

SUPPLEMENTAL MATERIALS

Supplemental Table 1. Exclusion criteria

| Criteria | Excluded | Remaining |
|--|-----------------|------------------|
| Nine cohorts selected | | 1,161,251 |
| Exclusions: | | |
| Men | 504,145 | 657,106 |
| Missing height | 28,092 | 629,014 |
| Missing age at menarche | 7,326 | 621,688 |
| No follow-up time | 55,385 | 566,303 |
| History of cancer diagnosis reported at baseline | 29,853 | 536,450 |

Supplemental Table 2. Retrospective ascertainment of the age at menarche by cohort

| Cohort | Question | Response |
|--------|---|---|
| AARP | How old were you when you had your <u>first</u> menstrual period? | <input type="checkbox"/> 10 or younger <input type="checkbox"/> 11 to 12 <input type="checkbox"/> 13 to 14 <input type="checkbox"/> 15 or older |
| BCDDP | How old were you when you started your menstrual period? | -- |
| CPSII | How old were you when menstruation began? | --- |
| IWHS | Have you ever had a menstrual cycle or period? | <input type="checkbox"/> No <input type="checkbox"/> Yes |
| | How old were you when you menstruated for the first time (had your first period)? | ___ years old |
| PLCO | How old were you when you had your first menstrual period? | <input type="checkbox"/> Less than 10 <input type="checkbox"/> 10-11 <input type="checkbox"/> 12-13 <input type="checkbox"/> 14-15 <input type="checkbox"/> 16 or older |
| SMC | How old were you when you got your first period? (translated from Swedish) | ___ years <input type="checkbox"/> I Don't Remember |
| USRT | How old were you when your first menstrual period started? | -- 00 11 22 33 44 55 66 77 88 99 |
| WHS | At what age did your menstrual periods begin? | <input type="checkbox"/> 9 or younger <input type="checkbox"/> 10 <input type="checkbox"/> 11 |

-
- 12
 - 13
 - 14
 - 15
 - 16
 - 17 or older
-

WLH

At which age did you have your first menstruation?

___ years

Abbreviations: AARP, National Institutes of Health–AARP Diet and Health Study; BCDDP, Breast Cancer Detection and Demonstration Project; CPS II, Cancer Prevention Study II; IWHS, Iowa Women’s Health Study; PLCO, Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial; SMC, Swedish Mammography Cohort; USRT, US Radiologic Technologists Cohort; WHS, Women’s Health Study; WLH, Women’s Lifestyle and Health Study.

Supplemental Table 3. *International Classification of Diseases for Oncology, 3rd Ed.* Codes for each cancer site used in ascertainment of primary incident invasive cancers across cohorts.

| Cancer site | ICD-O-3 codes and, if applicable, ICD-O-3 histology [†] |
|---------------------------|---|
| Esophageal adenocarcinoma | C150-159& histologies: 8140, 8142, 8144, 8261, 8310, 8480, 8481, 8570 |
| Gallbladder | C239 |
| Liver* | C220 and C221 |
| Lung | C340-C349 |
| Kidney | C649 and C659 |
| Small intestine | C170-179 |
| Gastric cardia | C160 |
| Endometrial | C540-C549 and C559 |
| Esophageal squamous | C150-159 & histologies: 8041, 8070, 8071, 8072, 8074 |
| Myeloid leukemia | Acute myeloid leukemia: any histology of 9840, 9861, 9865-9867, 9869, 9871-9874, 9895-9897, 9898, 9910-9911, 9920 Acute monocytic leukemia: any histology of 9891 Chronic myeloid leukemia: any histology of 9863, 9875-9876, 9945-9946 Other myeloid/monocytic leukemia: any histology of 9860, 9930 |
| Myeloma | Any histology of 9731-9732, 9734 |
| Colon | C180-C189, C260 |
| Head and neck | Lip: C000-C009 Tongue: C019-C029, Salivary gland: C079-C089 Floor of mouth: C040-C049 Gum and other mouth: C030-C039, C050-C059, C060-C069 Nasopharynx: C110-C119 Tonsil: C090-C099 Oropharynx: C100-C109 Hypopharynx: C129, C30-C139 Other oral cavity and pharynx: C140, C142, C148 Larynx: C320-C329 |
| Rectum | C199, C209 |

| | |
|---|--|
| Bladder | C670-C679 |
| Breast | C500-C509 |
| Non-Hodgkin's Lymphoma | NHL-nodal: C024, C098, C099, C111, C142, C379, C422, C770-C779 & histologies: 9590-9597, 9670-9671, 9673, 9675, 9678-9680, 9684, 9687-9691, 9695, 9698-9702, 9705, 9708-9709, 9712, 9714-9719, 9724-9729, 9735, 9737-9738, 9811-9818, 9823, 9827, 9837 NHL-extranodal, definition 1: All sites except C024, C098-C099, C111, C142, C379, C422, C770-C779 & histologies of: 9590-9597, 9670-9671, 9673, 9675, 9678-9680, 9684, 9687, 9688, 9689-9691, 9695, 9698-9702, 9705, 9708-9709, 9712, 9714-9719, 9724-9729, 9735, 9737, 9738 NHL-extranodal, definition 2: All sites except C024, C098-C099, C111, C142, C379, C420-C422, C424, C770-C779 & histologies of: 9811-9818, 9823, 9827, 9837 |
| Thyroid | C739 |
| Gastric non-cardia | C161-169 |
| Soft tissue | C380, C470-C479, C490-C499 |
| Pancreas | C250-C259 |
| Lymphocytic leukemia | Acute lymphocytic leukemia, definition 1: Any histology of 9826, 9835-9836 Acute lymphocytic leukemia, definition 2: C420, C421, C424 & histologies: 9811-9818, 9837 Chronic lymphocytic leukemia: C420, C421, C424; histology 9823 Other lymphocytic leukemia: Any histology of 9820, 9832-9834, 9940. |
| Ovary | C569 |
| Brain | C710-C719 |
| Skin cancer, excluding basal and squamous | Melanoma: C440-C449; histologies 8720-8790 Other non-epithelial skin: C440-C449, excluding histologies 8000-8005, 8010-8046, 8050-8084, 8090-8110, 8720-8790, 9050-9055, 9140, 9590-9992 |

* A small proportion (17%) of the liver cancer classification consists of intrahepatic bile duct cancer cases

† A small proportion (9%) of the kidney cancer classification consists of renal pelvis cancer cases

