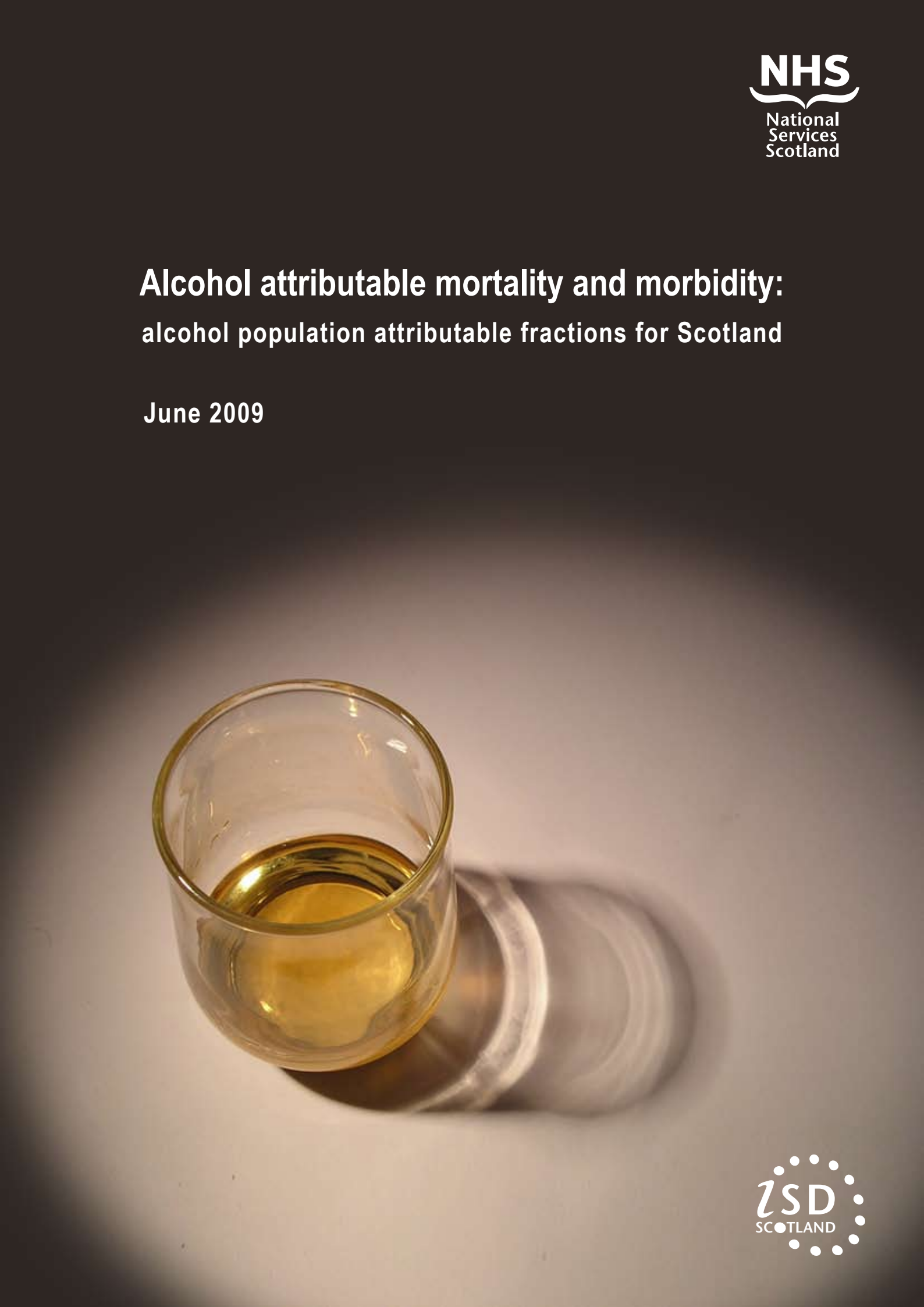
NHS National Services Scotland

Alcohol attributable mortality and morbidity:

alcohol population attributable fractions for Scotland

June 2009



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Executive Summary

Alcohol is linked to many disease conditions and is one of the major risk factors for burden of disease in established market economies. These conditions may be diseases, acute or chronic, or injuries. In order to measure the total burden of morbidity and mortality attributable to alcohol, all these conditions must be identified and the proportion attributable to alcohol calculated. Conditions where alcohol is 100% contributory are recognisable through the wording of ICD10 codes (e.g. alcohol dependence). The remaining conditions and the proportion attributable to alcohol (the population attributable fraction or PAF) can be determined through literature reviews or through primary analysis (or both). In Scotland, separate code-sets of conditions 100% attributable to alcohol have been defined and published by General Register Office for Scotland/Office of National Statistics and Information Services Division and are used to publish official statistics on alcohol mortality and morbidity respectively in Scotland. The aim of this study was to calculate alcohol PAFs for Scotland, using the best possible estimates based on the current evidence available in the epidemiological literature and specific estimates of population drinking in Scotland. These have been applied to mortality and morbidity data to estimate more fully the burden of alcohol related harm in Scotland.

Alcohol-attributable fractions were calculated for 53 conditions, of which 19 conditions were by definition wholly attributable to alcohol consumption and 34 conditions were partly attributable to alcohol consumption. The contribution of alcohol consumption varied across conditions. For example, it is estimated that 31% of male and 27% of female oesophageal cancer mortality and morbidity can be attributed to alcohol consumption. PAFs of over 50% for both men and women were calculated for non-alcoholic liver disease, cancer of the oral cavity and pharynx and epilepsy. Alcohol consumption is also estimated to be responsible for approximately 20% of breast cancer mortality and morbidity. Alcohol is also implicated in a range of injury related conditions including 34% of assaults, over 1 in 10 of suicide mortality and morbidity and in 35% of male and 20% of female road traffic fatalities and injuries. Alcohol consumption was found to have protective effects for three conditions: coronary heart disease; ischaemic stroke and cholelithiasis.

Applying these PAFs to mortality and morbidity data in 2003, the most recent year for which Scottish alcohol consumption data is available, we have estimated that 2,882 deaths were estimated to have occurred from alcohol attributable conditions, representing 1 in 20 (5.0%) of all deaths in Scotland in 2003. This is almost double the GROS figures of 1,525 alcohol-related deaths in 2003, calculated from the UK code-set defining alcohol related mortality. Men were at more risk of harm from their alcohol consumption than women; 6.8% of all male deaths were alcohol-attributable compared to 3.3% of all female deaths. Alcohol-attributable deaths also varied by age, with younger age groups more likely to be affected by their alcohol use. For example, over one in four (26.1%) of deaths in men and one in five of deaths (21.1%) in women aged 35-44 years old in 2003 were attributable to alcohol consumption. This compares to 2.0% (271/13,717) and 1.1% (239/20,966) in men and women aged 75 and over respectively. Below the age of 35, alcohol-attributable deaths were most likely to occur from the acute consequences of alcohol consumption, in particular, intentional self-harm and road traffic accidents. Beyond the age of 35, chronic diseases including mental and behavioral disorders due to alcohol use, alcoholic liver disease, cancer of the oesophagus and breast, colorectal cancer and hypertensive diseases were the more common causes of alcohol attributable deaths. A total of 1,492 deaths from partly attributable alcohol conditions were estimated to have been prevented by lower alcohol consumption, the majority from the prevention of Coronary Heart Disease (CHD) deaths in older age groups (i.e. 65 years and older).

Conditions either wholly or partly attributable to alcohol consumption also present a significant burden to the health care system. In 2003, there were 41,414 patient-specific discharges attributable to alcohol consumption, accounting for over one in twenty (7.3%) of all patient-specific discharges in Scotland among adults aged 16 and over. This is over one and a half times higher than the ISD 2003 report of 26,010 patient specific discharges based on the ISD code-set of wholly attributable alcohol conditions (Graham et al 2005). Unlike alcohol attributable mortality there was little variation by age in alcohol attributable patient specific discharges. Among men aged 16-64 yrs, approximately one in ten of all patient-specific discharges in Scotland were attributable to alcohol consumption, decreasing to 6.2% in men aged 75 years and over. In women, the highest proportion of alcohol attributable patient-specific discharges was found in those aged 45-54 years with approximately one in ten (9.2%) of all patient specific discharges alcohol attributable. Of the alcohol attributable patient-specific discharges, mental and behavioral disorders caused by alcohol use, hypertensive disease, cardiac arrhythmias, fall injuries and alcoholic liver disease were the most common conditions recorded. As with alcohol attributable mortality, the majority of the 13,618 patient-specific discharges prevented by lower alcohol consumption among both males and females were related to CHD.

In summary, alcohol plays a causal role in the development of a range of acute and chronic conditions. We have used the best risk estimates available from the epidemiological literature and the most recent alcohol consumption data available to calculate alcohol PAFs for Scotland. These calculations reveal that there were an estimated 2,882 deaths involving alcohol attributable conditions in 2003 and that there were 41,414 patient-specific discharges with an alcohol attributable condition. The figures presented here are a conservative estimate of the harm attributable to alcohol consumption given the limitations of the current evidence and the likely underestimation of population levels of alcohol consumption.

1. Background

There is a clear scientific consensus that alcohol consumption leads to a variety of harms to health and substantial agreement regarding many specific health consequences that result from alcohol consumption. Several recent reviews and meta-analyses provide surveys of the epidemiological evidence regarding alcohol effects for various health outcomes (English et al 1995, Corrao et al 1999, Gutjahr et al 2001, Ridolfo and Stevenson 2001, Rehm et al 2004, WCRF 2007). In 2003, the World Health Organisation undertook a study on the global burden of disease and estimated that alcohol consumption accounted for 3.2% of global mortality and 4.0% of global burden of disease (Rehm et al 2003).

These studies have estimated the disease burden from alcohol consumption through the calculation of population attributable fractions (PAFs). A population attributable fraction, also known as a population aetiological fraction, is an indirect quantification of morbidity and mortality due to a specified risk factor. For a particular disease or injury, it can be interpreted as the proportion of the total cases that would not have occurred in the absence of exposure to the risk factor (English et al 1995). In order to calculate alcohol PAFs, estimates of the relative risk of particular conditions/diseases for different levels of alcohol use are combined with prevalence data on the proportion of the adult population consuming alcohol at different levels of intake (WHO 2000).

In England, a number of studies have made estimates of alcohol-caused morbidity and mortality by using PAFs based on English consumption data (Britton and McPherson 2001, Cabinet Office 2003, Hughes et al 2004, Iyer et al 2006, Jones et al 2008). In addition, regional and local profiles of the public health effects of alcohol have been produced based on these alcohol PAFs and are now included in three key national indicators sets and performance management frameworks in England (Deacon et al 2007, NWPHO 2008). In Scotland, previous reports have quantified alcohol attributable mortality and morbidity using PAFs (Slatterly et al 2002, Scottish Public Health Observatory Collaboration 2008). However, the PAFs on which these estimates are based were not derived from Scottish alcohol consumption data. The purpose of this study was to calculate and present for the first time alcohol PAFs for Scotland based on alcohol consumption data for Scotland and best risk estimates from recent meta analyses, the epidemiological literature and primary data. The calculation of Scottish specific alcohol PAFs allow for the calculation of age and sex-specific attributable fractions and hence a more accurate means of estimating alcohol-attributable mortality and morbidity in Scotland. These estimates will augment current reporting of alcohol mortality and morbidity in Scotland.

An advisory group was established to advise on methodology, analysis, presentation of results and dissemination. The group comprised of representatives from the Scottish Government, NHS Health Scotland, Office for National Statistics, General Register Office for Scotland and Information Services Division (ISD) of National Services Scotland (see Appendix One for further information).

Box 1 Terminology

In this report the following terms, following practice established in recent reports, have been adopted: (WHO 2000, Rehm et al 2004, Walsh et al 2008, Jones et al 2008, Department of Health 2008).

Wholly attributable alcohol conditions: those conditions where alcohol is implicated in all cases of the condition; for example, alcohol-induced behavioural disorders and alcoholic liver cirrhosis. By definition, the PAF = 1, because no cases would be expected to arise in the absence of alcohol.

Partly attributable alcohol conditions: where alcohol is causally implicated in a proportion but not all cases of the condition. The PAF here is more than 0 but less than 1.

2. Alcohol attributable fractions: methods

The attributable fraction is the proportion of cases recorded in a population with a particular condition that is estimated to be solely caused by a particular risk factor (in this context, alcohol consumption) after controlling for the confounding effects of demographic variables and other risk factors such as smoking. The development of the alcohol PAFs involves a number of stages:

- Selecting the alcohol attributable conditions for inclusion
- Deriving estimates of relative risks from meta-analyses of large scale epidemiological studies of drinking at defined levels of intake (indirect method) or case series studies and/or routine statistics (direct method)
- Calculating prevalence of drinking alcohol at these defined levels of intake in the Scottish population
- Estimating the alcohol PAF as a positive function of the prevalence of drinking (the exposure) and the relative risk function for each alcohol attributable condition

2.1 Selection of alcohol attributable conditions

The selection of conditions wholly or partly attributable to alcohol consumption (see box 1 above) has been based on a review of meta-analyses and systematic literature reviews examining individual risk of disease associated with alcohol consumption. In addition, a number of reviews focusing on alcohol and cancer outcomes were also included. A list of these studies and the full literature review can be found in Appendix Two.

Following the methodological approach taken by Gutjahr et al (2001) and Rehm et al (2004), the decision on the inclusion of a particular disease or condition in the final list of alcohol-attributable conditions was taken where the weight of evidence from literature reviews and meta analyses has been consistent in concluding sufficient or some limited evidence for a causal relationship using established epidemiological causal verification criteria[1] (Rothman & Greenland 1998, IARC 1998). Greater weight was given to studies where established epidemiological criteria were used in the study itself to assess the causal relationship between alcohol and disease outcome (e.g. English et al 1995, IARC 1998, Corrao et al 1999, Gutjahr et al 2001, Rehm et al 2003, World Cancer Research Fund 2007).

Based on this review of existing systematic literature reviews, meta analytic studies and primary research, a list of conditions (based on version 10 of the WHO International Classification of Diseases (ICD)) considered wholly attributable or partly attributable to alcohol consumption was derived.

1 This judgement was made using standard criteria for establishing causality in epidemiology, with the most weight placed on the following four criteria (Rothman and Greenland 1988, IARC 1998): consistency across several studies; established biological mechanisms; strength of the association (effect size) and temporality (i.e. cause before effect).

2.1.1 Wholly attributable alcohol conditions

Conditions where alcohol is 100% contributory i.e. where the development of a condition necessarily requires the consumption of alcohol, are recognizable mostly through the wording of ICD codes (e.g. alcohol dependence, accidental poisoning by alcohol) and are shown in Table 1.

Table 1 Conditions wholly attributable to alcohol consumption.

Condition	ICD-10 codes
Alcohol induced pseudo Cushing's Syndrome	E24.4
Wernicke's encephalopathy	E51.2
Mental and behavioural disorders due to use of alcohol [2]	F10
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
Alcohol induced chronic pancreatitis	K86.0
Fetus and newborn affected by maternal use of alcohol	P04.3, O35.4
Fetal alcohol syndrome	Q86.0
Excessive blood level of alcohol	R78.0
Toxic effect of alcohol	T51.0, T51.9
Accidental poisoning by and 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
Evidence of alcohol involvement determined by level intoxication	Y91

In Scotland, official reporting of wholly attributable alcohol mortality and hospital discharges is undertaken by GROS and ISD respectively. Both of the afore-mentioned national bodies report annual statistics on deaths and hospital discharges based on agreed sets of wholly attributable alcohol conditions. The list of conditions in Table 1 above is broadly similar to those used by GROS and ISD but there are some differences which are as follows:

GROS

The following are not included in GROS reporting of wholly alcohol attributable mortality: Alcohol induced pseudo Cushing's Syndrome, Wernicke's encephalopathy, Alcoholic myopathy, Fetus and newborn affected by maternal use of alcohol, Fetal alcohol syndrome, Excessive blood level of alcohol, Toxic effect of alcohol and Evidence of alcohol involvement determined by blood alcohol level and level of intoxication. In addition, GROS report all chronic liver disease deaths as wholly alcohol attributable.

ISD

The ISD code list of wholly attributable alcohol conditions (2003 code-set) contained a number of conditions not included in Table 1 and these included: Toxic effect of methanol, Alcohol rehabilitation, Alcohol abuse counselling and surveillance and Alcohol use [3].

