# Risk relations between alcohol use and non-injury causes of death

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## Notes

This is an update of the Appendix of the overview paper of Rehm and colleagues on risk relations between alcohol use and mortality outcomes (1), and includes the relative risk of diseases, and conditions among former drinkers, which had been collected as part of the International Model of Alcohol Harms and Policies (InterMAHP; (2)). It contains risk relations for drinkers and former drinkers1 for all non-injury causes of death which had been determined as partially attributable to alcohol, i.e., where causality had been established (1, 6, 7). In addition, it denotes formulas for causes of death and burden of disease, which are 100% attributable to alcohol, but for which there had been no reliable global statistics either by World Health Organization (8) or by the Global Burden of Disease and Injury Studies (9). The original sources and full documentation of the formulas are given to comply with GATHER standards (10).

All functions are defined from 0 to 150 g/day pure alcohol/day (for reasoning (11, 12)). For any drinking level above 150g/day pure alcohol, please use the risk for 150 g/day (for sensitivity analyses please see (13)). If you would like to specify over a larger range of exposure, please use the already mentioned InterMAHP model for options (2).

In the function definitions, x refers to the average daily consumption of pure alcohol in g/day.

R-programs for the functions are available upon request from the first author under the conditions:

- that the original work for each formula is cited as per this report;
- that the source of the program is acknowledged as follows:
  The selection of causes of death attributable to alcohol use is based on Rehm et al., 2017 (1). Further documentation on the risk relations for current and former drinkers and R programs were made available by 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).

1 Please note, that the risk relations for former drinkers had been mainly derived from high-income countries where majority consumes alcohol, and quitting drinking is often after having consumed alcohol for decades (e.g., (3, 4)). There are problems in transposing these risks to countries where alcohol use is against the social norms, and former drinkers may have consumed alcohol only sporadically (see e.g., solution in (5) for potential modelling).

## Sources for determining causality

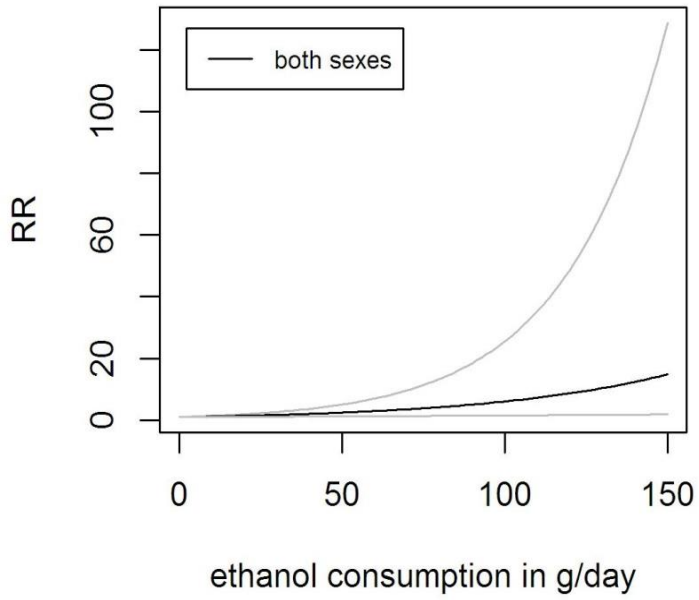
| Diseases or condition (ICD-10 code) | Source |
|---|---|
| Infectious disease [A00-B99] | |
| Tuberculosis [A15-19, B90] | Rehm et al., 2009 (14) |
| HIV/AIDS (effect via behavioural intentions) [B20-24] | Rehm et al., 2017 (15); Williams et al., 2016 (16) |
| Malignant neoplasms [C00-97] | |
| Oral cavity, salivary glands, oropharynx and hypopharynx cancer [C01-14] | International Agency for Research on Cancer (IARC) monograph (17, 18) |
| Oesophagus cancer [C15] | International Agency for Research on Cancer (IARC) monograph (17, 18) |
| Colon and rectum cancer [C18-20] | International Agency for Research on Cancer (IARC) monograph (17, 18) |
| Liver and intrahepatic bile duct cancer [C22] | International Agency for Research on Cancer (IARC) monograph (17, 18) |
| Larynx cancer [C32] | International Agency for Research on Cancer (IARC) monograph (17, 18) |
| Breast cancer (female) [C50] | International Agency for Research on Cancer (IARC) monograph (17, 18) |
| Diabetes mellitus [E10-14] | Howard et al., 2004 (19) |
| Diseases of the nervous system [G00-99] | |
| Epilepsy [G40-41] | Bartolomei, 2006 (20), Barclay et al., 2008 (21), Leach et al., 2012 (22) |
| Diseases of the circulatory system [I00-I99] | |
| Hypertensive heart diseases [I11-13] | Puddey and Beilin, 2006 (23); O'Keefe et al., 2014 (24) |
| Ischaemic Heart Disease [I20-25] | Mukamal & Rimm, 2001 (25), Collins et al., 2009 (26), Roerecke & Rehm, 2014 (27) |
| Atrial fibrillation and flutter [I48] | Rosenqvist, 1998 (28); |

| Diseases or condition (ICD-10 code) | Source |
|---|---|
| | Rosenberg & Mukamal, 2012 (29) |
| Haemorrhagic stroke and non-ischaemic stroke [I60-62, I69.0-2] | Puddey et al., 1999 (30); Mazzaglia et al., 2001(31) |
| Ischaemic stroke [I63-67, 69.3] | Puddey et al., 1999 (30); Mazzaglia et al., 2001(31); Collins et al., 2009 (26) |
| Diseases of the respiratory system [J00-99] | |
| Lower respiratory infections: pneumonia [J09–J22, J85, P23] | Samokhvalov et al., 2010 (32); Traphagen et al., 2015 (33), for heavy drinking und alcohol use disorders: Simet & Sisson, 2015 (34) |
| Diseases of the digestive system [K00-93] | |
| Fibrosis and cirrhosis of liver [K70, K73-74] | Gao & Bataller, 2011(35) |
| Pancreatitis [K85 K86.0-1] | Braganza et al., 2011(58); Yadav et al., 2013 (59); Lankisch et al., 2015 (60); Majumder & Chari, 2016 (61) |

## Infectious disease [A00-B99]

### Tuberculosis [A15-19, B90]

**Current drinkers**:



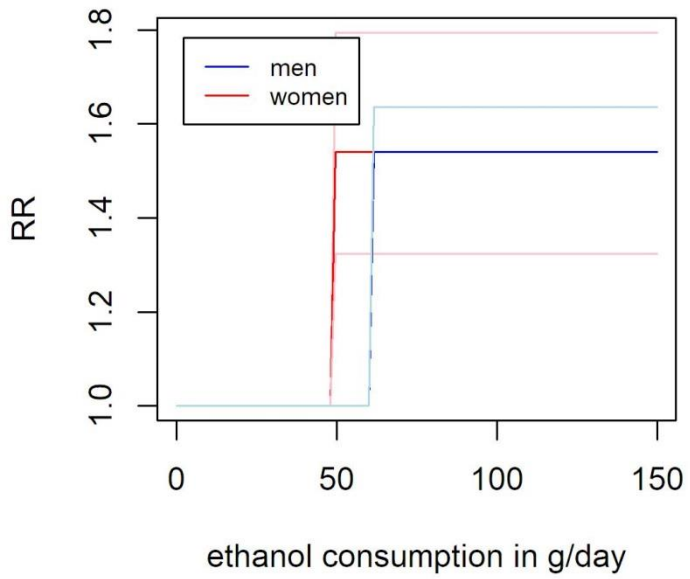

$$\ln(RR(x)) = 0.0179695 \cdot x$$

Source: Imtiaz et al., 2017 (36)

**Former drinkers:**
Women and men; $RR_{FD} = 1.0$*
* There is no increased risk of former drinkers, due to the biological pathways, which are based on infection due to acute consequences of use (14).

