Associations between prepregnancy body mass index, gestational weight gain and weight catch-up in small-for-gestational-age children

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Abstract
Inadequate gestational weight gain (GWG) was related with a higher incidence of small-for-gestational-age (SGA) births than appropriate GWG; however, the long-term association of maternal GWG with weight catch-up growth in SGA children remains unknown. The objective of this study is to evaluate the associations between prepregnancy body mass index (pBMI), GWG and weight catch-up patterns in SGA children. Data were from the Collaborative Perinatal Project, an American multicentre prospective cohort study. A total of 56,990 gravidas were recruited at the first prenatal visit, and children were followed up until school age. Maternal pBMI, GWG and physical growth of the offspring at birth, 4 months, 1 year, 4 years and 7 years old were recorded. The latent class analysis was employed to form weight catch-up growth patterns (appropriate, excessive, slow, regression and no catch-up patterns) in SGA children. SGA children who developed the ‘appropriate catch-up growth’ pattern and whose mothers had appropriate pBMI and GWG were chosen as the reference. Associations between GWG for different pBMI and weight catch-up patterns were analysed by multivariate logistic regression models. A total of 1619 infants (9.45%) were born term SGA. After adjusting for relevant confounders, compared with SGA children whose mothers had appropriate pBMI and GWG, SGA children with maternal prepregnancy underweight (for inadequate GWG, GWG below recommendations, adjusted OR: 2.88, 95% CI: 1.13–7.31; for appropriate/excessive GWG, adjusted OR: 3.07, 95% CI: 1.74–5.42) or with prepregnancy normal weight but inadequate GWG (adjusted OR: 2.14, 95% CI: 1.36–3.38) were at a higher risk of having the ‘no catch-up growth’ pattern. We suggest that SGA children with maternal prepregnancy underweight or inadequate GWG tend to have a poor weight catch-up growth at least until school age.

KEYWORDS
child, gestational gain, prepregnancy body mass index, small-for-gestational-age, weight, weight catch-up growth
INTRODUCTION

Although the prevalence of small-for-gestational-age (SGA) births has decreased (Campisi et al., 2019; Fujita et al., 2016), SGA babies still count a lot in developing and developed countries. The worldwide prevalence of SGA births is about 10% (Marzouk et al., 2017), ranging from 7% in industrialized countries (Campisi et al., 2019) to over 30% in South Asia or South Africa (Katz et al., 2014; Lavin et al., 2019; Lee et al., 2013).

Although quite a few studies emphasized the importance of appropriate catch-up growth, there were still 10% to 15% SGA children failing to develop the appropriate catch-up growth. Inappropriate postnatal catch-up growth in SGA infants was reported to be associated with problems in physical growth and cognitive/behavioural development in future life (Matthews et al., 2017; Perng et al., 2016; Pylipow et al., 2009; Takeuchi et al., 2018; Victora et al., 2003) and a significant burden for affected individuals, their families and the society (Li et al., 2013; Siega-Riz et al., 2009).

Previous studies showed that inadequate gestational weight gain (GWG, GWG below recommendations) was related with a higher incidence of SGA births than appropriate GWG (Goldstein et al., 2017; Li et al., 2013; Siega-Riz et al., 2009). In utero nutrition has deep associations with adult metabolic diseases (Carolan-Olah et al., 2015; Radford et al., 2014). Animal experiments also suggested the possibility of growth retardation induced by maternal low GWG (Wallace et al., 2015). A research found that inadequate GWG would increase the risk of stunting in SGA children (Goldstein et al., 2017; Xie et al., 2016). Therefore, we wonder whether GWG, an index of gestational energy intake, has effects on the physical growth in SGA children. However, related population studies are limited, and the long-term association of maternal GWG with weight catch-up growth in SGA children remains unknown and is not studied.

Therefore, we hypothesize that, in SGA children, inadequate maternal GWG might associate with inadequate weight catch-up growth, and maternal GWG with different prepregnancy body mass index (pBMI) may induce different weight catch-up patterns. In this study, we aim to evaluate the relationship between maternal pBMI, GWG and weight catch-up in SGA children using a multicentre long-running cohort study.

