**Proportion of U.S. Trends in Breast Cancer Incidence Attributable to Long-term Changes in Risk Factor Distributions**

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**Supplemental Material**

The supplemental material includes Supplemental Figures, Supplemental Tables, and Supplemental Material: Variance calculation for the percent relative difference (in that order).

**Supplemental Figures**

Supplemental Figure S1: Distribution of mean BMI, mean age-at-menarche, mean number of births, and mean age-at-first-live-birth among parous women from 1980 to 2008 for various age groups for white U.S. women. 

Supplemental Figure S2: Plot against calendar time of unadjusted breast cancer log10-incidence and estimated log10-incidence for women at the reference level of risk factors for a 40-44 year-old white woman and for a 40-44 year-old black women in the U.S.



Supplemental Figure S3: Plot against calendar time of unadjusted breast cancer log10-incidence and estimated log10-incidence for women at the reference level of risk factors for a 60-64 year-old white woman and for a 60-64 year-old black women in the U.S.



**Supplemental Tables**

Supplemental Table 1. Summary of surveys with corresponding sample sizes overall and by race

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Survey** | **Years covered** | **All women** | **White women** | **Black women** | **Women of other races/ethnicities** |
| **NHANES I** | 1971-1975 | 7040 | 5757 | 1178 | 105 |
| **NHANES II** | 1976-1980 | 4147 | 3550 | 514 | 83 |
| **NHANES III** | 1988-1994 | 7769 | 5026 | 2482 | 261 |
| **Continuous NHANES** | 1999-2008 | 12,309 | 9243 | 2570 | 496 |
| **NHIS 1987** | 1987 | 10,691 | 8671 | 1745 | 275 |
| **NHIS 2000** | 2000-2001 | 32,463 | 24782 | 4700 | 2981 |
| **NHIS 2005** | 2005-2006 | 17,283 | 13793 | 2639 | 851 |

Supplemental Table 2: Log-relative risk (log-RR) estimates for breast cancer incidence and 95% confidence intervals (CIs) from Poisson models that include each risk factor marginally, from separate models fit to women aged <50 and >=50.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor** | **Women ages <50** | | **Women ages ≥50** | |
|  | **Log-RR** | **StdErr** | **Log-RR** | **StdErr** |
| **BMI** | | | | |
| <25.3 | REF |  | EMPTY |  |
| (25.3, 25.9] | -0.0623 | 0.0213 | REF |  |
| (25.9, 26.4] | -0.0982 | 0.0267 | 0.0196 | 0.0204 |
| (26.4, 27.2] | -0.0864 | 0.0314 | 0.0007 | 0.0253 |
| (27.2, 28.1] | -0.0642 | 0.0386 | 0.0377 | 0.0271 |
|  | | | | |
| **Age at menarche** | | | | |
| [12.3, 12.6] | -0.0588 | 0.0432 | 0.0149 | 0.0141 |
| (12.6, 12.7] | -0.0605 | 0.0435 | 0.0241 | 0.0135 |
| (12.7, 12.8] | -0.0579 | 0.047 | -0.0196 | 0.0097 |
| (12.8, 13.1] | -0.0433 | 0.0444 | 0.0112 | 0.0199 |
| (13.1, 13.6] | REF |  | REF |  |
|  | | | | |
| **Number of births** | | | | |
| [0.29, 1.48] | 0.3096 | 0.0641 | EMPTY |  |
| (1.48, 2.01] | 0.2666 | 0.0522 | 0.0208 | 0.0169 |
| (2.01, 2.58] | 0.2385 | 0.051 | 0.0571 | 0.0119 |
| (2.58, 2.9] | 0.2192 | 0.0765 | 0.0442 | 0.0088 |
| (2.9,3.61] | REF |  | REF |  |
|  | | | | |
| **Age at first live birth\*** | | | | |
| [17.7,21.6] | REF |  | 0.0014 | 0.0146 |
| (21.6,22.1] | 0.0763 | 0.0303 | REF |  |
| (22.1, 22.9] | 0.1091 | 0.0289 | 0.0037 | 0.0092 |
| (22.9,23.5] | 0.1198 | 0.0299 | 0.01 | 0.0104 |
| (23.5,24.3] | 0.0759 | 0.0314 | 0.0011 | 0.0126 |
|  |  |  |  |  |

