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Whole milk compared with reduced-fat milk and childhood overweight: a systematic review and meta-analysis

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ABSTRACT

Background: The majority of children in North America consume cow-milk daily. Children aged >2 y are recommended to consume reduced-fat (0.1–2%) cow-milk to lower the risk of obesity.

Objectives: To evaluate the relation between cow-milk fat consumption and adiposity in children aged 1–18 y.

Methods: Embase (Excerpta Medica Database), CINAHL (Cumulative Index to Nursing and Allied Health Literature), MEDLINE, Scopus, and Cochrane Library databases from inception to August 2019 were used. The search included observational and interventional studies of healthy children aged 1–18 y that described the association between cow-milk fat consumption and adiposity. Two reviewers extracted data, using the Newcastle–Ottawa Scale to assess risk of bias. Meta-analysis was conducted using random effects to evaluate the relation between cow-milk fat and risk of overweight or obesity. Adiposity was assessed using BMI z-score (zBMI).

Results: Of 5862 reports identified by the search, 28 met the inclusion criteria: 20 were cross-sectional and 8 were prospective cohort. No clinical trials were identified. In 18 studies, higher cow-milk fat consumption was associated with lower child adiposity, and 10 studies did not identify an association. Meta-analysis included 14 of the 28 studies ($n = 20,897$) that measured the proportion of children who consumed whole milk compared with reduced-fat milk and direct measures of overweight or obesity. Among children who consumed whole (3.25% fat) compared with reduced-fat (0.1–2%) milk, the OR of overweight or obesity was 0.61 (95% CI: 0.52, 0.72; $P < 0.0001$), but heterogeneity between studies was high ($I^2 = 73.8\%$).

Conclusions: Observational research suggests that higher cow-milk fat intake is associated with lower childhood adiposity. International guidelines that recommend reduced-fat milk for children might not lower the risk of childhood obesity. Randomized trials are

needed to determine which cow-milk fat minimizes risk of excess adiposity. This systematic review and meta-analysis was registered with PROSPERO (registration number: CRD42018085075). *Am J Clin Nutr* 2020;111:266–279.

Keywords: cow-milk fat, children, overweight, obesity, meta-analysis

Introduction

Childhood obesity has tripled in the past 40 y, with nearly 1 in 3 North American children now overweight or obese (1–3). Over the same period, consumption of whole-fat cow-milk has halved (4). The American Academy of Pediatrics and the Canadian Paediatric Society recommend that children switch from whole-fat cow-milk (3.25%) to reduced-fat cow-milk (0.1 to 2%) at

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Supplemental Methods, Supplemental Tables 1 and 2, and Supplemental Figures 1–7 are available from the “Supplementary data” link in the online posting of the article and from the same link in the online table of contents at <https://academic.oup.com/ajcn/>.

Address correspondence to JLM (e-mail: jonathon.maguire@utoronto.ca). Abbreviations used: IOTF, International Obesity Task Force; NOS, Newcastle–Ottawa Scale; zBMI, body mass index z-score.

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2 y of age to limit fat intake and minimize the risk of childhood obesity (5, 6). European (7), British (8), and Australian (9) health authorities have provided similar recommendations. Healthcare providers (10) and families (11) frequently follow this guideline, and school and child-care nutrition policies (12–14) often reflect them. Since 1970 whole-cow-milk availability has dropped by 80% in North America, whereas reduced-fat milk purchases have tripled (15, 16).

Given that cow-milk is consumed daily by 88% of children aged 1 to 3 y and by 76% of children aged 4 to 8 y in Canada (17) and is a major dietary source of energy, protein, and fat for children in North America (17, 18), understanding the relation between cow-milk fat and risk of overweight or obesity is important. Systematic reviews and meta-analyses on the relation between total dairy consumption and child adiposity have had conflicting findings (**Supplemental Table 1**). According to these studies, higher cow-milk intake in children is associated with taller height and better bone and dental health (19–21). Although these studies evaluated total dairy consumption, they did not consider cow-milk fat specifically. The objectives of this study were to systematically review and meta-analyze the relation between whole-fat (3.25%) relative to reduced-fat (0.1 to 2%) cow-milk and adiposity in children.

Methods

A systematic review and meta-analysis of the literature was conducted. The study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA-P) (22) and registered as a PROSPERO systematic review and meta-analysis (registration number: CRD42018085075).

Inclusion criteria

Types of studies.

Studies included in the search were original works published in English in a peer-reviewed journal. Cross-sectional, cohort, case-control, and longitudinal studies, as well as intervention trials, both controlled and not controlled, were included in the search strategy. There were no restrictions on date or length of follow-up.

Population.

Studies that included healthy children aged 1–18 y with ≥ 10 human subjects were considered. Studies that examined undernourished or disease populations (other than asthma) were excluded.

Exposures.

The primary exposure was cow-milk fat, categorized as skim (0.1% fat), 1% fat, 2% fat, or whole or homogenized (3.25% fat). Measures of exposure included FFQ, multiday food record, 24-h food recall, or any other validated or nonvalidated dietary measurement tool. Dietary pattern analyses were not included.

Outcomes.

The primary outcome was childhood adiposity. These measures included BMI *z*-score (zBMI), BMI, weight for age, body fat mass, lean body mass, waist circumference, waist-to-hip ratio, body fat percentage, skinfold thickness, and prevalence of overweight or obesity as defined by the WHO (23), CDC (24), or International Obesity Task Force (IOTF) (25) cutoffs. When sufficient information was not available in the full text publication, study authors were contacted by email to obtain additional data.

Meta-analysis.

Meta-analysis included studies that reported the number of children who consumed whole (3.25%), 2%, 1%, or skim (0.1%) milk regularly (a priori defined as typically, daily, or ≥ 4 times per week), as well as the number of children from each of these groups who were classified as either healthy weight, or overweight or obese (overweight and obese were included as 1 category) assessed using BMI standardized according to the WHO (23), CDC (24), or IOTF (25) criteria.

Search methods

A comprehensive search strategy was developed by a research librarian (NT) with expertise in systematic reviews. From inception to August 2019, Embase, CINAHL (Cumulative Index to Nursing and Allied Health Literature), MEDLINE, Scopus, and the Cochrane Library were searched on March 23, 2018 and updated on August 2, 2019 using Medical Subject Headings (MeSH) and keywords (see **Supplemental Methods** for search strategies).

