



InterMAHP: The International Model of Alcohol Harms and Policies

A comprehensive guide to the estimation of alcohol-attributable morbidity and mortality

version 1.0 | December 2017

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For assistance

Please contact the first author for assistance in the understanding and use of the InterMAHP product.

The first author is available by correspondence or in-person to demonstrate the use of InterMAHP or assist with its use.

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For guidance on how to refer to the use of InterMAHP regarding changes to the default settings, please see Section 5 of this guide.

Contents

Introduction to InterMAHP Version 1.0	3
InterMAHP components	4
(1) InterMAHP: A comprehensive guide to the estimation of alcohol-attributable morbidity and mortality	4
(2) The InterMAHP program and user interface	4
(3) InterMAHP: User's manual	5
A note on replicability	5
Modularity of relative risk functions and estimates	6
GATHER compatibility	6
Section 1: General methods for calculating AA morbidity and mortality	7
1.1 Estimating exposure to alcohol, consumption and prevalence	9
1.1.1 Estimating total per capita consumption	9
1.1.2 Estimating drinking prevalences and relative consumption, by population subgroup	10
1.2 Causation and identifying alcohol-related conditions	10
1.3 Operationalizing alcohol-related conditions using ICD10 codes	11
1.4 Enumerating alcohol-related morbidity and mortality for each condition	16
1.4.1 Special considerations for oesophageal cancer	17
1.5 Assign alcohol-related conditions as 100% or partially attributable	18
1.6 Choose between direct and indirect AAFs for partially attributable conditions	18
1.7 Calculate AAFs for partially attributable conditions	19
1.8 Multiply morbidity and mortality counts by AAFs	19
Section 2: InterMAHP inputs	20
2.1 Consumption and prevalence input	20
2.2 Relative risk input	22

2.3 InterMAHP AAF calculator program: User interface	24
Section 3: Methods for calculating InterMAHP alcohol-attributable fractions	27
3.1 Modeling the continuous distribution of alcohol consumption	27
3.2 Relative risks associated with alcohol consumption	29
3.2.1 Continuous relative risk functions for current drinkers	29
3.2.2 Special case: choosing relative risk functions for ischaemic heart disease in males	35
3.2.3 Extrapolating relative risk functions in InterMAHP	37
3.2.4 Extrapolating relative risk functions for ischaemic heart disease	38
3.2.5 Categorical relative risk estimates for former drinkers	39
3.3 Considerations in matching per capita consumption to epidemiological studies	39
3.4 InterMAHP alcohol-attributable fraction methodology	40
3.5 Special cases of InterMAHP AAFs 1: Ischaemic heart disease and ischaemic stroke	41
3.6 Special cases of InterMAHP AAFs 2: Injuries	43
3.7 Section note	45
Section 4: Methods for additional InterMAHP functionality	46
4.1 Calculating InterMAHP AAFs by drinking categories: General case	46
4.2 Calculating InterMAHP AAFs by drinking categories: Special cases	48
4.3 Dynamic upper limit of consumption, z	50
Section 5: InterMAHP program defaults, suggested referencing and program restrictions .	52
5.1 Program defaults	52
5.2 Suggested referencing	52
5.3 Program restrictions	53
Section 6: Relative risk summary pages	54

Introduction to InterMAHP Version 1.0

The International Model of Alcohol Harms and Policies, Version 1.0 is intended to provide comprehensive methods and support to international alcohol epidemiologists in order to allow the calculation of alcohol-attributable fractions for their region, be it a country, province, state or city. Given a set of typically available data on alcohol exposure and prevalence, as well as count data on the number of hospitalizations and deaths within their region, InterMAHP allows users to calculate, using internationally standardized and well-documented methodologies, alcohol-attributable fractions (AAFs) for all alcohol-related conditions identified by InterMAHP.

It is the hope of the authors that this comprehensive guide and the accompanying InterMAHP AAF program will provide the international alcohol epidemiology community with a *standard set of methodologies* which, when adopted by a critical number of alcohol researchers, will result in more comparable estimates across global jurisdictions. Although InterMAHP comes with a default set of assumptions (such as which risk curves to use and which factors to apply to per capita consumption), it was also built from the ground up to be easily adaptable should researchers prefer to change these assumptions to meet their needs. For example, all relative risk functions are easily exchangeable at the input stage.

It is important to note that InterMAHP is a methodological supplement to, but not a replacement for, programs of work studying alcohol-attributable harms. There is a significant volume of work which cannot be generalized to the international level; this includes understanding the design of a region's administrative health databases, local area knowledge on surveys designed to capture drinking prevalence and relative consumption and information on captured alcohol sales data, all of which are necessary as inputs to the InterMAHP program.

In some regards, the InterMAHP guide and program comprise an updated version of the alcohol section of the well-recognized English and Holman publication [1]. Similarities between the two reports are significant: the relative risk relationship for each alcohol-related condition is studied and reported (though [1] completed many meta-analyses as part of the report), general considerations for estimating alcohol-attributable morbidity and mortality are treated and alcohol-attributable fraction methodologies are presented. However, an important extension of InterMAHP is the creation and distribution of a downloadable program tool which, given certain necessary input, automates the calculation of alcohol-attributable fractions.

InterMAHP also provides several novel functionalities to alcohol epidemiologists in the ability to (1) study the contribution to overall AAFs of four user-specified drinking groups (former, light, moderate and heavy drinkers) and (2) dynamically change the upper limit of consumption among the drinking population in their region. These functionalities are described in detail in Section 5.

InterMAHP components

The main components of the International Model of Alcohol Harms and Policies, Version 1.0 are the following three items, which are freely available for download at www.intermahp.cisur.ca.

(1) InterMAHP: A comprehensive guide to the estimation of alcohol-attributable morbidity and mortality

This document is created to provide an overview of the entire process of estimating alcohol-attributable morbidity and mortality in your region and a detailed, mathematically comprehensive description of the methods used by InterMAHP to calculate alcohol-attributable fractions based on standard input from your region.

This guide is intended to be fully-specified, i.e. given only this methodological description, it should be possible to completely replicate the functionality of the InterMAHP program (see also the Section: A note on replicability below).

(2) The InterMAHP program and user interface

The InterMAHP program and user interface are the tools used to calculate AAFs for your region; they are currently written using SAS software [2], with plans to replicate this software in the R programming language. The program is completely back-end, i.e. user's do not have to edit or interact with the code in anyway; however, it is freeware so it can be modified if you would like.

The InterMAHP interface page allows users to input their region-specific data, as well as to input dynamic consumption limits such as the definition of bingeing in their region and the upper limit of consumption. The interface is the only page in SAS which users must interact with in order to run the InterMAHP program. A screen shot and description of required inputs for the InterMAHP user interface is provided in Section 2.3; further, comprehensive instructions for

preparation of your input files and choices are provided in the accompanying InterMAHP User's manual.

(3) InterMAHP: User's manual

The accompanying InterMAHP User's manual provides a complete worked example of calculating the alcohol-attributable morbidity and mortality in the country of Canada and for one Canadian province, British Columbia.

A note on replicability

This guide is meant to make the InterMAHP AAF calculations completely replicable, i.e. given only this guide one should be able to re-build the InterMAHP AAF program given the detailed methodologies outlined herein. To our knowledge, a fully-specified method has never been collected in a single place; our aim is that every value, assumption, calculation, risk function and risk estimate is comprehensively sourced down to the article and table number, along with the citation of any personal correspondence between the authorship team of this guide and article authors, where acquiring unpublished information was necessary (such as the functional equation for a relative risk function, which are often not published).

It is likely that the least transparent methodology in this guide is the one given for injuries. Although the main relationship between chronic alcohol consumption and injury is taken from the published literature [3], a custom analysis was completed in order to calculate the risk of bingeing as compared to the risk of non-binge drinking, controlling for average drinking volume. This analysis has not been published and therefore the methods are described in Section 3.6. It is currently in preparation for publication and more information on the method is available upon request. We believe this is the only instance in this guide where a published source is not given for the assumptions and values involved in the methodologies.

In terms of full replicability, if you believe this is not the case for some aspect of the AAF methodologies described herein, please email the first author with your concerns and we will be sure to address them and, if necessary, build the comments into the next version of InterMAHP.

Modularity of relative risk functions and estimates

InterMAHP was built in order to make it a simple process to replace the relative risk functions representing the dose-response relationship for current drinkers and the categorical relative risk estimates for former drinkers. This was done to create a program that is easily adaptable to changes which users may wish to make. Although InterMAHP comes with a default set of relative risk functions and estimates (see summary Table 2 and expanded treatment in Section 6), should your team wish to change certain functions and values, they can simply be updated in the relative risk input spreadsheet (see Section 2.2 for more detail).

In this way, InterMAHP can be easily updated at the frontend, with no necessary changes to the backend code, when more recent meta-analyses for a certain condition become available or if your team would prefer to use a region-specific meta-analysis for certain relative risks.

GATHER compatibility

The Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) [4] “define best reporting practices for studies that calculate health estimates for multiple population” (pg.1). GATHER puts forward a checklist of 18 items which are necessary for best reporting practice.

InterMAHP is de facto GATHER compatible, except for item #16, uncertainty estimates. InterMAHP does not currently produce quantitative uncertainty estimates; however, note that subsequent versions of InterMAHP will be expanded to include uncertainty estimates using Monte Carlo simulations.

Section 1: General methods for calculating AA morbidity and mortality

This section provides an overview of the general, non-InterMAHP methods for calculating alcohol-attributable (AA) morbidity and mortality. Significant efforts in the field have previously tackled this issue [1, 5] and so this section provides only a general overview; readers may turn to more comprehensive treatments, if needed, depending on their familiarization with alcohol epidemiology.

The following list provides a step-by-step procedure which, when completed, will produce estimates of AA morbidity and mortality in your region. This list gives an overview, while the rest of this section expands on each step below.

Step, section reference, brief description	Source
(1) Estimate population exposure to alcohol. Described in Section 1.1, 1.1.1 and 1.1.2. Using data available in your region, information must be collected on per capita consumption, relative consumption among gender-age population subgroups and drinking and bingeing prevalences.	Your region
(2) Identify alcohol-related conditions. Described in Section 1.2. Comprehensively review the epidemiological literature to decide which conditions and diseases are definitively caused by alcohol consumption. The InterMAHP standard list is detailed in Table X.	InterMAHP provides standard list
(3) Operationalize alcohol-related conditions. Described in Section 1.3. Typically, medical diagnoses in health databases are represented by ICD10 codes. For each alcohol-related condition identified in Step 2, the ICD10 code(s) corresponding to the condition must be identified (e.g. liver cancer is identified by ICD10 code C22). The InterMAHP crosswalk is specified in Table 1.	InterMAHP provides standard ICD10 crosswalk

- | | |
|---|---|
| <p>(4) Enumerate alcohol-related morbidity and mortality for each condition. Described in Section 1.4. In order to apply AAFs, the total number of morbidities and mortalities for each alcohol-related condition must be enumerated in your region, by population subgroup. See Appendix A in the <i>User's manual</i> for a coded example of the assignment of alcohol-related conditions to record-level Canadian hospitalization data.</p> | <p>Your region</p> |
| <p>(5) Assign alcohol-related conditions as 100% attributable or partially attributable to alcohol. Described in Section 1.5. Wholly/100% attributable conditions have, by definition, AAFs = 1.0, while AAFs for partially attributable conditions must be calculated by either the direct or indirect method.</p> | <p>InterMAHP provides standard list</p> |
| <p>(6) Decide whether to calculate direct or indirect AAFs for partially attributable conditions. Described in Section 1.6.</p> | <p>Your region / InterMAHP provides advice</p> |
| <p>(7) Calculate AAFs for partially attributable conditions. Described comprehensively in Section 3 and briefly in Section 1.7. All partially attributable conditions will need AAFs. These may be either direct or indirect AAFs. InterMAHP will automatically calculate indirect AAFs for all partially attributable alcohol-related conditions.</p> | <p>InterMAHP automatically calculates based on your input</p> |
| <p>(8) Multiply the total number of morbidities and mortality by the appropriate AAFs to arrive at final estimates of harm. Described in Section 1.8. Once total numbers and AAFs are calculated, these two results are multiplied together to produce the burden of AA morbidity and mortality in your region.</p> | <p>Your region</p> |

1.1 Estimating exposure to alcohol, consumption and prevalence

Region-specific data will be required in order to drive the estimation of InterMAHP AAFs based on the unique input from your region. If your team has been working in alcohol research for some time, it is likely that you collectively have strong knowledge of the information sources necessary to estimate the consumption and prevalence data needed to run the InterMAHP program.

Specifically, you will need to acquire: (i) an estimate of per capita alcohol consumption (in litres ethanol per year) for the entire population aged 15+, (ii) a likely survey-based measure of the relative alcohol consumption in the six population subgroups defined by InterMAHP (gender by age groups 15 to 34, 35 to 64, 65+), (iii) by subgroup, the prevalence of current drinkers, (iv) by subgroup, the prevalence of binge drinkers, (v) by subgroup, the prevalence of former drinkers and (vi) by subgroup, the prevalence of lifetime abstainers. These variables are defined in more detailed in Section 2.1.

The calculation of these data requires specific knowledge of the sources of information used, for example the survey design and weighting schema for each prevalence source. It is currently beyond the scope of this document to discuss general survey calculations such as item nonresponse treatment and imputation or weighting and therefore this expertise falls to each region to understand their data sources comprehensively. Additional considerations for calculating these estimates are now discussed.

1.1.1 Estimating total per capita consumption

An estimate of per capita consumption (PCC) for the entire population aged 15 and older in each region and year of interest is necessary as input. There are two sources typically used as basis for these estimates: (1) official sales or tax receipts and (2) survey-based estimates of self-reported consumption. Each source has potential pros and cons, and a detailed review is beyond the scope of this document. However, briefly, official sales or tax receipts will not include spillage (i.e. wasted alcohol), tourist import/exports or alcohol made at home or in make-your-own stores. Conversely, it is well-known that there is significant underreporting of consumption in alcohol surveys, see [6, 7] among many and surveys may miss or under-sample certain drinking groups such as dependent drinkers and students. InterMAHP program is indifferent to your choice and so functionally supports the choice of either method.

Once one of these methods has been decided upon as an estimate basis, you should consider modifying this value based on any additional, region-specific information available on additional factors, such as known imports/exports, spillage, alcohol made at home or in make-your-own stores. These decisions are left to your team as the local-area experts.

The final estimate of PCC, in litres of ethanol per year, will include any of these adjustments which you decide to make and be inputted into InterMAHP as a single figure (e.g. 9.0 litres / year) for the entire population 15+ (not broken down by gender-age population subgroup). The decision was made to import this figure for the population 15+ as this is typically how government sources make the data available at the country, province or state.

The World Health Organizations produces national estimates of recorded + unrecorded alcohol consumption. These estimates are available as part of the Global Information System on Alcohol and Health: <http://www.who.int/gho/alcohol/en/>.

1.1.2 Estimating drinking prevalences and relative consumption, by population subgroup

Survey-based information on drinking prevalences and the relative consumption between population subgroup is necessary input for the InterMAHP program. There are five necessary variables which must be calculated for each of the six population subgroup. More detailed information on each of these variables is provided in Section 2.1 and in the accompanying InterMAHP user's manual.

1.2 Causation and identifying alcohol-related conditions

A foundational step in calculating AA morbidity and mortality is identifying which conditions are causally related to the consumption of alcohol and therefore need to be considered when estimating harms. Identifying alcohol-related conditions has been undertaken over decades by the alcohol epidemiological and medical communities and continues to evolve. Generally, in order for alcohol to be accepted as causative for a condition there must be an overwhelming consensus in the scientific literature on this association.

For InterMAHP v1.0, we have created our condition list from several articles and reports from members of the authorship group [8-10]. The InterMAHP alcohol-related condition list, with operationalizing ICD10 codes, InterMAHP number and condition category are shown in Table 1.

Table 1 is complete with comprehensive causation sourcing, taken from [10], as to the causative link between alcohol and each condition.

A necessary limitation of InterMAHP is the exclusion of Fetal Alcohol Spectrum Disorder (FASD) / Fetal Alcohol Syndrome (FAS) from the list of alcohol-related conditions for which AAFs can be calculated. It is known that mortality data due to FASD/FAS is not well recorded [10]; due to this reason harm estimates may instead be made based on prevalence estimates on drinking during pregnancy [11]. As this prevalence is very different from the more standardized forms of input necessary for InterMAHP, it was decided to omit FASD/FAD from InterMAHP Version 1.0 in order to keep the data limitations more reasonable for regions wishing to implement this methodology.

Additionally, we note that FASD/FAD is a condition which is not experienced by the drinker themselves and therefore falls into the category of harm-to-others. InterMAHP Version 1.0 is currently focused on providing methodologies for calculating harm to drinkers only; however, we note that this is a source of underestimation in the current iteration of InterMAHP.

1.3 Operationalizing alcohol-related conditions using ICD10 codes

Many countries have advanced administrative health data systems; i.e. when patients experience mortalities and morbidities it is commonplace to record their diagnoses and other information such as gender and age and make this information broadly available for researchers. To ensure international comparability, diagnoses are translated into International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD10) codes [12]. This classification is a comparable and comprehensive list of health diagnoses created and maintained by the World Health Organization. In InterMAHP, alcohol-related conditions (e.g. liver cirrhosis) are operationalized by their corresponding ICD10 codes (K70.* and K74.*). InterMAHP gives the example of ICD10 codes to operationalize alcohol-related conditions; however, it should be noted that it is possible to operationalize conditions using other categorizations such as ICD9, DSM-IV or DSM-5, but these definitions are not included in this methodological description of InterMAHP. InterMAHP ICD10 coding is provided in Table 1.

Table 1. InterMAHP alcohol-attributable conditions with groupings, ICD10 codes, and causation references.

Condition Group	Condition	IM #	ICD10 codes (Primary Dx)	ICD10 codes (External)	Partial or 100% attributable	Causation
(1) Communicable Diseases	Tuberculosis	(1).(1)	A15 – A19		Partial	Rehm et al. (2009) [13]
	HIV	(1).(2)	B20 – B24, Z21		Partial	Williams et al. (2016) [14] Rehm et al. (2017) [15]
	Lower respiratory tract infections	(1).(3)	J09 – J22		Partial	Samokhvalov et al. [16] Traphagen et al. [17] Simet & Sisson [18]
(2) Cancer	Oral cavity and pharynx cancer	(2).(1)	C00 – C05, C08 – C10, C12 – C14, D00.0		Partial	All but pancreatic: International Agency for Research on Cancer (2010) [19] International Agency for Research on Cancer (2012) [20] Bagnardi et al. (2016) [21] Pancreatic: Bagnardi et al. (2016) [21]
	Oesophageal cancer, squamous cell carcinoma	(2).(2)	C15, D00.1 (portional only)		Partial	
	Colorectal cancer	(2).(3)	C18 – C21, D01.0-D01.4		Partial	
	Liver cancer	(2).(4)	C22, D01.5		Partial	
	Pancreatic cancer	(2).(5)	C25, D01.7		Partial	
	Laryngeal cancer	(2).(6)	C32, D02.0		Partial	
	Breast cancer	(2).(7)	C50, D05		Partial	
(3) Endocrine conditions	Diabetes mellitus, Type 2	(3).(1)	E11, E13, E14		Partial	Howard et al. (2004) [22]
	Alcohol-induced pseudo-Cushing's syndrome	(3).(2)	E24.4		100%	Alcohol-caused by definition

(4) Neuropsychiatric conditions	Alcoholic psychoses	(4).(1)	F10.0, F10.3 – F10.9		100%	Alcohol-caused by definition
	Alcohol abuse	(4).(2)	F10.1		100%	Alcohol-caused by definition
	Alcohol dependence syndrome	(4).(3)	F10.2		100%	Alcohol-caused by definition
	Degeneration of nervous system due to alcohol	(4).(4)	G31.2		100%	Alcohol-caused by definition
	Epilepsy	(4).(5)	G40, G41		Partial	Bartolomei (2006) [23] Barclay et al. (2008) [24] Leach et al. (2012) [25]
	Alcoholic polyneuropathy	(4).(6)	G62.1		100%	Alcohol-caused by definition
	Alcoholic myopathy	(4).(7)	G72.1		100%	Alcohol-caused by definition
(5) Cardiovascular conditions	Hypertension	(5).(1)	I10 – I15		Partial	Puddey & Beilin (2006) [26] O’Keefe et al. (2014) [27]
	Ischaemic heart disease	(5).(2)	I20 – I25		Partial	Mukamal & Rimm (2001) [28] Collins et al. (2009) [29] Roerecke & Rehm (2014) [30] Zhao et al (2017) [31]
	Alcoholic cardiomyopathy	(5).(3)	I42.6		100%	Alcohol-caused by definition
	Atrial fibrillation and cardiac arrhythmia	(5).(4)	I47 – I49		Partial	Rosenqvist (1998) [32] Mukamal et al. (2012) [33]
	Haemorrhagic stroke	(5).(5)	I60 – I62, I69.0 – I69.2		Partial	Puddey et al. (1999) [34] Mazzaglia et al. (2001) [35]
	Ischaemic stroke	(5).(6)	I63 – I67, I69.3 – I69.4		Partial	Puddey et al. (1999) [34] Mazzaglia et al. (2001) [35] Collins et al. (2009) [29]
	Oesophageal varices	(5).(7)	I85		Partial	Typically caused by liver cirrhosis

(6) Digestive conditions	Alcoholic gastritis	(6).(1)	K29.2		100%	Alcohol-caused by definition
	Liver cirrhosis	(6).(2)	K70,K74		Partial	Gao & Bataller (2011) [36] Rehm et al. (2010) [37]
	Acute pancreatitis	(6).(3)	K85.0 – K85.1, K85.8 – K85.9		Partial	Yadav et al. (2013) [38] Lankisch et al. (2015) [39]
	Chronic pancreatitis	(6).(4)	K86.1 – K86.9		Partial	Lankisch et al. (2015) [39] Braganza et al. (2011) [40] Majumder & Chari (2016) [41]
	Alcohol-induced pancreatitis	(6).(5)	K85.2, K86.0		100%	Alcohol-caused by definition
(7) Motor vehicle collisions	Motor vehicle collisions	(7).(1)		V1*, Y85.0	Partial	Movig et al. (2004) [42] Skog (2001) [43]
(8) Unintentional injuries	Falls	(8).(1)		W00-W19, Y30	Partial	Smith et al. (1999) [44]
	Drowning	(8).(2)		W65 – W74	Partial	Smith et al. (1999) [44]
	Fires	(8).(3)		X00 – X09, Y26	Partial	Smith et al. (1999) [44]
	Accidental poisoning by substances other than alcohol	(8).(4)	T36-T50, T52-T65, T96-T97	X40-X44, X46- X49, Y10-Y14, Y16-Y19	Partial	Smith et al. (1999) [44]
	Accidental poisoning by alcohol	(8).(5)	T51	X45, Y15	100%	Alcohol-caused by definition
	Other unintentional injuries	(8).(6)		V2*, W20 – W64, W75 – W84, X10 – X33, Y20, Y22-Y25, Y27-Y29, Y31- Y34, Y85.9, Y86, Y87.2, Y89.9	Partial	Included in WHO Global Burden of Disease and Global Status Report on Alcohol and Health studies

(9) Intentional injuries	Intentional self-poisoning by substances other than alcohol	(9).(1)	T36-T50, T52-T65, T96-T97	X60-X64, X66-X69	Partial	Smith et al. (1999) [44]
	Intentional self-poisoning by alcohol	(9).(2)	T51	X65	100%	Alcohol-caused by definition
	Other intentional self-harm	(9).(3)		X70-X84, Y87.0	Partial	Included in WHO Global Burden of Disease and Global Status Report on Alcohol and Health studies
	Assault / homicide	(9).(4)		X85 – Y09 Y87.1	Partial	Smith et al. (1999) [44]
	Other intentional injuries	(9).(5)		Y35, Y89.0	Partial	Included in WHO Global Burden of Disease and Global Status Report on Alcohol and Health studies

V1*: V02.1, V02.9, V03.1, V03.9, V04.1, V04.9, V09.2, V09.3, V12.3 – V12.9, V13.3 – V13.9, V14.3 – V14.9, V19.4, V19.5, V19.6, V19.9, V20.3 – V20.9, V21.3 – V21.9, V22.3 – V22.9, V23.3 – V23.9, V24.3 – V24.9, V25.3 – V25.9, V26.3 – V26.9, V27.3 – V27.9, V28.3 – V28.9, V29.4, V29.5, V29.6, V29.9, V30.4 – V30.9, V31.4 – V31.9, V32.4 – V32.9, V33.4 – V33.9, V34.4 – V34.9, V35.4 – V35.9, V36.4 – V36.9, V37.4 – V37.9, V38.4 – V38.9, V39.4, V39.5, V39.6, V39.9, V40.4 – V40.9, V41.4 – V41.9, V42.4 – V42.9, V43.4 – V43.9, V44.4 – V44.9, V45.4 – V45.9, V46.4 – V46.9, V47.4 – V47.9, V48.4 – V48.9, V49.4, V49.5, V49.6, V49.9, V50.4 – V50.9, V51.4 – V51.9, V52.4 – V52.9, V53.4 – V53.9, V54.4 – V54.9, V55.4 – V55.9, V56.4 – V56.9, V57.4 – V57.9, V58.4 – V58.9, V59.4, V59.5, V59.6, V59.9, V60.4 – V60.9, V61.4 – V61.9, V62.4 – V62.9, V63.4 – V63.9, V64.4 – V64.9, V65.4 – V65.9, V66.4 – V66.9, V67.4 – V67.9, V68.4 – V68.9, V69.4, V69.5, V69.6, V69.9, V70.4 – V70.9, V71.4 – V71.9, V72.4 – V72.9, V73.4 – V73.9, V74.4 – V74.9, V75.4 – V75.9, V76.4 – V76.9, V77.4 – V77.9, V78.4 – V78.9, V79.4, V79.5, V79.6, V79.9, V80.3, V80.4, V80.5, V81.1, V82.1, V83.4, V84.4, V85.4, V86.0, V86.1, V86.3, V87.0 – V87.9, V89.2, V89.3, V89.9

V2*: All other ICD10 codes beginning with V.

1.4 Enumerating alcohol-related morbidity and mortality for each condition

This step requires region-specific knowledge on the sources and format of mortality and morbidity databases, the structure and access to which vary greatly by international jurisdiction. For example, in the Canadian context, counts of hospitalization discharges by year, region, condition, gender and age group must be requested from the Canadian Institute for Health Information, the national organizer of all Canadian hospital discharge information. In order to collate similar national mortality data, it is necessary to acquire access to Statistics Canada's Vital Statistics Database, or submit a data request resulting in the same summary. However, in Sweden for mortality, there exists a publicly accessible website called the Swedish Health and Welfare Database which can be used to enumerate mortalities by ICD10 condition code, year, gender and age group. In short, the ease and availability of access to morbidity and mortality is highly dependent on your region and requires varying degrees of analytic sophistication to acquire and analyze. It therefore falls to your local knowledge of your region's health data systems to complete this step.

What is necessary, for each population subgroup of interest, is to tally the number of mortalities and morbidities which occurred for each alcohol-related condition in a given year. Many databases allow for entry of more than one diagnosis on each record or discharge. We must consider when to include the diagnosis codes present in Table 1 in the enumeration of each condition. The default recommendation is, for all non-injury codes, to only count a record as an alcohol-related condition if the corresponding ICD10 code is the primary diagnosis of that record (sometime called most responsible diagnosis, depending on the region). In Table 1, these conditions have ICD10 codes in the ICD10 codes (Primary Dx) column. See Appendix A in the *User's manual* for a SAS-coded example of this assignment for a Canadian example.

Injury categories, and in particular poisonings, must be treated with more care as there are often multiple alcohol-related diagnoses on the same record and they do not necessarily appear in the primary diagnosis position. Consider the following example of a driver involved in a motor vehicle collision with another car (ICD10 code V43.5) which resulted in a broken leg (specifically a fracture of the upper end of the tibia, represented by S82.1). The primary diagnosis, the main reason why the patient is in hospital, is coded as S82.1; however, for our purposes, we require the information that the patient is in the hospital because of a motor vehicle collision. To our knowledge, this is virtually always coded elsewhere on the record; depending on the jurisdiction

this may be recorded as an external cause of injury code or a secondary diagnosis. Again, in short, knowledge of this coding structure, and how to interpret it in relation to alcohol-related injury codes, is a necessary component of any project detailing AA harms.

In our experience, it is best to follow these steps in order to categorize each record (discharge, death record, etc.) as alcohol-related, if necessary:

- (a) First categorize each record by primary diagnosis. This applies to all non-injury conditions, as well as injury poisonings with a primary diagnosis of T36-T65 or T95-T98.
- (b) For records classified as injury poisoning in (a), next search for intent, i.e. whether the poisoning was intentional or accidental. This is done by searching the other diagnoses on the record for the codes listed in Table 2 for (8).(4), (8).(5), (9).(1), (9).(2). Poisonings are often complex in terms of clinical causation and may have multiple ICD10 codes present from this list. We recommend using the first one present as diagnoses are typically listed, at least approximately, in order of importance.
- (c) For remaining records, which will be injury non-poisoning conditions, search for the first alcohol-related external cause code present on the record. These are the codes listed in Table 2, column ICD10 codes (External).

Note: it is important that each record only be counted in one alcohol-related condition category; otherwise it will lead to significant overestimation of alcohol harms, particularly in regards to injury poisonings. To avoid this, the above steps (a) to (c) should be created in a nested if-then coding structure which only allows each record to attain one alcohol-related condition category. See Appendix A in the *User's manual* for a SAS-coded example of this assignment for a Canadian example.

We note a conceptual difference between mortality and morbidity when enumerating these conditions. Mortality, by definition, can only occur once per individual. However, typically “morbidity” here is an event (such as an inpatient hospitalization or emergency department visit) that can be experienced more than once by an individual in a given region/year.

1.4.1 Special considerations for oesophageal cancer

From Table 2, we see a special consideration when operationalizing oesophageal cancer using ICD10 codes. Oesophageal cancer is comprised of two main sub-types: squamous cell

carcinoma (SCC) and adenocarcinoma (AC) [21]. However, alcohol is only causally related to oesophageal SCC [21]. Further, whether oesophageal cancer is SCC or AC cannot be differentiated by the ICD10 coding. It is therefore necessary to acquire a region-specific estimate of the percentage of all oesophageal cancers which are oesophageal SCC and apply this estimate to the enumerated quantity of oesophageal cancers. If this is not done, the number of alcohol-attributable oesophageal cancers will be significantly overestimated.

1.5 Assign alcohol-related conditions as 100% or partially attributable

Section 1.5 to 1.7 will describe three steps necessary to arrive at a comprehensive list of AAFs for each condition, gender and age group. First, alcohol-related conditions are divided into those which are 100% attributable to alcohol and those which are partially attributable to alcohol. 100% (or wholly) attributable conditions are those which are caused by alcohol by definition; conditions are categorized as 100% or partially attributable in Table 1. For example, for alcohol dependence syndrome, F10.2, consumption of alcohol is a necessary condition for development of this condition [45]. In the absence of alcohol, it would not be possible for anyone to develop alcohol dependence: therefore, by definition, the AAF of alcohol dependence syndrome is 1.00.

1.6 Choose between direct and indirect AAFs for partially attributable conditions

From Section 1.5, AAFs are easily defined for 100% attributable conditions. For some of the remaining partially attributable conditions, AAFs may be calculated by either the direct or indirect method. It may be possible to calculate direct AAFs for conditions/events where it is conceptually conceivable to simply test whether involved individuals have consumed alcohol (either by BAC level testing or self-reports) and therefore whether it is likely or certain that alcohol was the cause of the event [5]. Direct AAFs are only applicable to acute conditions, i.e. injuries, and are typically country- or region-specific, as it would be difficult to apply direct AAFs in another context unless the settings are broadly similar [5]. Note further the consideration that direct AAFs implicitly assume that a certain level of alcohol use (e.g. BACs above 0.05%) implies direct causation [5]. Despite these difficulties, it is recommended that, wherever possible by injury category, indirect AAFs calculated by InterMAHP be replaced with region-specific direct AAFs by your project team.

An example where direct AAFs can be calculated is provided by Canadian motor vehicle accident mortalities. A series of annual reports published by the Canadian Council of Motor Transport Administrators tallies the total number of motor vehicle accident fatalities and the proportion of these for which the driver tested positive for alcohol [46]. As we believe that this direct calculation, based on coroner's reports of the deaths in question and immediate testing of blood alcohol content, is more reliable than the calculation of an indirect AAF for motor vehicle collisions, we use this direct AAF when estimating the alcohol-attributable harm from motor vehicle collisions. This example is further illustrated in the InterMAHP user's manual.

1.7 Calculate AAFs for partially attributable conditions

For all other conditions, AAFs will be calculated using the indirect (or epidemiological) method of calculation. Indirect AAFs are calculated using the InterMAHP AAF formula, presented and fully treated in Section 3, which is of the same family of continuous current – categorical former alcohol-attributable fractions as that used by many studies, including the World Health Organization's Global Status Reports on Alcohol and Health [47] and Global Burden of Disease (of alcohol) [48]. Briefly, information on alcohol consumption and prevalence in a region is composed with meta-analyzed relative risk curves representing the dose-response relationship between alcohol and each related condition, as well as the relative risk of former drinkers (see Section 3).

An advancement of InterMAHP is that given the input from your region regarding alcohol consumption and prevalence, the InterMAHP program automates and standardizes the calculation of region-specific indirect AAFs using the detailed methodologies described in Sections 3 and 4. Resulting AAFs will be comparable to other international estimates created using the same set of InterMAHP methodologies, allowing for international benchmarking and comparability.