## HIV/AIDS (effect via behavioural intentions) [B20-24]

**Current drinkers**:




Women

$$\ln\big(RR(x)\big) = \begin{cases} 0 & , x \leq 49 \\ \ln(1.54), & x > 49 \end{cases}$$

Men

$$\ln\big(RR(x)\big) = \begin{cases} 0 & , x \leq 61 \\ \ln(1.54), & x > 61 \end{cases}$$

Source: Rehm et al., 2017 (15) based on Scott-Sheldon et al., 2016 (37); for the effect via medication adherence see Gmel et al., 2011 (38)

**Former drinkers:**

Women and men; $RR_{FD}$ = 1.0*

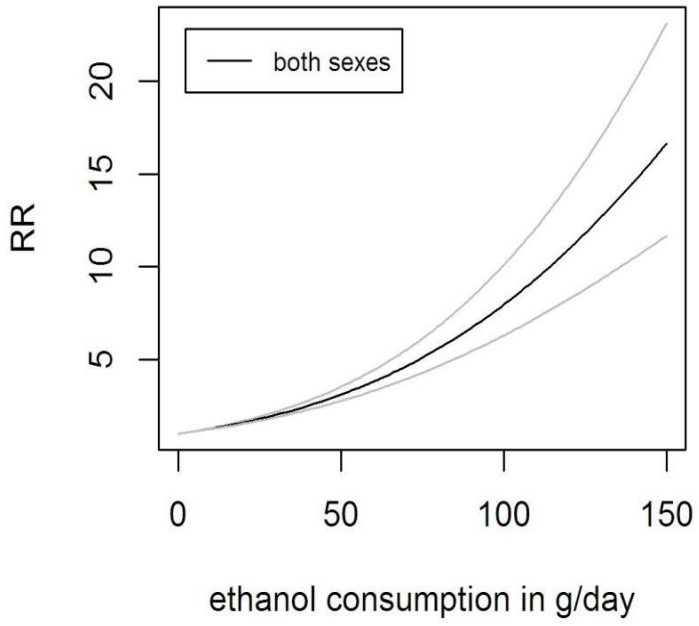
*There is no increased risk of former drinkers, due to the biological pathways, which are based on infection due to acute consequences of use (15, 16).

## Malignant neoplasms [C00-97]

For all alcohol-attributable cancers, causality has been determined by International Agency for Research on Cancer (IARC) monograph conferences (17, 18). Only cancers with the highest level of evidence for carcinogenicity in humans (group 1) were included (39).

### Oral cavity, salivary glands, oropharynx and hypopharynx cancer [C01-14]

**Current Drinkers:**



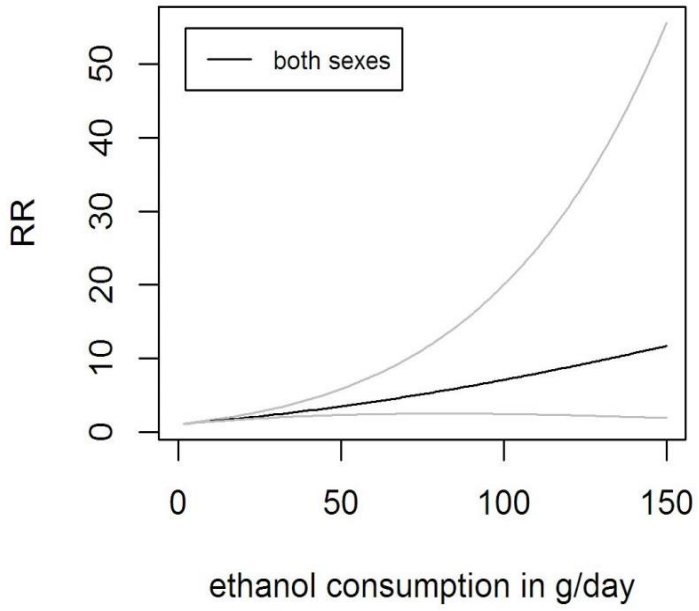

$$\ln(RR(x)) = 0.02474 \cdot x - 0.00004 \cdot x^2$$

Source: Bagnardi et al., 2015 (40)

**Former drinkers:**
Women and men; $RR_{FD}$= 1.20 (95% CI: 0.63-2.30)
Source: Marron et al., 2010 (41)

## Oesophagus cancer [C15]

**Current Drinkers:**



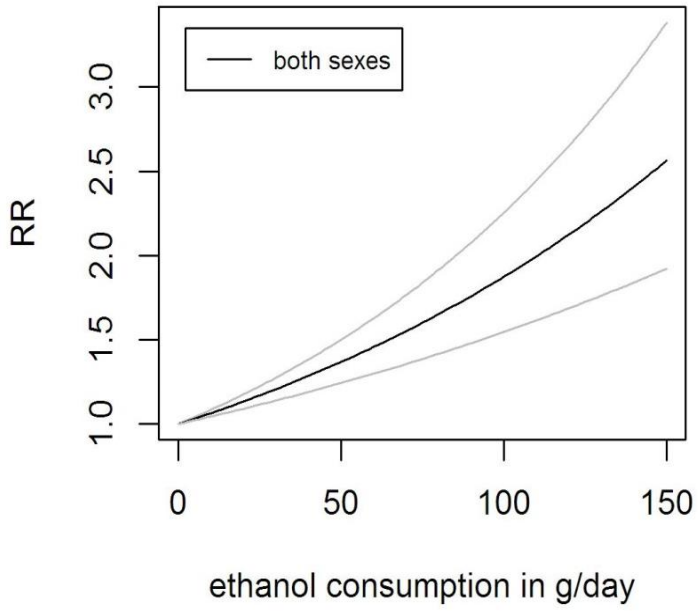

$$\ln(RR(x)) = 0.05593 \cdot x - 0.00789 \cdot x \cdot \ln(x)$$

Source: Bagnardi et al., 2015 (40)