Data extraction, management, and analysis

Study selection.

To evaluate study eligibility 2 reviewers (MA and SMV) independently reviewed study titles, abstracts, and full texts if needed. Both reviewers applied inclusion and exclusion criteria and differences were examined and resolved by consensus, which was achieved 100% of the time. Full-text articles were retrieved for potentially eligible studies and reviewed. Characteristics of included full-text studies were summarized.

Data extraction.

Two reviewers (MA and SMV) extracted data from eligible studies using standardized data extraction tables adapted from the Cochrane Data Extraction Template (26). Differences were resolved by consensus 100% of the time.

Data management.

Covidence (27) software was used to select studies, review results, and resolve discrepancies between reviewers. All included study records were kept in spreadsheet format.

Data synthesis.

Studies included in the analysis were described according to a standardized coding system that captured key elements of each study including descriptors of the study setting, population size and age (mean and range), exposure or intervention, comparator group, method of data collection, outcome measures, type of analysis, and results.

Risk of bias and study quality assessment

Risk of bias was assessed using the Newcastle–Ottawa Scale (NOS) (28) for nonrandomized analyses, which expresses the risk of bias on a numerical scale ranging from 0 to 9; scores <7 are considered low risk (28). (NOS criteria can be found in Table 2.) The NOS-guided review included an examination of participant selection, comparability of children consuming whole or reduced-fat milk, and exposure and outcome measure ascertainment (28). To allow sufficient follow-up time for a meaningful change in adiposity to occur, the minimum acceptable follow-up time was prespecified as 1 y. Study comparability, defined as whether studies adjusted for similar confounding variables, was specified a priori as studies that adjusted for important characteristics including: birth weight or baseline weight (for prospective cohort studies), milk volume consumed, and parent BMI. Studies that adjusted for each of these factors were awarded 2 points, whereas 1 point was allocated if adjustment was performed using ≥ 4 other covariates. Reports were assigned 1 point for ascertainment of exposure only when structured interviews or medical records were used for data collection (28). Risk of bias was assessed by 2 reviewers (MA and SMV) and consensus was achieved 100% of the time.

Statistical analysis

For each study, participant information, design, and results were summarized. We derived crude ORs and extracted adjusted ORs, whenever available, for overweight or obesity among children who consumed whole (3.25%) milk, compared with children who consumed reduced-fat (0.1–2%) milk regularly. A random effects model based on the restricted maximum likelihood estimator was decided a priori and used to separately pool crude and adjusted ORs of overweight or obesity. Each study was included as a random effect to account for between-study variation in this model. Sensitivity analyses were performed using the Knapp–Hartung method (29) and inverse-variance weights. Because prospective cohort studies can reveal different relations than cross-sectional studies, we performed a subgroup analysis according to study design. Additionally, we analyzed studies in subgroups according to risk of bias (high compared with low) and age (1–5 y, 6–11 y, and 12–18 y). Subgroup analyses were accompanied by tests for interaction between each subgroup and the main effect from the random-effects meta-regression, by using an interaction term in meta-regression models for study design (cross-sectional compared with prospective cohort), risk of bias (high compared with low), and age group (1–5 y, 6–11 y, and 12–18 y). Heterogeneity across included studies was estimated using the I^2 statistic (30). Heterogeneity was considered low (<40%), moderate (40–60%), or high (>60%) (31). Publication bias was assessed using a funnel plot and Egger test (32).

Finally, we conducted a dose–response meta-regression to quantify the association between percentage of fat in cow-milk consumed and the odds of overweight or obesity. Only studies that reported group-specific odds for ≥ 3 types of cow-milk fat were included in this analysis. For the dose–response analysis, we first used a fixed-effect approach to estimate the dose–response relations within each study. Then, we used a random-effects approach to combine across studies the dose–response estimates that were generated in the first step for each study (33) to obtain regression coefficients, and their respective standard errors. R software version 3.2.2 (34) was used for all analyses, using the “metafor” package (35).

Results

The database search identified 5862 potentially eligible studies. After exclusion of duplicates ($n = 1861$), 4001 reports underwent title and abstract review. Studies that did not meet inclusion criteria ($n = 3915$) were removed resulting in 86 published studies that underwent full text review (Figure 1). Reasons for exclusion included wrong exposure, wrong outcome, wrong patient population, dietary pattern analysis only, or wrong study design such as case reports or editorials. Twenty-eight studies met all inclusion criteria. Of these, 20 were cross-sectional and 8 were prospective cohort studies (see Table 1 for study characteristics). No interventional studies were identified. Most studies ($n = 23$) compared consumption of whole milk (3.25% fat) with reduced-fat milk (0.1%, 1%, or 2% fat). Four studies (36–39) compared whole and 2% milk with 1% and skim milk. One study compared whole milk with 2% milk (40).

Nineteen studies used zBMI, 4 prospective cohort studies used percentage body fat change, and 5 studies used overweight or obesity categories as the primary adiposity outcome. Three studies used 2008 WHO (23) growth standards, 14 studies used 2000 CDC (24) growth standards, 7 used 2000 IOTF (25) growth standards, and 4 studies either did not specify or used other standards for zBMI measurement.

Eighteen (36, 38, 39, 41–45, 47–49, 51, 52, 57, 58, 60, 63, 65) studies reported that higher cow-milk fat was associated with lower child adiposity. Ten studies (37, 40, 46, 50, 53–56, 59, 61) reported no association between cow-milk fat and child adiposity.

Risk-of-bias assessment

Risk of bias assessed using the NOS suggested that 1 of 8 prospective cohort studies and 0 of 20 cross-sectional studies were low risk of bias (Table 2). Common limitations that increased risk of bias included cross-sectional study design, nonstandardized dietary assessments that were either study specific or not validated, lack of adjustment for clinically important covariates (including volume of milk consumed, parent BMI, and child adiposity assessed prior to the outcome), and study duration too short to detect a meaningful change in adiposity (defined a priori as 1 y) (66).

