Supplemental (S) Material

Table S1 Comparison of children’s characteristics and health outcomes at age 3.5 years.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Allergy | 　 |  | Food allergy |  | Eczema | 　 |  | Wheezing | 　 |  | Infections | 　 |  | Otitis media |  | Respiratory infection |
|  |  |  | No | Yes |  | No | Yes |  | No | Yes |  | No | Yes |  | No | Yes |  | No | Yes |  | No | Yes |
| 　 | 　 | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) |
| Mother |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Age at delivery (years) |  | 31.1 ± 4.3 | 30.8 ± 4.7 |  | 31.0 ± 4.4 | 30.9 ± 4.6 |  | 31.2 ± 4.4 | 30.4 ± 4.6 |  | 31.0 ± 4.4 | 31.2 ± 4.6 |  | 31.3 ± 4.2 | 30.8 ± 4.6 |  | 31.3 ± 4.2 | 30.5 ± 4.7 |  | 31.1 ± 4.4 | 30.5 ± 4.7 |
|  | Pre-pregnancy BMI (kg/m2) |  | 20.9 ± 3.0 | 21.6 ± 3.4 |  | 21.1 ± 3.2 | 21.3 ± 3.2 |  | 21.2 ± 3.2 | 21.2 ± 3.2 |  | 21.0 ± 3.0 | 22.7 ± 4.2\*\* | 20.6 ± 3.3 | 21.5 ± 3.1\* |  | 20.8 ± 2.9 | 21.7 ± 3.5\* |  | 21.1 ± 3.2 | 21.5 ± 3.3 |
|  | Parity  | 0 | 97 (59.1) | 67 (40.9) |  | 129 (78.7) | 35 (21.3) |  | 128 (78.0) | 36 (22.0) |  | 148 (90.2) | 16 (9.8) |  | 67 (40.9) | 97 (59.1)\*\* |  | 102 (62.2) | 62 (37.8) |  | 127 (77.4) | 37 (22.6) |
|  |  | ≥1 | 93 (57.4) | 69 (42.6) |  | 125 (77.2) | 37 (22.8) |  | 129 (79.6) | 33 (20.4) |  | 136 (84.0) | 26 (16.0) |  | 41 (25.3) | 121 (74.7) |  | 89 (54.9) | 73 (45.1) |  | 133 (82.1) | 29 (17.9) |
|  | Educational level  | ≤12 years | 80 (63.0) | 47 (37.0) |  | 104 (81.9) | 23 (18.1) |  | 105 (82.7) | 22 (17.3) |  | 115 (90.6) | 12 (9.4) |  | 42 (33.1) | 85 (66.9) |  | 71 (55.9) | 56 (44.1) |  | 103 (81.1) | 24 (18.9) |
|  |  | >12 years | 111 (55.5) | 89 (44.5) |  | 151 (75.5) | 49 (24.5) |  | 153 (76.5) | 47 (23.5) |  | 170 (85.0) | 30 (15.0) |  | 66 (33.0) | 134 (67.0) |  | 120 (60.0) | 80 (40.0) |  | 158 (79.0) | 42 (21.0) |
|  | Tobacco smoking during pregnancy | No | 169 (58.5) | 120 (41.5) |  | 225 (77.9) | 64 (22.1) |  | 226 (78.2) | 63 (21.8) |  | 254 (87.9) | 35 (12.1) |  | 97 (33.6) | 192 (66.4) |  | 170 (58.8) | 119 (41.2) |  | 236 (81.7) | 53 (18.3)\* |
|  |  | Yes | 22 (57.9) | 16 (42.1) |  | 30 (78.9) | 8 (21.1) |  | 32 (84.2) | 6 (15.8) |  | 31 (81.6) | 7 (18.4) |  | 11 (28.9) | 27 (71.1) |  | 21 (55.3) | 17 (44.7) |  | 25 (65.8) | 13 (34.2) |
