

Supplementary material

Alcohol consumption and risks of more than 200 diseases in Chinese men

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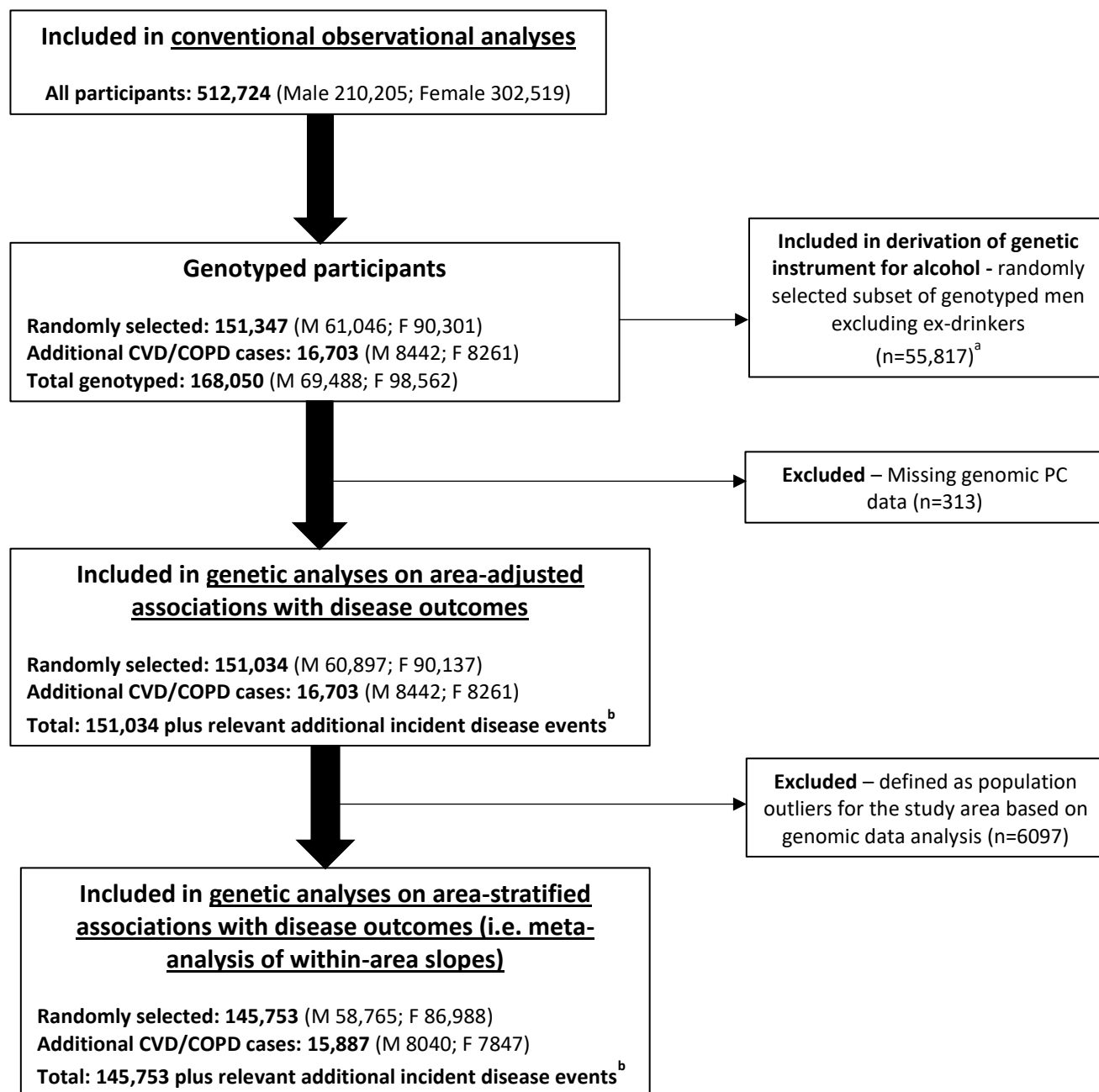
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Supplementary Figure 1. Study participant flowchart



^a The genetic instrument (six genetic categories C1-C6) was derived from the randomly selected subset of genotyped men excluding ex-drinkers (n=61,046 randomly selected, of whom n=5229 were ex-drinkers). The six genetic categories was then assigned to all genotyped men and women according to their genotype and area, regardless of individual drinking patterns.

^b To increase study power, additional recorded disease events (mainly but not limited to CVD/COPD) recorded during follow-up were selected from the subset of CVD/COPD cases and added to the genetic analyses of the corresponding disease outcome.
CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease; PC, principal components.

Supplementary Table 1. Self-reported alcohol intake at baseline and resurveys, by baseline alcohol grouping

| | Baseline (2004-2008) | | 1 st resurvey (2008) | | 2 nd resurvey (2013-2014) | | Average of 2 resurveys | Regression dilution ratio ^a |
|---------------------------|----------------------|------------------------|---------------------------------|------------------------|--------------------------------------|------------------------|---------------------------------|----------------------------------------------|
| Baseline alcohol grouping | N | Mean intake, g/week | N | Mean intake, g/week | N | Mean intake, g/week | Mean usual intake, g/week | |
| Men | | | | | | | | |
| Non-drinkers | 42779 | 0.0 | 1548 | 3.6 | 1845 | 4.2 | 3.9 | |
| Ex-drinkers | 18295 | 2.8 | 652 | 37.8 | 767 | 67.0 | 52.4 | |
| Occasional drinkers | 79231 | 5.0 | 2960 | 21.0 | 3659 | 33.6 | 27.3 | |
| Current drinkers | | | | | | | | |
| <140 g/week | 25093 | 79.5 | 987 | 97.1 | 1199 | 119.4 | 108.2 | |
| 140-279 g/week | 18907 | 222.6 | 659 | 185.0 | 888 | 233.1 | 209.1 | |
| 280-419 g/week | 12832 | 370.2 | 463 | 283.9 | 589 | 306.8 | 295.4 | |
| 420+ g/week | 13068 | 689.7 | 503 | 440.8 | 632 | 418.0 | 429.4 | 0.53 |
| Women | | | | | | | | |
| Non-drinkers | 192333 | 0.0 | 7602 | 0.8 | 9988 | 0.7 | 0.8 | |
| Ex-drinkers | 2657 | 2.5 | 113 | 13.4 | 151 | 11.8 | 12.6 | |
| Occasional drinkers | 101285 | 5.0 | 4036 | 4.6 | 4974 | 3.8 | 4.2 | |
| Current drinkers | | | | | | | | |
| <70 g/week | 3224 | 34.0 | 124 | 27.9 | 162 | 21.1 | 24.5 | |
| 70-139 g/week | 1587 | 112.5 | 69 | 89.9 | 93 | 66.0 | 77.9 | |
| 140+ g/week | 1433 | 302.5 | 70 | 199.4 | 94 | 136.5 | 167.9 | 0.53 |

Calculations assigned an intake of 5 g/week to those who drink sometimes but less than weekly at the time of survey (regardless of their past drinking patterns).

^aRegression dilution ratio is estimated among baseline current drinkers using baseline and usual alcohol intakes. It was calculated using the assumption-free, non-parametric McMahon-Peto method i.e. the ratio of the range of the usual alcohol intake levels to the range of the baseline alcohol intake levels of baseline-defined current drinker groups.

Supplementary Table 2. Baseline characteristics by drinking patterns, in male current drinkers

| | All current drinkers | Drinking days per week | | Heavy episodic drinking (> 60 g/session) | | Mealtime drinking | | Beverage type | | |
|-----------------------------------------|-------------------------|------------------------|-----------|---------------------------------------------|-----------|-------------------|---------------------|---------------|----------|-----------|
| | | 1-5 days | 6-7 days | No | Yes | With meals | Outside of meals | Beer | Wine | Spirits |
| | (N=69900) | (N=26521) | (N=43379) | (N=43891) | (N=26009) | (N=60043) | (N=9857) | (N=12723) | (N=8506) | (N=48671) |
| Sociodemographic characteristics | | | | | | | | | | |
| Mean age, years | 51.6 | 48.5 | 53.5 | 52.6 | 49.7 | 51.6 | 51.2 | 45.4 | 56.0 | 52.5 |
| Urban, % | 50.1 | 52.6 | 48.0 | 57.0 | 37.6 | 52.0 | 38.8 | 83.4 | 72.4 | 37.4 |
| Education > 6 years, % | 60.3 | 64.3 | 58.2 | 61.0 | 58.8 | 60.5 | 59.9 | 66.3 | 63.2 | 59.8 |
| Household income > 20,000 yuan/year, % | 51.5 | 54.4 | 49.4 | 51.2 | 51.9 | 52.0 | 48.6 | 59.7 | 59.8 | 50.7 |
| Alcohol drinking patterns | | | | | | | | | | |
| Mean weekly intake, g/week | 285.7 | 123.4 | 377.7 | 163.1 | 494.0 | 282.2 | 319.7 | 131.1 | 117.3 | 329.2 |
| Daily drinking, % | 62.1 | -- | -- | 56.7 | 69.8 | 61.7 | 63.4 | 43.3 | 57.3 | 66.2 |
| Heavy episodic drinking, % | 37.2 | 25.3 | 41.2 | -- | -- | 36.7 | 40.0 | 11.9 | 3.4 | 45.0 |
| Drinking outside of meals, % | 14.1 | 13.4 | 14.5 | 13.5 | 15.1 | -- | -- | 12.2 | 10.6 | 14.1 |
| Drinking spirits, % | 69.6 | 62.6 | 73.8 | 62.6 | 85.5 | 69.6 | 69.0 | -- | -- | -- |
| Flushing response, % | 17.9 | 22.4 | 15.5 | 22.3 | 11.6 | 17.9 | 18.3 | 22.9 | 16.8 | 17.3 |
| Duration of drinking, years | 23.0 | 21.9 | 23.5 | 22.0 | 24.9 | 22.9 | 23.8 | 21.6 | 20.3 | 23.3 |
| Age started drinking, years | 28.7 | 29.5 | 28.3 | 29.7 | 26.5 | 28.7 | 27.2 | 29.6 | 29.9 | 28.4 |
| Lifestyle risk factors | | | | | | | | | | |
| Current smokers, % | 71.3 | 67.3 | 73.8 | 68.0 | 76.8 | 71.2 | 71.0 | 62.9 | 63.4 | 74.0 |
| Infrequent fresh fruit intake, % | 77.2 | 73.8 | 79.4 | 75.2 | 81.1 | 77.1 | 76.7 | 68.2 | 56.8 | 79.0 |
| Physical activity, mean MET-h/d | 22.9 | 22.7 | 23.0 | 23.1 | 22.7 | 22.9 | 22.9 | 21.6 | 20.2 | 23.2 |
| Mean systolic blood pressure, mmHg | 134.2 | 132.7 | 135.1 | 133.0 | 136.4 | 134.3 | 132.8 | 129.5 | 127.9 | 135.2 |
| Mean body mass index, kg/m ² | 23.7 | 24.0 | 23.5 | 23.6 | 24.0 | 23.7 | 23.3 | 23.8 | 23.4 | 23.7 |
| Self-reported medical history, % | | | | | | | | | | |
| Poor self-reported health | 6.3 | 6.6 | 6.4 | 6.4 | 6.5 | 6.2 | 6.9 | 5.8 | 8.0 | 6.3 |
| Prior chronic disease ^a | 18.2 | 19.7 | 17.7 | 18.5 | 17.5 | 18.1 | 19.2 | 19.9 | 24.4 | 17.5 |

Means and percentages are adjusted for the age and study area structure of the CKB male current drinker population, using direct standardisation.

^a Chronic diseases included self-reported history of coronary heart disease, stroke, transient ischaemic attack, diabetes, tuberculosis, emphysema/chronic bronchitis, liver cirrhosis/chronic hepatitis, peptic ulcer, gallstone/gallbladder disease, kidney disease, rheumatoid arthritis, and cancer.

Supplementary Table 3. Mean duration of drinking by alcohol intake categories, in male and female current drinkers

| | < 140 (men) / < 70 (women) g per week | 140-279 (men) / 70-139 (women) g per week | 280-419 (men) / ≥ 140 (women) g per week | ≥ 420 (men) g per week | P value for trend |
|----------------------------------------------------|---------------------------------------------|-------------------------------------------------|------------------------------------------------|---------------------------|-------------------------|
| Men | | | | | |
| Adjusted mean duration of drinking (95% CI), years | 20.9 (20.8-21.0) | 23.0 (22.8-23.1) | 24.3 (24.1-24.4) | 25.6 (25.5-25.8) | < 1 x 10 ⁻¹⁰ |
| Women | | | | | |
| Adjusted mean duration of drinking (95% CI), years | 13.6 (13.1-14.0) | 16.0 (15.5-16.6) | 19.0 (18.4-19.6) | -- | < 1 x 10 ⁻¹⁰ |

Adjusted means and 95% CIs were estimated using multiple linear regression, adjusted for age (in ten-year intervals) and ten study areas, in male and female current drinkers respectively. P values for trend were obtained from multiple linear regression models assessing the dose-response per g/week increase in alcohol intake. All P values are two-sided. CI, confidence interval.

