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Relationship between oxidative balance score and prostate cancer: a cross-sectional study of NHANES, 1999–2010

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ABSTRACT

Objective Few studies have examined the relationship between systemic oxidative stress and prostate cancer (PCa) risk. This study aimed to explore potential correlations between PCa and oxidative balance score (OBS), which measures systemic oxidative stress.

Design A cross-sectional study.

Setting The National Health and Nutrition Examination Survey.

Participants A total of 8156 individuals were included in this study.

Primary and secondary outcome measures Weighted logistic regression with multivariable adjustment and restricted cubic splines (RCS) were used to assess the correlation between PCa and OBS. A sensitivity analysis was conducted specifically on patients with PCa to verify the results.

Results The prevalence of PCa was 2.55%. The multivariable logistic regression model revealed no correlation between OBS, dietary OBS, lifestyle OBS and PCa. Compared with the lowest quartile of OBS, the adjusted ORs for the highest quartile of OBS, dietary OBS and lifestyle OBS were 1.852 (95% CI 1.028–3.339), 1.565 (95% CI 0.841–2.913) and 1.575 (95% CI 0.915–2.710), respectively. Additionally, all p values for trend were greater than 0.05. Subgroup analysis revealed a consistent lack of association between OBS and PCa across various population settings. Furthermore, analysis using RCS confirmed this absence of association, indicating no significant relationship in either a linear or non-linear context. A sensitivity analysis focusing exclusively on patients with PCa showed a strong association (OR=2.737, p=0.008).

Conclusion This cross-sectional study reveals no significant association between systemic oxidative stress, measured by OBS, and PCa risk. Notably, a sensitivity analysis focusing solely on PCa patients suggested a potential link, warranting further investigation.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Comprehensive study using oxidative balance score index enhances depth of findings.
⇒ High-quality National Health and Nutrition Examination Survey sampling ensures representativeness.
⇒ Consideration of sample weights and confounders boosts analytical accuracy.
⇒ Lack of longitudinal data and potentially underpowered sample limit generalisability.

INTRODUCTION

Among males, prostate cancer (PCa) is the most common non-cutaneous cancer, with approximately 1.4 million new cases and 375 000 fatalities reported worldwide annually.[1] Among men worldwide, PCa ranked fifth as a cause of cancer-related deaths in 2020, while in the USA, it was the second most prevalent cause of cancer-related mortality.[2] After two decades of decline, the incidence of PCa, particularly at regional and distant stages, is resurging. Currently, the primary treatment modalities for clinically significant PCa include radical prostatectomy and radical radiotherapy. Additionally, focal treatments like high-intensity focused ultrasound are gaining traction for moderate and low-risk localised PCa. These methods have demonstrated effective therapeutic outcomes and are now recommended by clinical guidelines.[3 4] Despite advancements in PCa therapy, biochemical recurrence remains prevalent, affecting approximately 53% of patients post-treatment, posing a substantial threat to patient survival and well-being.[5] Therefore, preventing PCa is crucial.

Emerging evidence from migration studies indicates a significant correlation between environmental factors and the onset of prostate carcinogenesis.[6] Oxidative stress, resulting from an overproduction of reactive oxygen species (ROS) in response to harmful stimuli, leads to an imbalance between oxidation and antioxidant systems, causing tissue damage. Numerous studies have confirmed that tumour cells exhibit a higher redox state than normal cells and typically contain elevated ROS levels.[7] Oxidative stress plays a critical role in the initiation and progression of PCa through various mechanisms, including the modulation of

