**Supplemental Table 1. Summary of cohort studies included in the Liver Cancer Pooling Project**

| Study Name (Acronym) | Follow-up | Gender | Baseline cohort sample sizeN | Liver cancer case (HCC suspected)N | Baseline AgeMean (SD) | Baseline BMI (kg/m2)\*Mean (SD) | Baseline BMI ≥30 kg/m2\* % | Baseline Diabetes\*% | WC (cm)\*Mean (SD) | Baseline WC Men: ≥110 cmWomen: ≥90 cm\*% | Current cigarette smoker\*% | Non-alcohol drinker\*% |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| NIH-AARP Diet and Health Study (NIH-AARP) | 1995-2008 | Women | 226,705 | 322 | 61.5 (5.4) | 26.8 (5.4) | 23.1 | 7.7 | 84.6 (13.5) | 30.9 | 14.7 | 29.7 |
|  | Men | 339,615 | 1,058 | 61.8 (5.3) | 27.3 (4.1) | 21.2 | 10.4 | 97.9 (11.1) | 13.1 | 11.0 | 21.0 |
| Agricultural Health Study (AHS) | 1993-2008 | Women | 32,990 | 8 | 46.9 (12.1) | 26.0 (4.9) | 18.8 | 3.4 | -- | -- | 10.7 | 45.7 |
|  |  | Men | 54,279 | 36 | 46.3 (13.3) | 27.7 (4.2) | 23.8 | 3.3 | -- | -- | 16.8 | 32.2 |
| U.S. Radiologic Technologists (USRT) | 1994-2008 | Women | 56,263 | 39 | 48.0 (9.7) | 25.3 (5.0) | 15.4 | 2.6 | -- | -- | 12.6 | 24.4 |
|  |  | Men | 16,121 | 33 | 51.5 (10.5) | 27.1 (4.2) | 19.9 | 5.6 | -- | -- | 15.0 | 24.8 |
| The Breast Cancer Detection Demonstration Project (BCDDP) | 1987-1999 | Women | 51,105 | 39 | 62.0 (8.3) | 25.1 (4.5) | 13.0 | 5.6 | 82.1 (11.8) | 23.8 | 12.4 | 54.6 |
| Prostate, Lung, Colorectal, and Ovarian  | 1993-2010 | Women | 75,994 | 25 | 62.6 (5.4) | 27.0 (5.4) | 24.6 | 6.4 | -- | -- | 9.7 | 26.5 |
| Cancer Screening Trial (PLCO) |  | Men | 73,689 | 144 | 62.8 (5.3) | 27.5 (4.2) | 23.2 | 9.1 | -- | -- | 11.7 | 19.3 |
| Women’s Health Study (WHS) | 1993-2010 | Women | 39,781 | 8 | 54.1 (7.1) | 26.0 (5.0) | 18.2 | 2.4 | 89.6 (14.4) | 44.7 | 13.1 | 46.5 |
| Physicians’ Health Study (PHS) | 1981-2010 | Men | 28,961 | 33 | 55.1 (10) | 25.1 (3.0) | 6.0 | 3.0 | 96.3 (9.6) | 7.8 | 9.1 | 16.2 |
| Health Professionals Follow-Up Study (HPFS) | 1986-2011 | Men | 51,437 | 88 | 54.3 (9.9) | 25.5 (3.2) | 8.2 | 3.6 | 95.2 (9.2) | 6.3 | 10.0 | 24.2 |
| New York University Women’s’ Health Study (NYUWHS) | 1985-2010 | Women | 14,224 | 14 | 50.4 (8.7) | 24.9 (4.5) | 12.6 | 2.1 | 75.2 (11.7) | 11.1 | 18.2 | 58.2 |
| Cancer Prevention Study-II (CPS-II)  | 1992-2007 | Women | 84,280 | 26 | 62.2 (6.6) | 25.6 (4.7) | 15.7 | 6.1 | 86.4 (13.1) | 35.8 | 8.8 | 39.5 |
|  | Men | 76,265 | 89 | 64.0 (6.1) | 26.4 (3.7) | 14.5 | 9.1 | 98.8 (10.2) | 12.8 | 9.4 | 24.4 |
| Iowa Women’s Health Study (IWHS) | 1986-2007 | Women | 28,533 | 32 | 61.6 (4.2) | 26.9 (4.9) | 22.6 | 6.2 | 87.5 (13.9) | 37.9 | 13.5 | 55.2 |
| Black Women’s Health Study (BWHS) | 1995-2009 | Women | 56,790 | 14 | 38.8 (10.7) | 27.7 (6.2) | 29.3 | 3.3 | 81.6 (13.8) | 25.2 | 16.1 | 56.7 |
| Women’s Health Initiative (WHI) | 1993-1998/variable | Women | 160,768 | 73 | 63.3 (7.2) | 27.8 (5.6) | 29.7 | 5.0 | 86.5 (13.7) | 36.2 | 7.0 | 10.9 |
| Nurses’ Health Study (NHS) | 1980-2010 | Women | 102,223 | 81 | 47.0 (7.2) | 24.4 (4.5) | 11.3 | 2.4 | -- | -- | 29.0 | 20.1 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| All Women |  | Women | 929,656 | 681 | 57.2 (10.6) | 26.4 (5.3) | 21.3 | 5.2 | 85.3 (13.7) | 33.2 | 13.6 | 30.8 |
|  N (%) missing |  |  | -- | -- | -- | 3.2 | 3.2 | 1.4 | 49.2 | 49.2 | 1.9 | 4.9 |
| All Men |  | Men | 640,367 | 1,481 | 59.7 (8.9) | 27.0 (4.0) | 19.0 | 8.5 | 97.6 (10.6) | 11.8 | 11.3 | 22.3 |
|  N (%) missing |  |  | -- | -- | -- | 4.2 | 4.2 | 0.4 | 58.5 | 58.5 | 2.8 | 5.1 |
| All Combined |  | All | 1,570,023 | 2,162 | 58.2 (10.0) | 26.6 (4.8) | 20.4 | 6.5 | 89.8 (14.0) | 25.5 | 12.7 | 27.4 |
|  N (%) missing |  |  | -- | -- | -- | 3.6 | 3.6 | 1.0 | 53.0 | 53.0 | 2.2 | 5.0 |

