

Prevalence and Association between Obesity and Iron Deficiency in Children

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Background: Excessive body fat accumulation is a known risk factor for a variety of comorbidities including iron-related disorders such as iron deficiency and iron deficiency anemia. However, only minor investigations, particularly in Thailand, have established a link between obesity and iron-related disorders among children.

Objective: To examine the association between weight status, specifically overweight, obese, and morbidly obese children, and their iron levels, as well as to determine the prevalence of children who were overweight/obese and having iron deficiency and iron deficiency anemia.

Materials and Methods: The authors conducted a cross-sectional-research at Naresuan University Hospital in Phitsanulok, Thailand, on 99 overweight and obese pediatric outpatients aged 5 to 15 years between July 2020 and March 2021. Baseline characteristics and anthropometric measurements of the subjects were recorded, and blood samples were collected to determine hemoglobin concentration (Hb), serum iron (SI) levels, serum ferritin (SF), total iron-binding capacity (TIBC), mean corpuscular volume (MCV), and transferrin saturation. All data were entered into SPSS software and evaluated using analyses of variance (ANOVA), chi-square, Fisher's exact, Pearson's correlation, and odds ratio to identify the relationship between overweight/obesity and iron status.

Results: The findings revealed a 51.52% (95% CI 41.25 to 61.68) prevalence of iron deficiency in the study population, whereas 3% (95% CI 0.60 to 8.60) of the participants had iron deficiency anemia. The present research demonstrates unequivocally that individuals with iron deficiency and iron deficiency anemia had low SI level and low transferrin saturation. Additionally, all overweight and obese subjects had elevated SF levels but normal TIBC.

Conclusion: Iron deficiency is significantly more common in overweight and obese children. Serum iron and transferrin saturation levels serve as indicators of iron deficiency and iron deficiency anemia. Excess body fat results in elevated SF levels and normal TIBC levels. Therefore, SF and TIBC levels are not indicative of iron deficiency.

Keywords: Overweight; Obesity; Children; Iron deficiency; Iron deficiency anemia; Serum iron; Serum ferritin; Serum TIBC; Thalassemia, Anemia

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Iron-related disorders and obesity are major health concerns affecting people across the world. Although high body fat is a significant risk factor for serious health conditions, iron-related disorders such as iron deficiency and iron deficiency anemia are two of the most prevalent micronutrient deficiencies worldwide, particularly among the children. These conditions may have an etiology associated with nutritional deficits and changes in dietary habits and

lifestyle. Researchers have investigated these issues, as iron deficiency is particularly frequent among children. The World Health Organization (WHO) reported that 20.1% of children aged 0 to 4 years in industrialized countries and 39% in developing countries had iron deficiency, while 5.9% of children aged 5 to 14 years in industrialized countries and 48.1% in developing nations had iron deficiency⁽¹⁾.

The food industry has evolved over the years because of advancements in food processing and technology that enable consumers to acquire fast, convenient, and affordable meals that are highly processed and may be deficient in essential macro and micronutrients. As a result, the risk of weight gain and obesity along with malnutrition, are increased. According to the National Health and Nutrition Examination survey conducted in the US between 2015 and 2016, 18.5% of children were obese, with adolescents aged 12 to 19 years at 20.6%, children aged 6 to 11 years at 18.4%, and children aged 2 to

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5 years at 13.9%⁽²⁾. In Thailand, 9.1% of children and adolescents aged 3 to 18 years were overweight with 2.6% in the 3 to 5 years, 4.2% in the 6 to 11 years, and 2.4% in the 12 to 18 years. Furthermore, 6.5% were obese with 2.9% in the 3 to 5 years, 2.7% in the 6 to 11 years, and 0.9% in the 12 to 18 years groups⁽³⁾. Given the importance of iron deficiency in public health, exploring its correlation is critical for research. Obesity has been implicated in previous studies as a risk factor for iron-related disorders. However, the relationship between iron deficiency and obesity is often misconstrued, since iron deficiency is a type of micronutrient deficiency that usually occurs in individuals with poor nutritional status, while in contrast, obesity is a condition associated with excessive intake of nutrients that typically appears in individuals with good nutritional status.

