**Supplementary Table 1**. Age-and sex-adjustedmean values (95% CI) and proportion (95% CI) of baseline characteristics of study participants according to liver-related mortality

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | Liver related mortality (-) | Liver related mortality (+) | *p* value |
| Number | 608,745 | 554 |  |
| Age (years) | 39.5 (39.5-39.5) | 53.8 (53.0-54.7) | <0.001 |
| BMI (kg/m2) | 23.4 (23.3-23.4) | 22.9 (22.7-23.2) | 0.001 |
| Male (%) | 52.5 (52.4-52.6) | 82.0 (78.8-85.2) | <0.001 |
| Current smoker (%) | 23.2 (23.1-23.3) | 31.9 (29.0-34.8) | <0.001 |
| Alcohol intake (%)a | 18.9 (18.8-19.0) | 23.6 (20.6-26.5) | 0.001 |
| Regular exercise (%)b | 14.8 (14.7-14.9) | 14.0 (11.5-16.6) | 0.549 |
| Highest education level (%)c | 73.5 (73.3-73.6) | 54.4 (49.8-59.1) | <0.001 |
| Obesity (%)d | 28.9 (28.8-29.0) | 25.3 (22.3-28.4) | 0.029 |
| Diabetes (%) | 3.9 (3.9-4.0) | 6.3 (5.1-7.5) | <0.001 |
| Hypertension (%) | 14.6 (14.5-14.7) | 15.9 (13.8-18.0) | 0.199 |
| Family history of cancer | 3.0 (2.9-3.0) | 6.1 (3.5-8.6) | 0.001 |
| Systolic BP (mmHg) | 112.0 (111.9-112.0) | 115.0 (113.9-116.0) | <0.001 |
| Diastolic BP (mmHg) | 71.9 (71.9-71.9) | 73.1 (72.3-73.8) | 0.002 |
| Glucose (mg/dL) | 94.7 (94.7-94.8) | 98.7 (97.4-100.0) | <0.001 |
| Total cholesterol (mg/dL) | 193.6 (193.5-193.7) | 181.1 (178.3-184.0) | <0.001 |
| LDL-C (mg/dL) | 116.5 (116.4-116.6) | 98.2 (95.7-100.8) | <0.001 |
| HDL-C (mg/dL) | 57.7 (57.6-57.7) | 61.8 (60.7-62.9) | <0.001 |
| Triglycerides (mg/dL) | 116.9 (116.7-117.1) | 99.3 (92.8-105.7) | <0.001 |
| AST (U/l) | 23.6 (23.6-23.7) | 50.8 (49.2-52.3) | <0.001 |
| ALT (U/L) | 24.9 (24.9-25.0) | 46.6 (44.6-48.6) | <0.001 |
| GGT (U/L) | 30.2 (30.1-30.3) | 149.1 (145.8-152.3) | <0.001 |
| Albumin (g/dL) | 4.6 (4.6-4.6) | 4.3 (4.3-4.3) | <0.001 |
| Platelet count (×109/L) | 254.4 (254.2-254.5) | 194.9 (190.4-199.4) | <0.001 |
| hsCRP (mg/L) | 1.12 (1.11-1.13) | 2.13 (1.86-2.40) | <0.001 |
| HOMA-IRb, | 1.73 (1.73-1.73) | 2.44 (2.33-2.55) | <0.001 |
| FIB-4 | 0.82 (0.82-0.82) | 2.43 (2.40-2.47) | <0.001 |
| APRI | 0.27 (0.27-0.27) | 0.97 (0.95-0.99) | <0.001 |

Abbreviations: BMI, body mass index; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein-cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyltransferase; hsCRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; FIB-4, fibrosis-4; APRI, aspartate aminotransferase-to-platelet ratio.

a ≥20 g/day; b ≥ 3 times/week; c ≥ college graduate; d BMI ≥ 25 kg/m2

**Supplementary Table 2.** Trend of hepatitis B serologic markers according to year of birth

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Year of birth | HBsAg (-) & anti-HBc (-) | HBsAg (-), anti-HBc (+) & anti-HBs (+) | HBsAg (-), anti-HBc (+) & anti-HBs (-) | HBsAg (+) & anti-HBc (+) | Total number |
| ~1949 | 13,074 (33.95%) | 18,030 (46.82%) | 6,239 (16.2%) | 1,168 (3.03%) | 38,511 (100%) |
| 1950-1959 | 28,649 (41.04%) | 31,900 (45.69%) | 6,266 (8.98%) | 2,999 (4.30%) | 69,814 (100%) |
| 1960-1969 | 78,407 (56.15%) | 48,050 (34.41%) | 6,988 (5.00%) | 6,182 (4.43%) | 139,627 (100%) |
| 1970-1979 | 164,535 (77.72%) | 36,564 (17.27%) | 3,367 (1.59%) | 7,246 (3.42%) | 211,712 (100%) |
| 1980-1989 | 126,563 (90.21%) | 9,899 (7.06%) | 485 (0.35%) | 3,350 (2.39%) | 140,297 (100%) |
| 1990~ | 9,080 (97.24%) | 159 (1.70%) | 54 (0.58%) | 45 (0.48%) | 9,338 (100%) |
| Total number | 420,308 (68.98%) | 144,602 (23.73%) | 23,399 (3.84%) | 20,990 (3.44%) | 609,299 (100%) |

Data are presented as number and percentages of individuals with hepatitis B serologic markers according to year of birth

Abbreviations: HBsAg, hepatitis B surface antigen; Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody.