Association between cow-milk fat and child overweight or obesity

Fourteen (38, 42–44, 46, 47, 49, 51, 52, 57, 58, 60, 62, 65) studies met the meta-analysis inclusion criteria; 11 were cross-

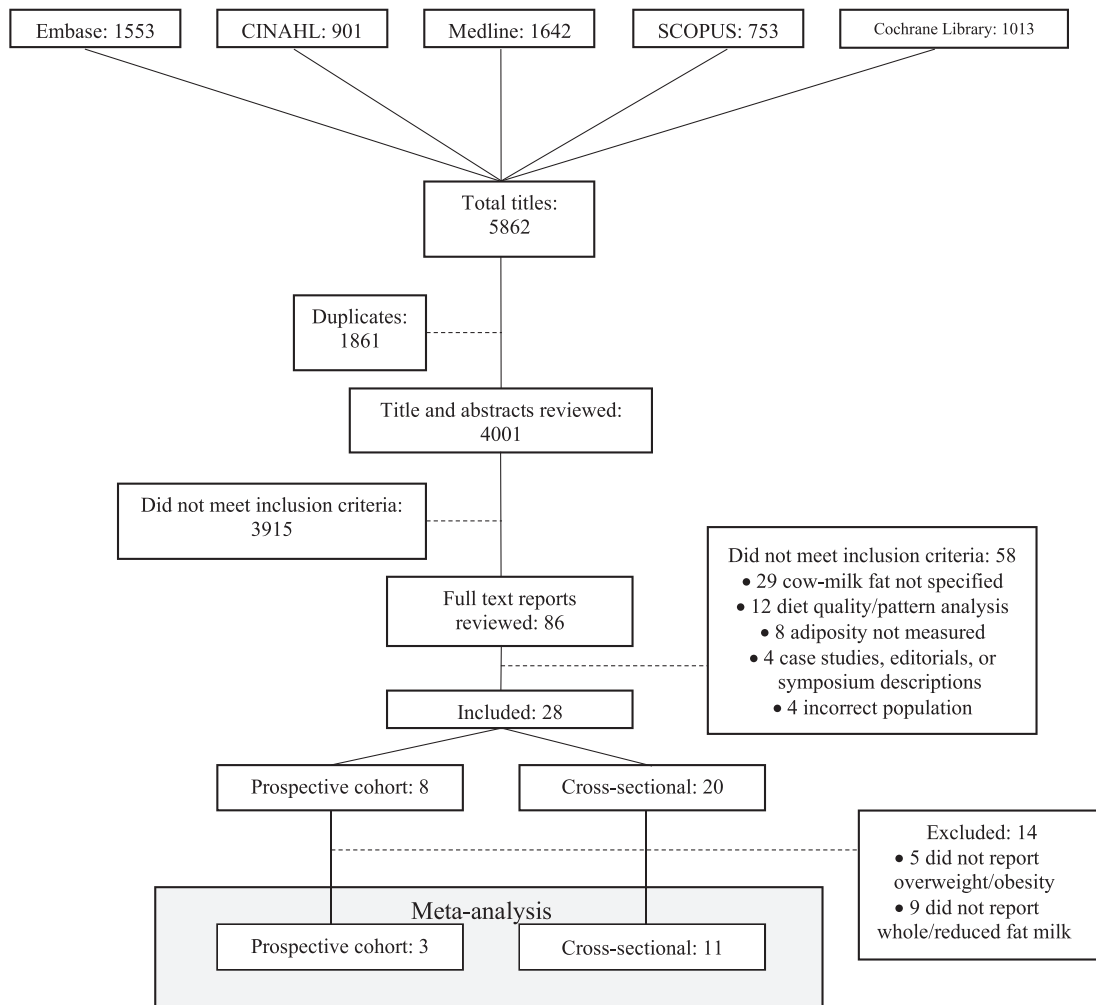


FIGURE 1 Systematic review study selection process.

sectional and 3 were prospective cohort studies. All studies included in the meta-analysis compared whole (3.25% fat) milk with reduced-fat (0.1–2%) milk consumption, allowing an OR to be calculated. A total of 20,897 healthy children aged 1–18 y were included in the meta-analysis. Children were from 7 countries (United States, United Kingdom, Canada, Brazil, Sweden, New Zealand, and Italy). Anthropometric standards used to determine overweight or obesity categories included the WHO (23), CDC (24), or IOTF (25) growth standards in 6, 5, and 3 studies respectively.

Crude analysis of all 14 studies revealed that among children who consumed whole milk compared with reduced-fat milk, the pooled OR for overweight or obesity was 0.61 (95% CI: 0.52, 0.72; $P < 0.0001$) (Figure 2). Heterogeneity measured by the I^2 statistic was 73.8% ($P < 0.0001$). A sensitivity analysis using inverse-variance weights did not reveal different results. Subgroup analysis by study design revealed no significant interaction between cross-sectional and prospective cohort studies ($P = 0.07$; Supplemental Table 2). For the 11 cross-sectional studies ($n = 9413$), the pooled OR of overweight or obesity was 0.56 (95% CI: 0.46, 0.69; $P = 0.0001$), and for the 3 prospective cohort studies ($n = 11,484$) it was 0.76 (95% CI: 0.63, 0.92; $P = 0.006$).

Risk of bias (high compared with low) and age group were also not significant modifiers of the relation between cow-milk fat and child adiposity (Supplemental Table 2 and Supplemental Figures 1–5). Analyses of 5 studies (49, 51, 52, 57, 58) that reported adjusted ORs did not show differences between crude and adjusted estimates (adjusted OR: 0.53; 95% CI: 0.44, 0.63; crude OR: 0.55; 95% CI: 0.46, 0.66); see Supplemental Figure 6. Results of the sensitivity analysis using the Knapp–Hartung method (29) to pool the 14 studies (crude OR: 0.62; 95% CI: 0.52, 0.73) were similar to the main results (crude OR: 0.61; 95% CI: 0.52, 0.72)). Publication bias, visualized using a funnel plot (Supplemental Figure 7), was difficult to ascertain given the high heterogeneity ($I^2 = 73.8\%$) and relatively low number of included studies.

The dose–response meta-analysis results are shown in Figure 3. Data were available from 7 studies (38, 39, 44, 52, 57, 58, 65) which included 14,582 children aged 2 to 11 y, and demonstrated a linear association between higher cow-milk fat and lower child adiposity. For each 1% higher cow-milk fat consumed, the overall crude OR for overweight or obesity was 0.75 (95% CI: 0.65, 0.87; $P = 0.004$; $\tau^2 = 0.01$; $I^2 = 64\%$).

