

Body Mass Index and Attention-Deficit/Hyperactivity Disorder in U.S. youth: a reverse J-shaped association

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Abstract

Background

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent neurodevelopmental disorder among children and adolescents. Most prior research assumed a linear dose-response between body mass index (BMI) and ADHD, but the shape of this association and potential biological mediators remain poorly characterized.

Methods

Using NHANES 1999–2004 and 2013–2018 cycles, we analyzed 18,383 children and adolescents (< 18years) with survey weights applied for national representativeness. Multivariable logistic regression estimated odds ratios across BMI tertiles. We identified a BMI threshold using generalized additive models (GAM) with restricted cubic splines (RCS) and two-piecewise regression. Mediation analysis quantified the proportion of the BMI-ADHD association mediated by Red cell distribution width (RDW). Sensitivity analyses incorporated alternative ADHD definitions and subgroup analyses confirmed robustness.

Results

BMI showed an inverse dose-response association with ADHD across tertiles (high vs. low: OR = 0.64; 95%CI 0.52–0.78; P -trend < 0.001). Adjusted GAM revealed a reverse J-shaped relationship with a non-linear threshold at BMI = 21.03kg/m² (LRT P < 0.001). Below this threshold, each 1-kg/m² increase corresponded to a 9% reduction in ADHD odds (OR = 0.91; 95%CI 0.88–0.95, P < 0.0001); above it, the association was null (OR = 1.00; 95%CI 0.98–1.02, P = 0.8949). Sensitivity analyses using questionnaire-based ADHD or ADHD medication as alternative outcomes yielded consistent threshold patterns. Mediation analysis indicated that RDW explained 11.4% (95%CI 0.1–47.8%, P = 0.044) of the total association.

Conclusions

This study reveals a non-linear BMI-ADHD relationship in U.S. children and adolescents, characterized by a critical threshold at 21.03 kg/m². RDW-mediated inflammation-iron pathways may underlie adverse neurocognitive outcomes, implicating erythrocyte homeostasis as a novel mechanistic target.

What is Known - What is New

What is Known:

1. Prior studies assumed a linear dose-response relationship between BMI and ADHD with contradictory findings.
2. The biological mediators linking adiposity to ADHD remain poorly characterized.

What is New:

1. First identification of a reverse J-shaped BMI-ADHD threshold at 21.03 kg/m² in a nationally representative U.S. pediatric sample.
2. RDW mediates 11.4% of the BMI-ADHD association, implicating inflammation-iron pathways.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent neurodevelopmental conditions in childhood^[1–3], affecting approximately 9% of U.S. children and adolescents^[4–6] and imposing substantial burdens on academic achievement, social functioning, and long-term mental health outcomes^[7, 8]. While its etiology is multifactorial, emerging evidence suggests that metabolic and inflammatory pathways may intersect with neurodevelopmental processes in ADHD pathophysiology^[9].

Body mass index (BMI), as a readily accessible indicator of metabolic and nutritional status, has been implicated in ADHD risk, yet epidemiologic findings remain contradictory^[10, 11]. Some studies report positive associations between obesity and ADHD symptoms^[12, 13], whereas others observe null or even inverse relationships^[14]. Such inconsistencies may stem from methodological limitations: reliance on linear models assuming a uniform dose-response gradient, insufficient adjustment for confounding, and use of non-representative samples^[15–17]. Virtually all prior investigations, however, assumed a uniform linear dose-response relationship without formal non-linearity testing, which may obscure clinically meaningful inflection points-thresholds at which the direction or magnitude of risk changes.

Red cell distribution width (RDW) is a quantitative measure of erythrocyte volume heterogeneity elevated in states of systemic inflammation, oxidative stress, and iron deficiency-all conditions implicated in neuroinflammatory disruption of dopaminergic neurotransmission. Epidemiological evidence links elevated RDW to frontal-striatal hypoperfusion and impaired executive function, hallmarks of ADHD pathophysiology^[18–20]. Positioning RDW as a downstream marker of metabolic dysregulation and an upstream contributor to neuroinflammatory injury, we hypothesized that RDW may partially mediate the BMI-ADHD association.

To address these gaps, we analyzed data from the National Health and Nutrition Examination Survey (NHANES), a nationally representative dataset enabling robust, survey-weighted inference. We hypothesized that (1) the BMI-ADHD association follows a non-linear threshold pattern rather than a simple linear gradient, and (2) RDW mediates a modest but significant proportion of this association. We additionally examined whether the BMI threshold and RDW mediation differ across demographic

subgroups defined by sex, age, and race/ethnicity, and validated findings against alternative ADHD definitions.

Materials and Methods

Data Source and Study Population

We analyzed publicly available NHANES data (CDC/NCHS), pooling 1999–2004 and 2013–2018 cycles to ensure adequate sample size and contemporary representation. The sample included children and adolescents < 18years who completed both interview and mobile examination center (MEC) components (n = 18,383 after excluding 5,803 with missing BMI and 1,318 with missing ADHD status from 25,504 total participants)(Fig. 1). All analyses applied MEC exam weights to account for selection probability, non-response, and post-stratification. As NHANES data are publicly available and de-identified, no additional institutional review board approval was required.

BMI Assessment

Weight and height were measured through standardised physical examination procedures at MECs. BMI was calculated as weight in kilograms divided by height in meters squared^[21]. In the analysis, BMI was treated both as a continuous variable and categorised into tertiles.

Definition of ADHD via diagnosis and medication records

ADHD was ascertained using cycle-specific proxy measures due to questionnaire modifications across NHANES waves. For 1999–2004, ADHD status was defined by parental or self-report of a clinical diagnosis via affirmative response to the household interview question: “Has a doctor or other health professional ever told {you/SP} that {you/s/he} had attention deficit disorder?”^[22]. For 2013–2018, ADHD was defined by documented use of ADHD-specific prescription medications reported in the prescription medication questionnaire^[23]. Both definitions have been validated in prior NHANES mental health research as reliable indicators of clinically significant ADHD.

We acknowledge that the two ADHD definitions employed in this study capture partially distinct constructs, and therefore may not be directly interchangeable. Diagnostic definition and treatment receipt overlap substantially but imperfectly. To evaluate the impact of this heterogeneity, we performed sensitivity analyses using each definition separately, and the threshold pattern remained consistent across both approaches.

Covariates

Covariates included: age (continuous, years); sex (male/female); race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, other); poverty income ratio (PIR, tertiles: 0-1.01, 1.02-2.38, 2.39-5.00); education (below high school, high school, above high school); physical activity (< 600 MET-min/week, $\geq$ 600 MET-min/week); secondhand smoke exposure (serum cotinine > 0.1 ng/mL or household smoking); maternal smoking during pregnancy; and WIC participation (ever/never). Missing data were retained as separate categories to preserve the weighted sample.

