**Table S1. Characteristics of eligible participants at baseline, by cohort**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **BWHS**n=51,452 | **NHS II**n=116,415 | **SIS**n=24,028 | **SCCS**n=30,144 | **WLHS** n=49,010 | **Overall** n=271,049 |
| **Age, years**; Mean (SD) | 36.7 (8.6) | 34.8 (4.7) | 47.9 (4.9) | 47.3 (4.2) | 39.2 (5.8) | 38.5 (7.5) |
| **Young adult BMIa, kg/m2**; Mean (SD) | 21.5 (4.1) | 21.1 (3.3) | 23.9 (4.7) | 23.2 (5.6) | 20.5 (2.6) | 21.7 (4.0) |
| Missing | 858 | 1,524 | 142 | 1,264 | 3,450 | 7,238 |
| **Baseline BMI, kg/m2**; Mean (SD) | 27.8 (6.7) | 24.1 (5.0) | 27.6 (6.5) | 32.0 (8.3) | 23.5 (3.7) | 25.9 (6.4) |
| Missing | 1,584 | 1,059 | 11 | 464 | 1,532 | 4,650 |
| **Race/Ethnicity**; N (%) |  |  |  |  |  |  |
| non-Hispanic white | 0 (0) | 106,563 (93) | 19,392 (82) | 8,247 (27) | 49,010 (100) | 183,212 (68) |
| African American | 51,452 (100) | 2,101 (2) | 2,397 (10) | 20,573 (68) | 0 (0) | 76,523 (29) |
| Other | 0 (0) | 5,401 (5) | 1,780 (8) | 1238 (4) | 0 (0) | 8,419 (3) |
| Missing | 0 | 2,350 | 459 | 86 | 0 | 2,895 |
| **Education**; N (%) |  |  |  |  |  |  |
| High school or less | 8,983 (17) | 0 (0) | 3,153 (13) | 17,744 (59) | 28,170 (59) | 58,050 (22) |
| Some college | 19,010 (37) | 0 (0) | 8,249 (34) | 8,594 (29) | 9,195 (19) | 45,048 (17) |
| Completed college | 23,374 (46) | 116,415 (100) | 12,619 (52) | 3,720 (12) | 10,559 (22) | 166,687 (62) |
| Missing | 85 | 0 | 7 | 86 | 1,086 | 1,264 |
| **Breast cancer family history**  |  |  |  |  |  |  |
| No 1st degree | 48,285 (94) | 97,974 (84) | 1003 (4) | 26,445 (90) | 44,533 (91) | 218,240 (81) |
| 1st degree | 3,167 (6) | 18,441 (16) | 23,022 (96) | 2,852 (10) | 4,477 (9) | 51,959 (19) |
| Missing | 0 | 0 | 3 | 947 | 0 | 850 |
| **Menopausal statusb at baseline** |  |  |  |  |  |  |
| Premenopausal | 45,859 (89) | 81,500 (70) | 16,238 (68) | 14,391 (48) | 47,651 (97) | 205,639 (76) |
| Postmenopausal | 5,593 (11) | 34,915 (30) | 7,790 (32) | 15,753 (52) | 1,359 (3) | 65,410 (24) |
| **Parity** |  |  |  |  |  |  |
| Nulliparous | 19,593 (38) | 33,578 (29) | 5,199 (22) | 3,393 (11) | 6,230 (13) | 67,993 (25) |
| 1 birth | 11,722 (23) | 22,185 (19) | 3,925 (16) | 4,775 (16) | 7,990 (16) | 50,597 (19) |
| 2 births | 11,621 (23) | 38,790 (33) | 9,162 (38) | 8,481 (28) | 21,336 (44) | 89,390 (33) |
| 3 or more births  | 8,516 (17) | 21,862 (19) | 5,742 (24) | 13,495 (45) | 13,454 (27) | 63,069 (23) |
| **Age at first birth (among parous)** |  |  |  |  |  |  |
| <20 | 10,887 (35) | 5,918 (7) | 2,592 (14) | 14,334 (54) | 7,977 (18) | 41,708 (21) |
| 20-<25 | 11,217 (36) | 27,557 (34) | 5,430 (29) | 7,966 (30) | 17,471 (41) | 69,641 (35) |
| 25-<30 | 6,330 (20) | 35,225 (44) | 5,990 (32) | 2,828 (11) | 12,631 (30) | 63,004 (31) |
| >30 | 3,018 (10) | 12,276 (15) | 4,814 (26) | 1,571 (6) | 4,700 (11) | 26,379 (13) |
| Missing | 407 | 1,861 | 3 | 52 | 1 | 2,324 |
| **Age at most recent birth (among parous)** |  |  |  |  |  |  |
| <20 | 3,170 (10) | 1,419 (2) | 527 (3) | 2,453 (9) | 1,130 (3) | 8,699 (4) |
| 20-<25 | 8,749 (28) | 9,491 (12) | 2,551 (14) | 6,990 (26) | 7,321 (17) | 35,102 (18) |
| 25-<30 | 10,048 (32) | 34,860 (43) | 5,245 (28) | 7,529 (28) | 16,244 (38) | 73,926 (37) |
| >30 | 9,084 (29) | 35,206 (43) | 10,502 (56) | 9,608 (36) | 18,059 (42) | 84,459 (41) |
| Missing | 808 | 1,861 | 4 | 171 | 26 | 2,870 |
| **Time since most recent birth (among parous)** |  |  |  |  |  |  |
| 0-<5 years | 6,548 (21) | 38,034 (47) | 1,141 (6) | 714 (3) | 10,852 (25) | 57,289 (29) |
| 5-<10 years | 5,876 (19) | 21,750 (27) | 2,235 (12) | 1,995 (8) | 9,417 (22) | 41,273 (21) |
| 10-<20 years | 10,738 (35) | 19,967 (25) | 7,754 (41) | 10,442 (39) | 16,370 (38) | 65,271 (33) |
| >20 years | 7,889 (25) | 1,225 (2) | 7,695 (41) | 13,441 (51) | 6,115 (14) | 36,365 (18) |
| Missing | 808 | 1,861 | 4 | 159 | 26 | 2,858 |

