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Original Research

The association between comprehensive dietary antioxidant index and erectile dysfunction in adult men: a cross-sectional study from the 2001-2004 U.S. National Health and Nutrition Examination Survey

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Abstract

Background: Increasing evidence suggests that a diet rich in antioxidants may prevent erectile dysfunction (ED), but the impact of comprehensive dietary antioxidants on ED has been little studied.

Aim: To investigate the association between the composite dietary antioxidant index (CDAI) and ED risk in adult men.

Methods: The study performed a cross-sectional analysis using data from the 2001-2004 National Health and Nutrition Examination Survey to investigate the association between the composite dietary antioxidant index (CDAI) and ED. The connection between the CDAI and ED was assessed using univariate and multivariate weighted logistic regression models, as well as the restricted cubic spline.

Outcomes: Association between the CDAI and the prevalence of ED.

Results: The study included a total of 3699 participants, among whom 1042 were diagnosed with ED, resulting in a prevalence of 28.17%. Multivariate weighted logistic regression consistently showed a negative association between the CDAI and ED (OR = 0.95, 95% CI: 0.92-0.98, $P = .005$). The group with the highest CDAI (Q4) had a 33% reduced risk of ED than the group with the lowest CDAI (Q1) when the CDAI was regarded as a categorical variable (OR = 0.67, 95% CI: 0.49-0.91, $P = .014$). Restricted cubic spline analysis showed that the CDAI was linearly related to the risk of ED (non-linearity $P = .652$). Furthermore, subgroup analysis indicated that the inverse relationship between CDAI and ED was more pronounced in individuals under 60 years of age, those with diabetes, and those without hypertension.

Clinical Implications: Dietary strategies to increase antioxidant intake might offer a potential approach to reducing ED risk and supporting men's sexual health.

Strengths and Limitations: This is a large-scale study investigating the association between the CDAI and ED. However, as a cross-sectional study, the timeliness of the dataset and the recall bias inherent in dietary data somewhat limit the reliability of the results.

Conclusion: This study identified a significant inverse association between the CDAI and ED risk among adult men in the United States; however, as a cross-sectional study, this research cannot establish causation, and further longitudinal studies are needed to validate these findings and provide more definitive evidence.

Keywords: CDAIerectile dysfunction; NHANESantioxidant; oxidative stress.

Introduction

Erectile dysfunction (ED) is a prevalent condition defined by the persistent or recurrent inability to achieve or sustain an erection sufficient for satisfactory sexual performance.[1] ED affects a substantial number of men, especially those over 40, significantly impairing their quality of life and mental well-being. Studies show that the prevalence of ED among males over the age of 40 is 46.1% in the United States, 42.1%-52.5% in Europe, and 47.4% in China, creating a significant societal burden due to its high prevalence.[2] The etiology of ED is multifactorial, including psychological, neurological, hormonal, and vascular factors. Currently, oxidative stress has been identified as a significant factor in the onset and progression of ED.[3,4] It arises from the generation of reactive oxygen species (ROS) coupled with a disruption in the organism's antioxidant defense systems, resulting in cellular impairment, endothelial dysfunction, and pathological inflammation.[5,6] Studies indicate that antioxidants can neutralize ROS, thereby fulfilling a vital function in maintaining vascular health and averting oxidative damage.[7-9] Therefore, increasing antioxidant intake through dietary adjustments may help prevent or treat ED.

The composite dietary antioxidant index (CDAI) constitutes a novel nutritional metric that offers a thorough estimate of an individual's aggregate exposure to dietary antioxidants.[10] It considers the following 6 particular antioxidants: zinc; carotenoids; selenium; and vitamins A, C, and E and provides a comprehensive assessment of their intake.[11] Previous epidemiological studies have shown that CDAI is significantly associated with a reduced risk of various chronic

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diseases, including metabolic syndrome and cardiovascular diseases.[12-16] However, Although some studies have investigated the link between specific antioxidant consumption and ED, the association between the CDAI and ED has not been explored.

In this study, we analyzed data from the National Health and Nutrition Examination Survey (NHANES) to investigate the potential association between the CDAI and ED, with the aim of providing reference for dietary guidance on male sexual health.