Statistical Analysis

All the statistical analyses were performed using the EmpowerStats (www.empowerstats.com, X&Y solutions, Inc. Boston MA) and R software version 4.2.0 (<http://www.r-project.org>). A two-tailed alpha of 0.05 denoted statistical significance.

Baseline characteristics were summarized separately for overweight and non-overweight participants. Continuous variables were reported as survey-weighted means with 95% confidence intervals (CI), while categorical variables were expressed as survey-weighted percentages with 95% CI. Group differences were tested using survey-weighted linear regression for continuous outcomes and Rao-Scott chi-square tests for categorical variables, with missing data retained as distinct categories to preserve the complete weighted sample and mitigate selection bias^[24].

Survey-weighted logistic regression models estimated odds ratios (OR) and 95% CI for the cross-sectional association between BMI and ADHD. BMI was examined both as a continuous variable (per 1-kg/m² increment) and in tertiles (low: 7.99-17.09 kg/m²; middle: 17.10-21.45 kg/m²; high: 21.46-62.73 kg/m²). Two nested adjustment models were constructed: Adjust I included age, sex, race/ethnicity, and poverty-income ratio (PIR); Adjust II additionally adjusted for total physical activity (MET/week), secondhand smoke exposure, maternal smoking during pregnancy, and WIC participation. The Adjust II model served as the primary analytic framework. Linear trend was assessed by modeling ordinal tertiles as a continuous term.

To relax the linearity assumption, GAM with restricted cubic splines (RCS) was used to visualize the BMI-ADHD relationship. Two-piecewise logistic regression identified a data-driven threshold (turning point K) by scanning candidate values across the 10th-90th BMI percentile range and selecting the value yielding the minimum model deviance^[25]. A likelihood ratio test (LRT) compared the piecewise model against a simple linear model; a *P*-value < 0.05 indicated that the threshold model provided superior fit. The final two-piecewise model estimated separate ORs for BMI below and above K, adjusted for all covariates in Adjust II.

Robustness was evaluated through multiple sensitivity checks. First, we refitted primary and threshold models using two alternative ADHD definitions: (1) questionnaire-based report only; (2) documented ADHD medication use only. Visual inspection of GAM plots stratified by definition confirmed consistent

non-linear patterns. Second, we conducted stratified analyses across demographic and clinical subgroups.

To test whether the identified BMI threshold differed across key subgroups, we performed interaction analyses by including product terms between BMI (below vs. above threshold) and effect modifiers (sex, race/ethnicity, and age group) in piecewise regression models. Likelihood ratio tests compared models with and without interaction terms. Statistical significance was defined as $P < 0.05$. Stratified threshold effects were estimated for subgroups showing significant interactions.

Mediation analysis quantified the indirect effect of BMI on ADHD through RDW using nonparametric bootstrap approach (1,000 resamples). The outcome model was a survey-weighted probit regression; the mediator model was a linear regression of RDW on BMI and covariates. Proportion mediated was calculated as the ratio of the average natural indirect effect to the average total effect.

Results

Participant Characteristics

The analytic sample comprised 18,383 children and adolescents (weighted to represent 58.0 million U.S. children and adolescents). Weighted prevalence of overweight (BMI $\geq$ 85th percentile) was 34.94% ($n = 6,826$), within this group, 55.20% ($n = 3,768$) had obesity (BMI $\geq$ 95th percentile). Children and adolescents with overweight were older (mean = 10.65 y vs. 9.83 y, $P < 0.0001$), had higher BMI (24.85 vs. 17.49 kg/m²), and were more likely to be non-Hispanic Black (16.2% vs. 13.5%) or Mexican American (17.9% vs. 12.2%) compared with non-overweight peers (all $P < 0.0001$). ADHD prevalence did not differ by overweight status (6.14% vs. 6.65%, $P = 0.38$) (Table 1).

Table 1
Weighted baseline characteristics of U.S. children and adolescents by overweight status

Overweight	No	Yes	P-value
Age (years)	9.83 (9.69 ,9.97)	10.65 (10.52 ,10.78)	< 0.0001
Poverty income ratio	2.56 (2.45 ,2.66)	2.24 (2.15 ,2.32)	< 0.0001
Body Mass Index(kg/m²)	17.49 (17.41 ,17.57)	24.85 (24.66 ,25.04)	< 0.0001
Waist(cm)	62.37 (62.06 ,62.67)	81.80 (81.25 ,82.35)	< 0.0001
Height(cm)	138.67 (137.91 ,139.43)	146.79 (146.07 ,147.51)	< 0.0001
Weight(kg)	36.08 (35.57 ,36.59)	57.16 (56.35 ,57.97)	< 0.0001
Age (years)			0.0152
< 14	73.19 (71.86 ,74.49)	70.67 (69.13 ,72.17)	
≥ 14	26.81 (25.51 ,28.14)	29.33 (27.83 ,30.87)	
Gender			0.2767
Male	50.19 (49.07 ,51.31)	51.29 (49.61 ,52.96)	
Female	49.81 (48.69 ,50.93)	48.71 (47.04 ,50.39)	
Ethnicity			< 0.0001
Non-Hispanic White	58.30 (54.76 ,61.76)	49.70 (45.65 ,53.76)	
Non-Hispanic Black	13.52 (11.72 ,15.56)	16.20 (13.85 ,18.87)	
Mexican American	12.17 (10.25 ,14.39)	17.88 (15.23 ,20.88)	
Other Hispanic	6.83 (5.60 ,8.31)	8.64 (7.18 ,10.37)	
Other Race	9.18 (8.04 ,10.47)	7.57 (6.46 ,8.84)	
Education level			0.4465
Below high school	77.58 (76.17 ,78.93)	78.69 (77.32 ,80.00)	
High school	22.33 (20.98 ,23.73)	21.23 (19.90 ,22.61)	
Above high school	0.09 (0.04 ,0.22)	0.09 (0.03 ,0.25)	
ADHD, Attention deficit hyperactivity disorder			

Overweight	No	Yes	P-value
Poverty income ratio			< 0.0001
Poor	20.02 (18.32 ,21.84)	24.32 (22.56 ,26.16)	
Nearly poor	21.92 (20.33 ,23.60)	24.78 (22.75 ,26.93)	
Middle income	27.27 (25.41 ,29.21)	27.07 (24.93 ,29.33)	
High income	24.34 (21.79 ,27.09)	16.73 (14.77 ,18.89)	
Missing	6.44 (5.56 ,7.45)	7.10 (6.09 ,8.25)	
Total physical activity(MET/week)			0.0034
< 600	14.27 (12.98 ,15.67)	14.17 (12.96 ,15.47)	
≥ 600	13.56 (12.43 ,14.77)	15.97 (14.54 ,17.51)	
Missing	72.17 (70.75 ,73.55)	69.86 (68.23 ,71.44)	
ADHD medications			0.1443
No	94.94 (93.81 ,95.87)	95.98 (94.59 ,97.02)	
Yes	5.06 (4.13 ,6.19)	4.02 (2.98 ,5.41)	
Questionnaire-based definition of ADHD			0.7748
No	91.55 (90.42 ,92.56)	91.27 (89.46 ,92.79)	
Yes	8.45 (7.44 ,9.58)	8.73 (7.21 ,10.54)	
Attention-deficit/hyperactivity disorder (ADHD)			0.3817
No	93.35 (92.57 ,94.06)	93.86 (92.80 ,94.78)	
Yes	6.65 (5.94 ,7.43)	6.14 (5.22 ,7.20)	
Obesity			< 0.0001
No	100.00 (100.00 ,100.00)	46.35 (44.73 ,47.98)	
Yes	0.00 (0.00 ,0.00)	53.65 (52.02 ,55.27)	
Secondhand Smoke			< 0.0001
No	40.25 (37.78 ,42.78)	39.72 (37.18 ,42.31)	
ADHD, Attention deficit hyperactivity disorder			

