Mortality and morbidity risks from alcohol consumption in the UK:

Analyses using the Sheffield Alcohol Policy Model (v.2.7) to inform the UK Chief Medical Officers' review of the UK lower risk drinking guidelines

Final report

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John Holmes

Colin Angus

Penny Buykx

Abdallah Ally

Tony Stone

Petra Meier

Alan Brennan

1. Executive Summary

1.1. Main conclusions

This study estimates the alcohol consumption levels associated with two definitions of 'low risk' drinking which were developed when selecting guideline thresholds in Canada and Australia. These definitions are applied to UK data on alcohol consumption, hospitalisation and mortality alongside international epidemiological study evidence within the Sheffield Alcohol Policy Model (v.2.7). The following conclusions for setting a mean daily or mean weekly consumption guideline were found:

- The Canadian approach sets the guideline threshold at the consumption level where population risks and possible benefits of drinking are balanced. That is, the same number of total deaths would occur in the population at this level of drinking as if every person were an abstainer, or in other words the net deaths due to alcohol would be zero. Using this approach, the implied threshold for males should be between 1.4 and 3.4 units per day depending on whether drinkers consume daily or once per week. The implied threshold for females should be between 1.9 and 10.0 units per day. The latter figure is higher because females have low mortality risk for causes which are associated with intoxication.
- The Australian approach sets the guideline threshold at the consumption level where if everyone drank at this level 1% of population deaths would be due to alcohol. Using this approach, the implied threshold for males should be between 2.0 and 6.0 units per day depending on whether drinkers consume daily or once per week. The implied threshold for females should be between 2.2 and 12.0 units per day.
- These estimated implied thresholds are subject to several uncertainties arising from sources including underestimation of alcohol consumption, uncertainty over cardioprotective effects of moderate drinking and necessary assumptions within the modelling undertaken here. The nature and scale of that uncertainty is discussed in this report. A number of expert judgements will be required to select an appropriate guideline threshold based on the wide range of evidence available.
- The estimated thresholds are based on aggregating results from age and gender specific risks for all males and all females. Using the same approaches to derive thresholds for specific population groups, such as young adults, is problematic and the research team would currently not recommend doing so. This is because of the different health risks each group faces. For example, while aged 18-24, males have a low absolute risk of mortality and a particularly low risk of mortality from chronic disease. A large proportion of deaths which do occur in this age group are due to acute causes (e.g. falls, road traffic accidents) and many of these are attributable to alcohol. As a result, alcohol-attributable deaths would be a large proportion of all deaths in this age group even if everyone in the group drank at a low level. Thus the implied guideline under the Australian approach would be very low. Similar problems using the Canadian approach are described in the main report.

1.2. Background to this report

This report was commissioned by Public Health England to inform the UK Chief Medical Officers' review of the country's lower risk drinking guidelines. A key challenge in developing such guidelines is selecting the consumption level above which drinking is not recommended. Previous guideline development processes in the UK and internationally have often relied on the judgement of expert committees, with limited transparency on how evidence informed decision-making. Seeking to address this problem, recent updates of drinking guidelines in Canada and Australia adopted more transparent methods. Guideline consumption thresholds were derived by applying objective and clearly stated definitions of 'lower risk' to analyses of the risks associated with drinking at different levels. These moves towards greater transparency inform the present report in which the Canadian and Australian approaches are adapted and expanded to derive potential guideline thresholds for the UK.

In Canada, the guideline was based around epidemiological evidence suggesting that low levels of alcohol consumption are associated with reduced annual risk of mortality when compared with not drinking (i.e. there is some evidence that low levels of alcohol consumption provide a 'protective effect'). The Canadian guidelines for average daily consumption were thus set at the level at which risks of drinking were equivalent to those of abstaining from alcohol. In other words, the threshold level was chosen such that, at the population level, the estimated harmful effects and the estimated protective effects were counterbalanced equally against each other and net annual mortality risk was the same as if everyone abstained from alcohol.

In Australia, an alternative approach was used which focused on the absolute mortality risk due to drinking compared to the mortality risks from other causes. Thus the Australian guideline was set such that if the population all drank at that level, 1% of annual deaths would be attributable to alcohol. Selection of this 1% level was informed by guidance and regulations relating to other environmental and health risks and also by risks which appear to be acceptable to the public for other activities (e.g. the risk associated with driving a car regularly).

Although these approaches have the merit of providing a transparent and objective means of deriving a guideline threshold, each can be criticised. For example, the Canadian approach is based around protective effects of moderate drinking which are disputed and the Australian approach uses a somewhat arbitrary threshold of 1% of deaths being attributable to alcohol. This report does not recommend one approach ahead of the other and instead presents results for both approaches. It also presents additional results based on expansions of each approach (e.g. results are presented for the point at which risk reduction relative to abstainers are greatest and the point at which 2% of deaths are alcohol attributable).

1.3. Purpose of this report

This report has three main aims:

1. To provide quantified risk estimates for the mortality and morbidity (defined as person-specific hospital admissions) associated with different levels and patterns of alcohol consumption for drinkers in the UK.

2. To report the guideline thresholds derived when applying the Canadian and Australian approaches to UK mortality and morbidity risk estimates.

3. To provide commentary on the limitations of the available evidence and considerations for its use in proposing new lower risk drinking guidelines for the UK.

Recommendation of specific guideline thresholds is not the responsibility of the authors of this report. The report is intended to be used alongside other evidence to inform the deliberations of the Guideline Development Group.

The specific research questions are:

- For males and females, what would be the estimated relative risk of alcohol-related mortality and morbidity associated with different levels and patterns of alcohol consumption in the UK population?
- For males and females, what would be the proportion of all annual mortalities that are alcohol attributable for different levels and patterns of alcohol consumption in the UK population?
- What considerations should inform the use of the results in developing new lower risk drinking guidelines for the UK general adult population?

1.4. Overview of methods

Risk estimates are produced using the Sheffield Alcohol Policy Model (SAPM) v.2.7; a mathematical simulation model previously used to appraise UK and international alcohol policy options. The key data inputs into SAPM are baseline levels of current UK alcohol consumption, current levels of alcohol-related mortality and morbidity (defined as person-specific hospital admissions) and, most importantly, international and UK-specific evidence relating different levels and patterns of alcohol consumption to risk of mortality or morbidity from 43 health conditions causally related to alcohol consumption. This evidence is taken from a combination of published meta-analyses of risk relationships, analyses of the proportion of cases of alcohol-related conditions attributable to alcohol and UK mortality and morbidity rates for the 43 conditions.

The 43 conditions are divided into four types:

1. *Wholly-attributable, chronic*: conditions which cannot occur in the absence of alcohol consumption and for which risk of occurrence changes with chronic exposure to alcohol, measured here as mean weekly consumption (e.g. alcoholic liver disease).
2. *Wholly-attributable, acute*: conditions which cannot occur in the absence of alcohol consumption and for which risk of occurrence changes with acute exposure to alcohol including intoxication, measured here as peak daily consumption over the previous seven days (e.g. ethanol poisoning).
3. *Partially-attributable, chronic*: conditions which can occur without alcohol consumption but for which the risk of occurrence changes with chronic exposure to alcohol (e.g. cancer of the oesophagus). For a number of primarily cardiovascular conditions within this category, lower levels of alcohol consumption are associated with reduced disease risk relative to abstainers (a so-called 'protective effect') and this is accounted for within SAPM.
4. *Partially-attributable, acute*: conditions which can occur without alcohol consumption but for which the risk of occurrence changes with acute exposure to alcohol including intoxication (e.g. falls).

Three sets of risk estimates are derived separately for males and females describing the relationship between:

- Mean weekly consumption and risk of chronic alcohol-related conditions;
- Peak daily consumption and risk of acute alcohol-related conditions;
- Mean weekly consumption distributed evenly over one to seven days and risk of all alcohol-related health conditions.

Importantly, the analysis accounts for frequency of drinking (which was incorporated into the analysis of mean consumption in Australia but not Canada). Thus there are seven risk curves drawn for males and seven for females, and these curves correspond to whether a given level of mean weekly consumption is drunk across 7, 6, 5, 4, 3, 2, or 1 day(s). The number of drinking days across which consumption is distributed affects the balance of chronic risk (due to the mean weekly consumption) and acute risk (due to the intoxication effects of drinking on a single day). Drinking ten units per week will accrue more acute risk if consumed on one day as opposed to across several days.

1.5. Summary of main findings

Table 1 presents the implied lower risk drinking guideline thresholds derived when using the Canadian and Australian approaches to analyse mortality risks. Thresholds are presented as both units per week and also units per day as the latter more intuitively demonstrates the effect of consumption frequency on the guideline threshold.

Table 1: Implied lower risk drinking guidelines under different approaches by number of drinking days and based on mortality data

		Units per week		Units per day	
Threshold	**Drinking days per week**	**Males**	**Females**	**Males**	**Females**
Canadian: RR=1.0	1	3.4	10.0	3.4	10.0
	2	5.8	12.0	2.9	6.0
	3	7.4	12.8	2.5	4.3
	4	8.2	13.2	2.1	3.3
	5	8.9	13.4	1.8	2.7
	6	9.4	13.6	1.6	2.3
	7	9.8	13.6	1.4	1.9
Australian: Proportion deaths attributable alcohol=1%	1	6.0	12.0	6.0	12.0
	2	9.4	14.0	4.7	7.0
	3	11.3	14.8	3.8	4.9
	4	12.3	15.2	3.1	3.8
	5	13.1	15.4	2.6	3.1
	6	13.7	15.6	2.3	2.6
	7	14.1	15.7	2.0	2.2

To increase understanding of the absolute alcohol-attributable mortality risk associated with different patterns of consumption, Table 2 and Table 3 show for males and females respectively the absolute lifetime risk of death as a result of drinking for a range of mean consumption levels and frequencies of drinking.

Table 2: Absolute lifetime risk of male alcohol-attributable mortality by consumption frequency and quantity

Mean consumption (units/week)	Drinking days per week						
	7	6	5	4	3	2	1
7	-0.0052	-0.0047	-0.0039	-0.0027	-0.0012	0.0027	0.0142
14	0.0095	0.0106	0.0121	0.0144	0.0178	0.0252	0.0465
21	0.0285	0.0300	0.0322	0.0355	0.0409	0.0514	0.0814
28	0.0511	0.0531	0.0558	0.0599	0.0670	0.0802	0.1178
35	0.0773	0.0796	0.0829	0.0877	0.0960	0.1114	0.1550
42	0.1070	0.1097	0.1133	0.1187	0.1277	0.1449	0.1928
49	0.1403	0.1431	0.1471	0.1529	0.1621	0.1806	0.2312

Table 3: Absolute lifetime risk of female alcohol-attributable mortality by consumption frequency and quantity

Mean consumption (units/week)	Drinking days per week						
	7	6	5	4	3	2	1
7	-0.0231	-0.0228	-0.0224	-0.0218	-0.0208	-0.0188	-0.0130
14	0.0018	0.0023	0.0031	0.0043	0.0061	0.0099	0.0205
21	0.0367	0.0374	0.0384	0.0400	0.0425	0.0476	0.0625
28	0.0776	0.0785	0.0797	0.0816	0.0846	0.0907	0.1089
35	0.1230	0.1240	0.1254	0.1275	0.1309	0.1377	0.1582
42	0.1720	0.1731	0.1746	0.1768	0.1806	0.1880	0.2096
49	0.2239	0.2251	0.2267	0.2290	0.2330	0.2408	0.2626

Black text, green background - overall protective effect
Red text, light orange background - overall lifetime risk less than 1 in 100
Black text, orange background - overall lifetime risk at least 1 in 100, but below 1 in 10
White text, red background - overall lifetime risk at least 1 in 10

F1: Using the Canadian approach, the implied drinking guideline for males is between 1.4 units per day if drinking every day and 3.4 units per day if drinking once per week (see Figure 6 for the male total alcohol-related mortality relative risk curve).

F2: Using the Canadian approach, the implied drinking guideline for females is 1.9 units per day if drinking every day (slightly higher than the male figure of 1.4 units per day) and 10.0 units per day if drinking only once per week (see Figure 7 for the female total alcohol-related mortality relative risk

curve). This figure of 10.0 units per day is estimated to be much higher for females than males (3.4 units per day) and this is because females have much lower absolute risk of acute conditions than males, even at high consumption levels. Thus the implied female threshold differs from the male threshold by being more strongly influenced by chronic risks, which are associated with mean weekly consumption, and less affected by acute risks, which are influenced by consumption frequency. More generally, it should be noted that acute risks are related to drinking on a single occasion and are partly attributable to factors including the drinking context (e.g. at home or in a bar) and the characteristics of the drinker. Thus the estimated threshold of 10.0 units if drinking once per week reflects the drinking contexts and drinker characteristics of an average female in the population rather than those of specific female drinkers at which any guideline may be targeted.

F3: The implied thresholds using the Australian approach are all marginally higher than those implied using the Canadian approach. This should be expected as the Canadian approach is based around the consumption level at which no deaths are attributable to alcohol and the Australian approach is defined by the consumption level at which 1% of annual deaths are attributable to alcohol.

F4: Using the Australian approach, the implied drinking guideline for males is between 2.0 units per day if drinking every day and 6.0 units per day if drinking once per week (see Figure 8 for the male total alcohol-related mortality curve showing the estimated proportion of annual deaths which are alcohol-related).

F5: Using the Australian approach, the implied drinking guideline for females is 2.2 units per day if drinking every day and 12.0 units per day if drinking once per week (see Figure 9 for the female total alcohol-related mortality curve showing the estimated proportion of annual deaths which are alcohol-related). As with the Canadian approach, the 12.0 units per day figure is estimated to be much higher than the male equivalent (6.0 units) due to low absolute risk of acute alcohol-related mortality among females and the resulting different trade-off of chronic and acute risks when compared to males.

F6: These implied guideline thresholds for males are generally lower than those in the current UK lower risk drinking guidelines (assuming at least three drinking days per week) whereas for females they are similar to the current guidelines. The implied guidelines thresholds are also lower than those selected in Canada and Australia.

F7: The current UK guidelines are higher for males than for females whereas the results presented here suggest the reverse – that guidelines should be slightly lower for males than females if targeted at those drinking on most days (i.e. four or more days a week). Using the Australian approach, the differences between males and females are small and this aligns with the conclusions reached in Australia where risks for males and females were found to not be significantly different at the consumption levels of interest. As a result, the resulting Australian guidelines did not distinguish between males and females.

F8: Findings F1 to F5 all consider the male or female population as a group and essentially average the different risks faced by people aged 18 through to 89. Risk curves actually vary substantially by age and there are particular age differences in both the balance of acute vs. chronic risks and the underlying absolute level of health risk. These differences create problems for the Canadian and

Australian approaches and suggest they are not well-suited to deriving age group-specific guideline thresholds.

For example, younger age groups (i.e. 18-24, 25-34) have very low absolute mortality risk and particularly low chronic disease mortality risk, including for cardiovascular diseases. This means potential cardioprotective effects have only a minor effect at very low consumption levels when calculating this age group's mortality risk across all alcohol-related conditions. Instead, the alcohol-related mortality risk curve is dominated by the acute risks which account for most alcohol-related mortality at younger ages. Therefore, any guideline threshold derived for the under-35s using the Canadian approach would be very low. Similarly, under the Australian approach, younger age groups' combination of very low absolute mortality risk but relatively high acute alcohol-attributable mortality risk means alcohol-attributable deaths account for a large percentage of total deaths in this age group. An age-specific guideline threshold derived using the Australian approach which is based on the ratio of alcohol-attributable deaths and total deaths, would therefore also be very low.

If the Guideline Development Guide wished to derive age-specific guideline thresholds, then one alternative would be to consider methods based around each age group's absolute *annual* risk of mortality. However, the appropriate method for deriving a guideline threshold under such an approach is unclear. The Australian 1 in 100 mortality risk could be adapted, although it is questionable whether the conceptual rationale underlying this definition of acceptable *lifetime* risk can be considered equally valid for annual risk and for risk at specific ages.

F9: Evidence that lower levels of alcohol consumption are associated with reduced mortality risks for cardiovascular disease exerts a strong influence on implied guideline thresholds derived under the Canadian and Australian approaches. This is because the apparent cardioprotective effects of moderate drinking influence the shape of the overall alcohol-related mortality risk curve. However, beyond this, potential health benefits of moderate drinking have only limited relevance when selecting population-level lower risk drinking guidelines. This conclusion is based on balancing four findings.

First, although reduced alcohol-attributable mortality risks at lower consumption levels remain after accounting for risks from other alcohol-related conditions where there is no evidence of protective effects, the level of risk reduction relative to abstainers is low. The lowest relative risk of mortality compared to abstainers is 0.97 for females and 0.99 for males. This risk reduction is associated with very low levels of consumption, namely 2.4 units per week for males drinking daily and 3.4 units per week for females drinking daily (see Table 14).

Second, the Canadian approach derives a guideline threshold from the consumption level where there are no further reduced mortality risks. The analyses presented here suggest very small risk reductions for alcohol-related mortality persist up to 9.8 units per week for males drinking daily and 13.6 units per week for females drinking daily (see Figure 6 and Figure 7).

Third, independent of alcohol consumption, people of each age and sex are at a different level of baseline risk for mortality from any cause and from each specific alcohol-related cause. This means risk reductions related to cardiovascular disease are of different importance to each demographic group's overall mortality risk. Analysis of variation in alcohol-related risk by age suggests that cardioprotective effects are only sufficient to provide substantial risk reductions from low levels of

drinking for females aged over 55 (see Figure 15). For other groups, risk reductions for cardiovascular conditions are either largely or wholly outweighed by risk increases for other conditions.

Fourth, strong concerns over the robustness of the evidence base for cardioprotective effects mean that, even for older females, mortality risk reductions from moderate alcohol consumption may be minimal or absent.

F10: The sensitivity analyses suggest the implied guideline thresholds and the risk curves from which they are derived are sensitive to the use of alternative assumptions within the modelling which underpins them. For most sensitivity analyses (e.g. modelling a ten year time period, assuming lower CVD mortality rates, varying the threshold within the Australian approach) the size of variation in implied guideline thresholds from the base case is of the order of three units per week. However, for other sensitivity analyses (e.g. reintroducing threshold effects used in previous versions of SAPM, assuming no cardioprotective effects from moderate alcohol consumption) the variation in results from the base case are larger and of the order of ten units per week. These results suggest the base case should not be accepted uncritically as the implied guideline thresholds are sensitive to alternative assumptions and baseline data and there are not strong arguments for preferring the base case specifications over those used in the sensitivity analyses.

1.6. Considerations for using the results to inform selection of new lower risk drinking guideline thresholds

It is beyond the scope of this project report to make specific recommendations on appropriate guideline thresholds or to specify the processes the Guideline Development Group should follow when using this report. Nonetheless, a number of expert judgements will be required by the group to translate the model results and other available evidence into a proposed guideline threshold. Despite the recent shift in international guideline development processes away from 'opaque collective expert opinion' and toward transparent empirically-driven methods, such judgements cannot be avoided and any guidelines which emerge from the review process will reflect considerations beyond the numerical analyses presented in this report. Thus, the final guideline should represent a holistic expert judgement by the Guideline Development Group accounting for the modelling results, the various points of discussion raised throughout this report and further evidence sources and considerations identified in the group's wider deliberations.

Based on analysis of the limitations of the research literature on alcohol epidemiology and of SAPM itself, the following considerations should usefully inform that judgement.

C1: Clear and scientifically-robust conclusions can be drawn regarding the broad levels of risk associated with different levels and patterns of alcohol consumption. The level of risk for a given level of mean weekly consumption varies depending on the consumption pattern (e.g. weekly vs. daily) as this alters the balance of acute and chronic risks the drinker is exposed to.

C2: Despite this, the consumption levels at which the Canadian and Australian definitions of low risk drinking are exceeded are subject to uncertainty due to limitations in the available evidence. In some cases expert judgements can be made to assess the likely direction of effect on risk estimates

of these limitations. In other cases, evidence available in the research literature offers a partial understanding of the nature and scale of uncertainty. This evidence can be considered alongside the results presented here when selecting lower risk drinking guideline thresholds.

C3: The nature and level of risk associated with a given consumption level or pattern varies markedly across the population. Results presented here demonstrate this for gender and age but similar points apply to other characteristics (e.g. socioeconomic status, health status, genetic profile). As a result, it is not recommended that either the Canadian or Australian approach are used to derive age-specific guidelines. The Guideline Development Group may also wish to consider whether the rationale for these approaches is undermined if the population guideline is derived from averaging highly diverse risks across the population and does not correspond to the risk profile of some groups of interest.

C4: Public health guidelines must inevitably strike a balance between being specific enough to reflect variations in risk across the population and remaining sufficiently broad to be communicable via population-level health promotion campaigns. One approach to addressing heterogeneity in risks is for the Guideline Development Group to consider who the key target populations for each guideline are and, where population-level guidelines are used (e.g. on bottle labels or television advertising where space is limited), ensure the guidelines are appropriate for those target populations.

