**Supporting information**

# Low levels of alcohol consumption, obesity and development of fatty liver with and without evidence of advanced fibrosis

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## Supplementary methods

### Comparison of baseline characteristics of participants included in the analysis and those who were excluded from the analysis due to missing data

When we compared characteristics of participants included in the analysis and those who were excluded from the analysis due to missing data (**Supplementary Table 1**), participants with missing data were more likely to be older, female, have a history of treatment of dyslipidemia, and have a lower level of HOMA-IR than those included in the analysis. Otherwise, there were very small differences in most variables between the two groups. Although these small differences were statistically significant with our large sample size, they are highly unlikely to be clinically relevant.

### Assessment of alcohol intake

Current alcohol use was assessed as the frequency of alcohol drinking per week and amount of alcohol consumed per drinking day using the following questions: “How often do you drink alcohol in a week on average (please fill in the details that apply to your current situation)?” and “How much alcohol do you usually drink per drinking day?” (see further details in the supporting information). Amount of alcohol consumed per drinking day was recorded in units of ‘soju,’ which is the most popular alcoholic beverage in Korea. The alcoholic content in *soju* was estimated to be 25% at the time of enrollment before 2006; thereafter, the amount was assumed to be 20%. The traditional unit of *jan* of soju (1 *jan* of *soju*=50 mL) contained 10 g of ethanol before 2006 and 8 g of ethanol thereafter (11). The questionnaire listed the volume of alcoholic beverages that contained the equivalent quantity of ethanol to one unit (*jan)* of soju, and the subjects referred to this chart when recording the alcohol amount consumed per drinking day.

### Alcohol flushing question

Alcohol flushing, a proxy for aldehyde dehydrogenase 2 (ALDH2) deficiency was

assessed using the following question: ‘Do you have a tendency to develop facial flushing immediately after drinking as little as one alcoholic drink?’ The choice of answers was: yes or no. Participants who answered ‘yes’ to the alcohol flushing question were classified as alcohol flushers and those who answered ‘no’ were classified as alcohol non-flushers. The alcohol flushing response is associated with high acetaldehyde levels and predominantly results from an inherited deficiency in the ALDH2 enzyme among East Asians (1). Questions about alcohol flushing have been used to identify ALDH2-deficient subjects in East Asian countries, including South Korea (1, 2).

**Assessment of binge drinking**

Binge drinking was assessed in two ways. A specific question about binge drinking is included in the Alcohol Use Disorders Identification Test (AUDIT) which was developed by the WHO as a simple method for screening individuals with harmful alcohol consumption (3); however, in our center, we started to use Korean version of AUDIT from 2011. Because the specific question about binge drinking was not available until 2011, we estimated binge drinking based on a question about the number of drinks consumed in a typical drinking day for overall population. We also have performed a sensitivity analysis using AUDIT-3 for defining binge drinking (“how often do you have six or more drinks on one occasion?”). To exclude the effect of binge drinking, we performed analyses of participants who answered “never” to the AUDIT-3 question.

References

1. Brooks PJ, Enoch MA, Goldman D, Li TK, Yokoyama A. The alcohol flushing response: an unrecognized risk factor for esophageal cancer from alcohol consumption. PLoS Med 2009;6:e50.
2. Kim JS, Kim YJ, Kim TY, Song JY, Cho YH, Park YC, Chung HW. Association of ALDH2 polymorphism with sensitivity to acetaldehyde-induced micronuclei and facial flushing after alcohol intake. Toxicology 2005;210:169-174.
3. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction 1993;88:791-804.

**Supplementary Table 1.** Comparison of baseline characteristics of participants included in the analysis and those who were excluded from the analysis due to missing data.