Supplementary Table 4. Baseline characteristics by drinking patterns, in female current drinkers

| | All current drinkers | Drinking days per week | | Heavy episodic drinking (> 40 g/session) | | Mealtime drinking | | Beverage type | | |
|-----------------------------------------|-------------------------|------------------------|----------------------|---------------------------------------------|----------------|------------------------|--------------------------------|------------------|------------------|---------------------|
| | (N=6244) | 1-5 days (N=3418) | 6-7 days (N=2826) | No (N=5656) | Yes (N=588) | With meals (N=5384) | Outside of meals (N=860) | Beer (N=1387) | Wine (N=1001) | Spirits (N=3856) |
| Sociodemographic characteristics | | | | | | | | | | |
| Mean age, years | 53.2 | 51.2 | 56.2 | 53.4 | 49.5 | 53.0 | 55.8 | 46.5 | 55.4 | 54.5 |
| Urban, % | 45.1 | 53.3 | 32.7 | 46.7 | 27.5 | 43.7 | 53.6 | 89.1 | 77.5 | 21.3 |
| Education > 6 years, % | 47.5 | 49.1 | 46.3 | 47.8 | 42.1 | 47.9 | 41.4 | 54.4 | 58.2 | 44.6 |
| Household income > 20,000 yuan/year, % | 39.4 | 40.6 | 38.0 | 39.2 | 34.1 | 40.1 | 40.9 | 42.0 | 66.8 | 36.8 |
| Alcohol drinking patterns | | | | | | | | | | |
| Mean weekly intake, g/week | 115.6 | 58.9 | 168.9 | 90.7 | 328.8 | 115.7 | 92.1 | 49.2 | 36.2 | 138.9 |
| Daily drinking, % | 45.3 | -- | -- | 43.9 | 49.4 | 44.0 | 43.2 | 20.8 | 37.2 | 48.6 |
| Heavy episodic drinking, % | 9.4 | 5.8 | 10.6 | -- | -- | 9.4 | 6.7 | 2.9 | 0.1 | 12.0 |
| Drinking outside of meals, % | 13.8 | 12.3 | 15.4 | 13.7 | 11.6 | -- | -- | 6.9 | 13.7 | 14.0 |
| Drinking spirits, % | 61.8 | 59.3 | 65.0 | 60.9 | 76.3 | 61.5 | 61.2 | -- | -- | -- |
| Flushing response, % | 23.6 | 23.9 | 23.5 | 24.5 | 15.4 | 23.3 | 26.5 | 24.9 | 24.3 | 24.0 |
| Duration of drinking, years | 15.4 | 15.1 | 15.4 | 15.1 | 17.9 | 15.8 | 12.4 | 13.9 | 14.5 | 15.8 |
| Age started drinking, years | 37.7 | 37.8 | 37.9 | 38.1 | 30.5 | 37.3 | 40.1 | 34.2 | 36.0 | 37.4 |
| Lifestyle risk factors | | | | | | | | | | |
| Current smokers, % | 15.7 | 12.0 | 18.2 | 14.4 | 24.1 | 15.8 | 9.5 | 7.1 | 5.6 | 17.8 |
| Infrequent fresh fruit intake, % | 59.1 | 58.0 | 60.1 | 58.8 | 62.0 | 58.8 | 64.1 | 50.8 | 24.4 | 62.6 |
| Physical activity, mean MET-h/d | 20.0 | 20.1 | 19.8 | 20.0 | 18.7 | 20.1 | 17.3 | 18.0 | 15.8 | 20.0 |
| Mean systolic blood pressure, mmHg | 128.2 | 127.8 | 128.4 | 128.0 | 121.8 | 128.1 | 122.8 | 116.7 | 114.4 | 128.6 |
| Mean body mass index, kg/m ² | 23.7 | 23.9 | 23.6 | 23.7 | 22.3 | 23.7 | 22.9 | 22.5 | 22.4 | 23.8 |
| Self-reported medical history, % | | | | | | | | | | |
| Poor self-reported health | 10.2 | 10.0 | 10.9 | 10.1 | 8.7 | 9.9 | 5.9 | 9.2 | 4.9 | 10.6 |
| Prior chronic disease ^a | 22.2 | 23.1 | 23.2 | 22.3 | 17.5 | 21.8 | 27.3 | 24.2 | 23.8 | 22.7 |

Means and percentages are adjusted for the age and study area structure of the CKB female current drinker population, using direct standardisation.

^a Chronic diseases included self-reported history of coronary heart disease, stroke, transient ischaemic attack, diabetes, tuberculosis, emphysema/chronic bronchitis, liver cirrhosis/chronic hepatitis, peptic ulcer, gallstone/gallbladder disease, kidney disease, rheumatoid arthritis, and cancer.

Supplementary Table 5. Summary of number of diseases associated with alcohol consumption by ICD-10 chapter, in women

| ICD-10 Chapter | No of diseases | Total No of events | No of events in current drinkers | Ever-regular vs. occasional drinking | | Dose-response associations among current drinkers | | Total ^a | |
|---------------------------------------------------|----------------|--------------------|----------------------------------|--------------------------------------|----------|---------------------------------------------------|----------|----------------------|----------------------|
| | | | | Positive | Negative | Positive | Negative | Positive | Negative |
| I Infectious and parasitic | 2 | 10858 | 283 | 0 | 0 | 0 | 0 | 0 | 0 |
| II Neoplasms | 2 | 29510 | 619 | 0 | 0 | 0 | 0 | 0 | 0 |
| III Blood and immune-related | 1 | 2831 | 71 | 0 | 0 | 0 | 0 | 0 | 0 |
| IV Endocrine, nutritional and metabolic | 3 | 28424 | 625 | 0 | 0 | 0 | 0 | 0 | 0 |
| V Psychiatric and behavioural | 1 | 3556 | 90 | 0 | 0 | 0 | 0 | 0 | 0 |
| VI Nerve-related | 2 | 12518 | 282 | 0 | 0 | 0 | 0 | 0 | 0 |
| VII Eye and adnexa | 2 | 18012 | 380 | 0 | 0 | 0 | 0 | 0 | 0 |
| VIII Ear and mastoid process | 2 | 5099 | 125 | 0 | 0 | 0 | 0 | 0 | 0 |
| IX Circulatory | 7 | 135578 | 3136 | 2 | 0 | 0 | 0 | 2 | 0 |
| X Respiratory | 5 | 51675 | 1537 | 0 | 1 | 0 | 0 | 0 | 1 |
| XI Digestive | 7 | 52823 | 1438 | 0 | 0 | 0 | 0 | 0 | 0 |
| XII Skin and subcutaneous tissue | 1 | 2329 | 80 | 0 | 0 | 0 | 0 | 0 | 0 |
| XIII Musculoskeletal | 5 | 47022 | 1224 | 0 | 1 | 0 | 0 | 0 | 1 |
| XIV Genitourinary | 2 | 27202 | 589 | 0 | 0 | 0 | 0 | 0 | 0 |
| XV Pregnancy-related | 1 | 1299 | 18 | 0 | 0 | 0 | 0 | 0 | 0 |
| XVIII Other symptoms, signs and abnormal findings | 3 | 28829 | 780 | 0 | 0 | 0 | 0 | 0 | 0 |
| XIX Injury, poisoning and other external causes | 1 | 17732 | 472 | 0 | 0 | 0 | 0 | 0 | 0 |
| XX External causes | 1 | 1689 | 24 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 48 | 476986 | 11773 | 2 | 2 | 0 | 0 | 2^b | 2^c |

ICD-10, International Classification of Diseases, 10th Revision; WHO, World Health Organization; FDR, false discovery rate.

^a Included disease associations from Cox regression analyses either significant ($p < 0.05$ for diseases classified as alcohol-related by the WHO, FDR-adjusted $p < 0.05$ for other diseases; two-sided) from the comparison of ever-regular vs. occasional drinking or dose-response association analyses within current drinkers.

^b The 2 diseases were intracerebral haemorrhage (ICD-10 code: I61) (HR 1.20, 95% CI 1.03-1.40) and essential primary hypertension (I10) (HR 1.08, 95% CI 1.01-1.16), both of which were classified as alcohol-related by the WHO and showed nominally significant associations with ever-regular drinking (i.e. P value < 0.05).

^c The 2 diseases were other acute lower respiratory infections (J20-J22) (HR 0.88, 95% CI 0.78-0.99) which was classified as alcohol-related by the WHO and showed nominal association with ever-regular drinking, and spondylosis (M47) (HR 0.87, 95% CI 0.80-0.95) which was significantly associated with ever-regular drinking after multiple testing correction (i.e. FDR-adjusted P value < 0.05).

Supplementary Table 6. Adjusted HRs for overall and specific morbidities associated with alcohol drinking status, by ICD-10 chapter in men