C5: Alcohol consumption is associated with a wide range of risks. This report addresses mortality and morbidity from alcohol-related health conditions; however, alcohol is also strongly associated with outcomes including crime, income and employment, family well-being, individual well-being (in both positive and negative ways) and child development. The Guideline Development Group should give consideration to these factors alongside the risks for health conditions modelled here.

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2. Introduction

In 2012 the UK Chief Medical Officers (CMO) began a review of the country's lower risk drinking guidelines. An expert advisory group, hereafter the 'Guideline Development Group', was appointed to provide scientific guidance, make recommendations on whether new guidelines should be developed and, if so, advise on what they should be. To inform the Guideline Development Group's considerations, Public Health England commissioned the University of Sheffield to conduct analyses quantifying the risks to UK drinkers associated with different levels and patterns of alcohol consumption. This report presents the methods and findings for those analyses alongside advisory commentary on their limitations and considerations for their use in developing revised lower risk drinking guidelines.

2.1. Current use of lower risk drinking guidelines

Public health guidance on alcohol consumption is provided by Government bodies in most developed countries.[1] Such guidance is argued to serve multiple functions including informing the public about scientific evidence on the risks of drinking, encouraging lower levels of consumption and providing a standard against which health professionals can assess patient behaviour and discuss it with them.[1,2] Guidance usually takes the form of guidelines regarding 'low risk', 'no risk' or 'safe' levels of alcohol consumption over a given time period, usually a day or week. The current UK drinking guidelines for the general population state:

> *"Men should not regularly drink more than 3-4 units a day and women 2-3 units a day where regularly means drinking this amount most or every day."*[1]

In some countries, separate guidelines are provided for regular consumption and consumption on a single occasion, for men and women and for high risk groups such as the young, the elderly and pregnant women.[3] The focus of this report is on providing evidence to inform gender-specific low risk guidelines for both regular and single occasion drinking within the UK general adult population.

2.2. Setting guideline levels

A key challenge for those developing or revising lower risk drinking guidelines, is selecting the consumption level at which the guideline should be set. No internationally-agreed threshold exists and variations between countries in drinking patterns, underlying risks to health and population demographics mean an international standard is not recommended.[4] However, there is also no agreement on the appropriate processes for setting a threshold in a single country, although steps towards this have been taken in recent years and these are briefly summarised below.

The terms 'no risk' and 'safe' drinking guidelines have largely been abandoned in favour of 'low risk' drinking guidelines. This reflects increased evidence of associations between low-level alcohol consumption and several diseases such as cancers of the mouth, throat, breast and digestive system.[5] However, adoption of the term 'low risk' creates a problem as definitions of what constitutes a low risk are subjective and risks are also context-specific. For example, different drinkers may be willing to accept greater or lesser degrees of risk and the risks of consumption on a single occasion depend on where the drinking takes place and the characteristics of the drinker.

Commentary on previous guideline development processes acknowledges that when attempting to define low risk and select a guideline consumption level, the opinions and values of health experts

have often played an important role. For example, public health researchers involved in developing guidelines for Australia have argued:

> *"For most specific diseases and for injuries, there is no basis at all in the data for a particular cut-off [threshold]… Committees seem to have drawn a deep collective breath and simply voted for specific cut-off levels. Particularly for cut-offs for single-occasion drinking… drawing the line is a matter of opaque collective expert opinion"*.[5 p.137]

In light of these concerns, recent drinking guideline review processes in Canada and Australia sought to develop more transparent and empirically-based approaches.

2.2.1. The Canadian approach

The Canadian approach was based around the 'j-curve' seen when plotting all-cause mortality risks against levels of alcohol consumption.[6] The j-shape is attributable to the purported protective effect of moderate drinking against heart disease and other cardiovascular conditions (see Figure 1 and Box 1). To derive a guideline threshold, the Canadian group argued that low risk could be defined as the point "where potential benefits and risks were balanced for the average person in comparison with lifetime abstainers".[7 p.126] As shown in Figure 1, the threshold was thus set at the point where the j-curve crosses the Relative Risk = 1 line. In other words, the point where drinking more alcohol would lead to a higher risk compared to an abstainer and drinking less alcohol would lead to a lower risk compared to an abstainer.

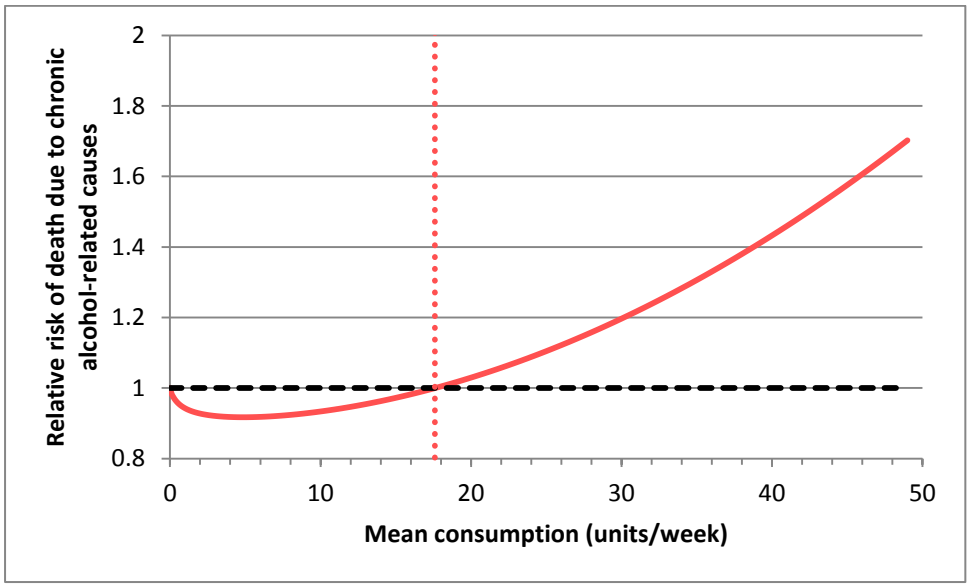

Figure 1: Example of the j-curve for relative risks of alcohol consumption

Box 1: The j-curve.

The j-curve refers to the shape of the curve formed by a graph plotting mean grams of alcohol consumed per day against risk of mortality from alcohol-related causes and particularly from cardiovascular diseases. At low levels of consumption, the mortality risk for many cardiovascular diseases is consistently observed to be less than the risk for abstainers. This suggests that moderate drinking may protect against cardiovascular disease. However, this interpretation of the finding is contested by many researchers who point to a lack of well-evidenced biological processes which could explain the effect. There are also concerns about the research methods which lead to the finding and these are discussed in the Discussion section of this report.

2.2.2. The Australian approach

A different approach was used in Australia where low risk was defined with reference to: (a) other official standards on environmental and health risks and (b) evidence on the risks associated with other everyday activities such as driving a car. A full discussion of these considerations is available in the Australian guideline development group's report.[8] Briefly, most environmental risk thresholds permit only very small risks. For example, in Australia, water toxins are not permitted in concentrations which would lead to more than one additional cancer per million people if consumed across a life time (i.e. a 1 in 1,000,000 risk threshold).[5] Application of such thresholds to alcohol consumption would lead to advising virtually no drinking. However, most of these environmental risk thresholds are set to ensure industry does not harm the public. An alternative threshold is one aimed at preventing individuals from harming themselves, such as thresholds determining the point at which Government should intervene and remove the public's choice to make their own risk decisions. The Australian guideline development group referred to Australian regulations allowing the forcible removal of people from their homes to avoid radioactive contamination if the risk of death was 1 in 100. However, as this threshold determines when risk is sufficiently high for Government to remove people's freedom to make their own health decision, it is still an imperfect basis for deriving a lower risk drinking guideline. Finally, the Australian group noted that a 1996 paper found the lifetime risk of dying in a traffic accident in the US for someone who drives 10,000 miles a year was estimated to be 1 in 60,[8,9] suggesting this is perceived by the public, to the extent they are aware of it, as an acceptable risk. Based on these public behaviour and environmental safety standards, it was concluded that an acceptable risk, and thus 'low risk', for voluntary activities such as drinking can reasonably be defined as a 1 in 100 lifetime risk of dying from the activity. For the present purposes, this can be alternatively phrased as the consumption level within the population below which no more than 1% of all deaths are attributable to alcohol.

2.2.3. Comparison and critique of the Canadian and Australian approaches

Although both approaches are more transparent than many previous guideline development processes, neither the Canadian or Australian approach is wholly satisfactory. For example, the Australian approach retains considerable subjectivity in its selection of the 1 in 100 threshold[3] and relies for this on the limited available evidence on acceptable risks. There is also no particular reason why low risk should be defined using a round number and not 1 in 82 or 1 in 137 and using these alternative but equally valid thresholds may affect the guideline consumption levels. Moreover, the Australian group acknowledge that their definition of low risk is partly based on previous environmental standards.[8] These relate imperfectly to the nature and purpose of public

health guidance and are also themselves somewhat arbitrary in their selection of threshold values; as evidenced by the consistent use of round numbers.

Furthermore, neither approach provides a method for selecting a guideline for single drinking occasions (also known as a binge drinking guideline). Under the Canadian approach, there is no j-curve for risks linked to single occasions (e.g. risks of injuries) and the report of the Canadian Guideline Development Group offers no rationale linking the evidence reviewed on single occasion drinking and the guideline eventually selected.[6] The Australian approach also cannot be straightforwardly used to derive a single occasion drinking guideline as it relies on modelling which combines adding up risks across multiple drinking occasions into an annual or lifetime risk. The Australian Guideline Development Group reverted to reviewing the literature when selecting a single occasion guidelines and identified an apparent threshold effect whereby risks from a single drinking occasion began to increase more rapidly above 4 Australian standard drinks (5 UK units) for both males and females.

Both approaches also prompt questions regarding how they would be applied if emerging evidence substantially revises estimated health risks and thus the derived guideline threshold. This problem is perhaps clearest for the Canadian approach which explicitly links the drinking guideline to evidence of cardioprotective effects from moderate drinking. These effects are disputed,[10-13] may be overestimated[14-17] and are probably limited to particular groups within society[18] (see Section 5.4.1.2). If, as appears possible, scientific opinion develops to conclude cardioprotective effects are in fact overestimated and only occur up to very low levels of consumption (e.g. 5 units per week); one of the researchers responsible for the Canadian approach concluded that this would leave the Canadian guideline "in trouble".[19 p.1547]

A further point of debate is whether it is more appropriate to set public health guidance using a 'relative risk' approach, as in Canada, or an 'absolute risk' approach, as is used in Australia (see Box 2). The Canadian relative risk approach suggests judgements of whether drinking is risky should be made with reference to the risk experienced by abstainers. However, the public may wish to know what their absolute level of risk is rather than considering how much extra risk they are willing to accept compared to 'the average abstainer'. This is particularly the case given the average abstainer is a statistical construct rather than a real person and one which represents a group (i.e. alcohol abstainers) who tend to be different from the general population in ways which extend beyond not consuming alcohol.[20-25] In contrast, the Australian approach is, to an extent, based on the absolute level of risk experienced by drinkers. However, many different guidelines would be required to satisfactorily account for the substantial variation in absolute risk which is seen across the population. For example, the risk of alcohol-related mortality in the next ten years is much higher for a 60-year-old compared to a 20-year-old drinking at the same level. Further large variations depend on characteristics such as social status, genetic profile, psychological predispositions and engagement in other healthy or unhealthy behaviours.

Despite these limitations, the Canadian and Australian approaches are currently regarded as the best available methods for deriving guideline thresholds from evidence on alcohol-related health risks. This is largely because they provide a transparent and empirical basis for selecting the threshold rather than relying on the "opaque collective expert opinion"[5 p.137] which has been acknowledged in previous public debate[26] and potentially undermines public faith in guidelines.

Box 2: Relative risk and absolute risk

Levels of risk can be presented in different ways and two of the most common ways are relative and absolute risk.

Absolute risks describe the risk (or probability) of experiencing an outcome over a given time period. Someone drinking 10 units a week might have an absolute risk of 0.05 (i.e. a 5% or 1 in 20 chance) of dying in any given year.

Relative risks are used to compare risk of a particular outcome in two groups of people. In alcohol research, this usually means comparing the risk of drinking at a particular level to the risk of not drinking. For example, drinking 10 units a week may be associated with a relative risk of 1.7 for dying in any given year. This would usually mean people drinking 10 units a week are 1.7 times more likely than abstainers to die in any given year. If drinking is less risky than not drinking, the relative risk will be less than one. For example, a relative risk of 0.5 for drinking 10 units a week would mean people drinking that amount are half as likely to experience the outcome as abstainers.

Both ways of presenting risks are useful for alcohol research. Absolute risks tell us something about whether we are likely to experience an outcome as a result of different levels of drinking (e.g. if you drink that amount you have a 12% risk of dying from your drinking). Relative risks are useful because they provide a way of comparing risks across different levels of behaviour (e.g. if you increase your drinking by that amount, you are doubling your risk of dying from it).

2.3. Purpose of this report

To inform the considerations of the Guideline Development Group, this report provides estimates of the health risks associated with different levels and patterns of alcohol consumption for UK drinkers. It also provides commentary on the limitations of those estimates and considerations for their use in proposing new lower risk drinking guidelines for the UK. Recommendation of specific guideline thresholds is outside of the scope of the report, but the guideline thresholds derived from applying the Canadian and Australian approaches to the risk estimates will be indicated. A limited set of further analyses are conducted examining the sensitivity of the results to alternative evidence, assumptions and methodologies. Sensitivity analyses will also examine how alternative versions of the Canadian and Australian approaches affect the derived guideline thresholds (e.g. if the Australian threshold is set at 2% of annual deaths being alcohol attributable instead of 1%).

The specific research questions answered are:

1. For males and females, what levels of relative risk of alcohol-related mortality and morbidity are associated with different levels and patterns of alcohol consumption in the UK population?
2. For males and females, what proportions of all annual mortalities are alcohol attributable for different levels and patterns of alcohol consumption in the UK population?
3. What considerations should inform the use of the results in developing new lower risk drinking guidelines for UK general adult population?

3. Methodology

3.1. Overview of the modelling approach

The Sheffield Alcohol Policy Model (SAPM) v.2.7 is used to estimate risk curves (similar to Figure 1) describing the relationship between alcohol consumption and risks of mortality or morbidity from alcohol-related health conditions. Morbidity is defined here as person-specific hospital admissions which means if an individual is hospitalised for more than one cause or more than once in a year, they are only counted once.

SAPM is a mathematical simulation model which has previously been used for appraising UK and international alcohol policy options.[27-32] It comprises two main components. The first component estimates the impact of policy changes on alcohol consumption (P2C) and the second component estimates the impact of consumption changes on rates of alcohol-related harm including health conditions, crime and workplace absenteeism (C2H). For the present analysis, only the C2H model examining health conditions is required.

The risk curves are created by using the C2H component of SAPM to estimate the absolute level of mortality and morbidity for alcohol-related conditions occurring in a single year under the assumption that the UK population all drink at the same level. The results are then converted into risk estimates by comparing the results when the level the population all drinks at is varied.

Risk curves are derived describing the relationship between:

- Mean weekly consumption and risk of chronic alcohol-related conditions (see Table 4);
- Single occasion consumption and risk of acute alcohol-related conditions (see Table 4);
- Mean weekly consumption distributed over one to seven days and risk of all alcohol-related health conditions.

For each of the above, separate risk curves are derived for males and females and, where available data permit, for mortality and morbidity. In all cases, risks curves are derived allowing for the Canadian approach to be used to identify an implied guideline threshold, as described in the Introduction (Section 2.2.1). This means risk curves where the y-axis is the modelled population's average annual relative risk of mortality or morbidity for the relevant alcohol-related conditions. For the third set of risk curves (mean weekly consumption distributed over one to seven days and risk of all alcohol-related health conditions), risk curves are derived which allow the Australian approach to be used to derive an implied guideline threshold via the method described in the Introduction (Section 2.2.2). For the Australian approach, the y-axis broadly relates to the proportion of mortalities which are alcohol attributable although the exact definition of the y-axis varies depending on the outcome under examination. Morbidity risk curves using the Australian approach are not derived as the necessary data are not held by the University of Sheffield (see Section 3.2.2).

A small number of adaptations to the previously published SAPM v.2.6[27] are required to enable these analyses to be performed for the UK. These adaptations are:

- A UK-wide version of SAPM is required as previous analyses have used separate models for each UK country.[27,33-35]

- Variations in alcohol-related health risk by socioeconomic status are not accounted for as socioeconomic status measures which are comparable between countries are not available within the input data used.
- Time lags describing the delay between changes in population-level consumption and changes in rates of alcohol-related health outcomes are not modelled as how population health changes over time is not a focus of the present analysis
- A revised model of the relationship between single occasions of drinking and health outcomes described by Hill-McManus et al.[36,37] is not used here although it is included in other forthcoming reports based on SAPM analyses. This is because the revised model accounts for a range of sociodemographic variables (e.g. education, ethnicity, number of children) in estimating annual drinking patterns. The modelling approach used for this report requires that all individuals in the population of interest (i.e. all men or all women) have the same consumption patterns.

Sensitivity analyses are described in Section 3.7 and examine:

- The effect of alternative assumptions regarding the consumption level above which risks for acute alcohol-related harms begin to increase;
- The effect of assuming alcohol consumption at any level does not reduce risks of any health condition;
- The effect of modelling different time periods;
- The effect of accounting for recent trends in cardiovascular mortality;
- The effect of using alternative thresholds linked to the Canadian and Australian approaches.

3.2. Data

The present analyses estimate risk curves under hypothetical scenarios where uniform consumption levels are assigned to the population. However, recent datasets detailing individual-level alcohol consumption and incidence of alcohol-related mortality and morbidity are still required to derive inputs to the model. Data on population demographics are also required to create accurate weighted averages of risk levels across the population.

Previous versions of SAPM have built separate country-specific model adaptations using data from each UK country (i.e. England, Scotland, Wales and Northern Ireland).[27,33-35] In the present analysis, a UK-wide SAPM is required meaning country-specific data must be combined or UK-wide datasets sourced.

3.2.1. Consumption data

Prior to 2011, the General Lifestyle Survey (GLF) provided large sample, nationally-representative individual self-report data on alcohol consumption in the UK. These data have been the key input to previous version of SAPM. However, funding for the alcohol questions in the GLF was discontinued with immediate effect in mid-2011, meaning the last full year sample was 2010. No suitable alternative UK-wide dataset was available, therefore UK-wide consumption data are obtained by combining data from the most recent large sample surveys in each UK country. These are:

- England: Health Survey for England, 2012.
- Scotland: Scottish Health Survey, 2012.

- Wales: General Lifestyle Survey, 2008-2011 (pooled, Welsh samples only) – used because the Welsh Health Survey does not measure mean weekly alcohol consumption and the sample size is increased by using three surveys.
- Northern Ireland: Health Survey Northern Ireland, 2010/11 and 2011/12 (pooled) – two surveys are used to increase the sample size.

To obtain an analytical dataset containing consumption data representative of the UK population, the existing weights in the survey datasets are adjusted to match the population distribution across age, sex and UK country based on Office for National Statistics (ONS) mid-year 2013 population estimates.[38]

Each survey provides data on respondents' mean weekly alcohol consumption in UK units (1 unit = 8g/10ml pure ethanol). These data are derived using beverage-specific quantity frequency questions which ask (a) how often respondents drink each of a set of beverage types (frequency) and (b) how much of each beverage type they consume on a typical occasion when they drink it (quantity). Quantities are converted into units of alcohol using standard ONS assumptions[39] and the frequency and quantity are multiplied and then summed across beverages to give mean weekly consumption. Consumption is capped at a maximum value of 300 units per week as the evidence used on health risks is less robust for those drinking at extremely high levels.

With the exception of the Health Survey Northern Ireland (HSNI), each survey also provides data on respondents' heaviest drinking day in the week preceding the survey. This is collected by identifying the day in the preceding week on which the respondent consumed the most and asking how much they consumed on that day of each of a set of beverage types. Consumption on the heaviest drinking day in the preceding week (hereafter peak daily consumption) provides a measure of binge or single occasion drinking behaviour.

For Northern Ireland, peak daily consumption is imputed using Predictive Mean Matching[40] within the combined survey data for England, Scotland and Wales. Under this method, individuals in the HSNI are allocated the peak daily consumption of the individual in the combined English, Scottish and Welsh dataset who provides the closest match in terms of mean weekly consumption, and a set of sociodemographic variables. Where multiple closest matches are identified, one is selected at random. All analyses were performed in Stata 12[41] using the *mi impute pmm* command. Whilst this process introduces additional uncertainty into the baseline data used in the modelling, the overall impact of this is likely to be small as Northern Ireland accounts for less than 3% of the baseline modelled population

3.2.2. Alcohol-related health condition data

The University of Sheffield hold data providing mortality and morbidity rates for alcohol-related health conditions in each UK country corresponding with the years of the consumption surveys. For England, all-cause and condition-specific mortality rates are derived from ONS mortality statistics for England and Wales,[42] while alcohol-related condition-specific morbidity rates are based on person-specific hospitalisations from the Hospital Episodes Statistics (HES) database as calculated by Jones and Bellis.[43] For Scotland, Wales and Northern Ireland, equivalent mortality and morbidity data were provided by the respective devolved governments.

