

## Gender Modify the Effect of Birth Weight on Later Obesity Risk among Primary School Pupils: A Community-Based Case-Control Study

Dariush Bastam<sup>1</sup>, \*Reza Vazirinejad<sup>2</sup>, Golnaz Sharifnia<sup>3</sup>, Mohsen Rezaeian<sup>4</sup>, Hasan Ahmadiania<sup>5</sup>

<sup>1</sup>MSc of Epidemiology, Medical school, Yasuj University of Medical Sciences, Yasuj, Iran. <sup>2</sup>Prof. Dept. of Social Medicine, Social Determinants of Health Research center, Medical school, Rafsanjan University of Medical Sciences, Rafsanjan, Iran. <sup>3</sup>Department of Epidemiology, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. <sup>4</sup>Prof. Dept. of Epidemiology, Occupational Environmental Research Center, Medical school, Rafsanjan University of Medical Sciences, Rafsanjan, Iran. <sup>5</sup>PhD Student of Biostatistics, Hamadan University of Medical Science, Hamadan, Iran.

### Abstract

#### Background

The researchers do not prove the effect of birth weight on childhood obesity, so far. This study aimed at providing evidence on the effect of birth weight on obesity and overweight among primary school pupils.

**Materials and Methods:** This case-control study was conducted on 508 primary school pupils. Multistage sampling technique was applied to increase the accuracy of risk calculation. Pupils were divided into the two groups of case (170 pupils with a Z-score  $\geq 1$  as overweight and obese) and control (338 pupils with a Z-score between -2 to 1 as not being obese or overweight) based on WHO reference data, For each case, two controls were matched and selected based on age, gender, and type of school. Demographic, physical activity as well as 24-hour dietary program and amount of energy expenditure data were collected. All data analyses were performed using SPSS. Odds ratio with 95% confidence interval was estimated.

**Results:** The risk of obesity and overweight among girls who had a birth weight  $> 3,500\text{g}$ , was 2.51 times higher than that in girls with a birth weight  $\leq 3,500\text{g}$  (OR=2.51, 95% CI: 1.2-5.25). However, not only this risk among boys was not higher than unity, but also it was less than one showing a reverse not-significant association (OR=0.715, 95% CI: 0.369-1.39).

#### Conclusion

Birth weight was an independent risk factor for obesity and overweight during childhood only among girls. Gender had a moderating effect on the relation between birth weight and obesity during childhood.

**Key Words:** Birth weight, Gender, Obesity, Overweight, Pupils.

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#### \*Corresponding Author:

Prof. Reza Vazirinejad, Dept. of Social Medicine, Social Determinants of Health Research center, Medical school, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

Email: rvazirinejad@yahoo.co.uk

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## 1- INTRODUCTION

Obesity is defined as an excessive fat accumulation in the body tissues that compromises the health of the individual (1). Nowadays, the obesity epidemic is one of the most important public health issues in most of the countries across the world, affecting both developed and developing countries. In 2016, 1.9 billion people over the age of 18 years were obese or overweight (2). In the same vein, there is a particular concern about this trend among children and adolescents, especially in developing countries (2). Accordingly, in Iran, obesity increased from 0.5% in 1975 to 11.5% in 2016 among the 5 to 9-year-old children (3). Enhancement of obesity prevalence has turned this issue into one of the major public health concerns. Based on the current evidence, childhood obesity increases the risk of obesity during adulthood (4, 5).

The obese children are at the high risk of developing multiple non-communicable diseases, such as type II diabetes mellitus, cardiovascular diseases, hypertension, metabolic syndrome, high cholesterol, and renal problems (6-9). As a result, obesity has imposed a high financial burden on the communities (9), and increased mortality (10, 11). The main concern is that the obese children may have shorter life spans than their parents (12). It seems that the current methods of obesity prevention and control are unsuccessful; accordingly, they should be implemented from embryonic and infancy periods during which many non-communicable diseases originate (13).

