

Alcohol-attributable diseases and dose-response curves

Version 1.1.1

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The code that accompanies this vignette can be found in the tobalcepi R package https://stapm.github.io/tobalcepi/ (Github code repository https://github.com/STAPM/tobalcepi).

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Therefore the citation above should be used for the content of this vignette. This vignette differs from the report cited above in being produced by the code within the tobalcepi R package. This vignette therefore presents the risk functions and acts as a means to quality assure the code in the tobalcepi R package.

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References

1 Introduction

This document presents the list of health conditions related to alcohol which are included in the most recent version (4.0) of the Sheffield Alcohol Policy Model (SAPM). It also presents the corresponding dose-response curves (the mathematical relationships between volume of alcohol consumed and risk of morbidity/mortality) for all included conditions which are not wholly-attributable to alcohol. This is based on recent reviews by Rehm et al. (2017; 2017) and Sherk et al. (2020), as well as previous versions of the Sheffield Model (Meier et al. 2016) supplemented with additional evidence as appropriate. Note that SAPM considers only conditions which affect the drinker and therefore several conditions related to alcohol, such as Foetal Alcohol Spectrum Disorders, are therefore not included.

2 Acknowledgements

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Category	Condition	ICD-10 code(s)	Condition type*
	Oropharyngeal cancer	C00-06, C09-10, C12-C14	
	Oesophageal cancer	C15	_
	Colorectal cancer	C18-C20	_
Cancer	Cancer of the liver and intrahepatic bile ducts	C22	– – _ Partial chronic –
	Pancreatic cancer	C25	
	Laryngeal cancer	C32	
	Breast cancer	C50	
	Hypertensive diseases	I10-I14	
	Ischaemic heart disease	120-125	
	Alcoholic cardiomyopathy	I42.6	100% chronic
Cardiovascular	Cardiac arrhythmias	I47-I49	– – – – –
Cardiovascular	Haemorrhagic stroke	I60-I62	
	Ischaemic stroke	I63-I67	
	Cirrhosis of the liver (excluding alcoholic liver disease)	K70 (excl. K70.0-K70.4, K70.9), K73-K74	
	Alcoholic Gastritis	K29.2	– _ 100% chronic
	Alcoholic liver disease	K70.0-K70.4, K70.9	
Digestive	Acute pancreatitis (alcohol induced)	K85.2	
	Acute pancreatitis	K85 (excl. K85.2, K85.3)	Partial chronic
	Chronic pancreatitis (alcohol induced)	K86.0	100% chronic
	Chronic pancreatitis	K86 (excl. K86.0)	Partial chronic
	Accidental poisoning by exposure to noxious substances	X40-X49 (excl. X45), Y10-Y14, Y16-Y19, T36-T50, T52-T65	Partial acute

Table 1: List of alcohol-attributable diseases.

Category	Condition	ICD-10 code(s)	Condition type*	
	Excessive Blood Level of Alcohol	R78.0		
	Toxic effect of alcohol	T51.0, T51.1, T51.8, T51.9	_	
Poisoning	Alcohol poisoning	X45, X65, Y15	– 100% acute	
	Evidence of alcohol involvement determined by blood alcohol level	Y90	_	
	Transport injuries (including road traffic accidents)	V01-V98, Y85.0		
	Fall injuries	W00-W19	_	
	Exposure to mechanical forces (including machinery accidents)	W20-W52	_	
	Drowning	W65-W74, Y21	_	
	Fire injuries	X00-X09, Y26	_ _ Partial acute _	
Iniuries	Other Unintentional Injuries	W75-W99, X10-X33, Y20, Y22-Y25, Y27-Y29, Y31-Y34		
mjarros	Intentional self-harm	X60-X84 (excl. X65), Y87.0		
	Assault	X85-Y09, Y87.1		
	Other intentional injuries	Y35		
	Diabetes (Type II)	E11	Partial chronic	
Endocrine	Alcohol-induced pseudo-Cushing's syndrome	E24.4	100% chronic	
	Acute intoxication	Y35 E11 E24.4 F10.0 F10.1-F10.9	100% acute	
Mental Health	Mental and behavioural disorders due to use of alcohol	F10.1-F10.9		
	Degeneration	G31.2	= 100% chronic	
	Epilepsy and status epilepticus	G40-G41	Partial chronic	
Nervous System	Alcoholic polyneuropathy	G62.1		
5,50011	Alcoholic myopathy	G72.1	- 100% chronic	
Other	Maternal care for (suspected) damage to foetus from alcohol	O35.4	_ 10070 0110110	
	Tuberculosis	A15-A19	Partial chronic	
Respiratory	Lower respiratory tract infections	J09-J18		

