Supplemental Information

MSMS

MSMs are a new class of causal models that distinguishes between confounder and mediators in the analysis, reducing the gap left by conventional regression methods to assess mediation.[40] Furthermore, by dealing with potential confounding by measured covariates through weighting rather than conditioning on covariates, MSMs allow for the identification of direct effects even in settings in which conventional approaches are biased.[22]

This technique is also considerably relevant for observational studies when exposures cannot be randomly allocated, such as breastfeeding, because it simulates a randomized controlled trial scenario. Moreover, in the absence of unmeasured confounding and measurement error, the results from an observational inverse probability treatment weight analysis may have causal interpretation and can overcome the issue of selection bias.[41] Thus, a MSM was used to estimate the CDE of PB on severe dental caries considering the sugar consumption pattern, whereas the CDE is defined as the effect of breastfeeding on dental caries at age 5 years regardless of sugar consumption during the life course. In the absence of interaction between breastfeeding and sugar consumption, the CDE may be interpreted as the total natural direct effect..[42] Stabilized weights are more efficient than inverse-probability-to-treatment weights, because stabilized weight precludes extreme differences in weights for the exposed and unexposed groups. Moreover, it maintains the original sample size in the weighted data set and provides a robust CI.[43] Stabilized weights (SW) were calculated for breastfeeding (1) and sugar consumption (2) separately according to the following formulas:

$$SW_i^{breastfeeding} = \frac{f(BF)}{f(BF|C)}; \quad (1)$$

$$SW_i^{sugar} = \frac{f(sugar|BF)}{f(sugar|BF,L,C)}, \quad (2)$$

where BF is PB; sugar is sugar consumption; C represents baseline confounders; and L represents the sugar consumption-dental caries confounder. Also, in the formula, f(BF) is the function of breastfeeding (BF), and f(BF|C) is the function of breastfeeding (BF) conditional on baseline confounders (C); whereas f(sugar|BF) is the function of sugar consumption (sugar) conditional on breastfeeding (BF), and f(sugar|BF, L,C) is the function of sugar consumption (sugar) conditional on breastfeeding (BF), baseline (C), and sugar consumption-dental caries (L) confounders.

The final stabilized weight was computed as:

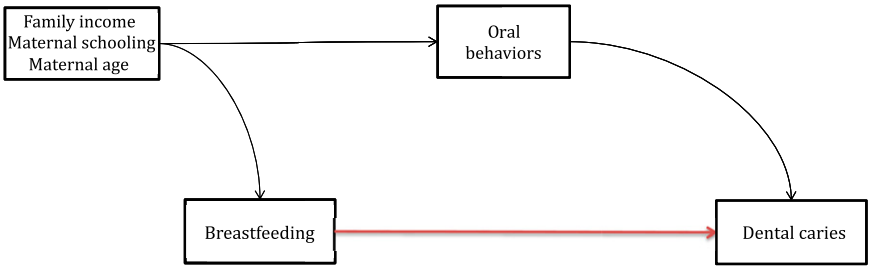
$$SW = SW_i^{breastfeeding} \times SW_i^{sugar}.$$

The distribution of stabilized weights was: stabilized weight for BF: mean = 1.00; range = 0.59 to 1.76; interquartile range = 0.93 to 1.05; stabilized weight for sugar consumption: mean = 1.00; range = 0.57 to 2.46; interquartile range = 0.93 to 1.06; and final stabilized weight: mean = 1.00; range = 0.48 to 2.66; interquartile range = 0.87 to 1.09. All analyses were conducted by using Stata version 13.0 (Stata Corp, College Station, TX).

SENSITIVITY ANALYSES FOR U

MSMs rely on the assumption that there is no unmeasured confounding between the mediator and outcome, exposure and mediator, and exposure and outcome. Although these assumptions may not be analytically verified, some alternatives have been suggested for conducting sensitivity analysis for unmeasured confounding (U).[15] For conducting this analysis, following VanderWeele,[15] we needed to assume 2 aspects, (1) the prevalence of U and (2) the effect of U on the outcome. We also assumed there was no relative excess risk due to interaction between exposure and U. The parameters of U, such as γ (conditional increase in the risk of dental caries), P1 [P(U = 1|BF, sugar, C)], and P2 [P(U = 1|BF*, sugar, C)] were specified from systematic reviews. We used the following model given by VanderWeele[15] to calculate the bias introduced by U that could invalidate the CDE:

$$Bias\ CDE_{BF,\,BF^*|c}^{RR}(sugar) = \frac{1 + (\gamma - 1)P1(U = 1|BF, sugar, C)}{1 + (\gamma - 1)P2(U = 1|BF^*, sugar, C)}$$



SUPPLEMENTAL FIGURE 2
Directed acyclic graph displays the backdoor path of oral behaviors blocked by socioeconomic variables.

SUPPLEMENTAL TABLE 3 Multiplicative Interaction Between Breastfeeding and Sugar Consumption

Parameter	Estimate	95% CI	SE	*P*
S-ECC				
Sugar#BF	−0.14	−0.32 to 0.07	0.11	.192
Intercept	−1.91	−260 to −1.21	0.35	<.001
Dental caries				
Sugar#BF	−0.07	−0.21 to 0.08	0.09	.403
Intercept	0.78	0.22 to 1.35	0.29	<.001

signifies interaction between conditions.

