

Protecting and improving the nation's health

Alcohol-attributable fractions for England: An update

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Executive summary

Background

Alcohol is a major risk factor for a range of chronic diseases. However, the estimated risks for developing diseases associated with drinking alcohol, compared to the risks for those who do not drink, have not been updated for a number of years. Therefore, this study aimed to identify the most recent and robust evidence on the relative risks (RRs) of disease that is associated with alcohol consumption. In addition, the proportion of disease cases that can be attributable to alcohol - alcohol attributable fractions (AAFs) - have been calculated, which updates the AAF estimates that were last published in 2013 (Jones & Bellis, 2013).

Methods

A literature review was carried out in PubMed from 2013 onwards to update the alcohol RRs previously used by (Jones & Bellis, 2013). In addition, the previous relative risks used by (Jones & Bellis, 2013) were used to update the AAFs, in cases where there were no updates to the RRs. The same method employed previously was used to replicate the study as far as was possible and the same diseases were included (with the addition of heart failure). Twenty-nine updates were found in the literature for alcohol RRs, though for some diseases there were multiple updates eg 8 updates for breast cancer. Excluding diseases wholly attributable to alcohol, the largest relative risks were for oral cancers (eg RR=5.13 (4.28-6.83) for heavy drinking males and females combined) and oesophageal squamous cell carcinoma (SCC) (eg RR=4.69 (3.49-6.31) for heavy drinking males and females combined).

Results in line with previous findings:

- alcohol continues to contribute to the increased risk of a large number of chronic and acute diseases
- alcohol consumption has the greatest impact on developing morbidities such as cancer and digestive diseases, compared to other morbidities
- evidence suggests the risk of type 2 diabetes and hypertensive disease for females is lower for low risk drinkers than abstainers

 there were age and gender differences in AAFs for all diseases. Differences in alcohol consumption level, number of current drinkers and variation in relative risks explain these differences

What this publication adds:

- an update to AAFs based on updated alcohol consumption rates and the latest evidence linking alcohol consumption to disease outcomes
- in comparison to the previously published AAFs (Jones & Bellis, 2013), 64%
 of estimated AAFs for chronic conditions are smaller in magnitude, while 3%
 have remained constant and 33% are larger. The changes are mainly due to
 changes in reported patterns of alcohol consumption in the English population
- 98% of estimated AAFs for acute conditions are smaller compared to Jones & Bellis, 2013, while 2% are larger. This change is due to changes in reported patterns of alcohol consumption and binge drinking
- a change in the upshift assumption that adjusts the distribution of alcohol consumption for under-reporting from 59% to 40% also has an effect on the results, but this is small in comparison to the effect of the change in patterns of alcohol consumption

Recommendations for future work:

- future work could calculate the AAFs by drink type
- future work could also explore differences in alcohol risk by different socioeconomic groups, local areas, and incorporate confidence intervals around each AAF estimate

Introduction

Alcohol consumption is a significant risk factor for major chronic diseases (eg coronary heart disease and stroke). In 2018 there were around 5,680 alcohol-specific deaths and during 2018/19 approximately 357,660 hospital admissions in England related to alcohol (narrow measure); the latter represents 2.1% of total hospital admissions, 62% of which were male and over half (57%) were aged between 45 and 74 years old (Public Health England, LAPE, 2020).

The relative risks¹ for developing diseases and causes of mortality amongst those who drink alcohol have not been updated for a number of years. As such, important new evidence has not been taken into account, resulting in figures that may misrepresent the potential burden of alcohol on mortality and hospital admissions (and other statistics related to these).

This study sets out to review the current literature and update the relative risks associated with alcohol and the resulting attributable fractions. Evidence has been selected from reviews or meta-analyses as these were assumed to be the most robust data sources.

Following a consultation on methods for measuring alcohol-related admissions, Public Health England (PHE) has updated the England alcohol-related conditions and relative risks ratios from the previous publication in 2013, taking account of the volume of new evidence that has emerged during this time. In addition to extracting the most recent RRs for alcohol, the alcohol attributable fractions (AAFs) were also calculated using these updated RRs to exactly replicate the diseases included in the last update of these AAFs in 2013 (Jones & Bellis, 2013).

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¹ Relative risks refer to the probability of an outcome in an exposed group (eg drinkers) to the probability of an outcome in an unexposed group (eg non-drinkers)

Methods

Literature review of alcohol RRs

Using the list of diseases included in the 2013 report (see Table 1 for disease list) a rapid literature review was carried out using PubMed to identify new systematic reviews and meta-analyses for relative risks linking alcohol consumption with disease. Publication dates for retrieval were restricted to 1st January 2013 to 31st December 2018. Searches were run by individual disease type, filtered by 'meta-analysis and review'. An example of a search string is as follows:

(disease/s) **AND** ("alcohol"[MeSH Terms] OR beer [Title/Abstract]) OR wine[Title/Abstract]) **AND** ((("relative risk"[Title/Abstract] OR "risk"[MeSH Terms]) OR "odds ratio"[Title/Abstract]) OR "hazards ratio"[Title/Abstract])

Synonyms for diseases were included where appropriate to ensure the review was as comprehensive as possible. A full search strategy can be found in Appendix 1.

The following limits were applied to the search: English language, humans only, 01/01/2013-2018. To supplement the PubMed search, reference lists within articles were also searched. Each disease is summarised in Table 1 with their corresponding medical classification code (ICD-10), also known as 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD) which has been developed by the World Health Organisation (WHO).

Table 1: Chronic and acute conditions related to alcohol that were included in the review (replicated from (Jones & Bellis, 2013): Table 2)

Condition	ICD10 code(s)
Infectious and parasitic diseases	
Tuberculosis	A15-A19
Malignant neoplasm of:	
Lip, oral cavity and pharynx	C00-C14
Oesophagus	C15
Colon	C18
Rectum	C20
Liver and intrahepatic bile ducts	C22
Larynx	C32
Breast	C50

Condition	ICD10 code(s)
Diabetes mellitus	
Diabetes mellitus (type II)	E11
Diseases of the nervous system	
Epilepsy and Status epilepticus	G40-G41
Cardiovascular diseases	
Hypertensive diseases	I10-I15
Ischaemic heart disease	120-125
Cardiac arrhythmias	147-148
Heart failure	150-151
Lla amarrhagia atraka	160-162
Haemorrhagic stroke	l69 (x.0-x.2 only) ²
Ischaemic stroke	163-166
ischaemic stroke	l69 (x.3-x.4 only)
Oesophageal varices	185
Respiratory infections	
	J10-J11 (x.0 only)
Pneumonia	J12-J15
	J18
Digestive diseases	
Gastro-oesophageal laceration haemorrhage syndrome	K22.6
Unspecified liver disease	K73-K74
Cholelithiasis (gall stones)	K80
Acute and chronic pancreatitis	K85
Acute and emonic panerealitis	K86.1
Skin diseases	
Psoriasis	L40 (excl. x.5)
Pregnancy and childbirth	
Spontaneous abortion	O03
Low birth weight	P05-P07
Unintentional injuries	
	V02-V04 (x.1 and x.9 only)
Road/pedestrian traffic accidents	V09 (x.2 and x.3 only)
	V12-V14 (x.3-x.9 only)

 $^{^{2}}$ x.0-x.2 refer to the ICD-10 subdivisions – thus here we are referring to the ICD-10 codes I69.0, I69.1 and I69.2

Condition	ICD10 code(s)
	V19 (x.4-x.6 only)
	V20-V28 (x.3-x.9 only)
	V29-V79 (x.4-x.9 only)
	V80 (x.3-x.5 only)
	V81-V82 (x.1 only)
	V83-V86 (x.0-x.3 only)
	V87 (excl. x.9)
	V89.2
Poisoning	X40-X49 (excl. X45)
Fall injuries	W00-W19
Fire injuries	X00-X09
Drowning	W65-W74
	V01
	V09 (x.0, x.1 and x.9 only)
	V10-V11
	V12-V14 (x.0-x.2 only)
	V15-V18
	V19 (x.1-x.3 only)
	V20-V28 (x.1 and x.2 only)
	V29 (x.0-x.3 only)
	V30-V38 (x.1 and x.2 only)
	V39 (x.0-x.3 only)
	V40-V48 (x.1 and x.2 only)
Other unintentional injuries	V49 (x.0-x.3 only)
	V50-V48 (x.1 and x.2 only)
	V59 (x.0-x.3 only)
	V60-V48 (x.1 and x.2 only)
	V69 (x.0-x.3 only)
	V70-V48 (x.1 and x.2 only)
	V79 (x.0-x.3 only)
	V80 (excl. x.2-x.5)
	V81-V82 (excl. x.1)
	V83-V86 (x.4-x.9 only)
	V87.9
	V88

Condition	ICD10 code(s)
	V89 (excl. x.2)
	V90-V99
	W20-W52
	W75-W99
	X10-X33
	X50-X59
	Y40-Y89 (excl. Y87)
Intentional injuries	
Intentional self-harm	X60-X84 (excl. X65)
mentional self-manni	X87.0
Event of undetermined intent	Y10-Y34 (excl. Y15)
Event of undetermined intent	Y87.2
Assault	X85-Y09
Assault	Y87.1

For reference, the conditions wholly attributable to alcohol are described in Table 2, however these were not included in the review since it was not necessary to calculate AAFs for these conditions (as they are all 1).

