## human

## SUPPLEMENTARY DATA

## Supplementary Table SI Characteristics of women with and without children.

| Characteristic | Had children$N=35479$ |  | Had no children $\mathbf{N}=\mathbf{7 6 5 6}$ |  |
| :---: | :---: | :---: | :---: | :---: |
|  | N | \% | N | \% |
| Education |  |  |  |  |
| High school or less | 6074 | 17.1 | 605 | 7.9 |
| Some college | 12732 | 35.9 | 1921 | 25.1 |
| Bachelor degree | 8977 | 25.3 | 2309 | 30.2 |
| Master's/PhD | 7693 | 21.7 | 2821 | 36.8 |
| Missing | 3 | 0.0 | 0 | - |
| Marital status at interview |  |  |  |  |
| Never legally married | 370 | 1.0 | 1717 | 22.4 |
| Ever married/ cohabiting | 35106 | 99.0 | 5936 | 77.5 |
| Currently married ${ }^{\text {a }}$ | 26482 | 75.4 | 3975 | 67.0 |
| Living as married ${ }^{\text {a }}$ | 1055 | 3.0 | 636 | 10.7 |
| Widowed ${ }^{\text {a }}$ | 2084 | 5.9 | 268 | 4.5 |
| Separated/divorced ${ }^{\text {a }}$ | 5485 | 15.6 | 1057 | 17.8 |
| Missing | 3 | 0.0 | 3 | 0.0 |
| Household income at interview |  |  |  |  |
| <\$20000 | 1535 | 4.3 | 341 | 4.5 |
| \$20 000-\$49 999 | 7238 | 20.4 | 1604 | 21.0 |
| \$50 000-\$99 999 | 13852 | 39.0 | 3020 | 39.4 |
| \$100 000-\$200 000 | 8938 | 25.2 | 1874 | 24.5 |
| > \$200 000 | 2478 | 7.0 | 550 | 7.2 |
| Missing | 1438 | 4.1 | 267 | 3.5 |
| Homosexual | 120 | 0.3 | 407 | 5.3 |
| Missing | 9 | 0.0 | 10 | 0.1 |
| Tried for > I year without conceiving | 3689 | 10.4 | 1327 | 17.3 |
| Missing ${ }^{\text {b }}$ | 4636 | 13.1 | 810 | 10.6 |
| Ever took fertility medications | 2274 | 6.4 | 740 | 9.7 |
| Missing | 17 | 0.0 | 13 | 0.2 |
| Prenatal exposure to DES ${ }^{\text {c }}$ | 731 | 2.1 | 291 | 3.8 |
| Missing | 5181 | 14.6 | 1257 | 16.4 |

${ }^{\text {aP Percent values are calculated excluding women who reported never having been }}$ married.
${ }^{\mathrm{b}}$ In total, $8 \%$ of the women did not take part in the follow-up in which this question was asked. Among those who did, 5.3 and $3.8 \%$ of those with and without children, respectively, did not answer the question.
${ }^{\text {c}}$ DES $=$ diethylstilbestrol. Women reported whether mother had taken DES while pregnant with them. Options were: definitely yes, probably yes (categorized as yes) and definitely not, or probably not (categorized as no).

Supplementary Table SII Sibling-matched analysis of 802 pairs of full sisters discordant for childlessness. Odds ratio (OR) and $95 \% \mathrm{Cl}$ from conditional logistic regression.

| Mother's age at birth | OR | $\mathbf{( 9 5 \% ~ C I )}$ |
| :--- | :---: | :---: |
| 20 | 0.77 | $(0.40-1.51)$ |
| $20-24$ | 1.00 |  |
| $25-29$ | 1.18 | $(0.89-1.56)$ |
| $30-34$ | 1.36 | $(1.00-1.84)$ |
| $35+$ | 1.71 | $(1.20-2.43)$ |

Test for trend (I d.f.): $P=0.00 \mathrm{I} 3$.

## Supplementary Table SIII Sibling-matched analysis

 restricted to 47 I pairs of sisters born $\leq 5$ years apart. OR and $95 \% \mathrm{Cl}$ from conditional logistic regression.| Mother's age at birth | OR | $\mathbf{( 9 5 \% ~ C I )}$ |
| :--- | :---: | :---: |
| $<20$ | 0.63 | $(0.26-1.52)$ |
| $20-24$ | 1.00 |  |
| $25-29$ | 1.56 | $(1.04-2.35)$ |
| $30-34$ | 1.89 | $(1.09-3.28)$ |
| $35+$ | 2.12 | $(0.98-4.57)$ |

Test for trend (I d.f.): $P=0.0163$
d.f. $=$ Degrees of freedom.


Supplementary Figure S I Identification of analytic sample.