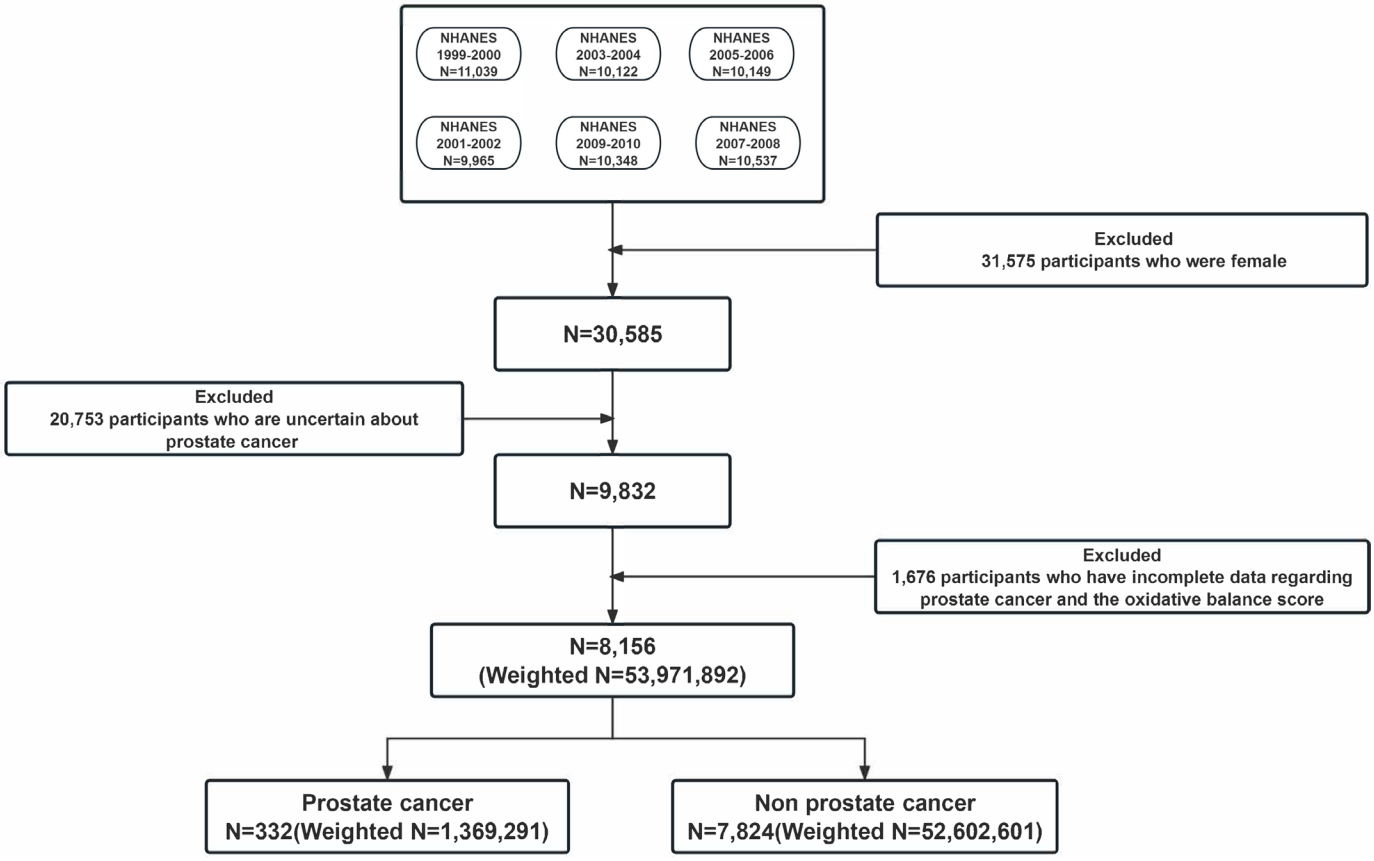

Figure 1 Flow diagram of participant selection. NHANES, National Health and Nutrition Examination Survey.

androgen receptor signalling and cellular proliferation. Chronic oxidative stress can induce somatic mutations and neoplastic transformation, contributing to the initiation of PCa.[8] High oxidative stress markers, such as F2-isoprostanes, are elevated in patients with advanced PCa, indicating the role of oxidative stress in disease progression.[9] Androgen receptor signalling, crucial for PCa cell survival, is modulated by oxidative stress.[10] Androgens can increase ROS production, leading to mitochondrial modifications and enhanced oxidative stress in PCa cells. This interaction promotes resistance to treatments such as androgen deprivation therapy.[11]

Antioxidant mechanisms involve various enzymes and substances that scavenge free radicals. However, findings from observational epidemiological studies and clinical trials examining the relationship between individual antioxidants and PCa risk have yielded inconsistent results.[12 13] To thoroughly evaluate the effects of various dietary and lifestyle elements on the overall balance between oxidation and antioxidants, the oxidative balance score (OBS) was created. This metric quantifies an individual's exposure to pro-oxidants and antioxidants.[14] Individuals with a higher OBS score were found to have elevated levels of antioxidants compared with pro-oxidants. Previous studies have found that OBS was negatively associated with PCa risk.[15] Nevertheless, there is still a lack of consensus on the relationship between oxidative stress and PCa.