aBMI ages 18-24 (BWHS, NHS II, SCCS, WLHS) or in 30s (SIS)

bIf missing menopausal status, assumed to be premenopausal (all age<51)

**Table S2. Characteristics of eligible participants at baseline, by GDM history**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Nulliparous** n=67,993 | **Parous, no GDM**n=192,291 | **Parous, GDM**n=10,765 |
| **Age, years**; Mean (SD) | 35.0 (7.7) | 39.6 (7.1) | 40.3 (7.3) |
| **Young adult BMIa**; Mean (SD) | 22.1 (4.5) | 21.5 (3.7) | 22.7 (5.0) |
| Missing | 1,603 | 5,348 | 287 |
| **Baseline BMI**; Mean (SD) | 25.5 (6.5) | 25.9 (6.2) | 29.0 (7.8) |
| Missing | 1,229 | 3,240 | 181 |
| **Race/Ethnicity**; N (%) |  |  |  |
| non-Hispanic white | 42,067 (63) | 134,702 (71) | 6,443 (61) |
| African American | 22,768 (34) | 50,125 (26) | 3,630 (34) |
| Other | 2,326 (3) | 5,530 (3) | 563 (5) |
| Missing | 832 | 1,934 | 129 |
| **Education**; N (%) |  |  |  |
| High school or less | 6,739 (10) | 48,639 (25) | 2,672 (25) |
| Some college | 9,655 (14) | 33,203 (17) | 2,190 (20) |
| Completed college | 51,375 (76) | 109,434 (57) | 5,878 (55) |
| Missing | 224 | 1,015 | 25 |
| **Breast cancer family history**  |  |  |  |
| No 1st degree | 55,686 (82) | 154,078 (80) | 8,476 (79) |
| 1st degree | 12,216 (18) | 37,527 (20) | 2,216 (21) |
| Missing | 91 | 686 | 73 |
| **Menopausal statusb** |  |  |  |
| Premenopausal | 49,790 (73) | 148,291 (77) | 7,558 (70) |
| Postmenopausal | 18,203 (27) | 44,000 (23) | 3,207 (30) |
| **Parity** |  |  |  |
| Nulliparous | 67,993 (100) | 0 (0) | 0 (0) |
| 1 birth | 0 (0) | 48,441 (25) | 2,156 (20) |
| 2 births | 0 (0) | 85,088 (44) | 4,302 (40) |
| 3 or more births  | 0 (0) | 58,762 (31) | 4,307 (40) |
| **Age at first birth (among parous)** |  |  |  |
| <20 | -- | 39,395 (21) | 2,313 (22) |
| 20-<25 | -- | 66,385 (35) | 3,256 (31) |
| 25-<30 | -- | 59,764 (31) | 3,240 (30) |
| ≥30 | -- | 24,526 (13) | 1,853 (17) |
| Missing |  | 2,221 | 103 |
| **Age at recent birth (among parous)** |  |  |  |
| <20 | -- | 8,473 (5) | 226 (2) |
| 20-<25 | -- | 33,789 (18) | 1,313 (12) |
| 25-<30 | -- | 70,738 (37) | 3,188 (30) |
| ≥30 | -- | 76,556 (40) | 5,903 (56) |
| Missing |  | 2,735 | 135 |
| **Time since most recent birth (among parous)** |  |  |  |
| 0-<5 years | -- | 53,559 (28) | 3,718 (35) |
| 5-<10 years | -- | 39,182 (21) | 2,091 (20) |
| 10-<20 years | -- | 61,989 (33) | 3,282 (31) |
| ≥20 years | -- | 34,826 (18) | 1,539 (14) |
| Missing |  | 2,735 | 135 |

