Lactose-reduced infant formula with corn syrup solids and obesity risk among participants in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC)

Christopher E Anderson,[1] *Shannon E Whaley,*[1] *and Michael I Goran*[2]

[1]Division of Research and Evaluation, Public Health Foundation Enterprises (PHFE) WIC, a program of Heluna Health, Irwindale, CA, USA; and [2]Department of Pediatrics, Children's Hospital Los Angeles, University of Southern California, Los Angeles, CA, USA

ABSTRACT

Background: The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), a federal nutrition assistance program supporting low-income families, serves half of United States–born infants, most of whom are issued infant formula by age 2 mo. Obesity prevalence is high among children of low-income households, particularly formula-fed children.

Objectives: This study was conducted to determine whether glucose-based lactose-reduced infant formula made with corn syrup solids (CSSF) is associated with increased obesity risk compared with non-CSSFs that are lactose based.

Design: WIC administrative data on infant formula issuance and child weights and lengths were collected prospectively in Southern California between 2012 and 2020. Included children stopped breastfeeding by 3 mo, were issued cow's milk–based formula through 12 mo, and were enrolled through the final year of WIC eligibility at age 4 y (n = 15,246). CSSF issuance was assessed continuously (range 0–13 mo) and dichotomously (any, none). Poisson and linear risk regression with robust SE estimates generated risk ratios (RRs), risk differences, and CIs for child obesity [BMI for age (in kg/m ^{2}) ≥95th percentile].

Results: Any CSSF was issued to 23% of children, and 25% were obese at age 4 y. Children with any CSSF issuance had 10% higher obesity risk (RR: 1.10; 95% CI: 1.02, 1.20) than children with no CSSF issuance at age 2 y. Associations remained significant through age 4 y (RR: 1.07; 95% CI: 1.01,1.14), independent of maternal weight status, total formula issued and breastfeeding duration, and were not modified by child race or sex. Obesity risk increased with additional mo of CSSF exposure, reaching 16% higher risk (RR: 1.16; 95% CI: 1.05, 1.28) at age 2 y for children with 12 mo of CSSF.

Conclusions: CSSF issuance is associated with increased obesity risk in the first 5 y life in a dose dependent manner, independently of maternal weight status, breastfeeding duration, and total formula issuance. *Am J Clin Nutr* 2022;0:1–8.

Keywords: infant formula, lactose, glucose, child obesity, WIC, corn syrup solids

Introduction

A substantial proportion of children in the United States are obese (1, 2), and the prevalence of severe obesity continues to increase (3). Obesity prevalence is higher among children from low-income households (4, 5). In Los Angeles, the prevalence of childhood obesity is 35% in low-income communities compared with 5% in the most affluent communities (6). Data collected during the COVID-19 pandemic suggest that rates of weight gain among young children continue to accelerate (7), adding urgency to primary prevention efforts to reduce childhood obesity. Rapid weight gain in the first 2 y of life increases obesity risk in later childhood (8), and childhood obesity increases obesity risk in adulthood (9). Infant feeding contributes to increased risk of obesity (10) from the early introduction of complementary foods and beverages (11), bottle feeding instead of breastfeeding (12), and feeding formula instead of breastmilk (13). The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) is a federal nutrition assistance program that issues benefits redeemable for healthy foods, nutrition education, breastfeeding support, and referrals to health and social services for pregnant or postpartum females and their children <5 y old who live in households with incomes below 185% of the federal poverty level (14). WIC serves >6 million participants every month (15) and half of infants born the United States (16). Despite increases in breastfeeding initiation and duration over the last 20 y (17), a majority of participating infants begin receiving formula from WIC by 2 mo of age (18). State WIC agencies

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Supplemental Figure 1 and Supplemental Table 1 are available from the "Supplementary data" link in the online posting of the article at https://academic.oup.com/ajcn/.

Address correspondence to CEA (e-mail: christophera@phfewic.org).

Abbreviations used: CSSF, lactose-reduced infant formula made with corn syrup solids; LAZ, length-for-age z-score; RR, risk ratio; WAZ, weight-for-age z-score; WIC, Special Supplemental Nutrition Program for Women, Infants, and Children; WLZ, weight-for-length z-score

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sign multiyear contracts with infant formula manufacturers to provide all nontherapeutic formulas to WIC-participating infants, and various formula types are provided, including cow's milk-based, soy-based, lactose-reduced, and specialty formulas (19).