Abbreviations: BMI, body mass index; WC, waist circumference

\*Among non-missing responders

**Supplemental Table 2. Joint effect of diabetes and body mass index (BMI) on risk of liver cancer in the Liver Pooling Project**

|  |  |  |  |
| --- | --- | --- | --- |
|  | No. cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ |
| Normal BMI (18.5-<25 kg/m2) |  |  |  |
|  No diabetes | 506 | 1.00 (ref) | 1.00 (ref) |
|  Diabetes | 71 | 3.18 (2.48-4.09) | 2.93 (2.28-3.77) |
| Overweight BMI (25-<30 kg/m2) |  |  |  |
|  No diabetes | 681 | 1.15 (1.03-1.30) | 1.18 (1.05-1.32) |
|  Diabetes | 177 | 3.50 (2.94-4.17) | 3.31 (2.77-3.95) |
| Obese BMI (≥30 kg/m2) |  |  |  |
|  No diabetes | 433 | 1.81 (1.59-2.07) | 1.86 (1.63-2.12) |
|  Diabetes | 184 | 4.46 (3.75-5.30) | 4.28 (3.59-5.10) |

Abbreviations: BMI, body mass index; HR, hazard risk ratio; CI, confidence interval

\*Some counts do not add to totals because of missing data

†Adjusted for age, sex, and study

‡Adjusted for age, sex, study, alcohol, cigarette smoking, and race

**Supplementary Table 3. Associations of BMI, WC, and diabetes with liver cancer**

**excluding the 1st 2 years and 1st 5 years in the Liver Cancer Pooling Project**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Overall Multivariable-Adjusted HR (95% CI)\* | Excluding 1st 2 yearsMultivariable-Adjusted HR (95% CI)\* | Excluding 1st 5 yearsMultivariable-Adjusted HR (95% CI)\* |
| BMI per 5 kg/m2 | 1.33 (1.27-1.39) | 1.34 (1.28-1.40) | 1.34 (1.27-1.40) |
| WC per 5 cm | 1.08 (1.04-1.13) | 1.08 (1.04-1.13) | 1.07 (1.02-1.12) |
| Diabetes |  |  |  |
|  No | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
|  Yes | 2.61 (2.34-2.91) | 2.58 (2.30-2.90) | 2.33 (2.04-2.65) |