2 Mental and behavioural disorders due to alcohol use (ICD-10) contain a wide variety of disorders that differ in severity and clinical form but that are all attributable to the use of alcohol. They are: Acute Intoxication, Harmful Use, Dependence Syndrome, Withdrawal State (including with delirium), Psychotic Disorder, Amnesic syndrome, Residual and late-onset psychotic disorder, Other and unspecified mental and behavioural disorders.

3 ICD code list used for reporting alcohol related discharges from Scottish hospitals was revised in 2008. Further information is available at http://www.alcoholinformation.isdscotland.org/alcohol_misuse/3986.html

2.1.2 Partly attributable alcohol conditions

Table 2 lists conditions that are not wholly attributable to alcohol but where the majority of meta-analyses and literature reviews found a contributory significant relationship to alcohol. These conditions have been categorised into five broad groupings; neoplasms, cardiovascular diseases, gastrointestinal, metabolic and endocrine conditions, other chronic and acute conditions and injuries. While the majority of effects from alcohol are detrimental to health, alcohol intake at lower levels can provide protective effects for some diseases (i.e. Coronary Heart Disease (CHD), ischaemic stroke and cholelithiasis) compared to individuals who abstain from alcohol.

Table 2 Conditions partly attributable to alcohol consumption.

Condition	ICD10 codes
Neoplasms	
Cancer of the lip	C00
Cancer of the oral cavity and pharynx	C01-C06, C09-10, C12-14
Oesophageal cancer	C15
Colorectal cancer	C18-C20
Cancer of the liver and intrahepatic bile ducts	C22
Laryngeal cancer	C32
Breast cancer	C50
Cardiovascular Diseases	
Hypertensive diseases	I10-I15
Coronary heart disease	I20-25
Cardiac arrhythmias	I47, I48
Haemorrhagic stroke	I60-I62
Ischaemic stroke	I63-I66
Gastrointestinal, metabolic and endocrine conditions	
Oesophageal varices	I85, I98.2
Mallory-Weiss syndrome	K22.6
Unspecified liver disease	K73, K74.0-2, K76.0, K76.9
Portal hypertension	K76.6
Cholelithiasis	K80
Acute and other chronic pancreatitis	K85, K86.1
Other chronic and acute conditions	
Psoriasis	L40 excl. L40.5
Spontaneous abortion	O03
Epilepsy and Status epilepticus	G40-G41
Injuries	
Road traffic accidents - non pedestrian	V$ (see table footnote)
Pedestrian traffic accidents	V$$ (see table footnote)
Water transport injuries	V90-V94
Fall injuries	W00-W19
Occupational work/machine injuries	W24-W31, W45
Firearm injuries	W32-W34
Drowning	W65-W74
Inhalation and ingestion of food causing obstruction of respiratory tract	W78-W79
Fire injuries	X00-X09
Accidental excessive cold	X31
Accidental poisoning by and exposure to noxious substances	X40-X49 excl. X45
Intentional self-harm\Event of undetermined intent	X60-X84, Y10-Y34, Y87.0, Y87.2 excl. X65, Y15
Assault	X85-Y09, Y87.1

V$: V12-V14 (.3 -.9), V19.4-V19.6, V19.9, V20-V28 (.3 -.9), V29-V79 (.4 -.9), V80.3-V80.5, V81.1, V82.1, V82.9, V83.0-V86 (.0 -.3), V87.0-V87.9, V89.2, V89.3, V89.9
V$$: V02-V04 (.1, .9), V06.1, V09.2, V09.3

2.1.3 Excluded conditions

In addition, a number of conditions, where alcohol is suspected of being a risk factor, were also considered for inclusion in the study (Table 3). Following the inclusion criteria established for this study, the evidence was considered currently to be too limited or inconsistent and/or inconclusive for these conditions to be included in the study (see Appendix Two). It may be that as more studies are carried out on the relation of alcohol as a risk factor for these conditions, the causality of alcohol can be reconsidered.

Table 3 Excluded conditions

Condition: (Neoplasms)	Condition: (Other)
Gastric cancer	Respiratory tuberculosis
Pancreatic cancer	Diabetes
Endometrial cancer	Heart failure
Ovarian cancer	Pneumonia and Influenza
Bladder cancer	Gastric and duodenal ulcer
Renal cancer	Unipolar major depression
Lung cancer	Low birth weight
Prostate cancer	Intrauterine growth restriction

2.2 Deriving estimates of 'risk'

To calculate an attributable fraction for each alcohol partly attributable condition in Table 2, estimates of the risk associated with alcohol use are required. These estimates come mainly in the form of pooled relative risks (RRs) from meta-analyses of epidemiological studies of the comparative rates of death and illness of people exposed and not exposed, or exposed at varying levels, to alcohol. For alcohol attributable injury conditions, insufficient epidemiological studies have been conducted to derive reliable estimates of relative risks. In these instances, the population attributable fraction may be calculated 'directly' from pooled case series studies from the proportion of cases at hazardous or harmful levels of drinking (WHO 2000, Chikritzhs et al 2002a). Estimates of risk for alcohol attributable injuries are presented in section 2.2.2.

2.2.1 Pooled relative risks for non-injury diseases

For conditions considered wholly attributable to alcohol consumption, no statistical procedures are necessary to estimate risk relationship as all deaths or hospitalisations from alcohol are considered wholly attributable to alcohol i.e. PAF =1.

For non-injury conditions considered partly attributable to alcohol consumption, established practice was followed (Rehm et al 2004, Jones et al 2008) in drawing pooled RRs from two meta-analyses: Corrao et al (2004), Gutjahr, Gmel and Rehm (2001). Table 4a presents the pooled relative risks for each partly attributable alcohol condition, at specified levels of alcohol intake per day, where the RR is a ratio of the probability of developing a disease in the exposed group (i.e. alcohol drinkers) versus the non-exposed group (i.e. non-drinkers). For example, an individual drinking 25g of alcohol per day [4], would have a risk of dying from laryngeal cancer 1.43 times higher than that of someone who does not drink at all. Drinking 100 grams per day, their risk of death is nearly four times higher than that of a non-drinker.

4 In the international literature it is assumed that one standard drink = 10-12 grams of pure alcohol therefore 25g/day would be equivalent to 2-2.5 drinks/day, 50g / day equivalent to 4-5 drinks per day and 100g/day equivalent to between 8-10 drinks/day. In the UK, however, the alcohol unit used in surveys is equivalent to 8 grams per day therefore the equivalent unit consumption of 25, 50 and 100 grams per day would be approximately 3, 6 and 12 units per day.

Where alcohol has a protective effect against a specific disease, usually at low to moderate levels of consumption, (e.g. Coronary Heart Disease (CHD), Cholelithiasis), the RR will be less than 1. For CHD, the pooled relative risks have been drawn from Corrao et al (2000); in this meta-analysis sex-specific RRs for CHD were presented, which demonstrated evidence of a different shaped relationship between alcohol consumption and CHD by gender. In women, the major protective effect occurred at lower levels of consumption (i.e. 10 g/day) compared to 25 g/day in men. Significant evidence of harmful effects was found at 52 g/day among women compared to 114 g/day in men (see Table 4b).

Table 4a Conditions partly attributable to alcohol consumption – Relative risks for selected daily doses of alcohol intake compared to reference group of non-drinkers (i.e. 0 –0-25grams /day)

	25g	50g	100g
Neoplasms			
Cancer of the lip oral cavity and pharynx	1.86	3.11	6.45
Oesophageal cancer	1.39	1.93	3.59
Colon cancer	1.05	1.10	1.21
Rectal cancer	1.09	1.19	1.42
Cancer of the liver and intrahepatic bile ducts	1.19	1.40	1.81
Laryngeal cancer	1.43	2.02	3.86
Breast cancer	1.25(f)	1.55(f)	2.41(f)
Cardiovascular Diseases			
Hypertensive diseases	1.43	2.04	4.15
Cardiac arrhythmias[2]	1.51	2.23	2.23
Haemorrhagic stroke	1.19	1.82	4.70
Ischaemic stroke	0.90	1.17	4.37
Gastrointestinal, metabolic and endocrine conditions			
Oesophageal varices[1]	1.26	9.54	9.54
Unspecified liver disease	1.26	9.54	9.54
Portal hypertension[1]	1.26	9.54	9.54
Cholelithiasis[2]	0.82	0.68	0.50
Acute and other chronic pancreatitis	1.34	1.78	3.19
Other chronic and acute conditions			
Psoriasis[2]	1.58	1.60	2.20
Spontaneous abortion[2]	1.20(f)	1.76(f)	1.76(f)
Epilepsy and Status epilepticus[2]	1.23(m)/1.34(f)	7.52(m)/7.22(f)	6.83(m)/7.52(f)

1 Apart from some rare conditions such as portal or hepatic vein occlusion due to thrombosis or portal lymphadenopathy, virtually all oesophageal varices are a result of liver cirrhosis. On this basis, English et al. (1995) recommended applying the overall liver disease fraction to oesophageal varices.

2 Relative risks taken from Gutjahr Gmel and Rehm (2001) are based on intakes of <40g, 40-60g and >61g/day

Table 4b, Pooled relative risks for Coronary Heart Disease for selected daily doses of alcohol intake compared to a reference group of non-drinkers

	25g	87g	114g
Men	0.77	0.94	1.09
	10g	**31g**	**52g**
Women	0.85	0.93	1.12

2.2.2 Risk estimates for alcohol attributable injuries

Alcohol use has been associated with increased risk of injury and death in a wide variety of settings, including road vehicle accidents (including those involving pedestrians), falls, fires, self-inflicted injuries and injuries resulting from interpersonal violence. There is no general consensus regarding estimates of risk for these outcomes and the risks of injury are likely to be linked to both the average volume of alcohol consumption and to patterns of drinking, especially heavy drinking occasions with intoxication (Rehm et al 2003). There is also evidence that risk estimates for alcohol attributable injuries vary between different geographic regions and by time and place (Rehm et al 2004). To account for this variation, Rehm et al (2004), as part of WHO Global Burden of Disease Study, modelled the relationship between volume and patterns of drinking by including a drinking pattern weighting factor in the derivation of their alcohol PAFs to estimate the risk of certain types of injury from alcohol consumption. This study has applied alcohol attributable injury risk estimates directly from the work of Rehm with the exception of falls, fire and drowning injuries where either risk estimates were not provided or where UK/Scottish data were available (see below).

Falls

Risk estimates for fall injuries were extracted from the work of Ridolfo and Stevenson (2001) since neither age or gender specific estimates were provided by Rehm et al (2004). Based on hazardous/harmful levels of alcohol consumption compared to low alcohol consumption, they determined separate risk estimates for fall injuries for males and females aged less than 65 years and 65 years or more. They found that among people aged less than 65 years, 22% of male falls and 14% of female falls were attributable to alcohol, compared to 12% and 4% of falls among male and females aged 65 years and over respectively.

Fires

Risk estimates for fire injuries caused by alcohol consumption were not provided by Rehm et al (2004). Previous alcohol PAF studies have used estimates provided by either Single et al (1999) or English et al (1995) which were based on official data sources in Canada and Australia respectively. In order to provide an up to date estimate, the risk estimate for fire injuries was derived from the Scottish Fire Service data, averaged over an eight year period (1999/00-2006/07), where alcohol was recorded as a direct contributory factor in fire fatalities (see Table 5).

Table 5 Summary of fatal fire incidents in dwellings where alcohol was a direct contributory factor: Scotland, 1999/00 to 2006/07

	Number of incidents	Number of fatal fires where alcohol was a direct contributory factor
1999/00	111	41
2000/01	78	29
2001/02	84	27
2002/03	84	32
2003/04	53	25
2004/05	74	27
2005/06	54	14
2006/07	39	12
Total	577	207 (36%)

Source: HMCI of Fire Services for Scotland, Annual Reports, TSO, Edinburgh

The Scottish figure of 36% compares with 44% in English et al (1995) and 38% in Single et al (1999). A recent UK government report estimated that in England and Wales, between 2002 and 2005, alcohol was implicated in 33% of fire deaths (Arson Control Forum 2006).

Drowning
Available risk estimates for drowning injuries, as with fire estimates above, are based on data derived from country specific national data sources (English et al 1995, Single et al 2006). Although Scottish data is not available for drowning injuries, a UK study on drowning fatalities by the Department of Trade and Industry (2001) provides estimates of alcohol's involvement in drowning fatalities. As these figures are UK specific, it was decided that they better described alcohol's role in drowning fatalities for Scotland than data from other countries. The UK figure of 13% compares with a figure of 34% in English et al (1995) and Rehm et al (2004).

2.3 Alcohol consumption data

The next step in calculating attributable fractions is to derive prevalence data on the number of persons consuming at different levels of alcohol intake.

The age and sex specific distribution of alcohol consumption for adults aged 16 and over in Scotland was derived from the adjusted 2003 Scottish Health Survey (Scottish Government 2008), which takes into account the revised alcohol unit conversion factors published by ONS (Goddard 2007). As the Scottish Health Survey reports levels of alcohol consumption in terms of units consumed per week, it was necessary to convert this measure into grams per day, which is the standard alcohol measurement used in medical epidemiological research on alcohol related health outcomes. A standard unit of alcohol is defined, in the UK as containing 8g (10ml) of pure alcohol. In the 1980's, this was the alcohol content of a half pint of beer or one small glass of wine (Miller et al 1991). To convert Scottish Health Survey prevalence data from units per week to grams per day for each respondent, weekly unit consumption was multiplied by 8 (grams per unit) and divided by 7 (days per week).

Categorical levels of average volume of alcohol per day to relate consumption to chronic and acute disease were selected to be consistent with previous meta-analyses (English et al. 1995, Gutjahr et al. 2001, Ridolfo and Stevenson 2001, Rehm et al 2003) and were defined as follows:

- non-drinker, a person not having had a drink containing alcohol within the last year (this includes those who drink ≤0.25 g/day);
- average volume drinking category I: for females >0.25–19.99g/day pure alcohol daily; for males >0.25–39.99g/day pure alcohol daily;
- average volume drinking category II: for females 20–39.99g/day pure alcohol daily; for males 40–59.99g/day pure alcohol daily; and
- average volume drinking category III: for females 40g/day or more pure alcohol daily; for males 60g/day or more pure alcohol daily.

Estimates of the proportion of adults aged 16 and over in Scotland within these drinking categories, based on revised 2003 Scottish Health Survey data as described above, are provided in Table 6 (men) and Table 7 (women).

Table 6 Males: age-specific distribution of alcohol consumption, Scotland 2003 (Source; Scottish Health Survey 2003 revised estimates, 2008)								
Grams per day	16 to 24 %	25 to 34 %	35 to 44 %	45 to 54 %	55 to 64 %	65 to 74 %	75 + %	16+ %
0 - ≤0.25	12.3	9.6	10.3	9.3	11.9	17.6	31.6	13.5
>0.25 – 39.99	70.2	73.5	70.4	72.3	70	68	59.4	69.7
40.00 – 59.99	8.1	10.3	9.9	8.9	8.4	8.7	5.0	8.7
60.00+	9.4	6.5	9.4	9.5	9.7	5.7	4.0	8.1

Table 7 Females: age-specific distribution of alcohol consumption, Scotland 2003 (Source; Scottish Health Survey 2003 revised estimates, 2008)								
Grams per day	16-24 %	25-34 %	35-44 %	45- 54 %	55-64 %	65-74 %	75 + %	16+ %
0 - ≤0.25	15.1	15.9	16.6	16.5	26.7	37.5	55.1	25.1
>0.25 – 19.99	58.6	61.4	62.7	61.9	58.5	55.1	41.3	58
20 – 39.99	17.3	17.2	15.7	15.2	11.9	5.9	3.3	12.6
40+	9.0	5.5	5.0	6.3	2.8	1.6	0.4	4.3

2.4. Alcohol attributable fraction formula

The alcohol PAF for a given disease is a function of the relative risks for non-drinkers and average volume drinking categories I, II and III (see section 2.3) and the percentages of the population falling within those groups.

For the above four groups, the PAF for each group is calculated as follows:

$$AF_i = \frac{p_i(RR_i - 1)}{\sum_{i=0}^{k} p_i(RR_i - 1) + 1}$$

where,
i = 0 is the baseline category (abstinent)
k = 3 (the number of categories)
AFi is the population attributable fraction for a particular category of exposure i (0=abstinent, 1=low, 2=moderate, 3=high alcohol consumption)
pi = the estimated prevalence of the ith category of exposure in the total population,
RRi = the Relative Risk (or estimate of Relative Risk) for the ith category of exposure.