| Characteristics | Overall | Participants included in final analysis | Participants excluded from analysis due to missing data | *P* value |
|---|---|---|---|---|
| Number | 202,537 | 190,074 | 12,463 | |
| Age (years) [a] | 35.6 (6.6) | 35.5 (6.5) | 37.2 (7.9) | <0.001 |
| Male (%) | 42.7 | 44.2 | 20.0 | <0.001 |
| Current smoker (%) | 17.9 | 18.5 | 8.1 | <0.001 |
| Regular exercise (%)[d] | 13.3 | 13.3 | 14.1 | 0.015 |
| High education level (%)[e] | 80.7 | 80.9 | 78.3 | <0.001 |
| Hypertension (%) | 6.5 | 6.6 | 5.6 | <0.001 |
| Diabetes (%) | 0.7 | 0.7 | 0.8 | 0.029 |
| Medication for dyslipidemia (%) | 0.5 | 0.4 | 1.1 | <0.001 |
| Systolic BP (mmHg)[a] | 108.4 (12.7) | 108.4 (12.7) | 107.3 (12.7) | <0.001 |
| Diastolic BP (mmHg)[a] | 69.4 (9.4) | 69.5 (9.4) | 68.1 (9.1) | <0.001 |
| Glucose (mg/dl) [a] | 90.9 (9.7) | 90.9 (9.7) | 90.3 (9.3) | <0.001 |
| Total cholesterol (mg/dl) [a] | 186.9 (32.0) | 186.9 (32.0) | 186.9 (32.7) | 0.924 |
| LDL-C (mg/dl) [a] | 108.9 (28.3) | 109.0 (28.3) | 108.4 (28.9) | 0.021 |
| HDL-C (mg/dl) [a] | 59.9 (13.8) | 59.8 (13.8) | 61.7 (14.0) | <0.001 |
| Triglycerides (mg/dl) [b] | 81 (60-113) | 81 (60-114) | 74 (57-102) | <0.001 |
| AST (U/l)[b] | 19 (16-23) | 19 (16-23) | 18 (16-21) | <0.001 |
| ALT (U/l) [b] | 16 (12-22) | 16 (12-22) | 14 (11-19) | <0.001 |
| GGT (U/l) [b] | 15 (11-23) | 15 (11-23) | 13 (10-18) | <0.001 |
| Albumin (g/dL) [b] | 4.6 (0.2) | 4.6 (0.2) | 4.5 (0.2) | <0.001 |
| Platelet ($\times 10^9$/L) [a] | 256.1 (52.2) | 255.9 (52.0) | 258.9 (54.1) | <0.001 |
| hsCRP (mg/l) [b] | 0.3 (0.2-0.7) | 0.3 (0.2-0.7) | 0.3 (0.2-0.7) | <0.001 |
| HOMA-IR [b] | 1.37 (0.92-1.56) | 1.39 (0.94-1.90) | 1.09 (0.72-1.56) | <0.001 |

Data are expressed as [a]mean (standard deviation), [b]median (interquartile range) or percentage.
[c] ≥ 10 g/day; [d] ≥ 3 times/week; [e] ≥ College graduate; [f] BMI ≥25kg/m$^2$.
The $\chi^2$-test and one-way analysis of variance were used to compare the characteristics of the study participants at baseline by category.
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BP, blood pressure; GGT, gamma-glutamyl transpeptidase; HDL-C, high-density lipoprotein-cholesterol; hsCRP, high sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance. LDL-C, low-density lipoprotein cholesterol.

**Supplementary Table 2.** Baseline characteristics according to development of hepatic steatosis and hepatic steatosis plus intermediate/high probability of advanced fibrosis based on FIB-4 index levels among 190,048 participants between 2002 and 2016.