|  | Alcohol consumption during pregnancy | No | 136 (59.6) | 92 (40.4) |  | 186 (81.6) | 42 (18.4)\* |  | 179 (78.5) | 49 (21.5) |  | 201 (88.2) | 27 (11.8) |  | 81 (35.5) | 147 (64.5) |  | 137 (60.1) | 91 (39.9) |  | 181 (79.4) | 47 (20.6) |
|  |  | Yes | 55 (55.6) | 44 (44.4) |  | 69 (69.7) | 30 (30.3) |  | 79 (79.8) | 20 (20.2) |  | 84 (84.8) | 15 (15.2) |  | 27 (27.3) | 72 (72.7) |  | 54 (54.5) | 45 (45.5) |  | 80 (80.8) | 19 (19.2) |
|  | Shoreline fish | <once/week | 109 (60.9) | 70 (39.1) |  | 143 (79.9) | 36 (20.1) |  | 147 (82.1) | 32 (17.9) |  | 157 (87.7) | 22 (12.3) |  | 62 (34.6) | 117 (65.4) |  | 107 (59.8) | 72 (40.2) |  | 143 (79.9) | 36 (20.1) |
|  |  | ≥once/week | 82 (55.4) | 66 (44.6) |  | 112 (75.7) | 36 (24.3) |  | 111 (75.0) | 37 (25.0) |  | 128 (86.5) | 20 (13.5) |  | 46 (31.1) | 102 (68.9) |  | 84 (56.8) | 64 (43.2) |  | 118 (79.7) | 30 (20.3) |
|  | Pelagic fish | <once/week | 88 (58.7) | 62 (41.3) |  | 118 (78.7) | 32 (21.3) |  | 116 (77.3) | 34 (22.7) |  | 133 (88.7) | 17 (11.3) |  | 50 (33.3) | 100 (66.7) |  | 83 (55.3) | 67 (44.7) |  | 127 (84.7) | 23 (15.3)\* |
|  |  | ≥once/week | 103 (58.2) | 74 (41.8) |  | 137 (77.4) | 40 (22.6) |  | 142 (80.2) | 35 (19.8) |  | 152 (85.9) | 25 (14.1) |  | 58 (32.8) | 119 (67.2) |  | 108 (61.0) | 69 (39.0) |  | 134 (75.7) | 43 (24.3) |
|  | Allergic history | No | 146 (62.4) | 88 (37.6)\* |  | 186 (79.5) | 48 (20.5) |  | 190 (81.2) | 44 (18.8) |  | 212 (90.6) | 22 (9.4)\*\* |  | 78 (33.3) | 156 (66.7) |  | 143 (61.1) | 91 (38.9) |  | 188 (80.3) | 46 (19.7) |
|  |  | Yes | 45 (48.4) | 48 (51.6) |  | 69 (74.2) | 24 (25.8) |  | 68 (73.1) | 25 (26.9) |  | 73 (78.5) | 20 (21.5) |  | 30 (32.3) | 63 (67.7) |  | 48 (51.6) | 45 (48.4) |  | 73 (78.5) | 20 (21.5) |
|  | Blood sampling period | <28 weeks | 9 (45.0) | 11 (55.0) |  | 15 (75.0) | 5 (25.0) |  | 16 (80.0) | 4 (20.0) |  | 16 (80.0) | 4 (20.0) |  | 10 (50.0) | 10 (50.0) |  | 12 (60.0) | 8 (40.0) |  | 15 (75.0) | 5 (25.0) |
|  |  | 28 to <36 weeks | 87 (59.6) | 59 (40.4) |  | 112 (76.7) | 34 (23.3) |  | 119 (81.5) | 27 (18.5) |  | 128 (87.7) | 18 (12.3) |  | 44 (30.1) | 102 (69.9) |  | 76 (52.1) | 70 (47.9) |  | 113 (77.4) | 33 (22.6) |