Estimated relative risks (RRs) have been reported in the literature covering a range of alcohol intakes from 0-100 g/day compared to a reference group of non-drinkers defined as those drinking between 0 to ≤0.25 grams per day (Corrao et al 2004). These RRs are neither age nor sex specific but can be used as an approximation for all ages and for both sexes. The estimated RR is expressed as a function of alcohol dose (g/day). For the purposes of calculating attributable fractions, the population was divided into 4 consumption groups (see page 15). An appropriate representative RR was assigned to each group. The average RR was applied taking into account the shape of the estimated RR curve over the relevant range of

consumption. The range for the high intake group was truncated at 100g/day for this purpose. The risk for each specified condition was assumed to be constant within these consumption bands i.e. those drinking 2g/day or 18g/day share the same RR. This may introduce some bias into the PAF estimates. Bofetta et al (2006) estimated that the excess risk in the 1 to 19 g/day category to be half of that reported for 25g/day for selected cancers, though no details were provided in the paper on how this was derived.

The calculation of the PAF is a function of the RR estimates and population drinking estimates and therefore relies on accuracy of population estimates of alcohol consumption and the availability and quality of the relative risk estimates reported in the epidemiological literature. There is therefore a degree of uncertainty surrounding the estimates presented which we have been unable to quantify. This limitation is one common to all studies calculating alcohol PAFs (Johansson et al 2002, Rehm et al 2004, Jones et al 2008).

3. Analysis and Results

3.1 Scottish specific alcohol attributable fractions

Tables 8a and 8b report the estimated age and sex specific alcohol-population attributable fractions for each wholly or partly alcohol attributable condition, caused or avoided by alcohol consumption in Scotland in 2003, derived from the formula in section 2.4. As previously discussed, attributable fractions for alcohol attributable injuries are taken directly from case series and other primary sources of data and the age and sex specific PAFs for these conditions are listed in Table 9.

Since wholly attributable conditions are by definition entirely caused by alcohol consumption, the attributable fraction for these conditions is '1'. Of the partly attributable alcohol conditions, unspecified liver disease and cirrhosis, cancer of the lip, oral cavity and pharynx and epilepsy were the conditions with the highest age-standardised [5] attributable fractions. For example, it is estimated that about half (51% for men and 48% for women) of deaths or hospitalisations for cancer of lip, oral cavity and pharynx are attributable to alcohol consumption; for deaths and hospitalisations attributable to unspecified liver disease and cirrhosis, the alcohol PAFs are 73% and 67% for men and women respectively.

Although there is considerable variation in the size of the alcohol PAFs across the spectrum of partly attributable alcohol conditions e.g. ranging from an alcohol PAF for cancer of the lip, oral cavity and pharynx of 48% among women to that of 19% for breast cancer, the overall burden caused by alcohol will be determined by how common mortality and hospitalisations are for each specified alcohol attributable condition. Therefore, since breast cancer is one of the largest causes of death (n=1062 in 2007 [6]) in Scotland in women, it may be expected that the number of cases attributable to alcohol consumption will be higher, despite one of the lowest PAFs, than the number of deaths from cancer of the lip, oral cavity and pharynx (n=99 in 2007 [7]). It should also be noted that, in some cases, where alcohol has a protective effect for a specific disease (e.g. CHD, cholelithiasis), the alcohol PAF will have a negative value. This gives an estimate of the number of prevented cases attributable to alcohol consumption. As with breast cancer, although the PAF for alcohol attributable CHD is small, the overall alcohol attributable figures will be high because of the high levels of mortality and hospitalisation associated with CHD.

The alcohol PAF estimates for each condition, however, also vary by age group and gender because of the differing levels of alcohol consumption in each group and by sex. The PAFs tend to decrease as people get older reflecting the lower levels of alcohol consumption in these age groups e.g. for men aged 16-64, the estimated alcohol PAF for cancer of the lip, oral cavity and pharynx is approximately 55% and this decreases to 48% and 41% for men aged 65-74 and ≥75. For women, the PAF in these age groups decreases to 37% and 27% respectively. To reflect the variation by age in alcohol consumption levels, the age specific estimates (as opposed to age standardised PAFs) have been used to calculate estimates of mortality and morbidity by sex.

5 Age standardised AAF is the weighted sum of the age specific AFs, weighted by proportions of Scottish population (>=16) within each age group (Source: GROS 2006 population estimates)

6 Source: ISD: http://www.isdscotland.org/isd/1508.html#Summary%20statistics%20for%20all%20cancers

7 Source: ISD: http://www.isdscotland.org/isd/1508.html#Summary%20statistics%20for%20all%20cancers

Table 8a Age and sex specific PAFs for alcohol partly attributable (non-injury) conditions																
	16-24		25-34		35-44		45-54		55-64		65-74		75+		Total	
Partly Attributable	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Lip oral cavity and pharyngeal cancer	0.52	0.58	0.51	0.55	0.55	0.54	0.55	0.55	0.54	0.47	0.48	0.37	0.41	0.27	0.51	0.48
Oesophageal cancer	0.32	0.34	0.31	0.31	0.33	0.31	0.33	0.31	0.33	0.26	0.29	0.21	0.24	0.15	0.31	0.27
Colon cancer	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.04	0.04	0.03	0.04	0.02	0.05	0.04
Rectal cancer	0.09	0.1	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.07	0.08	0.06	0.06	0.04	0.09	0.08
Liver cancer	0.17	0.18	0.17	0.17	0.18	0.16	0.18	0.17	0.17	0.14	0.15	0.11	0.12	0.08	0.16	0.14
Laryngeal cancer	0.34	0.36	0.33	0.33	0.35	0.33	0.35	0.33	0.35	0.28	0.31	0.22	0.26	0.16	0.33	0.29
Breast cancer	n/a	0.24	n/a	0.22	n/a	0.21	n/a	0.22	n/a	0.18	n/a	0.14	n/a	0.10	n/a	0.19
Hypertension	0.35	0.37	0.34	0.34	0.36	0.33	0.36	0.34	0.35	0.28	0.31	0.23	0.26	0.16	0.33	0.29
Cardiac arrhythmias	0.36	0.38	0.37	0.37	0.37	0.36	0.37	0.37	0.37	0.32	0.34	0.27	0.29	0.20	0.35	0.33
Ischaemic stroke	0.08	0.09	0.04	0.05	0.08	0.04	0.08	0.06	0.08	0.01	0.03	-0.01	0.01	-0.02	0.06	0.03
Haemorrhagic stroke	0.28	0.30	0.25	0.26	0.28	0.25	0.28	0.26	0.28	0.20	0.23	0.14	0.18	0.09	0.26	0.22
Coronary heart disease	-0.16	-0.09	-0.17	-0.10	-0.16	-0.10	-0.16	-0.10	-0.16	-0.09	-0.16	-0.08	-0.14	-0.06	-0.16	-0.09
Oesophageal varices	0.75	0.77	0.73	0.74	0.76	0.73	0.76	0.74	0.75	0.67	0.71	0.59	0.64	0.47	0.73	0.67
Mallory-Weiss syndrome*	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47
Unspecified liver disease	0.75	0.77	0.73	0.74	0.76	0.73	0.76	0.74	0.75	0.67	0.71	0.59	0.64	0.47	0.73	0.67
Portal hypertension	0.75	0.77	0.73	0.74	0.76	0.73	0.76	0.74	0.75	0.67	0.71	0.59	0.64	0.47	0.73	0.67
Epilepsy	0.55	0.65	0.55	0.62	0.58	0.6	0.57	0.61	0.56	0.53	0.51	0.4	0.41	0.27	0.53	0.53
Cholelithiasis	-0.25	-0.26	-0.25	-0.24	-0.26	-0.23	-0.26	-0.24	-0.25	-0.19	-0.22	-0.14	-0.17	-0.10	-0.24	-0.20
Acute and other chronic pancreatitis	0.29	0.31	0.28	0.28	0.30	0.27	0.30	0.28	0.29	0.23	0.26	0.18	0.21	0.13	0.28	0.24
Spontaneous abortion	n/a	0.24	n/a	0.23	n/a	0.22	n/a	0.22	n/a	0.19	n/a	0.14	n/a	0.10	n/a	0.19
Psoriasis	0.36	0.35	0.36	0.34	0.37	0.34	0.37	0.34	0.36	0.31	0.34	0.27	0.30	0.21	0.35	0.28

* Not based on meta-analysis but clinically documented therefore PAF obtained by direct method (English et al 1995)

Table 8b Age and sex specific PAFs for alcohol wholly attributable (non-injury) conditions																
	16-24		25-34		35-44		45-54		55-64		65-74		75+		Total	
Wholly Attributable	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Alcohol induced pseudo Cushing's Syndrome	BY DEFINITION THESE CONDITIONS ARE WHOLLY ATTRIBUTABLE TO ALCOHOL CONSUMPTION, THEREFORE PAF=1															
Wernicke's encephalopathy																
Mental and behavioural disorders due to use of alcohol																
Degeneration of nervous system due to alcohol																
Alcoholic polyneuropathy																
Alcoholic myopathy																
Alcoholic cardiomyopathy																
Alcoholic gastritis																
Alcoholic liver disease																
Alcohol induced chronic pancreatitis																
Fetus and newborn affected by maternal use of alcohol																
Fetal alcohol syndrome																
Excessive blood level of alcohol																
Toxic effect of alcohol																
Accidental and Intentional poisoning by and exposure to alcohol incl. NOS																
Evidence of alcohol involvement determined by blood alcohol level																
Evidence of alcohol involvement determined by level intoxication																
Poisoning by and exposure to alcohol, undetermined intent																

Table 9 Age and sex specific PAFs for alcohol attributable injuries																
	16-24		25-34		35-44		45-54		55-64		65-74		75+		Total	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Motor vehicle accidents including pedestrian accidents	0.46	0.18	0.50	0.25	0.50	0.25	0.27	0.21	0.27	0.21	0.22	0.15	0.22	0.15	0.35	0.20
Falls	0.22	0.14	0.22	0.14	0.22	0.14	0.22	0.14	0.22	0.14	0.12	0.04	0.12	0.04	0.18	0.13
Fire injuries	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36
Drowning	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13
Accidental poisoning by and exposure to noxious substances	0.38	0.31	0.22	0.21	0.22	0.21	0.22	0.21	0.22	0.21	0.22	0.21	0.12	0.10	0.23	0.21
Other unintentional injuries*	0.38	0.31	0.38	0.31	0.38	0.31	0.32	0.26	0.32	0.26	0.32	0.26	0.32	0.26	0.35	0.28
Intentional self-harm**	0.21	0.14	0.21	0.14	0.21	0.14	0.16	0.12	0.16	0.12	0.16	0.12	0.07	0.07	0.17	0.12
Assault	0.19	0.19	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.34	0.34

* Includes Water transport accidents, Work/machine injuries, Firearm injuries, Inhalation of gastric contents, Accidental excessive cold.
** Includes suicide and undetermined injury.

3.2 Alcohol Attributable Mortality

The age and sex specific alcohol PAFs have been applied to the number of deaths for each cause by age and by gender, to estimate mortality, wholly and partly attributable to alcohol consumption in Scotland in 2003. The number of deaths which occurred in 2003 in men and women aged 16 years and over, were obtained from the GROS. Data included deaths by sex, 10-year age group and cause, using WHO's 10th version of the International Classification of Diseases (ICD-10). Only those causes of deaths which had an alcohol condition recorded as the underlying cause were included in the analysis. The ICD-10 rules for recording of deaths aims to derive a single cause of death based on strict criteria for determining the underlying cause from the sequence of events leading to death. This single underlying cause of death is therefore used as the basis for applying the alcohol PAF in this study (Ridolfo and Stevenson 2001). This approach has also been chosen because, in the main, the PAFs are derived assuming single-cause coding (English et al 1995). Applying PAFs to multiple causes assumes that the cause recorded in the underlying position is equal in weight to other causes recorded in other positions in the sequence of events leading to the cause of death which is not the case based on ICD rules. Mortality data was extracted for 2003, because that year corresponds to the latest prevalence estimates there are of population alcohol consumption in Scotland from the SHeS 2003. Applying the alcohol PAFs generated in this study, which are based on drinking estimates in 2003, to more current vital statistics on cause-specific problems in more recent years, may potentially bias the estimates generated. This may arise as the PAFs could change over time due to changes in population prevalence, age and sex and of drinking at particular levels (Bloss 2005).

Table 10 provides an estimate of the number of deaths attributable to alcohol consumption in Scotland by age group and gender for 2003. Overall, there were an estimated 2,882 deaths attributable to alcohol consumption in 2003, equivalent to 5.0% of all deaths (n=58,064) in Scotland among adults aged 16 and over. This is almost double the GROS's report of 1,525 wholly attributable alcohol deaths in 2003, which were derived by applying the definition which is currently used for national mortality statistics [8]. The effect is greater for men than women; deaths in men from alcohol attributable conditions accounted for 6.8% of all male deaths recorded in Scotland in 2003, compared to 3.3% of all female deaths. Alcohol attributable deaths also varied by age. Although the highest numbers of deaths were seen in older age groups, younger age groups were more likely to be affected by their alcohol use as a proportion of overall deaths. For example, among 16-24 year old males, 17.5% of all deaths in this age group were estimated to be caused by attributable alcohol conditions. Over one in four (26.1%) of deaths in men and one in five of deaths (21.1%) in women aged 35-44 years old in 2003 were attributable to alcohol consumption. This compares to 2.0% (271/13,717) and 1.1% (239/20,966) in men and women aged 75 and over respectively. Tables showing estimated numbers of deaths by each alcohol attributable condition by gender are presented in Appendix Four.

8 For further information on GROS reporting of alcohol related deaths see http://www.gro-scotland.gov.uk/statistics/deaths/alcohol-related-deaths/index.html

Table 10 Number (and as a % of all deaths in each age group) of alcohol-attributable deaths

Age	Males		Females		Total	
	No. of alc. attrib. deaths (%)	No of all deaths*	No. of alc. attrib. deaths (%)	No of all deaths*	No. of alc. attrib. deaths (%)	No of all deaths *
16-24	54 (17.5)	308	12 (9.9)	121	66 (15.4)	429
25-34	96 (20.5)	469	29 (16.0)	181	125 (19.2)	650
35-44	233(26.1)	893	103 (21.1)	489	336 (24.3)	1,382
45-54	390 (23.9)	1,634	203 (19.1)	1,062	593 (22.0)	2,696
55-64	503 (13.3)	3,787	242 (9.9)	2,446	745 (12.0)	6,233
65-74	339 (5.0)	6,797	170 (3.3)	5,194	509 (4.2)	11,991
75+	271 (2.0)	13,717	239(1.1)	20,966	510 (1.5)	34,683
All ages	1,885 (6.8)	27,605	997 (3.3)	30,459	2,882 (5.0)	58,064

*(Data from 2003)

Overall, men were as likely to die from a condition wholly attributable to alcohol consumption as from a partly attributable condition: in 2003 there were 960 wholly alcohol attributable and 925 partly alcohol attributable deaths among men. In contrast, women were more likely to die from a condition partly attributable (n=597) than from a wholly attributable (n=400) condition. Among younger age groups (<35 years) the majority of deaths in both men and women occurred from consequences partly attributable to alcohol consumption mainly alcohol related injuries i.e., intentional self-harm and road traffic accidents. This was more pronounced in men than women. Between the ages of 35-74 yrs among men and 35-64 yrs among women, the majority of deaths occurred from chronic conditions wholly attributable to alcohol consumption (Figures 1 and 2).

