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ARTICLE

Cow's milk fat and child adiposity: a prospective cohort study

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BACKGROUND: International guidelines recommend children aged 9 months to 2 years consume whole (3.25%) fat cow's milk, and children older than age 2 years consume reduced (0.1–2%) fat cow's milk to prevent obesity. The objective of this study was to evaluate the longitudinal relationship between cow's milk fat (0.1–3.25%) intake and body mass index z-score (zBMI) in childhood. We hypothesized that higher cow's milk fat intake was associated with lower zBMI.
METHODS: A prospective cohort study of children aged 9 months to 8 years was conducted through the TARGet Kids! primary care research network. The exposure was cow's milk fat consumption (skim (0.1%), 1%, 2%, whole (3.25%)), measured by parental report. The outcome was zBMI. Height and weight were measured by trained research assistants and zBMI was determined according to WHO growth standards. A linear mixed effects model and logistic generalized estimating equations were used to determine the longitudinal association between cow's milk fat intake and child zBMI.
RESULTS: Among children aged 9 months to 8 years ($N = 7467$; 4699 of whom had repeated measures), each 1% increase in cow's milk fat consumed was associated with a 0.05 lower zBMI score (95% CI −0.07 to −0.03, $p < 0.0001$) after adjustment for covariates including volume of milk consumed. Compared to children who consumed reduced fat (0.1–2%) milk, there was evidence that children who consumed whole milk had 16% lower odds of overweight (OR = 0.84, 95% CI 0.77 to 0.91, $p < 0.0001$) and 18% lower odds of obesity (OR = 0.82, 95% CI 0.68 to 1.00, $p = 0.047$).
CONCLUSIONS: Guidelines for reduced fat instead of whole cow's milk during childhood may not be effective in preventing overweight or obesity.

INTRODUCTION

One in three children in North America are living with overweight or obesity [1]. Childhood obesity also tracks into adulthood [2], increasing the risk of cardiovascular disease over the life course [3]. Current nutritional guidelines recommended limiting dietary fat in childhood, but evidence to support these guidelines is lacking [4]. The American Academy of Pediatrics and American Heart Association [5, 6], the Canadian Pediatric Society [7], and National Health Service (UK) [8] have recommended since the 1990's that children consume whole (3.25% milk fat) cow's milk until 2 years of age and then switch to reduced (0.1–2% milk fat) cow's milk to lower the risk of overweight or obesity.

Cow's milk is widely consumed in childhood [9, 10] and contains nutrients which support growth and development, such as protein, fat, calcium, phosphorous, and vitamin D. Cow's milk has nutritional properties distinct from other dairy products such as yogurt, which often contains added sugar, or cheese, which contains a different quantity of fat and type of protein than fluid milk, and may have a unique relationship with adiposity [11, 12]. Two recent systematic reviews revealed that whole milk was associated with lower risk of child overweight or obesity among children aged 9 months to 18 years [13, 14]. These findings were largely based on low quality cross-sectional studies which did not adjust for potential confounding factors such as volume of milk consumed or previous child weight. Several systematic reviews have highlighted the need for additional high quality prospective cohort studies on this topic [15, 16]. This study is a longitudinal cohort study, including participants with and without multiple observations, in order to achieve the largest possible sample size and statistical power from this cohort. In contrast, our previous publication in this cohort was a cross-sectional analysis [17]. The current study was designed to overcome weaknesses of previous analyses and minimize risk of bias through a large prospective cohort study with adjustment for important potentially confounding factors.

The objective of this study was to evaluate the relationship between cow's milk fat consumption and child adiposity, measured by body mass index z-score (zBMI) among healthy children aged 9 months to 8 years. We hypothesized that children who consumed higher intakes of cow's milk fat would have lower zBMI and be less likely to be classified as overweight or obese compared to children who had lower intakes of cow's milk fat.