This study aimed to evaluate the link between oxidative stress potential, as reflected by OBS, and PCa risk. The assessment used data from the National Health and Nutrition Examination Survey (NHANES), representing the civilian population of the USA. By leveraging comprehensive NHANES data, incorporating a wide range of oxidative stress markers, identifying specific influential factors, conducting stratified analyses and evaluating long-term effects, this study significantly advances the understanding of the relationship between OBS and PCa. These novel contributions provide valuable insights that can inform prevention and management strategies for PCa.

MATERIALS AND METHODS

Data sources and study population

This study obtained data from the NHANES, a nationwide cross-sectional survey that assesses the health and nutritional well-being of the non-institutionalised population in the USA.[16] Data from six consecutive 2-year cycles of the NHANES, NHANES, spanning 1999–2010, were used. This specific period was selected because individuals who participated in these cycles answered the question, 'Has a doctor or healthcare provider ever informed you that you have prostate cancer?'. The exclusion criteria were as follows: (1) female participants; (2) participants lacking complete information on any components required

for OBS calculation; (3) participants with missing data for PCa definition; (4) participants without C reactive protein (CRP), poverty, education and diabetes. Male participants with energy intakes of less than 800 kcal/day or more than 4200 kcal/day were categorised as having improper energy consumption. Figure 1 presents the flow chart illustrating the process of selecting participants.

Oxidative balance score (exposure)

The determination of OBS in this study involved examining 16 nutrients and 4 lifestyle factors. The analysis included 5 substances that promote oxidation and 15 substances that prevent oxidation. These elements were chosen based on previously established data concerning the connection between oxidative stress and various nutrients or lifestyle factors.[14] The OBS was generated using dietary information obtained from the initial dietary review interview. The 16 nutrients included dietary fibre, carotene, riboflavin, niacin, vitamin B6, folate, vitamin B12, vitamin C, vitamin E, calcium, magnesium, zinc, copper, selenium, and total fat and iron (online supplemental table 1). The analysis also considered four lifestyle factors: exercise, body mass index (BMI), alcohol intake and tobacco use, with smoking intensity quantified using cotinine levels. Pro-oxidants included total fat, iron, BMI, alcohol consumption and smoking, while the remaining factors were classified as antioxidants. The OBS calculation followed the protocol presented by Zhang *et al*.[14] Based on their method, alcohol consumption was categorised into three groups: heavy drinkers (≥30 g/day for men), non-heavy drinkers (0–30 g/day for men) and non-drinkers, assigned 0, 1 and 2 points, respectively. Other components were divided into tertiles, with antioxidants scoring 0–2 and pro-oxidants scoring 2–0 (online supplemental table 1). For missing components, a score of 0 was assigned, regardless of being an antioxidant or pro-oxidant. A higher OBS indicated greater exposure to antioxidants.[17]

Covariates

In our research, we included covariates that were previously demonstrated or hypothesised to have associations with either PCa or OBS. The variables in this research included race (Mexican American, non-Hispanic Black, white, other Hispanic and other race), age group (under 65 years, 65 years or older), education level (above high school, high school or General Educational Development, and less than high school), family income (low, medium or high) and marital status (single, married or with partner). CRP was used to reflect inflammatory markers. Overall dietary quality was assessed by total energy intake and carbohydrate, protein and cholesterol intake. Physical activity levels were classified into three categories—less than moderate, moderate and vigorous—based on responses collected through the NHANES physical activity questionnaire. In NHANES, the cigarette-use questionnaire was replaced with serum cotinine. Comorbidities included hypertension and diabetes. Individuals were categorised as having hypertension if they met any of the following conditions: systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg or a self-reported diagnosis of hypertension as mentioned in the Blood Pressure & Cholesterol section of the survey. The diagnosis of diabetes was determined by measuring blood glucose levels, using medication and self-reporting.[18]

Statistical analysis

To comply with NHANES' analytical guidelines, the R package 'survey' was used to calculate individual sample weights. These weights were determined by considering the NHANES recommended sample weight for dietary day 1 records and the complex sampling design of NHANES. According to the Central Limit Theorem, the continuous variables, after weighting, follow a normal distribution.[19] Continuous variables are represented using weighted means (SEs), while categorical variables are expressed as sample numbers (weighted percentages). The Rao-Scott χ^2 test was used to evaluate variations in variable characteristics among different OBS groups (divided into quartiles), while the Kruskal-Wallis test was employed for non-normal continuous variables.