Between 1976 and 2003, the National Health and Nutrition Examination (NHANES II-IV) survey in the USA examined the epidemiology of iron deficiency in overweight and normal-weight children aged 1 to 3 years. They determined that children who were overweight and normal weight accounted for 20.3% to 24% and 7.2% to 9% of the population, respectively⁽⁴⁾. In addition, Carol Hutchinson's study (2016), found a high prevalence of iron deficiency and an association between iron deficiency and obesity in children and adolescents⁽⁵⁾. Zhu et al⁽⁶⁾ (2019) discovered that 8.9% of obese children in China suffered from iron deficiency, low serum iron levels, and high serum ferritin (SF). A study conducted by Phisek et al (2013) in Thailand revealed that 8% of obese children were diagnosed with iron deficiency anemia⁽⁷⁾. The authors now recognize that obesity, which relates to iron deficiency, may be induced by a nutritional imbalance from foods high in carbohydrates and fats but low in essential nutrients such as iron. Increased blood volume occurs because of weight gain in obese children, who require more iron supplementation than normal-weight children. Reduced physical activity, which decreases myoglobin, the protein that binds iron in muscles, contributes to obesity. Furthermore, chronic inflammation causes the reduction in iron absorption. Over the last decade, the connection between being overweight/obese and iron deficiency has received significantly less attention and examining this correlation has proven to be challenging. Laboratory investigations, including complete blood count, SF, serum transferrin saturation, serum iron, and total iron-binding capacity (TIBC) have been used to determine iron deficiency, but there is no consensus regarding which tests are

more appropriate for diagnosing iron deficiency and iron deficiency anemia, particularly in overweight and obese children. Thus, the primary objective of the present study was to investigate the relationship between childhood overweight/obesity and iron status, as well as to determine the prevalence of iron deficiency in the overweight and obese population.

Materials and Methods

Ethical statement

The protocol was approved by the Naresuan University Institutional Review Board (NU-IRB) (No. P3-0041/2563). Prior to initiating the research, the researchers informed and obtained consents from all participants or their parents. All data were collected solely for the purpose of statistical analyses. Personal information was safeguarded.

Sample collection

The present study was a cross-sectional study. It enrolled children aged 5 to 15 years in the outpatient pediatrics clinic at Naresuan University Hospital, Thailand between July 2020 and March 2021. The subjects were classified as overweight, obese, and morbidly obese. Patients with a chronic hematologic disorder, history of iron supplementation during the previous six months, a history of infection within the preceding two weeks, and those who were unable to provide a blood sample were excluded from the present study.

Basic information and anthropometric measurements

Demographic data such as gender, age, blood pressure, history of menarche in the case of adolescent females, underlying disease, obesity-related complications, history of infection, and history of iron supplement intake, were collected using a screening form and a recording form, both approved by the NU-IRB. Blood pressure levels were classified in accordance with the American Academy of Pediatrics (AAP) clinical practice guideline⁽⁸⁾. The height in centimeters was determined using a wall-mounted stadiometer, and the weight in kilograms was recorded following the usual methodology with zero calibrated equipment. The waist circumference was measured in a standing posture at the midpoint of the lower end of the rib cage and the top of the iliac crest using a non-elastic waist tape with an accuracy of 0.1 cm, which was conducted by the same researcher.

The definitions of overweight, obesity, and morbid obesity are based on the 2014 Clinical Practice

Guideline for the Prevention and Management of Childhood Obesity (the Royal College of Pediatricians of Thailand and the Pediatric Society of Thailand). The authors classified obese children into three categories based on their percent weight-for-height (%W/H), which is defined as body weight expressed as a percentage of the ideal weight for height, gender, and age suggested by the Thai Society for Pediatric Endocrinology (TSPE). These categories are 120% above ideal W/H, 140% above ideal W/H, and 200% above ideal W/H, respectively.

Iron status indicators measurement

Blood samples were taken from participants at Naresuan University Hospital by a qualified technician for complete blood count, hemoglobin (Hb) typing, alpha thalassemia deletion by multiplex gap polymerase chain reaction (PCR), and assessment of serum iron, SF and TIBC levels, and calculated transferrin saturation (%TS).