Figure 1. Males, alcohol attributable mortality by attributable status and age

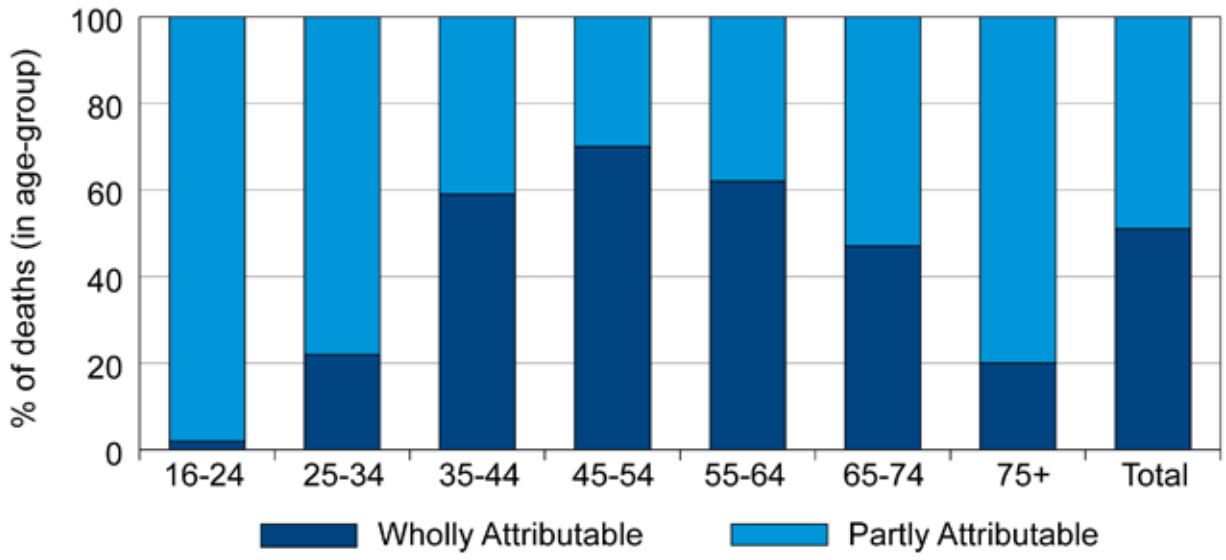
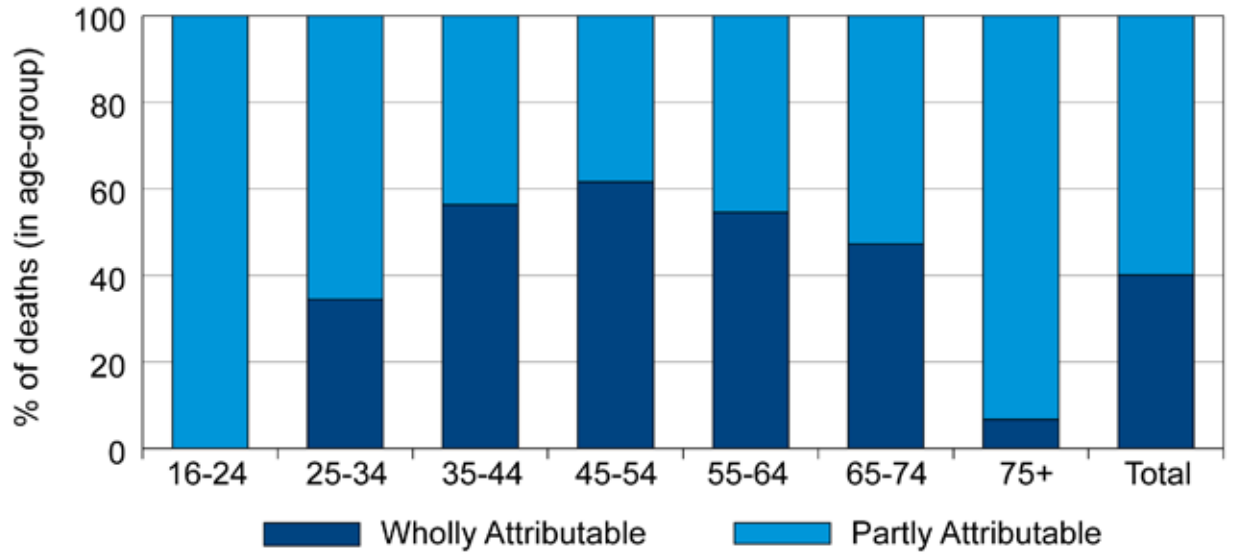


Figure 2. Females, alcohol attributable mortality by attributable status and age



Of the specific causes of death attributable to alcohol consumption in 2003, alcoholic liver disease (n=980), mental and behavioural disorders due to alcohol use (n=357), oesophageal cancer (n=191) and breast cancer (n=164) were the most common (Table 11). For men and women aged 16-34 years, road traffic accidents, intentional self harm and epilepsy [9] were among the most common causes of death and deaths from alcoholic liver disease were the largest cause of alcohol attributable mortality in women aged 25-34 years (3.3% of all deaths in Scotland in that age group). In women and men aged 35 years and over, alcoholic liver disease, mental and behavioural disorders due to alcohol use, oesophageal cancer and breast cancer (women only) were the most common causes of death attributable to alcohol consumption. Specifically, approximately one in ten of all deaths among men and women, aged between 35 and 44, were caused by alcoholic liver disease. The top three causes of death attributable to alcohol consumption, by age and sex, are shown in Table 11.

9 Excessive drinking can make seizures more likely because of the effect of alcohol on the brain. It can also interact with anti-epileptic drugs making them less effective. The commonest cause of alcohol related seizures are tonic-clonic convulsions (grand mal in nature) occurring either singly or in short series on withdrawal of alcohol after a period of chronic intoxication. Previous research has estimated that over one in ten of alcohol dependent discharges are attributable to epilepsy (Hanke et al 1997).

Table 11 Top three causes of alcohol attributable deaths by age and sex				
	Men	% of all deaths in age-group	Women	% of all deaths in age-group
	Condition	%	**Condition**	%
16-24	Road traffic accidents	7.6	Intentional self-harm	3.0
	Intentional self-harm	4.8	Road traffic accidents	2.8
	Assault	1.2	Epilepsy	1.7
25-34	Road traffic accidents	5.7	Alcoholic liver disease	3.3
	Intentional self-harm	5.5	Intentional self-harm	2.8
	Epilepsy	1.7	Epilepsy	2.4
35-44	Alcoholic liver disease	11.0	Alcoholic liver disease	9.8
	Mental & behavioural disorders	4.3	Breast cancer	2.5
	Intentional self-harm	3.4	Mental & behavioural disorders	2.0
45-54	Alcoholic liver disease	11.6	Alcoholic liver disease	8.2
	Mental & behavioural disorders	5.1	Mental & behavioural disorders	3.4
	Unspecified liver disease	1.0	Breast cancer	2.7
55-64	Alcoholic liver disease	5.9	Alcoholic liver disease	4.1
	Mental & behavioural disorders	2.2	Breast cancer	1.6
	Oesophageal cancer	1.0	Mental & behavioural disorders	1.3
65-74	Alcoholic liver disease	1.8	Alcoholic liver disease	1.0
	Oesophageal cancer	0.7	Breast cancer	0.7
	Mental & behavioural disorders	0.5	Haemorrhagic stroke	0.3
75+	Oesophageal cancer	0.3	Breast cancer	0.2
	Alcoholic liver disease	0.2	Cardiac arrhythmias	0.2
	Cardiac arrhythmias	0.2	Oesophageal cancer	0.1

3.3 Hospital patient-specific discharges for alcohol attributable conditions

The alcohol PAFs were used to calculate the number of individuals (patient-specific discharges) admitted to hospital in Scotland in 2003 with a condition wholly or partly attributable to alcohol consumption. To calculate the number of patient-specific hospital discharges in Scotland attributable to alcohol consumption in 2003, patient-specific data on relevant conditions were obtained from the Scottish Morbidity Record (SMR01). Data included hospital discharges by sex, 10 year age group and cause, using ICD-10. Hospital discharges relating to the same individual were linked using an unique personal identifier. An individual may have more than one alcohol attributable discharge in any given year, and within a discharge, more than one alcohol attributable diagnosis. To avoid double counting, an individual was assigned only one alcohol attributable diagnosis as follows:

1. For each individual, identify all alcohol attributable diagnosis codes from their discharge records
2. For each individual, identify the earliest hospital discharge in the year
3. In the event of there being two or more alcohol attributable diagnoses within the same discharge, select the condition on with the highest position within discharge record (i.e. first choose those conditions recorded in main position on discharge record, then second and so on).

Table 12 provides an estimate of the number of patient-specific discharges which were caused by alcohol attributable conditions, by age and sex. Overall in 2003, an estimated 41,414 patient-specific discharges were caused by alcohol (wholly and partly) attributable conditions, 25,688 among men and 15,716 among women, equivalent to over 1 in 20 (7.3%) of all patient-specific discharges (n= 569,269) in Scotland among adults aged 16 and over. As with alcohol attributable mortality, men were more likely to be discharged than women; male patient-specific discharges from alcohol attributable conditions accounted for 9.9% of all male patient-specific discharges recorded in Scotland in 2003, compared to 5.1% of female patient-specific discharges. Among men aged 16-64 yrs, approximately one in ten of all patient-specific discharges in Scotland were attributable to alcohol consumption. For men aged 65 years and over, the burden of alcohol consumption on the health care system decreased with increasing age, from 8.0% among 55-64 years to 6.2% among those aged 75+. In women, the highest proportion of alcohol attributable patient-specific discharges was found in those aged 45-54 years, approximately one in ten, (9.2%), of all patient specific discharges were alcohol attributable. Tables showing number of patient-specific discharges by alcohol attributable conditions are presented in Appendix Four.

Table 12 Number (and as a % of all patient-specific discharges in each age group) of alcohol-attributable hospital patient-specific discharges

	Males		Females		Total	
	No. of alc. patient specific discharges (%)	All patient specific discharges (n=)*	No. of alc. patient specific discharges (%)	All patient specific discharges (n=)*	No. of alc. patient specific discharges (%)	All patient specific discharges (n=)*
16-24	2,319 (11.4)	20,343	1,115 (4.2)	26,441	3,445 (7.4)	46,784
25-34	2,867 (11.1)	25,889	1,423 (4.2)	33,708	4,302 (7.2)	59,597
35-44	4,057 (11.3)	35,784	2,337 (5.5)	42,541	6,405 (8.2)	78,325
45-54	4,468 (11.9)	37,557	2,739 (6.7)	40,782	7,219 (9.2)	78,339
55-64	4,768 (10.5)	45,500	2,867 (6.5)	44,357	7,645 (8.5)	89,857
65-74	3,907 (8.0)	48,687	2,499 (5.0)	49,636	6,413 (6.5)	98,323
75+	2,881 (6.2)	46,386	2,742 (3.8)	71,658	5,629 (4.8)	118,044
Total	25,688 (9.9)	260,146	15,716 (5.1)	309,123	41,414 (7.3)	569,269

* (Data from 2003)

Overall, men were more likely to be discharged from hospital with a condition partly attributable to alcohol consumption: in 2003 there were 9,948 wholly attributable and 15,740 partly attributable patient-specific discharges among men. Women were more than twice as likely to be discharged for a partly attributable alcohol condition as a wholly attributable alcohol condition; (11,614 and 4,101) respectively. As shown in Figures 3 and 4, among younger age groups (<35 years), the majority of patient-specific discharges involved acute consequences partly attributable to alcohol consumption, in particular, intentional self-harm and road traffic accidents. This was more pronounced in men. Between the ages of 35-74 yrs among men and 35-54 yrs among women, the majority of patient-specific discharges involved chronic conditions wholly attributable to alcohol consumption (Figures 3 and 4).

Figure 3. Males, alcohol attributable patient-specific discharges by attributable status and age

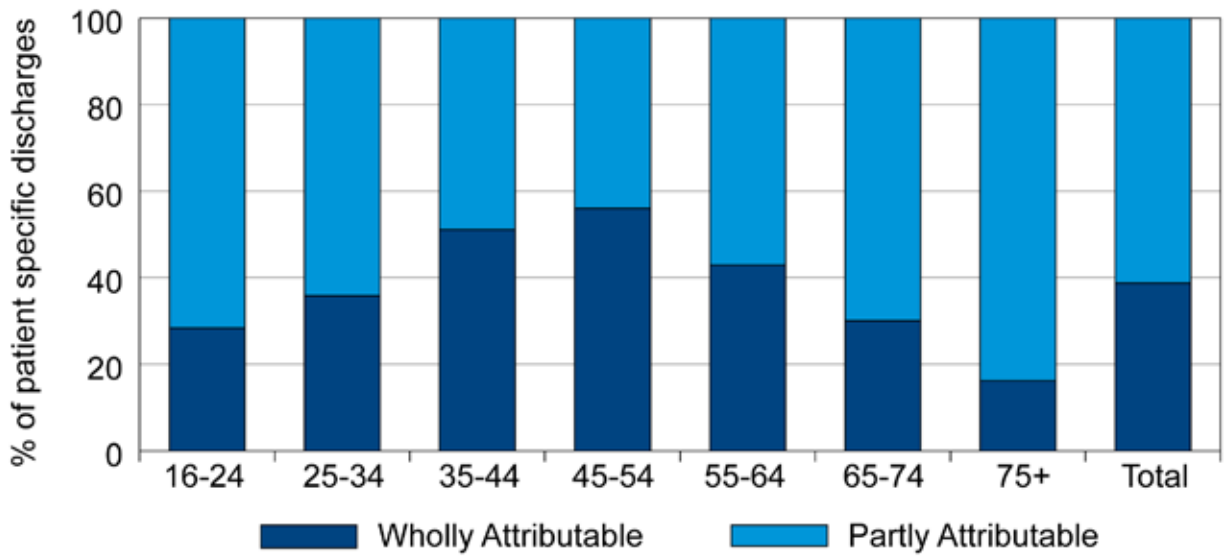
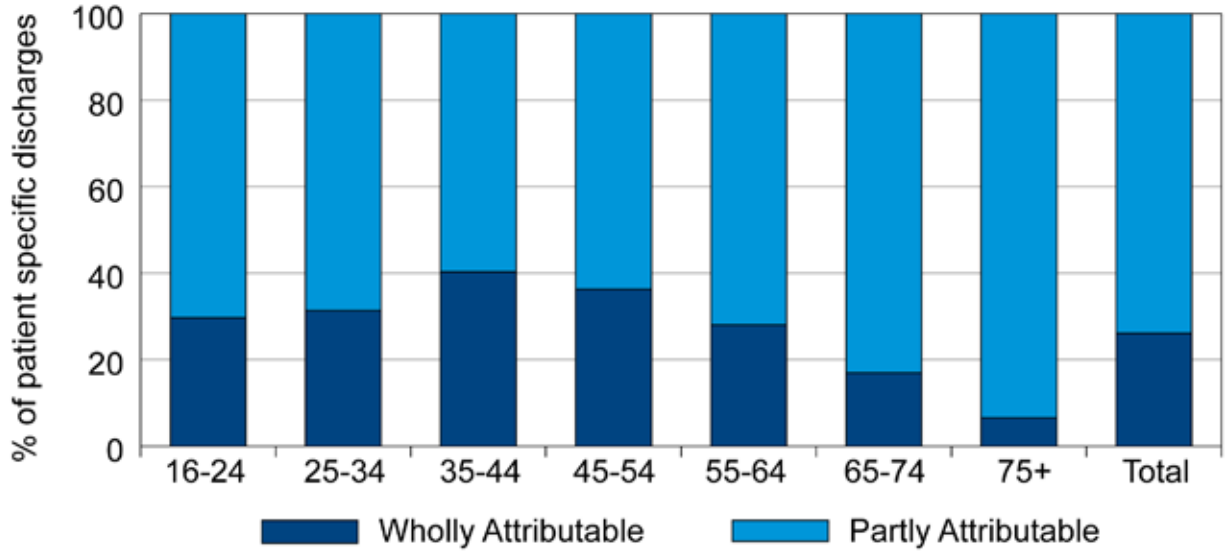


Figure 4. Females, alcohol attributable patient-specific discharges by attributable status and age



Of the alcohol attributable conditions, patient-specific discharges relating to mental and behavioural disorders caused by alcohol use (25.6%, n= 10,584), hypertensive disease (16.7%, n=6,894), cardiac arrhythmias (10.4%, n= 4,304), fall injuries (6.6%, n= 2,722) and alcoholic liver disease (5.3%, n= 2,174) were the most common (Table 13). For young men aged 16-34, mental and behavioural disorders due to alcohol use and assaults were the most common causes of discharge from hospital. For women aged 16-34 years, mental and behavioral disorders due to alcohol use, intentional self harm and epilepsy were the most common reasons for hospital discharge. After the age of 35, the highest number of alcohol attributable alcohol patient-specific discharges for men and women occurred from mental and behavioural disorders, and cardiovascular conditions such as hypertensive diseases and cardiac arrhythmias. The top three reasons for patient-specific discharges attributable to alcohol consumption, by age and sex are shown in Table 13. A table showing the number of patient-specific discharges, by gender, for each alcohol attributable condition are presented in Appendix Four.