Evaluations of the associations between formula intake and child obesity have focused on the duration and amount of formula received and have found that longer durations and more exclusive formula feeding are associated with increased obesity risk compared with breastfeeding (20). This may conceal important differences in growth patterns between infants receiving different types of formula (19), because lactose-reduced infant formulas made with corn syrup solids (CSSFs) as an alternative carbohydrate source are lower in lactose and higher in glucose and therefore more glycemic (21, 22). Recent studies have identified associations between consumption of CSSFs and the infant gut microbiome at 6 mo of age (23), and associations between infant gut microbiome and growth characteristics from birth to 12 mo of age (24). Because CSSFs are included among the contract formula options in many states, allowing mothers a reduced-lactose milk-based infant formula option, the current study was undertaken to evaluate the relation between receipt of a CSSF and obesity risk among WIC-participating children in Southern California. It was hypothesized that the risk of child obesity would increase with increasing duration of issuance of a CSSF.

Subjects and Methods

Subjects

Data used in this study were administrative data collected by a large local WIC agency in Southern California for children born between September 2012 and March 2016. Children were included in this study if: the child was enrolled in WIC within 42 days of birth, had complete WIC infant food package issuance data for 12 or more of the first 13 mo of life, received only cow's milk-based formula (excluding soy-based formula which differs in both protein and carbohydrate source), received the fully formula feeding infant package from 3 mo of age through the remainder of the infant year (indicating breastfeeding had ceased by 3 mo of age), had at least 1 height and weight measurement annually through age 4 y, and had complete sociodemographic covariate data (n, children = 15,246; **Supplemental Figure 1**). No sample size calculation was done for this study. This study was approved by the California Department of Health and Human Services Institutional Review Board.

Infant formula issuance

Infant formula exposure during the first year was characterized using WIC infant food package issuance data. WIC-participating infants receive food packages from 0 to 12 mo of age that are assigned based upon the amount of breastfeeding a mother reports, to ensure that the infant's nutritional needs are met. Infants receive one of four packages: fully breastfeeding (0 mL of infant formula monthly), mostly breastfeeding (up to 5,323 mL monthly), some breastfeeding (6,624 to 11,918 mL monthly), or fully formula feeding (9,227 to 13,071 mL monthly). The amount of formula in infant packages varies by child age to accommodate the portion of nutritional needs expected to be met by complementary foods after 6 mo of age (25). Infant formula is more likely than other WIC food items to be fully-redeemed (26), and WIC infant food package data are a valid proxy for infant feeding practices (kappa = 0.76 and 0.84 for infants 0–6 mo and 7–12 mo respectively) (27). In infant food packages that include formula, mothers can select a formula for their infant from among WIC contract infant formulas (28).

Infant feeding was summarized for each child over the first 13 mo by the: 1) age (in mo) at last reported breastfeeding, 2) the total number of mo any infant package containing formula was issued by WIC, and 3) the number of mo a CSSF was issued.

Months of CSSF issuance was the primary exposure of interest, and was explored as a continuous variable (the number of mo issued, range: 0 to 13) and a dichotomous variable (any, none).

Outcome

Child obesity was assessed with height and weight measurements collected during certification of a child's WIC program eligibility by WIC staff. These measurements have been reported to be of high validity (29). BMI-for-age z-scores were calculated from measurements between 24 and <60 mo of age, using sex-specific CDC growth curves (30). Obesity was defined at each measurement at ≥2 y of age as a BMI-for-age z-score ≥the 95th percentile (n = 64,767 observations).

Covariates

WIC administrative data, collected during routine program services, contained information on child, maternal, and household characteristics. Covariates for this study included the child's age, date of birth, sex, and maternally reported language preference (English, Spanish, or other language) and race/ethnicity (reported as Asian, Black, Hispanic, non-Hispanic White, or Other; language and race/ethnicity categorized together for analysis as English-speaking Asian, non–English-speaking Asian, Black, English-speaking Hispanic, Spanish-speaking Hispanic, White, or Other); maternal postpartum weight status from weights and heights measured by WIC staff between 0 and 6 mo after delivery [BMI (in kg/m^2), dichotomized as ≥25 and <25) and educational attainment (less than high school, completed high school, or more than high school), and household poverty (categorized as <100% or ≥100% of the federal poverty level). Maternal prepregnancy weight status was unavailable due to WIC program eligibility, and maternal postpartum weight status was identified as the best option to minimize missing data. Infant growth status at baseline was assessed as the weight-for-length z-score (WLZ), weight-for-age z-score (WAZ), and length-for-age z-score (LAZ) from the first length and weight measurement available for each infant, calculated using sex-specific CDC growth curves (30).

