Early Infant Feeding and Adiposity Risk: From Infancy to Adulthood

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**Key Words**
Adiposity · Breast-feeding · Formula-feeding · Obesity · Raine Study

**Abstract**

**Introduction:** Systematic reviews suggest that a longer duration of breast-feeding is associated with a reduction in the risk of later overweight and obesity. Most studies examining breast-feeding in relation to adiposity have not used longitudinal analysis. In our study, we aimed to examine early infant feeding and adiposity risk in a longitudinal cohort from birth to young adulthood using new as well as published data. **Methods:** Data from the Western Australian Pregnancy Cohort (Raine) Study in Perth, W.A., Australia, were used to examine associations between breast-feeding and measures of adiposity at 1, 2, 3, 6, 8, 10, 14, 17, and 20 years. **Results:** Breast-feeding was measured in a number of ways.

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**Key Points**

- Stopping breast-feeding before 6 months may lead to an increased risk of overweight and obesity later in life.
- Introducing a milk other than breast milk before 6 months may lead to an increased risk of obesity 20 years later.

**To Summarize Our Current Knowledge**

- Overweight infants are more likely to become overweight children, adolescents, and adults.
- Breast-feeding, preferably of long duration and for at least 6 months and beyond, and late introduction of formula milk are recommended for protection against increased adiposity in childhood, adolescence, and adulthood.
- Increasing the prevalence of exclusive breast-feeding to 6 months would be a worthwhile public health measure.
- A possible adverse effect of formula feeding on postnatal weight gain and infant health remains of contemporary public health significance.
Longer breast-feeding (in months) was associated with reductions in weight z-scores between birth and 1 year ($\beta = -0.027; p < 0.001$) in the adjusted analysis. At 3 years, breast-feeding for <4 months increased the odds of infants experiencing early rapid growth (OR 2.05; 95% CI 1.43–2.94; $p < 0.001$). From 1 to 8 years, children breast-fed for ≤4 months compared to ≥12 months had a significantly greater probability of exceeding the 95th percentile of weight. The age at which breast-feeding was stopped and a milk other than breast milk was introduced (introduction of formula milk) played a significant role in the trajectory of the BMI from birth to 14 years; the 4-month cutoff point was consistently associated with a higher BMI trajectory. Introduction of a milk other than breast milk before 6 months compared to at 6 months or later was a risk factor for being overweight or obese at 20 years of age (OR 1.47; 95% CI 1.12–1.93; $p = 0.005$). **Discussion:** Breast-feeding until 6 months of age and beyond should be encouraged and is recommended for protection against increased adiposity in childhood, adolescence, and young adulthood. Adverse long-term effects of early growth acceleration are fundamental in later overweight and obesity. Formula feeding stimulates a higher postnatal growth velocity, whereas breast-feeding promotes slower growth and a reduced likelihood of overweight and obesity. Biological mechanisms underlying the protective effect of breast-feeding against obesity are based on the unique composition and metabolic and physiological responses to human milk.

Introduction

Metabolic syndrome represents a cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus that includes central adiposity, impaired fasting glucose tolerance, hypertriglyceridemia, decreased high-density lipoprotein cholesterol, hypertension [1], and often a proinflammatory state [2], oxidative stress, and fatty liver disease [3]. Population-based surveys have shown that metabolic risk factors are increasingly prevalent among children and adolescents and progress into adulthood [4]. This phenomenon is increasing worldwide largely as a consequence of the ongoing obesity epidemic [5].

Gale et al. [6] recently showed that formula feeding affects the fat mass in childhood and that, compared to the body composition of breast-fed infants, formula-fed infants had an altered body composition in infancy. Systematic reviews have shown strong associations between early infant feeding and obesity risk [7–9]; however, so-ciodemographic, psychological, behavioral, ethnic, and cultural influences also impact childhood obesity emergence [10]. We have reported that breast-feeding protects against childhood obesity in a population cohort [11–13].