Iron measurement in laboratories was performed using fully automated cell clinical analyzers from the cobas® 6,000 analyzer series. Protein-based indicators such as SF were determined using an electrochemiluminescence immunoassay analyzer (ECLIA), while serum iron and TIBC were measured using a colorimetric reaction with ferene or ferrozine as a chromogen to form a color complex with iron. To obtain the percentage of transferrin saturation, the serum iron concentration was divided by the TIBC and then multiplied by 100.

According to the WHO guidelines, iron deficiency is defined as serum transferrin saturation of less than 16%, SF of less than 15 mg/mL, or serum iron of less than 60 mcg/dL in the absence of anemia. Iron deficiency anemia is characterized as a condition in which there is both anemia and iron deficiency. In consonance with the WHO criteria, anemia is the concentration of Hb lower than 11.5 g/dL or 12 g/dL in children aged 5 to 11 years and 12 to 15 years, respectively.

Sample size and statistical analysis

All statistical calculations in the present cross-sectional study were performed using SPSS Statistics, version 17.0 (SPSS Inc., Chicago, IL, USA), which showed continuous data with normal distribution represented by the mean and standard deviation (SD). Categorical data were shown as frequency and percentage. The chi-square, Fisher's exact, and analyses of variance (ANOVA) tests were employed to determine the association between excess weight and

iron status, which is classified into three categories, normal, iron deficiency, and iron deficiency anemia. Pearson correlation coefficient was utilized to examine the relationship between laboratory results and body mass index (BMI) or %W/H. A p-value of less than 0.05 is statically significant.

The sample size was calculated using infinite population proportion estimate as introduced by Brotanek et al⁽⁴⁾ (2018). The prevalence of iron deficiency in patients classified as overweight (95th percentile) based on their weight-for-height ratio was 20.3 when proportion=0.203, error=0.08, alpha=0.05, and a total sample size of 98 patients were used.

Results

Between July 2020 and March 2021, the present study enrolled 99 participants, 65 (65%) males and 34 (34%) females. The study population was made up of 17% overweight individuals, 69% obese individuals, and 13% morbidly obese individuals. Participants were distributed into three age groups, 40% in the 5 to 8 years, 48% in the 9 to 12 years, 11% in the 13 to 15 years groups. The prevalence of iron deficiency was 51.52% (95% CI 41.25 to 61.68), and iron deficiency anemia was 3.00% (95% CI 0.60 to 8.60). The %W/H and BMI in three groups are shown as mean±SD. The prevalence of iron deficiency was high among males at 68.63% versus 31.37%. Iron deficiency was highest in the age group of 9 to 12 years at 54.90%. Seventy-six-point-fourty seven percent of the participants with iron deficiency and 100% of the participants with iron deficiency anemia (100%) were obese (Table 1). However, laboratory findings indicated low serum iron levels in both iron deficiency 98.04% (p<0.001) and iron deficiency anemia 100% (p<0.001) groups. All participants had normal SF levels despite having iron deficiency and iron deficiency anemia. The range and mean of TIBC levels were normal at 330.83±41.16 and 341.53±42.97 for iron deficiency and iron deficiency anemia, respectively. Low serum transferrin saturation was found in 72.25% of the iron deficiency group and in 100% of the iron deficiency anemia group (p<0.001) (Table 2). Pearson correlation linear regression analysis revealed a significant positive association between BMI and SF (r=0.27, p=0.008), but a negative correlation between %W/H and serum iron (r=-0.206, p=0.041) (Table 3, Figure 1).

Discussion

The present study examined the prevalence and factors associated between iron deficiency and