For the present analyses, the denominators of the mortality and morbidity rates are adjusted to match the population distribution across age, sex and UK country given by ONS mid-year 2013 population estimates.[38]

Northern Ireland data were not available for three health conditions: (1) maternal care for (suspected) damage to foetus from alcohol, (2) tuberculosis and (3) lower respiratory infections: pneumonia. Therefore, UK mortality and morbidity rates for these conditions are calculated as rates for England, Scotland and Wales only. The impact of this on the model results is likely to be small as these three conditions have a relatively small number of alcohol-attributable cases.

3.3. Model structure

An epidemiological approach is used within SAPM to model the relationship between alcohol consumption and related harm. Therefore, risk functions relating mean weekly and peak daily consumption to level of risk for a set of 43 alcohol-related health conditions are the fundamental components of the model.

3.4. Health conditions included in the model

Table 4 presents the 43 alcohol-related health conditions included within SAPM and for which evidence suggests alcohol plays a contributory role. This has been adapted from recent global meta-analyses and burden of disease studies.[44,45] The conditions are divided into four categories delineating those which are wholly or partly due to alcohol and those which are primarily due to chronic or acute alcohol consumption:

1. *Wholly-attributable, chronic*: conditions which cannot occur in the absence of alcohol consumption and for which risk of occurrence changes with chronic exposure to alcohol, measured here as mean weekly consumption (e.g. alcohol liver disease).
2. *Wholly-attributable, acute*: conditions which cannot occur in the absence of alcohol consumption and for which risk of occurrence changes with acute exposure to alcohol including intoxication, measured here as peak daily consumption over the previous seven days (e.g. ethanol poisoning).
3. *Partially-attributable, chronic*: conditions which can occur without alcohol consumption but for which the risk of occurrence changes with chronic exposure to alcohol (e.g. cancer of the oesophagus). For a number of primarily cardiovascular conditions within this category, lower levels of alcohol consumption are associated with reduced disease risk relative to abstainers (a so-called 'protective effect') and this is accounted for within SAPM.
4. *Partially-attributable, acute*: conditions which can occur without alcohol consumption but for which the risk of occurrence changes with acute exposure to alcohol including intoxication (e.g. falls).

3.5. Derivation of risk functions

The relationship between alcohol consumption and health outcomes was examined differently for each of the four health condition categories.

3.5.1. Relative risk functions for partially-attributable chronic conditions - available in the published research literature

The relative risk functions linking mean weekly consumption to all chronic conditions that are partially attributable to alcohol are shown in Figure 2 and sources from within the published

research literature are shown in Table 4. These risk functions are taken from studies which systematically review and meta-analyse the evidence base. Where available, separate risk functions by gender and for mortality and morbidity were extracted from the literature and these are shown in Figure 2, otherwise the same risk function was assumed for both genders and/or outcomes.

Table 4: Health conditions included in SAPM v.2.7 and sources for risk functions

Category	Disease or injury	ICD-10 codes	Source for risk function
Wholly attributable to alcohol, chronic (10)	Alcohol-induced pseudo-Cushing's syndrome	E24.4	
	Degeneration of nervous system due to alcohol	G31.2	
	Alcoholic polyneuropathy	G62.1	
	Alcoholic myopathy	G72.1	
	Alcoholic cardiomyopathy	I42.6	
	Alcoholic gastritis	K29.2	
	Alcoholic liver disease	K70.0-K70.4, K70.9	
	Acute pancreatitis (alcohol induced)	K85.2	
	Chronic pancreatitis (alcohol induced)	K86.0	
	Maternal care for (suspected) damage to foetus from alcohol	O35.4	
Wholly attributable to alcohol, acute (7)	Mental and behavioural disorders due to use of alcohol	F10	
	Excessive Blood Level of Alcohol	R78.0	
	Toxic effect of alcohol	T51.0, T51.1, T51.8, T51.9	
	Accidental poisoning by exposure to alcohol	X45	
	Intentional self-poisoning by and exposure to alcohol	X65	
	Poisoning by and exposure to alcohol, undetermined intent	Y15	
	Evidence of alcohol involvement determined by blood alcohol level	Y90	
Partially attributable to alcohol, chronic (14)	Tuberculosis	A15-A19, B90	Lonnroth *et al* 2008 [46]
	Malignant neoplasm of lip, oral cavity and pharynx	C00-C14	Tramacere *et al* 2010 [47]
	Malignant neoplasm of oesophagus	C15	Rota *et al* 2009 [48]
	Malignant neoplasm of colon and rectum	C18-C21	Fedirko *et a*l 2011 [49]
	Malignant neoplasm of liver and intrahepatic bile ducts	C22	Corrao *et al* 2004 [50]
	Malignant neoplasm of larynx	C32	Islami *et al* 2011 [51]
	Malignant neoplasm of breast	C50	Key *et al* 2006 [52]
	Epilepsy and status epilepticus	G40-G41	Samokhvalov *et al* 2010 [53]
	Hypertensive diseases	I10-I14	Taylor *et al* 2009 [54]
	Cardiac arrhythmias	I47-I48	Kodama *et al* 2011 [55]
	Haemorrhagic and other non-ischaemic stroke	I60-I62, I69.0-I69.2	Patra *et al* 2010 [56]
	Lower respiratory infections: pneumonia	J09-J22, J85, P23	Samokhvalov *et al* 2010 [57]
	Cirrhosis of the liver (excluding alcoholic liver disease)	K70 (excl. K70.0-K70.4, K70.9), K73-K74	Rehm *et al* 2010 [58]
	Acute and chronic pancreatitis	K85-K86 excl. K85.2, K86.0	Irving *et al* 2009 [59]
Partially attributable to alcohol, chronic, beneficial effect (3)	Diabetes mellitus (type II)	E10-E14	Baliunas *et al* 2009 [60]
	Ischaemic heart disease	I20-I25	Roerecke and Rehm 2010, 2012 [18,61] Shield et al. 2014[62]
	Ischaemic stroke	I63-I67, I69.3	Patra *et al* 2010 [56]
Partially attributable to alcohol, acute (9)	Transport injuries (including road traffic accidents)	V01-V98, Y85.0	Ridolfo & Stevenson, 1998[63]
	Fall injuries	W00-W19	
	Exposure to mechanical forces (including machinery accidents)	W20-W52	Single et al. 1996[64]
	Drowning	W65-W74	
	Other Unintentional Injuries	W75-W99, X30-X33, X50-X58	
	Accidental poisoning by exposure to noxious substances	X40-X49 excl. X45	
	Intentional self-harm	X60-X84, Y87.0 excl. X65	
	Assault	X85-Y09, Y87.1	
	Other intentional injuries	Y35	

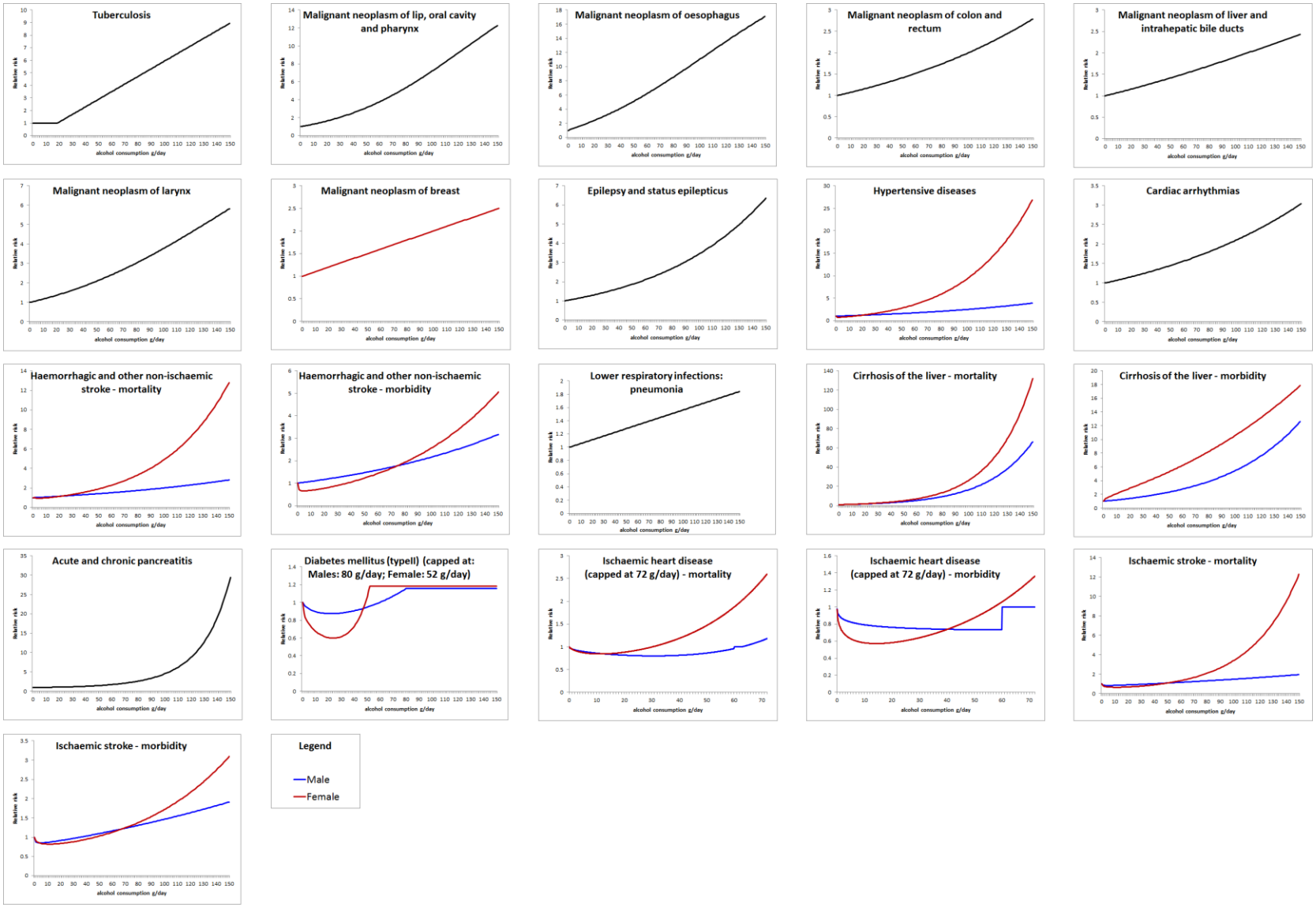

Figure 2: Relative risk functions for chronic conditions partially attributable to alcohol

3.5.1.1. Ischaemic heart disease and binge drinking

Ischaemic heart disease (IHD) represents a special case in SAPM v.2.7 as it is the only condition where a literature-based risk function is adjusted to reflect additional evidence. The source for the main risk functions suggests drinking up to approximately 8 units a day for males and 4 units a day for females is associated with a reduced risk of IHD relative to abstainers.[18] However, an earlier study by the same authors finds this reduced risk is substantially attenuated or eliminated for those engaging in heavy episodic drinking (defined as consuming at least 7.5 units on a single day) at least once a month.[61] As the present analysis does not consider frequency of heavy episodic drinking, this additional evidence is incorporated using a method employed by Shield et al.[62] whereby the risk function for IHD is adjusted such that drinkers consuming more than 7.5 units per day on average (52.5 units per week) are assumed to (a) have an IHD relative risk of 1.0 when the original risk function is less than RR=1.0 and (b) follow the original risk function when RR≥1.0. This limited adjustment means cardioprotective effects are likely to be overestimated within the model as many individuals with mean consumption less than 7.5 units per day are likely to be drinking this amount at least once a month.

3.5.2. Relative risk functions derived from the alcohol-attributable fraction for partially-attributable, acute conditions

For partially-attributable acute conditions, risk functions are typically not available in published meta-analyses. Therefore, an alternative method for deriving risk functions which links peak daily consumption to risk of these conditions is used. This method is based around the alcohol attributable fraction (AAF) for the condition.

In general, attributable fractions describe the proportion of cases of a condition which would not occur if the population were not subject to an exposure of interest (e.g. the proportion of lung cancer cases which would not occur if the population were entirely never smokers). More specifically, attributable fractions are the difference between the overall average risk (or incidence rate) of a disease in the entire population and the average risk in those without the exposure factor under investigation, expressed as a fraction of the overall average risk. For the present analyses, the AAF is used to describe the proportion of partially-attributable acute harms which would not occur if the population's peak daily consumption was zero.

The AAF can be calculated using the following formula:

$$AF = \frac{\sum_{i=1}^{n} p_i \left(RR_i - 1\right)}{1 + \sum_{i=1}^{n} p_i \left(RR_i - 1\right)} \qquad \textit{Equation 1}$$

Where RR_i is the relative risk due to exposure to alcohol at consumption state *i*, p_i is the proportion of the population exposed to alcohol at consumption state *i* and *n* is the number of consumption states. Thus the numerator is the excess expected cases of the condition due to alcohol exposure and the denominator is the total expected cases.

AAFs for partially-attributable acute conditions in the UK have been recently calculated by Jones and Bellis.[43] This evidence and Equation 1 are used to compute risk functions for these conditions.

Two assumptions are necessary to compute a relative risk function from an AAF. First, assumptions regarding the functional form (e.g. linear, various curvilinear forms). Linear functions were selected for the present analyses due to the lack of data on functional forms within the literature. Second, assumptions are also required regarding any consumption threshold below which the relative risk is equal to that of abstainers. An example of risk functions with and without threshold effects is shown in Figure 3. For the present analysis, the commissioners (Public Health England) requested a risk function with no threshold effect be used to reflect evidence that, for motor vehicle accidents, there is increased risk relative to abstention at any level of consumption.[65] In previous versions of SAPM, thresholds of four units for males and three units for females were selected and the rationale for this is described elsewhere.[32] As described below, threshold effects normally included within SAPM were also removed for wholly-attributable acute and chronic conditions. Sensitivity analyses investigating the impact of using the alternative specification where threshold effects are included are presented in Section 4.5.1 of the Results.

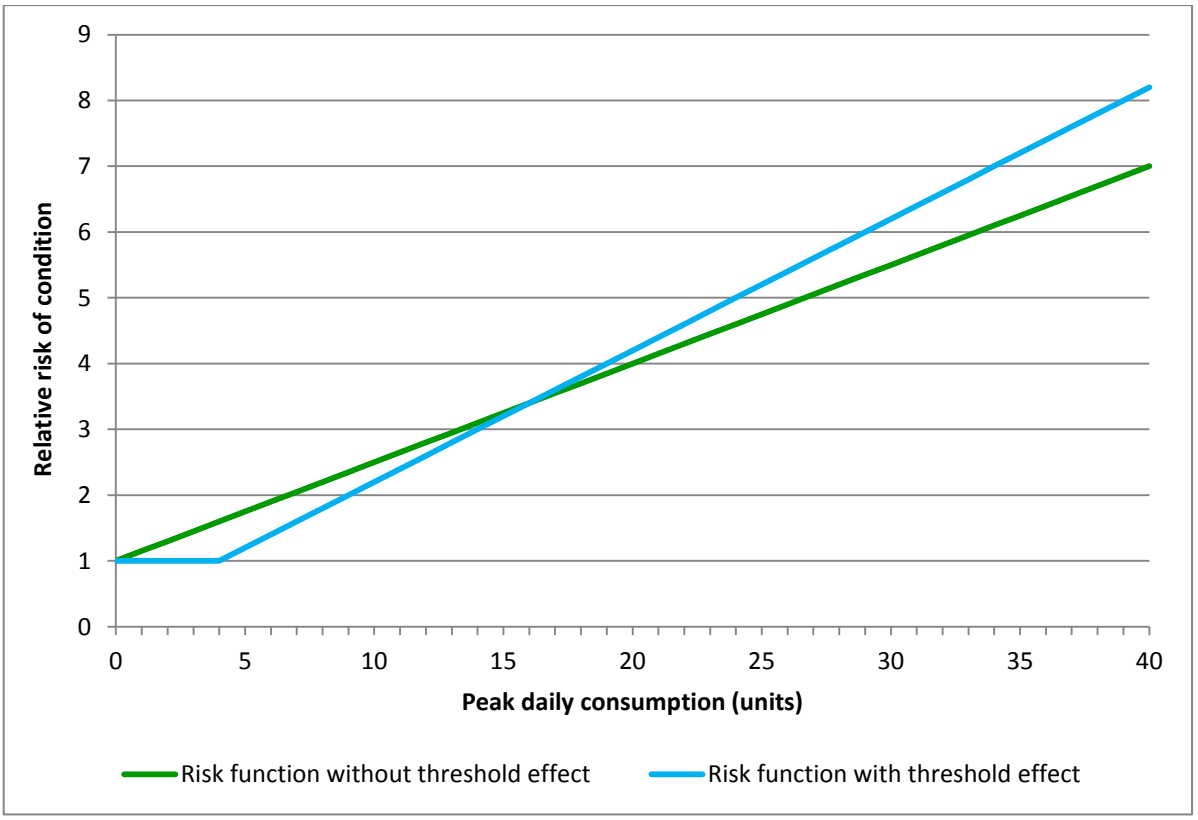

Figure 3: Illustrative linear relative risk function for a partially attributable acute harm with and without a threshold effect of 4 units.

3.5.3. Absolute risk functions for wholly-attributable acute conditions

While it is possible to estimate relative risk functions for most conditions, it is impossible to derive such functions linking peak daily consumption to risk of wholly alcohol-attributable acute harms (i.e. those with an AAF of 100%). This is because there is no reference group for the function to be relative to as abstainers, by definition, have zero risk of suffering wholly-attributable conditions.

Thus, an alternative approach is adopted whereby absolute risk functions are calculated for eight age and sex groups (male and female, ages: 16-24, 25-34, 35-54, 55+) based on the mortality rate or morbidity prevalence of the condition, the prevalence of different peak daily consumption levels and the population size of the age-sex group. As with the relative risk functions derived in Section 3.5.2, assumptions are necessary regarding the functional form and peak daily consumption threshold above which risk starts to increase. For consistency, the same linear form and lack of threshold effect was assumed and sensitivity analyses are used to examine the impact of modelling an alternative scenario where a threshold effect is included.

3.5.4. Absolute risk functions for wholly-attributable chronic conditions

Risk functions for wholly-attributable chronic conditions were calculated in the same way as for the acute equivalent with mean weekly consumption substituted for peak daily consumption. As with acute conditions, an assumption of no threshold before risk starts to increase was made.

3.6. Modelling procedure

3.6.1. Modelling current drinking, zero drinking and points in-between

To estimate the number of deaths (and hospitalisations) per annum which would accrue under different levels of alcohol consumption, a three step process is undertaken.

First, the current levels of alcohol consumption and current levels of risk of mortality for each age/gender group are inputted to SAPM to derive the risk functions as described in Sections 3.5.2 and 3.5.3. If the model is then run with input consumption at current levels alongside these calibrated risk functions, it returns as a result the current number of deaths per annum in each age-gender group, and for all males, all females, and the whole population aged 16+. The resulting number of deaths can be thought of as being made up of five components:

1. C1: Deaths for chronic alcohol-related conditions which are attributable to alcohol (e.g. deaths from oral cancers caused by alcohol);
2. C0: Deaths for chronic alcohol-related conditions which are not attributable to alcohol (e.g. deaths from oral cancers not caused by alcohol);
3. A1: Deaths from acute alcohol-related conditions which are attributable to alcohol (e.g. deaths from injuries caused by alcohol);
4. A0: Deaths from acute alcohol-related conditions which are not attributable to alcohol (e.g. deaths from injuries not caused by alcohol);
5. OD: Other deaths from causes unrelated to alcohol (e.g. deaths from lung cancer).

Second, an extreme what-if scenario where there is no drinking in the UK is then run in SAPM using the same risk functions. This what-if analysis estimates mortality levels if every person in the UK were drinking zero units of alcohol per week and gives a resulting number of deaths that is lower than in the first step as there are no deaths due to alcohol. The interpretation of the result of this model run is that it quantifies (C0+A0) the number of deaths in the 43 alcohol related conditions that are not currently caused by alcohol and (OD) deaths from other disease causes that are not related to alcohol at all, but has eliminated all of (C1 and A1) deaths in the 43 alcohol related conditions that are actually caused by alcohol. The number of deaths in this second step is therefore C0+A0+OD.

Third, SAPM is then repeatedly rerun for a set of what-if analyses. Each analysis obtains results for a scenario where every person in the UK is drinking at an exact specified level (e.g. all drinking one unit of alcohol per week, all drinking two units per week, etc.). This enables graphs to be drawn with the specified level of drinking on the x-axis and the number of deaths per annum on the y-axis.

3.6.2. What-if analyses separating effects for chronic and acute conditions and combining all alcohol-related conditions

For the present analyses, three sets of risk curves were derived describing relationships between mean weekly consumption and chronic alcohol-related health conditions, peak daily consumption and acute alcohol-related health conditions and mean weekly consumption spread over one to seven days and all alcohol-related health conditions. The processes for estimating mortality and morbidity risks associated with given consumption levels using SAPM is described below followed by a description of the process for converting mortality and morbidity point estimates into the required risk curves.

