**Supplementary Data**

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| **Supplementary Table S1. Baseline characteristics of premenopausal controls in the New England Case Control Study (NEC) and European Prospective Investigation into Nutrition and Cancer Study (EPIC)** |
| **Variables** | NEC  | EPIC  |
| **N** | 815 | 473 |
| **CA125, U/ml (SD)** | 17.3 (10.4) | 14.9 (8)b |
| **Age, years (SD)** | 42 (8) | 46(6) |
| **White race (%)** | 95 | 100 |
| **BMI, kg/m2 (SD)** | 25 (5) | 25 (4) |
| **Height, cm (SD)** | 164 (7) | 162 (6) |
| **Smoking (%)** | 48 | 44 |
| **Age at menarche, years (SD)** | 12.6 (2.0) | 12.9 (1.5) |
| **Oral contraceptive use (%)** | 78 | 69 |
| **Current hormone usec (%)** | 18 | 9 |
| **Blood drawn at early follicular phase (%)** | 15 | 15 |
| **Infertility (%)** | 20 | 5 |
| **Miscarriages (%)** | 23 | 22 |
| **Ectopic pregnancy (%)** | 2 | NA |
| **Parous (%)** | 74 | 89 |
| **Tubal ligation (%)** | 17 | 37d |
| **Intrauterine device use (%)** | 15 | NA |
| **Unilateral oophorectomy (%)** | 1 | 2 |
| **Endometriosis (%)** | 6 | NA |
| **Fibroids (%)** | 10 | NA |
| **Prior personal cancer diagnosis (%)** | 5 | 0 |
| **Family history of ovarian cancer (%)** | 2 | NA |
| **Genital powder use (%)** | 41 | NA |
| **Caffeine intake, mg (SD)**  | 215 (177) | NA |
| aMean and standard deviation (SD) is shown for continuous variables and percentage is shown for dichotomous variables |
| brecalibrated CA125 value |  |  |
| c includes oral contraceptives and injections |  |  |
| dmissing 84% |  |  |

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| **Supplementary Table S2. Association between predictors and high vs low CA125 in premenopausal women in the New England Case Control Study (n=815)** |
|  | **CA125 < 35 U/ mL (n=769)** | **CA125 ≥ 35 U/ mL (n=46)** | **Age-adjusted Odds Ratio[95%CI]** |
| **Variables** | **N(%)** | **N(%)** |   |
| **Age, years** |  |  |  |
|  < 30 | 67 (9) | 2 (4) | ref |
|  30- 39 | 195 (25) | 20 (43) | 3.44 [0.78, 15.09] |
|  40- 49 | 357 (46) | 17 (37) | 1.60 [0.36, 7.07] |
|  50+ | 150 (20) | 7 (15) | 1.56 [0.32, 7.72] |
|  P-trend |  |  | 0.33 |
| **Race** |  |  |  |
|  white | 36 (5) | 1 (2) | ref |
|  non-white | 733 (95) | 45 (98) | 0.43 [0.06, 3.22] |
| **BMI, kg/m2** |  |  |  |
|  < 20 | 70 (9) | 6 (13) | 1.40 [0.55, 3.57] |
|  20- < 25 | 391 (51) | 23 (50) | ref |
|  25- < 30 | 197 (26) | 9 (20) | 0.80 [0.36, 1.76] |
|  30- < 35 | 79 (10) | 5 (11) | 1.12 [0.41, 3.05] |
|  35+ | 32 (4) | 3 (7) | 1.69 [0.48, 6.00] |
|  P-trend |  |  | 0.84 |
| **Height, cm** |  |  |  |
|  < 160 | 176 (23) | 6 (13) | ref |
|  160- < 165 | 205 (27) | 13 (28) | 1.90 [0.71, 5.12] |
|  165- < 170 | 219 (28) | 12 (26) | 1.66 [0.61, 4.52] |