Statistical analysis

Participating children were characterized with means and standard deviations or frequencies and percentages. Comparisons between children by CSSF issuance (any, none) were performed with chi-square or t-tests for categorical and continuous variables, respectively.

TABLE 1 Characteristics of WIC-participating infants born between September 2012 and March 2016 by issuance of CSSF in Southern California ($n = 15,246$)[1]

Variable	Any CSSF ($n = 3548$)	No CSSF ($n = 11,698$)	P value
Male	1886 (53.2)	5903 (50.5)	0.005
Race/ethnicity and language			<0.001
Asian, non–English speaking	59 (1.7)	696 (6.0)	
Asian, English speaking	30 (0.9)	288 (2.5)	
Black	156 (4.4)	346 (3.0)	
Hispanic, English speaking	2234 (63.0)	5396 (46.1)	
Hispanic, Spanish speaking	966 (27.2)	4,739 (40.5)	
White	54 (1.5)	104 (0.9)	
Other	49 (1.4)	129 (1.1)	
Maternal education			<0.001
<High school degree	565 (16.0)	2656 (22.9)	
High school degree	851 (24.1)	3092 (26.7)	
>High school degree	2115 (59.9)	5854 (50.5)	
Income <100% federal poverty level	2783 (78.8)	9352 (80.6)	0.02
Maternal postpartum BMI ≥25	2743 (77.3)	8569 (73.3)	<0.001
Age at last breastfeeding, mo	1 ± 1	1 ± 1	0.55
Total formula, mo	12 ± 1	12 ± 1	<0.001
Total CSSF, mo	9 ± 4	0 ± 0	<0.001
Age at first CSSF, mo	2 ± 2	—	—
Baseline measurements			
Age, y	0.36 ± 0.22	0.37 ± 0.21	0.10
WLZ	0.55 ± 1.07	0.62 ± 1.05	0.006
WAZ	0.30 ± 1.07	0.35 ± 1.00	0.006
LAZ	−0.06 ± 1.04	−0.07 ± 0.97	0.71
Last measurements			
Age, mo	4.36 ± 0.35	4.37 ± 0.39	0.10
WLZ	0.81 ± 1.10	0.74 ± 1.07	0.02
WAZ	0.80 ± 1.17	0.70 ± 1.15	<0.001
LAZ	0.38 ± 1.00	0.30 ± 1.01	<0.001
Obese	953 (26.9)	2,879 (24.6)	0.007

[1] Values are presented as n (%) or means ± SDs unless otherwise indicated. CSSF, lactose-reduced infant formula made with corn syrup solids; LAZ, length-for-age z-score; WAZ, weight-for-age z-score; WIC, the Special Supplemental Nutrition Program for Women, Infants, and Children; WLZ, weight-for-length z-score.

A piecewise linear spline mixed model was used to evaluate mean WLZ trajectories by CSSF exposure and sex from birth to age 5 y (31, 32). Mixed effects models included random intercepts and random slopes for each age interval (0–0.5, 0.5–1.0, 1.0–1.5, 1.5–2.0, 2.0–3.0, 3.0–4.0, 4.0–5.0 y) and individual. The associations of infant CSSF issuance with child obesity were evaluated in modified Poisson regression models with robust standard error estimation, which were used to estimate risk ratios (RRs) for obesity at ages 2, 3, and 4 y while accommodating repeated measurements for children (33), and linear risk regression with robust standard error estimation which were used to estimate absolute risk and risk difference (RD) for obesity at ages 2, 3 and 4 y while accommodating repeated measurements for each child (34). Models were fitted separately for the dichotomous and continuous CSSF issuance variables. Mixed effects, linear risk, and Poisson regression models contained terms for independent variables, including household poverty, maternal postpartum weight status, educational attainment, race/ethnicity and language preference; child age, sex, age (months) at last reported breastfeeding; and total months of any formula issued by WIC; issuance of CSSF (any compared with none, or number of months issued). Linear risk and Poisson models included baseline WLZ, age (linear and quadratic), and 2-way interactions of child age (linear and quadratic) with issuance of CSSF (any compared with none, or number of months issued). The mixed effects model included interaction terms between age (and age spline variables) with CSSF issuance and child sex, and between-child sex and CSSF issuance. Effect modification by race/ethnicity and sex was evaluated in linear risk and Poisson regression models by the inclusion of 2-way interaction terms between race/ethnicity or sex and CSSF issuance. No significant interaction was identified, so the interactions with race/ethnicity and sex were removed from the final models (data not shown). A sensitivity analysis was conducted among a sample restricted to children of Hispanic mothers. Statistical significance was determined by P values < 0.05. All analyses were conducted using SAS 9.4 (SAS Institute Inc.).