Morbidity estimates are not produced using the Australian approach as the University of Sheffield do not hold the required data on all-cause morbidities. Similarly, risk curves relating to the Australian approach (i.e. the proportion of all deaths attributable to alcohol) are not estimated when examining chronic or acute alcohol-related conditions separately. This is because the risk estimates underpinning the curve are calculated as a proportion of the total annual number of deaths. Using the terminology above, this would be:

$$\%Deaths\ which\ are\ C1 = \frac{C1}{C1 + C0 + A1 + A0 + OD}$$

Equation 2

When examining chronic alcohol-related deaths, an estimate of the number of A1 deaths would be required and this can only be obtained by assuming a level of peak daily consumption in the population. There is no sound basis for such an assumption under the hypothetical scenario that the population all has the same mean weekly consumption. An alternative approach would be to calculate the proportion of deaths from chronic alcohol-related causes which are attributable to alcohol (i.e. the AAF for these deaths) which can be expressed as:

$$\%Deaths\ which\ are\ C1 = \frac{C1}{C1 + C0}$$

Equation 3

However, it was judged that this was a significant departure from the absolute risk focus which informs the Australian approach. The same problem exists when examining risks for acute alcohol-related conditions. Consequently, the Australian approach is applied only when considering total mortality risk from all alcohol-related causes simultaneously. This approach involves assuming a range of peak daily consumption levels and comparing the implied guideline across those levels.

3.6.2.1. Mean weekly consumption and chronic alcohol-related health conditions

Mean weekly consumption is set to be uniform across the population and the level of mortality and morbidity for chronic alcohol-related conditions are estimated using SAPM. As there is no relationship in the C2H component of SAPM between peak daily consumption and chronic alcohol-

related health conditions, peak daily consumption data are not considered. The process is repeated for values of mean weekly consumption ranging from 0 to 49 units.

Annual risks relative to abstainers of mortality and morbidity due to chronic alcohol-related conditions are estimated.

3.6.2.2. Peak daily consumption and acute alcohol-related health conditions

Peak daily consumption for the population is set to be uniform across the population and the level of mortality and morbidity for acute alcohol-related conditions is estimated using SAPM. As there is no relationship in the C2H component of SAPM between mean weekly consumption and acute alcohol-related conditions, mean weekly consumption data are not considered. The process is repeated for values of peak daily consumption ranging from 0 to 49 units.

Annual risks relative to abstainers of mortality and morbidity due to acute alcohol-related conditions are estimated.

3.6.2.3. Mean weekly consumption distributed across one to seven days and all alcohol-related health conditions.

Mean weekly consumption for the population is set to be uniform across the population and the level of mortality and morbidity for all alcohol-related health conditions is estimated. However, for each level of mean weekly consumption modelled, the analysis follows the Australian drinking guidelines review by exploring a range of alternative assumptions regarding how consumption is distributed across the week.[8] Specifically, the scenarios modelled in SAPM assume that consumption is distributed evenly across 1, 2, 3, 4, 5, 6 or 7 days. For example, a mean weekly consumption of 20 units would be modelled seven times with peak daily consumption set to 20, 10, 6.7, 5, 4, 3.3 and 2.9 units. Although a range of alternative distributions of consumption across drinking days are possible, the modelled options crucially include those with the highest and lowest peak daily consumption (i.e. all on one day and evenly distributed across seven days). These extreme cases will provide estimates of the maximum and minimum levels of total alcohol-related health risk associated with a given mean weekly consumption.

The process is repeated for values of mean weekly consumption ranging between 0 and 49 units per week.

Annual risks relative to abstainers of mortality and morbidity due to alcohol-related conditions are estimated. Also estimated for each level of consumption is the annual proportion of mortality for all causes which is attributable to alcohol.

3.6.3. Converting mortality and morbidity estimates into risk curves

Relative risk estimates are derived by comparing estimated mortality levels when the population drink at values above zero with estimated mortality levels when the population do not drink. Risk curves describing the proportion of mortalities which are alcohol attributable and for the relevant conditions can be derived by comparing, for a given level of consumption, estimated mortality for alcohol-related causes with estimated total mortality in the population. Similar processes can be used to derive morbidity estimates and separate estimates for males and females.

In order to calculate the precise levels of consumption which correspond to the Canadian and Australian approaches (i.e. RR=1 and AR=1/100), fractional polynomials are fitted to the model

results[66] using the Stata 12[41] command *fracpoly* and the resulting polynomial equations are solved as required. These polynomials are also used directly in order to derive absolute risks of alcohol-attributable mortality at different levels of consumption.

3.7. Sensitivity analyses

To assess the impact of alternative assumption, evidence and methodologies on the results, five sensitivity analyses are conducted which examine:

- The effect of alternative assumptions regarding the threshold consumption level above which risks for acute alcohol-related harms begin to increase (see Section 3.5.2);
- The effect of assuming alcohol consumption at any level does not reduce risks of any health condition;
- The effect of modelling different time periods;
- The effect of accounting for recent trends in cardiovascular mortality;
- The effect of using alternative versions of the Canadian and Australian approaches.

3.7.1. Sensitivity analysis 1: Assuming an alternative threshold for acute risks

As described in Section 3.5.2, previous analyses using SAPM have included threshold effects within risk functions for acute conditions and wholly-attributable chronic conditions such that risk only begins to increase above a pre-specified consumption level. At the request of the commissioners (Public Health England), this threshold effect was removed for the base case analysis meaning there is no threshold mean weekly or peak daily alcohol consumption level below which risks of acute alcohol-related mortality or morbidity are equivalent to that of abstainers.

To test the impact of this revised assumption, a sensitivity analysis was conducted with the assumed thresholds used in previous version of SAPM reinstated. These thresholds assume for acute conditions that risks are equivalent to abstainers when peak daily consumption is equal to or less than four units for males and three units for females. For wholly-attributable chronic conditions, risks are assumed to be equivalent to abstainers when mean weekly consumption is equal to or less than two units for females and three units for males.

3.7.2. Sensitivity analysis 2: Assuming alcohol consumption at any level does not reduce health risks

Risk functions for the following conditions all include reduced mortality or morbidity risk relative to abstainers at some levels of mean weekly alcohol consumption for males and/or females (see Figure 2):

- Ischaemic heart disease
- Ischaemic stroke
- Haemorrhagic stroke
- Hypertensive diseases
- Type II diabetes

These apparent protective effects are subject to considerable scientific debate and, therefore, the effect of removing them is examined by a sensitivity analysis setting relative risks at all consumption levels where RR<1 to RR=1. Relative risks for consumption levels where RR≥1 are left unadjusted.

3.7.3. Sensitivity analysis 3: Modelling different time periods

SAPM can model the effects of the population distribution of consumption on mortality and morbidity for a number of years specified by the user. In the present analysis, the modelled period is a single year. Running the model for a longer time period (e.g. 20 years) would alter the results. This is because the demographic structure of the population is based on ONS 2013 mid-year population estimates which are partly a product of the population's current (and previous) alcohol consumption. Within the present analysis, consumption is set to uniform levels for the whole population and over time the mortality consequences of drinking at these levels will gradually alter the demographic structure of the population with a greater extent of restructuring as the number of modelled years increases. This demographic restructuring means there are different absolute mortalities and morbidities for each condition in each age-sex group over time meaning the population risk curves for mortality and morbidity for all alcohol-related conditions are also different.

The effect of this is examined in a sensitivity analysis modelling a longer time period, specifically 10 years.

3.7.4. Sensitivity analysis 4: Exploring impact of trends in cardiovascular mortality

Cardiovascular diseases (CVD) are one of the leading causes of death in the UK; however, mortality rates from these conditions has been falling consistently over the past 30 years and are forecast to continue to fall into the future.[67] Alcohol is both a key risk factor for cardiovascular conditions and, at low consumption levels, may provide protective effects against these conditions. Therefore, changes in mortality rates for cardiovascular conditions are likely to impact on the implied guideline thresholds derived from SAPM.

To examine the potential effect of these changes in a sensitivity analysis, we update the baseline cardiovascular mortality rates used in the base case to those reported in the latest published figures for 2013 from England and Wales, Scotland and Northern Ireland.[42,68,69] These show an overall reduction of just over 9% in cardiovascular deaths, although these changes vary between health conditions as shown in Table 5.

Table 5: Changes in cardiovascular mortality rates from baseline years to 2013

Condition	% change in overall mortality
Hypertension	-17.2%
Cardiac arrhythmias	-5.4%
Haemorrhagic and other non-ischaemic stroke	-7.1%
Ischaemic heart disease	-13.5%
Ischaemic stroke	6.8%
All cardiovascular conditions	-9.2%

3.7.5. Sensitivity analysis 5: Using alternative thresholds under the Canadian and Australian approach

As noted in the Introduction, the Australian approach of setting the drinking guideline at the consumption level where 1% of all annual deaths are attributable to alcohol is somewhat arbitrary. Guidelines derived by applying thresholds of 0.5%, 1.5% and 2.0% of all annual deaths being attributable to alcohol are examined to assess the sensitivity of the implied guideline to alternative thresholds.

Also examined is an alternative to the Canadian approach whereby the nadir of the risk curve (i.e. the consumption level associated with the largest risk reductions relative to abstainers) is used to derive a guideline threshold.

3.8. Methodological differences compared to the Canadian and Australian analyses

Although informed by the Canadian and Australian approaches, there are importance differences between the analyses undertaken in those countries and in the present report. The key differences are listed below:

- The present report takes account of frequency of consumption when applying the Canadian approach for total alcohol-attributable mortality. This was not done in the Canadian analyses.
- Evidence of protective effects are included in all analyses here except Sensitivity Analysis 2. In Australia, protective effects were excluded from the base case.
- The alcohol-related health conditions modelled vary between each of the analyses. This reflects a range of consideration including the scope of the analyses, evidence available at the time the work was conducted and the methodological decisions of the researchers. The full lists of conditions modelled are included in each country's report.[6,8]
- SAPM and the Australian modelling both incorporate simultaneous analyses of both acute and chronic risks. In Canada these two types of risk were analysed separately.
- The Australian report discusses lifetime risks whereas here risks are referred to as annual risks. However, where risks are averaged across the population, these are identical.

4. Results

The results below are presented in five sections. First, the baseline mortality and morbidity data for the population are presented to illustrate how health risks and alcohol-related health risks are distributed across the population. This has important implications for the applicability of different risk thresholds to particular groups with the population. Next, the results for mortality risks are presented and describe in turn (a) mean weekly consumption and its relationship to chronic alcohol-related conditions, (b) peak daily consumption and its relationship to acute alcohol-related conditions and (c) mean weekly consumption distributed across one to seven days and its relationship to all alcohol-related conditions. A summary of morbidity results are then presented followed by an analysis of mortality risk by age group which illustrates some of the conceptual and analytical challenges of considering age group-specific risk thresholds. Finally the results of the sensitivity analyses are presented.

4.1. Baseline mortality and morbidity

4.1.1. Baseline mortality rates

Table 6 shows the baseline annual mortality rates used in the model by age, sex and different causes. This highlights four important differences in cause of death by age and sex.

Table 6: Baseline annual mortality rates by age, sex and attribution

Mortalities per 100,000 population	16-24		25-34		35-54		55+		Total		All
	M	F	M	F	M	F	M	F	M	F	
Acute alcohol-attributable[1]	10.1	1.8	12.9	1.8	17.3	4.2	18.2	7.6	15.8	4.6	10.2
Chronic alcohol-attributable[1]	0.5	0.2	3.7	2.6	24.1	16.2	53.9	21.3	27.0	13.2	20.1
Total alcohol-attributable	10.6	2.1	16.6	4.4	41.4	20.4	72.1	28.9	42.8	17.8	30.3
Total non-alcohol attributable	43.5	26.3	58.1	36.0	192.5	148.2	2,741.1	3,083.5	1,000.0	1,082.2	1,041.0
% mortalities alcohol-attributable	19.6	7.3	22.2	10.9	17.7	12.1	2.6	0.9	4.1	1.6	2.8

[1]Acute and chronic refer to types of conditions listed in Table 4. Chronic deaths are those assumed to be associated with mean weekly consumption over time and acute deaths are those assumed to be associated with a single drinking occasion.

First, at all ages and for both acute and chronic conditions, alcohol-attributable mortality rates are higher for males than females.

Second, alcohol-attributable mortality rates for both chronic and acute conditions increase substantially with age for both males and females.

Third, at age 16-24, alcohol-attributable deaths account for a large minority of all deaths and the proportion is greater for males than females (19.6% vs. 7.3%). With increasing age, this proportion declines and the gap between males and females diminishes in absolute terms. By age 55 and over the proportions are 2.6% for males and 0.9% for females. This mainly reflects much greater risks of non-alcohol-attributable mortality for older age groups which are not present at younger ages.

Finally, the balance of mortalities from acute vs. chronic conditions changes with age. At age 16-24, mortalities from acute conditions dominate for both sexes and for males in particular. Although the mortality rate for acute conditions increases with age, the rate for chronic conditions increases more sharply. By age 35-54, there are more mortalities from chronic conditions than acute conditions for both sexes and the gap widens further among those aged 55 and over.

4.1.2. Baseline morbidity rates

Table 7 presents baseline annual morbidity data by age, sex and attribution. Due to the data limitations discussed in Section 3.2.2, morbidity rates for other causes are not presented. The patterns are similar to those identified for mortality with consistently higher alcohol-attributable morbidity rates for males and higher alcohol-attributable morbidity for acute conditions and lower morbidity for chronic conditions at younger ages.

Table 7: Baseline annual morbidity rates by age, sex and attribution

Morbidities[1] per 100,000 population	**16-24**		**25-34**		**35-54**		**55+**		**Total**		**All**
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	
Acute alcohol-attributable[2]	683	456	642	331	848	453	781	323	2,129	1,218	3,347
Chronic alcohol-attributable[2]	66	50	124	99	549	488	2,913	333	1,412	400	1,812
Total alcohol-attributable	749	506	766	429	1,397	941	3,694	656	3,542	1,617	5,159

[1]Morbidity defined as person-specific hospital admissions.

[2]Acute and chronic refer to types of conditions listed in Table 4. Chronic morbidities are those assumed to be associated with mean weekly consumption over time and acute morbidities are those assumed to be associated with a single drinking occasion.

4.2. Mortality risks

The mortality risk results are presented below. In each case, fitted fractional polynomial curves are presented in the Figures and are used to derive implied guideline thresholds using the Canadian and, when considering all mortalities (Section 4.2.3), the Australian approach.

4.2.1. Mortality risks for chronic alcohol-related conditions

Figure 4 presents the estimated relative risk curves relating mean weekly consumption to relative risk of mortality from chronic alcohol-related causes. Curves for each gender are presented. The implied guideline threshold for males and females using the Canadian approaches is highlighted and summarised in Table 8 along with the relative risk associated with this consumption level.

Both of the risk curves are j-shaped, primarily as a result of the association between reduced cardiovascular risk and moderate levels of alcohol consumption. The nadir of the curve (i.e. the point of lowest risk) is 0.5 units greater per week for females compared to males (3.9 vs 3.4) and the reduction in risk relative to abstainers at this point is greater for females (RR=0.92 vs. 0.97). However, above the nadir, risk increases at a steeper rate for females than males. This suggests that any overall protective effects afforded by moderate drinking are greater for women and peak at very low consumption levels (i.e. less than one unit per day).

The guideline threshold which would be selected using the Canadian approach (i.e. where female drinkers have higher risks than female abstainers) is 14.1 units per week. The equivalent threshold for males is lower at 12.5 units per week. Above this threshold the male and female curves continue to diverge due to the steeper risk increases for females.

Table 8: Implied guideline mean weekly consumption thresholds for chronic alcohol-related mortality

	Guideline threshold in units per week		
Threshold	**Males**	**Females**	**Population**
Canadian: RR=1.0	12.5	14.1	13.7
Lowest possible risk (nadir of curve)	3.4	3.9	3.8
Relative risk at the nadir	0.97	0.92	0.94

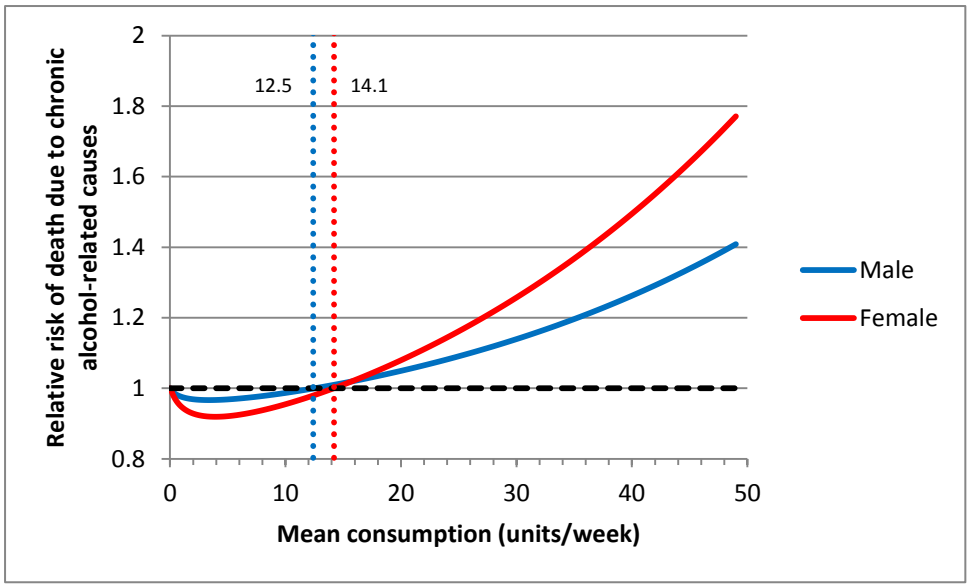

Figure 4: Relative risk of death due to chronic alcohol-related causes by mean weekly consumption level

4.2.2. Mortality risks for acute alcohol-related conditions

Figure 5 presents the estimated relative risk curves relating peak daily consumption and relative risk of mortality from acute alcohol-related causes. As with chronic conditions, curves are presented for both genders. As there is no evidence of reduced risk relative to abstainers for any consumption level, the Canadian approach provides no means of deriving a guideline threshold (or, under a different interpretation, implies that the guideline threshold should be zero).

The risk curve for males is steeper than females meaning risk relative to abstainers increases with rising peak daily consumption at a faster rate for males than females. Relative risks are also greater than those observed in the graph for chronic alcohol-related conditions. For example, the male relative risk for acute alcohol-related mortality relative to abstainers is 2.2 for a peak daily consumption of 10 units whereas the relative risk of mortality for chronic alcohol-related conditions when consuming 49 units per week is 1.4.

These results suggest mortality risks for acute alcohol-related conditions are likely to notably influence overall alcohol-related mortality risks where drinking patterns include heavy drinking and that this influence will be greater for males than females.

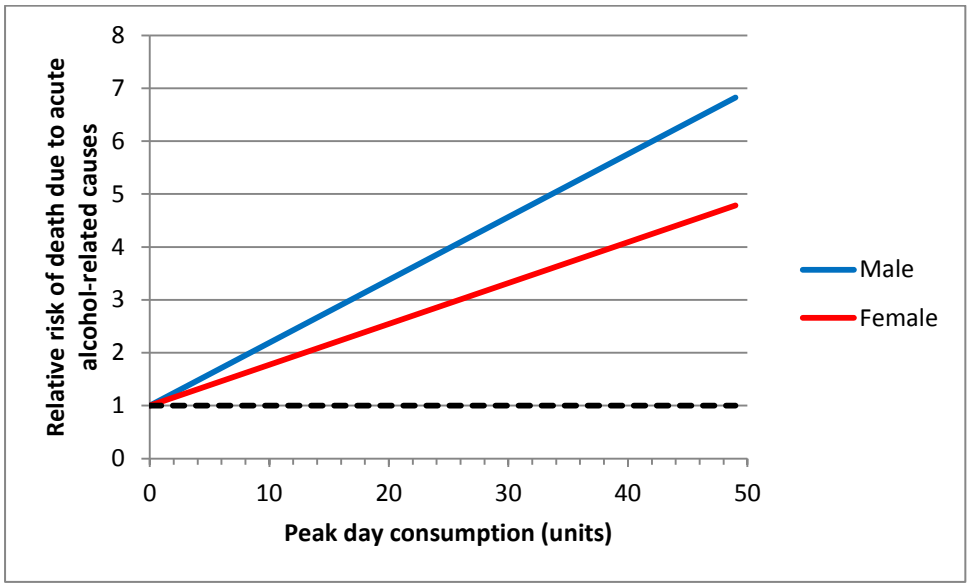

Figure 5: Relative risk of death due to acute alcohol-related causes by peak daily consumption level

4.2.3. Mortality risks for all alcohol-related conditions

Figure 6 and Figure 7 present the male and female estimated relative risk curves relating mean weekly consumption spread across one to seven days to total alcohol-related mortality risk. Figure 8 and Figure 9 present the equivalent estimated risk curves for the proportion of all deaths which are alcohol attributable. The Canadian and Australian approaches provide no specific guidance for selecting a guideline threshold from among these curves; however, the minimum (units consumed all on one day) and maximum (units evenly spaced across seven days) guideline thresholds are highlighted in each figure and thresholds for each scenario are summarised in Table 9.

