Supplemental Table 1 Comparison of participants’ characteristics between those who included into this study and full cohort population.

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics |  | This study (n=2,553) | Full population (n=18,131) |
|  |  | N （%）or mean ± S.D. | |
| **Maternal age（years）** |  | 30.9 ± 4.7 | 30.3 ± 4.8 |
| **Paternal age（years）** |  | 33.0 ± 5.6 | 32.1 ± 5.7 |
| **Maternal pre-pregnancy BMI（kg/m2）** | | 21.1 ± 3.3 | 21.1 ± 3.3 |
| **Parity** | Primipara | 959 (37.6) | 7761 (42.8) |
| Multipara | 1310（51.3） | 6799 (37.5) |
| Missing | 284 (11.1) | 3655 (20.2) |
| **Maternal drinking during pregnancy** | Yes | 271 （10.6） | 2019 (11.1) |
| No | 2193 (85.9) | 15192 (83.8) |
| Missing | 89 (3.5) | 1004 (5.5) |
| **Maternal cotinine levels (ng/ml)** | ≦ 0.21 (non-smokers) | 1210 (47.4) | 6040 (33.3) |
| 0.22-11.48 (passive smokers) | 776 (30.4) | 6869 (37.9) |
| ≧ 11.48 (active smokers) | 199 (7.8) | 2298 (12.7) |
| Missing | 368 (14.4) | 3008 (16.6) |
| **Maternal education** | Middle school | 87（3.4） | 937 (5.2) |
|  | High School | 921（36.1） | 7548 (41.6) |
|  | Community college, vocational school | 1108（43.3） | 6990 (38.6) |
|  | College or above | 383（15.0） | 1860 (10.3) |
|  | Missing | 54 (2.1) | 880 (4.9) |
| **Paternal education** | Middle school | 122（4.8） | 1333 (7.4) |
|  | High School | 939（36.8） | 7188 (39.6) |
|  | Community college, vocational school | 611（23.9） | 4027 (22.2) |
|  | College or above | 815（31.9） | 4530 (25.0) |
|  | Missing | 66 (2.6) | 1137 (6.3) |
| **Family income during pregnancy**  **(million yen/year)** | < 3 | 451（17.7） | 3420 (18.9) |
| 3-5 | 952（37.3） | 6613 (36.5) |
| 5-8 | 643（25.2） | 3751 (20.7) |
| ≧ 8 | 186（7.3） | 1093 (6.0) |
| Missing | 321 (12.6) | 3338 (18.4) |
| **Infant sex** | Boy | 1283（50.3） | 9143 (50.4) |
| **Gestational age (days)** |  | 274 ± 11 | 274 ± 11 |
| **Birth weight　（g）** |  | 3014 ± 419 | 3039 ± 412 |

Supplemental Table 2 Odds ratio of likelihood of behavioral problems stratified by child sex.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Univariate OR (95% CI) | | Multivariate OR (95% CI) | |
|  | Boys | Girls | Boys | Girls |
| **Maternal age (year)** |  |  |  |  |
| ≦ 25 | 1.3 (0.9, 1.9) | 2.1 (1.3, 3.3)\*\*\* | 0.9 (0.5, 1.4) | 1.2 (0.6, 2.2) |
| 26-30 | 1.0 (0.7, 1.4) | 1.5 (1.0, 2.1)\* | 0.9 (0.6, 1.2) | 1.3 (0.9, 20.) |
| 31-35 | Reference | Reference | Reference | Reference |
| ≧ 36 | 0.9 (0.6, 1.4) | 1.0 (0.6, 1.6) | 1.1 (0.7, 1.6) | 1.2 (0.7, 2.0) |
| **Paternal age (year)** |  |  |  |  |
| ≦ 25 | 1.4 (0.9, 2.2) | 2.0 (1.2, 3.5)\* | 1.1 (0.6, 2.0) | 1.3 (0.7, 2.7) |
| 26-30 | 1.2 (0.9, 1.7) | 1.3 (0.9, 1.9) | 1.1 (0.8, 1.7) | 1.0 (0.7, 1.6) |
| 31-35 | Reference | Reference | Reference | Reference |
| ≧ 36 | 0.9 (0.7, 1.3) | 0.7 (0.5, 1.1) | 0.9 (0.6, 1.4) | 1.4 (1.0, 2.0) |
| **Maternal BMI (kg/m2)** |  |  |  |  |
| < 18.5 | 0.7 (0.5, 1.1) | 1.1 (0.7, 1.6) | 0.7 (0.5, 1.1) | 1.0 (0.7, 1.5) |
| 18.5-25.0 | Reference | Reference | Reference | Reference |
| 25.0-30.0 | 1.3 (0.8, 2.1) | 1.1 (0.7, 1.6) | 1.2 (0.8, 2.0) | 1.1 (0.6, 2.0) |
| ≧ 30 | 1.8 (0.8, 4.1) | 1.9 (0.8, 4.4) | 2.2 (1.0, 4.9) | 2.2 (1.0, 5.0) |
| **Parity** |  |  |  |  |
| Primipara | 1.2 (0.9, 1.5) | 1.5 (1.1, 2.0)\* | 1.2 (0.9, 1.6) | 1.4 (1.0, 2.0)\* |
| Multipara | Reference | Reference | Reference | Reference |
| **Maternal cotinine level (ng/ml)** | | | | |
| ≦ 0.21 (non-smokers) | Reference | Reference | Reference | Reference |
| 0.22-11.48  (passive smokers) | 1.2 (0.9, 1.6) | 1.1 (0.8, 1.5) | 1.1 (0.8, 1.4) | 0.9 (0.6, 1.2) |
| ≧ 11.49 (active smokers) | 1.9 (1.2, 2.9)\*\* | 1.4 (0.8, 2.4) | 1.4 (0.9, 2.3) | 1.1 (0.6, 2.0) |
| **Maternal education** |  |  |  |  |
| Middle school | 2.6 (1.4, 4.9)\*\*\* | 1.7 (0.8, 3.4) | 2.3 (1.2, 4.6)\* | 1.4 (0.7, 3.0) |
| High School | Reference | Reference | Reference | Reference |
| Community college, vocational school | 0.8 (0.6, 1.0) | 0.7 (0.5, 1.0) | 0.9 (0.6, 1.2) | 0.8 (0.6, 1.2) |
| College or above | 0.6 (0.4, 1.0)\* | 0.8 (0.5, 1.2) | 0.8 (0.5, 1.3) | 1.2 (0.7, 2.0) |
| **Family income during pregnancy (million yen/year)** | | | | |
| < 3 | 1.6 (1.1, 2.2)\* | 2.3 (1.6, 3.3)\*\*\* | 1.3 (0.9, 1.9) | 2.1 (1.4, 3.1)\*\*\* |
| 3-5 | Reference | Reference | Reference | Reference |
| 5-8 | 0.8 (0.6, 1.1) | 0.9 (0.6, 1.3) | 0.9 (0.6, 1.2) | 0.9 (0.6, 1.4) |
| ≧ 8 | 0.6 (0.4, 1.1) | 0.6 (0.3, 1.2) | 0.8 (0.4, 1.6) | 0.7 (0.3, 1.5) |
| **Marital status** |  |  |  |  |
| Married | Reference | Reference | Reference | Reference |
| Single parent | 1.8 (1.1, 2.8)\*\* | 1.3 (0.8, 2.3) | 1.4 (0.8, 2.3) | 1.0 (0.5, 2.0) |

