Supplementary Material for

“Alcohol consumption and risk of liver cirrhosis: a systematic review and meta-analysis” by

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**Supplementary Table 1.** Search strategy forMedline(R) (1946-most recent) and Embase (Embase+Embase Classic)

|  |  |
| --- | --- |
| 1 | human/ |
| 2 | humans/ |
| 3 | 1 or 2 |
| 4 | (bibliography or case reports or clinical conference or clinical trial, all or comment or congresses or editorial or guideline or in vitro or letter or meta analysis or "review" or systematic reviews).pt. |
| 5 | 3 not 4 |
|  | **Method terms** |
| 6 | exp Case-Control Studies/ or case control.mp. |
| 7 | exp cohort studies/ or exp follow-up studies/ or exp longitudinal studies/ or exp prospective studies/ or exp retrospective studies/ or cohort study.mp. |
| 8 | 6 or 7 |
| 9 | 5 and 8 |
|  | **Alcohol terms** |
| 10 | exp alcohol drinking/ |
| 11 | exp alcoholic intoxication/ |
| 12 | exp binge drinking/ |
| 13 | (alcohol\* adj3 (drink\* or consum\* or intake)).mp. |
| 14 | heavy drinking.mp. |
| 15 | alcoholic beverages/ |
| 16 | 10 or 11 or 12 or 13 or 14 or 15 |
|  | **Disease terms** |
| 17 | liver diseases/ |
| 18 | liver cirrhosis/ or exp liver cirrhosis, alcoholic/ or exp liver cirrhosis, biliary/ |
| 19 | fatty liver/ or exp fatty liver, alcoholic/ or exp non-alcoholic fatty liver disease/ |
| 20 | steatohepatitis.mp. |
| 21 | steato-hepatitis.mp. |
| 22 | exp liver cirrhosis/ |
| 23 | exp liver fibrosis/ |
| 24 | ((hepatic or liver) and (fibrosis or cirrhosis)).mp. |
| 25 | 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 |
| 26 | 9 and 16 and 25 |
| 27 | remove duplicates from 26 |

Search was done on March 6th 2019 with no date restrictions.

**Supplementary Table 2.** The Risk of Bias in Non-randomized Studies – of Interventions (ROBINS-I) assessment tool

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Bias due to confounding** | **Bias in selection of participants into the study** | **Bias in classification of exposures** | **Bias due to missing data** | **Bias in measurement of outcomes** | **Bias in selection of the reported result** | **Overall risk of bias** |
| Askgaard et al, 2015(1) | Moderate | Moderate | Low | Low | Low | Low | Moderate |
| Boffetta et al, 1990(2) | Moderate | Low | Low | Low | Low | Low | Moderate |
| Corrao et al, 1993(3) | Moderate | Low | Moderate | Low | Low | Low | Moderate |
| Corrao et al, 1997(4) | Moderate | Low | Moderate | Low | Low | Low | Moderate |
| Fuchs et al, 1995(5) | Moderate | Low | Low | Unclear | Low | Low | Moderate |
| Garfinkel et al, 1988(6) | Serious | Low | Low | Unclear | Low | Low | Serious |
| Klatsky et al, 2003(7) | Moderate | Low | Low | Low | Low | Low | Moderate |
| Liu et al, 2009(8) | Moderate | Low | Moderate | Low | Low | Low | Moderate |
| Yang et al, 2012(9) | Moderate | Low | Low | Low | Low | Low | Moderate |

**Supplementary Fig. 1.** Funnel plot for cohort studies in drinkers of 1 or 2 drinks per day, both sexes, 1988-2017



**Supplementary Fig. 2.** Influence of omitting a single study for cohort studies in drinkers of 1 or 2 drinks per day, both sexes, 1988-2017



**Supplementary Fig. 3.** Forest plot of liver cirrhosis risk by alcohol consumption (in comparison to long-term abstainers) in cohort studies in women, 1988-2017



Adjusted for age, smoking, and body weight.

**Supplementary Fig. 4.** Dose-response relationship of liver cirrhosis risk by alcohol consumption in relation to long-term abstainers in men in cohort studies, 1988-2017

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CI = confidence interval.

**Supplementary Fig. 5.** Dose-response relationship of liver cirrhosis risk by alcohol consumption in relation to long-term abstainers in women in cohort studies, 1988-2017

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CI = confidence interval.

**Supplementary Fig. 6.** Forest plot of liver cirrhosis risk by alcohol consumption (in comparison to long-term abstainers) in case-control studies in men, 1988-2017



Relative risk on the log scale. 1 standard drink = 12 grams pure ethanol per day. RR = relative risk.

**Supplementary Fig. 7.** Forest plot of liver cirrhosis risk by alcohol consumption (in comparison to long-term abstainers) in case-control studies in women, 1988-2017



Relative risk on the log scale. 1 standard drink = 12 grams pure ethanol per day. RR = relative risk.

**Supplementary References**

1. Askgaard G, Gronbaek M, Kjaer MS, et al. Alcohol drinking pattern and risk of alcoholic liver cirrhosis: a prospective cohort study. J Hepatol 2015;62:1061-7.

2. Boffetta P, Garfinkel L. Alcohol drinking and mortality among men enrolled in an American Cancer Society prospective study. Epidemiology 1990;1:342-8.

3. Corrao G, Arico S, Lepore R, et al. Amount and duration of alcohol intake as risk factors of symptomatic liver cirrhosis: a case-control study. J Clin Epidemiol 1993;46:601-7.

4. Corrao G, Arico S, Zambon A, et al. Female sex and the risk of liver cirrhosis. Collaborative Groups for the Study of Liver Diseases in Italy. Scand J Gastroenterol 1997;32:1174-80.

5. Fuchs CS, Stampfer MJ, Colditz GA, et al. Alcohol consumption and mortality among women. N Engl J Med 1995;332:1245-50.

6. Garfinkel L, Boffetta P, Stellman SD. Alcohol and breast cancer: a cohort study. Prev Med 1988;17:686-93.

7. Klatsky AL, Friedman GD, Armstrong MA, et al. Wine, liquor, beer, and mortality. Am J Epidemiol 2003;158:585-95.

8. Liu B, Balkwill A, Roddam A, et al. Separate and joint effects of alcohol and smoking on the risks of cirrhosis and gallbladder disease in middle-aged women. Am J Epidemiol 2009;169:153-60.

9. Yang L, Zhou M, Sherliker P, et al. Alcohol drinking and overall and cause-specific mortality in China: nationally representative prospective study of 220,000 men with 15 years of follow-up. International J Epidemiol 2012;41:1101-1113.