1.8 Multiply morbidity and mortality counts by AAFs

Lastly, by each year, region, condition, gender and age group, the enumerated count of morbidities and mortalities is multiplied by the AAF for the same cell. The product is the number of alcohol-attributable morbidities and mortalities; these results can then be aggregated any number of ways to provide summary tables and overall estimates of alcohol-attributable harm in your region.

Section 2: InterMAHP inputs

In order to run the InterMAHP program, you will have to understand the input needed. Input is taken into InterMAHP in two spreadsheets (one that is related to alcohol consumption and drinking prevalence and one that is related to relative risk relationships), which must be in .csv format in order to be read into the InterMAHP interface. Each of these spreadsheets, as well as the InterMAHP program interface is now described.

2.1 Consumption and prevalence input

The consumption and prevalence input spreadsheet collects the necessary information from your region regarding per capita consumption, relative drinking between population subgroups and prevalences of current, binge and former drinkers, as well as lifetime abstainers.

The .xls spreadsheet is shown in Figure 1 as it is more readable than the .csv spreadsheet; however, the inputted spreadsheet must be in .csv format. Each variable is then described. It is important to note that the headings, order of the variables and column formatting must be exactly as shown below for InterMAHP to run properly.

Figure 1: Screenshot of InterMAHP consumption and prevalence input spreadsheet

Region	Year	Gender	Age_Group	Population	PCC_litres_year	Correction_factor	Relative_consumption	P_LA	P_FD	P_CD	P_BD
Your region	2013	Female	15 to 34	1193	9.00	0.8	5.6208	0.1004	0.0416	0.858	0.3432
Your region	2013	Female	35 to 64	1823	9.00	0.8	3.5191	0.0753	0.0307	0.894	0.2128
Your region	2013	Female	65+	1009	9.00	0.8	1.8913	0.1346	0.0504	0.815	0.1353
Your region	2013	Male	15 to 34	1254	9.00	0.8	10	0.0995	0.0215	0.879	0.4817
Your region	2013	Male	35 to 64	1863	9.00	0.8	7.1547	0.0321	0.0429	0.925	0.457
Your region	2013	Male	65+	844	9.00	0.8	3.8947	0.0803	0.0417	0.878	0.3415

- (1) **Region** – region name. This is the name of the country, province, state, city or other subregion for which you have the necessary data and would like to study AA morbidity and mortality. Note that multiple regions can be run concurrently.
- (2) **Year** – year of study. Note that multiple years can be run concurrently.
- (3) **Gender** – information is divided by gender
- (4) **Age Group** – information is divided by age group (15 to 34, 35 to 64, 65+)
- (5) **Population** – the population in each of the six gender-age group-defined population subgroups

- (6) **PCC_litres_year** – the best estimate of per capita consumption for the population 15+ in litres of ethanol per year. Notice, this figure is not broken down by population subgroup, it is for the entire population 15+. This was done as this number is typically available in aggregate, i.e. from government sources; it is then automatically divided amongst the population subgroups by the InterMAHP program.

This figure is your region's best estimate of per capita consumption, e.g. for Canadian provinces we begin with government alcohol sales figures and add on estimates of unrecorded alcohol, such as U-Brew, U-Vin and homemade alcohol [49].

Recommendation: the authors highly recommend the use of alcohol sales estimates instead of self-reported, survey-based estimates of per capita consumption; see expanded treatment in Section 1.1.

- (7) **Correction_factor** – a correction factor is applied to per capita consumption to account for the potential overestimate when using recorded + unrecorded consumption values as the epidemiological studies (from which relative risk functions and values are taken) typically have some degree of per capita consumption undercoverage. See Section 3.3 for an expanded treatment including the default value approved by the WHO methodological committee.

- (8) **Relative_consumption** – taken from surveys, this is the relative per person alcohol consumption in each of the six gender-age population subgroups. This information is necessary to apportion the per capita consumption into the six subgroups. In the screenshot above, for example, females aged 15 to 34 are estimated to drink $5.62/10.00 = 56.2\%$ as much as males aged 15 to 34 on a per person basis. In practice, this variable typically comes from surveys which may collect information on the number of standard drinks (SD) per day, SD/week, SD/year, grams/day or any measure of drinking amount per unit time. The unit does not matter, only the relative per person amount in each of the groups.

- (9) **P_LA** – in each population subgroup, the prevalence of lifetime abstainers. Lifetime abstainers are defined as people who have never consumed one standard drink.

- (10) **P_FD** – in each population subgroup, the prevalence of former drinkers. Former drinkers are defined as people who have consumed one standard drink or more in their lifetime, but have not consumed at least one standard drink in the past year.

(11) **P_CD** – in each population subgroup, the prevalence of current drinkers. Defined as people who have consumed one standard drink or more in the past year.

Note: as $P_{LA} + P_{FD} + P_{CD} = 1.00$, by definition, you must only find sources for two of these variables. You could then calculate the third.

(12) **P_BD** – in each population subgroup, the prevalence of binge drinkers among the population (not among drinkers). Defined as people who have consumed at or above the binge drinking level in the past month. The binge drinking level (in grams per day) may be dynamically defined for your region and may be differential by gender. See Section 2.3 for inputting the binge drinking levels in the InterMAHP program interface.

Note on all prevalence values: these must be presented as prevalence proportions (i.e. 0.50) and not percentages (i.e. 50% or 50.0)

2.2 Relative risk input

The relative risk input spreadsheet collects virtually all relative risk information, both for continuous dose-response curves and former drinker RR values, in one location for ease of use, adaptability and transparency.

The .xls spreadsheet is shown in Figure 2 as it is more readable than the .csv spreadsheet; however, the inputted spreadsheet must be in .csv format. Each variable is then described. If this spreadsheet is modified, it is important to keep all formats and the order of variables consistent or it will lead to unpredictable results upon running InterMAHP.

Figure 2: Two-part screenshot of InterMAHP relative risk input spreadsheet

IM	Condition	Gender	Outcome	RR_FD	BingeF	Function	B1	B2	B3	B4
(1).(1)	Tuberculosis	Male	Combined	1.000000	.	FP	0.0000000	0.0000000	0.0000000	0.0000000
(1).(1)	Tuberculosis	Female	Combined	1.000000	.	FP	0.0000000	0.0000000	0.0000000	0.0000000
(1).(2)	HIV	Male	Combined	1.000000	.	Step
(1).(2)	HIV	Female	Combined	1.000000	.	Step

B5	B6	B7	B8	B9	B10	B11	B12	B13	B14	B15	B16
0.0000000	0.0179695	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000
0.0000000	0.0179695	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000
.
.

(1) **IM** – InterMAHP condition number. See Table 1 for correspondence between all alcohol-related conditions and their InterMAHP numbers.

(2) **Condition** – name of alcohol-related condition

- (3) **Gender** - male or female. As many conditions have differential estimates of relative risks for former drinkers, all conditions have one line in the spreadsheet for males and one for females. These can be identical, e.g. tuberculosis, but are often different, e.g. colorectal cancer (different function and RR former value) and liver cancer (same function, but different RR former value).
- (4) **Outcome** – this may be morbidity, mortality or combined. Where supported by the meta-analyses used, relationships are divided by mortality and morbidity; however, for many conditions this division is not present and therefore the curves and values are identical for mortality and morbidity.
- (5) **RR_FD** – for each condition, gender and outcome, the relative risk of former drinkers as compared to lifetime abstainers. For comprehensive sourcing, see Table 2 and Section 6.
- (6) **BingeF** – binge factor which only applies to the three injury categories. All other values are left blank. The binge factor represents the risk ratio of bingers to non-bingers at the same average consumption level; see Section 3.6 for a more comprehensive description.
- (7) **Function** – represents the functional form of the continuous dose-response relationship between alcohol and each condition/gender/outcome. FP stands for the two-term fractional polynomial technique [50, 51] used by the vast majority of authors of alcohol dose-response meta-analyses (see Section 3.2.1 for expanded treatment). There are three exceptions to this: HIV is defined as a step function, while hypertension and acute pancreatitis (women) are defined by splines.

Note: As InterMAHP uses this input spreadsheet to read in RR functions in FP form, they are easily modifiable by simply changed in the form to the function you would like to use using the formula below. However, the relative risk functions for HIV, hypertension and acute pancreatitis are necessarily hardcoded into the SAS backend program due to their complexity and are therefore more difficult to update.
- (8) **B1 to B16** – these 16 variables represents the betas in *Formula 2.1* below. FP2 fractional polynomials must fit the form represented by the formula below, where either one or two of the betas is non-zero. It is therefore easy to represent FP2 functional equations as a series of 16 betas. For example, tuberculosis has $\beta_6 = 0.0179695$, while all other betas are zero. Therefore, from *Formula 2.1*, for tuberculosis, $\ln RR(x) = 0.0179695x$.

$$\begin{aligned}
\ln RR(x) = & \beta_1 x^{-2} + \beta_2 x^{-1} + \beta_3 x^{-\frac{1}{2}} + \beta_4 \ln x + \beta_5 x^{\frac{1}{2}} + \beta_6 x + \\
& \beta_7 x^2 + \beta_8 x^3 + \beta_9 x^{-2} \ln x + \beta_{10} x^{-1} \ln x + \beta_{11} x^{-\frac{1}{2}} \ln x + \\
& \beta_{12} (\ln x)^2 + \beta_{13} x^{\frac{1}{2}} \ln x + \beta_{14} x \ln x + \beta_{15} x^2 \ln x + \beta_{16} x^3 \ln x
\end{aligned}$$

Formula 2.1

2.3 InterMAHP AAF calculator program: User interface

InterMAHP is written in SAS with a graphical user interface as the frontend and the functional code as the backend. The input spreadsheets and AAF program were designed in such a way that is rarely or never necessary for users to modify the backend program. Therefore, no familiarity with the SAS programming language is necessary in order to run InterMAHP; however, SAS must be installed on the computer or server which will be used to run InterMAHP.

Detailed instructions on preparing the input spreadsheet and on the use of the InterMAHP interface are also provided in the User's manual (reference, when ready). This section will provide an overview and screenshot of the interface for a general introduction.

Figure 3: Screenshot of the InterMAHP AAF Calculator program user interface

The screenshot shows the 'InterMAHP AAF Calculator' interface. It includes the following elements:

- File Selection:** Three input fields for file paths, each with a folder icon to the right. They are labeled 'Prevalence and consumption spreads', 'Relative risk spreadsheet', and 'Output directory'. These are numbered 1, 2, and 3 respectively.
- Drinking definitions (g/day):** A section with two columns for 'Women' and 'Men'. Each column has four rows for 'Light', 'Moderate', 'Heavy', and 'Binge' drinking levels. Each row has two input fields (one for the lower limit and one for the upper limit) and a number. These are numbered 4 through 9.
- Upper limit of consumption:** A single input field with the value '250' and a number '10' next to it.
- Dose response extrapolation method:** A section with two radio buttons: 'Capped' and 'Linear'. The 'Linear' option is selected. This section is numbered 11.
- Buttons:** A 'Submit and Run' button at the bottom right.
- Logo:** A circular logo on the right side with the text 'InterMAHP' at the top and 'INTERNATIONAL MODEL OF ALCOHOL HARMS & POLICIES' around the bottom. The center features a world map.
- Version:** 'Version 1.0' is displayed at the bottom left.

As is evident in Figure 3, there are 11 inputs required when you run the InterMAHP program and interact with the program interface.

- (1) Input prevalence and consumption .csv spreadsheet you have prepared for your region(s). Hit the browse button on the right hand side and locate the .csv.
- (2) Input relative risk .csv spreadsheet. Choose to use the InterMAHP- provided relative risk functions and values, or update the ones you have chosen to update. Locate using the browse button on the right hand side.
- (3) Choose an output directory for the program output. For example, desktop or project folder.
- (4) Define the light drinking group for women as the lower limit of consumption (0.03 g/day) to this inputted value in g/day. Throughout the rest of this guide, the value you choose is denoted a_w . The lower limit of consumption (0.03 g/day) is defined as current drinkers are those who have had one standard drink or more in the past year (12g/365=0.03g/day).
- (5) Define the moderate drinking group for women as a_w (as above) to this inputted value in g/day. Throughout the guide, this value is denoted b_w .
- (6) Define the binge level definition for women in your region (or in the survey you are using). Throughout the guide, this value is denoted c_w .
- (7) Identical to (4), except for men. Inputted value denoted a_m .
- (8) Identical to (5), except for men. Inputted value denoted b_m .
- (9) Identical to (6), except for men. Inputted value denoted c_m .
- (10) Define the theoretical upper limit of average daily consumption in your region, based on the best available information. See also Section 4.3. Throughout the guide, this value is denoted z .
- (11) Choose the method used to extrapolate relative risk functions above 150 g/day. See Section 3.2.2 for a comprehensive discussion of this choice.

The logical application of the limits between light and moderate drinkers above leads to the following program restriction:

$$\begin{aligned} a_w &< b_w \\ a_m &< b_m \end{aligned}$$

Program Restriction 1

Note: the difficulty in functional implementing the complex spline function representing the dose-response curve for acute pancreatitis in women leads to the following program restriction. This should not affect your choice of a_w or a_m , as 3g/day is only about one quarter of one drink per day, a very low threshold to divide light and moderate drinkers.

$$a_w \geq 3.0$$

$$a_m \geq 3.0$$

Program Restriction 2

Section 3: Methods for calculating InterMAHP alcohol-attributable fractions

Whereas Section 1 gave a general overview of all necessary steps required for estimating AA morbidity and mortality, this section will give a detailed description of the specific methods used by InterMAHP to calculate AAFs. As discussed in the introduction under replicability, the intent of this guide is to provide methods and sources to the extent that the functionality of the InterMAHP program could be entirely replicated based only the contents presented here. The methods are therefore necessarily comprehensive; to our knowledge, this is the most comprehensive description of continuous current – categorical former AAFs provided in one source.

3.1 Modeling the continuous distribution of alcohol consumption

Methods for modeling the prevalence distribution of alcohol consumption in a population given only per capita consumption have recently been described using the Gamma distribution [52, 53], which is in the same family of distributions as the Lognormal distribution. In effect, this is a functional application of Ledermann's single distribution theory [54], a foundational theory in alcohol research, applied to six population subgroups as opposed to the entire population. In [53], the authors modeled the relationship between the mean (μ) and standard deviation (σ) of per capita consumption in 66 countries and reported that they formed a consistent ratio, by gender. Using this ratio ($\sigma / \mu = 1.258$ for women; $\sigma / \mu = 1.171$ for men) allows us to collapse the usually two-parameter Gamma distribution to a one-parameter distribution [53]. For more information on the choice of the Gamma distribution and the relationship between the mean and standard deviation, read [52, 53]. Note that the Gamma distribution is typically defined through the use of a shape and scale parameter; however, these parameters can also be expressed as formulas containing only the mean, μ , and standard deviation, σ . It is therefore possible, given the gender-specific ratios above, to reduce the shape and scale parameters to expressions containing only μ ; effectively collapsing the Gamma distribution to a single parameter and allowing us to model the prevalence distribution within a defined population subgroup using only the per capita consumption within the subgroup.

This advance allows us to define a Gamma distribution-based prevalence curve, which represents the continuous distribution of current drinkers in a population subgroup, by the following specification:

$$P(x) = \frac{P_{CD}}{nc} f(x; \mu) \quad \textbf{Formula 3.1}$$

where x is average ethanol consumption in grams/day, P_{CD} is the prevalence of current drinkers, for each population subgroup in your region, $f(x; \mu)$ is the probability density function of the Gamma distribution with a given mean μ , nc is a normalizing correction as shown in *Formula 2.2* below and defined in [55] and z is the user-defined upper limit of consumption in your region. If desired, see [52] for the mathematical formulation of the Gamma distribution. For a more detailed treatment of the normalizing constant, nc , and an example in Latvian men, a group with high consumption, see [55].

$$nc = \int_{0.03}^z f(x; \mu) dx \quad \textbf{Formula 3.2}$$

In words, $P(x)$ is the continuous prevalence of drinking at each average daily drinking level x (in grams/day). The normalizing constant, nc , is applied because the usual range of the Gamma distribution is $(0, \infty)$; however, since we restrict the range to $(0.03, z)$ we make a small adjustment so the integration of $P(x)$ over the selected range will equal P_{CD} , the prevalence of current drinkers, which is a requirement of the formulation.

Given this formula and for each population subgroup, we can now mathematically specify the prevalence of drinking at each drinking level x in g/day given only P_{CD} , the prevalence of current drinkers and μ , the mean consumption among drinkers in that subgroup. The resulting drinking prevalence curve for each population subgroup is necessary for the calculation of the InterMAHP AAF, described in section 3.4.

3.2 Relative risks associated with alcohol consumption

There are two risk relationships needed in order to fully specify the InterMAHP AAF formula: (i) for current drinkers - a continuous dose-response relationship between average daily alcohol consumption and the relative risk of conditions morbidity or mortality and (ii) for former drinkers - a categorical relative risk estimate. For each of these relationships, the risk is relative to that of a lifetime abstainer.

3.2.1 Continuous relative risk functions for current drinkers

For each partially attributable alcohol-related condition, a continuous dose-response relationship between average daily ethanol consumption and risk is estimated by using the most up-to-date, comprehensive meta-analysis existing in the alcohol epidemiological literature. This work builds on the foundational work of members of the authorship group, e.g. [8-10] among many. A comprehensive update of continuous relative risk relationships, as well as the categorical risk experience by former drinkers, was recently undertaken by members of the authorship group for the purposes of InterMAHP and updating methodology for the upcoming 2018 Global Status Report on Alcohol and Health, see [10].

This guide necessarily leans heavily on the methods used by the authors of each meta-analysis in regards to modeling the dose-response relationship; however, it is noted that the vast majority of meta-analyses in alcohol epidemiology use the two-term fractional polynomial method of modeling dose-response relationships, described in detail in [51] and initially described in [50]. Briefly, the two-term fractional polynomial (FP2) method tests 36 two-term and 8 one-term polynomials, with coefficients taken from the limited set $[-2, -1, -0.5, 0, 0.5, 1, 2, 3]$ where 0 represents $\ln(x)$ and for a two-term polynomial with powers $p_1 = p_2 = p$, x is represented by the vector $x^p = (x^p, x^p \ln x)$. Two-term polynomials must show statistical preference as compared to the one-term linear model to be selected. More detailed explanations are provided in references [50, 51], as well as in many of the meta-analyses which use the FP2 method.

Table 2 provides a summary table of all partially-attributable alcohol-related conditions in InterMAHP, along with the associated sources for continuous relative risk functions for current drinkers and categorical relative risk values for former drinkers. Notice that for some conditions, there are distinct RR functions by gender, by outcome, or by both. This is based significantly on the amount of epidemiological research that has been done between alcohol consumption and

the condition in question. For example, among the seven cancers for which alcohol is definitively causative, only two (colorectal cancer and breast cancer) have differential dose-response relationships by gender. The meta-analysis used to drive relative risk functions for cancer [21], tested for differential effects by each cancer type; however, only colorectal and breast were differential.

Table 2. Continuous and categorical relative risk sources for partially-attributable alcohol-related conditions

Condition Group	Condition	InterMAHP Number	Gender (Men vs. Women)	Outcome (Morbidity vs. Mortality)	Source for dose-response for current drinkers	Source for RR former drinkers
(1) Communicable diseases	Tuberculosis	(1).(1)	Combined	Combined	Imtiaz et al. (2017) [56] Table 2	N/A as $RR_{FD} = 1.0$
	HIV	(1).(2)	Men	Combined	Rehm et al. (2017) [15]	N/A as $RR_{FD} = 1.0$
			Women	Combined	Rehm et al. (2017) [15]	N/A as $RR_{FD} = 1.0$
	Lower respiratory tract infections	(1).(3)	Combined	Combined	Samokhvalov et al. (2010) [16] Figure 3	N/A as $RR_{FD} = 1.0$
(2) Cancer	Oral cavity and pharynx cancer	(2).(1)	Combined	Combined	Bagnardi et al. (2015) [21] Figure 3	Marron et al. (2009) [57] Table 2
	Oesophageal cancer	(2).(2)	Combined	Combined	Bagnardi et al. (2015) [21] Figure 3	Marron et al. (2009) [57] Table 2
	Colorectal cancer	(2).(3)	Men	Combined	Bagnardi et al. (2015) [21] Table 3	Schütze et al. (2011) [58] Table 2
			Women	Combined	Bagnardi et al. (2015) [21] Table 3	Schütze et al. (2011) [58] Table 2
	Liver cancer	(2).(4)	Combined	Combined	Corrao et al. (2004) [59] Figure 3	Schütze et al. (2011) [58] Table 2
	Pancreatic cancer	(2).(5)	Combined	Combined	Bagnardi et al. (2015) [21] Figure 3	Schütze et al. (2011) [58] Table 2
	Laryngeal cancer	(2).(6)	Combined	Combined	Bagnardi et al. (2015) [21] Figure 3	Marron et al. (2009) [57] Table 2
	Breast cancer	(2).(7)	Combined	Combined	Bagnardi et al. (2015) [21] Figure 3	Schütze et al. (2011) [58] Table 2

(3) Endocrine conditions	Diabetes mellitus, Type 2	(3).(1)	Men	Combined	Knott et al. (2015) [60] Figure 3	Reported in Rehm et al. (2010) [8] from Baliunas et al. (2009) [61]
			Women	Combined	Knott et al. (2015) [60] Figure 3	Reported in Rehm et al. (2010) [8] from Baliunas et al. (2009) [61]
(4) Neuropsychiatric conditions	Epilepsy	(4).(5)	Combined	Combined	Samokhvalov et al. (2010) [62] Figure 3	N/A as $RR_{FD} = 1.0$
(5) Cardiovascular conditions	Hypertension	(5).(1)	Men	Combined	Roerecke et al. (in press)	Roerecke et al. (in press)
			Women	Combined	Roerecke et al. (in press)	Roerecke et al. (in press)
	Ischaemic heart disease	(5).(2)	Men	Mortality two options	Zhao et al. (2017) [31] Table 3	Roerecke & Rehm (2010) [63] Table 3
			Men	Mortality two options	Roerecke & Rehm (2012) [30] Figure 2	Roerecke & Rehm (2010) [63] Table 3
			Women	Mortality	Roerecke & Rehm (2012) [30] Figure 2	Roerecke & Rehm (2010) [63] Table 3
			Men	Morbidity two options	Zhao et al. (2017) [31] Table 3	Roerecke & Rehm (2010) [63] Table 3
			Men	Morbidity two options	Roerecke & Rehm (2012) [30] Figure 2	Roerecke & Rehm (2010) [63] Table 3
			Women	Morbidity	Roerecke & Rehm (2012) [30] Figure 2	Roerecke & Rehm (2010) [63] Table 3
	Atrial fibrillation and cardiac arrhythmia	(5).(4)	Combined	Combined	Samokhvalov et al. (2010) [64] Figure 3	Larsson et al. (2014) [65] Table 1

	Haemorrhagic stroke	(5).(5)	Men	Mortality	Patra et al. (2010) [66] Figure 6	Larsson et al. (2016) [67] Table S2
			Women	Mortality	Patra et al. (2010) [66] Figure 6	Larsson et al. (2016) [67] Table S2
			Men	Morbidity	Patra et al. (2010) [66] Figure 6	Larsson et al. (2016) [67] Table S2
			Women	Morbidity	Patra et al. (2010) [66] Figure 6	Larsson et al. (2016) [67] Table S2
	Ischaemic stroke	(5).(6)	Men	Mortality	Patra et al. (2010) [66] Figure 7	Larsson et al. (2016) [67] Table S2
			Women	Mortality	Patra et al. (2010) [66] Figure 7	Larsson et al. (2016) [67] Table S2
			Men	Morbidity	Patra et al. (2010) [66] Figure 7	Larsson et al. (2016) [67] Table S2
			Women	Morbidity	Patra et al. (2010) [66] Figure 7	Larsson et al. (2016) [67] Table S2
(6) Digestive conditions	Liver cirrhosis	(6).(2)	Men	Mortality	Rehm et al. (2010) [37] Figure 2	Roerecke et al. (in press)
			Women	Mortality	Rehm et al. (2010) [37] Figure 2	Roerecke et al. (in press)
			Men	Morbidity	Rehm et al. (2010) [37] Figure 2	Roerecke et al. (in press)
			Women	Morbidity	Rehm et al. (2010) [37] Figure 2	Roerecke et al. (in press)
	Acute pancreatitis	(6).(3)	Men	Combined	Samokhvalov et al. (2015) [68] Figure 3, Table 2	Samokhvalov et al. (2015) [68] In discussion
			Women	Combined	Samokhvalov et al. (2015) [68] Figure 4, Table 2	Samokhvalov et al. (2015) [68] In discussion
	Chronic pancreatitis	(6).(4)	Combined	Combined	Samokhvalov et al. (2015) [68] Figure 2, Table 2	Samokhvalov et al. (2015) [68] In discussion

(7) Motor vehicle accidents	Motor vehicle accidents	(7).(1)	Combined	Mortality	Dose-response relationship: Corrao et al. (1999) [3] Table 8 Binge-modified factor: custom analysis from NHIS	N/A as $RR_{FD} = 1.0$
			Combined	Morbidity		N/A as $RR_{FD} = 1.0$
(8) Unintentional injuries	Fires, poisonings, falls, drowning, other unintentional	(8).(1) (8).(2) (8).(4) (8).(5) (8).(6)	Combined	Mortality	Dose-response relationship: Corrao et al. (1999) [3] Table 8 Binge-modified factor: custom analysis from NHIS	N/A as $RR_{FD} = 1.0$
			Combined	Morbidity		N/A as $RR_{FD} = 1.0$
(9) Intentional injuries	Self-inflicted injuries, assault/homici de other intentional	(9).(1) (9).(3) (9).(4)	Combined	Mortality	Dose-response relationship: Corrao et al. (1999) [3] Table 8 Binge-modified factor: custom analysis from NHIS	N/A as $RR_{FD} = 1.0$
			Combined	Morbidity		N/A as $RR_{FD} = 1.0$

Section 6 presents a comprehensive treatment of all partially attributable alcohol-related conditions with comprehensive sourcing for continuous dose-response relationships and categorical relative risks for former drinkers. The section provides a detailed one-page report for each condition (possibly divided by gender and outcome differences), including comprehensive sourcing, graphs depicting continuous RR curves and notes on methods and abstainer biases.

Note that for oesophageal varices, which are usually caused by scar tissue in the liver due to liver disease, the same AAF as that used for liver cirrhosis is used, by subgroup. For this reason, the condition oesophageal varices does not have a separate page summary in Section 6. This method of estimation is also described in the worked example in the User's manual.

3.2.2 Special case: choosing relative risk functions for ischaemic heart disease in males

As can be seen from Table 2, for virtually all conditions InterMAHP provides a default source for dose-response and categorical former relative risk relationships. However, an important and potentially controversial choice is the source of the dose-response relationship between alcohol drinking and ischaemic heart disease (IHD) morbidity and mortality in males.

To recognize and encourage this debate, we provide two options for each of IHD morbidity in men and IHD mortality in men. Project teams can decide among the options below based on their interpretation and understanding of the literature of the cardioprotective effect of alcohol. The two options are Zhao et al. [31] and Roerecke & Rehm [30]. Zhao et al. is a more recent meta-analysis studying the relationship between consumption and IHD mortality. Further, this article explicitly accounts for abstainer biases and there is also accounting for the mean age of the epidemiological cohorts which constitute the meta-analysis as a means of controlling for other forms of lifetime selection bias. However, continuous, gender-differential relative risk functions were not calculated as part of the article. Upon request, J. Zhao produced a continuous risk function based on the results presented in the top panel of Table 3 for IHD mortality in men. This shows no cardioprotection at any level of alcohol intake but, rather, a continuous increasing risk of IHD with rising consumption. Due to the small number of studies studying women, an analogous curve could not be created for women. Nonetheless, the categorical risk relationship for women indicated some cardioprotection for low volume alcohol intake, consistent with Roerecke and Rehm [30]. Roerecke & Rehm [30] does not explicitly account for abstainer biases at the study design stage; however, the authors account for abstainer bias by reweighting relative

risk results from studies which pooled former and never drinkers together. They do not take account of other potential lifetime selection biases however that may come into play with studies recruiting participants later in life.

It is the responsibility of your project team to understand these possible sources and to decide among them based your understanding of the literature. Note that it may be prudent to choose a primary method and also a secondary method, which may then be used as a sensitivity analysis.

These choices lead to the following options:

- (1) Use Zhao et al. [31] for IHD mortality in men and Roerecke & Rehm [30] for IHD morbidity in men. This is the option which comes pre-loaded into the InterMAHP relative risk spreadsheet. However, unlike other conditions, this does not represent the InterMAHP default (there is no InterMAHP default for IHD mortality and morbidity in men). This choice results in a consistent pattern of gender-based risk relationships to those reported by Knott et al [60] in relation to Diabetes Mellitus, one other condition where protective effects of low volume alcohol use are sometimes observed: i.e. some protection for women but not men.
- (2) Use Zhao et al. [31] for both IHD mortality and morbidity in men. The IHD mortality curve calculated by J. Zhao would here be used for IHD morbidity. This may result in a overestimate of IHD morbidity in men as, in most conditions, mortality RRs tend to be higher than for morbidity at equivalent consumption levels. However, it assumes that controlling for lifetime selection bias has a more profound effect resulting in more accurate estimates overall.
- (3) Use Roerecke & Rehm [30] for both IHD mortality and morbidity in men. Separate curves for mortality and morbidity are taken from Figure 2. This choice has the advantage of providing a consistent source for continuous risk relationships for both mortality and morbidity, for both men and women. However, it assumes cardio-protection for males at all levels of alcohol consumption.

Both options for IHD mortality and IHD morbidity are included in the relative risk one-pagers presented in Section 6. Recall, also, that changing between relative risk functions for IHD mortality and morbidity is as simple as replacing one line in the relative risk input spreadsheet. All

calculations will then follow through the InterMAHP AAF calculations. This choice has significant implications for the final estimate of overall alcohol-attributable harm as IHD is the one of the most common causes of mortality and morbidity and the two methods may give significantly different estimates depending on consumption and prevalence in the region under study. We note that, in addition to Zhao et al. [31], multiple skeptical perspectives on alcohol and cardioprotection [69-74], as well as alcohol and protection from all-cause mortality [75-77] have been recently published. This is balanced by meta-analyses [30, 63, 78, 79] and most observational studies, which do show a cardioprotective effect. It is critical that your team understand this literature and make a final decision which best suits interpretation in your region.

3.2.3 Extrapolating relative risk functions in InterMAHP

Previous WHO Global Burden of Disease (of alcohol) [48] and Global Status Reports on Alcohol and Health [47, 80, 81] have defined the upper limit of consumption at 150 g/day, which necessarily has the effect of truncating relative risk functions above 150g/day. However, research has suggested that truncating the consumption distribution and relative risk functions at 150 g/day can lead to significant underestimation of AAFs [55]. In [55], the authors conclude that restricting the upper limit of consumption to 150g/day may have led to the underestimation of alcohol-attributable mortality in the European Union by as much as 25.5% in men and 8.0% in women.

This, combined with evidence from Canada showing that individuals taking part in Managed Alcohol Programs (MAPs) chronically consume *on average* about 250 g/day ethanol [82], suggests that providing users with the ability to increase their region's upper limit of consumption beyond 150g/day may be wise. We have therefore built the ability into the InterMAHP program for the user to dynamically define the upper limit of consumption based on region-specific information.

If an upper limit of consumption above 150g/day is chosen, it is necessary to outline the methodology used to define relative risk curves above 150 g/day.

Firstly, consider using the functional equation representing the relative risk curve at consumption levels above 150 g/day. As can be seen by a detailed study of the relative risk one-pagers in Section 6, for some conditions this would result in an extremely steep, nearly vertical

relative risk function above 150 g/day (see (6).(2) liver cirrhosis mortality, men for example). The authors of the fractional polynomial modeling technique, in [51], describe how the FP2 technique should not be used to extrapolate relative risk values too far outside the range of observed data; this is also a general statistical principle. We have therefore decided not to allow relative risks to be extrapolated using the functional relative risk equations themselves, in order to err on the side of the conservative.

InterMAHP therefore allows the user to decide between two different methods of extrapolation for relative risk curves above 150 g/day. These are:

- (1) Capped – in this method, the continuous relative risk function is simply capped at the value it reaches at 150 g/day. It takes on this value of $RR(150)$ for all consumption levels above 150 g/day. See the relative risk one-pagers for each condition/gender/outcome in Section 6 for graphs of this method.
- (2) Linear – based on linear extrapolation of the slope calculated between 100 and 150 g/day. Here, the average slope of the relative risk function between 100 and 150 g/day is calculated using *Formula 3.3* below. For values above 150 g/day, the relative risk is then calculated using *Formula 3.4*.

$$slope = \frac{RR(150) - RR(100)}{150 - 100} \quad \textbf{Formula 3.3}$$

$$RR(x > 150) = RR(150) + slope(x - 150) \quad \textbf{Formula 3.4}$$

We note that the default choice in InterMAHP is the more conservative capped method. The linear extrapolation method is based loosely on the online appendix of [55]; however, all functions are extrapolated beginning at 150 g/day for consistency.

3.2.4 Extrapolating relative risk functions for ischaemic heart disease

The methodology above applies to all conditions, except for ischaemic heart disease. Due to the volatile nature of several IHD relative risk functions beginning at approximately 125g/day, the methodology above is modified by capping IHD functions at $RR(100)$ for the capped method and extrapolating the linear slope from $x=50$ to $x=100$ beyond $RR(100)$ for the linear method.