Table 1: List of alcohol-attributable diseases. (continued)

^{*} 100% conditions are those which are wholly-attributable to alcohol (i.e. which would not exist if nobody drank). Partial conditions are those which are partly attributable to alcohol but which would still exist, albeit with reduced prevalence, if nobody drank. Acute conditions are those which are related to intoxication. Chronic conditions are those which are related to chronic alcohol consumption in the longer term.

3 Dose-response curves for partially alcohol attributable chronic conditions

Relative risk of harm for drinkers at consumption level x, measured in grams of ethanol per day, versus lifetime abstainers. Due to small sample sizes, published risk functions are not stable above 150g/day, so we assume $RR(x) = RR(150) \forall x > 150$ for all conditions. All risk functions are applied to both genders and for both mortality and morbidity except where stated otherwise.

3.1Cancers

3.1.1Oropharyngeal (C00-06, C09-10, C12-14)



 $\ln(RR(x)) = 0.02474x - 0.00004x^2$

(1)

(2)

Figure 1: Relative risk for Oropharyngeal cancer by the average daily consumption of alcohol.

Source (Bagnardi et al. 2015)

Oesophageal (C15) 3.1.2



Figure 2: Relative risk for Oesophageal cancer by the average daily consumption of alcohol.

Source (Bagnardi et al. 2015)

Notes: Oesophageal cancer has two main histological types: Squamous Cell Carcinoma (SCC) and Adenocarcinoma (AC). Alcohol is only associated with SCC, not AC (Bagnardi et al. 2015). The relative prevalence of SCC and AC varies widely between countries and within population subgroups (Arnold et al. 2015) and it may therefore be necessary to apportion overall oesophageal cancer prevalence between SCC and AC using external data such as that from cancer registries.

3.1.3 Colorectal (C18-C20)

$$\ln(RR(x)) = 0.006279x \tag{3}$$



Figure 3: Relative risk for Colorectal cancer by the average daily consumption of alcohol.

3.1.4 Liver and intrahepatic bile ducts (C22)

$$\ln(RR(x)) = 0.4100701(y - 0.6728571429) + 0.6101417(y^2 - 0.4527367347), \tag{4}$$

$$y = \frac{x+12}{100}$$
(5)



Figure 4: Relative risk for Liver cancer by the average daily consumption of alcohol.

Source (Chuang et al. 2015)

Notes: Bagnardi et al. (2015), which we use as the source for all other cancer risk curves do provide a curve for liver cancer, however this has extremely high Relative Risks at high levels of consumption (RR=45 at 150g/day), driven by high risks from a small number of case-control studies. Alternative meta-analyses from Chuang et al (2015) and Turati et al (2014) have found lower risks at high levels of consumption (Chuang et al. 2015; Turati et al. 2014), however these risk curves are still quite divergent. It may therefore be advisable to present modelled estimates using several alternative sources to illustrate the impact of this uncertainty.

3.1.5 Pancreatic (C25)

$$\ln(RR(x)) = 0.002089x \tag{6}$$



Figure 5: Relative risk for Pancreatic cancer by the average daily consumption of alcohol.

Source (Bagnardi et al. 2015)

3.1.6 Laryngeal (C32)

$$\ln(RR(x)) = 0.01462x - 0.00002x^2 \tag{7}$$



Figure 6: Relative risk for Laryngeal cancer by the average daily consumption of alcohol.