TABLE 1 Data summary¹

Cross-sectional studies						
Author, year	No. of children; age range; location	Exposure; method	Outcome	Variables adjusted for	Adjusted result	P value
Acharya et al., 2011 (41)	770; 3–5 y; USA	Frequency of low- or high-fat milk intake; 24-h recall and FFQ with trained interviewers	zBMI (CDC)	Energy intake	Reduced-fat milk was positively associated with 0.52 (95% CI: 0.29, 0.75) higher zBMI. Children who consumed reduced-fat milk were more likely to be OB (OR = 2.98; 95% CI: 1.46, 6.05)	0.03
Barba et al., 2005* (42)	884; 3–11 y; Italy	Frequency of milk consumption by milk fat content; parent-completed questionnaire	zBMI (IOTF)	Age, birth weight, parental OW/OB, parental education level, physical activity, frequency of consumption of the other groups of foods (dairy foods, fish, cereals, meat, fruit, vegetables, sweet beverages, snacks)	Whole milk was associated with 0.112 lower zBMI (95% CI: -0.19, -0.33). Children who consumed whole milk least often were more likely to be OW than those who consumed it most often (OR = 2.18; 95% CI: 1.30, 3.66)	0.005
Barbiero et al., 2008* (43)	405; 10–18 y; Brazil	OW/OB (WHO)	Dietary habits, food intake by parent-completed questionnaire	None	Reduced-fat milk greater among children with OB Whole milk: normal-weight 91.7%, OW 89.7%, OB 61.1% Skimmed milk: normal-weight 8.3%, OW 10.3%, OB 38.9%	0.08
Beck et al., 2017* (44)	135; 3 y; USA	Milk fat, 24-h recall by trained research assistant	OW/OB (CDC)	Gender, maternal BMI, maternal education, maternal marital status, mother's preferred language, and mother's total years in the USA	Children with severe OB had a lower intake of cow-milk fat and were more likely to consume skim (0.1%) milk (OR = 0.89; 95% CI: 0.81, 0.97)	0.01
Charvet and Huffman, 2019* (39)	197; 3–4 y; USA	Beverage intake, measured using a nutrition and sociodemographic characteristics questionnaire	BMI percentile (CDC), measured by trained Women, Infants, and Children staff	None	A higher proportion of children with OW or OB consumed reduced-fat cow-milk than children with underweight or normal weight	0.014
Dodd et al., 2013* (37)	2314; 6–18 y; USA	Weight status (OW/OB), measured by field interviewers using standardized procedures (CDC)	Beverage consumption, child- and parent-completed 24-h recall interviews	NR	No significant differences in cow-milk fat and weight status. Normal-weight elementary and middle-school children were more likely to consume 2%/whole milk. Among high-school children, OW/OB children were more likely to consume reduced-fat milk (effect sizes NR)	NR
Eriksson and Strandvik, 2010 (45)	114; 8 y; Sweden	Food intake, parent- and child-completed 24-h recall with registered dietitian	BMI (IOTF)	None	Children who never/seldom consumed whole milk had a mean BMI of 17.7, whereas children who consumed 1 serving/d of whole milk had a mean BMI = 16.2, > 1 serving/d mean BMI = 15.4. Overall difference of 2.3 BMI	BMI, <0.001
Gaylis et al., 2017* (46)	598; 13–19 y; USA	Self-reported BMI, categorized into healthy, OW, OB (CDC)	Frequency of whole and low-fat milk consumption, child-completed FFQ	None	No difference in cow-milk fat intake between weight categories (effect size NR)	NR

(Continued)

TABLE 1 (Continued)

Cross-sectional studies						
Author, year	No. of children; age range; location	Exposure; method	Outcome	Variables adjusted for	Adjusted result	P value
Kim and Mallo, 2019 (47)	529; 3–4 y; USA	BMI percentile (CDC), measured by trained Women, Infants, and Children staff	Cow-milk fat consumed, assessed during telephone interview	None	A higher proportion of children with OW or OB consumed reduced-fat cow-milk than children with normal weight	<0.01
LaRowe et al., 2007 (48)	1334; 2–11 y; USA	Beverage intake patterns, interview by caregiver	BMI (CDC)	Age, sex, ethnicity, household income, Healthy Eating Index score, physical activity, birth weight	Among children aged 6–11 y, those who consumed whole milk had lowest BMI and higher healthy eating scores. BMI was significantly higher in the water, sweetened drinks, and soda patterns (adjusted mean BMI = 19.9, 18.7, and 18.7, respectively) compared with the mix/light and whole-milk patterns (adjusted mean BMI = 18.2 and 17.8, respectively) ($P < 0.05$) Proportion of children aged 6–11 y with OW/OB: whole milk 22.1%, soda 35.2%, mix/light drinker 28%, water 42.6%, sweetened drinks 35.4% Proportion of children aged 2–5 y with OW/OB: whole milk 26.9%, mix/light drinker 15.0%, water 25.8%, fruit juice 19.6% In children aged 2–5 y, no significant association between milk fat content and BMI (effect size NR)	BMI, <0.05; >85th percentile (both age groups), <0.0001
Mazahery et al., 2018* (49)	1155; 2–4 y; New Zealand	Frequency and fat content of milk consumption (questionnaire)	BMI, measured by trained testers (IOTF)	NR	Higher odds of consuming reduced-fat milk among OW/OB (OR = 1.74; 95% CI: 1.20, 2.54 for OW; OR = 1.48; 95% CI: 0.73, 3.01 for OB), compared with normal-weight children OW/OB children were less likely to drink whole milk than thin or normal weight children	OW, <0.05; OB, >0.05
Milla Tobarra et al., 2014 (50)	373; 9–11 y; Spain	Beverage intake, child-completed 24-h recall	BMI (IOTF)	Age, cardiovascular fitness	Thin girls consumed a mean 2.9 mL/kg/d more whole milk than OW/OB girls; thin boys 2.8 mL/kg/d more whole milk than OW/OB boys Children who consumed whole milk were less likely (OR = 0.50; 95% CI: 0.31, 0.80) to be OW/OB	Girls, 0.002; boys, 0.043
Nelson et al., 2004* (51)	451; 2–4 y; USA	BMI, measured by a medical provider (CDC)	Nutrition and sociodemographic characteristics	Race/ethnicity, age, sex, birthplace of the parent, fat content of milk consumed by children in family, fruit/vegetable consumption, exercise		<0.01