Table 13 Top 3 causes of alcohol attributable patient-specific discharges by age and sex				
	Males		Females	
	Condition	n	Condition	n
16-24	Mental and behavioral disorders Assault Fall injuries	587 368 270	Mental and behavioral disorders Intentional self-harm Epilepsy	257 232 154
25-34	Mental and behavioral disorders Assault Intentional self-harm	850 491 238	Mental and behavioral disorders Epilepsy Intentional self-harm	310 193 190
35-44	Mental and behavioral disorders Assault Epilepsy	1,701 317 265	Mental and behavioral disorders Epilepsy Intentional self-harm	666 230 213
45-54	Mental and behavioral disorders Hypertensive diseases Alcoholic liver disease	1,859 502 454	Mental and behavioral disorders Hypertensive diseases Breast cancer	666 485 278
55-64	Mental and behavioral disorders Hypertensive diseases Cardiac arrhythmias	1,509 900 496	Hypertensive diseases Mental and behavioral disorders Breast cancer	778 487 280
65-74	Hypertensive diseases Mental and behavioral disorders Cardiac arrhythmias	1,029 889 728	Hypertensive diseases Cardiac arrhythmias Mental and behavioral disorders	914 485 290
75+	Cardiac arrhythmias Hypertensive diseases Fall injuries	880 801 248	Hypertensive diseases Cardiac arrhythmias Fall injuries	929 894 308

3.4 Protective effects of alcohol consumption

Estimates of deaths and hospital patient-specific discharges prevented as a result of alcohol consumption by age and gender are presented in Tables 14 and 15 respectively. Overall, an estimated 1,492 deaths (998 males and 494 females) and 13,618 patient-specific discharges (8,804 men and 4,813 women) may have been prevented by lower levels of alcohol consumption.

Table 14 Number of alcohol preventable deaths in 2003								
	16-24	25-34	35-44	45-54	55-64	65-74	75+	All ages
Men	0	-2	-18	-52	-144	-271	-422	-998
Women	0	0	-2	-8	-28	-82	-293	-494
Total	0	-2	-20	-60	-172	-353	-715	-1,492

Table 15 Number of alcohol preventable patient-specific discharges in 2003								
	16-24	25-34	35-44	45-54	55-64	65-74	75+	All ages
Men	-6	-56	-324	-1,050	-2,031	-2,664	-2,198	-8,804
Women	-102	-238	-368	-601	-829	-1,121	-1,259	-4,813
Total	-108	-294	-692	-1,651	-2,860	-3,786	-3,457	-13,618

Of these deaths and patient-specific discharges preventable by alcohol consumption, coronary heart disease (CHD) is by far the most common condition; 98.4% of all alcohol preventable mortality among women and 99.7% among men can be attributed to CHD. For patient-specific discharges the corresponding figures are 88.5% among men and 65% among women.

4. Discussion

Alcohol is linked to many disease conditions and is one of the major risk factors for burden of disease in established market economies (Rehm et al 2003). The aim of this study was to calculate alcohol population attributable fractions for Scotland, using the best possible estimates based on the current evidence available in the epidemiological literature augmented where necessary by primary data and specific estimates of population drinking in Scotland. These were then applied to mortality and morbidity data to estimate more fully the burden of alcohol related harm in Scotland.

Alcohol-attributable fractions were calculated for 53 conditions, of which 19 conditions were by definition wholly attributable to alcohol consumption and 34 conditions were partly attributable to alcohol consumption. The contribution of alcohol consumption varied across conditions. PAFs over 50% were calculated for four conditions; unspecified liver disease, oesophageal varices, malignant neoplasm of the lip, oral cavity and pharynx, and epilepsy. Alcohol consumption was found to have protective effects for three conditions: coronary heart disease; ischaemic stroke and cholelithasis, though this effect was only apparent at lower levels of alcohol consumption. Overall in 2003, 2,882 deaths were estimated to have occurred from alcohol attributable conditions, representing 5.0% of all deaths in 2003. This is almost double GROS's estimate of 1,525 alcohol-related deaths in 2003, which was produced by applying the definition which is currently used for national statistics. Men were as likely to die from a wholly attributable alcohol condition as they were from a partly attributable condition though women were more likely to die from a partly attributable alcohol condition. Men were at more harm from alcohol consumption than women; 6.8% of all male deaths were alcohol-attributable compared to 3.3% of all female deaths. Alcohol-attributable deaths also varied by age: For example, over one in four (26.1%) of deaths in men and one in five of deaths (24.3%) in women aged 35-44 years old in 2003 were attributable to alcohol consumption. This compares to 2.0% (271/13,717) and 1.5% (239/20,966) in men and women aged 75 and over respectively. Below the age of 35, alcohol-attributable deaths were most likely to occur from the acute consequences of alcohol consumption, in particular, intentional self-harm and road traffic accidents. After the age of 35, chronic diseases were more predominant including, mental and behavioral disorders due to alcohol use, alcoholic liver diseases, malignant neoplasm of the oesophageal, breast and colorectal cancer and hypertensive diseases were the most common causes of alcohol attributable deaths. A total of 1,492 deaths from partly attributable alcohol conditions were estimated to have been prevented by alcohol consumption, the majority from the prevention of CHD deaths in the older age group (i.e. 65 years and older).

Conditions either wholly or partly attributable to alcohol consumption also present a significant burden to the health care system. In 2003, there were 41,414 patient-specific discharges attributable to alcohol consumption, over one in twenty (7.3%) of all patient-specific discharges in Scotland among adults aged 16 and over. This is over one and half times higher than ISD 2003 estimate of 26,010 patient-specific discharges based on a list of wholly attributable alcohol conditions (Graham et al 2005). Among men aged 16-64 yrs, approximately one in ten of all patient-specific discharges in Scotland were attributable to alcohol consumption. For men aged 65 years and over, the burden of alcohol consumption on the health care system decreased with increasing age, from 8.0% among 55-64 years to 6.2% among those aged 75+. In women, the highest proportion of alcohol attributable patient-specific discharges was found in those aged 45-54 years approximately one in ten (9.2%) of all patient specific discharges were alcohol attributable. Of the alcohol attributable patient-specific discharges, mental and behavioral disorders caused by alcohol use, hypertensive disease, cardiac arrhythmias, fall injuries and alcoholic liver disease were the most common conditions reported. As with alcohol attributable mortality, the majority of the 13,618 patient-specific discharges prevented by lower alcohol consumption among both males and females, were related to coronary heart disease.

There are limitations to the methods used to calculate PAFs. The calculation is a function of relative risk estimates and population drinking estimates and relies on the accuracy of population estimates of alcohol consumption and the availability and quality of the relative risk estimates reported in the epidemiological literature. Estimates of alcohol consumption derived from national population surveys are likely to be an underestimate of the true levels of consumption in the general population, therefore the estimates of alcohol attributable mortality and patient-specific discharges will probably be higher than those reported in this study. Furthermore, the majority of the relative risks used in this analysis have not been modified according to age. This is largely because the data on which such modifications would be based are sparse. To assume that the relative risks apply to all ages for each disease equally may be an unreasonable assumption, but one commonly assumed in epidemiology (Britton and McPherson 2001). There is also evidence that the risks of similar levels of alcohol use may not be equivalent for men and women (Graham et al 1998, Britton and McPherson 2001). It was not possible to consistently account for gender differences across the majority of conditions examined, as relative risk estimates were not reported separately in the most recent meta-analysis by Corrao et al (2004). Where sex-specific relative risk estimates were available for CHD, there was evidence of a different shaped dose response relationship between alcohol consumption and CHD by gender (Corrao et al 2000).

Where possible Corrao et al (2004) used studies in their meta-analysis that were adjusted for known confounders, particularly smoking for upper aero-digestive tract cancers, breast cancer and stroke. It is not possible to completely rule out the interaction between alcohol and other risk factors, however, the best estimates available have been utilised. If meta-analysis estimates do not adjust for all confounders then it is possible that some or all of the apparent protective or detrimental effects of alcohol are due to unmeasured or residual confounding. Ideally, estimates of numbers of cases caused by alcohol consumption would be based on relative risks obtained from studies of the relevant outcome. In the case of mortality, the epidemiological studies would have death as the outcome, whereas if hospitalisation were the measure of interest, the relative risks would come from studies of hospitalised cases, or perhaps all incident cases (English et al. 1995, Corrao et al 1999). However, and common to all studies of alcohol attributable mortality, the relative risk estimates used in the calculation of alcohol PAFs were based on pooled data from studies of both incidence and mortality. There is, therefore, a degree of uncertainty surrounding the estimates presented but as with other calculations of alcohol PAFs (e.g. Rehm et al 2006, Ridolfo & Stevenson 2001) this study has not developed methodologies for calculating confidence intervals for each PAF.

There are a number of caveats surrounding estimates of CHD preventable mortality and CHD preventable patient–specific discharges. Firstly, in our estimates, over 50% of alcohol preventable CHD mortality occurs in people aged 75 years and over, yet some studies that have examined how the risks of CHD change with increasing age have noted that in general, relative risks for CHD risk factors converge towards 1 (i.e. no protective effect) (Jones et al 2008). Abbot et al (2002) found no evidence of any protective effect from alcohol consumption in a cohort of Japanese men aged 75+ though Rehm et al (2006) reported no reduction in the beneficial effects of alcohol consumption among older people. If adults aged 75 years and over were to be excluded from the analysis, the estimates of CHD preventable patient-specific discharges would, among men decrease by 25.4% (7,975 to 5,347) and among women by 34.9% (3,130 to 2,037). For CHD preventable mortality, estimates would decrease in men by 40.2% (996 to 596) and in women by 44.4% (446 to 198). Since the evidence is inconsistent, we have not applied age-cut offs to our estimates of alcohol attributable CHD mortality and morbidity. This approach is also in line with the estimates for all the other conditions. Secondly, although the relationship between lower levels of alcohol consumption and reduced risk of coronary heart disease is found in many studies, it is not found in all (Fillmore et al 1998, Leino et al 1998). Concern still remains that the size of the effect may have been overestimated due to alcohol measurement problems and confounders that have not been adequately controlled in all studies. A meta-analysis of 54 published studies tested the extent to which a systematic

misclassification error was committed by including as 'abstainers' many people who had reduced or stopped drinking, a phenomenon associated with ageing and ill health (which could also be attributed to former dependence on alcohol). Only two studies were judged to be error free, and they found no significant all-cause or cardiac protection, suggesting that the cardiac protection afforded by alcohol may have been over-estimated (Fillmore et al 2006). However, as reported in Fillmore's et al paper, this finding is based on the results of only two studies therefore the study itself could be subject to bias. Although concerns about bias and error in estimates of alcohol's protective effect remain, the general consensus is that alcohol still offers a protective role against coronary heart disease when drunk at lower levels (Anderson and Baumberg 2006, Rimms and Moates 2007). What is unknown is the size of this protective effect and how it varies with age and gender and even by drinking patterns (Bagnardi et al 2008). Therefore, while estimates of preventable mortality and patient-specific discharges are presented in this report, caution should be observed in interpreting them. They should also not be considered in isolation, in that any protective effect can be mitigated by the risks from alcohol consumption for other conditions.

Relative risk estimates to calculate alcohol morbidity and mortality can be calculated using a number of reference points, reference categories or 'counterfactual scenarios' (Murray et al 2003); such as zero consumption of alcohol (abstinence) or 'unsafe' drinking (e.g. low risk drinking defined as not more than four drinks per day for men and two drinks per day for women or drinking less than the weekly limits). There are arguments for and against using either reference point. English et al (1995) argued that since, in general, the object of public health intervention in the alcohol field is to reduce 'unsafe' drinking, it stands to reason that the exposure contrast of greatest interest in the underlying epidemiology should be that between the unsafe drinker and the responsible drinker; not between the drinker and non-drinker. It therefore follows that a population attributable fraction of alcohol attributable mortality and morbidity should ideally pertain to unsafe alcohol consumption and should estimate the proportion of deaths that would be prevented if all unsafe drinkers were to reduce their exposure to a responsible level (WHO 2000). However, even at low levels of consumption, alcohol increases the risk of some conditions e.g. breast cancer (Ridolfo and Stevenson 2001). The use of 'low risk' drinking as a reference category also does not allow for the quantification of conditions apparently prevented as a result of low levels of alcohol consumption e.g. coronary heart disease. Furthermore, the relative risk estimates from epidemiological studies also use abstainers as their reference category. Of the two approaches, abstainers as a reference category is the more common approach in studies estimating alcohol attributable morbidity and mortality (Britton and McPherson 2001, Ridolfo and Stevenson 2001, Corrao et al 2002, Rehm et al 2003, Jones et al 2008) and a similar approach has been adopted in this study. This single, constant baseline, although illustrating the total magnitude of the risk, does not provide visions of population health under other alternative exposure distribution scenarios and future studies in this area should examine more sophisticated scenarios e.g. using a theoretical minimum, or feasible or plausible distributions of exposure in a population as counterfactual scenarios (Rehm et al 2001).

Average volume of consumption has been the usual measure of exposure in alcohol epidemiology. Both average volume of alcohol consumption and patterns of drinking, however, have been shown to influence alcohol related burden of disease. Patterns of drinking were found to influence CHD and liver cirrhosis outcomes and many kinds of accidents and injury (Rehm et al 2001, Rehm et al 2004, Dawson 2008). It is likely that additional disease outcomes are influenced by patterns of drinking, however, there has been relatively little focus on drinking patterns in medical epidemiological research to date and many potential links have not yet been explored. Even in studies in which patterns were explored no standardised measure of drinking pattern has been adopted, thus making comparisons and pooling of studies difficult (Rehm et al 2003). This study focuses on current consumption and does not consider previous levels or patterns of drinking. It is probable that an exposure over several years is needed for some conditions to develop and more longitudinal studies are needed in which changes in alcohol consumption (both levels and patterns) are measured. In addition, estimates of population consumption levels based on self-report may

underestimate true consumption in the general population. It has been suggested that self reported alcohol use in population surveys covers only 50%–60% of alcohol sales and individuals who are very heavy drinkers are unlikely to participate in the surveys (Goddard 2007, Catto and Gibb 2008). If the Scottish Health Survey underestimates the actual consumption, overall alcohol attributable mortality and morbidity will have been under estimated in this analysis (even accounting for revised estimates of consumption).

Estimates of alcohol attributable mortality and patient-specific discharges in this study are based on 2003 data from the Scottish Health Survey as this year corresponds to the most recent prevalence estimates of population alcohol consumption in Scotland. This approach was chosen because of the possible variation in levels of drinking over time which may affect the estimated PAF for each of the conditions included in this study. This in turn could affect the overall estimates of mortality and patient-specific discharges either positively or negatively. The data presented in this study therefore is illustrative of the burden of harm caused by alcohol consumption in Scotland in 2003 only and it is recommended that the PAFs produced in this report are updated when more current and up-to-date alcohol consumption information is available from the Scottish Health Survey.

Quantifying the level of disability and morbidity related to alcohol can be difficult in large part because few standardised measures exist. Full accounting of morbidity outcomes must confront a range of qualitative considerations encompassing illness, pain and disability though most studies have used indicators of health care utilisation e.g. hospitalisations, hospital days, health care expenditures (Murray et al 2003). One way to quantify the relationship between alcohol and health related consequences is to use a measure called the Disability Adjusted Life Year (DALY) which may prove useful in summarising the effects of alcohol in the full spectrum of health outcomes. Murray and Lopez (1996, 1997) combined years of life lost and years lived with disability into a single indicator, DALY, in which each year lived with a disability was adjusted according to severity of the disability. This approach was beyond the remit of the present study though future studies could incorporate DALYs into methods used to quantify the level of disability and mortality related to alcohol.

In summary, alcohol plays a causal role in the development of a range of acute and chronic conditions. Despite the limitations of the evidence, this study has used the best risk estimates from the epidemiological literature and primary data and the most recent alcohol consumption data available to calculate alcohol PAFs for Scotland. These calculations reveal that there were an estimated 2,882 deaths involving alcohol attributable conditions in 2003 and that there were 41,414 patient-specific discharges with an alcohol attributable condition. The figures presented here are a conservative estimate of the harm attributable to alcohol consumption given the limitations of the current evidence and the likely underestimation of population levels of alcohol consumption.