To examine the connections between OBS and PCa, weighted linear models and weighted logistic regression models were used, incorporating three hierarchical adjustments. The p value for trend was calculated. Model 1 (unadjusted model) performed weighted linear regression between OBS and PCa. Model 2 (moderately adjusted model) accounted for age group, race, marital status, education level and family income. Model 3 (fully adjusted model) adjusted for age group, race, energy and protein intake, education level, family income, marital status, smoking status, physical activity, hypertension, diabetes and CRP. OBS was transformed into a categorical variable by quartiles based on weighted distributions for regression. To investigate their correlation with PCa, OBS was categorised into dietary OBS and lifestyle OBS. Subgroup and interaction analyses were carried out using logistic regressions with full adjustments. To investigate the non-linear correlation between OBS and PCa, restricted cubic splines (RCS) were used in every model, incorporating four knots. A sensitivity analysis that exclusively includes patients diagnosed with PCa was conducted. Wald tests, executed through the 'ANOVA' command in R, provided both the overall and non-linear p values in the RCS. Statistical analyses were performed using R V.4.0.5 (http://www.R-project.org; The R Foundation). Statistical significance was determined based on a two-sided p value of less than 0.05.

Consent to participate

Surveys protocols were reviewed and approved by Centre for Disease Control and Prevention, and written informed consent was obtained from each participant.

Table 1 The baseline characteristics by quartiles of the OBS: National Health and Nutrition Examination Survey 1999–2010

Characteristic	Total n=53 971 892	Q1 (3, 12) n=11 349 527	Q2 (12, 18) n=13 524 910	Q3 (18, 24) n=15 097 311	Q4 (24, 36) n=14 000 145	P value
OBS, mean (SE)	19.19±0.15	9.37±0.06	15.54±0.06	21.49±0.06	28.17±0.08	<0.0001
CRP, mean (SE)	0.37±0.01	0.52±0.03	0.39±0.02	0.34±0.01	0.27±0.01	<0.0001
Total energy intake, mean (SE)	2436.21±15.78	1582.71±20.30	2126.16±22.76	2552.31±22.32	3302.46±36.86	<0.0001
Protein, mean (SE)	94.25±0.66	56.05±0.64	79.69±0.85	99.32±0.95	133.80±1.47	<0.0001
Carbohydrate, mean (SE)	286.12±2.24	189.28±3.34	248.72±3.03	295.33±3.63	390.83±4.99	<0.0001
Cholesterol, mean (SE)	341.71±3.59	225.34±4.40	304.63±6.87	366.07±6.77	445.59±9.82	<0.0001
Age (year), mean (SE)	55.46±0.22	56.88±0.36	56.24±0.34	55.05±0.39	54.00±0.36	<0.0001
Age group,n (%)						<0.0001
<65	40 792 207 (75.58)	8 150 519 (71.81)	9 928 711 (73.41)	11 597 235 (76.82)	11 115 743 (79.40)	
≥65	13 179 685 (24.42)	3 199 007 (28.19)	3 596 199 (26.59)	3 500 076 (23.18)	2 884 402 (20.60)	
Race, n (%)						<0.0001
Mexican American	3 140 871 (5.82)	657 340 (5.79)	948 342 (7.01)	861 027 (5.70)	674 162 (4.82)	
Other Hispanic	2 016 279 (3.74)	536 870 (4.73)	530 556 (3.92)	529 289 (3.51)	419 565 (3.00)	
Non-Hispanic White	41 929 025 (77.69)	7 746 803 (68.26)	10 280 341 (76.01)	12 068 260 (79.94)	11 833 621 (84.52)	
Non-Hispanic Black	4 837 898 (8.96)	1 847 821 (16.28)	1 203 012 (8.89)	1 014 114 (6.72)	772 950 (5.52)	
Other race	2 047 819 (3.79)	560 692 (4.94)	562 659 (4.16)	624 620 (4.14)	299 848 (2.14)	
Education level, n (%)						<0.0001
Less than high school	10 407 499 (19.28)	3 194 423 (28.15)	3 109 465 (22.99)	2 407 761 (15.95)	1 695 850 (12.11)	
High school grad or GED	13 580 429 (25.16)	3 182 185 (28.04)	3 498 079 (25.86)	3 826 558 (25.35)	3 073 607 (21.95)	
Above high school	29 983 964 (55.55)	4 972 918 (43.82)	6 917 366 (51.15)	8 862 992 (58.71)	9 230 688 (65.93)	
Marital status, n (%)						<0.0001
Married or with partner	40 967 678 (75.91)	7 887 562 (69.50)	10 208 012 (75.48)	11 649 498 (77.16)	11 222 607 (80.16)	
Single	13 004 215 (24.09)	3 461 965 (30.50)	3 316 898 (24.52)	3 447 814 (22.84)	2 777 538 (19.84)	
Family income, n (%)						<0.0001
Low	8 332 604 (15.44)	2 482 216 (21.87)	2 277 821 (16.84)	1 935 070 (12.82)	1 637 496 (11.70)	
Medium	18 026 029 (33.40)	4 610 896 (40.63)	4 625 229 (34.20)	4 852 721 (32.14)	3 937 183 (28.12)	
High	27 613 259 (51.16)	4 256 414 (37.50)	6 621 860 (48.96)	8 309 520 (55.04)	8 425 465 (60.18)	
Hypertension, n (%)						<0.0001
No	28 255 084 (52.35)	5 124 880 (45.16)	6 797 499 (50.26)	8 048 907 (53.31)	8 283 799 (59.17)	
Yes	25 716 808 (47.65)	6 224 647 (54.84)	6 727 411 (49.74)	7 048 404 (46.69)	5 716 346 (40.83)	
Diabetes mellitus, n (%)						<0.0001