3.2.5 Categorical relative risk estimates for former drinkers

The second piece of the relative risk puzzle for each condition/gender/outcome is a relative risk estimate for former drinkers. Table 2 shows a summary table of all former drinker relative risk sources. Section 6 provides relative risk one-pagers which comprehensively describe the source and, if necessary, calculations or justifications for our choices of former drinker relative risks

3.3 Considerations in matching per capita consumption to epidemiological studies

A final discussion before moving to the calculation of InterMAHP AAFs concerns the applicability of the gathered per capita consumption data to that used by epidemiological studies to calculate relative risk estimates and functions. The per capita consumption estimate in the consumption and prevalence input spreadsheet used by InterMAHP should be the most comprehensive estimate of PCC available in your region. However, we note that self-reported consumption in epidemiological studies may be underreported as compared to a measure of recorded + unrecorded consumption and this may affect the comparability of this estimate with consumption estimates used to produce epidemiological relative risks.

Authors TS and AS are currently working on a study, in international context, which will estimate the coverage of self-reported consumption in epidemiological studies as compared with figures of recorded and unrecorded consumption. However, this research is not yet complete. We therefore revert to precedent for InterMAHP Version 1.0: previous iterations of the Global Status Reports on Alcohol and Health [47] and the Global Burden of Disease (of alcohol) studies [48] have used a correction factor of 0.8 in order to marginally deflate the measure of PCC to be more in line with that captured by the epidemiological studies producing relative risk estimate. This value of 0.8 has been based on the recommendation of the technical advisory committee for the World Health Organization.

Note, however, that this correction factor, as it is called in the consumption and prevalence input spreadsheet (see Section 2.1), is easily modifiable and so if your region has other data on which to rely, the input value is easily modified.

3.4 InterMAHP alcohol-attributable fraction methodology

The continuous drinking curves and dose-response relationships, as well as the categorical prevalence of former drinkers and relative risks, described in the preceding sections, are now composed together to calculate InterMAHP alcohol-attributable fractions.

The specification of the InterMAHP indirect AAF is the following formulation which uses a continuous distribution of current drinkers and a categorical definition of former drinkers. It is of the same family of continuous current – categorical former alcohol-attributable fractions as that used by the World Health Organization to produce the Global Status Reports on Alcohol and Health [47] and the Global Burden of Disease (of alcohol) studies [48]. Previous research by members of the authorship team has suggested that continuous attributable fractions are more mathematically appropriate than categorical attributable fractions where the data exists to model continuous exposures and relative risks [53]. Further, we note that a continuous attributable fraction is the natural formulation; clearly, natural exposure to alcohol occurs in a continuous and not categorical manner.

The following specification is therefore used for all partially attributable alcohol-related conditions, except for three conditions which are modified by bingeing behaviour: (1) ischaemic heart disease and (2) ischaemic stroke and (3) injuries (these are discussed later). The InterMAHP AAF for all other conditions is specified by the following general form (for each population subgroup):

$$AAF = \frac{P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx}{1 + P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx} \quad \textbf{Formula 3.5}$$

where P_{FD} is the prevalence of former drinkers, RR_{FD} is the categorical relative risk of former drinkers, $P(x)$ is the distribution of current drinking at level x in grams of ethanol per day as defined in *Formula 3.1*, $RR(x)$ is the continuous relative risk for each condition-gender-outcome, 0.03 is the lower limit of consumption (defined as one standard drink in the previous year = 12g/365) and z is the user-defined upper limit of daily consumption.

Formula 3.5 is an excess risk (also called classical or Levin) formulation of the AAF [83], using the excess risk quantity of $RR - 1$, multiplied by population prevalences, to arrive at the

attributable fraction result. We note that this formula, save for differing limits of integration, is mathematically identical to the second formula presented in [53]; however, composition of the formula is significantly altered and so this may be difficult to discern. We suggest InterMAHP's *Formula 3.5* is a more intuitive and flexible formulation of a continuous current – categorical former AAF and we therefore use this formulation throughout this document. Specifically, preserving the denominator value as the total risk experienced by the population in regards to a particular condition (i.e. 1 + the excess risk of alcohol consumption), allows the unique decomposition of the numerator in order to study different drinking groups, such as light, moderate and heavy drinkers. This additional functionality is given more detailed treatment in Section 4.

Note further that in [53], the $\frac{P_{CD}}{nc}$ term is implicitly defined as a component of $P(x)$, while in *Formula 3.1* it is explicitly defined. However, it is important to state that this adjustment must always be present in the calculation of any continuous AAF calculation using the Gamma distribution.

3.5 Special cases of InterMAHP AAFs 1: Ischaemic heart disease and ischaemic stroke

The dose-response risk relationships between ischaemic heart disease (IHD) and ischaemic stroke (IS) and alcohol drinking are modified by bingeing behaviour by the removal of the protective effect for persons engaged in binge drinking [30, 84, 85]. The removal of this protective effect for ischaemic conditions is paralleled in recent versions of the WHO's Global Burden of Disease studies [48, 86] and Global Status Reports on Alcohol and Health [47]. *Formula 3.5* is therefore modified for these two conditions by the following steps:

1. For each gender-age subgroup, the prevalence of current drinkers who drink above the threshold which defines binge drinking is calculated. These drinkers are guaranteed to be bingers since their daily consumption is above the binge level. We define the prevalence of these drinkers as P_{BAT} , where BAT stands for bingers above threshold. The prevalence is calculated as:

$$P_{BAT} = \int_c^z P(x)dx \quad \textbf{Formula 3.6}$$

where c is the gender-specific, user-defined binge level, other quantities are as defined in *Formula 3.5*.

Note: Although quite rare, it is possible that the Gamma-calculated P_{BAT} is greater than the survey-defined P_{BD} for a particular region and population subgroup. In testing using dozens of global regions, this occurred only for region-subgroups with a very low prevalence of current drinkers. Further, the effects on the AAFs were exceedingly small. However, for accuracy, the following automatic check and correction is completed by InterMAHP:

- a) InterMAHP checks to ensure that the Gamma-calculated P_{BAT} is less than the survey- and input-defined P_{BD} . If this is not the case, InterMAHP sets $P_{BAT}=P_{BD}$.
- b) Further, if $P_{BAT}>P_{BD}$, mathematically it means that the integral portion

$\int_c^z P(x)[RR_{BD}(x) - 1]dx$ in *Formula 3.6* below has been overestimated. It is

therefore deflated by a factor of $\frac{P_{BD}}{P_{BAT}}$.

2. The remaining prevalence of *bingers below threshold* (drinkers who binge, but do not consume above the binge threshold daily) is then found as $P_{BBT} = P_{BD} - P_{BAT}$. where P_{BD} is the survey-defined prevalence of binge drinking in your region and is from the consumption and prevalence input spreadsheet.
3. Now that the prevalence of bingeing has been divided into those above and below threshold, the AAF formula is modified in the following way for IHD and IS, where the AAF numerator becomes:

$$\begin{aligned}
AAF(numerator) = & P_{FD}[RR_{FD} - 1] \\
& + \left[\frac{P_{CD} - P_{BD}}{P_{CD} - P_{BAT}} \right] \int_{0.03}^c P(x)[RR(x) - 1] dx \\
& + \left[\frac{P_{BD} - P_{BAT}}{P_{CD} - P_{BAT}} \right] \int_{0.03}^c P(x)[RR_{BD}(x) - 1] dx \\
& + \int_c^z P(x)[RR_{BD}(x) - 1] dx
\end{aligned}
\tag{Formula 3.7}$$

and the complete alcohol-attributable fraction is calculated by:

$$AAF = \frac{AAF(numerator)}{1 + AAF(numerator)}
\tag{Formula 3.8}$$

All quantities in *Formula 3.6* have been previously defined in *Formula 3.5*, except for:

$$RR_{BD}(x) = \max(RR(x), 1)
\tag{Formula 3.9}$$

Formula 3.9 has the straightforward effect of removing the protective effect for binge drinkers when $RR(x) < 1$.

3.6 Special cases of InterMAHP AAFs 2: Injuries

The current InterMAHP method for injuries was formulated and tested at an Alcohol and Injury Working Group including authors JR, KDS and AS, as well as members of Alcohol Research Group (ARG). The method is a distributional method based on the relationship between average alcohol consumption and the meta-analyzed risk of injury [3]. It is similar in concept and builds upon methods recently used by the World Health Organization [87] and members of the authorship team; however, the binge-specific component of the formula will now be based on region-specific and user-inputted data regarding the prevalence of binge drinking, instead of on a scaling constant as previously.

The modified structure of the attributable fraction formula is identical to that discussed above for IHD and IS in Section 2.5 where the prevalence of certain bingers is first calculated from the gender-specific binge definition and the Gamma distribution. For injuries, however, there is no excess risk for former drinkers and the binge-modified AAF becomes:

$$\begin{aligned}
 AAF(numerator) &= \left[\frac{P_{CD} - P_{BD}}{P_{CD} - P_{CB}} \right] \int_{0.03}^c P(x) [RR(x) - 1] dx \\
 &+ \left[\frac{P_{BD} - P_{CB}}{P_{CD} - P_{CB}} \right] \int_{0.03}^c P(x) [RR_{BD,i}(x) - 1] dx \quad \textbf{Formula 3.9} \\
 &+ \int_c^z P(x) [RR_{BD,i}(x) - 1] dx
 \end{aligned}$$

where $RR(x)$ is the general risk of injury at consumption level x , from [3]. All other quantities in have been previously defined in *Formula 3.5*, except:

$$RR_{BD,i}(x) = BingeFactor_i * RR(x) \quad \textbf{Formula 3.10}$$

where i represents each of three injury categories.

In InterMAHP, injuries are divided into three categories: motor vehicle collisions, intentional injuries and unintentional injuries. See also the relative risk section for more information on the relative risk curves representing injuries. The complete attributable fraction is again calculated using *Formula 3.8*.

InterMAHP binge factors ($BingeFactor_i$ above) represent the ratio of the relative risk of bingers divided by non-bingers at the same average consumption level, and so conceptually capture the risk of bingeing over and above that of non-binge consumption. Risk ratios were calculated for this project using linked data on drinking, bingeing and mortality from 134,237 individuals in the National Health Interview Survey, a representative survey conducted in the United States by the U.S. Census Bureau. The calculated binge factors were 1.49 for MVCs, 1.70 for intentional injury and 1.48 for unintentional injury.

3.7 Section note

It is important to note that throughout Section 3 and 4, there are many formulas which use the user-defined limits a , b and c . Recall that for each of these, there are actually two values, differentiated by gender: $a_w, b_w, c_w, a_m, b_m, c_m$.

For each formula presented in these sections, these are generalized by dropping the subscript terms and only using a , b and c ; however, functionally in the InterMAHP program there are two formulas, one specific to women and one to men, for each formula presented here which includes one or more of these terms. This is done for ease of presentation and description in the guide.

Section 4: Methods for additional InterMAHP functionality

This section treats several added components to functionality in InterMAHP which are more specific than the general methods described above. To our knowledge, these functional additions are novel to continuous current – categorical former formulations of alcohol-attributable fractions in the literature.

4.1 Calculating InterMAHP AAFs by drinking categories: General case

A significant advance of InterMAHP is the built-in functionality to calculate the alcohol-attributable harm experienced by different categories of drinkers. This built-in ability allows users to dynamically specify drinking categories and receive as output alcohol-attributable fractions for four drinking categories: former drinkers, light drinkers, moderate drinkers and heavy drinkers. Users state, on the input screen of the InterMAHP user interface, the average consumption level in grams per day which defines low, moderate and heavy drinkers in their jurisdiction. More details on specifying the limits of light, moderate and heavy drinkers can be found in the InterMAHP User's Manual.

Recall from Formula 2.2 that InterMAHP's AAF formula is defined as the excess risk formulation of the population attributable fraction formula (repeated here as *Formula 3.5* for ease of reference):

$$AAF = \frac{P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx}{1 + P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx} \quad \textbf{Formula 4.1}$$

Defined in this way, it is possible to decompose the numerator into constituent pieces and describe different proportions of the total alcohol-attributable fraction. For example, let the user-specified drinking define light drinkers as those who drink between 0.03 and a grams/day ethanol, moderate drinkers as those who drink between a and b and heavy drinkers those who drink between b and z , where z is the user-defined upper limit of consumption. The integral in the AAF formula can be decomposed as follows to study four drinking groups, as below. Note, the numerator and denominator are presented separately only for readability, as the formula is difficult to read when collapsed into one.

$$\begin{aligned}
AAF(numerator) &= P_{FD}[RR_{FD} - 1] \\
&+ \int_{0.03}^a P(x)[RR(x) - 1] dx \\
&+ \int_a^b P(x)[RR(x) - 1] dx + \int_b^z P(x)[RR(x) - 1] dx
\end{aligned}$$

Formula 4.2

$$\begin{aligned}
AAF(denominator) \\
&= 1 + P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx
\end{aligned}$$

Formula 4.3

$$AAF = \frac{AAF(numerator)}{AAF(demoninator)}$$

Formula 4.4

Studying *Formula 4.2* allows us to define this decomposition more explicitly; we have the following attributable fraction formulas for the four drinking groups:

$$AAF_{FD} = \frac{P_{FD}[RR_{FD} - 1]}{1 + P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx}$$

Formula 4.5

$$AAF_{LD} = \frac{\int_{0.03}^a P(x)[RR(x) - 1] dx}{1 + P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx}$$

Formula 4.6

$$AAF_{MD} = \frac{\int_a^b P(x)[RR(x) - 1] dx}{1 + P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx}$$

Formula 4.7

$$AAF_{HD} = \frac{\int_b^z P(x)[RR(x) - 1] dx}{1 + P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx} \quad \textbf{Formula 4.8}$$

Where, for each gender, AAF_{FD} is the attributable fraction for former drinkers, AAF_{LD} is the attributable fraction for light drinkers (defined between 0.03 and a_w for women and between 0.03 and a_m for men, AAF_{MD} is the attributable fraction for moderate drinkers (defined between a_w and b_w for women and a_m and b_m for men) and AAF_{HD} is the attributable fraction for heavy drinkers (defined between b_w and z for women and b_m and z for men).

It is then important to note that the four components above sum to the whole as below, meaning we can choose to study drinking groups, but if this is not our objective, the components may be ignored and the sum total used to study total alcohol-attributable harm.

$$AAF_{Total} = AAF_{FD} + AAF_{LD} + AAF_{MD} + AAF_{HD} \quad \textbf{Formula 4.9}$$

4.2 Calculating InterMAHP AAFs by drinking categories: Special cases

As the specification of AAF components for the three AAF binge-modified cases are the most mathematically complex scenario, a program restriction is introduced into InterMAHP to make the programming possible (described below). Note that the special cases of IHD, IS and injuries are nearly identical except for a differing $RR_{BD}(x)$ function within them. Recalling the differing definition of $RR_{BD}(x)$ from *Formula 3.7* and *Formula 3.9* allows us to define the below decomposition for all three special cases together; the AAF numerator components for the four drinking categories become:

$$AAF_{FD}(\text{numerator}) = P_{FD}[RR_{FD} - 1] \quad \textbf{Formula 4.10}$$

$AAF_{LD}(\text{numerator})$

$$= \left[\frac{P_{CD} - P_{BD}}{P_{CD} - P_{BAT}} \right] \int_{0.03}^a P(x)[RR(x) - 1] dx$$

$$+ \left[\frac{P_{BD} - P_{BAT}}{P_{CD} - P_{BAT}} \right] \int_{0.03}^a P(x)[RR_{BD}(x) - 1] dx$$

Formula 4.11

$AAF_{MD}(\text{numerator})$

$$= \left[\frac{P_{CD} - P_{BD}}{P_{CD} - P_{BAT}} \right] \int_a^b P(x)[RR(x) - 1] dx$$

$$+ \left[\frac{P_{BD} - P_{BAT}}{P_{CD} - P_{BAT}} \right] \int_a^b P(x)[RR_{BD}(x) - 1] dx$$

Formula 4.12

$AAF_{HD}(\text{numerator})$

$$= \left[\frac{P_{CD} - P_{BD}}{P_{CD} - P_{BAT}} \right] \int_b^c P(x)[RR(x) - 1] dx$$

$$+ \left[\frac{P_{BD} - P_{BAT}}{P_{CD} - P_{BAT}} \right] \int_b^c P(x)[RR_{BD}(x) - 1] dx$$

$$+ \int_c^z P(x)[RR_{BD}(x) - 1] dx$$

Formula 4.13

Lastly, the AAF for each of the four drinking groups is calculated using the following formula and by replacing the numerator with each of the four drinking groups - only the example of former drinkers(AAF_{FD}) is shown, but the other three are exactly analogous.

$$AAF_{FD} = \frac{AAF_{FD}(numerator)}{1 + AAF_{FD}(num) + AAF_{LD}(num) + AAF_{MD}(num) + AAF_{HD}(num)} \quad \mathbf{F\,4.14}$$

Recall, in *Formula 4.13*, that b is the user-defined boundary between moderate and heavy drinkers in grams per day and c is the user-defined and gender-specific definition of bingeing. Due to this calculation, a program restriction is introduced to ensure the programming is possible: the user-defined boundary between moderate and heavy drinking, b , must be less than or equal to the definition of binge drinking, c (for each gender):

$$\begin{aligned} b_w &< c_w \\ b_m &< c_m \end{aligned} \quad \mathbf{Program\,Restriction\,3}$$

4.3 Dynamic upper limit of consumption, z

To our knowledge, an AAF calculator with a dynamic upper limit of consumption has not previously been created. InterMAHP allows, on the AAF calculator input screen, the user to define the upper limit of consumption which is most appropriate for their region, based on available evidence.

As discussed in Section 3.2.2, previous studies by the WHO [47, 80, 81, 86] have defined the upper limit of consumption at 150 g/day. However, research suggests that capping the alcohol consumption distribution and relative risk functions can lead to significantly lower AAFs [55]. Combined with evidence from Canada showing that individuals taking part in Managed Alcohol Programs (MAPs) chronically consume *on average* about 250 g/day ethanol [82], it is necessary to provide InterMAHP users with the ability to increase their region's upper limit of consumption beyond 150g/day may be wise.

Therefore, users have the ability to define the upper limit of consumption, z in the formula below (reproduction of *Formula 3.5* for ease of reference):

$$AAF = \frac{P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx}{1 + P_{FD}[RR_{FD} - 1] + \int_{0.03}^z P(x)[RR(x) - 1] dx} \quad \textbf{Formula 4.15}$$

Since all relative risk curves are monotonically increasing after approximately 60g/day ethanol, increasing the upper limit of consumption, z , will produce higher AAF values. However; the value z in your region should be chosen based on available region-specific evidence regarding the upper limit of chronic daily consumption.

Section 5: InterMAHP program defaults, suggested referencing and program restrictions

5.1 Program defaults

The following is a list of default InterMAHP settings. These are included towards comparability (i.e. results produced using these settings are the “base case” and may be more comparable to those produced by other jurisdictions) and ease of referencing InterMAHP.

- 1) Relative risk functions and values. Default relative risk functions and values are included in the downloaded package as the relative risk input spreadsheets (.xls and .csv). This applies to all conditions *except* for the two relative risk functions representing IHD mortality and morbidity in men. There is no default InterMAHP function for these two categories and so your choice must always be described in the statement referencing the use of InterMAHP.
- 2) Correction factor = 0.8. Described in Section 3.3, a factor of 0.8 is used as the default to align with the decision made by the World Health Organization’s technical advisory committee.
- 3) Upper limit of consumption, $z=250\text{g/day}$. Described in Section 4.3, evidence from Canada suggests this may be an appropriate upper limit of consumption in the Canadian context.
- 4) Relative risk extrapolation method = capped. Described in Sections 3.2.3 and 3.2.4, choosing the capped method of extrapolation will result in more conservative estimates of alcohol harms.

There are no program defaults for the values a_w , b_w , c_w , a_m , b_m or c_m . The choices of these variables must always be described in the methods section which references InterMAHP.

5.2 Suggested referencing

Suggested citations for InterMAHP products (program suite, this *Guide* and the *User’s manual*) are as shown before the table of contents in this document.

This section is about referencing the use of InterMAHP in the methods section of reports and articles produced using InterMAHP methodology, specifically changes to the program defaults above and how to reference additional decisions that must be made.

It is most clear if each decision made when running InterMAHP is explicitly referenced. For example, when running the default settings above to calculate total AAFs, the following could be written: “To calculate AAFs for this project, we used the International Model of Alcohol Harms and Policies (reference). For the relative risk function relating IHD mortality in males and consumption we used Zhao et al. [31], while for IHD morbidity in men we used Roerecke & Rehm [30]. (Provide your rationale for this choice). We used the following dynamic parameters when running the InterMAHP program: a correction factor of 0.8, an upper limit of consumption of 250g/day and the capped relative risk extrapolation method described in (reference). The definition of bingeing used was 53.8g/day for women and 67.3g/day for men (note: these are Canadian values of 4+/5+ standard drinks).”

It is left to your discretion in what detail the general methodologies within this guide are described in calculating AAFs. Further, if you are using InterMAHP to apportion harm to drinking groups (former, light, moderate and heavy drinkers), you will need to detail your choices of a_w , b_w , a_m and b_m ; which divide drinking categories

5.3 Program restrictions

Collecting the program restrictions described in this guide in Sections 2.3 and 4.2 allows us to collapse the separate restrictions into the following relationship, by gender. We also add an upper limit above which the binge level, c , cannot be set. It is a very high level of consumption, though, and so should not affect your choices of limits.

$$3.0 \leq a_w < b_w < c_w \leq 150$$

$$3.0 \leq a_m < b_m < c_m \leq 150$$

Overall Program Restrictions

Section 6: Relative risk summary pages

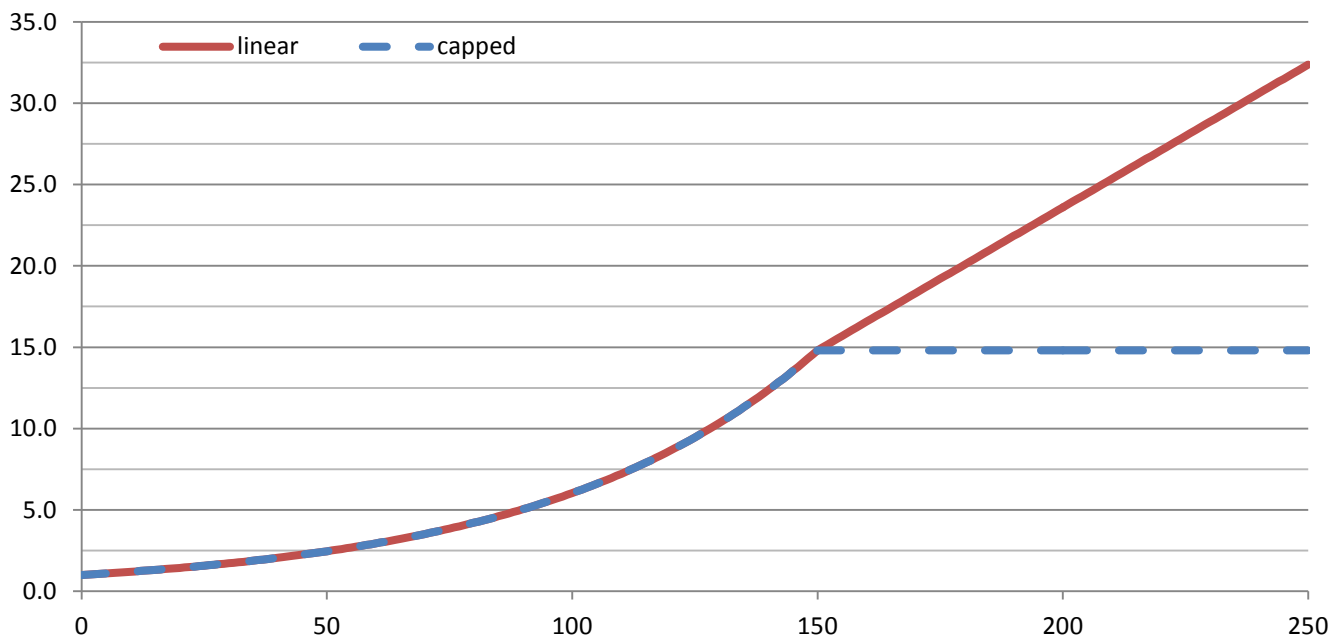
For each partially-attributable alcohol-related condition, the following section provides a one page reference with all source information, relative risk functions and values, ICD10 codes, comments and considerations regarding how studies controlled for abstainer biases, as well as figures depicting the dose-response relative risk functions.

Note that for the figures, the vertical and horizontal axes are not labeled due to space restrictions: the horizontal axis represents average alcohol consumption in grams per day and the vertical axis corresponds to the relative risk as compared to lifetime abstainers.

(1).(1) Tuberculosis

Condition category: (1) Communicable diseases
ICD10 codes: A15 to A19

	Current drinkers	Former drinkers
Source	Imtiaz et al. (2017) Table 2	There is no increased risk for former drinkers
Relative risk Equation or estimate	$\ln RR(x) = 0.0179695x$ $RR(x) = \exp(0.0179695x)$	$RR_{FD} = 1.00$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Note coefficient presented in Table 2 is $\exp(0.0179695) = \text{round}(1.0181)$.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Not applicable. There is no increased risk for former drinkers.	



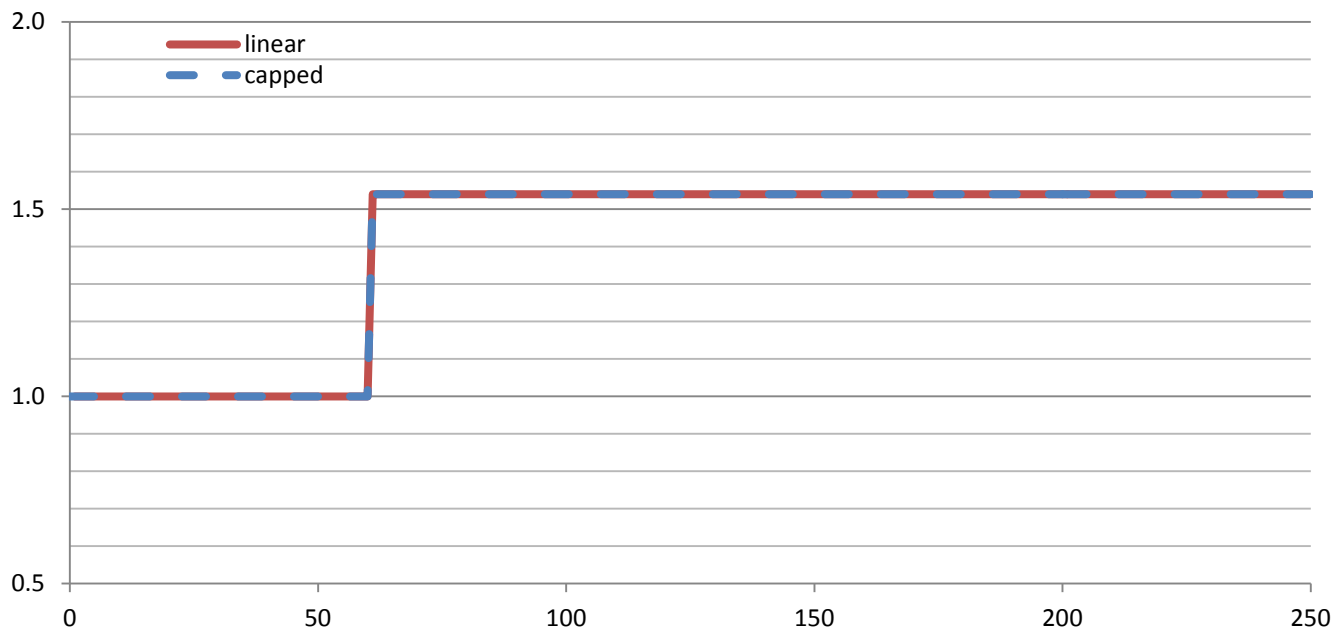
Source

Imtiaz, S., Shield, K. D., Roerecke, M., Samokhvalov, A. V., Lönnroth, K., & Rehm, J. (2017). Alcohol consumption as a risk factor for tuberculosis: meta-analyses and burden of disease. *European Respiratory Journal*, 50(1), 1700216.

(1).(2) HIV, men

Condition category: (1) Communicable diseases
ICD10 codes: B20 to B24, Z21

	Current drinkers	Former drinkers
Source	Rehm et al. (2017) Presented in article section entitled <i>Quantification of the effect of alcohol use on HIV</i>	There is no increased risk for former drinkers
Relative risk Equation or estimate	Step function: $RR = \begin{cases} 1.00, & 0 < x < 61 \\ 1.54, & 61 \leq x \leq z \end{cases}$	$RR_{FD} = 1.00$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	Note: HIV is the only condition for which step functions are present in InterMAHP. For step functions, the linear and capped methods are equivalent.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Not applicable. There is no increased risk for former drinkers.	



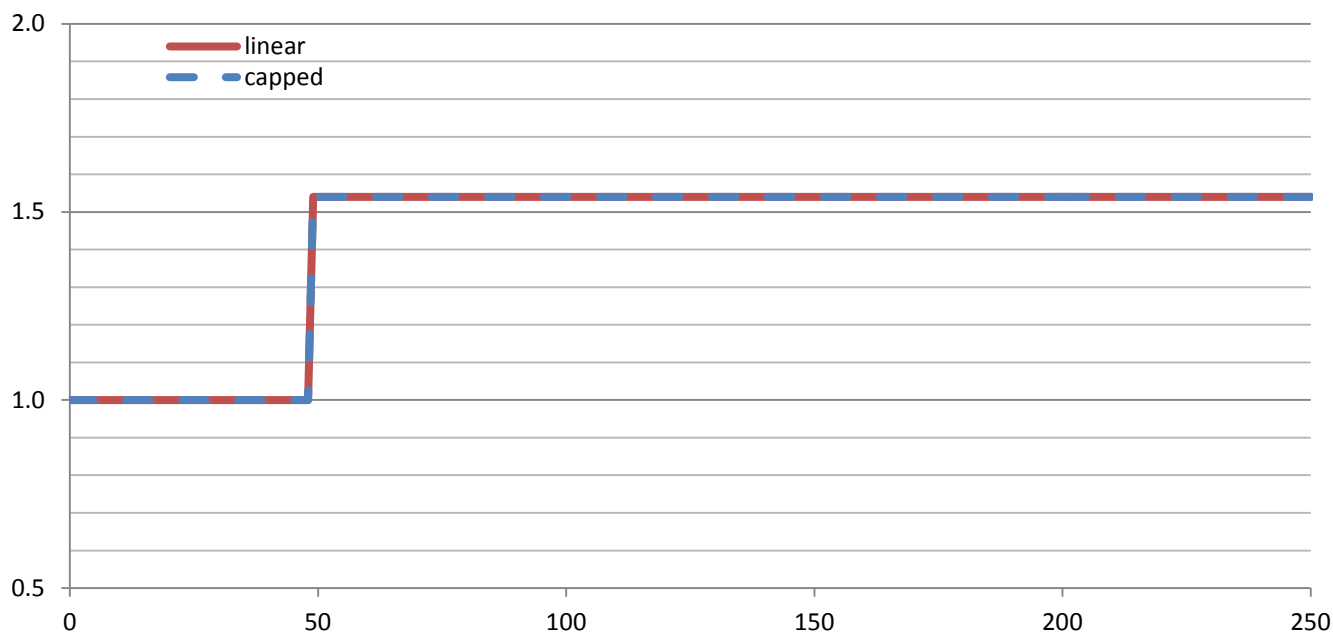
Source

Rehm, J., Probst, C., Shield, KD, Shuper, PA. (2017). Does alcohol use have a causal effect on HIV incidence and disease progression? A review of the literature and a modeling strategy for quantifying the effect. *Population Health Metrics*, 15(4). doi10.1186/s12963-017-0121-9

(1).(2) HIV, women

Condition category: (1) Communicable diseases
ICD10 codes: B20 to B24, Z21

	Current drinkers	Former drinkers
Source	Rehm et al. (2017) Presented in article section entitled <i>Quantification of the effect of alcohol use on HIV</i>	There is no increased risk for former drinkers
Relative risk Equation or estimate	Step function: $RR = \begin{cases} 1.00, & 0 < x < 49 \\ 1.54, & 49 \leq x \leq z \end{cases}$	$RR_{FD} = 1.00$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	Note: HIV is the only condition for which step functions are present in InterMAHP. For step functions, the linear and capped methods are equivalent.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Not applicable. There is no increased risk for former drinkers.	



