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# Association between dietary oxidative balance scores and myocardial infarction in diabetic patients: insights from NHANES 1999–2018

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## Abstract

**Background** Myocardial infarction (MI) poses a serious health threat to diabetic patients, who are particularly vulnerable due to heightened oxidative stress. The dietary oxidative balance score (DOBS) quantifies the overall oxidative profile of the diet and may reflect diet-related cardiovascular risk.

**Objective** This study aimed to evaluate the association between DOBS and the risk of MI among diabetic individuals using a nationally representative U.S. population.

**Methods** We analyzed data from 5,002 diabetic participants in the NHANES 1999–2018 cycles. DOBS was calculated based on 16 pro- and antioxidant nutrients using two 24-hour dietary recalls. Logistic regression models and 1:1 propensity score matching (PSM) were employed to assess the association between DOBS and self-reported history of MI, adjusting for demographic, clinical, and lifestyle covariates. Restricted cubic spline (RCS) models were used to evaluate potential nonlinear relationships.

**Results** A one-point increase in DOBS was associated with a 3% lower odds of MI in both unadjusted and fully adjusted models (adjusted OR=0.97, 95% CI: 0.95–0.99). Participants in the highest DOBS tertile had a 38% lower odds of MI compared to the lowest tertile (OR=0.62, 95% CI: 0.43–0.87), and this association remained consistent in the matched cohort (OR=0.72, 95% CI: 0.48–0.88). While formal tests for nonlinearity were not significant, RCS curves suggested a threshold effect with diminishing benefits at higher DOBS levels. Subgroup and sensitivity analyses confirmed the robustness of the findings.

**Conclusion** Higher DOBS is associated with a lower likelihood of MI among diabetic patients. These findings highlight the potential value of antioxidant-rich dietary patterns in cardiovascular risk assessment. However, given geographic and cultural variability in diet, further validation is needed in diverse populations and prospective study settings.

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**Keywords** DOBS, Oxidative stress, Myocardial infarction, Diabetes, NHANES, Antioxidant diet, Propensity score matching

## Introduction

Myocardial infarction (MI), commonly known as a heart attack, is a type of acute coronary artery disease caused by the sudden interruption of the blood supply to the heart muscle, leading to the death of myocardial cells. It is one of the leading causes of death and disability worldwide. As of 2024, it is estimated that approximately 3 million people worldwide will be affected by MI, with an incidence rate of 100–200 cases per 100,000 people [1]. In the United States alone, approximately 605,000 new cases are reported each year, underscoring the significant burden of this disease [1]. The risk of MI is significantly increased in individuals with diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia and associated with various cardiovascular complications [2, 3]. Previous studies have indicated that individuals with diabetes face a 2- to 4-fold greater risk of experiencing MI than do those without diabetes [4, 5]. Managing and mitigating the risk factors contributing to MI in diabetic patients is crucial for improving outcomes and reducing the burden of cardiovascular disease (CVD) in this high-risk population.

Oxidative stress has emerged as a critical factor in the pathogenesis of cardiovascular diseases, including MI [6–8]. Oxidative stress refers to an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense mechanisms. This imbalance promotes the development and progression of atherosclerosis, which is the primary underlying cause of myocardial infarction [7, 9]. In individuals with diabetes, oxidative stress is exacerbated by chronic hyperglycemia, further increasing the risk of MI [10, 11].

Diet plays a pivotal role in modulating oxidative stress. Diets rich in antioxidants, such as fruits, vegetables, and whole grains, have been shown to reduce oxidative stress, whereas diets high in pro-oxidants, including processed foods and those rich in saturated fats, may increase oxidative stress [12, 13]. The dietary oxidative balance score (DOBS) is an index that quantifies the balance between pro-oxidant and antioxidant components of the diet [14–16]. A higher concentration of DOBS reflects a diet with greater antioxidant potential, which could mitigate oxidative stress and reduce the risk of MI. Previous studies have explored the relationships among diet, oxidative stress, and cardiovascular outcomes [17–19], but there is limited evidence specifically examining the associations between DOBS and MI in diabetic patients. Given the high oxidative stress burden in individuals with diabetes [10, 20] and the critical role of diet in managing this

stress, investigating the impact of DOBS on MI risk in this population is highly important for public health.

This study aimed to explore the association between dietary oxidative balance scores and the prevalence of myocardial infarction in diabetic patients via data from the National Health and Nutrition Examination Survey (NHANES) 1999–2018. By providing insights into the relationship between diet-induced oxidative stress and MI risk, this research could inform dietary recommendations and interventions aimed at reducing the cardiovascular burden in diabetic individuals.

## Methods

### Study design and data source

This study is an observational study based on cross-sectional data, with data sourced from the publicly available National Health and Nutrition Examination Survey (NHANES) from 1999 to 2018. The NHANES is a nationally representative health survey aimed at assessing the health and nutritional status of the U.S. population. The survey employs a stratified multistage probability sampling design to ensure the representativeness of the sample. This study analyzed data from adult diabetic patients who participated in the NHANES survey between 1999 and 2018. The NHANES data used in this study are publicly available and were utilized for secondary data analysis. All participants provided informed consent. The analysis process of this study adhered to ethical review standards and received an exemption from the Ethics Review Board of the National Center for Health Statistics, USA.

### Study population

The study included individuals aged 18 years and older diagnosed with diabetes from the 1999–2018 NHANES database, excluding individuals with missing diet, diabetes, and MI data. Diabetes was defined on the basis of a self-reported physician diagnosis (doctors tell you that you have diabetes?), a fasting blood glucose level  $\geq 7.0$  mmol/L or a random blood glucose level  $\geq 11.1$  mmol/L.

### Variable definitions

#### Exposure variable

Dietary Oxidative Balance Scores (DOBS): DOBS were calculated by integrating the intake of 16 dietary nutrients, including 14 antioxidants (total dietary fiber, riboflavin, niacin, vitamin B6, total folate, vitamin B12, vitamin C, vitamin E, carotene, calcium, magnesium, zinc, copper, and selenium) and 2 pro-oxidants (total fat and iron). Dietary intake data were obtained based on

the average of two 24-hour dietary recalls, and each participant's DOBS were calculated via established dietary scoring methods [14, 21]. Each nutrient was categorized into low, medium, and high groups on the basis of tertiles, with oxidative stress scores assigned to each group accordingly. The final DOBS was calculated by summing these scores. Higher scores indicate a relatively higher intake of antioxidants in the diet. The detailed scoring criteria can be found in Table 1.

### Outcome variable

**Myocardial Infarction (MI):** MI was defined on the basis of participants' self-reported response to the following question [22]: "Has a doctor or other health professional ever told you that you had a heart attack or myocardial infarction?"