Obesity is a complex multifactorial disease with genetic and environmental etiologies (14, 15). Therefore, the prevention of this disease requires the identification of the associated risk factors and critical periods facilitating disease progression (16, 17). Childhood is known as a critical period for obesity (18) during which environmental risk factors, such as intrauterine

environment, physical activity, lifestyle, eating habits, and family history play a role in the development of the disease. The early life factors, such as the intrauterine growth, may contribute to the disease progression. In this regard, birth weight is an intrauterine index (19), the relationship of which with obesity and overweight in children and adolescents has been investigated in various studies (20-22). Most of the cross-sectional studies have indicated a statistically significant relationship between birth weight and obesity/overweight (23, 24).

However, the results of the mentioned studies are contradictory due to a number of factors, including small sample size, use of available sampling, nonrandomization in group allocation, use of non-matched groups in terms of age, gender, and economic and social status, non-consideration of the variables intervening with birth weight, and measurement of a limited number of environmental variables affecting obesity (e.g., eating habits, physical activity, and energy intake). With this background in mind, the present study was conducted to investigate the effect of birth weight as an independent risk factor on obesity and overweight among the first-grade primary school pupils in Rafsanjan, Iran. In this study, an effort was given to select a representative sample of pupils and eliminate the aforementioned defects of other studies.

## 2- MATERIALS AND METHODS

### 2-1. Study design and population

This community-based case-control study was conducted on 508 eligible randomly selected first grade primary school pupils in Rafsanjan, one of the cities of Kerman province, Iran. To calculate the sample size, all the values in the following formula were used according to the previous studies (25, 26).

$$n_1 = \left( \frac{Z_{(1-\frac{\alpha}{2})} \sqrt{\bar{p}\bar{q}} \left(1 + \frac{1}{k}\right) + Z_{(1-\beta)} \sqrt{p_1q_1 + \frac{p_2q_2}{k}}}{|p_2 - p_1|} \right)^2$$

$$\bar{q} = 1 - \bar{p} \quad \text{and} \quad \bar{p} = \frac{p_1 + kp_2}{1+k} \quad \text{and} \quad \beta = 0.2, \quad \text{and} \quad \alpha = 0.05$$

$$p_1 = \frac{OR \times p_2}{1 + (OR - 1)p_2} \quad p_2 = 0.3, \quad (9) \quad OR = 3.14, \quad (6)$$

Where,

$n_1$  = Sample size in the case group

$n_2$  = Sample size in the control group

$$\left(z_{1-\frac{\alpha}{2}}\right) = 1.96, \quad \left(z_{1-\beta}\right) = 0.85$$

$\bar{p}$  = The weighted average of the desired ratio in the two groups.

$$\bar{q} = 1 - \bar{p}$$

$p_1$  = The ratio of obesity and overweight in the case group.

$p_2$  = The ratio of obesity and overweight in the control group.

$$q_1 = 1 - p_1$$

$$q_2 = 1 - p_2$$

OR = Odds ratio

$$K = \frac{n_2}{n_1}$$

$|p_2 - p_1|$  = Absolute value of mean difference between case and control groups.

The study population was assigned into two groups of case, including 170 pupils with obesity or overweight, and control, entailing 338 pupils with a normal weight, after measuring their weight. The height and weight of all pupils were measured upon entering the school by the Student Assessment Team of the Ministry of Health using the Seca weight scale made in Germany and stadiometer made in US Hapkins medical products company. A student assessment team consisting of a physician, a health care provider and a medical expert measured the height and weight of all pupils. Accordingly, body mass index (BMI) was calculated through dividing the weight in kilograms by height in meters squared. These data, along with other results related to medical examinations, were recorded in the pupils' health records.

## 2-2. Ethical consideration

Study approval was obtained from the University Council granting an ethics code (ID-code: IR.RUMS.REC.1395.98). Furthermore, the permission to enter the schools was obtained from the education department of the city. For the purpose of sampling, the primary schools of Rafsanjan were divided into five geographical districts out of which 12 schools were selected. In each school, the BMI-for-age (5-19 years; Z-score) was calculated for all pupils in the first grade based on the World Health Organization child growth chart (27). All pupils with obesity or overweight (Z-score  $\geq 1$ ) were identified in each of the classes. Subsequently, for each case, two controls with normal weights (Z-score of -2 to 1) were selected based on age, gender, and type of school.

