Additional file 1 Education, K6 score, household income of the 2-year questionnaire respondents (N=80,468)

\*Chi-square test

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | 2-year questionnaire respondents | |  | Analyzed participants | |
|  | (N=80,468) | |  | (N=93,643) | |
|  | N | % |  | N | % |
| Mother’s education |  |  |  |  |  |
| EDC1 | 3,096 | 3.9 |  | 4,389 | 4.7 |
| EDC2 | 24,059 | 29.9 |  | 28,664 | 30.6 |
| EDC3 | 34,092 | 42.4 |  | 38,499 | 41.1 |
| EDC4 | 18,267 | 22.7 |  | 19,910 | 21.3 |
| Missing | 954 | 1.2 |  | 2,181 | 2.3 |
| Household income (10 thousand yen/year) |  |  |  |  |  |
| -199 | 3,785 | 4.7 |  | 4,820 | 5.2 |
| 200-399 | 25,287 | 31.4 |  | 29,378 | 31.4 |
| 400-599 | 24,894 | 30.9 |  | 28,177 | 30.1 |
| 600-799 | 12,251 | 15.2 |  | 13,642 | 14.6 |
| 800-999 | 5,102 | 6.3 |  | 5,677 | 6.1 |
| 1000- | 3,261 | 4.1 |  | 3,652 | 3.9 |
| Missing | 5,888 | 7.3 |  | 8,297 | 8.9 |
| Mother’s psychological distress |  |  |  |  |  |
| No | 76,519 | 95.1 |  | 88,072 | 94.1 |
| Yes | 2,624 | 3.3 |  | 3,231 | 3.5 |
| Missing | 1,325 | 1.7 |  | 2,340 | 2.5 |

EDC1: junior high school, EDC2: high school, EDC3: technical junior college, technical/vocational college, or EDC4: associate degree bachelor’s degree or postgraduate degree.

Additional file 2 Relationships between the variables and infant congenital heart defect