### Covariates

To control for potential confounding factors, the following covariates were considered in this study: age, sex, ethnicity, education level, marital status, body mass index (BMI), drinking status, smoking status, sedentary time, diabetes drugs, myocardial infarction drugs and history of hypertension, hyperlipidemia and chronic kidney disease (CKD). BMI was calculated on the basis of body mass (kilograms) and height (m [2]). Drinking status was categorized as follows: "Never drinker" was defined as someone who has never consumed more than 12 alcoholic drinks in their lifetime; "Former drinker" was defined as someone who has consumed at least 12 alcoholic drinks in their lifetime but has not consumed any alcoholic drinks in the past year; "Current drinker" was defined as someone who has consumed at least 12

alcoholic drinks in their lifetime and has also consumed alcohol in the past year. Smoking status was categorized as follows: "Never smoker" was defined as someone who has never smoked more than 100 cigarettes in their lifetime; "Former smoker" was defined as someone who has smoked at least 100 cigarettes in their lifetime but is not currently smoking; "Current smoker" was defined as someone who has smoked at least 100 cigarettes in their lifetime and is currently smoking. Sedentary time was assessed by asked participants to report the average amount of time spent sitting during a typical day. This included time spent sitting at school, home, or in transit, as well as time spent reading, using a computer, or watching television, but excluded time spent sleeping. The total sedentary time was recorded in minutes and converted to hours for analysis. Use of diabetes and myocardial infarction medications was identified based on the NHANES prescription medication dataset using free-text matching of drug names in the RXDDRUG variable. Antidiabetic medications included biguanides, sulfonylureas, meglitinides, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, and insulin or its analogues. Medications related to myocardial infarction included antiplatelet agents, statins, beta-blockers, ACE inhibitors, and angiotensin II receptor blockers (ARBs). Participants were classified as medication users if any relevant drug was recorded in their prescription history. A history of hypertension, hyperlipidemia, or chronic kidney disease was defined through self-reported responses to the following question: "Have you ever been told by a doctor or other health professional that you have ~?"

### Multiple imputation for missing data

To manage missing values in the covariates, we applied multiple imputation using chained equations (MICE). This method operates under the assumption that data are missing at random (MAR), utilizing all available information to minimize bias. We generated 20 imputed datasets and conducted the analyses independently on each. The results were then combined following Rubin's rules to produce final estimates, with standard errors appropriately adjusted. All covariates were incorporated into the imputation process.

### Statistical analysis

Data analysis was conducted via Stata 17.0 software. All analyses accounted for the complex sampling design of the NHANES and applied appropriate weighting to ensure the national representativeness of the results. The DOBS were categorized into tertiles, and baseline characteristics were compared across different groups. Means, standard deviations (SDs), and percentages were calculated for all study variables. One-way ANOVA and chi-square tests were used to examine whether there

**Table 1** Assignment scheme for dietary oxidative balance scores

DOBS components	Property	Score		
		0	1	2
Dietary fiber (g/d)	A	< 10.81	10.81–17.90	≥ 17.90
Riboflavin (mg/d)	A	< 1.35	1.35–2.07	≥ 2.07
Niacin (mg/d)	A	< 17.49	17.49–24.52	≥ 24.52
Vitamin B6 (mg/d)	A	< 1.20	1.20–1.92	≥ 1.92
Total folate (mcg/d)	A	< 245.95	245.95–398.03	≥ 398.03
Vitamin B12 (mcg/d)	A	< 2.33	2.33–4.71	≥ 4.71
Vitamin C (mg/d)	A	< 28.02	28.02–82.10	≥ 82.10
Vitamin E (mg/d)	A	< 4.40	4.40–7.81	≥ 7.81
Carotene (mcg/d)	A	< 392.01	392.01–1489.05	≥ 1489.05
Calcium (mg/d)	A	< 544.78	544.78–924.05	≥ 924.05
Magnesium (mg/d)	A	< 201.00	201.00–302.00	≥ 302.00
Zinc (mg/d)	A	< 6.99	6.99–11.33	≥ 11.33
Copper (mg/d)	A	< 0.84	0.84–1.23	≥ 1.23
Selenium (mcg/d)	A	< 74.61	74.61–115.47	≥ 115.47
Total fat (g/d)	P	≥ 82.05	49.75–82.05	< 49.75
Iron (mg/d)	P	≥ 15.11	9.54–15.11	< 9.54

Abbreviations: DOBS=dietary oxidative balance score, A=antioxidant and P=pro-oxidant

were significant differences between the groups. Step-wise adjusted logistic regression models were used to assess the relationship between DOBS and MI in diabetic patients. The models were as follows: Model 1 was unadjusted; Model 2 was adjusted for age, sex, and ethnicity; Model 3 was further adjusted for education level, marital status, BMI, drinking, smoking, hypertension, hyperlipidemia, and CKD. Restricted cubic splines (RCS) were used to evaluate the nonlinear relationship between DOBS and MI among diabetic patients, and a joint Wald test was conducted on the spline terms beyond the linear component. Subgroup analysis was conducted according to sex, age, BMI, smoking status, drinking status, hypertension status, hyperlipidemia status, and CKD status to further explore effect heterogeneity across different populations. Sensitivity analysis was performed using diabetic patients from the 2009–2018 cycle for internal validation to ensure the robustness of the results. All the statistical analyses were conducted via two-sided tests, with  $p < 0.05$  considered statistically significant.

### Propensity score matching (PSM)

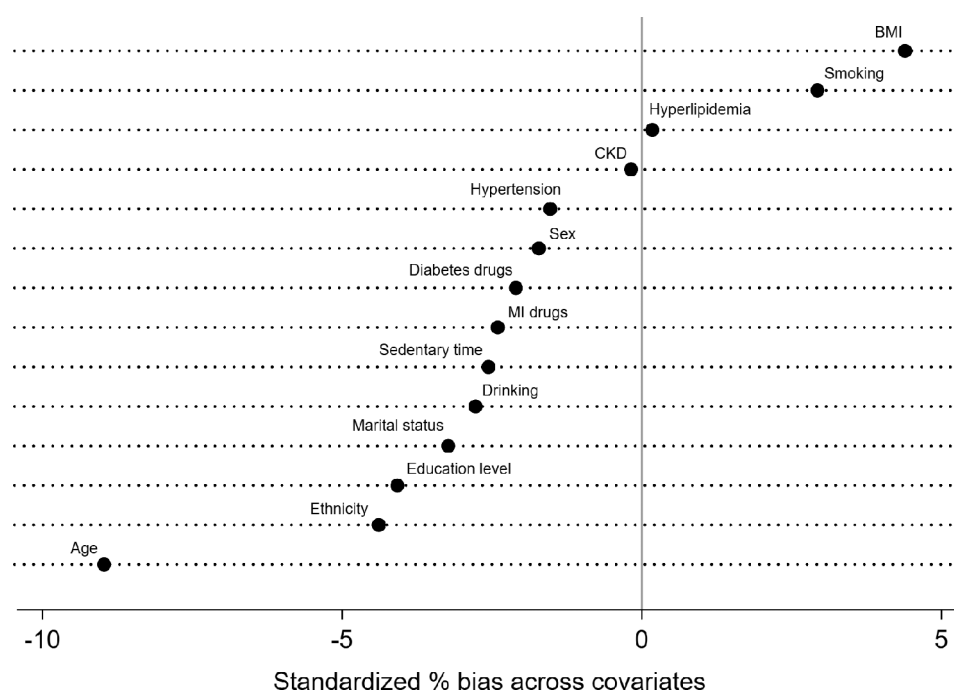
To further reduce potential confounding and simulate a quasi-randomized comparison, propensity score matching (PSM) was conducted as a sensitivity analysis. The propensity score for each participant was estimated using a logistic regression model that included age, sex, ethnicity, education level, marital status, BMI, smoking status, drinking status, sedentary time, diabetes drugs,

myocardial infarction drugs, hypertension, hyperlipidemia, and CKD. Participants in the higher DOBS tertile were matched 1:1 with those in the lowest tertile using nearest-neighbor matching with a caliper of 0.2 without replacement. Covariate balance after matching was assessed using standardized mean differences (SMDs), with values below 0.1 considered acceptable. All covariates demonstrated adequate balance ( $\text{SMD} < 10\%$ , Fig. 1). The association between DOBS and MI was then re-evaluated in the matched cohort using logistic regression.