Source (Bagnardi et al. 2015)

3.1.7 Breast (C50)



Figure 7: Relative risk for Laryngeal cancer by the average daily consumption of alcohol.

Source (Bagnardi et al. 2015)

3.2 Cardiovascular diseases

3.2.1 Hypertensive diseases (I10-I14)

$$\mathbf{Male} \ \ln(RR(x)) = \begin{cases} 0.0150537x - 0.0156155\frac{x^3}{75^2}, & \text{if } 0 \le x < 21\\ 0.0150537x - 0.0156155\frac{x^3 - \frac{(x-21)^3 \times 75}{(75-21)}}{75^2}, & \text{if } 21 \le x < 75\\ 0.0150537x - 0.0156155\frac{x^3 - \frac{(x-10)^3 \times 20 - (x-20)^3 \times 10}{(75-21)}}{75^2}, & \text{if } 75 \le x \end{cases}$$
(9)

$$\mathbf{Female} \ \ln(RR(x)) = \begin{cases} 0, & \text{if } 0 \le x < 18.9517 \\ -0.0154196x + 0.0217586 \frac{x^3 - \frac{(x-10)^3 \times 20 - (x-20)^3 \times 10}{(20-10)}}{20^2}, & \text{if } 18.9517 \le x < 75 \\ 0.9649937, & \text{if } 75 \le x \end{cases}$$
(10)



Figure 8: Relative risk for Hypertensive diseases by the average daily consumption of alcohol.

Source (J. Rehm et al. 2017)

3.2.2 Ischaemic heart disease (I20-I25)

3.2.2.1 Mortality

$$\mathbf{Male, 16-34} \ \ln(RR(x)) = \begin{cases} 1.111874(-0.4870068\sqrt{y} + 1.550984y^3), & \text{if } 0 \le x \le 60\\ 0, & \text{if } 60 < x < 100\\ 0.012(x - 100), & \text{if } 100 \le x \end{cases}$$
(11)

$$\mathbf{Male, 35-64} \ \ln(RR(x)) = \begin{cases} 1.035623(-0.4870068\sqrt{y} + 1.550984y^3), & \text{if } 0 \le x \le 60\\ 0, & \text{if } 60 < x < 100\\ 0.012(x - 100), & \text{if } 100 \le x \end{cases}$$
(12)

$$\mathbf{Male, 65+} \ln(RR(x)) = \begin{cases} 0.757104(-0.4870068\sqrt{y} + 1.550984y^3), & \text{if } 0 \le x \le 60\\ 0, & \text{if } 60 < x < 100\\ 0.012(x - 100), & \text{if } 100 \le x \end{cases}$$
(13)

Female, 16-34
$$\ln(RR(x)) = \begin{cases} 1.111874(1.832441y + 1.538557y\ln(y)), & \text{if } 0 \le x < 30.3814\\ 0.01(x - 30.3814), & \text{if } 30.3814 \le x \end{cases}$$
 (14)

Female, 35-64
$$\ln(RR(x)) = \begin{cases} 1.035623(1.832441y + 1.538557y\ln(y)), & \text{if } 0 \le x < 30.3814\\ 0.0093(x - 30.3814), & \text{if } 30.3814 \le x \end{cases}$$
 (15)

Female, 65+
$$\ln(RR(x)) = \begin{cases} 0.757104(1.832441y + 1.538557y \ln(y)), & \text{if } 0 \le x < 30.3814\\ 0.0068(x - 30.3814), & \text{if } 30.3814 \le x \end{cases}$$
 (16)



Figure 9: Relative risk for mortality from Ischaemic heart disease by the average daily consumption of alcohol.

Source (Jürgen Rehm et al. 2016)

Notes: All protective effects are removed for drinkers who consume more than 60g in a single drinking occasion at least once per month, as per (Roerecke and Rehm 2010)

3.2.2.2 Morbidity

$$\mathbf{Male} \ \ln(RR(x)) = \begin{cases} -0.1178113\sqrt{x} + 0.0189\sqrt{x}\ln(x), & \text{if } 0 \le x < 60\\ 0, & \text{if } 60 \le x \end{cases}$$
(18)

Female
$$\ln(RR(x)) = -0.296842\sqrt{x} + 0.0392805x$$
 (19)



Figure 10: Relative risk for mortality from Ischaemic heart disease by the average daily consumption of alcohol.

