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Original Article

# Maternal smoking during pregnancy and rapid weight gain from birth to early infancy

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A B S T R A C T

*Background:* Although several studies have focused on the association between maternal smoking during pregnancy and rapid weight gain (RWG) during infancy, the dose-response relationship has not yet been confirmed, and very few studies have included Asian populations. Using a record-linkage method, we examined the association between maternal smoking during pregnancy and RWG in infants at around 4 months of age to clarify the dose-response relationship.
*Methods:* Two databases were used: maternal check-ups during pregnancy and early infancy check-ups (between April 1, 2013 and March 31, 2014 in Okinawa, Japan) were linked via IDs and provided to us after unlinkable anonymizing. For 10,433 subjects (5229 boys and 5204 girls), we calculated the change in infants' weight z-score by subtracting the z-score of their birth weight from their weight at early infancy check-ups. Smoking exposure was categorized into five groups. We used Poisson regression to examine the association of maternal smoking during pregnancy with RWG in early infancy.
*Results:* Overall, 1524 (14.6%) were ex-smoker and 511 (4.9%) were current smoker. Compared with the reference category of non-smokers, the adjusted risk ratio of RWG was 1.18 (95% confidence interval [CI], 1.06–1.32) for ex-smokers, 1.18 (95% CI, 0.93–1.50) for those who smoked 1–5 cigarettes per day, 1.57 (95% CI, 1.24–2.00) for those who smoked 6–10 cigarettes per day, and 2.13 (95% CI, 1.51–3.01) for those who smoked ≥11 cigarettes per day. There was a clear dose-response relationship.
*Conclusion:* Our study suggests that maternal smoking during pregnancy is associated in a dose-dependent manner with increased risk of RWG in early infancy.



## 1. Introduction

Maternal smoking during pregnancy is known to restrict intrauterine growth, leading to low birth weight. Studies have also indicated that maternal smoking during pregnancy can lead to overweight or obesity in infancy and childhood,[1–4] and that rapid weight gain (RWG) in early infancy can increase the risk of cardiovascular disease and type 2 diabetes in early adulthood.[5,6] Ong et al. have shown an association between RWG during the first 2 years of life and subsequent obesity, suggesting that this 2-year postnatal period is an important opportunity to prevent the later development of obesity and metabolic disease.[7]

Several studies have focused on the association of maternal smoking during pregnancy and RWG during infancy.[8–10] However, the dose-response relationship, which is important for inferring a causal relationship, has not yet been confirmed. Second, very few recent studies have included Asian populations. Japanese women generally have lower BMI, lower gestational weight gain, and offspring with lower birth weight than Western women[11–14]; they also tend to smoke less. The association between maternal smoking during pregnancy and RWG would be strengthened if it were also

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observed in a Japanese population. Moreover, low birth weight is known to be an independent risk factor for RWG within the first 2 years of life.[7] Therefore, our study tried to assess the direct effect of maternal smoking on RWG in early infancy in a population without low birth weight.

Health check-ups are provided free of charge in Japan for infants at around 4 months of age, and almost all Japanese infants receive them. We can use the unique resulting dataset to investigate the association between maternal smoking and RWG in early infancy in a community setting via cross-referencing with data collected on the mothers at check-ups during pregnancy. Obtaining data during early infancy also helps minimize the effects of lifestyle factors, such as patterns of movement (e.g., crawling and standing), diet, and sleep habits.

The purpose of this study was to use a record-linkage method to examine the association of maternal smoking during pregnancy with RWG in infants at around 4 months of age and to clarify the dose-response relationship.

## 2. Methods

### *2.1. Study subjects*

All 41 municipalities in Okinawa prefecture provide to free four check-ups for pregnant women and infants (at early and late infancy, 18 months, and 36 months) using the same standardized questionnaire. Pregnant women received maternal health check-ups at a medical institute, with questionnaires distributed at municipalities' health centers. Infants received infant check-ups, with questionnaire mailed to each family from municipalities' health centers.