aBMI ages 18-24 (BWHS, NHS II, SCCS, WLHS) or in 30s (SIS)

bIf missing menopausal status, assumed to be premenopausal (all age<51)

**Table S3. Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between gestational diabetes mellitus (GDM) and risk of breast cancer, adjusted for young adult body mass index.a**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **History of GDM** | **All breast cancersb** **HR (95% CI)** | **Invasive breast cancersb****HR (95% CI)** | **ER+ breast cancerb** **HR (95% CI)** | **ER- breast cancerb** **HR (95% CI)** |
| **All women** |  |  |  |  |
| Nulliparous  | 1.00 | 1.00 | 1.00 | 1.00 |
| Parous, no GDM | 0.83 (0.80, 0.88) | 0.88 (0.83, 0.94) | 0.83 (0.76, 0.89) | 0.98 (0.85, 1.13) |
| Parous, GDM  | 0.76 (0.66, 0.88) | 0.85 (0.72, 1.00) | 0.81 (0.66, 0.99) | 1.04 (0.75, 1.44) |
| **Parous women only** |  |  |  |  |
| Never  | 1.00 | 1.00 | 1.00 | 1.00 |
| Ever  | 0.91 (0.80, 1.05) | 0.95 (0.81, 1.12) | 0.98 (0.80, 1.18) | 1.05 (0.77, 1.43) |

aRestricted to women with complete covariate information.

bStratified by cohort and adjusted for age (as the time scale) and young adult BMI (continuous).

**Table S4: Pooled results for GDM status at baseline and risk of incident
breast cancer, leaving out one study at a time**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Hazard Ratio (95% CI): all breast cancersb** | **Hazard Ratio (95% CI): invasive breast cancers** | **Between-cohort Heterogeneity p-values**all cases/ invasive cases |
| **All women** (referent = nulliparous women) |  |  |
| Leaving out BWHS | 0.74 (0.63, 0.87) | 0.82 (0.67, 0.99) | 0.34 / 0.37 |
| Leaving out NHS II | 0.98 (0.79, 1.21) | 1.02 (0.80, 1.31) | 0.53 / 0.07 |
| Leaving out SIS | 0.75 (0.63, 0.88) | 0.79 (0.65, 0.96) | 0.10 / 0.04 |
| Leaving out SCCS | 0.77 (0.66, 0.90) | 0.84 (0.70, 1.01) | 0.20 / 0.03 |
| Leaving out WLHS | 0.78 (0.67, 0.93) | 0.86 (0.71, 1.04) | 0.08 / 0.09 |
| **Overall** | **0.79 (0.68, 0.91)** | **0.85 (0.72, 1.02)** | **0.17 / 0.06** |
|  |  |  |  |
| **Parous women** (referent = parous women with no GDM) |  |  |
| Leaving out BWHS | 0.89 (0.77, 1.04) | 0.96 (0.81, 1.15) | 0.11 / 0.09 |
| Leaving out NHS II | 1.03 (0.85, 1.24) | 1.04 (0.84, 1.29) | 0.50 / 0.16 |
| Leaving out SIS | 0.85 (0.73, 0.99) | 0.87 (0.73, 1.04) | 0.72 / 0.86 |
| Leaving out SCCS | 0.89 (0.77, 1.03) | 0.93 (0.78, 1.10) | 0.12 / 0.07 |
| Leaving out WLHS | 0.90 (0.78, 1.04) | 0.95 (0.80, 1.12) | 0.12 / 0.07 |
| **Overall** | **0.90 (0.78, 1.03)** | **0.94 (0.80, 1.10)** | **0.19 / 0.13** |

Adjusted for age (as the time scale), race/ethnicity (non-Hispanic White, African American, other), attained education (high school or less, some college, college graduate), parity (0, 1, 2, 3 or more), age at first birth (continuous, centered at 25), age at most recent birth (continuous, centered at 25), an interaction term between parity (yes or no) and age at first birth, an interaction term between parity (yes or no) and age at most recent birth, and young adult BMI (continuous). For analyses limited to parous women, age at first birth and age at most recent birth are included as continuous variables with no interaction terms. Pooled estimate includes stratification by cohort.