Abbreviations: BMI, body mass index; WC, waist circumference; HR, hazard risk ratio; CI, confidence interval

\*BMI models adjusted for age, sex, study, alcohol, cigarette smoking, and race. WC and diabetes models adjusted for age, sex, study, alcohol, cigarette smoking, race, and BMI

**Supplementary Table 4. Associations of body mass index (BMI) with confirmed incident HCC in the Liver Cancer Pooling Project**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All** |  | **Women** |  | **Men** |
| BMI (kg/m2) | No.cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-Adjusted HR (95% CI)§ |  | No.cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-Adjusted HR (95% CI)§ |  | No.cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-Adjusted HR (95% CI)§ |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <18.5  | 9 | 1.87 (0.96-3.65) | 1.67 (0.86-3.25) | 1.70 (0.87-3.30) |  | 6 | 2.63 (1.15-6.03) | 2.33 (1.01-5.35) | 2.37 (1.03-5.46) |  | 3 | 1.18 (0.38-3.71) | 1.06 (0.34-3.32) | 1.07 (0.34-3.37) |
| 18.5-<25  | 236 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |  | 79 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |  | 157 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 25-<30  | 401 | 1.27 (1.08-1.50) | 1.31 (1.11-1.54) | 1.24 (1.05-1.46) |  | 77 | 1.19 (0.87-1.63) | 1.17 (0.85-1.60) | 1.10 (0.80-1.51) |  | 324 | 1.30 (1.07-1.57) | 1.35 (1.12-1.64) | 1.28 (1.05-1.55) |
| 30-<35 | 223 | 2.16 (1.80-2.61) | 2.22 (1.84-2.68) | 1.91 (1.58-2.31) |  | 59 | 2.09 (1.49-2.93) | 1.99 (1.41-2.81) | 1.72 (1.21-2.44) |  | 164 | 2.19 (1.76-2.74) | 2.29 (1.83-2.87) | 1.96 (1.56-2.46) |
| 35-<40 | 64 | 2.64 (2.00-3.49) | 2.65 (2.00-3.51) | 2.08 (1.57-2.77) |  | 27 | 2.79 (1.80-4.34) | 2.59 (1.66-4.06) | 2.07 (1.31-3.26) |  | 37 | 2.53 (1.76-3.63) | 2.60 (1.81-3.74) | 2.02 (1.40-2.91) |
| ≥40  | 21 | 2.75 (1.75-4.30) | 2.66 (1.69-4.17) | 1.96 (1.25-3.09) |  | 11 | 2.73 (1.45-5.15) | 2.45 (1.29-4.67) | 1.86 (0.97-3.56) |  | 10 | 2.75 (1.45-5.23) | 2.74 (1.44-5.22) | 1.96 (1.03-3.74) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <18.5  | 9 | 1.87 (0.96-3.64) | 1.67 (0.86-3.25) | 1.69 (0.87-3.30) |  | 6 | 2.63 (1.15-6.03) | 2.33 (1.01-5.35) | 2.38 (1.03-5.46) |  | 3 | 1.18 (0.38-3.71) | 1.06 (0.34-3.32) | 1.07 (0.34-3.37) |
| 18.5-<25 | 236 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |  | 79 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |  | 157 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 25-<30  | 401 | 1.27 (1.08-1.50) | 1.31 (1.11-1.54) | 1.24 (1.05-1.46) |  | 77 | 1.19 (0.87-1.63) | 1.17 (0.85-1.60) | 1.10 (0.80-1.51) |  | 324 | 1.30 (1.07-1.57) | 1.35 (1.12-1.64) | 1.28 (1.05-1.55) |
| ≥30  | 308 | 2.28 (1.92-2.71) | 2.32 (1.95-2.77) | 1.94 (1.63-2.32) |  | 97 | 2.31 (1.71-3.12) | 2.17 (1.59-2.95) | 1.81 (1.32-2.48) |  | 211 | 2.27 (1.84-2.80) | 2.36 (1.91-2.92) | 1.97 (1.59-2.44) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Per 5 kg/m2 5 |  | 1.41 (1.32-1.51) | 1.41 (1.32-1.51) | 1.30 (1.22-1.39) |  |  | 1.40 (1.26-1.55) | 1.37 (1.23-1.52) | 1.27 (1.14-1.42) |  |  | 1.42 (1.31-1.55) | 1.44 (1.32-1.56) | 1.31 (1.21-1.43) |
| p-value for trend¶ |  | <0.001 | <0.001 | <0.001 |  |  | <0.001 | <0.001 | <0.001 |  |  | <0.001 | <0.001 | <0.001 |
| p-interaction with sex# |  | 0.67 | 0.42 | 0.60 |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Abbreviations: BMI, body mass index; HR, hazard risk ratio; CI, confidence interval; HCC, hepatocellular carcinoma