Source

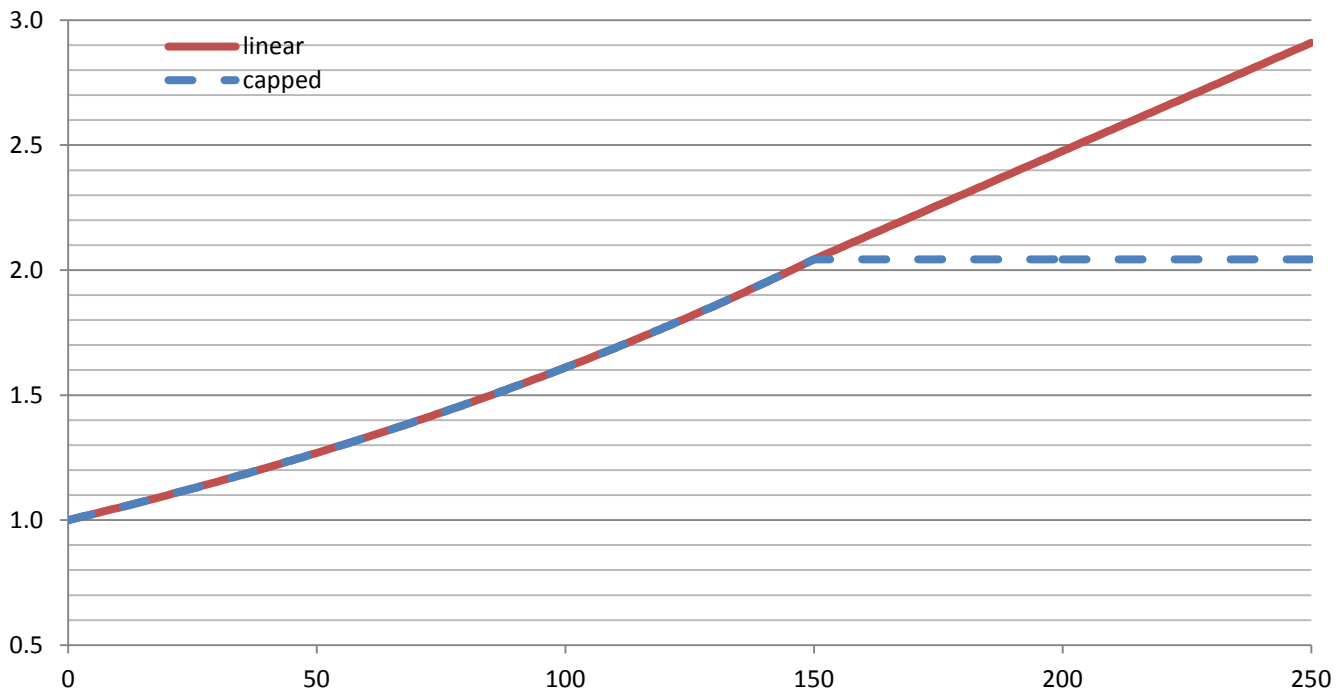
Rehm, J., Probst, C., Shield, KD, Shuper, PA. (2017). Does alcohol use have a causal effect on HIV incidence and disease progression? A review of the literature and a modeling strategy for quantifying the effect. *Population Health Metrics*, 15(4). doi10.1186/s12963-017-0121-9

(1).(3) Lower respiratory tract infections

Condition category: (1) Communicable diseases

ICD10 code(s): J09 to J22

	Current drinkers	Former drinkers
Source	Samokhvalov et al. (2010) Figure 3	There is no increased risk for former drinkers
Relative risk Equation or estimate	$\ln RR(x) = 0.004764038x$ $RR(x) = \exp(0.004764038x)$	$RR_{FD} = 1.00$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Not applicable. There is no increased risk for former drinkers.	



Source

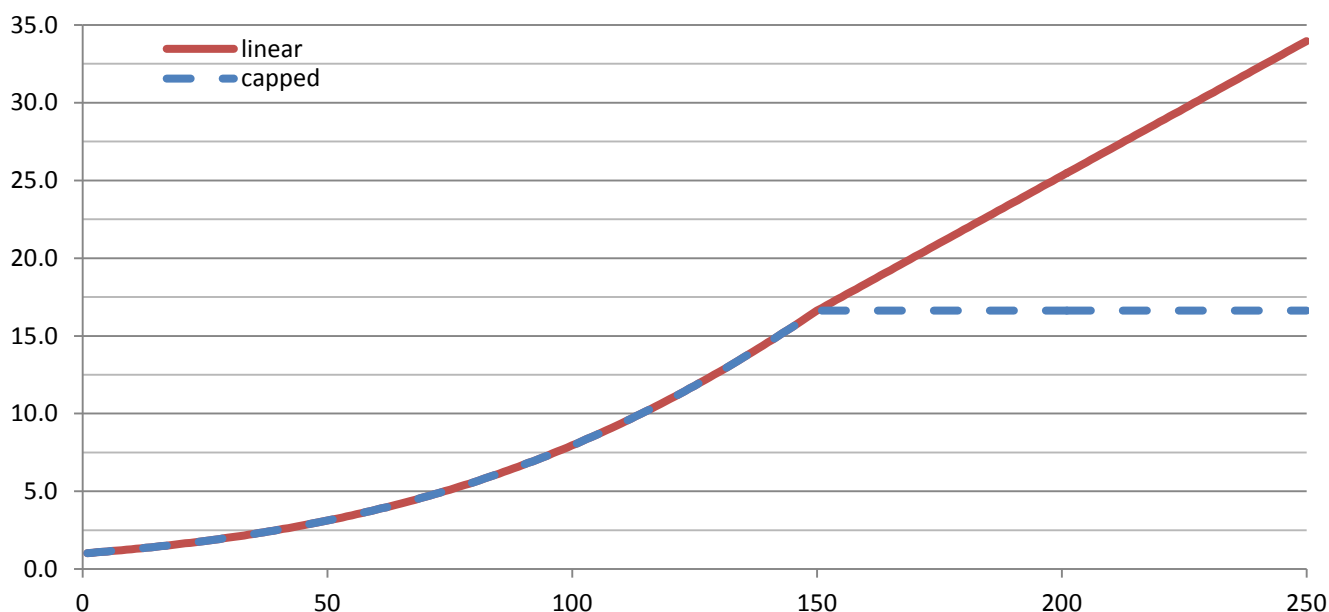
Samokhvalov, A. V., Irving, H. M., & Rehm, J. (2010). Alcohol consumption as a risk factor for pneumonia: a systematic review and meta-analysis. *Epidemiology & Infection*, 138(12), 1789-1795.

(2).(1) Oral cavity and pharynx cancer

Condition category: (2) Cancer

ICD10 codes: C00 to C05; C08 to C10; C12 to C14, D00.0

	Current drinkers	Former drinkers
Source	Bagnardi et al. (2015) Figure 3	Marron et al. (2009) Table 2, top panel of results
Relative risk Equation or estimate	$\ln RR(x) = 0.02474x - 0.00004x^2$ $RR(x) = \exp(0.02474x - 0.00004x^2)$	$RR_{FD} = 1.16$
Comments	Functional equation for continuous curve depicted in Figure 3 obtained through personal correspondence between AS and V. Bagnardi, dated 25-July-2017. Bagnardi et al. tested for differential dose-response relationship by gender and found none.	RR_{FD} rescaled as current drinkers were the referent in Table 2. $RR_{FD} = 0.85/0.73 = 1.16$ Estimate from "head and neck" category used as oral cavity and oro/hypopharynx were separated. Pooled analysis from broad international sources.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The meta-analysis does not explicitly control for abstainer bias in the meta-regression.	Yes. As this article was concerned with the cessation of drinking, lifetime abstainers and former drinkers were separated in the study design.



Sources

Bagnardi, V., Rota, M., Botteri, E., Tramacere, I., Islami, F., Fedirko, V., Scotti, L., Jenab, M., Turati, F., Pasquali, E., Pelucchi, C., Galeone, C., Belloco, R., Negri, E., Corrao, G., Boffetta, P. & La Vecchia, C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *British journal of cancer*, 112(3), 580.

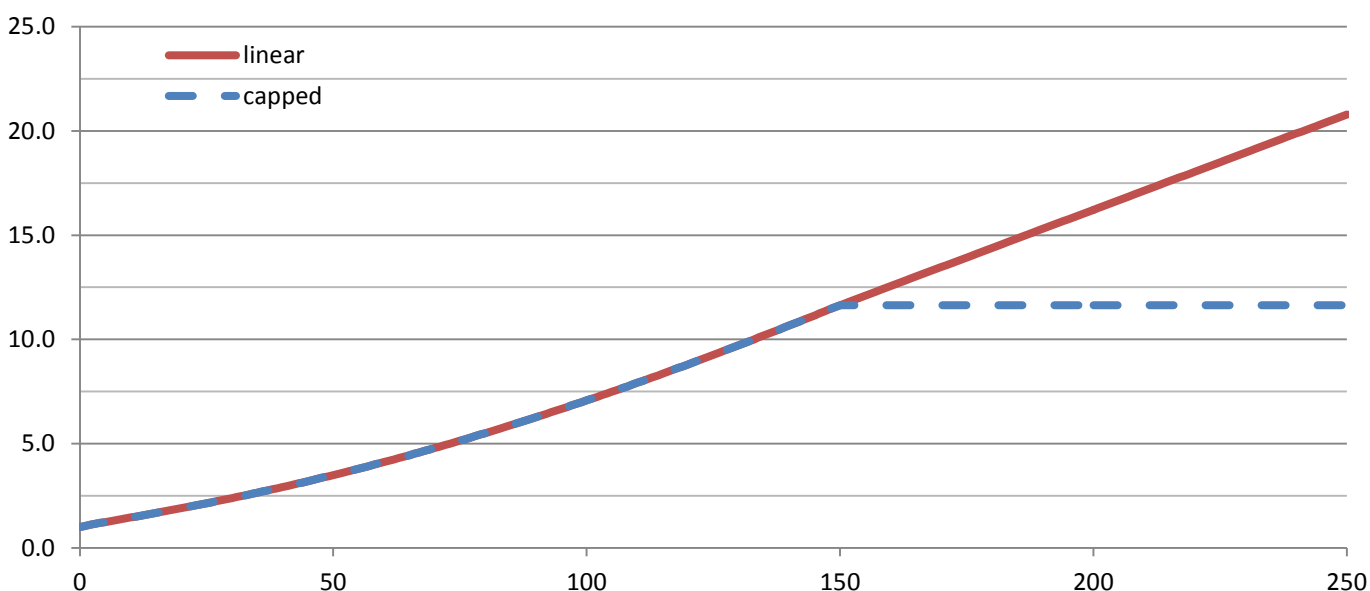
Marron, M., Boffetta, P., Zhang, Z. F., Zaridze, D., Wünsch-Filho, V., Winn, D. M., ... & Smith, E. (2009). Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. *International journal of epidemiology*, 39(1), 182-196.

(2).(2) Oesophageal cancer, squamous cell carcinoma (SCC)

Condition category: (2) Cancer

ICD10 codes: C15, D00.1 (portional - only SCC and not adenocarcinoma)

	Current drinkers	Former drinkers
Source	Bagnardi et al. (2015) Figure 3	Marron et al. (2009) Table 2, top panel of results
Relative risk Function or estimate	$\ln RR(x) = 0.0559x - 0.00789x \ln x$ $RR(x) = \exp(0.0559x - 0.00789x \ln x)$	$RR_{FD} = 1.16$
Comments	Functional equation for continuous curve depicted in Figure 3 obtained through personal correspondence between AS and V. Bagnardi, dated 25-July-2017. Bagnardi et al. tested for differential dose-response relationship by gender and found none.	RR_{FD} rescaled as current drinkers were the referent in Table 2. $RR_{FD} = 0.85/0.73 = 1.16$ Estimate from "head and neck" category used as oral cavity and oro/hypopharynx were separated. Pooled analysis from broad international sources.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The meta-analysis does not explicitly control for abstainer bias in the meta-regression.	Yes. As this article was concerned with the cessation of drinking, lifetime abstainers and former drinkers were separated in the study design.



Sources

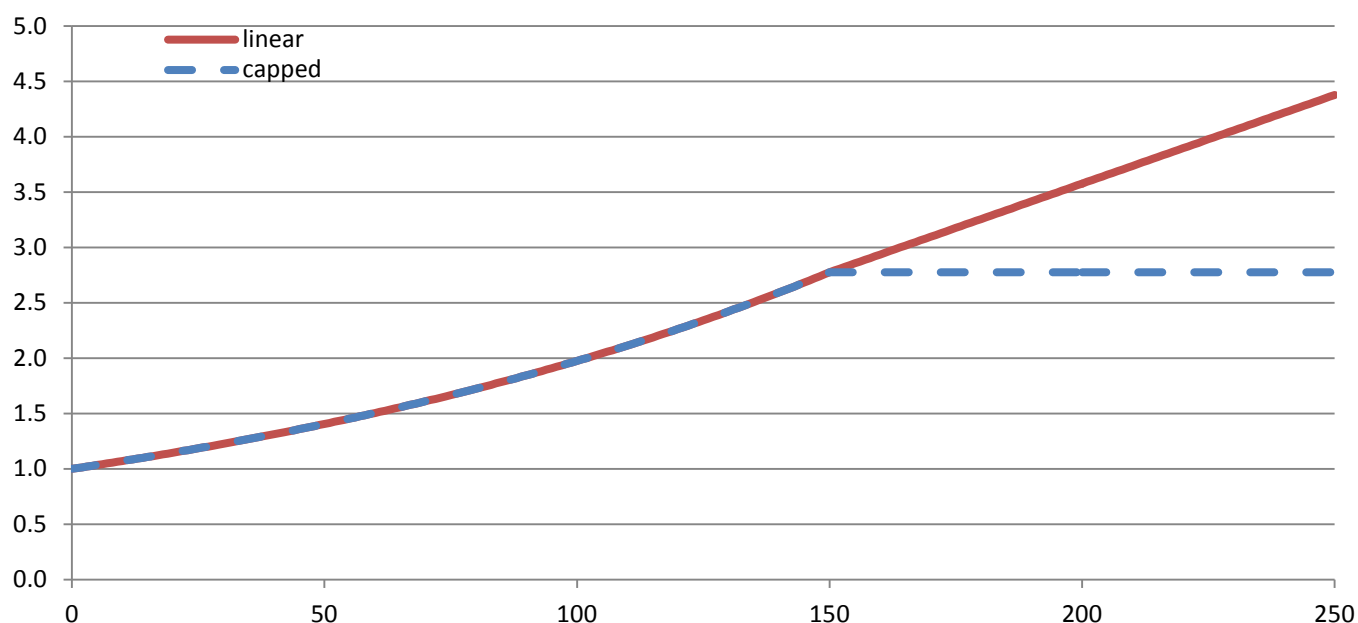
Bagnardi, V., Rota, M., Botteri, E., Tramacere, I., Islami, F., Fedirko, V., Scotti, L., Jenab, M., Turati, F., Pasquali, E., Pelucchi, C., Galeone, C., Belloco, R., Negri, E., Corrao, G., Boffetta, P. & La Vecchia, C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *British journal of cancer*, 112(3), 580.

Marron, M., Boffetta, P., Zhang, Z. F., Zaridze, D., Wünsch-Filho, V., Winn, D. M., ... & Smith, E. (2009). Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. *International journal of epidemiology*, 39(1), 182-196.

(2).(3) Colorectal cancer, men

Condition category: (2) Cancer
ICD10 codes: C18 to C21, D01.0 to D01.4

	Current drinkers	Former drinkers
Source	Bagnardi et al. (2015) Table 3	Schütze et al. (2011) Table 2
Relative risk Function or estimate	$\ln RR(x) = 0.006806x$ $RR(x) = \exp(0.006806x)$	$RR_{FD} = 2.19$
Comments	Test for heterogeneity showed differential effect for men and women. Continuous relative risk function based on the categorical information presented in Table 3 obtained through personal correspondence between AS and V. Bagnardi, dated 25-July-2017.	Based on the prospective cohort EPIC study (European Prospective Investigation into Cancer and Nutrition). Data analyzed from eight western European countries; context therefore not as broad as a large meta-analysis.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The meta-analysis does not explicitly control for abstainer bias in the meta-regression.	Yes. EPIC asks respondents their alcohol use at ages 20,30,40,50 and recruitment. Accurate measure of lifetime abstention.



Sources

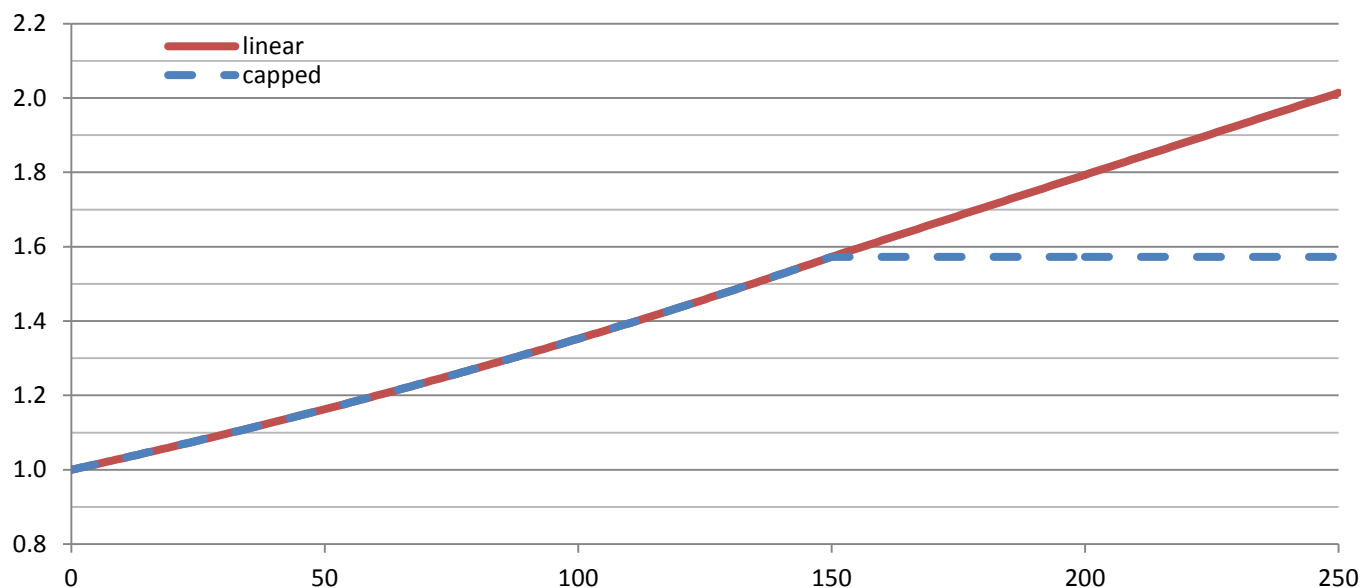
Bagnardi, V., Rota, M., Botteri, E., Tramacere, I., Islami, F., Fedirko, V., Scotti, L., Jenab, M., Turati, F., Pasquali, E., Pelucchi, C., Galeone, C., Bellocco, R., Negri, E., Corrao, G., Boffetta, P. & La Vecchia, C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *British journal of cancer*, 112(3), 580.

Schütze, M., Boeing, H., Pischon, T., Rehm, J., Kehoe, T., Gmel, G., ... & Clavel-Chapelon, F. (2011). Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. *Bmj*, 342, d1584.

(2).(3) Colorectal cancer, women

Condition category: (2) Cancer
ICD10 codes: C18 to C21, D01.0 to D01.4

	Current drinkers	Former drinkers
Source	Bagnardi et al. (2015) Table 3	Schütze et al. (2011) Table 2
Relative risk Function or estimate	$\ln RR(x) = 0.003020x$ $RR(x) = \exp(0.003020x)$	$RR_{FD} = 1.05$
Comments	Test for heterogeneity showed differential effect for men and women. Continuous relative risk function based on the categorical information presented in Table 3 obtained through personal correspondence between AS and V. Bagnardi, dated 25-July-2017.	Based on the prospective cohort EPIC study (European Prospective Investigation into Cancer and Nutrition). Data analyzed from eight western European countries; context therefore not as broad as a large meta-analysis.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The meta-analysis does not explicitly control for abstainer bias in the meta-regression.	Yes. EPIC asks respondents their alcohol use at ages 20,30,40,50 and recruitment. Accurate measure of lifetime abstention.



Sources

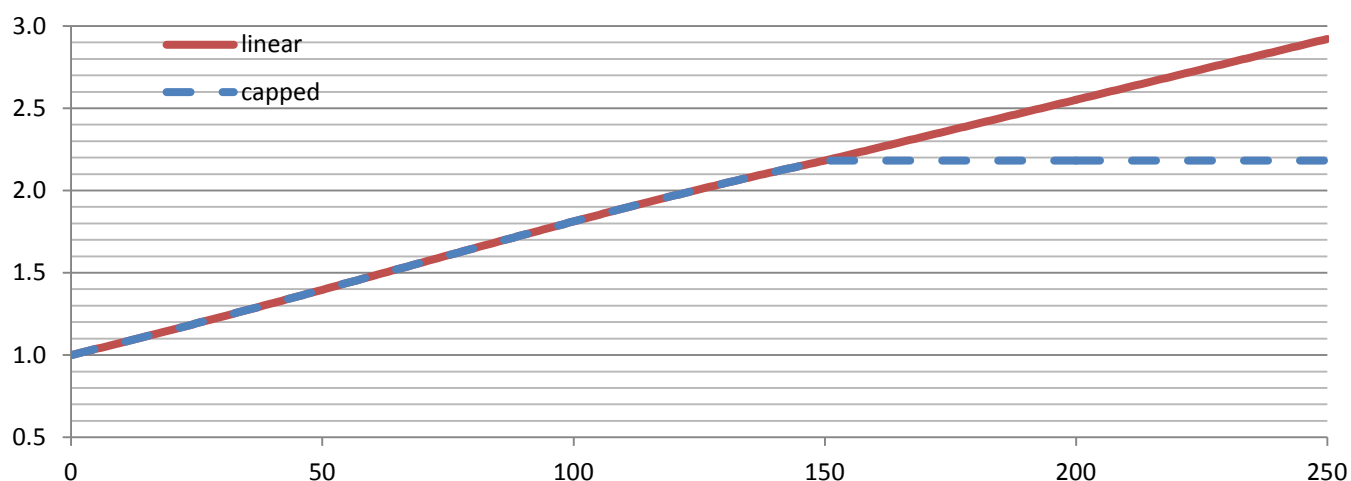
Bagnardi, V., Rota, M., Botteri, E., Tramacere, I., Islami, F., Fedirko, V., Scotti, L., Jenab, M., Turati, F., Pasquali, E., Pelucchi, C., Galeone, C., Bellocco, R., Negri, E., Corrao, G., Boffetta, P. & La Vecchia, C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *British journal of cancer*, 112(3), 580.

Schütze, M., Boeing, H., Pischon, T., Rehm, J., Kehoe, T., Gmel, G., ... & Clavel-Chapelon, F. (2011). Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. *Bmj*, 342, d1584.

(2).(4) Liver cancer

Condition category: (2) Cancer
ICD10 codes: C22, D01.5

	Current drinkers	Former drinkers
Source	Corrao et al. (2004) Figure 1	Schütze et al. (2011) Table 2
Relative risk Function or estimate	$\ln RR(x) = 0.00742949x - 0.0000148593x^2$ $RR(x) = \exp(0.00742949x - 0.0000148593x^2)$	$RR_{FD}(\text{men}) = 1.54$ $RR_{FD}(\text{women}) = 2.28$
Comments	Functional equation for continuous curve depicted in Figure 1 obtained previously from Corrao et al. by JR. Corrao et al. (2004) is used instead of Bagnardi et al. (2015) due to the instability of the function for liver cancer. It has a cubic term and therefore increases dramatically above 100g/day. The decision to use Corrao is the same as is expected to be used by the WHO 2018 Global Status Report on Alcohol and Health.	Based on the prospective cohort EPIC study (European Prospective Investigation into Cancer and Nutrition). Data analyzed from eight western European countries; context therefore not as broad as a large meta-analysis. $RR_{FD}(\text{men})$ same as that for total cancer as there were not enough cases to uniquely estimate for liver cancer.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The meta-analysis does not explicitly control for abstainer bias in the meta-regression.	Yes. EPIC asks respondents their alcohol use at ages 20,30,40,50 and recruitment. Accurate measure of lifetime abstention.



Sources

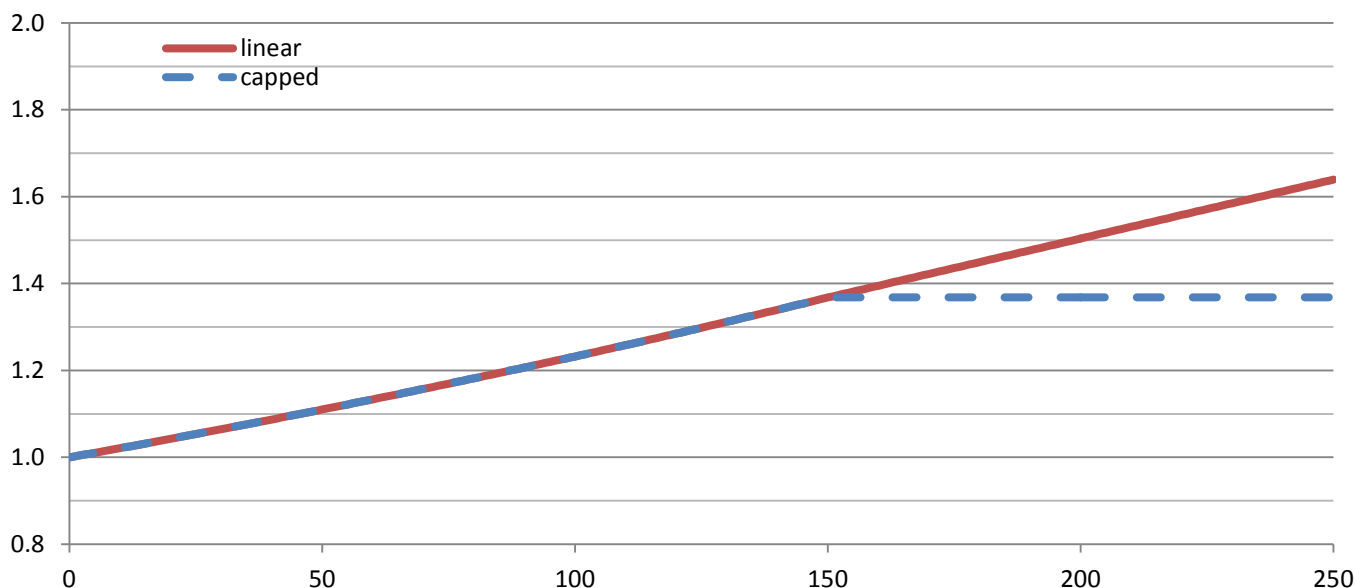
Corrao, G., Bagnardi, V., Zambon, A., & La Vecchia, C. (2004). A meta-analysis of alcohol consumption and the risk of 15 diseases. *Preventive medicine*, 38(5), 613-619.

Schütze, M., Boeing, H., Pischon, T., Rehm, J., Kehoe, T., Gmel, G., ... & Clavel-Chapelon, F. (2011). Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. *Bmj*, 342, d1584.

(2).(5) Pancreatic cancer

Condition category: (2) Cancer
ICD10 codes: C25, D01.7

	Current drinkers	Former drinkers
Source	Bagnardi et al. (2015) Figure 3	Schütze et al. (2011) Table 2
Relative risk Function or estimate	$\ln RR(x) = 0.002089x$ $RR(x) = \exp(0.002089x)$	$RR_{FD}(\text{men}) = 1.54$ $RR_{FD}(\text{women}) = 1.10$
Comments	Functional equation for continuous curve depicted in Figure 3 obtained through personal correspondence between AS and V. Bagnardi, dated 25-July-2017. Bagnardi et al. tested for differential dose-response relationship by gender and found none.	Results for total cancer used as no condition-specific results available. Based on the prospective cohort EPIC study (European Prospective Investigation into Cancer and Nutrition). Data analyzed from eight western European countries; context therefore not as broad as a large meta-analysis.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The meta-analysis does not explicitly control for abstainer bias in the meta-regression.	Yes. EPIC asks respondents their alcohol use at ages 20,30,40,50 and recruitment. Accurate measure of lifetime abstention.



Sources

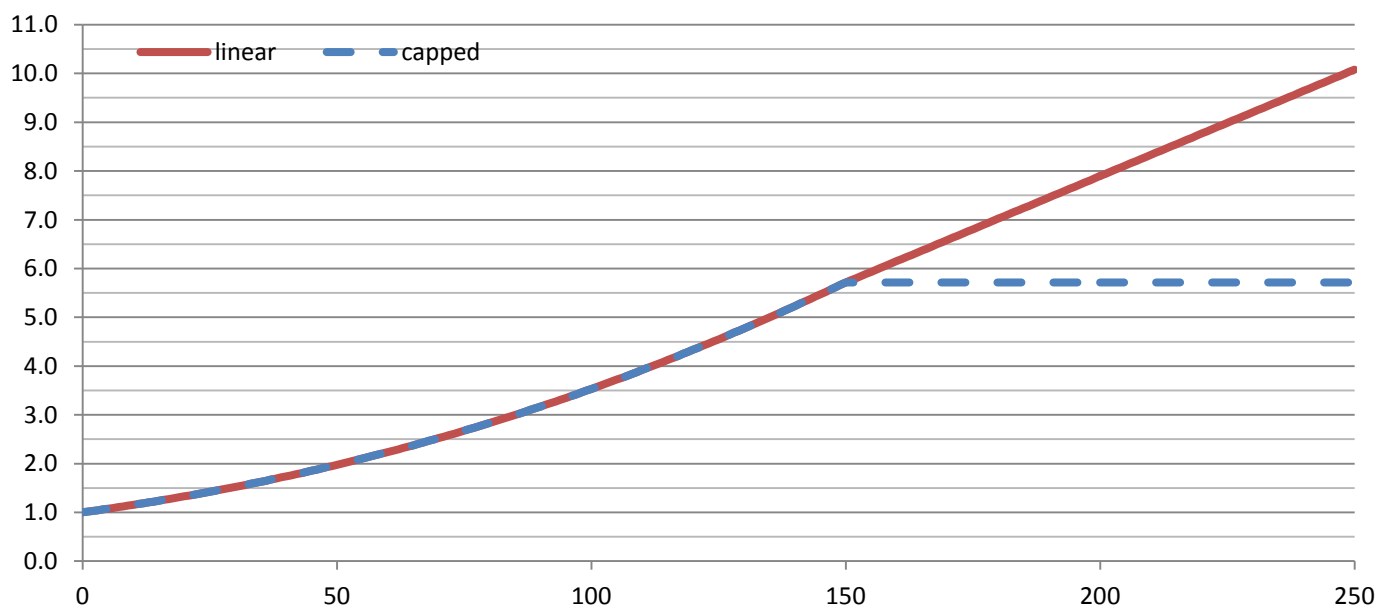
Bagnardi, V., Rota, M., Botteri, E., Tramacere, I., Islami, F., Fedirko, V., Scotti, L., Jenab, M., Turati, F., Pasquali, E., Pelucchi, C., Galeone, C., Bellocco, R., Negri, E., Corrao, G., Boffetta, P. & La Vecchia, C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *British journal of cancer*, 112(3), 580.

Schütze, M., Boeing, H., Pischon, T., Rehm, J., Kehoe, T., Gmel, G., ... & Clavel-Chapelon, F. (2011). Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. *Bmj*, 342, d1584

(2).(6) Laryngeal cancer

Condition category: (2) Cancer
ICD10 codes: C32, D02.0

	Current drinkers	Former drinkers
Source	Bagnardi et al. (2015) Figure 3	Marron et al. (2009) Table 2, top panel of results
Relative risk Function or estimate	$\ln RR(x) = 0.01462x - 0.00002x^2$ $RR(x) = \exp(0.01462x - 0.00002x^2)$	$RR_{FD} = 1.18$
Comments	Functional equation for continuous curve depicted in Figure 3 obtained through personal correspondence between AS and V. Bagnardi, dated 25-July-2017. Bagnardi et al. tested for differential dose-response relationship by gender and found none.	RR_{FD} rescaled as current drinkers were the referent in Table 2. $RR_{FD} = 0.79/0.67 = 1.18$ Estimate from “head and neck” category used as oral cavity and oro/hypopharynx were separated. Pooled analysis from broad international sources.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The meta-analysis does not explicitly control for abstainer bias in the meta-regression.	Yes. As this article was concerned with the cessation of drinking, lifetime abstainers and former drinkers were separated in the study design.



Sources

Bagnardi, V., Rota, M., Botteri, E., Tramacere, I., Islami, F., Fedirko, V., Scotti, L., Jenab, M., Turati, F., Pasquali, E., Pelucchi, C., Galeone, C., Bellocco, R., Negri, E., Corrao, G., Boffetta, P. & La Vecchia, C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *British journal of cancer*, 112(3), 580.

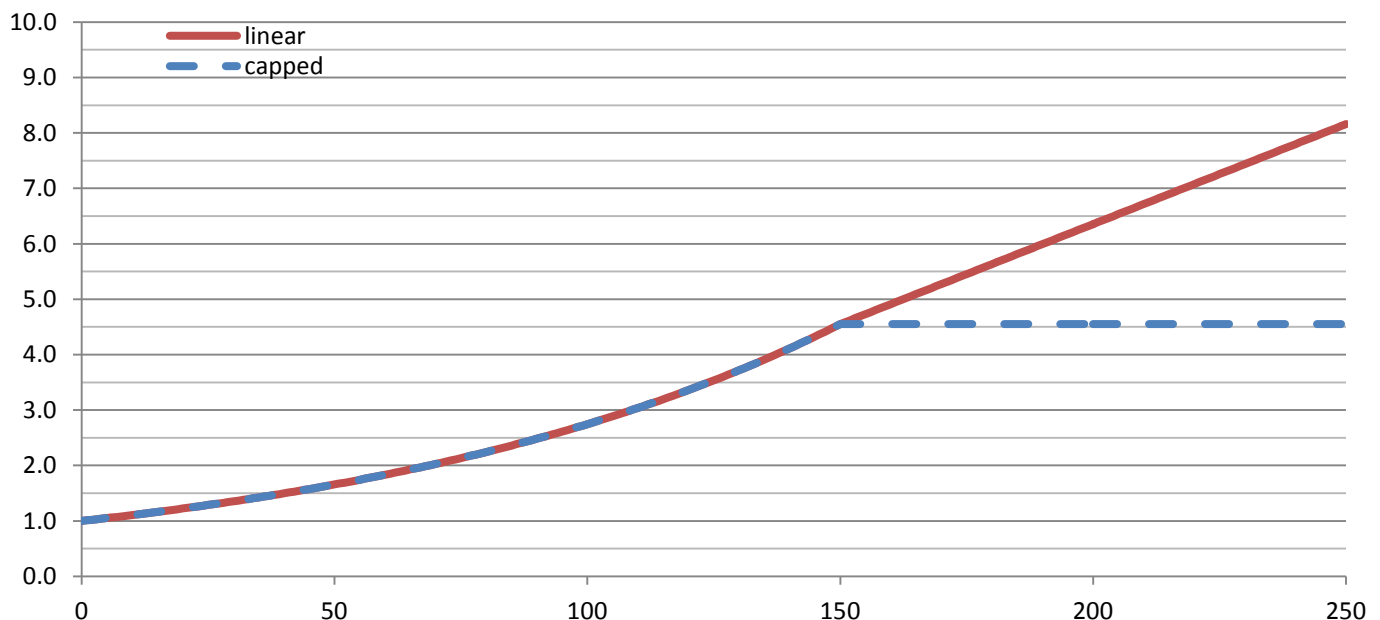
Marron, M., Boffetta, P., Zhang, Z. F., Zaridze, D., Wunsch-Filho, V., Winn, D. M., ... & Smith, E. (2009). Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. *International journal of epidemiology*, 39(1), 182-196.