**Table S5. GDM status at baseline and risk of invasive versus in situ breast cancer**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Breast Cancer Cases**Invasive / in situ | **Hazard Ratio (95% CI): invasive breast cancers** | **Hazard Ratio (95% CI): in situ breast cancers** | **Between-cohort Heterogeneity****p-valuesa**  |
| **All women** (referent = nulliparous women) |
| BWHS | 926 / 205 | 0.90 (0.58, 1.39) | 1.19 (0.53, 2.67) |  |
| NHS II | 2,409 / 860 | 0.70 (0.54, 0.90) | 0.55 (0.34, 0.89) |  |
| SIS | 471 / 191 | 1.21 (0.76, 1.94) | 0.49 (0.20, 1.20) |  |
| SCCS | 172 / 0 | 0.76 (0.37, 1.59) | -- |  |
| WLHS | 890 / 204 | 0.72 (0.41, 1.28) | 1.18 (0.39, 3.54) |  |
| **Pooled Sample** | **4,868 / 1,460** | **0.85 (0.72, 1.02)** | **0.66 (0.46, 0.94)** | **0.42** |
|  |  |  |  |  |
| **Parous women** (referent = parous women with no GDM) |
| BWHS | 609 / 119 | 0.82 (0.55, 1.24) | 1.28 (0.59, 2.76) |  |
| NHS II | 1,679 / 574 | 0.85 (0.67, 1.07) | 0.67 (0.43, 1.05) |  |
| SIS | 357 / 137 | 1.38 (0.95, 1.99) | 0.77 (0.36, 1.65) |  |
| SCCS | 149 / 0 | 1.09 (0.66, 1.80) | -- |  |
| WLHS | 747 / 179 | 0.88 (0.52, 1.49) | 1.02 (0.38, 2.75) |  |
| **Pooled Sample** | **3,541 / 1,009** | **0.94 (0.80, 1.10)** | **0.79 (0.57, 1.10)** | **0.35** |

Restricted to women with complete covariate information for the adjusted models (257,290 total [49,745 in BWHS; 110,780 in NHS II; 23,429 in SIS; 28,660 in SCCS; 44,676 in WLHS] and 191,847 total parous [30,487 in BWHS; 78,415 in NHS II; 18,342 in SIS; 25,462 in SCCS; 39,139 in WLHS])

Adjusted for age (as the time scale), race/ethnicity (non-Hispanic White, African American, other), attained education (high school or less, some college, college graduate), parity (0, 1, 2, ≥3), age at first birth (continuous, centered at 25), age at most recent birth (continuous, centered at 25), an interaction term between parity (yes or no) and age at first birth, an interaction term between parity (yes or no) and age at most recent birth, and BMI at ages 18-24 (continuous). For analyses limited to parous women, age at first birth and age at most recent birth are included as continuous variables with no interaction terms. Pooled estimate includes stratification by cohort.

aFor test of heterogeneity between invasive and in situ breast cancer from joint Cox model.

**Table S6. Pooled, multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between gestational diabetes mellitus (GDM) and risk of breast cancer among women with exactly two births.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **History of GDM** | **Person-years at risk**a | **Casesa** **(all / invasive)** | **All breast cancersb** **HR (95% CI)** | **Invasive breast cancersb****HR (95% CI)** | **ER+ invasivecancersb** | **ER- invasivecancersb** |
| **Cases** | **HR (95% CI)** | **Cases** | **HR (95% CI)** |
| Never  | 1,135,764 | 2,221 / 1,632 | 1.00 | 1.00 | 1,085 | 1.00 | 361 | 1.00 |
| Ever  | 54,416 | 106 / 82 | 0.97 (0.80, 1.19) | 1.04 (0.83, 1.30) | 55 | 1.04 (0.79, 1.36) | 21 | 1.20 (0.77, 1.87) |

aRestricted to women with complete covariate information.

bStratified by cohort and adjusted for age (as the time scale), race/ethnicity (non-Hispanic White, African American, other), attained education (high school or less, some college, college graduate), parity (1, 2, 3 or more), age at first birth (continuous, centered at 25), age at most recent birth (continuous, centered at 25), and young adult BMI (continuous).