### 2-3. Inclusion and exclusion criteria

The case and control group definition was according to the WHO definitions on obesity and overweight. As such, overweight is BMI-for-age greater than 1 standard deviation above the WHO Growth Reference median; and obesity is greater than 2 standard deviations above the WHO Growth Reference median (28). Control groups were children with normal weight according to the WHO Growth Reference median (28). The exclusion criteria included: 1) a lower than normal weight, 2) disease-related obesity, 3) congenital hypothyroidism, 4) use of hormonal medicines, 5) affliction with diabetes mellitus, 6) unavailability of birth information, and 7) parental unwillingness to cooperate with the research.

### 2-4. Measuring tools

The data were collected using a demographic form, a valid checklist covering data related to physical activity and dietary habits, as well as the 24-hour dietary recall questionnaire. Additionally, the 24-hour dietary recall questionnaire measures the type of food, food components, amount of eaten foods, and timing of the main meal and snack for three days (29, 30). The demographic form, which made by the research team (Cronbach's alpha=0.76) covered such data as parental education level (i.e., illiteracy, elementary, junior high school, diploma, and above diploma), maternal occupation (i.e., housewife/employed), maternal age at pregnancy, history of obesity in the first-degree relatives (yes/no), child's birth rank, length of breastfeeding, use of complementary foods other than breastfeeding in the first six months of life (yes/no), age of starting complementary foods, gestational age at birth (in weeks), delivery type, household size, and housing status. The checklist of physical activity and healthy dietary habits included items that measured the duration of indoor and

outdoor physical activities (e.g., cycling, skating, jumping rope, running, and gymnastics), sedentary activities (e.g., watching T.V and playing commuter or mobile games), and sleeping during the day. Furthermore, the items related to healthy dietary habits covered such data as the regular consumption of breakfast, eating speed, regular consumption of homemade meals, and parental supervision on the child's eating behavior. The school staff called the parents, and their informed consents were obtained. Birth weight data were extracted from the children's growth cards and health records by the investigator. In addition, such variables as maternal age at pregnancy, gestational age at birth, and delivery type were obtained based on the health records. The information about other variables was obtained through interviews with the pupils' parents.

### 2-5. Data Analyses

The data were analyzed by SPSS software (version 21.0). The data obtained through the 24-hour dietary recall questionnaire were first entered into Nutrition software (version 4.0). Subsequently, the three-day mean of energy intake in terms of calorie consumption was entered into the SPSS software. The relationship of the normally and non-normally distributed quantitative variables with obesity and overweight was examined using t-test and Mann-Whitney U test, respectively. The quantitative data were reported using the first and third quartiles, while the qualitative data were presented as numbers and percentages. In addition, the Chi-square test was used to examine the relationship of multilevel qualitative variables with obesity and overweight. In order to measure the risk of being obese and overweight based on birth weight and other variables, Odds Ratio (OR) was calculated using the logistic regression with a confidence interval of 95%.

### 3- RESULTS

In this study, the case group (obesity or overweight children) consisted of 85 females and 85 males, and the control group (normal weight children) entailed 168 females and 170 males. As indicated in **Table.1**, there was no significant difference between the two groups in terms of male to female ratio; in other words, the two groups were comparable in this regard. Furthermore, the frequency distributions of paternal and maternal education levels, maternal occupation, and housing status were comparable between the two groups (**Table.1**). This indicated

that the two groups were properly matched based on these factors. The two groups were compared in terms of the mean calorie intake calculated based on the data related to food intake (**Table.2**). The results revealed no statistically significant difference between the two groups regarding this variable. Furthermore, there was no significant difference between the two groups in terms of maternal age at pregnancy, and length of playing, watching television, and sleeping during a day, indicating a similar situation of pupils in the two groups based on physical activities and energy expenditure.

**Table-1:** Frequency distribution of students in the case and control groups based on demographic variables, n=170 for case group, and 337 for control group.