| Characteristics | Overall | No incident hepatic steatosis (a) | Incident hepatic steatosis (b) | Incident hepatic steatosis plus intermediate/high FIB(c) | *P* value[g] | Multiple comparisons[h] |
|---|---|---|---|---|---|---|
| Number | 190,048 | 146,582 | 40,483 | 2,983 | | |
| Age (years) [a] | 35.5 (6.5) | 35.3 (6.5) | 35.7 (6.1) | 41.9 (8.4) | <0.001 | a≠b, a≠c, b≠c |
| Male (%) | 44.2 | 36.7 | 69.1 | 73.4 | <0.001 | a≠b, a≠c, b≠c |
| Current smoker (%) | 18.4 | 14.7 | 30.9 | 32.7 | <0.001 | a≠b, a≠c |
| Alcohol intake [c] | 23.9 | 21.0 | 33.1 | 40.2 | <0.001 | a≠b, a≠c, b≠c |
| Regular exercise (%)[d] | 13.3 | 12.9 | 14.2 | 20.5 | <0.001 | a≠b, a≠c, b≠c |
| High education level (%)[e] | 80.9 | 81.0 | 81.2 | 71.6 | <0.001 | a≠c, b≠c |
| Hypertension (%) | 6.6 | 5.2 | 10.6 | 18.7 | <0.001 | a≠b, a≠c, b≠c |
| Diabetes (%) | 0.7 | 0.5 | 1.1 | 1.7 | <0.001 | a≠b, a≠c, b≠c |
| Medication for dyslipidemia (%) | 0.4 | 0.4 | 0.6 | 0.9 | <0.001 | a≠b, a≠c |
| Obesity (%)[f] | 13.7 | 9.1 | 28.8 | 31.2 | <0.001 | a≠b, a≠c, b≠c |
| Body mass index (kg/m$^2$) | 22.1 (2.7) | 21.6 (2.5) | 23.8 (2.5) | 23.9 (2.4) | <0.001 | a≠b, a≠c, b≠c |
| Systolic BP (mmHg)[a] | 108.4 (12.7) | 107.0 (12.4) | 113.0 (12.5) | 115.5 (13.3) | <0.001 | a≠b, a≠c, b≠c |
| Diastolic BP (mmHg)[a] | 69.5 (9.4) | 68.5 (9.1) | 72.9 (9.4) | 75.0 (9.8) | <0.001 | a≠b, a≠c, b≠c |
| Glucose (mg/dl) [a] | 90.9 (9.7) | 90.4 (9.3) | 92.7 (10.7) | 93.0 (12.4) | <0.001 | a≠b, a≠c |
| Total cholesterol (mg/dl) [a] | 186.9 (32.0) | 184.6 (31.3) | 194.5 (32.9) | 199.9 (34.4) | <0.001 | a≠b, a≠c, b≠c |
| LDL-C (mg/dl) [a] | 109.0 (28.3) | 106.5 (27.7) | 117.4 (28.5) | 118.2 (29.1) | <0.001 | a≠b, a≠c |
| HDL-C (mg/dl) [a] | 59.8 (13.8) | 61.6 (13.9) | 53.9 (11.6) | 53.2 (11.8) | <0.001 | a≠b, a≠c, b≠c |
| Triglycerides (mg/dl) [b] | 81 (60-114) | 75 (57-103) | 107 (78-149) | 119 (86-169) | <0.001 | a≠b, a≠c, b≠c |
| AST (U/l)[b] | 19 (16-23) | 19 (16-22) | 21 (18-24) | 23 (20-27) | <0.001 | a≠b, a≠c, b≠c |
| ALT (U/l) [b] | 16 (12-22) | 15 (12-20) | 20 (15-28) | 22 (17-29) | <0.001 | a≠b, a≠c, b≠c |
| GGT (U/l) [b] | 15 (11-23) | 14 (10-20) | 20 (14-31) | 23 (15-37) | <0.001 | a≠b, a≠c, b≠c |
| Albumin (g/dL) [b] | 4.6 (0.2) | 4.6 (0.2) | 4.6 (0.2) | 4.5 (0.2) | <0.001 | a≠b, a≠c, b≠c |
| Platelet ($\times 10^9$/L) [a] | 255.9 (52.0) | 254.3 (51.8) | 263.3 (52.4) | 234.7 (47.5) | <0.001 | a≠b, a≠c, b≠c |
| hsCRP (mg/l) [b] | 0.3 (0.2-0.7) | 0.3 (0.1-0.6) | 0.5 (0.2-1.0) | 0.5 (0.3-1.0) | <0.001 | a≠b, a≠c |
| HOMA-IR [b] | 1.39 (0.94-1.90) | 1.31 (0.88-1.80) | 1.65 (1.19-2.18) | 1.70 (1.28-2.19) | <0.001 | a≠b, a≠c, b≠c |
| Fib4 [a] | 0.69 (0.20) | 0.70 (0.21) | 0.65 (0.19) | 0.91 (0.21) | <0.001 | a≠b, a≠c, b≠c |

Data are expressed as [a]mean (standard deviation), [b]median (interquartile range) or percentage.
[c] ≥ 10 g/day; [d] ≥ 3 times/week; [e] ≥ College graduate; [f] BMI ≥25kg/m$^2$.
Participants who developed hepatic steatosis as well as a change to intermediate/high probability of advanced fibrosis were exclusively categorized as hepatic steatosis plus intermediate/high FIB (c); thus, incident hepatic steatosis (b) indicates hepatic steatosis with low probability of advanced fibrosis.