Table 2: Wholly attributable conditions

Condition	ICD10 code(s)
Alcohol-induced pseudo-Cushing's syndrome	E24.4
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	142.6
Alcoholic gastritis	K29.2
Alcoholic liver disease	K70
Alcohol-induced chronic pancreatitis	K86.0
Ethanol poisoning	T51.0
Methanol poisoning	T51.1
Toxic effect of alcohol, unspecified	T51.9
Accidental poisoning by and exposure to alcohol	X45
Intentional self-poisoning by and exposure to alcohol	X65

Condition	ICD10 code(s)
Poisoning by and exposure to alcohol, undetermined intent	Y15
Alcohol-induced acute pancreatitis	K85.2
Fetal alcohol syndrome (dysmorphic)	Q86.0
Excess alcohol blood levels	R78.0
Evidence of alcohol involvement determined by blood alcohol level	Y90
Evidence of alcohol involvement determined by level of intoxication	Y91

Alcohol consumption in England

Individual level alcohol consumption data were extracted from Health Survey for England, 2016 (HSE2016). The data were aggregated to estimate the distribution of drinkers for the following age groups by gender, 16-24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years, 65-74 years, 75-84 years and 85+ years. At the same time, the aggregated data were used to calculate the mean and variance alcohol consumption (in grams per day) for current drinkers of each age and gender specific group.

Relative risks for alcohol consumption

New sources of relative risks for alcohol consumption (RRs) identified in the literature review were combined with the alcohol consumption data and used to update the AAFs. RRs identified in an earlier report were used in cases where new data sources did not exist (Jones & Bellis, 2013). Diseases that used RRs from the earlier report were epilepsy and status epilepticus, ischaemic stroke, ischaemic heart disease, oesophageal varices, gastro-oesophageal laceration-haemorrhage, pneumonia, unspecified liver disease, spontaneous abortion, low birth weight, motor vehicle accidents and non-motor vehicle accidents. Diseases were excluded from the analysis in cases where no updates were available or the RRs were not provided in an earlier report (Jones & Bellis, 2013). Diseases were also excluded if new evidence revealed no association between alcohol consumption and the disease. Table 4 shows the final RRs used in this analysis.

Alcohol attributable fractions for chronic conditions

AAFs for a specific age and gender groups were calculated using the following continuous approach:

$$AAF = \frac{P_{abs}RR_{abs} + P_{former}RR_{former} + P_{current}\left(\int_{>0}^{150} p(x)rr(x)dx\right) - 1}{P_{abs}RR_{abs} + P_{former}RR_{former} + P_{current}\left(\int_{>0}^{150} p(x)rr(x)dx\right)}$$
(1)

This equation uses the proportion of lifetime abstainers, P_{abs} , former drinkers, P_{former} , current drinkers, $P_{current}$, and the probability distribution of drinkers, p(x), where x refers to the levels of alcohol consumption in grams per day and dx refers to an infinitely small range in alcohol consumption (Jones & Bellis, 2013). P_{abs} and P_{former} were estimated directly by extracting the proportion of abstainers and former drinkers from the 2016 HSE dataset. Exposure is capped at 150g of alcohol per day to provide a conservative estimate in line with the international literature and the previous report (Jones & Bellis, 2013; J. Rehm, Kehoe, et al., 2010). The probability distribution of current drinkers, p(x), was sampled at 0.5 gram/day discrete intervals, dx. between 0 and 150g/day, ie, the proportion of the population consuming between 0 and 0.5 g/day; the proportion of the population consuming between 0.5g/day and 1q/day etc. The term rr(x) is the relative risk of disease associated with consuming x grams of alcohol per day. In general, the relative risk for lifetime abstainers, RR_{abs} , is assumed to be 1. Although this was driven by the evidence available and in some cases the relative risk associated with lifetime abstainers was higher than individuals who consume very low levels of alcohol for instance, in the case of heart disease. The equation also uses the relative risks for former drinkers, RR_{former} . If RR_{former} was not available, we set its value equal to 1 and assumed it was associated with the same risk as abstainers. In the literature abstainers tended to be the reference group (therefore $RR_{abs} = 1$). Further technical details are provided in Appendix 2.

Alcohol attributable fractions for acute conditions

To calculate the morbidity AAFs for acute conditions (AAF_{injury}) the combination of the results from equations (2) and (4) were used (Jones & Bellis, 2013; B. J. Taylor, Shield, & Rehm, 2011).

$$AAF_{injury} = \frac{(1 - P_{binge}) + P_{binge} \left(\int_{>0}^{150} p(x) r r_{binge}(x) dx \right) - 1}{(1 - P_{binge}) + P_{binge} \left(\int_{>0}^{150} p(x) r r_{binge}(x) dx \right)}$$
 (2)

where

$$1 = P_{abs} + P_{former} + P_{nonbinge} + P_{binge}$$
 (3)

This first equation uses the proportions of lifetime abstainers, former drinkers, current drinkers who do not engage in binge drinking and current drinkers who do engage in binge drinking (the four terms on the right-hand side of (3) respectively). This also uses the probability of drinking at level x, p(x). The relative risk for the acute condition at a binge drinking level x was adjusted for the time at risk in order to calculate the risk ratio, $rr_{binge}(x)$. These adjustments require the time at risk per drinking occasion for each quantity of alcohol (1 drink³ = 30 minutes; 3 drinks = 2 hours; 5 drinks = 3 hours; 7 drinks = 4.8 hours)(Jones & Bellis, 2013). An upper level (or cap) for alcohol consumption was set to 150g to remain consistent with the previous report.

$$AAF_{injury} = \frac{P_{abs} + P_{former} + P_{nonbinge} + P_{binge}RR_{binge} - 1}{P_{abs} + P_{former} + P_{nonbinge} + P_{binge}RR_{binge}}$$
(4)

This second equation is much simpler than the first one as all binge drinkers are given a fixed RR_{binge} . However, it should be noted that the relative risk in this equation has been adjusted for both time at risk and number of drinking occasions. The statistical analysis was performed using R statistical software. Further technical details are provided in Appendix 2.

Adjustment for mortality

To calculate the mortality AAFs for acute conditions, AAF_{death} , we used the scaling discussed in (Jürgen Rehm et al., 2004). For road/pedestrian accidents, the ratio of AAF for morbidity is set as two thirds of the AAF for mortality. The ratio for other kinds of injury is lower, set conservatively as four ninths (or two thirds of the ratio for road/pedestrian accidents).

This gives the following formula for road/pedestrian accidents:

³ Equivalent to ~10g of alcohol

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$$AAF_{death} = \frac{3}{2}AAF_{injury} \tag{5}$$

And for other kinds of injury:

$$AAF_{death} = \frac{9}{4}AAF_{injury} \tag{6}$$

Based on the reported AAFs published within (Jones & Bellis, 2013), we have assumed that the ratio between mortality and morbidity for acute conditions used this scaling (subject to rounding) – although it is not explicitly referenced, the author mentions the use of a scaling decided through personal communication with Rehm and colleagues, thus we assume this to be the case and have proceeded with this method.

Results

Literature review of alcohol RRs

The results of the literature review are summarised in Figure 1 and described more fully in Table 3 and Table 4. The first table presents the list of chronic conditions, the source used in the previous study, the updated source from the present review, and the updated relative risk values. In total 29 papers contained data that updated the previous RRs used in (Jones & Bellis, 2013). Based on the previous list of diseases included in (Jones & Bellis, 2013), there were updated RRs for a number of cancers, type 2 diabetes, cardiovascular diseases, and liver diseases, but no updates for epilepsy, pneumonia, early infant death, low birth weight and accidents. There was one update for psoriasis; however, this review confirmed that the causality between alcohol and psoriasis is still uncertain, therefore this was not included in the AAF calculation. For some diseases there was more than one update, for example for breast cancer there were 8 updates. When this was the case, the most recent update or the study with the most robust evidence/methodology (meta-analysis), and/or the most granular data was chosen for inclusion. This selection was agreed with the project steering group.

Excluding the conditions which are wholly attributable to alcohol, the largest risks are for oral cancers (eg RR=5.13 (4.28-6.83) for heavy drinking males and females combined) and oesophageal SCC (eg RR=4.69 (3.49-6.31) for heavy drinking males and females combined). No relative risks were disaggregated by age group. However, some relative risks by drink type (eg wine, beer, spirits) were found.

The second table presents the list of acute conditions, the source used in the previous study, the updated source from the present review, and the ratio used between the AAFs for morbidity and mortality (Jürgen Rehm et al., 2004).