Source (Roerecke and Rehm 2012)

Notes: All protective effects are removed for drinkers who consume more than 60g in a single drinking occasion at least once per month, as per (Roerecke and Rehm 2010)

3.2.3 Cardiac arrhythmias (I47-I49)



Figure 11: Relative risk for mortality from Cardiac arrhythmias by the average daily consumption of alcohol.

Source (A. V. Samokhvalov, Irving, and Rehm 2010)

3.2.4 Haemorrhagic and other non-ischaemic stroke (I60-I62)

3.2.4.1 Mortality

$$\mathbf{Male} \ \ln(RR(x)) = \begin{cases} \ln(1 - x(1 - 1.006943)), & \text{if } 0 \le x \le 1\\ 0.6898937 \times \frac{x + 0.0028572082519531}{100}, & \text{if } x > 1 \end{cases}$$
(21)

Female
$$\ln(RR(x)) = \begin{cases} \ln(1 - x(1 - 1.014815)), & \text{if } 0 \le x \le 1\\ 1.466406 \times \frac{x + 0.0028572082519531}{100}, & \text{if } x > 1 \end{cases}$$
 (22)



Figure 12: Relative risk for mortality from Haemorrhagic and other non-ischaemic stroke by the average daily consumption of alcohol.

Source (Patra et al. 2010)

3.2.4.2 Morbidity

Male
$$\ln(RR(x)) = 0.007695021x$$
 (23)

Female
$$\ln(RR(x)) = -0.340861\sqrt{x} + 0.0944208\sqrt{x}\ln(x)$$
 (24)



Figure 13: Relative risk for morbidity from Haemorrhagic and other non-ischaemic stroke by the average daily consumption of alcohol.

Source (Patra et al. 2010)

3.2.5 Ischaemic stroke (I63-I67)

3.2.5.1 Mortality

$$\mathbf{Male, 16-34} \ \ln(RR(x)) = \begin{cases} \ln(1 - x(1 - e^{-0.03521})), & \text{if } 0 \le x \le 1\\ 1.111874 \times (0.4030081\sqrt{y} + 0.3877538\sqrt{y}\ln(y)), & \text{if } x > 1 \end{cases}$$
(25)

$$\mathbf{Male, 35-64} \ \ln(RR(x)) = \begin{cases} \ln(1 - x(1 - e^{-0.03279})), & \text{if } 0 \le x \le 1\\ 1.035623 \times (0.4030081\sqrt{y} + 0.3877538\sqrt{y}\ln(y)), & \text{if } x > 1 \end{cases}$$
(26)

$$\mathbf{Male, 65+} \ln(RR(x)) = \begin{cases} \ln(1 - x(1 - e^{-0.02397})), & \text{if } 0 \le x \le 1\\ 0.757104 \times (0.4030081\sqrt{y} + 0.3877538\sqrt{y}\ln(y)), & \text{if } x > 1 \end{cases}$$
(27)

Female, 16-34
$$\ln(RR(x)) = \begin{cases} \ln(1 - x(1 - e^{-0.37987})), & \text{if } 0 \le x \le 1\\ 1.111874 \times (-2.48768\sqrt{y} + 3.708724y), & \text{if } x > 1 \end{cases}$$
 (28)

Female, 35-64
$$\ln(RR(x)) = \begin{cases} \ln(1 - x(1 - e^{-0.35382})), & \text{if } 0 \le x \le 1\\ 1.035623 \times (-2.48768\sqrt{y} + 3.708724y), & \text{if } x > 1 \end{cases}$$
 (29)

Female, 65+
$$\ln(RR(x)) = \begin{cases} \ln(1 - x(1 - e^{-0.25866})), & \text{if } 0 \le x \le 1\\ 0.757104 \times (-2.48768\sqrt{y} + 3.708724y), & \text{if } x > 1 \end{cases}$$
 (30)

$$y = \frac{x + 0.0028572082519531}{100} \tag{31}$$



Figure 14: Relative risk for mortality from Ischaemic stroke by the average daily consumption of alcohol.