These curves are composites of the chronic and acute risks and the results reflect this. For example, risk curves are steeper when the same volume of alcohol is consumed on fewer days. This reflects the increased risk of acute mortality associated with increased intoxication on drinking days. Similarly, the steeper acute risk curves for males (see Figure 5) and the greater incidence of acute alcohol-related mortality for males (see Table 6) mean the seven curves in each of Figure 6 to Figure 9 are more affected by number of drinking days for males than females.

The effect of number of drinking days on the male curves has important impacts on the j-curve and therefore the implied guideline thresholds.

Figure 6 shows that, for males, the nadir of the curve is reached at 1.2 units per week if consumption occurs on a single day but 2.4 units per week if the individual drinks every day. The maximum reduction in risk relative to abstainers is, however, small in both cases (RR=0.99 in both cases) demonstrating that any cardioprotective from moderate drinking have little impact on overall risks for males and particularly males whose drinking patterns include episodes of heavy drinking. The implied male guideline under the Canadian approach is also sharply different across the seven curves, being 3.4 units per week if alcohol is consumed once a week and 9.8 units per week if alcohol is consumed every day.

For females, the relative risk results are less affected by the number of drinking days reflecting the reduced importance of acute risks. The nadir of the j-curve is reached at 2.8 and 3.4 units per week for drinking once a week and drinking daily respectively and the corresponding maximum reductions in risk relative to abstainers are RR=0.98 and RR=0.97 respectively. Although greater than observed for males, these risk reductions remain modest and peak at very low levels of alcohol consumption, suggesting again that the importance of any cardioprotective effects of alcohol at the population level should not be over-emphasised when considered in the context of all other risks. The implied female mean weekly consumption guidelines using the Canadian approach are 10.0 units per week if alcohol is consumed once a week and 13.6 units per week if alcohol is consumed every day.

Under the Australian approach, the implied guidelines for both males and females are higher reflecting a definition of low risk which is necessarily above that used in the Canadian approach. For males drinking once a week and drinking daily the implied guideline threshold would be 6.0 and 14.1 units per week and the equivalent implied guidelines for females would be 12.0 and 15.7 units per week.

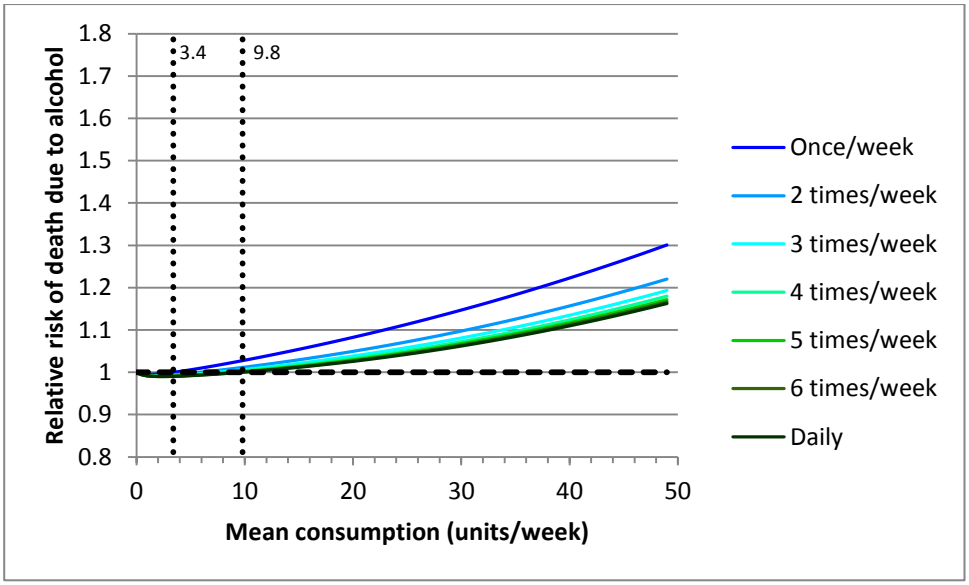

Figure 6: Male relative risk of death from alcohol-related causes by mean weekly consumption and number of drinking days

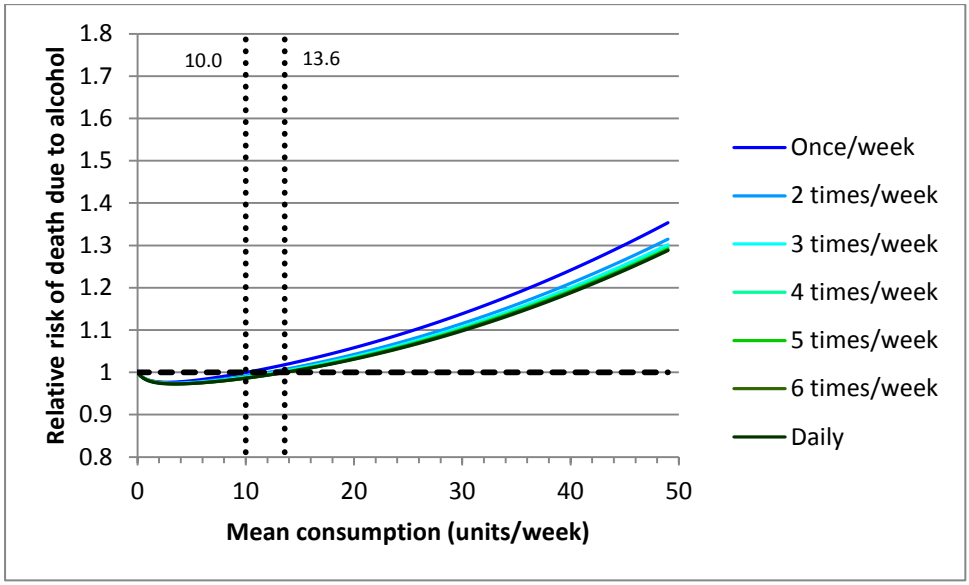

Figure 7: Female relative risk of death from alcohol-related causes by mean weekly consumption and number of drinking days

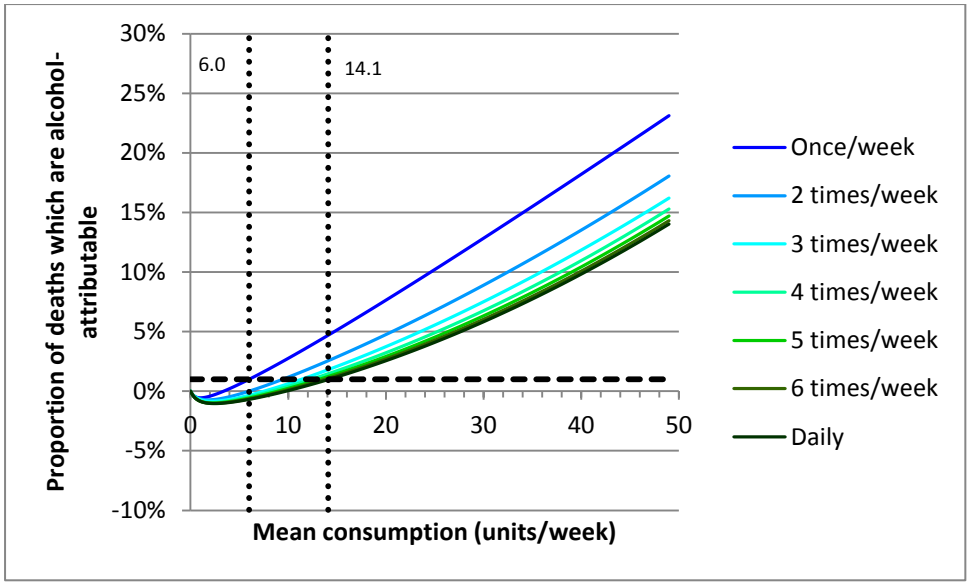

Figure 8: Male proportion of deaths which are alcohol-attributable by mean weekly consumption and number of drinking days

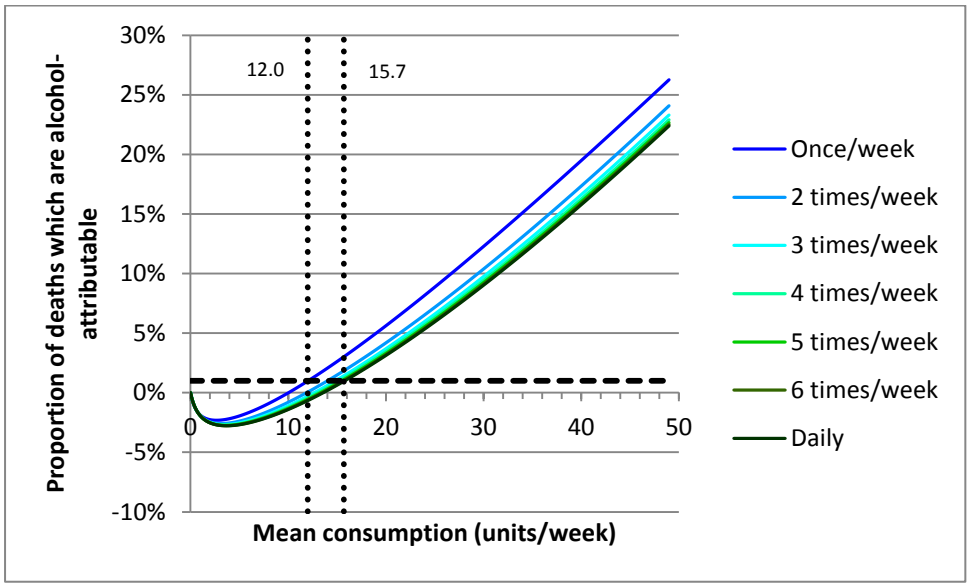

Figure 9: Female proportion of deaths which are alcohol-attributable by mean weekly consumption and number of drinking days

Table 9: Implied guideline for mean weekly consumption for total alcohol-related mortality by number of drinking days per week

		Units per week	
Threshold	**Drinking days per week**	**Males**	**Females**
Canadian: RR=1.0	1	3.4	10.0
	2	5.8	12.0
	3	7.4	12.8
	4	8.2	13.2
	5	8.9	13.4
	6	9.4	13.6
	7	9.8	13.6
Australian: Proportion=1%	1	6.0	12.0
	2	9.4	14.0
	3	11.3	14.8
	4	12.3	15.2
	5	13.1	15.4
	6	13.7	15.6
	7	14.1	15.7

4.2.3.1. Absolute lifetime alcohol-attributable mortality risk

The absolute lifetime risk of alcohol-attributable mortality for males and females drinking at different quantities and frequencies is shown in Table 10 and Table 11. For males drinking 21 units per week across five drinking days (roughly equivalent to the current UK guidelines), absolute mortality lifetime risk is 0.03 and for females drinking 14 units per week across five drinking days (again roughly equivalent to the current UK guidelines), absolutealcohol-attributable mortality risk is 0.003 – ten times lower than males.

Table 10: Absolute lifetime risk of male alcohol-attributable mortality by consumption frequency and quantity

Mean consumption (units/week)	**Drinking days per week**						
	7	**6**	**5**	**4**	**3**	**2**	**1**
7	-0.0052	-0.0047	-0.0039	-0.0027	-0.0012	0.0027	0.0142
14	0.0095	0.0106	0.0121	0.0144	0.0178	0.0252	0.0465
21	0.0285	0.0300	0.0322	0.0355	0.0409	0.0514	0.0814
28	0.0511	0.0531	0.0558	0.0599	0.0670	0.0802	0.1178
35	0.0773	0.0796	0.0829	0.0877	0.0960	0.1114	0.1550
42	0.1070	0.1097	0.1133	0.1187	0.1277	0.1449	0.1928
49	0.1403	0.1431	0.1471	0.1529	0.1621	0.1806	0.2312

Table 11: Absolute lifetime risk of female alcohol-attributable mortality by consumption frequency and quantity

Mean consumption (units/week)	Drinking days per week						
	7	6	5	4	3	2	1
7	-0.0231	-0.0228	-0.0224	-0.0218	-0.0208	-0.0188	-0.0130
14	0.0018	0.0023	0.0031	0.0043	0.0061	0.0099	0.0205
21	0.0367	0.0374	0.0384	0.0400	0.0425	0.0476	0.0625
28	0.0776	0.0785	0.0797	0.0816	0.0846	0.0907	0.1089
35	0.1230	0.1240	0.1254	0.1275	0.1309	0.1377	0.1582
42	0.1720	0.1731	0.1746	0.1768	0.1806	0.1880	0.2096
49	0.2239	0.2251	0.2267	0.2290	0.2330	0.2408	0.2626

Black text, green background - overall protective effect
Red text, light orange background - overall lifetime risk less than 1 in 100
Black text, orange background - overall lifetime risk at least 1 in 100, but below 1 in 10
White text, red background - overall lifetime risk at least 1 in 10

4.3. Morbidity risks

Morbidity results using the Canadian approach are presented for the relationship between mean weekly consumption and chronic alcohol-related conditions and between peak daily consumption and acute alcohol-related conditions. Due to the data limitations discussed in Section 3.2.2, no results are presented for total morbidity or using the Australian approach. As with mortality, fitted fractional polynomial curves are shown in the figures and implied guideline thresholds are shown in the tables.

4.3.1. Morbidity risks for chronic alcohol-related conditions

Figure 10 shows the relative risk of chronic alcohol-related morbidity (defined as person-specific admission to hospital for chronic alcohol-related conditions) by mean weekly alcohol consumption. Curves are shown for both genders and the implied guideline threshold using the Canadian approach is highlighted and summarised in Table 12 along with information on the nadir of the curve.

The risk curves are markedly different for males and females. For males, there is no j-curve, with the relative risk for those who consume alcohol relative to abstainers equalling 1.0 at 0 units per week, and rising thereafter. The absence of a j-curve presents a problem for using the Canadian approach to derive a guideline threshold as it implies either the guideline should be set at zero units per week or that no threshold can be derived.

A j-curve is observed for females although the nadir is again at a very low consumption level of 2.5 units per week. However, the relative risk estimate associated with the nadir is 0.80, implying a meaningful morbidity risk reduction relative to abstainers. Following the nadir, the female curve is steeper than the male curve implying a faster rate of increase in risk with rising consumption. The implied guideline threshold for females using the Canadian approach is 16.6 units per week. Above

24.8 units per week, relative risks for females are greater than for males for chronic alcohol-related causes.

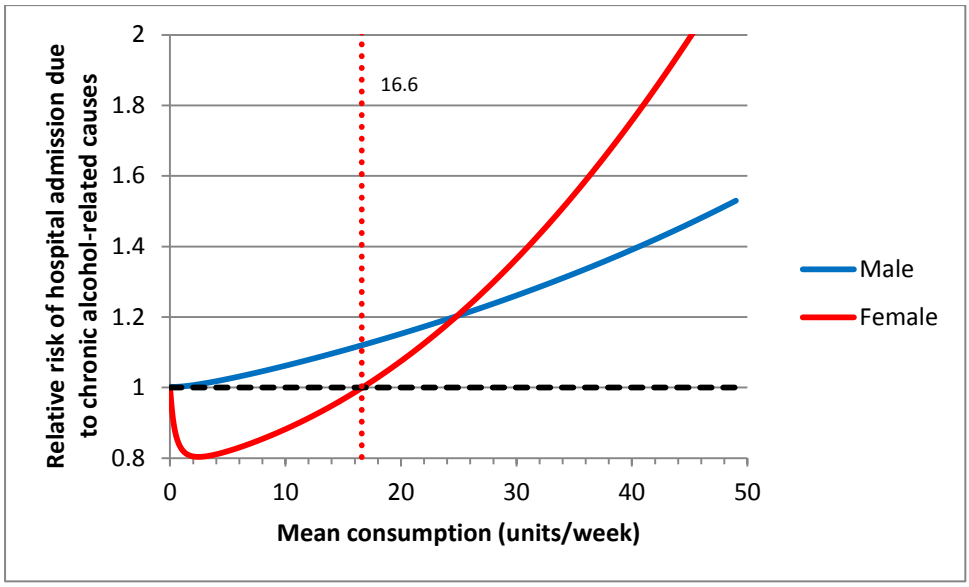

Figure 10: Relative risk of chronic alcohol-related morbidity by mean weekly consumption

Table 12: Implied guideline mean weekly consumption thresholds for chronic alcohol-related morbidity

	Guideline threshold in units per week		
Threshold	**Males**	**Females**	**Population**
Canadian: RR=1.0	0	16.6	12.9
Lowest possible risk (nadir of curve)	0	2.5	2.3
Relative risk at the nadir	1.00	0.80	0.90

4.3.2. Morbidity risks for acute alcohol-related conditions

Figure 11 shows the estimated relative risk of acute alcohol-related morbidity by peak daily consumption for males and females. As with the equivalent mortality graph, there is no j-curve for acute alcohol-related conditions and, therefore, the Canadian approach cannot be used to derive a drinking guideline.

Acute morbidity risk increases more rapidly for males than females although the difference is smaller than for mortality risk (see Figure 5). As with mortality, the risk estimates are sufficiently large that they can be expected to influence the overall morbidity risk, attenuating observed risk reductions relative to abstainers at low levels of consumption and making risk estimate sensitive to how many days mean weekly consumption is distributed across. This is particularly the case for males who have higher baseline rates of acute alcohol-related morbidity,

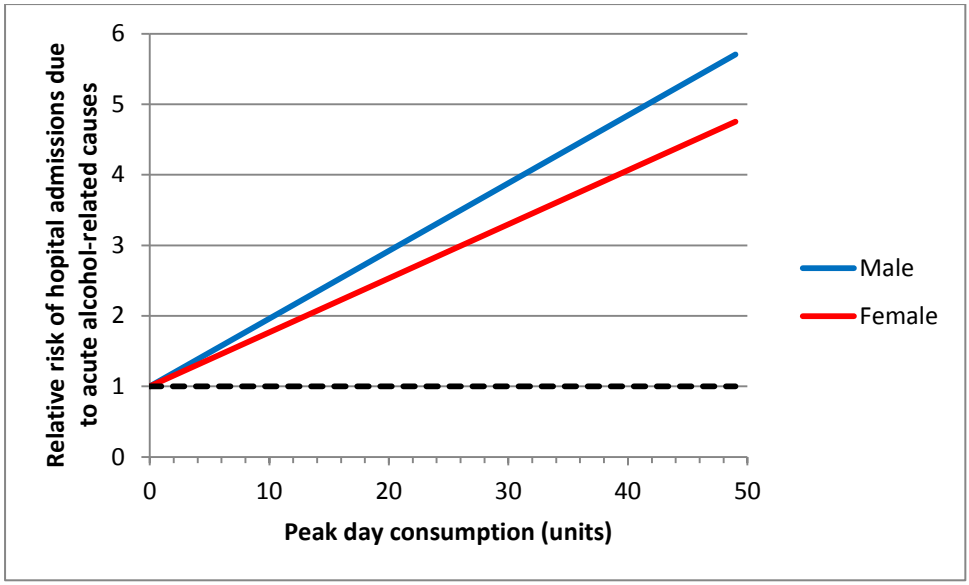

Figure 11: Relative risk of acute alcohol-related morbidity by peak daily consumption

4.4. Analysis of variation in risk by age

Figure 12 to Figure 15 shows alcohol-related mortality risks by mean weekly consumption but separated by gender, age and the extremes of number of drinking days (i.e. drinking once a week or drinking daily). When interpreting these figures, it should be remembered that SAPM estimates risks within each age group and not risks experienced by age groups across their whole life course. Therefore, the mortality risks for 18-24 year olds are not lifetime mortality risks starting from age 18-24 but mortality risks while aged 18-24. These figures illustrate several important points regarding age-related risks.

First, implied guideline thresholds differ starkly depending on the age group under examination. This is largely a result of the very different risks to which each group is subject. In short, younger age groups have high risk of acute alcohol-related mortality but very low risk of chronic alcohol-related mortality. Older age groups have much higher risk of mortality for chronic conditions but similar acute condition mortality risk (see Table 6). As a result, the risk curves for younger age groups are strongly influenced by acute risks whereas the risk curves for older age groups are more influenced by chronic risks. Two features of the acute risk curve are salient: (a) there is no evidence of reduced mortality risk for acute alcohol-related conditions and (b) it is linear and has no threshold effect meaning risk increases consistently across all levels of consumption including very low levels. As a results of these points, the Canadian approach to deriving guideline thresholds gives mean weekly consumption thresholds close to zero for younger age groups. Similarly, the low overall mortality risk for younger age groups means a substantial proportion of deaths in this group are alcohol attributable. Consequently, the Australian approach also implies a drinking guideline close to zero.

Second, it is clear from all of the figures that reduced risks from moderate drinking among males and females aged under 55 are negligible or non-existent reflecting the low risk of cardiovascular disease in these groups. For males aged 55 and over, these reduced risks are also very small and correspond to very low levels of consumption. For females aged 55 and over, reduced risks are larger; however, the greatest risk reductions again correspond to low levels of mean weekly alcohol consumption (approximately five units per week).