Results

Characteristics of the study participants are presented in **Table 1**. Most children were Hispanic (87.5%) and lived in a household with an income below 100% of the federal poverty level (79.6%). Children with any CSSF issuance were significantly more likely than those with no issuance to be male (53.2% compared with 50.5%, $P = 0.005$), to be Black (4.4% compared with 3.0%) or English-speaking Hispanic (63.0% compared with 46.1%, $P < 0.001$ for race/ethnicity and language), and to have a

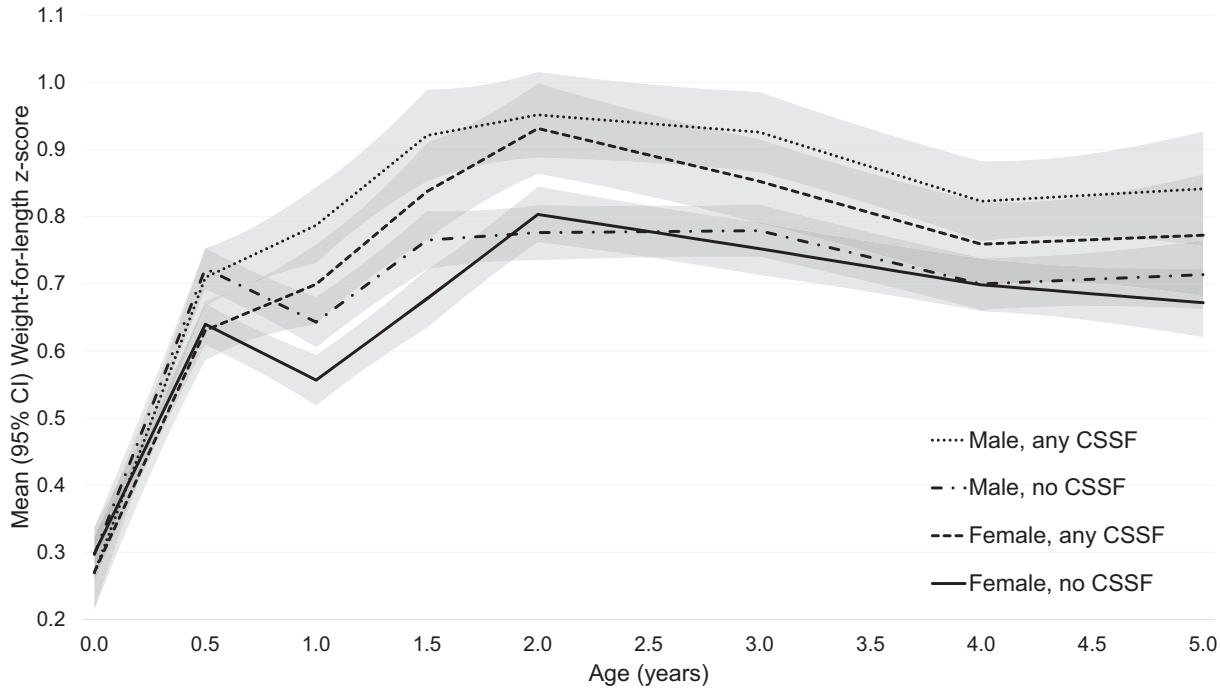

FIGURE 1 Mean WLZ trajectories by CSSF and sex among WIC-participating infants of born September 2012 to March 2016 in Southern California ($n = 15{,}246$). Mean WLZ and 95% CIs were obtained from a piecewise linear spline mixed effects regression model that included random intercepts, random slopes in each age interval (0.0–0.5, 0.5–1.0, 1.0–1.5, 1.5–2.0, 2.0–3.0, 3.0–4.0, 4.0–5.0 y), and terms for household poverty; maternal postpartum weight status, educational attainment; infant sex, race/ethnicity, age (in months) at last reported breastfeeding, total months of any formula issued by WIC, any CSSF issued by WIC, age at weight/length measurement (and age spline variables), 2-way interaction between any CSSF and child sex, 2-way interactions between any CSSF issued and age (and age spline variables), 2-way interactions between child-sex and age (and age spline variables), and 3-way interactions between child sex, any CSSF issuance, and age (and age spline variables). Mixed models accommodated repeated observations clustered within each child. Groups included the following number of children: male, any CSSF, $n = 1886$; female, any CSSF, $n = 1662$; male, no CSSF, $n = 5903$; female, no CSSF, $n = 5795$. CSSF, lactose-reduced infant formula made with corn syrup solids; WIC, the Special Supplemental Nutrition Program for Women, Infants, and Children; WLZ, weight-for-length *z*-score.

mother with more than a high school degree (59.9% compared with 50.5%, $P < 0.001$). Children with any CSSF issuance had significantly lower WLZ and WAZ at baseline (P values 0.006 and 0.006, respectively), and significantly higher WLZ, WAZ, and LAZ at the last measurement (P values 0.02, <0.001, and <0.001, respectively). Over one-quarter of study participants were obese at 4 y of age, and the proportion with obesity was higher among children with any CSSF issuance than among children with no CSSF issuance (26.9% compared with 24.6%, P value = 0.007).