## Results

### Participant characteristics

A total of 5002 diabetic patients were included in the study, and their baseline characteristics were stratified by tertiles of DOBS (Table 2). Differences in demographic, lifestyle, and health-related factors were observed across DOBS tertiles. The participants in the highest tertile (Q3) of DOBS had a mean age of 60.64 years, whereas those in the lowest tertile (Q1) had a mean age of 63.01 years ( $p < 0.001$ ). The gender distribution also differed notably, with 66.0% of the participants in Q3 being male, whereas 38.1% were in Q1 ( $p < 0.001$ ). Smoking and hypertension rates decreased with increasing DOBS. For example, current smokers comprised 13.7% of Q3, compared with 18.5% in Q1 ( $p < 0.001$ ), and the prevalence of hypertension was lower in Q3 (66.9%) than in Q1 (73.2%) ( $p < 0.001$ ). CKD and MI also tended to decrease with increasing DOBS. CKD was present in



**Fig. 1** Standardized mean differences (SMD) across covariates after 1:1 propensity score matching. All covariates demonstrated adequate balance ( $\text{SMD} < 10\%$ )

**Table 2** Baseline characteristics stratified by DOBS tertiles

Factor	Q1 (N = 1776)	Q2 (N = 1632)	Q3 (N = 1594)	P value
DOBS	8.85 ± 2.85	16.98 ± 2.00	24.08 ± 2.20	< 0.001
Age, year	63.01 ± 12.83	62.15 ± 12.99	60.64 ± 13.06	< 0.001
Sex				< 0.001
Male	676 (38.1%)	830 (50.9%)	1052 (66.0%)	
Female	1100 (61.9%)	802 (49.1%)	542 (34.0%)	
Ethnicity				< 0.001
Mexican American	300 (16.9%)	313 (19.2%)	336 (21.1%)	
Other Hispanic	175 (9.9%)	171 (10.5%)	118 (7.4%)	
Non-Hispanic White	578 (32.5%)	574 (35.2%)	645 (40.5%)	
Non-Hispanic Black	579 (32.6%)	425 (26.0%)	347 (21.8%)	
Other Race	144 (8.1%)	149 (9.1%)	148 (9.3%)	
Education Level				< 0.001
Less than high school	744 (42.0%)	567 (34.8%)	468 (29.4%)	
High school graduate	418 (23.6%)	377 (23.1%)	351 (22.1%)	
More than high school	610 (34.4%)	686 (42.1%)	772 (48.5%)	
Marital Status				< 0.001
Married	873 (49.2%)	913 (56.0%)	979 (61.5%)	
Never Married	173 (9.7%)	145 (8.9%)	119 (7.5%)	
Others	729 (41.1%)	573 (35.1%)	494 (31.0%)	
BMI, kg/m <sup>2</sup>	32.44 ± 7.54	32.39 ± 7.78	32.38 ± 7.38	0.960
Drinking				0.150
Never	338 (52.5%)	259 (49.1%)	179 (47.5%)	
Former	185 (28.7%)	177 (33.5%)	113 (30.0%)	
Current	121 (18.8%)	92 (17.4%)	85 (22.5%)	
Smoking				< 0.001
Never	892 (50.2%)	813 (49.8%)	765 (48.0%)	
Former	556 (31.3%)	571 (35.0%)	609 (38.2%)	
Current	328 (18.5%)	248 (15.2%)	219 (13.7%)	
Hypertension	1296 (73.2%)	1136 (69.8%)	1064 (66.9%)	< 0.001
Hyperlipidemia	1056 (63.5%)	984 (63.4%)	963 (63.4%)	0.990
CKD	225 (12.7%)	160 (9.8%)	112 (7.0%)	< 0.001
Sedentary time, hours	7.07 ± 13.14	6.61 ± 9.53	7.31 ± 13.69	0.340
Diabetes drugs	1440 (81.1%)	1331 (81.6%)	1300 (81.6%)	0.920
MI drugs	1363 (76.7%)	1223 (74.9%)	1201 (75.3%)	0.430
MI	259 (14.6%)	182 (11.2%)	158 (9.9%)	< 0.001

Continuous variables are presented as the means ± SDs, and categorical variables are presented as percentages. Abbreviations: DOBS = Dietary oxidative balance score; BMI = Body mass index; CKD = Chronic kidney disease; MI = Myocardial infarction

7.0% of the participants in Q3, compared with 12.7% in Q1 ( $p < 0.001$ ), whereas the MI incidence was 9.9% in Q3, compared with 14.6% in Q1 ( $p < 0.001$ ). Other factors, such as hyperlipidemia, sedentary time, diabetes drugs, MI drugs, did not significantly differ across the tertiles.

#### Associations between DOBS and myocardial infarction

For each one-point increase in DOBS, the odds of MI decreased by 3% in the unadjusted model (Model 1: OR = 0.97, 95% CI: 0.96–0.99) (Table 3). This association became slightly stronger after adjusting for age, sex, and ethnicity (Model 2: OR = 0.96, 95% CI: 0.94–0.98) and remained consistent even after further adjustment for additional covariates, including education level, marital

status, BMI, smoking, drinking, sedentary time, diabetes drugs, MI drugs, hypertension, hyperlipidemia, and CKD (Model 3: OR = 0.97, 95% CI: 0.95–0.99).

When comparing the DOBS tertiles, participants in the highest tertile (Q3) had significantly lower odds of MI than did those in the lowest tertile (Q1) (Table 3). In the unadjusted model, the odds of MI for Q3 versus Q1 were reduced by 36% (OR = 0.64, 95% CI: 0.50–0.84). This reduction in MI risk was even more pronounced in the fully adjusted model (Model 3: OR = 0.62, 95% CI: 0.43–0.87). Similarly, participants in the second tertile (Q2) also presented a significantly lower risk of MI than did those in Q1, with odds ratios of 0.72 (95% CI: 0.54–0.97)



**Table 3** ORs and 95% CIs for the associations between DOBS and MI in diabetic patients

DOBS	Model 1	Model 2	Model 3	PSM Model
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Per score increase	0.97(0.96–0.99)	0.96(0.94–0.98)	0.97(0.95–0.99)	-
Per tertile increase				
Q1	1(Ref.)	1(Ref.)	1(Ref.)	1(Ref.)
Q2	0.72(0.54–0.97)	0.65(0.48–0.88)	0.69(0.50–0.93)	0.66(0.47–0.93)
Q3	0.64(0.50–0.84)	0.54(0.40–0.74)	0.62(0.43–0.87)	0.72(0.48–0.88)

Model 1 is unadjusted. Model 2 is adjusted for age, sex, and ethnicity. Model 3 was further adjusted for education level, marital status, BMI, drinking, smoking, sedentary time, diabetes drugs, MI drugs, hypertension, hyperlipidemia, and CKD. The PSM Model was based on separate 1:1 nearest-neighbor matching (caliper = 0.2) for Q2 vs. Q1 and Q3 vs. Q1, using the same covariates as Model 3. Abbreviations: DOBS = Dietary oxidative balance score, OR = Odds ratio, CI = Confidence interval

in the unadjusted model and 0.69 (95% CI: 0.50–0.93) in the fully adjusted model.

These associations remained robust in the propensity score-matched analysis, where Q3 and Q2 were each compared separately with Q1 using 1:1 nearest-neighbor matching. In the matched samples, the odds of MI were significantly lower in both Q2 (OR = 0.66, 95% CI: 0.47–0.93) and Q3 (OR = 0.72, 95% CI: 0.48–0.88) compared with Q1.