(Continued)

TABLE 1 (Continued)

Cross-sectional studies							
Author, year	No. of children; age range; location	Exposure; method	Outcome	Variables adjusted for	Adjusted result	P value	
Nilsen et al., 2017* (52)	2104; 7–9 y; Sweden	Food and beverage intake frequency, parent-completed questionnaire	OW/OB (WHO)	Gender, parental weight status, parents' education level and area of living	Odds of being OW/OB were higher among those who consumed reduced-fat milk (OR = 1.90; 95% CI: 1.40, 2.48) compared with those who consumed whole milk. Inverse association between odds of OW/OB and whole milk consumption (OR = 0.60; 95% CI: 0.39, 0.78)	0.001	
O'Connor et al., 2006 (53)	1160; 2–5 y; USA	Beverage consumption, parent-completed 24-h recall interview	BMI percentile	Age, ethnicity, gender, income, energy consumed, physical activity	No significant association between cow-milk fat and weight status (effect size NR)	NR	
Papandreou et al., 2013 (54)	607; 7–15 y; Greece	Beverage intake 24-h recall × 3 d by registered dietitian	BMI, OW/OB (IOTF)	Age, gender, income, energy intake, physical activity	Cow-milk fat was not significantly associated with weight status (effect size NR)	NR	
Ruxton et al., 1996 (55)	136; 7–8 y; Scotland	Milk intake, 7-d food record by parents	zBMI	NR	No significant relation between fat content or volume of milk and anthropometry or growth (effect size NR)	NR	
Schroeder et al., 2014 (56)	1149; 10–18 y; Spain	Beverage consumption, 24-h recall by child	zBMI	Age, energy underreporting, mother's educational level, physical activity, television viewing, energy intake	Comparison between reduced-fat and whole milk on zBMI not significant. For boys, OR = 1.21; 95% CI: 0.95, 1.56; for girls, OR = 10.4; 95% CI: 0.79, 1.37 for higher zBMI	Boys, 0.199; girls, 0.792	
Tovar et al., 2012* (57)	217; 6–11 y; USA	OW and OB prevalence (CDC)	Diet quality, parent completed questionnaire	Age, gender, race/ethnicity, state of residence, number of members in the household, family government assistance	OW (OR = 0.90; 95% CI: 0.40, 1.80) and OB children less likely (OR = 0.40; 95% CI: 0.20, 0.70) to consume whole milk than normal-weight children	OW, 0.80; OB, 0.001	
Vanderhout et al., 2016* (58)	2738; 1–5 y; Canada	Milk fat content consumed, parent-completed FFQ	zBMI (WHO)	Age, sex, vitamin D supplementation, minutes per day of both outdoor free play and screen time, milk and SSB volume consumed daily, maternal BMI, skin pigmentation, family income, maternal ethnicity, date	Participants who consumed whole milk had 0.72 (95% CI: 0.68, 0.76) lower zBMI score than children who consumed reduced-fat milk	<0.0001	
Prospective cohort studies							
Author, year	No. of children; age range; location	Duration	Exposure	Outcome	Variables adjusted for	P value	
Berkey et al., 2005 (59)	12,829; 9–14 y; USA	3 y	Dietary intake, self-administered FFQ	BMI (CDC)	Prior-year BMI z-score, physical activity and inactivity, race or ethnicity, sex, age and maturational stage, height growth	Among boys, 0.027 higher BMI (95% CI: 0.002, 0.053) with every daily serving of 1% milk, and girls 0.021 higher BMI per daily serving of reduced-fat milk (95% CI: 0.001, 0.04). BMI gains among children who consumed whole milk were nonsignificant. Dairy fat (cheese, butter, etc.) was nonsignificantly associated with BMI (effect NR)	<0.05, dairy fat NR

(Continued)

TABLE 1 (Continued)

Prospective cohort studies							
Author, year	No. of children; age range; location	Duration	Exposure	Outcome	Variables adjusted for	Adjusted result	P value
Bigornia et al., 2014* (60)	2282; 10–13 y; UK	3 y	Dairy fat, parent-assisted 3-d food records	Body fat %, BMI (IOTF)	Sex, volume of dairy intake, age, height, maternal education, maternal OW status, physical activity, pubertal stage, dieting at follow-up, baseline intakes of cereal, total fat, total protein, fiber, 100% fruit juice, fruit and vegetables, SSBs, dietary reporting errors at follow-up	Children who consumed the most whole-fat dairy compared with the least whole-fat dairy at age 10 and 13 had the lowest risk of excess fat mass (OR = 0.64; 95% CI: 0.41, 1.00), and a lower risk of OW (OR = 0.65; 95% CI: 0.40, 1.06) at age 13	Fat mass, 0.03; OW, 0.24; BMI gains, <0.01; Reduced fat NR
DeBoer et al., 2015 (36)	8950; 4–5 y; USA	1 y	Volume and fat content of milk, parent online interview	zBMI (CDC)	Sex, race/ethnicity, SES	High vs. low whole-fat dairy consumption also had the smallest gains in BMI: 2.5 kg/m ² (95% CI: 2.2, 2.7) vs. 2.8 kg/m ² (95% CI: 2.5, 3.0). Reduced-fat dairy associations with adiposity were nonsignificant	<0.001
DuBois et al., 2016 (61)	304; 9–14 y; Canada	5 y	Dietary intake, 2 × 24-h recalls by parent and child with registered dietitian	BMI (IOTF)	Each twin served to balance characteristics of other twin	Every 1% increase in milk fat was associated with 0.176 (95% CI: -0.197, -0.155) lower zBMI among 4-y-olds and 0.139 lower zBMI (95% CI: -0.173, -0.105) among 5-y-olds	<0.05
						Heavier boy twins consumed more whole milk and alternatives than their leaner twin; heavier girl twins consumed less whole milk than their leaner twin. Reduced-fat milk consumption among girls was associated with a 0.32 higher BMI from age 9 to 14 y; whole milk did not have a significant relation with BMI	

(Continued)

TABLE 1 (Continued)