Figure 1: Results of the literature search for alcohol relative risks

	References following search: N = 472+1								
Tuberculosis N = 5	Cancers N = 142	Type II Diabetes N = 38	Epilepsy N = 8	Cardiovascular N = 90+1	Pneumonia N = 7	Digestive N = 153	Psoriasis N = 11	Pregnancy & Childbirth N = 5	Accidents & Injuries N = 13
	References included for full-text review following title/abstract review: N = 104+13								
Tuberculosis N = 2+1	Cancers N = 35+6	Type II Diabetes N = 6+2	Epilepsy N = 2	Cardiovascular N = 26+4	Pneumonia N = 3	Digestive N = 19	Psoriasis N = 7	Pregnancy & Childbirth N = 2	Accidents & Injuries N = 2
	Total references included for extraction follow full-text review: 19+10								
Tuberculosis N = 1	Cancers N = 7+5	Type II Diabetes N = 1	Epilepsy N = 0	Cardiovascular N = 7+4	Pneumonia N = 0	Digestive N = 3	Psoriasis N = 1	Pregnancy & Childbirth N = 0	Accidents & Injuries N = 0

Table 3: Sources of alcohol RRs for chronic conditions

Condition	Previous Sources	New Sources	Value(s) in New Sources ⁴				
Infectious and parasitic diseases							
			RR 1.35 (1.09–1.68) for 'alcohol use'				
			RR 1.57 (1.10-2.23) at 25 g/day				
			RR 2.46 (1.21-4.98) at 50 g/day				
			RR 3.85 (1.33-11.11) at 75 g/day				
	(Lonnroth, Williams,		RR 6.03 (1.47-24.81) at 100 g/day				
Tuberculosis	Stadlin, Jaramillo, & Dye,	(Imtiaz et al., 2017)					
	2008)		<u>Male</u>				
			RR 1.50 (0.70–3.20) for former drinkers				
			<u>Female</u>				
			RR 5.30 (1.40–19.80) for former drinkers				
Malignant neoplasm of:							
			RR 1.13 (1.00–1.26) for light drinking ⁵				
Lip, oral cavity and pharynx	(Tramacere et al., 2010)	(Bagnardi et al., 2015)	RR 1.83 (1.62–2.07) for moderate drinking ⁶				
			RR 5.13 (4.31–6.10) for heavy drinking ⁷				

⁴ Values are given as combined male and female where available. RRs compared to baseline (no alcohol consumption, unless otherwise stated). Includes values for relative risk (RR), hazard ratio (HR) and odds ratio (OR). Parentheses indicate 95% confidence intervals. Values for former drinkers given where appropriate – if not explicitly stated, these are assumed to be equal to those for non-drinkers.

⁵ Defined as ≤12.5 g/day

⁶ Defined as between 12.5 and 50 g/day

⁷ Defined as >50 g/day

Condition	Previous Sources	New Sources	Value(s) in New Sources ⁴
			RR 1.26 (1.06–1.50) for light drinking ⁵
Oesophagus	(Islami et al., 2011)	(Bagnardi et al., 2015) ⁸	RR 2.23 (1.87–2.65) for moderate drinking ⁶
			RR 4.95 (3.86–6.34) for heavy drinking ⁷
Colon	(Fedirko et al., 2011)		RR 0.99 (0.95–1.04) for light drinking ⁵
Dootum	(Fodirko et al. 2011)	(Bagnardi et al., 2015) ⁹	RR 1.17 (1.11–1.24) for moderate drinking ⁶
Rectum	(Fedirko et al., 2011)		RR 1.44 (1.25–1.65) for heavy drinking ⁷
Liver and introhanatio hile	(Corrao, Bagnardi,		RR 1.00 (0.85–1.18) for light drinking ⁵
Liver and intrahepatic bile	Zambon, & La Vecchia,	(Bagnardi et al., 2015)	RR 1.08 (0.97–1.20) for moderate drinking ⁶
ducts	2004)		RR 2.07 (1.66–2.58) for heavy drinking ⁷
			RR 0.87 (0.68–1.11) for light drinking ⁵
Larynx	(Islami et al., 2011)	(Bagnardi et al., 2015)	RR 1.44 (1.25–1.66) for moderate drinking ⁶
			RR 2.65 (2.19–3.19) for heavy drinking ⁷
			RR 1.04 (1.01–1.07) for light drinking ⁵
Breast	(Hamajima et al., 2002)	(Bagnardi et al., 2015)	RR 1.23 (1.19–1.28) for moderate drinking ⁶
			RR 1.61 (1.33–1.94) for heavy drinking ⁷
Diabetes mellitus			
	(Baliunas et al., 2009)	(Knott, Bell, & Britton, 2015)	RR <1 for consumption level of <63 g/day
Diabetes mellitus (type II)			RR 1 for consumption level of 63 g/day
			RR >1 for consumption level of >63 g/day
Diseases of the nervous sys	tem		

Oesophagus squamous cell carcinoma only.
 Results are given for malignant neoplasm of colorectum.

Condition	Previous Sources	New Sources	Value(s) in New Sources⁴
Epilepsy and Status	(Samokhyalov, Irving		RR 1.37 (1.28-1.47) at 25 g/day
epilepticus	(Samokhvalov, Irving,	No update	RR 1.86 (1.62-2.13) at 50 g/day
ерперисиз	Mohapatra, & Rehm, 2010)		RR 3.44 (2.61-4.52) at 100 g/day
Cardiovascular diseases			
			<u>Male</u>
			RR 0.82 (0.65-1.02) at <2.5 g/day
			RR 0.77 (0.65-0.92) at 2.5 to 12 g/day
	(B. Taylor et al., 2009)		RR 0.75 (0.64-0.88) at 12 to 24 g/day
			RR 0.74 (0.53-1.02) at 24 to 36 g/day
		(Briasoulis, Agarwal, & Messerli,	RR 0.99 (0.90–1.08) for former drinkers ¹¹
Hypertensive diseases			
		2012) ¹⁰	<u>Female</u>
			RR 0.91 (0.78–1.07) at <2.5 g/day
			RR 0.54 (0.45-0.65) at 2.5 to 12 g/day
			RR 0.61 (0.38-0.99) at 12 to 24 g/day
			RR 0.40 (0.14-1.13) at 24 to 36 g/day
			RR 1.11 (0.94–1.32) for former drinkers ¹²
	(Pagragka & Bahm 2010		Male
Ischaemic heart disease	(Roerecke & Rehm, 2010, 2012; Ronksley, Brien,		RR 0.82 (0.65-1.02) at <2.5 g/day
			RR 0.77 (0.65-0.92) at 2.5 to 12 g/day

<sup>Results are given for hypertension.
(Jones & Bellis, 2013)
(Jones & Bellis, 2013)</sup>

Condition	Previous Sources	New Sources	Value(s) in New Sources ⁴	
	Turner, Mukamal, & Ghali,	(Angus, Henney, Webster, &	RR 0.75 (0.64-0.88) at 12 to 24 g/day	
	2011)	Gillespie, 2019; Roerecke &	RR 0.74 (0.53-1.02) at 24 to 36 g/day	
		Rehm, 2012)		
			<u>Female</u>	
			RR 0.91 (0.78-1.07) at <2.5 g/day	
			RR 0.54 (0.45-0.65) at 2.5 to 12 g/day	
			RR 0.61 (0.38-0.99) at 12 to 24 g/day	
			RR 0.40 (0.14-1.13) at 24 to 36 g/day	
	(Kodama et al., 2011;		HR 1.17 (0.86–1.60) per 100 g/week higher	
Cardiac arrhythmias	Samokhvalov, Irving,	(Wood et al., 2018)	, , , , , ,	
	Mohapatra, et al., 2010)		consumption	
	Not included; risk estimates		HR 1.09 (1.03–1.15) per 100 g/week higher	
Heart failure	not available from meta-	(Wood et al., 2018)	consumption	
	analyses		Consumption	
Haemorrhagic stroke	(Patra et al., 2010)	(Wood et al., 2018)	HR 1.17 (1.12–1.23) per 100 g/week higher	
Tiaemornagic stroke	(Falla et al., 2010)	(WOOd et al., 2010)	consumption	
Ischaemic stroke	(Patra et al., 2010)	(Wood et al., 2018; Zheng et al.,	HR 1.13 (1.09–1.18) per 100 g/week higher	
ischaeniic shoke	(1 atia et al., 2010)	2015) ¹³	consumption	
	Applied new estimate for			
Oesophageal varices	unspecified liver disease (J.	No update	See unspecified liver disease	
	Rehm, Taylor, et al., 2010)			

¹³ In (Zheng et al., 2015), results are given by gender.