|  170- < 175 | 115 (15) | 13 (28) | 3.35 [1.24, 9.08] |
|  175+ | 54 (7) | 2 (4) | 1.12 [0.22, 5.73] |
|  P-trend |  |  | 0.17 |
| **Smoking** |  |  |  |
|  never | 402 (52) | 19 (41) | ref |
|  former | 245 (32) | 24 (52) | 2.21 [1.18, 4.16] |
|  current | 122 (16) | 3 (7) | 0.49 [0.14, 1.69] |
| **Smoking status and duration** |  |  |  |
|  never smokers | 402 (52) | 19 (41) | ref |
|  < 15 packyears among former | 198 (26) | 21 (46) | 2.35 [1.23, 4.49] |
|  15+ packyears among former | 47 (6) | 3 (7) | 1.60 [0.44, 5.73] |
|  < 15 packyears among current | 68 (9) | 1 (2) | 0.27 [0.04, 2.07] |
|  15+ packyears among current | 54 (7) | 2 (4) | 0.82 [0.19, 3.63] |
| **Age at menarche, years** |  |  |  |
|  ≤ 12  | 357 (46) | 29 (63) | ref |
|  13+ | 411 (54) | 17 (37) | 0.51 [0.28, 0.95] |
| **Oral contraceptive use** |  |  |  |
|  Never | 171 (22) | 9 (20) | ref |
|  Ever | 598 (78) | 37 (80) | 1.19 [0.56, 2.51] |
| **Duration of oral contraceptive use among ever users, years** |  |  |  |
|  < 2 | 128 (21) | 12 (32) | ref |
|  2 - 3 | 127 (21) | 6 (16) | 0.48 [0.18, 1.33] |
|  4 - 5 | 97 (16) | 6 (16) | 0.67 [0.24, 1.86] |
|  6 - 9 | 117 (20) | 8 (22) | 0.66 [0.26, 1.69] |
|  10+ | 129 (22) | 5 (14) | 0.42 [0.14, 1.23] |
|  P-trend |  |  | 0.22 |
| **Current hormone usea** |  |  |  |
|  no | 401 (81) | 26 (96) | ref |
|  yes | 93 (19) | 1 (4) | 0.16 [0.02, 1.22] |
| **Menstrual phase at time of blood draw (days)** |  |  |  |
|  early follicular (0 - 7) | 116 (15) | 10 (22) | ref |
|  late follicular (8 - 11) | 50 (7) | 6 (13) | 1.42 [0.49, 4.12] |
|  peri-ovulatory (12 - 16) | 71 (9) | 2 (4) | 0.32 [0.07, 1.52] |
|  luteal (17 - 35) | 150 (20) | 5 (11) | 0.38 [0.13, 1.15] |
|  long cycle (36+) | 60 (8) | 3 (7) | 0.64 [0.17, 2.43] |
|  irregular | 64 (8) | 1 (2) | 0.17 [0.02, 1.38] |
|  missing | 258 (34) | 19 (41) | 0.84 [0.38, 1.86] |
| **Infertility** |  |  |  |
|  none/male factor | 631 (82) | 38 (83) | ref |
|  endometriosis | 10 (1) | 3 (7) | 4.85 [1.28, 18.41] |
|  tubal/uterus/ovulatory | 26 (3) | 1 (2) | 0.67 [0.09, 5.05] |
|  unknown | 102 (13) | 4 (9) | 0.68 [0.24, 1.95] |
| **Number of miscarriages** |  |  |  |
|  0 | 583 (76) | 42 (91) | ref |
|  1 | 134 (17) | 3 (7) | 0.32 [0.10, 1.04] |
|  2+ | 52 (7) | 1 (2) | 0.27 [0.04, 2.02] |
| **Ectopic pregnancy** |  |  |  |
|  no | 750 (98) | 45 (98) | ref |
|  yes | 19 (2) | 1 (2) | 0.92 [0.12, 7.01] |
| **Parity** |  |  |  |
|  0 | 195 (25) | 19 (41) | ref |
|  1 | 135 (18) | 5 (11) | 0.38 [0.14, 1.08] |
|  2 | 251 (33) | 13 (28) | 0.54 [0.25, 1.18] |
|  3+ | 188 (24) | 9 (20) | 0.51 [0.21, 1.20] |
| **Tubal ligation** |  |  |  |
|  no | 630 (82) | 44 (96) | ref |
|  yes | 139 (18) | 2 (4) | 0.21 [0.05, 0.90] |
| **Intrauterine device use** |  |  |  |
|  never | 650 (85) | 39 (85) | ref |