Univariate model was adjusted for age at SDQ (month). Multivariate model was adjusted for all the variates shown in the table and age at SDQ (month). Missing values were replaced by mean value (continuous variables) and by most frequent answer (categorical variables). \* p < 0.050 \*\* p < 0.010, \*\*\* p < 0.005.

Supplemental Table 3 Associated factors of child behavioral problems by multivariable regression analysis excluding participants with any missing values (N=1686).

|  |  |  |
| --- | --- | --- |
|  | N | OR of behavioral problems (95% CI) |
| **Maternal age (year)** | | |
| ≦ 25 | 211 | 0.9 (0.6, 1.5) |
| 26-30 | 563 | 1.0 (0.7, 1.4) |
| 31-35 | 651 | Reference |
| ≧ 36 | 261 | 1.1 (0.7, 1.6) |
| **Paternal age (year)** |  |  |
| ≦ 25 | 124 | 1.0 (0.6, 1.8) |
| 26-30 | 461 | 1.2 (0.9, 1.7) |
| 31-35 | 605 | Reference |
| ≧ 36 | 496 | 0.9 (0.6, 1.2) |
| **Maternal pre-pregnancy BMI (kg/m2)** |  |  |
| < 18.5 | 288 | 1.0 (0.7, 1.3) |
| 18.5-25.0 | 1228 | Reference |
| 25.0-30.0 | 137 | 1.2 (0.8, 1.9) |
| ≧ 30 | 33 | 1.6 (0.7, 3.6) |
| **Parity** |  |  |
| 0 | 674 | 1.5 (1.2, 2.0)\*\*\* |
| ≧ 1 | 1012 | Reference |
| **Maternal cotinine level (ng/ml)** | | |
| ≦ 0.21 (non-smokers) | 929 | Reference |
| 0.22-11.48 (passive smokers) | 602 | 1.2 (0.9, 1.5) |
| ≧ 11.49 (active smokers) | 155 | 1.7 (1.1, 2.6)\* |
| **Maternal education** | | |
| Middle school | 66 | 1.8 (1.1, 3.2)\* |
| High School | 624 | Reference |
| Community college, vocational school | 744 | 0.8 (0.6, 1.1) |
| College or above | 252 | 0.8 (0.5, 1.2) |
| **Family income during pregnancy (million yen/year)** | | |
| < 3 | 350 | 1.5 (1.1, 2.0)\* |
| 3-5 | 723 | Reference |
| 5-8 | 485 | 0.7 (0.5, 1.0)\* |
| ≧ 8 | 128 | 0.8 (0.4, 1.3) |
| **Marital status** |  |  |
| Married | 1574 | Reference |
| Single parent | 108 | 1.2 (0.8, 1.9) |
| **Child sex** |  |  |
| Boys | 845 | 1.7 (1.3, 2.2)\*\*\* |
| Girls | 841 | Reference |

Multivariate model was adjusted for all the variates shown in the table and age at SDQ (month). \* p < 0.050, \*\* p < 0.010, \*\*\* p < 0.005

Supplemental Figure 1 Selection of study participants.