The $\chi^2$-test and one-way analysis of variance were used to compare the characteristics of the study participants at baseline by category.
[g] p value refers to between group differences
[h] Post-hoc multiple comparison analysis was performed with Bonferroni correction
Abbreviations: ALT, alanine aminotransferase; APRI, aspartate transaminase to platelet ratio index; AST, aspartate aminotransferase; BP, blood pressure; FIB-4, fibrosis-4; GGT, gamma-glutamyl transpeptidase; HDL-C, high-density lipoprotein-cholesterol; hsCRP, high sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance. LDL-C, low-density lipoprotein cholesterol; NAFLD, nonalcoholic fatty liver disease; NFS, NAFLD fibrosis score

**Supplementary Table 3.** Development of hepatic steatosis plus intermediate/high probability of advanced fibrosis based on NFS by alcohol consumption category among 190,048 NAFLD free participants with a low probability of advanced fibrosis at baseline.

| Categories of alcohol consumption [a] | Person-years (PY) | Incident cases | Incidence (per $10^3$ PY) | Cumulative Incidence (per $10^3$ person) | | Multivariable-adjusted HR[b] (95% CI) | | | HR (95% CI)[c] in model using time-dependent variables |
|---|---|---|---|---|---|---|---|---|---|
| | | | | 2-Year | 5-Year | Model 1 | Model 2 | Model 3 | |
| Non-drinkers | 431,409.9 | 1,369 | 3.2 | 1.6 | 8.0 | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| Light drinkers | 463,180.5 | 1,749 | 3.8 | 1.8 | 8.4 | 1.18 (1.09-1.28) | 1.18 (1.09-1.28) | 1.16 (1.08-1.26) | 1.02 (0.93-1.11) |
| Moderate drinkers | 271,638.5 | 2,058 | 7.6 | 4.2 | 19.6 | 1.64 (1.51-1.77) | 1.60 (1.47-1.73) | 1.33 (1.23-1.45) | 1.29 (1.18-1.42) |
| *P* for trend | | | | | | <0.001 | <0.001 | <0.001 | <0.001 |

[a] Non-drinking, light drinking, and moderate drinking were defined as 0 g/day, 1-<10 g/day, and 10-<20 g/day for women and 0 g/day, 1-<10 g/day, and 10-<30 g/day for men, respectively

[b] Estimated from parametric proportional hazard models. Multivariable model 1 was adjusted for age, sex, center and year of screening exam; model 2: model 1 plus adjustment for smoking status, regular exercise, education level, history of diabetes, medication for diabetes, history of hypertension, medication for diabetes and medication for dyslipidemia; model 3: model 2 plus adjustment for BMI

[c] Estimated from parametric proportional hazard models with alcohol intake, smoking status, regular exercise, diabetes and hypertension as a time-dependent categorical variables and baseline age, sex, center, year of screening exam, and education level as time-fixed variables.

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; NFS, NAFLD fibrosis score

**Supplementary Table 4.** Development of hepatic steatosis and hepatic steatosis plus intermediate/high probability of advanced fibrosis (defined by FIB-4 or NFS) according to alcohol consumption category, among 149,690 participants without reported binge drinking, based on a question about the number of drinks consumed in a typical drinking day, who underwent a comprehensive examination between 2002 and 2016.

| Categories of alcohol consumption[a] | Multivariate-adjusted HR[b] (95% CI) | | |
|---|---|---|---|
| | Hepatic steatosis | Hepatic steatosis plus Intermediate /high based on FIB4 | Hepatic steatosis plus Intermediate /high based on NFS |
| Non-drinker | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| Light drinker | 0.94 (0.91-0.96) | 1.15 (1.03-1.28) | 1.13 (1.04-1.23) |
| Moderate drinker | 0.89 (0.86-0.93) | 1.49 (1.26-1.75) | 1.34 (1.18-1.53) |
| *P* for trend | <0.001 | <0.001 | <0.001 |

[a] Non-drinking, light drinking, and moderate drinking were defined as 0 g/day, 1-<10 g/day, and 10-<20 g/day for women and 0 g/day, 1-<10 g/day, and 10-<30 g/day for men, respectively

[b] Estimated from parametric proportional hazard models. Multivariable model was adjusted for age, sex, center, year of screening exam, smoking status, regular exercise, education level, history of diabetes, medication for diabetes, history of hypertension, medication for diabetes, medication for dyslipidemia and body mass index

Abbreviations: CI, confidence interval; HR, hazard ratio.