**Former drinkers:**
Women and men; $RR_{FD}$ = 1.16 (95% CI: 0.72-1.87)
Source: Marron et al., 2010 (41)

## Colon and rectum cancer [C18-20]

**Current drinkers:**



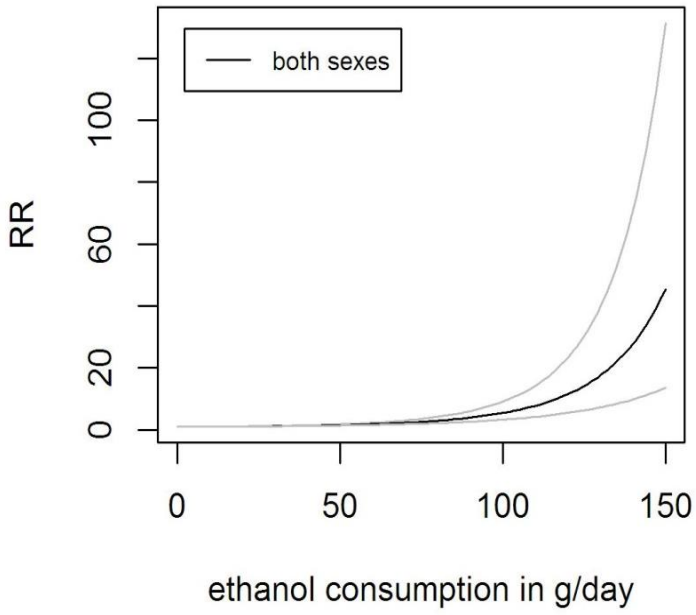

$$\ln(RR(x)) = 0.006279 \cdot x$$

Source: Bagnardi et al., 2015 (40)

**Former drinkers:**
Women; $RR_{FD}$ = 1.05 (95% CI: 0.79-1.40)
Men; $RR_{FD}$ = 2.19 (95% CI: 0.99-4.83)
Source: Schütze et al., 2011 (42)

## Liver and intrahepatic bile duct cancer [C22]

**Current drinkers:**



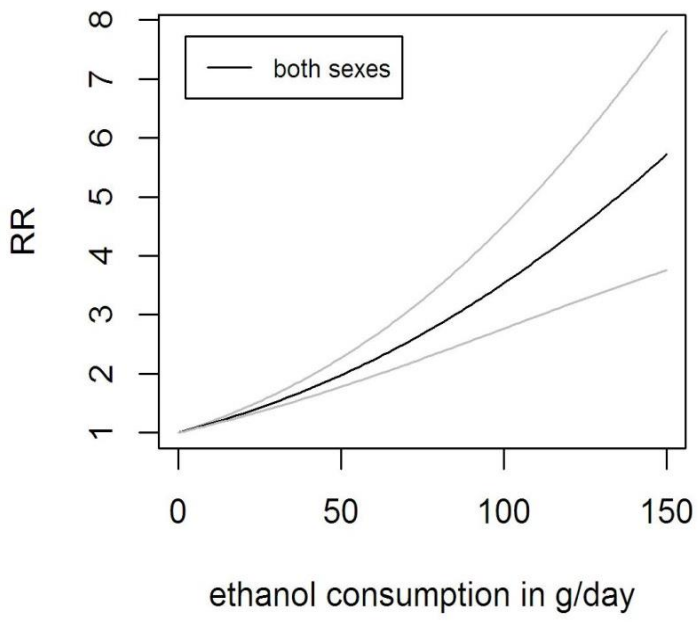

$$\ln(RR(x)) = 0.00017 \cdot x^2 - 0.00069 \cdot x^{0.5}$$

Source: Bagnardi et al., 2015 (40)

**Former drinkers:**
Women; $RR_{FD}$ = 2.28 (95% CI: 0.88-5.85)
Men; $RR_{FD}$ = 1.54 (95% CI: 1.20-1.98)
***Source:*** Schütze et al., 2011 (42)

## Larynx cancer [C32]

**Current drinkers:**



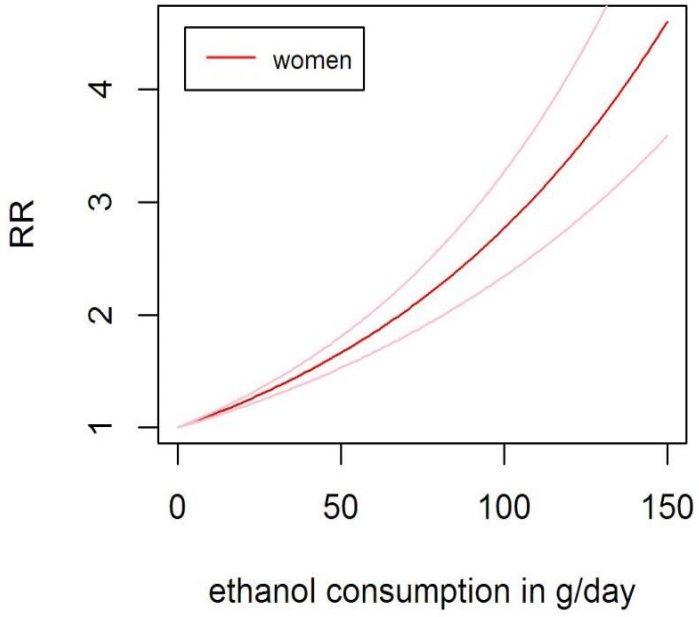

$$\ln(RR(x)) = 0.01462 \cdot x - 0.00002 \cdot x^2$$

Source: Bagnardi et al., 2015 (40)

**Former drinkers:**
Women and men: $RR_{FD}$ = 1.18 (95% CI: 0.67-2.08)
Source: Marron et al., 2010 (41)

## Female breast cancer [C50]

**Current drinkers:**




$$\ln(RR(x)) = 0.01018 \cdot x$$

Source: Bagnardi et al., 2015 (40)

**Former drinkers:**

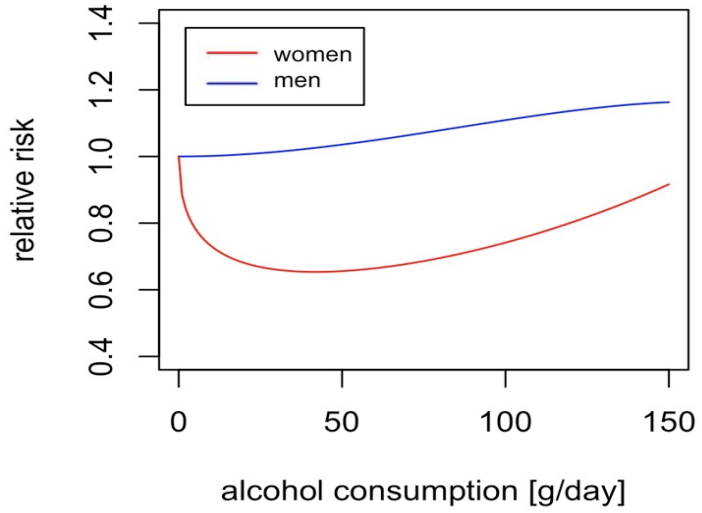
Women and Men $RR_{FD}$ = 1.00*

* The $RR_{FD}$ = 1.03 (0.88-1.21) as measured by Schütze et al., 2011 (42) falls inside the range of 0.95 and 1.05 where the former drinker RRs were not modelled.