|  ever | 119 (15) | 7 (15) | 1.08 [0.46, 2.52] |
| **Unilateral oophorectomy** |  |  |  |
|  no | 763 (99) | 45 (98) | ref |
|  yes | 6 (1) | 1 (2) | 2.76 [0.32, 23.46] |
| **Endometriosis** |  |  |  |
|  no | 725 (94) | 39 (85) | ref |
|  yes | 44 (6) | 7 (15) | 2.99 [1.26, 7.07] |
| **Fibroids** |  |  |  |
|  no | 696 (91) | 41 (89) | ref |
|  yes | 73 (9) | 5 (11) | 1.27 [0.48, 3.36] |
| **Prior personal cancer diagnosis** |  |  |  |
|  no | 740 (96) | 38 (83) | ref |
|  yes | 29 (4) | 8 (17) | 5.91 [2.49, 14.02] |
| **Family history of ovarian cancer** |  |  |  |
|  no | 753 (98) | 42 (91) | ref |
|  yes | 16 (2) | 4 (9) | 4.66 [1.49, 14.64] |
| **Genital powder use** |  |  |  |
|  no use | 455 (59) | 29 (63) | ref |
|  body use | 146 (19) | 11 (24) | 1.22 [0.59, 2.50] |
|  genital use | 168 (22) | 6 (13) | 0.58 [0.24, 1.45] |
| **Caffeine intake, mg** |  |  |  |
|  < 72 | 187 (25) | 11 (24) | ref |
|  72- < 171 | 189 (25) | 9 (20) | 0.84 [0.34, 2.08] |
|  171- < 348.9 | 186 (25) | 12 (27) | 1.16 [0.50, 2.72] |
|  348.9+ | 185 (25) | 13 (29) | 1.25 [0.54, 2.87] |
|  P-trend |   |   | 0.46 |
| aincludes oral contraceptives and injections |  |  |

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| **Supplementary Table 3. Linear CA125 prediction model among premenopausal women applied in complete case and multiple imputed datasets in the New England Case Control Study (NEC)** |
| **Selected predictors** | Complete case in NEC (n=498)a b | Multiple imputation in NEC(n=815)a |
|  | % change | SE | *p*-value | % change | SE | *p*-value |
| **Age, years** |   |   |   |   |   |   |
|  **<30** | -19% | 0.09 | 0.02 | -19% | 0.07 | 0.003 |
|  **30-<40** | ref |  |  | ref |  |  |
|  **40-<50** | -6% | 0.05 | 0.29 | -7% | 0.04 | 0.11 |
|  **50+** | -7% | 0.06 | 0.29 | -9% | 0.05 | 0.06 |
| **Non-white race** | -26% | 0.11 | 0.01 | -12% | 0.08 | 0.13 |
| **Tubal ligation** | -10% | 0.06 | 0.08 | -11% | 0.05 | 0.01 |
| **Endometriosis** | 40% | 0.09 | 0.0002 | 20% | 0.07 | 0.01 |
| **Menstrual phase at time of blood draw** |  |  |  |  |  |  |
|  **on hormonal contraceptives** | -28% | 0.07 | <.0001 | -29% | 0.07 | <.0001 |
|  **regular menstruation + blood draw at early follicular phase** | ref |  |  | ref |  |  |
|  **regular menstruation  + blood draw at other phase** | -17% | 0.05 | 0.001 | -17% | 0.06 | 0.001 |
|  **irregular menstrual cycle** | -28% | 0.10 | 0.002 | -27% | 0.11 | 0.004 |
|  **missing time at blood draw**  |   |   |   |   |   |   |
| **Fibroids** | 17% | 0.07 | 0.03 | 12% | 0.06 | 0.06 |
| **R-square** | 0.11c | 0.07 |
| aadjusted for study and center |  |  |  |  |  |  |
| bexclude missing age at menarche(n=1), caffeine intake(n=23), and menstrual cycle length(n=23), menstrual phase at time at (n=270) |