‡ Unless otherwise stated, cancer definitions exclude the histologies 9050-9055, 9140, 9590-9992

† A small proportion (4%) of the skin cancer classification consists of non-epithelial malignant skin cancer cases

Supplemental Table 4. Site-specific cancer diagnoses by cohort*

| | AARP | BCDDP | CPSII | IWHS | PLCO | SMC | USRT | WHS | WLH | Included |
|----------------------------|------|---------------|-------|------|------|---------------|------|------|---------------|----------|
| Endometrial cancer | 1604 | 249 | 824 | 562 | 238 | 280 | 153 | 420 | 9 | 4330 |
| Liver cancer | 130 | 29 | 54 | 49 | 18 | 23 | 4 | 20 | 2 | 323 |
| Melanoma | 1305 | 292 | 786 | 276 | 168 | 108 | 238 | 257 | 67 | 3497 |
| Bladder cancer | 640 | 79 | 294 | 185 | 78 | 72 | 48 | 87 | 17 | 1500 |
| Myeloid leukemia | 182 | 31 | 121 | 113 | 30 | 31 | 9 | 46 | 10 | 564 |
| Thyroid cancer | 326 | 35 | 127 | 67 | 37 | 14 | 120 | 102 | 8 | 814 |
| Colon cancer | 1871 | 325 | 1044 | 1088 | 218 | 286 | 132 | 344 | 52 | 5360 |
| Lung cancer | 3607 | 322 | 1050 | 877 | 390 | 199 | 76 | 420 | 57 | 6998 |
| Breast cancer | 9484 | 1522 | 5458 | 2694 | 1443 | 973 | 1029 | 2029 | 436 | 25,068 |
| Ovarian cancer | 739 | 61 | 441 | 269 | 121 | 123 | 72 | 200 | 4 | 2026 |
| Non-Hodgkin's lymphoma | 1010 | 107 | 620 | 391 | 134 | 90 | 87 | 231 | 14 | 2670 |
| Head & Neck cancers | 443 | 43 | 129 | 150 | 27 | 42 | 28 | 47 | 8 | 909 |
| Kidney cancer | 553 | 48 | 235 | 177 | 73 | 68 | 37 | 97 | 4 | 1288 |
| Pancreatic cancer | 618 | 84 | 281 | 233 | 98 | 88 | 5 | 88 | 15 | 1505 |
| Lymphocytic leukemia | 225 | 14 | 167 | 122 | 66 | 47 | 20 | 66 | 5 | 713 |
| Rectal cancer | 617 | 58 | 295 | 283 | 47 | 111 | 22 | 100 | 34 | 1567 |
| Brain cancer | 226 | 2 | 146 | 108 | 32 | 38 | 4 | 47 | 22 | 619 |
| Gastric cancer, non-cardia | 164 | 0 | 63 | 49 | 18 | 52 | 7 | 0 | 0 | 346 |
| Myeloma | 282 | 11 | 169 | 124 | 43 | 56 | 18 | 60 | 11 | 752 |

*Where cohorts have been excluded for particular outcomes due to low case numbers, the sample size is crossed out. Abbreviations: AARP, National Institutes of Health–AARP Diet and Health Study; BCDDP, Breast Cancer Detection and Demonstration Project; CPS II, Cancer Prevention Study II; IWHS, Iowa Women's Health Study; PLCO, Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial; SMC, Swedish Mammography Cohort; USRT, US Radiologic Technologists Cohort; WHS, Women's Health Study; WLH, Women's Lifestyle and Health Study.

Supplementary Table 5. Prevalence of demographic and lifestyle characteristics by age at menarche among pooled participants from 9 cohorts

| Characteristic | All participants, % | Age at menarche (y), % | | | |
|---|---------------------|------------------------|-------|-------|------|
| | | ≤ 10 | 11-12 | 13-14 | 15+ |
| Age, y | | | | | |
| <60 | 50.4 | 59.4 | 52.2 | 48.2 | 47.4 |
| 60-69.9 | 42.8 | 37.3 | 42.1 | 4.9 | 44.4 |
| 70+ | 6.8 | 3.3 | 5.7 | 8.0 | 8.3 |
| Smoking status | | | | | |
| Never | 51.7 | 49.2 | 51.6 | 52.2 | 51.5 |
| Former | 34.2 | 35.7 | 34.6 | 33.9 | 33.2 |
| Current | 14.1 | 15.1 | 13.8 | 13.9 | 15.3 |
| Alcohol intake, g/d | | | | | |
| 0 | 34.7 | 37.8 | 35.0 | 33.6 | 36.5 |
| 0.1-14.9 | 56.5 | 54.5 | 56.3 | 57.3 | 54.5 |
| 15.0-29.9 | 5.3 | 4.5 | 5.2 | 5.6 | 5.4 |
| ≥ 30 | 3.5 | 3.2 | 3.5 | 3.5 | 3.5 |
| Race | | | | | |
| White | 95.3 | 94.0 | 95.3 | 95.8 | 93.7 |
| Black | 3.3 | 4.7 | 3.3 | 2.9 | 4.2 |
| Other | 1.5 | 1.4 | 1.4 | 1.4 | 2.2 |
| Education | | | | | |
| Less than high school | 13.2 | 7.2 | 10.8 | 15.4 | 16.4 |
| High school graduate | 23.5 | 20.0 | 23.1 | 23.6 | 26.6 |
| Post-high school training | 15.9 | 20.5 | 17.1 | 14.6 | 14.1 |
| Some college | 18.6 | 19.8 | 18.9 | 18.2 | 19.2 |
| College degree of greater | 28.9 | 32.5 | 30.2 | 28.2 | 24.7 |
| Postmenopausal hormone therapy use | | | | | |
| Ever | 50.2 | 50.8 | 50.6 | 49.9 | 49.5 |
| Never | 49.8 | 49.2 | 49.5 | 50.1 | 50.5 |
| Oral contraceptive use | | | | | |
| Ever | 47.2 | 50.1 | 47.6 | 47.0 | 44.6 |
| Never | 52.8 | 49.9 | 52.4 | 53.0 | 55.4 |
| Age at menopause, y | | | | | |
| Premenopausal | 20.4 | 20.6 | 20.8 | 19.3 | 18.3 |
| <40 | 11.4 | 17.1 | 12.2 | 10.0 | 10.9 |
| 40-44 | 11.2 | 13.6 | 11.9 | 10.4 | 11.0 |
| 45-49 | 20.4 | 19.0 | 20.5 | 20.6 | 19.8 |
| 50-54 | 28.9 | 22.8 | 27.3 | 30.5 | 29.5 |
| 55+ | 7.9 | 6.9 | 7.3 | 8.3 | 9.5 |