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METHODS

Participants and setting

A prospective cohort study was conducted through the TARGet Kids! (The Applied Research Group for Kids) primary care research network in Toronto, Ontario, Canada. Children who were participating in regularly scheduled well-child visits, which occur at ages 2, 4, 6, 9, 12, 18, and 24 months, and annually thereafter, at 12 pediatric and family practices were recruited by trained research assistants in the clinic waiting room between August 2008 and April 2019 [18]. In TARGet Kids!, recruitment occurs between ages 0 and 5 years, and children are followed through subsequent well-child visits. Healthy children aged 9 months to 8 years who reported consuming cow's milk were included in this analysis, in the interest of generating evidence about cow's milk fat for children of all ages. Exclusion criteria were children with severe developmental delay, birth weight <2500 grams, chronic illness impacting metabolism (e.g., cystic fibrosis). All exposures, outcomes and covariates were measured at each well-child visit following enrollment in TARGet Kids!. All parents of children participating in this study provided informed written consent, and ethics approval was obtained from the Hospital for Sick Children (#10000-12436) and Unity Health Toronto (#17-335).

Exposure

The exposure was cow's milk fat consumption. This was measured through a parent-completed dietary questionnaire, administered at a well-child visit, based on the Canadian Community Health Survey which has been in use since 2008 [19]. Parents were asked, "Please specify your child's diet for the past 3 days: skim (0.1%), 1%, 2%, homo (3.25%) milk. Circle how many cups your child has currently in a typical day: 0, ½, 1, 2, 3, 4, 5+." If parents indicated more than one milk fat, the mean cow's milk fat intake was calculated. We also measured cow's milk fat dichotomously as whole (3.25%) vs. reduced (0.1–2%) fat cow's milk consumption.

Outcome

The outcome was body mass index z-score (zBMI), which is an age and sex adjusted measure of body weight. Trained research assistants measured child weight in kilograms and height in meters using a Healthometer digital baby scale and standardized recumbent length board (SECA, FL), respectively, for children younger than 2 years of age. Weight and height were measured using a Healthometer stadiometer (SECA, FL) for older children, according to standardized procedures [20]. Body mass index was calculated by dividing weight (kg) by height squared (m^2) and z-scores were determined according to the World Health Organization (WHO) [21] growth standards. Categories for normal weight, overweight, and obesity were defined as: $-2 \leq zBMI \leq 1$ normal weight, $1 < zBMI \leq 2$ overweight, $zBMI > 2$ obesity, consistent with WHO recommended weight status categorization [21]. For the purpose of this manuscript and consistency across ages, we applied WHO weight classifications for children over age 5 years to all children in our sample [22, 23]. There is evidence that children younger than 5 years of age in the TARGet Kids! cohort exhibit functional outcomes of overweight, obesity, and severe obesity [24].

Covariates

Clinically relevant covariates which have been proposed in the literature to have a relationship with cow's milk fat or childhood adiposity were specified a priori through a detailed literature review. These included volume of cow's milk, volume of sugary drinks (including 100% juice, fruit drinks, and soft drinks) consumed in 250 ml cups per day, maternal ethnicity, self-reported family income, birth weight in kilograms, breast-feeding duration in months, and parent BMI. Dietary information, maternal ethnicity, family income, breastfeeding duration, and birth weight were collected using the same questionnaire as used to measure cow's milk fat consumption. Volume of cow's milk and sugary drinks was measured with the question, "Circle how many cups of each drink your child has currently in a typical day: 0, ½, 1, 2, 3, 4, 5+." Daily physical activity was considered as a covariate [17] but our previous research [17] demonstrated that it may not be a confounder in this relationship. Trained research assistants measured parental height and weight using a Healthometer stadiometer (SECA, FL) and BMI was calculated as weight (kg) divided by height squared (m^2).

Statistical analysis

Descriptive statistics were used to characterize participants. To determine the longitudinal association between cow's milk fat consumption and child zBMI as continuous variables, a linear mixed effects model was used. Linear mixed effects models have the advantage that all repeated measures provided by each participant can be used and within-subject correlation can be accounted for using subject specific random intercepts. Unadjusted and adjusted (see "Covariates" above) models were created with cow's milk fat as the exposure and zBMI as the outcome. Restricted cubic splines for age with five knots were used to evaluate non-linear trajectories of the observed relationships in keeping with previous research in the same cohort [25]. Multinomial logistic generalized estimating equations (GEE) were used to examine the relationship between cow's milk fat and odds of overweight excluding obesity ($1 < zBMI \leq 2$) and obesity ($zBMI > 2$) relative to normal weight ($-2 \leq zBMI \leq 1$), also adjusting for all covariates.