Supplemental Table 3: Log-relative risk (log-RR) estimates for breast cancer incidence and 95% confidence intervals (CIs) from Poisson models that include each risk factor marginally, from separate models fit to white women and black women.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor** | **Women ages <50** | | **Women ages ≥50** | |
|  | **White** | **Black** | **White** | **Black** |
|  | **Log-RR (StdErr)** | **Log-RR (StdErr)** | **Log-RR (StdErr)** | **Log-RR (StdErr)** |
| **BMI** | | | | |
| [21.8,25.3] | REF | REF | EMPTY | REF |
| (25.3, 25.9] | -0.06 (0.02) | -0.18 (0.05) | REF | 0.02 (0.05) |
| (25.9, 26.4] | -0.06 (0.03) | -0.17 (0.06) | 0.01 (0.02) | 0.02 (0.04) |
| (26.4, 27.2] | -0.03 (0.03) | -0.15 (0.07) | 0.01 (0.03) | 0.05 (0.04) |
| (27.2, 28.1] | -0.05 (0.05) | -0.23 (0.10) | 0.05 (0.03) | 0.04 (0.05) |
| **Age at menarche** | | | | |
| [12.3, 12.6] | -0.02 (0.03) | -0.04 (0.05) | 0.03 (0.02) | 0.05 (0.03) |
| (12.6, 12.7] | -0.04 (0.03) | -0.01 (0.05) | 0.03 (0.02) | -0.04 (0.03) |
| (12.7, 12.8] | -0.05 (0.03) | 0.02 (0.05) | 0.03 (0.02) | -0.02 (0.02) |
| (12.8, 13.1] | -0.07 (0.03) | -0.01 (0.06) | -0.01 (0.01) | -0.01 (0.02) |
| (13.1, 13.6] | REF | REF | REF | REF |
| **Number of births** | | | | |
| [0.29, 1.48] | 0.30 (0.06) | 0.48 (0.15) | EMPTY | -0.15 (0.05) |
| (1.48, 2.01] | 0.28 (0.05) | 0.48 (0.15) | -0.01 (0.02) | -0.06 (0.03) |
| (2.01, 2.58] | 0.24 (0.05) | 0.49 (0.15) | 0.04 (0.01) | 0.01 (0.02) |
| (2.58, 2.9] | 0.16 0(.06) | 0.34 (0.14) | 0.03 (0.01) | 0.01 (0.02) |
| (2.9,3.61] | REF | REF | REF | REF |
| **Age at first live birth\*** | | | | |
| [17.7,21.6] | -0.06 (0.04) | -0.02 (0.07) | 0.03 (0.01) | 0.01 (0.02) |
| (21.6,22.1] | REF | REF | REF | REF |
| (22.1, 22.9] | 0.04 (0.02) | 0.03 (0.04) | 0.00 (0.01) | 0.04 (0.02) |
| (22.9,23.5] | 0.07 (0.02) | 0.06 (0.05) | 0.01 (0.01) | 0.05 (0.02) |
| (23.5,24.3] | 0.01 (0.02) | 0.00 (0.05) | -0.01 (0.01) | 0.01 (0.02) |

Supplemental Table 4: Values of percent relative difference in incidence,  , for black women, with standard errors in parentheses.a