|  |  | ≥36 weeks | 33 (49.3) | 34 (50.7) |  | 52 (77.6) | 15 (22.4) |  | 46 (68.7) | 21 (31.3) |  | 57 (85.1) | 10 (14.9) |  | 21 (31.3) | 46 (68.7) |  | 42 (62.7) | 25 (37.3) |  | 54 (80.6) | 13 (19.4) |
|  |  | After delivery | 62 (66.0) | 32 (34.0) |  | 76 (80.9) | 18 (19.1) |  | 77 (81.9) | 17 (18.1) |  | 84 (89.4) | 10 (10.6) |  | 33 (35.1) | 61 (64.9) |  | 61 (64.9) | 33 (35.1) |  | 79 (84.0) | 15 (16.0) |
| Father |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Allergic history  | No | 167 (62.8) | 99 (37.2)\*\* |  | 215 (80.8) | 51 (19.2)\* |  | 213 (80.1) | 53 (19.9) |  | 241 (90.6) | 25 (9.4)\*\* |  | 91 (34.2) | 175 (65.8) |  | 157 (59.0) | 109 (41.0) |  | 219 (82.3) | 47 (17.7)\* |
|  |  | Yes | 24 (39.3) | 37 (60.7) |  | 40 (65.6) | 21 (34.4) |  | 45 (73.8) | 16 (26.2) |  | 44 (72.1) | 17 (27.9) |  | 17 (27.9) | 44 (72.1) |  | 34 (55.7) | 27 (44.3) |  | 42 (68.9) | 19 (31.1) |
| Living environment |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Environmental tobacco exposure  | No | 76 (55.1) | 62 (44.9) |  | 103 (74.6) | 35 (25.4) |  | 105 (76.1) | 33 (23.9) |  | 122 (88.4) | 16 (11.6) |  | 52 (37.7) | 86 (62.3) |  | 86 (62.3) | 52 (37.7) |  | 119 (86.2) | 19 (13.8)\* |
|  |  | Yes | 115 (60.8) | 74 (39.2) |  | 152 (80.4) | 37 (19.6) |  | 153 (81.0) | 36 (19.0) |  | 163 (86.2) | 26 (13.8) |  | 56 (29.6) | 133 (70.4) |  | 105 (55.6) | 84 (44.4) |  | 142 (75.1) | 47 (24.9) |
|  | Keeping pets  | No | 162 (58.9) | 113 (41.1) |  | 215 (78.2) | 60 (21.8) |  | 216 (78.5) | 59 (21.5) |  | 242 (88.0) | 33 (12.0) |  | 94 (34.2) | 181 (65.8) |  | 165 (60.0) | 110 (40.0) |  | 226 (82.2) | 49 (17.8)\* |
|  |  | Yea | 29 (55.8) | 23 (44.2) |  | 40 (76.9) | 12 (23.1) |  | 42 (80.8) | 10 (19.2) |  | 43 (82.7) | 9 (17.3) |  | 14 (26.9) | 38 (73.1) |  | 26 (50.0) | 26 (50.0) |  | 35 (67.3) | 17 (32.7) |
|  | Annual household income during pregnancy | ≤5 million yen | 124 (58.5) | 88 (41.5) |  | 162 (76.4) | 50 (23.6) |  | 166 (78.3) | 46 (21.7) |  | 185 (87.3) | 27 (12.7) |  | 71 (33.5) | 141 (66.5) |  | 128 (60.4) | 84 (39.6) |  | 166 (78.3) | 46 (21.7) |
|  |  | >5 million yen | 67 (58.3) | 48 (41.7) |  | 93 (80.9) | 22 (19.1) |  | 92 (80.0) | 23 (20.0) |  | 100 (87.0) | 15 (13.0) |  | 37 (32.2) | 78 (67.8) |  | 63 (54.8) | 52 (45.2) |  | 95 (82.6) | 20 (17.4) |