In this paper, we collate the evidence of this association between early infant feeding and adiposity risk in a longitudinal analysis from infancy to 20 years of age, with a presentation of already published as well as new data from the West Australian Pregnancy Cohort Study.

Methods

The West Australian Pregnancy Cohort (Raine) Study commenced in 1989 with the recruitment of 2,900 pregnant women between 16 and 20 weeks of gestation [14]. A total of 2,868 live infants (96%) available for follow-up at birth provided a wide range of maternal and offspring data during pregnancy and at 1, 2, 3, 6, 8, 10, 14, 17, and 20 years of age. The 20-year follow-up was complete by December 2012.

**Exposures**

**Duration of Breast-Feeding**

Diaries were maintained by the mother during the first 3 years of life. The age at which another milk was introduced and the age at which breast-feeding was stopped were recorded, providing good prospectively collected measures of infant feeding as continuous variables in months. Breast-feeding duration was dichotomized using 4 months as the cutoff point, which is consistent with the recommendation of the World Health Organization prior to 2004 for mothers to exclusively breast-feed their infants for 4 months, although this has since been increased to 6 months [15]. Full breast-feeding was defined as breast-feeding without the regular introduction of milk other than breast milk, but it did not preclude the intake of solid foods.

**Other Factors**

Comprehensive medical and obstetric data were obtained at recruitment. Questionnaires ascertained demographic information and maternal factors including the usual prepregnancy weight. Antenatal information was obtained from maternal records and maternal height was measured at the first visit. Infant birth weight (in g) and gestational age (GA; in days) were obtained from medical notes. The maternal prepregnancy BMI was calculated as weight (kg)/height$^2$ (m). Social, demographic, and family data including family income, structure, and parental education during the mother’s pregnancy were prospectively collected via questionnaire.

**Outcomes Measured at 1-, 2-, 3-, 6-, 8-, 10-, 14-, 17-, and 20-Year Follow-Ups**

At the ages of 1, 2, 3, 6, 8, 10, 14, and 17 years, participants underwent clinical assessment at the Telethon Kids Institute (formerly known as the Telethon Institute for Child Health Research), initially with the primary caregiver and then independently from age 17 years on. At 20 years, participants attended the clinical as-

Short Breast-Feeding Duration and Adiposity Risk

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sessement at an adult health facility. Weight was measured to the nearest 100 g using Wedderburn digital chair scales, with children wearing light clothing, and height was measured to the nearest 0.1 cm with a Holtain stadiometer. The BMI was calculated as weight (kg)/height$^2$ (m). Additional anthropometric measures at all follow-up visits included calibrated measurements of waist, hip, and arm circumferences and skinfolds (suprailiac, triceps, and abdominal) using Holtain skinfold calipers (Holtain, Crymlyn, UK). Blood pressure was taken at all follow-up visits according to a standardized methodology and venous blood samples were taken after an overnight fast for serum insulin, glucose, triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, and high-sensitivity C-reactive protein. HOMA-IR was calculated as insulin (µU/ml) × glucose (mmol/l)/22.5. These additional anthropometric and metabolic results have previously been reported [16].

**Statistical Analyses**

**One Year**

At 1 year of age, the population for analysis was defined as unrelated, full-term, singleton births of European descent with no congenital abnormalities. Weights at birth and at 1 year of age were standardized for sex and age (age at birth was represented by a single time point) using WHO growth standards [17, 18]. These reflect ideal growth patterns in children who have been breast-fed exclusively for 4 months and are still breast-fed at 12 months. Weight z-scores were calculated using the formula \( \frac{(X/M)^{(L+S)} – 1}{L} \), where X is the weight measurement and L, M, and S are the age- and sex-specific values for power in the Box-Cox transformation, the median, and the coefficient of variation, respectively [19]. The difference in weight z-scores from 0 to 1 year was calculated as the birth weight z-score minus the 1-year weight z-score. Fewer sex-specific summary statistics were calculated for maternal anthropometrics, pregnancy, and early-life factors using means and SD for symmetric distributions and medians and interquartile ranges (Q1 to Q3) for asymmetric distributions.