Condition	Previous Sources	New Sources	Value(s) in New Sources ⁴
Respiratory infections			
	(Samokhvalov, Irving, &		RR 1.12 (1.02–1.23) for 24 g/day
Pneumonia	Rehm, 2010)	No update	RR 1.33 (1.06–1.67) for 60 g/day
	(Netitii, 2010)		RR 1.76 (1.13–2.77) for 120 g/day
Digestive diseases			
Gastro-oesophageal	Not included; risk estimates		
laceration haemorrhage	not available from meta-	No update	N/A
syndrome	analyses		
			Male
			RR 1.0 (0.6–1.6) for 0 to 12 g/day
			RR 1.6 (1.4–2.0) for 12 to 24 g/day
			RR 2.8 (2.3–3.4) for 24 to 36 g/day
			RR 5.6 (4.5–7.0) for 36 to 48 g/day
			RR 7.0 (5.8–8.5) for 48 to 60 g/day
Unspecified liver disease	(J. Rehm, Taylor, et al., 2010)	No update	RR 14.0 (11.7–16.7) for >60 g/day
			<u>Female</u>
			RR 1.9 (1.1–3.1) for 0 to 12 g/day
			RR 5.6 (4.5-6.9) for 12 to 24 g/day
			RR 7.7 (6.3–9.5) for 24 to 36 g/day
			RR 10.1 (7.5–13.5) for 36 to 48 g/day
			RR 14.7 (11.0–19.6) for 48 to 60 g/day

Condition	Previous Sources	New Sources	Value(s) in New Sources⁴
			RR 22.7 (17.2–30.1) for >60 g/day
Cholelithiasis (gall stones)	Not available; used (Gutjahr, Gmel, & Rehm, 2001)	(Shabanzadeh, Sorensen, & Jorgensen, 2016)	OR 0.99 (0.98; 1.00)
Acute and chronic	(Irving, Samokhvalov, &	(Shabanzadeh et al., 2016)	RR 0.91 (0.70, 1.18) for 0.1 to 40 g/day
pancreatitis	Rehm, 2009)	(Shabanzadon of all, 2010)	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Skin diseases			
Psoriasis	Not included; insufficient evidence for causal relationship	No update	N/A
Pregnancy and childbirth			
Spontaneous abortion	Not available; used (Gutjahr et al., 2001)	No update	RR 1.20 for <16 g/day RR 1.76 for >16 g/day
Low birth weight	(Patra et al., 2011)	No update	RR 1.03 (0.96-1.11) at 12 g/day RR 1.23 (1.10–1.36) at 24 g/day RR 1.50 (1.30–1.73) at 36 g/day RR 1.86 (1.54–2.24) at 48 g/day RR 2.32 (1.83–2.93) at 60 g/day RR 2.91 (2.18-3.88) at 72 g/day RR 3.67 (2.60-5.17) at 84 g/day

Table 4: Sources of data for acute morbidity outcomes

Condition	Previous Sources	New Sources	Ratio Between AAFs ¹⁴
Unintentional injuries			
Road/pedestrian traffic accidents	(B. Taylor et al., 2010)	No update	0.66
Poisoning	(B. Taylor et al., 2010)	No update	0.44
Fall injuries	(B. Taylor et al., 2010)	No update	0.44
Fire injuries	(B. Taylor et al., 2010)	No update	0.44
Drowning	(B. Taylor et al., 2010)	No update	0.44
Other unintentional injuries	(English & Holman, 1995; Single, Robson, Xie, & Rehm, 1996)	No update	0.44
Intentional injuries			
Intentional self-harm	(B. Taylor et al., 2010)	No update	0.44
Event of undetermined intent	(B. Taylor et al., 2010)	No update	0.44
Assault	(B. Taylor et al., 2010)	No update	0.44

¹⁴ From (Jürgen Rehm et al., 2004)

The age- and gender-specific distribution of alcohol consumption

Individual level alcohol consumption data was extracted from HSE2016 and aggregated to estimate mean alcohol consumption and variance for each age and gender specific group. It has been debated that national surveys underestimate population levels of alcohol consumption (Catto & Gibbs, 2008; Corrao, Bagnardi, Zambon, & Arico, 1999; Jones & Bellis, 2013; Meier et al., 2013; Parkin, 2011; J. Rehm, Kehoe, et al., 2010). The mean and variance were upshifted by 40% to reflect the actual alcohol consumption level, due to the evidence suggesting that reported consumption was an under-estimate of true consumption (Boniface, Kneale, & Shelton, 2013; Boniface & Shelton, 2013; Meier et al., 2013). Detailed upshifting methods are provided in Appendix 2. In Table 5, the upshifted mean alcohol consumption levels from HSE2016 for each age and gender group are presented. The results are compared against alcohol consumption from the General Lifestyle Survey 2010 (GLS 2010) which was used in the previous report, however we have upshifted this by 40% in line with the present analysis.

Table 5: Upshifted mean alcohol consumption levels (g/day) and standard deviations by age and gender specific groups in GLS2010 and HSE2016 and difference between them

	16-24	25-34	35-44	45-54	55-64	65-74	75-84	85+		
Upshifted	d mean (sto	d. dev.) ald	cohol cons	umption in	g/day fron	n HSE2016	6			
Male	18.8	22.7	27.1	28.0	31.8	27.8	22.2	15.8		
iviale	(22.0)	(26.6)	(31.8)	(32.9)	(37.3)	(32.6)	(26.1)	(18.5)		
Fomolo	11.2	12.3	14.8	19.1	17.1	13.5	11.1	7.5		
Female	(14.2)	(15.4)	(18.4)	(23.5)	(21.1)	(16.8)	(14.0)	(9.8)		
Upshifted	d mean (sto	d. dev.) ald	cohol cons	umption in	g/day fron	n GLS2010)			
Male	28.0	29.5	30.6	31.9	31.9	26.1	18	3.1		
iviale	(32.9)	(34.7)	(35.9)	(37.5)	(37.4)	(30.6)	(21	.2)		
Famala	16.8	14.1	17.3	17.8	16.2	12.3	9	.0		
Female	(20.7)	(17.5)	(21.3)	(21.9)	(20.0)	(15.5)	(11	.6)		
Difference in mean alcohol consumption in g/day										
Male	-9.2	-6.8	-3.5	-3.9	-0.1	+1.7	+4.1	-2.3		
Female	-5.6	-1.8	-2.5	+1.3	+0.9	+1.2	+2.1	-1.5		

In HSE2016, the highest levels of alcohol consumption for males were observed in the 55 to 64 year old age group and for females the highest level was observed in the 45 to 54 year old age group. This is consistent with results in GLS2010 however, the highest levels of alcohol consumption covered a wider age group in the 45 to 64 year old male age group in GLS2010. The mean alcohol consumption level is lower in HSE2016 compared with GLS2010 (in 16 to 64 year old males). In contrast, increases in alcohol consumption are observed in males older than 65 years across the two time periods. A similar pattern is observed in females such that alcohol consumption is higher in GLS2010 compared with HSE2016 (in 16 to 44 year olds), while mean alcohol consumption is lower in GLS 2010 compared with HSE 2016 in females older than 45 years old. The largest decrease in alcohol is observed in the 16 to 24 year old age group. Further details about the data extraction and methods employed to determine these mean values are provided in Appendix 2.

Updated AAFs for chronic and acute conditions

The AAFs for chronic and acute conditions are listed in Table 6. Compared to (Jones & Bellis, 2013) psoriasis was excluded because the rapid review confirmed that the causality between alcohol and this condition is still unclear. In the earlier report of (Jones & Bellis, 2013) separate mortality and morbidity AAFs were calculated for haemorrhagic stroke, ischaemic stroke, unspecified liver disease and all acute conditions and our aim was to update this analysis in the same format. A detailed comparison between these results and the results estimated by (Jones & Bellis, 2013) is provided in Appendix 3.

The updated AAFs by age for selected conditions for males and females are presented in Figure 2 and Figure 3 respectively.

Table 6: AAFs for chronic and acute conditions

							Αg	je/Gend	der Gro	up						
Condition	16	-24	25	-34	35	-44	45	-54	55	-64	65	-74	75	-84	8	5 +
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Wholly attributable cond	litions															
Alcohol-induced																
pseudo-Cushing's	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
syndrome																
Mental and																
behavioural disorders	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
due to use of alcohol																
Degeneration of																
nervous system due to	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
alcohol																
Alcoholic	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
polyneuropathy	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Alcoholic myopathy	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Alcoholic	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
cardiomyopathy	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Alcoholic gastritis	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Alcoholic liver disease	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Alcohol-induced	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
chronic pancreatitis	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

	Age/Gender Group															
Condition	16-	-24	25	-34	35	-44	45	-54	55	-64	65	-74	75	-84	85	5+
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Ethanol poisoning	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Methanol poisoning	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Toxic effect of alcohol, unspecified	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Accidental poisoning																
by and exposure to	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
alcohol																
Intentional self-																
poisoning by and	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
exposure to alcohol																
Poisoning by and																
exposure to alcohol,	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
undetermined intent																
Alcohol-induced acute	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
pancreatitis	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Fetal alcohol																
syndrome	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
(dysmorphic)																
Excess alcohol blood	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
levels	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