Continued

Table 1 Continued

Characteristic	Total	Q1 (3, 12)	Q2 (12, 18)	Q3 (18, 24)	Q4 (24, 36)	P value
	n=53 971 892	n=11 349 527	n=13 524 910	n=15 097 311	n=14 000 145	
DM	9 204 333 (17.05)	2 493 103 (21.97)	2 600 836 (19.23)	2 198 389 (14.56)	1 912 007 (13.66)	
IFG	3 227 056 (5.98)	613 247 (5.40)	711 467 (5.26)	937 961 (6.21)	964 382 (6.89)	
IGT	1 314 525 (2.44)	272 174 (2.40)	376 645 (2.78)	426 280 (2.82)	239 427 (1.71)	
No	40 225 977 (74.53)	7 971 003 (70.23)	9 835 963 (72.72)	11 534 682 (76.40)	10 884 329 (77.74)	
PCa prevalence rate (%)	2.55					

CRP, C reactive protein; DM, diabetes mellitus; GED, General Educational Development; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OBS, oxidative balance score; PCa, prostatae cancer.

Patient and public involvement

Patients and the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

From NHANES 1999 to 2010, a total of 62 160 comprehensive individual interviews were conducted, with 31 575 female participants subsequently excluded. Additionally, 1676 participants were eliminated due to insufficient data on PCa and OBS (figure 1). Our final analysis included 8156 participants, of whom 332 were diagnosed with PCa, resulting in a prevalence rate of 2.55% (95% CI 2.11–3.00). Table 1 lists the differences among participants across the four OBS quartiles. Based on weighted analysis, the average age was 55.46±0.22 years. Compared with individuals in the first quartile of OBS, those in the fourth quartile were younger (54.00±0.36 years vs 56.88±0.36 years) and had a higher likelihood of being non-Hispanic White (84.52% vs 68.26%). In OBS quartile 4, the occurrence rates of high blood pressure (40.83% vs 54.84%) and diabetes (13.66% vs 21.97%) were lower than in OBS quartile 1. Conversely, OBS quartile 4 exhibited higher values for total energy intake (3302.46±36.86 vs 1582.71±20.30 kcal), education level (65.93% vs 43.82%) and income (60.18% vs 37.50%) compared with OBS quartile 1. The results from online supplemental table 2, displaying baseline characteristics from NHANES (1999–2010) grouped by PCa status, show significant demographic and health differences between individuals with and without PCa. Notably, the PCa group had a higher mean age of 72.29 years compared with 55.02 years in the non-PCa group, indicating a strong age correlation with PCa incidence. Dietary intake differed significantly between the groups; the PCa group consumed less total energy, protein and carbohydrates but had a higher mean cholesterol intake. Health-wise, the prevalence of hypertension and diabetes mellitus was significantly higher in the PCa group.

Table 2 summarises the outcomes of logistic regressions with weights applied. When considering the OBS as a continuous factor, model 1 (the unadjusted model) showed no significant association between OBS and PCa (OR 1.001, 95% CI 0.984–1.019, p>0.05). This result was consistent with the findings from Model 3 (OR 1.038, 95% CI 1.005–1.071, p>0.05). In the sensitivity analysis, after dividing OBS into quartiles and comparing relative to OBS quartile 1, we found that the odds of PCa for individuals in the third or fourth quartile of OBS were not statistically significant in the full model (Q3: OR 1.127, 95% CI 0.694–1.829, p for trend >0.05; Q4: OR 1.852, 95% CI 1.028–3.339, p for trend >0.05).