Table 1. Baseline characteristics of the study population

Characteristics	Normal (n=45)	Iron deficiency (n=51)	Iron deficiency anemia (n=3)	p-value
Sex; n (%)				0.445
Male	29 (64.44)	35 (68.63)	1 (33.33)	
Female	16 (35.56)	16 (31.37)	2 (66.67)	
Age (years); n (%)				0.528
5 to 8	20 (44.44)	19 (37.25)	1 (33.33)	
9 to 12	18 (40.00)	28 (54.90)	2 (66.67)	
13 to 15	7 (15.56)	4 (7.84)	0 (0.00)	
Weight-for-height (%); n (%)				0.370
Overweight (120 to 140)	11 (24.44)	6 (11.76)	0 (0.00)	
Obese (140 to 200)	27 (60.00)	39 (76.47)	3 (100)	
Morbidly obese (≥200)	7 (15.56)	6 (11.76)	0 (0.00)	
Weight-for-height (%); mean±SD	165.27±31.00	170.58±29.64	173.51±16.65	0.658
Body mass index (kg/m ²); mean±SD	27.72±5.92	28.22±5.78	29.16±1.57	0.862
Blood pressure; n (%)				0.497
Normal	24 (53.33)	31 (60.79)	2 (66.67)	
Elevated	3 (6.67)	6 (11.76)	0 (0.00)	
Stage 1 hypertension	14 (31.11)	10 (19.61)	0 (0.00)	
Stage 2 hypertension	4 (8.89)	4 (7.84)	1 (33.33)	
Underlying diseases; n (%)				0.623
No	34 (75.56)	39 (76.47)	3 (100)	
Yes	11 (24.44)	12 (23.53)	0 (0.00)	
Allergic rhinitis	6 (13.33)	7 (13.73)	0 (0.00)	0.790
Other	7 (15.56)	6 (11.76)	0 (0.00)	0.681
• Gastrointestinal disorder	3 (6.67)	1 (1.96)	0 (0.00)	0.416
• Development disorder	2 (4.44)	0 (0.00)	0 (0.00)	0.264
• Oncology	1 (2.22)	0 (0.00)	0 (0.00)	0.485
• Atopic dermatitis	1 (2.22)	2 (3.92)	0 (0.00)	0.847
• Neurocutaneous syndrome	1 (2.22)	0 (0.00)	0 (0.00)	0.485
• Bone and joint disorder	0 (0.00)	2 (3.92)	0 (0.00)	0.527
• Eye disease	0 (0.00)	1 (1.96)	0 (0.00)	0.622
Complications of obesity; n (%)				0.449
No	18 (40.00)	22 (43.14)	0 (0.00)	
Yes	27 (60.00)	29 (56.86)	3 (100)	
Obstructive sleep apnea	13 (28.89)	13 (25.49)	1 (33.33)	0.920
Asthma	6 (13.33)	5 (9.80)	1 (33.33)	0.399
Pulmonary hypertension	0 (0.00)	1 (1.96)	0 (0.00)	0.622
Hypertension	4 (8.89)	3 (5.88)	0 (0.00)	0.762
Attention deficit hyperactivity disorder	7 (15.56)	9 (17.65)	0 (0.00)	0.714
Non-alcoholic fatty liver disease	5 (11.11)	4 (7.84)	0 (0.00)	0.798
Gallstone	1 (2.22)	0 (0.00)	0 (0.00)	0.485
Gastroesophageal reflux disease	0 (0.00)	2 (3.92)	0 (0.00)	0.527
Diabetes mellitus	3 (6.67)	4 (7.84)	0 (0.00)	0.867
Dyslipidemia	1 (2.22)	2 (3.92)	1 (33.33)	0.157
Precocious puberty	1 (2.22)	1 (1.96)	0 (0.00)	0.965
Polycystic ovary syndrome	0 (0.00)	1 (1.96)	0 (0.00)	0.622

SD=standard deviation

obesity. There were 99 patients included in the study, which exceeded the projected population by one participant. Results showed an unexpectedly

high prevalence of iron deficiency, accounting for 51.52% of the participants, plus an additional 3% with iron deficiency anemia. Iron deficiency was

Table 2. Laboratory Findings

	Normal (n=45); n (%)	Iron deficiency (n=51); n (%)	Iron deficiency anemia (n=3); n (%)	p-value
Hemoglobin level (g/dL); mean±SD	13.13±1.09	12.90±0.91	10.30±0.98	<0.001*
Unknown cause of anemia	3 (6.67)	0 (0.00)	0 (0.00)	0.180
Serum iron (mcg/dL); mean±SD	79.75±20.98	44.33±12.30	30.10±9.00	<0.001*
>60	44 (97.78)	1 (1.96)	0 (0.00)	
<60	1 (2.22)	50 (98.04)	3 (100)	
Serum ferritin (mg/mL); mean±SD	96.49±9.35	75.90±5.04	48.64±18.11	0.065
>15	45 (100)	51 (100)	3 (100)	
<15	0 (0.00)	0 (0.00)	0 (0.00)	
TIBC; mean±SD	314.75±56.37	330.83±41.16	341.53±42.97	0.227
MCV; mean±SD	74.95±6.72	75.04±5.44	62.33±9.00	0.003*
Transferrin saturation (%); mean±SD	26.44±9.63	13.73±4.04	9.00±3.67	<0.001*
>16	45 (100)	14 (27.45)	0 (0.00)	
<16	0 (0.00)	37 (72.55)	3 (100)	