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | No CHD | | CHD | | P |
|  | N | % | N | % |  |
| Maternal age at delivery |  |  |  |  | 0.026 |
| -24 | 9,273 | 98.88 | 105 | 1.12 |  |
| 25-29 | 25,474 | 98.91 | 281 | 1.09 |  |
| 30-34 | 32,680 | 98.96 | 342 | 1.04 |  |
| 35-39 | 20,952 | 99.02 | 207 | 0.98 |  |
| 40- | 4,251 | 98.45 | 67 | 1.55 |  |
| Pre-pregnancy BMI |  |  |  |  | <0.001 |
| -18.4 | 14,463 | 98.71 | 189 | 1.29 |  |
| 18.5-24.9 | 68,009 | 99.02 | 674 | 0.98 |  |
| 25- | 10,042 | 98.64 | 138 | 1.36 |  |
| Mother’s education |  |  |  |  | 0.409 |
| EDC1 | 4,333 | 98.72 | 56 | 1.28 |  |
| EDC2 | 28,371 | 98.98 | 293 | 1.02 |  |
| EDC3 | 38,097 | 98.96 | 402 | 1.04 |  |
| EDC4 | 19,702 | 98.96 | 208 | 1.04 |  |
| Father’s education |  |  |  |  | 0.174 |
| EDC1 | 6,483 | 99.04 | 63 | 0.96 |  |
| EDC2 | 32,949 | 98.87 | 376 | 1.13 |  |
| EDC3 | 20,320 | 99.06 | 192 | 0.94 |  |
| EDC4 | 30,165 | 98.96 | 316 | 1.04 |  |
| Household income (thousand yen/year) |  |  |  |  | 0.518 |
| -199 | 4,764 | 98.84 | 56 | 1.16 |  |
| 200-399 | 29,057 | 98.91 | 321 | 1.09 |  |
| 400-599 | 27,885 | 98.96 | 292 | 1.04 |  |
| 600-799 | 13,500 | 98.96 | 142 | 1.04 |  |
| 800-999 | 5,628 | 99.14 | 49 | 0.86 |  |
| 1000- | 3,607 | 98.77 | 45 | 1.23 |  |
| Marital status |  |  |  |  | 0.045 |
| Married | 86,879 | 99.0 | 925 | 1.05 |  |
| Unmarried, divorced or bereavement | 4,131 | 98.6 | 58 | 1.38 |  |
| Mother’s alcohol intake |  |  |  |  | 0.016 |
| Non-drinker | 45,116 | 98.87 | 516 | 1.13 |  |
| Drinker during early pregnancy | 45,163 | 99.03 | 441 | 0.97 |  |
| Mother’s smoking status |  |  |  |  | 0.430 |
| Non-, ex-smoker | 74,089 | 98.95 | 789 | 1.05 |  |
| Smoker during pregnancy | 16,651 | 98.88 | 189 | 1.12 |  |
| Father’s smoking status |  |  |  |  | 0.587 |
| Non-, ex-smoker | 45,280 | 98.95 | 480 | 1.05 |  |
| Smoker during pregnancy | 44,109 | 98.91 | 485 | 1.09 |  |
| Parity |  |  |  |  | 0.142 |
| 0 | 38,478 | 98.85 | 447 | 1.15 |  |
| 1 | 33,808 | 99.00 | 343 | 1.00 |  |
| >2 | 17,996 | 98.97 | 187 | 1.03 |  |
| Infant’s sex |  |  |  |  | 0.003 |
| Girl | 45,054 | 98.83 | 533 | 1.17 |  |
| Boy | 47,572 | 99.03 | 466 | 0.97 |  |
| Plurality |  |  |  |  | <0.001 |
| Singleton | 91,766 | 99.0 | 972 | 1.05 |  |
| Multiplet | 875 | 96.7 | 30 | 3.31 |  |
| Fertility treatment |  |  |  |  | 0.011 |
| Spontaneous | 85,817 | 98.95 | 907 | 1.05 |  |
| Ovulation induction through medication | 2,561 | 98.58 | 37 | 1.42 |  |
| Artificial insemination or in vitro fertilization | 3,760 | 98.53 | 56 | 1.47 |  |
| Hypertensive disorder during pregnancy |  |  |  |  | <0.001 |
| No | 87,788 | 98.97 | 915 | 1.03 |  |
| Yes | 3,318 | 97.67 | 79 | 2.33 |  |
| Thyroid diseases during pregnancy |  |  |  |  | 0.051 |
| No | 89,393 | 98.93 | 969 | 1.07 |  |
| Yes | 1,223 | 98.31 | 21 | 1.69 |  |
| Diabetes mellitus during pregnancy /gestational diabetes | |  |  |  | <0.001 |
| No | 88,228 | 98.95 | 932 | 1.05 |  |
| Yes | 2,878 | 97.89 | 62 | 2.11 |  |
| Folic acid supplement at early pregnancy |  |  |  |  | 0.668 |
| No | 65,587 | 98.94 | 703 | 1.06 |  |
| Yes | 25,305 | 98.91 | 280 | 1.09 |  |
| Anti-depressant/anti-anxiety drug intake at early pregnancy | |  |  |  | 0.094 |
| No | 90,673 | 98.93 | 978 | 1.07 |  |
| Yes | 219 | 97.77 | 5 | 2.23 |  |
| Congenital heart diseases in the mother |  |  |  |  | 0.013 |
| No | 91,142 | 98.94 | 977 | 1.06 |  |
| Yes | 281 | 97.23 | 8 | 2.77 |  |
| Psychological distress in the mother |  |  |  |  | 0.036 |
| No | 87,145 | 98.95 | 927 | 1.05 |  |
| Yes | 3,184 | 98.55 | 47 | 1.45 |  |

EDC1: junior high school, EDC2: high school, EDC3: technical junior college, technical/vocational college, or EDC4: associate degree bachelor’s degree or postgraduate degree.

