Is Associated With Better Cognitive Function Among Older Male Veterans Receiving Primary Care." *J Geriatr Psychiatry Neurol* **19**(2): 98-105.
- Renaud, S. (1984). "Risk factors for coronary heart disease and platelet functions." *Advances in experimental medicine and biology* **164**: 129-144.
- Renaud, S. C., A. D. Beswick, A. M. Fehily, D. S. Sharp and P. C. Elwood (1992). "Alcohol and platelet aggregation: the Caerphilly Prospective Heart Disease Study." *American Journal of Clinical Nutrition* **55**(5): 1012-1017.
- Renaud, S. C. and J.-C. Ruf (1996). "Effects of alcohol on platelet functions." *Clinica Chimica Acta* **246**(1-2): 77-89.
- Ridolfo, B. and C. Stevenson (2001). The quantification of drug-caused morbidity and mortality in Australia, 1998, AIHW.
- Rimm, E. B., J. Chan, M. J. Stampfer, G. A. Colditz and W. C. Willett (1995). "Prospective study of cigarette smoking, alcohol use, and the risk of diabetes in men." *BMJ : British Medical Journal* **310**(6979): 555-559.

- Rimm, E. B., P. Williams, K. Fosher, M. Criqui and M. J. Stampfer (1999). "Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors." *BMJ : British Medical Journal* **319**(7224): 1523-1528.
- Roche, A. M., K. Watt, R. McClure, D. M. Purdie and D. Green (2001). "Injury and alcohol: a hospital emergency department study." *Drug and Alcohol Review* **20**(2): 155-166.
- Saunders, J. B., M. Davis and R. Williams (1981). "Do women develop alcoholic liver disease more readily than men?" *British Medical Journal (Clinical Research Edition)* **282**(6270): 1140-1143.
- Scherr, P. A., A. Z. LaCroix, R. B. Wallace, L. Berkman, J. D. Curb, J. Cornoni-Huntley, D. A. Evans and C. H. Hennekens (1992). "Light to moderate alcohol consumption and mortality in the elderly." *Journal of the American Geriatrics Society* **40**: 651-657.
- Simons, L. A., J. McCallum, Y. Friedlander, M. Ortiz and J. Simons (2000). "Moderate alcohol intake is associated with survival in the elderly: the Dubbo Study." *The Medical journal of Australia* **173**(3): 121-124.
- Simons, L. A., J. McCallum, Y. Friedlander and J. Simons (1996). "Alcohol intake and survival in the elderly: a 77 month follow-up in the Dubbo study." *Australian and New Zealand journal of medicine* **26**(5): 662-670.
- Simons, L. A., J. McCallum, Y. Friedlander, J. Simons, I. Powell and R. Heller (1991). "Dubbo study of the elderly: sociological and cardiovascular risk factors at entry." *Australian & New Zealand Journal of Medicine* **21**: 701-709.
- Simons, L. A., J. Simons, J. McCallum and Y. Friedlander (2006). "Lifestyle factors and risk of dementia: Dubbo Study of the elderly." *The Medical journal of Australia* **184**(2): 68-70.
- Singh, R. B., H. Mori, J. Chen, S. Mendis, M. Moshiri, S. Zhu, S. H. Kim, R. G. Sy and A. M. Faruqui (1996). "Recommendations for the prevention of coronary artery disease in Asians: a scientific statement of the International College of Nutrition." *Journal of cardiovascular risk* **3**(6): 489-494.
- Single, E., L. Robson, J. Rehm, X. Xie and X. Xi (1999). "Morbidity and mortality attributable to alcohol, tobacco, and illicit drug use in Canada." *American Journal of Public Health* **89**(3): 385-390.
- Single, E. and T. Rohl (1997). The National Drug Strategy: Mapping the Future. Evaluation of the National Drug Strategy 1993-1997. Canberra, AGPS.
- Smith, W. and P. Mitchell (1996). "Alcohol intake and age-related maculopathy." *American Journal of Ophthalmology* **122**(5): 743-745.
- Solomon, C. G., F. B. Hu, M. J. Stampfer, G. A. Colditz, F. E. Speizer, E. B. Rimm, W. C. Willett and J. E. Manson (2000). "Moderate Alcohol Consumption and Risk of Coronary Heart Disease Among Women With Type 2 Diabetes Mellitus." *Circulation* **102**(5): 494-499.

