**Supplementary materials**

**Maternal intake of one-carbon metabolism-related B vitamins and**

**anorectal malformations in the Japan Environment and Children’s Study**

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**Table S1.** Baseline characteristics of mothers who delivered infants with anorectal malformation (ARM), Japan Environment and Children's Study (2011-2014)

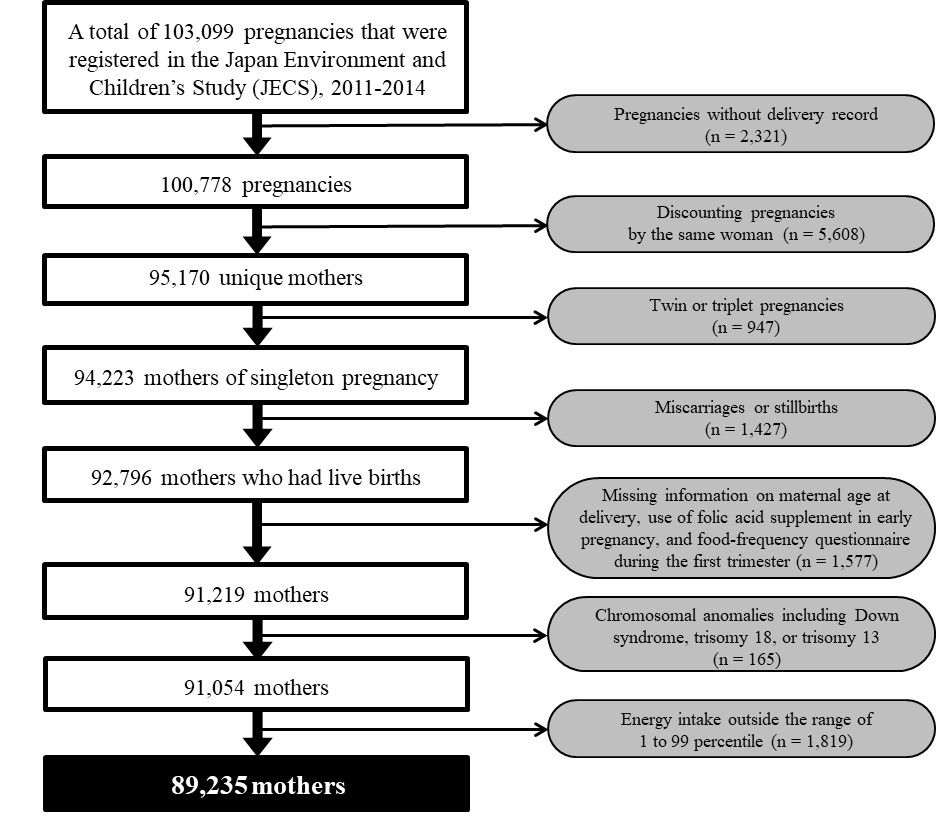
|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | No. of women\* | Frequency (%) |  | ARM (n = 43) | |
|  |  |  | No. of cases | /10,000 live births |
|  |  |  |
| No. of women | | 89,235 | 100 |  | 43 | 4·8 |
|  |  |  |  |  |  |  |
| Dietary and supplemental intake of folate in early pregnancy (μg/day) | | | |  |  |  |
|  | Low (< 400 μg/day) | 59,573 | 66·8 |  | 29 | 4·9 |
|  | High (≥ 400 μg/day) | 29,662 | 33·2 |  | 14 | 4·7 |
| Dietary intake of vitamin B6 in early pregnancy (mg/day) | | | |  |  |  |
|  | Low | 44,617 | 50·0 |  | 27 | 6·1 |
|  | High | 44,618 | 50·0 |  | 16 | 3·6 |
| Dietary intake of vitamin B12 in early pregnancy (μg/day) | | | |  |  |  |
|  | Low | 44,615 | 50·0 |  | 25 | 5·6 |
|  | High | 44,620 | 50·0 |  | 18 | 4·0 |
| Age at delivery (years) | |  |  |  |  |  |
|  | < 25 | 8,603 | 9·6 |  | 4 | 4·6 |
|  | 25-29 | 24,537 | 27·5 |  | 10 | 4·1 |
|  | 30-34 | 31,680 | 35·5 |  | 16 | 5·1 |
|  | ≥ 35 | 24,415 | 27·4 |  | 13 | 5·3 |
| Smoking habits | |  |  |  |  |  |
|  | Never smoked | 51,999 | 58·3 |  | 30 | 5·8 |
|  | Ex-smokers/smokers | 37,113 | 41·7 |  | 13 | 3·5 |
| Alcohol consumption | |  |  |  |  |  |
|  | Never drank | 30,713 | 34·4 |  | 17 | 5·5 |
|  | Ex-drinkers/drinkers | 58,505 | 65·6 |  | 26 | 4·4 |
| Pre-pregnancy body mass index | |  |  |  |  |  |
|  | < 18·5 kg/m2 | 14,406 | 16·2 |  | 9 | 6·2 |
|  | 18·5-24·9 kg/m2 | 65,370 | 73·3 |  | 32 | 4·9 |
|  | ≥ 25·0 kg/m2 | 9,421 | 10·5 |  | 2 | 2·1 |
| Current history of diabetes or gestational diabetes | | |  |  |  |  |
|  | No | 86,429 | 96·9 |  | 41 | 4·7 |
|  | Yes | 2,806 | 3·1 |  | 2 | 7·1 |
| Infertility treatment | |  |  |  |  |  |