## Diabetes mellitus [E10-14]

### Diabetes mellitus [E10-14]

**Current drinkers:**




Women

$$\ln\left(RR(x)\right) = -1.3133910 \cdot \left(\frac{x}{100}\right)^{0.5} + 0.0728256 \cdot \left(\frac{x}{100}\right)^{3}$$

Men

$$\ln\left(RR(x)\right) = 0.1763703 \cdot \left(\frac{x}{100}\right)^{2} - 0.0728256 \cdot \left(\frac{x}{100}\right)^{3}$$

Source: Knott et al. (2015) (43)

**Former drinkers:**

Women: $RR_{FD}$ = 1.14 (95% CI: 0.99-1.31)

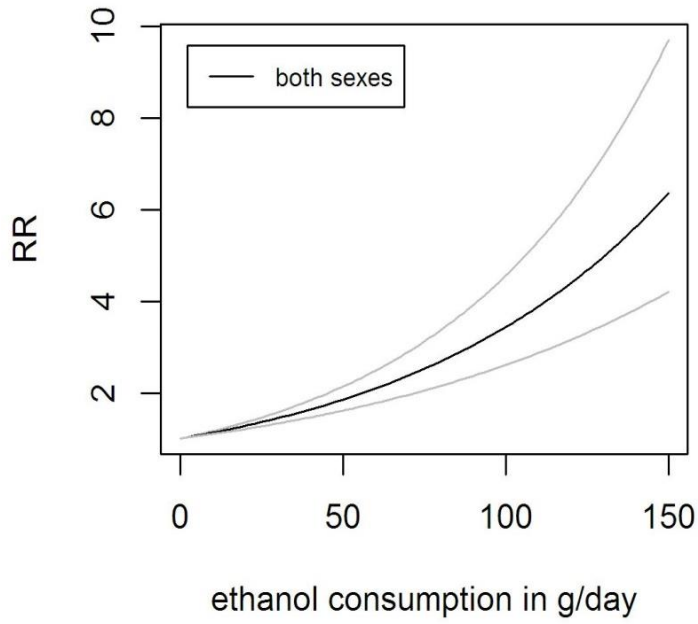
Men: $RR_{FD}$ = 1.18 (95% CI: 0.89-1.52)

Source: Rehm et al., 2010 (6)

## Diseases of the nervous system [G00-99]

### Epilepsy [G40-41]

**Current drinkers:**




$$\ln(RR(x)) = 1.22861 \cdot \frac{x + 0.5}{100}$$

Source: Samokhvalov et al., 2010 (44)

**Former drinkers:**

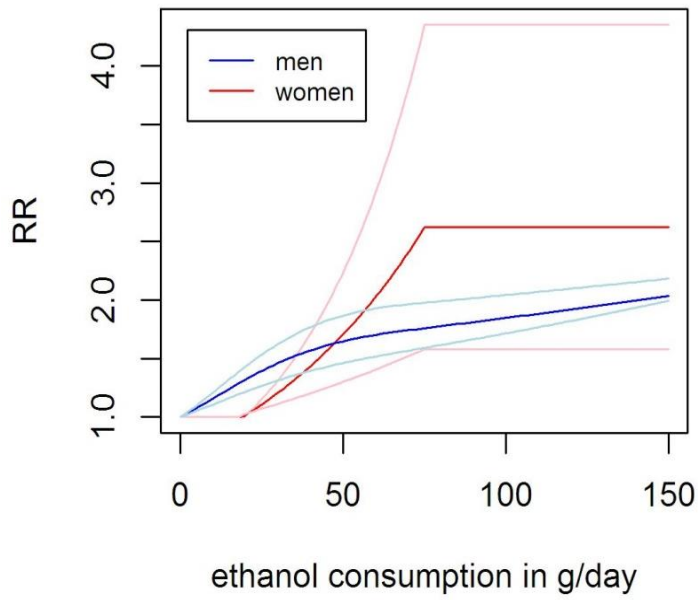
Men and women: $RR_{FD}$ = 1.00*

* The observed $RR_{FD}$ were 0.9 (95% CI: 0.1, 5.0) for women and 0.9 (95% CI: 0.2, 3.0) for men as measured by Leone et al., 1997 (45). However, there is no evidence that former drinking is correlated to the risk of an epileptic seizure.

## Diseases of the circulatory system [I00-I99]

### Hypertensive heart diseases [I11-13]

**Current drinkers:**




Women

$$\ln\big(RR(x)\big) = \begin{cases} 0 & ,x < 18.9517 \\ -0.0154196 \cdot x + 0.0217586 \cdot \dfrac{x^3 - \dfrac{(x-10)^3 \cdot 20 - (x-20)^3 \cdot 10}{(20-10)}}{20^2} & ,18.9517 \le x < 75 \\ 0.9649937 & ,x \ge 75 \end{cases}$$

Men

$$\ln\big(RR(x)\big) = \begin{cases} 0.0150537 \cdot x - 0.0156155 \cdot \dfrac{x^3}{75^2} & ,0 \le x < 21 \\ 0.0150537 \cdot x - 0.0156155 \cdot \dfrac{x^3 - \dfrac{(x-21)^3 \cdot 75}{(75-21)}}{75^2} & ,21 \le x < 75 \\ 0.0150537 \cdot x - 0.0156155 \cdot \dfrac{x^3 - \dfrac{(x-21)^3 \cdot 75 - (x-75)^3 \cdot 21}{(75-21)}}{75^2} & ,75 \le x \end{cases}$$

Source: Roerecke et al., personal communication

**Former drinkers:**

Women: $RR_{FD}$ = 1.00*

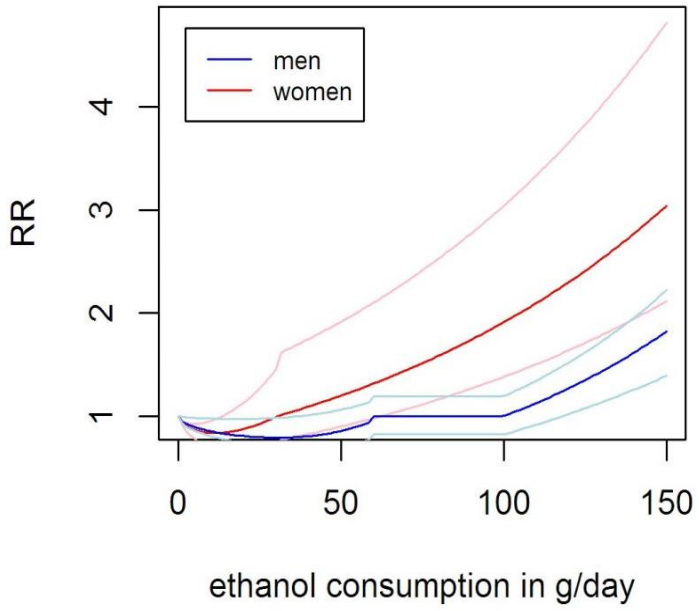
Men: $RR_{FD}$ = 1.05 (95% CI: 0.85, 1.30)

Source Roerecke et al., personal communication

* The $RR_{FD}$ = 1.03 (95% CI: 0.78, 1.33) for women falls inside the range of 0.95 and 1.05 where the former drinker RRs were not modelled.

