Association between high-density lipoproteins and prostate specific antigen: A cross-sectional study from NHANES database

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Abstract. According to increasing evidence, high-density lipoproteins (HDLs) may raise prostate-specific antigen (PSA) levels in the prostate. The link between HDL-cholesterol (C) and PSA, on the other hand, is debatable and challenging. Hence, the present study examined the relationship between HDL-C and PSA in men using the National Health and Nutrition Examination Survey (NHANES) database. NHANES data were extracted for five cycles from 2001 to 2010. The data used for analysis included PSA concentrations, sociodemographic and laboratory data. After the screening, 6,669 out of 52,195 participants were included in the present study. Participants were divided into four groups based on HDL-C quartiles. Categorical and continuous variables using weighted chi-square tests and linear regression models were analysed to compare differences between groups. A total of three weighted multivariate linear regression models were constructed and the association between HDL-C and PSA using a smoothed curve fit was assessed. In the present study, unadjusted and adjusted multivariate linear regression models revealed a significant positive association between PSA concentrations and serum HDL-C levels. Specifically, each unit increase in HDL-C ratio was associated with an increase in PSA concentration by 0.470 ng/ml (P<0.001) in the unadjusted model. In minimally adjusted models, accounting for socioeconomic and demographic factors, this association remained significant, with an increase of 0.408 ng/ml per unit increase in serum HDL-C (P<0.001). Furthermore, the stratified analysis revealed various impacts based on socioeconomic status and HDL-C levels, with a significant interaction between household income and HDL-C levels (P=0.037). Exclusion of subjects with low HDL-C levels strengthened the association, revealing a significant increase in PSA concentration with higher HDL-C levels (0.50 ng/ml per 1 mmol/l increase, P=0.009). The findings of the present study suggest a nuanced relationship between HDL-C levels, socioeconomic factors, and PSA concentrations, highlighting the potential importance of considering these factors in prostate cancer (Pca) screening and risk assessment. The present study found a positive association between serum HDL-C and PSA concentrations in adult men in the United States without a Pca diagnosis.

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Abbreviations: Pca, prostate cancer; HDL-C, high-density lipoprotein cholesterol; PIR, poverty income ratio; PSA, prostate-specific antigen

Key words: PSA, HDL, Pca, triglycerides, national health and nutrition examination survey

Introduction

Prostate cancer (Pca) is the second most commonly diagnosed cancer and the fifth leading cause of cancer-related deaths among men worldwide (1). In the United States of America (USA) alone it is estimated that there were ~288,300 new cases of Pca and 34,700 deaths from the disease in 2021, and this number increased to 3,523,230 in 2022 (2,3). Therefore, Pca remains the most frequently diagnosed cancer among men (2). Early detection and treatment are crucial for improving prognosis and survival rates in patients with Pca (4).

Prostate-specific antigen (PSA) is a protein produced by the prostate gland, and its levels can be measured through a simple blood test. The PSA test is widely used for Pca screening (5,6); however, its effectiveness in reducing mortality from Pca remains controversial (7). Elevated PSA levels can also be caused by non-cancerous conditions such as prostatitis and benign prostatic hyperplasia, which can lead to false-positive results and unnecessary biopsies (6,8-10).

High-density lipoprotein cholesterol (HDL-C) is a lipoprotein that transports cholesterol from peripheral tissues to the liver for excretion. HDL-C is commonly referred to as 'good' cholesterol because it has been revealed to have protective effects against cardiovascular disease (11). Previously, several studies have investigated the association between HDL-C levels and Pca risk. Several hypotheses have been proposed to explain the potential link between HDL-C levels and Pca. One theory is that high levels of HDL-C may be protective against Pca by removing excess cholesterol from prostate cells and reducing oxidative stress (12). Conversely, another hypothesis posits low HDL-C levels may be a result of inflammation, which has been linked to the development and progression of Pca (13).

In addition to its potential role in Pca risk, HDL-C levels may also be related to PSA levels. An inverse association between HDL-C levels and PSA levels has been reported, suggesting that men with higher HDL-C levels may have lower PSA levels (14). However, the relationship between HDL-C and PSA levels is not fully understood, and additional research is needed to clarify this association. Therefore, the purpose of the present study was to examine the relationship between HDL-C and PSA in men from USA using the National Health and Nutrition Examination Survey (NHANES) database and to discuss the potential implications of this relationship for Pca screening and diagnosis.

Materials and methods

Data availability. The NHANES, initially established in 1960, is a survey conducted by the National Center for Disease Control and the Prevention National Center for Health Statistics. The objective of this assessment is to evaluate the physical well-being and dietary condition of both adults and children living in USA. Demographic and methodological information were searched in the NHANES website [www.cdc.gov/nchs/nhanes (15)], viewed on October 7, 2022. The NHANES protocols have been authorized by the National Center for the Health Statistics Research Ethics Review Board.

Study population. NHANES employs a stratified, multi-stage random sampling design, serving as a nationally representative nutrition survey of the broader USA population. For the present study, five cycles of NHANES data were incorporated covering the period from 2001 to 2010. The dataset utilized for the secondary analysis encompasses PSA concentrations, socio-demographic data and laboratory information.