**Supplementary Table 5.** Development of hepatic steatosis and hepatic steatosis plus intermediate/high probability of advanced fibrosis (defined by FIB-4 or NFS) according to alcohol consumption category, among 41,882 participants between 2011 and 2016 without reported binge drinking based on the relevant AUDIT-3 question.

| Categories of alcohol consumption[a] | Multivariate-adjusted HR[b] (95% CI) | | |
|---|---|---|---|
| | Hepatic steatosis | Hepatic steatosis plus Intermediate /high based on FIB4 | Hepatic steatosis plus Intermediate /high based on NFS |
| Non-drinker | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| Light drinker | 0.94 (0.88-1.06) | 1.43 (0.90-2.27) | 0.92 (0.64-1.31) |
| Moderate drinker | 0.90 (0.82-0.99) | 1.81 (1.01-3.24) | 1.08 (0.69-1.69) |
| *P* for trend | 0.037 | 0.045 | 0.743 |

[a] Non-drinking, light drinking, and moderate drinking were defined as 0 g/day, 1-<10 g/day, and 10-<20 g/day for women and 0 g/day, 1-<10 g/day, and 10-<30 g/day for men, respectively

[b] Estimated from parametric proportional hazard models. Multivariable model was adjusted for age, sex, center, year of screening exam, smoking status, regular exercise, education level, history of diabetes, medication for diabetes, history of hypertension, medication for diabetes, medication for dyslipidemia and body mass index

Abbreviations: CI, confidence interval; HR, hazard ratio.

**Supplementary Table 6.** Development of hepatic steatosis and hepatic steatosis plus intermediate/high probability of advanced fibrosis (defined by FIB-4 or NFS) according to alcohol consumption category among 190,048 participants between 2002 and 2016

| Categories of alcohol consumption[a] | Multivariate-adjusted HR[b] (95% CI) | | |
|---|---|---|---|
| | Hepatic steatosis | Hepatic steatosis plus Intermediate /high based on FIB4 | Hepatic steatosis plus Intermediate /high based on NFS |
| Non-drinker | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| Light drinker | | | |
| 1-3 times a month | 0.96 (0.93-1.00) | 1.13 (0.99-1.29) | 1.13 (1.03-1.25) |
| ≥ once a week | 0.91 (0.88-0.94) | 1.16 (1.01-1.34) | 1.14 (1.02-1.27) |
| Moderate drinker | 0.88 (0.85-0.92) | 1.49 (1.26-1.76) | 1.34 (1.18-1.53) |
| P for trend | 0.004 | 0.738 | 0.962 |

[a] Non-drinking, light drinking, and moderate drinking were defined as 0 g/day, 1-<10 g/day, and 10-<20 g/day for women and 0 g/day, 1-<10 g/day, and 10-<30 g/day for men, respectively. Light drinkers were further divided into two groups according to drinking frequency: 1-3 times a month and ≥ once a week. Median (interquartile range) of alcohol quantity consumed per drinking day was 3.5 drinks (3.5-3.5) for infrequent light drinkers (1-3 times a month), 2.5 drinks (1.6-3.5) for regular light drinkers (at least once a week) and 6 drinks (4-7) for moderate drinkers.

[b] Estimated from parametric proportional hazard models. The multivariable model was adjusted for age, sex, center, year of screening exam, smoking status, regular exercise, education level, history of diabetes, medication for diabetes, history of hypertension, medication for diabetes, medication for dyslipidemia and body mass index

Abbreviations: CI, confidence interval; HR, hazard ratio.