**Supplementary Table 3.** Trend of hepatitis B serologic markers according to year of birth

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Birth year | HBsAg (-), anti-HBc (-) & anti-HBs (-) | HBsAg (-), anti-HBc (-) & anti-HBs (+) | HBsAg (-), anti-HBc (+) & anti-HBs (+) | HBsAg (-), anti-HBc (+) & anti-HBs (-) | HBsAg (+) & anti-HBc (+) | Total |
| ~1949 | 7,184 (18.65%) | 5,890 (15.29%) | 18,030 (46.82%) | 6,239 (16.2%) | 1,168 (3.03%) | 38,511 (100%) |
| 1950-1959 | 12,884 (18.45%) | 15,765 (22.58%) | 31,900 (45.69%) | 6,266 (8.98%) | 2,999 (4.30%) | 69,814 (100%) |
| 1960-1969 | 33,618 (24.08%) | 44,789 (32.08%) | 48,050 (34.41%) | 6,988 (5.00%) | 6,182 (4.43%) | 139,627 (100%) |
| 1970-1979 | 53,233 (25.14%) | 111,302 (52.57%) | 36,564 (17.27%) | 3,367 (1.59%) | 7,246 (3.42%) | 211,712 (100%) |
| 1980-1989 | 27,770 (19.79%) | 98,793 (70.42%) | 9,899 (7.06%) | 485 (0.35%) | 3,350 (2.39%) | 140,297 (100%) |
| 1990~ | 4,928 (52.77%) | 4,152 (44.46%) | 159 (1.70%) | 54 (0.58%) | 45 (0.48%) | 9,338 (100%) |
| Total | 139,617 (22.91%) | 280,691 (46.07%) | 144,602 (23.73%) | 23,399 (3.84%) | 20990 (3.44%) | 609299 (100%) |

Data are presented as numbers and percentages of individuals with hepatitis B serologic markers according to year of birth.

Abbreviations: HBsAg, hepatitis B surface antigen; Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody.

**Supplementary Table 4.** Liver related and liver cancer mortality by hepatitis B serologic markers after further adjustment for alcohol intake and diabetes

|  |  |
| --- | --- |
| Group | Multivariable-adjusted HRa (95% CI) |
| Liver related mortality |  |
| HBsAg (-) & anti-HBc (-) | 1.00 (reference) |
| HBsAg (-), anti-HBc (+) & anti-HBs (+) | 0.98 (0.74-1.29) |
| HBsAg (-), anti-HBc (+) & anti-HBs (-) | 1.63 (1.18-2.26) |
| HBsAg (+) & anti-HBc (+) | 27.53 (21.85-34.68) |
| Liver cancer mortality |  |
| HBsAg (-) & anti-HBc (-) | 1.00 (reference) |
| HBsAg (-), anti-HBc (+) & anti-HBs (+) | 1.04 (0.71-1.51) |
| HBsAg (-), anti-HBc (+) & anti-HBs (-) | 2.24 (1.50-3.36) |
| HBsAg (+) & anti-HBc (+) | 50.62 (37.47-68.39) |

a Cox proportional hazard model with age as a time scale was used to estimate HRs and 95% CIs. The multivariable model was adjusted for age (time scale), sex, year of screening exam, center, educational level, use of antiviral agents, alcohol intake and diabetes.

**Supplementary Table 5.** Liver related and liver cancer mortality by hepatitis B serologic markers after further adjustment for FIB-4 or APRI index

|  |  |
| --- | --- |
| Group | Multivariable-adjusted HRa (95% CI) |
| Model 1 | Model 2 |
| Liver related mortality |  |  |
| HBsAg (-) & anti-HBc (-) | 1.00 (reference) | 1.00 (reference) |
| HBsAg (-), anti-HBc (+) & anti-HBs (+) | 0.98 (0.74-1.29) | 0.96 (0.73-1.26) |
| HBsAg (-), anti-HBc (+) & anti-HBs (-) | 1.69 (1.22-2.33) | 1.68 (1.21-2.32) |
| HBsAg (+) & anti-HBc (+) | 25.30 (20.05-31.92) | 26.27 (20.85-33.10) |
| Liver cancer mortality |  |  |
| HBsAg (-) & anti-HBc (-) | 1.00 (reference) | 1.00 (reference) |
| HBsAg (-), anti-HBc (+) & anti-HBs (+) | 1.04 (0.71-1.51) | 1.02 (0.70-1.48) |
| HBsAg (-), anti-HBc (+) & anti-HBs (-) | 2.31 (1.54-3.46) | 2.30 (1.53-3.44) |
| HBsAg (+) & anti-HBc (+) | 47.63 (35.23-64.40) | 48.93 (36.21-66.10) |