Overall, these points demonstrate that the population-level risk curves reflect not only variations in degrees of risk across age groups but also substantial variation in the nature of risks to which different aged drinkers are exposed. As these different risks have very different relationships to alcohol consumption (e.g. linear, j-shaped, curvilinear), this means a highly heterogeneous set of age-specific risks curves are being averaged to produce the population-level curve. Neither the Australian nor Canadian approaches cope well with this heterogeneity when the approaches are applied to attempt to derive age-specific lower risk drinking guidelines.

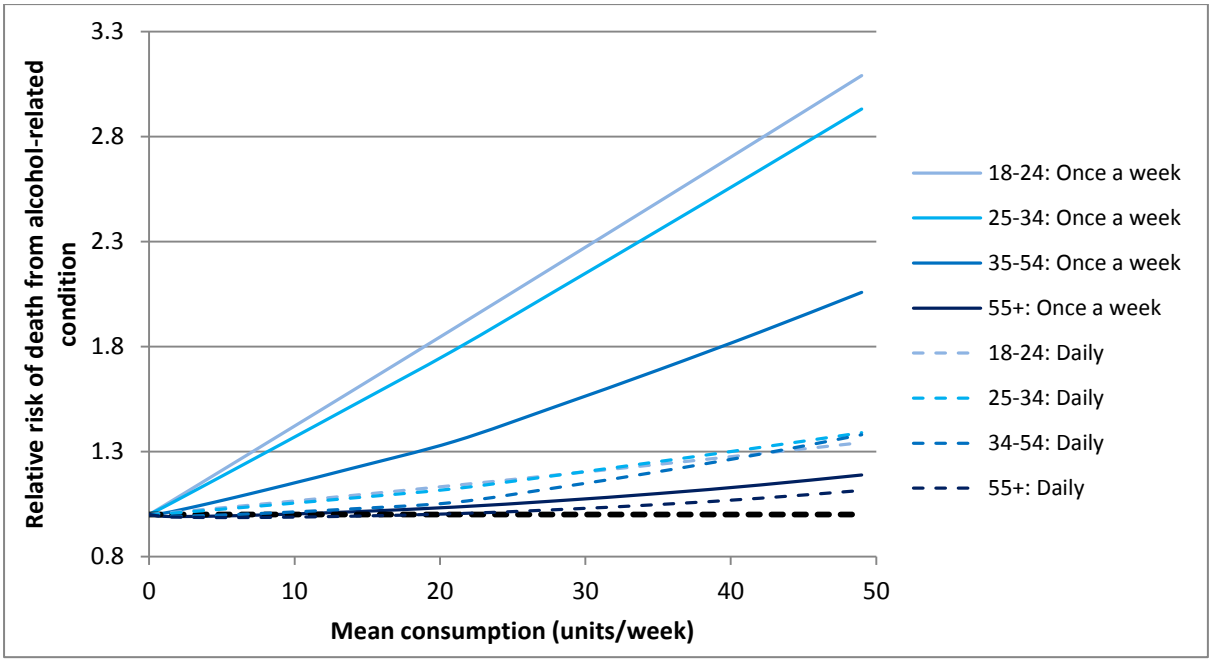

Figure 12: Male relative risk of alcohol-related mortality by mean weekly consumption, number of drinking days and age

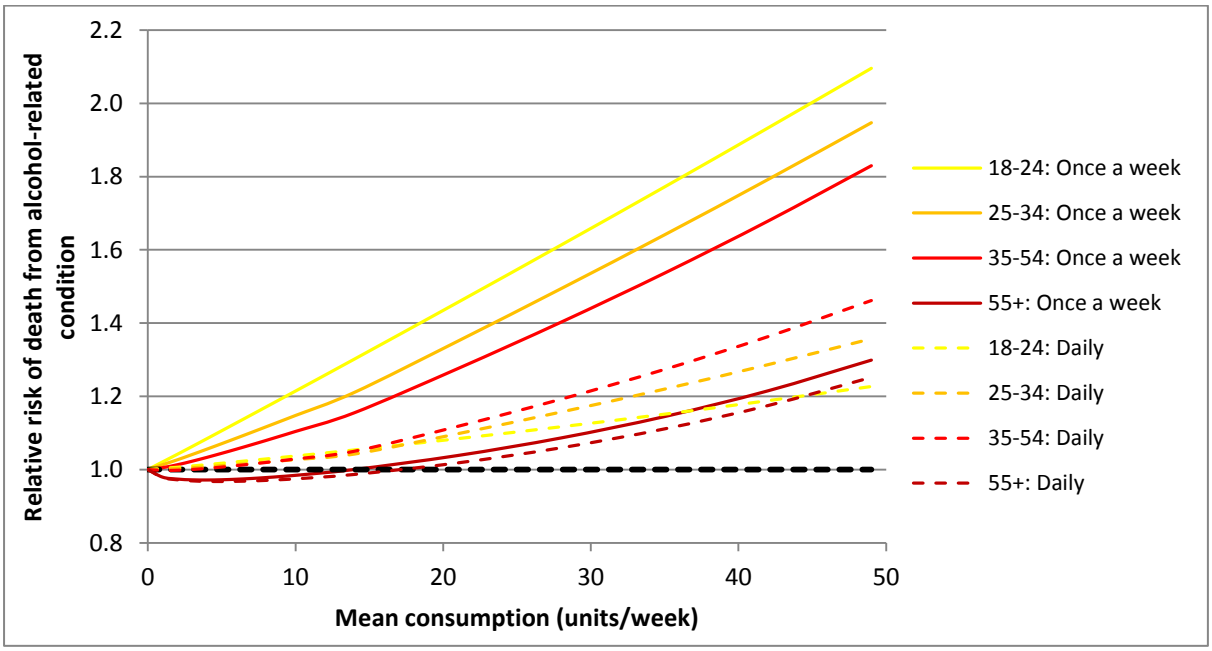

Figure 13: Female relative risk of alcohol-related mortality by mean weekly consumption, number of drinking days and age

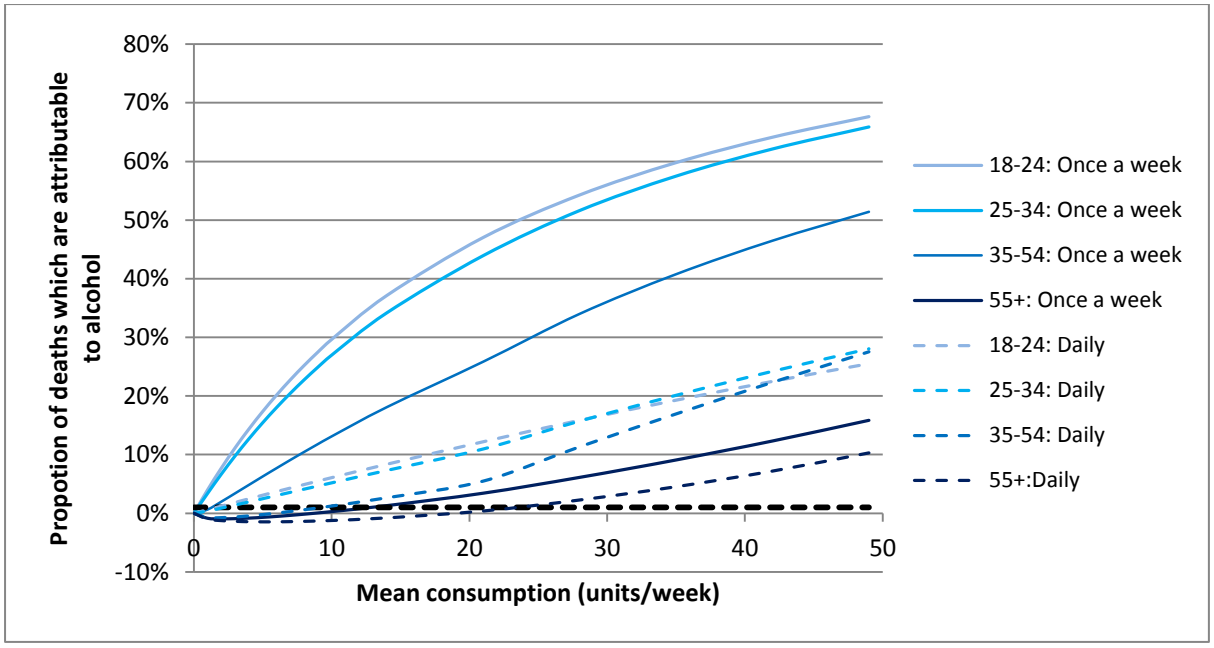

Figure 14: Male proportion of deaths attributable to alcohol by mean weekly consumption, number of drinking days and age

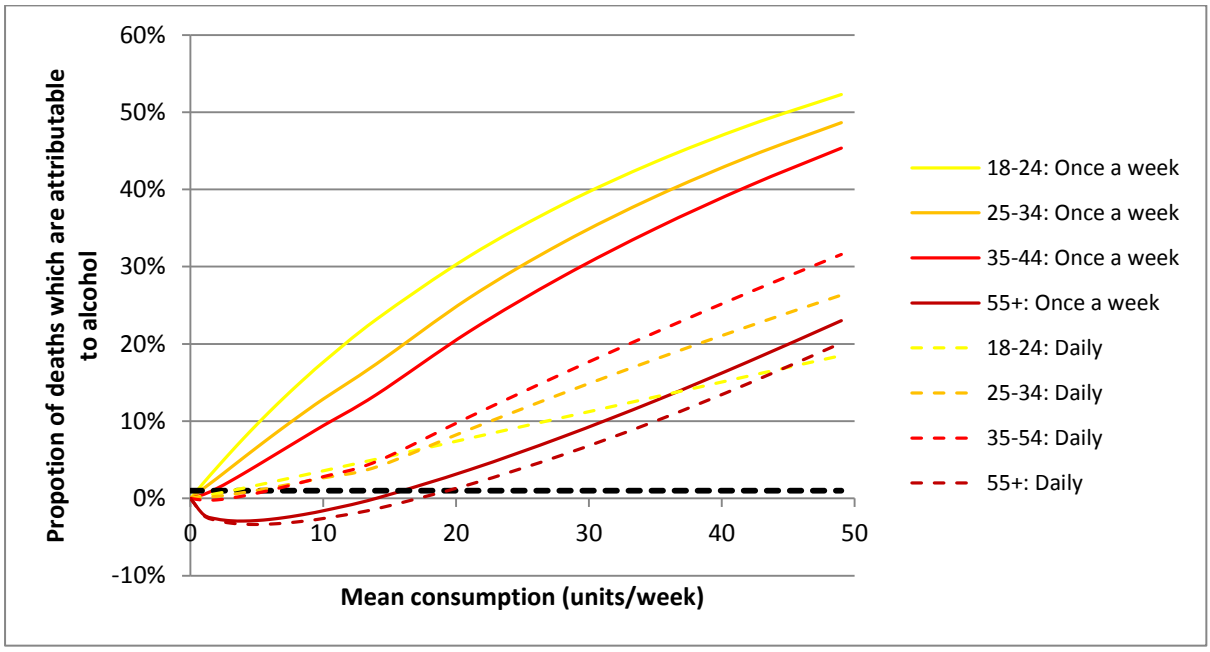

Figure 15: Female proportion of deaths attributable to alcohol by mean weekly consumption, number of drinking days and age

4.5. Sensitivity analyses

Sensitivity analyses are presented in two sections: analyses of key assumptions and analyses of alternative thresholds for deriving implied guidelines.

4.5.1. Analyses of key assumptions

Four sets of sensitivity analyses were undertaken to understand the extent to which the results are affected by key assumptions. The sensitivity analyses examined:

- SA1: The impact of assuming a threshold effect in the function relating peak daily consumption to risk for acute alcohol-related conditions. The modelled threshold assumed risk equivalent to abstainers up to three units for females and four units for males.[70]
- SA2: The impact of assuming no protective effects for cardiovascular conditions. Where consumption levels are associated with reduced risk relative to abstainers, the risk function is adjusted so risk is equal to abstainers (i.e. Relative Risk = 1.0).
- SA3: The impact of modelling a longer time period; namely 10 years. This allows shifts in the demographic structure of the population to occur following reduced premature mortality.
- SA4: The impact of accounting for recent trends in mortality rates from cardiovascular conditions, using the most recent available figures from 2013.

The implied guideline thresholds for mortality under each sensitivity analysis and the base case are presented in Table 13. The results show that assumptions regarding the presence of absence of threshold effects have a substantial impact on the implied guidelines, particularly for males and when using the Canadian approach. Implied guideline thresholds for men are approximately twice as high as in the base case when using the Canadian approach, and around 60% higher under the Australian approach. The thresholds for women are 10-15% higher under either approach.

Modelling a ten year period to allow the demographic structure of the population to change in response to new drinking behaviours and accounting for recent trends in cardiovascular mortality both have moderate impacts on the implied guidelines. In general modelling a longer time period leads to slightly higher implied guideline thresholds, while accounting for reductions in cardiovascular death rates leads to slightly lower implied guidelines thresholds. In the latter case, this is because the impact of cardioprotective effects on overall death rates is reduced. To illustrate the scale of these differences, the implied guideline threshold for males drinking daily using the Canadian approach is 9.8 units per week in the base case, 10.2 units per week when modelling a ten year time period and 9.5 units per week when modelling lower baseline CVD mortality rates.

Crucially, assuming no protective effects substantially lowers the implied guideline. The Canadian approach relies on the presence of protective effects so no guideline is derived; however, under the Australian approach the implied guideline threshold is below four units per week in all instances. This highlights that although observed protective effects are small, they exert a strong influence on overall risk estimates.

Table 13: Implied guideline for mean weekly consumption under different sensitivity analyses

		Units per week									
		Males					Females				
Threshold	Drinking days per week	Base case	SA1: Threshold effect	SA2: No protective	SA3: 10 yrs	SA4: CVD risks	Base case	SA1: Threshold effect	SA2: No protective	SA3: 10 yrs	SA4: CVD risks
Canadian RR=1.0	1	3.4	6.4	-	3.5	3.6	10.0	9.7	-	10.3	6.8
	2	5.8	12.4	-	6.1	6.0	12.0	13.1	-	12.1	8.5
	3	7.4	15.8	-	7.6	7.4	12.8	14.6	-	12.6	9.2
	4	8.2	17.7	-	8.6	8.2	13.2	15.1	-	13.0	9.6
	5	8.9	18.7	-	9.3	8.7	13.4	15.4	-	13.2	9.8
	6	9.4	19.3	-	9.8	9.2	13.6	15.6	-	13.4	10.0
	7	9.8	19.2	-	10.2	9.5	13.6	15.8	-	13.5	10.1
Australian Proportion =1%	1	6.0	8.2	1.5	6.4	6.0	12.0	11.2	2.3	12.4	9.2
	2	9.4	14.9	2.1	10.0	9.3	14.0	14.6	2.8	14.4	11.1
	3	11.3	18.5	2.4	11.8	10.9	14.8	16.2	3.1	15.1	11.9
	4	12.3	20.1	2.6	13.0	11.9	15.2	16.9	3.2	15.5	12.3
	5	13.1	21.5	2.7	13.8	12.6	15.4	17.2	3.3	15.8	12.6
	6	13.7	22.1	2.8	14.6	13.2	15.6	17.5	3.3	15.9	12.8
	7	14.1	22.2	2.9	15.1	13.5	15.7	17.6	3.4	16.0	12.9

4.5.2. Analysis of alternative thresholds

Both the Canadian and Australian approach could be applied differently to derive guideline thresholds. Under the Canadian approach, instead of defining low risk as the consumption level at which risks are equal to those of abstainers, an alternative application is to define low risk as the consumption level at which the greatest risk reduction is seen relative to abstainers (i.e. the nadir of the curve). Under the Australian approach, alternative proportions of mortalities or morbidities which are alcohol-attributable could be used (e.g. 2.0% instead of 1.0% of deaths being alcohol-attributable).

Table 14 presents estimated guideline thresholds for mortality comparing the base case Canadian results and results if the nadir of the curve is used instead. By definition the implied thresholds are lower under the sensitivity analysis than in the base case. Maximum risk reductions typically occur at very low levels of consumption and do not increase substantially if drinking is spread over a larger number of days. For males, the nadir of the curve is estimated to occur at 1.2 units per week if drinking once per week and 4.3 units per week if drinking daily. For females, the equivalent estimates are 3.2 units and 4.3 units.

Table 14: Estimated guideline thresholds for mortality under different applications of the Canadian approach (SA5)

		Units per week			
		Males		Females	
Threshold	**Drinking days per week**	**Base case RR=1.0**	**Sensitivity analysis Nadir of curve**	**Base case**	**Sensitivity analysis Nadir of curve**
Canadian	1	3.4	1.2	10.0	2.8
	2	5.8	1.7	12.0	3.2
	3	7.4	2.1	12.8	3.4
	4	8.2	2.0	13.2	3.5
	5	8.9	2.2	13.4	3.6
	6	9.4	2.3	13.6	3.6
	7	9.8	2.4	13.6	3.4

Table 15 compares alternative estimated guideline thresholds using the Australian approach. Thresholds are derived which correspond to consumption levels when the proportion of deaths which are alcohol-attributable is 0.5%, 1.0%, 1.5% and 2.0%.

The use of these alternative cut-off points has a moderate impact on the estimated guideline threshold. For males, the threshold varies between 4.7 and 8.3 units per week if drinking once per week and between 12.0 and 18.0 units per week if drinking daily. Similar differences are seen for females where the threshold varies between 11.0 and 13.9 units per week if drinking once per week and 14.7 and 17.8 units per week if drinking daily.

Table 15: Estimated guideline thresholds for mortality under different applications of the Australian approach

		Units per week							
		Males				Females			
Threshold	**Drinking days per week**	**SA 0.5%**	**Base case 1.0%**	**SA 1.5%**	**SA 2.0%**	**SA 0.5%**	**Base case 1.0%**	**SA 1.5%**	**SA 2.0%**
Australian	1	4.7	6.0	7.1	8.3	11.0	12.0	12.9	13.9
	2	7.7	9.4	10.9	12.4	12.9	14.0	15.0	16.0
	3	9.5	11.3	13.0	14.7	13.7	14.8	15.8	16.8
	4	10.3	12.3	14.2	15.9	14.1	15.2	16.2	17.2
	5	11.1	13.1	15.0	16.8	14.4	15.4	16.5	17.5
	6	11.6	13.7	15.7	17.5	14.5	15.6	16.7	17.7
	7	12.0	14.1	16.1	18.0	14.7	15.7	16.8	17.8

5. Discussion

5.1. Summary of results

Table 16 summarises the implied guideline consumption thresholds derived using different approaches. Thresholds are presented as both units per week and units per day as the latter more clearly illustrates how the number of days on which alcohol is consumed affects the estimated guideline threshold using either the Canadian or Australian approaches. These risk estimates and the sensitivity analyses point to five key findings described below.

Table 16: Implied guideline consumption thresholds using different approaches

		Units per week		Units per day	
Threshold	**Drinking days per week**	**Males**	**Females**	**Males**	**Females**
Canadian: RR=1.0	1	3.4	10.0	3.4	10.0
	2	5.8	12.0	2.9	6.0
	3	7.4	12.8	2.5	4.3
	4	8.2	13.2	2.1	3.3
	5	8.9	13.4	1.8	2.7
	6	9.4	13.6	1.6	2.3
	7	9.8	13.6	1.4	1.9
Australian: Proportion=1%	1	6.0	12.0	6.0	12.0
	2	9.4	14.0	4.7	7.0
	3	11.3	14.8	3.8	4.9
	4	12.3	15.2	3.1	3.8
	5	13.1	15.4	2.6	3.1
	6	13.7	15.6	2.3	2.6
	7	14.1	15.7	2.0	2.2

First, using the Canadian approach, the implied drinking guideline for males is between 1.4 units per day if drinking every day and 3.4 units per day if drinking once per week. The implied drinking guideline for females is 1.9 units per day if drinking every day (0.5 units greater than the male figure) and 10.0 units per day if drinking only once per week. The estimate for drinking once per week is much higher for females than males (10.0 units per day vs. 3.4 units per day) because the absolute risk of acute injury, even at high consumption levels, is much lower for females than males. Thus the implied female differs from the male threshold by being more strongly influenced by chronic risks, which are associated with mean weekly consumption, and less affected by acute risks, which are influenced by consumption frequency. More generally, it should be noted that acute risks are related to drinking on a single occasion and are partly attributable to factors including the drinking context (e.g. at home or in a bar) and the characteristics of the drinker. Thus the estimated threshold of 10.0 units if drinking once per week reflects the drinking contexts and drinker characteristics of an average female in the population rather than those of specific female drinkers at which any guideline may be targeted.

Second, the implied thresholds using the Australian approach are all marginally higher than those implied using the Canadian approach. Using the Australian approach, the implied drinking guideline

for males is between 2.0 units per day if drinking every day and 6.0 units per day if drinking once per week. The implied drinking guideline for females is 2.2 units per day if drinking every day and 12.0 units per day if drinking once per week (again much higher than the equivalent estimate for males).