| Child |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Gender | Male | 89 (55.6) | 71 (44.4) |  | 122 (76.3) | 38 (23.8) |  | 128 (80.0) | 32 (20.0) |  | 139 (86.9) | 21 (13.1) |  | 54 (33.8) | 106 (66.3) |  | 90 (56.3) | 70 (43.8) |  | 135 (84.4) | 25 (15.6)\* |
|  |  | Female | 102 (61.1) | 65 (38.9) |  | 133 (79.6) | 34 (20.4) |  | 130 (77.8) | 37 (22.2) |  | 146 (87.4) | 21 (12.6) |  | 54 (32.3) | 113 (67.7) |  | 101 (60.5) | 66 (39.5) |  | 126 (75.4) | 41 (24.6) |
|  | Duration of breast-feeding | <4 months | 33 (63.5) | 19 (36.5) |  | 43 (82.7) | 9 (17.3) |  | 42 (80.8) | 10 (19.2) |  | 47 (90.4) | 5 (9.6) |  | 17 (32.7) | 35 (67.3) |  | 32 (61.5) | 20 (38.5) |  | 41 (78.8) | 11 (21.2) |
|  |  | ≥4 months | 155 (57.0) | 117 (43.0) |  | 209 (76.8) | 63 (23.2) |  | 213 (78.3) | 59 (21.7) |  | 235 (86.4) | 37 (13.6) |  | 90 (33.1) | 182 (66.9) |  | 158 (58.1) | 114 (41.9) |  | 218 (80.1) | 54 (19.9) |
|  | Daycare attendance | No | 89 (58.2) | 64 (41.8) |  | 118 (77.1) | 35 (22.9) |  | 120 (78.4) | 33 (21.6) |  | 140 (91.5) | 13 (8.5)\* |  | 64 (41.8) | 89 (58.2)\*\* |  | 102 (66.7) | 51 (33.3)\*\* |  | 131 (85.6) | 22 (14.4)\* |
| 　 | 　 | Yes | 102 (58.6) | 72 (41.4) | 　 | 137 (78.7) | 37 (21.3) | 　 | 138 (79.3) | 36 (20.7) | 　 | 145 (83.3) | 29 (16.7) | 　 | 44 (25.3) | 130 (74.7) | 　 | 89 (51.1) | 85 (48.9) | 　 | 130 (74.7) | 44 (25.3) |

\*p<0.05, \*\*p<0.01 by t-test, and chi-squared test.

Table S2 Comparison of children’s characteristics and health outcomes at age 7 years.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Allergy | 　 |  | Food allergy |  | Eczema | 　 |  | Wheezing | 　 |  | Infections | 　 |  | Otitis media |  | Respiratory infection |
|  |  |  | No | Yes |  | No | Yes |  | No | Yes |  | No | Yes |  | No | Yes |  | No | Yes |  | No | Yes |
| 　 | 　 | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) | 　 | Mean ±SD or N (%) | Mean ± SD or N (%) |
| Mother |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Age at delivery (years) |  | 30.9 ± 4.2 | 31.6 ± 4.5 |  | 31.3 ± 4.4 | 31.3 ± 4.3 |  | 31.2 ± 4.4 | 31.5 ± 4.2 |  | 31.1 ± 4.2 | 31.7 ± 4.8 |  | 30.8 ± 4.2 | 31.5 ± 4.4 |  | 31.4 ± 4.2 | 31.2 ± 4.6 |  | 31.4 ± 4.4 | 31.0 ± 4.1 |