Appendix One

AAF Advisory Group

Information Services Division:	Dr Lesley Graham (Chair), (January 2007 to June 2009) Stephen Pavis (January 2007 to October 2007) succeeded by Anthea Springbett (November 2007 to June 2009)
GROS:	Graham Jackson (January 2007 to November 2007) succeeded by Frank Dixon (December 2007 to June 2009)
NHS Health Scotland:	David Gordon (December 2007 to June 2009)
Scottish Government:	Julie Ramsay (January 2007 to November 2007) succeeded by Iain MacAllister (December 2007 to June 2009)
Office for National Statistics:	Allan Baker (January 2007 to June 2009)

Remit of the AAF advisory group:

To advise and guide the work of the study in terms of its:

- Methodology
- Analysis and Presentation of Results
- Dissemination

Appendix Two

Alcohol and related disease outcomes – a review of the evidence

1. Introduction

Since the early 1990s, an extensive body of literature on alcohol and health has developed. Today, the list of diseases and health effects associated with alcohol consumption is still growing and changing as new scientific evidence accumulates. The objective of this evidence review is to elaborate a comprehensive and updated list of alcohol attributable medical conditions for the Scottish population attributable fraction (PAF) study.

The first comprehensive review (including a meta-analysis) to consider the entire spectrum of conditions considered to be related to alcohol was carried out by Australian researchers in mid 1990s (English et al 1995). From their research over forty conditions were identified as having sufficient or some limited evidence to consider a causal association with alcohol consumption based on established epidemiological criteria for causality. This was a seminal piece of work and has provided the framework of alcohol attributable conditions considered by many subsequent reviews and meta-analyses on alcohol disease outcomes (Single et al 1999, Sjogren et al 2000, Ridolfo & Stevenson 2001, Gutjahr et al 2001, Rehm et al 2003, CDC 2004). As the epidemiological evidence grows, many of these studies have reviewed and updated English's original list of conditions though not all necessarily agreed on the extent of causality.

2. Methods

2.1 Selection of alcohol conditions

The selection of conditions wholly or partly attributable to alcohol is based on a set of comprehensive meta-analyses and literature reviews. These reviews mainly examine alcohol consumption and disease outcome and include a number of reviews which focus specifically on alcohol consumption and cancer outcomes.

The disease conditions related to alcohol will be grouped into three categories, reflecting the nature of the conditions and the nature of the aetiologic influence of alcohol on those conditions: (Rehm et al 2003a)

- Conditions wholly attributable to alcohol
- Conditions where alcohol is a contributory cause (both harmful and protective)
- Injuries where alcohol is a contributory cause.

The decision to include a particular condition in the final list was taken where the weight of evidence from literature reviews and meta-analyses have been consistent in concluding sufficient or limited evidence for a causal relationship. Greater weight is given to studies where established epidemiological criteria were used to assess the causal relationship between alcohol and disease outcome (English et al 1995, IARC 1998, Corrao et al 1999, Gutjahr & Gmel 2001, Rehm et al 2003). It should be noted that biological mechanisms have historically been the most important criteria in establishing the causal link between alcohol consumption and health outcomes (Rehm et al 2003).

2.2 Alcohol diagnostic categories and codes

The alcohol attributable conditions considered in this report are based on the diagnostic categories and codes used in the current version of the International Classification of Diseases, ICD-10. Much of the initial work on alcohol attributable conditions was carried out utilizing the ICD-9 version of conditions and codes. Published conversion tables to convert the codes to ICD-10 have, therefore, been used where possible (WHO 2002, Chikritzhs et al 2002b, CDC 2004, Hughes et al 2004). While a straightforward translation from ICD-9 to ICD-10 is accepted for many of the alcohol attributable diagnoses, the creation

of new disease classifications and codes in ICD-10 has led to different interpretations of which ICD-10 codes should be assigned to certain alcohol conditions. Where this has arisen in the studies reviewed, the most commonly defined sets of ICD-10 codes used for these new conditions have been used.

3. Wholly alcohol attributable conditions

Table A2.1 gives an overview of the wholly attributable conditions, i.e. those by definition considered to be 100% attributable to alcohol consumption, which have been included in the lists of published literature reviews and meta-analysis.

Table A2.1 Wholly alcohol attributable consequences – a review of study lists.

	Meta Analyses and Literature Reviews*						
Wholly attributable conditions	Eng	Sin	Sjo	Rid	Gut	Reh	CDC
	95	99	00	01	01	03	04
Mental and behavioural disorders due to alcohol use	Y	Y	Y	Y	Y	Y	Y
Alcoholic polyneuropathy	Y	Y	Y	Y	Y	Y	Y
Alcoholic cardiomyopathy	Y	Y	Y	Y	Y	Y	Y
Alcoholic gastritis	Y	Y	Y	Y	Y	Y	Y
Excessive blood level of alcohol	-	Y	-	-	Y	Y	Y
Alcoholic liver disease	Y	-		Y	Y	-	Y
All chronic liver disease	See section 3.2						
Fetal alcohol syndrome	-	-	-	-	-	Y	Y
Toxic effect of alcohol	Y	-	Y	Y	Y	Y	Y
Accidental poisoning not elsewhere specified	Y	Y	-	Y	-	-	Y
Poisoning to alcohol undetermined	-	-	-	-	-	-	Y
Intentional self poisoning by and exposure to alcohol	-	-	-	-	-	-	Y
Alcoholic myopathy	-	-	-	-	-	-	Y
Degeneration of nervous system due to alcohol	-	-	-	-	-	-	Y
Alcohol induced chronic pancreatitis	-	-	-	-	-	-	Y
Fetus and newborn affected by maternal use of alcohol	-	-	-	-	-	-	Y
Evidence of alcohol involvement determined by blood alcohol level	Y	-	-	-	-	-	-
Evidence of alcohol involvement determined by level intoxication	Y	-	-	-	-	-	-

*English et al (Eng) 1995, Single et al (Sin) 1999, Gurr (Gur) 1999, Sjogren et al (Sjo) 2000, Bagnardi (Bag) et al 2001, Ridolfo & Stevenson (Rid) 2001, Gutjahr & Gmel (Gut) 2001, Rehm et al (Reh) 2003b, CDC 2004.
Y= included in study list.

3.1 Recommended set of wholly alcohol attributable conditions

The conditions considered to be 100% attributable to alcohol and to be included in this study are listed in table A2.2 along with the recommended ICD-10 codes. Conditions have been included if they were listed in wholly alcohol attributable lists of at least two of the literature reviews/meta analyses. In addition, a number of other conditions recently identified in only one review/meta analysis but also included in recent alcohol morbidity and mortality studies have been recommended for inclusion i.e. poisoning from alcohol undetermined; intentional self poisoning by and exposure to alcohol; alcoholic myopathy; alcohol-induced pseudo-Cushing's syndrome; degeneration of nervous system due to alcohol; alcohol induced chronic

pancreatitis, and fetus and newborn affected by maternal use of alcohol. Most of these latter conditions were new diagnostic groupings in ICD-10 (and therefore not included in the majority of studies reviewed in this paper). Given the significant contribution of alcoholic liver disease to estimates of overall alcohol attributable mortality/morbidity, a more detailed discussion is provided in Section 3.2 of how alcoholic liver disease and liver disease from other causes are dealt with by the literature.

Table A2.2. Recommended list of wholly alcohol attributable conditions

Condition	ICD10 code(s)
Alcohol-induced pseudo-Cushing's syndrome	E24.4
Wernicke's encephalopathy	E51.2
Mental and behavioural disorders due to use of alcohol	F10
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
Alcohol induced chronic pancreatitis	K86.0
Fetus and newborn affected by maternal use of alcohol	P04.3, O35.4
Fetal alcohol syndrome	Q86.0
Excessive blood level of alcohol	R78.0
Toxic effect of alcohol	T51.0, T51.9
Accidental poisoning by and 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
Evidence of alcohol involvement determined by level intoxication	Y91

3.2 Alcoholic liver disease and liver disease 'unspecified'

The treatment of alcoholic liver disease (ALD) and liver disease from other causes varies across the studies reviewed as to what is defined as wholly attributable to alcohol. The most common approach identified in the literature is to consider alcoholic liver disease and liver disease from other causes separately and to assign the appropriate attributable fraction to both. English et al (1995) distinguished ALD from liver diseases from other causes, by considering ALD only (i.e. ICD-9: 571.0–571.3) as 100% alcohol attributable (PAF=1). Liver disease from other causes (i.e. ICD-9: 571.5-571.9), on the other hand, was included in the 'alcohol partly attributable' list and the proportion of these cases attributable to alcohol was estimated as a function of prevalence of alcohol exposure and relative risk. The majority of studies since English's work have also followed this approach and recommended distinguishing between the two (Ridolfo & Stevenson 2001, Gutjahr & Gmel 2001, Rehm et al 2003, CDC 2004). In contrast, a Swedish meta-analysis combined ALD and liver diseases from other causes into one liver cirrhosis category and defined the category as wholly alcohol attributable (Sjorgen et al 2000). This method was also used in a comprehensive costing study in the UK (COSU 2003). Routine national statistics for alcohol related mortality in the UK also adopt this approach in their definition (ONS 2006). Corrao et al (1999, 2004) Johansson et al (2006) and Single et al (1999) also combined ALD and liver disease into one cirrhosis category but defined the category as partly attributable.

Assuming all liver disease to be entirely attributable to alcohol will likely overestimate alcohol's contribution although evidence from America, Europe and the UK indicates that an appreciable proportion (but not all) of deaths from cirrhosis without mention of alcohol were in fact attributable to alcohol (Gutjahr & Gmel 2001, Fisher et al 2002). In contrast, separating ALD from liver disease from other causes is likely to underestimate alcohol's contribution to overall liver disease mortality and morbidity. It has been argued that since the pooled estimate of the alcohol caused proportion of liver disease from other causes is itself based on relative risks from studies that included both alcoholic and non-alcoholic cirrhosis cases, this actually may result in an overestimation of alcohol's role in unspecified liver disease deaths/cases (English et al 1995). It is worth noting that Single et al (1999) found little difference in either including or excluding unspecified liver disease as a 100% attributable condition when calculating alcohol attributable mortality in Canada, though this may not be transferable to other countries in the world due to difference in recording of the role of alcohol in the cause of death.

Even though the Australian method i.e. separating ALD from liver disease from other causes, is the most common approach in studies estimating alcohol attributable mortality and morbidity, it is also widely acknowledged that it is extremely difficult to separate ALD from unspecified liver disease and ultimately the distinction is solely a matter of technical assessment in autopsies (English et al 1995, Gutjahr & Gmel 2001, Rehm et al 2003b). Although, empirically, there is good evidence to suggest including one liver cirrhosis category only, it is proposed, that in this study only ALD is regarded as wholly attributable and an appropriate PAF be calculated for liver disease from other causes. The rationale for this is that the weight of evidence on alcohol's contribution to unspecified liver disease though suggestive is based on a small number of studies and still only assigns a proportion of cases to alcohol consumption. Equally on the basis of the evidence reviewed for this paper, separating ALD from unspecified liver diseases is the most common approach in attributable fraction studies.

4. Conditions where alcohol is a potential contributory cause

As more epidemiological evidence becomes available, the list of conditions considered potentially attributable to alcohol has continued to evolve since the seminal work by English et al (1995). Tables A2.3a (cancers) and A2.3b (other conditions) provide an overview of these conditions where the studies reviewed in this study have considered a possible relationship with alcohol consumption.

Table A2.3a Cancers where alcohol is a potential contributory cause: a review of study lists [10]

	Eng	Gur	IARC	Cor	Bag	Rid	Gut	Sjo	Bur	Reh	Cor	CDC	Bof	Wcrf
	1995	1996	1998	1999	2001	2001	2001	2002	2004	2004	2004	2004	2006	2007
Cancer														
Lip	-	-	-	Y	-	-	Y	-	-	Y	-	-	-	Y
Oral & Pharyngeal	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Oesophagus	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Liver	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Gastric	N	N	N	-	N	-	N	-	N	N	-	-	-	Y
Colon	N	N	N	Y	Y	-	N	-	Y	N	Y	-	Y	Y
Rectal	N	N	N	Y	Y	-	N	-	Y	N	Y	-	Y	Y
Pancreatic	N	N	N	-	N	-	N	-	N	N	-	-	-	-
Lung	N	-	N	-	N		N	-	-	N	-	-	-	-
Laryngeal	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Breast	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Ovarian	-	-	N	N	Y	-	-	-	-	N	-	-	N	-
Prostate	-	-	N	-	N	-	N	-	-	N	-	Y	N	-
Endometrial	-	-	-	-	-	-	N	-	-		-	-	N	-
Bladder	N	-	N	N	N	-	N	-	-	N	-	-	N	-
Renal	N	-	N	N	N	-	-	-	-		-	-	N	-

Y = studies that have concluded that there is sufficient or limited evidence of causality, N = studies that have rejected condition because evidence is inconsistent or inadequate

10 English et al (Eng) 1995, Single et al (Sin) 1999, Gurr (Gur) 1999, Sjogren et al (Sjo) 2000, Bagnardi (Bag) et al 2001, Ridolfo & Stevenson (Rid) 2001, Gutjahr & Gmel (Gut) 2001, Rehm et al (Reh) 2003b, CDC 2004, Burger et al (Bur) 2004, Corrao (Cor) et al1999, 2004, Bofetta & Hashibe (Bof) 2006, World Cancer Research Fund (Wcrf) 2007, International Agency Research Cancer (IARC) 1998.

Table A2.3b Other conditions where alcohol is a contributory cause: a review of study lists										
	Eng	Gur	Cor	Rid	Gut	SJo	Bur	Reh	Cor	CDC
	1995	1996	1999	2001	2001	2002	2004	2004	2004	2004
Respiratory Tuberculosis	-	-	N	-	N	-	-	-	-	-
Unipolar major depression	-	-	-	-	-	-	-	Y	-	-
Diabetes	N	-	-	N	Y	-	-	Y	-	-
Epilepsy	Y	-	-	Y	Y	Y	-	Y	-	Y
Hypertension	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Coronary heart disease	N	Y	Y	N	Y	Y	Y	Y	Y	Y
Cardiac arrhythmias	Y	-	-	Y	Y	Y	-	Y	-	Y
Heart failure	N	-	-	N	Y	Y	-	Y	-	-
Hemorrhagic stroke	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Ischaemic stroke	Y	N	N	Y	Y	Y	Y	Y	Y	Y
Oesopahageal varices	Y	-	-	Y	Y	Y	-	Y	-	Y
Pneumonia and Influenza	-	N	N	-	N	-	-	-	-	-
Gastric and duodenal ulcer	N	-	N	N	N	-	-	-	N	-
Gastro-oesophageal haemorrhage	Y	-	-	Y	Y	Y	-	Y	-	Y
Unspecified liver cirrhosis	Y	Y	Y	Y	Y	Y	-	Y	Y	Y
Cholelithiasis	Y	-	-	Y	Y	Y	N	Y	-	Y
Portal hypertension	-	-	-	-	-	-	-	-	-	Y
Acute pancreatitis	Y	-	N	Y	Y	Y	N	Y	-	Y
Chronic pancreatitis	Y	-	Y	Y	Y	Y	N	Y	Y	Y
Spontaneous abortion	Y	N	-	Y	Y	-	-	Y	-	Y
Low birth weight	Y	N	-	Y	Y	-	-	Y	-	Y
Psoriasis	Y	N	-	Y	Y	-	-	Y	-	Y

Y = studies that have concluded that there is sufficient or limited evidence of causality, N = studies that have rejected condition because evidence is inconsistent or inadequate

4.1 Code-set of conditions where alcohol is a contributory cause selected for this study.

Table A2.4 provides an overview of the selected chronic conditions with accompanying ICD-10 codes that are not wholly attributable to alcohol but where the weight of evidence from literature reviews and meta analyses have been consistent in concluding sufficient or limited evidence for a causal relationship. Conditions that have been found to have a significant protective effect of alcohol are in bold. A short summary of the evidence from the reviews and the rationale for the inclusion of the condition in the final list of alcohol-attributable conditions is provided in Section 4.1.1.