| ICD-10 coded disease | Overall N of events | Ex-drinkers | | Non-drinkers | | Occasional drinkers | | Current drinkers | | | | | | | |
|-------------------------------------------------------------------------------------------------------|---------------------------|-------------|------------------|--------------|------------------|---------------------|------------------|------------------|------------------|----------------|------------------|----------------|------------------|-------------|------------------|
| | | N | HR (95% CI) | N | HR (95% CI) | N | HR (95% CI) | <140 g/week | | 140-279 g/week | | 280-419 g/week | | 420+ g/week | |
| | | N | HR (95% CI) | N | HR (95% CI) | N | HR (95% CI) | N | HR (95% CI) | N | HR (95% CI) | N | HR (95% CI) | N | HR (95% CI) |
| I Infectious and parasitic | | | | | | | | | | | | | | | |
| A15-A19, B90 Tuberculosis | 1794 | 222 | 1.35 (1.18-1.54) | 442 | 1.27 (1.15-1.40) | 575 | 1.00 (0.92-1.09) | 207 | 1.02 (0.89-1.17) | 146 | 1.02 (0.87-1.21) | 85 | 1.02 (0.82-1.27) | 117 | 1.51 (1.25-1.83) |
| Any | 7647 | 975 | 1.30 (1.22-1.39) | 1791 | 1.20 (1.14-1.26) | 2476 | 1.00 (0.96-1.04) | 849 | 1.00 (0.93-1.07) | 600 | 0.92 (0.85-1.00) | 416 | 0.98 (0.89-1.08) | 540 | 1.16 (1.06-1.27) |
| II Neoplasms | | | | | | | | | | | | | | | |
| C00-C14 Lip, oral cavity & pharynx cancer | 531 | 64 | 1.34 (1.05-1.72) | 98 | 0.95 (0.77-1.17) | 168 | 1.00 (0.85-1.18) | 38 | 0.68 (0.49-0.93) | 63 | 1.42 (1.11-1.82) | 33 | 1.07 (0.76-1.51) | 67 | 1.92 (1.49-2.48) |
| C15 Oesophageal cancer | 2017 | 208 | 1.39 (1.21-1.59) | 317 | 1.09 (0.97-1.23) | 689 | 1.00 (0.92-1.09) | 135 | 0.94 (0.79-1.11) | 173 | 1.49 (1.29-1.74) | 178 | 2.18 (1.88-2.53) | 317 | 3.51 (3.10-3.98) |
| C16 Stomach cancer | 2720 | 304 | 1.18 (1.05-1.33) | 614 | 1.13 (1.04-1.23) | 868 | 1.00 (0.93-1.07) | 288 | 1.10 (0.98-1.23) | 239 | 1.08 (0.95-1.23) | 221 | 1.43 (1.25-1.64) | 186 | 1.20 (1.03-1.39) |
| C18 Colon cancer | 1085 | 147 | 1.45 (1.23-1.71) | 223 | 1.08 (0.94-1.24) | 328 | 1.00 (0.89-1.12) | 128 | 1.07 (0.90-1.27) | 115 | 1.34 (1.12-1.62) | 74 | 1.37 (1.09-1.73) | 70 | 1.37 (1.07-1.74) |
| C19-C20 Rectal cancer | 1131 | 142 | 1.29 (1.09-1.53) | 225 | 1.07 (0.93-1.22) | 335 | 1.00 (0.89-1.12) | 126 | 1.00 (0.84-1.20) | 135 | 1.39 (1.17-1.65) | 78 | 1.26 (1.01-1.58) | 90 | 1.41 (1.13-1.75) |
| C22 Liver cancer | 2246 | 315 | 1.73 (1.55-1.94) | 527 | 1.36 (1.24-1.50) | 661 | 1.00 (0.92-1.08) | 219 | 1.02 (0.89-1.17) | 178 | 1.08 (0.93-1.26) | 156 | 1.44 (1.23-1.69) | 190 | 1.69 (1.45-1.96) |
| C32 Larynx cancer | 208 | 26 | 1.83 (1.24-2.70) | 27 | 0.91 (0.61-1.35) | 42 | 1.00 (0.73-1.38) | 22 | 1.35 (0.89-2.07) | 27 | 2.05 (1.40-3.00) | 23 | 2.83 (1.87-4.28) | 41 | 4.95 (3.52-6.96) |
| C34 Lung cancer | 4297 | 557 | 1.40 (1.29-1.52) | 1102 | 1.38 (1.30-1.47) | 1074 | 1.00 (0.94-1.06) | 478 | 1.09 (1.00-1.20) | 457 | 1.27 (1.16-1.39) | 310 | 1.33 (1.18-1.48) | 319 | 1.29 (1.15-1.45) |
| C80 Malignant neoplasm, without specification of site | 1575 | 208 | 1.31 (1.14-1.51) | 288 | 1.06 (0.93-1.19) | 434 | 1.00 (0.91-1.10) | 166 | 0.97 (0.83-1.14) | 199 | 1.35 (1.17-1.55) | 142 | 1.26 (1.07-1.49) | 138 | 1.41 (1.18-1.68) |
| D38 Neoplasm of uncertain or unknown behaviour of middle ear and respiratory and intrathoracic organs | 479 | 48 | 1.31 (0.98-1.75) | 103 | 1.22 (0.99-1.50) | 146 | 1.00 (0.84-1.19) | 69 | 1.32 (1.04-1.68) | 51 | 1.38 (1.04-1.82) | 33 | 1.37 (0.97-1.94) | 29 | 1.27 (0.87-1.85) |
| Any | 19450 | 2287 | 1.30 (1.25-1.36) | 4228 | 1.15 (1.11-1.18) | 6028 | 1.00 (0.97-1.03) | 2110 | 1.01 (0.97-1.06) | 1880 | 1.16 (1.11-1.21) | 1332 | 1.24 (1.18-1.31) | 1585 | 1.45 (1.38-1.53) |
| III Blood and immune-related | | | | | | | | | | | | | | | |
| D64 Other anaemias | 587 | 96 | 1.45 (1.18-1.78) | 155 | 1.72 (1.45-2.04) | 139 | 1.00 (0.84-1.19) | 53 | 1.03 (0.78-1.36) | 44 | 0.91 (0.67-1.22) | 35 | 1.03 (0.74-1.44) | 65 | 1.37 (1.06-1.78) |
| D69 Purpura and other haemorrhagic conditions | 293 | 39 | 1.25 (0.90-1.72) | 74 | 1.53 (1.20-1.96) | 84 | 1.00 (0.80-1.25) | 24 | 0.77 (0.52-1.17) | 19 | 0.68 (0.43-1.08) | 15 | 0.81 (0.49-1.35) | 38 | 1.44 (1.03-2.04) |
| Any | 1449 | 210 | 1.33 (1.15-1.52) | 356 | 1.40 (1.25-1.57) | 418 | 1.00 (0.90-1.11) | 141 | 0.93 (0.79-1.10) | 105 | 0.78 (0.64-0.95) | 77 | 0.85 (0.68-1.06) | 142 | 1.17 (0.99-1.40) |
| IV Endocrine, nutritional and metabolic | | | | | | | | | | | | | | | |
| E04 Other nontoxic goitre | 351 | 32 | 0.88 (0.62-1.25) | 58 | 0.84 (0.64-1.11) | 149 | 1.00 (0.85-1.18) | 50 | 0.76 (0.57-1.01) | 27 | 0.57 (0.39-0.83) | 22 | 0.70 (0.46-1.08) | 13 | 0.53 (0.31-0.93) |
| E10-E14 Diabetes mellitus | 12610 | 1713 | 1.54 (1.46-1.61) | 2867 | 1.25 (1.20-1.3) | 3957 | 1.00 (0.97-1.03) | 1346 | 0.86 (0.81-0.91) | 1099 | 0.91 (0.86-0.96) | 818 | 1.01 (0.95-1.09) | 810 | 1.02 (0.95-1.09) |
| E88 Other metabolic disorders | 216 | 42 | 1.60 (1.17-2.18) | 35 | 1.52 (1.08-2.14) | 39 | 1.00 (0.72-1.38) | 11 | 0.72 (0.40-1.30) | 18 | 0.90 (0.56-1.43) | 31 | 2.03 (1.43-2.90) | 40 | 1.50 (1.09-2.07) |
| Any | 14938 | 2029 | 1.48 (1.41-1.54) | 3273 | 1.22 (1.17-1.26) | 4697 | 1.00 (0.97-1.03) | 1600 | 0.86 (0.82-0.91) | 1320 | 0.90 (0.85-0.95) | 988 | 1.00 (0.94-1.07) | 1031 | 1.00 (0.94-1.06) |
| V Psychiatric and behavioural | | | | | | | | | | | | | | | |
| Less common psychiatric and behavioural ICD-10 codes combined† | 1197 | 137 | 1.43 (1.21-1.70) | 289 | 1.36 (1.20-1.54) | 387 | 1.00 (0.90-1.11) | 119 | 0.82 (0.69-0.99) | 104 | 0.98 (0.81-1.20) | 74 | 1.10 (0.87-1.38) | 87 | 1.32 (1.06-1.65) |
| Any | 1611 | 179 | 1.41 (1.21-1.63) | 361 | 1.36 (1.22-1.53) | 509 | 1.00 (0.91-1.10) | 201 | 0.96 (0.84-1.11) | 154 | 1.04 (0.88-1.22) | 102 | 1.14 (0.94-1.39) | 105 | 1.28 (1.05-1.56) |
| VI Nerve-related | | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | |
|-----------------------------------------------------------------|-------|------|------------------|-------|------------------|-------|------------------|------|------------------|------|------------------|------|------------------|------|------------------|
| G40-G41 Epilepsy | 487 | 64 | 1.92 (1.50-2.47) | 122 | 1.66 (1.37-2.01) | 144 | 1.00 (0.84-1.19) | 52 | 1.07 (0.81-1.42) | 34 | 0.97 (0.69-1.37) | 32 | 1.49 (1.05-2.12) | 39 | 1.80 (1.29-2.5) |
| G45 Transient cerebral ischaemic attacks and related syndromes | 3758 | 402 | 1.25 (1.14-1.39) | 563 | 1.10 (1.01-1.20) | 1388 | 1.00 (0.95-1.06) | 594 | 1.08 (0.99-1.17) | 410 | 1.03 (0.93-1.13) | 229 | 1.06 (0.93-1.21) | 172 | 1.03 (0.89-1.21) |
| Any | 7355 | 864 | 1.32 (1.24-1.42) | 1442 | 1.15 (1.09-1.22) | 2564 | 1.00 (0.96-1.04) | 985 | 1.02 (0.96-1.09) | 698 | 1.01 (0.94-1.09) | 424 | 1.09 (0.99-1.2) | 378 | 1.10 (0.99-1.22) |
| VII Eye and adnexa | | | | | | | | | | | | | | | |
| H25-H26 Cataract | 6328 | 756 | 1.11 (1.03-1.19) | 1533 | 1.01 (0.96-1.07) | 2011 | 1.00 (0.95-1.05) | 685 | 0.96 (0.89-1.03) | 588 | 1.10 (1.02-1.20) | 351 | 1.14 (1.02-1.27) | 404 | 1.22 (1.10-1.35) |
| Any | 9323 | 1083 | 1.09 (1.03-1.16) | 2143 | 0.96 (0.92-1.00) | 3120 | 1.00 (0.96-1.04) | 1031 | 0.94 (0.88-1.00) | 859 | 1.07 (1.00-1.14) | 534 | 1.14 (1.05-1.24) | 553 | 1.13 (1.04-1.24) |
| VIII Ear and mastoid process | | | | | | | | | | | | | | | |
| Any | 2097 | 208 | 1.05 (0.91-1.20) | 407 | 1.06 (0.95-1.17) | 828 | 1.00 (0.93-1.08) | 265 | 0.99 (0.88-1.12) | 177 | 0.93 (0.80-1.07) | 111 | 0.85 (0.70-1.03) | 101 | 0.75 (0.62-0.92) |
| IX Circulatory | | | | | | | | | | | | | | | |
| I10 Essential (primary) hypertension | 13950 | 1905 | 1.50 (1.43-1.57) | 3176 | 1.21 (1.16-1.25) | 4340 | 1.00 (0.97-1.03) | 1660 | 1.06 (1.01-1.11) | 1246 | 1.11 (1.05-1.17) | 747 | 1.13 (1.05-1.22) | 876 | 1.27 (1.18-1.36) |
| I11 Hypertensive heart disease | 750 | 138 | 1.90 (1.60-2.26) | 239 | 1.45 (1.27-1.67) | 177 | 1.00 (0.85-1.17) | 67 | 1.17 (0.92-1.49) | 42 | 0.85 (0.63-1.15) | 36 | 1.07 (0.77-1.48) | 51 | 1.25 (0.94-1.67) |
| I25 Chronic ischaemic heart disease | 17973 | 2424 | 1.44 (1.39-1.50) | 4056 | 1.23 (1.19-1.27) | 6084 | 1.00 (0.97-1.03) | 2258 | 0.94 (0.90-0.98) | 1567 | 0.96 (0.91-1.01) | 852 | 0.98 (0.91-1.05) | 732 | 1.02 (0.95-1.10) |
| I42 Cardiomyopathy | 447 | 79 | 2.18 (1.73-2.74) | 106 | 1.15 (0.94-1.41) | 124 | 1.00 (0.83-1.21) | 42 | 1.02 (0.75-1.38) | 36 | 1.07 (0.77-1.49) | 35 | 1.58 (1.13-2.22) | 25 | 1.02 (0.68-1.53) |
| I51 Complications and ill-defined descriptions of heart disease | 1083 | 164 | 1.69 (1.45-1.98) | 236 | 1.32 (1.15-1.51) | 350 | 1.00 (0.89-1.12) | 99 | 0.85 (0.70-1.04) | 97 | 1.07 (0.87-1.31) | 74 | 1.23 (0.98-1.55) | 63 | 1.13 (0.88-1.46) |
| I61 Intracerebral haemorrhage | 6409 | 888 | 1.67 (1.56-1.78) | 1891 | 1.37 (1.31-1.44) | 1851 | 1.00 (0.95-1.05) | 547 | 1.00 (0.92-1.09) | 495 | 1.27 (1.16-1.39) | 342 | 1.49 (1.33-1.65) | 395 | 1.70 (1.53-1.88) |
| I63 Cerebral infarction | 24260 | 3010 | 1.51 (1.45-1.56) | 5479 | 1.25 (1.22-1.29) | 8460 | 1.00 (0.98-1.02) | 2929 | 0.99 (0.96-1.03) | 2103 | 1.10 (1.06-1.15) | 1232 | 1.19 (1.13-1.26) | 1047 | 1.27 (1.20-1.36) |
| I64 Stroke, not specified as haemorrhage or infarction | 1087 | 169 | 1.50 (1.29-1.75) | 250 | 1.22 (1.07-1.40) | 311 | 1.00 (0.89-1.12) | 121 | 0.89 (0.74-1.07) | 97 | 1.02 (0.83-1.24) | 70 | 1.27 (1.00-1.62) | 69 | 1.49 (1.17-1.91) |
| I65 Occlusion and stenosis of precerebral arteries | 333 | 70 | 1.74 (1.37-2.22) | 60 | 1.36 (1.04-1.77) | 78 | 1.00 (0.79-1.26) | 30 | 0.90 (0.62-1.29) | 34 | 0.99 (0.70-1.38) | 27 | 1.07 (0.73-1.57) | 34 | 0.93 (0.66-1.32) |
| I66 Occlusion and stenosis of cerebral arteries | 1235 | 174 | 1.59 (1.36-1.85) | 360 | 1.32 (1.18-1.48) | 377 | 1.00 (0.90-1.11) | 127 | 0.87 (0.73-1.04) | 89 | 0.90 (0.73-1.11) | 54 | 1.21 (0.92-1.59) | 54 | 1.60 (1.21-2.10) |
| I67 Other cerebrovascular diseases | 12623 | 1526 | 1.26 (1.20-1.32) | 2517 | 1.10 (1.05-1.14) | 4553 | 1.00 (0.97-1.03) | 1800 | 1.04 (0.99-1.09) | 1135 | 1.00 (0.94-1.06) | 612 | 1.03 (0.95-1.11) | 480 | 0.97 (0.88-1.06) |
| I69 Sequelae of cerebrovascular disease | 3892 | 662 | 1.93 (1.78-2.08) | 951 | 1.33 (1.25-1.43) | 1264 | 1.00 (0.94-1.06) | 371 | 0.97 (0.87-1.07) | 267 | 1.03 (0.91-1.17) | 187 | 1.26 (1.09-1.46) | 190 | 1.45 (1.25-1.68) |
| I80 Phlebitis and thrombophlebitis | 348 | 41 | 1.46 (1.07-1.99) | 55 | 0.91 (0.69-1.20) | 118 | 1.00 (0.82-1.21) | 53 | 1.32 (1.00-1.73) | 34 | 1.31 (0.93-1.85) | 19 | 1.24 (0.79-1.96) | 28 | 2.17 (1.47-3.21) |
| Less common circulatory ICD-10 codes combined† | 2448 | 354 | 1.54 (1.38-1.71) | 540 | 1.16 (1.06-1.27) | 785 | 1.00 (0.93-1.08) | 252 | 0.91 (0.80-1.03) | 222 | 1.06 (0.92-1.21) | 148 | 1.10 (0.93-1.29) | 147 | 1.00 (0.84-1.18) |
| Any | 62339 | 7558 | 1.46 (1.43-1.49) | 14525 | 1.23 (1.21-1.26) | 21055 | 1.00 (0.99-1.01) | 7319 | 0.99 (0.97-1.02) | 5387 | 1.05 (1.03-1.08) | 3302 | 1.13 (1.09-1.17) | 3193 | 1.18 (1.13-1.22) |
| X Respiratory | | | | | | | | | | | | | | | |
| J12-J18 Pneumonia | 14353 | 1880 | 1.24 (1.18-1.30) | 3468 | 1.19 (1.14-1.23) | 4407 | 1.00 (0.97-1.03) | 1513 | 0.95 (0.90-1.00) | 1270 | 1.01 (0.96-1.07) | 831 | 1.02 (0.95-1.09) | 984 | 1.06 (0.99-1.13) |
| J42 Unspecified chronic bronchitis | 4097 | 687 | 1.50 (1.39-1.62) | 1416 | 1.51 (1.43-1.59) | 898 | 1.00 (0.93-1.07) | 334 | 1.00 (0.90-1.12) | 301 | 1.02 (0.91-1.14) | 234 | 1.24 (1.09-1.41) | 227 | 0.99 (0.87-1.13) |
| J44 Other chronic obstructive pulmonary disease | 8497 | 1464 | 1.46 (1.38-1.53) | 2746 | 1.51 (1.45-1.57) | 1919 | 1.00 (0.95-1.05) | 684 | 0.94 (0.87-1.01) | 699 | 1.03 (0.96-1.11) | 423 | 0.94 (0.85-1.04) | 562 | 0.87 (0.80-0.95) |
| Any | 30560 | 4076 | 1.31 (1.27-1.36) | 7752 | 1.25 (1.22-1.28) | 9097 | 1.00 (0.98-1.02) | 3142 | 0.97 (0.93-1.00) | 2707 | 1.03 (0.99-1.07) | 1728 | 1.00 (0.96-1.05) | 2058 | 1.00 (0.96-1.05) |
| XI Digestive | | | | | | | | | | | | | | | |
| K21 Gastro-oesophageal reflux disease | 323 | 49 | 1.67 (1.25-2.22) | 85 | 1.25 (1.00-1.58) | 100 | 1.00 (0.81-1.23) | 29 | 0.95 (0.65-1.37) | 21 | 0.94 (0.61-1.45) | 17 | 1.29 (0.80-2.09) | 22 | 1.36 (0.88-2.13) |