|  | Pre-pregnancy BMI (kg/m2) |  | 21.1 ± 2.8 | 21.2 ± 3.2 |  | 21.2 ± 2.9 | 20.9 ± 3.4 |  | 21.1 ± 3.0 | 21.2 ± 3.1 |  | 20.9 ± 2.8 | 21.6 ± 3.3 |  | 20.9 ± 3.1 | 21.2 ± 3.0 |  | 20.9 ± 2.7 | 21.4 ± 3.3 |  | 21.1 ± 3.0 | 21.3 ± 3.3 |
|  | Parity  | 0 | 61 (47.3) | 68 (52.7) |  | 103 (79.8) | 26 (20.2) |  | 92 (71.3) | 37 (28.7) |  | 92 (71.3) | 37 (28.7) |  | 31 (24.0) | 98 (76.0) |  | 66 (51.2) | 63 (48.8) |  | 104 (80.6) | 25 (19.4) |
|  |  | ≥1 | 55 (41.0) | 79 (59.0) |  | 102 (76.1) | 32 (23.9) |  | 91 (67.9) | 43 (32.1) |  | 82 (61.2) | 52 (38.8) |  | 29 (21.6) | 105 (78.4) |  | 82 (61.2) | 52 (38.8) |  | 111 (82.8) | 23 (17.2) |
|  | Educational level  | ≤12 years | 47 (51.6) | 44 (48.4)\* |  | 78 (85.7) | 13 (14.3)\* |  | 67 (73.6) | 24 (26.4) |  | 62 (68.1) | 29 (31.9) |  | 24 (26.4) | 67 (73.6) |  | 49 (53.8) | 42 (46.2) |  | 75 (82.4) | 16 (17.6) |
|  |  | >12 years | 69 (39.9) | 104 (60.1) |  | 128 (74.0) | 45 (26.0) |  | 116 (67.1) | 57 (32.9) |  | 113 (65.3) | 60 (34.7) |  | 36 (20.8) | 137 (79.2) |  | 100 (57.8) | 73 (42.2) |  | 141 (81.5) | 32 (18.5) |
|  | Tobacco smoking during pregnancy | No | 104 (44.1) | 132 (55.9) |  | 184 (78.0) | 52 (22.0) |  | 162 (68.6) | 74 (31.4) |  | 160 (67.8) | 76 (32.2) |  | 55 (23.3) | 181 (76.7) |  | 134 (56.8) | 102 (43.2) |  | 192 (81.4) | 44 (18.6) |
|  |  | Yes | 12 (42.9) | 16 (57.1) |  | 22 (78.6) | 6 (21.4) |  | 21 (75.0) | 7 (25.0) |  | 15 (53.6) | 13 (46.4) |  | 5 (17.9) | 23 (82.1) |  | 15 (53.6) | 13 (46.4) |  | 24 (85.7) | 4 (14.3) |
|  | Alcohol consumption during pregnancy | No | 77 (42.8) | 103 (57.2) |  | 142 (78.9) | 38 (21.1) |  | 124 (68.9) | 56 (31.1) |  | 119 (66.1) | 61 (33.9) |  | 45 (25.0) | 135 (75.0) |  | 103 (57.2) | 77 (42.8) |  | 145 (80.6) | 35 (19.4) |
|  |  | Yes | 39 (46.4) | 45 (53.6) |  | 64 (76.2) | 20 (23.8) |  | 59 (70.2) | 25 (29.8) |  | 56 (66.7) | 28 (33.3) |  | 15 (17.9) | 69 (82.1) |  | 46 (54.8) | 38 (45.2) |  | 71 (84.5) | 13 (15.5) |
|  | Shoreline fish | <once/week | 63 (42.9) | 84 (57.1) |  | 116 (78.9) | 31 (21.1) |  | 101 (68.7) | 46 (31.3) |  | 98 (66.7) | 49 (33.3) |  | 29 (19.7) | 118 (80.3) |  | 81 (55.1) | 66 (44.9) |  | 119 (81.0) | 28 (19.0) |
|  |  | ≥once/week | 53 (45.3) | 64 (54.7) |  | 90 (76.9) | 27 (23.1) |  | 82 (70.1) | 35 (29.9) |  | 77 (65.8) | 40 (34.2) |  | 31 (26.5) | 86 (73.5) |  | 68 (58.1) | 49 (41.9) |  | 97 (82.9) | 20 (17.1) |