Materials and methods

Study population

The NHANES is a national health survey conducted by the Centers for Disease Control and Prevention and the National Center for Health Statistics (NCHS), aimed at collecting data from a nationally representative sample, including demographics and individual nutritional status and more (www.cdc.gov/nchs/nhanes/). Since the erectile function of adult male participants was only surveyed between 2001 and 2004, this study used data from the 2001-2002 and 2003-2004 NHANES cycles. The study protocol was approved by the NCHS Research Ethics Review Board, and all participants provided written informed consent.

Initially, the study identified 21 161 participants from the NHANES dataset (2001-2004). Of these, 17 045 participants had missing, "do not know," or refused responses to erectile function questions; 89 participants lacked complete data for the 6 dietary antioxidants required to calculate the CDAI; 2 participants were missing education-level data; 2 participants were missing marital status data; 220 participants lacked poverty–income ratio (PIR) data; 99 participants lacked body mass index (BMI) data; 3 participants were missing hypertension data; and 2 participants were missing alcohol consumption data. We excluded these participants. As a result, the study comprised 3699 participants in total (Figure 1).

Assessment of CDAI

Diet-derived intake information was obtained from the Detailed Dietary Interview component, which estimated the types and amounts of foods and beverages consumed in the 24 hours prior to the interview. In this study, we assessed the CDAI using data from the first 24-hour recall interview. The assessment of CDAI takes into account 6 dietary antioxidants, namely, carotenoids, vitamin A, vitamin C, vitamin E, zinc, and selenium. The calculation formula is as follows:

$$\mathrm{CDAI} = \sum_{i=1}^{n=6} \frac{\text{Individual intake} - \text{Mean}}{\text{SD}}$$

Assessment of ED

The evaluation of ED as a dependent variable was conducted using the NHANES self-report questionnaire, which inquired, "How would you describe your ability to develop and maintain an erection sufficient for sexual intercourse?" Participants had the option to select from 4 categories: "never," "sometimes," "usually," or "always or almost always." Those who answered "sometimes" or "never" to sustain an erection on this questionnaire were classified as having ED. This questionnaire item was adapted from the Massachusetts Male Aging Study. Previous studies have shown that using this item to assess ED yields results highly consistent with the IIEF-5 and that it is an effective tool for population-based research.[17]

Assessment of covariates

The covariates in this study include age, race, degree of education, BMI, PIR, marital status, drinking and smoking status, diabetes, and hypertension, all of which may be potential confounding factors influencing the relationship between the CDAI and ED. Race was divided into Mexican American, non-Hispanic White, and non-Hispanic Black groups. Age was further separated into categories of <60 and ≥ 60 years. Marital status was classified as either married/living with a partner or widowed/divorced/separated/never married. Education levels were divided into 3 categories: less than high school, completed high school, and more than high school. BMI was categorized as <25, 25-29.99, and ≥ 30 kg/m^2. PIR is categorized as <1.30, 1.31-3.49, or ≥ 3.50, corresponding to "low income," "middle income," and "high income," respectively. If a person had smoked at least 100 cigarettes over their lives, they were classified as smokers. Individuals who had drunk at least 12 alcoholic beverages in any given year of their lives were classed as drinkers. An average systolic blood pressure of at least 140 mmHg and/or an average diastolic blood pressure of at least 90 mmHg, as well as self-reported diagnosis of hypertension and antihypertensive drug use, were considered hypertension.[18,19] Participants were defined as diabetic if they had been diagnosed by a physician, had a hemoglobin A1c level above 6.5%, fasting blood glucose level ≥ 7.0 mmol/L, random blood glucose level ≥ 11.1 mmol/L, or were using diabetes medications or insulin.[20]