| | | | | | | | | | | | | | | | |
|------------------------------------------------------------|-------|------|------------------|------|------------------|-------|------------------|------|------------------|------|-------------------|------|-------------------|------|-----------------------------------------|
| K25 Gastric ulcer | 1236 | 147 | 1.28 (1.08-1.51) | 256 | 1.12 (0.98-1.28) | 370 | 1.00 (0.90-1.11) | 139 | 1.10 (0.93-1.31) | 127 | 1.21 (1.01-1.44) | 85 | 1.21 (0.98-1.51) | 112 | 1.32 (1.08-1.61) |
| K40 Inguinal hernia | 3808 | 411 | 1.00 (0.91-1.11) | 824 | 0.93 (0.86-1.00) | 1327 | 1.00 (0.94-1.06) | 435 | 0.98 (0.89-1.08) | 355 | 1.01 (0.91-1.12) | 218 | 0.89 (0.78-1.02) | 238 | 0.86 (0.75-0.98) |
| K61 Abscess of anal and rectal regions | 640 | 52 | 1.29 (0.98-1.71) | 82 | 1.02 (0.81-1.28) | 202 | 1.00 (0.86-1.16) | 99 | 1.14 (0.93-1.39) | 85 | 1.32 (1.06-1.63) | 71 | 1.80 (1.42-2.28) | 49 | 1.24 (0.92-1.66) 26.24 (21.28-32.34) |
| K70 Alcoholic liver disease | 305 | 30 | 4.99 (3.46-7.19) | 12 | 0.83 (0.47-1.48) | 21 | 1.00 (0.64-1.55) | 36 | 4.77 (3.42-6.66) | 55 | 9.16 (7.03-11.94) | 41 | 11.2 (8.24-15.21) | 110 | |
| K74 Fibrosis and cirrhosis of liver | 1212 | 165 | 2.14 (1.83-2.51) | 290 | 1.74 (1.53-1.98) | 340 | 1.00 (0.89-1.12) | 95 | 0.82 (0.67-1.00) | 116 | 1.32 (1.10-1.59) | 82 | 1.47 (1.18-1.84) | 124 | 2.26 (1.88-2.73) |
| K75 Other inflammatory liver diseases | 410 | 55 | 1.92 (1.47-2.52) | 65 | 1.26 (0.97-1.63) | 133 | 1.00 (0.83-1.20) | 59 | 1.22 (0.94-1.58) | 45 | 1.36 (1.01-1.83) | 28 | 1.29 (0.89-1.88) | 25 | 1.39 (0.92-2.08) |
| K76 Other diseases of liver | 770 | 112 | 1.54 (1.27-1.87) | 119 | 1.23 (1.01-1.48) | 208 | 1.00 (0.87-1.15) | 74 | 0.83 (0.66-1.05) | 91 | 1.15 (0.93-1.41) | 48 | 0.88 (0.66-1.17) | 118 | 1.58 (1.30-1.91) |
| K85-K86 Pancreatitis | 968 | 112 | 1.34 (1.11-1.61) | 218 | 1.21 (1.05-1.39) | 298 | 1.00 (0.89-1.13) | 117 | 1.07 (0.89-1.28) | 77 | 0.86 (0.68-1.07) | 53 | 0.88 (0.67-1.16) | 93 | 1.36 (1.10-1.69) |
| K92 Other diseases of digestive system | 2513 | 314 | 1.42 (1.27-1.59) | 587 | 1.26 (1.16-1.38) | 762 | 1.00 (0.93-1.08) | 268 | 1.02 (0.90-1.15) | 212 | 1.07 (0.93-1.22) | 157 | 1.19 (1.02-1.40) | 213 | 1.54 (1.34-1.77) |
| Any | 30836 | 3374 | 1.22 (1.18-1.27) | 6425 | 1.13 (1.10-1.16) | 10343 | 1.00 (0.98-1.02) | 3648 | 1.02 (0.99-1.05) | 2838 | 1.01 (0.97-1.05) | 1957 | 1.04 (0.99-1.08) | 2251 | 1.08 (1.03-1.13) |
| XII Skin and subcutaneous tissue | | | | | | | | | | | | | | | |
| L08 Other local infections of skin and subcutaneous tissue | 515 | 68 | 1.24 (0.98-1.59) | 126 | 1.22 (1.01-1.47) | 138 | 1.00 (0.84-1.19) | 52 | 0.98 (0.75-1.30) | 33 | 0.70 (0.49-0.98) | 38 | 1.13 (0.82-1.56) | 60 | 1.34 (1.02-1.75) |
| Any | 2139 | 250 | 1.30 (1.15-1.48) | 486 | 1.17 (1.07-1.29) | 651 | 1.00 (0.92-1.08) | 263 | 1.10 (0.97-1.24) | 198 | 1.05 (0.91-1.21) | 135 | 1.10 (0.92-1.30) | 156 | 1.12 (0.95-1.32) |
| XIII Musculoskeletal | | | | | | | | | | | | | | | |
| M10 Gout | 1010 | 149 | 1.84 (1.56-2.16) | 209 | 1.16 (1.01-1.34) | 250 | 1.00 (0.88-1.14) | 111 | 1.25 (1.04-1.51) | 109 | 1.82 (1.50-2.20) | 79 | 2.22 (1.77-2.78) | 103 | 2.73 (2.22-3.36) |
| M19 Other arthrosis | 2006 | 228 | 1.18 (1.03-1.35) | 440 | 1.00 (0.90-1.11) | 653 | 1.00 (0.92-1.08) | 233 | 1.09 (0.96-1.24) | 191 | 1.19 (1.03-1.37) | 120 | 1.18 (0.99-1.42) | 141 | 1.18 (0.99-1.41) |
| M87 Osteonecrosis | 304 | 26 | 1.46 (0.99-2.16) | 48 | 1.47 (1.08-2.00) | 75 | 1.00 (0.79-1.27) | 27 | 1.01 (0.69-1.48) | 39 | 1.91 (1.39-2.62) | 37 | 2.85 (2.05-3.95) | 52 | 3.77 (2.80-5.07) |
| Any | 17404 | 1870 | 1.13 (1.08-1.18) | 3769 | 1.00 (0.96-1.03) | 6118 | 1.00 (0.97-1.03) | 1936 | 0.99 (0.95-1.04) | 1566 | 1.04 (0.99-1.09) | 952 | 0.99 (0.93-1.06) | 1193 | 1.04 (0.98-1.11) |
| XIV Genitourinary | | | | | | | | | | | | | | | |
| N40 Hyperplasia of prostate | 3782 | 532 | 1.14 (1.05-1.25) | 990 | 1.06 (0.99-1.13) | 1260 | 1.00 (0.94-1.06) | 442 | 0.99 (0.90-1.08) | 258 | 0.76 (0.67-0.86) | 147 | 0.69 (0.59-0.82) | 153 | 0.63 (0.53-0.74) |
| Any | 15105 | 1915 | 1.24 (1.18-1.30) | 3578 | 1.10 (1.07-1.14) | 5099 | 1.00 (0.97-1.03) | 1641 | 0.93 (0.88-0.98) | 1253 | 0.90 (0.85-0.95) | 754 | 0.83 (0.77-0.89) | 865 | 0.81 (0.75-0.86) |
| XVIII Other symptoms, signs and abnormal findings | | | | | | | | | | | | | | | |
| R53 Malaise and fatigue | 208 | 34 | 1.45 (1.03-2.05) | 40 | 0.91 (0.66-1.26) | 52 | 1.00 (0.75-1.33) | 14 | 0.69 (0.41-1.18) | 22 | 1.16 (0.76-1.76) | 18 | 1.03 (0.65-1.64) | 28 | 1.80 (1.22-2.65) |
| R69 Unknown and unspecified causes of morbidity | 8156 | 1354 | 1.38 (1.31-1.46) | 1436 | 1.23 (1.16-1.29) | 2047 | 1.00 (0.96-1.05) | 914 | 1.00 (0.93-1.07) | 854 | 0.97 (0.91-1.04) | 733 | 1.05 (0.98-1.13) | 818 | 1.09 (1.01-1.17) |
| R94 Abnormal results of function studies | 340 | 39 | 1.71 (1.24-2.35) | 68 | 1.78 (1.38-2.30) | 72 | 1.00 (0.78-1.27) | 41 | 1.50 (1.09-2.05) | 37 | 1.58 (1.14-2.19) | 28 | 1.62 (1.11-2.35) | 55 | 2.53 (1.91-3.36) |
| R99 Other ill-defined and unspecified causes of mortality | 380 | 47 | 1.41 (1.06-1.89) | 105 | 1.54 (1.25-1.90) | 120 | 1.00 (0.83-1.20) | 37 | 0.77 (0.56-1.07) | 30 | 1.13 (0.79-1.63) | 21 | 1.49 (0.96-2.30) | 20 | 1.85 (1.17-2.93) |
| Any | 17617 | 2519 | 1.33 (1.28-1.39) | 3631 | 1.17 (1.13-1.21) | 5110 | 1.00 (0.97-1.03) | 1960 | 0.96 (0.92-1.00) | 1670 | 0.98 (0.93-1.02) | 1300 | 1.04 (0.98-1.09) | 1427 | 1.07 (1.02-1.13) |
| XIX Injury, poisoning and other external causes | | | | | | | | | | | | | | | |
| S22 Fracture of rib(s), sternum and thoracic spine | 1023 | 105 | 1.07 (0.88-1.31) | 211 | 0.92 (0.80-1.06) | 274 | 1.00 (0.88-1.13) | 93 | 1.01 (0.82-1.24) | 95 | 1.07 (0.87-1.30) | 96 | 1.40 (1.14-1.71) | 149 | 1.56 (1.32-1.85) |
| S42 Fracture of shoulder and upper arm | 688 | 64 | 1.21 (0.94-1.55) | 142 | 1.16 (0.97-1.37) | 199 | 1.00 (0.86-1.16) | 75 | 1.18 (0.94-1.48) | 68 | 1.25 (0.98-1.59) | 50 | 1.19 (0.90-1.57) | 90 | 1.60 (1.29-1.99) |
| S72 Fracture of femur | 1077 | 139 | 1.38 (1.16-1.63) | 285 | 1.19 (1.05-1.34) | 294 | 1.00 (0.89-1.13) | 115 | 1.10 (0.92-1.33) | 92 | 1.21 (0.98-1.48) | 56 | 1.11 (0.85-1.45) | 96 | 1.77 (1.43-2.19) |

| | | | | | | | | | | | | | | | |
|--------------------------------------------------------------------------------|-------|------|------------------|------|------------------|------|------------------|------|------------------|------|------------------|-----|------------------|------|------------------|
| Less common injury, poisoning and other external causes ICD-10 codes combined† | 3137 | 297 | 1.13 (1.01-1.27) | 705 | 1.07 (0.99-1.16) | 1031 | 1.00 (0.94-1.07) | 309 | 1.04 (0.93-1.17) | 308 | 1.29 (1.16-1.45) | 216 | 1.28 (1.12-1.47) | 271 | 1.34 (1.18-1.52) |
| Any | 11517 | 1146 | 1.14 (1.07-1.21) | 2592 | 1.02 (0.98-1.07) | 3784 | 1.00 (0.97-1.03) | 1127 | 1.01 (0.95-1.07) | 1049 | 1.15 (1.08-1.22) | 775 | 1.18 (1.10-1.27) | 1044 | 1.30 (1.22-1.39) |
| XX External causes | | | | | | | | | | | | | | | |
| V01-V99 Transport accidents | 917 | 90 | 1.15 (0.93-1.42) | 204 | 1.09 (0.94-1.26) | 296 | 1.00 (0.88-1.13) | 81 | 0.98 (0.78-1.22) | 86 | 1.20 (0.97-1.49) | 64 | 1.25 (0.97-1.60) | 96 | 1.56 (1.26-1.92) |
| W00-W19 Falls | 417 | 47 | 1.50 (1.12-2.01) | 136 | 1.57 (1.30-1.89) | 127 | 1.00 (0.83-1.21) | 30 | 0.89 (0.62-1.27) | 28 | 1.11 (0.76-1.61) | 21 | 1.22 (0.79-1.88) | 28 | 1.50 (1.02-2.21) |
| X60-X84 Intentional self-harm | 274 | 28 | 1.47 (1.00-2.14) | 87 | 1.55 (1.23-1.96) | 76 | 1.00 (0.79-1.27) | 23 | 1.20 (0.79-1.81) | 18 | 1.19 (0.75-1.90) | 14 | 1.49 (0.88-2.54) | 28 | 2.61 (1.75-3.91) |
| Rest of V-Y | 696 | 81 | 1.54 (1.23-1.92) | 152 | 1.15 (0.97-1.36) | 217 | 1.00 (0.86-1.16) | 62 | 1.05 (0.82-1.35) | 69 | 1.54 (1.21-1.95) | 42 | 1.40 (1.03-1.90) | 73 | 2.12 (1.66-2.71) |
| Any | 2302 | 246 | 1.36 (1.20-1.54) | 578 | 1.25 (1.14-1.36) | 716 | 1.00 (0.92-1.08) | 195 | 1.00 (0.87-1.16) | 201 | 1.29 (1.12-1.48) | 141 | 1.32 (1.12-1.56) | 225 | 1.81 (1.57-2.08) |

Cox models were stratified by age-at-risk and study area, and were adjusted for education and smoking.

