

# Risk Factors for Childhood Obesity in the First 1,000 Days

## A Systematic Review

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**Context:** Mounting evidence suggests that the origins of childhood obesity and related disparities can be found as early as the “first 1,000 days”—the period from conception to age 2 years. The main goal of this study is to systematically review existing evidence for modifiable childhood obesity risk factors present from conception to age 2 years.

**Evidence acquisition:** PubMed, Embase, and Web of Science were searched for studies published between January 1, 1980, and December 12, 2014, of childhood obesity risk factors present during the first 1,000 days. Prospective, original human subject, English-language research with exposure occurrence during the first 1,000 days and with the outcome of childhood overweight or obesity (BMI  $\geq$  85th percentile for age and sex) collected between age 6 months and 18 years were analyzed between December 13, 2014, and March 15, 2015.

**Evidence synthesis:** Of 5,952 identified citations, 282 studies met inclusion criteria. Several risk factors during the first 1,000 days were consistently associated with later childhood obesity. These included higher maternal pre-pregnancy BMI, prenatal tobacco exposure, maternal excess gestational weight gain, high infant birth weight, and accelerated infant weight gain. Fewer studies also supported gestational diabetes, child care attendance, low strength of maternal–infant relationship, low SES, curtailed infant sleep, inappropriate bottle use, introduction of solid food intake before age 4 months, and infant antibiotic exposure as risk factors for childhood obesity.

**Conclusions:** Modifiable risk factors in the first 1,000 days can inform future research and policy priorities and intervention efforts to prevent childhood obesity.

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### Context

High obesity prevalence persists in all age groups in the U.S., and one third of U.S. children aged 2–19 years are affected by overweight or obesity (sex-specific BMI  $\geq$  85th percentile for age).<sup>1</sup>

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Approximately 8.1% of U.S. children younger than age 2 years have weight-for-length  $\geq$  95th percentile, predisposing them to obesity. The first 1,000 days describes the period from conception through age 2 years, which is increasingly recognized as a critical period for development of childhood obesity and its adverse consequences.<sup>2</sup>

Childhood obesity, and its disparate impact on underserved populations, originates in early life.<sup>3,4</sup> Among children aged 2–5 years, Hispanic children have almost fivefold and non-Hispanic black children have threefold higher obesity prevalence compared with their non-Hispanic white counterparts.<sup>1,5–7</sup> During the first years of life, racial/ethnic differences in modifiable risk factors for childhood obesity contribute substantially to racial/ethnic disparities in later childhood obesity.<sup>8–13</sup>

Despite mounting evidence that the first 1,000 days are important in the prevention of childhood obesity and in the reduction in obesity disparities, no systematic review

has focused on risk factors from conception through age 2 years. Identifying current evidence for childhood obesity risk factors during the first 1,000 days will advance understanding of the origins of obesity and inform future research priorities and efforts to prevent childhood obesity.

The goal of this study is to systematically review existing evidence for modifiable childhood obesity risk factors that are present from conception to age 2 years. This review focuses on prospective studies and uses a conceptual framework that incorporates individual, family, community, and systems levels to highlight future research needs.

## Evidence Acquisition

### Conceptual Framework

The Glass and McAtee<sup>14</sup> model of multi-level influences on behavior and health informed the overarching conceptual framework (Figure 1). The model outlines macro (environmental); mezzo (community); and micro (parent/family/caregiver) levels of “above water” influences, and individual-level health behaviors at the “waterline.” This study focuses on potentially modifiable risk factors for childhood obesity during two life-course stages:

1. from conception to delivery; and
2. from birth to age 2 years.

“Under water” metabolic and genetic risk factors are briefly summarized.