METHODS

Study population

The Collaborative Perinatal Project (CPP, 1959–1976) was a prospective birth-cohort study that recruited pregnant women who received prenatal care at 12 US academic medical centres. Information about maternal behaviour and physical examination was collected at entry and at each prenatal follow-up visit with standardized CPP operation procedures, and offspring were followed up until school age with physical growth assessments at birth, 4 months, 1 year, 4 years and 7 years of age (Hardy, 2003; Klebanoff, 2009). There were 56,990 pregnancies enrolled in CPP at first, and the percentages of surviving children successfully followed was 88% at 1 year old, 75% at 4 years old and 79% at 7 years old (Hardy, 2003; Klebanoff, 2009). Former researches using CPP data reported that, at follow-up evaluations, most of the children failed to return because of mothers having other young children to care for, illness of other family members or other problems, rather than the reasons related to the presence or absence of abnormalities of the study child or characteristics of the subject (Natus, 2015). The study obeyed with all applicable requirements to conduct research in humans, women gave oral informed consent prior to the CPP study and use of publicly available de-identified data was exempt from the review by our Institutional Review Board.

Exposure

GWG plus pBMI was used as the independent variable in this study. Maternal data were collected at enrolment (gestational weeks of their first prenatal-care visit, median [IQR]: 21 [15–27] weeks) using a
A questionnaire including self-reported prepregnancy weight, age, race, number of cigarettes smoked per day, number of siblings in the household and number of previous pregnancies (Wrotniak et al., 2008). Previous studies have noted that women's recall was highly accurate for their prepregnancy weight even after 30 or more years (Tomeo et al., 1999). Maternal weight and height were measured at the time of delivery. All obstetric examinations and procedures were conducted by trained study staff. GWG was determined as the difference between measured weight at delivery and self-reported prepregnancy weight. According to pBMI, we divided mothers into three groups including prepregnancy underweight (<18.5 kg/m²), normal weight (18.5 ≤ BMI < 25 kg/m²) and overweight/obesity (BMI ≥ 25 kg/m²). Because women with prepregnancy overweight and obesity were limited in numbers (11.6% and 4.6%, respectively), we merged overweight and obese women into the prepregnancy overweight/obesity group (BMI ≥ 25 kg/m²). Mothers were further classified into three groups based on GWG according to the 2009 National Institution of Medicine Guideline (Yaktine, 2009), including excessive GWG, appropriate GWG and inadequate GWG groups (the GWG recommendations for prepregnancy underweight, normal weight, overweight and obesity are 12.5–18.0, 11.5–16.0, 7.0–11.5 and 5–9 kg, respectively). Therefore, mothers were classified into nine groups including prepregnancy underweight and inadequate or appropriate or excessive GWG; prepregnancy normal weight and inadequate or appropriate or excessive GWG; prepregnancy overweight/obesity and inadequate or appropriate or excessive GWG groups.

### 2.4 | Outcome

The main outcome in this study was the post-natal weight growth pattern. In our former study, we used the latent class analysis (LCA) to explore the catch-up growth patterns for term SGA children and formed five catch-up growth trajectories including the appropriate, slow, no, excessive catch-up growth patterns and the regression after 4 months pattern (Lei et al., 2015). Sex- and age-specific weight z-scores were calculated, because z-scores could reflect the relative
position of a child on the growth chart. The ‘appropriate catch-up growth’ pattern (with a rapid weight catch-up growth at the first 4 months that was from less than the 10th percentile at birth to the 30th percentile at 4 months; modest catch-up thereafter that was from the 30th percentile at 4 months to the 50th percentile at 1 year old; then keeping around the 50th percentile from 1 to 7 years of age).