Overweight	No	Yes	P-value
Yes	36.14 (33.82 ,38.53)	43.34 (40.66 ,46.06)	
Missing	23.61 (22.16 ,25.11)	16.94 (15.53 ,18.46)	
Mother smoked when pregnant			< 0.0001
No	73.97 (72.63 ,75.27)	69.78 (67.79 ,71.69)	
Yes	11.44 (10.26 ,12.74)	15.38 (13.90 ,16.99)	
Missing	14.59 (13.61 ,15.62)	14.84 (13.80 ,15.95)	
ADHD, Attention deficit hyperactivity disorder			

For continuous variables: survey-weighted mean (95% CI), -value was by survey-weighted linear regression (svyglm)

For continuous variables: survey-weighted mean (95% CI), *P*-value was by survey-weighted linear regression (svyglm)

For categorical variables: survey-weighted percentage (95% CI), *P*-value was by survey-weighted Chi-square test (svytable)

Primary Association Between BMI and ADHD

In the fully adjusted survey-weighted model (Adjust II), each 1-kg/m² increase in BMI was associated with a 2% lower odds of ADHD (OR = 0.98; 95%CI 0.96–0.99; *P* = 0.0006). When BMI was modeled in tertiles, a graded inverse association emerged (*P*-trend < 0.0001): children and adolescents in the high BMI tertile had 36% lower odds of ADHD versus those in the low tertile (OR = 0.64; 95%CI 0.52–0.78; *P* < 0.0001) (Table 2).

Table 2
Association between BMI and ADHD among U.S. children and adolescents

Exposure	Adjust I ^a		Adjust II ^b	
	OR (95% CI)	P-value	OR (95% CI)	P-value
BMI ^c	0.98 (0.96, 0.99)	0.0017	0.98 (0.96, 0.99)	0.0006
BMI tertile				
Low	1.0		1.0	
Middle	0.77 (0.64, 0.93)	0.0062	0.73 (0.60, 0.88)	0.0009
High	0.68 (0.55, 0.83)	0.0002	0.64(0.52, 0.78)	< 0.0001
P for trend	0.0003		< 0.0001	
^a Adjust I model adjust for: Age (years); Gender; ETH; PIR				
^b Adjust II model adjust for: Age (years); Gender; ETH; PIR; Total physical activity (MET/week);				

Secondhand Smoke; Mother smoked when pregnant; WIC

^cBMI, Body Mass Index; ADHD, Attention deficit hyperactivity disorder

Threshold Effect Analysis

GAM revealed a non-linear, threshold-type relationship between BMI and ADHD(Fig. 2). Visual inspection and piecewise regression identified an inflection point at BMI = 21.03 kg/m². Below this threshold, each 1-kg/m² increase corresponded to a 9% reduction in ADHD odds (OR = 0.91; 95%CI 0.88–0.95; $P < 0.0001$). Above 21.03 kg/m², the association was null (OR = 1.00; 95%CI 0.98–1.02; $P = 0.89$). The LRT confirmed the threshold model's superior fit over the simple linear model (LRT $\chi^2=14.8$, $P < 0.001$) (Table 3).

Table 3
Threshold effect analysis of BMI and ADHD

Outcome	OR (95% CI)	P-value
Model I		
One linear effect	0.98 (0.96, 0.99)	0.0006
Model II^a		
Turning point (K)	21.03	
BMI ^b < K	0.91 (0.88, 0.95)	< 0.0001
BMI > K	1.00(0.98, 1.02)	0.8949
P value for LRT test [*]		< 0.001
^a Adjust II model adjust for: Age (years); Gender; ETH; PIR; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC		
^b BMI, Body Mass Index; ADHD, Attention deficit hyperactivity disorder		
[*] LRT, logarithm likelihood ratio test. <i>P</i> < 0.05 indicates that model II is significantly different from Model I. Restricted cubic spline smoothing were applied		

Subgroup and Sensitivity Analyses

Stratified analyses demonstrated heterogeneity across key subgroups (Table 4). The BMI-ADHD association was positive in females (OR = 1.04; 95%CI 1.02–1.06; *P* < 0.0001) but null in males (OR = 1.01; 95%CI 0.99–1.02; *P* = 0.41). By race/ethnicity, non-Hispanic White (OR = 1.04; 95%CI 1.02–1.06; *P* < 0.0001) and other race (OR = 1.06; 95%CI 1.02–1.10; *P* = 0.005) children and adolescents showed modest positive associations, while Mexican American, non-Hispanic Black, and other Hispanic subgroups showed no significant association. Socioeconomic stratification revealed stronger associations among high-income children and adolescents (OR = 1.04; 95%CI 1.01–1.07; *P* = 0.008) compared with lower-income groups. Sensitivity analyses affirmed the robustness of the threshold finding. When ADHD was defined solely by questionnaire-based report, the piecewise model yielded comparable ORs below the threshold (OR = 0.92; 95%CI 0.88–0.96). Using only medication-based ADHD definition preserved the null association above K (OR = 1.01; 95%CI 0.98–1.03) and the steep inverse gradient below K (OR = 0.90; 95%CI 0.85–0.95) (Figs. 3–4).