SD=standard deviation; TIBC=total iron-binding capacity; MCV=mean corpuscular volume

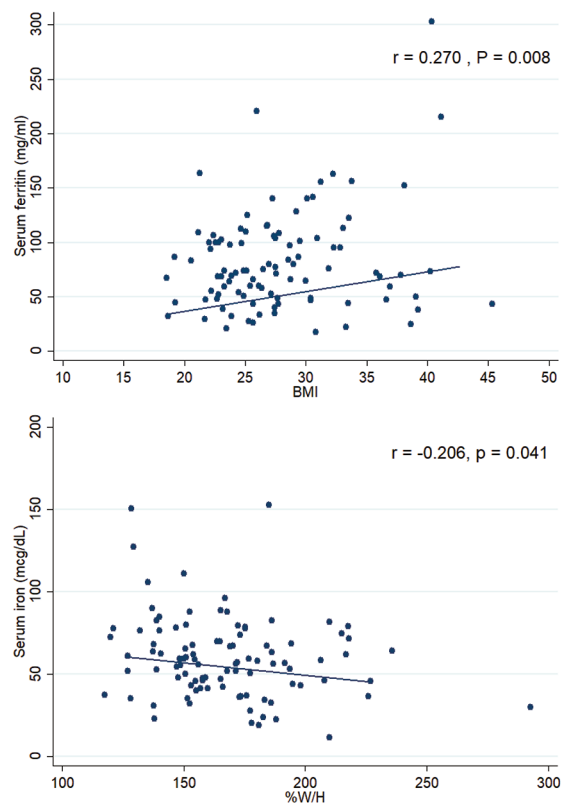
Table 3. Correlations between serum parameters in BMI and %W/H

	BMI		%W/H	
	r	p-value	r	p-value
Hemoglobin level (g/dL)	0.177	0.080	0.074	0.466
Serum iron (mcg/dL)	-0.077	0.449	-0.206	0.041*
Serum ferritin (mg/mL)	0.270	0.008*	0.157	0.122
Transferrin saturation (%)	-0.019	0.852	-0.158	0.118
TIBC	-0.119	0.239	-0.088	0.385

BMI=body mass index; W/H=weight-for-height; TIBC=total iron-binding capacity

more prevalent in males than females between the ages of 9 and 12, which corresponds to a prior study conducted by Phisek et al (2013) in Khon Kaen Hospital, Thailand, wherein results revealed the highest prevalence among obese children aged 3 to 16⁽⁷⁾.

According to WHO in 2020, SF level is a good marker of iron stores and should be used to assess and diagnose iron deficiency in otherwise healthy individuals⁽⁹⁾. However, the iron panel in the present study detected elevated SF levels in all participants, although the serum iron and transferrin saturation levels were significantly lower in patients with iron deficiency and iron deficiency anemia. These findings corroborate the observation of Ghadimi et al (2015), that a rise in BMI would lead to an elevated TIBC, and that serum iron and transferrin saturation levels were inversely associated with BMI⁽¹⁰⁾. The same result with Zhu, et al (2019) study showed lowest serum iron and the highest SF in obese 7 to 18 years old participants⁽⁶⁾.

**Figure 1.** Correlation coefficients between body mass index (BMI) and serum ferritin, as well as %W/H and serum iron.

Serum TIBC is a protein that transports iron to the body that tends to increase when iron stores are diminished but has low sensitivity⁽¹¹⁾. It is an important parameter in diagnosing iron deficiency, but the normal values vary among laboratories. Serum

Table 4. Type of thalassemia

	Normal (n=45); n (%)	Iron deficiency (n=51); n (%)	Iron deficiency anemia (n=3); n (%)	p-value
Thalassemia				0.079
HbE trait	8 (17.78)	8 (15.69)	0 (0.00)	
Hb CS	3 (6.67)	0 (0.00)	1 (33.33)	
Beta thalassemia trait	1 (2.22)	0 (0.00)	0 (0.00)	0.485
Alpha thalassemia 1 trait	3 (6.67)	1 (1.96)	1 (33.33)	0.070
Homozygous alpha thalassemia 2	2 (4.44)	7 (13.73)	0 (0.00)	0.376
Alpha thalassemia 2 trait	5 (11.11)	5 (9.80)	0 (0.00)	0.822

TIBC levels in the present study were normal and were not used in general diagnosis iron deficiency. TIBC's normal values used in the present research is 250 to 410 ug/dL.