### TABLE 1  Maternal and offspring characteristics of the study mother–SGA pairs based on GWG

| Characteristics                          | Inadequate GWG (n = 1195) | Appropriate GWG (n = 331) | Excessive GWG (n = 93) | P*  |
|------------------------------------------|---------------------------|----------------------------|------------------------|-----|
| Mother                                   |                           |                            |                        |     |
| Age mean (SD)                            | 23.9 (6.5)                | 23 (6.1)                   | 24.9 (6.8)             | <0.05|
| Race, Caucasian, N (%)                   | 443 (37.1)                | 112 (33.8)                 | 27 (29)                | 0.20 |
| Education, N (%)                         |                           |                            |                        | 0.22 |
| ≥13 years                                | 102 (8.5)                 | 18 (5.4)                   | 10 (10.8)              |      |
| 10–12 years                              | 715 (59.8)                | 201 (60.7)                 | 59 (63.4)              |      |
| ≤9 years                                 | 378 (31.6)                | 112 (33.8)                 | 24 (25.8)              |      |
| Prepregnancy BMI, mean (SD)              | 21.5 (3.7)                | 22.4 (3.8)                 | 26 (6.4)               | <0.05|
| Prepregnancy BMI, N (%)                  |                           |                            |                        | <0.05|
| Underweight                              | 184 (81.8)                | 36 (16)                    | 5 (2.2)                |      |
| Normal weight                            | 886 (77.7)                | 215 (18.8)                 | 40 (2.5)               |      |
| Overweight/obesity                       | 125 (49.4)                | 80 (31.6)                  | 48 (19)                |      |
| Smoking, N (%)                           |                           |                            |                        | 0.17 |
| 0 pipes per day                          | 464 (38.8)                | 139 (42)                   | 39 (42)                |      |
| 1–19 pipes per day                       | 439 (36.7)                | 119 (36)                   | 36 (38.7)              |      |
| ≥20 pipes per day                        | 234 (19.6)                | 68 (20.5)                  | 15 (16.1)              |      |
| Unknown                                  | 58 (4.9)                  | 5 (1.5)                    | 3 (3.2)                |      |
| Social economic status, N (%)            |                           |                            |                        | 0.99 |
| 1 (lowest)                               | 136 (11.4)                | 42 (12.7)                  | 10 (10.8)              |      |
| 2                                        | 417 (34.9)                | 110 (33.2)                 | 34 (36.6)              |      |
| 3                                        | 349 (29.2)                | 99 (29.9)                  | 26 (28)                |      |
| 4                                        | 204 (17.1)                | 58 (17.5)                  | 18 (19.4)              |      |
| 5 (highest)                              | 73 (6.1)                  | 18 (5.4)                   | 5 (5.4)                |      |
| Unknown                                  | 16 (1.3)                  | 4 (1.2)                    | 0 (0)                  |      |
| Offspring                                |                           |                            |                        |     |
| Boys, N (%)                              | 570 (47.7)                | 181 (54.7)                 | 52 (55.9)              | <0.05|
| Gestational age at birth (weeks)         | 39.3 (1.2)                | 39.3 (1.3)                 | 39.3 (1.1)             | 0.69 |
| Birthweight, kg, mean (SD)               | 2.2 (0.3)                 | 2.5 (0.2)                  | 2.5 (0.3)              | <0.05|
| z-score                                  | −1.6 (0.5)                | −1.5 (0.4)                 | −1.6 (0.5)             | <0.05|
| Weight at 4 months, kg, mean (SD)        | 5.6 (0.8)                 | 5.7 (0.7)                  | 5.8 (0.9)              | <0.05|
| z-score                                  | −0.9 (0.9)                | −0.8 (0.8)                 | −0.7 (1)               | <0.05|
| Weight at 1 year, kg, mean (SD)          | 8.9 (1.1)                 | 9.1 (1.2)                  | 9.3 (1.3)              | <0.05|
| z-score                                  | −0.8 (0.9)                | −0.6 (0.9)                 | −0.5 (1)               | <0.05|
| Weight at 4 years, kg, mean (SD)         | 15.1 (2)                  | 15.5 (1.9)                 | 16 (2.9)               | <0.05|
| z-score                                  | −0.6 (0.9)                | −0.5 (0.9)                 | −0.2 (1.3)             | <0.05|
| Weight at 7 years, kg, mean (SD)         | 21.9 (4)                  | 22.8 (4.1)                 | 23.7 (5.4)             | <0.05|
| z-score                                  | −0.4 (0.9)                | −0.2 (1)                   | 0 (1.3)                | <0.05|

Note: Continuous variables were shown in mean (SD), and categorical variables were shown in N (%). Chi-square was used for categorical variables, and ANOVA was used for continuous variables.