Variables	Research groups				*P-value	
	Case, n=170		Control, n=337			
	Number	%	Number	%		
Gender	Female	85	50	167	49.6	0.975
	Male	85	50	170	50.4	
	Total	170	100	337	100	
Paternal education level	Elementary and lower	15	8.9	29	8.8	0.920
	Junior high school	33	19.6	74	22.4	
	Diploma	70	41.7	134	40.5	
	Above diploma	50	29.8	94	28.4	
	Total	168	100	331	100	
Maternal education level	Elementary and lower	8	4.8	20	6.5	0.811
	Junior high school	20	11.9	42	12.5	
	Diploma	89	53	163	48.7	
	Above diploma	51	30.4	110	32.8	
	Total	168	100	335	100	
Maternal occupation	Housewife	136	80	285	84.3	0.222
	Employed	34	20	53	15.7	
	Total	170	100	338	100	
Housing status	Owner	141	83.9	269	80.1	0.528
	Tenant	22	13.1	57	17	
	Others	5	3	10	3	
	Total	168	100	336	100	

\*Chi-square test.

**Table-2:** Mean values of physical activity and calorie intake in the case and control groups.

Variables	Case, n=170	Control, n=337	Statistical test	P-value
Maternal age at pregnancy (year)	26.38±4.87	26.60±5.68	t-test	0.679
Duration of playing during a day (hour)	3(2.17,4.75)	3(2,5)	Mann-Whitney	0.732
Length of watching television (hour)	2.37±1.25	2.30±1.29	t-test	0.543
Length of sleep (hour)	8.97±1.33	9.9±1.45	t-test	0.378
Calorie intake (Kilo calorie)	1702.69±240.26	1726.22±378.06	t-test	0.463
Duration of breastfeeding (month)	20.31±7.17	20.05 ± 6.73	t-test	0.694
Initiating complementary (month)	5.99±0.77	5.95±0.70	t-test	0.557

\*The two groups were compared using t-test and Mann-Whitney U test for normally and non-normally distributed data, respectively.

**Table.3** presents the frequency distributions of the case and control groups based on eating speed, family history of obesity, and type of delivery. As the results indicated, the case and control groups were comparable in terms of breakfast consumption; parental supervision on child’s eating behavior, and taking food to school. However, the two

groups showed a significant difference regarding the regular consumption of meals, eating speed, family history of obesity, and type of delivery. The effect of these factors on the association between birth weight and obesity was controlled in further analysis using logistic regression method.

**Table-3:** Frequency distribution of the case and control groups based on eating speed, family history of obesity, and type of delivery.

Variables	Research group						P-value (Chi-square test)
	Case		Control				
	Number	%	Number	%			
Breakfast consumption	Yes	117	69.2	236	70.4		
	No	52	30.8	99	29.6		
	Total	169	100	335	100		
Supervision on Child’s eating behavior	Yes	132	78.1	263	78.5	0.918	
	No	37	21.9	72	21.5		
	Total	169	100	335	100		
Taking food to School	Yes	86	50.9	180	53.9	0.524	
	No	83	49.1	154	46.1		
	Total	169	100	334	100		
Regular consumption of meals	Yes	155	91.7	252	75.2	<0.001	
	No	14	8.3	83	24.8		
	Total	169	100	335	100		
Eating speed	Slow	111	65.7	288	86.7	<0.001	
	Fast	58	34.3	44	13.3		
	Total	169	100	332	100		
Family history of obesity	Yes	79	47.3	75	22.5	<0.001	
	No	88	52.7	259	77.5		
	Total	167	100	334	100		
Type of delivery	Cesarean	118	69.4	190	56.2	0.004	
	Normal	52	30.6	148	43.8		
	Total	170	100	338	100		

The boys in the case and control groups had a similar frequency distribution in terms of birth weight; however, this variable was significantly different among the girls in the case and control groups.

Overall, there was no statistically significant difference between the two groups regarding the birth weight (**Table.4**).

**Table-4:** Comparison of the frequency distribution of birth weight between the case and control groups based on gender.

Variables	Research groups				P-value*	
	Case		Control			
	Number	%	Number	%		
Birth weight of boys (gram)	<-3500 gr	62	72.9	119	70	0.626
	>3500 gr	23	27.1	51	30	
	Total	85	100	170	100	
Birth weight of girls (gram)	<-3500 gr	60	71.4	141	84.4	0.013
	>3500 gr	24	27.6	26	15.6	
	Total	84	100	167	100	
Birth weight in both control and case groups (gram)	<-3500 gr	122	72.2	260	77.2	0.222
	>3500 gr	47	27.8	77	22.8	
	Total	169	100	337	100	

\*Chi-square test.