The cross-sectional analysis of the difference in weight z-score from 0 to 1 year was performed using multivariate linear regression. Covariates were selected for the multivariate model using both forward and backward stepwise procedures. Covariates included: maternal (prepregnancy) age, height, weight, and BMI, maternal smoking (at any time during the pregnancy), family income, parity (coded as an ordered categorical variable), pregnancy weight gain up to 34 weeks' gestation, maternal self-reported diabetes and hypertension during pregnancy, GA at birth, and duration of breast-feeding. All analyses were performed using the statistical graphics software R version 2.6.2 [18].

**Growth Trajectories to Three Years**

Longitudinal increases in BMI over the first 3 years of life and the influence of breast-feeding duration, maternal prepregnancy BMI, parental educational status, and maternal smoking during pregnancy were analyzed via latent growth mixture modeling (LGMM) (P.R., B.K., and W.H.O.). Using this random-effects extension of a latent class growth curve model, we identified homogeneous subgroups of typical BMI trajectory classes among the heterogeneous individual growth curves. The number of BMI trajectory classes was identified by test statistics. Use of this model allowed the effects of breast-feeding duration and other predictors of our identified typical BMI trajectory classes to be estimated. Detailed information on the LGMM is available [20]. The significance of breast-feeding duration was evaluated by 95% CI around the OR and the size of the OR or mean outcomes and related p values. Gender was not included in any LGMM as WHO standardized BMI SD scores are standardized to age- and sex-specific ‘ideal growth’. All statistical analyses were performed using either SAS 9.3 or Mplus 7.1 statistics software.

**Years One to Eight**

Using the National Center for Health Statistics/Centers for Disease Control and Prevention website (http://www.cdc.gov/nchs/), the weight-for-length was calculated for 1-year-olds, BMI z-scores were calculated for 3-, 6-, and 8-year-olds, and overweight was defined according to the sex-specific 95th percentiles [11]. Categories of breast-feeding were defined as: never breast-fed, breast-fed for ≤4 months, breast-fed for 5–8 months, breast-fed for 9–12 months, and breast-fed for >12 months. These categories were used in mixed-effects models with the BMI z-score as the response variable and age as the explanatory variable. Final models included adjustment for birth weight, GA, ethnicity, sex, maternal BMI, smoking status during pregnancy, parity, and educational level. Generalized estimating equations modeled overweight from the ages of 1 to 8 years using the sets of covariates. p = 0.05 was considered statistically significant.

**At Fourteen Years**

We have reported adiposity rebound, defined as the last minimum (nadir) BMI before a continuous increase with age [21] and calculated in a subset of individuals (n = 171) for whom a complete set of BMI data were available for all 8 measured time points (birth to 14 years), based on the child’s age in months. We used linear mixed modeling which accounted for correlated errors normally associated with repeated, continuous, and correlated observations. The variables for the age at which breast-feeding was stopped and the age at which another milk was introduced were categorized using a 4-month cutoff point. These were compared across weight status groups [22]. The effect of the duration of breast-feeding (based on the 4-month cutoff point) was assessed across the age range based on group mean differences tested using Pearson’s $\chi^2$ test. Adjustment for potential socioeconomic status confounding was based on maternal education.

**At Seventeen Years**

A longitudinal analysis was performed (n = 1,009) using multivariate linear regression models with continuous BMI as the response variable and breast-feeding duration and age at 17 years of age which milk other than breast milk was introduced (in months) as dichotomized explanatory variables, adjusting for child gender and the following maternal factors: prepregnancy BMI, education, age, and family income.

**At Twenty Years**

The nonrandom loss of disadvantaged participants is to be expected in a longitudinal cohort and may decrease the generalizability of any findings. We developed a method that could be applied to account for such attrition bias using inverse probability weighting [23].