|  | Pelagic fish | <once/week | 49 (42.6) | 66 (57.4) |  | 94 (81.7) | 21 (18.3) |  | 82 (71.3) | 33 (28.7) |  | 76 (66.1) | 39 (33.9) |  | 24 (20.9) | 91 (79.1) |  | 66 (57.4) | 49 (42.6) |  | 97 (84.3) | 18 (15.7) |
|  |  | ≥once/week | 67 (45.0) | 82 (55.0) |  | 112 (75.2) | 37 (24.8) |  | 101 (67.8) | 48 (32.2) |  | 99 (66.4) | 50 (33.6) |  | 36 (24.2) | 113 (75.8) |  | 83 (55.7) | 66 (44.3) |  | 119 (79.9) | 30 (20.1) |
|  | Allergic history | No | 85 (46.2) | 99 (53.8) |  | 148 (80.4) | 36 (19.6) |  | 132 (71.7) | 52 (28.3) |  | 126 (68.5) | 58 (31.5) |  | 40 (21.7) | 144 (78.3) |  | 105 (57.1) | 79 (42.9) |  | 154 (83.7) | 30 (16.3) |
|  |  | Yes | 31 (38.8) | 49 (61.3) |  | 58 (72.5) | 22 (27.5) |  | 51 (63.8) | 29 (36.3) |  | 49 (61.3) | 31 (38.8) |  | 20 (25.0) | 60 (75.0) |  | 44 (55.0) | 36 (45.0) |  | 62 (77.5) | 18 (22.5) |
|  | Blood sampling period | <28 weeks | 4 (23.5) | 13 (76.5) |  | 12 (70.6) | 5 (29.4) |  | 11 (64.7) | 6 (35.3) |  | 7 (41.2) | 10 (58.8)\*\* |  | 2 (11.8) | 15 (88.2) |  | 8 (47.1) | 9 (52.9)\* |  | 12 (70.6) | 5 (29.4) |
|  |  | 28 to <36 weeks | 50 (42.0) | 69 (58.0) |  | 92 (77.3) | 27 (22.7) |  | 81 (68.1) | 38 (31.9) |  | 84 (70.6) | 35 (29.4) |  | 25 (21.0) | 94 (79.0) |  | 57 (47.9) | 62 (52.1) |  | 98 (82.4) | 21 (17.6) |
|  |  | ≥36 weeks | 20 (38.5) | 32 (61.5) |  | 42 (80.8) | 10 (19.2) |  | 36 (69.2) | 16 (30.8) |  | 25 (48.1) | 27 (51.9) |  | 14 (26.9) | 38 (73.1) |  | 34 (65.4) | 18 (34.6) |  | 41 (78.8) | 11 (21.2) |
|  |  | After delivery | 42 (55.3) | 34 (44.7) |  | 60 (78.9) | 16 (21.1) |  | 55 (72.4) | 21 (27.6) |  | 59 (77.6) | 17 (22.4) |  | 19 (25.0) | 57 (75.0) |  | 50 (65.8) | 26 (34.2) |  | 65 (85.5) | 11 (14.5) |
| Father |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Allergic history  | No | 105 (48.8) | 110 (51.2)\*\* | 175 (81.4) | 40 (18.6)\* |  | 154 (71.6) | 61 (28.4) |  | 152 (70.7) | 63 (29.3)\*\* |  | 48 (22.3) | 167 (77.7) |  | 123 (57.2) | 92 (42.8) |  | 180 (83.7) | 35 (16.3) |
|  |  | Yes | 11 (22.4) | 38 (77.6) |  | 31 (63.3) | 18 (36.7) |  | 29 (59.2) | 20 (40.8) |  | 23 (46.9) | 26 (53.1) |  | 12 (24.5) | 37 (75.5) |  | 26 (53.1) | 23 (46.9) |  | 36 (73.5) | 13 (26.5) |