Statistical analyses

To mitigate the effects associated with the intricate multistage sampling design employed by NHANES, we utilized the day 1 dietary sample weight (WTDRD1) as delineated by the guidelines established by NHANES and performed weighted analyses to augment the precision of the data. Continuous variables are presented as median with interquartile range, and categorical variables are presented as counts with corresponding percentages. Subsequently, participants' baseline features were assessed based on ED status using the Kruskal–Wallis and chi-square tests. To estimate the adjusted odds ratio (OR) and their 95% confidence interval (CI) for CDAI quartiles, weighted logistic regression models were employed. The study constructed 3 weighted logistic regression models: Model 1 had no adjustments; Model 2 was adjusted for age, race, marital status, education level, and PIR; and Model 3 included further adjustments for BMI, hypertension, diabetes, smoking status, and alcohol consumption. Additionally, the study applied weighted restricted cubic splines (RCSs) to clarify the dose–response relationship between the CDAI and ED risk, adjusting for potential confounders. In order to investigate any potential differential connections between subgroups, we subsequently stratified the patients by age, race, BMI, smoking status, alcohol intake, hypertension, and diabetes and performed interaction analyses. Statistical analyses were performed using R software (version 4.4.1; R Foundation, Vienna, Austria; http://www.R-project.org), with statistical significance set at a 2-sided P value of less than .05.

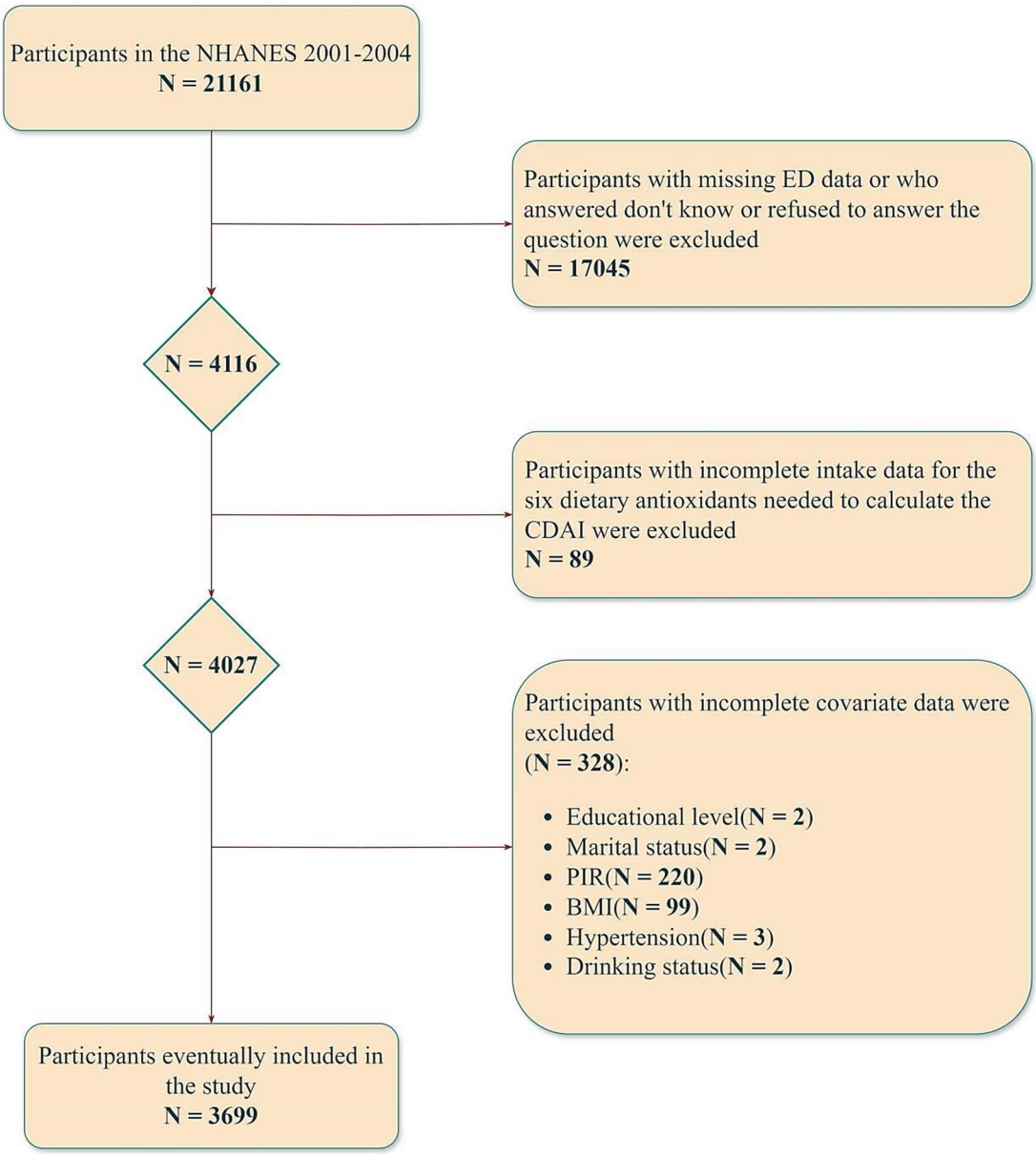

Figure 1. Flowchart of participant selection procedure.