Threshold effect

Restricted cubic spline (RCS) analyses were conducted to examine the association between DOBS and the odds of MI (Fig. 2). Although all models demonstrated a statistically significant overall inverse association ( $P$  for overall < 0.01), the formal tests for nonlinearity were not significant ( $P > 0.89$  in all models), indicating that the relationship did not statistically deviate from linearity.

However, the spline curves showed a steep reduction in MI odds at lower DOBS levels, followed by a flattening of the association at higher values. This visual trend suggests the presence of a potential threshold effect, beyond which further increases in DOBS yield a smaller incremental association with MI. To further explore this, we performed a threshold-based analysis using a DOBS cut-off of 7—the approximate point of minimal predicted risk on the spline curve. The results confirmed that participants with DOBS > 7 had significantly lower odds of MI compared to those with DOBS ≤ 7 (Table 4), supporting the presence of a threshold effect, even in the absence of statistically significant nonlinearity.

Subgroup analysis

The subgroup analyses, as shown in Fig. 3, highlight the associations between DOBS and MI across various demographic and clinical subgroups in diabetic patients. These models were fully adjusted for potential confounders, the same as Model 3 in Table 3. The results indicate that the inverse relationship between DOBS and MI was generally consistent across most subgroups, with higher DOBS being associated with a lower risk of MI. Notably, the inverse association between higher DOBS and MI appeared to be more pronounced in certain subgroups,

such as current smokers, where the odds ratios were significantly lower than those observed in other subgroups. However, the interaction tests revealed that there was no statistically significant difference in the effect of DOBS on MI across the subgroups, suggesting that the association between DOBS and MI is robust and broadly applicable across different populations.

Sensitivity analysis

The sensitivity analysis results, presented in Table 5, confirm the robustness of the association between DOBS and MI among diabetic patients and indicate that this relationship remains consistent across different NHANES survey cycles.

Discussion

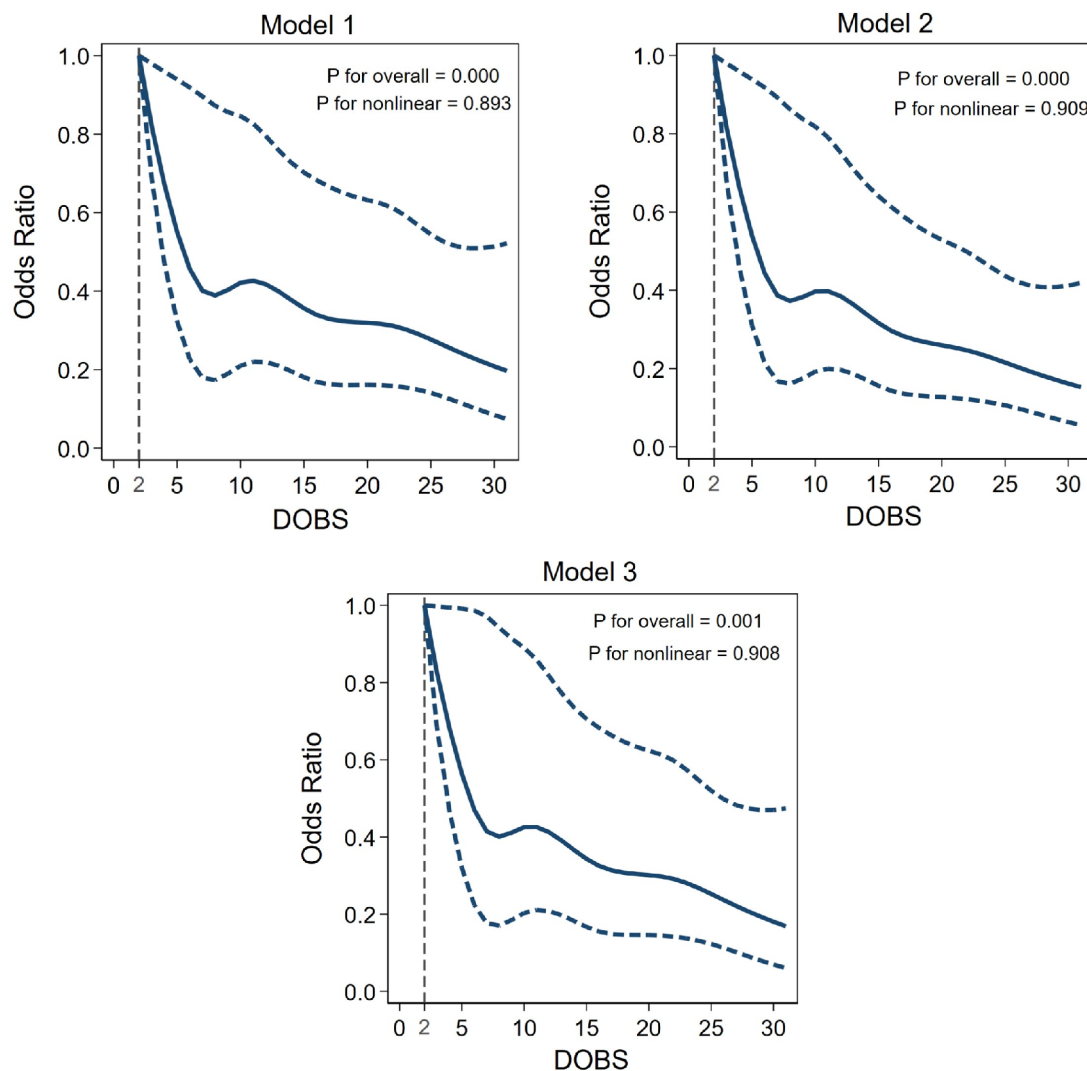
Study context

Myocardial infarction (MI), a leading cause of mortality and disability globally, poses an even greater risk to individuals with diabetes mellitus because of their elevated oxidative stress and metabolic abnormalities [23]. These factors accelerate the development of atherosclerosis [24, 25], the primary cause of MI. Diet plays a critical role in modulating oxidative stress, making it a key factor in managing cardiovascular risk in diabetic patients. The dietary oxidative balance score (DOBS) is an index that captures the balance between pro-oxidant and antioxidant dietary components and can be used in the assessment of cardiovascular risk [26]. A relatively high concentration of DOBS reflects a diet with greater antioxidant potential, which could reduce MI risk.

This study utilized data from the 1999–2018 National Health and Nutrition Examination Survey (NHANES) to explore the association between DOBS and the incidence of MI in diabetic patients. DOBS were calculated on the basis of the intake of antioxidant and pro-oxidant components in the diet, and their relationship with MI was assessed via a cross-sectional study design and multivariable regression models.