\*Some counts do not add to totals because of missing data

†Adjusted for age, sex, and study

‡Adjusted for age, sex, study, alcohol, cigarette smoking, and race

§Adjusted for age, sex, study, alcohol, cigarette smoking, race, and diabetes

ǁContinuous BMI models exclude those <18.5 kg/m2

|  |
| --- |
|  ¶p-value for trend from Wald tests |
|  #p-interaction with sex from log likelihood ratio tests |

**Supplementary Table 5. Associations of waist circumference with confirmed incident HCC in the Liver Cancer Pooling Project**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All** |  | **Women** |  | **Men** |
| Waist Circumference (cm) | No.cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-AdjustedHR (95% CI)§ |  | No.cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-AdjustedHR (95% CI)§ |  | No.cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-AdjustedHR (95% CI)§ |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| M:<90, F:<70 cm | 52 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |  | 8 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |  | 44 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| M:90-100, F:70-80 cm | 117 | 1.07 (0.77-1.49) | 1.16 (0.83-1.61) | 0.98 (0.70-1.39) |  | 27 | 1.11 (0.50-2.44) | 1.14 (0.52-2.52) | 1.09 (0.48-2.45) |  | 90 | 1.07 (0.75-1.54) | 1.15 (0.80-1.66) | 0.92 (0.62-1.37) |
| M:100-110,F:80-90 cm | 114 | 1.43 (1.03-2.00) | 1.56 (1.11-2.17) | 1.07 (0.73-1.58) |  | 43 | 1.59 (0.74-3.39) | 1.59 (0.75-3.40) | 1.31 (0.57-3.03) |  | 71 | 1.38 (0.95-2.01) | 1.49 (1.02-2.19) | 0.92 (0.59-1.46) |
| M:≥110, F: ≥90 cm | 120 | 2.08 (1.48-2.91) | 2.20 (1.56-3.09) | 1.13 (0.72-1.77) |  | 69 | 2.17 (1.04-4.54) | 2.12 (1.01-4.43) | 1.34 (0.55-3.27) |  | 51 | 2.08 (1.39-3.12) | 2.19 (1.46-3.30) | 1.05 (0.61-1.80) |
|  | . |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Per 5 cm |  | 1.13 (1.09-1.18) | 1.14 (1.09-1.18) | 1.07 (1.01-1.13) |  |  | 1.15 (1.09-1.21) | 1.14 (1.08-1.20) | 1.12 (1.03-1.21) |  |  | 1.12 (1.07-1.18) | 1.13 (1.07-1.19) | 1.03 (0.95-1.11) |
| p-value for trend¶ |  | <0.001 | <0.001 | 0.03 |  |  | <0.001 | <0.001 | 0.009 |  |  | <0.001 | <0.001 | 0.51 |
| p-interaction with sex# |  | 0.51 | 0.75 | 0.60 |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Abbreviations: HR, hazard risk ratio; CI, confidence interval; M, males; F, females; HCC, hepatocellular carcinoma

\*Some counts do not add to totals because of missing data. Only 10 of the 14 cohorts in the Liver Cancer Pooling Project contributed to waist circumference analyses.