Results

Baseline characteristics of participants

In total, 3699 eligible participants, aged 20-85 years, were included in the final analysis. As shown in Table 1, among these participants, 1042 self-reported ED, and 2657 reported normal erectile function, resulting in an ED prevalence of 28.17%. In the ED group, approximately 73% of participants were aged ≥60 years, 23% had an education level below high school, 27% had a household income classified as low, and 31% had a BMI ≥30 kg/m^2; 70% of the subjects exhibited a prior history of smoking, while 81% demonstrated a background of alcohol consumption. In addition, 23% were diagnosed with diabetes, and 67% were found to have hypertension in the ED group. Significant statistical differences were noted between the 2 cohorts in terms of age, race, marital status, PIR, level of education, BMI, smoking status, drinking status, and the prevalence of hypertension, diabetes, and CDAI ($P < .05$).

Association of CDAI with ED

Weighted multivariable logistic regression analysis was employed to investigate the association between CDAI levels and the risk of ED across different models. As shown in Table 2, both univariate and multivariate weighted logistic regression models indicated a negative association between CDAI and the risk of ED. Furthermore, we converted CDAI into a categorical variable represented by quartiles for enhanced analytical scrutiny. In Model 3, subsequent to the adjustment for all conceivable covariates, participants situated in the uppermost quartile (Q4) of CDAI exhibited a 33% diminished risk of experiencing ED in comparison to their counterparts in the lowest quartile (Q1) (Q4 vs Q1, OR: 0.67; 95% CI: 0.49-0.91; $P = .014$, trend $P = .008$).

The dose–response curve analysis using RCSs demonstrated a linear relationship between the CDAI and ED risk, showing that as the CDAI increases, the risk of ED decreases (overall $P = .004$; non-linearity $P = .652$; Figure 2).

Table 1. Characteristics of the study participants.

Variable	Total 3699 (100 %)	Non-ED 2657 (71.83 %)	ED 1042 (28.17 %)	*P* value
Age				<.001
20-59	2464 (66.61%)	2190 (82.42%)	274 (26.30%)	
≥60	1235 (33.39%)	467 (17.58%)	768 (73.70%)	
Race				<.001
Mexican American	750 (20.28%)	540 (20.32%)	210 (20.15%)	
Non-Hispanic White	2016 (54.50%)	1397 (52.58%)	619 (59.40%)	
Non-Hispanic Black	699 (18.90%)	541 (20.36%)	158 (15.16%)	
Other race	234 (6.33%)	179 (6.74%)	55 (5.28%)	
Marital status				<.001
Married/Living with a partner	1156 (31.25%)	885 (33.31%)	271 (26.01%)	
Widowed/Divorced/Separated/Never married	2543 (68.75%)	1772 (66.69%)	771 (73.99%)	
Education level				<.001
Less than high school	477 (12.90%)	237 (8.920%)	240 (23.03%)	
Completed high school	547 (14.79%)	373 (14.04%)	174 (16.70%)	
Above high school	2675 (72.32%)	2047 (77.04%)	628 (60.27%)	
PIR				<.001
Low income	880 (23.79%)	600 (22.58%)	280 (26.87%)	
Middle income	1452 (39.25%)	998 (37.56%)	454 (43.57%)	
High income	1367 (36.96%)	1059 (39.86%)	308 (29.56%)	
BMI				.038
<25	1105 (29.87%)	821 (30.90%)	284 (27.26%)	
25-29.99	1547 (41.82%)	1110 (41.78%)	437 (41.94%)	
≥30	1047 (28.30%)	726 (27.32%)	321 (30.81%)	
Smoking status				<.001
No	1497 (40.47%)	1184 (44.56%)	313 (30.04%)	
Yes	2202 (59.53%)	1473 (55.44%)	729 (69.96%)	
Drinking status				.036
No	640 (17.30%)	438 (16.48%)	202 (19.39%)	
Yes	3059 (82.70%)	2219 (83.52%)	840 (80.61%)	
Diabetes				<.001
No	3327 (89.94%)	2524 (94.99%)	803 (77.06%)	
Yes	372 (10.06%)	133 (5.01%)	239 (22.94%)	
Hypertension				<.001
No	2015 (54.47%)	1674 (63.00%)	341 (32.73%)	
Yes	1684 (45.53%)	983 (37.00%)	701 (67.27%)	
CDAI (continuous)	-0.7 (-2.4, 1.4)	-0.4 (-2.2, 1.8)	-1.3 (-2.7, 0.4)	<.001
CDAI (categorical)				<.001
Q1	1054 (28.49%)	691 (26.01%)	363 (34.84%)	
Q2	931 (25.17%)	630 (23.71%)	301 (28.89%)	
Q3	875 (23.66%)	651 (24.50%)	224 (21.50%)	
Q4	839 (22.68%)	685 (25.78%)	154 (14.78%)	