|  | No | 83,193 | 93·3 |  | 36 | 4·3 |
|  | Yes | 6,015 | 6·7 |  | 7 | 11·6 |
| Educational background (years) | |  |  |  |  |  |
|  | < 13 | 31,496 | 35·8 |  | 11 | 3·5 |
|  | ≥ 13 | 56,490 | 64·2 |  | 32 | 5·7 |
| Household income (million Japanese-yen/year) | | |  |  |  |  |
|  | < 6 | 60,086 | 73·0 |  | 30 | 5·0 |
|  | ≥ 6 | 22,192 | 27·0 |  | 10 | 4·5 |
| Occupation in early pregnancy | |  |  |  |  |  |
|  | Administrative, managerial, professional, and engineering | 20,568 | 23·2 |  | 9 | 4·4 |
|  | Clerical | 15,224 | 17·2 |  | 10 | 6·6 |
|  | Sales and service | 19,438 | 21·9 |  | 12 | 6·2 |
|  | Homemaker | 24,686 | 27·9 |  | 7 | 2·8 |
|  | Other | 8,657 | 9·8 |  | 5 | 5·8 |
| Use of multi-vitamin supplements | | |  |  |  |  |
|  | No | 82,059 | 92·4 |  | 41 | 5·0 |
|  | Yes | 6,797 | 7·6 |  | 2 | 2·9 |
| Week of pregnancy at delivery | |  |  |  |  |  |
|  | < 37 weeks (preterm) | 4,143 | 4·6 |  | 6 | 14·5 |
|  | ≥ 37 weeks | 85,092 | 95·4 |  | 37 | 4·3 |
| Parity | |  |  |  |  |  |
|  | 0 | 38,938 | 43·8 |  | 24 | 6·2 |
|  | ≥ 1 | 49,995 | 56·2 |  | 19 | 3·8 |
| Infant sex | |  |  |  |  |  |
|  | Boys | 45,808 | 51·3 |  | 25 | 5·5 |
|  | Girls | 43,419 | 48·7 |  | 18 | 4·1 |

\* Subgroup totals do not equal the overall number because of missing data.

**Table S2.** Spearman’s correlation coefficients between dietary B vitamin intake in early pregnancy and that in mid-late pregnancy

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Early pregnancy | | | Mid-late pregnancy | | |
|  | | Folate | Vitamin B6 | Vitamin B12 | Folate | Vitamin B6 | Vitamin B12 |
| Early pregnancy | |  |  |  |  |  |  |
|  | Folate | 1 |  |  |  |  |  |
|  | Vitamin B6 | 0·70\* | 1 |  |  |  |  |
|  | Vitamin B12 | 0·28\* | 0·53\* | 1 |  |  |  |
| Mid-late pregnancy | |  |  |  |  |  |  |
|  | Folate | 0·57\* | 0·46\* | 0·19\* | 1 |  |  |
|  | Vitamin B6 | 0·45\* | 0·58\* | 0·29\* | 0·70\* | 1 |  |
|  | Vitamin B12 | 0·19\* | 0·32\* | 0·48\* | 0·31\* | 0·54\* | 1 |

\* *P*-value < 0.01



**Fig. S1.** Flow of Study Population