† Included less common ICD-10 codes within the corresponding ICD-10 chapter which were not individually investigated in the present study. “Less common psychiatric and behavioural ICD-10 codes” consisted of ICD-10 codes F00-F99, excluding F32, F33, and F99. “Less common circulatory ICD-10 codes” consisted of ICD-10 codes I00-I99, excluding I10, I11, I20, I21, I24, I25, I27, I42, I46, I48-I51, I60-I67, I69, I70, I80, and I83. “Less common injury, poisoning and other external causes ICD-10 codes” consisted of ICD-10 codes S00-T98, excluding S06, S09, S22, S32, S42, S52, S62, S72, S82, S92, and T14.

Supplementary Table 7. Outcome classifications of pre-specified major diseases and aggregate endpoints

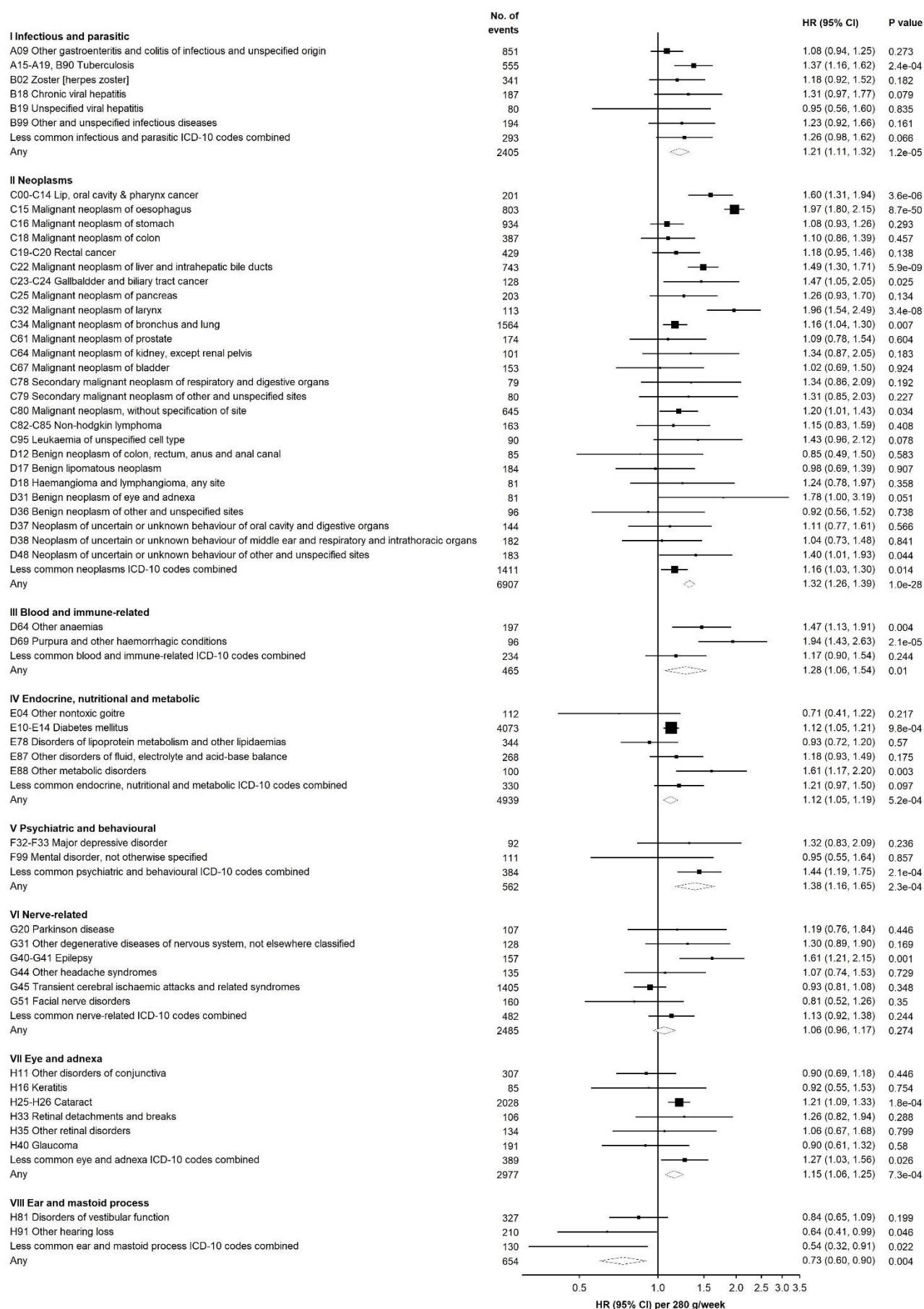
| ICD-10 codes | Disease description |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| C00-C14, C15, C18-C20, C22, C32, C50 (women only) | Alcohol-related cancers (lips, oral cavity and pharynx, oesophagus, colon-rectum, liver, larynx, female breast) |
| E10-E14 | Diabetes mellitus |
| I20-I25 | Ischaemic heart disease |
| I60, I61, I63, I64 | Stroke |
| K70, K74 | Liver cirrhosis |
| V01-Y98 | External causes |
| A15-A19, B90, C00-C14, C15, C18-C20, C22, C32, E10-E14, G40-G41, G45, I10, I11, I25, I42, I61, I63, I65, I66, I67, I69, J12-J18, K70, K74, K85-K86, V01-Y98 | 28 CKB WHO alcohol-related diseases ^a |
| C16, C34, C80, D38, D64, D69, E88, H25-H26, J42, J44, K21, K25, K61, K75, K76, K92, L08, M10, M19, M87, S00-T98 (excluding S06, S09, S32, S52, S62, S82, S92, T14), R53, R69, R94, R99, F00-F99 (excluding F32, F33, F99), I00-I99 (excluding I10, I11, I20, I21, I24, I25, I27, I42, I46, I48-I50, I60-I63, I65-I67, I69, I70, I83) | 33 CKB new alcohol-associated diseases ^b |
| Any coded or uncoded disease events | All morbidity |
| All morbidity minus CKB WHO alcohol-related diseases, CKB new alcohol-associated diseases, and diseases negatively associated with alcohol in men or women | Non alcohol-related diseases |

CKB, China Kadoorie Biobank; ICD-10, International Classification of Diseases, 10th Revision; WHO, World Health Organisation; FDR, false discovery rate.

^a Diseases which were considered to be alcohol-related by the WHO and showed significant adverse associations at two-sided $p < 0.05$ with alcohol drinking in the CKB were combined as “CKB WHO alcohol-related” diseases.

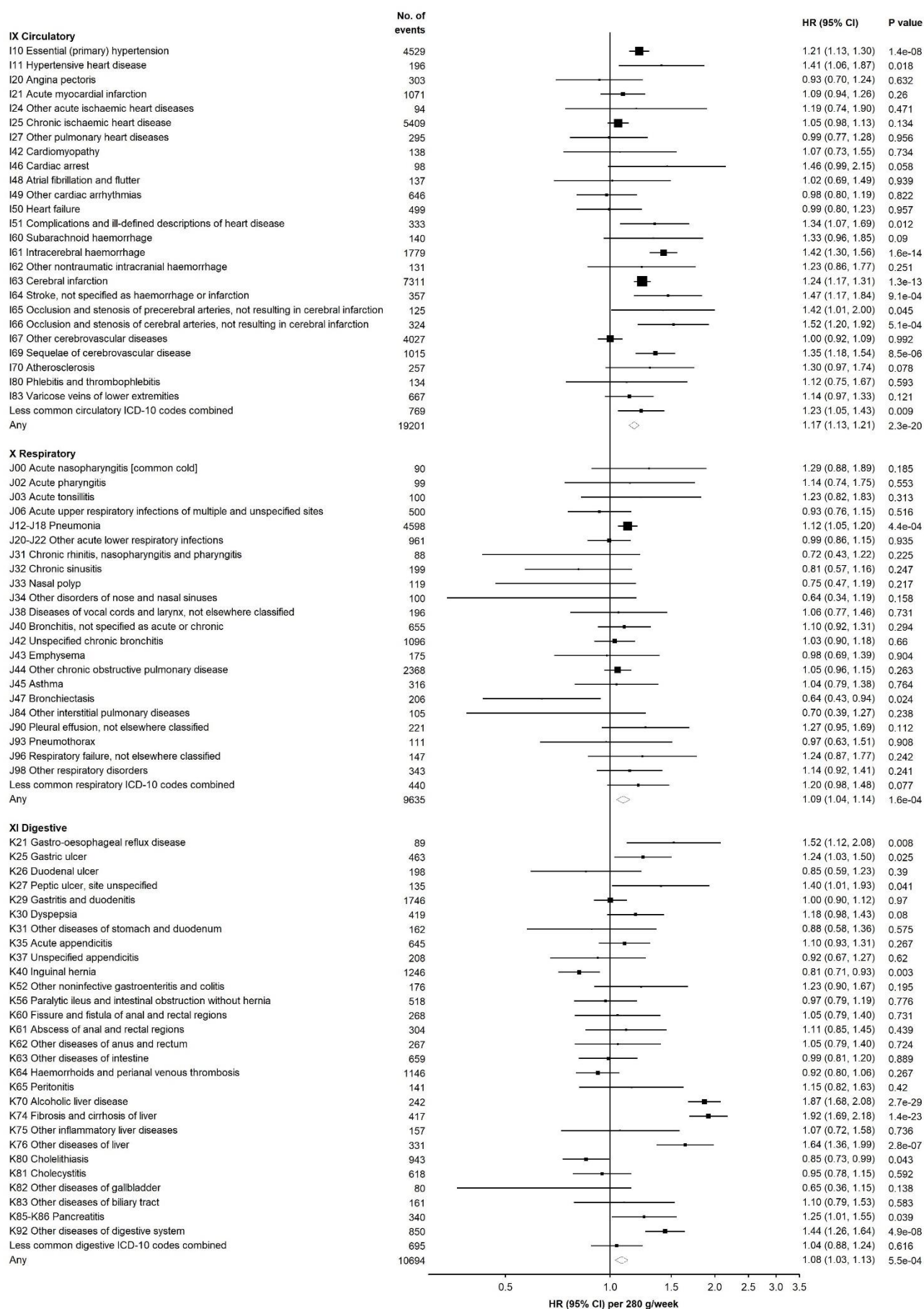
^b Diseases showing significant adverse associations with alcohol drinking in men in CKB after multiple testing correction (FDR-adjusted $p < 0.05$), but had not been classified as alcohol-related by WHO, were combined as “CKB new alcohol-associated diseases”.

Supplementary Figure 2. Adjusted HRs for ICD-10 Chapters I to VIII associated with usual alcohol intake, in male current drinkers



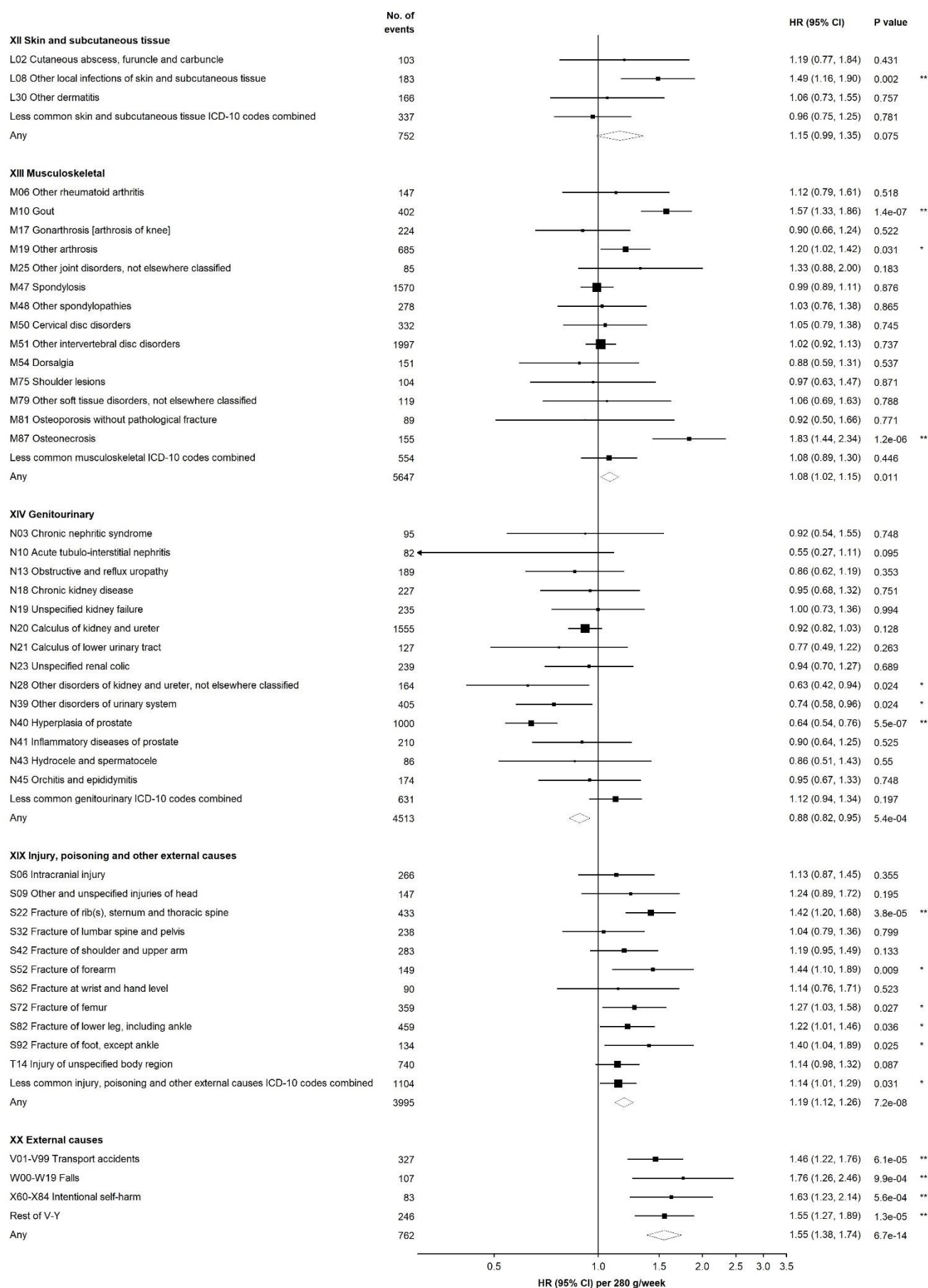
Cox models were stratified by age-at-risk and study area, and adjusted for education and smoking. Each solid square or diamond represents HR per 280 g/week higher usual alcohol intake among male current drinkers, with the area inversely proportional to the variance of the log HR. The horizontal lines indicate 95% CIs. All P values are two-sided. * indicate $p < 0.05$; ** indicate FDR-adjusted $p < 0.05$. CI, confidence interval; HR hazard ratio; ICD-10, International Classification of Diseases, 10th Revision.