Table 2. The association between CDAI and ED.

Characteristics	Model1		Model2		Model3	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
CDAI (continuous)	0.91 (0.89, 0.94)	<.001	0.94 (0.91, 0.97)	<.001	0.95 (0.92, 0.98)	.005
CDAI (quartile)						
Q1	Ref	Ref	Ref	Ref	Ref	Ref
Q2	0.93 (0.71, 1.22)	.594	1.07 (0.75, 1.50)	0.705	1.06 (0.74, 1.53)	.731
Q3	0.65 (0.50, 0.85)	.003	0.73 (0.53, 1.01)	0.054	0.76 (0.55, 1.07)	.108
Q4	0.45 (0.35, 0.59)	<.001	0.63 (0.46, 0.86)	0.006	0.67 (0.49, 0.91)	.014
P for trend		<.001		0.002		.008

Subgroup analysis

We conducted a stratified analysis to evaluate whether the relationship between the CDAI and ED differs across various subgroups (Figure 3). Our findings indicated interactions between age, drinking status, hypertension, and CDAI (*P* for interaction <.05). Specifically, the effect of CDAI in reducing ED risk was more pronounced among participants under 60 years old, those who consumed alcohol, and those without hypertension, after adjusting for covariates. In other subgroup analyses, there was no significant difference in the relationship between CDAI and ED risk (*P* for interaction >.05).

Discussion

This study explored the relationship between CDAI and ED risk using data from the NHANES public database and found

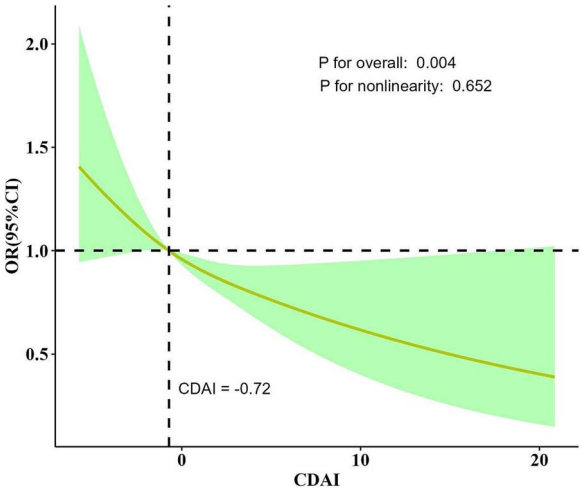

Figure 2. The dose–response relationship of the CDAI with the risk of ED.

that whether CDAI was quantified as a continuous variable or as quartiles, both univariable and multivariable models indicated an inverse relationship between CDAI levels and ED risk. Additionally, we found noteworthy interactions between CDAI and certain ED risk variables in the subgroup analysis. Specifically, it was found that most groups had a negative link between CDAI and ED; this relationship was more pronounced in people under 60, those with diabetes, and people without hypertension.