Two databases were used for this study, one including data collected on mothers at check-ups during pregnancy (maternal check-ups) and the other including information on infants receiving check-ups at around 4 months of age (early infancy check-ups). Okinawa Prefecture collected data of both check-ups from 41 municipalities and linked data cross-referenced via IDs in maternity record books. Data were provided to us after unlinkable anonymizing. Between April 1, 2013 and March 31, 2014, 15,781 (91.6%) of the 17,229 infants entitled to early infancy check-ups in Okinawa Prefecture received them. After the linkage to the maternal check-up database, 12,373 subjects (6162 boys and 6211 girls) were singleton and had complete data at the first (around 8–11 weeks of gestation) and the last (around 34–37 weeks of gestation) maternal check-ups. Further, we excluded 1940 subjects falling into one or more of the following categories: preterm gestational age <37 weeks ($n = 443$), birth weight <2500 g ($n = 695$) or $\geq$4000 g ($n = 79$), no information about maternal smoking status during pregnancy or anthropometric data ($n = 303$), and age at check-ups <3 months or >5 months ($n = 420$). Analyses were carried out on the remaining 10,433 subjects (5229 boys and 5204 girls).

### *2.2. Information on maternal smoking during pregnancy*

The mothers were asked about maternal smoking status during pregnancy using a self-reported questionnaire at their first maternal check-ups. This questionnaire included questions about their smoking status before and during pregnancy (current or not) and the number of cigarettes they smoked per day. Those mothers who had smoked before but not during pregnancy were classified as ex-smokers. Current smokers during pregnancy were classified according to the number of cigarettes smoked daily, in multiples of five: 1–5, 6–10, and $\geq$11 cigarettes per day (there were only three groups because few subjects smoked $\geq$16 cigarettes per day).

### *2.3. Rapid weight gain*

Data on the subjects' weight in early infancy (age 3–5 months) were collected at the early infancy check-ups. Data on the subjects' birthweight and gestational age were transcribed from maternal record books by nurses or public health nurses at the same check-ups. We calculated weight z-score (observed value − mean/standard deviation [SD]) at birth. Calculating weight z-score at birth, Ong et al. adjusted for gestational age and sex,[7] and Project Koshu adjusted only for sex, without adjusting for gestational age.[15] We used the latter method, though both gave us a similar results in this study. We calculated weight z-score at early infancy according to sex and month of age. The mean and SD were based on the available data on all of the infants receiving early infancy check-ups in the study period ($n = 15,781$), according to Project Koshu.[15] The weight distribution in our data was similar to that found in Japan's 2000 survey on growth of infants and preschool children[16] and was not skewed, so we calculated direct z-scores. RWG in early infancy was assessed on the basis of changes in weight z-score from birth to early infancy, with a change exceeding +0.67 defined as RWG. According to Ong et al., a z-score of 0.67 represent the width of each percentile band on standard growth charts (2nd, 10th, 25th, 50th, 75th, 90th, and 98th percentile lines); thus, a weight gain exceeding +0.67 SD indicates an increase across at least one of these percentile bands.[7]

### *2.4. Covariates*

Information was collected at the maternal check-ups on age, pre-pregnancy body mass index (BMI; weight [kg]/length [m]$^2$), and weight gain during pregnancy (subtracting the pre-pregnancy weight from the weight at the last maternal check-up). At the early infancy check-ups, information was collected on sex, gestational age at birth, birth order, birth weight, and paternal smoking during pregnancy. We also collected information on how the infants had been fed between birth and the early infancy check-ups and divided them into three feeding categories: exclusive breast-feeding, mixed feeding, and exclusive bottle-feeding.

### *2.5. Statistical analysis*

We used Stata 12 for Windows (STATA Corporation, College Station, TX, USA) software for statistical analysis, and we used Poisson regression analysis to estimate crude and adjusted risk ratios (RRs) and 95% confidence intervals (CIs) for RWG during early infancy according to maternal smoking status during pregnancy. We found no statistical interaction according to infant sex ($p = 0.44$), so we constructed combined models for both sexes. Our multivariable model included potential confounders identified in previous studies: infants' sex, birth order (first, second, or later), maternal age ($\leq$26 years [25th percentile], 27–33 years [25th-75th percentile], or $\geq$34 years [75th percentile]), paternal smoking during pregnancy (current or not), gestational age (continuous), and maternal pre-pregnancy BMI (<18.5, 18.5–22.9, 23–24.9, or $\geq$25 kg/m$^2$). The inclusion of age in days from birth to infancy check-ups in the multivariable model did not alter the results substantially, so we did not adopt this factor as a covariate. This multivariable model was further adjusted individually for type of feeding between birth and the early infancy check-ups (exclusive breast-feeding, mixed feeding, or exclusive bottle-feeding), maternal weight gain (<5, 5–6.9, 7–8.9, 9–10.9, 11–12.9, or $\geq$13 kg), and birth weight (continuous). A previous study had found interaction between maternal smoking and type of feeding between birth and early infancy check-ups in the risk of RWG,[17] but we found no interaction ($p = 0.39$). Therefore, we treated feeding as a covariate. For trend analysis, Poisson regression analysis was repeated, with smoking categories given integer values.