Table 4
Stratification analysis for the association between BMI and ADHD

Subgroups	Total	OR (95%CI)	P-value
Age (years)			
<14	13010	1.01 (1.00, 1.03)	0.1295
≥14	5373	1.00 (0.98, 1.02)	0.8593
Gender			
Male	9230	1.01 (0.99, 1.02)	0.4108
Female	9153	1.04 (1.02, 1.06)	< 0.0001
Ethnicity			
Non-Hispanic White	4992	1.04 (1.02, 1.06)	< 0.0001
Non-Hispanic Black	5193	1.01 (0.99, 1.03)	0.3175
Mexican American	4984	1.00 (0.97, 1.03)	0.8651
Other Hispanic	1324	0.97 (0.92, 1.03)	0.3240
Other Race	1890	1.06 (1.02, 1.10)	0.0047
Poverty income ratio group			
0–1.01	5576	1.01 (0.99, 1.03)	0.1711
1.02–2.38	5634	1.00 (0.98, 1.02)	0.9118
2.39–5	5650	1.03 (1.01, 1.05)	0.0018
Education level			
Below high school	11515	0.99 (0.97, 1.00)	0.0506
High school	3395	1.00 (0.98, 1.02)	0.9077
Above high school	12	0.85 (0.52, 1.37)	0.4996
Poverty income ratio			
Poor	5456	1.01 (0.99, 1.03)	0.1940
Nearly poor	4676	1.00 (0.98, 1.02)	0.9521
Middle income	4072	1.02 (1.00, 1.04)	0.0739
High income	2656	1.04 (1.01, 1.07)	0.0082
Adjusting variables: Age (years); Ethnicity; Poverty income ratio; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC; Gender			

Subgroups	Total	OR (95%CI)	P-value
Age (years)			
Missing	1523	1.01 (0.96, 1.05)	0.7506
Total physical activity(MET/week)			
<600	3432	0.99 (0.97, 1.01)	0.4657
≥600	2488	0.98 (0.95, 1.01)	0.1951
Missing	12463	1.01 (1.00, 1.03)	0.1381
Body Mass Index(kg/m²) group			
7.99–17.09	6123	1.01 (0.89, 1.14)	0.9281
17.1–21.45	6130	1.01 (0.92, 1.09)	0.9017
21.46–62.73	6130	1.00 (0.98, 1.02)	0.8980
Waist(cm) group			
32–60.1	5913	0.89 (0.80, 0.98)	0.0182
60.2–74.6	5928	0.93 (0.88, 0.98)	0.0110
74.7–159.2	5933	1.00 (0.98, 1.02)	0.7062
Height(cm) group			
78.3–130.3	6127	0.90 (0.83, 0.98)	0.0184
130.4–157.7	6113	0.95 (0.93, 0.97)	< 0.0001
157.8–200.7	6143	0.99 (0.98, 1.01)	0.3608
Weight(kg) group			
9.1–29	6096	0.76 (0.69, 0.85)	< 0.0001
29.1–53.6	6148	0.90 (0.86, 0.94)	< 0.0001
53.7–191.7	6139	0.98 (0.97, 1.00)	0.1021
Overweight			
No	11557	1.05 (1.02, 1.08)	0.0028
Yes	6826	1.03 (1.01, 1.04)	0.0016
Obesity			
Adjusting variables: Age (years); Ethnicity; Poverty income ratio; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC; Gender			

Subgroups	Total	OR (95%CI)	P-value
Age (years)			
No	14615	1.03 (1.01, 1.05)	0.0149
Yes	3768	1.03 (1.01, 1.05)	0.0048
Secondhand Smoke			
No	7015	0.99 (0.97, 1.01)	0.3564
Yes	7659	1.01 (0.99, 1.02)	0.2917
Missing	3709	1.04 (1.01, 1.07)	0.0053
Mother smoked when pregnant			
No	13516	1.01 (1.00, 1.03)	0.1706
Yes	1967	1.01 (0.98, 1.03)	0.5402
Missing	2900	0.99 (0.97, 1.02)	0.5510
Adjusting variables: Age (years); Ethnicity; Poverty income ratio; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC; Gender			

Interaction test

Piecewise regression interaction models revealed significant heterogeneity in the BMI threshold effect across demographic subgroups (Table 5). Sex significantly modified the threshold effect (P -interaction = 0.039): Males experienced an 11% risk reduction per BMI unit below 21.03 kg/m² (OR = 0.89; 95%CI 0.85–0.93, $P < 0.0001$), whereas no threshold effect was observed in females (OR = 0.99; 95%CI 0.92–1.07, $P = 0.77$). Race/ethnicity also modified the threshold (P -interaction = 0.035): Other Hispanic youth exhibited the strongest effect (OR = 0.66; 95%CI 0.56–0.78, $P < 0.0001$), non-Hispanic Whites also showed a pronounced threshold effect (OR = 0.89; 95%CI 0.84–0.95, $P = 0.0004$), but absent in other groups. Age group did not significantly modify the threshold effect (P -interaction = 0.211).

Table 5
Threshold Effect Modification by Demographics

Subgroup	N	OR below K (95%CI)	OR above K (95%CI)	P-interaction
Overall	18,383	0.91 (0.88–0.95)	1.00 (0.98–1.02)	
Gender				0.039
Male	9,230	0.89 (0.85–0.93)	0.99 (0.97–1.01)	
Female	9,153	0.99 (0.92–1.07)	1.02 (0.99–1.05)	
Race/Ethnicity				0.035
Non-Hispanic White	4,992	0.89 (0.84–0.95)	1.01 (0.98–1.04)	
Non-Hispanic Black	5,193	0.97 (0.91–1.04)	1.00 (0.97–1.03)	
Mexican American	4,984	0.94 (0.85–1.03)	0.97 (0.92–1.02)	
Other Hispanic	1,324	0.66 (0.56–0.78)	1.04 (0.96–1.13)	
Other Race	1,890	0.91 (0.79–1.05)	0.99 (0.92–1.07)	
Age				0.211
< 14 years	13,010	1.02 (0.97–1.06)	0.98 (0.95–1.02)	
≥ 14 years	5,373	0.96 (0.87–1.05)	1.02 (0.99–1.04)	

P-interaction from likelihood ratio test comparing piecewise models with and without product terms $P < 0.05$ indicates subgroups with significant threshold effects

Mediation Analysis

RDW mediated 11.4% (95%CI 0.1%–47.8%; $P = 0.044$) of the total BMI-ADHD association (Table 6). The average natural indirect effect was -0.00082 (95% CI -0.0017 to -0.00003 ; $P = 0.034$), while the average direct effect remained significant (-0.00637 ; 95% CI -0.0123 to -0.0011 ; $P = 0.018$) (Figs. 5). Bootstrap diagnostics indicated stable estimates, and the correlation of residuals from mediator and outcome models was negligible ($r = -0.00008$).

Table 6
Mediation Analysis for red cell distribution width for the association between BMI and ADHD

Total effect	Estimate	95% CI lower	95% CI upper	P-value
	-0.007187	-0.013179	-0.001980	0.0100
Mediation effect	-0.000819	-0.001685	-0.000026	0.0340
Direct effect	-0.006368	-0.012277	-0.001085	0.0180
Propotion mediated	0.113974	0.001071	0.477777	0.0440

Mediator variable: Red Cell Distribution Width

Adjusting variables: Age (years); Ethnicity; Poverty income ratio; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC; Gender

Nonparametric Bootstrap (resamples = 1000) Confidence Intervals with the Percentile Method

Correlation of residuals from mediator model with residuals from outcome model: -0.000085

Discussion

This study is the first to characterize a non-linear threshold relationship between BMI and ADHD in a nationally representative U.S. pediatric sample. Rather than a uniform linear gradient, we observed a pronounced inverse association below a BMI of 21.03kg/m² that attenuated to null beyond this point. Our threshold model explains why prior studies report conflicting linear associations. Investigations limited to leaner populations may detect inverse relationships, whereas those focused on obese cohorts may observe null or positive associations.