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Values of | | | | |
| **Risk factor** | **Age** | **1980-1994** | **1995-2011** | **1980-2011** |
| **BMI** | 35-39 | -12.59 (3.65) | -18.75 (8.10) | -15.84 (5.78) |
|  | 40-44 | -14.69 (4.76) | -20.97 (9.57) | -18.00 (7.15) |
|  | 45-49 | -15.77 (5.18) | -22.11 (10.18) | -19.12 (7.69) |
|  | 50-54 | 1.15 (2.39) | 2.61 (3.28) | 1.98 (2.84) |
|  | 55-59 | 1.52 (2.56) | 2.97 (3.47) | 2.35 (3.03) |
|  | 60-64 | 0.97 (2.56) | 2.43 (3.35) | 1.80 (2.95) |
|  | 65-69 | 0.94 (2.44) | 2.41 (3.43) | 1.78 (2.95) |
| **Age at menarche** | 35-39 | -0.47 (4.35) | -1.41 (4.71) | -0.96 (4.53) |
|  | 40-44 | -0.53 (3.96) | -1.47 (4.33) | -1.02 (4.14) |
|  | 45-49 | -0.62 (4.19) | -1.55 (4.53) | -1.11 (4.36) |
|  | 50-54 | -0.98 (1.10) | -2.33 (1.74) | -1.76 (1.46) |
|  | 55-59 | -1.17 (1.29) | -2.52 (1.97) | -1.95 (1.67) |
|  | 60-64 | -1.02 (1.08) | -2.37 (1.74) | -1.79 (1.45) |
|  | 65-69 | 0.74 (1.09) | -0.59 (1.48) | -0.02 (1.28) |
| **Number of births** | 35-39 | 37.36 (8.88) | 38.49 (9.13) | 37.95 (9.01) |
|  | 40-44 | 37.11 (8.81) | 38.24 (9.03) | 37.702 (8.92) |
|  | 45-49 | 37.36 (8.86) | 38.48 (9.08) | 37.95 (8.97) |
|  | 50-54 | -2.28 (1.68) | -4.08 (2.39) | -3.308 (2.08) |
|  | 55-59 | -0.31 (1.08) | -2.08 (1.76) | -1.33 (1.46) |
|  | 60-64 | 2.13 (1.04) | 0.40 (1.31) | 1.14 (1.14) |
|  | 65-69 | 1.97 (0.70) | 0.24 (0.93) | 0.98 (0.75) |
| **Age at first live birth\*** | 35-39 | 1.38 (3.70) | 1.49 (5.21) | 1.44 (4.54) |
| \* starts in 1983 | 40-44 | 1.39 (3.48) | 1.50 (4.96) | 1.45 (4.29) |
|  | 45-49 | 3.04 (2.79) | 3.15 (4.01) | 3.10 (3.43) |
|  | 50-54 | 2.30 (1.11) | 2.45 (1.30) | 2.39 (1.20) |
|  | 55-59 | 1.75 (0.95) | 1.90 (0.95) | 1.84 (0.91) |
|  | 60-64 | 1.97 (0.91) | 2.12 (0.99) | 2.06 (0.92) |
|  | 65-69 | 2.73 (1.16) | 2.88 (1.12) | 2.82 (1.11) |

aResults in the table were based on separate models for black women aged <50 and >=50 years.

Supplemental Table 5: Values of percent relative difference in incidence,  , for white women, with standard errors in parentheses.a