(2).(7) Breast cancer, women

Condition category: (2) Cancer

ICD10 codes: C50, D05

	Current drinkers	Former drinkers
Source	Bagnardi et al. (2015) Table 3	Schütze et al. (2011) Table 2
Relative risk Function or estimate	$\ln RR(x) = 0.0101018x$ $RR(x) = \exp(0.0101018x)$	$RR_{FD} = 1.03$
Comments	Functional equation for continuous curve depicted in Figure 3 obtained through personal correspondence between AS and V. Bagnardi, dated 25-July-2017. Bagnardi et al. tested for differential dose-response relationship by gender and found none.	Based on the prospective cohort EPIC study (European Prospective Investigation into Cancer and Nutrition). Data analyzed from eight western European countries; context therefore not as broad as a large meta-analysis.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The meta-analysis does not explicitly control for abstainer bias in the meta-regression.	Yes. EPIC asks respondents their alcohol use at ages 20,30,40,50 and recruitment. Accurate measure of lifetime abstention.



Sources

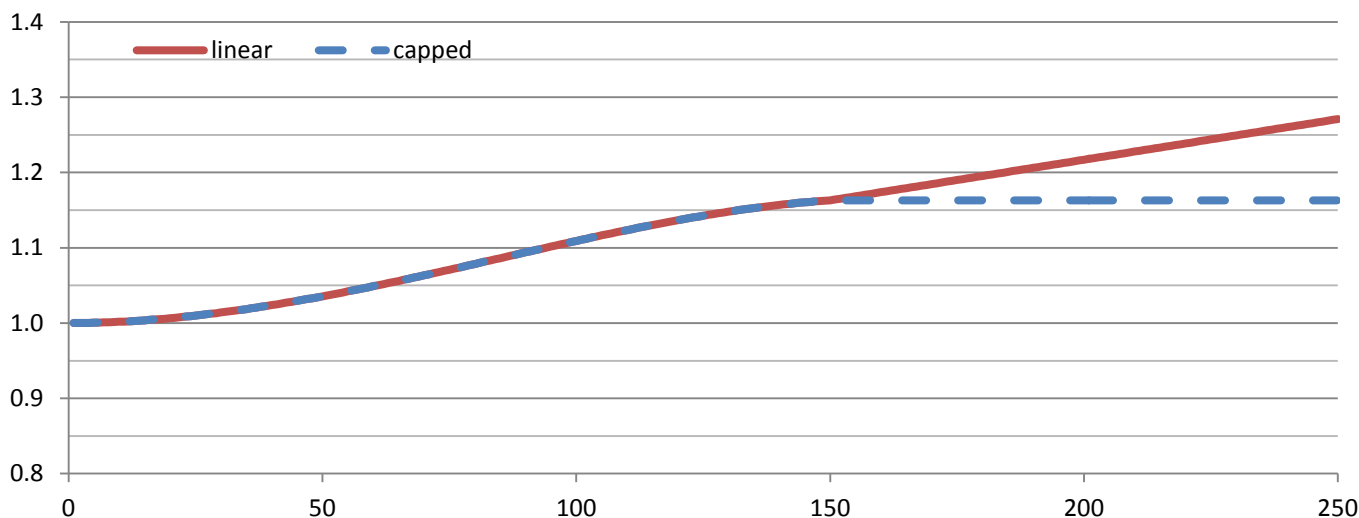
Bagnardi, V., Rota, M., Botteri, E., Tramacere, I., Islami, F., Fedirko, V., Scotti, L., Jenab, M., Turati, F., Pasquali, E., Pelucchi, C., Galeone, C., Belloco, R., Negri, E., Corrao, G., Boffeta, P. & La Vecchia, C. (2015). Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *British journal of cancer*, 112(3), 580.

Schütze, M., Boeing, H., Pischon, T., Rehm, J., Kehoe, T., Gmel, G., ... & Clavel-Chapelon, F. (2011). Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. *Bmj*, 342, d1584.

(3).(1) Type 2 diabetes mellitus, men

Condition category: (3) Endocrine conditions
ICD10 codes: E11,E13, E14

	Current drinkers	Former drinkers
Source	Knott et al. (2015) Figure 3	Reported in Rehm et al. (2010), Table 4; calculated as part of Baliunas et al. (2009) but not presented
Relative risk Function or estimate	$\ln RR(x) = 0.00001763703x^2 - 0.0000000728256x^3$ $RR(x) = \exp(0.00001763703x^2 - 0.0000000728256x^3)$	$RR_{FD} = 1.18$
Comments	Functional equation for continuous curve depicted in Figure 3 obtained through personal correspondence between AS and C. Knott, dated 31-July-2017.	Relative risks for former drinkers were calculated as a component of Baliunas et al. (2009); however, they were not reported in that article. They were later reported in Rehm et al. (2010), an article produced by many of the same authors.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. An analysis restricted to strictly-defined lifetime abstainers was completed by Knott et al. and presented in Suppl.Fig.S1. It was decided not to use these results due to the small number of included studies.	Yes. Baliunas et al. reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.



Sources

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.

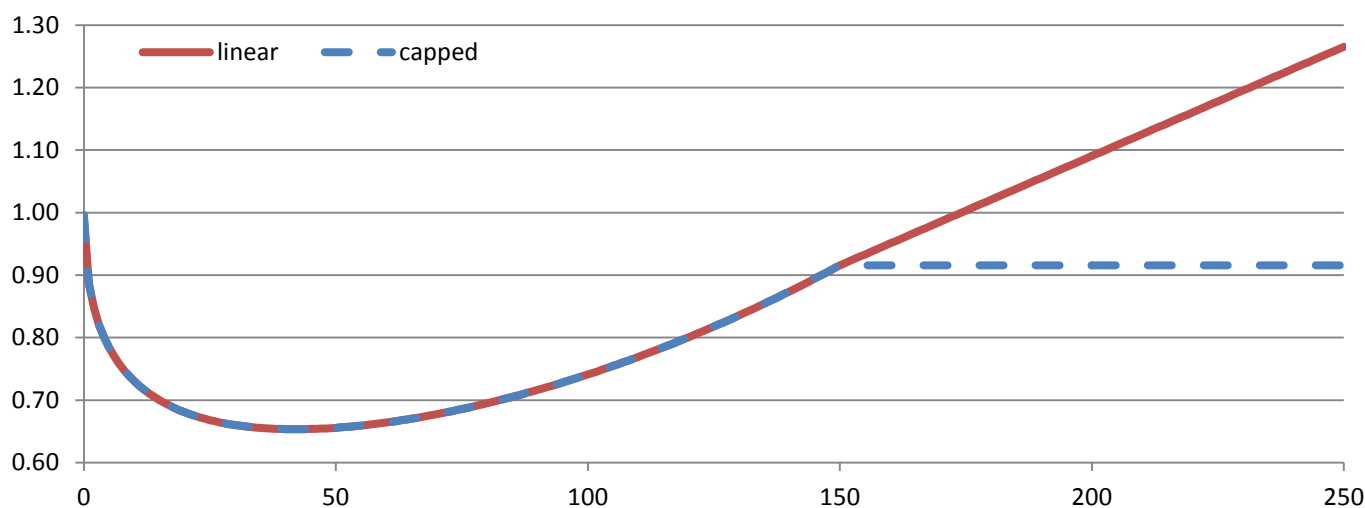
Rehm, J., Baliunas, D., Borges, G. L., Graham, K., Irving, H., Kehoe, T., ... & Roerecke, M. (2010). The relation between different dimensions of alcohol consumption and burden of disease: an overview. *Addiction*, 105(5), 817-843.

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. *Diabetes care*, 32(11), 2123-2132.

(3).(1) Type 2 diabetes mellitus, women

Condition category: (3) Endocrine conditions
ICD10 codes: E11,E13, E14

	Current drinkers	Former drinkers
Source	Knott et al. (2015) Figure 3	Reported in Rehm et al. (2010), Table 4; calculated as part of Baliunas et al. (2009) but not presented.
Relative risk Function or estimate	$\ln RR(x) = -0.1313991\sqrt{x}$ + 0.01014239x $RR(x) = \exp(-0.1313991\sqrt{x} +$ 0.01014239x)	$RR_{FD} = 1.14$
Comments	Functional equation for continuous curve depicted in Figure 3 obtained through personal correspondence between AS and C. Knott, dated 31-July-2017.	Relative risks for former drinkers were calculated as a component of Baliunas et al. (2009); however, they were not reported in that article. They were later reported in Rehm et al. (2010), an article produced by many of the same authors.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. An analysis restricted to strictly-defined lifetime abstainers was completed by Knott et al. and presented in Suppl.Fig.S1. It was decided not to use these results due to the small number of included studies.	Yes. Baliunas et al. reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.



Sources

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.

Rehm, J., Baliunas, D., Borges, G. L., Graham, K., Irving, H., Kehoe, T., ... & Roerecke, M. (2010). The relation between different dimensions of alcohol consumption and burden of disease: an overview. *Addiction*, 105(5), 817-843.

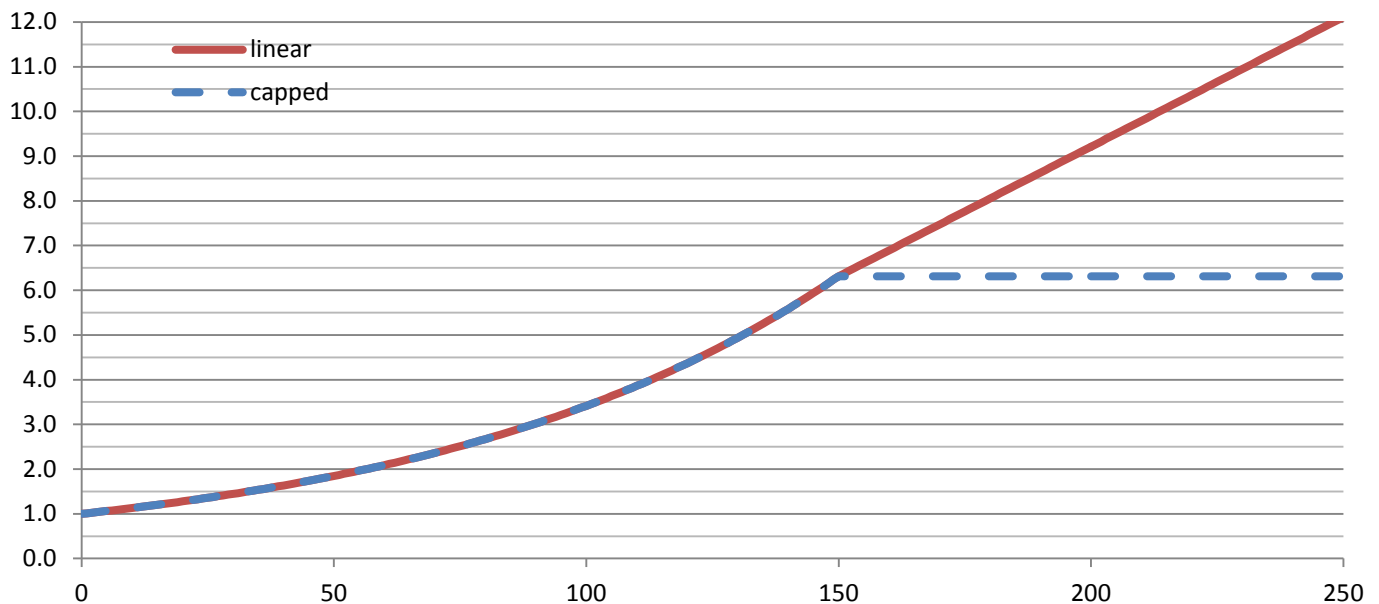
Baliunas, D. O., Taylor, B. J., Irving, H., Roerecke, M., Patra, J., Mohapatra, S., & Rehm, J. (2009). Alcohol as a risk factor for type 2 diabetes. *Diabetes care*, 32(11), 2123-2132.

(4).(5) Epilepsy

Condition category: (4) Neuropsychiatric conditions

ICD10 code(s): G40,G41

	Current drinkers	Former drinkers
Source	Samokhvalov et al. (2010) Figure 3	Leone et al. (1997) Rehm et al. (2017)
Relative risk Function or estimate	$\ln RR(x) = 0.0122861x$ $RR(x) = \exp(0.0122861x)$	$RR_{FD} = 1.00$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	There is no evidence that former drinking is correlated to the risk of an epileptic seizure: see interpretation in Rehm et al. (2017) of Leone et al. (1997)
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. It does not appear that the meta-analysis specifically quantified whether constituent studies were affected by abstainer biases.	



Sources

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.

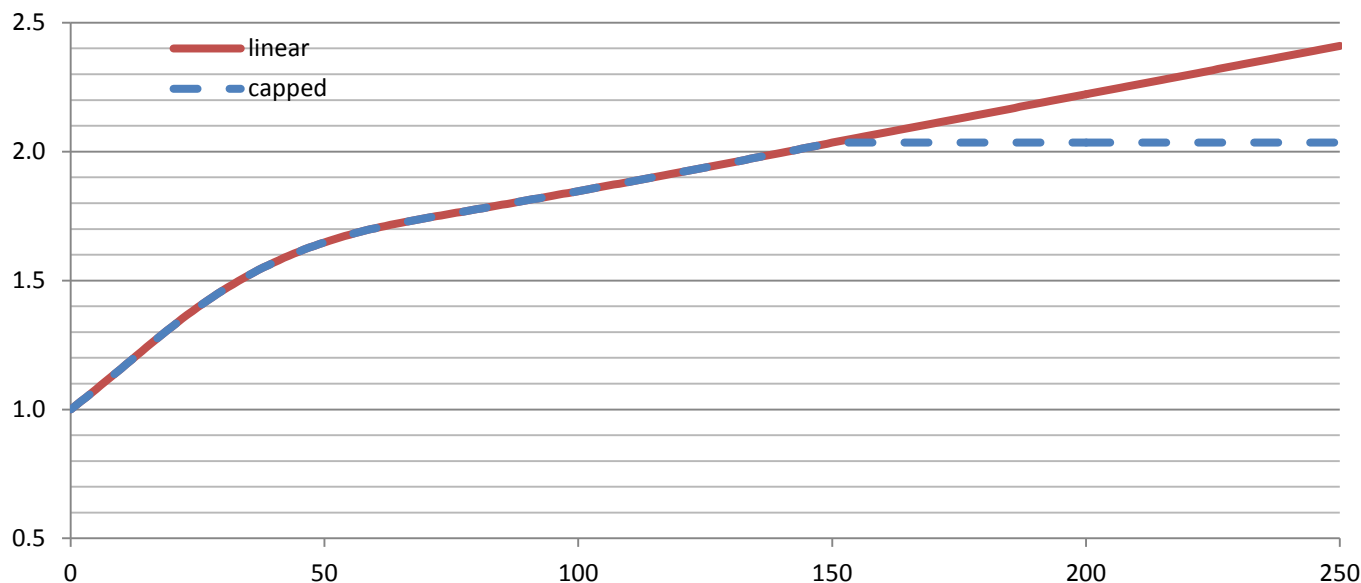
Rehm, J., Sherk, A., Shield, K.D., & Gmel, G. (2017). Risk relations between alcohol use and non-injury causes of death. Version 2: September 2017. Toronto, Canada: Centre for Addiction and Mental Health. ISBN: [978-1-77114-399-8](https://doi.org/10.1007/978-1-77114-399-8).

Leone, M., Bottacchi, E., Beghi, E., Morgando, E., Mutani, R., Amedeo, G., ... & Ceroni, L. R. (1997). Alcohol use is a risk factor for a first generalized tonic-clonic seizure. *Neurology*, 48(3), 614-620.

(5).(1) Hypertension, men

Condition category: (5) Cardiovascular conditions
ICD10 codes: I10 to I15

	Current drinkers	Former drinkers
Source	Roerecke et al. (in press) Also reported in Rehm et al. (2017)	Roerecke et al. (in press) Rehm et al. (2017)
Relative risk Function or estimate	$\ln RR(x) = \begin{cases} 0.0150537x - \frac{0.0156155x^3}{75^2}, & 0 < x < 21 \\ 0.0150537x - 0.0156155 \frac{x^3 - \frac{75(x-21)^3}{(75-21)^3}}{75^2}, & 21 \leq x < 75 \\ 0.0150537x - 0.0156155 \frac{x^3 - \frac{75(x-21)^3 - 21(x-75)^3}{(75-21)^3}}{75^2}, & x \geq 75 \end{cases}$	$RR_{FD} = 1.03$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Article in press at the time of InterMAHP publication.	Article in press at the time of InterMAHP publication.
Control for abstainer bias	Unknown. Article not yet published.	Unknown. Article not yet published.



Sources

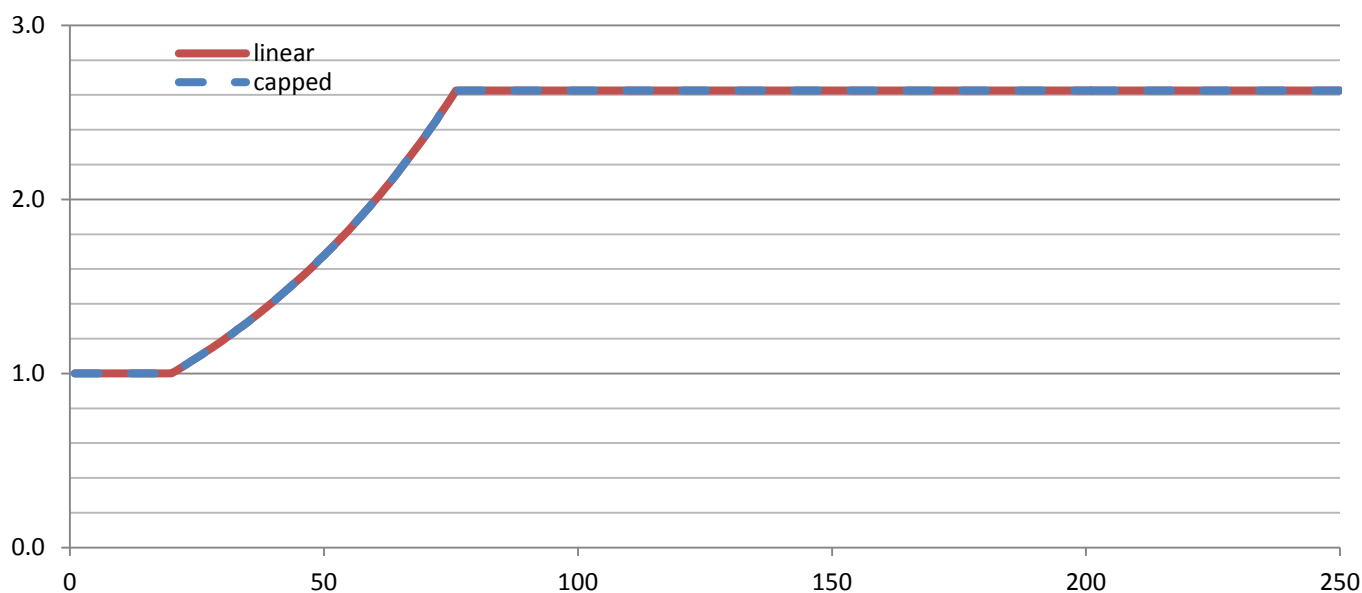
Roerecke, M., Tobe, S., Kaczorowski, J., Bacon, SL, Vafaei, A., Hasan, OSM, Krishnan, RJ, Raifu, AO, Rehm, J. (in press). The relationship between alcohol consumption and sex-specific incidence of hypertension: a systematic review and meta-analysis of cohort studies. Centre for Addiction and Mental Health. Toronto, Canada: CAMH.

Rehm, J., Sherk, A., Shield, K.D., & Gmel, G. (2017). Risk relations between alcohol use and non-injury causes of death. Version 2: September 2017. Toronto, Canada: Centre for Addiction and Mental Health. ISBN: [978-1-77114-399-8](https://doi.org/10.1007/978-1-77114-399-8).

(5).(1) Hypertension, women

Condition category: (5) Cardiovascular conditions
ICD10 codes: I10 to I15

	Current drinkers	Former drinkers
Source	Roerecke et al. (in press) Also reported in Rehm et al. (2017)	Roerecke et al. (in press)
Relative risk	$\ln RR(x)$	$RR_{FD} = 1.05$
Function or estimate	$= \begin{cases} 0, & 0 < x < 18.9517 \\ -0.0154196x + 0.0217586 \frac{x^3 - \frac{20(x-10)^3 - 10(x-20)^3}{(20-10)}}{20^2}, & 18.9517 \leq x < 75 \\ 0.9649937, & x \geq 75 \end{cases}$	
Comments	Relative risk function received directly from members of authorship group who are members of this project. Article in press at the time of InterMAHP publication.	Article in press at the time of InterMAHP publication.
Control for abstainer bias	Unknown. Article not yet published.	Unknown. Article not yet published.



Sources

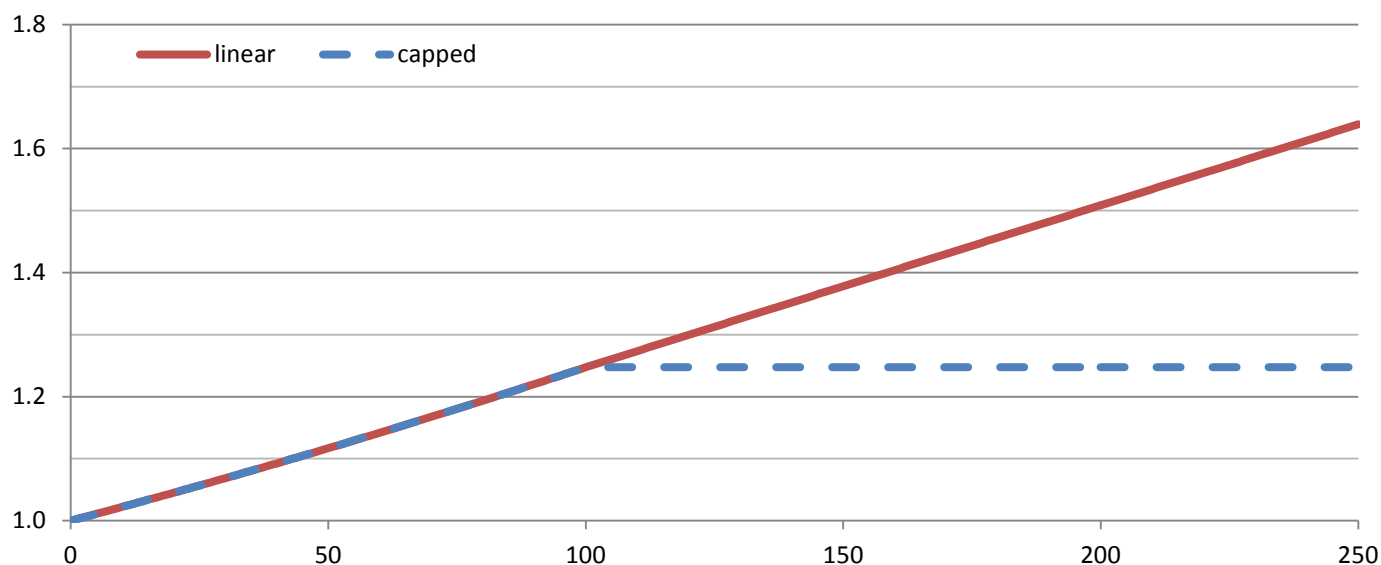
Roerecke, M., Tobe, S., Kaczorowski, J., Bacon, SL, Vafaei, A., Hasan, OSM, Krishnan, RJ, Raifu, AO, Rehm, J. (in press). The relationship between alcohol consumption and sex-specific incidence of hypertension: a systematic review and meta-analysis of cohort studies. Centre for Addiction and Mental Health. Toronto, Canada: CAMH.

Rehm, J., Sherk, A., Shield, K.D., & Gmel, G. (2017). Risk relations between alcohol use and non-injury causes of death. Version 2: September 2017. Toronto, Canada: Centre for Addiction and Mental Health. ISBN: [978-1-77114-399-8](https://doi.org/10.1007/978-1-77114-399-8).

(5).(2) Ischaemic heart disease mortality, men (two options)

Condition category: (5) Cardiovascular conditions
ICD10 codes: I20 to I25

	Current drinkers	Former drinkers
Source	Zhao et al. (2017) Table 3, top panel, fully-adjusted results, custom analysis (see comments)	Roerecke & Rehm (2010b) Table 3
Relative risk Function or estimate	$\ln RR(x) = 0.002211x$ $RR(x) = \exp(0.002211x)$	$RR_{FD} = 1.25$
Comments	Fully-adjusted model for the younger age cohort in Table 3 was re-analyzed by the first author upon request to include a gender breakdown and to provide a continuous relationship. Results received through personal correspondence between AS, TS and J. Zhao (dated 14-Oct-17).	Results stratified by gender and endpoint (outcome) used.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study explicitly controlled for abstainer biases selecting studies with no bias and selecting younger cohorts, among other methods. See article for full methodology.	Yes, considered. The reference group was operationalized as "long-term abstainers or very light drinkers."



Sources

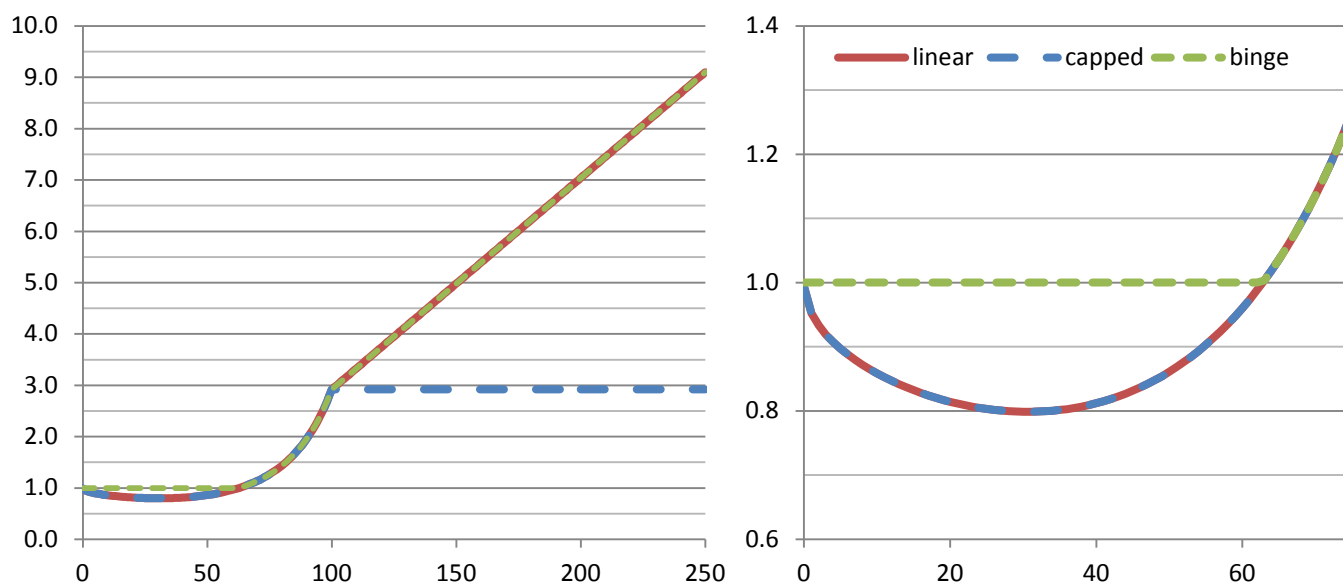
Zhao, J., Stockwell, T., Roemer, A., Naimi, T., Chikritzhs, T. (2017). Alcohol consumption and mortality from coronary heart disease: An updated meta-analysis of cohort studies. *Journal of Studies on Alcohol and Drugs*, 78, 375-386.

Roerecke, M., & Rehm, J. (2010b). Ischemic heart disease mortality and morbidity rates in former drinkers: a meta-analysis. *American journal of epidemiology*, 173(3), 245-258.

(5).(2) Ischaemic heart disease mortality, men (two options)

Condition category: (5) Cardiovascular conditions
ICD10 codes: I20 to I25

	Current drinkers	Former drinkers
Source	Roerecke & Rehm (2012) Figure 2 Roerecke & Rehm (2010a) From text, e.g. in abstract	Roerecke & Rehm (2010b) Table 3
Relative risk Function or estimate	$\ln RR(x) = -0.04870068\sqrt{x} + 0.000001559x^3$ $RR(x) = \exp(-0.04870068\sqrt{x} + 0.000001559x^3)$	$RR_{FD} = 1.25$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Roerecke & Rehm (2010a) modifies the RR curve for bingers by removing the protective effect (i.e. $RR=1.0$).	Results stratified by gender and endpoint(outcome) used. Note: In the figure below, the binge level is set at 60g/day; therefore $RR=1.0$ above this as this portion of the population is guaranteed to binge.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	Yes, considered. The reference group was operationalized as "long-term abstainers or very light drinkers."



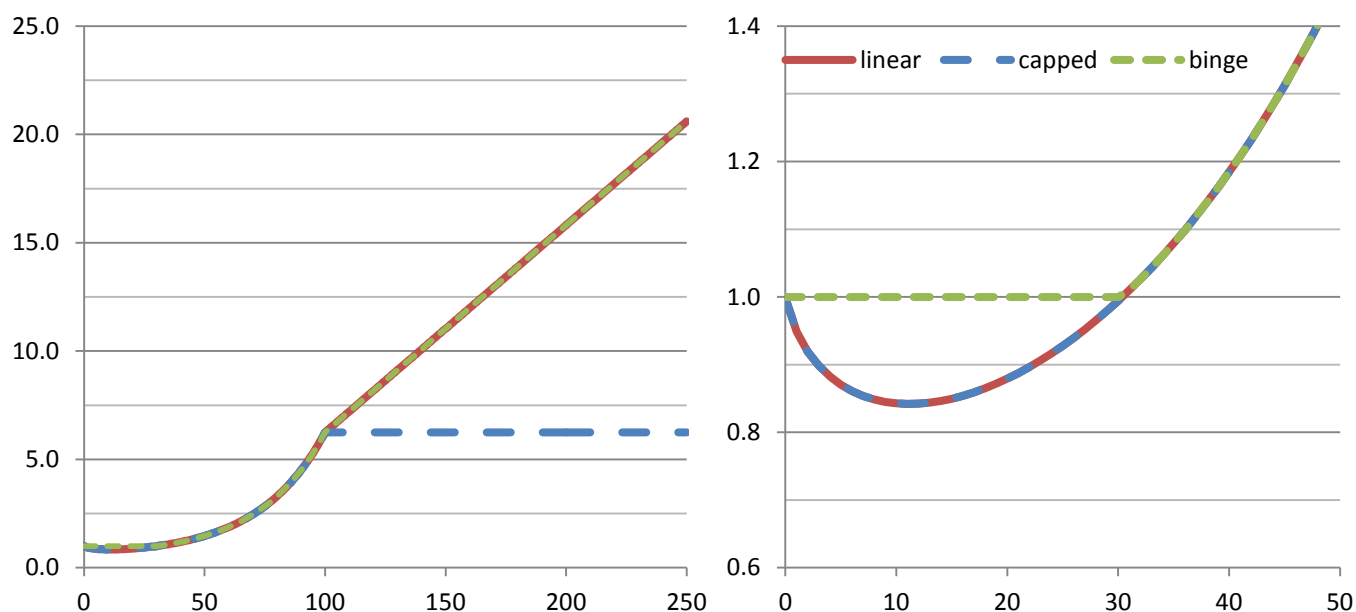
Sources

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.
 Roerecke, M., & Rehm, J. (2010a). Irregular heavy drinking occasions and risk of ischemic heart disease: a systematic review and meta-analysis. *American journal of epidemiology*, 171(6), 633-644.
 Roerecke, M., & Rehm, J. (2010b). Ischemic heart disease mortality and morbidity rates in former drinkers: a meta-analysis. *American journal of epidemiology*, 173(3), 245-258.

(5).(2) Ischaemic heart disease mortality, women

Condition category: (5) Cardiovascular conditions
ICD10 codes: I20 to I25

	Current drinkers	Former drinkers
Source	Roerecke & Rehm (2012) Figure 2 Roerecke & Rehm (2010a) From text, e.g. in abstract	Roerecke & Rehm (2010b) Table 3
Relative risk Function or estimate	$\ln RR(x) = -0.0525288x + 0.0153856x \ln x$ $RR(x) = \exp(-0.0525288x + 0.0153856x \ln x)$	$RR_{FD} = 1.54$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Roerecke & Rehm (2010a) modifies the RR curve for bingers by removing the protective effect (i.e. $RR=1.0$).	Results stratified by gender and endpoint (outcome) used. Current: In the figure below, the binge level is set at 60g/day; therefore $RR=1.0$ above this as this portion of the population is guaranteed to binge.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	Yes, considered. The reference group was operationalized as "long-term abstainers or very light drinkers."