a Cox proportional hazard model with age as a time scale was used to estimate HRs and 95% CIs. The multivariable model 1 was adjusted for age (time scale), sex, year of screening exam, center, educational level, use of antiviral agents and FIB-4 index; model 2: model 1 plus adjustment for APRI index instead of FIB-4 index

**Supplementary Table 6.** Overall accuracy for liver related or cancer mortality by degree of fibrosis based on each fibrosis score (Fib4 and APRI) among isolated HBcAb positivity

|  |  |
| --- | --- |
|  | AUROC (95% CI) |
| **Fib4** | **APRI** |
| Liver related mortality | 0.921 (0.907-0.935) | 0.866 (0.845-0.888) |
| Liver cancer mortality | 0.921 (0.907-0.935) | 0.866 (0.845-0.888) |

Each statistic is the area under the receiver-operating characteristic curve (AUROC) with 95% confidence intervals (CI) for liver-related mortality and liver cancer mortality stratified by age groups (liver cancer and liver-related mortality, separately in each model).

**Supplementary Table 7.** Age at baseline and the time of death among the decedents

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | HBsAg (–) and anti-HBc (–) | HBsAg (–), anti-HBc (+), and anti-HBs (+) | HBsAg (–), anti-HBc (+), and anti-HBs (–) | HBsAg (+) and anti-HBc (+) |
| Death (%) | 0.68 | 1.93 | 4.65 | 2.63 |
| Liver-related death (%) | 0.02 | 0.07 | 0.27 | 1.34 |
| Age at baseline (years) | 49.8 (37.1-62.9) | 59.9 (49.0-67.3) | 63.9 (56.5-69.7) | 49.4 (42.0-59.4) |
| Age at the time of all-cause death (years) | 57.5 (45.1-70.8) | 67.7 (56.7-75.9) | 72.1 (63.5-78.6) | 56.4 (49.5-65.7) |
| Age at the time of liver-related death (years) | 64.2 (49.4-73.0) | 65.7 (56.8-74.0) | 70.1 (62.1-76.3) | 56.9 (51.0-64.1) |
| Cause of death among decedents | n = 2859 | n = 2791 | n = 1088 | n = 551 |
|  Injury-related (S00-T98) | 635 (22.2) | 443 (15.9) | 134 (12.3) | 55 (10.0) |
|  Cardiovascular disease (I00-I99) | 436 (15.3) | 467 (16.7) | 180 (16.5) | 37 (6.7) |
|  Liver cancer (C22) | 52 (1.8) | 61 (2.2) | 47 (4.3) | 268 (48.6) |
|  Other neoplasm (C00-D48, except C22) | 1223 (42.8) | 1204 (43.1) | 433 (39.8) | 115 (20.9) |
|  Liver-related disease except liver cancer | 50 (1.8) | 47 (1.7) | 16 (1.5) | 13 (2.4) |

The median ages (interquartile range) are presented. The most common cause of cancer death among group 1 was lung cancer, followed by stomach cancer, pancreas cancer, and colorectal cancer. The most common cause of cancer death among HBsAg positive group was liver cancer, followed by lung cancer, and stomach cancer.

**Supplementary Table 8.** Changes in HBV serological markers at first follow-up

|  |  |
| --- | --- |
| Status at first follow-up | Baseline status |
| HBsAg (-) & anti-HBc (-) | HBsAg (-), anti-HBc (+) & anti-HBs (+) | HBsAg (-), anti-HBc (+) & anti-HBs (-) | HBsAg (+) & anti-HBc (+) |
| HBsAg (-) & anti-HBc (-) (n=290,071) | 285,578 (98.91%) | 3,300 (3.97%) | 1,168 (10.43%) | 25 (0.18%) |
| HBsAg (-), anti-HBc (+) & anti-HBs (+) (n=83,281) | 2,471 (0.86%) | 77,482 (93.23%) | 3,245 (28.97%) | 83 (0.61%) |
| HBsAg (-), anti-HBc (+) & anti-HBs (-) (n=9,960) | 653 (0.23%) | 2,319 (2.79%) | 6,776 (60.49%) | 212 (1.57%) |
| HBsAg (+) & anti-HBc (+) (n=13,231) | 16 (0.01%) | 4 (0.00%) | 12 (0.11%) | 13,199 (97.63%) |
| Total | 288,718 (100%) | 83,105 (100%) | 11,201 (100%) | 13,519 (100%) |