According to the RCS analysis, despite slight increasing trends in the OBS, there was no overall or non-linear association between OBS and PCa (figure 2).

Online supplemental table 3 displays the outcomes of a logistic regression analysis examining the connection

Table 2 Weighted logistic regression analysis models showing the associations between OBS and prostate cancer

	Model 1		Model 2		Model 3	
OBS	OR (95% CI)	P for trend	OR (95% CI)	P for trend	OR (95% CI)	P for trend
Q1	Ref	0.974	Ref	0.090	Ref	0.071
Q2	0.974 (0.677, 1.400)		1.064 (0.716, 1.579)		1.154 (0.746, 1.784)	
Q3	0.839 (0.576, 1.221)		0.995 (0.667, 1.486)		1.127 (0.694, 1.829)	
Q4	1.035 (0.733, 1.460)		1.462 (0.987, 2.165)		1.852 (1.028, 3.339)	
Continue	1.001 (0.984, 1.019)		1.020 (1.000, 1.041)		1.038 (1.005, 1.071)	

Model 1: unadjusted.
Model 2: adjusted for age group, race, marital status, education level and family income.
Model 3: Additionally, adjusted for C reactive protein, total energy intake, protein, carbohydrate, cholesterol, hypertension and diabetes mellitus.
OBS, oxidative balance score.

between dietary and lifestyle OBS and PCa. There was no correlation between PCa and either dietary OBS or lifestyle OBS. For dietary OBS, the association with PCa was statistically insignificant after adjusting for all variables (OR=1.565, 95% CI 0.841–2.913, p for trend=0.245). Similarly, lifestyle OBS showed no association with PCa after adjusting for all confounders (OR=1.575, 95% CI 0.915–2.710, p for trend=0.090). Table 3 summarises the findings of the subgroup analysis. Although there were variations in population settings (subgroups), we did not observe a substantial correlation between OBS and PCa, indicating a minimal likelihood of heterogeneities (p for interaction >0.05).

The weighted logistic regression analysis from online supplemental table 4 reveals the association between OBS and PCa across three models in a sensitivity test, which excludes 721 patients with other types of tumours, focusing exclusively on those diagnosed with PCa. The unadjusted model 1 shows no significant trend (OR for Q4=1.167, 95% CI 0.767–1.776, p=0.517). Model 2, adjusted for sociodemographic factors, indicates a moderate increase in PCa risk in the highest OBS quartile (OR=1.749, 95% CI 1.072–2.854, p=0.022). Model 3, additionally adjusted for health and dietary factors, shows a robust association (OR=2.737, 95% CI 1.304–5.746, p=0.008), suggesting a significant link between higher OBS and increased PCa risk.

DISCUSSION

This study investigated the link between OBS and PCa in a large, random, nationwide sample of American individuals. Surprisingly, no correlation was discovered between OBS and PCa in either continuous or categorical models, suggesting that the influence of oxidative stress on PCa remains unclear. Furthermore, the analysis that examined dietary OBS and lifestyle OBS individually yielded comparable results.

Numerous research studies have examined the correlation between combined oxidative scores of antioxidant exposure levels and the likelihood of developing colorectal, prostate and lung cancer.[20–22] The findings of our study were largely in line with a cohort investigation conducted in 2011 using data from the Canadian Study of Diet, Lifestyle and Health cohort. This study did not identify any connection between OBS and the overall likelihood of developing PCa or advanced disease.[23] In the study conducted by Geybels *et al* in the Netherlands Cohort, a wider range of OBS elements were analysed compared with previous research. This expanded list included α-carotene, zinc, flavonoids and glucosinolates, all of which have potential antioxidant properties. The findings revealed no significant association between OBS and the risk of PCa.[24] Several other studies investigated the correlation between OBS and PCa, yielding contradictory