Oxidative stress is characterized by an imbalance in the production of antioxidants and pro-oxidants, resulting in oxidative damage to DNA, proteins, carbohydrates, and lipids, leading to apoptosis, organ dysfunction, and ultimately a range of health issues.[21,22] Oxidative stress plays a critical role in the pathogenesis of ED. Studies have shown that penile tissues in patients with ED exhibit significant oxidative stress, characterized by elevated levels of ROS and reduced activity of antioxidant defense systems. This state of oxidative stress leads to cellular damage in penile tissues, subsequently impairing erectile function. On one hand, oxidative stress can damage vascular endothelial cells and hinder the production of nitric oxide (NO), thereby affecting smooth muscle relaxation and the erection process.[23] Nitric oxide is a crucial signaling molecule that promotes penile blood flow and plays a key role in the normal functioning of erectile processes.[24] The reduction in NO production caused by oxidative stress directly affects penile blood flow, thus impairing erectile function.[25] On the other hand, oxidative stress can also trigger inflammatory responses, leading to vascular and nerve damage, which further impairs erectile response. Numerous studies have proven the link between ED and chronic inflammation, with oxidative stress serving as a major mediator in this process.[24,26] Furthermore, oxidative stress plays a crucial role in the pathogenesis of metabolic syndrome and cardiovascular diseases.[27] Studies have shown that individuals with metabolic syndrome or cardiovascular diseases are more likely to develop ED. This association may arise from shared pathophysiological mechanisms, including vascular damage, chronic inflammation, and neural injury, with oxidative stress potentially being a key factor in this process.[28,29] Exogenous antioxidants like carotenoids, polyphenols, vitamins C and E, and flavonoids help reduce oxidative stress by scavenging free radicals and ROS.[30,31] This helps to protect cellular lipids, proteins, and nucleic acids from oxidative damage.[32] Consuming a diet rich in antioxidants is associated with a lower risk of developing chronic diseases like cardiovascular disease, cancer, diabetes, and neurodegenerative disorders.[32,33]

Previous research has assessed the association between the consumption of specific antioxidants and ED, finding that the consumption of antioxidants such as flavonoids, carotenoids, zinc, selenium, and vitamin E is inversely correlated with the risk of developing ED.[34-38] These studies primarily focus on the effects of individual dietary antioxidants on ED. While individual antioxidants might be helpful in preventing the onset of ED, considering the natural nutritional combinations found in foods and potential biological interactions among dietary antioxidants, evaluating the total intake of antioxidants may offer a more complete picture. As a composite response indicator of the level of dietary antioxidant intake, the CDAI has been found to be associated with a reduced risk of a number of diseases, including stroke, coronary heart disease, and hypertension.[15,39,40] Nevertheless, no studies have been found to have examined the relationship between the CDAI and ED. Our findings complement and support the favorable effect of increased CDAI in lowering the risk of ED in men.

However, our study has certain limitations. One of the primary limitations of this study is the time frame of the data used. The dataset from the 2001-2004 NHANES represents information from more than 20 years ago. While this dataset remains one of the most comprehensive sources for exploring the relationship between dietary factors and ED, its age may limit the generalizability of the findings to current populations due to potential changes in dietary patterns, healthcare access, and population demographics over time. Future research utilizing more recent data would be valuable to confirm and extend these findings. Another important limitation arises from the cross-sectional design of the study, which allows us to infer only an association between the CDAI and ED, rather than establish a causal relationship. Additionally, dietary intake was assessed using 24-hour dietary recalls, which, although widely used, are still susceptible to recall bias and measurement errors. Future studies that use multiple dietary recalls or food frequency questionnaires could improve the accuracy and comprehensiveness of dietary assessments. Moreover, observational studies are susceptible to residual confounding. Even though this study used multivariable models to adjust for potential confounders, the results may still be influenced by unaccounted confounding factors. Finally, since the study population consisted of Americans, the findings may not be generalizable to other populations. Further research is required to ascertain if the effects of CDAI on ED are applicable to diverse populations.

Conclusion

Our findings suggest a significant inverse association between CDAI and ED risk in adult men. While these results highlight the potential importance of antioxidant-rich diets in supporting erectile function, further research is needed to establish causality and provide clearer guidance for clinical and public health practice.