## Stratified by highest household education, childhood ${ }^{\text {a }}$



Supplementary Figure S2 Relative risk (RR) and $95 \% \mathrm{Cl}$ of childlessness as a function of mother's age at birth, by highest household education when the participant was 13 . Vertical dashed lines at 0.77 and I .3 are included to facilitate comparisons. ${ }^{\text {a Models include: total number of siblings, birth }}$ order, race/ethnicity, income level growing up, and 5 -year birth cohort. ${ }^{\text {b }}$ Adjusted predictive marginal probabilities of childlessness (in \%). 'Includes associate degree.


Supplementary Figure S3 Association of mother's age at birth with selected predictors of childlessness in daughters. Left panel: RR (95\% CI) of never having been legally married (top); RR ( $95 \% \mathrm{Cl}$ ) of having obtained a postgraduate diploma (bottom). Right panel: RR ( $95 \% \mathrm{Cl}$ ) of having ever tried to conceive without success for $>$ I year (top); RR ( $95 \% \mathrm{Cl}$ ) of having ever taken fertility medications (bottom). Vertical dashed lines at 0.77 and 1.3 are included to facilitate comparisons. ${ }^{\text {a }}$ Models include: total number of siblings, birth order, race/ethnicity, income level growing up, highest household education when participant was 13 , and 5 -year birth cohort. ${ }^{\text {b }}$ Adjusted predictive marginal probabilities of the outcome (in \%) ${ }^{\text {C Logistic regression }}$ model. RR and $95 \% \mathrm{Cl}$ estimated from predictive marginal probabilities and standard errors. ${ }^{\circ}$ Women who reported never having been married were excluded. The question ('Have you ever tried for more than one year to become pregnant and did not get pregnant?') was asked at the triennial follow-up. ${ }^{e}$ Women born before 1945 and those who had never married were excluded from this analysis. The outcome is having used fertility medication on at least one occasion.

Different subsets of women ${ }^{\text {a }}$
(\%) ${ }^{\text {b }} \quad$ RR $(95 \% \mathrm{Cl})$
Age 56+ at follow-up, no breast cancer $\mathbf{d x}(\mathrm{n}=35,844)^{\text {C }}$


Never married $(\mathrm{n}=2,040)^{\text {d }}$


With prenatal/early-life factors

$$
(\%)^{b} \quad \text { RR }(95 \% \mathrm{Cl})
$$

Adjusted for prenatal esposure: to DES \& maternal smoking ( $\mathrm{n}=35,434)^{\text {e }}$


Adjusted for feeding as an infant (breastfed, soy formula) ( $n=34,139)^{f}$


Supplementary Figure S4 Relative risk (RR) and $95 \% \mathrm{Cl}$ of childlessness as a function of mother's age at birth. Left panel: Analysis restricted to women with reproductive history updated at age 56 or later who remained free of breast cancer through age 55 (top); analysis restricted to women who reported never having been married (bottom). Right panel: Adjusted for prenatal exposure to DES and maternal smoking (top); adjusted for having been breastfed as an infant and having been fed soy formula (bottom). Vertical dashed lines at 0.77 and 1.3 are included to facilitate comparisons. ${ }^{\text {a }}$ Models include: total number of siblings, birth order, race/ethnicity, income level growing up, highest household education when participant was I3, and 5 -year birth cohort. ${ }^{\text {b }}$ Adjusted predictive marginal probabilities of childlessness (in \%). ${ }^{\text {c } 6998}$ women were excluded because the most recent information on pregnancy referred to before age 56, and 293 because they had developed breast cancer (or in situ lobular lesions) before age 56. ${ }^{\text {d Logistic }}$ regression model. RR and $95 \% \mathrm{Cl}$ estimated from predictive marginal probabilities and standard errors. ${ }^{\text {e Model includes factors listed in ' } a \text { ', plus pre- }}$ natal exposure to DES (yes/no, see footnote 'c' to Supplementary Table SI) and maternal smoking (4 levels: definitely yes, probably yes, probably not, definitely not). Exposure to DES and smoking was missing for 15 and $4.9 \%$, respectively. 'Model includes factors listed in 'a', plus breastfeeding (missing for $7.6 \%$ ) and having received soy formula (missing for 17.3\%). Both factors were categorized as yes (definitely yes + probably yes) or no (definitely not + probably not).


Supplementary Figure S5 Proportion childess as a function of the number of older sisters, stratified by total number of older siblings (brothers + sisters), full siblings. ${ }^{\text {a }}$ Category includes 111 women (out of 4429 with 3 older siblings), 18 of whom were childless. ${ }^{\text {b }}$ Category includes 42 women (out of 5320 with $4+$ older siblings), II of whom were childless.