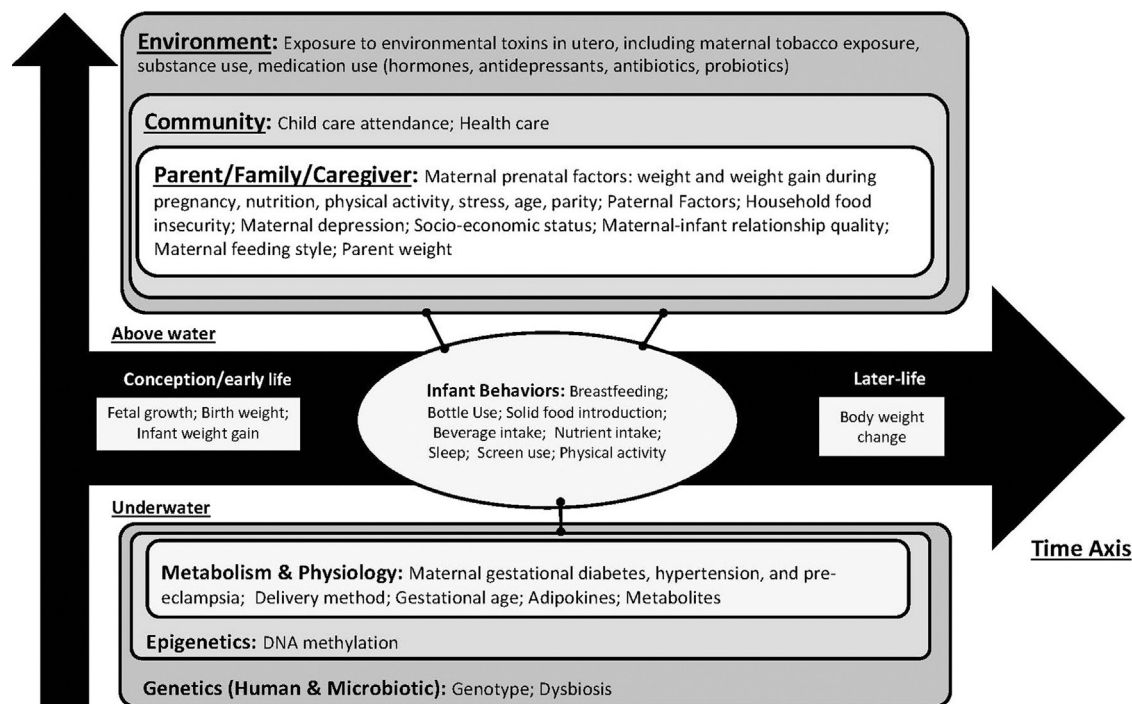
### Search Strategy and Data Extraction

Methods followed the IOM and Patient-Centered Outcomes Research Institute standards.<sup>15,16</sup> Studies published between January 1, 1980, and December 12, 2014, were included. PubMed, Embase, and Web of Science were searched, and references of systematic reviews published in the past 3 years were reviewed. In PubMed, the Medical Subject Headings *pregnancy* and *infancy* were separately included with the combined terms of *pediatric overweight*, *childhood overweight*, *child overweight*, *children overweight*, *infancy overweight*, *pediatric obesity*, *childhood obesity*, *child obesity*, *children obesity*, *infancy obesity*, *pediatric obese*, *childhood obese*, *child obese*, *children obese*, and *infancy obese*.

Prospective, English-language studies were included if they had

1. human subjects;
2. original quantitative evidence;
3. exposure occurrence during the first 1,000 days; and
4. a main outcome measure of childhood overweight or obesity collected between age 6 months and 18 years, herein described as “overweight.”<sup>17-19</sup>

For age 2–18 years, studies reporting child BMI  $\geq$ 85th percentile for age and sex on 2000 CDC growth charts,<sup>17</sup> BMI corresponding to adult BMI  $\geq$ 25 per International Obesity Task Force guidelines,<sup>18</sup> or country-specific standards were included. For age 6 months and age 2 years, studies reporting child weight-for-length or BMI  $\geq$ 97.7th percentile on WHO charts and weight-for-length  $\geq$ 95th percentile on CDC growth charts were included.<sup>19</sup> Because this review focuses on risk factors for child overweight, studies that only reported continuous



**Figure 1.** Conceptual framework for systematic review of childhood obesity risk factors from conception through age 2 years. Adapted from Glass and McAtee.<sup>14</sup>

outcomes were excluded. To reduce individual study bias, studies using cross-sectional data, parental recall after child age 2 years of exposure measures, and self-report of anthropometric outcomes were excluded. Studies of children with specific or rare medical conditions (e.g., Prader-Willi syndrome) were not included, as they do not represent the general population.

Data analysis occurred between December 13, 2014, and March 15, 2015. Independent initial screen based on title and abstract (JWB, LL, TBL, MEP, and EMT) was performed. Two authors then independently reviewed full-text articles based on eligibility criteria (JWB or EC and LL, TBL, or MEP). Data were extracted from articles using a structured data collection form. Key findings were qualitatively summarized with consideration of number of studies addressing individual risk factors, as well as the strength and direction of association of the risk factor with child overweight across studies (Appendix Table 1, available online). Bias was considered within and across studies, taking into account study type, sample size, and loss to follow-up. Generalizability was appraised based on region of study, income level of country and participants, and racial/ethnic diversity of sample populations. Given the wide range of exposures, outcome variability, and multiple research designs, quantitative or meta-analysis of the reviewed literature was not feasible.