Source (Jürgen Rehm et al. 2016)

Notes: All protective effects are removed for drinkers who consume more than 60g in a single drinking occasion at least once per month, as per (Jürgen Rehm et al. 2016)

3.2.5.2 Morbidity

Male
$$\ln(RR(x)) = -0.132894\sqrt{x} + 0.03677422\sqrt{x}\ln(x)$$
 (32)

Female
$$\ln(RR(x)) = -0.114287\sqrt{x} + 0.01680936x$$
 (33)



Figure 15: Relative risk for morbidity from Ischaemic stroke by the average daily consumption of alcohol.

Source (Patra et al. 2010)

Notes: All protective effects are removed for drinkers who consume more than 60g in a single drinking occasion at least once per month, as per (Jürgen Rehm et al. 2016)

3.3 Digestive diseases

3.3.1 Cirrhosis of the liver (K70 (excl. K70.0-K70.4, K70.9), K73-K74)

3.3.1.1 Mortality

$$\mathbf{Male} \ \ln(RR(x)) = \begin{cases} \ln(1 + x(1.033224 - 1)), & \text{if } 0 \le x \le 1\\ 2.793524 \times \frac{x + 0.1699981689453125}{100}, & \text{if } x > 1 \end{cases}$$
(34)

Female
$$\ln(RR(x)) = \begin{cases} \ln(1 + x(1.421569 - 1)), & \text{if } 0 \le x \le 1\\ 3.252035 \times \frac{x + 0.1699981689453125}{100}, & \text{if } x > 1 \end{cases}$$
 (35)



Figure 16: Relative risk for mortality from Cirrhosis of the liver by the average daily consumption of alcohol.

3.3.1.2 Morbidity

Male
$$\ln(RR(x)) = 0.01687111x$$
 (36)

$$\mathbf{Female} \ \ln(RR(x)) = 0.2351821\sqrt{x} \tag{37}$$



Figure 17: Relative risk for morbidity from Cirrhosis of the liver by the average daily consumption of alcohol.

Source (Jürgen Rehm et al. 2010)

3.3.2 Acute pancreatitis (K85 (excl. K85.2, K85.3))

$$Male \ln(RR(x)) = 0.013x \tag{38}$$

$$\mathbf{Female} \ \ln(RR(x)) = \begin{cases} -0.0272886x, & \text{if } 0 \le x < 3\\ -0.0272886x + 0.0611466 \times \frac{(x-3)^3}{(40-3)^2}, & \text{if } 3 \le x < 15\\ -0.0272886x + 0.0611466 \times \frac{(x-3)^3 - \frac{(x-15)^3 \times (40-3)}{40-15}}{(40-3)^2}, & \text{if } 15 \le x < 40\\ -0.0272886x + 0.0611466 \times \frac{(x-3)^3 - \frac{(x-15)^3 \times (40-3)}{40-15}}{(40-3)^2}, & \text{if } 40 \le x < 108\\ 2.327965, & \text{if } 108 \le x \end{cases}$$

$$(39)$$



Figure 18: Relative risk for Acute pancreatitis by the average daily consumption of alcohol.

Source (A. V. Samokhvalov, Rehm, and Roerecke 2015)

3.3.3 Chronic pancreatitis (K86 (excl. K86.0))

$$\ln(RR(x)) = 0.018x \tag{40}$$



Figure 19: Relative risk for Acute pancreatitis by the average daily consumption of alcohol.

Source (A. V. Samokhvalov, Rehm, and Roerecke 2015)

3.4 Endocrine diseases

3.4.1 Diabetes mellitus (type II) (E11)

Male
$$\ln(RR(x)) = 0.00001763703x^2 - 0.0000000728256x^3$$
 (41)



Female $\ln(RR(x)) = -0.1313991\sqrt{x} + 0.01014239x$ (42)

Figure 20: Relative risk for Diabetes mellitus (type II) by the average daily consumption of alcohol.