| Living environment |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Environmental tobacco exposure  | No | 48 (42.9) | 64 (57.1) |  | 81 (72.3) | 31 (27.7) |  | 77 (68.8) | 35 (31.3) |  | 79 (70.5) | 33 (29.5) |  | 32 (28.6) | 80 (71.4) |  | 67 (59.8) | 45 (40.2) |  | 96 (85.7) | 16 (14.3) |
|  |  | Yes | 61 (43.3) | 80 (56.7) |  | 115 (81.6) | 26 (18.4) |  | 99 (70.2) | 42 (29.8) |  | 88 (62.4) | 53 (37.6) |  | 27 (19.1) | 114 (80.9) |  | 75 (53.2) | 66 (46.8) |  | 109 (77.3) | 32 (22.7) |
|  | Keeping pets  | No | 90 (42.3) | 123 (57.7) |  | 167 (78.4) | 46 (21.6) |  | 149 (70.0) | 64 (30.0) |  | 141 (66.2) | 72 (33.8) |  | 52 (24.4) | 161 (75.6) |  | 124 (58.2) | 89 (41.8) |  | 178 (83.6) | 35 (16.4)\* |
|  |  | Yea | 19 (47.5) | 21 (52.5) |  | 29 (72.5) | 11 (27.5) |  | 27 (67.5) | 13 (32.5) |  | 26 (65.0) | 14 (35.0) |  | 7 (17.5) | 33 (82.5) |  | 18 (45.0) | 22 (55.0) |  | 27 (67.5) | 13 (32.5) |
|  | Annual household income during pregnancy | ≤5 million yen | 71 (44.1) | 90 (55.9) |  | 128 (79.5) | 33 (20.5) |  | 113 (70.2) | 48 (29.8) |  | 103 (64.0) | 58 (36.0) |  | 35 (21.7) | 126 (78.3) |  | 95 (59.0) | 66 (41.0) |  | 130 (80.7) | 31 (19.3) |
|  |  | >5 million yen | 45 (43.7) | 58 (56.3) |  | 78 (75.7) | 25 (24.3) |  | 70 (68.0) | 33 (32.0) |  | 72 (69.9) | 31 (30.1) |  | 25 (24.3) | 78 (75.7) |  | 54 (52.4) | 49 (47.6) |  | 86 (83.5) | 17 (16.5) |
| Child |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | Gender | Male | 55 (41.0) | 79 (59.0) |  | 102 (76.1) | 32 (23.9) |  | 95 (70.9) | 39 (29.1) |  | 84 (62.7) | 50 (37.3) |  | 30 (22.4) | 104 (77.6) |  | 70 (52.2) | 64 (47.8) |  | 114 (85.1) | 20 (14.9) |
|  |  | Female | 61 (46.9) | 69 (53.1) |  | 104 (80.0) | 26 (20.0) |  | 88 (67.7) | 42 (32.3) |  | 91 (70.0) | 39 (30.0) |  | 30 (23.1) | 100 (76.9) |  | 79 (60.8) | 51 (39.2) |  | 102 (78.5) | 28 (21.5) |
|  | Duration of breast-feeding | <4 months | 15 (37.5) | 25 (62.5) |  | 31 (77.5) | 9 (22.5) |  | 24 (60.0) | 16 (40.0) |  | 25 (62.5) | 15 (37.5) |  | 7 (17.5) | 33 (82.5) |  | 20 (50.0) | 20 (50.0) |  | 33 (82.5) | 7 (17.5) |
| 　 | 　 | ≥4 months | 94 (44.1) | 119 (55.9) | 　 | 165 (77.5) | 48 (22.5) | 　 | 152 (71.4) | 61 (28.6) | 　 | 142 (66.7) | 71 (33.3) | 　 | 52 (24.4) | 161 (75.6) | 　 | 122 (57.3) | 91 (42.7) | 　 | 172 (80.8) | 41 (19.2) |

\*p<0.05, \*\*p<0.01 by t-test, and chi-squared test.