## Evidence Synthesis

The initial search identified 5,952 articles. After screening and full-text review, a total of 282 articles met criteria for inclusion (Appendix Figure 1, available online).

### Conception Through Delivery

Biological, community, family, and environmental risk factors were examined from conception through delivery (Table 1). Of the 33 studies that examined the relationship between gestational diabetes and childhood overweight, 22 noted significant associations between maternal gestational diabetes and childhood overweight,<sup>20-41</sup> and 11 found no association.<sup>42-52</sup> Two additional studies<sup>53,54</sup> found an association between maternal Type 1 diabetes and later childhood overweight/obesity.

One study<sup>55</sup> identified any maternal hypertension during pregnancy as a risk factor for child overweight. In two studies<sup>40,43</sup> of maternal pre-eclampsia, no increased risk of child overweight was found.

Of the 11 articles that investigated method of delivery at birth, six<sup>56-61</sup> reported associations between cesarean delivery and offspring overweight. Five studies<sup>62-66</sup> reported null associations.

Three studies<sup>67-69</sup> found a positive correlation between higher fetal ultrasound measurements and later childhood obesity. Three studies<sup>68,70,71</sup> investigated gestational age at delivery as a risk factor for childhood overweight, with mixed results.

Higher maternal pre-pregnancy BMI had a consistent relationship with offspring overweight later in childhood, noted in 34 of 38 articles.<sup>30,40,42,45,47,49,68,72-98</sup> The four

studies reporting null associations were not generalizable as they reported results from a limited population,<sup>99</sup> only among multi-fetal gestations,<sup>100</sup> or within the context of a clinical trial.<sup>101,102</sup>

Excess gestational weight gain consistently increased risk for childhood overweight among the 21 studies examining maternal gestational weight gain, with only two studies<sup>68,103</sup> reporting null associations with child overweight. The remaining 19 studies<sup>49,72,74,76,98,104-117</sup> reported significant associations between excess (defined by IOM criteria) or high (defined by various cut-points) weight gain during pregnancy and offspring overweight.

Four studies<sup>68,118-120</sup> examined the influence of various aspects of maternal prenatal diet, and one<sup>121</sup> of physical activity, on child overweight. Two<sup>68,120</sup> found no relationship between maternal carbohydrate, fat, or protein intake with child overweight, but one<sup>120</sup> reported a positive correlation between maternal sugar intake and offspring overweight. In Project Viva, a pre-birth cohort in Massachusetts, higher maternal fatty acid intake during pregnancy was associated with childhood overweight.<sup>119</sup> Another study<sup>118</sup> of U.S. children found that > 150 mg of maternal caffeine intake during pregnancy was associated with offspring overweight. One study<sup>121</sup> examined maternal physical activity during pregnancy and found no association with offspring weight status.

Other studies of maternal factors examined stress, age, and parity. Three studies<sup>122-124</sup> of maternal self-report of stress during pregnancy found higher odds of later childhood overweight with higher stress levels, but another study<sup>125</sup> found no association between salivary cortisol levels and childhood overweight. In two large European cohorts, maternal age was not a risk factor for childhood overweight.<sup>68,126</sup> Two studies<sup>79,127</sup> found that children of multiparous mothers had lower odds of overweight than those of nulliparous mothers.

For paternal factors, two studies<sup>68,77</sup> found an association between higher paternal BMI and measures of childhood overweight. In four studies,<sup>68,128-130</sup> prenatal paternal smoking was not associated with child overweight, but one study<sup>131</sup> found a positive association. In another study,<sup>132</sup> the association between paternal stress and child overweight was reported to be null.

Two studies<sup>49,133</sup> of maternal prenatal health care during pregnancy in the Fragile Families and Wellbeing Study, a multi-city cohort mostly composed of children from single-parent families, did not find any association between maternal receipt of health care during pregnancy and offspring overweight.

Among 11 studies, maternal exposure to several environmental pollutants was associated with childhood overweight, including dichlorodiphenyldichloroethylene,<sup>134,135</sup>

