**Supplementary Table 1.** Hazard ratios for associations between alcohol consumption and the risk of **colorectal polyp or cancer** for DNA mismatch repair gene germline mutation carriers

|  |  |  |
| --- | --- | --- |
|  |  | Multivariable model (complete case analysis)a |
|  | Cases | Person-years  | HR (95% CI) | *P* value  |
| Average daily ethanol intake from any alcoholic beverage  |  |  |  |  |
|  Abstainer | 283 | 13258.5 | 1 [Reference] |  |
|  Ever user | 690 | 24702 | 1.26 (1.09 – 1.47) | 0.002 |
| >0 to ≤14 grams  | 423 | 15340.5 | 1.25 (1.07 – 1.46) | 0.01 |
| >14 grams to ≤28 grams  | 123 | 4662.5 | 1.21 (0.96 – 1.52) | 0.11 |
| >28 grams  | 144 | 4699 | 1.46 (1.15 – 1.86) | 0.002 |
| Average daily ethanol intake from any alcoholic beverage (14 grams/day)  | 973 | 37960.5 | 1.03 (0.99 – 1.07) | 0.14 |
| Average daily ethanol intake from beer b |  |  |  |  |
|  Abstainer | 495 | 21864 | 1 [Reference] |  |
|  Ever user | 531 | 18012.5 | 1.18 (1.00 – 1.38) | 0.05 |
| Average daily ethanol intake from beer (14 grams/day)  | 1026 | 39876.5 | 1.01 (0.97 – 1.06) | 0.51 |
| Average daily ethanol intake from wine c |  |  |  |  |
|  Abstainer | 660 | 27673 | 1 [Reference] |  |
|  Ever user | 385 | 12565.5 | 1.08 (0.93 – 1.25) | 0.29 |
| Average daily ethanol intake from wine (14 grams/day)  | 1045 | 40238.5 | 1.07 (0.86 – 1.32) | 0.55 |
| Average daily ethanol intake from spirits d |  |  |  |  |
|  Abstainer | 631 | 26204 | 1 [Reference] |  |
|  Ever user | 386 | 13331.5 | 1.14 (1.00 – 1.31) | 0.05 |
| Average daily ethanol intake from spirits (14 grams/day)  | 1017 | 39535.5 | 1.04 (0.92 – 1.17) | 0.54 |

Abbreviation: HR, hazard ratio; CI, confidence interval a All multivariable models were adjusted for country (categorical, time-fixed), education (categorical, time-fixed l), ascertainment (binary, time-fixed), sex (binary, time-fixed), BMI at age 20 (categorical, time-fixed), diabetes status (binary, time-varying), regular physical activity (binary, time-varying), and smoking status (categorical, time-varying). b Multivariable models additionally adjusted for average daily ethanol intake from wine (binary, time-varying) and from spirits (binary, time-varying) c Multivariable models additionally adjusted for average daily ethanol intake from beer (binary, time-varying) and from spirits (binary, time-varying) d Multivariable models additionally adjusted for average daily ethanol intake from beer (binary, time-varying) and from wine (binary, time-varying)

**Supplementary Table 2.** Hazard ratios for associations between alcohol consumption and the risk of **colorectal cancer** for DNA mismatch repair gene germline mutation carriers; **analyses limited to mutation carriers diagnosed with colorectal cancer or censored within 5 years before baseline interview**

