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Introduction

Obesity's link to midlife cognition is inconsistent, and may depend on sex.

- Obesity is a major driver of global morbidity, yet its cognitive link is inconsistent – some studies report a paradoxical link to preserved cognition [1,2]
- BMI is an imprecise proxy for adiposity; the Lancet Commission's framework distinguishes non-obesity, preclinical, and clinical obesity [5]
- Most prior studies capture only a single snapshot, not obesity's cumulative burden across adulthood [6]
- This study tests whether cumulative obesity burden predicts midlife cognition, and whether this differs by sex

Bogalusa Heart Study Sample

A 50-year cohort tracks obesity from childhood into midlife.

- White and Black American children followed since 1972
- This study draws upon a 20 year window of cross-sectional study surveys with obesity classification roughly every 5 years
- Included: ≥2 cardiometabolic exams (1985–2010) + cognitive assessment (2013–2016) (Figure 1)

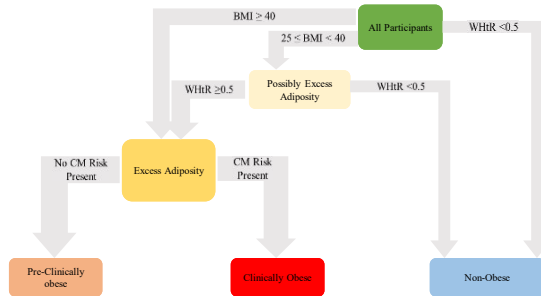


Figure 1. Lancet Commission obesity classification algorithm.

Key terms:

- GCS – sum of 9 standardized neuropsych z-scores (age/sex/race-adjusted); higher = better
- Cumulative obesity burden (AUC) – time-weighted area under the obesity classification curve, z-scored

Neuropsychological Battery: 4 Domains, 9 Tests

Attention & Processing Speed	Executive Function	Episodic Memory	Language
WAS-IV Digit Span Forward	Trail Making Test, Part B	WMS-IV Delayed Free Recall	WRAT-4 Word & Letter Reading
Trail Making Test, Part A	WAS-IV Digit Symbol Coding	WMS-IV Delayed Recognition	WAS-IV Vocabulary

Quantifying Life-Course Obesity Burden

AUC captures obesity trajectories across adulthood.

- Classified non-obese (0), preclinical (1), or clinical (2) at each of up to 6 exams; integrated across age and z-scored

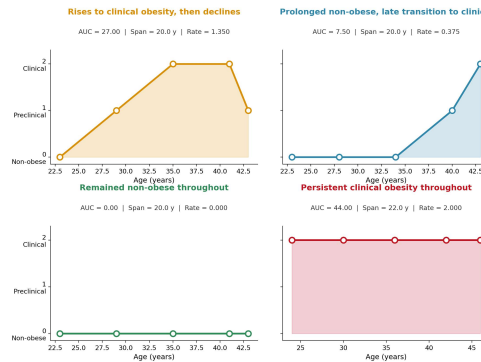


Figure 2. Trapezoidal AUC calculation for four example participants.

Cognition was scored from 9 tests across 4 domains.

- 4 domains (attention/speed, executive function, episodic memory, language); standardized for age/sex/race into a global score (GCS)

Statistical Analysis

OLS models tested whether obesity burden predicts cognition, and whether education explains it.

- OLS regression sequentially adjusted for education (Model 2), lifestyle (Model 3), both (Model 4)
- Post hoc sex-interaction and sex-stratified analyses used the same framework
- AUC–education association examined separately

Sample Characteristics

The sample (N = 965) was mostly female and White.

- 60.0% female; 65.9% White; mean age 43.2 ± 4.4y
- Clinical obesity occurred in 63.4%; preclinical-only was rare (5.0%) (Table 1)

Table 1. Participant Characteristics by Sex					
Variable	All (N=965)	Female (n=576)	Male (n=388)	Variable	All (N=965)
Demographics				Anthropometrics	
Age ± cognitive exam, y	43.18 ± 4.39	42.95 ± 4.40	43.58 ± 4.33	Height, cm	168.4 ± 9.4
Race, n (%)				BMI, kg/m²	30.7 ± 7.4
White	652 (65.9%)	370 (65.9%)	282 (67.9%)	Waist circum., cm	96.4 ± 16.4
Black	313 (34.1%)	206 (36.0%)	128 (32.7%)	Clinical conditions	
Education level, n (%)				Hypertension, n (%)	295 (30.6%)
< High school	97 (10.1%)	52 (9.0%)	45 (11.6%)	Diabetes, n (%)	36 (3.7%)
High school	461 (48.2%)	261 (45.3%)	200 (51.9%)	Cognitive measures	
Some college	112 (11.6%)	72 (12.5%)	40 (10.3%)	Global cognitive score	-0.18 ± 5.89
Bachelor's or higher	295 (30.7%)	190 (33.2%)	105 (27.2%)	Study characteristics	
				Years contributing to AUC	4.18 ± 1.49

Values are mean (SD) for continuous variables and n (%) for categorical variables. Sample restricted to participants with non-missing global cognitive score and all cross-sectional measurements contributing to the AUC calculation.

Results

Cumulative obesity burden reveals a complex, sex-specific relationship with cognition.

- Overall (N=965): no significant link to cognition, unadjusted ($\beta = -0.335$, $p = 0.062$) or fully adjusted ($\beta = -0.151$, $p = 0.342$)
- A striking AUC × sex interaction emerged unadjusted/lifestyle-adjusted ($p = 0.001$, 0.005), fading after adjusting for education ($p = 0.085$, 0.142)
- Females: higher burden linked to lower cognition, unadjusted ($\beta = -0.777$, $p < 0.001$) and fully adjusted ($\beta = -0.368$, $p = 0.050$); males: no link, positive estimates throughout – the obesity paradox (Figure 3)
- Greater obesity burden independently predicted lower educational attainment ($\beta = -0.067$, $p = 0.042$)

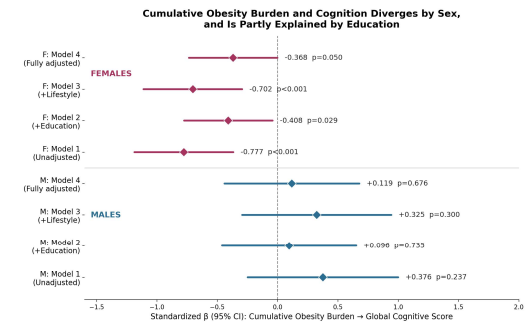


Figure 3. Cumulative obesity burden and global cognition, by sex and adjustment model.

Conclusion

Obesity's cognitive cost is sex-specific, and partly explained by education.

- No independent link overall; sex-stratified analyses revealed a borderline female-specific association after adjustment
- Education explained much of the sex difference; male pattern matched the obesity paradox

References, Contact Info, and Funding

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