Additional file 3 Crude and adjusted ORs of combined maternal education and psychological distress

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Proportion\* | OR | 95%CI | | | P |  | OR | 95%CI | | | P |  | OR | 95%CI | | | P |
| Psychological distress(-) + ECD2-4 | 92.0% | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |
| Psychological distress(-) + ECD1 | 4.5% | 1.19 | 0.88 | - | 1.60 | 0.253 |  | 1.14 | 0.83 | - | 1.57 | 0.420 |  | 1.14 | 0.83 | - | 1.57 | 0.425 |
| Psychological distress(+) + ECD2-4 | 3.2% | 1.32 | 0.96 | - | 1.83 | 0.088 |  | 1.28 | 0.92 | - | 1.77 | 0.138 |  | 1.27 | 0.91 | - | 1.75 | 0.157 |
| Psychological distress(+) + ECD1 | 0.4% | 2.02 | 0.97 | - | 4.24 | 0.062 |  | 1.86 | 0.87 | - | 3.97 | 0.107 |  | 1.82 | 0.85 | - | 3.89 | 0.121 |

Junior high school: EDC1

\*Mean proportion of each category in the imputed 25 datasets

(Multiple imputation, N=93,643)

Model 1: All listed variables, maternal age, mother BMI, household income, father education, marital status, mother drinking habit, mother smoking, paternal smoking, parity, infant sex, plurality, fertility treatment, hypertensive disorder during pregnancy, thyroid diseases during pregnancy, diabetes mellitus during pregnancy /gestational diabetes, folic acid supplementation during early pregnancy, and mother congenital heart diseases are introduced.

Model 2: All the variables in Model 1 and anti-depressant intake are introduced.

Additional file 4 Crude and adjusted ORs of maternal education, psychological distress, and household income with 2-year outcomes

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Crude | | | | |  | Model 1 | | | | |  | Model 2 | | | | |
|  | Proportion\* | OR | 95%CI | | | P |  | OR | 95%CI |  |  | P |  | OR | 95%CI | | | P |
| Mother’s education |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| EDC1 | 4.9% | 1.03 | 0.78 | - | 1.36 | 0.829 |  | 0.92 | 0.67 | - | 1.26 | 0.608 |  | 0.92 | 0.67 | - | 1.26 | 0.599 |
| EDC2 | 31.5% | 1.05 | 0.91 | - | 1.23 | 0.501 |  | 0.96 | 0.81 | - | 1.15 | 0.669 |  | 0.96 | 0.81 | - | 1.15 | 0.667 |
| EDC3 | 42.0% | 1.01 | 0.87 | - | 1.17 | 0.886 |  | 0.96 | 0.83 | - | 1.12 | 0.647 |  | 0.96 | 0.83 | - | 1.12 | 0.648 |
| EDC4 | 21.7% | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |
| Household income (10 thousand yen/year) | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| -199 | 5.9% | 1.03 | 0.73 | - | 1.46 | 0.861 |  | 1.01 | 0.70 | - | 1.45 | 0.972 |  | 1.01 | 0.70 | - | 1.45 | 0.974 |
| 200-399 | 35.0% | 1.01 | 0.77 | - | 1.34 | 0.923 |  | 1.03 | 0.78 | - | 1.38 | 0.823 |  | 1.03 | 0.78 | - | 1.38 | 0.825 |
| 400-599 | 32.7% | 0.95 | 0.72 | - | 1.25 | 0.706 |  | 0.97 | 0.73 | - | 1.29 | 0.853 |  | 0.97 | 0.73 | - | 1.29 | 0.854 |
| 600-799 | 15.7% | 0.96 | 0.71 | - | 1.30 | 0.788 |  | 0.98 | 0.73 | - | 1.33 | 0.900 |  | 0.98 | 0.73 | - | 1.33 | 0.902 |
| 800-999 | 6.5% | 0.81 | 0.57 | - | 1.15 | 0.228 |  | 0.82 | 0.58 | - | 1.17 | 0.269 |  | 0.82 | 0.58 | - | 1.17 | 0.270 |
| 1000- | 4.2% | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |
| Psychological distress in the mother |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| No | 96.4% | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |
| Yes | 3.6% | 1.30 | 1.00 | - | 1.69 | 0.046 |  | 1.26 | 0.97 | - | 1.64 | 0.081 |  | 1.25 | 0.96 | - | 1.63 | 0.094 |

(Multiple imputation, N=93,643)

EDC1: junior high school, EDC2: high school, EDC3: technical junior college, technical/vocational college, or EDC4: associate degree bachelor’s degree or postgraduate degree.