|  |  |  |
| --- | --- | --- |
|  |  | Multivariable model (complete case analysis)a |
|  | Cases | Person-years  | HR (95% CI) | *P* value  |
| Average daily ethanol intake from any alcoholic beverage  |  |  |  |  |
|  Abstainer | 92 | 7485.5 | 1 [Reference] |  |
|  Ever user | 262 | 17109.5 | 1.26 (0.81 – 1.97) | 0.30 |
| >0 to ≤14 grams  | 168 | 10842.5 | 1.31 (0.84 – 2.04) | 0.23 |
| >14 grams to ≤28 grams  | 42 | 3030 | 0.98 (0.53 – 1.81) | 0.96 |
| >28 grams  | 52 | 3237 | 1.29 (0.65 – 2.53) | 0.46 |
| Average daily ethanol intake from any alcoholic beverage (14 grams/day)  | 354 | 24595 | 0.96 (0.86 – 1.08) | 0.50 |
| Average daily ethanol intake from beer b |  |  |  |  |
|  Abstainer | 159 | 13276.5 | 1 [Reference] |  |
|  Ever user | 211 | 12267.5 | 1.01 (0.67 – 1.52) | 0.95 |
| Average daily ethanol intake from beer (14 grams/day)  | 369 | 25544 | 0.89 (0.76 – 1.05) | 0.17 |
| Average daily ethanol intake from wine c |  |  |  |  |
|  Abstainer | 241 | 17110 | 1 [Reference] |  |
|  Ever user | 136 | 8889 | 0.90 (0.61 – 1.33) | 0.60 |
| Average daily ethanol intake from wine (14 grams/day)  | 377 | 25999 | 0.48 (0.22 – 1.05) | 0.07 |
| Average daily ethanol intake from spirits d |  |  |  |  |
|  Abstainer | 222 | 16433.5 | 1 [Reference] |  |
|  Ever user | 152 | 9293.5 | 1.51 (1.05 – 2.17) | 0.03 |
| Average daily ethanol intake from spirits (14 grams/day)  | 374 | 25727 | 1.14 (0.95 – 1.38) | 0.17 |

Abbreviation: HR, hazard ratio; CI, confidence interval a All multivariable models were adjusted for country (categorical, time-fixed), education (categorical, time-fixed l), ascertainment (binary, time-fixed), sex (binary, time-fixed), BMI at age 20 (categorical, time-fixed), diabetes status (binary, time-varying), regular physical activity (binary, time-varying), and smoking status (categorical, time-varying). b Models additionally adjusted for average daily ethanol intake from wine (binary, time-varying) and from spirits (binary, time-varying) c Models additionally adjusted for average daily ethanol intake from beer (binary, time-varying) and from spirits (binary, time-varying) d Models additionally adjusted for average daily ethanol intake from beer (binary, time-varying) and from wine (binary, time-varying)

**Supplementary Table 3.** Hazard ratios for associations between alcohol consumption and the risk of **colorectal cancer** for DNA mismatch repair gene germline mutation carriers by smoking status, body mass index (BMI) at age 20 years, and history of having received sigmoidoscopy or colonoscopy