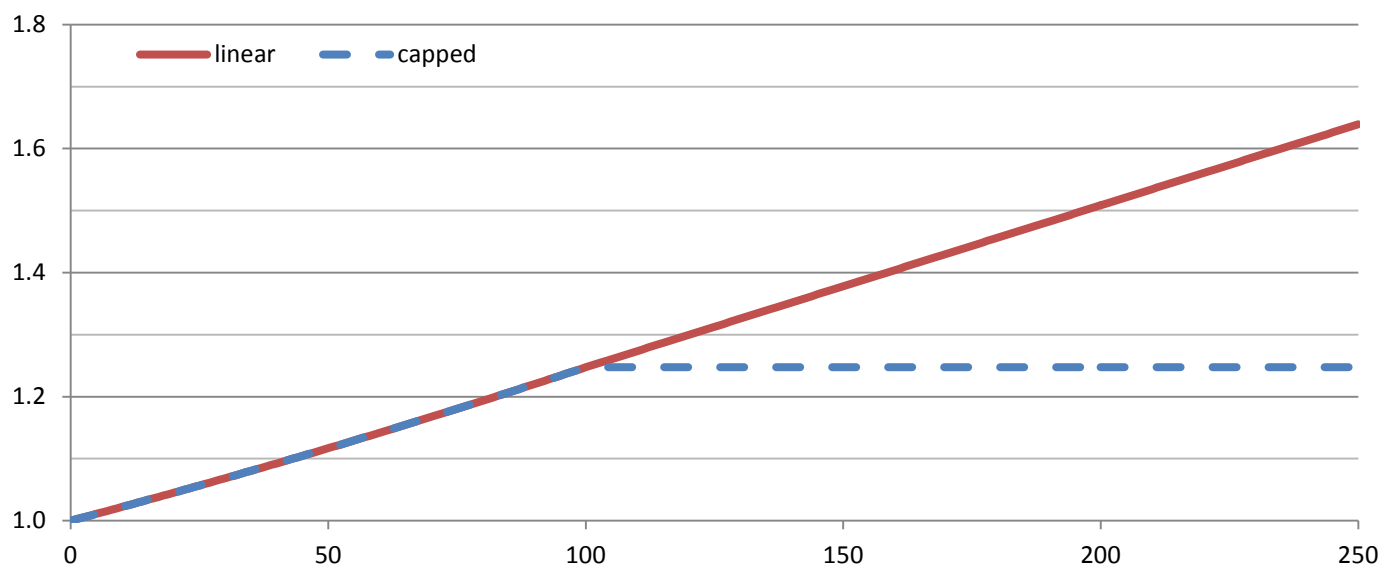
Sources

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.
 Roerecke, M., & Rehm, J. (2010a). Irregular heavy drinking occasions and risk of ischemic heart disease: a systematic review and meta-analysis. *American journal of epidemiology*, 171(6), 633-644.
 Roerecke, M., & Rehm, J. (2010b). Ischemic heart disease mortality and morbidity rates in former drinkers: a meta-analysis. *American journal of epidemiology*, 173(3), 245-258.

(5).(2) Ischaemic heart disease morbidity, men (two options)

Condition category: (5) Cardiovascular conditions
ICD10 codes: I20 to I25

	Current drinkers	Former drinkers
Source	Zhao et al. (2017) Table 3, top panel, fully-adjusted results, custom analysis (see comments)	Roerecke & Rehm (2010b) Table 3
Relative risk Function or estimate	$\ln RR(x) = 0.002211x$ $RR(x) = \exp(0.002211x)$	$RR_{FD} = 1.25$
Comments	Fully-adjusted model for the younger age cohort in Table 3 was re-analyzed by the first author upon request to include a gender breakdown and to provide a continuous relationship. Results received through personal correspondence between AS, TS and J. Zhao (dated 14-Oct-17).	Results stratified by gender and endpoint (outcome) used. Note: in this option, the RR function from IHD mortality in men, calculated by J. Zhao from the article below, is used as the RR function for IHD morbidity in men.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study explicitly controlled for abstainer biases selecting studies with no bias and selecting younger cohorts, among other methods. See article for full methodology.	Yes, considered. The reference group was operationalized as "long-term abstainers or very light drinkers."



Sources

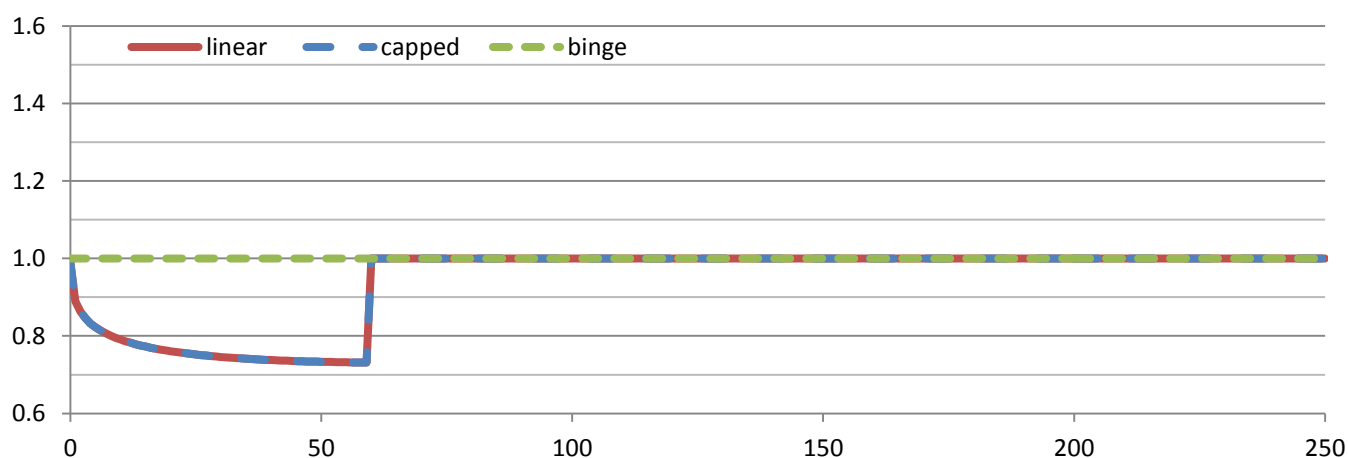
Zhao, J., Stockwell, T., Roemer, A., Naimi, T., Chikritzhs, T. (2017). Alcohol consumption and mortality from coronary heart disease: An updated meta-analysis of cohort studies. *Journal of Studies on Alcohol and Drugs*, 78, 375-386.

Roerecke, M., & Rehm, J. (2010b). Ischemic heart disease mortality and morbidity rates in former drinkers: a meta-analysis. *American journal of epidemiology*, 173(3), 245-258.

(5).(2) Ischaemic heart disease morbidity, men (two options)

Condition category: (5) Cardiovascular conditions
ICD10 codes: I20 to I25

	Current drinkers	Former drinkers
Source	Roerecke & Rehm (2012) Figure 2 Roerecke & Rehm (2010a) From text, e.g. in abstract	Roerecke & Rehm (2010b) Table 3
Relative risk Function or estimate	$\ln RR(x) = -0.1178113\sqrt{x} + 0.0189\sqrt{x} \ln x$ $RR(x) = \exp(-0.1178113\sqrt{x} + 0.0189\sqrt{x} \ln x)$	$RR_{FD} = 0.85$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Roerecke & Rehm (2010a) modifies the RR curve for bingers by removing the protective effect (i.e. $RR=1.0$). In the figure below, the binge level is set at 60g/day; therefore $RR=1.0$ above this as this portion of the population is guaranteed to binge.	Results stratified by gender and endpoint(outcome) used. Note: linear and capped curves are identical.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	Yes, considered. The reference group was operationalized as "long-term abstainers or very light drinkers."



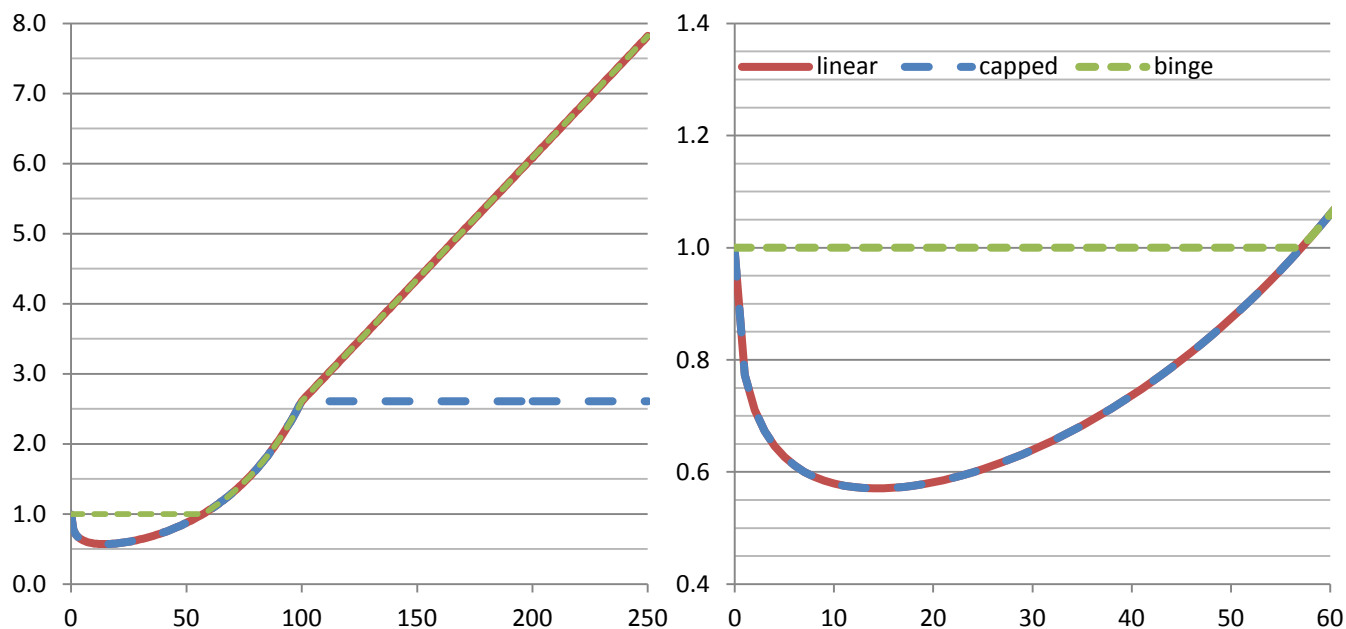
Sources

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.
 Roerecke, M., & Rehm, J. (2010a). Irregular heavy drinking occasions and risk of ischemic heart disease: a systematic review and meta-analysis. *American journal of epidemiology*, 171(6), 633-644.
 Roerecke, M., & Rehm, J. (2010b). Ischemic heart disease mortality and morbidity rates in former drinkers: a meta-analysis. *American journal of epidemiology*, 173(3), 245-258.

(5).(2) Ischaemic heart disease morbidity, women

Condition category: (5) Cardiovascular conditions
ICD10 codes: I20 to I25

	Current drinkers	Former drinkers
Source	Roerecke & Rehm (2012) Figure 2 Roerecke & Rehm (2010a) From text, e.g. in abstract	Roerecke & Rehm (2010b) Table 3
Relative risk Function or estimate	$\ln RR(x) = -0.296842\sqrt{x} + 0.0392805x$ $RR(x) = \exp(-0.296842\sqrt{x} + 0.0392805x)$	$RR_{FD} = 1.05$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Roerecke & Rehm (2010a) modifies the RR curve for binge drinkers by removing the protective effect (i.e. $RR=1.0$).	Results stratified by gender and endpoint used. Current: In the figure below, the binge level is set at 60g/day; therefore $RR=1.0$ above this as this portion of the population is guaranteed to binge.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	Yes, considered. The reference group was operationalized as "long-term abstainers or very light drinkers."



Sources

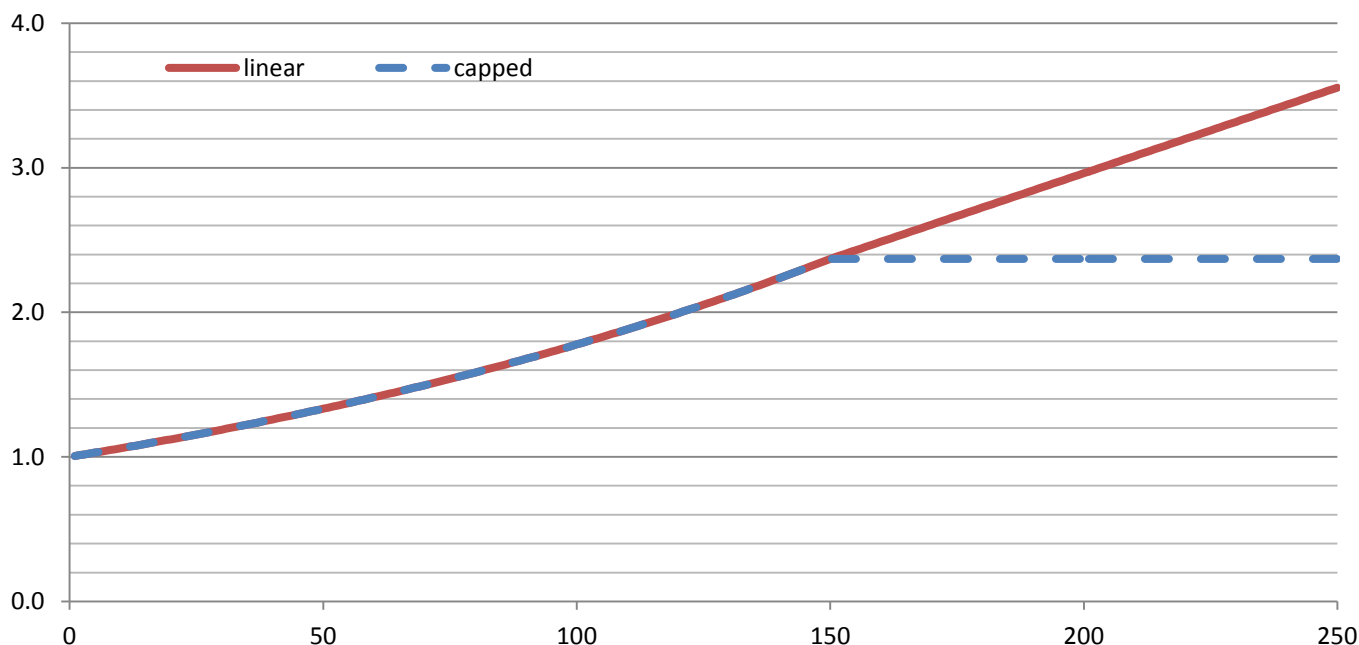
Roerecke, M., & Rehm, J. (2012). The cardioprotective association of average alcohol consumption and ischaemic heart disease: a systematic review and meta-analysis. *Addiction*, 107(7), 1246-1260.
 Roerecke, M., & Rehm, J. (2010a). Irregular heavy drinking occasions and risk of ischemic heart disease: a systematic review and meta-analysis. *American journal of epidemiology*, 171(6), 633-644.
 Roerecke, M., & Rehm, J. (2010b). Ischemic heart disease mortality and morbidity rates in former drinkers: a meta-analysis. *American journal of epidemiology*, 173(3), 245-258.

(5).(4) Atrial fibrillation and cardiac arrhythmia

Condition category: (5) Cardiovascular conditions

ICD10 codes: I47 to I49

	Current drinkers	Former drinkers
Source	Samokhvalov et al. (2010) Figure 3	Larsson et al. (2014) Table 1, right column of results Also reported in Rehm et al. (2017)
Relative risk Function or estimate	$\ln RR(x) = 0.00575183x$ $RR(x) = \exp(0.00575183x)$	$RR_{FD} = 1.01$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	No. The methods of this article do not describe a methodology for controlling for potential abstainer bias in the constituent studies.	No. The methods of this article do not describe a methodology for controlling for potential abstainer bias in the constituent studies.



Sources

Samokhvalov, A. V., Irving, H. M., & Rehm, J. (2010). Alcohol consumption as a risk factor for atrial fibrillation: a systematic review and meta-analysis. *European Journal of Cardiovascular Prevention & Rehabilitation*, 17(6), 706-712.

Larsson, S. C., Drca, N., & Wolk, A. (2014). Alcohol consumption and risk of atrial fibrillation: a prospective study and dose-response meta-analysis. *Journal of the American College of Cardiology*, 64(3), 281-289.

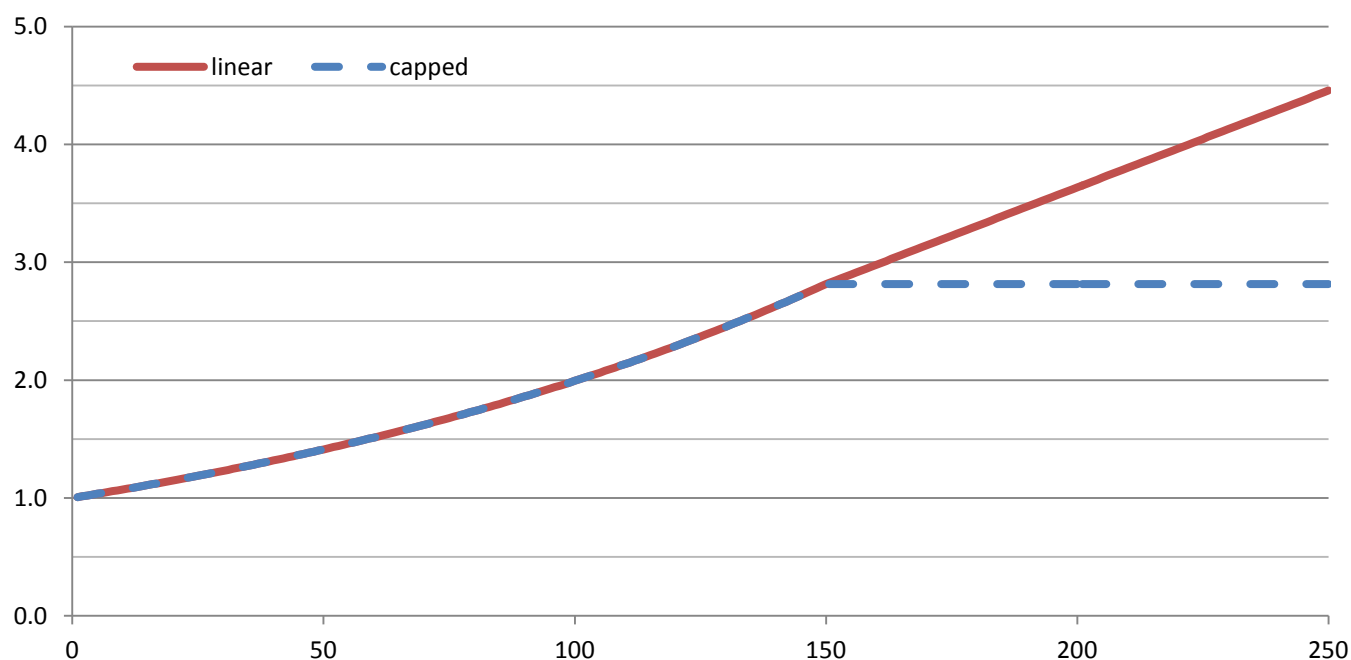
Rehm, J., Sherk, A., Shield, K.D., & Gmel, G. (2017). Risk relations between alcohol use and non-injury causes of death. Version 2: September 2017. Toronto, Canada: Centre for Addiction and Mental Health. ISBN: [978-1-77114-399-8](https://doi.org/10.1111/9781771143998).

(5).(5) Haemorrhagic stroke mortality, men

Condition category: (5) Cardiovascular conditions

ICD10 codes: I60 to I62, I69.0 to I69.2

	Current drinkers	Former drinkers
Source	Patra et al. (2010) Figure 6	Larsson et al. (2016) Supplementary Table S2, pooled analysis
Relative risk Function or estimate	$\ln RR(x) = 0.006898937x$ $RR(x) = \exp(0.006898937x)$	$RR_{FD} = 1.36$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	No. This study does not explicitly account for abstainer bias.



Sources

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(1), 258.

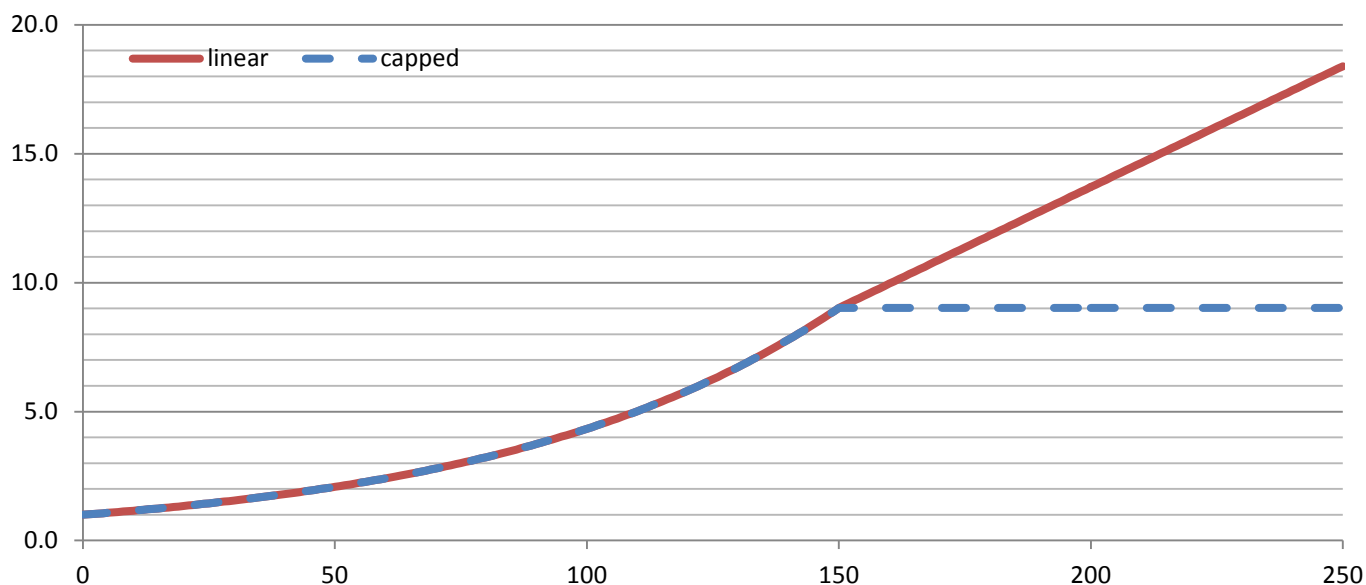
Larsson, S. C., Wallin, A., Wolk, A., & Markus, H. S. (2016). Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. *BMC medicine*, 14(1), 178.

(5).(5) Haemorrhagic stroke mortality, women

Condition category: (5) Cardiovascular conditions

ICD10 codes: I60 to I62, I69.0 to I69.2

	Current drinkers	Former drinkers
Source	Patra et al. (2010) Figure 6	Larsson et al. (2016) Supplementary Table S2, pooled analysis
Relative risk Function or estimate	$\ln RR(x) = 0.01466406x$ $RR(x) = \exp(0.01466406x)$	$RR_{FD} = 1.36$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	Note: the functional form of this curve is misreported in Patra et al. (2010) as $\beta_1 \ln x + \beta_2 x$. The correct functional form used here was received by KDS from first author on 29-Aug-17.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	No. This study does not explicitly account for abstainer bias.



Sources

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(1), 258.

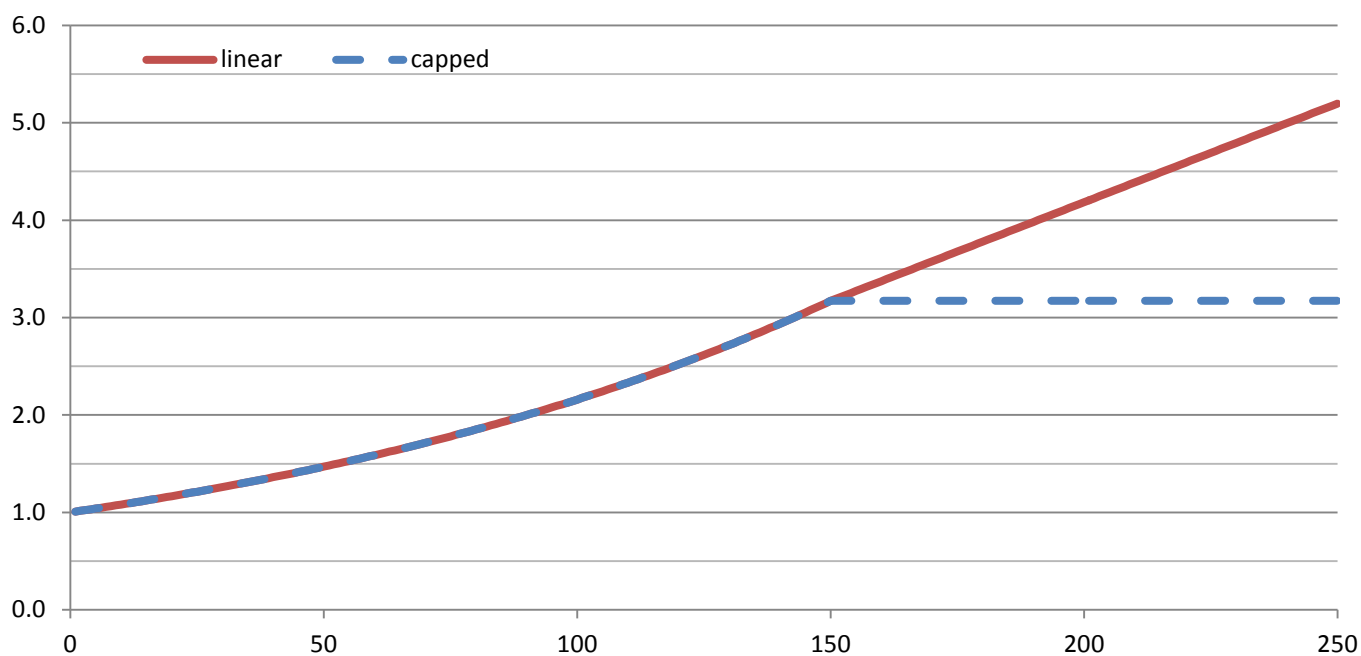
Larsson, S. C., Wallin, A., Wolk, A., & Markus, H. S. (2016). Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. *BMC medicine*, 14(1), 178.

(5).(5) Haemorrhagic stroke morbidity, men

Condition category: (5) Cardiovascular conditions

ICD10 codes: I60 to I62, I69.0 to I69.2

	Current drinkers	Former drinkers
Source	Patra et al. (2010) Figure 6	Larsson et al. (2016) Supplementary Table S2, pooled analysis
Relative risk Function or estimate	$\ln RR(x) = 0.007695021x$ $RR(x) = \exp(0.007695021x)$	$RR_{FD} = 1.36$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	No. This study does not explicitly account for abstainer bias.



Sources

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(1), 258.

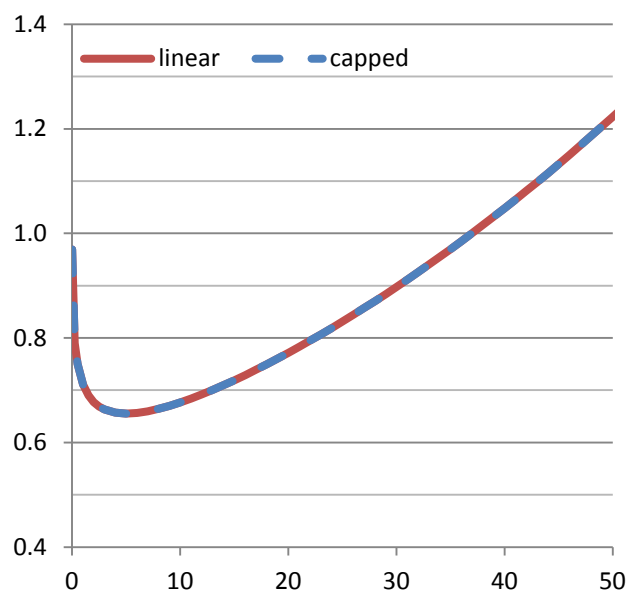
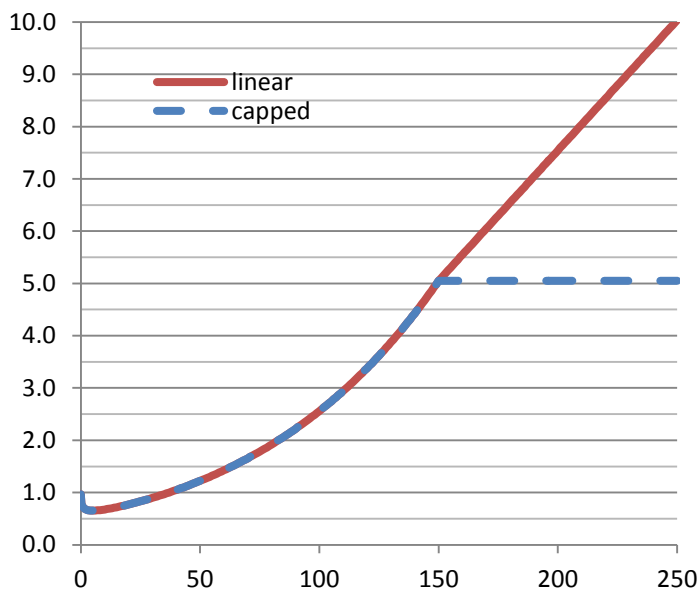
Larsson, S. C., Wallin, A., Wolk, A., & Markus, H. S. (2016). Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. *BMC medicine*, 14(1), 178.

(5).(5) Haemorrhagic stroke morbidity, women

Condition category: (5) Cardiovascular conditions

ICD10 codes: I60 to I62, I69.0 to I69.5

	Current drinkers	Former drinkers
Source	Patra et al. (2010) Figure 6	Larsson et al. (2016) Supplementary Table S2, pooled analysis
Relative risk Function or estimate	$\ln RR(x) = -0.340861\sqrt{x} + 0.0944208\sqrt{x} \ln x$ $RR(x) = \exp(-0.340861\sqrt{x} + 0.0944208\sqrt{x} \ln x)$	$RR_{FD} = 1.36$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	No. This study does not explicitly account for abstainer bias.



Sources

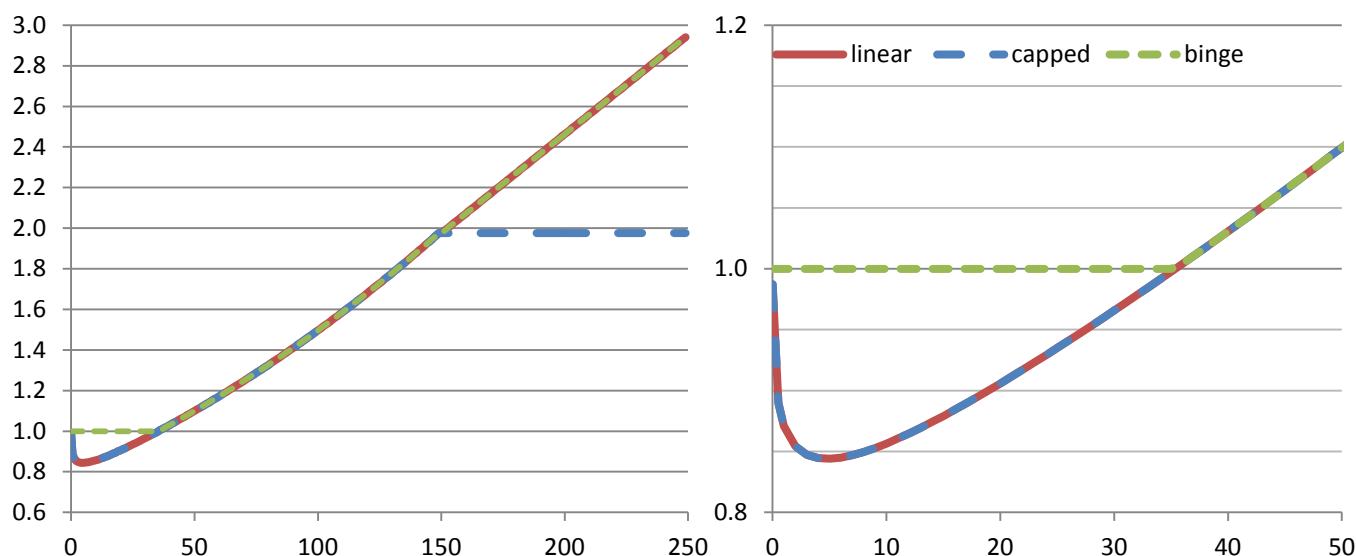
Patra, J., Taylor, B., Irving, H., Roerecke, M., Baliunas, D., Mohapatra, S., & Rehm, J. (2010). Alcohol consumption and the risk of morbidity and mortality for different stroke types-a systematic review and meta-analysis. *BMC public health*, 10(1), 258.

Larsson, S. C., Wallin, A., Wolk, A., & Markus, H. S. (2016). Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. *BMC medicine*, 14(1), 178.

(5).(6) Ischaemic stroke mortality, men

Condition category: (5) Cardiovascular conditions
ICD10 codes: I63 to I67, I69.3

	Current drinkers	Former drinkers
Source	Patra et al. (2010) Figure 7 Rehm et al. (2016) From text, in methods	Larsson et al. (2016) Supplementary Table S2, pooled analysis
Relative risk Function or estimate	$\ln RR(x) = -0.1382664\sqrt{x} + 0.03877538\sqrt{x} \ln x$ $RR(x) = \exp(-0.1382664\sqrt{x} + 0.03877538\sqrt{x} \ln x)$	$RR_{FD} = 0.97$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Rehm et al. (2016) modifies the RR curve for bingers by removing the protective effect (i.e. $RR=1.0$).	Note: In the figure below, the binge level is set at 60g/day; therefore $RR=1.0$ above this as this portion of the population is guaranteed to binge.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	No. This study does not explicitly account for abstainer bias.



Sources

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(1), 258.