Infants with and without any CSSF issuance were issued an average of 12 mo of any formula by WIC and breastfed for an average of 1 mo (Table 1). Children with any CSSF issuance were issued an average of 9 mo of the CSSF. The proportion of children issued a CSSF increased from 0 to 3 mo of age, and a CSSF was issued to >18% of infants per mo from 3 to 12 mo of age (**Supplemental Table 1**).

Trajectories in mean WLZ by CSSF issuance separated between 0.5 and 1.0 y of age for both sexes (**Figure 1**), with CSSF recipients remaining at a higher average WLZ through age 5 y. Children with any CSSF issuance had elevated risk of obesity compared with children with no CSSF issuance (**Table 2**). Absolute risk of obesity at age 2 y was 1.94% points higher for children with any CSSF issued by WIC compared with children with no CSSF issued (RD: 1.94%; 95% CI: 0.18, 3.70), equating to 10% higher obesity risk for children with any CSSF issued by WIC than for children with no CSSF issued by WIC (RR: 1.10; 95% CI 1.02, 1.20). RRs and RDs for obesity associated with any CSSF issuance remained statistically significant through 4 y of age. Children with any CSSF issuance had 7% higher relative and 1.97% points higher absolute risk of obesity than children with no CSSF issuance at age 4 y (RR: 1.07; 95% CI: 1.01, 1.14; RD: 1.97; 95% CI: 0.42, 3.53). Results of the sensitivity analysis among Hispanic children were nearly identical to those in the full sample (Table 2). Each additional month of CSSF issuance was associated with a small increase in risk of obesity, reaching 16% higher risk of obesity at 2 y of age among children with 12 mo compared to those with 0 mo of CSSF issuance, and the association attenuated slightly but remained statistically significant at ages 3 and 4 y (**Figure 2**).

Discussion

This study was conducted to evaluate whether CSSF issuance was associated with differences in childhood obesity among WIC participants from 2 to 4 y of age. Obesity risk was 10% higher at age 2 y among children with any CSSF issuance than among children who were issued other WIC contract formulas, independent of maternal weight status, breastfeeding duration, and total months of formula issued by WIC. This higher risk of

TABLE 2 Absolute risk, risk difference, and RRs for obesity by issuance of any CSSF by WIC at ages 2, 3, and 4 y among WIC-participating children in Southern California (total, $n = 15,246$; Hispanic, $n = 13,335$)[1]