- Stampfer, M. J., J. H. Kang, J. Chen, R. Cherry and F. Grodstein (2005). "Effects of moderate alcohol consumption on cognitive function in women." *The New England journal of medicine* **352**(3): 245-253.
- Stockley, C.S. (2007). "Recommendations on Alcohol Consumption: An International Comparison". Accepted for publication in *Contemporary Drug Problems* November 2007.
- Stockwell, T., D. Hawks, E. Lang and P. Rydon (1996). "Unravelling the preventive paradox for acute alcohol problems." *Drug and Alcohol Review* **15**(1): 7 - 15.
- Stockwell, T. R., D. Heale, T. N. Chikritzhs, P. Dietze and P. Catalano (2002). "How much alcohol is drunk in Australia in excess of the new Australian alcohol guidelines?" *Medical Journal of Australia* **176**: 91-92.
- Substance Abuse and Mental Health Services Administration (2003). Co-Occurring Disorders: Integrated Dual Disorders Treatment: Implementation Resource Kit. Rockville, Maryland, Center for Mental Health Services.
- Substance Abuse and Mental Health Services Administration (2003). National Household Survey on Drug Abuse, 2001, Office of National Drug Control Policy.
- Suhonen, O., A. Aromaa, A. Reunanen and P. Knekt (1987). "Alcohol consumption and sudden coronary death in middle-aged Finnish men." *Acta medica Scandinavica* **221**(4): 335-341.
- Tagawa, M., M. Kano, N. Okamura, M. Itoh, E. Sakurai, W. T and K. Yanai (2000). "Relationship between effects of alcohol on psychomotor performances and blood alcohol concentrations." *Japanese Journal of Pharmacology* **83**: 253-260.
- Tanaka, E. (1999). "Gender-related differences in pharmacokinetics and their clinical significance." *Journal of Clinical Pharmacy and Therapeutics* **24**(5): 339-346.
- Tanasescu, M., F. B. Hu, W. C. Willett, M. J. Stampfer and E. B. Rimm (2001). "Alcohol consumption and risk of coronary heart disease among men with type 2 diabetes mellitus." *Journal of the American College of Cardiology* **38**(7): 1836-1842.
- Teri, L., J. P. Hughes and E. B. Larson (1990). "Cognitive deterioration in Alzheimer's disease: behavioural and health factors." *J Gerontol* **42**: 3-10.
- Thadhani, R., C. A. Camargo, Jr., M. J. Stampfer, G. C. Curhan, W. C. Willett and E. B. Rimm (2002). "Prospective Study of Moderate Alcohol Consumption and Risk of Hypertension in Young Women." *Archives of internal medicine* **162**(5): 569-574.
- The Gut Foundation (1984). Alcohol and the liver. Sydney, Gut Foundation.
- Thygesen, L. C., N. Keiding, C. Johansen and M. Grønbaek (2007). "Changes in alcohol intake and risk of upper digestive tract cancer." *Acta Oncologica* **46**(8): 1085-1089.
- Tjønneland, A., J. Christensen, A. Olsen, C. Stripp, B. Thomsen, K. Overvad, P. Peeters, C. van Gils, H. Bueno-de-Mesquita, M. Ocké, et al. (2007). "Alcohol intake and breast cancer risk: the

- European Prospective Investigation into Cancer and Nutrition (EPIC)." *Cancer Causes and Control* **18**(4): 361-373.
- Tolstrup, J. S., M. K. Jensen, A. Tjønneland, K. Overvad and M. Grønbaek (2004). "Drinking pattern and mortality in middle-aged men and women." *Addiction* **99**(3): 323-330.
- Tolvanen, E., K. Seppä, T. Lintonen, P. Paavilainen and M. Jylhä (2005). "Old people, alcohol use and mortality. A ten-year prospective study." *Aging clinical and experimental research* **17**(5): 426-433.
- Trichopoulou, A. and E. Critselis (2004). "Mediterranean diet and longevity." *European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP)* **13**(5): 453-456.