Continued

| Characteristic | All participants, % | Age at menarche (y), % | | | |
|--|---------------------|------------------------|-------|-------|------|
| | | ≤ 10 | 11-12 | 13-14 | 15+ |
| Parity | | | | | |
| 0 | 12.9 | 14.6 | 13.3 | 12.4 | 11.7 |
| 1 | 10.8 | 11.3 | 10.8 | 10.7 | 11.0 |
| 2 | 29.8 | 28.9 | 29.7 | 30.1 | 29.6 |
| 3+ | 46.5 | 45.2 | 46.1 | 46.8 | 47.7 |
| Height | | | | | |
| Bottom tertile | 35.3 | 45.9 | 38.2 | 32.4 | 30.7 |
| Middle tertile | 31.7 | 29.1 | 31.5 | 32.4 | 30.5 |
| Top tertile | 33.0 | 25.1 | 30.3 | 35.3 | 38.9 |
| Physical activity level | | | | | |
| Bottom tertile | 33.9 | 36.8 | 34.4 | 32.9 | 33.4 |
| Middle tertile | 31.6 | 29.0 | 31.1 | 32.5 | 31.1 |
| Top tertile | 34.6 | 34.2 | 34.5 | 34.6 | 34.9 |
| Body mass index, kg/m² | | | | | |
| <20 | 6.1 | 3.5 | 5.2 | 6.7 | 8.5 |
| 20-29.9 | 75.6 | 64.2 | 73.6 | 78.1 | 78.2 |
| 30+ | 18.4 | 32.3 | 21.2 | 15.2 | 13.4 |

Supplemental Table 6. Selected characteristics of study participants by cohort

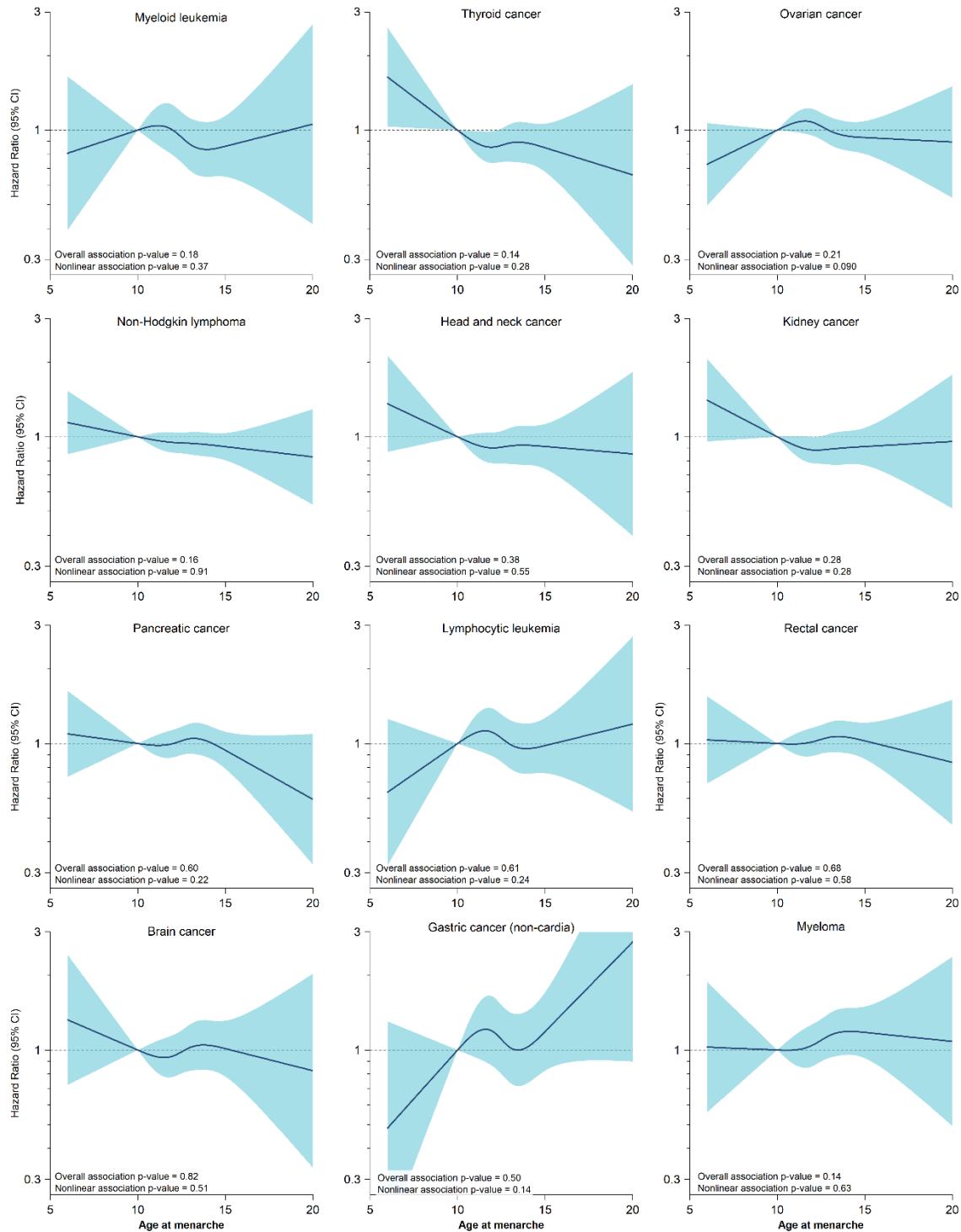
| | Nulliparous | Smoking Status | | | Hormone therapy use | | |
|--------|-------------|----------------|--------|---------|---------------------|---------|--------|
| | % | Never | Former | Current | Never | Current | Former |
| AARP | 15% | 46% | 40% | 15% | 46% | 44% | 9% |
| BCDDP | 8% | 57% | 30% | 13% | 31% | 68% | |
| CPS II | 9% | 55% | 36% | 9% | 42% | 47% | 5% |
| IWHS | 5% | 66% | 19% | 15% | 61% | 27% | 11% |
| PLCO | 4% | 57% | 34% | 9% | 25% | 40% | 13% |
| SMC | 4% | 54% | 23% | 23% | 53% | 37% | 10% |
| USRT | 14% | 57% | 30% | 12% | 69% | 24% | 6% |
| WHS | 7% | 51% | 36% | 13% | 50% | 41% | 9% |
| WLH | 5% | 48% | 33% | 20% | 62% | 19% | 17% |

Abbreviations: AARP, National Institutes of Health–AARP Diet and Health Study; BCDDP, Breast Cancer Detection and Demonstration Project; CPS II, Cancer Prevention Study II; IWHS, Iowa Women’s Health Study; PLCO, Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial; SMC, Swedish Mammography Cohort; USRT, US Radiologic Technologists Cohort; WHS, Women’s Health Study; WLH, Women’s Lifestyle and Health Study.