Overall comparison (boys and girls) showed no statistically significant association between childhood obesity and birth weight after controlling the effect of known confounding variables. However, the separate assessment of the risk in each gender group indicated the moderating effect of this factor (**Table.5**). Furthermore, despite controlling the effect of confounding variables (i.e., type of delivery, family history of obesity, regular food consumption, and eating speed) using the logistic regression model, there was no

significant difference between the weight of pupils with birth weight > 3500 gr, compared to pupils with birth weight < 3500 gr among boys (OR=0.866, 95% CI: 0.485-1.54). Whereas, among girls, the risk of being obese or/and overweight during childhood in pupils with birth weight > 3500 gr was 151% more than the risk of being obese or/and overweight during childhood in pupils with birth weight < 3500 gr (OR=2.16, 95% CI: 1.53-4.08) (**Table. 5**).

**Table-5:** Unadjusted and adjusted odds ratios of obesity based on birth weight, delivery type, family history of obesity, regular food consumption, and eating speed in the students in each gender.

Variables		Unadjusted odds ratio (95%CI)	Adjusted odds ratio (95% CI)	P-value*	$\beta^*$	
Boys	Birth weight (gr)	$\leq 3500$	1	1	.331	-.330
		>3500	.866(.485, 1.54)	.719(.369, 1.39)		
	Delivery type	Normal	1	1	.019	.770
		Cesarean section	1.93(1.09, 3.40)	2.16(1.13, 4.10)		
	Family history of obesity	No	1	1	.002	.976
		Yes	2.75(1.56, 4.83)	2.65(1.42, 4.93)		

	Regular food consumption	No	1	1	.094	.698
		Yes	2.07(1.002, 4.27)	2.009(.888, 4.54)		
	Eating speed	Slow	1	1	<.001	1.33
		Fast	3.64(2.01, 6.59)	3.81(1.98, 7.33)		
Girls	Birth weight	≤3500 gr	1	1	.014	.921
		>3500 gr	2.16(1.53, 4.08)	2.51(1.02, 5.25)		
	Delivery type	Normal	1	1	.021	.739
		Cesarean section	1.62(.943, 2.79)	2.09(1.12, 3.91)		
	Family history of obesity	Do not have	1	1	<.001	1.16
		Has	3.37(1.92, 5.94)	3.19(1.69, 6.04)		
	Regular food consumption	No	1	1	<.001	2.34
		Yes	9.29(2.78, 31)	1.43(2.97, 36.68)		
Eating speed	Slow	1	1	.009	1.08	
	Fast	3.28(1.61, 6.66)	2.94(1.31, 6.63)			

\*Adjusted odds ratio, CI: Confidence interval.

#### 4- DISCUSSION

The present study aimed at to investigate the effect of birth weight as an independent risk factor on obesity and overweight among the first-grade primary school pupils in Rafsanjan, Iran. Considering that the case and control groups in this study were in the first grade of the same primary schools, they were almost comparable in terms of age, gender, behavioral characteristics such as daily physical activities (at school and somewhat at home), diet, sleeping status, and duration of watching television. The main reason of these similarities was that the social economic situation of pupils' families was mostly the same. Our comparison indicated no significant difference between the two groups (case and control) in terms of these variables. The comparability of the aforementioned variables reflects the use of appropriate sampling method and optimal school programs, including the consideration of equal time for sports and recreation for all pupils, parental supervision on sleeping status, playing computer games, and watching television, as well as proper interaction between school officials and pupils' parents. The results also do not demonstrate a positive correlation between obesity/overweight and the duration of

breastfeeding, age of initiating complementary foods and maternal age at pregnancy (Table.3), which is not in line with the results of other studies (31-33). It should be mentioned that these variables were measured for homogeneity, which greatly increased the validity of the assessment of the effect of birth weight on obesity and overweight among children in our study. In current study, efforts were made to control the confounding effect of the majority of the important and influential variables during study design or/and data analysis using proper statistical methods. Our results showed that the case group had a higher frequency of birth weight > 3500gr comparing to the control group; however, this difference was not statistically significant. This shows that, overall pupils who were obese or overweight had a mean birth weight higher than that among pupils who were not obese or overweight which these results are in line with those obtained by Kalantari et al. (31), Ochoa et al. (34), Bhuiyan et al. (32), and Rathnayake et al. (33), investigating the effect of birth weight on childhood obesity. In our study the difference was not statistically different. Takahashi et al. (35), and Ribervo et al. (36) have also confirmed the effect of birth weight on obesity during childhood. In