The inflection point at BMI = 21.03kg/m² corresponds approximately to the 75th percentile of BMI for U.S. children and adolescents, straddling the overweight-obesity boundary. Below this threshold, each incremental rise in BMI may reflect improved nutrition, neurodevelopmental resilience, or hormonal milieu that attenuates ADHD risk^[26, 27]. Modest adiposity ensures adequate energy reserves and essential fatty acids critical for myelination and synaptic plasticity^[28], whereas underweight status may signal malnutrition, chronic illness, or heightened hypothalamic-pituitary-adrenal axis activation linked to inattention and executive dysfunction^[29–31]. Conversely, the null association above 21.03kg/m² suggests that the adverse neuroinflammatory and metabolic consequences of excess adiposity counterbalance any early protective effects^[32], aligning with literature implicating obesity-related inflammation in dopaminergic dysregulation^[33]. The mediation analysis indicates that RDW—a biomarker of systemic inflammation and erythropoietic homeostasis-mediated 11.4% of the total BMI-ADHD association. The

proportion, while modest, is clinically meaningful: RDW is inexpensive, universally measured in primary care, and modifiable through targeted interventions such as iron supplementation, anti-inflammatory dietary modifications, and sleep optimization^[34, 35]. Nevertheless, approximately 90% of the BMI-ADHD association operated through pathways not captured by RDW, including direct neurodevelopmental programming by adipose-derived hormones, psychosocial stressors linked to body image, sedentary behavior effects on dopaminergic circuits, and genetic pleiotropy^[36]-underscoring that effective prevention requires integrated strategies addressing nutritional, environmental, and neurobiological determinants simultaneously. It should be noted that the wide confidence interval (95% CI: 0.1%–47.8%) around the mediation proportion indicates limited statistical precision for this modest effect, underscoring the need for replication in larger samples.

Formal interaction tests confirmed that the BMI threshold effect differed significantly by sex ($P = 0.039$) and race/ethnicity ($P = 0.035$). The striking sex heterogeneity-wherein females exhibited a modest positive BMI-ADHD association while males showed a pronounced protective threshold-may reflect differential psychosocial pressures, diagnostic biases, or neurohormonal influences^[37]. Similarly, race/ethnicity findings underscore that the BMI-ADHD relationship is not universal: non-Hispanic White children and adolescents demonstrated stronger associations, whereas Mexican American and non-Hispanic Black children and adolescents showed null effects. Other Hispanic children and adolescents despite not demonstrating a linear association, exhibited the strongest protective threshold effect (OR = 0.66), suggesting that conventional linear models may obscure subgroup-specific inflection points. This could reflect cultural or metabolic differences in obesity distribution or nutritional adaptation within this population, or indicate that unmeasured confounding factors in immigrant identity or dietary culture adaptation patterns amplified the neuroprotective effects of moderate obesity^[38, 39]. Although Mexican-American children and adolescents showed higher obesity prevalence, their threshold effect was zero, indicating that metabolic elasticity in this population may reach saturation at lower BMI levels. These differential patterns emphasize that the "Hispanic" racial group is not a homogeneous entity. These findings require validation in cohorts with more comprehensive ADHD phenotypic characteristics. Future studies must employ larger sample sizes and culturally specific ADHD measurement methods to conduct subgroup analyses of these populations, underscoring the necessity of developing culturally adaptive screening strategies. The null age interaction ($P = 0.211$) may reflect inadequate power to detect modest effect differences between younger ($< 14y$) and older ($\geq 14y$) sample, given the reduced sample size in the older group ($n = 5,373$). Alternatively, the threshold may truly be developmentally stable, supporting its utility across pediatric age ranges.

Our findings suggest that pediatric BMI screening may inform mental health risk stratification, but only within specific adiposity ranges. Clinicians should recognize that low BMI confers risk in males (who lack the protective threshold), whereas markedly elevated BMI confers risk across all groups. Males and Other Hispanic youth may benefit from low-BMI targeted assessment, while females and non-Hispanic Whites require continuous BMI monitoring given their linear dose-response relationship. Beyond sex and race/ethnicity, we observed notable heterogeneity across socioeconomic and environmental strata. The

BMI-ADHD association was amplified among youth from high-income households compared with those from poorer families, suggesting that socioeconomic context may shape vulnerability to BMI-related neurodevelopmental effects^[40, 41]. These patterns indicate that the BMI-ADHD relationship is not uniform across the pediatric population and may be contingent on broader environmental conditions.

This study leverages a large, nationally representative sample with rigorous survey-weighting, ensuring high generalizability. We employed advanced statistical techniques-GAM splines, piecewise regression, and mediation-which are underutilized in pediatric obesity-psychiatric comorbidity research. Sensitivity analyses across ADHD definitions and extensive subgroup stratification bolster internal validity. Nevertheless, several limitations merit consideration. First, the cross-sectional design precludes causal inference; reverse causation (ADHD symptoms influencing weight through appetite suppression or sedentary behavior) remains plausible^[42–45]; longitudinal studies are needed to confirm these associations and explore underlying mechanisms. Second, residual confounding by unmeasured variables (e.g., parental ADHD, dietary quality, sleep disorders) may persist despite robust covariate adjustment; RDW mediation assumes no unmeasured confounding of the mediator-outcome relationship, while residual correlation was negligible, this cannot be definitively proven. Third, the substantial missing data for physical activity (71.36%) may have limited our ability to detect true effect modification, particularly in interaction analyses where subgroup sample sizes were further reduced. Fourth, the Other Hispanic subgroup comprised only 1,324 participants, limiting statistical stability of the pronounced threshold effect. This finding requires replication in larger, ethnically disaggregated cohorts.

Longitudinal studies are needed to establish temporal directionality and test whether crossing the BMI threshold of 21.03kg/m² during development predicts ADHD symptom trajectories. Mechanistic research should integrate neuroimaging, inflammatory biomarker panels, and gut microbiome analyses to clarify why excess adiposity ceases to be protective beyond this inflection point. Interventional trials targeting inflammation could evaluate whether reducing RDW attenuates ADHD risk in youth with low-to-normal BMI. Finally, replication in diverse international cohorts is necessary to determine if the BMI threshold is culturally or nutritionally determined.

Conclusions

Using nationally representative data, we identified a reverse J-shaped, threshold-type BMI-ADHD association in U.S. children and adolescents, characterized by a critical threshold at BMI = 21.03 kg/m² that demarcates an association of modest adiposity on ADHD risk. RDW mediated 11.4% of this association, implicating inflammation-iron pathways linking metabolic status to neurocognitive outcomes. These findings challenge linear paradigms and highlight the need for precision phenotyping in pediatric obesity-mental health research.