Our aim was to investigate exclusive breast-feeding and the prevalence of a high BMI, overweight, and obesity at 20 years. Of the original cohort (n = 2,868), 73% were available at the 20-year follow-up. Our follow-up response rate was 46% of those available.
for follow-up (n = 1,053). Participants at 20 years were compared to nonparticipants to identify a priori candidates to predict missingsness [24]. A missingness model was defined based on sociodemographic factors that predicted continued participation (maternal factors of age, education, BMI before pregnancy, and family income at birth). Final models (i.e. overweight and obesity vs. breast-feeding) incorporated generalized estimating equations and our final predictive model provided an OR and 95% CI.

Results

At One Year

By the time their infant was 6 months of age, 39% of the mothers had stopped breast-feeding and 55% had introduced a milk other than breast milk. At 1 year of age, a longer duration of breast-feeding was independently associated with reductions in weight z-scores between birth and the first year of life (β = –0.027; SE 0.004; p < 0.001) following adjustment for maternal factors, increasing weight gain up to 34 weeks of gestation, birth order, and duration of gestation (table 1).

At Three Years

Using BMI SD scores, the growth pattern of infants identified in a class 2 pattern – comprising 35.8% of the cohort – began at 0.3 SD above the ideal growth standard and gained almost 1 SD within the first 2 years (fig. 1). The curve remained 1 SD above the ideal, normative growth development up to 3 years of age. We showed that breast-feeding for <4 months significantly increased the odds of infants being assigned to early rapid growth class 2 (OR 2.05; 95% CI 1.43–2.94; p < 0.001) following adjustment for maternal BMI before pregnancy, socioeconomic status, and GA. Although the growth patterns of infants identified in a class 1 or class 3 pattern showed an even stronger increase in BMI SD score deviation from ideal growth within the first 2 years compared to those in class 2, breast-feeding was not significantly associated with these growth patterns.

At One, Three, Six, and Eight Years

As reported previously [11], at 1 year infants breast-fed for >12 months were the leanest group (mean z-score –0.16, 95% CI –0.28 to –0.04; not breast-fed: mean z-score 0.16, 95% CI 0.02–0.29; breast-fed for ≤4 months: mean z-score 0.31, 95% CI 0.22–0.40; breast-fed for 5–8 months: mean z-score 0.17, 95% CI 0.06–0.27; and breast-fed for 9–12 months: mean z-score 0.11, 95% CI 0.01–0.22). From 1 to 8 years, children breast-fed for ≤4 months compared to those breast-fed

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Table 1. Analysis of changes in weight z-scores from birth to 1 year

<table>
<thead>
<tr>
<th>Estimate</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of gestation (days)</td>
<td>–0.037</td>
<td>0.003</td>
</tr>
<tr>
<td>Parity 0</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>–0.287</td>
<td>0.072</td>
</tr>
<tr>
<td>Maternal smoker No</td>
<td>1</td>
<td>0.319</td>
</tr>
<tr>
<td>Yes</td>
<td>0.180</td>
<td>0.302</td>
</tr>
<tr>
<td>Maternal diabetes No</td>
<td>1</td>
<td>–0.435</td>
</tr>
<tr>
<td>Yes</td>
<td>0.123</td>
<td>0.057</td>
</tr>
<tr>
<td>Maternal hypertension No</td>
<td>1</td>
<td>–0.015</td>
</tr>
<tr>
<td>Yes</td>
<td>0.019</td>
<td>0.006</td>
</tr>
<tr>
<td>Pregnancy weight gain (kg)</td>
<td>–0.027</td>
<td>0.004</td>
</tr>
<tr>
<td>Prepregnancy maternal BMI</td>
<td>–0.015</td>
<td>0.004</td>
</tr>
<tr>
<td>Duration of breast-feeding (months)</td>
<td>–0.027</td>
<td>0.004</td>
</tr>
<tr>
<td>Family income &lt;AUD 11,999</td>
<td>1</td>
<td>0.070</td>
</tr>
<tr>
<td>AUD 12,000–23,999</td>
<td>0.084</td>
<td>0.086</td>
</tr>
<tr>
<td>AUD 24,000–35,999</td>
<td>0.207</td>
<td>0.087</td>
</tr>
</tbody>
</table>

a Continuous covariates were centered prior to analysis: length of gestation minus 280 days, pregnancy weight gain minus 14 kg, and pre-pregnancy maternal BMI minus 22 kg/m².