Third, the above results all consider the male or female population as a group and use average estimated risks from ages 18 through to 89. Risk curves actually vary substantially by age and there are particular differences by age in the balance of acute vs. chronic risks and the underlying absolute level of health risk. These differences create problems for the Canadian and Australian approaches and suggests they are not well-suited to deriving age group-specific guideline thresholds. For example, younger age groups (i.e. 18-24, 25-34) have very low absolute mortality risk and particularly low chronic disease mortality risk, including for cardiovascular diseases. This means potential cardioprotective effects have only a minor influence when calculating this age group's average mortality risk across all alcohol-related conditions. Instead, the average risk curve is dominated by the acute risks which account for most alcohol-related mortality at younger ages. These acute risks increase linearly from zero and thus outweigh the small contribution of cardioprotective effects except at very low consumption levels. Consequently, any guideline threshold derived from the under-35s average risk curve using the Canadian approach would be correspondingly very low. Similarly, under the Australian approach, the very low chronic disease mortality risk at younger ages means acute deaths, including alcohol-attributable acute deaths, account for a large percentage of total deaths in this age group. An age-specific guideline threshold derived using the Australian approach (based on the consumption level where 1% of deaths are alcohol-attributable) would, therefore, also be very low.

If the Guideline Development Guide wished to derive age-specific guideline threshold, then one alternative would be to consider methods based around each age group's absolute annual risk of mortality. This may draw on Spiegelhalter's 'Micromorts' and 'Microlifes' approaches;[71] however, the appropriate method for deriving a guideline threshold under such an approach is unclear. The Australian 1 in 100 mortality risk could be adapted, although it is questionable whether the conceptual rationale underpinning this definition of acceptable *lifetime* risk can be considered equally valid for *annual* risk and for risk within all age groups.

Fourth, associations between reduced mortality risks for cardiovascular disease and lower levels of alcohol consumption have only limited relevance for selecting population-level lower risk drinking guidelines. The following points inform this conclusion:

- Although reduced alcohol-attributable mortality risks at lower consumption levels remain after accounting for risks from other alcohol-related conditions where there is no evidence of protective effects, the level of risk reduction relative to abstainers is low. The lowest relative risk of mortality compared to abstainers is 0.97 for females and 0.99 for males. This risk reduction is associated with very low levels of consumption, namely 2.4 units per week for males drinking daily and 3.4 units per week for females drinking daily (see Table 14).
- The Canadian approach derives a guideline threshold from the consumption level where there are no further reduced alcohol-attributable mortality risks. The analyses presented here suggest very small risk reductions for alcohol-related mortality persist up to 9.8 units per week for males drinking daily and 13.6 units per week for females drinking daily (see Figure 6 and Figure 7).

- Independent of alcohol consumption, people of each age and sex are at a different level of baseline risk for mortality from any cause and from each specific alcohol-related cause. This means risk reductions related to cardiovascular disease are of different importance to each demographic group's overall mortality risk. Analysis of variation in alcohol-related risk by age suggests that cardioprotective effects are only sufficient to provide substantial risk reductions from low levels of drinking for females aged over 55 (see Figure 15). For other groups, risk reductions for cardiovascular conditions are either largely or wholly outweighed by risk increases for other conditions.
- Strong concerns over the robustness of the evidence base for cardioprotective effects mean that, even for older females, mortality risk reductions from moderate alcohol consumption may be minimal or absent.

Fifth, the sensitivity analyses suggest the results are sensitive to alternative assumptions. For most sensitivity analyses (e.g. modelling a ten year time period, assuming lower CVD mortality rates, varying the threshold within the Australian approach) the size of variation from the base case in implied guideline thresholds is of the order of three units per week. However, for other sensitivity analyses (e.g. reintroducing threshold effects used in previous versions of SAPM, assuming no cardioprotective effects from moderate alcohol consumption) the variation in results from the base case are larger and of the order of ten units per week. These results suggest the base case should not be accepted uncritically as the implied guideline thresholds are sensitive to alternative assumptions and baseline data and there are not strong arguments for preferring the base case specifications over those used in the sensitivity analyses. In particular the strong influence of assumptions regarding the veracity of observed cardioprotective effects is demonstrated. Section 5.4.1.2 of this report discusses the scientific debate regarding whether observed associations between moderate drinking and reduced cardiovascular mortality risk reflect a causal relationship and depending on one's position on this debate, the implied guideline thresholds in the base case should be interpreted with particular caution.

5.1.1. Results for single occasion drinking and acute risks

As with the Canadian and Australian approaches on which it draws, this report provides no clear basis for selecting a single occasion drinking guideline. This is because the Canadian approach relies on a j-curve which is not present when considering risks associated with an individual occasion of drinking. Similarly, the Australian approach relies on modelling (in the present case using SAPM) which combines multiple heterogeneous occasions into an annual risk of alcohol-related mortality which can be compared to annual mortality risk from other occasions.

To resolve this problem, the Guideline Development Group may consider that one motivation for having a single occasion threshold is that drinkers may not spread their consumption evenly across the week. Thus drinkers may consume a large proportion of the mean consumption guideline on one or two occasions, increasing their acute risk. In the context of this motivation, considering Table 16 alongside information on the drinking patterns of those at greatest risk of acute harms may inform the selection of a single occasion guideline. For example, if the groups at greatest risk of acute harms typically drink twice per week, the Australian approach would suggest a single occasion guideline of the order of 5 units for males and 7 units for females (while bearing in mind SAPM assumes equal consumption on each occasion).

For clarity, this approach does not permit a guideline to be straightforwardly extracted from the analyses presented above. Instead, it relies on the Guideline Development Group considering and balancing the information in Table 16 and evidence on the typical drinking patterns of those at whom a single occasion guideline would be aimed. The Group may also wish to factor into these considerations alternative literature-based evidence which speaks more directly to the risks of single occasion consumption. Examples of this literature can be seen in the reports of the Canadian and Australian Guideline Development Groups and a more recent report by the RARHA project.[6,8,72]

5.2. Comparison with previous analyses and guidelines

In the base case, the implied guideline thresholds are lower than those in the current UK lower risk drinking guidelines and the guidelines which resulted from the Canadian and Australian reviews. The current UK guidelines are daily guidelines and recommend not drinking every day. Assuming a maximum of five drinking days per week, the current UK guidelines imply maximum limits of 20 units per week for males and 15 units per week for females. The Canadian and Australian mean weekly guideline levels equate to approximately 25 and 17 units per week for males and 17 units per week in both countries for females. Assuming drinkers consume alcohol between three and five times a week, the implied weekly guidelines in this report vary between 7 and 13 units per week for males and 13 and 15 units per week for females.

The current Australian guidelines give the same consumption threshold for both males and females, reflecting their Guideline Development Group's conclusion that alcohol-attributable mortality risks do not significantly differ at the consumption levels of interest. Although the UK Guideline Development Group may wish to take further evidence into account, Table 16 points toward a similar conclusion for males and females drinking on four or more days per week in the UK, although implied guidelines for females are slightly higher than males.

Methodological differences between the analyses in each country should be borne in mind when comparing implied guidelines. A key difference between the present analysis and that in Australia is that protective effects were excluded from the Australian modelling. When protective effects were removed in the present analysis, very low guideline thresholds were derived (approximately two to three units per week). There are a number of differences between the modelling approaches in this report and in Australia which may contribute to this difference; however, a key explanation appears to be differences in the baseline mortality rates for individual health conditions in the UK and Australia. These differences lead to higher risk estimates at lower consumption levels in the UK and become particularly salient when any cardioprotective effects which counteract these risks are removed. Results are particularly affected if conditions where relative risks are high for moderate consumption are more prevalent in the UK compared to Australia or, conversely, if conditions where relative risks are low for moderate consumption are less prevalent.

A recent report by the EU-funded RARHA project investigated for seven European countries the consumption levels associated with lifetime alcohol-attributable mortality risks of 1 in 1,000 and 1 in 100. The analysis was largely based on the Australian approach; however, there were a number of methodological differences. Four of these are particularly salient. First, protective effects were included in the RARHA analysis. Second, analyses are only presented for mean consumption and not number of drinking days. Third, the RARHA analysis only considers risks for those aged under 75 and argues mortality data for those 75 and older is less accurate with respect to cause of death. Fourth,

it is noted that females have a higher life expectancy and this will exert a downward influence on female alcohol-attributable mortality risk up to age 74. To ensure implied guideline thresholds are driven by alcohol-attributable mortality risks rather than overall mortality risks, the RARHA base case analysis assumes males and females have the same overall mortality risk. The alternative scenario of different overall mortality risks is examined in a sensitivity analysis and demonstrates implied guideline thresholds are lower for males and higher for females when differences in life expectancy by sex are included in the analysis. This sensitivity analysis is the most similar to the analyses presented here and the average results across all seven countries for the 1 in 100 threshold give implied guideline thresholds which are higher than those in the present report. The RARHA implied thresholds for daily drinkers are 15 units per week for females and 21 units per week for males.

Confidence in the results presented here is generally increased by a degree of consistency in the implied guideline thresholds across studies and countries. Although the implied guidelines thresholds presented here are lower than those within previous studies, they remain of the same order of magnitude and different assumptions examined within the sensitivity analyses, particularly the reinstatement of threshold effects used in previous versions of SAPM, bring the implied guideline thresholds close to those found elsewhere. The methodological differences described should not be overlooked as these may, in part, be responsible for both the lower estimates presented here and the general similarity of findings in terms of order of magnitude. Had the present analysis followed the Australian approach of excluding protective effects, the implied guideline thresholds would have been starkly different to those found elsewhere (see Sensitivity Analysis 2). Similarly, the decision in the RARHA project to exclude mortality at ages 75 and over from the analysis is a major methodological differences from other studies given a large proportion of mortality occurs in this older age group. The impact of this exclusion on implied guideline thresholds is difficult to infer as it is dependent on the balance of mortality rates within this age group between conditions unrelated to alcohol, conditions related to alcohol but having no potential protective effect and conditions related to alcohol and having a potential protective effect. Cardiovascular diseases, which have a potential protective effect, tend to be more prevalent in older age groups and this suggests that by excluding those aged 75 and over the RARHA analysis may bias downwards implied guideline thresholds.

Overall, the conclusion drawn from comparison with previous studies is that although implied guideline thresholds are of similar orders of magnitude, there are a significant number of methodological decisions which can impact on the results in different ways depending on the country and baseline data under examination.

5.3. Strengths of the analysis

The analyses presented here are based on the best available evidence on the relationship between alcohol consumption and risks of alcohol-related health conditions. These are (a) systematic reviews and meta-analyses of international evidence published in scientific journals, (b) UK-specific evidence on the proportion of mortalities and morbidities attributable to alcohol for a set of conditions where alcohol has been shown to play a causal role and (c) UK Government datasets detailing alcohol consumption, mortality, morbidity and population demographic data.

These data are synthesised to produce risk estimates using the Sheffield Alcohol Policy Model (SAPM), a well-established modelling framework which has previously been used in influential analyses of alcohol policies published by the National Institute for Health and Care Excellence[32] and in leading scientific journals.[27,28,31] A particular strength of SAPM is the simultaneous consideration of a wide range of alcohol-related health conditions arising from both regular long-term alcohol consumption and episodes of heavy drinking. A range of sensitivity analyses are provided for consideration by readers to aid understanding of how the results vary when using alternative assumptions, evidence or methodologies. Further narrative discussion of uncertainty to aid readers' understanding of the results is provided in Sections 5.4 and 0 below.

Analyses of risk are presented in several ways, allowing consideration of different alcohol consumption patterns, different outcomes (mortality and morbidity) and different metrics of risk (relative risk, proportion of deaths attributable to particular causes). Separate analyses are presented for males and females and the effects and challenges of separating analyses by age are also shown.

5.4. Limitations

When using the results presented above, it is important to be aware of limitations in both the underlying epidemiological evidence base which provides the inputs to SAPM and the SAPM methodology itself. Given their importance to the application of the Canadian and Australian methods, the key limitations are discussed in some detail below; focusing first on general limitations of the epidemiological evidence followed by limitations specific to SAPM.

5.4.1. Limitations of epidemiological evidence

The epidemiological evidence detailing relationships between alcohol consumption and risks to health is primarily derived from meta-analyses of case control and cohort studies. Evidence used in SAPM was identified via a systematic review of reviews to identify the most recent high quality meta-analyses. Those studies provide detailed information on the risks associated with alcohol and play an important role in public health analyses such as the Global Burden of Disease studies.[73] However, the studies also have widely acknowledged limitations relating to the underestimation of alcohol consumption and further biases which some scientists argue are key reasons for the observation of cardioprotective effects from moderate drinking. These points are discussed in turn.

5.4.1.1. Underestimation of alcohol consumption

SAPM requires as model inputs survey data on alcohol consumption and also draws on evidence linking consumption to health risks. In both cases, the alcohol consumption data typically underestimate levels of drinking when compared with more robust aggregate data (e.g. tax or sales data). Depending on the country and the survey method used, this underestimation can be such that surveys only account for between 40% and 70% of alcohol known to be sold in a given year.[74,75] The UK surveys used within SAPM account for approximately 60-70% of alcohol cleared for sale by HMRC.[76] This means risks of drinking are commonly derived from data which significantly underestimate the levels of alcohol consumption taking place. There are a number of reasons for this underestimation and, in particular, surveys are potentially subject to bias from four main sources.

First, cohort studies estimating risks of alcohol consumption using surveys often exclude certain population groups whose drinking differs from the general population. For example, surveys of

private households exclude those in nursing homes, psychiatric institutions, prisons and the military, students living in halls of residence and the homeless. Other groups are included in the sample but are substantially under-represented. A key example of this are dependent drinkers and a recent analysis estimated that, after weighting, the 2006 UK General Lifestyle Survey under-represented dependent drinkers by approximately 50%.[76] Surveys of UK clinical populations also suggest that dependent drinkers sampled in general population surveys have lower alcohol consumption levels than the wider dependent drinker population.[77,78]

Second, studies estimating risks from alcohol consumption vary in the questions they use to measure that consumption. This variation in survey questions used leads to markedly different levels of underestimation of consumption relative to aggregate sales or tax data.[79] For example, all of the following have been shown to alter substantially consumption estimates: asking about consumption for each beverage type in turn, asking about frequency of consuming at different consumption levels, extending the reference period for the question (e.g. over the last week, month, 6 months or year) and asking about both typical and heavy drinking occasions.[80]

Third, there may be inaccuracies in self-reports of drinking behaviour even when sampling and questionnaires are well-designed. People may over- or under-report their drinking for reasons of social desirability,[81] inaccurately recall how much they drank or lack of sufficient knowledge to provide accurate reports.[82-84] For example, a consistent finding is that drinkers underestimate the volume of liquid in self-poured drinks of spirits. Self-reports of consuming one unit of spirits are seen to correspond to drinks which contain on average two or more units.[85-87] This is particularly significant as it suggests a relationship between the beverages people drink, the locations they drink them (as self-poured spirits will typically not be drunk in bars or restaurants) and the extent of error in self-reported consumption data. This means self-report error is likely to vary across the population.

Fourth, after collecting data on drinks consumed, it must then be converted into units of alcohol as detailed information on alcoholic content are rarely collected from respondents. Where data have not been collected for each beverage type separately, there is a high risk of measurement error as participants or researchers attempt to convert a potentially diverse portfolio of drinks (e.g. strong beer, double whisky, large red wine, small white wine) into an estimate of total units consumed. Even where beverage-specific data have been collected, this still requires researchers to apply assumptions regarding average alcoholic strengths of drinks. These assumptions may be appropriate for the total population but if certain population groups tend to prefer stronger or weaker variants of beer, wine or spirits, their consumption estimates are likely to be biased

The above biases are near-ubiquitous within alcohol epidemiology and methods for adjusting data to account for them are not well-developed. In particular, methods accounting for variation in underestimation across the population are lacking.[76,88,89] Key barriers are a lack of gold standard individual-level data against which to assess surveys and resultant limited understanding of the extent to which consumption is under- or overestimated for different groups within the population.[90]

These biases do not fundamentally undermine the wide range of research undertaken using alcohol consumption data to investigate the impact of alcohol on health. The 43 alcohol-related health conditions selected for use within SAPM are chosen because there is robust evidence that alcohol

plays a causal role in their occurrence.[44] Although epidemiological evidence of the kind discussed here is crucial for quantifying associations between alcohol consumption and each condition, it is only one of several kinds of evidence which are used to assess whether alcohol is playing a causal role.[91] Other types of evidence (e.g. plausible biological mechanisms, findings from laboratory studies and the coherence and consistency of findings across all research) also play an important role. Similarly important is the consistent dose-response nature of the findings whereby, after accounting for any cardioprotective effects (see Section 5.4.1.2) risk typically increases in line with consumption. Although the precise level of risk associated with a given level of consumption may be subject to uncertainty, evidence that high levels of consumption entail greater risk than low levels of consumption is robust. Finally, analyses of alcohol consumption data have shown that, while consumption levels may be underestimated, many survey techniques are still able to reliably identify drinkers who are heavier and lighter drinkers and, consequently, those at lower and higher risk from their drinking.[92,93]

In conclusion, the limitations discussed above do mean that caution must be applied when interpreting individual quantifications of risk associated with a particular level of consumption. However, those quantifications remain of value as indicators of the level of risk associated with a particular consumption level or pattern and, particularly, as indicators of how that level of risk compares to alternative consumption levels or patterns. Moreover, they represent the best available evidence of risk levels from alcohol consumption and should form part of any consideration of what constitutes low risk drinking.

5.4.1.2. Debate regarding cardioprotective effects

An extensive literature including well-executed meta-analyses of high quality primary studies have found an association between moderate drinking and reduced risk of cardiovascular disease and particularly ischaemic heart disease. For example, a systematic review and meta-analysis of 24 studies found male mortality risk for ischaemic heart disease was lowest among those drinking an average of four units of alcohol per day and risk remained lower than that of abstainers up to approximately eight units per day. Other health conditions included in SAPM where there is evidence of protective effects are ischaemic and haemorrhagic stroke, type II diabetes and hypertensive diseases (i.e. diseases arising from high blood pressure).

This literature has attracted substantial debate regarding whether evidence is sufficient to conclude that low levels of alcohol consumption have a causal relationship with improved cardiovascular health. The debate includes detailed critique of both observational and meta-analytic studies, exploration of potential biological mechanisms explaining observed cardioprotective effects and arguments regarding the public health relevance of establishing the veracity of cardioprotective effects given alcohol's undisputed risk for other diseases and the various alternative options for reducing cardiovascular risk.[10,12,13,17,94] The key arguments suggesting cardioprotective effects may be over-estimated by standard epidemiological analyses are outlined below.

First, there is evidence that participants in epidemiological cohort studies may differ with regard to their underlying health status compared to the general population. One reason for this is such studies often recruit participants with no underlying health conditions at baseline.[13,95] The resulting potential for bias was demonstrated in a major European prospective cohort study which included at baseline people with chronic disease. Risk estimates were calculated for both the whole cohort and

for a subsample of the cohort who were free of chronic disease at enrolment.[14] Relative risk of cardiovascular mortality was lowest in those with light to moderate alcohol use; however, this was only the case among the subsample free from chronic disease at enrolment. This suggests sample selection processes for typical cohort studies may disproportionately exclude those at cardiovascular risk from moderate drinking leading to overestimation of any cardioprotective effect.

Second, estimates of risk relationships between alcohol consumption and health conditions are commonly quantified by calculating the risk of a given level of consumption relative to the risk of zero consumption (i.e. abstention). In practice, this means assuming that, after controlling for a range of confounding factors such as age and gender, drinkers and abstainers only meaningfully differ in terms of their alcohol consumption and a narrow set of other factors. This assumption has been questioned and the characteristics of abstainers and their similarity to the general population have been closely scrutinised.[20-25,96] Most significantly, the classification of former drinkers as abstainers has raised particular concerns, particularly where those former drinkers have stopped drinking due to health problems. Meta-analyses which disaggregate abstainers (e.g. never drinkers, former drinkers, occasional drinkers) have concluded that using a single abstainer category leads to overestimation of the cardioprotective effect of alcohol.[15,16,18]

Third, alcohol consumption is typically measured in epidemiological studies of long-term health risks as average daily consumption. However, recent evidence incorporating data on frequency of heavy drinking occasions (defined as more than 7.5 units on a single day) has shown an elevated ischaemic heart disease risk for moderate drinkers who have heavy drinking occasions at least once per month when compared to moderate drinkers with fewer heavy drinking occasions.[61] Further analyses suggest any cardioprotective effect from moderate drinking may be attenuated or no longer present among those who have heavy drinking occasions at least monthly.[97,98]

Fourth, alcohol consumption is only one of many variables which have a positive or negative association with an individual's cardiovascular risk and it has been argued that "groups with different drinking habits differ in several other ways than their drinking, making it difficult to separate the effects of drinking habits from other factors".[10 p.2] For example, both increasing age and smoking status increase individual risk of ischaemic heart disease and estimated risk relationships for alcohol consumption can be adjusted to account for these confounding factors.[97] However, a recent major meta-analysis noted substantial unexplained heterogeneity in risk estimates suggesting other important confounding factors were not controlled for.[18]

Evidence that cardioprotective effects may be overestimated is relevant here for three reasons: (1) the results presented above are highly sensitive to the removal of any protective effects; (2) potential cardiovascular effects of moderate drinking have informed previous guideline development processes[1,6] and (3) many of the studies which suggest cardioprotective effects are overestimated identify biases which are equally present in most epidemiological analyses of this kind (i.e. in estimated risk relationships between alcohol consumption and other non-cardiovascular health conditions). Indeed protective effects have been found for a plethora of unrelated health conditions with little evidence of plausible biological mechanisms to explain many of the associations.[10]

Given these critiques, there is little consensus in the scientific community regarding the presence or size of any cardioprotective effect. Evidence supporting the effects undoubtedly exists and the

association between moderate drinking and reduced cardiovascular risk is consistently observed within epidemiological analyses. However, interpretations of this finding vary and there are strong reasons to conclude the effect is, at the least, overestimated within standard epidemiological analyses and limited to certain groups within the population (e.g. those with fewer heavy drinking occasions, particular demographic characteristics and particular health behaviours). Crucially, the methodological issues which give rise to these beliefs are not limited to studies of cardiovascular risk. They apply equally, creating greater or lesser degrees of bias, to studies of other health conditions. The potential effect of those further biases has not been quantified in the present report.