## Ischaemic Heart Disease [I20-25] (ages 35-64)

**Current drinkers:**




Women

$$\ln\big(RR(x)\big) = \begin{cases} 1.897718 \cdot y + 1.593365 \cdot y * log(y) \,, x < 30.3814 \\ 0.0093 \cdot (x - 30.3814) \qquad\qquad\quad \,, x \geq 30.3814 \end{cases}$$

$$where\ y = \frac{x\ +\ 0.0099999997764826}{100}$$

Men

$$\ln\big(RR(x)\big) = \begin{cases} -0.5043554 \cdot \sqrt{y} + 1.606235 \cdot y^3, x \leq 60 \\ 0 \qquad\qquad\qquad\qquad\qquad\quad ,60 < x < 100 \\ 0.012 \cdot (x - 100) \qquad\qquad\quad ,x \geq 100 \end{cases}$$

$$where\ y = \frac{x\ +\ 0.0099999997764826}{100}$$

The risk relations between alcohol use and ischemic stroke are age-dependent (5). We only show exemplary functions for one age group. In addition, the relative risk is 1 for all people, who consume on average less then 60g of pure alcohol per day, but have at least one heavy drinking occasion per month (27, 46).
Source: Rehm et al., 2016(5) based on Roerecke & Rehm, 2012(47)

**Former drinkers:**

Women: $RR_{FD}$ = 1.54 (95% CI: 1.17-2.03)
Men: $RR_{FD}$ = 1.25 (95% CI: 1.15-1.36)
Source: Roerecke & Rehm (2011) (48)

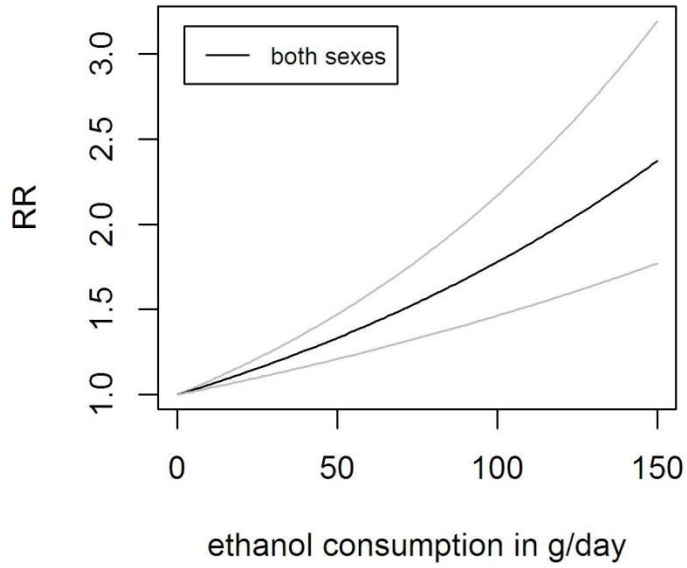
## Cardiomyopathy [I42]

**Causality**: Not necessary, as there is a distinct category call alcoholic cardiomyopathy [I42.6]; for an on overview see Rehm et al., 2017(49)

**Meta-analysis and modelling**: No meta-analysis possible due to lack of epidemiological data (49). An alternative strategy to model the data can be found in Manthey et al., 2017 (50).

## Atrial fibrillation and flutter [I48]

**Current drinkers:**




$$\ln\big(RR(x)\big) = 0.0575183 \cdot y$$
$$where\ y = \frac{x + 0.0499992370605469}{10}$$

Source: Samokhvalov et al., 2010 (51)

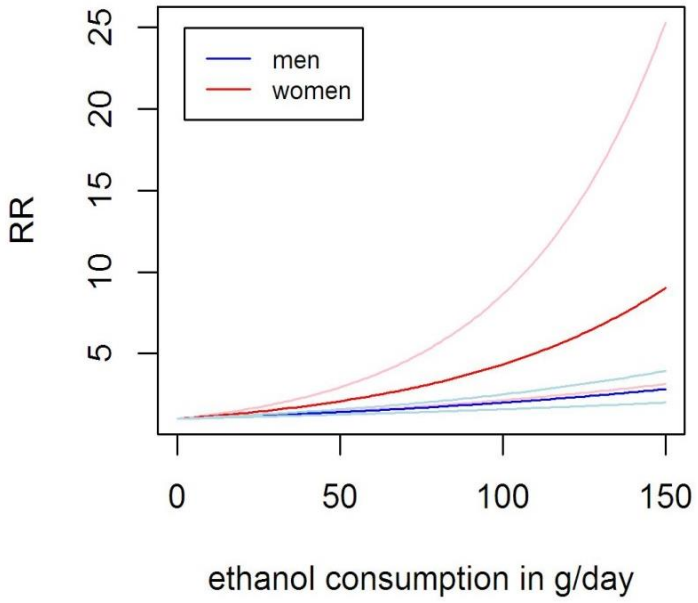
**Former drinkers:**

Women and men: $RR_{FD} = 1.00$*

*The $RR_{FD} = 1.01$ (95% CI: 0.88-1.16) measured Larsson et al., 2014 (52), falls inside the range of 0.95 and 1.05 where the former drinker RRs were not modelled.

## Haemorrhagic stroke and non-ischaemic stroke [I60-62, I69.0-2]

**Current drinkers:**




Women

$$\ln\big(RR(x)\big) = \begin{cases} \ln\big(1 - x \cdot (1 - 1.014815)\big) & , x \leq 1 \\ 1.466406 \cdot \dfrac{x + 0.0028572082519531}{100} & , x > 1 \end{cases}$$

Men

$$\ln\big(RR(x)\big) = \begin{cases} \ln\big(1 - x \cdot (1 - 1.006943)\big) & , x \leq 1 \\ 0.6898937 \cdot \dfrac{x + 0.0028572082519531}{100} & , x > 1 \end{cases}$$

Source: Patra et al., 2010(53)