| cr-square taking away the effect of center and study phase |  |  |  |  |  |

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| **Supplementary Table 4. Dichotomous CA125 prediction model of high CA125 ( ≥ 35 U/ mL) applied in complete case, multiple imputed datasets, and using collapsed menstrual phase variables in premenopausal women in the New England Case Control Study (NEC)** |
| **Selected predictors** | Complete case in NEC (n=498)a b | Multiple imputation in NEC (n=815)a | Model in NEC using collapsed variable(n=768)a c |
|  | OR | 95%CI | OR | 95%CI | OR | 95%CI |
| **Age, years\*** |   |   |   |   |   |   |
|  **< 30** | 0.46 | 0.05, 4.36 | 0.34 | 0.07, 1.63 | 0.33 | 0.07, 1.52 |
|  **30- < 40** | ref |  | ref |  | ref |  |
|  **40- < 50** | 0.51 | 0.17, 1.55 | 0.34 | 0.16, 0.75 | 0.38 | 0.17, 0.82 |
|  **50+** | 0.56 | 0.15, 2.07 | 0.36 | 0.14, 0.94 | 0.39 | 0.14, 1.11 |
| **Tubal ligation** | 0.12 | 0.01, 1.12 | 0.17 | 0.04, 0.77 | 0.16 | 0.03, 0.73 |
| **Endometriosis** | 7.07 | 1.96, 25.54 | 2.93 | 1.05, 8.14 | 2.92 | 1.06, 8.05 |
| **Prior personal cancer diagnosis** | 6.03 | 1.56, 23.35 | 5.66 | 1.92, 16.63 | 5.92 | 1.88, 18.62 |
| **Family history of ovarian cancer** | 11.09 | 1.91, 64.47 | 12.50 | 3.34, 46.86 | 11.08 | 2.98, 41.14 |
| **Number of miscarriages** |  |  |  |  |  |  |
|  **0** | ref |  | ref |  | ref |  |
|  **1** | 0.35 | 0.08, 1.59 | 0.20 | 0.06, 0.71 | 0.25 | 0.07, 0.92 |
|  **2+** | 0.36 | 0.04, 3.70 | 0.18 | 0.03, 1.07 | 0.19 | 0.02, 1.61 |
| **Menstrual phase at time of blood draw** |  |  |  |  |  |  |
|  **regular menstruation + blood draw at early follicular phase** | ref |  | ref |  | ref |  |
|  **on hormonal contraceptivesd** | 0.07 | 0.01, 0.69 | 0.07 | 0.01, 0.59 | 0.37 | 0.15, 0.93 |
|  **regular menstruation + blood draw at other phase /irregular menstrual cycle** | 0.45 | 0.17, 1.18 | 0.45 | 0.15, 1.33 |
|  **missing time at blood draw**  |   |   |   |   | 0.59 | 0.08, 4.54 |
| **Smoking status** |  |  |  |  |  |  |
|  **Never** | ref |  | ref |  | ref |  |
|  **Former** | 1.19 | 0.39, 3.63 | 2.33 | 1.09, 5.01 | 2.05 | 0.93, 4.52 |
|  **Current** | 0.06 | <0.001, 3.79 | 0.09 | 0.01, 0.74 | 0.13 | 0.01, 1.58 |
|  **Pack-years among former smokers** | 1.00 | 0.91, 1.10 | 0.99 | 0.95, 1.03 | 0.99 | 0.94, 1.05 |
|  **Pack-years among current smokers** | 1.12 | 1.00, 1.26 | 1.10 | 1.03, 1.17 | 1.09 | 1.00, 1.18 |
| **AUC (95%CI)** | 0.84 (0.76, 0.93) | 0.84 | 0.82 (0.75, 0.89) |
| aadjusted for study and center |  |  |  |  |  |  |
| bexclude missing age at menarche(n=1), caffeine intake(n=23), and menstrual cycle length(n=23), menstrual phase at time at (n=270) |
| cexclude missing age at menarche(n=1), caffeine intake(n=23), and menstrual cycle length(n=23) |