**Supplementary Table 7.** Development of hepatic steatosis and hepatic steatosis plus intermediate/high probability of advanced fibrosis (defined by FIB-4 or NFS) according to alcohol consumption category by flushing response among 71,905 participants between 2011 and 2016.

| Categories of alcohol consumption[a] | Multivariate-adjusted HR[b] (95% CI) | | | | |
|---|---|---|---|---|---|
| | Hepatic steatosis | Intermediate/high probability of advanced fibrosis based on Fib4 | Hepatic steatosis plus Intermediate /high based on FIB4 | Intermediate/high probability of advanced fibrosis based on NFS | Hepatic steatosis plus Intermediate /high based on NFS |
| Non-flushers (N= 48,014) | | | | | |
| Non-drinker | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| Light drinker | 0.94 (0.86-1.03) | 1.03 (0.86-1.23) | 0.88 (0.46-1.70) | 0.92 (0.77-1.10) | 0.96 (0.56-1.65) |
| Moderate drinker | 0.97 (0.88-1.07) | 1.18 (0.97-1.44) | 1.30 (0.67-2.49) | 1.10 (0.91-1.33) | 1.36 (0.79-2.33) |
| *P* for trend | 0.823 | 0.032 | 0.098 | 0.049 | 0.048 |
| Flushers (N= 23,891) | | | | | |
| Non-drinker | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| Light drinker | 0.92 (0.83-1.01) | 1.09 (0.88-1.35) | 1.72 (0.73-4.08) | 1.03 (0.84-1.28) | 1.09 (0.63-1.89) |
| Moderate drinker | 0.86 (0.77-0.97) | 1.29 (0.99-1.69) | 1.49 (0.57-3.84) | 1.40 (1.10-1.80) | 1.17 (0.63-2.17) |
| P for trend | 0.015 | 0.056 | 0.660 | 0.004 | 0.616 |
| P for interaction | 0.130 | 0.849 | 0.193 | 0.233 | 0.580 |

[a] Non-drinking, light drinking, and moderate drinking were defined as 0 g/day, 1-<10 g/day, and 10-<20 g/day for women and 0 g/day, 1-<10 g/day, and 10-<30 g/day for men, respectively

[b] Estimated from parametric proportional hazard models. Multivariable model was adjusted for age, sex, center, year of screening exam, smoking status, regular exercise, education level, history of diabetes, medication for diabetes, history of hypertension, medication for diabetes, medication for dyslipidemia and body mass index

Abbreviations: CI, confidence interval; HR, hazard ratio.

**Supplementary Table 8.** Development of hepatic steatosis and hepatic steatosis plus intermediate/high probability of advanced fibrosis (defined by FIB-4 or NFS) according to drinking pattern among 190,048 participants between 2002 and 2016.

| Drinking pattern | Multivariate-adjusted HR[a] (95% CI) | | |
|---|---|---|---|
| | **Hepatic steatosis** | **Hepatic steatosis plus Intermediate /high based on FIB4** | **Hepatic steatosis plus Intermediate /high based on NFS** |
| 6.1 Frequency of drinking days per week (days) | | | |
| 0 | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| 1-2 | 0.86 (0.78–0.95) | 1.04 (0.44-2.42) | 0.74 (0.43-1.29) |
| 3-4 | 0.81 (0.73-0.91) | 1.61 (0.68-3.82) | 0.93 (0.53-1.64) |
| 5-7 | 0.74 (0.60-0.91) | 1.69 (0.62-4.62) | 0.69 (0.30-1.58) |
| *P* for trend | <0.001 | <0.001 | 0.021 |
| 6.2 alcohol quantity consumed per drinking day (drinks/drinking-day) | | | |
| 0 | 1.00 (reference) | 1.00 (reference) | 1.00 (reference) |
| 1-2 | 1.06 (0.96-1.18) | 0.98 (0.41-2.33) | 1.30 (0.74-2.28) |
| 3-5 | 1.08 (0.98-1.20) | 1.12 (0.48-2.64) | 1.56 (0.90-2.71) |
| ≥6 | 1.05 (0.95-1.16) | 1.28 (0.54-3.00) | 1.74 (1.001-3.02) |
| *P* for trend | 0.237 | 0.004 | <0.001 |

[a] Estimated from parametric proportional hazard models. Multivariable model included frequency of drinking and alcohol quantity consumed per drinking day simultaneously as well as age, sex, center, year of screening exam, smoking status, regular exercise, education level, history of diabetes, medication for diabetes, history of hypertension, medication for diabetes, medication for dyslipidemia, and body mass index

Abbreviations: CI, confidence interval; HR, hazard ratio.