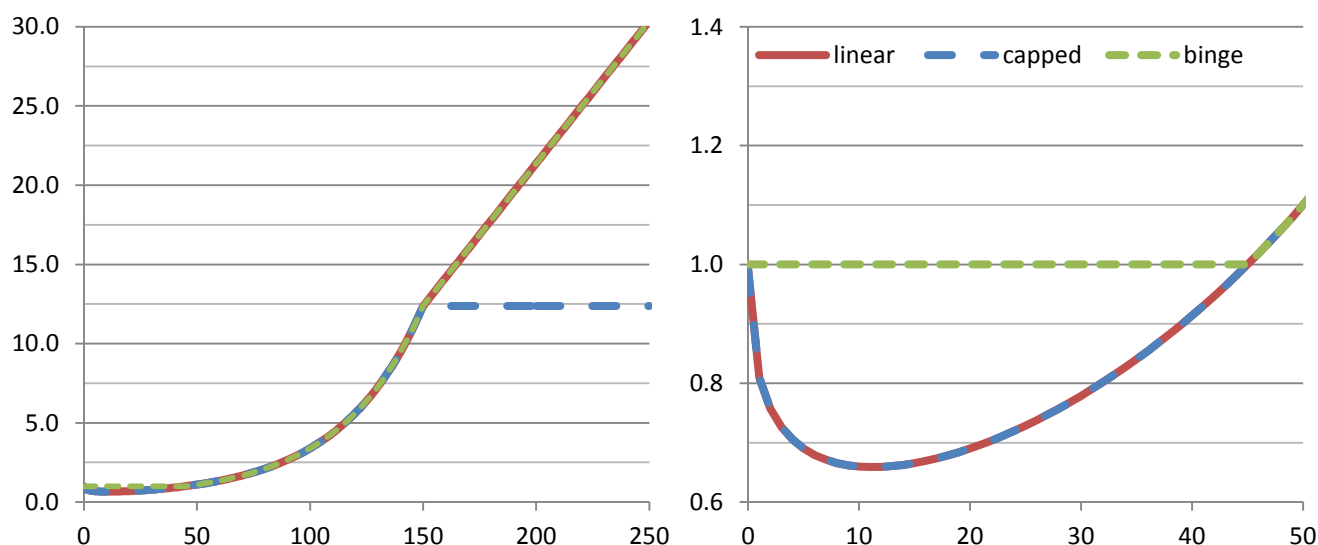
Larsson, S. C., Wallin, A., Wolk, A., & Markus, H. S. (2016). Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. *BMC medicine*, 14(1), 178.

Rehm, J., Shield, K. D., Roerecke, M., & Gmel, G. (2016). Modelling the impact of alcohol consumption on cardiovascular disease mortality for comparative risk assessments: an overview. *BMC Public Health*, 16(1), 363.

(5).(6) Ischaemic stroke mortality, women

Condition category: (5) Cardiovascular conditions
ICD10 codes: I63 to I67, I69.3

	Current drinkers	Former drinkers
Source	Patra et al. (2010) Figure 7 Rehm et al. (2016) From text, in methods	Larsson et al. (2016) Supplementary Table S2, pooled analysis
Relative risk Function or estimate	$\ln RR(x) = -0.248768\sqrt{x} + 0.03708724x$ $RR(x) = \exp(-0.248768\sqrt{x} + 0.03708724x)$	$RR_{FD} = 0.97$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Rehm et al. (2016) modifies the RR curve for bingers by removing the protective effect (i.e. $RR=1.0$).	Note: In the figure below, the binge level is set at 60g/day; therefore $RR=1.0$ above this as this portion of the population is guaranteed to binge.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	No. This study does not explicitly account for abstainer bias.



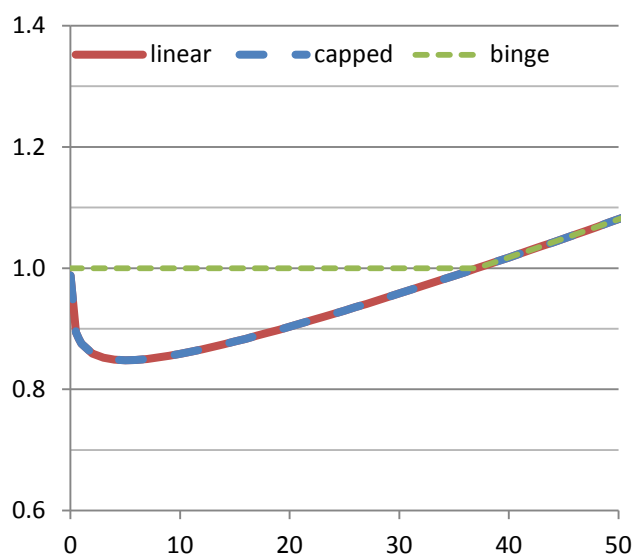
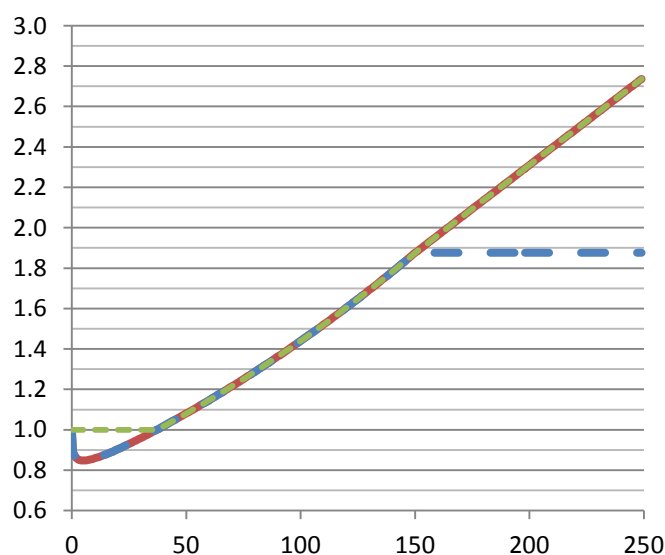
Sources

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(1), 258.
 Larsson, S. C., Wallin, A., Wolk, A., & Markus, H. S. (2016). Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. *BMC medicine*, 14(1), 178.
 Rehm, J., Shield, K. D., Roerecke, M., & Gmel, G. (2016). Modelling the impact of alcohol consumption on cardiovascular disease mortality for comparative risk assessments: an overview. *BMC Public Health*, 16(1), 363.

(5).(6) Ischaemic stroke morbidity, men

Condition category: (5) Cardiovascular conditions
ICD10 codes: I63 to I67, I69.2

	Current drinkers	Former drinkers
Source	Patra et al. (2010) Figure 7 Rehm et al. (2016) From text, in methods	Larsson et al. (2016) Supplementary Table S2, pooled analysis
Relative risk Function or estimate	$\ln RR(x) = -0.132894\sqrt{x} + 0.03677422\sqrt{x} \ln x$ $RR(x) = \exp(-0.132894\sqrt{x} + 0.03677422\sqrt{x} \ln x)$	$RR_{FD} = 0.97$
Comments	RR function received directly from members of authorship group who are members of this project. Rehm et al. (2016) modifies the RR curve for bingers by removing the protective effect (i.e. $RR=1.0$).	Note: In the figure below, the binge level is set at 60g/day; therefore $RR=1.0$ above this as this portion of the population is guaranteed to binge.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	No. This study does not explicitly account for abstainer bias.



Sources

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(1), 258.

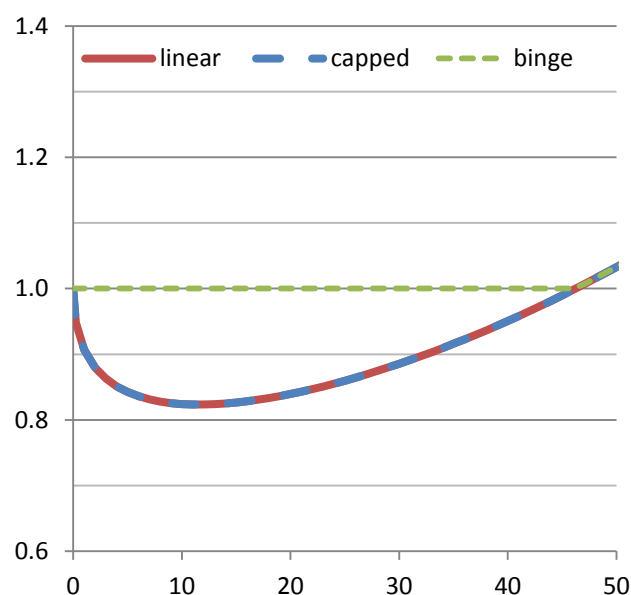
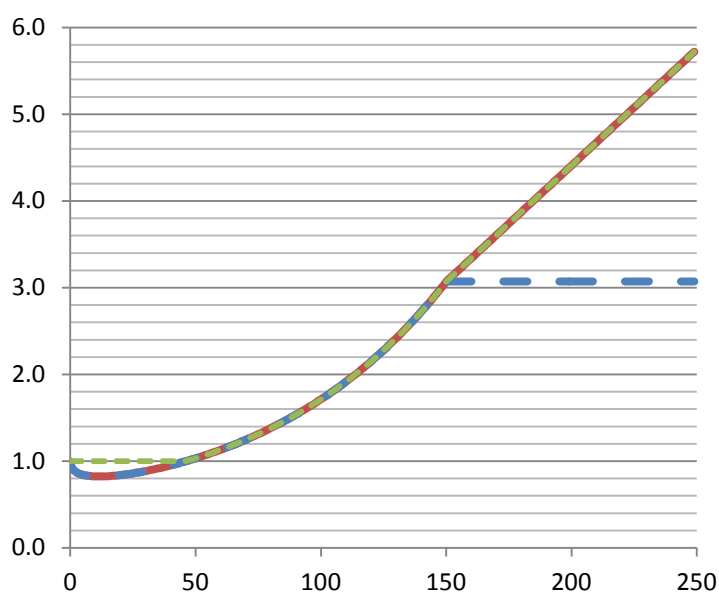
Larsson, S. C., Wallin, A., Wolk, A., & Markus, H. S. (2016). Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. *BMC medicine*, 14(1), 178.

Rehm, J., Shield, K. D., Roerecke, M., & Gmel, G. (2016). Modelling the impact of alcohol consumption on cardiovascular disease mortality for comparative risk assessments: an overview. *BMC Public Health*, 16(1), 363.

(5).(6) Ischaemic stroke morbidity, women

Condition category: (5) Cardiovascular conditions
ICD10 codes: I63 to I67, I69.2

	Current drinkers	Former drinkers
Source	Patra et al. (2010) Figure 7 Rehm et al. (2016) From text, in methods	Larsson et al. (2016) Supplementary Table S2, pooled analysis
Relative risk Function or estimate	$\ln RR(x) = -0.114287\sqrt{x} + 0.01680936x$ $RR(x) = \exp(-0.114287\sqrt{x} + 0.01680936x)$	$RR_{FD} = 0.97$
Comments	Relative risk function received directly from members of authorship group who are members of this project. Rehm et al. (2016) modifies the RR curve for bingers by removing the protective effect (i.e. $RR=1.0$).	Note: In the figure below, the binge level is set at 60g/day; therefore $RR=1.0$ above this as this portion of the population is guaranteed to binge.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. This study reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	No. This study does not explicitly account for abstainer bias.



Sources

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(1), 258.

Larsson, S. C., Wallin, A., Wolk, A., & Markus, H. S. (2016). Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. *BMC medicine*, 14(1), 178.

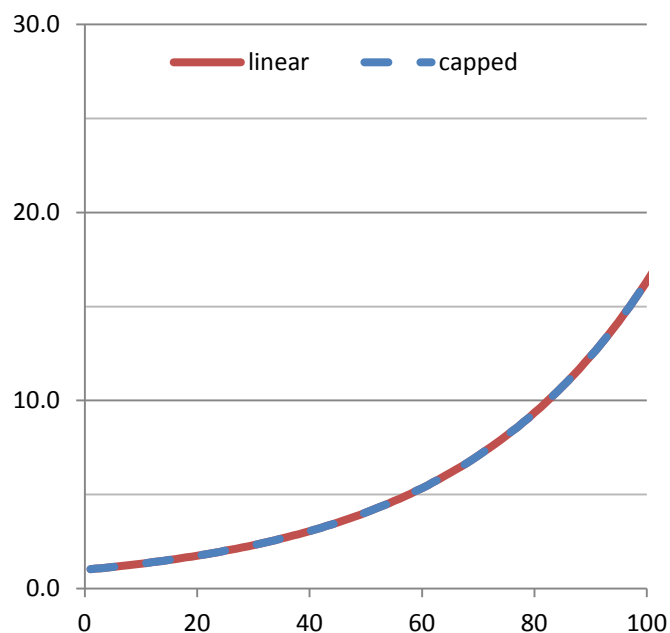
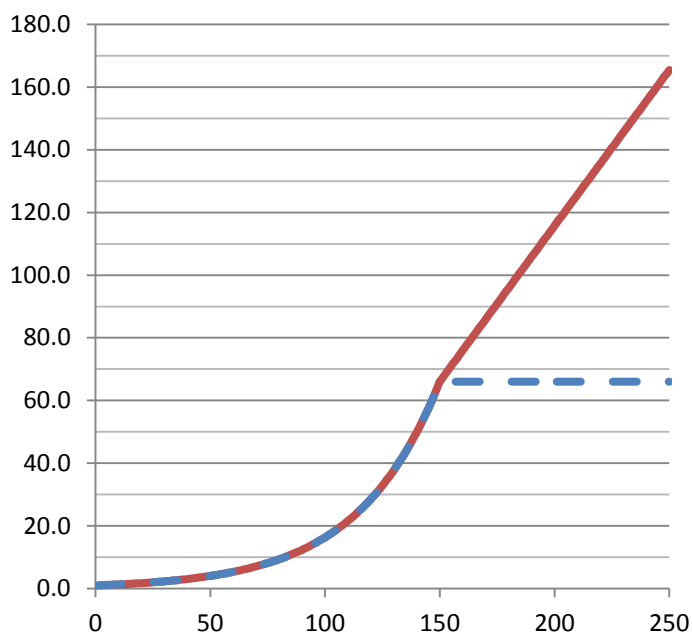
Rehm, J., Shield, K. D., Roerecke, M., & Gmel, G. (2016). Modelling the impact of alcohol consumption on cardiovascular disease mortality for comparative risk assessments: an overview. *BMC Public Health*, 16(1), 363.

(6).(2) Liver cirrhosis mortality, men

Condition category: (6) Digestive conditions

ICD10 codes: K70,K74

	Current drinkers	Former drinkers
Source	Rehm et al. (2010) Figure 2	Roerecke et al. (2017) CAMH working report Also reported in Rehm et al. (2017)
Relative risk Function or estimate	$\ln RR(x) = 0.02793524x$ $RR(x) = \exp(0.02793524x)$	$RR_{FD} = 3.26$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. Rehm et al. (2010a) reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	Not known – not yet finalized.



Sources

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 and alcohol review*, 29(4), 437-445.

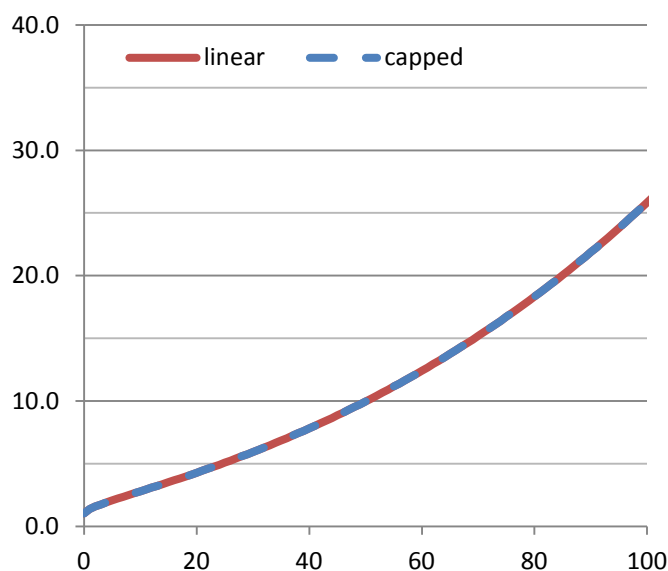
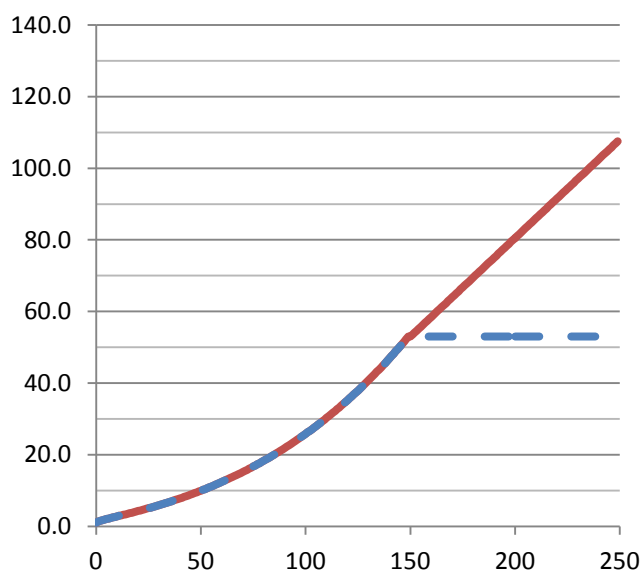
Roerecke et al. (2017) CAMH working paper.

Rehm, J., Sherk, A., Shield, K.D., & Gmel, G. (2017). Risk relations between alcohol use and non-injury causes of death. Version 2: September 2017. Toronto, Canada: Centre for Addiction and Mental Health. ISBN: [978-1-77114-399-8](https://doi.org/10.1007/978-1-77114-399-8).

(6).(2) Liver cirrhosis mortality, women

Condition category: (6) Digestive conditions
ICD10 codes: K70,K74

	Current drinkers	Former drinkers
Source	Rehm et al. (2010) Figure 2	Roerecke et al. (2017) CAMH working report Also reported in Rehm et al. (2017)
Relative risk Function or estimate	$\ln RR(x) = 0.32520349\sqrt{x}$ $RR(x) = \exp(0.32520349\sqrt{x})$	$RR_{FD} = 3.26$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. Rehm et al. (2010a) reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	Not known – not yet finalized.



Sources

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 and alcohol review*, 29(4), 437-445.

Roerecke et al. (2017) CAMH working paper.

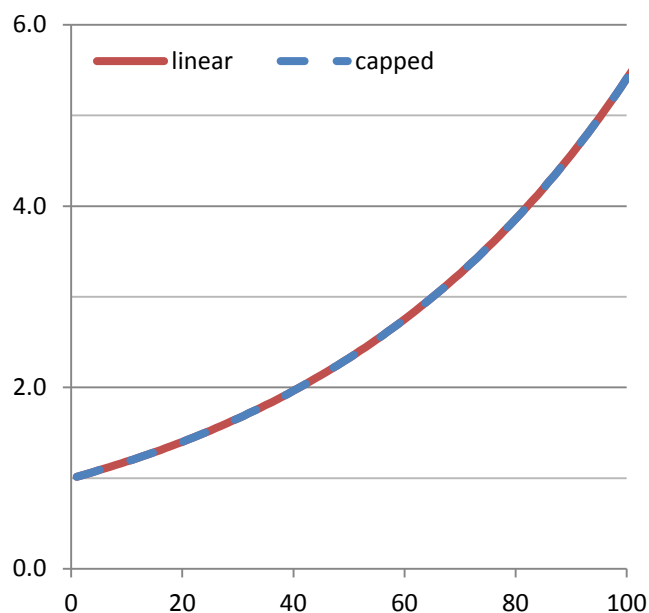
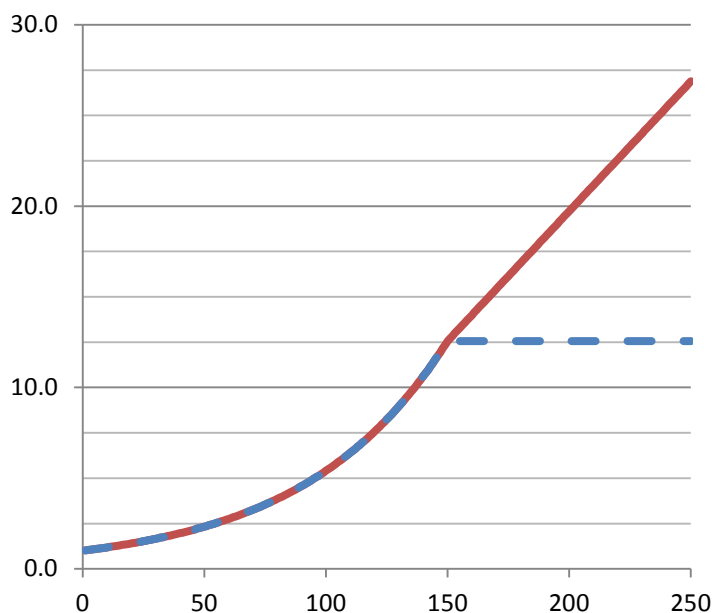
Rehm, J., Sherk, A., Shield, K.D., & Gmel, G. (2017). Risk relations between alcohol use and non-injury causes of death. Version 2: September 2017. Toronto, Canada: Centre for Addiction and Mental Health. ISBN: [978-1-77114-399-8](https://doi.org/10.1007/978-1-77114-399-8).

(6).(2) Liver cirrhosis morbidity, men

Condition category: (6) Digestive conditions

ICD10 codes: K70,K74

	Current drinkers	Former drinkers
Source	Rehm et al. (2010) Figure 2	Roerecke et al. (2017) CAMH working report Also reported in Rehm et al. (2017)
Relative risk Function or estimate	$\ln RR(x) = 0.01687111x$ $RR(x) = \exp(0.01687111x)$	$RR_{FD} = 3.26$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. Rehm et al. (2010a) reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	Not known – not yet finalized.



Sources

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 and alcohol review*, 29(4), 437-445.

Roerecke et al. (2017) CAMH working paper.

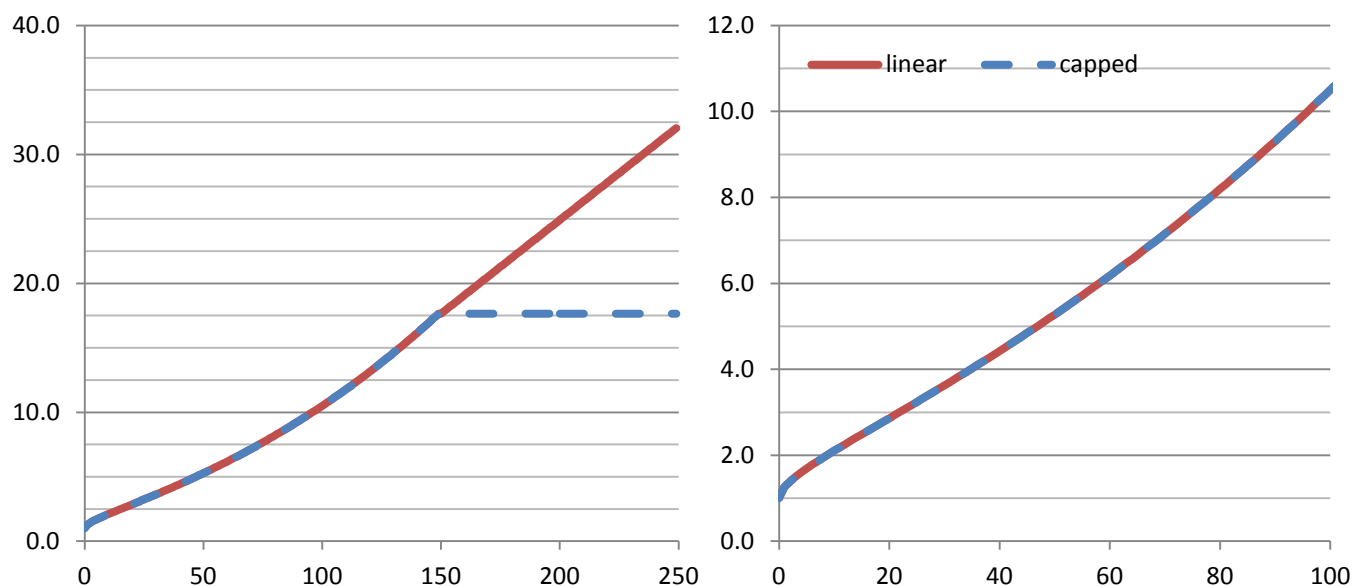
Rehm, J., Sherk, A., Shield, K.D., & Gmel, G. (2017). Risk relations between alcohol use and non-injury causes of death. Version 2: September 2017. Toronto, Canada: Centre for Addiction and Mental Health. ISBN: [978-1-77114-399-8](https://doi.org/10.1007/978-1-77114-399-8).

(6).(2) Liver cirrhosis morbidity, women

Condition category: (6) Digestive conditions

ICD10 codes: K70,K74

	Current drinkers	Former drinkers
Source	Rehm et al. (2010) Figure 2	Roerecke et al. (2017) CAMH working report Also reported in Rehm et al. (2017)
Relative risk Function or estimate	$\ln RR(x) = 0.2351821\sqrt{x}$ $RR(x) = \exp(0.2351821\sqrt{x})$	$RR_{FD} = 3.26$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. Rehm et al. (2010a) reweighted relative risk results from studies which pooled former and never drinkers as abstainers using a standard methodology.	Not known – not yet finalized.



Sources

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 and alcohol review*, 29(4), 437-445.

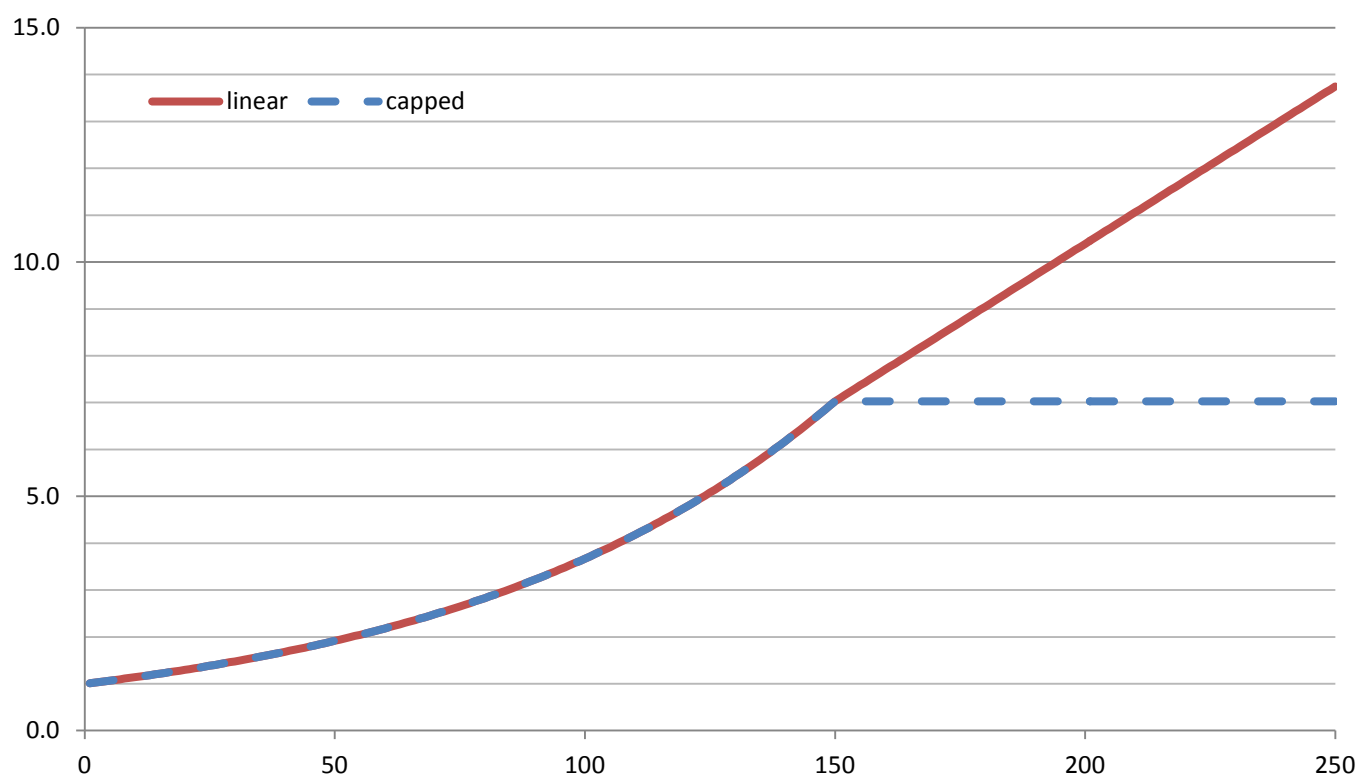
Roerecke et al. (2017) CAMH working paper.

Rehm, J., Sherk, A., Shield, K.D., & Gmel, G. (2017). Risk relations between alcohol use and non-injury causes of death. Version 2: September 2017. Toronto, Canada: Centre for Addiction and Mental Health. ISBN: [978-1-77114-399-8](#)

(6).(3) Acute pancreatitis, men

Condition category: (6) Digestive conditions
ICD10 codes: K85.0, K85.1, K85.8, K85.9

	Current drinkers	Former drinkers
Source	Samokhvalov et al. (2015) Figure 3, Table 2	Samokhvalov et al. (2015) Reported in discussion
Relative risk Function or estimate	$\ln RR(x) = 0.013x$ $RR(x) = \exp(0.013x)$	$RR_{FD} = 2.20$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. Samokhvalov et al. (2015) gave priority to studies where lifetime abstainers were the risk reference group.	Yes. Samokhvalov et al. (2015) gave priority to studies where lifetime abstainers were the risk reference group.



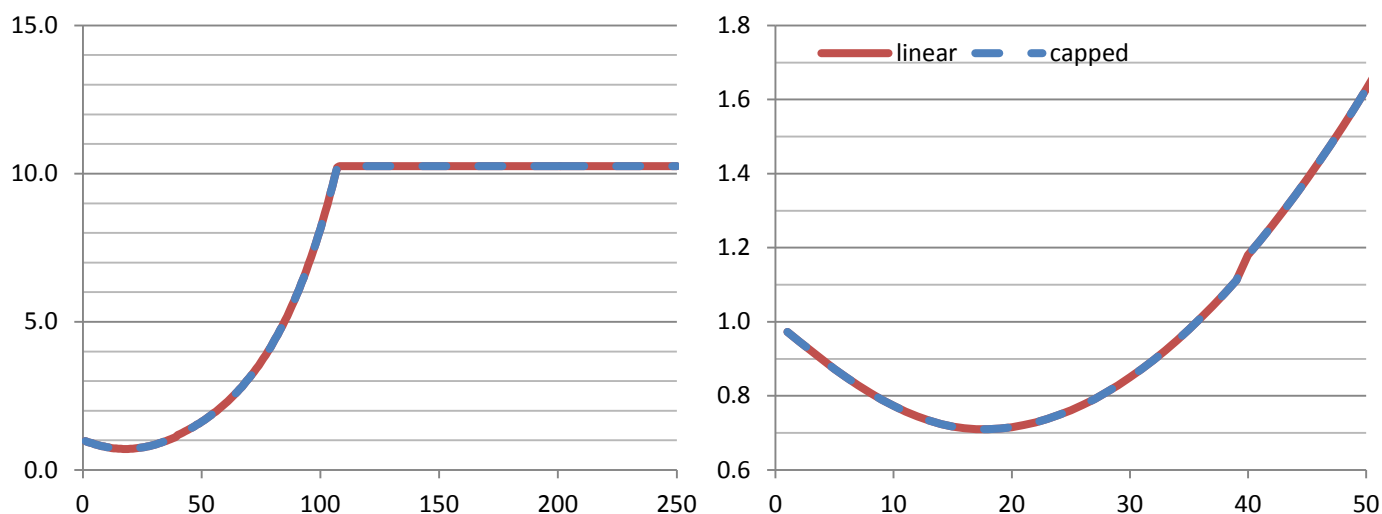
Sources

Samokhvalov, A. V., Rehm, J., & Roerecke, M. (2015). Alcohol consumption as a risk factor for acute and chronic pancreatitis: a systematic review and a series of meta-analyses. *EBioMedicine*, 2(12), 1996-2002.

(6).(3) Acute pancreatitis, women

Condition category: (6) Digestive conditions
ICD10 codes: K85.0, K85.1, K85.8, K85.9

	Current drinkers	Former drinkers
Source	Samokhvalov et al. (2015) Figure 4, Table 2	Samokhvalov et al. (2015) Reported in discussion $RR_{FD} = 2.20$
Relative risk Function or estimate	$\ln RR(x) = \begin{cases} -0.0272886x, & 0 < x < 3 \\ -0.0272886x + 0.0611466 \frac{(x-3)^3}{37^2}, & 3 \leq x < 15 \\ -0.0272886x + 0.0611466 \frac{(x-3)^3 - \frac{37(x-15)^3}{25}}{37^2}, & 15 \leq x < 40 \\ -0.0272886x + 0.0611466 \frac{(x-3)^3 - \frac{37(x-15)^3 - 12(x-40)^3}{25}}{37^2}, & 40 \leq x < 108 \\ 2.327965, & x \geq 108 \end{cases}$	
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias	Yes, for both current and former drinkers. Samokhvalov et al. (2015) gave priority to studies where lifetime abstainers were the risk reference group.	