All covariates had <15% missing data. Missing data were handled using multiple imputation using 18 imputed datasets using all covariates [26]. Sensitivity analyses were conducted among children with and without missing data to assess for consistency of results. For all statistical tests, an alpha level of 0.05 was used and 95% confidence intervals were calculated. As the secondary objectives were hypothesis-generating, no adjustments for multiple comparisons were performed. The sample size for this analysis was dictated by the number of children enrolled in the ongoing registry. Multicollinearity was measured using the variance inflation factor, which remained under 1.5 for all covariates [27]. All analyses were conducted using the geepack [28], multgee [29], nlme [30], and lme4 [31] packages in R version 3.5.1 [32]. Statistical code used to produce the analysis is available upon request.

RESULTS

A total of 7467 children aged 9 months to 8 years were included in the analysis (Fig. 1). Baseline characteristics of participating children are described in Table 1. Sixty-three percent (4699/7467) of children had repeated measures. At baseline, the mean child age was 2.6 (SD 1.5) years, and 53% of participants were male. The mean zBMI at baseline was 0.18 (SD 1.1); 77% of children had normal weight, 16% had overweight excluding obesity, 5% had obesity, and 2% had underweight. The majority (56%) of children consumed whole cow's milk at baseline, followed by 2% milk (34% of children), 1% milk (8% of children), and skim milk (3% of children). On average, children consumed 1.9 (SD 1.2) 250-ml cups of cow's milk per day at baseline. The mean follow-up duration was 2.7 years (SD 1.7).
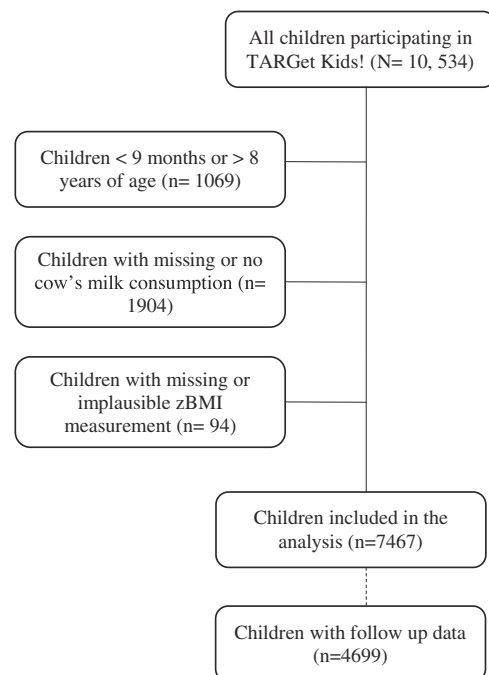

Fig. 1 Participant flow diagram. Children who were participating in regularly scheduled well-child visits, which occur at ages 2, 4, 6, 9, 12, 18, and 24 months, and annually thereafter.

Table 1. Participant characteristics ($n = 7467$) at baseline.

Child characteristics	
Age, years, mean (SD)	2.6 (1.5)
Gender, male, n (%)	3930 (53)
zBMI, mean (SD)	0.18 (1.1)
Thinness (zBMI < −2), n (%)	170 (2)
Normal weight (−2 ≤ zBMI ≤ 1), n (%)	5764 (77)
Overweight (excluding obesity; 1 < zBMI ≤ 2), n (%)	1173 (16)
Obesity (zBMI > 2), n (%)	355 (5)
Cow's milk consumed in the past 3 days[a]	
Skim (0.1%), n (%)	226 (3)
1%, n (%)	562 (8)
2%, n (%)	2501 (33)
Whole (3.25%), n (%)	4178 (56)
Typical cow's milk volume consumed, cups/day, mean (SD)	1.9 (1.2)
Parent BMI, mean (SD)	25.3 (4.9)
Maternal ethnicity, n (%)[a]	
European	4425 (59)
East Asian	458 (6)
South Asian	587 (8)
Southeast Asian	239 (3)
Arab or African	486 (7)
Latin American	208 (3)
Mixed ethnicity	383 (5)
Other	22 (0.3)
Self-reported household income ($), n (%)[b]	
<30,000	719 (10)
30,000–79,999	1222 (16)
80,000–150,000	3584 (48)
>150,000	251 (3)
Sugary drink intake, cups/day, mean (SD)	0.7 (1.1)
Serum 25-hydroxyvitamin D, nmol/l, mean (SD)	87.9 (29.4)
Birth weight, kg, mean (SD)	3.3 (0.6)
Breastfeeding duration, months, mean (SD)	10.7 (7.5)
Follow-up duration, years, mean (SD)[c]	2.7 (1.7)

[a]$n = 659$ children with missing maternal ethnicity.
[b]$n = 1691$ children with missing household income.
[c]Not a baseline characteristic.