### 2.6. Ethical considerations

All data provided by Okinawa Prefecture were anonymized in an unlinkable fashion, and the researchers were blinded to personal information about the mothers and infants. This study was approved by the Ethics Committee of Toho University (approval number: 25124).

## 3. Results

Table 1 shows the maternal smoking status during pregnancy of the study subjects. In total, 8398 (80.5%) were non-smokers, 1524 (14.6%) were ex-smokers, and 511 (4.9%) reported smoking during pregnancy. A majority (52.8%) of the current smokers smoked 1–5 cigarettes per day. The current smokers tended to be younger, to be overweight, to gain less weight during pregnancy, and to have husbands who smoked during pregnancy. The infants whose mothers smoked were likely to be second or later children and to have received mixed feeding.

Table 2 shows the anthropometric data of the infants by sex and maternal smoking status. In both sexes, average birth weight and z-score at birth tended to decrease as the number of cigarettes smoked by their mothers increased. In contrast, average weight and z-score during early infancy tended to increase in line with the number of cigarettes smoked by the mothers. Thus, changes in weight z-score and the incidence of RWG in early infancy increased in line with increased maternal smoking: around 20% of the infants with non-smoking mothers experienced RWG, whereas the proportion was almost 40% among infants whose mothers smoked ≥11 cigarettes per day.

Table 3 shows the dose-response relationship between the smoking category (based on the number of cigarettes smoked by mothers during pregnancy) and the risk of RWG in early infancy, as determined by Poisson regression analysis. Compared with non-smokers, the multivariable-adjusted RRs for RWG were 1.18 (95% CI, 1.06–1.32) for ex-smokers, 1.18 (95% CI, 0.93–1.50) for those who smoked 1–5 cigarettes per day, 1.57 (95% CI, 1.24–2.00) for those who smoked 6–10 cigarettes per day, and 2.13 (95% CI, 1.51–3.01) for those who smoked ≥11 cigarettes per day. Further adjustment for type of feeding between birth and early infancy, and for maternal weight gain during pregnancy, did not change the RRs substantially (Table 3). In contrast, adjustment for birth weight attenuated the RRs, although a statistically significant association between maternal smoking status and RWG remained. When smoking categories were treated as integer values, upward trends across smoking statuses were observed (p for trend<0.05 for each model).

In order to minimize the influence of the difference in days between birth and early infancy check-ups, we limited to infants who received check-ups at 4 months of age and repeated the analysis, with similar results (eTable 1).

## 4. Discussion

This study showed an increased risk of RWG in early infancy for infants exposed to maternal smoking during pregnancy, and a clear dose-response relationship was observed between the number of