Fig. 1. Identified BMI trajectory classes from birth to 3 years by LGMM in the Raine Study.

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for >12 months had the greatest probability of exceeding the 95th percentile for BMI (OR 1.87; 95% CI 1.21–2.89; p = 0.005), and this was associated with the highest prevalence of maternal obesity, smoking, and lower education.

At Fourteen Years
The age at which breast-feeding was stopped and a milk other than breast milk was introduced played significant roles in the trajectory of BMI from birth to 14 years, especially at the 4-month cutoff point; differences in BMI peaks were apparent at 1 year of age, and these differences were consistent over time and into adolescence (fig. 2a, b).

At Seventeen Years
Cessation of breast-feeding before 6 months and introduction of a milk other than breast milk before 6 months compared to at 6 months or later were associated with an increased BMI at 17 years. The BMI was consistently associated with early cessation of breast-feeding following adjustment for gender, maternal age, maternal education, family income at birth, and maternal prepregnancy BMI (table 2).

At Twenty Years
In recent work [13] at 20 years, our final predictive weighted model showed that cessation of exclusive breast-feeding before 6 months, compared to at 6 months or later, was associated with an increased prevalence of overweight and obesity (BMI 25+) at 20 years (OR 1.47; 95% CI 1.12–1.93; p = 0.005). The full multivariate generalized estimating equation model for being overweight or obese

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**Table 2.** Multivariate linear regression models for continuous BMI at 17 years, with breast-feeding duration and age at which a milk other than breast milk was introduced (in months), as dichotomized variables

<table>
<thead>
<tr>
<th>BMI at 17 years&lt;sup&gt;a&lt;/sup&gt;</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast-feeding stopped by</strong>&lt;sup&gt;*&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>1.26 (0.43–2.10)</td>
</tr>
<tr>
<td>4 months</td>
<td>1.14 (0.37–1.92)</td>
</tr>
<tr>
<td>5 months</td>
<td>1.01 (0.26–1.75)</td>
</tr>
<tr>
<td>6 months</td>
<td>0.95 (0.23–1.67)</td>
</tr>
<tr>
<td><strong>Milk other than breast milk was introduced before</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>1.17 (0.43–1.91)</td>
</tr>
<tr>
<td>4 months</td>
<td>1.15 (0.45–1.84)</td>
</tr>
<tr>
<td>5 months</td>
<td>1.11 (0.42–1.80)</td>
</tr>
<tr>
<td>6 months</td>
<td>1.07 (0.37–1.76)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Values represent unstandardized β-coefficient (95% CI).  
<sup>*</sup> Adjusted for gender, maternal age <20 years, maternal education <12 years, family income <AUD 12,000 at birth, and maternal prepregnancy BMI ≥25.

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![Fig. 2. Mean BMI by mean age based on the age at which breast-feeding was stopped (a; n = 1,330) and the age at which another milk was introduced (b; n = 1,320) [12]. Error bars show 95% CI of the mean.](image-url)
compared to normal weight at 20 years, by milk introduced before 6 months of age, is shown in Table 3. Supplementary tables provide further information about the West Australian Pregnancy Cohort Study.

**Discussion**

Breast-feeding, preferably of a long duration (>6 months), and late introduction of formula milk are recommended for protection against increased adiposity in childhood, adolescence, and young adulthood. Our results provide an opportunity to examine the influence of infant feeding on weight status, the relationship with adiposity rebound, and subsequent adolescent and young-adult BMI. Overall, our findings suggest that formula feeding compared to breast-feeding results in accelerated weight gain in the infant, with likely upward BMI centile crossing [25]. Our results support other studies that showed overweight in adolescence increased as the duration of exclusive breast-feeding decreased [26], and they extend the findings of Burke et al. [11] which showed a higher BMI at 8 years in children breast-fed for ≤4 months. Statistical modeling [12] showed that breast-feeding and the age at which another milk was introduced play an important role and may contribute to the timing of the adiposity rebound.