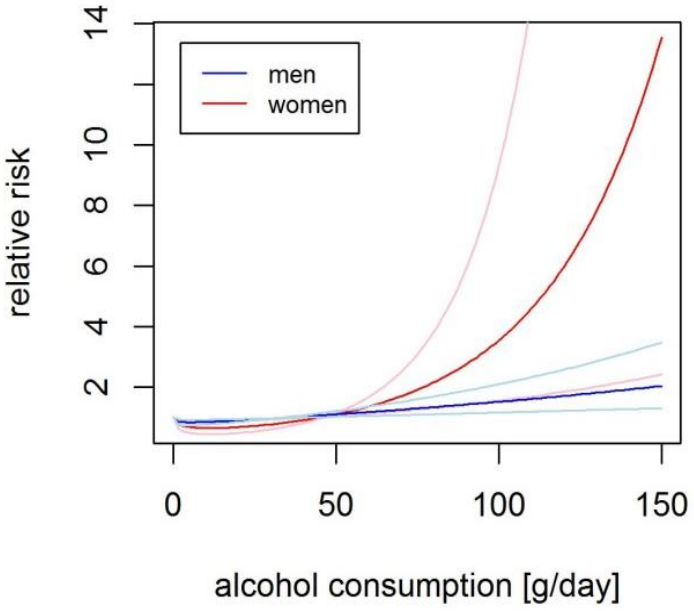
**Former drinkers:**

Women and men: $RR_{FD}$ = 1.36 (95% CI: 0.92-2.02)

Source: Larsson et al., 2016 (54)

## Ischaemic stroke [I63-67, 69.3] (ages 35-65)

**Current drinkers:**




Women

$$\ln\big(RR(x)\big) = \begin{cases} \ln\big(1 - x \cdot (1 - 0.8029366)\big) & , x \leq 1 \\ 1.035623 \cdot (-2.48768 \cdot y^{0.5} + 3.7087240 \cdot y), x > 1 \end{cases}$$

$$where\ y = \frac{x + 0.0028572082519531}{100}$$

Men

$$\ln\big(RR(x)\big) = \begin{cases} \ln\big(1 - x \cdot (1 - 0.8665101)\big) & , x \leq 1 \\ 1.035623 \cdot (0.4030081 \cdot y^{0.5} + 0.3877538 \cdot y^{0.5} \cdot \ln(y)), x > 1 \end{cases}$$

$$where\ y = \frac{x + 0.0028572082519531}{100}$$

The risk relations between alcohol use and ischemic stroke are age-dependent (5). We only show exemplary functions for one age group. In addition, the relative risk is 1 for all people, who consume on average less then 60g of pure alcohol per day, but have at least one heavy drinking occasion per month (55, 56).
Source: Rehm et al., 2016(5) based on Patra et al., 2010 (53)

**Former drinkers:**

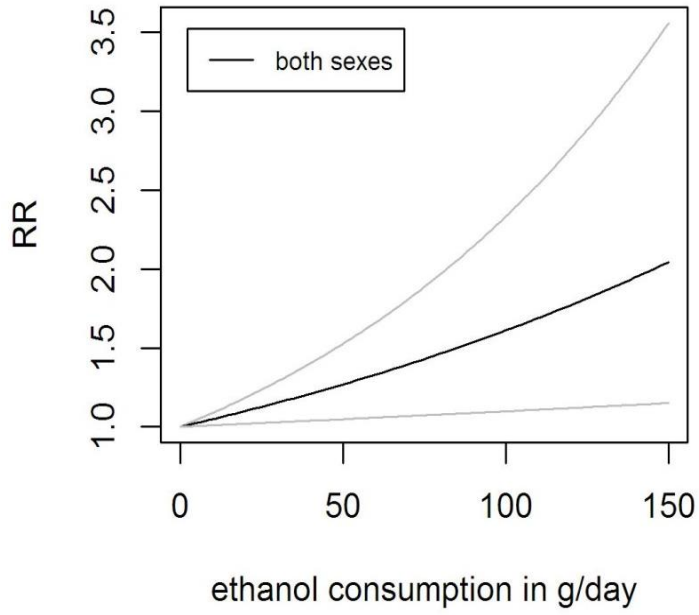
Women and men : $RR_{FD}$ = 1.00*

* The $RR_{FD}$ = 0.97 (0.83-1.14) measured Larsson et al., 2016 (54), falls inside the range of 0.95 and 1.05 where the former drinker RRs were not modelled.

## Diseases of the respiratory system [J00-99]

### Lower respiratory infections: pneumonia [J09–J22, J85, P23]

Current drinkers:




$$\ln(RR(x)) = 0.4764038 \cdot \left(\frac{x + 0.0399999618530273}{100}\right)$$

Source: Samokhvalov et al., 2010 (32)

Former drinkers:

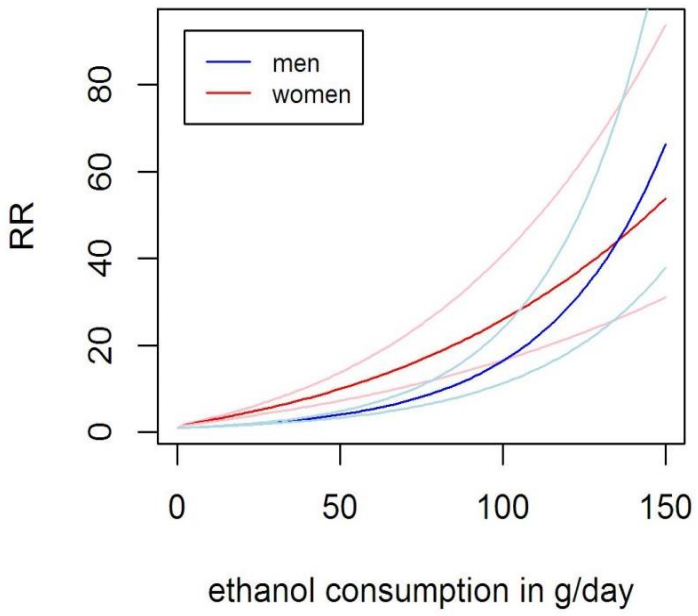
Women and men: $RR_{FD} = 1.00$ *

*There is no increased risk of former drinkers, due to the biological pathways, which are based on infection due to acute consequences of use (32, 33).

## Diseases of the digestive system [K00-93]

### Fibrosis and cirrhosis of liver [K74]

**Current drinkers:**




Women

$$\ln\big(RR(x)\big) = \begin{cases} \ln\big(1 + x \cdot (1.421569 - 1)\big) & , x \leq 1 \\ 3.252035 \cdot \sqrt{\dfrac{x + 0.1699981689453125}{100}} & , x > 1 \end{cases}$$

Men

$$\ln\big(RR(x)\big) = \begin{cases} \ln\big(1 + x \cdot (1.033224 - 1)\big) & , x \leq 1 \\ 2.793524 \cdot \dfrac{x + 0.1699981689453125}{100} & , x > 1 \end{cases}$$

Source: Rehm et al., 2010 (57)