**Table 1.** Conception to Birth: Key Findings and Research Needs Based on Systematic Review and Evidence Synthesis

Risk factor	No.	Key findings	Research needs
<b>Biologic</b>			
Maternal diabetes mellitus (DM)—gestational or Type 1	35	Most studies suggest maternal gestational diabetes is a risk factor for offspring overweight; Type 1 DM may also be a risk factor	Independent and combined effects of maternal insulin, glucose, and BMI on offspring overweight; effects of prevention and reversal of gestational diabetes effects
Pregnancy complications	3	One of three studies found maternal hypertension as a risk factor for child overweight	Relationship of maternal health conditions related to maternal excess weight on child health
Method of delivery	11	Moderate evidence that cesarean delivery is a risk factor for overweight in childhood	Plausible mechanisms
Fetal growth	3	Some evidence to support an association between high estimated fetal weight and increased likelihood of childhood obesity	Standardized measures of fetal growth and how they relate to postnatal growth parameters
Gestational age at birth	3	Mixed evidence for a relationship between gestational age and later childhood overweight	Additional prospective studies and plausible mechanisms
<b>Parent/family/caregiver</b>			
Maternal pre-pregnancy BMI	38	Consistent findings of maternal pre-pregnancy BMI as a risk factor for offspring overweight	Effective interventions to reduce maternal overweight/obesity in the pre-conceptual period, and their long-term impacts on maternal-child outcomes
Gestational weight gain	21	Consistent findings of maternal gestational weight gain as a risk factor for offspring overweight; emerging evidence that this relationship might vary by trimester of exposure	Identification of critical periods to intervene and long-term maternal-child outcomes of interventions
Maternal diet and nutrition	4	Limited evidence for fatty acid, caffeine, and sugar intake; no evidence for energy and macronutrient intake	Additional prospective studies of prenatal dietary patterns and plausible mechanisms
Maternal physical activity	1	No association for maternal report of recreational exercise during pregnancy and offspring BMI	Identification of physical activity patterns that safely promote healthy weight gain during pregnancy
Maternal stress	4	Inconsistent evidence for an association between maternal stress and childhood overweight	Prospective studies with self-report of maternal stress complemented with biological stress measures
Maternal age at delivery	2	No evidence to support an association between maternal age and offspring overweight	
Maternal parity	2	Lower parity associated with increased odds of childhood overweight in both studies	Mechanisms through which prior pregnancies may influence future offspring overweight risk
Paternal factors	4	Limited evidence of paternal influences to offspring adiposity measures	Prospective studies of the influences through which partners and fathers modify child overweight risk
<b>Community</b>			
Prenatal health care	2	Insufficient evidence of associations for prenatal care and offspring adiposity	Processes and systems through which health care during pregnancy can reduce risk factors
<b>Environmental</b>			
Environmental pollutant exposure	11	Inconsistent associations between environmental pollutants and child overweight	Impact of change in environmental exposure levels on child weight outcomes

*(continued on next page)*

**Table 1.** Conception to Birth: Key Findings and Research Needs Based on Systematic Review and Evidence Synthesis (continued)

Risk factor	No.	Key findings	Research needs
Maternal tobacco use	31	Consistent evidence that smoking during pregnancy is a risk factor for increased offspring adiposity	Effect of interventions aimed at tobacco cessation prior to pregnancy
Maternal prenatal substance use	5	Limited evidence suggests maternal cocaine use during pregnancy may promote childhood overweight	Long-term maternal child effects of programs to reduce maternal substance abuse
Prenatal medication	2	Insufficient evidence	Additional prospective studies

hexachlorobenzene,<sup>134,136</sup> dichlorodiphenyltrichloroethane,<sup>137</sup> bisphenol A,<sup>138</sup> polycyclic aromatic hydrocarbon,<sup>139</sup> and polychlorinated biphenyls.<sup>135</sup> However, findings were inconsistent, with other studies<sup>134,140-144</sup> finding null results.

In 23 studies,<sup>40,78,84,112,128,130,145-161</sup> prenatal maternal tobacco smoking was associated with increased odds of offspring overweight. Eight additional studies<sup>49,68,98,103,129,131,162,163</sup> did not find statistically significant associations between maternal tobacco smoking during pregnancy and offspring overweight. Among three studies of alcohol use, one<sup>112</sup> found lower odds of obesity among offspring whose mothers drank alcohol during pregnancy, and two<sup>68,98</sup> did not find significant associations. Two studies of maternal cocaine use found an association with child overweight in subgroup analyses among mothers who did not drink alcohol<sup>164</sup> and term infants.<sup>165</sup>

Two studies examined maternal medication intake during pregnancy. One<sup>166</sup> found a reduced risk of obesity among female, but not male, children of women with depression who took selective serotonin reuptake inhibitors during pregnancy. Another study<sup>167</sup> found that maternal report of oral contraceptive or diethylstilbestrol use during pregnancy was associated with later child overweight.