Table A2.4. Selected set of conditions where alcohol is a contributory cause		
Condition	**Strength of evidence***	**ICD10 code(s)**
Lip cancer	L	C00
Oral cavity and pharyngeal cancer	S	C01-C06, C09-C10, C12-C14
Oesophageal cancer	S	C15
Liver cancer	S	C22
Colon cancer	L	C18
Rectal cancer	L	C20
Laryngeal cancer	S	C32
Breast cancer	L	C50
Epilepsy	L	G40-G41
Hypertension	S	I10-I15
Coronary (Ischaemic) heart disease	S	I20-I25
Cardiac arrhythmias	S	I47.1, I47.9, I48
Haemorrhagic stroke	S	I60-I62
Ischaemic stroke	L	I63-I66
Oesopahageal varices	S	I85, I98.2*
Mallory-Weiss Syndrome	S	K226
Unspecified liver disease	S	K74.3-K74.6, K76.0, K76.9
Portal hypertension	L	K76.6
Cholelithiasis	S	K80
Acute pancreatitis	S	K85
Other Chronic pancreatitis	S	K861
Spontaneous abortion	L	O03
Psoriasis	L	L40 excl L40.5

S= sufficient evidence of causality, L= limited evidence of causality

4.1.1 Summary of Evidence

Cancers

Multiple studies of varying design have consistently found a relationship between alcohol and the risk of cancers of the mouth, pharynx, larynx, oesophagus, and liver. The association appears to be dose dependent, following a linear trend. The weight of evidence is clear in respect of the cancers outlined in Table A2.3a. Less straightforward is the treatment of lip cancer. Assessment of the association between alcohol and lip cancer is complicated in that most of the studies on cancer of the upper aero-digestive tract do not distinguish between specific cancer sites. Reviews carried out by IARC (1998) and English et al (1995) either did not consider lip cancer or excluded it because of confusion over the its exact anatomical location. Subsequent reviews however have argued that lip cancer by definition is part of malignant neoplasms involving the oral cavity. In two studies updating English's work both concluded that there was sufficient epidemiological evidence to differ from English and included lip cancer in their list (Gutjahr & Gmel 2001, Rehm et al 2003b). It is therefore recommended that lip cancer be included in the list of chronic alcohol attributable conditions.

The exact relationship between alcohol consumption and development of breast cancer has been the subject of much epidemiological research over the last 20 years. Reviews of the literature published up until 1995 observed that though the available data did indicate a positive association between alcohol and breast cancer, a firm conclusion about a causal relationship could not be made at that time partly due to

the risk being associated with high levels of alcohol consumption only (English et al 1995, Gurr 1996, IARC 1998). From 1998 onwards, however, reviews have been consistent in their assessment that sufficient epidemiological evidence now exists for a causal association between alcohol and breast cancer, even at low levels of alcohol intake. (Ridolfo & Stevenson 2001, Gutjahr & Gmel 2001, Rehm et al 2003b, World Cancer Research Fund 2007). Meta-analytic and pooled analyses have also confirmed a dose response relationship between alcohol consumption and breast cancer (Smith-Warner et al 1998, Bagnardi et al 2001, Hamajima et al 2002, Corrao et al 2004). Despite the modest increase in risk associated with alcohol and doubts concerning the effect of low levels of alcohol intake, there is a consensus in the literature that alcohol constitutes a risk factor for breast cancer. The public health implications of even a moderate effect of alcohol consumption on breast cancer are significant given the high prevalence of this cancer (Bofetta & Hashibe 2006). In line with published reviews, breast cancer has been selected for inclusion on the list of alcohol attributable conditions.

The evidence from the literature as to whether there is limited or sufficient evidence of causal relationship between alcohol and colorectal cancers is mixed. A number of reviews have considered that the epidemiological evidence is suggestive but too weak to allow for a conclusion to be drawn about the role of alcohol consumption in the causation of colon and rectal cancers (English et al 1995, Gurr 1996, IARC 1988, Gutjahr & Gmel 2001). Doubts have also been raised about the consistency of findings on the biological pathways by which alcohol acts as a carcinogen (Rehm et al 2003b). Meta analyses by Bagnardi et al (2001), and Corrao et al (1999, 2004) have since observed significant borderline increases in risk for both cancers. However, whilst Bagnardi concluded that an inference on a causal relationship for these two cancers was still not possible, Corrao's interpretation was that there was limited evidence of causality and he subsequently included both cancers in a study of alcohol attributable mortality and morbidity in Italy (Corrao et al 2002). A pooled analyses study has also observed an association between alcohol and colorectal cancers though this risk is only apparent at moderate to high levels of alcohol consumption (Cho et al 2004). Boffetta & Hashibe (2006) in their review of alcohol and related cancers also concluded that although the effects may be moderate there seems to be a causal relation between alcohol consumption and risk of colorectal cancer. Recent studies have also observed some highly convincing biological mechanisms through which alcohol acts as a carcinogen (Pedersen et al 2003, Su & Arab 2004). A restricted search of current research lends support for limited evidence of a causal association. A strong dose response relationship between alcohol consumption and rectal cancer has been reported in the majority of recent studies (Sharpe et al 2002, Pedersen et al 2002, Murtagh et al 2004). The evidence for colon cancer is slightly more mixed, split between studies observing no effect of alcohol (Flood et al 2002, Pedersen et al 2003) and those observing a dose response relationship (Sharpe et al 2002, Shimizu et al 2003, Otani et al 2003, Su & Arab 2004). However, two major reviews published recently by the International Agency for Research on Cancer (2006) and the World Cancer Research Fund (2007) have concluded that there is a definite causal relationship between colorectal cancer and alcohol consumption among men, and a probable relationship among women. Based on this current evidence, colon and rectal cancer have been selected for the list of alcohol attributable conditions.

Gastrointestinal conditions

English et al (1995) originally concluded that oesophageal varices, gastro-oesophageal haemorrhage, chronic and acute pancreatitis were partly attributable to alcohol consumption though their observations were based entirely on clinical case studies. The lack of epidemiological research establishing dose response relationships has often led to these conditions being excluded from meta-analytic studies (Corrao et al 1999, Sjogren et al 2000, Burger et al 2004). Nevertheless, the causal role of alcohol in these conditions seems to be clear and supported by the vast majority of studies reviewed (Table 3b). With regard to cholelithiasis, reviews have consistently reported a moderately strong, statistically significant and coherent protective effect of alcohol consumption. These conditions have therefore been included on list of alcohol partly attributable conditions.

Cardiovascular Diseases

The role of alcohol as both a risk and protective factor for cardiovascular diseases such as hypertension, stroke, arrhythmias and coronary heart disease, has been investigated for many years and the epidemiological evidence of causality for a number of conditions is strong for some though less convincing for others.

For conditions such as hypertension, cardiac arrhythmias and coronary (ischaemic) heart disease (CHD), the epidemiological evidence of a causal relationship with alcohol is convincing with the risk of these conditions increasing in a dose dependent manner. These conditions are routinely included in lists of alcohol attributable conditions (Table 3b). CHD, however, differs slightly from other conditions in its relationship to alcohol. Although the epidemiological evidence is clear that low to moderate levels of alcohol consumption are protective against CHD, heavy drinking occasions, even when coupled with average light or moderate consumption, are associated with an increase in CHD risk (Rehm et al 2003a). Unlike most other alcohol attributable conditions which follow a dose response relationship, the relative risk curve for CHD is more J-shaped i.e. higher risks for abstainers than for light drinkers.

Although the relationship between lower levels of alcohol consumption and reduced risk of coronary heart disease is found in many studies, it is not found in all (Fillmore et al 1998a, Fillmore et al 1998b; Leino et al 1998). Concern still remains that the size of the effect may have been overestimated due to alcohol measurement problems and confounders that have not been adequately controlled in all studies. A meta-analysis of 54 published studies tested the extent to which a systematic misclassification error was committed by including as 'abstainers' many people who had reduced or stopped drinking, a phenomenon associated with ageing and ill health. The studies judged to be error free found no significant all-cause or cardiac protection, suggesting that the cardiac protection afforded by alcohol may have been over-estimated (Fillmore et al 2006). However, as reported in Fillmore's et al paper, this finding is based on the results of only two studies therefore the study itself could be subject to bias. Although concerns about bias and error in estimates of alcohol's protective effect remain, the general consensus is that alcohol still offers a protective role against coronary heart disease when drunk at low to moderate levels (Anderson and Baumberg 2006, Rimms and Moates 2007). What is unknown is the size of this protective effect and how it varies with age and gender and even by drinking patterns (Bagnardi et al 2008). Furthermore, the decision to include CHD in calculations of alcohol attributable morbidity and mortality, has tended to flow directly from the choice of abstention or low consumption as the study's baseline (reference) category. For example, English et al (1995) and Single et al (1999) concluded that there was inadequate evidence that the marginal exposure between low and hazardous or harmful alcohol intake is either a cause of, or protective against ischaemic heart disease. Since this marginal risk was the focus of both their studies, they did not calculate a PAF for alcohol and CHD. In contrast, the majority of studies which have focused on both the harms and the benefits of alcohol consumption, relative to abstaining from alcohol, have included coronary heart disease in their calculations of alcohol attributable mortality and morbidity (Ridolfo & Stevenson 2001, Gutjahr & Gmel 2001, Rehm et al 2003b).

Stroke is also routinely included in the review lists based on the epidemiological evidence though a distinction needs to be made between hemorrhagic stroke and ischaemic stroke (Table 3b). Studies in the last 10 years have confirmed that alcohol consumption has a distinctively different association with hemorrhagic stroke as opposed to ischaemic stroke. In the main, they have shown an increased risk of hemorrhagic stroke associated with increasing alcohol consumption in a dose-dependent fashion, so that even moderate levels of drinking increase the risk of hemorrhagic stroke. For ischemic stroke, the predominant type of stroke, the weight of evidence suggests similar effects as for CHD, namely that low to moderate consumption may offer some protection against the disease (Ridolfo & Stevenson 2001, Gutjahr & Gmel 2001).

Conditions arising during pregnancy and birth

In their comprehensive literature review of alcohol attributable morbidity, English et al (1995) derived risk ratios for spontaneous abortion, low birth weight and premature/intrauterine growth-retardation and alcohol and found a small increase in risk due to hazardous and harmful consumption in pregnancy, relative to low consumption. Based on this, they concluded that there was some limited evidence of causality for these conditions as a result of moderate to high levels of alcohol intake. This association has been accepted by subsequent alcohol attributable studies and often an update of the research published since English et al's work has produced evidence supporting this causal association (e.g. Gutjahr et al 2001, Rehm et al 2004). However, in all these studies, the association between alcohol and the above prenatal conditions was based on an assessment of a very small number of studies.

A more recent and comprehensive review on the fetal effects of prenatal alcohol exposure commissioned by the Department of Health (Gray and Henderson 2006) concluded that there was no consistent evidence of adverse effects from low to moderate prenatal alcohol consumption for low birth weight and intrauterine growth restriction, whilst there was evidence of an adverse effect of alcohol on spontaneous abortion. A brief summary of the study results are provided below and on the basis of the report's findings reported by Gray and Henderson (2006), only spontaneous abortion will be included in the list of alcohol attributable conditions for this study:

- Spontaneous abortion - eight studies, seven of which reported a statistically significant association
- Low Birth weight - 20 studies, only 1 reported a significant excess in risk, however, the result was inconsistent in that heavy alcohol consumption was not associated with increased risk. Small amounts of alcohol appeared to exert a mildly protective effect. However Johansson et al (2006) argue that there is no biological evidence for a protective effect of low consumption.
- Intrauterine growth retardation – of seven studies, only one found a positive association, a further two found low to moderate alcohol consumption to be mildly protective but this was of borderline statistical significance.

Epilepsy

The majority of reviews include epilepsy as an alcohol attributable condition. It was included by English et al (1995) based on the observations of both clinical cases studies and epidemiological research and subsequent literature reviews have supported this association. Although none of the meta-analyses reviewed in this study included epilepsy in their lists this will in part be due to the lack of epidemiological research establishing clear dose response relationships. Excessive drinking can make seizures more likely because of the effect of alcohol on the brain. It can also interact with anti-epileptic drugs making them less effective. The commonest cause of alcohol related seizures are tonic-clonic convulsions (grand mal in nature) occurring either singly or in short series on withdrawal of alcohol after a period of chronic intoxication. Previous research has estimated that over one in ten of alcohol dependent discharges are attributable to epilepsy (Hanke et al 1997). In view of epilepsy's inclusion in the majority of alcohol attributable studies, this condition has been included on list of alcohol partly attributable conditions.

5. Injuries where alcohol is a contributory cause

Alcohol use has been associated with increased risk of traumatic injury in a variety of settings such as traffic accidents, accidents in professional and recreational contexts, falls, arson, but also self-inflicted injury (including suicide) and injuries resulting from violence. The assessment of causality is often difficult and needs triangulation by different sources, such as time series analyses, natural experiments, case-control studies, accident and emergency studies, general population surveys, and experimental designs. The context of drinking, social and cultural environment, and drinking patterns, however, is probably as important as the amount of alcohol consumed.

With respect to certain acute conditions, most researchers agreed on causality (English et al 1995, Single et al 1996, 1999, Sjögren et al 2000, Gutjahr & Gmel 2001, Ridolfo & Stevenson 2001, Rehm et al 2003b), and these conditions are listed in Table A2.5 along with the recommended ICD-10 codes. It should be noted that while the researchers from most studies agree on causality, there is no general consensus regarding PAFs for these outcomes, as there is good reason to expect the PAFs to vary by time and place. This should be carefully considered when assigning estimates of the proportion of deaths/cases that can be attributed to alcohol drawing on studies that are either UK based or countries that share similar levels of alcohol consumption.

Table A2.5 Injuries where alcohol is a contributory cause

Condition	ICD10 code(s)
Road injuries/Motor vehicle accidents	V01-V89
Fall injuries	W00-W19
Fire injuries	X00-X09
Occupational and machine injuries	W21, W22-W24, W29-W31, W49, W52
Intentional self-harm	X60-X84, Y87.0 excl.X65
Undetermined injury	Y10-Y34, Y87.2 excl. Y15
Assaults	X85-Y09, Y87.1
Aspiration	W78-W79
Water transport accident injuries	V90-V94
Drowning	W65-W74
Additional excessive cold (hypothermia)	X31
Accidental firearm missile injuries	W32-W34

6. Conditions excluded from selection of alcohol attributable conditions

There are a number of other disease outcomes, especially cancers, which have been examined for their relationship to alcohol consumption and these are summarised in Table A2.6. These are conditions where alcohol is suggested as a possible risk factor but for which the literature has concluded that the evidence of a causal association with alcohol is inconsistent, inconclusive or there is a lack of epidemiological evidence. Biological evidence also plays a key role here as many of the associations are currently excluded because of the lack of biological plausibility. A short summary of the evidence from the reviews is provided in Section 6.1.

Table A2.6 Excluded conditions

Condition	ICD10 code(s)
Respiratory tuberculosis	(011-012)
Gastric cancer	C16
Pancreatic cancer	C56
Endometrial cancer	C54
Ovarian cancer	C56
Bladder cancer	C67
Renal cancer	C64, C65
Lung cancer	C33-34
Prostate cancer	C61
Hepatitis C	B15
Diabetes	E11
Pneumonia and Influenza	J12-J18
Gastric and duodenal ulcer	K25-K27
Depression	F32-F33
Low birth weight	P05, P07, 036.5

6.1 Summary of evidence for excluded conditions

Cancers

There is some limited evidence to suggest borderline increases in risk between alcohol and bladder, endometrial, gastric, ovarian, pancreatic and lung cancer (English et al 1995, Bagnardi et al 2001, Zeegers et al 2001, Zaridze et al 2000), though other studies have observed that there is insufficient or inconclusive evidence of a causal association (Weiderpass & Baron 2001, Michaud et al 2001, Goodman & Tung 2003, Djousse et al 2004, Barstad et al 2005, WCRF 2007). The majority of reviews have concluded that evidence of causal associations between alcohol and these cancers is inconsistent and/or inconclusive and that further data is required before any association between alcohol and these cancers can be confirmed. More recently, studies have observed a possible protective effect of ovarian cancer at moderate levels of alcohol intake which require further investigation (Schouten et al 2004, Bofetta & Hashibe 2006).

There are a limited number of studies on renal cancer and alcohol consumption preventing any conclusive assessment of the role alcohol in renal carcinogenesis. Recent reviews and primary studies have observed that a possible protective effect of alcohol consumption on development of renal cancer needs to be further investigated (Bagnardi et al 2001, Parker et al 2002, Mahabir et al 2005, Bofetta & Hashibe 2006).

Studies on the relationship between prostate cancer and alcohol consumption have continued to produce mixed results. Slight borderline increases in risk particularly at moderate levels of alcohol intake have

been observed (Sharpe et al 2001, Platz et al 2004) though the majority of recent studies have confirmed the absence of an appreciable role for alcohol drinking on the risk of prostate carcinogenesis (Ellison 2000, Sesso et al 2001, Barba et al 2004, Crispo et al 2004). Causality of relationship between alcohol consumption and prostate cancer is not yet clear and whilst the CDC (2004) scientific review concluded that prostate cancer should be regarded as alcohol attributable, the majority of reviews consider the evidence too weak.