Declarations

Data Availability Statement

Publicly available datasets were analyzed in this study. The datasets supporting the conclusions of this study are available in the National Health and Nutrition Examination Survey repository, maintained by the Centers for Disease Control and Prevention (CDC), at <https://wwwn.cdc.gov/nchs/nhanes/default.aspx>.

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Author Contributions

JS: Conceptualization, Formal analysis, Writing-original draft. XC: Writing-review & editing, Methodology, Investigation. DL: Resources, Data curation, software. HL: Conceptualization, Supervision, Writing-review & editing, Project administration.

Conflict of Interest

The authors have no relevant financial or non-financial interests to disclose.

Ethics Statement

Our study used NHANES data was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Review Board of National Center for Health Statistics. No additional ethical approval was required to perform secondary analyses. Publicly available datasets were analyzed in this study, patient consent was not required.

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Figures

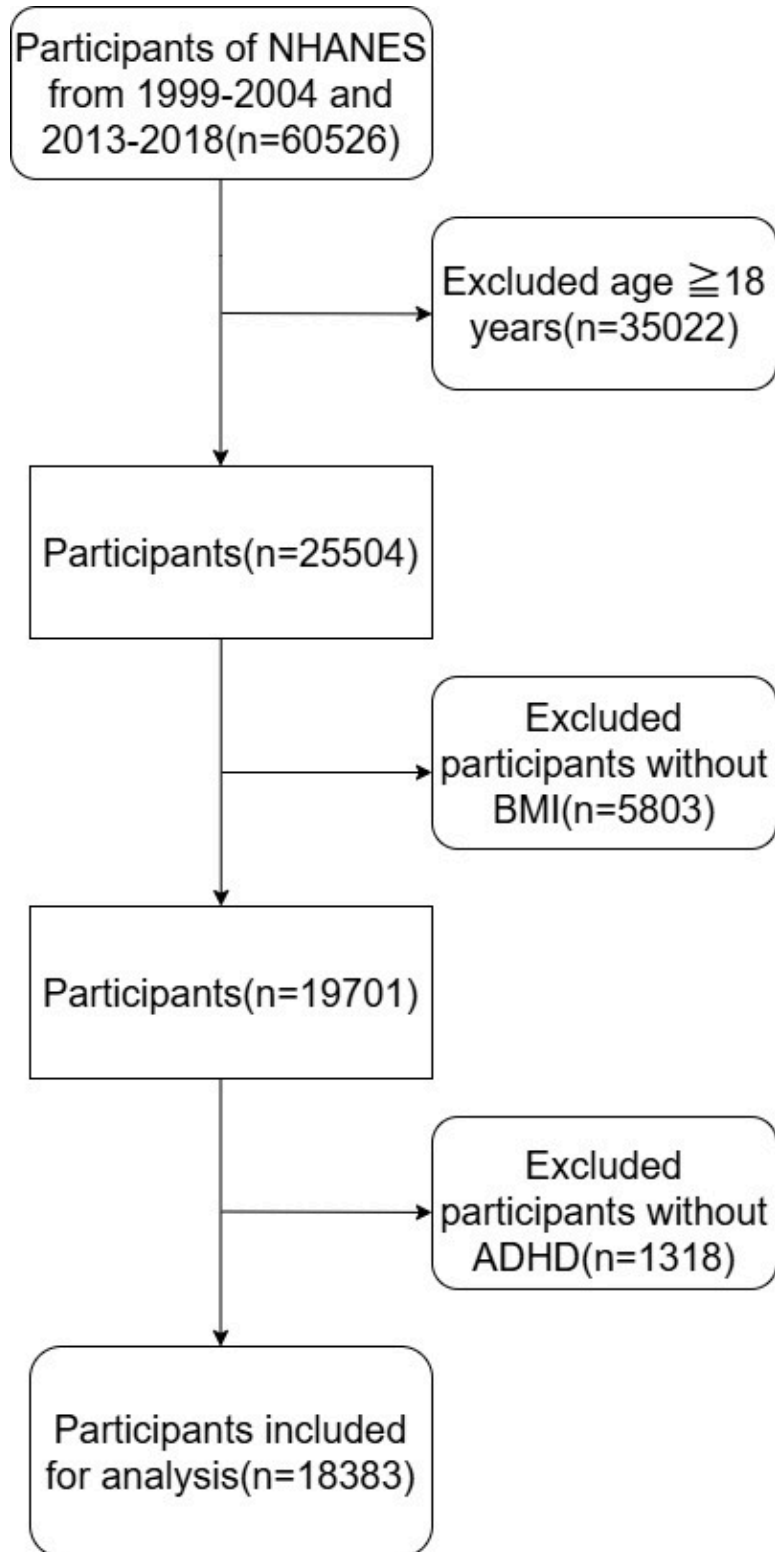


Figure 1

Flow chart of study population. NHANES, National Health and Nutrition Examination Survey; BMI,Body Mass Index; ADHD, Attention deficit hyperactivity disorder