### Birth Through Age 2 Years

Table 2 summarizes findings for birth through age 2 years. Twenty-eight studies<sup>40,42,53,62,68,69,78,79,90,98,163,168-184</sup> examined the association between birth weight and later child overweight. Higher birth weight was consistently associated with later childhood overweight, with 24 studies<sup>40,42,53,68,69,78,79,90,98,163,168-175,177-181,184</sup> identifying an association between higher birth weight and later overweight. Studies defined birth weight as a continuous measure, as categorical absolute weight (e.g., macrosomia), or in reference to gestational age (e.g., large for gestational age). Of these 28 studies, one additionally

examined higher infant birth length and found it to be a risk factor for later child overweight.<sup>177</sup> Regardless of exposure definition, higher birth weight and later childhood overweight were consistently linked.

Of the 46 studies examining rapid weight gain and higher absolute weight-for-length during the first 2 years of life, 45 found an association between higher infancy weight or weight gain and later childhood overweight.<sup>25,62,68,73,79,90,96,147,169,182,185-219</sup> Definitions for weight and weight gain varied, including absolute weight as a continuous measure, change in weight, crossing percentiles on growth charts, weight-for-length using either CDC or WHO charts, or BMI based on WHO charts. Only one study<sup>220</sup> did not report a significant association between infant weight gain and later overweight.

Three studies examined early-life metabolic influences on later childhood overweight. One<sup>221</sup> found an inverse relationship between adiponectin concentration in breast milk and overweight status among breastfed children, but another<sup>222</sup> found a positive correlation. Neither article reported child blood levels of adipokines. Another study<sup>223</sup> of metabolites at age 6 months found a potential role for serum LPCaC14:0 in childhood overweight at age 6 years.

In two nested case-control studies<sup>221,224</sup> examining the fecal microbiome of children with mothers enrolled in a Finnish probiotic RCT, a greater number of *Staphylococcus aureus* bacteria in the infant microbiome was associated with later childhood overweight, and more bifidobacteria was associated with later normal weight.

Two studies<sup>225,226</sup> found associations between placental or cord blood methylation levels of insulin growth factor 2 genes and higher birth weight or infant weight, but there were no epigenetic studies of later childhood overweight outcomes. Two studies<sup>227,228</sup> found evidence for genetic components to childhood overweight, implicating a role for variants in several genes, including *FTO*, *TMEM18*, *POMC*, and *MC4R*.



**Table 2.** Birth to 2 Years: Key Findings and Research Needs From Systematic Review and Evidence Synthesis

Risk factor	No.	Key findings	Research needs
Biologic			
Birth weight	28	Consistent association with later childhood overweight	Mechanisms that lead to higher risk of childhood obesity among higher birth weight children
High infant weight and weight gain	46	Consistent association with later childhood overweight despite inconsistent exposure definitions.	Thresholds for infant “overweight” and “obese” and approaches to prevent excess infant weight gain
Adipokines and Metabolites	3	Inconsistent association of adiponectin levels in breast milk with childhood overweight.	Influence of breast milk composition on child metabolic pathways and obesity risk
Microbiome	2	Inconsistent findings in 2 studies of same nested case-control study.	Longitudinal studies of infancy microbiome profiles associated with normal and excess weight gain
Epigenetics/genetics	2	No epigenetic studies. Genetic components likely contribute to some cases of childhood obesity.	Genetic studies in racial/ethnic groups at highest risk for obesity; Longer-term epigenetic outcomes
Infant behaviors			
Child screen time	1	Insufficient evidence to quantify early life screen use effect on child overweight/obesity	Studies of infant screen exposure and its downstream effects
Child sleep	4	In a U.S. geographic pre-birth cohort, curtailed infant sleep found to be risk factor; inconsistent effect in other studies	Valid measurements of infant sleep that expand beyond duration to include quality and timing; consistency in exposure reporting
Child active play/physical activity	0	No studies	Valid measurements and norms of physical activity; Association with health outcomes
Multiple behaviors	4	Targeting multiple behaviors for intervention development shows promise for obesity prevention	Larger sample sizes and longer follow-up of interventions
Nutrition/feeding	(see Table 3)		
Parent/family/caregiver			
Household food insecurity	3	May act indirectly through parenting and feeding practices to act as a childhood obesity risk factor	Effect of interventions targeting parenting skills and feeding practice in food-insecure families
Maternal depression	3	Insufficient evidence	
Cumulative social stressors	1	Limited evidence to suggest an additive effect of social stressors on childhood obesity risk	Effect of interventions aimed at coping with and reducing social stressors on child overweight
SES	3	Consistent evidence for SES as risk factor, but mechanisms unclear	Mechanisms for obesity risk in low-income families and effective interventions in low-income populations
Maternal-infant relationship	3	Low strength of maternal-child relationship is a likely risk factor	Ways to strengthen maternal-infant relationships and the effect this has on childhood obesity
Parental weight	3	Limited information supports link between parental post-partum weight to childhood overweight	Role of family members other than mothers; mechanisms of association between parental weight and childhood overweight
Community			
Child care attendance	2	Child care attendance was a risk factor in both studies	Individual-level outcomes in evaluation of best practices to promote obesity prevention
Environment			
Antibiotic and probiotic exposure	5	Any infant antibiotic exposure was risk factor; insufficient evidence for probiotic use	Plausible mechanisms for antibiotic effect, such as microbiome change; robust longer-term studies of probiotic use