Supplemental Table 7. Age at cancer diagnosis by type of cancer among pooled participants from nine cohorts

| Cancer | Median age at diagnosis (25 th and 75 th percentiles) |
|----------------------------|---|
| Endometrial cancer | 68.0 (63.0-73.0) |
| Liver cancer | 71.7 (66.5-76.0) |
| Melanoma | 68.0 (62.4-73.0) |
| Bladder cancer | 70.5 (65.0-75.0) |
| Myeloid leukemia | 70.0 (64.8-75.4) |
| Thyroid cancer | 65.9 (59.7-71.0) |
| Colon cancer | 70.9 (65.8-75.6) |
| Lung cancer | 70.0 (65.1-74.0) |
| Breast cancer | 67.7 (62.2-72.6) |
| Ovarian cancer | 68.3 (62.7-73.5) |
| Non-Hodgkin's lymphoma | 69.9 (64.3-74.5) |
| Head & Neck cancers | 69.0 (63.8-73.9) |
| Kidney cancer | 69.7 (64.0-74.4) |
| Pancreatic cancer | 71.1 (66.2-75.8) |
| Lymphocytic leukemia | 70.2 (65.0-75.0) |
| Rectal cancer | 69.0 (64.0-74.0) |
| Brain cancer | 68.2 (63.0-73.5) |
| Gastric cancer, non-cardia | 72.4 (68.1-76.3) |
| Myeloma | 70.9 (65.9-75.7) |

Supplementary Figure 1. Splines describing cancer risk by the age at menarche (y)



Non-linear associations of selected site-specific cancer risks with the age at menarche among middle-aged women drawn from 9 cohorts. Separate models were fit for each cancer type using cubic restricted splines in samples stratified by cohort. Models adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplemental Table 8. Change in summary estimates of multivariable-adjusted* hazard ratios for site-specific cancers associated with the age at menarche in models additionally adjusted for young adult body mass index (BMI)

| Site specific cancer | Percent change |
|----------------------------|----------------|
| Liver Cancer | -1.9% |
| Melanoma | -0.5% |
| Bladder Cancer | -0.2% |
| Myeloid Leukemia | -0.7% |
| Thyroid cancer | -0.6% |
| Colon Cancer | -0.6% |
| Lung Cancer | -0.3% |
| Breast Cancer | 0.7% |
| Ovarian cancer | 0.5% |
| Non-Hodgkin's lymphoma | -1.3% |
| Head & Neck | -0.8% |
| Kidney Cancer | -1.4% |
| Pancreatic cancer | -0.2% |
| Lymphocytic Leukemia | -0.5% |
| Rectal cancer | -0.7% |
| Brain Cancer | -0.2% |
| Gastric cancer, non-cardia | -2.2% |
| Myeloma | -0.8% |

*Base models adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height. The percent difference reflects change in the summary estimate for the HR

Supplementary Table 9. Summary estimates of multivariable-adjusted* relative risks for site-specific cancers associated with the age at menarche in strata defined by birth cohort

| | Stratified by Birth Year | | | | | | Percent difference in HR | P for interaction |
|----------------------------|--------------------------|-----------------------|------|-----------------------|-----------------------|------|--------------------------|-------------------|
| | Born before 1934 | | | Born in 1934 or later | | | | |
| | HR | 95% confidence limits | | HR | 95% confidence limits | | | |
| | Lower | Upper | | Lower | Upper | | | |
| Endometrial cancer | 0.91 | 0.88 | 0.95 | 0.92 | 0.90 | 0.95 | 1.1% | 0.64 |
| Liver cancer | 0.92 | 0.85 | 1.01 | . | . | . | | |
| Melanoma | 0.92 | 0.87 | 0.97 | 0.99 | 0.96 | 1.02 | 7.1% | 0.01 |
| Bladder cancer | 0.97 | 0.93 | 1.01 | 0.94 | 0.88 | 1.00 | -3.2% | 0.39 |
| Myeloid leukemia | 0.97 | 0.90 | 1.04 | 0.95 | 0.85 | 1.06 | -2.1% | 0.79 |
| Thyroid cancer | 1.02 | 0.95 | 1.10 | 0.95 | 0.89 | 1.01 | -7.4% | 0.11 |
| Colon cancer | 0.98 | 0.96 | 1.00 | 0.97 | 0.93 | 1.01 | -1.0% | 0.73 |
| Lung cancer | 0.98 | 0.95 | 1.01 | 0.96 | 0.94 | 0.99 | -2.1% | 0.43 |
| Breast cancer | 0.97 | 0.96 | 0.98 | 0.98 | 0.97 | 0.99 | 1.0% | 0.57 |
| Ovarian cancer | 0.98 | 0.95 | 1.02 | 0.97 | 0.93 | 1.02 | -1.0% | 0.69 |
| Non-Hodgkin lymphoma | 0.98 | 0.95 | 1.01 | 0.99 | 0.93 | 1.05 | 1.0% | 0.84 |
| Head and neck cancer | 0.98 | 0.93 | 1.03 | 1.00 | 0.93 | 1.07 | 2.0% | 0.69 |
| Kidney cancer | 0.98 | 0.94 | 1.03 | 0.98 | 0.92 | 1.04 | 0.0% | 0.98 |
| Pancreas cancer | 0.99 | 0.95 | 1.03 | 0.99 | 0.92 | 1.06 | 0.0% | 0.87 |
| Lymphocytic leukemia | 0.99 | 0.93 | 1.05 | 0.99 | 0.92 | 1.08 | 0.0% | 0.97 |
| Rectal cancer | 1.00 | 0.96 | 1.04 | 1.01 | 0.96 | 1.07 | 1.0% | 0.73 |
| Brain cancer | 1.02 | 0.95 | 1.09 | 0.99 | 0.92 | 1.08 | -3.0% | 0.68 |
| Gastric cancer, non-cardia | 1.03 | 0.95 | 1.12 | . | . | . | | |
| Myeloma | 1.05 | 0.99 | 1.11 | 1.00 | 0.87 | 1.14 | -5.0% | 0.50 |

*Adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplementary Table 10. Summary estimates of multivariable-adjusted* relative risks for site-specific cancers associated with the age at menarche in strata defined by the median age

| | HR | Age < 60 y | | HR | Age ≥ 60 y | | Percent difference in HR | P for interaction |
|----------------------|------|-----------------------|-------|------|-----------------------|-------|--------------------------|-------------------|
| | | 95% confidence limits | | | 95% confidence limits | | | |
| | | Lower | Upper | | Lower | Upper | | |
| Endometrial | 0.92 | 0.89 | 0.96 | 0.91 | 0.88 | 0.94 | -1.1% | 0.75 |
| Liver | 0.97 | 0.85 | 1.12 | 0.85 | 0.71 | 1.02 | -14.1% | 0.23 |
| Melanoma | 0.98 | 0.95 | 1.02 | 0.93 | 0.89 | 0.97 | -5.4% | 0.05 |
| Bladder | 0.95 | 0.90 | 1.01 | 0.96 | 0.92 | 1.01 | 1.0% | 0.69 |
| Myeloid leukemia | 0.98 | 0.89 | 1.07 | 0.92 | 0.79 | 1.07 | -6.5% | 0.47 |
| Thyroid | 0.97 | 0.91 | 1.03 | 0.94 | 0.81 | 1.09 | -3.2% | 0.75 |
| Colon | 0.96 | 0.93 | 0.99 | 0.98 | 0.95 | 1.00 | 2.0% | 0.28 |
| Lung | 0.97 | 0.94 | 0.99 | 0.98 | 0.95 | 1.01 | 1.0% | 0.54 |
| Breast | 0.97 | 0.96 | 0.99 | 0.98 | 0.97 | 0.99 | 1.0% | 0.59 |
| Ovarian | 0.96 | 0.92 | 1.00 | 1.00 | 0.96 | 1.04 | 4.0% | 0.2 |
| Non-Hodgkin lymphoma | 0.99 | 0.93 | 1.04 | 0.98 | 0.94 | 1.02 | -1.0% | 0.85 |
| Head and neck | 0.98 | 0.92 | 1.05 | 0.98 | 0.93 | 1.04 | 0.0% | 0.96 |
| Kidney | 1.01 | 0.94 | 1.08 | 0.99 | 0.93 | 1.05 | -2.0% | 0.71 |
| Pancreas | 0.99 | 0.93 | 1.05 | 0.98 | 0.94 | 1.03 | -1.0% | 0.89 |
| Lymphocytic leukemia | 1.01 | 0.93 | 1.09 | 0.99 | 0.92 | 1.06 | -2.0% | 0.73 |
| Rectum | 1.01 | 0.96 | 1.07 | 1.01 | 0.97 | 1.06 | 0.0% | 0.97 |
| Brain | 0.98 | 0.90 | 1.05 | 1.05 | 0.97 | 1.14 | 6.7% | 0.18 |
| Gastric, non-cardia | 1.02 | 0.86 | 1.21 | 1.03 | 0.94 | 1.13 | 1.0% | 0.92 |
| Myeloma | 1.01 | 0.89 | 1.14 | 1.07 | 1.01 | 1.14 | 5.6% | 0.38 |

*Adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplementary Table 11. Summary estimates of multivariable-adjusted* relative risks for site-specific cancers associated with the age at menarche in strata defined by overweight and obese (body mass index > 25)

| | Stratified by body mass index | | | | | | Percent difference in HR | P for interaction |
|----------------------|-------------------------------|-----------------------|------|--------------------------|-----------------------|------|--------------------------|-------------------|
| | < 25 kg / m ² | | | ≥ 25 kg / m ² | | | | |
| | HR | 95% confidence limits | | HR | 95% confidence limits | | | |
| | Lower | Upper | | Lower | Upper | | | |
| Endometrial | 0.94 | 0.91 | 0.97 | 0.93 | 0.91 | 0.96 | -1.1% | 0.74 |
| Liver | 0.98 | 0.85 | 1.12 | 0.91 | 0.81 | 1.03 | -7.7% | 0.48 |
| Melanoma | 0.96 | 0.92 | 1.00 | 0.95 | 0.92 | 0.98 | -1.1% | 0.86 |
| Bladder | 1.01 | 0.96 | 1.06 | 0.96 | 0.89 | 1.03 | -5.2% | 0.23 |
| Myeloid leukemia | 0.94 | 0.85 | 1.04 | 1.02 | 0.91 | 1.15 | 7.8% | 0.31 |
| Thyroid | 1.02 | 0.92 | 1.12 | 0.94 | 0.88 | 0.99 | -8.5% | 0.15 |
| Colon | 0.99 | 0.95 | 1.03 | 0.98 | 0.95 | 1.00 | -1.0% | 0.60 |
| Lung | 0.97 | 0.95 | 0.99 | 0.97 | 0.93 | 1.02 | 0.0% | 0.88 |
| Breast | 0.98 | 0.97 | 1.00 | 0.98 | 0.97 | 0.99 | 0.0% | 0.49 |
| Ovarian | 0.98 | 0.94 | 1.02 | 0.98 | 0.93 | 1.02 | 0.0% | 0.98 |
| Non-Hodgkin lymphoma | 0.98 | 0.94 | 1.03 | 0.98 | 0.95 | 1.02 | 0.0% | 0.93 |
| Head and neck | 0.98 | 0.93 | 1.04 | 0.98 | 0.92 | 1.05 | 0.0% | 0.98 |
| Kidney | 0.98 | 0.92 | 1.05 | 1.03 | 0.97 | 1.11 | 4.9% | 0.30 |
| Pancreas | 0.99 | 0.94 | 1.04 | 1.00 | 0.95 | 1.06 | 1.0% | 0.66 |
| Lymphocytic leukemia | 1.00 | 0.92 | 1.10 | 0.98 | 0.91 | 1.04 | -2.0% | 0.62 |
| Rectum | 0.99 | 0.94 | 1.04 | 1.03 | 0.98 | 1.07 | 3.9% | 0.28 |
| Brain | 1.03 | 0.95 | 1.11 | 0.97 | 0.90 | 1.05 | -6.2% | 0.32 |
| Gastric, non-cardia | 1.00 | 0.90 | 1.11 | 1.03 | 0.92 | 1.16 | 2.9% | 0.68 |
| Myeloma | 1.02 | 0.92 | 1.13 | 1.07 | 1.00 | 1.14 | 4.7% | 0.42 |

*Adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplementary Table 12. Summary estimates of multivariable-adjusted* relative risks for site-specific cancers associated with the age at menarche in strata defined by parity

| | Parous | | | Nulliparous | | | Percent difference | P for interaction |
|----------------------|--------|-----------------------|-------|-------------|-----------------------|-------|--------------------|-------------------|
| | HR | 95% confidence limits | | HR | 95% confidence limits | | | |
| | | Lower | Upper | | Lower | Upper | | |
| Endometrial | 0.90 | 0.88 | 0.92 | . | . | . | | |
| Liver | 0.92 | 0.83 | 1.02 | 0.99 | 0.95 | 1.04 | 7.1% | 0.18 |
| Melanoma | 0.95 | 0.92 | 0.98 | . | . | . | | |
| Bladder | 0.96 | 0.92 | 0.99 | 1.01 | 0.87 | 1.17 | 5.0% | 0.51 |
| Myeloid leukemia | 0.97 | 0.91 | 1.03 | . | . | . | | |
| Thyroid | 0.97 | 0.92 | 1.02 | 0.96 | 0.90 | 1.03 | -1.0% | 0.90 |
| Colon | 0.97 | 0.95 | 0.99 | 0.99 | 0.94 | 1.05 | 2.0% | 0.43 |
| Lung | 0.97 | 0.96 | 0.99 | . | . | . | | |
| Breast | 0.98 | 0.97 | 0.98 | 0.97 | 0.95 | 1.00 | -1.0% | 0.91 |
| Ovarian | 0.98 | 0.95 | 1.01 | 0.98 | 0.88 | 1.09 | 0.0% | 0.97 |
| Non-Hodgkin lymphoma | 0.98 | 0.96 | 1.01 | 0.96 | 0.88 | 1.04 | -2.1% | 0.52 |
| Head and neck | 0.98 | 0.94 | 1.03 | 0.98 | 0.86 | 1.11 | 0.0% | 0.93 |
| Kidney | 0.98 | 0.94 | 1.02 | . | . | . | | |
| Pancreas | 0.99 | 0.96 | 1.03 | 0.94 | 0.85 | 1.04 | -5.3% | 0.29 |
| Lymphocytic leukemia | 1.01 | 0.96 | 1.06 | 0.95 | 0.74 | 1.21 | -6.3% | 0.62 |
| Rectum | 1.02 | 0.98 | 1.05 | 0.94 | 0.89 | 1.01 | -8.5% | 0.05 |
| Brain | 1.01 | 0.95 | 1.07 | . | . | . | | |
| Gastric, non-cardia | 1.03 | 0.93 | 1.15 | 0.96 | 0.83 | 1.12 | -7.3% | 0.48 |
| Myeloma | 1.03 | 0.98 | 1.09 | 1.00 | 0.89 | 1.13 | -3.0% | 0.67 |

*Adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplementary Table 13. Summary estimates of multivariable-adjusted* relative risks for site-specific cancers associated with the age at menarche in strata defined by the median height

| | Height < 162.5 cm | | | Height ≥ 162.5 cm | | | Percent difference in HR | P for interaction |
|----------------------|-------------------|-----------------------|-------|-------------------|-----------------------|-------|--------------------------|-------------------|
| | HR | 95% confidence limits | | HR | 95% confidence limits | | | |
| | | Lower | Upper | | Lower | Upper | | |
| Endometrial | 0.90 | 0.87 | 0.93 | 0.92 | 0.90 | 0.95 | 2.2% | 0.21 |
| Liver | 0.92 | 0.81 | 1.05 | 0.94 | 0.84 | 1.06 | 2.1% | 0.81 |
| Melanoma | 0.92 | 0.86 | 0.98 | 0.97 | 0.94 | 1.00 | 5.2% | 0.11 |
| Bladder | 0.95 | 0.90 | 1.00 | 0.96 | 0.92 | 1.01 | 1.0% | 0.67 |
| Myeloid leukemia | 0.92 | 0.83 | 1.02 | 0.99 | 0.91 | 1.07 | 7.1% | 0.31 |
| Thyroid | 0.97 | 0.87 | 1.08 | 0.97 | 0.92 | 1.03 | 0.0% | 0.99 |
| Colon | 1.00 | 0.97 | 1.02 | 0.96 | 0.94 | 0.99 | -4.2% | 0.08 |
| Lung | 0.97 | 0.94 | 0.99 | 0.97 | 0.94 | 1.01 | 0.0% | 0.83 |
| Breast | 0.97 | 0.95 | 0.98 | 0.98 | 0.97 | 0.99 | 1.0% | 0.16 |
| Ovarian | 1.05 | 0.98 | 1.12 | 0.92 | 0.87 | 0.98 | -14.1% | 0.01 |
| Non-Hodgkin lymphoma | 0.99 | 0.94 | 1.04 | 0.97 | 0.94 | 1.01 | -2.1% | 0.64 |
| Head and neck | 0.97 | 0.90 | 1.03 | 1.00 | 0.94 | 1.05 | 3.0% | 0.47 |
| Kidney | 0.94 | 0.89 | 1.00 | 1.01 | 0.96 | 1.07 | 6.9% | 0.07 |
| Pancreas | 1.02 | 0.97 | 1.07 | 0.96 | 0.91 | 1.02 | -6.3% | 0.18 |
| Lymphocytic leukemia | 1.00 | 0.92 | 1.09 | 0.98 | 0.92 | 1.04 | -2.0% | 0.66 |
| Rectum | 1.02 | 0.95 | 1.09 | 1.02 | 0.95 | 1.09 | 0.0% | 1.00 |
| Brain | 1.01 | 0.93 | 1.11 | 1.00 | 0.93 | 1.07 | -1.0% | 0.76 |
| Gastric, non-cardia | 1.06 | 0.91 | 1.25 | 0.99 | 0.87 | 1.11 | -7.1% | 0.46 |
| Myeloma | 1.02 | 0.95 | 1.10 | 1.03 | 0.95 | 1.13 | 1.0% | 0.83 |

*Adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplementary Table 14. Summary estimates of multivariable-adjusted* relative risks for site-specific cancers associated with the age at menarche in strata defined by smoking status

| | Never smokers | | | Ever smokers | | | Percent difference | P for interaction |
|----------------------|---------------|-----------------------|-------|--------------|-----------------------|-------|--------------------|-------------------|
| | HR | 95% confidence limits | | HR | 95% confidence limits | | | |
| | | lower | upper | | lower | upper | | |
| Endometrial | 0.96 | 0.93 | 0.99 | 0.95 | 0.92 | 0.98 | 0.4% | 0.86 |
| Liver | 0.94 | 0.84 | 1.05 | 0.96 | 0.83 | 1.12 | -2.9% | 0.77 |
| Melanoma | 0.95 | 0.92 | 0.99 | 0.97 | 0.94 | 1.00 | -1.2% | 0.64 |
| Bladder | 0.95 | 0.89 | 1.01 | 0.97 | 0.93 | 1.01 | -1.8% | 0.63 |
| Myeloid leukemia | 1.02 | 0.93 | 1.11 | 0.97 | 0.90 | 1.06 | 4.3% | 0.47 |
| Thyroid | 0.91 | 0.85 | 0.97 | 1.08 | 1.00 | 1.17 | -19.2% | 0.00 |
| Colon | 1.00 | 0.96 | 1.03 | 0.98 | 0.95 | 1.01 | 1.5% | 0.50 |
| Lung | 0.99 | 0.92 | 1.07 | 0.97 | 0.95 | 0.99 | 2.6% | 0.49 |
| Breast | 0.98 | 0.97 | 0.99 | 0.99 | 0.98 | 1.01 | -1.7% | 0.05 |
| Ovarian | 0.98 | 0.94 | 1.03 | 0.98 | 0.94 | 1.03 | 0.1% | 0.97 |
| Non-Hodgkin lymphoma | 0.98 | 0.95 | 1.02 | 1.00 | 0.96 | 1.03 | -1.3% | 0.62 |
| Head and neck | 1.03 | 0.95 | 1.12 | 0.97 | 0.92 | 1.02 | 6.1% | 0.20 |
| Kidney | 1.02 | 0.97 | 1.08 | 1.02 | 0.95 | 1.10 | 0.3% | 0.95 |
| Pancreas | 0.99 | 0.93 | 1.05 | 1.00 | 0.95 | 1.07 | -1.7% | 0.71 |
| Lymphocytic leukemia | 0.99 | 0.92 | 1.06 | 1.01 | 0.94 | 1.09 | -2.6% | 0.62 |
| Rectum | 1.01 | 0.97 | 1.06 | 1.01 | 0.95 | 1.07 | 0.5% | 0.89 |
| Brain | 1.01 | 0.94 | 1.09 | 1.01 | 0.94 | 1.09 | -0.3% | 0.96 |
| Gastric, non-cardia | 1.02 | 0.92 | 1.13 | 1.02 | 0.92 | 1.13 | 0.7% | 0.93 |
| Myeloma | 1.07 | 1.01 | 1.14 | 0.97 | 0.85 | 1.11 | 9.3% | 0.19 |

*Adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplementary Table 15. Summary estimates of multivariable-adjusted* relative risks for site-specific cancers associated with the age at menarche in strata defined by history of menopausal hormone use

| | Never users | | | Current users | | | Former users | | | Never vs. Current | | Never vs. Former | |
|----------------------|-------------|-----------------------|-------|---------------|-----------------------|-------|--------------|-----------------------|-------|--------------------|-------------------|--------------------|-------------------|
| | HR | 95% confidence limits | | HR | 95% confidence limits | | HR | 95% confidence limits | | Percent difference | P for interaction | Percent difference | P for interaction |
| | | Lower | Upper | | Lower | Upper | | Lower | Upper | | | | |
| Endometrial | 0.89 | 0.86 | 0.93 | 0.96 | 0.93 | 0.99 | 0.93 | 0.85 | 1.03 | 7.7% | 0.006 | 4.9% | 0.57 |
| Liver | 0.88 | 0.76 | 1.03 | 0.89 | 0.70 | 1.13 | 1.00 | 0.84 | 1.19 | 0.2% | 0.99 | 13.3% | 0.11 |
| Melanoma | 0.93 | 0.90 | 0.96 | 0.98 | 0.94 | 1.02 | 0.98 | 0.93 | 1.03 | 5.2% | 0.045 | 5.3% | 0.97 |
| Bladder | 0.95 | 0.90 | 0.99 | 0.97 | 0.92 | 1.03 | 0.96 | 0.94 | 0.99 | 2.7% | 0.49 | 1.4% | 0.77 |
| Myeloid leukemia | 0.98 | 0.90 | 1.07 | 0.94 | 0.86 | 1.04 | | | | -4.2% | 0.51 | | |
| Thyroid | 0.95 | 0.89 | 1.02 | 0.98 | 0.88 | 1.10 | 1.06 | 0.91 | 1.23 | 3.4% | 0.61 | 11.1% | 0.36 |
| Colon | 0.97 | 0.95 | 1.00 | 0.98 | 0.95 | 1.01 | 1.05 | 0.99 | 1.11 | 0.7% | 0.73 | 7.6% | 0.85 |
| Lung | 0.97 | 0.95 | 0.99 | 0.96 | 0.92 | 1.01 | 0.98 | 0.88 | 1.09 | -0.9% | 0.72 | 0.8% | 0.02 |
| Breast | 0.97 | 0.95 | 0.98 | 0.99 | 0.97 | 1.00 | 1.09 | 0.88 | 1.35 | 2.2% | 0.02 | 12.9% | 0.82 |
| Ovarian | 0.97 | 0.92 | 1.02 | 0.99 | 0.94 | 1.04 | 1.04 | 0.85 | 1.28 | 2.2% | 0.56 | 7.8% | 0.79 |
| Non-Hodgkin lymphoma | 0.99 | 0.95 | 1.02 | 0.98 | 0.91 | 1.07 | 1.08 | 0.92 | 1.26 | -0.3% | 0.95 | 9.6% | 0.72 |
| Head and neck | 0.99 | 0.93 | 1.05 | 0.94 | 0.88 | 1.02 | 0.98 | 0.81 | 1.20 | -4.4% | 0.35 | -0.4% | 0.43 |
| Kidney | 0.95 | 0.91 | 1.00 | 1.00 | 0.94 | 1.06 | 0.95 | 0.87 | 1.05 | 5.2% | 0.20 | 0.0% | 0.63 |
| Pancreas | 0.99 | 0.94 | 1.03 | 1.01 | 0.93 | 1.10 | 1.01 | 0.89 | 1.14 | 2.8% | 0.56 | 2.3% | 0.47 |
| Lymphocytic leukemia | 0.97 | 0.90 | 1.04 | 1.01 | 0.93 | 1.10 | 1.03 | 0.93 | 1.14 | 4.6% | 0.43 | 6.5% | 0.48 |
| Rectum | 0.98 | 0.94 | 1.03 | 1.02 | 0.96 | 1.08 | 1.06 | 0.96 | 1.18 | 4.2% | 0.28 | 8.5% | 0.17 |
| Brain | 1.04 | 0.96 | 1.12 | 1.00 | 0.92 | 1.10 | 0.93 | 0.82 | 1.07 | -3.0% | 0.61 | -9.9% | 0.72 |
| Gastric, non-cardia | 1.07 | 0.98 | 1.18 | 0.92 | 0.81 | 1.05 | | | | -14.0% | 0.06 | | |
| Myeloma | 0.99 | 0.88 | 1.12 | 1.05 | 0.94 | 1.18 | 1.03 | 0.87 | 1.22 | 5.9% | 0.50 | 3.9% | 0.41 |

*Adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplementary Table 16. Summary estimates of multivariable-adjusted* relative risks for site-specific cancers associated with the age at menarche in strata defined by geographic location (Sweden vs. America)

| | USA | | Sweden | | Percent difference | P-interaction |
|----------------------|------|--------------------------------------|--------|--------------------------------------|--------------------|---------------|
| | HR | 95% confidence limits lower upper | HR | 95% confidence limits lower upper | | |
| Endometrial | 0.92 | 0.89 0.95 | . | . | . | |
| Liver | 0.93 | 0.87 1.00 | . | . | . | |
| Melanoma | 0.96 | 0.93 0.99 | 1.00 | 0.84 | 1.20 | 4.0% 0.63 |
| Bladder | 0.96 | 0.93 0.99 | 1.08 | 0.91 | 1.28 | 11.1% 0.18 |
| Myeloid leukemia | 0.98 | 0.92 1.03 | . | . | . | |
| Thyroid | 0.97 | 0.93 1.02 | . | . | . | |
| Colon | 0.98 | 0.96 1.00 | 0.97 | 0.89 | 1.06 | -1.0% 0.80 |
| Lung | 0.98 | 0.95 1.00 | 0.97 | 0.88 | 1.07 | -1.0% 0.88 |
| Breast | 0.98 | 0.97 0.99 | 0.99 | 0.95 | 1.03 | 1.0% 0.63 |
| Ovarian | 0.98 | 0.95 1.01 | . | . | . | |
| Non-Hodgkin lymphoma | 0.98 | 0.96 1.01 | . | . | . | |
| Head and neck | 0.98 | 0.94 1.03 | . | . | . | |
| Kidney | 1.00 | 0.95 1.05 | . | . | . | |
| Pancreas | 0.99 | 0.96 1.02 | 1.03 | 0.87 | 1.21 | 3.9% 0.66 |
| Lymphocytic leukemia | 1.00 | 0.95 1.05 | . | . | . | |
| Rectum | 1.01 | 0.98 1.04 | 1.04 | 0.91 | 1.18 | 2.9% 0.70 |
| Brain | 1.01 | 0.96 1.07 | 1.01 | 0.81 | 1.25 | 0.0% 0.96 |
| Gastric, non-cardia | 1.05 | 0.97 1.12 | . | . | . | |
| Myeloma | 1.03 | 0.96 1.10 | . | . | . | |

*Adjusted for baseline age, smoking, alcohol, race/ethnicity, education, and hormone replacement therapy, oral contraceptive use, age at menopause, parity and height.

Supplemental Table 17. Comparison of multivariable hazard ratios per additional year of age at menarche, in all participants and after excluding those with extreme age at menarche (AAM) values¹

| Cancer | All participants | Excluding extremes of AAM ² | Percent Change in HR, % |
|----------------------------|------------------|--|-------------------------|
| Endometrial cancer | 0.91 (0.89-0.94) | 0.91 (0.89-0.93) | 0.0% |
| Liver cancer | 0.92 (0.85-0.99) | 0.88 (0.81-0.96) | -4.3% |
| Melanoma | 0.96 (0.93-0.99) | 0.94 (0.91-0.98) | -2.1% |
| Bladder cancer | 0.95 (0.93-0.98) | 0.97 (0.93-1.01) | 2.1% |
| Myeloid leukemia | 0.96 (0.91-1.02) | 0.94 (0.88-1.01) | -2.1% |
| Thyroid cancer | 0.97 (0.92-1.01) | 0.98 (0.92-1.04) | 1.0% |
| Colon cancer | 0.98 (0.97-0.98) | 0.98 (0.95-1.00) | 0.0% |
| Lung cancer | 0.98 (0.96-0.99) | 0.97 (0.95-0.99) | -1.0% |
| Breast cancer | 0.97 (0.96-0.99) | 0.97 (0.96-0.98) | 0.0% |
| Ovarian cancer | 0.98 (0.95-1.01) | 0.95 (0.92-0.99) | -3.1% |
| Non-Hodgkin's lymphoma | 0.98 (0.94-1.03) | 0.99 (0.96-1.02) | 1.0% |
| Head & Neck cancer | 0.98 (0.96-1.01) | 0.99 (0.95-1.05) | 1.0% |
| Kidney cancer | 0.99 (0.96-1.03) | 1.00 (0.96-1.05) | 1.0% |
| Pancreatic cancer | 0.99 (0.95-1.03) | 0.98 (0.94-1.02) | -1.0% |
| Lymphocytic leukemia | 0.99 (0.94-1.04) | 0.97 (0.91-1.03) | -2.0% |
| Rectal cancer | 1.01 (0.97-1.04) | 1.01 (0.98-1.05) | 0.0% |
| Brain cancer | 1.01 (0.96-1.06) | 1.03 (0.97-1.09) | 2.0% |
| Gastric cancer, non-cardia | 1.03 (0.96-1.11) | 0.99 (0.91-1.07) | -3.9% |
| Myeloma | 1.03 (0.98-1.10) | 1.03 (0.96-1.12) | 0.0% |

¹ Extreme values of AAM defined as values less than 10 years of age, or 17 or more years of age. This corresponds to data points more than 1.5 interquartile ranges below the 25th percentile or above the 75th percentile, which is one frequently used definition for outliers.

² This analysis includes 515,229 participants and 58,593 cancer cases, corresponding to 96% of the total participants and total cancer cases.

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