							Ag	e/Gend	der Gro	up						
Condition	16-	-24	25	-34	35	-44	45	-54	55	-64	65	-74	75	-84	8	5+
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Evidence of alcohol																
involvement	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
determined by blood	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
alcohol level																
Evidence of alcohol																
involvement	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
determined by level of	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
intoxication																
Infectious and parasitic	disease	es														
Tuberculosis	-0.01	0.29	0.11	0.25	0.23	0.27	0.26	0.33	0.33	0.34	0.26	0.37	0.13	0.39	-0.11	0.39
Malignant neoplasm of:																
Lip, oral cavity and	0.34	0.21	0.44	0.24	0.50	0.30	0.51	0.39	0.55	0.36	0.51	0.26	0.43	0.20	0.31	0.11
pharynx	0.01	0.21	0.11	0.21	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.20	0.10	0.20	0.01	0.11
Oesophagus	0.39	0.27	0.48	0.30	0.52	0.35	0.54	0.44	0.57	0.40	0.54	0.32	0.46	0.26	0.37	0.16
Colon	0.09	0.05	0.12	0.06	0.14	0.07	0.14	0.10	0.16	0.09	0.14	0.06	0.11	0.05	0.08	0.03
Rectum	0.09	0.05	0.12	0.06	0.14	0.07	0.14	0.10	0.16	0.09	0.14	0.06	0.11	0.05	0.08	0.03
Liver and intrahepatic	0.16	0.05	0.25	0.06	0.34	0.11	0.37	0.20	0.42	0.16	0.37	0.08	0.24	0.05	0.11	0.01
bile ducts	0.10	0.03	0.23	0.00	0.54	0.11	0.57	0.20	0.42	0.10	0.57	0.00	0.24	0.03	0.11	0.01
Larynx	0.19	0.12	0.26	0.14	0.30	0.17	0.31	0.23	0.34	0.20	0.31	0.15	0.25	0.11	0.18	0.06
Breast	N/A	0.08	N/A	0.10	N/A	0.12	N/A	0.17	N/A	0.15	N/A	0.11	N/A	0.08	N/A	0.04

	Age/Gender Group															
Condition	16-	-24	25	-34	35	-44	45	-54	55	-64	65	-74	75	-84	8	5+
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Diabetes mellitus																
Diabetes mellitus (type II)	-0.11	-0.12	-0.12	-0.13	-0.10	-0.13	-0.10	-0.13	-0.09	-0.14	-0.10	-0.13	-0.11	-0.12	-0.13	-0.10
Diseases of the nervous	systen	n														
Epilepsy and Status epilepticus	0.18	0.11	0.25	0.13	0.28	0.15	0.29	0.21	0.32	0.19	0.29	0.14	0.23	0.10	0.16	0.06
Cardiovascular diseases	S															
Hypertensive diseases	0.10	-0.01	0.14	0.00	0.15	0.02	0.16	0.07	0.17	0.05	0.16	0.01	0.13	-0.01	0.10	-0.02
Ischaemic heart disease	-0.15	-0.23	-0.18	-0.26	-0.18	-0.26	-0.18	-0.22	-0.18	-0.25	-0.18	-0.24	-0.17	-0.22	-0.17	-0.16
Cardiac arrhythmias	0.13	0.08	0.18	0.10	0.20	0.12	0.21	0.15	0.23	0.14	0.21	0.10	0.17	0.08	0.12	0.05
Heart failure	0.08	-0.03	0.11	-0.04	0.13	-0.05	0.13	-0.07	0.15	-0.06	0.13	-0.04	0.11	-0.03	0.08	-0.02
Haemorrhagic stroke - Mortality ¹⁵	0.08	0.03	0.12	0.05	0.14	0.10	0.15	0.20	0.16	0.15	0.15	0.07	0.11	0.03	0.07	0.00
Haemorrhagic stroke - Morbidity ¹⁶	0.13	0.08	0.18	0.10	0.20	0.12	0.21	0.15	0.23	0.14	0.21	0.10	0.17	0.08	0.12	0.05

¹⁵ I60-I62 ¹⁶ I69 (x.0 to x.2 only)

	Age/Gender Group															
Condition	16	-24	25	-34	35	-44	45	-54	55	-64	65	-74	75	-84	8	5+
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Ischaemic stroke - Mortality ¹⁷	0.02	0.01	0.02	0.01	0.03	0.01	0.03	0.02	0.03	0.02	0.03	0.01	0.02	0.01	0.02	0.01
Ischaemic stroke - Morbidity ¹⁸	0.10	0.06	0.14	0.08	0.16	0.09	0.17	0.12	0.18	0.11	0.17	0.08	0.13	0.06	0.10	0.03
Oesophageal varices - Mortality	0.52	0.64	0.63	0.68	0.67	0.73	0.69	0.78	0.72	0.77	0.69	0.70	0.61	0.64	0.47	0.50
Oesophageal varices - Morbidity	-0.17	-0.09	-0.03	-0.05	0.11	0.08	0.13	0.24	0.21	0.18	0.13	0.02	-0.04	-0.10	-0.34	-0.22
Respiratory infections																
Pneumonia	0.05	0.02	0.07	0.02	0.09	0.03	0.09	0.06	0.11	0.05	0.09	0.03	0.07	0.01	0.04	0.00
Digestive diseases																
Unspecified liver disease - Mortality	0.52	0.64	0.63	0.68	0.67	0.73	0.69	0.78	0.72	0.77	0.69	0.70	0.61	0.64	0.47	0.50
Unspecified liver disease - Morbidity	-0.17	-0.09	-0.03	-0.05	0.11	0.08	0.13	0.24	0.21	0.18	0.13	0.02	-0.04	-0.10	-0.34	-0.22
Cholelithiasis (gall stones)	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01

¹⁷ I63-I66 ¹⁸ I69 (x.3 to x.4 only)

							Αg	je/Gend	der Gro	up						
Condition	16	-24	25	-34	35	-44	45	-54	55	-64	65	-74	75	-84	8	5+
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Acute and chronic pancreatitis	0.28	0.16	0.37	0.19	0.43	0.24	0.44	0.32	0.48	0.29	0.44	0.21	0.35	0.15	0.25	0.08
Pregnancy and childbirt	h															
Spontaneous abortion	N/A	0.09	N/A	0.10	N/A	0.10	N/A	0.11	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Low birth weight	N/A	0.01	N/A	0.02	N/A	0.05	N/A	0.09	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Unintentional injuries																
Road/pedestrian traffic accidents - Mortality	0.12	0.02	0.22	0.03	0.31	0.05	0.33	0.10	0.38	0.06	0.24	0.01	0.10	0.00	0.01	0.00
Road/pedestrian traffic accidents - Morbidity	0.08	0.02	0.15	0.02	0.21	0.03	0.22	0.06	0.25	0.04	0.16	0.01	0.07	0.00	0.00	0.00
Poisoning - Mortality	0.07	0.02	0.12	0.02	0.17	0.03	0.18	0.06	0.20	0.04	0.12	0.01	0.05	0.00	0.00	0.00
Poisoning - Morbidity	0.03	0.01	0.05	0.01	0.07	0.01	0.08	0.03	0.09	0.02	0.06	0.00	0.02	0.00	0.00	0.00
Fall injuries - Mortality	0.07	0.02	0.12	0.02	0.17	0.03	0.18	0.06	0.20	0.04	0.12	0.01	0.05	0.00	0.00	0.00
Fall injuries - Morbidity	0.03	0.01	0.05	0.01	0.07	0.01	0.08	0.03	0.09	0.02	0.06	0.00	0.02	0.00	0.00	0.00
Fire injuries - Mortality	0.07	0.02	0.12	0.02	0.17	0.03	0.18	0.06	0.20	0.04	0.12	0.01	0.05	0.00	0.00	0.00
Fire injuries - Morbidity	0.03	0.01	0.05	0.01	0.07	0.01	0.08	0.03	0.09	0.02	0.06	0.00	0.02	0.00	0.00	0.00
Drowning - Mortality	0.07	0.02	0.12	0.02	0.17	0.03	0.18	0.06	0.20	0.04	0.12	0.01	0.05	0.00	0.00	0.00
Drowning - Morbidity	0.03	0.01	0.05	0.01	0.07	0.01	0.08	0.03	0.09	0.02	0.06	0.00	0.02	0.00	0.00	0.00

	Age/Gender Group															
Condition	16	-24	25	-34	35	-44	45	-54	55	-64	65	-74	75	-84	85	5+
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Other unintentional injuries - Mortality	0.07	0.02	0.12	0.02	0.17	0.03	0.18	0.06	0.20	0.04	0.12	0.01	0.05	0.00	0.00	0.00
Other unintentional injuries	0.03	0.01	0.05	0.01	0.07	0.01	0.08	0.03	0.09	0.02	0.06	0.00	0.02	0.00	0.00	0.00
Intentional injuries																
Intentional self-harm - Mortality	0.07	0.02	0.12	0.02	0.17	0.03	0.18	0.06	0.20	0.04	0.12	0.01	0.05	0.00	0.00	0.00
Intentional self-harm	0.03	0.01	0.05	0.01	0.07	0.01	0.08	0.03	0.09	0.02	0.06	0.00	0.02	0.00	0.00	0.00
Event of undetermined intent - Mortality	0.07	0.02	0.12	0.02	0.17	0.03	0.18	0.06	0.20	0.04	0.12	0.01	0.05	0.00	0.00	0.00
Event of undetermined intent	0.03	0.01	0.05	0.01	0.07	0.01	0.08	0.03	0.09	0.02	0.06	0.00	0.02	0.00	0.00	0.00
Assault - Mortality	0.07	0.02	0.12	0.02	0.17	0.03	0.18	0.06	0.20	0.04	0.12	0.01	0.05	0.00	0.00	0.00
Assault - Morbidity	0.03	0.01	0.05	0.01	0.07	0.01	0.08	0.03	0.09	0.02	0.06	0.00	0.02	0.00	0.00	0.00