- U.S. Department of Health and Human Services and U.S. Department of Agriculture (2005). *Dietary Guidelines for Americans*. U.S. Department of Health and Human Services and U.S. Department of Agriculture, U.S. Government Printing Office, Washington, DC.
- Van de Water, H. A. and H. C. Boshuizen (1995). The impact of substitute morbidity and mortality on public health policy. Leiden, TNA Prevention and Health, Division of Public Health and Prevention.
- van der Gaag, M. S., J. B. Ubbink, P. Sillanaukee, S. Nikkari and H. F. J. Hendriks (2000). "Effect of consumption of red wine, spirits, and beer on serum homocysteine.(Brief Article)(Statistical Data Included)." *The Lancet* **355**(9214): 1522.
- Voigt, L. F., T. D. Koepsell, J. L. Nelson, C. E. Dugowson and J. R. Daling (1994). "Smoking, Obesity, Alcohol Consumption, and the Risk of Rheumatoid Arthritis." *Epidemiology* **5**(5): 525-532.
- Wallgren, H. and H. Barry (1970). Actions of alcohol. Amsterdam, Elsevier.
- Waters, K. (2005). Precursors and consequences of heavy alcohol use in adolescence. Australian Institute of Family Studies, The University of Melbourne.
- Welch, G. N. and J. Loscalzo (1998). "Homocysteine and Atherothrombosis." *New England Journal of Medicine* **338**(15): 1042-1050.
- Wells, S. and S. Macdonald (1999). "The relationship between alcohol consumption patterns and car, work, sports and home accidents for different age groups." *Accident Analysis & Prevention* **31**(6): 663-665.
- Westerterp, K. R. (1995). "Alcohol calories do not count the same as other calories." *International Journal of Obesity* **19**(Suppl. 2): 14-15.
- White, I., Altmann, D., and Nanchahal, K. (2004) "Mortality in England and Wales attributable to any drinking, drinking above sensible limits and drinking above lowest risk-level." *Addiction* **99**: 749-756.

- White, I., Altmann, D., and Nanchahal, K. (2002) "Alcohol consumption and mortality: modelling risks for men and women at different ages. *British Medical Journal*. **325**.
- White, V. and J. Hayman (2006). Australian secondary school students' use of alcohol in 2005. D. S. B. Australian Government Department of Health and Ageing, Australian Government Printing Service:Canberra.
- Wietlisbach, V., F. Paccaud, M. Rickenbach and F. Gutzwiller (1997). "Trends in Cardiovascular Risk Factors (1984-1993) in a Swiss Region: Results of Three Population Surveys." *Preventive Medicine* **26**(4): 523-533.
- World Health Organisation (2001). Global Status Report: Alcohol and Young People, WHO.
- World Health Organisation (2001). WHO Regional Office for Europe Declaration on Young People and Alcohol. Geneva, WHO.
- World Health Organization (1999). Global Status Report on alcohol 1999. Geneva, WHO.
- World Health Organisation (2003). World Health Report. Shaping the Future, Geneva, WHO.
- World Health Organization (2005). Public health problems caused by harmful use of alcohol. 58th World Health Assembly. Geneva, WHO.
- World Health Organization. (2007). "World Health Statistics 2007." from www.who.int/whosis/.
- Wright, C. B., M. S. V. Elkind, T. Rundek, B. Boden-Albala, M. C. Paik and R. L. Sacco (2006). "Alcohol Intake, Carotid Plaque, and Cognition: The Northern Manhattan Study." *Stroke* **37**(5): 1160-1164.
- Young, A. and J. Powers (2005). Australian Women and Alcohol Consumption: Australian Longitudinal Study on Women's Health 1996-2003, Australian Government Department of Health and Ageing.
- Zimmet, P.Z., Alberti, K.G. and Shaw, J.E. (2005) Mainstreaming the metabolic syndrome: a definitive definition. This new definition should assist both researchers and clinicians. *Medical Journal of Australia* **183**:175-176.
- Zuccala, G., G. Onder, C. Pedone, M. Cesari, F. Landi, R. Bernabei and A. Cocchi (2001). "Dose-Related Impact of Alcohol Consumption on Cognitive Function in Advanced Age: Results of a Multicenter Survey." *Alcoholism: Clinical and Experimental Research* **25**(12): 1743-1748.