5.4.1.3. Further limitations of epidemiological analyses

In addition to those points raised in the debate regarding cardiovascular risk a further set of common limitations in primary epidemiological studies or meta-analyses of those studies are relevant. These include:

- Relating consumption at a single point in time to health outcomes rather than a trajectory of consumption across the period of time during which the health condition developed;[99]
- Not accounting for systematic differences in health risks between individuals with the same average daily consumption but different drinking patterns;[11]
- Synthesising within meta-analyses different measures of alcohol consumption from primary studies or creating categorical consumption measures (e.g. 1-3 units per day, 4-6 units per day) which reduce the precision of consumption estimates.[16,18]

5.4.1.4. Summary

The above discussion highlights that, as with all research, epidemiological analyses estimating risk relationships between alcohol consumption and health outcomes are subject to important limitations. As with self-reported alcohol consumption data, there is no suggestion in the research literature that the limitations discussed above fundamentally undermine evidence of causal relationships between alcohol consumption and the 43 alcohol-related health conditions modelled here. Again, a range of alternative evidence beyond epidemiological analyses supports the conclusion that alcohol is a causal agent for those conditions[44] and consistently observed dose-response relationships support conclusions that higher levels of risk occur for heavier drinkers. Moreover, research methods have developed to account for limitations as they have been identified (e.g. it is now common practice to attempt to exclude studies from meta-analyses if they do not disaggregate never drinkers from former drinkers). However, the limitations do imply that the estimated risk for any given level of alcohol consumption is subject to a degree of uncertainty beyond that provided by the confidence intervals or standard errors reported in most studies. The scale of this uncertainty is likely to be substantial as, for example, the evidence from available analyses described above suggests particular limitations can lead to large observed cardioprotective effects being called into question. The sensitivity analyses for this report further suggest that excluding those effects has a large impact on average risk estimates across all alcohol-related health conditions.

Quantifying the overall effect on risk estimates of the uncertainty in the data used by SAPM is challenging. Evidence is lacking on variation in underestimation of alcohol consumption across the population and on the influence of different drinking patterns on risk estimates for most diseases.

Although the effects of some limitations on risk estimates for ischaemic heart disease are reasonably well understood, [10,100] the effects of other limitations and the effects on risk estimates for other conditions are less widely researched. A small number of studies have attempted to model the effects of these limitations on various alcohol epidemiology metrics and provide indications of the potential scale of uncertainty around risk estimates. Examples of this approach include studies examining how the impact of different adjustments to alcohol consumption data affect levels of underestimation and estimated levels of alcohol-attributable mortality. Results have shown underestimation of alcohol consumption data may lead to the number of alcohol-attributable cases for a range of conditions (including key diseases such as liver cirrhosis) being underestimated by between 30% and 40%.[76,88,101] Note that this does not mean the results presented here are necessarily subject to the same 30-40% degree of uncertainty as there are a large number of steps between calculating numbers of alcohol-attributable mortalities and producing modelled estimates of risks relationships. The authors are, however, unaware of any modelling study which seeks to simultaneously account for a wide range of the limitations discussed above and thus produces a comprehensive quantified uncertainty estimate.

In the absence of quantification, evidence-based judgements can be made as to the broad effects of different biases. For example, while underestimation of alcohol consumption has been shown to lead to underestimation of AAFs, it is also likely to lead to overestimation of risks as each *measured* consumption level corresponds to a higher *actual* consumption level. Similarly, classifying former drinkers as abstainers will increase the mortality rate in this group and bias downwards risks for current drinkers leading to underestimation of consumption risks. Finally, quantified effects of limitations for one alcohol-related outcome can often be used to inform understanding of similar effects for other outcomes. A key example of this is considering how critiques of the epidemiology of cardioprotective effects may impact on other alcohol-related risk estimates. Overall, however, the absence of a comprehensive analysis of uncertainty means such judgements can only provide guidance for considering the results

The implications of these points for the Guideline Development Group's use of the results presented above will be discussed after outlining limitations in the SAPM methodology which also require consideration by the group.

5.4.2. Limitations of SAPM

SAPM is subject to a number of limitations which are discussed in previous technical reports.[32,70] These include many of the limitations outlined above but also include a number of limitations of particular relevance to the modelling undertaken for the present report. These are discussed in turn below.

First, modelling of the relationship between single occasion alcohol consumption and acute alcohol-related health conditions is limited by the available consumption data and previous evidence on such risks. UK datasets which include the large sample size and mean weekly consumption estimates required by SAPM only characterise single occasion consumption via the heaviest drinking day in the week preceding the survey. This measure is unusual internationally and thus links poorly to the wider epidemiological evidence base on acute alcohol-related health risks.[102-104] It also captures only one dimension of single occasion consumption (quantity) and does not capture important additional dimensions (e.g. frequency of heavy consumption or variability in consumption

across occasions).[80,105] To partially account for this, the analyses of mean weekly consumption by number of drinking days examines the extreme scenarios where a given mean weekly level is consumed evenly across seven days (thus minimising acute risk) and consumed on a single day (thus maximising acute risk). Assuming drinkers consume at least weekly, the risks for all possible drinking patterns fall between these minimum and maximum risk scenarios. Therefore, to the extent that risks for the extreme scenarios are correctly estimated, a range of possible values for the implied guideline threshold can be identified.

Second, the epidemiological evidence base on acute risks is also limited as, unlike chronic alcohol-related health risks, there are few meta-analyses deriving risk functions linking single occasion consumption measures to specific health risks. SAPM accounts for these limitations in the available evidence by calibrating risk functions to AAFs or absolute case numbers for health conditions as outlined in Section 3.5. These risk functions are assumed to be linear in the absence of compelling evidence for alternative specifications. This assumption is also applicable to risk functions calibrated for wholly-attributable chronic health conditions. Further assumptions are also required regarding thresholds below which risks are identical to those of abstainers. Sensitivity analyses around those assumptions are provided.

Third, there is evidence that risk of alcohol-related health harm varies by socioeconomic status independent of alcohol consumption.[106] Although this has been accounted for in recent versions of SAPM,[27] the present version does not do so due to inconsistencies in the definition of socioeconomic status across the mortality and morbidity data available for each country.

Fourth, as no data are available on condition-specific morbidity prevalence in the general population, risk curve estimates for morbidity are based on a more limited definition of morbidity; specifically morbidity leading to one or more hospital admission(s).

Fifth, no measures of statistical uncertainty are provided around the risk estimates presented in the results. This is because the modelling uses sources of evidence which often do not report confidence intervals. Further, the limitations in the evidence and in SAPM itself which are discussed above contribute additional and substantial methodological uncertainty. This means any confidence intervals presented would, in one sense, be misleading as they pertain to only one part of the uncertainty which is known to exist around any given risk estimate. Therefore, in addition to presenting a comprehensive discussion of this uncertainty for consideration by readers, the uncertainty is also examined via set of scenario analyses investigating the sensitivity of the results to particular alternative assumptions, evidence or modelling methodologies. These are presented in Section 4.5.

Finally, risk estimates are provided for mortality and morbidity separately with no single metric provided which integrates these (e.g. quality adjusted life years or QALYs). The potential life years lost at different consumption levels also not provided and this introduces uncertainty regarding the extent to which premature mortalities are at younger or older ages. SAPM is not currently able to produce these metrics for the present analyses and this point is discussed further in the directions for future research (Section 5.6.1).

5.5. Consideration for using the results to inform selection of new lower risk drinking guideline thresholds

It is beyond the scope of this project report to make specific recommendations on appropriate guideline thresholds or to specify the processes the Guideline Development Group should follow when using this report. However, alongside other evidence considered by the group, the following section should usefully inform consideration of the model results and the accompanying commentary.

A critical over-arching conclusion which informs this section is that a number of expert judgements will be required by the Guideline Development Group to translate the model results and other available evidence into proposed guideline thresholds. Despite the recent shift in guideline development processes away from 'opaque collective expert opinion'[5] and toward transparent empirically-driven methods,[3] the points made will highlight that expert judgement cannot be removed from the process. Therefore, those reading this report should not expect that any guideline which emerges from the review process is solely a product of the numerical analyses presented. The final decision on a guideline threshold must represent a holistic expert judgement by the Guideline Development Group accounting for the modelling results, the various points raised in this discussion and further evidence sources and considerations identified in the group's deliberations.

5.5.1. Considerations relating to limitations in the available evidence

The strengths and limitations in the epidemiological evidence base and in the SAPM methodology are discussed in Sections 5.4.1 and 5.4.2. Sensitivity analyses around assumption made in the modelling are also provided in Section 4.5. These highlight that:

- Clear and scientifically-robust conclusions can be drawn regarding the broad levels of risk associated with different levels and patterns of alcohol consumption. For example, it is clear that, above the level where any protective affects occur, mortality and morbidity risks increase with increasing consumption. Therefore, there is robust evidence that, for example, consuming 50 units of alcohol per week carries substantially greater mortality and morbidity risks than consuming 20 units of alcohol per week.
- The level of risk associated with a particular level of mean weekly consumption varies depending on the pattern of consumption (e.g. weekly vs. daily consumption) as this exposes the drinker to greater or lesser levels of intoxication-related risk and cardiovascular risk.[61,107] The extent of this variation is not consistent across the population and depends on each population group's balance of baseline risk for acute and chronic alcohol-related conditions.
- The consumption levels at which the Canadian or Australian definitions of low risk drinking are exceeded are subject to uncertainty due to limitations in the available evidence. Sensitivity analyses illustrate that some aspects of this uncertainty have a modest but noteworthy impact on risk estimates (e.g. uncertainty around threshold effects where risk functions are calibrated) and others aspects have large impacts (e.g. uncertainty around threshold effects within risk function and the veracity of cardioprotective effects from moderate drinking). Further evidence from studies examining this uncertainty does not provide quantifications of uncertainty around risk estimates based on simultaneous consideration of all principal sources of uncertainty; however, it does provide evidence on the effects of several individual sources of uncertainty.

This evidence can be considered alongside the results presented here when selecting lower risk drinking guideline thresholds.

5.5.2. Considerations relating to variations in risk across the population

The results present guidelines for males and females and an analysis of variation in risk by age. These results highlight that:

- Males and females and different age groups experience different types of risk and different degrees of risk as a result of alcohol consumption. This variation is reflected in the risk estimates presented above. The Guideline Development Group should consider whether the implied guideline thresholds support separate lower risk guidelines for males and females for mean weekly consumption.
- Using the Canadian or Australian approaches to derive lower risk drinking guidelines for each age group based on age-specific risk curves is not recommended. Sections 4.4 and 5.1 illustrate how this produces guideline thresholds which vary markedly and sometimes counter-intuitively by age. Some of the guideline thresholds which would be derived are likely to lack credibility with the public and other stakeholders. This occurs because both the Canadian and Australian approach rely on the averaging of very different risk profiles across age groups. These risk profiles emerge from different balances of acute and chronic health risks across the population and further differences in absolute levels of health risk from all causes.
- The rationale for both the Canadian and Australian approaches is to employ a transparent and conceptually robust definition of low risk in selecting the guideline threshold. In both cases, it is argued that the guideline corresponds to a defensible definition of low risk. The Guideline Development Group may wish to consider to what extent that rationale is undermined by (a) the difficulty of applying either definition of low risk to certain age groups and (b) the population guideline being based on the average of highly diverse risks across the population and thus not corresponding directly to any one group's risk profile.
- Similar arguments may be made with regard to other individual characteristics which are associated with health outcomes and not examined in this report. These include socioeconomic status, health status, psychological dispositions, engagement in other health-related behaviours, genetic profile and personal health and health behavioural history.
- Public health guidelines must inevitably strike a balance between being specific enough to reflect variations in risk across the population and remaining sufficiently broad to be communicable via population-level health promotion campaigns. One approach to addressing heterogeneity in risk across the population is for the Guideline Development Group to consider who the key target populations for each guideline are and, where population-level guidelines are used (e.g. on bottle labels or television advertising where space is limited), ensure the guidelines are appropriate for those target populations.

5.5.3. Considerations relating to alternative guidelines and alternative means of selecting guideline thresholds

This report has provided a number of risk curves presenting implied guideline thresholds (a) under the Canadian and Australian approaches, (b) for different measures of alcohol consumption and (c) for mortality and morbidity. These results highlight that:

- The differences between implied guideline thresholds across analyses are modest in most cases.
- The range of implied thresholds for mean weekly consumption are generally lower in the base case model than those used in the current UK lower risk drinking guidelines and in the Canadian and Australian drinking guidelines which are partly based on similar modelling exercises
- The current UK drinking guidelines do not include a single occasion guideline. As explained in the Summary of Results (Section 5.1.1), the Canadian and Australian approaches offer no straightforward means for deriving such a guideline and the Guideline Development Groups in those countries based their single occasion guidelines on reviews of the relevant literature.
- If the UK Guideline Development Group wishes to propose a single occasion drinking guideline, the authors of this report recommend the approach outlined in Section 5.1.1 which relies on the group balancing (a) evidence in Table 16 on mortality risks associated with consumption on different numbers of drinking days, (b) the drinking patterns including number of drinking days per week among the population at whom a single occasion guideline is targeted and (c) literature-based evidence such as that considered by the Canadian and Australian approach.
- The notion of 'drink-free days' is part of the UK Government's 'Change for Life' campaign.[108] The House of Commons Science and Technology Committee also noted it was an important aspect of drinking guidelines based on daily, as opposed to weekly, consumption limits.[1] The analyses provided here link implied guidelines thresholds to number of drinking days, but this is a means of examining the balance of risks associated with low level regular drinking vs. occasional heavy drinking. It does not account for any potential additional benefits directly resulting from drink-free days via, for example, allowing the liver to recover following a heavy drinking occasion or disrupting habitual drinking behaviours. Rehm et al. recently argued "the scientific basis for alcohol-free days is scarce, especially for light to moderate drinking" while also noting well-established links between daily drinking and increased alcohol use disorder risk and indications that drink-free days may contribute to reduced mortality among heavy drinkers as a result of relieved liver function.[72 p.37] Therefore, it is recommended that the Guideline Development Group focus any discussion of drink-free days on (a) clarifying that a daily drinking guideline does not imply one should drink daily and (b) potential but unproven benefits for reducing liver damage and habitual drinking risks among heavier drinkers.
- A number of important outcomes related to alcohol consumption are not modelled here and should be considered. These include social risks to the individual (e.g. risks of being a victim of crime, negative consequences for family well-being and for income and employment) and risks of others being harmed by an individual's drinking (e.g. alcohol-attributable crime, intimate partner violence, worsened child development and macroeconomic impacts through reduced productivity). Evidence relating to these risks is less well-developed than for health risks; however, evidence of varying strengths for a causal effect from alcohol consumption is present in many cases.[109-112]
- Finally, with the exception of any cardioprotective effects of moderate drinking, this report has focused exclusively on the negative consequences of drinking. The Guideline

Development Group may wish to give consideration to the positive reasons people choose to drink and any potential benefits to well-being they receive from doing so. There is very little quantitative evidence in this area which could be incorporated within SAPM and this reflects difficulties in quantifying such benefits.[113] However, there are qualitative and ethnographic literatures on the reasons people choose to drink and the positive consequences for well-being they report from doing so[114,115] The Group may wish to consider this literature alongside evidence on the negative consequences of drinking.

5.6. Directions for future research

5.6.1. Extensions to the present research

The analyses above could be extended in two main ways:

First, the present analysis relied on combining data sources already held by the University of Sheffield. This meant certain analyses, particularly of morbidity, were not possible due to the absence of necessary data which could be obtained if required.

Second, the analysis of mortality does not include in its results the distribution of mortalities across age groups (although this is modelled) and thus does not account for potential years of life lost (PYLL). Further, it treats mortality and morbidity separately rather than integrating them within a single metric such as that provided by QALYs (quality adjusted life years) which measures life years lost and also losses from years lived without full health. It is possible in theory to repeat analyses using the Canadian approach using PYLL or QALYs rather than mortalities; however, it would be more challenging to do this using the Australian approach. This is because substantial revisions to SAPM would be required to calculate the PYLL and QALYs for other causes. These calculations are required to estimate the proportion of PYLL and QALY losses attributable to alcohol.

5.6.2. Wider research needs

A key limitation of the research which is discussed extensively above is the uncertainty in the available evidence measuring alcohol consumption and quantifying risk relationships between alcohol consumption and health outcomes. Research is required to increase understanding of the impact of this uncertainty on risk estimates and, potentially, increase precision of risk estimates. Specific research needs include:

- Further investigation of the impact of underestimation of alcohol consumption on epidemiological evidence relating to alcohol consumption and in particular its effects on AAFs and risk estimates;
- Further investigation of the variation in underestimation of alcohol consumption across individuals and population groups;
- Investigation of how the biases which are shown to affect estimates of cardioprotective effects from moderate alcohol consumption also affect risk estimates for other conditions where no protective effects are observed;
- Further development of methods to synthesise statistical uncertainty estimates (i.e. confidence intervals) from multiple sources when undertaking modelling exercises such as SAPM;
- Development of methods for simultaneously addressing all or many components of the above and allowing for comprehensively adjusted risk estimates to be produced.

A further key area requiring development in alcohol epidemiology is the relationship between health outcomes and complex patterns of drinking (e.g. average consumption, frequency of consumption, peak consumption and variability in consumption across drinking occasions) and the shifting of these patterns across the life course. Research is beginning to emerge in this area;[36,37,61,65,99] however, further understanding is required across the broad range of health outcomes related to alcohol and in the detail of how different drinking patterns explain variation in risks across the population.

Also important for the tailoring of drinking guidelines and risk estimates is an improved understanding of the context-specificity of risks and how acute risks in particular are affected by the drinking context (e.g. company, location, type of occasion). Currently, alcohol epidemiology is strongly informed by an 'exposure-outcome' paradigm which is built around metrics of ethanol consumption and ICD codes. Although informative, this method does not given attention to the fact that drinking alcohol is a socially embedded behaviour where many risks of concern to policy makers (e.g. social disorder, family well-being) are less objectively defined than health conditions and which are rooted in the interaction between alcohol consumption and the contexts in which it occurs. Emerging research examining alcohol's harm to those other than the drinker[110,116-121] and the nature of drinking occasions[122] are examples of research moves in this direction.

With regard to data, the UK has a strong legacy of cohort studies permitting analyses of alcohol consumption-related risk; however, it is in a deteriorating position with regard to the general population surveys which underpin SAPM and other valuable research. The long-running General Lifestyle Survey (GLF) was discontinued in 2011, ending a time series on alcohol consumption which had run over 35 years. No annual, UK-wide, large sample survey has been established to collect equivalent data. Longitudinal panel data collected in the later years of the GLF has not been cleaned by the Office for National Statistics and is thus not being made available to researchers. The health surveys of the individual UK countries have smaller samples than the (GLF) and must be synthesised by the researcher for UK-wide analysis. This process is hindered as the same data are not collected in each country. In some cases the data collected are of poor quality and do not conform to international recommendations[102-104] (e.g. the Health Survey for Wales only collects data on the heaviest drinking day in the preceding week; a measure of little value for much alcohol research as the crucial measure of average daily or weekly consumption cannot be derived from it). The new UK-wide panel study, Understanding Society, will collect alcohol consumption data intermittently but, again, alcohol consumption measures used do not conform to international recommendations and will present difficulties for researchers seeking to work within established international research paradigms. A strong recommendation of this report is for the Office for National Statistics and others involved in the design of UK alcohol consumption surveys to give greater regard to the needs of researchers using those surveys. An important first step would be establishing consistent data collection standards conforming to international recommendations across all UK surveys collecting information on alcohol consumption.

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