Abbreviations: BMI, body mass index; GWG, gestational weight gain; mother–SGA, mother–small-for-gestational-age children; SGA, small for gestational age.
*Comparisons among SGA children in different GWG levels, P < 0.05 was set as statistically significant.
was used as the reference pattern because it had a lower risk of overweight/obesity and growth restriction at 7 years and did not show any increased risks of other adverse outcomes than the appropriate gestational-age children (Lei et al., 2015). Children's weight and height measurements were done by staff members with special training, strictly following the standardized CPP procedures (Hardy, 2003; Klebanoff, 2009).

### 2.5 | Confounders

Based on literature review and statistical analyses, the models were adjusted for confounders that may affect GWG and offspring physical growth including maternal age, education level, race, smoking during pregnancy, child sex, parity and economic status (Hack et al., 2003; Leger et al., 1998).

### 2.6 | Statistics analysis

Baseline characteristics of the study population among three GWG categories were examined by chi-square for categorical variables and ANOVA for continuous variables.

LCA is a statistical method used to identify a set of discrete, mutually exclusive latent classes of individuals based on their responses to a set of observed categorical variables (Lanza et al., 2007). The probability of belonging to which catch-up pattern was calculated for each individual and was estimated from the model parameters. For descriptive analyses and modelling-checking purposes, individuals could be assigned to the patterns to which they had the highest probability of belonging. We used LCA to group SGA children into different growth patterns by their weight percentiles (Lei et al., 2015). This was done in a probabilistic manner, using maximum likelihood, conducted by PROC LCA in SAS (version 9.4).

The exposure variable, GWG, was related to the growth patterns via a multivariate logistic regression model after adjusting for confounders mentioned above, using the appropriate GWG as reference. To elucidate the impact of pBMI on the association between GWG and weight catch-up patterns, we used the pBMI as a stratified variable and further analysed the association of GWG categories with weight catch-up patterns among women in different pBMI levels. Because very few prepregnancy underweight women developed excessive GWG ($n = 5$), prepregnancy underweight women with appropriate or excessive GWG were merged into one group ($n = 41$).

Odds ratios (ORs) and 95% confidence intervals (CIs) calculated for the ORs were analysed using SAS software (version 9.4, SAS Institute, Cary, NC). $P < 0.05$ was considered as a significant level.

### 3 | RESULTS

Table 1 showed maternal and offspring characteristics based on GWGs. A total of 1619 mother–SGA child pairs were included in this study, accounting for 9.5% of the whole investigated population, close to the prevalence of SGA children all over the world (Katz et al., 2014). The Caucasian accounted for 36.0%, and the boys accounted for 49.6%. Maternal age was $23.8 \pm 6.4$ years old, pBMI was $22.0 \pm 4.1 \text{ kg/m}^2$ and gestational age at birth was $39.3 \pm 1.2$ weeks based on the last menstrual period. Weights of the study SGA children were $2.5 \pm 0.2$ kg at birth, $5.6 \pm 0.8$ kg at 4 months old, $9.0 \pm 1.1$ kg at 1 year old, $15.2 \pm 2.1$ kg at 4 years old and $22.2 \pm 4.1$ kg at 7 years old. The prepregnancy underweight, normal weight and overweight/obesity accounted for 13.7%, 70.7% and 15.6%, respectively, based on maternal pBMI. Average GWG was $8.1 \pm 5.2$ kg, and inadequate, appropriate and excessive GWGs accounted for 73.7%, 20.6% and 5.8%, respectively.

Figure 2 displayed weight $z$-scores from birth to 7 years old by different GWG categories. SGA children in the inadequate GWG group got the lowest weight catch-up level, reached the lowest weights at birth, ages of 4 months, 1 year, 4 years and 7 years, and the differences were statistically significant at each follow-up stage.

![Figure 2](image-url)
compared with SGA children with appropriate or excessive maternal GWG (Table 1 and Figure 2).

Figure 3 depicted the results of LCA, dividing SGA children with different growth trajectories into five distinct patterns. The grouping method was based on our previous study (Lei et al., 2015). All SGA children had a similar starting weight percentile (the 10th percentile). The proportions of the ‘no catch-up growth’, ‘regression after 4 months’, ‘slow catch-up growth’, ‘excessive catch-up growth’ and ‘appropriate catch-up growth’ patterns were 23.4%, 16.2%, 17.0%, 9.3% and 34.2%, respectively.