Study participant age, y	Absolute obesity risk, %[2]		Risk difference, %[2]			RR[3]		
	Any CSSF	No CSSF	Any CSSF	No CSSF	*P* value	Any CSSF	No CSSF	*P* value
Full sample								
2	16.4 (14.2, 18.6)	14.4 (12.7, 16.2)	1.94 (0.18, 3.70)	0.00 (ref)	0.03	1.10 (1.02, 1.20)	1.00 (ref)	0.02
3	21.2 (19.2, 23.2)	19.3 (17.6, 21.0)	1.87 (0.37, 3.37)	0.00 (ref)	0.01	1.08 (1.02, 1.15)	1.00 (ref)	0.01
4	23.1 (21.1, 25.2)	21.1 (19.4, 22.9)	1.97 (0.42, 3.53)	0.00 (ref)	0.01	1.07 (1.01, 1.14)	1.00 (ref)	0.01
Hispanic								
2	21.3 (19.5, 23.0)	19.2 (18.1, 20.3)	2.09 (0.22, 3.97)	0.00 (ref)	0.03	1.10 (1.01, 1.20)	1.00 (ref)	0.03
3	26.2 (24.7, 27.7)	24.2 (23.3, 25.2)	1.95 (0.34, 3.55)	0.00 (ref)	0.02	1.08 (1.01, 1.15)	1.00 (ref)	0.02
4	28.2 (26.6, 29.7)	26.0 (25.1, 27.0)	2.13 (0.47, 3.79)	0.00 (ref)	0.01	1.08 (1.02, 1.15)	1.00 (ref)	0.01

[1]Values are presented as absolute risks, risk differences, and risk ratios (RRs) (95% CIs) unless otherwise indicated. CSSF, lactose-reduced infant formula made with corn syrup solids; ref, referent; WIC, the Special Supplemental Nutrition Program for Women, Infants, and Children. [2]Absolute obesity risk and risk differences were obtained from linear risk regression generalized estimating equation models with robustSE estimation that included terms for household poverty; maternal postpartum weight status; educational attainment; infant sex, race/ethnicity, baseline weight-for-length *z*-score, age (in months) at last reported breastfeeding, total months of any formula issued by WIC, any CSSF issued by WIC, age at weight/length measurement (linear and quadratic), and 2-way interactions between any CSSF issued and age (linear and quadratic). Regression accommodated repeated observations clustered within each child.

[3]RRs and 95% CIs were obtained from modified Poisson regression generalized estimating equation models with robust SE estimation that included terms for household poverty; maternal postpartum weight status; educational attainment; infant sex, race/ethnicity, baseline weight-for-length *z*-score, age (in months) at last reported breastfeeding, total months of any formula issued by WIC, any CSSF issued by WIC, age at weight/length measurement (linear and quadratic), and 2-way interactions between any CSSF issued and age (linear and quadratic). Regression models accommodated repeated observations clustered within each child.

obesity attenuated slightly but persisted as statistically significant through 4 y of age.

Prior research has identified associations between consumption of infant formula compared with breastfeeding and elevated risk of obesity (13). In the present study the sample was restricted to children receiving no breastmilk from 3 mo of age onward, and adjusted for duration of breastfeeding and total months of formula issued by WIC to control for possible confounding by total exposure to breastmilk and infant formula. The 7 to 10% higher RR for obesity from ages 2 to 4 y among infants with any CSSF