Figure 2: AAFs for males, showing new values for each age group and a variety of conditions

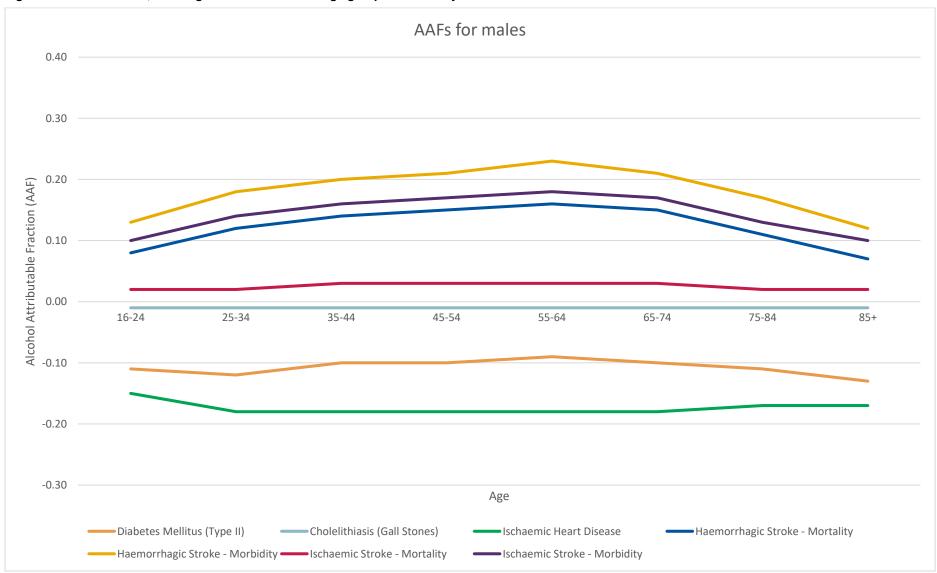
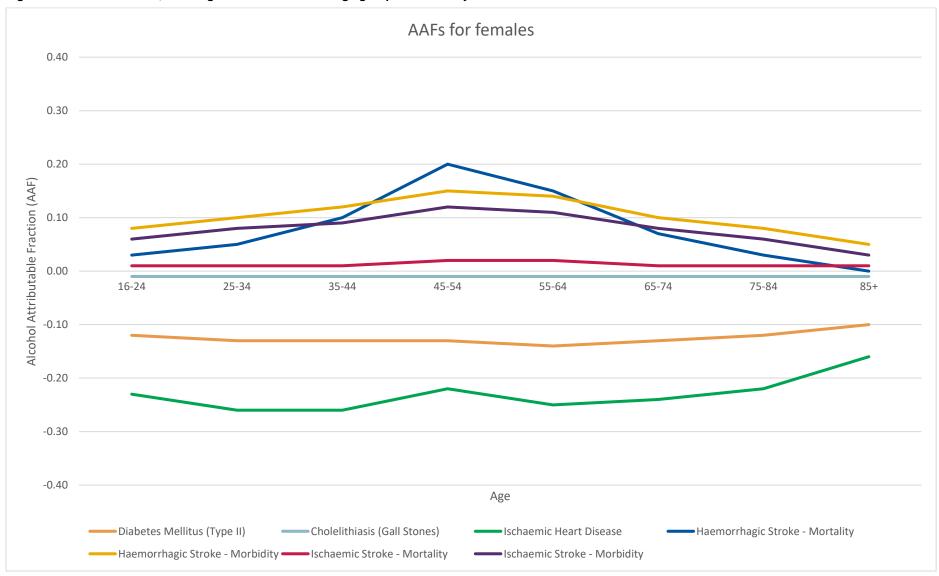


Figure 3: AAFs for females, showing new values for each age group and a variety of conditions



Discussion

Consistent with previous reviews there continues to be clear evidence for an association between alcohol consumption and a wide range of chronic and acute conditions. The UK Chief Medical Officer has recommended: "to keep health risks from alcohol to a low level it is safest not to drink more than 14 units a week on a regular basis (UK Chief Medical Officers' Low Risk Drinking Guidelines, 2016)."

Discussion related to results

Evidence suggests the alcohol attributable fractions for ischaemic heart disease, cholelithiasis, unspecified liver disease for age groups 16 to 34-year olds and 75+ year olds, hypertensive diseases for female age groups 16 to 24-year olds and 75+ year olds, heart failure across all female age groups and type 2 diabetes are negative. This is related to the relative risks being lower (less than one) for different categories of drinkers when compared to abstainers. In some cases, the relative risk is less than one for all drinkers for a given condition. Drink type might play a role in this effect. For example, in one study this effect of alcohol on type 2 diabetes was only observed for wine consumption, but no significant effect was observed for beer or spirits (Huang, Wang, & Zhang, 2017). Further, (Wood et al., 2018) found that for cardiovascular diseases, the RRs were higher in beer and spirit drinkers than in wine drinkers. Future work might calculate the alcohol attributable fraction for different drink types in order to quantify what drink type causes the largest burden of alcohol-related disease.

The alcohol consumption and alcohol attributable fractions varied by both age and sex for most conditions. It is important to note that the effect by age group could be overestimated particularly for the older age groups, since the sample size for 85+ is very small and the results are subject to high variance. Moreover, in this study, we have disaggregated the age group 75+ year olds into two groups 75 to 84 year olds and 85+ year olds. For that reason, the comparison between new alcohol attributable fractions for the age group 75 to 84 year olds and old alcohol attributable fractions for age group 75+ year olds in the Bellis report may not be equivalent. In addition, the uncertainty estimates around each alcohol attributable fraction has not been estimated based on the uncertainty from each relative risk. In some cases where the

attributable fraction is close to zero, the result is likely to have some uncertainty ranging between a negative and positive attributable fraction.

For all diseases, except for tuberculosis and unspecified liver disease mortality across all age groups and haemorrhagic stroke mortality for some age groups, the alcohol attributable fractions for males are larger than those for females. A likely reason is because the proportion of current drinkers and average alcohol consumption is higher in males than females. For tuberculosis, female former drinkers have a much higher relative risk than male former drinkers for the disease. alcohol attributable fractions for unspecified liver diseases mortality have a different pattern because female current drinkers have much higher relative risks than male current drinkers.

Comparison with previous estimates

The new alcohol attributable fractions are different in their magnitude compared to those in the Bellis report. Overall, 75% of all (acute and chronic) alcohol attributable fractions are lower, 2% have remained constant, and 23% are higher.

For example, the new morbidity alcohol attributable fractions for malignant neoplasm of the liver are significantly higher than the previous alcohol attributable fractions for all male age groups, but for females, the new alcohol attributable fractions are slightly lower than the old alcohol attributable fractions for most age groups. The new morbidity alcohol attributable fractions for hypertensive diseases for males or females are much lower than the previous alcohol attributable fractions for all age groups except for the 75-84 female age group. For ischaemic heart disease, the new morbidity alcohol attributable fractions for males and females are lower than old alcohol attributable fractions for all age groups.

For chronic conditions, 64% of alcohol attributable fractions for chronic conditions are lower than in the Bellis report, while 3% have stayed the same and 33% are higher. The main reason for these differences is related to the change in prevalence data on the proportion of drinkers in each age and gender group and the mean alcohol consumption in these groups. A lesser impact is due to a difference in the percentage upshift that has been applied to account for underreporting. In the original report, a 59% upshift was applied, based on a methodology that analysed the gap between data on alcohol purchased and alcohol reported to be consumed,

adjusting for waste. In this report we have applied an upshift of 40%, based on the same methodology as the Bellis report with more recent data applied.

For acute conditions, 98% of alcohol attributable fractions are lower, while 2% are higher. This is due to changes in prevalence of alcohol consumption and binge drinking.