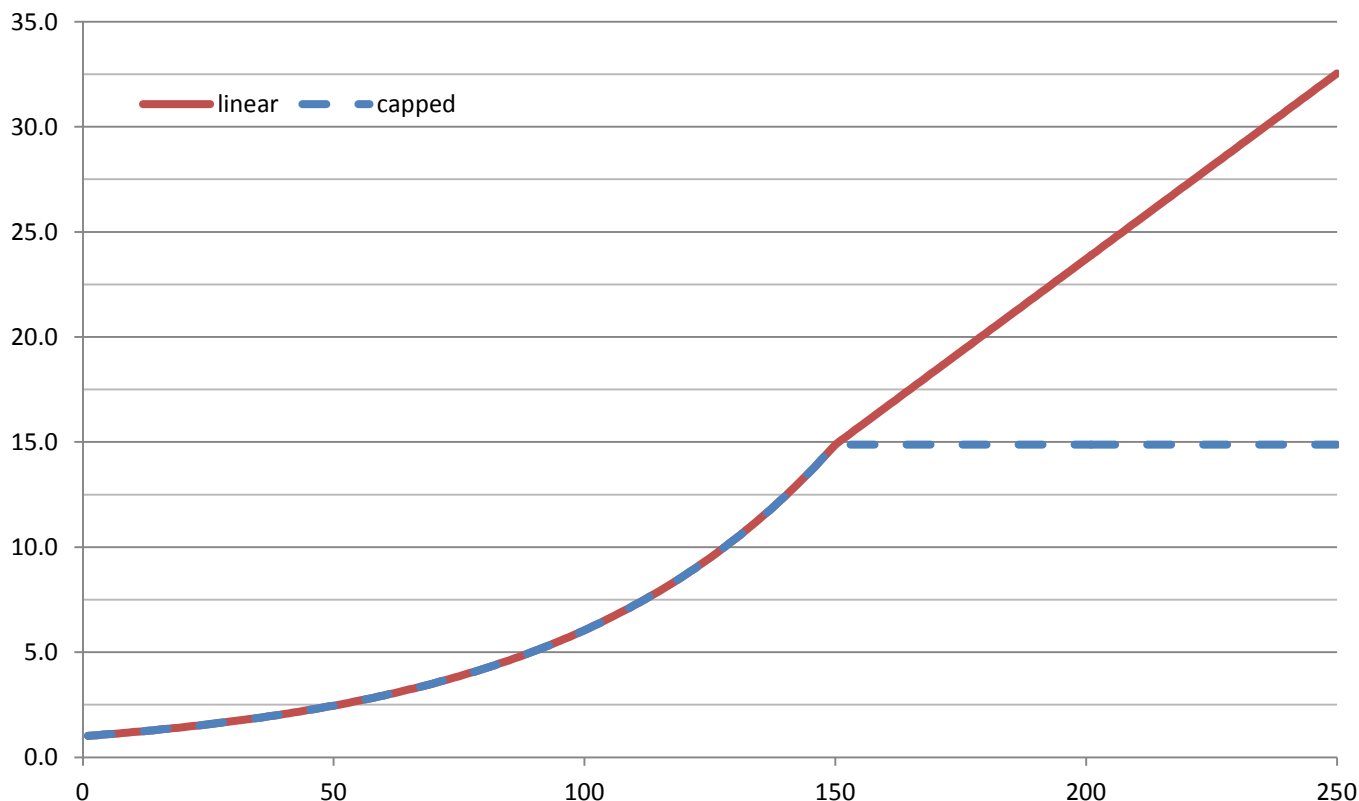
Sources

Samokhvalov, A. V., Rehm, J., & Roerecke, M. (2015). Alcohol consumption as a risk factor for acute and chronic pancreatitis: a systematic review and a series of meta-analyses. *EBioMedicine*, 2(12), 1996-2002.

(6).(4) Chronic pancreatitis

Condition category: (6) Digestive conditions
ICD10 codes: K86.1 to K86.9

	Current drinkers	Former drinkers
Source	Samokhvalov et al. (2015) Figure 2, Table 2	Samokhvalov et al. (2015) Reported in discussion
Relative risk Function or estimate	$\ln RR(x) = 0.018x$ $RR(x) = \exp(0.018x)$	$RR_{FD} = 2.20$
Comments	Relative risk function received directly from members of authorship group who are members of this project.	
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Yes. Samokhvalov et al. (2015) gave priority to studies where lifetime abstainers were the risk reference group.	Yes. Samokhvalov et al. (2015) gave priority to studies where lifetime abstainers were the risk reference group.



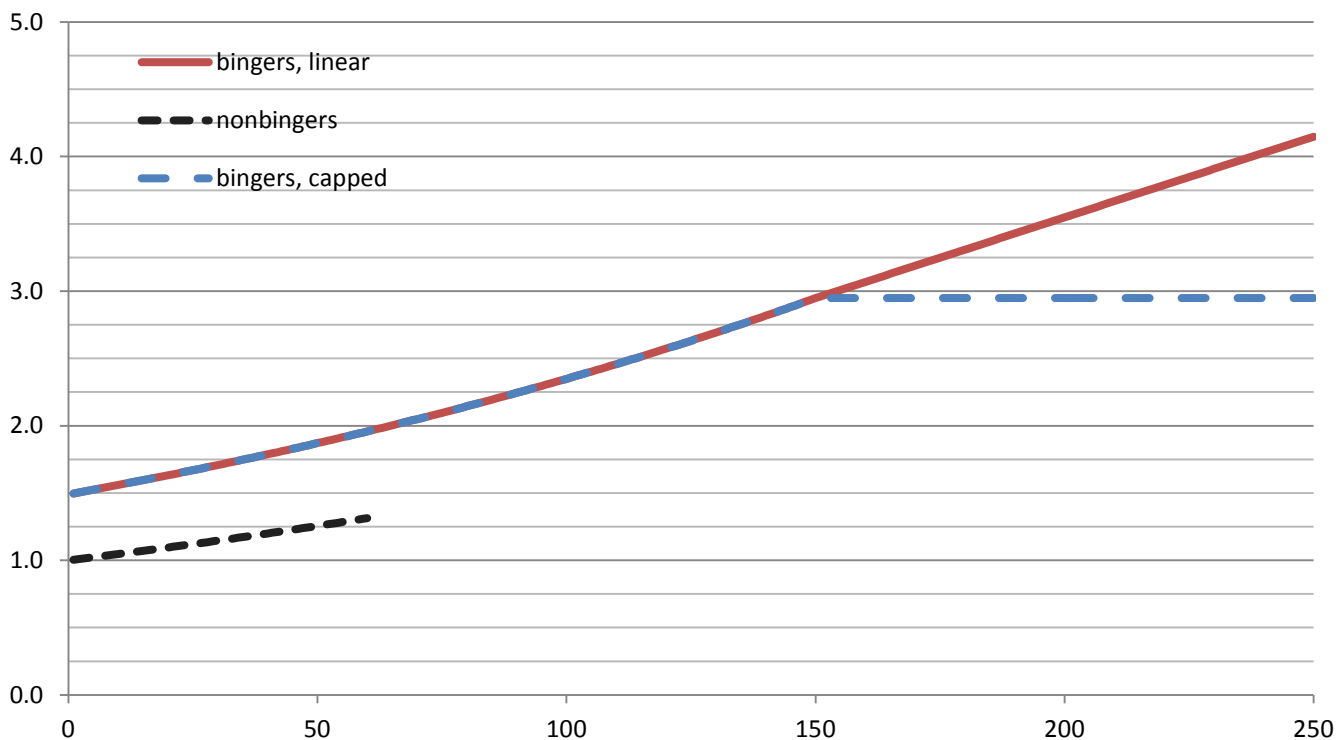
Sources

Samokhvalov, A. V., Rehm, J., & Roerecke, M. (2015). Alcohol consumption as a risk factor for acute and chronic pancreatitis: a systematic review and a series of meta-analyses. *EBioMedicine*, 2(12), 1996-2002.

(7).(1) Motor vehicle collisions

Condition category: (7) Injuries – motor vehicle collisions
ICD10 codes: V1* (shown in XXX), Y85.0

	Current drinkers, nonbinge	Current drinkers, binge
Source	Corrao et al. (1999) Table 2	Custom analysis from U.S. Census Bureau's National Health Interview Survey (see Section 2.6)
Relative risk Equation or estimate	$\ln RR(x) = 0.00455x$ $RR(x) = \exp(0.00455x)$	$RR(x) = 1.49 * \exp(0.00455x)$
Comments		In the graph below, the binge level is defined as 60 grams. Therefore, all drinkers above 60g/day are guaranteed to be bingers.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Not applicable. There is no increased risk for former drinkers.	Former drinkers. There is no increased risk for former drinkers, $RR_{FD} = 1.00$



Source

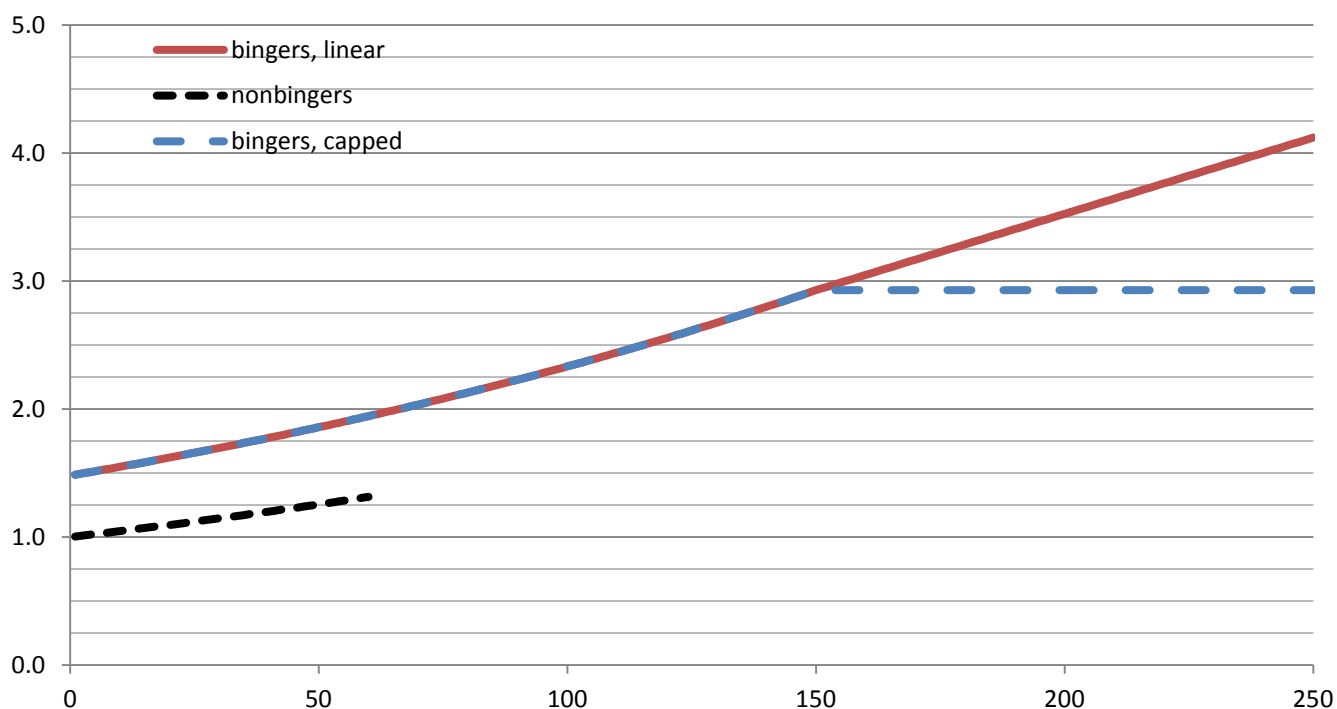
Corrao, G., Bagnardi, V., Zambon, A., & Arico, S. (1999). Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol-related conditions: a meta-analysis. *Addiction*, 94(10), 1551-1573.

(8).(1),(2),(3),(4),(6) Unintentional injuries

Condition category: (8) Injuries – unintentional injuries

ICD10 codes: Many, see Table 2

	Current drinkers, nonbinge	Current drinkers, binge
Source	Corrao et al. (1999) Table 2	Custom analysis from U.S. Census Bureau's National Health Interview Survey (see Section 2.6)
Relative risk Equation or estimate	$\ln RR(x) = 0.00455x$ $RR(x) = \exp(0.00455x)$	$RR(x) = 1.48 * \exp(0.00455x)$
Comments		In the graph below, the binge level is defined as 60 grams. Therefore, all drinkers above 60g/day are guaranteed to be bingers.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Not applicable. There is no increased risk for former drinkers.	Former drinkers. There is no increased risk for former drinkers, $RR_{FD} = 1.00$



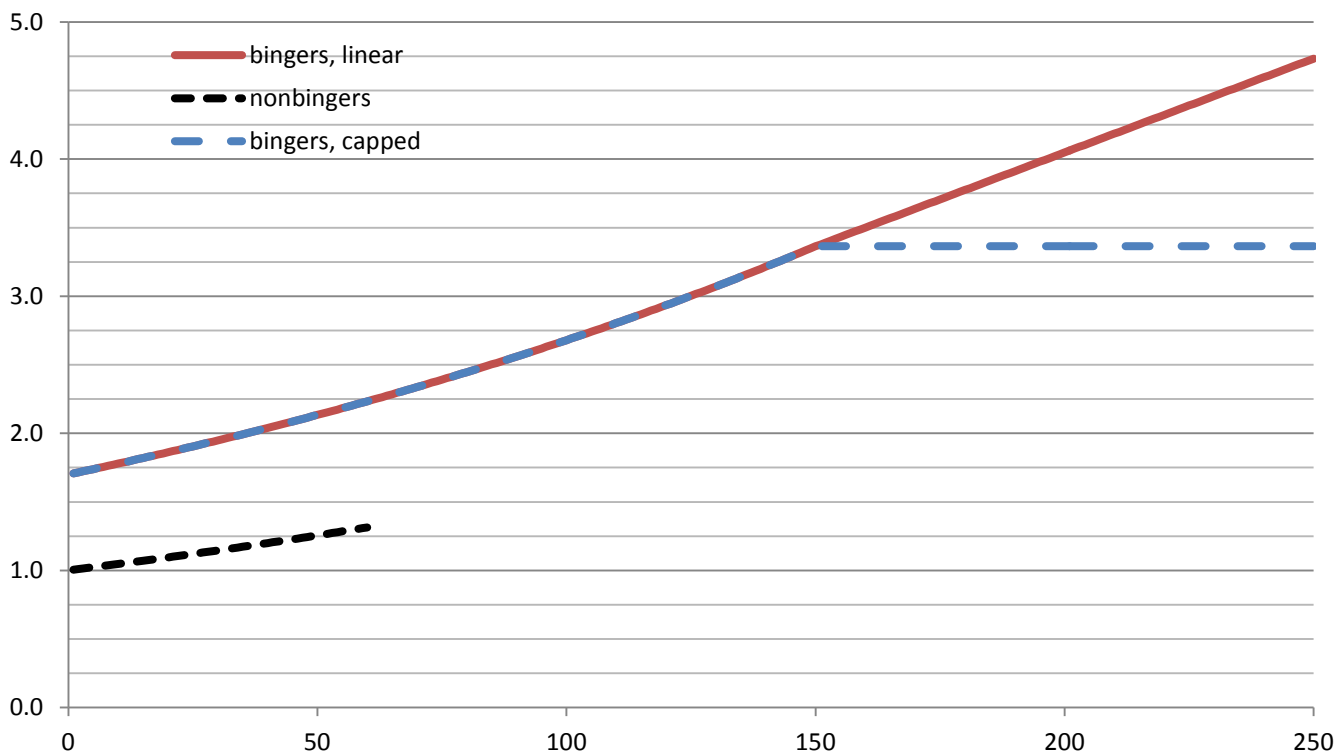
Source

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.

(9).(1),(3),(4),(5) Intentional injuries

Condition category: (9) Injuries – intentional injuries
ICD10 codes: Many, see Table 2

	Current drinkers, nonbinge	Current drinkers, binge
Source	Corrao et al. (1999) Table 2	Custom analysis from U.S. Census Bureau's National Health Interview Survey (see Section 2.6)
Relative risk Equation or estimate	$\ln RR(x) = 0.00455x$ $RR(x) = \exp(0.00455x)$	$RR(x) = 1.70 * \exp(0.00455x)$
Comments		In the graph below, the binge level is defined as 60 grams. Therefore, all drinkers above 60g/day are guaranteed to be bingers.
Control for abstainer bias Does the article control for abstainer bias? If so, how?	Not applicable. There is no increased risk for former drinkers.	Former drinkers. There is no increased risk for former drinkers, $RR_{FD} = 1.00$



Source

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.

References

1. English D, Holman C, Milne E, Winter M, Hulse G, Codde G, Bower G, Corti B, de Klerk N, Knuiman M, et al: **The Quantification of Drug caused Morbidity and Mortality in Australia 1995**. Canberra, Australia: Commonwealth Department of Human Services and Health; 1995.
2. SAS Institute: *SAS/STAT 9.3 user's guide*. Cary, NC: SAS Institute Inc. ; 2011.
3. Corrao G, Bagnardi V, Zambon A, Arico S: **Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol-related conditions: a meta-analysis**. *Addiction* 1999, **94**:1551-1573.
4. Stevens GA, Alkema L, Black RE, Boerma JT, Collins GS, Ezzati M, Grove JT, Hogan DR, Hogan MC, Horton R: **Guidelines for accurate and transparent health estimates reporting: the GATHER statement**. *PLoS medicine* 2016, **13**:e1002056.
5. Organization WH: **International guide for monitoring alcohol consumption and related harm**. 2000.
6. Stockwell T, Zhao J, Greenfield T, Li J, Livingston M, Meng Y: **Estimating under-and over-reporting of drinking in national surveys of alcohol consumption: identification of consistent biases across four English-speaking countries**. *Addiction* 2016, **111**:1203-1213.
7. Rehm J, Room R: **Monitoring of alcohol use and attributable harm from an international perspective**. *Contemporary Drug Problems* 2009, **36**:575-587.
8. Rehm J, Baliunas D, Borges GL, Graham K, Irving H, Kehoe T, Parry CD, Patra J, Popova S, Poznyak V: **The relation between different dimensions of alcohol consumption and burden of disease: an overview**. *addiction* 2010, **105**:817-843.
9. Rehm J, Gmel GE, Gmel G, Hasan OS, Imtiaz S, Popova S, Probst C, Roerecke M, Room R, Samokhvalov AV: **The relationship between different dimensions of alcohol use and the burden of disease—an update**. *Addiction* 2017.
10. Rehm J, Sherk A, Shield KD, Gmel G: **Risk relations between alcohol use and non-injury causes of death**. Toronto, Canada: Centre for Addiction and Mental Health; 2017.
11. Popova S, Lange S, Probst C, Gmel G, Rehm J: **Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis**. *The Lancet Global Health* 2017, **5**:e290-e299.
12. WHO: **International statistical classification of diseases and related health problems 10th revision**. Geneva: Switzerland: World Health Organization; 2016.
13. Rehm J, Samokhvalov AV, Neuman MG, Room R, Parry C, Lönnroth K, Patra J, Poznyak V, Popova S: **The association between alcohol use, alcohol use disorders and tuberculosis (TB). A systematic review**. *BMC public health* 2009, **9**:450.
14. Williams EC, Hahn JA, Saitz R, Bryant K, Lira MC, Samet JH: **Alcohol use and Human Immunodeficiency Virus (HIV) infection: Current knowledge, implications, and future directions**. *Alcohol Clin Exp Res* 2016, **40**:16.
15. Rehm J, Probst C, Shield KD, Shuper PA: **Does alcohol use have a causal effect on HIV incidence and disease progression? A review of the literature and a modeling strategy for quantifying the effect**. *Population Health Metrics* 2017, **15**.

16. Samokhvalov A, Irving H, Rehm J: **Alcohol consumption as a risk factor for pneumonia: a systematic review and meta-analysis.** *Epidemiology & Infection* 2010, **138**:1789-1795.
17. Traphagen N, Tian Z, Allen-Gipson D: **Chronic ethanol exposure: pathogenesis of pulmonary disease and dysfunction.** *Biomolecules* 2015, **5**:2840-2853.
18. Simet SM, Sisson JH: **Alcohol's Effects on Lung Health and Immunity.** *Alcohol research: current reviews* 2015, **37**:199-208.
19. Allen N, Anderson LM, Beland FA, Bénichou J, Beral V, Bloomfield K, Brooks PJ, Cai L, Cho SI, Crabb DW: **Alcohol consumption and ethyl carbamate.** *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* 2010, **96**:1-1379.
20. **IARC monographs on the evaluation of carcinogenic risks to humans. personal habits and indoor combustion.** In *Volume 100E*, vol. 100.
21. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, Scotti L, Jenab M, Turati F, Pasquali E: **Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis.** *British journal of cancer* 2015, **112**:580-593.
22. Howard AA, Arnsten JH, Gourevitch MN: **Effect of alcohol consumption on diabetes mellitusA systematic review.** *Annals of internal medicine* 2004, **140**:211-219.
23. Bartolomei F: **Epilepsy and alcohol.** *Epileptic disorders* 2006, **8**:72-78.
24. Barclay G, Barbour J, Stewart S, Day C, Gilvarry E: **Adverse physical effects of alcohol misuse.** *Advances in Psychiatric Treatment* 2008, **14**:139-151.
25. Leach JP, Mohanraj R, Borland W: **Alcohol and drugs in epilepsy: pathophysiology, presentation, possibilities, and prevention.** *Epilepsia* 2012, **53**:48-57.
26. Puddey IB, Beilin LJ: **Alcohol is bad for blood pressure.** *Clinical and Experimental Pharmacology and Physiology* 2006, **33**:847-852.
27. O'Keefe JH, Bhatti SK, Bajwa A, DiNicolantonio JJ, Lavie CJ: **Alcohol and cardiovascular health: the dose makes the poison... or the remedy.** In *Mayo Clinic Proceedings*. Elsevier; 2014: 382-393.
28. Mukamal KJ, Rimm EB: **Alcohol's effects on the risk for coronary heart disease.** *Alcohol Research and Health* 2001, **25**:255-262.
29. Collins MA, Neafsey EJ, Mukamal KJ, Gray MO, Parks DA, Das DK, Korthuis RJ: **Alcohol in moderation, cardioprotection, and neuroprotection: epidemiological considerations and mechanistic studies.** *Alcoholism: Clinical and Experimental Research* 2009, **33**:206-219.
30. Roerecke M, Rehm J: **The cardioprotective association of average alcohol consumption and ischaemic heart disease: a systematic review and meta-analysis.** *Addiction* 2012, **107**:1246-1260.
31. Zhao J, Stockwell T, Roemer A, Naimi TS, Chikritzhs T: **Alcohol consumption and mortality from coronary heart disease: An updated meta-analysis of cohort studies.** *Journal of Studies on Alcohol and Drugs* 2017, **78**:375-386.
32. Rosenqvist M: **Alcohol and cardiac arrhythmias.** *Alcoholism: Clinical and Experimental Research* 1998, **22**.
33. Mukamal KJ, Ding EL, Djoussé L: **Alcohol consumption, physical activity, and chronic disease risk factors: a population-based cross-sectional survey.** *BMC Public Health* 2006, **6**:118.
34. Puddey IB, Rakic V, Dimmitt S, Beilin L: **Influence of pattern of drinking on cardiovascular disease and cardiovascular risk factors-a review.** *Addiction* 1999, **94**:649-663.

35. Mazzaglia G, Britton AR, Altmann DR, Chenet L: **Exploring the relationship between alcohol consumption and non-fatal or fatal stroke: a systematic review.** *Addiction* 2001, **96**:1743-1756.
36. Gao B, Bataller R: **Alcoholic liver disease: pathogenesis and new therapeutic targets.** *Gastroenterology* 2011, **141**:1572-1585.
37. Rehm J, Taylor B, Mohapatra S, Irving H, Baliunas D, Patra J, Roerecke M: **Alcohol as a risk factor for liver cirrhosis: A systematic review and meta-analysis.** *Drug and alcohol review* 2010, **29**:437-445.
38. Yadav D, Lowenfels AB: **The epidemiology of pancreatitis and pancreatic cancer.** *Gastroenterology* 2013, **144**:1252-1261.
39. Lankisch P, Apte M, Banks P: **Acute pancreatitis.** *The Lancet* 2015, **386**:85-96.
40. Braganza JM, Lee SH, McCloy RF, McMahon MJ: **Chronic pancreatitis.** *The Lancet* 2011, **377**:1184-1197.
41. Majumder S, Chari ST: **Chronic pancreatitis.** *The Lancet* 2016, **387**:1957-1966.
42. Movig KL, Mathijssen M, Nagel P, Van Egmond T, De Gier JJ, Leufkens H, Egberts AC: **Psychoactive substance use and the risk of motor vehicle accidents.** *Accident Analysis & Prevention* 2004, **36**:631-636.
43. Skog OJ: **Alcohol consumption and mortality rates from traffic accidents, accidental falls, and other accidents in 14 European countries.** *Addiction* 2001, **96**:49-58.
44. Smith GS, Branas CC, Miller TR: **Fatal nontraffic injuries involving alcohol: a metaanalysis.** *Annals of emergency medicine* 1999, **33**:659-668.
45. Rothman KJ, Greenland S, Lash TL: *Modern epidemiology.* Lippincott Williams & Wilkins; 2008.
46. Brown SW, Vanlaar WGM, Robertson RD: **Alcohol and Drug-Crash Problem in Canada.** Ottawa, ON: The Traffic Injury Research Foundation of Canada; 2017.
47. WHO: **Global status report on alcohol and health.** In *World Health Organization.* Geneva, Switzerland: World Health Organization; 2014.
48. World Health Organization: **Global health risks. Mortality and burden of disease attributable to selected major risks.** Geneva, Switzerland: WHO Press; 2009.
49. Macdonald S: **Unrecorded alcohol consumption in Ontario, Canada: estimation procedures and research implications.** *Drug and Alcohol Review* 1999, **18**:21-29.
50. Royston P, Ambler G, Sauerbrei W: **The use of fractional polynomials to model continuous risk variables in epidemiology.** *International journal of epidemiology* 1999, **28**:964-974.
51. Royston P, Sauerbrei W: *Multivariable model-building: a pragmatic approach to regression analysis based on fractional polynomials for modelling continuous variables.* John Wiley & Sons; 2008.
52. Rehm J, Kehoe T, Gmel G, Stinson F, Grant B, Gmel G: **Statistical modeling of volume of alcohol exposure for epidemiological studies of population health: the US example.** *Population Health Metrics* 2010, **8**:1.
53. Kehoe T, Gmel G, Shield KD, Gmel G, Rehm J: **Determining the best population-level alcohol consumption model and its impact on estimates of alcohol-attributable harms.** *Population health metrics* 2012, **10**:1.
54. Skog O-J: **The historical roots of Ledermann's theory of the distribution of alcohol consumption.** *Contemporary Drug Problems* 2006, **33**:143-174.

55. Gmel G, Shield KD, Kehoe-Chan TA, Rehm J: **The effects of capping the alcohol consumption distribution and relative risk functions on the estimated number of deaths attributable to alcohol consumption in the European Union in 2004.** *BMC medical research methodology* 2013, **13**:24.
56. Imtiaz S, Shield KD, Roerecke M, Samokhvalov AV, Lönnroth K, Rehm J: **Alcohol consumption as a risk factor for tuberculosis: meta-analyses and burden of disease.** *European Respiratory Journal* 2017, **50**:1700216.
57. Marron M, Boffetta P, Zhang Z-F, Zaridze D, Wünsch-Filho V, Winn DM, Wei Q, Talamini R, Szeszenia-Dabrowska N, Sturgis EM: **Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk.** *International journal of epidemiology* 2009, **39**:182-196.
58. Schütze M, Boeing H, Pischon T, Rehm J, Kehoe T, Gmel G, Olsen A, Tjønneland AM, Dahm CC, Overvad K: **Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study.** *Bmj* 2011, **342**:d1584.
59. Corrao G, Bagnardi V, Zambon A, La Vecchia C: **A meta-analysis of alcohol consumption and the risk of 15 diseases.** *Preventive medicine* 2004, **38**:613-619.
60. Knott C, Bell S, Britton A: **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* 2015, **38**:1804-1812.
61. Baliunas DO, Taylor BJ, Irving H, Roerecke M, Patra J, Mohapatra S, Rehm J: **Alcohol as a risk factor for type 2 diabetes.** *Diabetes care* 2009, **32**:2123-2132.
62. Samokhvalov AV, Irving H, Mohapatra S, Rehm J: **Alcohol consumption, unprovoked seizures, and epilepsy: A systematic review and meta-analysis.** *Epilepsia* 2010, **51**:1177-1184.
63. Roerecke M, Rehm J: **Ischemic heart disease mortality and morbidity rates in former drinkers: a meta-analysis.** *American journal of epidemiology* 2010, **173**:245-258.
64. Samokhvalov AV, Irving HM, Rehm J: **Alcohol consumption as a risk factor for atrial fibrillation: a systematic review and meta-analysis.** *European Journal of Cardiovascular Prevention & Rehabilitation* 2010, **17**:706-712.
65. Larsson SC, Drca N, Wolk A: **Alcohol consumption and risk of atrial fibrillation: a prospective study and dose-response meta-analysis.** *Journal of the American College of Cardiology* 2014, **64**:281-289.
66. Patra J, Taylor B, Irving H, Roerecke M, Baliunas D, Mohapatra S, Rehm J: **Alcohol consumption and the risk of morbidity and mortality for different stroke types-a systematic review and meta-analysis.** *BMC public health* 2010, **10**:1.
67. Larsson SC, Wallin A, Wolk A, Markus HS: **Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis.** *BMC medicine* 2016, **14**:178.
68. Samokhvalov AV, Rehm J, Roerecke M: **Alcohol consumption as a risk factor for acute and chronic pancreatitis: a systematic review and a series of meta-analyses.** *EBioMedicine* 2015, **2**:1996-2002.
69. Chikritzhs T, Fillmore K, Stockwell T: **A healthy dose of scepticism: four good reasons to think again about protective effects of alcohol on coronary heart disease.** *Drug and alcohol review* 2009, **28**:441-444.

70. Juonala M, Viikari JS, Kähönen M, Laitinen T, Taittonen L, Loo B-M, Jula A, Marniemi J, Räsänen L, Rönkämaa T: **Alcohol consumption is directly associated with carotid intima-media thickness in Finnish young adults: The Cardiovascular Risk in Young Finns Study.** *Atherosclerosis* 2009, **204**:e93-e98.
71. Holmes MV, Dale CE, Zuccolo L, Silverwood RJ, Guo Y, Ye Z, Prieto-Merino D, Dehghan A, Trompet S, Wong A: **Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data.** *Bmj* 2014, **349**:g4164.
72. Naimi TS, Brown DW, Brewer RD, Giles WH, Mensah G, Serdula MK, Mokdad AH, Hungerford DW, Lando J, Naimi S: **Cardiovascular risk factors and confounders among nondrinking and moderate-drinking US adults.** *American journal of preventive medicine* 2005, **28**:369-373.
73. Naimi TS, Stockwell T, Zhao J, Xuan Z, Dangardt F, Saitz R, Liang W, Chikritzhs T: **Selection biases in observational studies affect associations between 'moderate' alcohol consumption and mortality.** *Addiction* 2017, **112**:207-214.
74. Pletcher MJ, Varosy P, Kiefe CI, Lewis CE, Sidney S, Hulley SB: **Alcohol consumption, binge drinking, and early coronary calcification: findings from the Coronary Artery Risk Development in Young Adults (CARDIA) Study.** *American Journal of Epidemiology* 2005, **161**:423-433.
75. Bergmann MM, Rehm J, Klipstein-Grobusch K, Boeing H, Schütze M, Drogan D, Overvad K, Tjønneland A, Halkjær J, Fagherazzi G: **The association of pattern of lifetime alcohol use and cause of death in the European Prospective Investigation into Cancer and Nutrition (EPIC) study.** *International journal of epidemiology* 2013, **42**:1772-1790.
76. Fillmore KM, Kerr WC, Stockwell T, Chikritzhs T, Bostrom A: **Moderate alcohol use and reduced mortality risk: Systematic error in prospective studies.** *Addiction Research & Theory* 2006, **14**:101-132.
77. Stockwell T, Zhao J, Panwar S, Roemer A, Naimi T, Chikritzhs T: **Do "moderate" drinkers have reduced mortality risk? A systematic review and meta-analysis of alcohol consumption and all-cause mortality.** *Journal of studies on alcohol and drugs* 2016, **77**:185-198.
78. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA: **Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis.** *Bmj* 2011, **342**:d671.
79. Brien SE, Ronksley PE, Turner BJ, Mukamal KJ, Ghali WA: **Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies.** *Bmj* 2011, **342**:d636.
80. World Health Organization: **Global status report on alcohol and health. Retrieved from.** Geneva, Switzerland: WHO Press; 2011.
81. World Health Organization: *Global status report on alcohol and health.* Geneva, Switzerland: World Health Organization; 2014.
82. Stockwell T, Pauly B, Chow C, Erickson R, Krysovaty B, Roemer A, Vallance K, Wettlaufer A, Zhao J: **Does managing the consumption of people with severe alcohol dependence reduce harm? A comparison of participants in six Canadian managed alcohol program with locally recruited controls.** *Drug and Alcohol review* in press.

83. Hanley J: **A heuristic approach to the formulas for population attributable fraction.** *Journal of epidemiology and community health* 2001, **55**:508-514.
84. Roerecke M, Rehm J: **Irregular heavy drinking occasions and risk of ischemic heart disease: a systematic review and meta-analysis.** *American journal of epidemiology* 2010, **171**:633-644.
85. Rehm J, Shield KD, Roerecke M, Gmel G: **Modelling the impact of alcohol consumption on cardiovascular disease mortality for comparative risk assessments: an overview.** *BMC Public Health* 2016, **16**:363.
86. GBD 2015 Risk Factors Collaborators: **Global, regional, and national comparative risk assessment of 79 behavioral, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015.** *Lancet* 2016, **388**:1659-1724.
87. Shield KD, Rylett M, Rehm J: *Public health successes and missed opportunities. Trends in alcohol consumption and attributable mortality in the WHO European Region, 1990-2014.* Copenhagen, Denmark: WHO European Region; 2016.



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