**Table 1**
Characteristics of the study population by maternal smoking during pregnancy.

| | Non-smoker | Ex-smoker | Current-smoker (number of cigarettes per day) | | | $p$-value[b] |
|---|---|---|---|---|---|---|
| | (n = 8398) n (%)[a] | (n = 1524) n (%)[a] | 1-5 cigarettes/day (n = 270) n (%)[a] | 6–10 cigarettes/day (n = 189) n (%)[a] | ≥11 cigarettes/day (n = 52) n (%)[a] | |
| **Parental** | | | | | | |
| Maternal age, years | | | | | | <0.001 |
| ≤26 (<25th percentile) | 1820 (21.7) | 645 (42.3) | 122 (45.2) | 64 (33.9) | 12 (23.1) | |
| 27-33 (25-75th percentile) | 3843 (45.8) | 556 (36.5) | 103 (38.2) | 82 (43.4) | 32 (61.5) | |
| ≥34 (>75th percentile) | 2731 (32.5) | 323 (21.2) | 45 (16.7) | 43 (22.8) | 8 (15.4) | |
| Maternal BMI | | | | | | <0.001 |
| <18.5 kg/m | 1240 (14.8) | 239 (15.7) | 53 (19.6) | 24 (12.8) | 7 (13.5) | |
| 18.5–22.9 kg/m | 5266 (62.8) | 865 (57.0) | 139 (51.5) | 102 (54.3) | 22 (42.3) | |
| 23–24.9 kg/m | 929 (11.1) | 187 (12.3) | 30 (11.1) | 23 (12.2) | 5 (9.6) | |
| ≥25 kg/m | 947 (11.3) | 228 (15.1) | 48 (17.8) | 29 (20.7) | 18 (34.6) | |
| Weight gain during pregnancy | | | | | | <0.001 |
| ≤4.9 kg | 913 (10.9) | 124 (8.1) | 25 (9.2) | 32 (14.9) | 14 (26.7) | |
| 5–6.9 kg | 1133 (13.5) | 133 (8.7) | 19 (7.0) | 18 (9.5) | 8 (15.4) | |
| 7–8.9 kg | 2032 (24.2) | 254 (16.7) | 53 (19.6) | 46 (24.3) | 12 (23.1) | |
| 9–10.9 kg | 2106 (25.1) | 283 (18.6) | 56 (20.7) | 31 (16.4) | 8 (15.4) | |
| 11–12.9 kg | 1310 (15.6) | 279 (18.3) | 58 (21.5) | 30 (15.9) | 5 (9.6) | |
| ≥13 kg | 904 (10.8) | 451 (29.6) | 59 (21.9) | 32 (16.9) | 5 (9.7) | |
| Paternal smoking during pregnancy | 2551 (33.1) | 945 (64.2) | 210 (80.2) | 151 (83.0) | 37 (74.0) | <0.001 |
| **Infancy** | | | | | | |
| Sex (boy) | 4223 (50.3) | 738 (48.4) | 145 (53.7) | 90 (47.6) | 33 (64.5) | 0.12 |
| Gestational age[c] | 39.0 (1.1) | 39.1 (1.1) | 39.1 (1.1) | 39.0 (1.1) | 38.8 (1.2) | 0.18 |
| Birth order | | | | | | <0.001 |
| First | 2913 (34.9) | 720 (47.5) | 119 (44.4) | 52 (28.8) | 15 (28.9) | |
| Second or later | 5430 (65.1) | 796 (52.5) | 149 (55.6) | 131 (71.25) | 37 (71.2) | |
| Feeding between birth and early infancy checkups | | | | | | <0.001 |
| Exclusive breast-feeding | 3011 (36.1) | 392 (25.9) | 67 (25.0) | 34 (18.2) | 16 (31.4) | |
| Mixed-feeding | 2923 (35.0) | 705 (46.7) | 141 (52.6) | 115 (61.5) | 27 (53.0) | |
| Exclusive bottled feeding | 2419 (29.0) | 414 (27.4) | 60 (22.4) | 38 (20.3) | 8 (15.7) | |

BMI, body mass index.
Due to missing values, the totals for the stratified subgroups are not equal.
[a] Column %.
[b] p-value for $\chi^2$ test or Analysis of variance or Fisher's exact test.
[c] Mean (standard deviation).