Prospective cohort studies							
Author, year	No. of children; age range; location	Duration	Exposure	Outcome	Variables adjusted for	Adjusted result	P value
Huh et al., 2010* (62)	852; 2–3 y; USA	1 y	Volume and fat content of milk consumed, parent-completed FFQ	zBMI (CDC)	Age, sex, race/ethnicity, energy intake, nondairy beverage intake, TV viewing, maternal BMI and education; paternal BMI, 2-y zBMI	Higher intake of whole milk at age 2 y associated with -0.09 unit per daily serving, (95% CI: -0.16 , -0.01) lower zBMI at age 3 y Cow-milk fat intake not related to OW, ORs for OW at age 3 were 1.04 (95% CI: 0.74, 1.44) for whole milk, 0.91 (95% CI: 0.20, 1.34) for 2% milk, and 0.95 (95% CI: 0.58, 1.55) for 1%/skim milk	zBMI, 0.02 OR for OW: whole milk, 0.84; 1%/skim, 0.83
Noel et al., 2011 (63)	2245; 10–13 y; UK	3 y	Milk fat, parent- and child- completed 3-d food records	Body fat %	Age, sex, height, physical activity, pubertal status, maternal BMI, maternal education, dietary intakes of total fat, ready-to-eat breakfast cereal, 100% fruit juice, and SSB intake, calcium, total energy intake, metabolic rate	At age 13, per daily serving of whole milk, a 1.32% lower body fat (95% CI: -2.36 , -0.27) was seen. Longitudinal relations were nonsignificant	0.01
Scharf et al., 2013 (38)	8350; 2–4 y; USA	2 y	Milk fat, parent-completed online questionnaire	zBMI (CDC)	Sex, race, SES, juice and SSB intake, number of glasses of milk daily, maternal BMI	Children who consumed reduced-fat (skim/1%) milk had higher odds of OW (age 2 OR = 1.64; 95% CI: 1.32, 2.03; age 4 OR = 1.63; 95% CI: 1.23, 1.86) or OB (age 2 OR = 1.57; 95% CI: 1.03, 2.42; age 4 OR = 1.64; 95% CI: 1.04, 2.60) than those consuming whole/2% milk. Children who were normal weight at age 2 who consumed skim/1% milk more likely to become OW/OB at age 4 (OR = 1.57; 95% CI: 1.03, 2.42)	OW age 2, 4, OB age 4: <0.0001; OW age 4: 0.002; becoming OW/OB age 4: 0.04
Wojcie et al., 2001 (40)	51; 1–2 y; USA	1 y	Milk fat consumption at 12, 18, and 24 mo, 3-d food record, parent completed	Weight, body fat change	NR	No difference in weight or body fat at 12, 18, or 24 mo, or changes in anthropometry between children consuming reduced-fat or whole milk (effect sizes NR)	NR

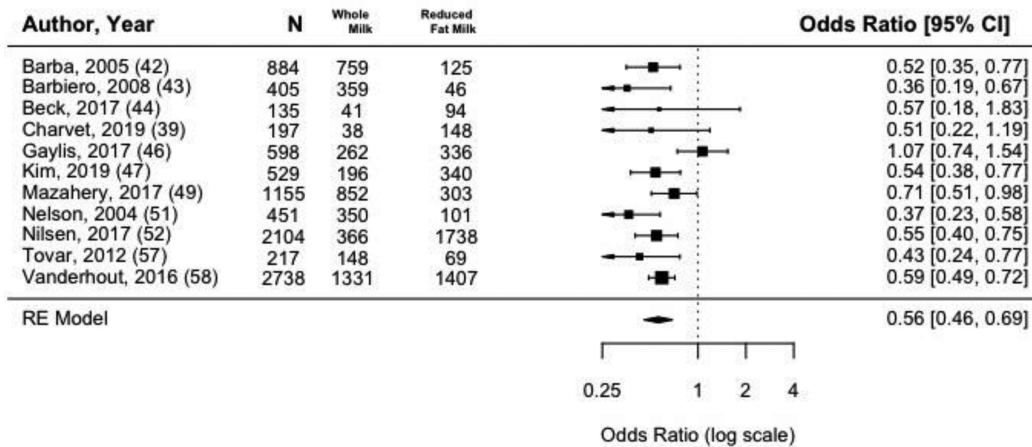
*Adiposity outcomes, where reported, were standardized according to WHO, CDC, or IOTF (International Obesity Task Force). *Studies included in the meta-analysis. NR, not reported, OB, obesity, defined as >95th percentile for BMI and >2 for zBMI (64); OW, overweight, defined by >85th percentile for BMI or >1 for zBMI; SES, socioeconomic status; SSB, sugar-sweetened beverage; zBMI, BMI z-score.

TABLE 2 Risk of bias according to the Newcastle–Ottawa Scale (28) for nonrandomized studies¹

	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Outcome of interest not present at start	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Duration sufficient for outcomes to occur (>1 y)	Adequacy of follow-up of cohorts	Total	Overall risk of bias
Cross-sectional studies (<i>n</i> = 20)										
Acharya et al., 2011 (41)	X	X	X	—	—	X	—	—	4	High
Barba et al., 2005 (42)	X	X	—	—	X	X	—	—	4	High
Barbiero et al., 2008 (43)	X	—	—	—	—	—	—	—	1	High
Beck et al., 2017 (44)	X	X	X	—	X	X	—	—	5	High
Charvet and Huffman, 2019 (39)	X	X	X	—	—	X	—	—	4	High
Dodd et al., 2010 (37)	X	X	X	—	—	X	—	—	4	High
Eriksson et al., 2010 (45)	X	X	X	—	—	—	—	—	2	High
Gaylis et al., 2017 (46)	X	X	—	—	—	—	—	—	2	High
Kim and Mallo, 2019 (47)	X	X	X	—	—	—	—	—	3	High
LaRowe et al., 2007 (48)	X	X	X	—	X	X	—	—	5	High
Mazahery et al., 2018 (49)	X	X	X	—	—	—	—	—	3	High
Milla Tobarra et al., 2014 (50)	—	X	—	—	—	X	—	—	2	High
Nelson et al., 2004 (51)	X	X	X	—	X	X	—	—	5	High
Nilsen et al., 2017 (52)	X	X	—	—	X	X	—	—	4	High
O'Connor et al., 2006 (53)	X	X	X	—	X	—	—	—	4	High
Papandreou et al., 2013 (54)	X	X	X	—	X	X	—	—	5	High
Ruxton et al., 1996 (55)	X	X	—	—	—	X	—	—	3	High
Schroeder et al., 2014 (56)	X	X	—	—	X	X	—	—	4	High
Tovar et al., 2012 (57)	X	X	—	—	X	X	—	—	4	High
Vanderhout et al., 2016 (58)	X	X	—	—	X	X	—	—	4	High
Total low risk (out of 20)									0	
Prospective cohort studies (<i>n</i> = 8)										
Berkey et al., 2005 (59)	—	X	—	X	XX	—	X	X	6	High
Bigornia et al., 2014 (60)	X	X	—	X	X	X	X	—	6	High
DeBoer et al., 2015 (36)	X	X	—	X	—	—	—	X	5	High
Dubois et al., 2016 (61)	X	X	X	X	—	—	X	—	5	High
Huh et al., 2010 (62)	X	X	—	X	XX	X	—	X	7	Low
Noel et al., 2011 (63)	X	X	—	X	X	X	X	—	6	High
Scharf et al., 2013 (38)	X	X	—	X	X	X	X	—	6	High
Wojcie et al., 2001 (40)	X	X	—	X	—	X	—	X	5	High
Total low risk (out of 8)									1	