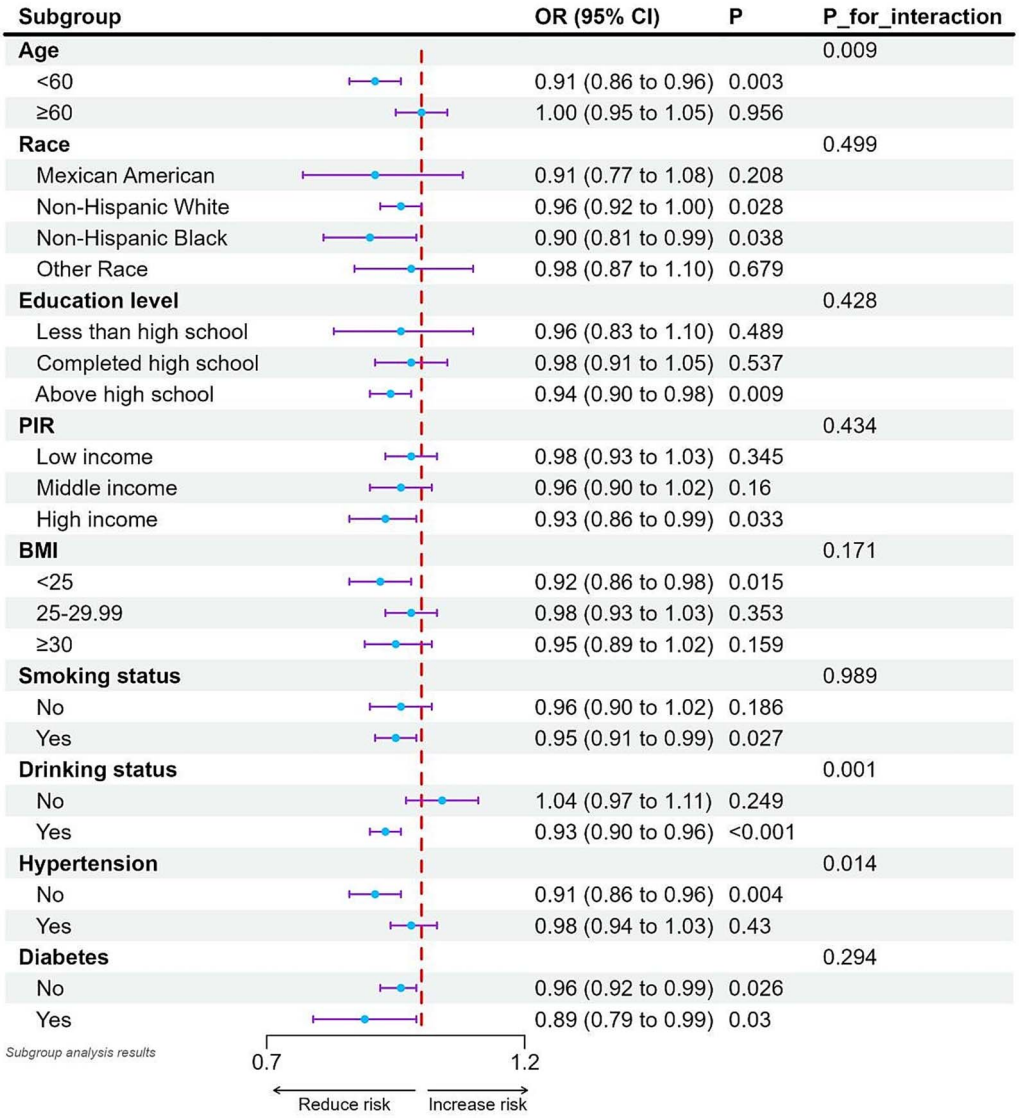

Figure 3. Relationship between the CDAI and ED in each subgroup. Each subgroup was adjusted for all factors except the grouping factor itself.

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Author contributions

Conceptualization, M.L.; Methods, M.L.; Formal Analysis, M.L.; Investigation, M.L.; Resources, P.Z. and M.L.; Data organization, M.L.; Writing—original draft preparation, P.Z. and M.L.; Writing—review and editing, P.Z. and M.L.; Visualization, M.L.; Supervision, P.Z.; Project management, P.Z. All authors have read and agreed to the published version of the manuscript.

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Conflicts of interest

None declared.

Data availability

All datasets used during the current study can be found on the NHANES website (https://www.cdc.gov/nchs/nhanes).

Ethics and informed consent statement

The NHANES is a publicly available, free database that has been approved by the NCHS Research Ethics Review Board and agreed to by all participants.

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