Source (Knott, Bell, and Britton 2015)

3.5 Diseases of the nervous system

3.5.1 Epilepsy and status epilepticus (G40-G41)

$$\ln(RR(x)) = 1.22861 \times \frac{x+0.5}{100} \tag{43}$$



Figure 21: Relative risk for Epilepsy and status epilepticus by the average daily consumption of alcohol.

Source (A. V. Samokhvalov et al. 2010)

3.6 Respiratory diseases

3.6.1 Tuberculosis (A15-A19)

$$\ln(RR(x)) = 0.0179695x \tag{44}$$



Figure 22: Relative risk for Tuberculosis by the average daily consumption of alcohol.

Source (Imtiaz et al. 2017)

3.6.2 Lower respiratory tract infections (J09-J18)



Figure 23: Relative risk for Lower respiratory tract infections by the average daily consumption of alcohol.

Source (A. Samokhvalov, Irving, and Rehm 2010)

4 Dose-response curves for partially alcohol attributable acute conditions

Relative risk of harm for drinkers at consumption level x, measured in grams of ethanol consumed on a single drinking occasion, versus non-drinkers. All risk functions are applied to both genders and for both mortality and morbidity except where stated otherwise.

4.1 Transport Injuries (V01-V98, Y85.0)

$$RR(x) = \frac{e^{0.837637 \times (\ln(y) + 3.973538882) + 1.018824 \times (y^3 - 0.00000665184)}}{0.370731 \times (1 + e^{0.837637 \times (\ln(y) + 3.973538882) + 1.018824 \times (y^3 - 0.00000665184)})}$$
(46)

$$y = \frac{\frac{x}{12.8} + 1}{100} \tag{47}$$



Figure 24: Relative risk for transport injuries by the amount of alcohol consumed on an occassion.

Source (Cherpitel et al. 2015)

4.2 Violent injuries (X85-Y09, Y87.1 & Y35)

$$RR(x) = \frac{e^{-0.42362 \times \left(\frac{1}{\sqrt{y} - 5.084489629}\right) + 0.562549 \times (y^3 - 0.0000578783)}}{0.110872 \times \left(1 + e^{-0.42362 \times \left(\frac{1}{\sqrt{y}} - 5.084489629\right) + 0.562549 \times (y^3 - 0.0000578783)}\right)}$$
(48)

$$y = \frac{\frac{x}{12.8} + 1}{100} \tag{49}$$



Figure 25: Relative risk for violence by the amount of alcohol consumed on an occassion.

Source (Cherpitel et al. 2015)

4.3 Falls (W00-W19)

$$RR(x) = \frac{e^{17.84434 \times (\sqrt{y} - 0.1398910338) - 17.6229 \times (y - 0.0195695013)}}{0.367446 \times (1 + e^{17.84434 \times (\sqrt{y} - 0.1398910338) - 17.6229 \times (y - 0.0195695013))}$$
(50)

(51)



Figure 26: Relative risk for falls by the amount of alcohol consumed on an occassion.

Source (Cherpitel et al. 2015)

4.4 Other injuries (W20-W52, W65-W74, Y21, X00-X09, Y26, W75-W99, X10-X33, Y20, Y22-Y25, Y27-Y29, Y31-Y34, X60-X84 (excl. X65), Y87.0)

$$RR(x) = \frac{e^{-0.28148 \times \left(\frac{1}{\sqrt{y}} - 0.1398910338\right) - 2.00946 \times (y - 0.015761462)}}{0.363279 \times \left(1 + e^{-0.28148 \times \left(\frac{1}{\sqrt{y}} - 0.1398910338\right) - 2.00946 \times (y - 0.015761462)}\right)}$$
(52)

where



Figure 27: Relative risk for other injuries by the amount of alcohol consumed on an occassion.

Source (Cherpitel et al. 2015)

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