Key findings

The study demonstrated a significant inverse association between DOBS and the likelihood of MI among



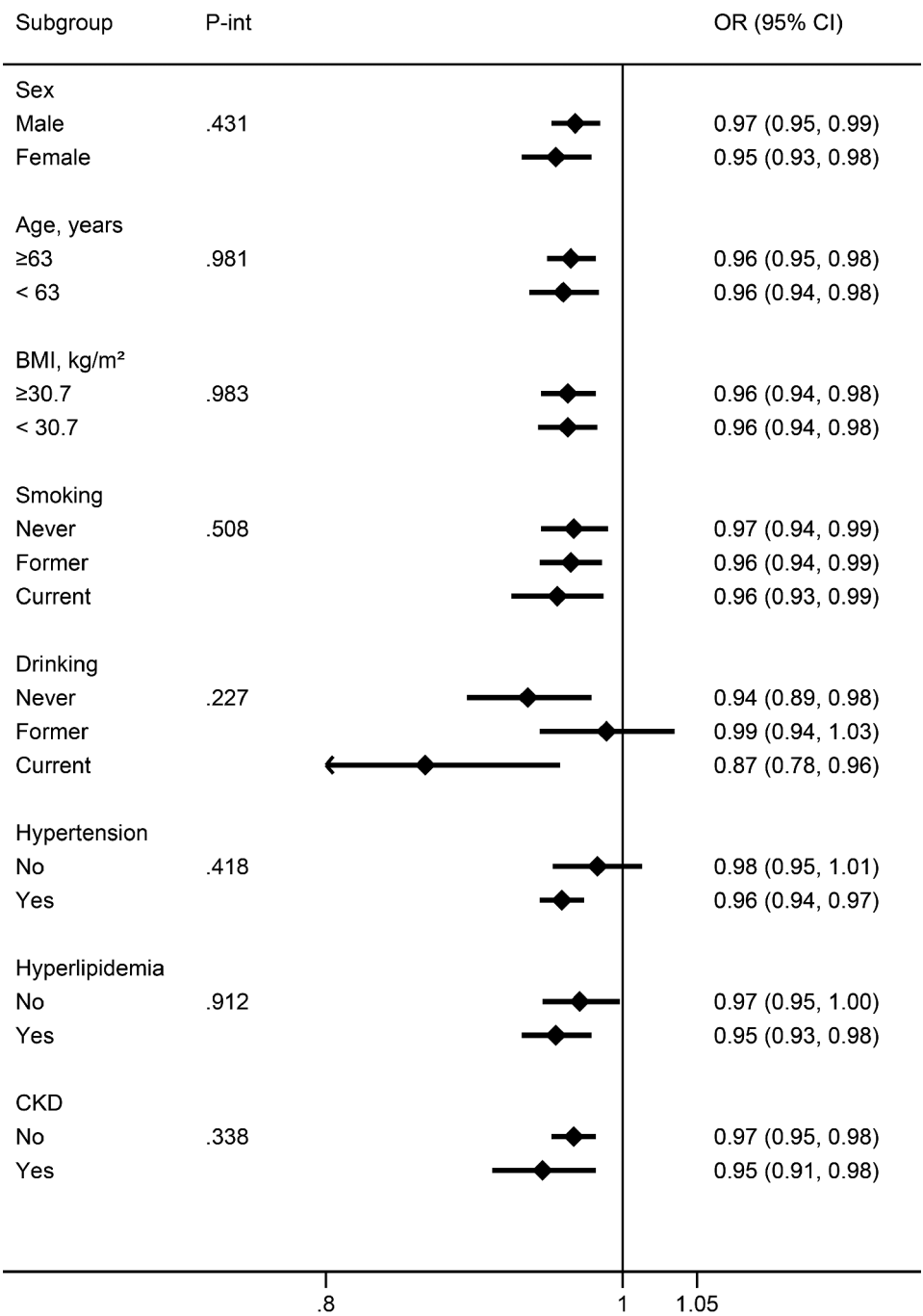
**Fig. 2** RCS curves for the associations between DOBS and MI in diabetic patients. Same models as those in Table 3. Reference: DOBS = 2

**Table 4** ORs and 95% CIs for the associations between DOBS (using cutoff value 7) and MI in diabetic patients

DOBS	Model 1	Model 2	Model 3	PSM Model
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Per score increase				
DOBS ≤ 7	0.94(0.92–0.97)	0.94(0.92–0.98)	0.92(0.88–0.95)	-
DOBS > 7	0.97(0.95–0.99)	0.96(0.93–0.98)	0.96(0.93–0.99)	-
Per tertile increase				
DOBS ≤ 7	1(Ref.)	1(Ref.)	1(Ref.)	1(Ref.)
DOBS > 7	0.71(0.52–0.96)	0.63(0.45–0.89)	0.71(0.48–0.93)	0.75(0.54–0.93)

Model 1 is unadjusted. Model 2 is adjusted for age, sex, and ethnicity. Model 3 was further adjusted for education level, marital status, BMI, drinking, smoking, sedentary time, diabetes drugs, MI drugs, hypertension, hyperlipidemia, and CKD. The PSM Model was based on separate 1:1 nearest-neighbor matching (caliper = 0.2) for Q2 vs. Q1 and Q3 vs. Q1, using the same covariates as Model 3. Abbreviations: DOBS = Dietary oxidative balance score, OR = Odds ratio, CI = Confidence interval

diabetic patients. Each one-point increase in DOBS was associated with approximately 3% lower odds of MI in the unadjusted model, and this association remained robust after adjustment for age, sex, ethnicity, education level, marital status, BMI, smoking, drinking, sedentary behavior, medication use, hypertension, hyperlipidemia, and chronic kidney disease (Model 3: OR = 0.97, 95% CI: 0.95–0.99). Importantly, the association persisted in the propensity score–matched (PSM) analysis, further confirming its robustness. Subgroup analyses also showed



**Fig. 3** Subgroup analyses for the association between DOBS and MI in diabetic patients. All the models were adjusted as in Model 3 in Table 3. Abbreviations: OR=odds ratio; CI=confidence interval; P-int =P-interaction

consistent associations across different demographic and clinical strata.

Although formal tests did not support a nonlinear association, visual inspection of spline curves suggested a threshold effect: the inverse association between DOBS and MI was more pronounced at lower DOBS levels and gradually flattened at higher levels. A secondary analysis using a cutoff of DOBS = 7 supported this trend,

showing significantly lower odds of MI in participants with DOBS > 7.

**Clinical and epidemiological evidence**

The findings of this study are consistent with and extend the results of previous studies exploring the relationships among diet, oxidative stress, and cardiovascular outcomes.



**Table 5** ORs and 95% CIs for the associations between DOBS and MI in diabetic patients. (NHANES 1999–2004, NHANES 2005–2010, NHANES 2011–2018)

Cycles	DOBS	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	PSM Model OR (95% CI)
1999-2004	Per score <sup>+</sup>	0.96(0.92–0.99)	0.94(0.88–0.99)	0.95(0.89–0.98)	-
	Per tertile <sup>+</sup>				
	Q1	1(Ref.)	1(Ref.)	1(Ref.)	1(Ref.)
	Q2	0.68(0.29–1.29)	0.59(0.18–1.18)	0.74(0.27–1.89)	0.80(0.15–1.15)
	Q3	0.63(0.38–0.98)	0.50(0.19–0.97)	0.56(0.25–1.03)	0.67(0.21–0.97)
2005-2010	Per score <sup>+</sup>	0.96(0.93–0.98)	0.94(0.91–0.97)	0.95(0.89–1.01)	-
	Per tertile <sup>+</sup>				
	Q1	1(Ref.)	1(Ref.)	1(Ref.)	1(Ref.)
	Q2	0.60(0.39–0.91)	0.51(0.32–0.83)	0.55(0.34–0.89)	0.45(0.29–0.71)
	Q3	0.53(0.34–0.82)	0.42(0.25–0.68)	0.52(0.31–0.87)	0.62(0.36–0.95)
2011-2018	Per score <sup>+</sup>	0.98(0.96–0.99)	0.97(0.95–0.99)	0.98(0.95–1.01)	-
	Per tertile <sup>+</sup>				
	Q1	1(Ref.)	1(Ref.)	1(Ref.)	1(Ref.)
	Q2	0.81(0.53–0.92)	0.75(0.50–1.13)	0.80(0.52–0.11)	0.76(0.46–1.12)
	Q3	0.71(0.48–0.95)	0.62(0.40–0.97)	0.67(0.42–0.98)	0.75(0.45–0.93)