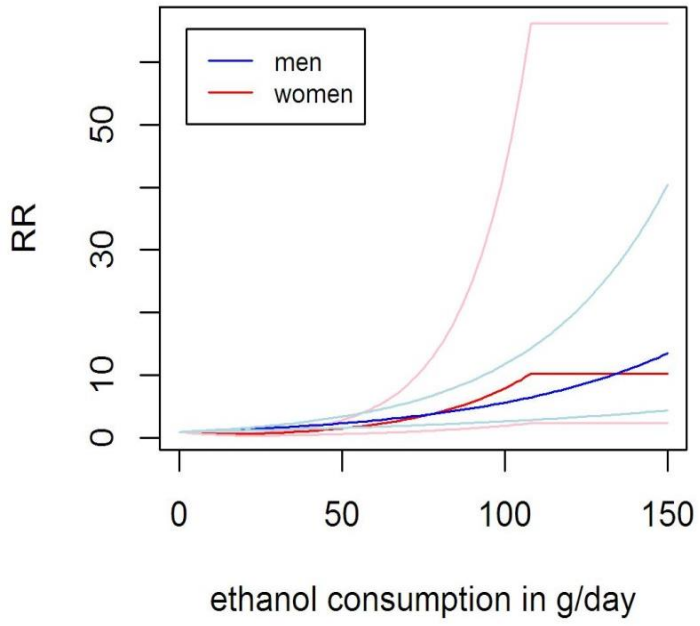
**Former drinkers:**

Women and men: $RR_{FD}$ = 3.26 (95% CI: 1.38-7.74)

Source: Roerecke et al., personal communication

## Pancreatitis [K85-86]

**Current data:**




Women

$$\ln\left(RR(x)\right) = \begin{cases} -0.0272886 \cdot x & ,x > 3 \\ -0.0272886 \cdot x + 0.0611466 \cdot \dfrac{(x-3)^3}{(40-3)^2} & ,3 \le x < 15 \\ -0.0272886 \cdot x + 0.0611466 \cdot \dfrac{(x-3)^3 - \dfrac{(x-15)^3 \cdot (40-3)}{(40-15)}}{(40-3)^2} & ,15 \le x < 40 \\ -0.0272886 \cdot x + 0.0611466 \cdot \dfrac{(x-3)^3 - \dfrac{(x-15)^3 \cdot (40-3) - (x-40)^3 \cdot (15-3)}{(40-15)}}{(40-3)^2} & ,40 \le x < 108 \\ 2.327965 & ,x \ge 108 \end{cases}$$

Men

$$\ln\left(RR(x)\right) = 0.0173451 \cdot x$$

Source: Samokvalov et al., 2015(58)

**Former drinkers:**

Women and men : $RR_{FD}$ = 2.20 (95% CI: 1.45-3.34)

Source: Samokvalov et al., 2015 (58)

## Fetal alcohol syndrome (FAS)

The fetal alcohol syndrome (FAS) is a condition which is per definition caused by alcohol (for all such conditions see (1)). However, mortality due to FAS is not routinely collected by either WHO (8) or IHME ((9); for more background see (59)). Mortality due to FAS will be calculated based on prevalence, which is calculated based on the number of pregnant women who consume alcohol (60).

## References


1. Rehm J, Gmel GE, Gmel G, Hasan OSM, Imtiaz S, Popova S, et al.(2017) The relationship between different dimensions of alcohol use and the burden of disease - an update. Addiction.112(6):968-1001.
2. Sherk A, Stockwell T, Rehm J, Dorocicz J, Shield KD.(2017) The International Model of Alcohol Harms and Policies (InterMAHP) v1.0: A comprehensive guide to the estimation of alcohol-attributable morbidity and mortality. Victoria, BC: Centre for Addictions Research of British Columbia, University of Victoria
3. Shaper A, Wannamethee G, Walker M.(1988) Alcohol and mortality in British men: explaining the U-shaped curve. Lancet.2(8623):1267-73.
4. Marmot MG, Brunner E.(1991) Alcohol and cardiovascular disease: the status of the U- shaped curve. BMJ.303:565-8.
5. Rehm J, Shield KD, Roerecke M, Gmel G.(2016) Modelling the impact of alcohol consumption on cardiovascular disease mortality for comparative risk assessments: an overview BMC Public Health.16:363.
6. Rehm J, Baliunas D, Borges GL, Graham K, Irving HM, Kehoe T, et al.(2010) The relation between different dimensions of alcohol consumption and burden of disease - An overview. Addiction.105(5):817-43.
7. Rehm J, Room R, Graham K, Monteiro M, Gmel G, Sempos C.(2003) The relationship of average volume of alcohol consumption and patterns of drinking to burden of disease - An overview. Addiction.98(10):1209-28.
8. Global Information System on Alcohol and Health (GISAH) [Internet]. World Health Organization. 2016 [cited 09/05/2017]. Available from: http://apps.who.int/gho/data/node.main.A1022?lang=en&showonly=GISAH.
9. Institute of Health Metrics Evaluation. Institute of Health Metrics Evaluation Global Burden of Disease (GBD). 2012 [cited 07/08/2017]. Available from: http://www.healthdata.org/gbd.
10. Stevens GA, Alkema L, Black RE, Boerma JT, Collins GS, Ezzati M, et al.(2016) Guidelines for accurate and transparent health estimates reporting: the GATHER statement. Lancet.388(No. 10062):e19-e23.
11. Rehm J, Room R, Monteiro M, Gmel G, Graham K, Rehn N, et al. Alcohol Use. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, editors. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva, Switzerland: World Health Organization; 2004. p. 959-1109.
12. Rehm J, Kehoe T, Gmel G, Stinson F, Grant B, Gmel G.(2010) Statistical modeling of volume of alcohol exposure for epidemiological studies of population health: the example of the US. Popul Health Metr.8:3.
13. Gmel G, Shield KD, Kehoe-Chan TAK, Rehm J.(2013) 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 Med Res Methodol.13(1):24.
14. Rehm J, Samokhvalov AV, Neuman MG, Room R, Parry CD, Lönnroth K, et al.(2009) The association between alcohol use, alcohol use disorders and tuberculosis (TB). A systematic review. BMC Public Health.9(1):450.
15. 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 modelling strategy for quantifying the effect. Popul Health Metr.15(1):4.
16. Williams EC, Hahn JA, Saitz R, Bryant K, Lira MC, Samet JH.(2016) Alcohol use and Human Immunodeficiency Virus (HIV) infection: Current knowledge, implications, and future directions. Alcohol Clin Exp Res.40(10):2056-72.
17. International Agency for Research on Cancer. IARC Monographs on the evaluation of carcinogenic risks to humans: Alcohol consumption and ethyl carbamate. Lyon, France: International Agency for Research on Cancer; 2010.
18. International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans 100E Personal Habits and Indoor Combustions. Lyon, France: International Agency for Research on Cancer; 2012.
19. Howard AA, Arnsten JH, Gourevitch MN.(2004) Effect of alcohol consumption on diabetes mellitus: a systematic review. Ann Intern Med.140(3):211-9.
20. Bartolomei F.(2006) Epilepsy and alcohol. Epileptic Disord.8:S72-S8.
21. Barclay GA, Barvour J, Stewart S, Day CP, Gilvarry E.(2008) Adverse physical effects of alcohol misuse. Adv Psychiatr Treat.14:139-51.