Supplementary Figure 3. Adjusted HRs for ICD-10 Chapters IX to XI associated with usual alcohol intake, in male current drinkers



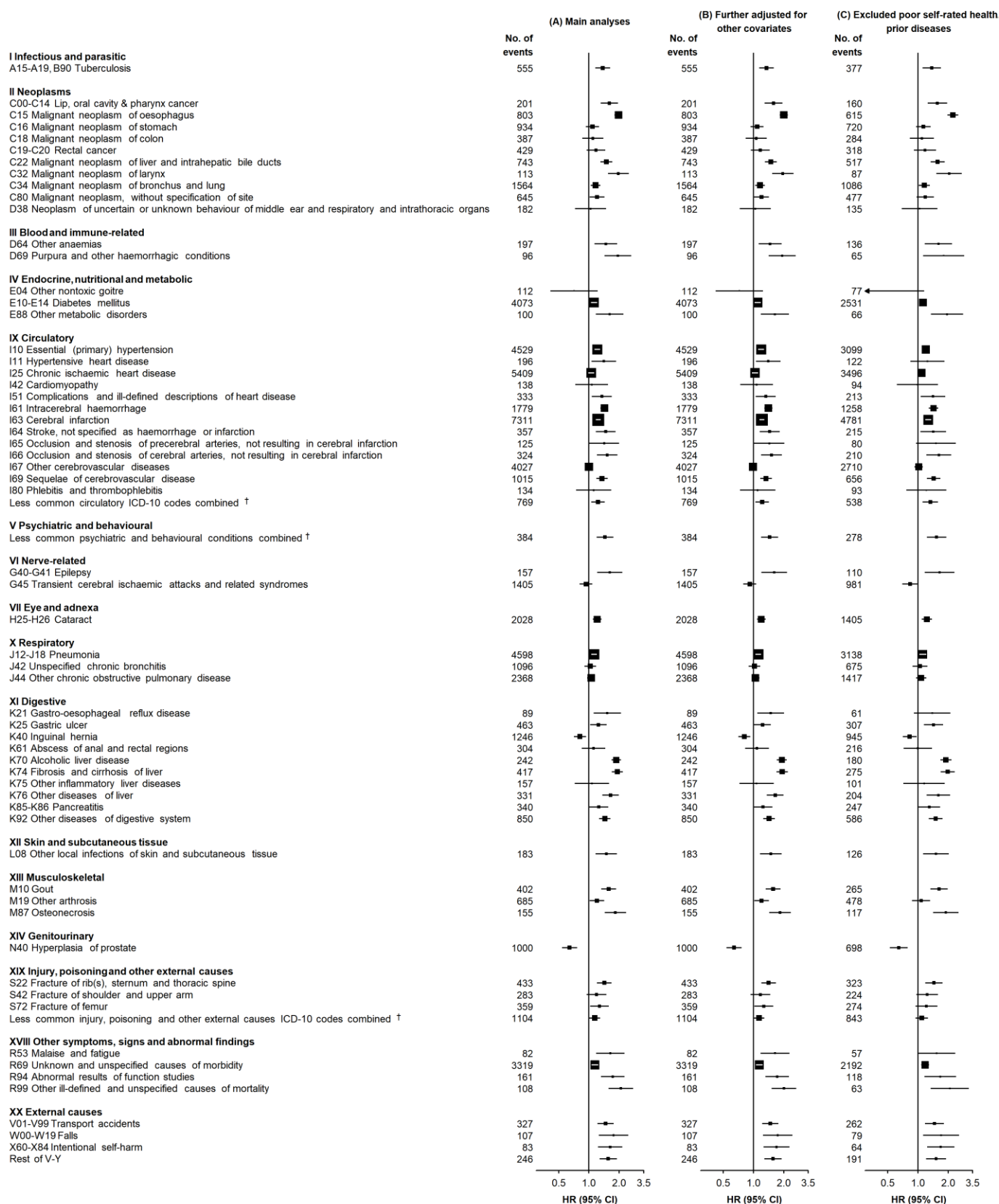
Cox models were stratified by age-at-risk and study area, and adjusted for education and smoking. Each solid square or diamond represents HR per 280 g/week higher usual alcohol intake among male current drinkers, with the area inversely proportional to the variance of the log HR. The horizontal lines indicate 95% CIs. All P values are two-sided. * indicate $p < 0.05$; ** indicate FDR-adjusted $p < 0.05$. CI, confidence interval; HR hazard ratio; ICD-10, International Classification of Diseases, 10th Revision.

Supplementary Figure 4. Adjusted HRs for ICD-10 Chapters XII to XX associated with usual alcohol intake, in male current drinkers



Cox models were stratified by age-at-risk and study area, and adjusted for education and smoking. Each solid square or diamond represents HR per 280 g/week higher usual alcohol intake among male current drinkers, with the area inversely proportional to the variance of the log HR. The horizontal lines indicate 95% CIs. All P values are two-sided. * indicate $p < 0.05$; ** indicate FDR-adjusted $p < 0.05$. CI, confidence interval; HR hazard ratio; ICD-10, International Classification of Diseases, 10th Revision.

Supplementary Figure 5. Adjusted HRs per 280 g/week higher usual alcohol intake for specific alcohol-associated diseases in male current drinkers, with further adjustments or exclusion of participants with baseline medical conditions



Cox models were stratified by age-at-risk and study area, and were adjusted for education and smoking in (A). (B) had the same model specification as in (A) plus further adjustments for income, physical activity, fruit intake, and body mass index. (C) had the same model specification as in (A) and excluded participants with poor self-rated health or prior chronic disease (i.e. self-reported history of coronary heart disease, stroke, transient ischaemic attack, diabetes, tuberculosis, emphysema/chronic bronchitis, liver cirrhosis/chronic hepatitis, peptic ulcer, gallstone/gallbladder disease, kidney disease, rheumatoid arthritis, and cancer) at baseline. Each solid square represents HR per 280 g/week higher usual alcohol intake among male current drinkers, with the area inversely proportional to the variance of the log HR. The horizontal lines indicate 95% CIs. † Included less common ICD-10 codes within the corresponding ICD-10 chapter which were not individually investigated in the present study. CI, confidence interval; HR hazard ratio; ICD-10, International Classification of Diseases, 10th Revision.

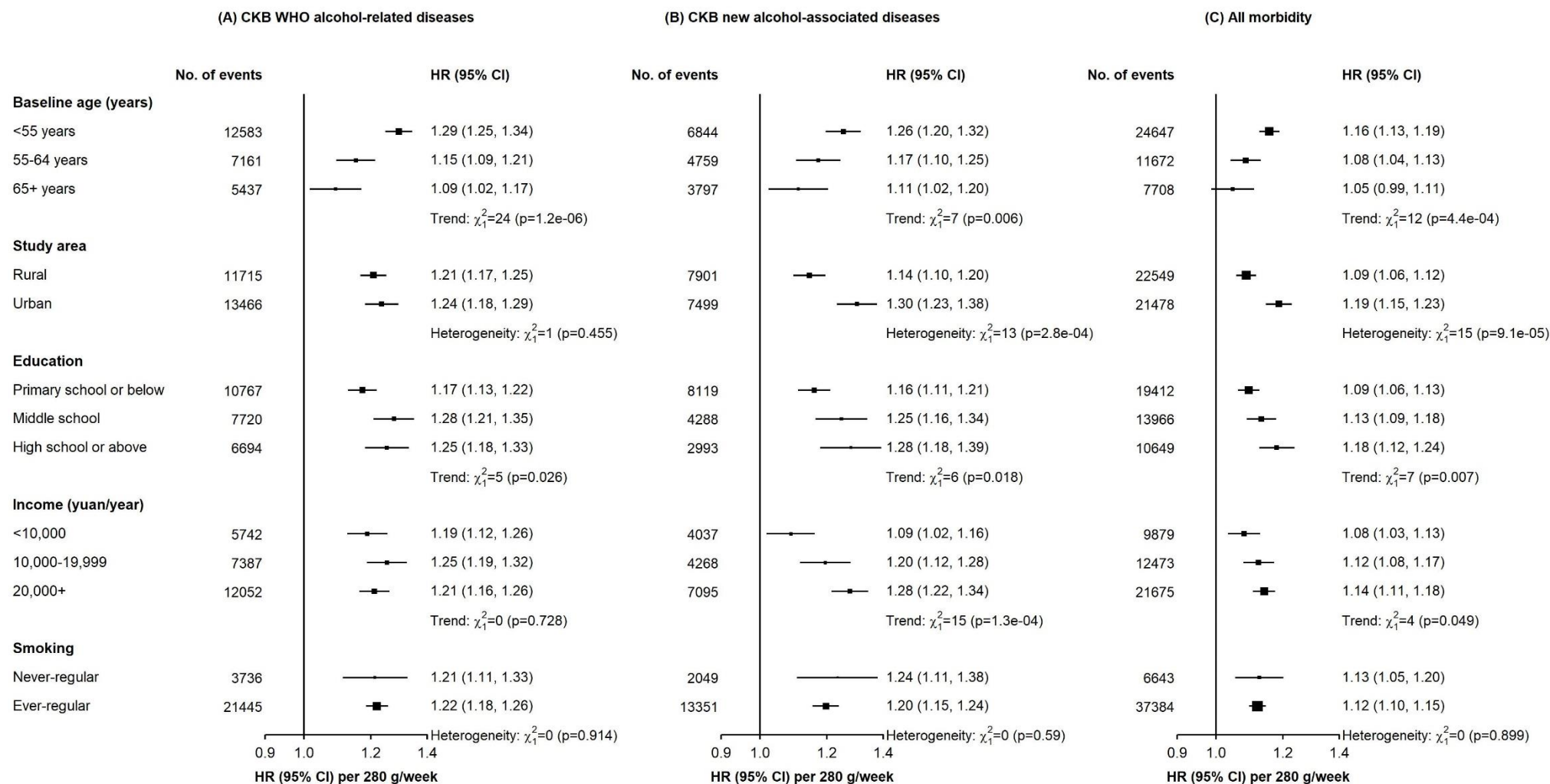
Supplementary Table 8. Adjusted HRs per 280 g/week higher usual alcohol intake for major diseases in male current drinkers, with further adjustments or exclusion of participants with baseline medical conditions

| | Main analyses | | Further adjusted for drinking duration | | Further adjusted for other covariates (income, physical activity, fruit intake, BMI) | | Excluded poor self-reported health / prior chronic diseases | |
|-------------------------------------|---------------|------------------|----------------------------------------|------------------|--------------------------------------------------------------------------------------|------------------|-------------------------------------------------------------|------------------|
| | N | HR (95% CI) | N | HR (95% CI) | N | HR (95% CI) | N | HR (95% CI) |
| Alcohol-related cancers | 2452 | 1.63 (1.53-1.75) | 2452 | 1.61 (1.50-1.73) | 2452 | 1.63 (1.52-1.74) | 1805 | 1.69 (1.56-1.83) |
| Diabetes mellitus | 4073 | 1.12 (1.05-1.21) | 4073 | 1.08 (1.01-1.16) | 4073 | 1.10 (1.03-1.18) | 2531 | 1.13 (1.03-1.23) |
| Ischaemic heart disease | 6212 | 1.08 (1.01-1.15) | 6212 | 1.07 (1.00-1.14) | 6212 | 1.06 (1.00-1.14) | 4054 | 1.11 (1.03-1.20) |
| Stroke | 8731 | 1.28 (1.22-1.34) | 8731 | 1.26 (1.19-1.32) | 8731 | 1.26 (1.20-1.32) | 5810 | 1.31 (1.24-1.39) |
| Liver cirrhosis | 605 | 1.86 (1.70-2.03) | 605 | 1.84 (1.68-2.01) | 605 | 1.89 (1.72-2.07) | 420 | 1.90 (1.71-2.11) |
| External causes | 762 | 1.55 (1.38-1.74) | 762 | 1.52 (1.35-1.71) | 762 | 1.56 (1.39-1.75) | 595 | 1.54 (1.35-1.76) |
| CKB new alcohol-associated diseases | 15400 | 1.20 (1.16-1.24) | 15400 | 1.19 (1.15-1.23) | 15400 | 1.20 (1.16-1.24) | 10750 | 1.22 (1.17-1.27) |
| CKB WHO alcohol-related diseases | 25181 | 1.22 (1.19-1.25) | 25181 | 1.20 (1.17-1.23) | 25181 | 1.20 (1.17-1.24) | 17631 | 1.24 (1.20-1.28) |
| All morbidity | 44027 | 1.12 (1.10-1.14) | 44027 | 1.11 (1.08-1.13) | 44026 | 1.11 (1.09-1.14) | 32508 | 1.13 (1.10-1.15) |

CKB, China Kadoorie Biobank; WHO, World Health Organisation; HR, hazard ratio; CI, confidence interval; BMI, body mass index.