The linear mixed model revealed that with every 1% increase in cow's milk fat consumed (for example, 2% vs. 1%, 1% vs. skim, etc.), children had 0.05 lower zBMI (95% CI −0.07 to −0.03, $p < 0.0001$), after adjustment for covariates including volume of milk consumed. Unadjusted and adjusted model results were unchanged (Table 2). For example, a 4-year-old child who consumed whole milk had on average 0.1 kg lower body weight than a 4-year-old child with the same height consuming reduced fat milk. Figure 2 shows the adjusted longitudinal relationship between cow's milk fat, dichotomized into reduced (0.1–2%) fat and whole (3.25%) fat milk, and child zBMI.

Odds ratios for overweight and obesity among children who consumed whole vs. skim (0.1%), 1 and 2% cow's milk were estimated (Table 3). When analyzed in a multinomial logistic GEE model, trends suggest that children who consumed whole cow's milk had 16% lower odds of overweight (OR = 0.84, 95% CI 0.77–0.91, $p < 0.0001$) and 18% lower odds of obesity (OR = 0.82,

Table 2. The relationship between cow's milk fat intake and child zBMI.

	Unadjusted		Adjusted[a]	
	Coefficient (95% CI)	p value	Coefficient (95% CI)	p value
Cow's milk fat (%)	−0.05 (−0.07 to −0.03)	<0.0001	−0.05 (−0.07 to −0.03)	<0.0001

$N = 7467$.
[a]A linear mixed model was used and adjusted for volume of cow's milk, volume of sugary drink intake (including 100% juice, fruit drinks, and soft drinks) consumed in 250 ml cups per day, maternal ethnicity, self-reported family income, birth weight in kilograms, breastfeeding duration in months, and parent BMI. Covariate coefficient estimates not shown.

95% CI 0.68–1.00, $p = 0.047$) compared to children who consumed reduced (0.1–2%) fat cow's milk, after adjustment.

To apply our analysis directly to current recommendations for children over age 2 years to consume reduced fat milk, we conducted a sensitivity analysis among children aged 2–8 years only. Among 6219 children aged 2–8 years of age, each 1% increase in cow's milk fat consumed was associated with a 0.07 lower zBMI score (95% CI −0.09 to −0.05, $p < 0.0001$). Compared to children who consumed reduced fat (0.1–2%) cow's milk, there was evidence that children who consumed whole cow's milk had 10% lower odds of overweight (OR = 0.90, 95% CI 0.80–1.00, $p = 0.05$).

DISCUSSION

In this prospective cohort study of 7467 healthy children aged 9 months to 8 years, higher cow's milk fat consumption was associated with lower child zBMI after controlling for potential confounding factors including volume of milk consumed, parent BMI, and birth weight. On average, children who consumed whole milk had a 0.1 lower zBMI than children who consumed reduced fat milk, which is similar in magnitude to other dietary interventions for preventing obesity among children [33]. These findings were further supported by the evidence that children who consumed whole milk had 16% lower odds of overweight and 18% lower odds of obesity relative to children who consumed reduced fat (0.1–2%) milk.

Professional recommendations from the American Academy of Pediatrics [6], Academy of Nutrition and Dietetics [34], American Heart Association [5, 35], Health Canada [36] and the Canadian Pediatric Society [36], the National Health Service (UK) [8] and the Australian National Health and Medical Research Council [37] recommend that children consume whole cow's milk until age 2 years, and then transition to reduced (0.1–2%) fat cow's milk to reduce the risk of excess adiposity. These guidelines are based on consensus opinion [38] and evidence from the 1990s supporting that reduced fat cow's milk is safe for children to consume [39, 40]. Our findings support the guideline for children aged 9 months to 2 years, but suggest that guidelines for older children may not be effective in preventing child overweight or obesity.