Table 2 displayed the association between GWG and weight catch-up growth patterns and analysed via multivariate logistic models. After adjusting for pBMI and other covariates, we found that compared with SGA children whose mothers had appropriate GWG, children whose mothers had inadequate GWG were at a higher odd of being classified in the ‘no catch-up growth’ pattern (adjusted OR: 1.79, 95% CI: 1.24–2.58). Children whose mothers had inadequate GWG were also at a marginally higher odd of being classified in the ‘regression after 4 months’ pattern (adjusted OR: 1.25, 95% CI: 0.83–1.82). Children whose mothers had excessive GWG had no significant associations with any of the catch-up growth patterns (all P values > 0.05).

Table 3 described the associations between GWG and weight catch-up growth patterns for different pBMI categories. Mothers with prepregnancy normal BMI and appropriate GWG were chosen as the reference group. Multivariate logistic models were used to calculate the risks of being classified in different patterns. Children with maternal prepregnancy underweight and any GWG were at higher odds of being classified in the ‘no catch-up’ pattern, and maternal prepregnancy underweight plus inadequate GWG had the highest odd of being classified in the ‘no catch-up growth’ pattern (adjusted OR: 3.07, 95% CI: 1.74–5.42). In SGA children with maternal prepregnancy normal weight but inadequate GWG, a higher odd of being classified in the ‘no catch-up growth’ pattern (adjusted OR: 2.14, 95% CI: 1.36–3.38) was found compared with the reference group. Among SGA children with maternal prepregnancy overweight/obesity, GWG had no significant associations with specific growth patterns.

However, it was interesting to note that if using the recommendations from the 1970s GWG guideline (maternal GWGs of 9.1–12.2 kg were considered appropriate for any pBMI level) (Abrams, 1993) and performing the same analyses, the results on the association of GWG with catch-up growth patterns would show a similar trend (Tables S1 and S2) but were ‘not quite the same’.
TABLE 3 Relationships between GWG and weight catch-up patterns in term SGA children with different maternal prepregnancy BMI

| Prepregnancy BMI | GWG      | No catch-up pattern (aOR, 95% CI) | Regression after 4-months pattern (aOR, 95% CI) | Excessive catch-up pattern (aOR, 95% CI) | Slow catch-up pattern (aOR, 95% CI) |
|-----------------|----------|----------------------------------|-----------------------------------------------|----------------------------------------|-----------------------------------|
|                  |          | P<0.05                           | P<0.05                                       | P<0.05                                 | P<0.05                           |
| Underweight     | Inadequate | 3.07 (1.74–5.42)                 | 1.73 (0.97–3.09)                             | 0.34 (0.12–0.94)                       | 1.28 (0.69–2.37)                 |
|                  | Appropriate/excessive | 2.88 (1.13–7.31)                 | 1.61 (0.60–4.31)                             | 0.89 (0.23–3.42)                       | 1.53 (0.55–4.24)                 |
| Normal weight   | Inadequate | 2.14 (1.36–3.38)                 | 1.12 (0.72–1.75)                             | 0.96 (0.57–1.61)                       | 1.23 (0.79–1.93)                 |
|                  | Excessive  | 1.77 (0.72–4.37)                 | 0.69 (0.24–2.05)                             | 0.80 (0.35–2.05)                       | 0.42 (0.06–1.35)                 |
| Overweight/obesity | Inadequate | 0.49 (0.15–1.57)                 | 0.56 (0.19–1.66)                             | 1.09 (0.36–3.30)                       | 0.99 (0.39–2.54)                 |
|                  | Appropriate | 1.36 (0.21–8.68)                 | 1.17 (0.19–7.42)                             | 2.40 (0.37–15.51)                      | 3.39 (0.75–15.26)                 |
|                  | Excessive  | 0.91 (0.50–1.64)                 | 0.59 (0.32–1.10)                             | 2.60 (0.63–2.99)                       | 1.08 (0.61–1.89)                 |

Note: SGA children with maternal appropriate GWG and prepregnancy BMI were chosen as the reference. Adjusted for maternal age, parity (0, ≥1 and unknown), education (>12, 10–12 and ≤9 years), race, smoking during pregnancy (0, 1–19, ≥20 cigarettes per day), social economic status (1–5, from the lowest to the highest) and child sex. Abbreviations: aOR, adjusted OR; BMI, body mass index; GWG, gestational weight gain; SGA, small for gestational age.