SUPPLEMENTAL TABLE 4 Relative Excess Risk Due to Interaction Between Breastfeeding and Sugar Consumption

Parameter	Estimate	95% CI	SE	*P*
S-ECC				
RERI	−0.37	−5.02 to 4.27	2.37	.875
BF (0 and 2)				
Sugar (0 and 3)				
RERI	−0.07	−0.49 to 0.35	0.21	.732
BF (1 and 2)				
Sugar (2 and 3)				
RERI	−0.27	−2.76 to 2.23	1.27	.833
BF (0 and 2)				
Sugar (1 and 3)				
Dental caries				
RERI	1.19	−2.39 to 4.47	1.82	.515
BF (0 and 2)				
Sugar (0 and 3)				
RERI	0.12	−0.35 to 0.59	0.24	.625
BF (1 and 2)				
Sugar (0 and 3)				
RERI	0.68	−1.59 to 2.95	1.16	.557
BF (0 and 2)				
Sugar (1 and 3)				

Numbers in parentheses in column 1 indicate the levels of each variable considered in the RERI analysis. BF, breastfeeding; RERI, relative excess risk due to interaction.

SUPPLEMENTAL TABLE 5 Sensitivity Analysis for U Considering the Estimates of PB on Severe Dental Carries

γ	P1	P2	P1 – P2	RR	γ	P1	P2	P1 – P2	RR	γ	P1	P2	P1-P2	RR
2	40	10	30	1.27	3	40	10	30	1.50	4	40	10	30	1.70
2	50	10	40	1.32	3	50	10	40	1.67	4[a]	50[a]	10[a]	40[a]	1.92[a,b]
2	60	10	50	1.45	3	60	10	50	1.83	4[a]	60[a]	10[a]	50[a]	2.15[a,b]
2	70	10	60	1.54	3[a]	70[a]	10[a]	60[a]	2.00[a,b]	4[a]	70[a]	10[a]	60[a]	2.38[a,c]
2	80	10	70	1.63	3[a]	80[a]	10[a]	70[a]	2.16[a,b]	4	80	10	70	2.60[a,c]
2	90	10	80	1.72	3[a]	90[a]	10[a]	80[a]	2.33[a,c]	4	90	10	80	2.80[a,c]
2	40	20	20	1.16	3	40	20	20	1.28	4	40	20	20	1.37
2	50	20	30	1.25	3	50	20	30	1.42	4	50	20	30	1.56
2	60	20	40	1.33	3	60	20	40	1.57	4	60	20	40	1.75
2	70	20	50	1.42	3	70	20	50	1.70	4[a]	70[a]	20[a]	50[a]	1.93[a,b]
2	80	20	60	1.50	3	80	20	60	1.85	4[a]	80[a]	20[a]	60[a]	2.10[a,b]
2	90	20	70	1.60	3[a]	90[a]	20[a]	70[a]	2.00[a,b]	4[a]	90[a]	20[a]	70[a]	2.30[a,b]
2	40	30	10	1.07	3	40	30	10	1.12	4	40	30	10	1.15
2	50	30	20	1.15	3	50	30	20	1.25	4	50	30	20	1.31
2	60	30	30	1.23	3	60	30	30	1.38	4	60	30	30	1.47
2	70	30	40	1.31	3	70	30	40	1.50	4	70	30	40	1.63
2	80	30	50	1.36	3	80	30	50	1.62	4	80	30	50	1.78
2	90	30	60	1.46	3	90	30	60	1.75	4[a]	90[a]	30[a]	60[a]	1.94[a,b]
2	50	40	10	1.07	3	50	40	10	1.10	4	50	40	10	1.13
2	60	40	20	1.14	3	60	40	20	1.20	4	60	40	20	1.27
2	70	40	30	1.21	3	70	40	30	1.30	4	70	40	30	1.41
2	80	40	40	1.28	3	80	40	40	1.44	4	80	40	40	1.54
2	90	40	50	1.36	3	90	40	50	1.55	4	90	40	50	1.68
2	60	50	10	1.06	3	60	50	10	1.10	4	60	50	10	1.12
2	70	50	20	1.13	3	70	50	20	1.20	4	70	50	20	1.24
2	80	50	30	1.20	3	80	50	30	1.30	4	80	50	30	1.36
2	90	50	40	1.27	3	90	50	40	1.40	4	90	50	40	1.48

It is noteworthy that U must be strongly associated with dental caries (γ should be at least 3) and unequally distributed among the exposed (P1) and nonexposed (P2) groups. This seems unlikely to be observed in the real world, because no condition related to breastfeeding and dental caries satisfy these parameters. Thus, it ensures the robustness of the observed findings. γ, conditional increase in the risk for dental caries; P1, prevalence in exposed group (breastfed for ≥24 months); P2, prevalence in nonexposed group (breastfed for ≤12 mo); P1 – P2, calculated differences in the probability of U; RR, relative risk.

[a] Indicates scenario where U would nullify the CDE of PB on dental caries.

[b] Results would eliminate the CDE of 24 months of breastfeeding on dental caries.

[c] Results would eliminate the CDE of 24 months of breastfeeding on S-ECC.

SUPPLEMENTAL REFERENCES

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