Findings from the present study are consistent with several other studies. A recent systematic review [14] and meta-analysis [13] identified observational studies which examined the relationship between cow's milk fat and child adiposity among children aged 9 months to 18 years. An association between higher cow's milk fat and lower adiposity was found in the majority of studies, and no study identified that reduced fat milk lowered the risk of child overweight or obesity. However, the majority of the studies were considered to have high risk of bias due to cross-sectional design or lack of adjustment for potential confounding factors such as volume of milk, prior measures of adiposity, and parent
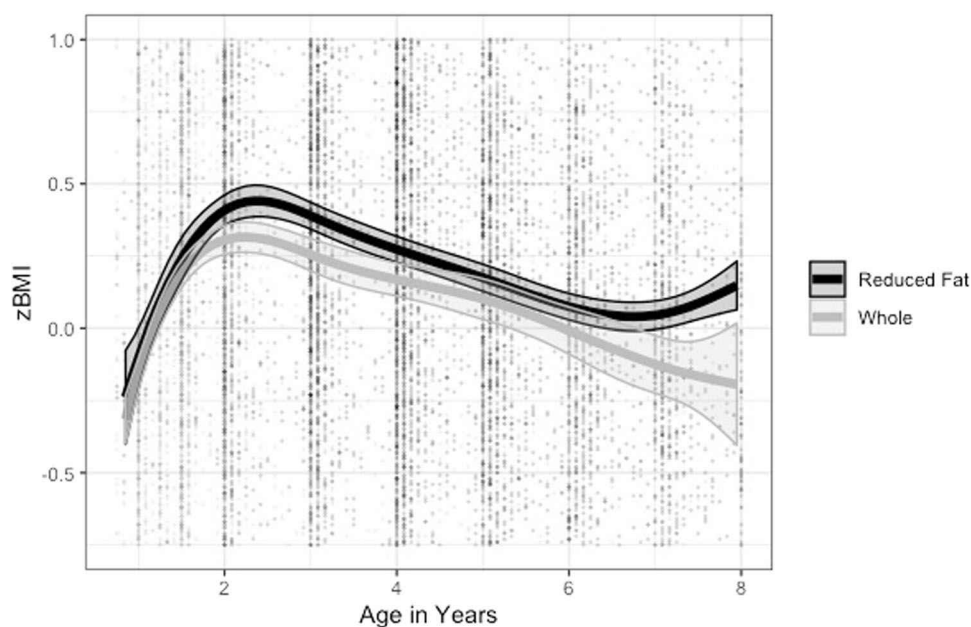
Fig. 2 The relationship between cow's milk fat and zBMI in children aged 9 months to 8 years, adjusted for clinically relevant covariates. Individual data points are represented by small circles in the background. Shades of circles correspond to cow's milk fat consumed by children according to the figure legend.

Table 3. The relationship between cow's milk fat intake and odds of overweight (excluding obesity) and obesity relative to normal weight ($-2 <$ zBMI ≤ 1), adjusted for clinically relevant covariates[a].

	Overweight (1 < zBMI ≤ 2)		Obesity (zBMI > 2)	
	aOR (95% CI)	p value	aOR (95% CI)	p value
Whole vs. 0.1–2%	0.84 (0.77–0.91)	<0.0001	0.82 (0.68–1.00)	0.047
Whole vs. 2%	0.81 (0.74–0.89)	<0.0001	0.83 (0.68–1.00)	0.05
Whole vs. 1%	0.96 (0.82–1.11)	0.57	0.87 (0.66–1.16)	0.35
Whole vs. 0.1%	0.83 (0.66–1.03)	0.09	0.69 (0.45–1.05)	0.08

Logistic generalized estimating equations were used and adjusted for volume of cow's milk, volume of sugary drink intake (including 100% juice, fruit drinks, and soft drinks) consumed in 250 ml cups per day, maternal ethnicity, self-reported family income, birth weight in kilograms, breastfeeding duration in months, and parent BMI. Covariate coefficient estimates not shown. For a family-wise error rate of 0.05, use a 0.01 level of significance.
aOR adjusted odds ratio.
[a]$N = 7467$.

BMI [13]. The current study was designed to overcome these weaknesses through a large prospective cohort study with adjustment for important potentially confounding factors. Our findings are also consistent with a RCT of children aged 4–13 years which showed no evidence of a relationship between dairy fat (including milk, cheese, and yogurt) intake and child adiposity [41].