¹Each study can be awarded a maximum of 1 X for each numbered item within the Selection and Exposure categories. A maximum of 2 Xs can be given for Comparability. Two Xs were awarded if studies accounted for volume of milk consumed, prior weight status (birth weight for cross-sectional studies), and parent BMI. One X was awarded for adjusting for ≥ 4 other covariates. By design, cross-sectional studies were considered unable to achieve comparable cohorts; a maximum of 1 X could only be awarded. The original NOS uses stars, which were replaced with Xs for ease of visual interpretation. We specified follow-up time to be adequate if study duration was > 1 y. If participants who were missing/lost to follow-up were not reported, no X was allocated. As per NOS guidelines, studies were considered low risk of bias if they received ≥ 7 Xs (28). NOS, Newcastle–Ottawa Scale.

A Cross-sectional studies only.



B Prospective cohort studies only.

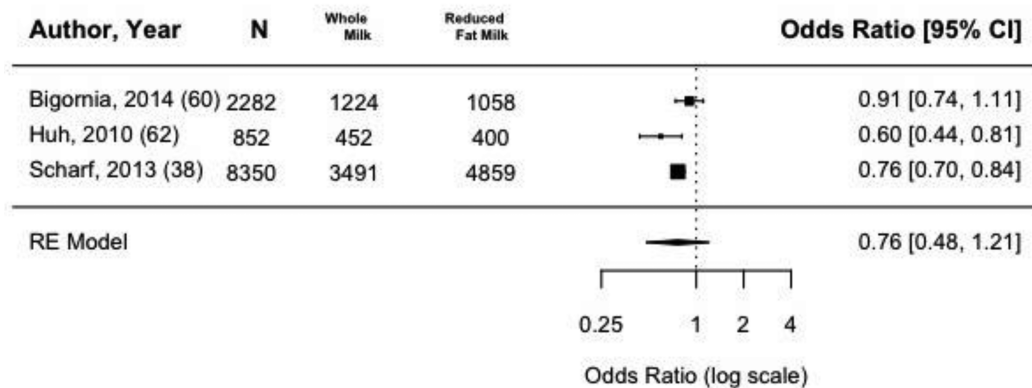


FIGURE 2 Crude OR of overweight/obesity comparing children consuming whole milk with children consuming reduced-fat milk. (A) Cross-sectional studies only; (B) prospective cohort studies only. Pooled effects were determined using random effects models; $I^2 = 73.8\%$. P values for pooled ORs: cross-sectional studies $P < 0.0001$; prospective cohort studies $P = 0.006$.

Discussion

This systematic review and meta-analysis has identified that relative to reduced-fat cow-milk, whole-fat cow-milk consumption was associated with lower odds of childhood overweight or obesity. The direction of the association was consistent across a range of study designs, settings, and age groups and demonstrated a dose effect. Although no clinical trials were identified, existing observational research suggests that consumption of whole milk compared with reduced-fat milk does not adversely affect body weight or body composition among children and adolescents. To the contrary, higher milk fat consumption appears to be associated with lower odds of childhood overweight or obesity.

Findings from the present study suggest that cow-milk fat, which has not been examined in previous meta-analyses, could play a role in the development of childhood overweight or obesity. Several mechanisms have been proposed that might explain why higher cow-milk fat consumption could result in lower childhood adiposity. One theory involves the replacement of calories from less healthy foods, such as sugar-sweetened beverages, with cow-milk fat (67). Consumption of beverages high in added sugar

has been associated with increased risk of overweight and obesity during childhood (68). Other theories involve satiety mechanisms such that higher milk fat consumption might induce satiety through the release of cholecystokinin and glucagon-like peptide 1 (69, 70) thereby reducing desire for other calorically dense foods. Another possibility is that lower satiety from reduced-fat milk could result in increased milk consumption causing higher weight gain relative to children who consume whole milk, as observed in the study by Berkey et al. (59).

Cow-milk fat might offer cardiometabolic benefits. The types of fat found in cow-milk, including *trans*-palmitoleic acid, could be metabolically protective. Higher circulating *trans*-palmitoleic acid has been associated with lower adiposity, serum LDL cholesterol and triglyceride concentrations, and insulin resistance, and higher HDL cholesterol in several large adult cohort studies (71–73). However, diets that replace dairy fat with unsaturated fatty acids might also offer cardiometabolic protection (74, 75)

Confounding by indication and reverse causality (76) are plausible alternate explanations. Parents of children who have lower adiposity might choose higher-fat milk to increase weight