22. Leach JP, Mohanraj R, Borland W.(2012) Alcohol and drugs in epilepsy: pathophysiology, presentation, possibilities, and prevention. Epilepsia.53 Suppl 4:48-57.
23. Puddey IB, Beilin LJ.(2006) Alcohol is bad for blood pressure. Clinical and Experimental Pharmacology and Physiology.33(9):847-52.
24. O'Keefe JH, Bhatti SK, Bajwa A, DiNicolantonio JJ, Lavie CJ.(2014) Alcohol and cardiovascular health: the dose makes the poison...or the remedy. Mayo Clin Proc.89(3):382-93.
25. Mukamal KJ, Rimm EB.(2001) Alcohol's effects on the risk for coronary heart disease. Alcohol Res Health.25:255-61.
26. Collins MA, Neafsey EJ, Mukamal KJ, Gray MO, Parks DA, Das DK, et al.(2009) Alcohol in moderation, cardioprotection, and neuroprotection: epidemiological considerations and mechanistic studies. Alcohol Clin Exp Res.33(2):206-19.
27. Roerecke M, Rehm J.(2014) Alcohol consumption, drinking patterns, and ischemic heart disease: a narrative review of meta-analyses and a systematic review and meta-analysis of the impact of heavy drinking occasions on risk for moderate drinkers. BMC Med.12:182.
28. Rosenqvist M.(1998) Alcohol and cardiac arrhythmias. Alcohol Clin Exp Res.22(7 Suppl):318s-22s.
29. Mukamal KJ, Ding EL, Djoussé L.(2012) Alcohol consumption, physical activity, and chronic disease risk factors: a population-based cross-sectional survey. BMC Public Health.6(1):118.
30. Puddey IB, Rakic V, Dimmitt SB, Beilin LJ.(1999) Influence of pattern of drinking on cardiovascular disease and cardiovascular risk factors - a review. Addiction.94:649-63.
31. Mazzaglia G, Britton R, Altmann DR, Chenet L.(2001) Exploring the relationship between alcohol consumption and non-fatal or fatal stroke: a systematic review. Addiction.96:1743-56.
32. Samokhvalov AV, Irving HM, Rehm J.(2010) Alcohol consumption as a risk factor for pneumonia: systematic review and meta-analysis. Epidemiol Infect.138(12):1789-95.
33. Traphagen N, Tian Z, Allen-Gipson D.(2015) Chronic ethanol exposure: pathogenesis of pulmonary disease and dysfunction. Biomolecules.5(4):2840-53.
34. Simet SM, Sisson JH.(2015) Alcohol's effects on lung health and immunity. Alcohol Res.37(2):199-208.
35. Gao B, Bataller R.(2011) Alcoholic liver disease: pathogenesis and new therapeutic targets. Gastroenterology.141(5):1572-85.
36. Imtiaz S, Shield KD, Roerecke M, Samokhvalov AV, Lönnroth K, Rehm J.(2017) Alcohol consumption as a risk factor for tuberculosis: meta-analyses and burden of disease. Euro Respir J.50(1):1700216.
37. Scott-Sheldon LA, Carey KB, Cunningham K, Johnson BT, Carey MP, MASH Research Team.(2016) Alcohol use predicts sexual decision-making: A systematic review and meta-analysis of the experimental literature. AIDS Behav.20; Suppl 1:S19-S39.
38. Gmel G, Shield K, Rehm J.(2011) Developing a methodology to derive alcohol-attributable fractions for HIV/AIDS mortality based on alcohol's impact on adherence to antiretroviral medication. Popul Health Metr.9(1):5.
39. International Agency for Research on Cancer, World Health Organization. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. 2016 [cited 09/05/2017]. Available from: http://monographs.iarc.fr/ENG/Preamble/currentb6evalrationale0706.php.
40. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al.(2015) Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Br J Cancer.112(3):580-93.
41. Marron M, Boffetta P, Zhang ZF, Zaridze D, Wunsch-Filho V, Winn DM, et al.(2010) Cessation of alcohol drinking, tobacco smoking and the reversal of head and neck cancer risk. Int J Epidemiol.39(1):182-96.
42. Schütze M, Boeing H, Pischon T, Rehm J, Kehoe T, Gmel G, et al.(2011) Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. BMJ.342:d1584.
43. 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):1804-12.
44. Samokhvalov AV, Irving H, Mohapatra S, Rehm J.(2010) Alcohol consumption, unprovoked seizures and epilepsy: a systematic review and meta-analysis. Epilepsia.51(7):1177-84.

45. Leone M, Bottachi E, Beghi E, Morgando E, Mutani R, Amedeo G, et al.(1997) Alcohol use is a risk factor for a first generalized tonic-clonic seizure. Neurology.48:614-20.
46. Roerecke M, Rehm J.(2010) Irregular heavy drinking occasions and risk of ischemic heart disease: a systematic review and meta-analysis. Am J Epidemiol.171(6):633-44.
47. 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):1246-60.
48. Roerecke M, Rehm J.(2011) Ischemic heart disease mortality and morbidity in former drinkers: a meta-analysis. Am J Epidemiol.173(3):245-58.
49. Rehm J, Hasan OSM, Imtiaz S, Neufeld M.(2017) Quantifying the contribution of alcohol to cardiomyopathy: a systematic review. Alcohol.61:9-15.
50. Manthey J, Imtiaz S, Neufeld J, Rylett M, Rehm J.(2017) Quantifying the global contribution of alcohol consumption to cardiomyopathy. Popul Health Metr.15(1):20.
51. Samokhvalov AV, Irving HM, Rehm J.(2010) Alcohol as a risk factor for atrial fibrillation: a systematic review and meta-analysis. Eur J Cardiov Prev R.17(6):706-12.
52. Larsson SC, Drca N, Wolk A.(2014) Alcohol consumption and risk of atrial fibrillation: a prospective study and dose-response meta-analysis. J Am Coll Cardiol.64(3):281-9.
53. Patra J, Taylor B, Irving H, Roerecke M, Baliunas D, Mohapatra S, et al.(2010) Alcohol consumption and the risk of morbidity and mortality from different stroke types - a systematic review and meta-analysis. BMC Public Health.10(1):258.
54. Larsson SC, Wallin A, Wolk A, Markus HS.(2016) Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis. BMC Med.14(1):178.
55. Mostofsky E, Chahal HS, Mukamal KJ, Rimm EB, Mittleman MA.(2016) Alcohol and immediate risk of cardiovascular events: a systematic review and dose-response meta-analysis. Circulation.133(10):979-87.
56. Guiraud V, Amor MB, Mas JL, Touzé E.(2010) Triggers of ischemic stroke: a systematic review. Stroke.41(11):2669-77.
57. Rehm J, Taylor B, Mohapatra S, Irving H, Baliunas D, Patra J, et al.(2010) Alcohol as a risk factor for liver cirrhosis - a systematic review and meta-analysis. Drug Alcohol Rev.29(4):437-45.
58. Samokhvalov AV, 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.
59. Rehm J, Imtiaz S.(2016) Alcohol consumption as a risk factor for global burden of disease. A narrative review. Subst Abuse Treat Prev Policy.11(1):37.
60. Popova S, Lange S, Probst C, Gmel G, Rehm J.(2017) Estimation of national, regional and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis. Lancet Glob Health.5(3):e290-e9.