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Values of | | | | |
| **Risk factor** | **Age** | **1980-1994** | **1995-2011** | **1980-2011** |
| **BMI** | 35-39 | -3.45 (1.37) | -3.51 (2.66) | -3.48 (2.03) |
|  | 40-44 | -3.97 (1.85) | -4.03 (3.14) | -4.01 (2.51) |
|  | 45-49 | -3.88 (2.22) | -3.94 (3.57) | -3.91 (2.92) |
|  | 50-54 | 1.89 (1.95) | 4.90 (2.69) | 3.56 (2.33) |
|  | 55-59 | 2.20 (2.14) | 5.20 (2.85) | 3.87 (2.50) |
|  | 60-64 | 2.05 (2.11) | 5.05 (2.82) | 3.72 (2.47) |
|  | 65-69 | 0.63 (2.03) | 3.68 (2.68) | 2.33 (2.35) |
| **Age at menarche** | 35-39 | -4.11 (2.85) | -4.50 (2.90) | -4.32 (2.87) |
|  | 40-44 | -3.69 (2.97) | -4.08 (3.01) | -3.90 (2.98) |
|  | 45-49 | -4.08 (2.76) | -4.48 (2.84) | -4.29 (2.79) |
|  | 50-54 | 1.10 (0.87) | 2.91 (1.61) | 2.11 (1.28) |
|  | 55-59 | 0.67 (0.76) | 2.49 (1.48) | 1.68 (1.15) |
|  | 60-64 | 0.52 (0.65) | 2.34 (1.37) | 1.53 (1.04) |
|  | 65-69 | -1.15 (0.46) | 0.71 (0.95) | -0.12 (0.66) |
| **Number of births** | 35-39 | 22.55 (3.76) | 25.17 (4.05) | 23.94 (3.90) |
|  | 40-44 | 21.60 (3.64) | 24.25 (3.92) | 23.01 (3.78) |
|  | 45-49 | 21.05 (3.62) | 23.72 (3.87) | 22.47 (3.74) |
|  | 50-54 | 1.78 (0.10) | 1.33 (1.32) | 1.53 (1.17) |
|  | 55-59 | 2.73 (0.73) | 2.28 (0.95) | 2.48 (0.84) |
|  | 60-64 | 3.30 (0.70) | 2.86 (0.82) | 3.06 (0.75) |
|  | 65-69 | 2.15 (0.54) | 1.70 (0.51) | 1.90 (0.49) |
| **Age at first live birth\*** | 35-39 | 3.68 (1.42) | 3.15 (2.27) | 3.38 (1.85) |
| \* starts in 1983 | 40-44 | 2.71 (1.35) | 2.18 (2.20) | 2.41 (1.78) |
|  | 45-49 | 2.63 (1.10) | 2.10 (1.90) | 2.33 (1.49) |
|  | 50-54 | -0.20 (0.71) | -0.07 (0.66) | -0.12 (0.67) |
|  | 55-59 | 0.52 (0.51) | 0.65 (0.56) | 0.60 (0.53) |
|  | 60-64 | 0.42 (0.40) | 0.55 (0.44) | 0.50 (0.41) |
|  | 65-69 | 0.48 (0.44) | 0.62 (0.39) | 0.56 (0.39) |

aResults in the table were based on separate models for white women aged <50 and >=50 years.

**Supplemental Material: Variance calculation for the percent relative difference**

Here we describe how to estimate the variance of, where parameters are replaced by their estimates from fitting nested Poisson models. We let  index the  cross-classified age x period units for age groupsand periods

We have independent Poisson counts . The mean levels of a covariate *X*, e.g. BMI, are categorized into levels  For age, period and the covariate, level 0 is the referent level. Let be a  vector of indicator variables, which are zero unless  corresponds to an age group  , in which case that indicator is 1. Similarly,  is a vector indicator variables, of which at most one is 1, if  corresponds to some period  Finally is a vector of indicator variables only one of which is 1 if the mean covariate level in cell  falls in some level  Let  be the  column vector of age parameters,  be the  column vector of period parameters, and  be the  column vector of covariate parameters. Let  be person-years in cell  that are included as an offset in the model. First, we fit Poisson models to the event data that only included age and period. The expected Poisson count is , where

 (1)

We then add terms for risk factor *X* for the age and cohort group that corresponds to index *i*:

 (2)

Under the full model (2), we obtain maximum likelihood estimates (MLEs) from PROC GENMOD, SAS 9.3., which also provides a scale parameter estimate, (option SCALE=PEARSON); standard errors of the parameters  have been multiplied by this scale to account for over-dispersion. The estimated covariance matrix of  is  where  is the unscaled estimated Fisher information from the full model in (2). Likewise,  for the model (1). The score equations for the full model are



For the restricted model given in (1) we have the same score equations (3)- (5) except that replaces  In the absence of over-dispersion, the estimated covariances of the unrestricted and restricted scores are given by the estimated Fisher information matrices,  and  Let  be a row vector for the null design matrix that corresponds to cell , and let  be the corresponding row vector for the full model. Note that the first elements of these vectors are 1 because they represent the intercepts. Then, under Poisson sampling, the  covariance between the restricted and unrestricted scores is estimated by  because  is an estimate of its Poisson variance, and are independent. Hence, under Poisson sampling without over-dispersion, the estimated covariance matrix for the scores from both models is Allowing for over-dispersion, this becomes.

From a Taylor expansion, and letting denote the  vector of all scores,

 , leading to 

The variance of  is then computed based on  and the delta method. We computed the row vector of partial derivatives  by numerical differentiation, and then calculated 