Cox models were stratified by age-at-risk and study area, and were adjusted for education and smoking in the main analyses. Prior chronic diseases included self-reported history of coronary heart disease, stroke, transient ischaemic attack, diabetes, tuberculosis, emphysema/chronic bronchitis, liver cirrhosis/chronic hepatitis, peptic ulcer, gallstone/gallbladder disease, kidney disease, rheumatoid arthritis, and cancer.

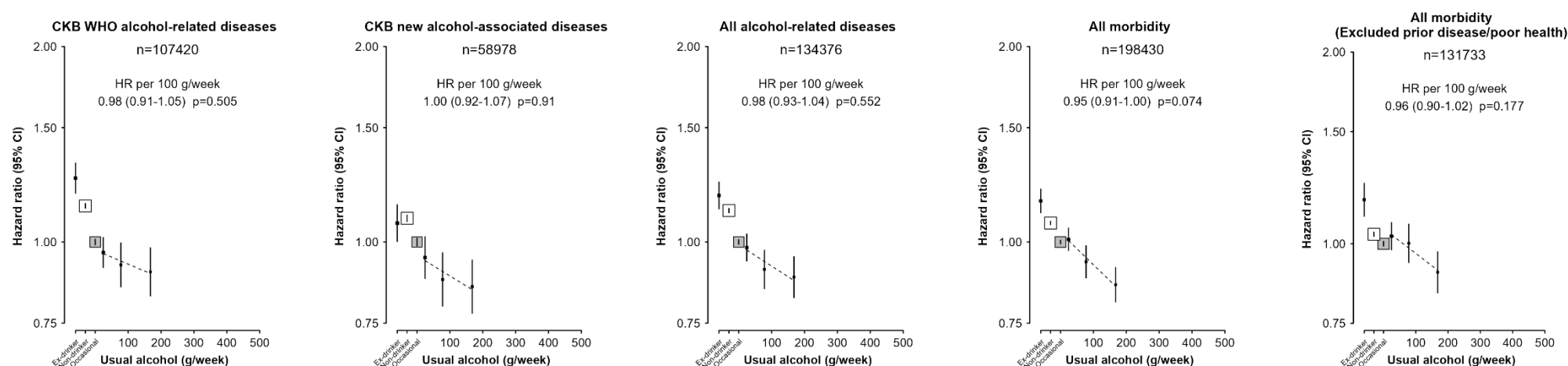
Supplementary Figure 6. Adjusted HRs for CKB WHO alcohol-related diseases, CKB new alcohol-associated diseases and all morbidity per 280 g/week higher usual alcohol intake, by population subgroups in male current drinkers



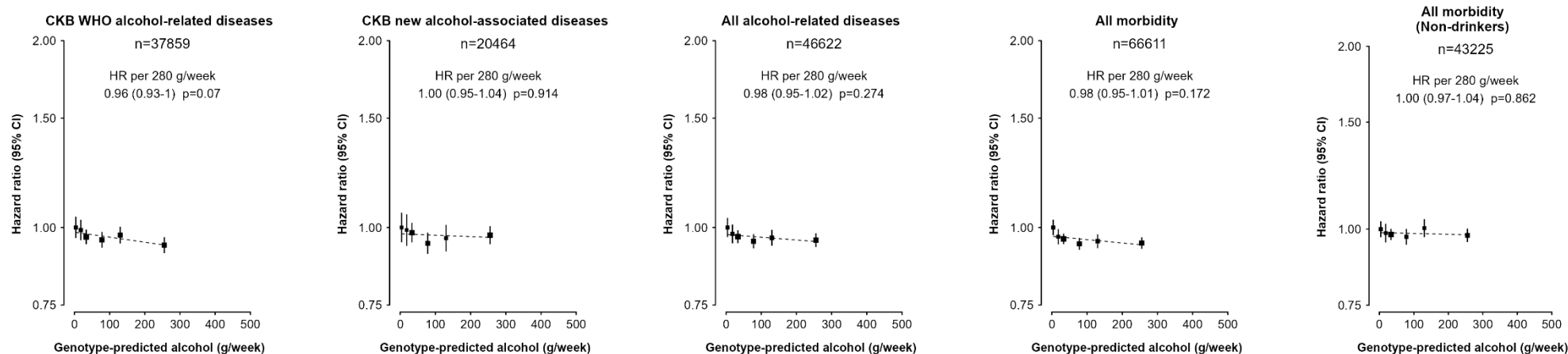
Cox models were stratified by age-at-risk and study area, and adjusted for education and smoking. Each solid square represents HR per 280 g/week higher usual alcohol intake among male current drinkers, with the area inversely proportional to the variance of the log HR. The horizontal lines indicate 95% CIs. All P values are two-sided. CI, confidence interval; HR hazard ratio; ICD-10, International Classification of Diseases, 10th Revision.

Supplementary Figure 7. Associations of aggregate disease categories with self-reported alcohol intake and with genotype-predicted mean male alcohol intake categories, in women

Conventional epidemiological analyses



Genetic epidemiological analyses



Conventional epidemiological analyses relate self-reported drinking patterns to risks of diseases (reference group = occasional drinkers), using Cox models stratified by age-at-risk and study area and adjusted for education and smoking. Within current drinkers, HRs were plotted against usual alcohol intake and were calculated per 100 g/week higher usual alcohol intake. Genetic epidemiological analyses relate genetic categories to risks of diseases (reference group = genotype group with lowest mean genotype-predicted mean male alcohol intake), using Cox models by age-at-risk and study area and adjusted for 11 genomic principal components. The HR per 280 g/week higher genotype-predicted mean male alcohol intake is calculated from the inverse-variance-weighted mean of the slopes of the fitted lines in each study area. Each box represents HR with the area inversely proportional to the variance of the group-specific log hazard within subplot. The vertical lines indicate group-specific 95% CIs. All P values are two-sided. CI, confidence interval; HR hazard ratio; CKB, China Kadoorie Biobank; ICD-10, International Classification of Diseases, 10th Revision; WHO, World Health Organisation.

Supplementary Table 9. Genotype distribution and allele frequencies of *ALDH2*-rs671 and *ADH1B*-rs1229984 across the ten study areas

| | No of men and women genotyped | <i>ALDH2</i> -rs671 | | | | <i>ADH1B</i> -rs1229984 | | | |
|-------------------------------|-------------------------------|---------------------|--------------|-------------|-----------------------------------|-------------------------|--------------|--------------|-----------------------------------|
| | | GG | AG | AA | A-allele frequency ^{a,b} | GG | AG | AA | A-allele frequency ^{a,b} |
| Study area^c | | | | | | | | | |
| Harbin (Urban) | 17879 | 12520 | 4876 | 483 | 0.16 | 1928 | 7976 | 7975 | 0.67 |
| Qingdao (Urban) | 11944 | 7957 | 3615 | 372 | 0.18 | 1190 | 5123 | 5631 | 0.69 |
| Suzhou (Urban) | 15189 | 9035 | 5389 | 765 | 0.23 | 1306 | 6226 | 7657 | 0.71 |
| Liuzhou (Urban) | 14018 | 8048 | 5118 | 852 | 0.24 | 1237 | 5840 | 6941 | 0.70 |
| Haikou (Urban) | 7693 | 3860 | 3160 | 673 | 0.29 | 538 | 2935 | 4220 | 0.74 |
| Gansu (Rural) | 16098 | 11833 | 3939 | 326 | 0.14 | 2083 | 7518 | 6497 | 0.64 |
| Henan (Rural) | 17762 | 13392 | 4073 | 297 | 0.13 | 2022 | 7982 | 7758 | 0.66 |
| Sichuan (Rural) | 16403 | 10725 | 5120 | 558 | 0.19 | 1687 | 7078 | 7638 | 0.68 |
| Zhejiang (Rural) | 18022 | 9378 | 7198 | 1446 | 0.28 | 1442 | 7336 | 9244 | 0.72 |
| Hunan (Rural) | 16339 | 8766 | 6453 | 1120 | 0.27 | 1270 | 6410 | 8659 | 0.73 |
| All areas | 151347 | 95514 | 48941 | 6892 | 0.21 | 14703 | 64424 | 72220 | 0.69 |

^a A-alleles decrease alcohol tolerability. Genotype distributions did not deviate from Hardy-Weinberg equilibrium within study areas.

^b Corresponding frequencies in European-origin populations (1KGP) are 0.00 (*ALDH2*-rs671) and 0.03 (*ADH1B*-rs1229984).

^c Within rural and urban level, the study areas are ordered from North to South.

Supplementary Table 10. Baseline characteristics and alcohol drinking patterns by *ALDH2*-rs671 genotype, and by *ADH1B*-rs1229984 genotype

| | Overall in CKB study | Genotyped subset | ALDH2-rs671 | | | P value for trend / G-allele | ADH1B-rs1229984 | | | P value for trend / G-allele |
|--------------------------------------------------|-------------------------|---------------------|-------------|-------|-------|------------------------------------|-----------------|-------|-------|------------------------------------|
| | | | AA | AG | GG | | AA | AG | GG | |
| Men | | | | | | | | | | |
| N | 210205 | 61046 | 2770 | 19905 | 38371 | | 29187 | 26104 | 5755 | |
| Mean age, years | 52.8 | 52.9 | 53 | 52.9 | 52.9 | 0.11 | 52.9 | 52.9 | 52.6 | 0.13 |
| Education > 6 years, % | 57.8 | 57.8 | 56.6 | 57.5 | 57.9 | 0.50 | 57.7 | 57.9 | 57.1 | 0.44 |
| Household income > 20,000 yuan/year, % | 45.6 | 44.7 | 44.5 | 44.9 | 44.7 | 0.37 | 45 | 44.4 | 44.6 | 0.16 |
| Current smokers, % | 61.1 | 60.9 | 59.8 | 61 | 60.9 | 0.33 | 61 | 60.7 | 61 | 0.53 |
| Infrequent fresh fruit intake, % | 77.0 | 76.5 | 73.5 | 74.2 | 77.9 | 2.6 x 10 ⁻¹⁸ | 76.3 | 76.7 | 76.9 | 0.90 |
| Physical activity, mean MET-h/d | 22.0 | 22.1 | 21.4 | 21.9 | 22.1 | 0.14 | 22 | 22.2 | 21.8 | 0.93 |
| Mean alcohol intake overall, g/week ^a | 106.1 | 108.4 | 2.4 | 37.4 | 162.4 | <1 x 10 ⁻¹⁰⁰ | 100.9 | 109 | 162.3 | 5.5 x 10 ⁻⁴¹ |
| Ever-regular drinking, % | 42.0 | 42.5 | 2.4 | 22.3 | 56.9 | <1 x 10 ⁻¹⁰⁰ | 41.1 | 42.1 | 52.4 | 8.7 x 10 ⁻³² |
| Women | | | | | | | | | | |
| N | 302519 | 90301 | 4122 | 29036 | 57143 | | 43033 | 38320 | 8948 | |
| Mean age, years | 51.5 | 51.5 | 51.9 | 51.5 | 51.4 | 0.17 | 51.4 | 51.5 | 51.4 | 0.30 |
| Education > 6 years, % | 43.3 | 43.3 | 43.7 | 43.4 | 43.1 | 0.04 | 43.6 | 43.1 | 42.4 | 9.7x10 ⁻⁴ |
| Household income > 20,000 yuan/year, % | 40.7 | 39.5 | 39.3 | 39.4 | 39.7 | 0.70 | 39.7 | 39.4 | 38.9 | 0.17 |
| Current smokers, % | 2.4 | 2.3 | 2.7 | 2.2 | 2.4 | 0.03 | 2.3 | 2.3 | 2.6 | 0.85 |
| Infrequent fresh fruit intake, % | 68.2 | 67.5 | 65.9 | 67.4 | 67.6 | 0.11 | 67.4 | 67.6 | 68 | 0.29 |
| Physical activity, mean MET-h/d | 20.4 | 20.5 | 20.5 | 20.5 | 20.5 | 0.58 | 20.4 | 20.5 | 20.3 | 0.97 |
| Mean alcohol intake overall, g/week ^a | 4.1 | 4.1 | 0.7 | 1.9 | 5.4 | 8.2 x 10 ⁻⁴⁷ | 3.7 | 4.1 | 6 | 1.8 x 10 ⁻⁶ |
| Ever-regular drinking, % | 2.9 | 2.9 | 0.3 | 1.2 | 4 | 4.2 x 10 ⁻⁴⁰ | 2.7 | 3 | 4.1 | 1.3 x 10 ⁻⁶ |

MET-h/d, metabolic equivalent of task per hour per day.

Prevalences and means are adjusted for study area and (where appropriate) age (in 10-year intervals) structure of the CKB randomly selected genotyped subset, using direct standardisation separately by sex.

The P value for trend is from an inverse-variance-weighted meta-analysis across ten areas, with within-area per G-allele effect adjusted (where appropriate) for age and genomic principal components using multiple linear regression models. All P values are two-sided.

^a Calculations assign an intake of 5 g/week to occasional drinkers, and exclude ex-drinkers.