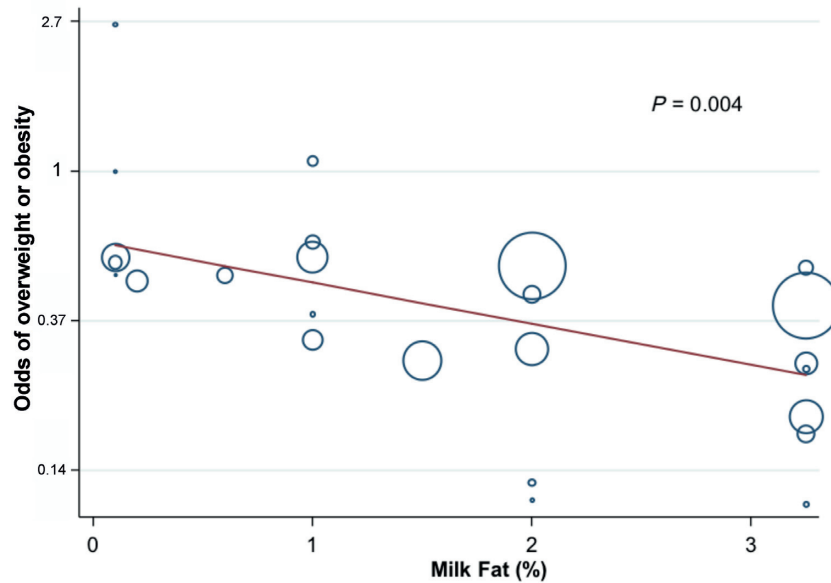


FIGURE 3 Dose–response relation between cow-milk fat and odds of overweight or obesity. Seven studies provided data on 14,582 participants and were included in this analysis. Each circle represents a group of participants in each study consuming different concentrations of cow-milk fat. The size of the circles represents the inverse of the variance of the group-specific log odds. *P* value is derived from a dose–response meta-regression with an OR of 0.75 (95% CI: 0.65, 0.87; $\tau^2 = 0.010$; $I^2 = 64\%$).

gain. Similarly, parents of children who have higher adiposity might choose lower-fat milk to reduce the risk of overweight or obesity (44, 48). The majority of children included in this systematic review were involved in prospective cohort studies, in which the potential for reverse causality is lower than in cross-sectional studies. Results from these 11,484 children were consistent with the overall findings. Two of the included prospective cohort studies (59, 62) attempted to address confounding by indication by adjusting for baseline BMI; 1 of these repeated the statistical analysis only among participants with normal-weight BMI values, with similar findings (62). Clinical trial data would have provided better evidence for the directionality of this relation; however, none were available.

This study had a number of strengths. The meta-analysis included a large, diverse sample of children from around the world. The number of potentially eligible studies was maximized by the comprehensive search strategy and contact with authors to obtain missing data. Also, study selection, data collection, and risk of bias assessment were performed by 2 independent reviewers, which improved accuracy and consistency. All studies included in the meta-analysis used trained individuals to obtain anthropometric measurements, and weight status was standardized using growth reference standards (WHO, CDC, and IOTF). Using meta-regression techniques, differences in study design, risk of bias, and age group were taken into account. Finally, a dose–response meta-analysis was conducted, which demonstrated a linear relation between higher cow-milk fat and lower child adiposity (Figure 3).

This study had a number of limitations. First, included studies were all observational. Only 1 study in this analysis was considered to have low risk of bias, and all studies in the meta-analysis had high risk of bias. Risk of bias included cross-sectional designs and lack of adjustment for clinically important

covariates. For example, cow-milk volume was accounted for in only 11 of 28 studies in the systematic review, and in 5 of 14 studies in the meta-analysis. Adjustment for volume in future studies would allow for a clearer understanding of whether higher cow-milk fat protects against higher adiposity, or reduced-fat cow-milk increases adiposity. However, among these studies, comparison of adjusted compared with crude odds demonstrated consistent findings. Residual confounding by variables not accounted for in the individual analyses is also possible; this is a common limitation for meta-analyses of observational studies. Heterogeneity was relatively high ($I^2 = 73.8\%$), which might have been attributable to a variety of factors including varied methods of ascertainment of exposure and outcome, and differences in study design and follow-up duration. Although subgroup analyses of prospective cohort studies revealed results comparable to the overall meta-regression, these comparisons might not have had sufficient power to detect clinically meaningful differences. However, 11,484 children were involved in prospective cohort studies making large differences in effect size unlikely. Although only studies with standardized dietary measurements were included, measurement error was possible due to recall bias or lack of validation of dietary assessment tool. Error in adiposity measurement could also have introduced bias, although weights and heights were measured by trained individuals and standardized protocols were used in all studies included in the meta-analysis. Differences in adiposity measurement (i.e., body fat percentage, zBMI, BMI), and different growth standards could have contributed to heterogeneity. For example, use of the WHO rather than IOTF or CDC standards could have resulted in a greater proportion of overweight or obese children being reported (77). Future studies using WHO growth standards, which are believed to represent optimal child growth (23), would help to minimize

heterogeneity and overcome these limitations. Consideration for relevant outcomes such as cardiovascular risk should be included in future analyses to understand other effects of cow-milk fat. Publication bias was also possible as demonstrated by a funnel plot and Egger test.

In conclusion, observational evidence supports that children who consume whole milk compared with reduced-fat milk have lower odds of overweight or obesity. Given that the majority of children in North America consume cow-milk on a daily basis, clinical trial data and well-designed prospective cohort studies involving large, diverse samples, using standardized exposure and outcome measurements, and with long study duration would help determine whether the observed association between higher milk fat consumption and lower childhood adiposity is causal.

The authors' responsibilities were as follows—SMV, JLM: conceptualized and designed the research study, performed initial statistical analyses, drafted the manuscript, approved the final manuscript as submitted, had full access to all the data in the study, and took responsibility for the integrity of the data and the accuracy of the data analysis; NT: developed and implemented the systematic review search strategy, generating the initial search results; MA, SMV: independently reviewed study titles, abstracts, and full texts to determine included studies, performed data extraction, and evaluated each study for risk of bias; CB, DO: assisted in refining the study design, reviewed and revised the manuscript, and approved the final manuscript as submitted; KT, BD, PJ: reviewed and revised statistical analysis as well as the manuscript, and approved the final manuscript as submitted; and all authors: read and approved the final manuscript. Author Disclosures: JLM received an unrestricted research grant for a completed investigator-initiated study from the Dairy Farmers of Canada (2011–2012), and Ddrops provided nonfinancial support (vitamin D supplements) for an investigator-initiated study on vitamin D and respiratory tract infections (2011–2015). All other authors report no conflicts of interest.

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