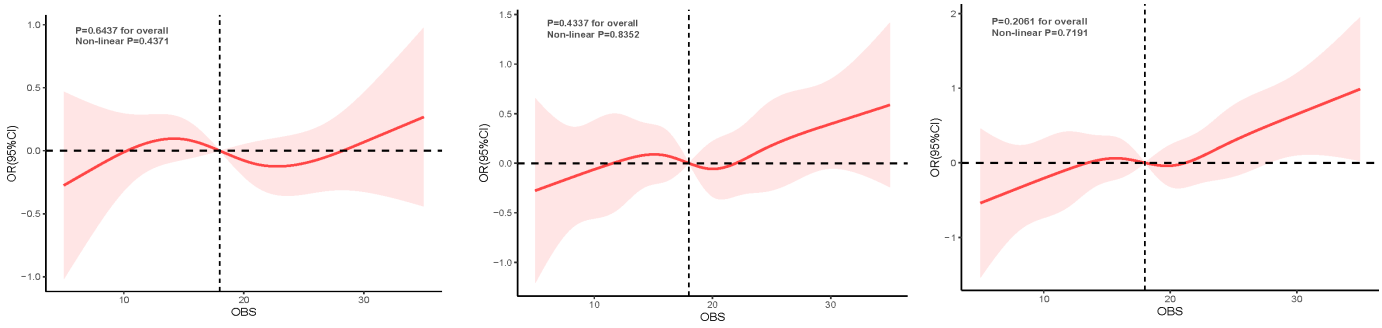

Figure 2 Association between oxidative balance score (OBS) and prostate cancer visualised by restricted cubic splines. Model 1: unadjusted; model 2: adjusted for age group, race, marital status, education level and family income; model 3: additionally, adjusted for C reactive protein, total energy intake, protein, carbohydrate, cholesterol, hypertension and diabetes mellitus.

Table 3 Subgroup analysis

	OR (95% CI)	P for interaction
Age group		0.701
<65	1.042 (0.956, 1.135)	
≥65	1.046 (1.011, 1.083)	
Race		0.793
Mexican American	1.044 (0.921, 1.184)	
Other Hispanic	0.904 (0.801, 1.020)	
Non-Hispanic White	1.053 (1.019, 1.088)	
Non-Hispanic Black	1.037 (0.974, 1.105)	
Other race	1.302 (0.658, 2.576)	
Marital status		0.925
Married or with partner	1.054 (1.013, 1.096)	
Single	1.038 (0.972, 1.108)	
Education level		0.238
Less than high school	1.007 (0.944, 1.075)	
High school grad or GED	1.114 (1.034, 1.201)	
Above high school	1.045 (1.003, 1.089)	
Family income		0.601
Low	1.003 (0.920, 1.094)	
Medium	1.048 (1.005, 1.093)	
High	1.066 (1.010, 1.125)	
Hypertension		0.575
No	1.055 (1.019, 1.092)	
Yes	1.038 (0.985, 1.095)	
Diabetes mellitus		0.100
DM	1.012 (0.989, 1.037)	
IFG	0.977 (0.945, 1.009)	
IGT	1.045 (0.954, 1.144)	
No	0.902 (0.801, 1.016)	

All presented covariates were adjusted (as in model 3) except the stratification variable itself.
DM, diabetes mellitus; GED, General Educational Development; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

findings. For example, Li *et al* conducted a previous observational study that found a negative correlation between antioxidant score (highest vs lowest category) and the risk of overall PCa (RR 0.60, 95% CI 0.39–0.88).[25] The initial investigation into the correlation between PCa and OBS revealed that OBS was also associated with a reduced likelihood of PCa (OR 0.28, p<0.05). However, it is important to note that this particular study was a small-scale case–control study (89 cases, 197 controls), which restricts the applicability of its findings to the broader population.[15] According to different research conducted by Lakkur *et al*, individuals with an elevated OBS might have a greater likelihood of developing or receiving a diagnosis of PCa.[26] Lakkur *et al* performed an analysis that considered family history of PCa and analysed the effects of individual polyunsaturated fatty acids instead of all polyunsaturated fatty acids. The utilisation of various classifications for incorporating components into the OBS differed among these three studies and the current study, potentially contributing to the inconsistent results observed across the studies.

In our research, we analysed a broader range of OBS elements compared with earlier studies, which omitted riboflavin, niacin, vitamin B6, overall folate, vitamin B12, magnesium, calcium or copper, all of which have potential antioxidant properties.[14] The involvement of various B vitamins contributes to the development of PCa risk, which should not be disregarded. Folate and vitamin B12, essential for DNA integrity, have been associated with a modest increase in PCa risk, a subject still under debate.[27] According to a comprehensive case–control study, higher levels of riboflavin in the bloodstream could potentially lead to a higher likelihood of developing PCa.[28] Additionally, research indicates that low levels of magnesium in the blood and a high ratio of calcium to magnesium are significantly linked to advanced PCa, while increased copper levels may have a notable impact on the onset of PCa.[29 30] Incorporating physical exercise into our lifestyle OBS components is important, as it can activate Nrf2 and promote the expression of antioxidant genes.[31–33] Numerous studies indicate that this could be a potential factor that can be modified to reduce the risk of PCa. Most prior research examining the influence of oxidative stress on PCa concentrated solely on a few antioxidant elements, neglecting the comprehensive oxidation balance patterns or the interactions between antioxidant and pro-oxidant elements. In other words, the OBS offered an effective means of assessing the overall potential for oxidative stress and its correlation with PCa, rather than examining each individual antioxidant element separately.