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Average daily ethanol intake from (ever vs. never users) |  | Cases/PY(ever vs. never users) | HR (95% CI) a | P value for interaction  b |
| Smoking status c | Any alcoholic beverage  | Never smoker | 194/10401.5 vs. 120/8812.5 | 1.49 (0.97 – 2.31) |  |
| Former smoker | 109/3734 vs. 25/1115 | 1.51 (0.75 – 3.04) |  |
| Current smoker | 183/10488.5 vs. 50/3293 | 1.27 (0.76 – 2.14) | 0.61 |
| Beer | Never smoker | 143/6765.5 vs. 186/13255.5 | 1.41 (0.91 – 2.19) |  |
| Former smoker | 93/3070 vs. 50/2149 | 1.66 (0.87 – 3.16) |  |
| Current smoker | 149/8165 vs. 94/6344.5 | 0.99 (0.61 – 1.61) | 0.17 |
| Wine | Never smoker | 120/6327 vs. 210/13789 | 1.02 (0.67 – 1.55) |  |
| Former smoker | 54/2138 vs. 93/3233 | 0.57 (0.32 – 1.02) |  |
| Current smoker | 79/4065.5 vs. 171/10517 | 1.23 (0.75 – 2.02) | 0.70 |
| Spirits | Never smoker | 100/5163 vs. 224/14691 | 1.06 (0.65 – 1.73) |  |
| Former smoker | 62/2079 vs. 82/3043 | 1.56 (0.90 – 2.69) |  |
| Current smoker | 115/6005.5 vs. 129/8408 | 1.21 (0.75 – 1.94) | 0.83 |
| BMI at age 20 years d | Any alcoholic beverage | Normal weight | 311/16798 vs. 122/8692.5 | 1.48 (1.02 – 2.13) |  |
| Overweight/obese | 130/5500 vs. 42/2195 | 0.99 (0.48 – 2.01) | 0.88 |
| Beer | Normal weight | 237/11778 vs. 220/15182.5 | 1.19 (0.84 – 1.69) |  |
| Overweight/obese | 116/4881.5 vs. 62/3140.5 | 0.99 (0.50 – 1.94) | 0.56 |
| Wine | Normal weight | 174/9174 vs. 288/17949.5 | 1.13 (0.79 – 1.62) |  |
| Overweight/obese | 53/2286 vs. 131/5946 | 0.55 (0.31 – 0.97) | 0.38 |
| Spirits | Normal weight | 172/8862 vs. 280/17619.5 | 1.09 (0.77 – 1.54) |  |
| Overweight/obese | 81/3171 vs. 100/4980 | 1.53 (0.87 – 2.69) | 0.61 |
| Received sigmoidoscopy or colonoscopy e | Any alcoholic beverage | Never | 108/19642 vs. 59/10464 | 1.10 (0.68 – 1.79) |  |
| Ever | 201/2065 vs. 72/658.5 | 0.70 (0.41 – 1.19) | 0.43 |
| Beer | Never | 86/14355.5 vs. 90/17072.5 | 1.11 (0.61 – 2.00) |  |
| Ever | 162/1499 vs. 125/1380.5 | 0.78 (0.48 – 1.27) | 0.41 |
| Wine | Never | 50/9530 vs. 128/22096 | 0.96 (0.58 – 1.58) |  |
| Ever | 116/1353 vs. 175/1584.5 | 0.73 (0.47 – 1.15) | 0.42 |
| Spirits | Never | 64/10435 vs. 111/20712 | 1.13 (0.70 – 1.81) |  |
| Ever | 113/1182 vs. 174/1654.5 | 1.00 (0.63 – 1.58) | 0.81 |

Abbreviation: PY, person-years; HR, hazard ratio; CI, confidence interval a All multivariable models were adjusted for country (categorical, time-fixed), education (categorical, time-fixed l), ascertainment (binary, time-fixed), sex (binary, time-fixed), diabetes status (binary, time-varying), regular physical activity (binary, time-varying) b *P value* from likelihood ratio test c Models additionally adjusted for BMI at age 20 years (categorical, time-fixed) c Models additionally adjusted for smoking status (categorical, time-varying) d Models additionally adjusted for BMI at age 20 years (categorical, time-fixed) and smoking status (categorical, time-varying) e Models additionally adjusted for average daily ethanol intake from wine (binary, time-varying) and from spirits (binary, time-varying) f Models additionally adjusted for average daily ethanol intake from beer (binary, time-varying) and from spirits (binary, time-varying) g Models additionally adjusted for average daily ethanol intake from beer (binary, time-varying) and from wine (binary, time-varying)

**Supplementary Table 4.** Assessment of interaction between main exposure variables and sex (binary), country (categorical), ascertainment method (binary), mutated gene (categorical), and folic acid supplement intake (binary)

|  |  |  |
| --- | --- | --- |
|  | P value for interaction a |  |
|  | Sex | Country | Ascertainment method | Mutated gene | Folic acid supplement intake |
| Average daily ethanol intake from any alcoholic beverage  (abstainer vs ever user) | 0.78 | 0.99 | 0.11 | 0.99 | 0.37 |
| Average daily ethanol intake from beer  (abstainer vs ever user) | 0.61 | 0.53 | 0.35 | 0.50 | 0.87 |
| Average daily ethanol intake from wine  (abstainer vs ever user) | 0.44 | 0.69 | 0.99 | 0.58 | 0.07 |
| Average daily ethanol intake from spirits (abstainer vs ever user) | 0.09 | 0.59 | - | 0.89 | 0.86 |

a *P value* from likelihood ratio test