Excluding chronic and acute conditions which are wholly attributable to alcohol consumption, the new results show that alcohol consumption is the largest contributor to new cases of cancers, digestive diseases and road/pedestrian traffic accidents, which are consistent with results in the earlier report (Jones & Bellis, 2013). For some diseases, the updated alcohol attributable fractions have different patterns across the age groups from those in Jones and Bellis' report. The alcohol attributable fractions in (Jones & Bellis, 2013) for most cardiovascular and liver diseases stayed at a relatively consistent level across all age groups, whilst in this update, alcohol attributable fractions for most diseases, except for tuberculosis, increase from age group 16-24, reaching their peak value at age group 55-64 for males and 45-54 for females and decrease thereafter. This can be explained by changes in the alcohol consumption distribution. The alcohol consumption in GLS2010 is consistent across all age groups for males and females, shown in Table 5. In contrast, alcohol consumption in HSE2016 increases from age group 16-24. reaching its peak value at age 55-64 for males and 45-54 for females and decreases thereafter (Table 5). Figure 4 compares the alcohol attributable fractions by age for selected conditions for men from the previous analysis and in this update, and Figure 5 presents the same but for women. For tuberculosis, the new alcohol attributable fractions have different patterns across the two reports because the relative risks for former drinkers against lifetime abstainers were applied in the alcohol attributable fraction calculation.

Limitations

A limitation of this project is that we have explored updates by gender and age only. However, there are likely to be important differences in relative risks across ethnic and socio-economic groups. For instance, there is much evidence of the 'alcohol harm paradox' such that people in more deprived socio-economic status groups are more susceptible to the harms of alcohol than those in less deprived groups (Beard

et al., 2016; Bellis et al., 2016; Lewer, Meier, Beard, Boniface, & Kaner, 2016). Future work might update alcohol attributable fractions for alcohol by SES group.

This work has also not incorporated sensitivity analysis, eg through the use of confidence intervals around each relative risk. Additionally, there is a limitation with the population attributable fraction methodology associated with the time lag between drinking and the occurrence of drinking-related harms. This work is based on relative risks and uses current distributions of alcohol consumption and therefore assumes that there is no time lag between exposure and outcome; this is unlikely to be the case.

Conclusion

In summary, our reviews of the literature confirmed the detrimental impact that alcohol has on a diverse number of chronic and acute conditions. Future work could explore alcohol attributable fractions in different socioeconomic groups, local areas, and by drink type. It could also incorporate confidence intervals around each alcohol attributable fraction estimate.

Figure 4: AAFs for males, showing previous values (dashed) against new values (solid) for each age group and a variety of conditions

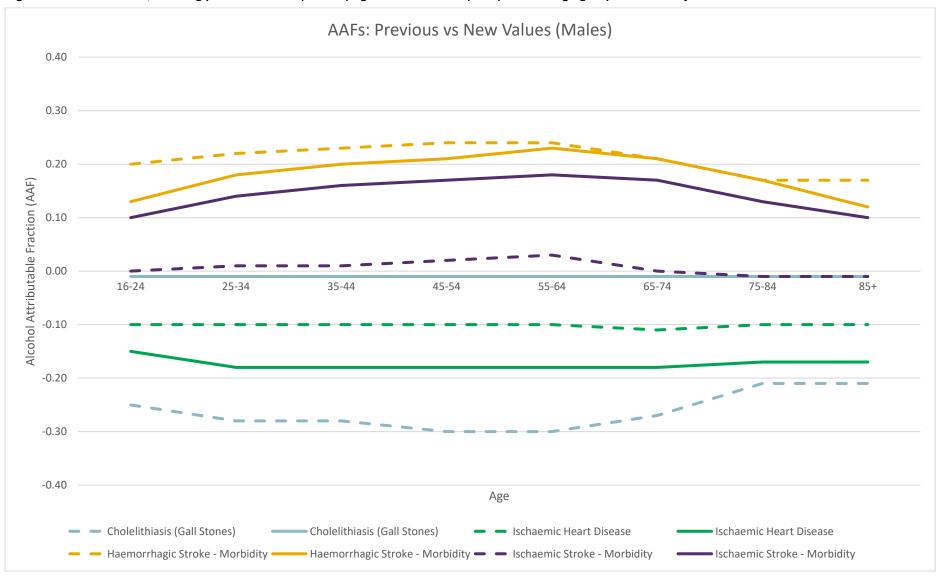
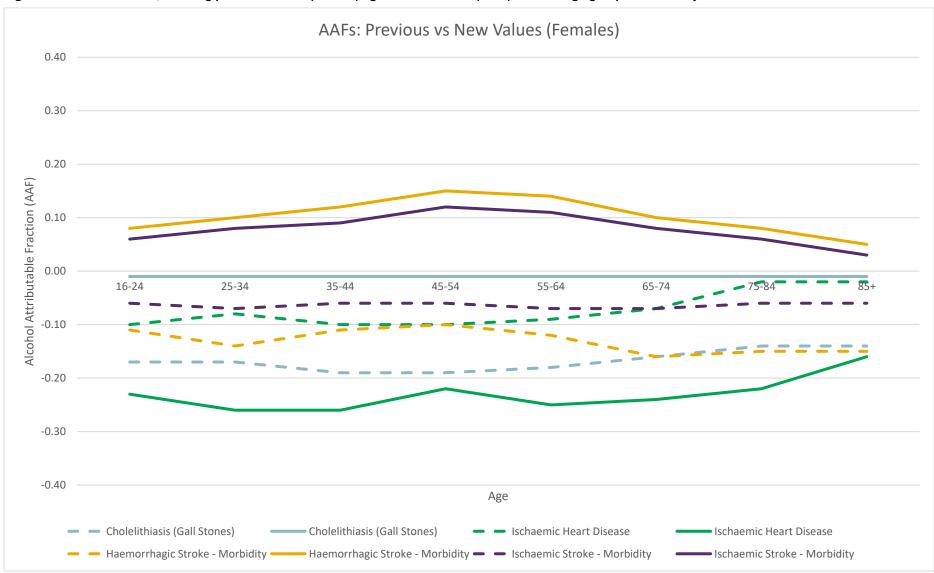


Figure 5: AAFs for females, showing previous values (dashed) against new values (solid) for each age group and a variety of conditions



Bibliography

- Angus, C., Henney, M., Webster, L., & Gillespie, D. (2019). Alcohol-attributable diseases and dose-response curves for the Sheffield Alcohol Policy Model version 4.0.
- Bagnardi, V., Rota, M., Botteri, E., Tramacere, I., Islami, F., Fedirko, V., . . . La Vecchia, C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer, 112*(3), 580-593. doi:10.1038/bjc.2014.579
- Baliunas, D. O., Taylor, B. J., Irving, H., Roerecke, M., Patra, J., Mohapatra, S., & Rehm, J. (2009). Alcohol as a risk factor for type 2 diabetes: A systematic review and meta-analysis. *Diabetes Care, 32*(11), 2123-2132. doi:10.2337/dc09-0227
- Beard, E., Brown, J., West, R., Angus, C., Brennan, A., Holmes, J., . . . Michie, S. (2016). Deconstructing the Alcohol Harm Paradox: A Population Based Survey of Adults in England. *PLoS One, 11*(9), e0160666. doi:10.1371/journal.pone.0160666
- Bellis, M. A., Hughes, K., Nicholls, J., Sheron, N., Gilmore, I., & Jones, L. (2016). The alcohol harm paradox: using a national survey to explore how alcohol may disproportionately impact health in deprived individuals. *BMC Public Health*, *16*, 111. doi:10.1186/s12889-016-2766-x
- Boniface, S., Kneale, J., & Shelton, N. (2013). Actual and perceived units of alcohol in a self-defined "usual glass" of alcoholic drinks in England. *Alcohol Clin Exp Res*, *37*(6), 978-983. doi:10.1111/acer.12046
- Boniface, S., & Shelton, N. (2013). How is alcohol consumption affected if we account for under-reporting? A hypothetical scenario. *Eur J Public Health*, 23(6), 1076-1081. doi:10.1093/eurpub/ckt016
- Briasoulis, A., Agarwal, V., & Messerli, F. H. (2012). Alcohol consumption and the risk of hypertension in men and women: a systematic review and meta-analysis. *J Clin Hypertens (Greenwich), 14*(11), 792-798. doi:10.1111/jch.12008
- Catto, S., & Gibbs, D. (2008). How much are people in Scotland really drinking? A review of data from Scotland's routine national surveys. Retrieved from
- Corrao, G., Bagnardi, V., Zambon, A., & Arico, S. (1999). Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol-related conditions: a meta-analysis. *Addiction, 94*(10), 1551-1573. doi:10.1046/j.1360-0443.1999.9410155111.x
- Corrao, G., Bagnardi, V., Zambon, A., & La Vecchia, C. (2004). A meta-analysis of alcohol consumption and the risk of 15 diseases. *Prev Med, 38*(5), 613-619. doi:10.1016/j.ypmed.2003.11.027
- English, D. R., & Holman, C. D. A. J. (1995). *The quantification of drug caused morbidity and mortality in Australia*: Australian Government Publishing Service.
- Fedirko, V., Tramacere, I., Bagnardi, V., Rota, M., Scotti, L., Islami, F., . . . Jenab, M. (2011). Alcohol drinking and colorectal cancer risk: an overall and doseresponse meta-analysis of published studies. *Ann Oncol, 22*(9), 1958-1972. doi:10.1093/annonc/mdq653