Model 1 is unadjusted. Model 2 is adjusted for age, sex, and ethnicity. Model 3 was further adjusted for education level, marital status, BMI, drinking, smoking, sedentary time, diabetes drugs, MI drugs, hypertension, hyperlipidemia, and CKD. The PSM Model was based on separate 1:1 nearest-neighbor matching (caliper = 0.2) for Q2 vs. Q1 and Q3 vs. Q1, using the same covariates as Model 3. Abbreviations: DOBS = Dietary oxidative balance score, OR = Odds ratio, CI = Confidence interval. Per score<sup>+</sup> = Per score increase

In a clinical trial, Jordi Salas-Salvadó and colleagues reported that intensive weight loss lifestyle interventions can significantly reduce long-term cardiovascular risk [27]. Obesity, oxidative stress, and diet are closely interconnected, with a diet rich in antioxidants being associated with a lower incidence of obesity [28–31]. Another clinical trial revealed a strong inverse association between the oxidative balance score (OBS) and cardiovascular disease (CVD) mortality. The hazard ratio (HR) for CVD mortality in the highest quartile (favoring antioxidants) compared with the lowest quartile (reference category) was 0.18, with a 95% confidence interval (CI) of 0.06–0.51 [32]. A cross-sectional study revealed that a decrease in OBS, which incorporates both dietary and lifestyle components, is positively associated with an increased risk of overall and specific cardiovascular diseases [33]. Similarly, Yingzi Li and colleagues reported a protective association between adherence to an antioxidant-rich diet and lifestyle and a reduced incidence and mortality of CVD among adults with nonalcoholic fatty liver disease (NAFLD) [34]. Kai Chen and colleagues reported a significant negative correlation between OBS and the risk of coronary artery disease (CAD) [35]. A recent Korean cohort study involving 5,181 participants revealed a negative correlation between OBS and the likelihood of developing new-onset hypertension [36]. A study from the NHANES analyzing 4,955 participants revealed a significant negative correlation between OBS and the 10-year risk of atherosclerotic cardiovascular disease (ASCVD). Continuous OBS was associated with an adjusted odds ratio (OR) of 0.97 (95% CI: 0.95–0.99) [37].

### Basic medical evidence

Numerous studies have consistently demonstrated that oxidative stress plays a critical role in promoting the development of atherosclerosis (AS) and MI, particularly in patients with diabetes. Reactive oxygen species (ROS) play crucial roles in all stages of atherosclerotic inflammation. In the initial stages of AS, endothelial dysfunction leads to a reduction in nitric oxide (NO) bioavailability and an increase in NO degradation, which promotes ROS production and triggers oxidative stress responses [38]. This oxidative stress facilitates the oxidation of low-density lipoprotein (LDL), leukocyte adhesion and migration, vascular smooth muscle cell (VSMC) proliferation, and platelet aggregation, all of which accelerate the formation of lipid plaques [39]. The primary redox-sensitive transcription factor involved in AS is nuclear factor- $\kappa$ B (NF- $\kappa$ B). NF- $\kappa$ B not only promotes the production of ROS but also induces the synthesis of pro-inflammatory cytokines, such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). This leads to increased infiltration of immune cells into the affected vascular regions, thereby exacerbating the vascular inflammatory response [40, 41]. Additionally, in the context of AS, the primary source of ROS within the vascular wall is attributed to NADPH oxidase (NOX). Toll-like receptor 2 (TLR2) signaling can promote the progression of AS by activating NOX, which enhances vascular smooth muscle cell migration and vascular remodeling [42–44]. Studies have shown that the iNOS/NO signaling pathway is closely linked to the pathogenesis of myocardial ischemia-reperfusion injury (MIRI). It is well documented that this pathway

can exacerbate cardiac damage and myocardial infarction by promoting oxidative stress [45]. ROS produced by NOX enzymes contribute to the disruption of the coronary microvascular structure and exacerbate coronary microvascular injury [46]. In diabetic patients, metabolic abnormalities and chronic hyperglycemia lead to the excessive production of mitochondrial ROS in the endothelial cells of both large and small vessels, as well as in the myocardium. This overproduction exacerbates oxidative stress, significantly increasing the likelihood of cardiovascular events [10, 20, 47].

### Geographic and regional variability in DOBS-Related dietary patterns

Although substantial evidence supports the role of dietary oxidative balance in reducing cardiovascular risk, the composition of DOBS-related nutrients varies markedly across countries and regions. A global analysis involving 195 countries revealed that the intake of antioxidant-rich components such as whole grains, fruits, and nuts is often inadequate worldwide, with striking regional differences driven by cultural and economic factors [48]. For example, Mediterranean diets are rich in monounsaturated fats and antioxidants, while Western diets tend to be higher in pro-oxidants such as saturated fats and sodium. These disparities imply that the distribution and health relevance of DOBS may differ significantly across populations.

Moreover, even within a single country, regional heterogeneity in dietary quality may influence DOBS. For instance, nationally representative studies in China have shown that urban populations typically consume more fruits, marine omega-3 fatty acids, and dietary fiber, whereas rural populations have higher intakes of refined carbohydrates and sodium [49]. These intranational variations suggest that DOBS values and their associations with disease outcomes may not be uniform even within a single national context. In addition, region-specific food sources, cooking habits, and environmental exposures may influence the physiological effects of similar nutrient intakes, further complicating the interpretation of DOBS across populations.

In the present study, DOBS was calculated based on U.S. dietary data. Although the observed inverse association with MI in diabetic patients was robust and consistent across subgroups, caution is warranted in generalizing these findings to populations with different dietary structures or nutrient sources.

### Clinical and public health implication

The findings of this study may have important clinical and public health relevance. As a simple dietary index, the DOBS may serve as a useful tool for evaluating cardiovascular risk profiles in diabetic patients and informing

dietary assessments. The consistent inverse association observed across demographic and clinical subgroups suggests that higher dietary antioxidant balance may be associated with more favorable cardiovascular status. Public health efforts encouraging antioxidant-rich diets—particularly among high-risk groups such as individuals with diabetes—may contribute to improved population-level cardiovascular outcomes, though causal relationships remain to be established.

To explore potential nonlinearity, we conducted an RCS analysis of the association between DOBS and MI. While the formal test for nonlinearity was not statistically significant, the spline curve revealed a possible threshold pattern around a DOBS value of 7. Specifically, participants with  $\text{DOBS} \leq 7$  showed a steeper decline in MI odds with increasing DOBS, whereas the association plateaued among those with  $\text{DOBS} > 7$ . This pattern suggests that dietary oxidative balance may be more strongly associated with cardiovascular risk in the lower DOBS range. If supported by future longitudinal studies, this threshold-like pattern may help refine dietary guidance by identifying individuals who might derive the greatest relative benefit from antioxidant-focused dietary improvement.