In Project Viva, children with <12 hours' daily sleep between age 6 and 24 months had almost twofold odds of obesity at age 3 years compared with those with  $\geq 12$  hours sleep.<sup>229</sup> In a follow-up study,<sup>230</sup> chronic curtailed sleep was associated with higher odds of obesity. In Generation R and an Australian RCT targeting infants with sleep difficulties, no association between infancy sleep duration and later childhood obesity was found.<sup>68,231</sup>

One study<sup>68</sup> quantified an effect between infant screen time and childhood overweight. This population-based study in the Netherlands did not find an association between TV viewing in infancy and child obesity.

Three RCTs targeted multiple behaviors during infancy. In the first, the Special Turku Coronary Risk Factor Intervention Project targeted avoidance of excessive saturated fat intake. At age 10 years, girls who were in the intervention arm had continuously lower prevalence of overweight.<sup>232</sup> In Healthy Beginnings, multiple diet and activity behaviors were targeted from the prenatal period until age 2 years in Australian families, with resultant lower mean BMI, but no difference in overweight, between intervention and control participants.<sup>233</sup> A third intervention in a Mohawk community found no significant difference in child overweight among children of participants in a parenting support group targeting healthy eating and physical activity compared to a parenting support group focused on active parenting, but sample sizes were small.<sup>234</sup>

Table 3 summarizes findings for infant feeding practices and mode. Forty-nine articles examined breastfeeding. Of these, 23 suggested that breastfeeding had a protective effect against later overweight.<sup>53,82,96,99,112,181,183,213,235-249</sup> The remaining 26 studies found no association between breastfeeding and childhood overweight.<sup>62,68,86,98,103,176,189,191,250-267</sup> Some studies strictly included exclusive breastfeeding in their exposure definition, whereas others included consumption of any breast milk.

Five U.S.-based articles<sup>49,73,268-270</sup> in ethnically diverse populations examined bottle use. One nationally representative study<sup>270</sup> did not find a difference in childhood overweight among children who drank breast milk from a bottle compared to those who breastfed. In the Early Childhood Longitudinal Study, Birth Cohort (ECLS-B), bottle use at 24 months and putting a child to sleep with a bottle at 9 months were associated with subsequent child overweight.<sup>73,269</sup> However, in the Fragile Families and Wellbeing Study,<sup>49</sup> sleeping with a bottle at 9 months was not associated with subsequent overweight. In a non-blinded RCT of infants in low-income families, a bottle-weaning intervention led to a reduction in bottle use and total calorie intake, but did not result in differences in overweight.<sup>268</sup>

Evidence from three prospective birth cohorts<sup>12,254,271</sup> supports a role for early timing of introduction of solid foods in the development of childhood overweight. One<sup>12</sup> of these found that introduction of solid food before age

**Table 3.** Birth to 2 Years—Feeding Practices and Mode: Key Findings and Research Needs

Risk factor	No.	Key findings	Research needs
Breastfeeding	49	Breastfeeding may be protective, but evidence is inconsistent.	Plausible mechanisms linking feeding style and breast milk composition with biologic changes (e.g., microbiome and adipokines)
Bottle use	5	Inappropriate bottle use and delayed transition from bottles to sippy cup may be risk factors for obesity	Messages and specific behavioral targets for appropriate bottle use; longer intervention follow-up
Early or late solid food introduction	8	Evidence in a few large prospective birth cohorts that introduction of solid foods younger than age 4 months is a risk factor for obesity, and this may be particularly true for children who are formula-fed; however, overall evidence is inconsistent	Optimal life course stages and messaging to target prevention of early introduction of solid foods
Beverage intake	4	Infant coffee and tea drinking may be a risk factor for obesity and severe obesity; no prospective studies of juice or SSB intake; only one study of milk intake, which did not show evidence for milk volume as a risk factor	Confirmation of coffee/tea findings; prospective studies of comprehensive beverage intake in this age group to determine the prevalence, effect on obesity risk, and specific behaviors to target for messaging
Nutrient intake	6	Insufficient information to suggest infant carbohydrate or fatty acid intake as risk factors; high infant protein intake may be a risk factor for child overweight	Comprehensive examinations of diet composition and child obesity and cardiometabolic outcomes
Feeding style	3	Insufficient evidence	Impact of parental feeding beliefs and behaviors with child growth in diverse populations.