- Gutjahr, E., Gmel, G., & Rehm, J. (2001). Relation between average alcohol consumption and disease: an overview. *Eur Addict Res, 7*(3), 117-127. doi:10.1159/000050729
- Hamajima, N., Hirose, K., Tajima, K., Rohan, T., Calle, E. E., Heath, C. W., Jr., . . . Meirik, O. (2002). Alcohol, tobacco and breast cancer--collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *Br J Cancer*, 87(11), 1234-1245. doi:10.1038/sj.bjc.6600596
- Huang, J., Wang, X., & Zhang, Y. (2017). Specific types of alcoholic beverage consumption and risk of type 2 diabetes: A systematic review and meta-analysis. *J Diabetes Investig*, 8(1), 56-68. doi:10.1111/jdi.12537
- Imtiaz, S., Shield, K. D., Roerecke, M., Samokhvalov, A. V., Lonnroth, K., & Rehm, J. (2017). Alcohol consumption as a risk factor for tuberculosis: meta-analyses and burden of disease. *Eur Respir J, 50*(1). doi:10.1183/13993003.00216-2017
- Irving, H. M., Samokhvalov, A. V., & Rehm, J. (2009). Alcohol as a risk factor for pancreatitis. A systematic review and meta-analysis. *JOP : Journal of the pancreas, 10*(4), 387-392.
- Islami, F., Fedirko, V., Tramacere, I., Bagnardi, V., Jenab, M., Scotti, L., . . . La Vecchia, C. (2011). Alcohol drinking and esophageal squamous cell carcinoma with focus on light-drinkers and never-smokers: a systematic review and meta-analysis. *Int J Cancer, 129*(10), 2473-2484. doi:10.1002/ijc.25885
- Jones, L., & Bellis, M. A. (2013). Updating England-specific alcohol-attributable fractions.
- Knott, C., Bell, S., & Britton, A. (2015). Alcohol Consumption and the Risk of Type 2 Diabetes: A Systematic Review and Dose-Response Meta-analysis of More Than 1.9 Million Individuals From 38 Observational Studies. *Diabetes Care*, 38(9), 1804-1812. doi:10.2337/dc15-0710
- Kodama, S., Saito, K., Tanaka, S., Horikawa, C., Saito, A., Heianza, Y., . . . Sone, H. (2011). Alcohol consumption and risk of atrial fibrillation: a meta-analysis. *J Am Coll Cardiol*, *57*(4), 427-436. doi:10.1016/j.jacc.2010.08.641
- Lewer, D., Meier, P., Beard, E., Boniface, S., & Kaner, E. (2016). Unravelling the alcohol harm paradox: a population-based study of social gradients across very heavy drinking thresholds. *BMC Public Health*, *16*, 599. doi:10.1186/s12889-016-3265-9
- Lonnroth, K., Williams, B. G., Stadlin, S., Jaramillo, E., & Dye, C. (2008). Alcohol use as a risk factor for tuberculosis a systematic review. *BMC Public Health, 8*, 289. doi:10.1186/1471-2458-8-289
- Meier, P. S., Meng, Y., Holmes, J., Baumberg, B., Purshouse, R., Hill-McManus, D., & Brennan, A. (2013). Adjusting for unrecorded consumption in survey and per capita sales data: quantification of impact on gender- and age-specific alcohol-attributable fractions for oral and pharyngeal cancers in Great Britain. *Alcohol Alcohol*, 48(2), 241-249. doi:10.1093/alcalc/agt001
- Parkin, D. M. (2011). 3. Cancers attributable to consumption of alcohol in the UK in 2010. *Br J Cancer, 105 Suppl 2*, S14-18. doi:10.1038/bjc.2011.476
- Patra, J., Bakker, R., Irving, H., Jaddoe, V. W., Malini, S., & Rehm, J. (2011). Doseresponse relationship between alcohol consumption before and during pregnancy and the risks of low birthweight, preterm birth and small for

- gestational age (SGA)-a systematic review and meta-analyses. *BJOG*, *118*(12), 1411-1421. doi:10.1111/j.1471-0528.2011.03050.x
- Patra, J., Taylor, B., Irving, H., Roerecke, M., Baliunas, D., Mohapatra, S., & Rehm, J. (2010). Alcohol consumption and the risk of morbidity and mortality for different stroke types--a systematic review and meta-analysis. *BMC Public Health*, 10, 258. doi:10.1186/1471-2458-10-258
- Rehm, J., Kehoe, T., Gmel, G., Stinson, F., Grant, B., & Gmel, G. (2010). Statistical modeling of volume of alcohol exposure for epidemiological studies of population health: the US example. *Popul Health Metr, 8*, 3. doi:10.1186/1478-7954-8-3
- Rehm, J., Room, R., Monteiro, M., Gmel, G., Graham, K., Rehn, N., . . . Jernigan, D. (2004). Addictive substances: Alcohol use. In M. Ezzati, A. D. Lopez, A. A. Rodgers, & C. J. L. Murray (Eds.), *Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors* (Vol. 1, pp. 959-1108).
- Rehm, J., Taylor, B., Mohapatra, S., Irving, H., Baliunas, D., Patra, J., & Roerecke, M. (2010). Alcohol as a risk factor for liver cirrhosis: a systematic review and meta-analysis. *Drug Alcohol Rev, 29*(4), 437-445. doi:10.1111/j.1465-3362.2009.00153.x
- Roerecke, M., & Rehm, J. (2010). Irregular heavy drinking occasions and risk of ischemic heart disease: a systematic review and meta-analysis. *Am J Epidemiol*, 171(6), 633-644. doi:10.1093/aje/kwp451
- Roerecke, M., & Rehm, J. (2012). The cardioprotective association of average alcohol consumption and ischaemic heart disease: a systematic review and meta-analysis. *Addiction*, 107(7), 1246-1260. doi:10.1111/j.1360-0443.2012.03780.x
- Ronksley, P. E., Brien, S. E., Turner, B. J., Mukamal, K. J., & Ghali, W. A. (2011). Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. *BMJ*, *342*, d671. doi:10.1136/bmi.d671
- Samokhvalov, A. V., Irving, H., Mohapatra, S., & Rehm, J. (2010). Alcohol consumption, unprovoked seizures, and epilepsy: a systematic review and meta-analysis. *Epilepsia*, *51*(7), 1177-1184. doi:10.1111/j.1528-1167.2009.02426.x
- Samokhvalov, A. V., Irving, H. M., & Rehm, J. (2010). Alcohol consumption as a risk factor for pneumonia: a systematic review and meta-analysis. *Epidemiol Infect*, 138(12), 1789-1795. doi:10.1017/S0950268810000774
- Shabanzadeh, D. M., Sorensen, L. T., & Jorgensen, T. (2016). Determinants for gallstone formation a new data cohort study and a systematic review with meta-analysis. *Scand J Gastroenterol*, *51*(10), 1239-1248. doi:10.1080/00365521.2016.1182583
- Single, E., Robson, L., Xie, X., & Rehm, J. (1996). The costs of substance abuse in Canada: a cost estimation study: highlights of a major study of the health, social and economic costs associated with the use of alcohol, tobacco and illicit drugs. Retrieved from Ottawa, ON:
- Taylor, B., Irving, H. M., Baliunas, D., Roerecke, M., Patra, J., Mohapatra, S., & Rehm, J. (2009). Alcohol and hypertension: gender differences in dose-response relationships determined through systematic review and meta-analysis. *Addiction*, 104(12), 1981-1990. doi:10.1111/j.1360-0443.2009.02694.x

- Taylor, B., Irving, H. M., Kanteres, F., Room, R., Borges, G., Cherpitel, C., . . . Rehm, J. (2010). The more you drink, the harder you fall: a systematic review and meta-analysis of how acute alcohol consumption and injury or collision risk increase together. *Drug Alcohol Depend, 110*(1-2), 108-116. doi:10.1016/j.drugalcdep.2010.02.011
- Taylor, B. J., Shield, K. D., & Rehm, J. T. (2011). Combining best evidence: a novel method to calculate the alcohol-attributable fraction and its variance for injury mortality. *BMC Public Health*, *11*, 265. doi:10.1186/1471-2458-11-265
- Tramacere, I., Negri, E., Bagnardi, V., Garavello, W., Rota, M., Scotti, L., . . . La Vecchia, C. (2010). A meta-analysis of alcohol drinking and oral and pharyngeal cancers. Part 1: overall results and dose-risk relation. *Oral Oncol*, *46*(7), 497-503. doi:10.1016/j.oraloncology.2010.03.024
- Wood, A. M., Kaptoge, S., Butterworth, A. S., Willeit, P., Warnakula, S., Bolton, T., . . . Danesh, J. (2018). Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. *The Lancet*, 391(10129), 1513-1523. doi:10.1016/s0140-6736(18)30134-x
- Zheng, Y. L., Lian, F., Shi, Q., Zhang, C., Chen, Y. W., Zhou, Y. H., & He, J. (2015). Alcohol intake and associated risk of major cardiovascular outcomes in women compared with men: a systematic review and meta-analysis of prospective observational studies. *BMC Public Health*, 15, 773. doi:10.1186/s12889-015-2081-y