Diabetes

The relationship between alcohol and diabetes has only recently been investigated. English et al. (1995) found two studies that met their inclusion criteria. Their pooled analysis of relative risks was statistically consistent with no effect. They reported evidence of a weak inverse relationship. Overall, they excluded it because of inconsistency of results. A review by Gutjahr et al (2001) concluded that there was sufficient evidence of a protective effect of moderate alcohol consumption and diabetes (though there was an increased risk with high levels of consumption) and included the condition in their study, despite the evidence being based on only four studies. Rehm et al (2004) as part of the WHO Global Burden of Disease study concluded that evidence for the relationship between alcohol consumption and diabetes is far from conclusive at present though it was included as a beneficial effect in their calculations for disease burden in western economies (the rationale being that the evidence from cohort studies and plausible biological mechanisms meant that in countries with beneficial drinking patterns, it was reasonable to include a beneficial effect for diabetes). A recent meta-analysis of 20 studies (mainly cohort in design) also concluded that moderate alcohol consumption (defined as between 5-30 grams per day) was protective against diabetes but the evidence at high levels of consumption was inconsistent neither proving a protective or detrimental effect of alcohol consumption (Carlsson et al 2005). Findings from a Swedish longitudinal study support the protective effect of moderate alcohol consumption on diabetes though in this study it was also reported that high levels of alcohol consumption did not increase risk of diabetes incidence (Lapidus et al 2005).

At the outset of the study, inclusion criteria were established which stated that for a condition to be included in this study it would have to fulfill the basic epidemiological criteria of causality as outlined by Hill et al (1965). The evidence to date would certainly suggest an association between alcohol consumption and diabetes but of course association does not imply causation or protection. There are too many unresolved questions concerning the relationship between alcohol consumption and diabetes; biological mechanisms facilitating the protective effect of light to moderate alcohol consumption on diabetes; the effect of body weight on an adverse effect of heavy drinking on diabetes, the relationship between alcohol consumption, coronary heart disease and diabetes (Wannamethee et al 2002, Lapidus et al 2005). In light of this, diabetes has not been included in the study.

Depression

Alcohol is implicated in a variety of mental disorders that are wholly alcohol attributable but until recently, no major overview on the alcohol attributable burden of disease has included depressive disorders. However, in a recent review of the literature, as part of the WHO Global Burden of Disease study, Rehm et al (2003b) concluded that there is now sufficient evidence of causality for the influence of alcohol dependence on depressive disorders though they acknowledged that the status of alcohol misuse as a causal agent in depression is not as clear. This study demonstrated that based on consistency across several studies, strength of association, temporal order and plausible biological mechanisms; there was a clear and consistent association between alcohol dependence and depressive disorders. Crucially, however, this assessment is based on a measure of alcohol dependence and not alcohol consumption (i.e. frequency and patterns) and the authors themselves acknowledge that the relationship between alcohol consumption and depressive disorders should be clarified in future research (Rehm et al 2003b). Despite the strong arguments by Rehm et al (2003b) on the causal relationship between alcohol and depressive disorders, this

condition has not been included in the study on the grounds that the evidence for alcohol consumption itself (as opposed to a diagnosis of alcohol dependence) and depression is still unclear.

Hepatitis C

Since Hepatitis C was first identified in the late 1980s, many of the reviews and meta-analyses used in this study, whose search strategies tended to be based on published literature between 1960s and mid 1990s, did not include Hepatitis C as an alcohol attributable condition. Since these reviews, increasing evidence has accumulated, mainly through case control studies, of heavy levels of alcohol consumption among Hepatitis C patients contributing to the acceleration of liver disease. The evidence concerning the negative effect of low to moderate alcohol consumption among Hepatitis C carriers, on the liver, however, is less convincing than that for heavy alcohol consumption (Everhart 2006). Despite a lack of consistent evidence of the effect of low to moderate levels of consumption on the liver of people with Hepatitis C, it is generally accepted among reviews of alcohol related health conditions that liver disease itself can be worsened even at low to moderate levels of alcohol consumption (English et al 1995, Gutjahr et al 2001, Rehm et al 2004). Hepatitis C does not, however, meet the established inclusion criteria for this study, since not all requirements for causality can be demonstrated e.g. consistency across studies, strength of association.

Heart Failure

One other possible relevant disease category considered by a number of reviews is based on the ICD diagnostic categories, 'heart failure and ill-defined descriptions and complications of heart disease'. English et al (1995) originally observed that 'heart failure and ill-defined descriptions and complications of heart disease' are non-specific categories underlying various manifestations of heart disease. Since they also considered CHD to be the predominant cause of heart failure, alcohol consumption was also seen as related to heart failure because of its association with CHD. Though this decision to consider heart failure as alcohol attributable is not based on any epidemiological evidence, subsequent reviews have followed this approach and included heart failure in their lists of alcohol attributable conditions (Table 3b). Since heart failure is an unspecific category with no identification of underlying pathology, the risk relationship between average volume consumption and outcome has not been determined. Heart failure does not strictly meet the epidemiological criteria of causality since the association is not based on epidemiological evidence. Furthermore, Johannsson et al (2006) evaluated the possible role of alcohol in heart failure by examining the aggregate level relationship between alcohol consumption and mortality in heart failure in Sweden in a time series analysis of annual data. The analysis showed no significant relationship and therefore the disease category of heart failure and ill-defined complications of heart disease was excluded from their study. Given the lack of evidence either from observational or correlation studies, heart failure will not be selected for inclusion in this study.

Other conditions

A small number of experimental and epidemiological studies have observed a possible relationship between alcohol consumption and tuberculosis, pneumonia and influenza, gastric and duodenal ulcers and Alzheimer's disease. Although some of these conditions have appeared in recent alcohol mortality and morbidity studies, the most recent studies to review the association between alcohol and the aforementioned conditions have recommended exclusion as alcohol attributable conditions because of a lack of epidemiological evidence or inconsistent or inconclusive evidence (Corrao et al 1999, Gutjahr & Gmel 2001). There is no evidence to suggest departing from this approach and they therefore have been excluded.

Appendix Three

Consumption data

This study uses the revised estimates of alcohol consumption from the 2003 Scottish Health Survey using updated conversion factors for converting drinks into units of alcohol (Scottish Government 2008). These figures were recalculated in response to reviews by ONS and NHS Health Scotland showing that surveys have increasingly underestimated the level of alcohol consumption by not taking account of increased strength and size of some drinks (Goddard 2007, Catto and Gibbs 2008). In order to provide a more accurate picture of drinking in Scotland, these reviews recommended recalculation of existing survey data to take account of these changes. The figures presented below (tables A3.2 and A3.3) are based on updated conversion factors (Table A3.1) published by the Office for National Statistics in December 2007, which are now being used to estimate alcohol consumption in England and Great Britain.

Table A3.1. Previous and revised factors for converting alcohol volume to units, Source: (Goddard 2007)

Drink	Original unit conversion factors	Usual volume (ml)	Strength	Revised no. of units
Normal beer/lager/cider				
half pint	1	284ml	4.5%	1
small can/bottle	1	330ml	4.5%	1.5
large can/bottle	1.5/2	440ml	4.5%	2
very large can	n/a	500ml	4.5%	2.5
Strong beer/lager/cider				
half pint	1.5	284ml	6.5%	2
small can/bottle	1.5	330ml	6.5%	2
large can/bottle	2.3/3	440ml	6.5%	3
very large can	n/a	500ml	6.5%	3.5
Table wine				
small glass	n/a	125ml	12.5%	1.5
medium glass	n/a	175ml	12.5%	2
large glass	n/a	250ml	12.5%	3
glass- size unspecified	1	n/a		
bottle	6	750ml	12.5%	9
Fortified wine				
small glass	1	50	17.0%	1
bottle	n/a	750	17.0%	13
litre	n/a	1000	17.0%	17
Spirits				
single shot	1	25ml	40.0%	1
bottle	n/a	750ml	40.0%	30
litre	n/a	1000	40.0%	40
Alcopops				
bottle	1.5/1.0	275ml	5.0%	1.5

Table A3.2 Men – age specific comparison of proportion drinking at given levels (grams of alcohol) based on old and new alcohol unit conversion factors

		16-24	25-34	35-44	45-54	55-64	65-74	75+
Abstainers	Old	12.3	10.1	11.0	9.5	12.4	18.7	31.6
	New	12.3	9.6	10.3	9.3	11.9	17.6	31.6
0.26 – 39.99g/day	Old	72.8	77.8	75.8	77.7	75.0	70.0	62.5
	New	70.2	73.5	70.4	72.3	70.0	68.0	59.4
40.00 – 59.99g/day	Old	7.8	6.7	7.4	6.9	6.5	7.3	3.7
	New	8.1	10.3	9.9	8.9	8.4	8.7	5.0
60.00+ g/day	Old	7.1	5.4	5.8	5.9	6.2	3.9	2.2
	New	9.4	6.5	9.4	9.5	9.7	5.7	4.0

Table A3.3 Women – age specific comparison of proportion drinking at given levels (grams of alcohol) based on old and new alcohol unit conversion factors

		16-24	25-34	35-44	45-54	55-64	65-74	75+
Abstainers	Old	15.3	17.1	17.2	17.9	29.1	38.7	57.1
	New	15.1	15.9	16.6	16.5	26.7	37.5	55.1
0-19.99g/day	Old	66.7	71.1	73.4	70.3	64.7	57.7	41.1
	New	58.6	61.4	62.7	61.9	58.5	55.1	41.3
20.00 – 39.99g/day	Old	13.4	9.4	7.5	9.9	5.2	2.9	1.6
	New	17.3	17.2	15.7	15.2	11.9	5.9	3.3
40.00+g/day	Old	4.6	2.5	1.9	1.9	1.0	0.7	0.2
	New	9.0	5.5	5.0	6.3	2.8	1.6	0.4

Appendix Four

Table A4.1 Number of deaths attributable to alcohol consumption by condition and gender, 2003		
Condition	**Men**	**Women**
Alcohol induced pseudo Cushing's Syndrome	0	0
Wernicke's encephalopathy	0	0
Mental and behavioural disorders due to use of alcohol	262	95
Degeneration of nervous system due to alcohol	2	0
Alcoholic polyneuropathy	1	0
Alcoholic myopathy	0	0
Alcoholic cardiomyopathy	8	2
Alcoholic gastritis	1	1
Alcoholic liver disease	679	301
Alcohol induced chronic pancreatitis	6	1
Fetus and newborn affected by maternal use of alcohol	n/a	0
Fetal alcohol syndrome	0	0
Excessive blood level of alcohol	0	0
Toxic effect of alcohol	0	0
Accidental poisoning by and exposure to alcohol	0	0
Intentional self poisoning by, and exposure to alcohol	1	0
Poisoning by and exposure to alcohol, undetermined intent	0	0
Evidence of alcohol involvement determined by blood alcohol level	0	0
Evidence of alcohol involvement determined by level intoxication	0	0
Road traffic accidents - non pedestrian	77	14
Pedestrian traffic accidents	10	3
Water transport accidents	2	0
Fall injuries	37	19
Occupational work/machine injuries	0	0
Firearm injuries	0	0
Drowning	1	0
Inhalation and ingestion of food causing obstruction of respiratory tract	7	5
Fire injuries	16	9
Accidental excessive cold	5	3
Accidental poisoning by and exposure to noxious substances	6	1
Intentional self-harm\Event of undetermined intent	106	27
Assault	27	4
Malignant neoplasm of lip	0	0
Malignant neoplasm of oral cavity and pharynx	77	27
Malignant neoplasm of oesophagus	142	49
Malignant neoplasm of the colorectum	63	38
Malignant neoplasm of liver and intrahepatic bile ducts	25	12
Malignant neoplasm of larynx	23	6
Malignant neoplasm of breast	n/a	164
Epilepsy and Status epilepticus	44	24
Psoriasis	1	0
Spontaneous abortion	n/a	0
Hypertensive diseases	44	32
Cardiac arrhythmias	33	48
Haemorrhagic stroke	81	69
Ischaemic stroke	26	n/a
Oesophageal varices	2	1
Mallory Weiss syndrome	1	1
Unspecified liver disease	59	33
Portal hypertension	2	0
Acute and other chronic pancreatitis	12	9

Table A4.2 Number of alcohol attributable patient-specific discharges by condition and gender, 2003		
Condition	**Men**	**Women**
Alcohol induced pseudo Cushing's Syndrome	0	0
Wernicke's encephalopathy	13	*
Mental and behavioural disorders due to use of alcohol	7,789	2,795
Degeneration of nervous system due to alcohol	20	*
Alcoholic polyneuropathy	17	7
Alcoholic myopathy	7	*
Alcoholic cardiomyopathy	36	*
Alcoholic gastritis	293	409
Alcoholic liver disease	1,431	743
Alcohol induced chronic pancreatitis	203	55
Fetus and newborn affected by maternal use of alcohol	n/a	*
Fetal alcohol syndrome	0	*
Excessive blood level of alcohol	0	0
Toxic effect of alcohol	47	48
Accidental poisoning by and exposure to alcohol	*	*
Intentional self poisoning by, and exposure to alcohol	8	17
Poisoning by and exposure to alcohol, undetermined intent	0	0
Evidence of alcohol involvement determined by blood alcohol level	37	11
Evidence of alcohol involvement determined by level of intoxication	42	18
Road traffic accidents - non pedestrian	1,031	196
Pedestrian traffic accidents	103	36
Water transport accidents	20	*
Fall injuries	1,656	1,066
Occupational work/machine injuries	772	153
Firearm injuries	25	*
Drowning	*	*
Inhalation and ingestion of food causing obstruction of respiratory tract	27	16
Fire injuries	62	30
Accidental excessive cold	11	10
Accidental poisoning by and exposure to noxious substances	206	173
Intentional self-harm\Event of undetermined intent	820	794
Assault	1,392	211
Malignant neoplasm of lip	8	6
Malignant neoplasm of oral cavity and pharynx	248	111
Malignant neoplasm of oesophagus	257	92
Malignant neoplasm of the colorectum	215	118
Malignant neoplasm of liver and intrahepatic bile ducts	32	16
Malignant neoplasm of larynx	94.	21
Malignant neoplasm of breast	n/a	984
Epilepsy and Status epilepticus	1,283	1,114
Psoriasis	202	188
Spontaneous abortion	n/a	346
Hypertensive diseases	3,522	3,372
Cardiac arrhythmias	2,461	1,843
Haemorrhagic stroke	176	136
Ischaemic stroke	137	n/a
Oesophageal varices	348	199
Mallory Weiss syndrome	125	73
Unspecified liver disease	213	177
Portal hypertension	63	42
Acute and other chronic pancreatitis	231	147

* indicates values that have been suppressed due to the potential risk of disclosure.

Glossary

Acute disease: a disease with either or both: a rapid onset and a short course (as opposed to a chronic course).
Chronic disease: a disease that is long-lasting or recurrent. The term chronic describes the course of the disease, or its rate of onset and development.
Hospital discharge: a period of hospital care/treatment. An individual patient may have more than one hospital discharge in any given year
Patient-specific discharge rate: the number of individuals discharged from hospital in a given year
Partly attributable alcohol condition: where alcohol is causally implicated in a proportion but not all cases of the condition.
Population attributable fraction: is an indirect quantification of morbidity and mortality due to a specified risk factor. It is also known as a population aetilogical fraction. For a particular disease or injury, it can be interpreted as the proportion of the total cases that would not have occurred in the absence of exposure to the risk factor (English et al 1995)
Relative Risk: the risk of an event (or of developing a disease) relative to exposure. Relative risk is a ratio of the probability of the event occurring in the exposed group versus a non-exposed group.
Wholly attributable alcohol condition: a condition where alcohol is implicated in all cases of the condition; for example, alcohol-induced behavioural disorders and alcoholic liver cirrhosis.

Abbreviations

CHD	Coronary Heart Disease
DoH	Department of Health
GROS	General Register Office for Scotland
ICD	International Classification of Diseases
ISD	Information Services Division
ONS	Office for National Statistics
PAF	Population Attributable Fraction
RR	Relative Risk
SHeS	Scottish Health Survey
WCRF	World Cancer Research Fund
WHO	World Health Organisation

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