### Limitations

Despite offering valuable insights, this study has several limitations. First, due to its cross-sectional design, the temporal relationship between DOBS and MI cannot be established, and causality cannot be inferred. Reverse causation is possible, as patients who had experienced MI may have subsequently changed their dietary habits, leading to altered DOBS values. Second, dietary intake data were collected using 24-hour self-reported recalls, which are subject to recall bias and day-to-day variability, particularly in diabetic populations. Although we used the average of two days to reduce this bias, limitations remain. Third, self-reported MI status may be subject to misclassification, especially among diabetic individuals who may experience atypical symptoms, potentially impacting the validity of our outcome assessment. Fourth, although multiple covariates were adjusted for, residual confounding from unmeasured factors (such as medication adherence, genetic predisposition, or psychosocial stress) cannot be ruled out. Fifth, the findings are based on the U.S. NHANES population and may not be generalizable to other ethnic or regional groups with distinct dietary structures and oxidative stress exposures. Future longitudinal studies and randomized controlled trials are needed to validate the observed associations and evaluate whether increasing dietary antioxidant balance through intervention can effectively reduce cardiovascular risk in diabetic individuals.

## Conclusion

This study identifies a consistent inverse association between the dietary oxidative balance score (DOBS) and the likelihood of myocardial infarction (MI) among diabetic patients. While causality cannot be inferred due to the cross-sectional design, the observed associations suggest that DOBS may serve as a useful marker for evaluating cardiovascular risk in this high-risk population. These findings support the need for prospective studies to further investigate the role of dietary antioxidant balance in cardiovascular health and inform dietary recommendations for individuals with diabetes.

## Abbreviations

MI	Myocardial infarction
DOBS	Dietary Oxidative Balance Score
CKD	Chronic kidney disease
CVD	Cardiovascular disease
NHANES	National Health and Nutrition Examination Survey
BMI	Body mass index
OR	Odds ratio
CI	confidence interval
SD	Standard deviations
RCS	Restricted cubic splines
HR	Hazard ratio
NAFLD	Non-alcoholic fatty liver disease
CAD	Coronary artery disease
ASCVD	Atherosclerotic cardiovascular disease
AS	Atherosclerosis
ROS	Reactive oxygen species
NO	Nitric oxide
LDL	low-density lipoprotein
NF-κB	Nuclear factor-κB
TNF-α	Tumor necrosis factor-α
NOX	NADPH oxidase
TLR2	Toll-like receptor 2
MIRI	Myocardial ischemia-reperfusion injury

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## Author contributions

The primary manuscript was written by Xu Li and Yashi Li. Zitong Chen provided statistical guidance on propensity score matching. Xinyi Yang and Zehao Jin assisted with data extraction and language editing, while Lan He provided statistical guidance and was responsible for the final revisions.

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## Data availability

All data used in this study were obtained from the NHANES database: <https://www.nchs.gov/nhanes/Default.aspx>.

## Declarations

### Ethics approval and consent to participate

The analysis process of this study adhered to ethical review standards and received an exemption from the Ethics Review Board of the National Center for Health Statistics, USA. All participants provided signed informed consent.

### Consent for publication

Not Applicable.

## Competing interests

The authors declare no competing interests.

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## References

- Martin SS et al. 2024 Heart Disease and Stroke Statistics: A Report of US and Global Data From the American Heart Association. *Circulation* 149, e347–e913 (2024). <https://doi.org/10.1161/cir.0000000000001209>
- Marenzi G, et al. Prognostic value of the acute-to-Chronic glycemic ratio at admission in acute myocardial infarction: A prospective study. *Diabetes Care*. 2018;41:847–53. <https://doi.org/10.2337/dc17-1732>.
- Yusuf S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364:937–52. [https://doi.org/10.1016/s0140-6736\(04\)17018-9](https://doi.org/10.1016/s0140-6736(04)17018-9).
- Liang H, et al. Increased risk of subsequent myocardial infarction in patients with type 2 diabetes: a retrospective cohort study using the U.K. General practice research database. *Diabetes Care*. 2014;37:1329–37. <https://doi.org/10.2337/dc13-1953>.
- Milazzo V, et al. Diabetes mellitus and acute myocardial infarction: impact on short and Long-Term mortality. *Adv Exp Med Biol*. 2021;1307:153–69. [https://doi.org/10.1007/5584\\_2020\\_481](https://doi.org/10.1007/5584_2020_481).
- Senoner T, Dichtl W. Oxidative stress in cardiovascular diseases: still a therapeutic target? *Nutrients*. 2019;11. <https://doi.org/10.3390/nu11092090>.
- Kattoor AJ, Pothineni NVK, Palagiri D, Mehta JL. Oxidative stress in atherosclerosis. *Curr Atheroscler Rep*. 2017;19:42. <https://doi.org/10.1007/s11883-017-0678-6>.
- Zhang Q, et al. Signaling pathways and targeted therapy for myocardial infarction. *Signal Transduct Target Ther*. 2022;7:78. <https://doi.org/10.1038/s41392-022-00925-z>.
- Förstermann U, Xia N, Li H. Roles of vascular oxidative stress and nitric oxide in the pathogenesis of atherosclerosis. *Circ Res*. 2017;120:713–35. <https://doi.org/10.1161/circresaha.116.309326>.
- Giacco F, Brownlee M. Oxidative stress and diabetic complications. *Circ Res*. 2010;107:1058–70. <https://doi.org/10.1161/circresaha.110.223545>.
- Yuan T, et al. New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. *Redox Biol*. 2019;20:247–60. <https://doi.org/10.1016/j.redox.2018.09.025>.
- Ávila-Escalante ML, Coop-Gamas F, Cervantes-Rodríguez M, Méndez-Iturbide D, Aranda G. The effect of diet on oxidative stress and metabolic diseases—Clinically controlled trials. *J Food Biochem*. 2020;44:e13191. <https://doi.org/10.1111/jfbc.13191>.
- Tan BL, Norhaizan ME. Effect of High-Fat diets on oxidative stress, cellular inflammatory response and cognitive function. *Nutrients*. 2019;11. <https://doi.org/10.3390/nu1112579>.
- Wang J, Xing F, Sheng N, Xiang Z. Associations of dietary oxidative balance score with femur osteoporosis in postmenopausal women: data from the National health and nutrition examination survey. *Osteoporos Int*. 2023;34:2087–100. <https://doi.org/10.1007/s00198-023-06896-3>.
- Slattery ML, et al. Angiogenesis genes, dietary oxidative balance and breast cancer risk and progression: the breast Cancer health disparities study. *Int J Cancer*. 2014;134:629–44. <https://doi.org/10.1002/ijc.28377>.
- Van Hoydonck PG, Temme EH, Schouten EG. A dietary oxidative balance score of vitamin C, beta-carotene and iron intakes and mortality risk in male smoking Belgians. *J Nutr*. 2002;132:756–61. <https://doi.org/10.1093/jn/132.4.756>.