Supplementary Table 11. Baseline characteristics and alcohol drinking patterns by six genetic categories (C1-C6)

| | Genotyped subset | Genetic category | | | | | | P value for trend by mean male intake |
|----------------------------------------------------|------------------|------------------|------|-------|-------|-------|-------|---------------------------------------|
| | | C1 | C2 | C3 | C4 | C5 | C6 | |
| Men | | | | | | | | |
| N | 61046 | 4269 | 6356 | 11984 | 13542 | 9057 | 15838 | |
| Mean age, years | 52.9 | 53.1 | 52.9 | 53.1 | 53.0 | 52.6 | 52.9 | 0.03 |
| Education > 6 years, % | 57.8 | 56.0 | 56.8 | 58.9 | 57.0 | 58.3 | 57.8 | 0.85 |
| Household income > 20,000 yuan/year, % | 44.7 | 43.6 | 45.8 | 44.7 | 45.1 | 43.7 | 44.5 | 0.85 |
| Current smokers, % | 60.9 | 59.6 | 60.7 | 61.6 | 60.7 | 61.1 | 60.8 | 0.94 |
| Infrequent fresh fruit intake, % | 76.5 | 73.5 | 73.3 | 75.3 | 75.5 | 78.5 | 79.6 | 6.3 x 10 ⁻¹⁶ |
| Physical activity, mean MET-h/d | 22.1 | 21.9 | 21.8 | 22.0 | 22.1 | 22.2 | 22.2 | 0.31 |
| Mean alcohol intake overall, g/week ^{a,b} | 108.4 | 4.0 | 18.3 | 33.5 | 78.2 | 130.2 | 255.4 | <1 x 10 ⁻¹⁰⁰ |
| Ever-regular drinking, % ^a | 42.5 | 3.0 | 15.1 | 20.4 | 39.1 | 59.9 | 74.0 | <1 x 10 ⁻¹⁰⁰ |
| Women | | | | | | | | |
| N | 90301 | 6454 | 9740 | 17191 | 20015 | 13075 | 23826 | |
| Mean age, years | 51.5 | 51.7 | 51.5 | 51.5 | 51.4 | 51.5 | 51.4 | 0.68 |
| Education > 6 years, % | 43.3 | 44.1 | 43.7 | 43.2 | 43.7 | 42.6 | 42.8 | 0.04 |
| Household income > 20,000 yuan/year, % | 39.5 | 38.8 | 39.2 | 39.4 | 39.8 | 39.1 | 39.7 | 0.32 |
| Current smokers, % | 2.3 | 2.4 | 2.1 | 2.4 | 2.1 | 2.3 | 2.7 | 0.08 |
| Infrequent fresh fruit intake, % | 67.5 | 66.3 | 68.1 | 67.3 | 67.5 | 67.3 | 68.2 | 0.09 |
| Physical activity, mean MET-h/d | 20.5 | 20.4 | 20.6 | 20.4 | 20.5 | 20.3 | 20.6 | 0.27 |
| Mean alcohol intake overall, g/week ^{a,b} | 4.1 | 0.6 | 1.9 | 1.2 | 3.5 | 5.4 | 7.8 | 1.1 x 10 ⁻⁵⁷ |
| Ever-regular drinking, % ^a | 2.9 | 0.2 | 0.8 | 0.8 | 2.1 | 4.5 | 5.8 | 1.2 x 10 ⁻⁷⁷ |

MET-h/d, metabolic equivalent of task per hour per day.

Prevalences or means (except for those for alcohol drinking) are adjusted for area, genomic principal components and (where appropriate) age, using multiple linear regression models.

The P value for trend is from an inverse-variance-weighted meta-analysis across ten areas, with within-area slopes adjusted (where appropriate) for age and genomic principal components using multiple linear regression models. All P values are two-sided.

^a Prevalences or means of alcohol consumption are unadjusted.

^b Calculations assign an intake of 5 g/week to occasional drinkers, and exclude ex-drinkers.

Supplementary Table 12. Adjusted HRs per 280 g/week higher genotype-predicted alcohol intake with alcohol-related diseases and overall morbidity, sensitivity analyses in men

| | Main approach | Main approach (area-adjusted) ^a | Area-stratified 2SLS (additive) approach ^b | Area-adjusted 2SLS (additive) approach ^c | Area-stratified 2SLS (genotype) approach ^d | Area-adjusted 2SLS (genotype) approach ^e |
|-------------------------------------|------------------|-----------------------------------------------|-------------------------------------------------------------|-----------------------------------------------------------|-------------------------------------------------------------|-----------------------------------------------------------|
| | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| CKB WHO alcohol-related diseases | 1.14 (1.09-1.20) | 1.15 (1.10-1.21) | 1.12 (1.07-1.18) | 1.16 (1.10-1.22) | 1.14 (1.09-1.20) | 1.17 (1.11-1.23) |
| CKB new alcohol-associated diseases | 1.06 (1.01-1.12) | 1.10 (1.03-1.17) | 1.07 (1.02-1.13) | 1.12 (1.04-1.20) | 1.07 (1.01-1.12) | 1.11 (1.04-1.18) |
| All alcohol-related diseases | 1.11 (1.07-1.16) | 1.13 (1.08-1.18) | 1.10 (1.05-1.15) | 1.14 (1.09-1.20) | 1.11 (1.07-1.15) | 1.15 (1.09-1.20) |
| All morbidity | 1.07 (1.03-1.11) | 1.09 (1.05-1.13) | 1.07 (1.03-1.10) | 1.10 (1.05-1.14) | 1.07 (1.03-1.11) | 1.10 (1.05-1.14) |

2SLS, two-stage least-squares; HR, hazard ratio; CI, confidence interval; PC, principal components.

^a Estimated using the same approach as the main approach but with an area-adjusted model, i.e. using Cox regression model stratified by age-at-risk and ten study areas and adjusted for 11 genomic PCs.

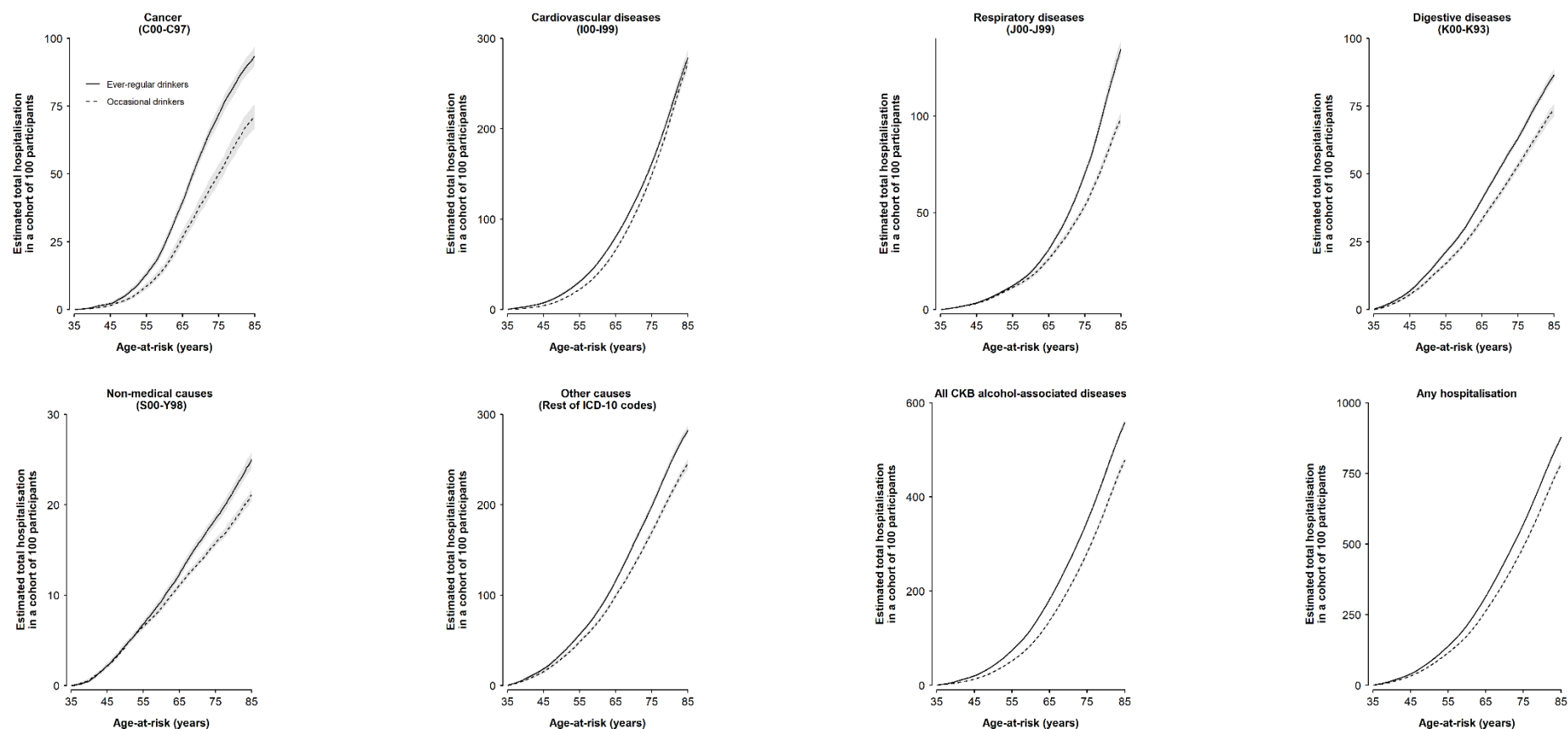
^b Estimated using 2SLS approach within each study area and meta-analysed with inverse-variance-weighted method across ten study areas. In the first stage, total alcohol intake (assigning 5 g/week to occasional drinkers and excluding ex-drinkers) was regressed against rs671 (continuous, per G allele), rs1229984 (continuous, per G allele) and covariates (age, genomic PCs) using linear regression in the population subset of genotyped men within each study area. In the second stage, genetically-predicted alcohol intake (assigned to all genotyped participants in the corresponding study area as a result of the first stage) was related to disease risk using Cox regression stratified by age-at-risk and adjusted for genomic PCs to yield area-specific effect estimates, which were then meta-analysed with inverse-variance-weighted method.

^c Estimated using 2SLS approach with an area-adjusted model. In the first stage, total alcohol intake (assigning 5 g/week to occasional drinkers and excluding ex-drinkers) was regressed against rs671 (continuous, per G allele), rs1229984 (continuous, per G allele) and covariates (age, ten study areas, 11 genomic PCs) using linear regression in the population subset of genotyped men. In the second stage, genetically-predicted alcohol intake (assigned to all genotyped participants as a result of the first stage) was related to disease risk using Cox regression stratified by age-at-risk and ten study areas and adjusted for 11 genomic PCs.

^d Estimated using 2SLS approach as described above in (b), except that rs671 and rs1229984 were modelled as categorical variables (each AA, AG, GG) in the first stage.

^e Estimated using 2SLS approach as described above in (c), except that rs671 and rs1229984 were modelled as categorical variables (each AA, AG, GG) in the first stage.

Supplementary Figure 8. Total expected hospitalisations overall and by major disease categories in ever- and never-regular drinkers from age-at-risk of 35 years among men



The solid and dashed lines indicate the estimated total hospitalisation of specific causes in a cohort of 100 participants in male ever-regular drinkers and male occasional drinkers, respectively. Grey bands show 95% confidence intervals. CKB, China Kadoorie Biobank; ICD-10, International Classification of Diseases, 10th Revision. "All CKB alcohol-related diseases" include disease events from "CKB WHO alcohol-related diseases" or "CKB new alcohol-associated diseases".

Supplementary Table 13. ICD-10 code mapping of CKB significant WHO alcohol-related diseases to alcohol-related diseases based on WHO-classifications

| WHO alcohol-related diseases | WHO codes | CKB codes* |
|-------------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| Tuberculosis | A15–A19, B90 | A15–A19, B90 |
| HIV/AIDS† | B20–B24 | |
| Lower respiratory infections | J09–J22, P23, U04 | J12–J18 |
| Lip, oral cavity and pharynx cancer | C00–C14 | C00–C14 |
| Oesophageal cancer | C15 | C15 |
| Colorectal cancer | C18–C21 | C18; C19–C20 |
| Liver cancer | C22 | C22 |
| Larynx cancer | C32 | C32 |
| Female breast cancer† | C50 | |
| Diabetes mellitus | E10–E14 (minus E10.2–E10.29, E11.2–E11.29, E12.2, E13.2–E13.29, E14.2) | E10–E14 |
| Alcohol use disorders† | F10, G72.1, Q86.0, X45 | |
| Epilepsy | G40–G41 | G40–G41 |
| Hypertensive heart disease | I10–I15 | I10; I11 |
| Ischaemic heart disease | I20–I25 | I25 (also significant when analysed as pre-specified major disease [I20–I25]) |
| Ischaemic stroke | G45–G46.8, I63–I63.9, I65–I66.9, I67.2–I67.848, I69.3–I69.4 | G45; I63; I65; I66; I67; I69 |
| Haemorrhagic stroke | I60–I62.9, I67.0–I67.1, I69.0–I69.298 | I61; I67; I69 |
| Cardiomyopathy, myocarditis, endocarditis | I30–I33, I38, I40, I42 | I42 |
| Cirrhosis of the liver | K70, K74 | K70; K74 |
| Pancreatitis | K85–K86 | K85–K86 |
| Road injury | V01–V04, V06, V09–V80, V87, V89, V99* | V01–V99 |
| Poisonings | X40, X43, X46–X48, X49 | Rest of V–Y |
| Falls | W00–W19 | W00–W19 |
| Fire, heat and hot substances | X00–X19 | Rest of V–Y |
| Drowning | W65–W74 | Rest of V–Y |
| Exposure to mechanical forces | W20–W38, W40–W43, W45, W46, W49–W52, W75, W76 | Rest of V–Y |
| Other unintentional injuries | Rest of V, W39, W44, W53–W64, W77–W99, X20–X29, X50–X59, Y40–Y86, Y88, Y89 | Rest of V–Y |
| Self-harm | X60–X84, Y870 | X60–X84 |
| Interpersonal violence | X85–Y09, Y871 | Rest of V–Y |

CKB, China Kadoorie Biobank; ICD-10, International Classification of Diseases, 10th Revision; WHO, World Health Organisation.

* CKB codes refer to ICD-10 codes that were significantly associated with alcohol intake in the present study.

† Recorded numbers of cases for these diseases were too low in the present study for these individual diseases to be investigated.