Obesity can increase SF level as an acute phase reactant due to chronic inflammation in the body. Hepcidin production increases in response to chronic inflammation due to obesity resulting in an elevated SF level and low serum iron level. Interleukin-6, which is released from visceral adipose tissue into portal blood, may dramatically stimulate hepatic hepcidin synthesis. The role of hepcidin is to reduce ferroportin, which is a transporter that mediates the export of iron from reticuloendothelial macrophages and duodenal enterocytes. As a result, intestinal absorption of dietary iron is reduced, lowering the serum iron levels⁽¹²⁾.

The present study also gathered data on obesity-related complications. As reported in Table 1, there were 89 complications in 59 children, with obstructive sleep apnea (OSA) being the most common, which is consistent with the previous research indicating a significantly higher prevalence of OSA at 44.6% in children with overweight/obesity compared with 9.1% in the normal-weight group⁽¹³⁾. Other complications include hypertension⁽¹⁴⁾, asthma, pulmonary hypertension, development disorder, non-alcoholic fatty liver disease, gallstones, gastroesophageal reflux disease, dyslipidemia, diabetes mellitus type 2, precocious puberty, and polycystic ovary syndrome (Table 1).

A study in India discovered that iron deficiency is one of the coexisting conditions in beta thalassemia trait. Since the symptoms of iron deficiency are similar to those of anemia and the blood picture mimics those of thalassemia, iron deficiency in this group is frequently neglected⁽¹⁵⁾. The present research had 19 participants with iron deficiency plus two participants with iron deficiency anemia. Different types of thalassemia found comprised of HbE trait, alpha thalassemia 1 trait, homozygous alpha

thalassemia, alpha thalassemia 2 trait, and Hb CS (Table 4). The present study also recorded unknown cause of anemia of three participants. Thalassemia and iron deficiency are two distinct disorders that require different treatments.

The present research has strengths and weaknesses. Despite publications highlighting the importance of this subject, Southeast Asia and Thailand are rarely studied. The present study is a cross-sectional that includes extensive data on blood and anthropometry, particularly thalassemia status, which is the leading cause of anemia in Thailand. The present study demonstrates a significant increase in the prevalence of iron deficiency. It is critical to assess iron status in obese patients and to treat iron deficiency according to established guidelines. Currently, no screening for iron deficiency is included in the National Clinical Practice Guideline for obese children. Because the participants' iron status resulted in significantly decreased serum iron and transferrin saturation levels, the researchers recommend that these tests be included in the national public health screening program. In contrast, SF and TIBC may be omitted from iron deficiency screening in obese children because they do not correlate with iron deficiency status.

The present research was not specifically designed to evaluate factors related to the nutritional intake and dietary analyses of the participants since the previous study suggested that differences in dietary factors were not associated with lower serum iron concentrations found in obese adults⁽¹⁶⁾. Other limitations include the absence of waist circumference measurements and the presence of diurnal variation in laboratories for TIBC and SF. The discussion about iron deficiency related to inadequate dietary iron intake and other significant inflammatory markers (IL-6, Hepcidin) will require additional evaluation.

Conclusion

The present study discovered high prevalence

of iron deficiency in obese Thai children. However, there are no present standard screening and indicator method to assess and diagnose iron deficiency related to obesity. The authors found that low serum iron and low transferrin saturation are the best parameters for diagnosis.

What is already known on this topic?

Iron deficiency is related with obesity. The National Clinical Practice Guideline Currently does not have a standard routine for care.

What this study adds?

Iron deficiency is highly prevalent in overweight and obese children. Transferrin saturation and serum iron are the best indicators to diagnose iron deficiency in obese/excess weight groups.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

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