†Adjusted for age, sex, and study

‡Adjusted for age, sex, study, alcohol, cigarette smoking, and race

§Adjusted for age, sex, study, alcohol, cigarette smoking, race, and body mass index

|  |
| --- |
|  ¶p-value for trend from Wald tests |
|  #p-interaction with sex from log likelihood ratio tests |

**Supplementary Table 6. Associations of diabetes with confirmed incident HCC in the Liver Cancer Pooling Project**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All** |  | **Women** |  | **Men** |
| Diabetes | No.cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-AdjustedHR (95% CI)§ |  | No.cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-AdjustedHR (95% CI)§ |  | No. cases\* | Minimally-Adjusted HR (95% CI)† | Multivariable-Adjusted HR (95% CI)‡ | Multivariable-AdjustedHR (95% CI)§ |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| No Diabetes | 728 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |  | 210 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |  | 518 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| Diabetes | 260 | 4.15 (3.59-4.79) | 3.74 (3.23-4.33) | 3.37 (2.90-3.92) |  | 57 | 4.37 (3.25-5.87) | 3.70 (2.73-5.01) | 3.25 (2.38-4.43) |  | 203 | 4.07 (3.46-4.80) | 3.74 (3.16-4.42) | 3.41 (2.87-4.04) |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| p-interaction with sex¶ |  | 0.57 | 0.71 | 0.94 |  |  |  |  |  |  |  |  |  |  |

Abbreviations: HR, hazard risk ratio; CI, confidence interval; HCC, hepatocellular carcinoma

\*Some counts do not add to totals because of missing data

†Adjusted for age, sex, and study

‡Adjusted for age, sex, study, alcohol, cigarette smoking, and race

§Adjusted for age, sex, study, alcohol, cigarette smoking, race, and body mass index

¶p-interaction with sex from log likelihood ratio tests

**Supplementary Table 7. Cohorts included in the LCPP**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cohort** | **Location** | **Recruitment/****Follow-up** | **Cohort Characteristics** | **Case Ascertainment** |
| NIH-AARP Diet and Health Study | Multiple states | 1995/2008 | AARP Members | Cancer registries and NDI |
| Agricultural Health Study | North Carolina/ Iowa | 1993/2008 | Farmers and Spouses | Cancer registries |
| United States Radiologic Technologists Study | Multiple states | 1994/2008 | US radiologic technologists | Cancer registries and NDI |
| The Breast Cancer Detection Demonstration Project Follow-up study | Multiple states | 1987/1999 | Breast cancer screening program | Self-report followed by medical record verification and cancer registries |
| Prostate. Lung, Colorectal, and Ovarian Cancer Screening Trial | Multiple states | 1993/2009 | Trial of cancer screening modalities | Self-report followed by medical record verification |
| Women’s Health Study | Multiple states | 1993/2010 | Trial of low-dose aspirin and vitamin E in prevention of CVD and cancer | Self-report followed by medical record verification |
| Physician’s Health Study | Multiple states | 1981/2010 | Physicians | Self-report followed by medical record verification |
| Health Professionals Follow-up Study  | Multiple states | 1986/2011 | Male health professionals nationwide, ages 40-75 | Medical record/pathology review |
| NYU Women’s Health Study | New York | 1985/2010 | Study of hormones and breast cancer | Cancer registry, medical records, NDI (rare) |
| Cancer Prevention Study II | Multiple states | 1992/2007 | General population recruited by American Cancer Society volunteers | Medical records or cancer registry |
| Iowa Women’s Health Study | Iowa | 1986/2007 | Postmenopausal women, ages 55-69 years | All from cancer registries |
| Black Women’s Health Study | Multiple states | 1995/2009 | General population, self-identified as black or African-American | Cancer registry, medical records, NDI (rare) |
| Women’s Health Initiative | Multiple states | 1993/variable | Postmenopausal women, ages 50-79 years | All medical record/pathology review |
| Nurses’ Health Study | Multiple states | 1980/2010 | Married female nurses, ages 30-55 | All medical record/pathology review |

Title to Supplemental Figure 1:

Supplementary Figure 1. Individual participant meta-analysis of body mass index (per 5 kg/m2) and liver cancer risk in the Liver Cancer Pooling Project

Footnote to Supplementary Figure 1.

Multivariable models include age, sex, study, alcohol, smoking, and race.

Title to Supplemental Figure 2:

Supplementary Figure 2. Individual participant meta-analysis of waist circumference (per 5 cm) and liver cancer risk in the Liver Cancer Pooling Project

Footnote to Supplementary Figure 2.

Multivariable models include age, sex, study, alcohol, smoking, race and body mass index.

Title to Supplemental Figure 3:

Supplementary Figure 3. Individual participant meta-analysis of diabetes (yes versus no) and liver cancer risk in the Liver Cancer Pooling Project

Footnote to Supplementary Figure 3.

Multivariable models include age, sex, study, alcohol, smoking, race and body mass index.