17. Zhang H, Tian W, Qi G, Zhou B, Sun Y. Interactive association of the dietary oxidative balance score and cardiovascular disease with mortality in older adults: evidence from NHANES. *Food Funct*. 2024;15:6164–73. <https://doi.org/10.1039/d4fo01515k>.
18. Liu J, Wang W, Wen Y. Association of dietary oxidative balance score and sleep duration with the risk of mortality: prospective study in a representative US population. *Public Health Nutr*. 2023;26:2066–75. <https://doi.org/10.1017/s136890023001155>.
19. Wang X, et al. Association of dietary inflammatory index and dietary oxidative balance score with All-Cause and Disease-Specific mortality: findings of 2003–2014 National health and nutrition examination survey. *Nutrients*. 2023;15. <https://doi.org/10.3390/nu15143148>.
20. González P, Lozano P, Ros G, Solano F. Hyperglycemia and oxidative stress: an integral, updated and critical overview of their metabolic interconnections. *Int J Mol Sci*. 2023;24. <https://doi.org/10.3390/ijms24119352>.
21. Kong SY, et al. Oxidative balance score as predictor of all-cause, cancer, and noncancer mortality in a biracial US cohort. *Ann Epidemiol*. 2015;25:256–e262251. <https://doi.org/10.1016/j.annepidem.2015.01.004>.
22. National Center for Health Statistics. NHANES Questionnaires, Datasets, and Related Documentation. Available online: (<https://www.cdc.gov/nchs/nhanes/Default.aspx> accessed on 30 June 2024).
23. Shah MS, Brownlee M. Molecular and cellular mechanisms of cardiovascular disorders in diabetes. *Circ Res*. 2016;118:1808–29. <https://doi.org/10.1161/circresaha.116.306923>.
24. Poznyak A, et al. The diabetes Mellitus-Atherosclerosis connection: the role of lipid and glucose metabolism and chronic inflammation. *Int J Mol Sci*. 2020;21. <https://doi.org/10.3390/ijms21051835>.
25. Wang C, et al. Endogenous protective factors and potential therapeutic agents for Diabetes-Associated atherosclerosis. *Front Endocrinol (Lausanne)*. 2022;13:821028. <https://doi.org/10.3389/fendo.2022.821028>.
26. Kawada T. Oxidative stress markers and cardiovascular disease: advantage of using these factors in combination with lifestyle factors for cardiovascular risk assessment. *Int J Cardiol*. 2012;157:119–20. <https://doi.org/10.1016/j.ijcard.2012.03.107>.
27. Salas-Salvado J, et al. Effect of a lifestyle intervention program with Energy-Restricted mediterranean diet and exercise on weight loss and cardiovascular risk factors: One-Year results of the PREDIMED-Plus trial. *Diabetes Care*. 2019;42:777–88. <https://doi.org/10.2337/dc18-0836>.
28. Fernández-Sánchez A, et al. Inflammation, oxidative stress, and obesity. *Int J Mol Sci*. 2011;12:3117–32. <https://doi.org/10.3390/ijms12053117>.
29. Zhu Z, et al. Association of the oxidative balance score with obesity and body composition among young and middle-aged adults. *Front Nutr*. 2024;11:1373709. <https://doi.org/10.3389/fnut.2024.1373709>.
30. Pérez-Torres I, et al. Oxidative stress, plant natural antioxidants, and obesity. *Int J Mol Sci*. 2021;22. <https://doi.org/10.3390/ijms22041786>.
31. Karam BS, Chavez-Moreno A, Koh W, Akar JG, Akar FG. Oxidative stress and inflammation as central mediators of atrial fibrillation in obesity and diabetes. *Cardiovasc Diabetol*. 2017;16:120. <https://doi.org/10.1186/s12933-017-0604-9>.
32. Talavera-Rodriguez I, et al. Association between an oxidative balance score and mortality: a prospective analysis in the SUN cohort. *Eur J Nutr*. 2023;62:1667–80. <https://doi.org/10.1007/s00394-023-03099-8>.
33. Chen X, et al. Interplay of sleep patterns and oxidative balance score on total cardiovascular disease risk: insights from the National health and nutrition examination survey 2005–2018. *J Glob Health*. 2023;13:04170. <https://doi.org/10.7189/jogh.14.04170>.
34. Li Y, Liu Y. Adherence to an antioxidant diet and lifestyle is associated with reduced risk of cardiovascular disease and mortality among adults with nonalcoholic fatty liver disease: evidence from NHANES 1999–2018. *Front Nutr*. 2024;11:1361567. <https://doi.org/10.3389/fnut.2024.1361567>.
35. Chen K, et al. Association between oxidative balance score, systemic inflammatory response index, and cardiovascular disease risk: a cross-sectional analysis based on NHANES 2007–2018 data. *Front Nutr*. 2024;11:1374992. <https://doi.org/10.3389/fnut.2024.1374992>.
36. Lee JH, Son DH, Kwon YJ. Association between oxidative balance score and new-onset hypertension in adults: A community-based prospective cohort study. *Front Nutr*. 2022;9:1066159. <https://doi.org/10.3389/fnut.2022.1066159>.
37. Wang R, et al. A cross-sectional study exploring the relationship between oxidative balance score and 10-year atherosclerotic cardiovascular disease risk based on the National health and nutrition examination survey (2011–2020). *Diab Vasc Dis Res*. 2024;21:14791641241244658. <https://doi.org/10.1177/14791641241244658>.
38. Fukai T, Ushio-Fukai M. Cross-Talk between NADPH oxidase and mitochondria: role in ROS signaling and angiogenesis. *Cells*. 2020;9. <https://doi.org/10.3390/cells9081849>.
39. Yan Q, et al. Targeting oxidative stress as a preventive and therapeutic approach for cardiovascular disease. *J Transl Med*. 2023;21:519. <https://doi.org/10.1186/s12967-023-04361-7>.
40. El Hadri K, Smith R, Duplus E, El Amri C. Inflammation. Oxidative stress, senescence in atherosclerosis: Thioredoxine-1 as an emerging therapeutic target. *Int J Mol Sci*. 2021;23. <https://doi.org/10.3390/ijms23010077>.
41. Forman HJ, Zhang H. Targeting oxidative stress in disease: promise and limitations of antioxidant therapy. *Nat Rev Drug Discov*. 2021;20:689–709. <https://doi.org/10.1038/s41573-021-00233-1>.
42. Schürmann C, et al. The NADPH oxidase Nox4 has anti-atherosclerotic functions. *Eur Heart J*. 2015;36:3447–56. <https://doi.org/10.1093/eurheartj/ehv460>.
43. Lee JH, et al. Interaction of NADPH oxidase 1 with Toll-like receptor 2 induces migration of smooth muscle cells. *Cardiovasc Res*. 2013;99:483–93. <https://doi.org/10.1093/cvr/cvt107>.
44. Marchio P, et al. Targeting early atherosclerosis: A focus on oxidative stress and inflammation. *Oxid Med Cell Longev*. 2019;2019(8563845). <https://doi.org/10.1155/2019/8563845>.
45. Yu X, et al. The dual role of inducible nitric oxide synthase in myocardial ischemia/reperfusion injury: friend or foe?? *Oxid Med Cell Longev*. 2018;2018(8364848). <https://doi.org/10.1155/2018/8364848>.
46. Chang X, et al. Coronary microvascular injury in myocardial infarction: perception and knowledge for mitochondrial quality control. *Theranostics*. 2021;11:6766–85. <https://doi.org/10.7150/thno.60143>.
47. An Y, et al. The role of oxidative stress in diabetes mellitus-induced vascular endothelial dysfunction. *Cardiovasc Diabetol*. 2023;22:237. <https://doi.org/10.1186/s12933-023-01965-7>.
48. Health effects of dietary risks. In 195 countries, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet*. 2019;393:1958–72. [https://doi.org/10.1016/s0140-6736\(19\)30041-8](https://doi.org/10.1016/s0140-6736(19)30041-8).
49. He Y, et al. The dietary transition and its association with cardiometabolic mortality among Chinese adults, 1982–2012: a cross-sectional population-based study. *Lancet Diabetes Endocrinol*. 2019;7:540–8. [https://doi.org/10.1016/s2213-8587\(19\)30152-4](https://doi.org/10.1016/s2213-8587(19)30152-4).

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