A number of observational studies and meta-analyses have shown small protective effects of breast-feeding on obesity. However, other studies have found no effect and raise the possibility of unknown confounders and publication bias [27]. Three comprehensive meta-analyses were conducted over the past decade. A meta-analysis that included 9 studies with over 69,000 participants [7] showed that breast-feeding has a consistent protective effect against childhood obesity (OR 0.78; 95% CI 0.71–0.85), with 4 studies showing a dose-response effect for the duration of breast-feeding. A meta-analysis of 17 studies in 2005 [8] found a dose-response relationship where an increased duration of breast-feeding was related to a decreased risk of overweight later in life. More specifically, that meta-analysis reported a 4% decrease in risk with each additional month of breast-feeding. When restricted to exclusive breast-feeding, the risk of overweight decreased by 6% per month [8] suggesting that exclusivity of breast-feeding may be central to the mechanism whereby it protects against obesity [28]. A meta-analysis by Owen et al. [9] concluded that breast-feeding reduces the risk of obesity compared to formula feeding (OR 0.87; 95% CI 0.85–0.89). However, the same authors have since suggested that any observed protective effect of breast-feeding on the BMI may be due to unadjusted confounding [27]. Beyerlein and von Kries [29] suggested that the discrepancy in the findings of studies examining breast-feeding and obesity may be due to the different effects of breast-feeding in normal-weight versus overweight populations, showing a protective effect of breast-feeding in those within the highest BMI percentiles (>90th) [30].

A German study of 9,357 children found that breast-feeding had a protective effect against obesity and overweight which remained significant after adjusting for social class and lifestyle [31]. A dose-response relationship was shown with the duration of breast-feeding, indicating a possible causal effect associated with a shorter duration.

A recent study of 822 young adults (aged 18–28 years) from the Netherlands [32] demonstrated that exclusive breast-feeding had a significant protective dose-response effect on measures of body fat mass and visceral fat mass.

### Table 3. Multivariate generalized estimating equation model for being overweight or obese compared to normal weight at 20 years, by milk introduced before 6 months of age

<table>
<thead>
<tr>
<th>Exposures</th>
<th>Overweight or obese at 20 years</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A milk other than breast milk was introduced before 6 months of age (yes vs. no)</td>
<td>1.47 (1.12–1.93)</td>
<td>0.005</td>
</tr>
<tr>
<td>Gender (male vs. female)</td>
<td>1.14 (0.87–1.49)</td>
<td>0.340</td>
</tr>
<tr>
<td>Maternal age at birth (&lt;20 vs. ≥20 years)</td>
<td>1.49 (0.80–2.80)</td>
<td>0.210</td>
</tr>
<tr>
<td>Maternal education (&lt;12 vs. ≥12 years)</td>
<td>1.27 (0.97–1.67)</td>
<td>0.080</td>
</tr>
<tr>
<td>Family income at birth (&lt;AUD 12,000 vs. ≥AUD 12,000)</td>
<td>1.59 (1.05–2.40)</td>
<td>0.030</td>
</tr>
<tr>
<td>Maternal BMI before pregnancy (≥25 vs. &lt;25)</td>
<td>3.11 (2.22–4.34)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The sample was weighted according to principles of inverse probability weighting [23].

a Values represent OR (95% CI).