\*Mean proportion of each category in the imputed 25 datasets

Model 1: All listed variables, maternal age, ma BMI, father education, marital status, mother drinking habit, mother smoking, paternal smoking, parity, infant sex, plurality, fertility treatment, hypertensive disorder during pregnancy, thyroid diseases during pregnancy, diabetes mellitus/gestational diabetes during pregnancy, folic acid supplementation during early pregnancy, and mother congenital heart diseases are introduced.

Model 2: All the variables in Model 1 and anti-depressant intake are introduced.

Additional file 5 Crude and adjusted ORs of maternal education, psychological distress, and household income without 2-y outcomes

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Crude | | | | |  | Model 1 | | | | |  | Model 2 | | | | |
|  | Proportion\* | OR | 95%CI | | | P |  | OR | 95%CI |  |  | P |  | OR | 95%CI | | | P |
| Mother’s education |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| EDC1 | 4.9% | 1.24 | 0.92 | - | 1.67 | 0.164 |  | 1.08 | 0.76 | - | 1.54 | 0.657 |  | 1.08 | 0.76 | - | 1.53 | 0.668 |
| EDC2 | 31.5% | 0.99 | 0.83 | - | 1.19 | 0.935 |  | 0.90 | 0.73 | - | 1.11 | 0.334 |  | 0.90 | 0.73 | - | 1.11 | 0.332 |
| EDC3 | 42.0% | 1.00 | 0.85 | - | 1.18 | 1.000 |  | 0.96 | 0.80 | - | 1.15 | 0.665 |  | 0.96 | 0.80 | - | 1.15 | 0.666 |
| EDC4 | 21.7% | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |
| Household income (10 thousand yen/year) | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| -199 | 5.9% | 0.98 | 0.66 | - | 1.45 | 0.918 |  | 0.93 | 0.61 | - | 1.41 | 0.728 |  | 0.93 | 0.61 | - | 1.41 | 0.725 |
| 200-399 | 35.0% | 0.91 | 0.67 | - | 1.24 | 0.548 |  | 0.93 | 0.67 | - | 1.29 | 0.661 |  | 0.93 | 0.67 | - | 1.29 | 0.659 |
| 400-599 | 32.7% | 0.86 | 0.63 | - | 1.17 | 0.337 |  | 0.89 | 0.65 | - | 1.22 | 0.472 |  | 0.89 | 0.65 | - | 1.22 | 0.473 |
| 600-799 | 15.7% | 0.85 | 0.61 | - | 1.20 | 0.364 |  | 0.88 | 0.63 | - | 1.24 | 0.466 |  | 0.88 | 0.63 | - | 1.24 | 0.468 |
| 800-999 | 6.5% | 0.72 | 0.48 | - | 1.08 | 0.116 |  | 0.74 | 0.50 | - | 1.11 | 0.149 |  | 0.74 | 0.50 | - | 1.11 | 0.150 |
| 1000- | 4.2% | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |
| Psychological distress in the mother |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| No | 96.4% | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |  | 1.00 |  |  |  |  |
| Yes | 3.6% | 1.39 | 1.03 | - | 1.87 | 0.029 |  | 1.32 | 0.98 | - | 1.79 | 0.066 |  | 1.31 | 0.97 | - | 1.77 | 0.080 |

EDC1: junior high school, EDC2: high school, EDC3: technical junior college, technical/vocational college, or EDC4: associate degree bachelor’s degree or postgraduate degree.