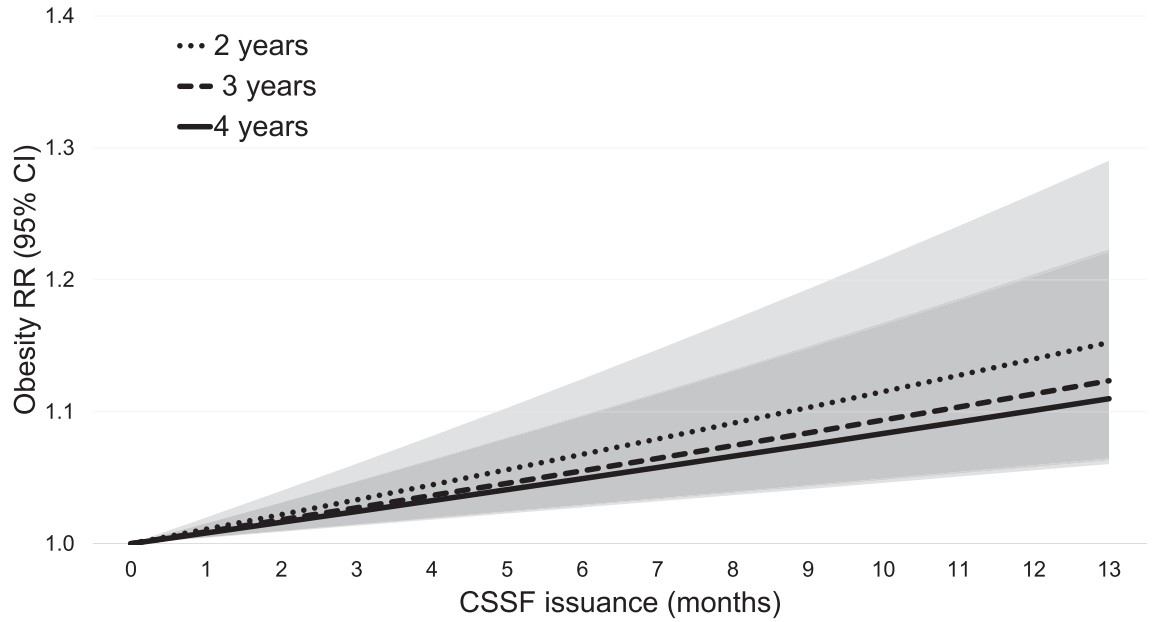

FIGURE 2 RRs for child obesity among WIC-participating children in Southern California by number of months CSSFs were issued by WIC ($n = 15,246$). RRs and 95% CIs were obtained from modified Poisson regression generalized estimating equation models with robust SE estimation that included terms for household poverty, maternal postpartum weight status, educational attainment; infant sex, race/ethnicity, baseline weight-for-length *z*-score, age (in months) at last reported breastfeeding, total months of any formula issued by WIC, months of CSSF issued by WIC, age at weight/length measurement (linear and quadratic), and 2-way interactions between months of CSSF issued and age (linear and quadratic). Regression models accommodated repeated observations clustered within each child. CSSF, lactose-reduced infant formula made with corn syrup solids; WIC, the Special Supplemental Nutrition Program for Women, Infants, and Children.

issuance compared with infants issued only non-CSSF formulas aligns with more rapid weight gain identified among females in a CSSF exposure group in a prior randomized trial (35). Lasekan et al. identified no significant deficiency in child growth over the 112-d duration of their study comparing lactose-free infant formula with lactose-containing infant formula (CSSF and non-CSSF) (35). The group who received the CSSF gained weight at a higher daily rate than the group who received lactose-containing formula, though this more rapid weight gain was only statistically significant among female infants. In contrast, in the present study, sex did not modify the association between CSSF issuance and obesity. While the results of the present study generally align with those of the randomized trial, differences between the results may be attributable to demographic differences in the study populations (much higher proportion of Hispanic infants in the WIC sample), the duration of exposure and follow-up (the infants in the intervention study were followed to 4 mo of age, while the WIC sample infants were followed to 4 y of age), and statistical methods (the randomized trial performed a 1-sided hypothesis test for the primary study endpoint).

Research has demonstrated that lactose-reduced infant formulas can be well tolerated by infants and do not appear to contribute to growth insufficiency (35, 36). However, concerns about growth in infancy are not restricted to insufficient weight gain. Recent research has revealed associations between infant consumption of CSSFs and characteristics of the infant gut microbiome (23, 37), including alpha diversity, which have also been associated with rapid growth during the first years of life (24), which is a well-established risk factor for later obesity (8). An analysis conducted in Canadian infants identified associations between infant formula consumption and elevated risk of overweight at 1 y of age, and this association was attenuated after adjustment for microbiome characteristics, demonstrating that effects on the infant gut microbiome may partially mediate associations between formula intake and child weight status (38). These prior results suggest that the association between CSSF (compared with other formulas) and elevated risk of obesity among WIC participants may be attributable to impacts of CSSFs on the gut microbiome. Other possible mechanisms for the association between CSSFs and obesity risk include CSSFs contributing to rapid weight gain in early infancy that predisposes infants to later risk of obesity (8, 35), CSSFs leading to adverse metabolic programming through a higher glycemic index compared with that for other formulas (21, 22), or that CSSFs contribute to learned preference for sweet tastes given the greater sweetness of glucose than lactose (39), and contribute to child preference for foods and beverages with added sugars (40).