**Table 2**
Anthropometric data by sex and maternal smoking during pregnancy.

| | Non-smoker Mean (SD) | Ex-smoker Mean (SD) | Current smoker 1-5 cigarettes/day Mean (SD) | Current smoker 6-10 cigarettes/day Mean (SD) | Current smoker ≥11 cigarettes/day Mean (SD) |
|---|---|---|---|---|---|
| **Total (n = 10,433)** | 8398 | 1524 | 270 | 189 | 52 |
| Birth weight | 3083.1 (317.4) | 3076.1 (312.5) | 3053.4 (298.6) | 3014.9 (306.6) | 2947.4 (251.3) |
| z-score at birth | 0.21 (0.76) | 0.20 (0.75) | 0.14 (0.71) | 0.05 (0.73) | −0.11 (0.60) |
| Weight at early infancy | 6960.7 (802.0) | 7052.0 (823.9) | 7048.1 (818.3) | 7165.8 (921.8) | 7147.8 (683.9) |
| z-score at early infancy | 0.04 (0.94) | 0.15 (0.96) | 0.12 (0.97) | 0.23 (1.07) | 0.26 (0.84) |
| Change in weight z-score from birth to early infancy | −0.17 (0.94) | −0.05 (0.93) | −0.02 (1.00) | 0.18 (0.99) | 0.38 (0.94) |
| Rapid weight gain (%) | 1527 (18.8) | 335 (22.0) | 57 (21.1) | 54 (28.6) | 20 (38.5) |
| **Boys (n = 5229)** | 4223 | 738 | 145 | 90 | 33 |
| Birth weight | 3114.7 (315.2) | 3109.3 (311.2) | 3082.4 (316.5) | 3067.0 (299.1) | 2923.6 (207.8) |
| z-score at birth | 0.19 (0.75) | 0.18 (0.73) | 0.12 (0.75) | 0.09 (0.71) | −0.26 (0.49) |
| Weight at early infancy | 7208.8 (780.8) | 7296.1 (801.3) | 7213.8 (769.7) | 7418.2 (882.6) | 7276.5 (770.9) |
| z-score at early infancy | 0.03 (0.94) | 0.14 (0.97) | −0.01 (0.95) | 0.23 (1.06) | 0.14 (0.93) |
| Change in weight z-score from birth to early infancy | −0.16 (0.94) | −0.04 (0.93) | −0.12 (0.98) | 0.14 (1.00) | 0.41 (0.84) |
| Rapid weight gain (%) | 783 (18.5) | 166 (22.5) | 25 (17.2) | 24 (26.7) | 13 (39.4) |
| **Girls (n = 5204)** | 4175 | 786 | 125 | 99 | 19 |
| Birth weight | 3051.2 (316.4) | 3044.8 (310.6) | 3019.9 (273.8) | 2964.8 (306.3) | 2988.6 (315.1) |
| z-score at birth | 0.24 (0.77) | 0.22 (0.76) | 0.16 (0.66) | 0.28 (0.75) | 0.09 (0.76) |
| Weight at early infancy | 6709.7 (743.0) | 6822.9 (778.1) | 6855.8 (833.9) | 6936.3 (900.4) | 6924.5 (431.0) |
| z-score at early infancy | 0.06 (0.94) | 0.20 (0.97) | 0.25 (1.05) | 0.29 (1.10) | 0.26 (0.61) |
| Change in weight z-score from birth to early infancy | −0.18 (0.95) | −0.03 (1.09) | 0.09 (1.09) | 0.26 (1.03) | 0.18 (1.03) |
| Rapid weight gain (%) | 744 (17.8) | 169 (21.5) | 32 (25.6) | 30 (30.3) | 7 (36.8) |

SD, standard deviation.

cigarettes smoked and RWG risk. The association remained after we adjusted for the type of feeding, maternal weight gain during pregnancy, and birth weight, so our results suggest that the association of maternal smoking status during pregnancy with RWG in early infancy is independent of these three factors.

Previous studies on the association between maternal smoking during pregnancy and weight gain in infancy have shown disparate results, perhaps largely because of differences in the study periods and outcome indicators.[8,9,18] However, most studies focusing on weight gain in early infancy have shown a positive association between maternal smoking during pregnancy and weight gain. In a cohort study of neonates carried out in Norway in 1992 and 1993, Nafstad et al. used weight gain during the first year as an outcome indicator and found that infants born to smoking mothers gained more weight, in a dose-dependent manner, than those born to non-smoking mothers.[9] They also investigated breast-feeding during the first 6 months and suggested that the observed weight gain could be partially explained by the shorter duration of breast-feeding by smoking mothers. In Canada, Dubois observed infants born in 1998 from birth to 5 months of age and found that those born to smoking mothers gained more weight than those born to non-smoking mothers.[18] Harrod et al. used air-displacement plethysmography to measure changes in the body composition of infants born in the United States between July 2010 and November 2013 from birth to 5 months.[19] They found that fat-free mass at 5 months was significantly greater in infants exposed to prenatal smoking than in those not exposed, but that the mean change in weight-for-length z-score of offspring between birth and 5 months was not significantly different.

Two other studies[20,21] investigated the association between maternal smoking during pregnancy and RWG in infancy using the same definition of RWG by Ong et al. used in our study. Wijlaars et al. analyzed 2402 infant/parent pairs in England and reported a positive association between maternal smoking during pregnancy and RWG at 3 months of age.[20] With non-smokers as the reference category, the odds ratio (OR) of RWG in infants of mothers who smoked during pregnancy was 1.34 (95% CI, 1.00–1.78). However, they did not investigate the dose-response relationship. Lyte et al. studied 11,134 children and parents in Ireland to investigate the

**Table 3**
Risk ratios of rapid weight gain at early infancy by maternal smoking during pregnancy, With calculated weight z-scores at birth adjusted for sex and gestational age.