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Short Breast-Feeding Duration and Adiposity Risk

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likely in breast-fed infants has been shown to promote slower growth, obesity is less well as formula-fed infants; however, as breast-feeding of life leads to an elevated risk of obesity in breast-fed as later in life. The theory is that a high-nutrient diet in in-

A crucial period during postnatal growth relating to obesity risk has been hypothesized. The timing of this period remains uncertain, with some suggesting that the first few days of life [34], the first few weeks [28], or up to the first 2 years may be the crucial period [35]. Plausible mechanisms for the development of fatness during this early sensitive window of exposure include permanent structural changes such as a decreased β-cell mass, accelerated cellular aging, telomere shortening with cell division and oxidative damage, and epigenetic programming changes from transcription to translation of proteins [36]. Our results demonstrate that the early months of life are the crucial period for the development of adiposity later in life.

We showed that, in terms of feeding patterns, the time period of greatest risk for obesity later in life was prior to 6 months, and this finding supports the recommendation of continued exclusive breast-feeding for up to 6 months and beyond. The theory is that a high-nutrient diet in infancy adversely programs the cardio-metabolic system by promoting growth acceleration (upward centile crossing) [37]. Therefore, a slower growth benefits later cardiovascular disease and its risk factors [33]. Early growth acceleration programs the abnormal vascular biology associated with early atherosclerosis. Therefore, infants who grow rapidly during infancy or are at the highest end of the weight or BMI distribution are at an increased risk for subsequent obesity [38]. The growth velocity may have a relevant influence on the causal pathway of obesity, as suggested for fetal programming of metabolic disease [39], with reported associations between protein intake, growth velocity, and weight gain [40, 41].

The theory of reverse causation in relation to growth suggests that infants who have lower growth trajectories, and therefore lower energy requirements, are satisfied with breast-feeding for longer. Children ‘programmed’ to be larger require and demand a higher energy intake, resulting in the mother supplementing with formula or solid food earlier [42]. Rapid growth in the first few months of life leads to an elevated risk of obesity in breast-fed as well as formula-fed infants; however, as breast-feeding has been shown to promote slower growth, obesity is less likely in breast-fed infants [43, 44].

Findings from recent randomised controlled studies followed up at 2 and 6 years, respectively [45, 46], compared the BMI of infants fed high-protein formula versus low-protein formula and a breast-feeding comparison group and were supportive of the early protein hypothesis. Those authors reported a higher BMI in the high-protein-formula group compared to the low-protein group which had BMI values closer to those of the breast-fed infants. With regard to the risk of later obesity, the most important differences between breast milk and formula appear to be related to the lower protein content and the presence of hormones, growth factors, and bioactive factors in breast milk [47]. In addition, the biological mechanisms underlying the protective effect of breast milk feeding compared to formula feeding are based on the unique composition of human milk and the metabolic and physiological responses to human milk [48]. Breast-fed infants may absorb less energy per volume than formula-fed infants, as well as receiving modifying growth factors that may inhibit adipocyte differentiation [48, 49].

Evidence exists for programming by nutrition in early infancy [50]. Feeding methods may prime offspring dietary behaviors, possibly by influencing the development of the hypothalamus which occurs through gestation and into the postnatal period and is thought to play an important role in appetite control [51]. In humans, breast-fed babies have been shown to exhibit better appetite control than bottle-fed babies [52]. This evidence supports the link between a longer duration of breast-feeding and a decreased risk of obesity later in life.

**Strengths**

Our study has a number of strengths that include the use of a prospective pregnancy cohort and early infant feeding data, and anthropometric data collected for up to 20 years. Breast-feeding data were collected close to the period of breast-feeding cessation and a diary card was maintained to improve data collection. The study design and large community sample are clear strengths, generating adequate statistical power to measure the association between dichotomized breast-feeding variables and anthropometric outcomes while controlling for possible confounders.

**Conclusion**

As with other programming effects, the effect of early diet on the later obesity risk may amplify over time. The early postnatal period is a particularly important time for the risk of the development of obesity and its cardio-metabolic sequelae which may potentially be addressed...
through the promotion of breast-feeding. Therefore, this period is particularly important for targeting interventions, and our findings suggest that the promotion of breast-feeding may have long-term protective benefits against future obesity.

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Disclosure Statement

No conflicts of interest are declared.

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