Infants carried to term produce sufficient lactase to digest up to 1 L of breastmilk daily (41), and lactase nonpersistence and subsequent low lactase activity are not thought to emerge in any racial group before 3 y of age (42, 43). CSSF products may be chosen by mothers who think their child is gassy or fussy due to lactose intolerance, but these products may have detrimental impacts on child growth and long-term health. Human milk is abundant in lactose with 55 to 70 g/L, and an additional 5 to 8 g/L of complex oligosaccharides (44). Substitution of lactose in infant formula with carbohydrates like corn syrup solids contributes to a glucose-based diet that may have differential effects on metabolism and appetite regulation due to the more rapid digestion and higher glycemic index of glucose compared with lactose as the primary carbohydrate source in infant formula (21, 22). Lower glycemic index diets have been associated with lower risk of developing obesity (45). Infant formulas with higher glycemic index values, such as those replacing lactose with glucose, may therefore contribute to adverse metabolic programming and obesity risk (21, 22).

This study was conducted in a large, well-characterized sample with prospectively collected exposure and outcome data and had child growth data for the full period of WIC eligibility through age 4 y. The study sample was restricted to children receiving the fully formula feeding infant package from 3 mo of age, and analyses controlled for the age at breastfeeding cessation and the total months of formula issuance, allowing reported associations between CSSF issuance and obesity to be independent of breastfeeding duration and the total duration of formula issuance, both of which have been previously associated with obesity risk in WIC participants (20, 46). Detailed data on infant package issuance each month from 0 to 12 mo of age allowed evaluation of the dose of CSSF issuance. Both infant package issuance data and height and weight measurements collected by WIC have been previously validated (27, 29). This study was limited by its observational nature, precluding causal inference, and allowing for possible residual confounding by unmeasured maternal or child characteristics. Administrative data used in this study have no data on intake of infant formula, which limits our ability to draw inferences regarding formula issued by WIC and potentially may lead to misclassifying infant formula exposure if formulas not issued by WIC are consumed. The data do not include complementary dietary intake information, meaning complementary feeding practices may confound identified associations. Maternal sensitivity, perception of child disposition (fussiness, gassiness), and feeding practices that might increase risk of obesity (such as using food to soothe a child) may be related to formula choices, and could contribute to the observed association between CSSF issuance and obesity (47, 48). Maternal weight status was assessed postpartum because WIC only serves (and weighs/measures) pregnant and postpartum women, meaning prepregnancy weight was unavailable. The final sample was a small subset of participating children due to restriction to those enrolled in WIC from age 0 to 5 y, which may limit the generalizability of the results.

In conclusion, any issuance of lactose-reduced infant formula made with corn syrup solids as an alternative glucose-only carbohydrate source was associated with 10% higher risk of obesity at age 2 y among WIC-participating children in Southern California, and this elevated risk persisted through age 4 y. Obesity risk was 16% higher at age 2 y among children who received lactose-reduced infant formula for 12 mo of their infant year compared to infants who received other formulas for the same duration. These associations were independent of other factors such as sex and maternal weight status. Given the tremendous impact that WIC formula contracts have on the formula consumed by infants across the United States (28), detailed evaluations of impacts on child growth should be considered when making decisions about formula contracts. WIC state agency decisions about formula contracts are limited by federal regulations and state contracting laws. Results of this and similar studies, coupled with less constrictive USDA regulations, could allow state-level formula contract decisions to benefit

participant health. Further research is necessary to understand why mothers select CSSFs for their infants; to compare the effects of CSSFs to those of lactose-reduced formulas without added corn syrup solids on child weight gain, metabolism, and appetite regulation; to evaluate mechanisms underlying the associations identified between CSSF issuance and obesity; and to evaluate what other health impacts CSSF issuance may have for children.

The authors' responsibilities were as follows—CEA, SEW, MIG: designed the research; SEW: provided essential materials; CEA: analyzed the data; CEA, SEW, MIG: wrote paper; CEA: had primary responsibility for the final content; and all authors read and approved the final manuscript. Dr Goran receives book royalties from Penguin Random House and is a scientific consultant for Yumi Foods and Else Nutrition. All other authors have no conflicts of interest to disclose.

Data Availability

Data described in the manuscript were derived from confidential administrative data and will not be made publicly available due to a memorandum of understanding with the California Department of Public Health WIC Division.

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