SSB, sugar-sweetened beverage.

4 months had a significant association with later obesity only among formula-fed children, and this effect was substantial (AOR=6.2, 95% CI=2.3, 16.3). Three cohorts<sup>263,267,272</sup> did not find any association of solid food introduction timing with obesity. For later introduction of solid foods, findings were inconsistent.<sup>62,189</sup>

Two articles examined ECLS-B data and found that child coffee or tea intake at age 2 years was associated with twofold higher odds of childhood overweight,<sup>73</sup> and threefold higher odds of severe obesity,<sup>25</sup> at Kindergarten entry. In Project Viva, higher milk consumption volume was not a risk factor for overweight.<sup>273</sup> A Swedish study<sup>250</sup> found children who consumed a milk cereal drink at age 6 months had higher odds of overweight.

Six studies examined the role of infant diet and nutrient intake in later overweight risk. One<sup>274</sup> study of children of low-income, African American mothers participating in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) found that inappropriate feeding was associated with higher energy intake and greater odds of high weight-for-length. In Generation R, higher infant polyunsaturated fat intake had a preventive effect on child overweight/obesity.<sup>68</sup> In a Danish RCT, obesity prevalence was higher in children of mothers randomized to fish oil supplementation during breastfeeding than in olive oil supplementation and high fish intake groups, but findings were not statistically significant.<sup>275,276</sup> Two studies<sup>277,278</sup> reported that higher protein intake during infancy was associated with later overweight or obesity.

In the ECLS-B,<sup>73</sup> maternal self-report of a belief that infants should be fed when hungry rather than on a regular schedule had a small magnitude of association with decreased overweight/obesity at Kindergarten entry. However, a birth cohort in the Netherlands did not find an association between on-demand feeding and later overweight.<sup>256</sup> In Project Viva, maternal feeding restriction at age 1 year was associated with obesity at age 3 years, but after models adjusted for weight at 1 year, findings were no longer significant.<sup>279</sup>

Of the three studies<sup>280-282</sup> addressing food insecurity, a Canadian study<sup>280</sup> found a nearly twofold increase in odds of obesity at age 4 years among children with any infant food insecurity compared with those without food insecurity. Among WIC participants,<sup>281</sup> food insecurity was an obesity risk factor but only among those with persistent food insecurity and with hunger. In a nationally representative U.S. study,<sup>282</sup> food insecurity had indirect effects through parenting practices on childhood obesity.

Three studies<sup>283-285</sup> examined the association of any maternal depression in the first 1,000 days with child overweight and reported inconsistent findings. Each

study used different exposure definitions and scales for measurement and different outcome measures for child overweight.

In a prospective cohort study<sup>286</sup> of 1,600 low-income U.S. families, female, but not male, children with two social adversity risk factors at age 12 months (maternal mental health, substance abuse, and intimate partner violence; housing and food insecurity; or paternal incarceration) had twice the odds of obesity at age 5 years than those with zero to one social adversity risk factors.

Three large, prospective U.S. studies<sup>79,287,288</sup> investigated SES during the first 1,000 days, and all found an association with later childhood overweight. One study<sup>287</sup> using the National Longitudinal Study of Youth found higher odds of overweight among children in middle-income households compared with high-income families. Another study<sup>288</sup> of National Longitudinal Study of Youth offspring found a small association of greater maternal hours worked per week with child overweight. In the ECLS-B, lower SES based on parent education and household income was a risk factor for child overweight.<sup>79</sup>

Five articles<sup>289-293</sup> examined the role of maternal-infant relationship quality with childhood overweight. In two<sup>289,290</sup> of these studies, insecure child attachment was associated with higher odds of overweight. In the ECLS-B, low maternal-infant relationship quality was associated with child overweight, but adjustment for sociodemographic characteristics accounted for results.<sup>291</sup> Two studies<sup>292,293</sup> found that lower maternal sensitivity, defined by observed maternal responsiveness to infant cues, was associated with later childhood overweight.

Two studies examined facets of parent weight between birth and child age 24 months. One<sup>147</sup> found that children aged 5 months with one obese parent had twofold higher odds of obesity at age 4.5 years and threefold odds of obesity if both parents were obese. Another<sup>294</sup> found a positive association between maternal attempt to lose weight at 6 months postpartum and later child obesity.