 Table S3 Comparison of the characteristics of included and excluded subjects in present study.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristics | Included participants at birth (n = 239) | Excluded participants at birth (n = 275) |  | Included participants at 3.5 years of age (n = 327) | Excluded participants at 3.5 years of age (n = 187) |  | Included participants at 7 years of age (n = 264) | Excluded participants at 7 years of age (n = 250) |
| Maternal characteristics  |  |  |  |  |  |  |  |  |
|  Age at delivery (years) | 30.3 ± 4.9 | 30.5 ± 4.9 |  | 31.0 ± 4.4 | 29.3 ± 5.5\* |  | 31.3 ± 4.4 | 29.4 ± 5.3\* |
|  Pre-pregnancy BMI (kg/m2) | 20.9 ± 3.0 | 21.5 ± 3.5\* |  | 21.2 ± 3.2 | 21.3 ± 3.3 |  | 21.1 ± 3.0 | 21.3 ± 3.5 |
|  Parity |  |  |  |  |  |  |  |  |
| 0 | 127 (53.1) | 113 (42.8)\* |  | 164 (50.3) | 76 (42.9) |  | 128 (48.9) | 112 (46.5) |
| ≥1 | 112 (46.9) | 151 (57.2) |  | 162 (49.7) | 101 (57.1) |  | 134 (51.1) | 129 (53.5) |
|  Education level (years) |  |  |  |  |  |  |  |  |
| ≤12 | 103 (43.1) | 122 (45.4) |  | 127 (38.8) | 98 (54.1)\*\* |  | 91 (34.6) | 134 (54.7)\*\* |
| ≥12 | 136 (56.9) | 147 (54.6) |  | 200 (61.2) | 83 (45.9) |  | 172 (65.4) | 111 (45.3) |
|  Tobacco smoking during pregnancy |  |  |  |  |  |  |  |  |  |
| No | 197 (82.4) | 208 (77.3) |  | 289 (88.4) | 116 (64.1)\*\* |  | 235 (89.4) | 170 (69.4)\*\* |
| Yes | 42 (17.6) | 61 (22.7) |  | 38 (11.6) | 65 (35.9) |  | 28 (10.6) | 75 (30.6) |
|  Alcohol consumption during pregnancy |  |  |  |  |  |  |  |  |
| No | 159 (66.5) | 192 (71.4) |  | 228 (69.7) | 123 (68.0) |  | 179 (68.1) | 172 (70.2) |
| Yes | 80 (33.5) | 77 (28.6) |  | 99 (30.3) | 58 (32.0) |  | 84 (31.9) | 73 (29.8) |
|  Annual household income (million yen) |  |  |  |  |  |  |  |  |
| <5 | 168 (70.3) | 177 (66.5) |  | 212 (64.8) | 133 (74.7)\* |  | 161 (61.2) | 184 (76.0)\*\* |
| ≥5 | 71 (29.7) | 89 (33.5) |  | 115 (35.2) | 45 (25.3) |  | 102 (38.8) | 58 (24.0) |
| Infant characteristics |  |  |  |  |  |  |  |  |
|  Sex |  |  |  |  |  |  |  |  |
| Male | 112 (46.9) | 130 (49.1) |  | 160 (48.9) | 82 (46.3) |  | 133 (50.6) | 109 (45.2) |
| Female | 127 (53.1) | 135 (50.9) |  | 167 (51.1) | 95 (53.7) |  | 130 (49.4) | 132 (54.8) |
|  |  |  |  |  |  |  |  |  |  |
|  Gestational age at birth (weeks) | 39.3 ± 1.0 | 38.4 ± 1.8\* |  | 38.9 ± 1.4 | 38.7 ± 1.7 |  | 39.0 ± 1.4 | 38.7 ± 1.6 |
|  Birth weight (g) | 3146.4 ± 335.9 | 2941.4 ± 440.5\* |  | 3064.7 ± 369.5 | 2990.5 ± 465.9 |  | 3079.6 ± 371.5 | 2994.0 ± 439.1\* |

Data are presented as the mean ± standard deviation or *n* (%).

\*p < 0.05, \*\*p < 0.01 by Student’s t-tests and χ2 tests.