Possible mechanisms underlying the observed relationship include reverse causality, where parents of leaner children provide higher cow's milk fat and vice versa. Another possibility is that children who consume higher cow's milk fat may be more satiated than those who consume reduced fat cow's milk, leading them to consume a lower quantity of cow's milk or other energy dense foods contributing to higher energy intake [42]. Hormones secreted in response to whole milk consumption such as cholecystokinin and glucagon-like peptide 1 may also play a role in this relationship [43, 44]. Cow's milk fat contains unique fatty acids such as trans-palmitoleic acid and conjugated linoleic acid [45], which may provide cardiometabolic benefits relative to other fatty acids [46]. This theory suggests that cow's milk fat may not contribute to energy storage and adipose tissue as significantly as

other types of dietary fat [47, 48]. Some evidence suggests that children who consume a lower proportion of dietary fat early in life may develop a "thrifty metabolism," where the body adapts by storing excess energy as fat [49]. Conversely, a higher fat diet may metabolically program higher energy utilization and lower energy storage [49, 50]. A lower fat diet in early life may program the body to favor energy storage over utilization, which may increase the risk of obesity over the life course [51–54]. Future studies are needed to understand the mechanism underlying the relationship between cow milk fat and child adiposity, including randomized controlled trials to mitigate influence of confounding factors and establish temporality.

This study had several strengths. The large, diverse cohort of healthy children who were followed over many years provided rich information about nutrition through early and middle childhood. In addition, a number of clinically relevant covariates were controlled for which reduced the risk of confounding. Complex statistical modeling using random effects models minimized within-subject correlation and improved model estimate accuracy. Restricted cubic splines allowed for evaluation of non-linear trends over time. Repeated measures data allowed us

to account for the directionality of this relationship, which improved upon the cross-sectional methods of previous studies by adding power and adjusting for within-subject measures, including changes in cow's milk fat intake from one observation to the next.

This study had a number of weaknesses. The clinical significance of small differences in zBMI in children is not clear. However, the observed difference in weight for a 4-year-old child who consumed whole vs. reduced fat milk seems meaningful. Although cow's milk volume and sugary drink consumption were accounted for, there were insufficient data to calculate total daily energy which would have improved our understanding of the mechanism underlying the observed relationship. The questionnaire used to capture participant diets was based on the Canadian Community Health Survey [55], but has not yet been validated. Though we were able to follow children over an average of 2.7 years, longer follow-up duration would have allowed a better understanding of the temporality of the observed relationships. While zBMI is a measure preferred by clinicians because it is simple to interpret and track over time, and the WHO growth standards are considered the gold standard for zBMI classification [56], BMI is not a direct measure of body composition [57]. Stadiometers used to measure height and weight in this study are routinely checked for accuracy but calibration protocols are not consistent across primary care practices, which may have led to measurement errors. Our sample included a relatively small proportion (5% of the total sample) of children with obesity, which may have limited our statistical power to explore the relationship between cow's milk fat and adiposity among these children, especially in our secondary analysis which estimated odds of overweight and obesity among children who consumed skim, 1%, and 2% compared to whole milk. Imbalance between groups was expected, because obesity was classified based on z-score cut-offs at the tails. While participants in this study were from an ethnically diverse population of healthy urban Canadian children, they may not be representative of other groups of children. Further, cow's milk with different fat contents may have been offered to children based on parent perception of body size. Data on reasons for milk fat choices would have helped to clarify whether reverse causality contributed to the observed results, but this was not available.

In this prospective cohort study of healthy children age 9 months to 8 years, higher cow's milk fat consumption was associated with lower zBMI and lower odds of overweight and obesity. Given that the majority of North American children consume cow's milk daily, this study raises the possibility that whole cow's milk may play a role in lowering the risk of childhood overweight or obesity. Randomized trial data showing the relationship between cow's milk fat and child adiposity is needed to confirm these findings.

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AUTHOR CONTRIBUTIONS

SMV and JLM conceptualized and designed the research study, performed initial statistical analyses, drafted the manuscript, approved the final manuscript as submitted, and had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. CSB and DLO assisted in refining the study design, reviewed and revised the manuscript, and approved the final manuscript as submitted. KET and CDGKS reviewed and revised statistical analysis as well as the manuscript, and approved the final manuscript as submitted.

COMPETING INTERESTS

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ADDITIONAL INFORMATION

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