contrast, studies of Bhuiyan MU et al., and Rathnayake KM et al. (3) rejected such an effect. The findings of the present study may explain the contradiction in the results of the aforementioned studies. Our results showed that the effect of birth weight on childhood obesity should be evaluated by considering the moderator role of gender. In this regard, after stratifying pupils based on their gender (boys and gender) the assessment of the effect of birth weight on childhood obesity showed interesting results. The calculation of Risk Ratio (Odds Ratio) in the emergence of childhood obesity because of high birth weight (>3500 gr) in boys showed no statistically significant results. Whereas, among girls, the results indicated that high birth weight (>3500 vs. ≤3500 gr) resulted in a statistically significant higher risk of childhood obesity (OR=2.16).

The risk ratio of childhood obesity as a result of high birth weight was further evaluated by a multivariate logistic regression model. This model enabled the controlling of the confounding variables (i.e., type of delivery, family history of obesity, regular consumption of food, and eating speed), which independently showed significant effects on childhood obesity and were not possible to be matched during the study design. Overall calculation of the risk ratio of childhood obesity due to high birth weight based on the regression model also showed no significant association.

The precise designing of the study and fulfillment of the principles of accurate statistical methods in calculating the risk ratio of childhood obesity because of high birth weight in both male and female groups, separately, highlight the novelty and importance of our findings. Therefore, future studies are recommended to consider these issues. In this study, obesity and overweight showed a statistically significant relationship with such latent variables as the type of delivery, family

history of obesity, eating speed, and regular food consumption. Given the significant effect of these variables on childhood obesity and overweight, the researcher decided to examine the odds ratio of obesity and overweight in both genders and different levels of these variables, and then separately examine the relationship between these variables and obesity/overweight. Our study also provided interesting results regarding these variables (i.e., type of delivery, family history of obesity, regular food consumption, and eating speed), which can be helpful in future programs and health education in this domain. For example, our results indicated that the girls who were born through cesarean section, had at least one obese individual in their first-class relatives, consumed food quickly, or took food regularly had a higher chance of childhood obesity.

Therefore, these issues should be taken into account by parents and physicians. The most important result of this study, which distinguishes it from the results of other studies, is that gender has a moderating effect on the relationship between birth weight and childhood obesity and overweight. In this regard, birth weight was considered as an independent risk factor for obesity and overweight among the female pupils; however, this trend was not observed in their male counterparts.

In our study, family history of obesity, cesarean section, and eating speed were identified as independent risk factors for obesity and overweight. This finding indicates that obesity is a multifactorial disease. Accordingly, genetics, intrauterine environment, as well as behavioral and environmental factors play a major role in the emergence of this condition. Therefore, it is necessary to recognize the interactive effects of these variables with birth weight on obesity and overweight.

#### 4-1. Study Limitations

Along with the strengths of the present study, it might be affected by some limitations. Although, the present study was a case-control study in design, the control group was not matched with the case group in terms of age. However, no significant difference was observed between the two groups in terms of age. In addition, non-random sampling might affect the results. Lastly, data on some socio-economic status of the family, and history of diseases or past history of growth failure in early childhood were not available, which should be considered a limitation of this study. Altogether, as the sample was selected from one province, the results of this study could not be generalized to all Iranian children. Future cohort or randomized clinical trials, with a larger sample size and selection of samples from different provinces, can add new findings to the results of the present study and provide researchers with a wider view toward this issue.

#### 5- CONCLUSION

The results of the present study revealed that, birth weight was an independent risk factor for obesity and overweight during childhood only among girls. Also, gender seems to have a moderating effect on the relation between birth weight and obesity during childhood. In our study, family history of obesity, and cesarean section were identified as independent risk factors for obesity and overweight among children. This finding indicates that obesity is a multifactorial disease among pupils.

#### 6- AUTHOR CONTRIBUTORS

The manuscript has been read and approved by all authors and they had significant cooperation with different sections of the work

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**8- CONFLICT OF INTEREST:** None.

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