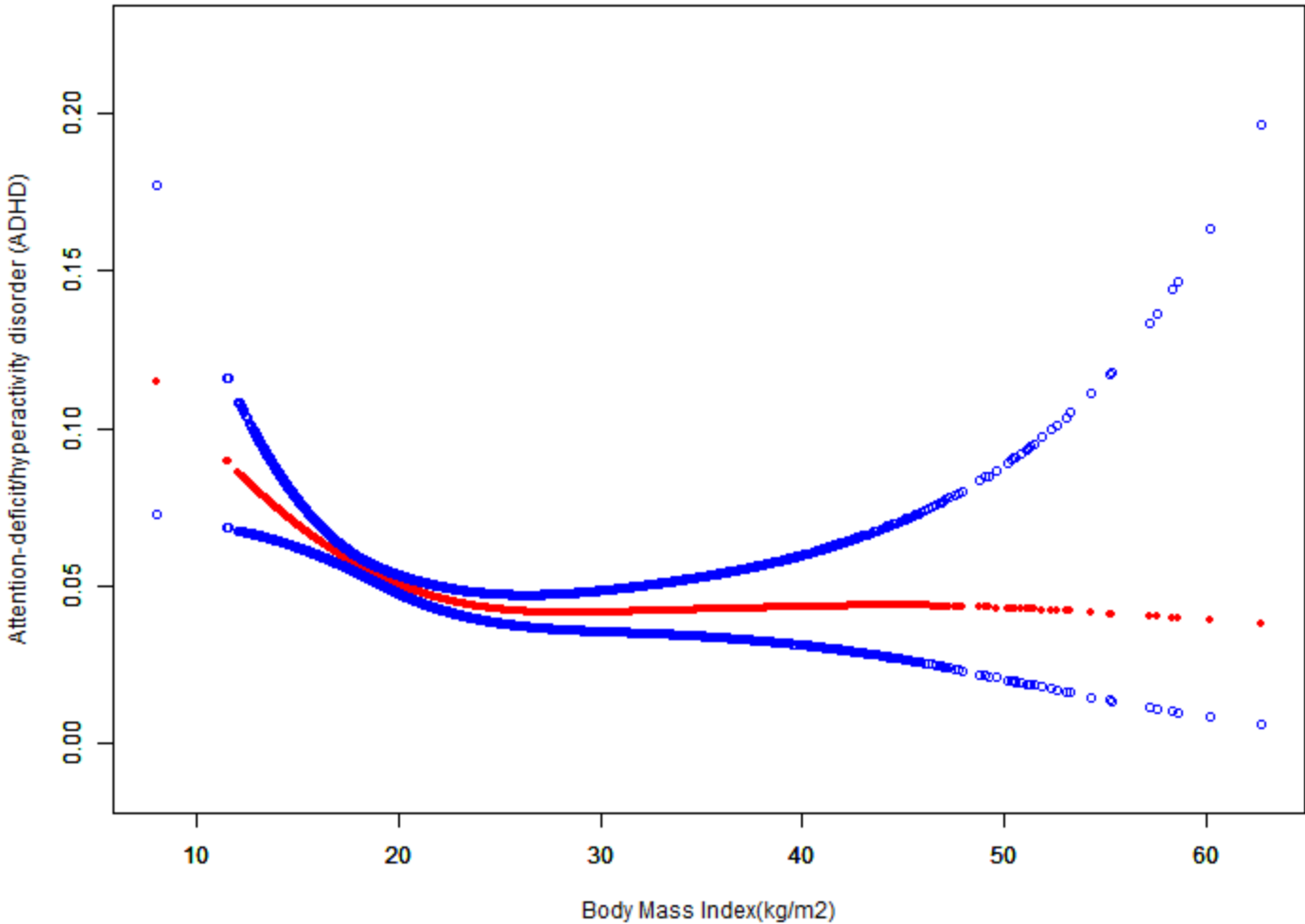


Figure 2

Associations between the BMI and ADHD, NHANES 1999-2004 and 2013-2018 (n=18,383). A threshold, nonlinear association between the BMI and ADHD was identified in a generalized additive model (GAM). The solid red line represents the smooth curve fit between the variables. The blue bands represent the 95% confidence interval derived from the fit. Adjusted for Age (years); Gender; ETH; PIR; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC

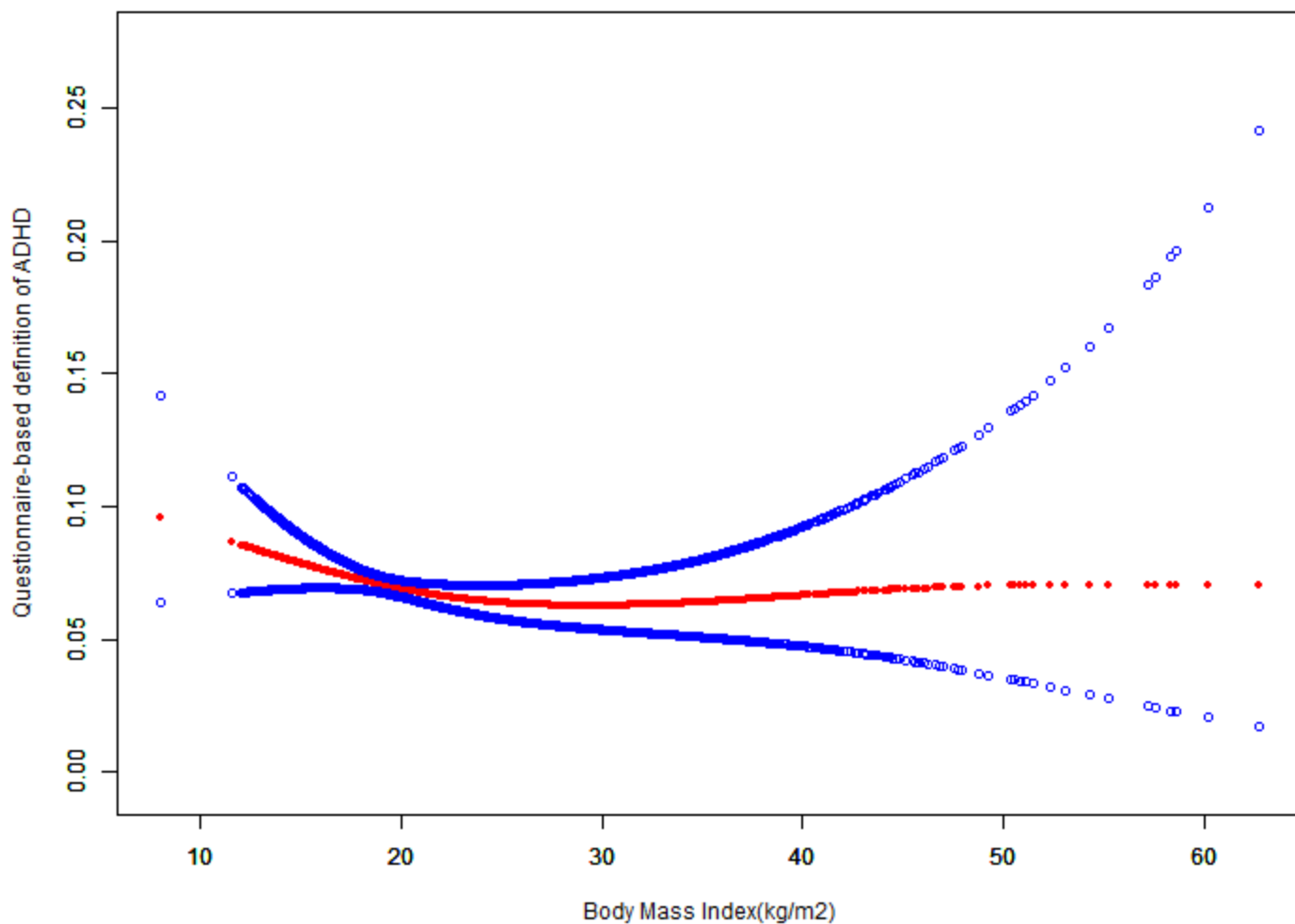


Figure 3

Associations between the BMI and ADHD stratified by Questionnaire-based definition of ADHD, using data from NHANES 1999-2004 and 2013-2018 (n=18,383). A generalized additive model (GAM) revealed a threshold, nonlinear relationship. The solid red line represents the smooth curve fit between the variables. The blue bands represent the 95% confidence interval derived from the fit. Adjusted for Age (years); Gender; ETH; PIR; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC

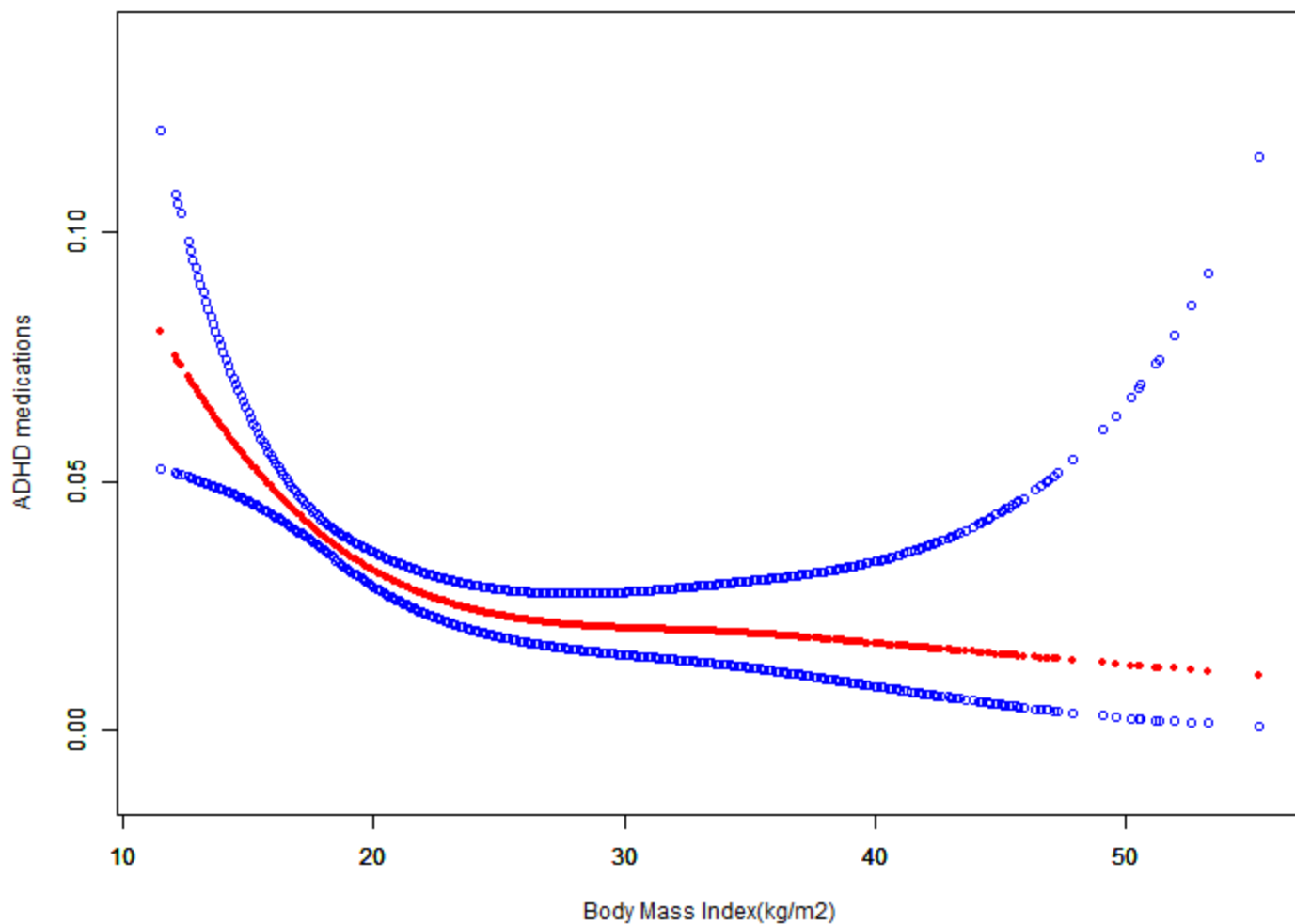


Figure 4

Associations between the BMI and ADHD stratified by ADHD medications use, using data from NHANES 1999-2004 and 2013-2018 (n=18,383). A generalized additive model (GAM) revealed a threshold, nonlinear relationship. The solid red line represents the smooth curve fit between the variables. The blue bands represent the 95% confidence interval derived from the fit. Adjusted for Age (years); Gender; ETH; PIR; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC

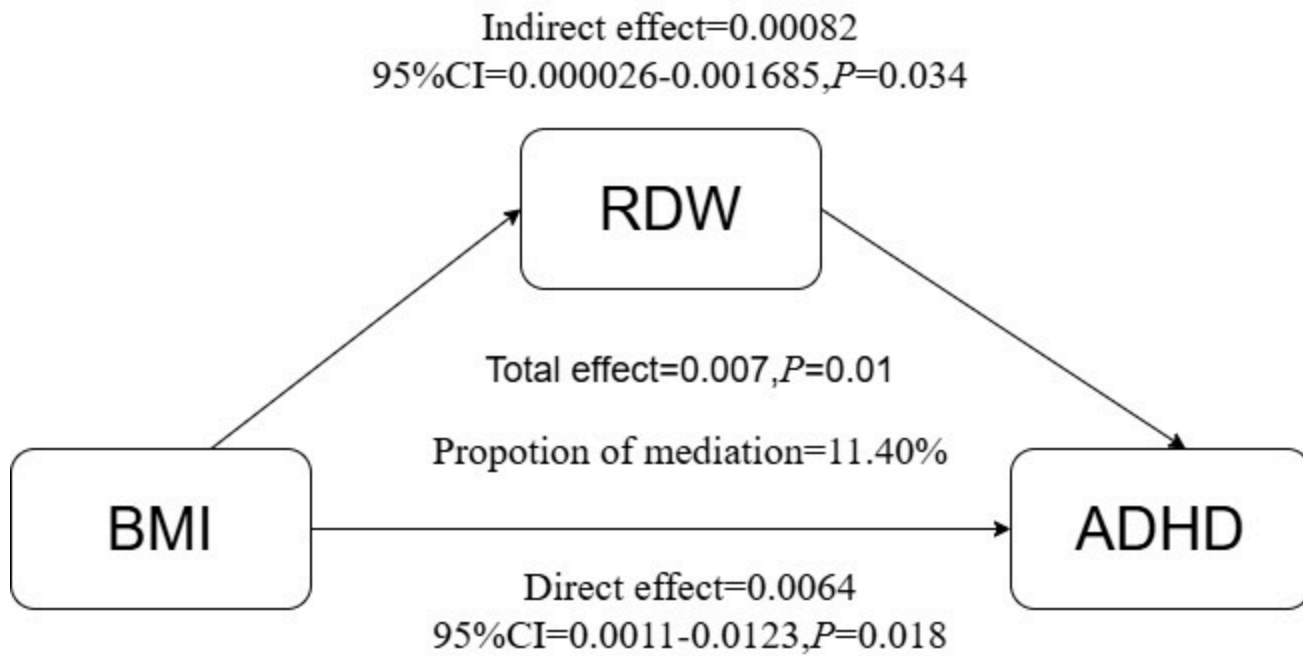


Figure 5

Path diagram of the mediation analysis of RDW on the relationship between BMI and ADHD. Adjusted for Age (years); Gender; ETH; PIR; Total physical activity (MET/week); Secondhand Smoke; Mother smoked when pregnant; WIC. BMI, Body Mass Index; ADHD, Attention deficit hyperactivity disorder; RDW, Red Cell Distribution Width