| | | n/N (%) | Crude risk ratio (95% CI) | Multivariable risk ratio[a] (95% CI) | Further adjusted by: Feeding between birth and early infancy checkups (95% CI) | Further adjusted by: Maternal weight gain during pregnancy (95% CI) | Further adjusted by: Birth weight (95% CI) |
|---|---|---|---|---|---|---|---|
| Non-smoker | | 1527/8398 (18.2) | ref | ref | ref | ref | ref |
| Ex-smoker | | 335/1524 (22.0) | 1.21 (1.09–1.34) | 1.18 (1.06–1.32) | 1.18 (1.05–1.32) | 1.19 (1.06–1.34) | 1.17 (1.05–1.32) |
| Current-smoker | 1–5 cigarettes/day | 57/270 (21.1) | 1.16 (0.91–1.47) | 1.18 (0.93–1.50) | 1.17 (0.92–1.48) | 1.18 (0.93–1.51) | 1.14 (0.89–1.44) |
| | 6–10 cigarettes/day | 54/189 (28.6) | 1.57 (1.25–1.98) | 1.57 (1.24–2.00) | 1.55 (1.22–1.98) | 1.58 (1.24–2.01) | 1.41 (1.10–1.80) |
| | ≥11 cigarettes/day | 20/52 (38.5) | 2.12 (1.50–2.99) | 2.13 (1.51–3.01) | 2.05 (1.43–2.93) | 2.13 (1.51–3.01) | 1.80 (1.30–2.50) |
| Risk ratio for one category increase | | | 1.17 (1.11–1.23) | 1.15 (1.10–1.21) | 1.16 (1.10–1.23) | 1.16 (1.09–1.22) | 1.13 (1.07–1.19) |

CI, confidence interval.
[a] Adjusted for infant' sex, birth order, maternal age, paternal smoking during pregnancy, gestational age, and pre-pregnant BMI.

risk of RWG at 9 months,[21] and their results suggested a positive association between prenatal exposure to smoking and RWG, with a dose-response relationship. The OR of RWG at 9 months of age for the children of mothers who smoked heavily (≥11cigarettes daily), after adjusting for birth weight and gestation, was 1.85 (95% CI not reported). In our study, the relative risk of RWG, after adjusting for birth weight, in infants whose mothers smoked ≥11 cigarettes per day was 1.80, which was close to Lyte's figure.

The mechanisms of the link between maternal smoking during pregnancy and RWG have not been fully clarified, but several hypotheses can be put forward. First, nicotine, which is transported across the placenta, may explain the physiologic effects of smoking during pregnancy.[22] In an animal study, rats prenatally exposed to low doses of nicotine were not smaller at birth but had higher fat levels.[23] It has also been suggested that maternal smoking during pregnancy may be associated with lower cord blood leptin,[22] and that a low concentration of this hormone at birth may provide a signal for catch-up growth by inhibiting satiety.[7] Thus, it is conceivable that the mechanisms linking prenatal smoking with RWG bypass birth weight and type of feeding.

The main strength of our study is that we had access to a large population-based dataset rather than a hospital-based dataset. Second, we collected information about maternal smoking status before and during pregnancy, and we had information on number of cigarettes smoked per day during pregnancy. Thus, we could observe increased risk of RWG in infants born to ex-smokers and light smokers (1–5 cigarettes per day), which allowed us to assess the dose-response relationship. Also, because we were able to examine the infants in early infancy (at 3–5 months of age), the influence of lifestyle factors was minimized.

The main limitation of our study is that maternal smoking status was assessed using self-report. Because of the self-report format of our study, the subjects in the ex-smoker group may actually have included some current smokers. Tong et al. reported that 10% of woman who claimed to have stopped smoking showed biochemical evidence of continued smoking.[24] It is possible that we overestimated the risk of RWG in the ex-smoker group, and that smoking cessation during pregnancy may have a greater effect on RWG in early infancy than the study results indicate. Next, a recent study on the relationship between the socioeconomic status of mothers and RWG in their infants is worthy of attention.[25] We did not have access to information on socio-economic status, such as maternal education, household income, and occupation. Further studies that include information on socio-economic status will be necessary. Last, our subjects were from Okinawa Prefecture, which has a distinct culture from the rest of Japan, including food and lifestyle. Therefore, our subjects might not be representative of pregnant Japanese woman.

In conclusion, our results from a large population-based dataset clearly show that maternal smoking during pregnancy results in dose-dependent increases in the risk of RWG in their offspring in early infancy. This finding is significant because previous studies of maternal smoking status and RWG in infants have not included Asian subjects, who differ physically from Western subjects.

## Conflicts of interest

None declared.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.je.2016.10.005.

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