(Multiple imputation, N=93,269)

\*Mean proportion of each category in the imputed 25 datasets

Model 1: All listed variables, maternal age, mother BMI, father education, marital status, mother drinking habit, mother smoking, paternal smoking, parity, infant sex, plurality, fertility treatment, hypertensive disorder during pregnancy, thyroid diseases during pregnancy, diabetes mellitus/gestational diabetes during pregnancy, folic acid supplementation during early pregnancy, and mother congenital heart diseases are introduced.

Model 2: All the variables in Model 1 and anti-depressant intake are introduced.

Additional file 6 Adjusted ORs of maternal education and psychological distress (2-y questionnaire outcome added)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Crude | | | | | |  | Model 1 | | | | | |  | Model 2 | | | | | |
|  | Proportion\* | OR | 95%CI | | | P | P for trend |  | OR | 95%CI | | | P | P for trend |  | OR | 95%CI | | | P | P for trend |
| Number of positive |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |
| 0 | 92.0% | 1.00 |  |  |  |  | 0.190 |  | 1.00 |  |  |  |  | 0.351 |  | 1.00 |  |  |  |  | 0.381 | |
| 1 | 7.6% | 1.10 | 0.91 | - | 1.35 | 0.323 |  |  | 1.07 | 0.87 | - | 1.32 | 0.502 |  |  | 1.07 | 0.87 | - | 1.32 | 0.530 |  | |
| 2 | 0.4% | 1.45 | 0.69 | - | 3.03 | 0.325 |  |  | 1.37 | 0.64 | - | 2.89 | 0.416 |  |  | 1.34 | 0.63 | - | 2.84 | 0.445 |  | |

\*Mean proportion of each category in the imputed 25 datasets

(Multiple imputation, M=93,643)

Model 1: All listed variables, maternal age, mother BMI, household income father education, marital status, mother drinking habit, mother smoking, paternal smoking, parity, infant sex, plurality, fertility treatment, hypertensive disorder during pregnancy, thyroid diseases during pregnancy, diabetes mellitus/gestational diabetes during pregnancy, folic acid supplementation during early pregnancy, and mother congenital heart diseases are introduced.

Model 2: All the variables in Model 1 and anti-depressant intake are introduced.

P for trend: The number of positives (0-2) is introduced into the model.

Additional file 7 Adjusted ORs of maternal education and psychological distress (only 2-y questionnaire outcome positive excluded)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Crude | | | | | |  | Model 1 | | | | | |  | Model 2 | | | | | |
|  | Proportion\* | OR | 95%CI | | | P | P for trend |  | OR | 95%CI | | | P | P for trend |  | OR | 95%CI | | | P | P for trend |
| Number of positive |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | |
| 0 | 92.0% | 1.00 |  |  |  |  | 0.011 |  | 1.00 |  |  |  |  | 0.044 |  | 1.00 |  |  |  |  | 0.052 | |
| 1 | 7.6% | 1.24 | 1.00 | - | 1.55 | 0.053 |  |  | 1.20 | 0.95 | - | 1.52 | 0.126 |  |  | 1.19 | 0.94 | - | 1.51 | 0.139 |  | |
| 2 | 0.4% | 2.02 | 0.96 | - | 4.22 | 0.063 |  |  | 1.87 | 0.88 | - | 3.97 | 0.106 |  |  | 1.82 | 0.86 | - | 3.89 | 0.120 |  | |

\*Mean proportion of each category in the imputed 25 datasets

(Multiple imputation, N=93,269)

Model 1: All listed variables, maternal age, mother BMI, household income father education, marital status, mother drinking habit, mother smoking, paternal smoking, parity, infant sex, plurality, fertility treatment, hypertensive disorder during pregnancy, thyroid diseases during pregnancy, diabetes mellitus/gestational diabetes during pregnancy, folic acid supplementation during early pregnancy, and mother congenital heart diseases are introduced.

Model 2: All the variables in Model 1 and anti-depressant intake are introduced.

P for trend: The number of positives (0-2) is introduced into the model.