Two large prospective U.S. birth cohorts<sup>295,296</sup> of primarily non-Hispanic white children examined child care attendance during the first 1,000 days. Both found a small but significant association of any child care attendance with child obesity.

All four studies<sup>66,297-299</sup> of antibiotic use during the first 6-12 months of life found any infant antibiotic use to be a risk factor for later child overweight. For probiotic use, intervention and control arms in an RCT of maternal *Lactobacillus rhamnosus* GG use found no difference in childhood overweight, but the prevalence of overweight in the study was low.<sup>300</sup>



## Discussion

In this systematic review of nearly 300 prospective studies, several risk factors during the first 1,000 days were consistently associated with later childhood overweight: higher maternal pre-pregnancy BMI, maternal excess gestational weight gain, prenatal tobacco exposure, high infant birth weight, and high infant weight gain. A smaller number of studies also supported gestational diabetes, child care attendance, low strength of maternal–infant relationship, low SES, curtailed infant sleep, inappropriate bottle use, introduction of solid food before age 4 months, and infant antibiotic exposure as risk factors for childhood overweight. Results for breastfeeding, food insecurity, and maternal depression were inconsistent.

Previous systematic reviews have focused either on pregnancy, infancy, or childhood risk factors for obesity, including a 2012 systematic review<sup>301</sup> of risk factors for child overweight during infancy. To the authors' knowledge, none have reviewed the literature for risk factors that span these important life periods. In this review, several prenatal risk factors for childhood obesity were identified but findings showed only two risk factors during infancy with consistent evidence to support their role in childhood overweight. Excess maternal gestational weight gain, infant birth weight, and accelerated infant weight gain were consistently associated with later childhood overweight. Future studies should examine modifiable determinants of these biological factors.

This review identified a number of gaps in the literature that should be filled to advance childhood obesity research during the first 1,000 days. First, many studies of pregnancy and birth risk factors or interventions do not extend beyond the first months of life. Future research during pregnancy should examine the mechanisms through which intrauterine risk factors lead to offspring risk of overweight and the impact of interventions to reduce childhood obesity risk factors during this time period, and include long-term follow-up of mothers and children.

Second, there is no single measure of adiposity that can be continuously used across fetal, infant, and early-childhood life course periods. Prenatal ultrasound estimates of fetal growth are not universally conducted and are subject to a wide range of measurement error. Although WHO BMI standards from birth to 24 months exist, CDC recommends clinical use of WHO weight-for-length charts rather than WHO BMI charts below age 2 years, and no accepted thresholds for infant "overweight" or "obesity" exist.<sup>302</sup> Standardized measures for reporting high fetal and infant weight are needed, and a continuous measure of child growth during the first years of life would facilitate future research.

Third, outcome measures and reporting of child weight category vary. Some studies report only on continuous BMI outcomes, overweight with obesity, only obesity, or overweight and obesity as separate outcomes. There is a need for consistent reporting of outcomes to compare findings across studies.

Fourth, the single risk factor with the largest number of studies examining its relationship with obesity was breastfeeding, which did not consistently protect against childhood overweight. To identify intervention targets during the first 1,000 days, comprehensive examinations of child dietary composition and feeding will advance understanding of their role in obesity development. Finally, many studies focus on maternal factors that contribute to obesity development. Future research should include information on the role of fathers, partners, and other caretakers on child weight outcomes.

Although substantial disparities in childhood obesity exist, the bulk of studies took place in high-income populations with predominantly non-Hispanic white participants. In the U.S., few prospective studies included low-income families in low-SES settings or racial/ethnic minorities to allow for generalizability. More research is needed to determine mechanisms of obesity development and feasible approaches to reduce obesity in diverse populations.

## Limitations

The current body of evidence for childhood obesity risk factors is largely observational, which limits the ability to draw conclusions about causality. Also, the body of evidence examined for each risk factor may have been limited by excluding cross-sectional studies and those with self-reported exposures and outcomes. However, by including only prospective studies, the potential for reverse causation interfering with interpretation of results is limited. Because the focus was specifically on risk factors for child overweight/obesity, articles that only used continuous weight outcomes in their reporting were not included, but a large number of prospective studies spanning conception through age 18 years were still examined.

## Conclusions

The first 1,000 days are a critical period for childhood obesity development, and thus prevention. Targeting healthy pre-conception weight and gestational weight gain, tobacco avoidance, and healthy infant weight gain with adherence to current infancy nutrition and sleep recommendations shows promise for childhood obesity prevention.

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## Appendix

### Supplementary data

Supplementary data associated with this article can be found at <http://dx.doi.org/10.1016/j.amepre.2015.11.012>.