**P < 0.05 was set as statistically significant.**
growth, which may help predict the future catch-up patterns of SGA neonates, in order to take proper and timely intervention measures and finally optimize SGA children’s growth. Furthermore, this study used growth trajectories (relating to our former study) as the outcome based on the LCA procedure (Hendryx & Luo, 2018; Zablotsky et al., 2018). Compared with one-point weight values, dynamically changing growth trajectories contained more development information.

Our study also had some limitations. First, we did not have data on Doppler ultrasound measurements to assess fetal well-being, which were methods evolving during the time of study (Gurugubelli Krishna & Vishnu Bhat, 2018; He et al., 2018; Pamidi et al., 2016; Reddy et al., 2008; Smith & Lees, 2008; Watkins et al., 2017). Therefore, we cannot differentiate SGA children between FGR/IUGR babies and genetically small babies in this study, and we have no evidence that the findings of this study are more suitable for FGR/IUGR or for genetically small babies. Besides, some secular changes (e.g., the rate of smoking during pregnancy decreased and women’s highest educational levels increased) have occurred after the completion of the CPP study (Tong et al., 2002; Torr, 2011). Although smoking and women’s highest educational levels were not statistically significant in our logistic models, caution should be taken when explaining the roles of these factors in the association of GWG with SGA catch-up growth. Interestingly, we found that the results on the association of GWG with catch-up growth patterns showed a similar trend if using the recommendations of the 1970s GWG guideline (Tables S1 and S2). Third, minority ethnicities were excluded because of lack of representativeness. Therefore, although our study had a relatively large sample size and was followed up for a long time, future studies are still warranted to confirm findings in our study, especially in other ethnicities. Fourth, in this study, women with prepregnancy underweight but excessive GWG were very few (n = 5), so we merged prepregnancy underweight women with appropriate and excessive GWGs into one group. In that way, the differences between the effects of appropriate and excessive GWGs in women with prepregnancy underweight may be concealed. Fifth, GWG is a total weight increase during the whole pregnancy. We have no data about weight gain in each trimester. Former study stated that GWGs in the second and third trimesters were risk factors for SGA or LGA whereas GWG in the first trimester was not (Gonzalez-Ballano et al., 2019; Pugh et al., 2017); we had no data for these factors in the association of GWG with SGA catch-up growth. Interestingly, we found that the results on the association of GWG with catch-up growth patterns showed a similar trend if using the recommendations of the 1970s GWG guideline (Tables S1 and S2). Third, minority ethnicities were excluded because of lack of representativeness. Therefore, although our study had a relatively large sample size and was followed up for a long time, future studies are still warranted to confirm findings in our study, especially in other ethnicities. Fourth, in this study, women with prepregnancy underweight but excessive GWG were very few (n = 5), so we merged prepregnancy underweight women with appropriate and excessive GWGs into one group. In that way, the differences between the effects of appropriate and excessive GWGs in women with prepregnancy underweight may be concealed. Fifth, GWG is a total weight increase during the whole pregnancy. We have no data about weight gain in each trimester. Former study stated that GWGs in the second and third trimesters were risk factors for SGA or LGA whereas GWG in the first trimester was not (Gonzalez-Ballano et al., 2019; Pugh et al., 2017); we had no data to examine trimester-specific associations between weight catch-up patterns and GWG. Although limitations existed, our study provided evidences on the potentially important roles of GWG and pBMI in the development of weight catch-up patterns in SGA children from birth to school age.

5 CONCLUSION

Gestation is a special time for pregnant women and an initial period of life. Nutrition intake in or even before gestation is essential for fetal health and has associations with post-natal growth. Our study releases that appropriate pBMI and GWG are related with an optimal post-natal catch-up growth pattern in SGA children besides what former studies have stated that inadequate GWG was associated with a higher risk of SGA births than appropriate GWG.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

LH, SJ and XL are responsible for the acquisition of data. LH and SJ are responsible for the data analysis and interpretation of data, carried out the initial analyses and wrote the paper. JX and JZ designed the research. JX has the primary responsibility for the final content. All authors have read and approved the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available through the US National Archives (http://www.archives.gov). The use of data is exempt from the review by our Institutional Review Board.

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