Our study has multiple strengths. First, a more thorough investigation result can be obtained by studying OBS as a comprehensive index. Moreover, the NHANES dataset employs a sophisticated, multi-phase random sampling methodology to select representative samples with excellent data quality. Our research involved a comprehensive cross-sectional analysis, examining the correlation between OBS and PCa, while accounting for sample weights to ensure a more accurate representation of the entire US population. Additionally, the research accounted for potential factors that could influence the results, such as demographic traits, energy consumption and CRP levels. CRP is extensively used as a biomarker for chronic inflammation, and its association with PCa has been the subject of multiple studies. Elevated CRP levels have been linked with an increased risk of several cancers, including PCa, supporting its utility in assessing chronic inflammation's role in cancer risk.[34] In the Atherosclerosis Risk in Communities study, Prizment *et al* found that plasma CRP levels were associated with an increased risk of PCa.[35] Another study by Stikbakke *et al* in the PROCA-life study observed that men with increased hs-CRP levels

had a 36% higher risk of developing PCa.[34] These findings collectively underscore CRP's adequacy as an indicator of chronic inflammation and its association with PCa risk. However, the non-specific nature of CRP implies that elevated levels could result from various inflammatory conditions, necessitating careful interpretation within the broader clinical context. Therefore, we included it in the multivariate regression to adjust for bias. Instead of using questionnaires, we used serum cotinine levels to reflect smoking status, effectively reducing recall bias.[36] Furthermore, stratified analysis was conducted based on dietary OBS and lifestyle OBS, yielding consistent results with the primary analysis and enhancing the specificity of the findings. Nevertheless, it is important to acknowledge certain constraints. Due to the nature of this cross-sectional study, it was not possible to establish a causal relationship between OBS and PCa. More qualitative longitudinal research in this area is recommended. Second, due to lack of information on PCa staging, we did not perform subgroup analyses according to localised PCa, progressive PCa, etc. What is more, our study revealed a significant age difference between PCa patients and controls, which is a major limitation. Age is a known risk factor for PCa, and this disparity could confound the relationship between OBS and PCa. Although we adjusted for age in our analysis, the observed difference suggests potential residual confounding. This limitation calls for cautious interpretation of our findings. Future studies should consider matching cases and controls by age or applying more rigorous adjustments. Furthermore, despite our study indicating no correlation between OBS and PCa risk, it is plausible that the magnitude of the impact is relatively minor and that our sample size may not be adequate to detect this distinction. Additionally, the study assumes a direct correlation between various antioxidants, pro-oxidants and oxidative stress. This overlooks the possibility of threshold effects in antioxidants and the fact that certain antioxidants might exhibit pro-oxidant properties under specific circumstances or at elevated concentrations, as observed with copper and carotenoids. Last but not least, the initial analysis included patients with multiple tumour histories, potentially confounding the results. To address this, a sensitivity analysis was conducted, including only patients with a singular history of PCa. This refined analysis suggested a potential link between higher oxidative stress and increased PCa risk. These findings highlight the importance of controlling for multiple tumour histories in research and suggest that further investigation is warranted. Future studies should focus on larger cohorts and longitudinal designs to better understand the role of oxidative stress in PCa development and to identify possible therapeutic interventions.

CONCLUSION

While an imbalance in oxidative control could impact the likelihood of developing tumours, the occurrence of PCa might not necessarily be linked to oxidative stress. Nevertheless, given the study's cross-sectional design, it is important to exercise caution when interpreting these results, emphasising the necessity for additional longitudinal research.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The survey protocols were reviewed and approved by the Institutional Review Board of the National Centre for Health Statistics of the Centre for Disease Control and Prevention (CDC) (protocol numbers: protocol #98-12 (NHANES 1999–2004); protocol #2005-06 (NHANES 2005–2010)). This investigation was approved by the Institutional Review Board of Beijing Hospital (Approval ID: 2022BJYYEC-198-02). Participants gave informed consent to participate in the study before taking part.

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