To ensure the accuracy and relevance of the present study's findings, participants based on specific criteria were systematically excluded: (i) Age below 40 years (n=34,634); (ii) individuals diagnosed with Pca (n=377); (iii) individuals with factors that could impact PSA levels, such as a prostatitis diagnosis, statin drug usage, a recent prostate biopsy within one week, or urinary system surgery within one month (n=492); and (iv) participants with missing PSA data (n=10,023); (v) Notably, there were no instances of missing HDL-C data (n=0).

After a thorough screening process, 6,669 individuals from the initial 52,195 participants were included in the present study, as illustrated in Fig. 1. Furthermore, the present study adheres to the ethical guidelines set by the world medical association's declaration of Helsinki for research design and conduct. The data analysis of the present study is based on the robust and representative NHANES data.

Statistical analysis. All statistical analyses were conducted by using the R Package and EmpowerStats (http://www.empowerstats.net), utilizing the complex weighted sampling design from NHANES. Participants were characterized according to the quartiles of HDL-C: Category 1 (19-40), Category 2 (40-46), Category 3 (46-56) and Category 4 (56-148). For categorical variables, percentages were used, while the means ± standard deviations were calculated for continuous variables.

To investigate group differences, weighted chi-square tests were performed for categorical variables and linear regression models for continuous variables. The link between HDL-C and PSA levels was assessed using a weighted multivariate linear regression model. A total of three models were established: An unadjusted model (Model 1), a minimally adjusted model (Model 2) accounting for factors such as poverty-income ratio, ethnicity, military participation, marriage and education, and a fully adjusted model (Model 3) with additional adjustments for triglycerides, low density lipoprotein cholesterol (LDL-C), monocyte count, neutrophil count, red blood cell count, haemoglobin, platelet count and C-reactive protein.

Stratified analyses were conducted based on age, family income, ethnicity, military status, marital status and education, with interactions examined. Additionally, assuming the normal reference value range of HDL-C as 1.04 mmol/l, a weighted multivariate linear regression analysis was performed, excluding individuals with HDL-C levels <1.04 μg/dl to limit the impact of very low HDL-C in men from USA. $P<0.05$ was considered to indicate a statistically significant deference.

Results

Baseline characteristics of the selected participant. A statistical analysis was performed on HDL-C, triglyceride and PSA levels. Grouping HDL-C into four quartiles (Q1-Q4), there were no significant differences in military participation or platelet count between the quartile groups. Participants with higher PSA, older age, higher household income, higher level of education, married, high in vitamin D, high LDL-C and high in total cholesterol present high HDL-C levels. Conversely, individuals with elevated serum HDL-C have lower triglycerides, lower white blood cell count, lower lymphocyte number, lower monocyte number, lower neutrophils, lower red blood cells, lower haemoglobin and lower C-reactive protein. As demonstrated in Table I, non-Hispanic whites were the main participants in the present study.

Link between PSA concentration and serum HDL-C. Univariate and multivariate analyses was performed using weighted linear models, resulting in three weighted univariate and multivariate linear regression models. First, in the unadjusted model, for each unit increase in the HDL-C ratio, PSA concentration increased by 0.470 ng/ml (0.281, 0.659) ($P<0.001$). In a minimum adjustment model, which accounted for factors such as poverty-income ratio, ethnicity, military

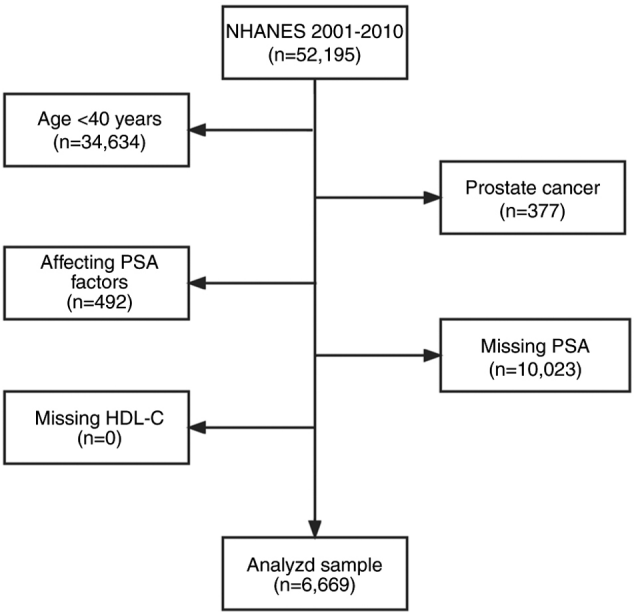

Figure 1. Study participant inclusion and exclusion criteria. According to the inclusion and exclusion criteria, a total of 6,669 eligible cases were included, and they were divided into four groups according to the HDL-C quartile. HDL-C, high-density lipoprotein cholesterol; PSA, prostate-specific antigen; NHANES, national health and nutrition examination survey.

enlistment, marriage and education, PSA concentrations increased by 0.408 ng/ml (0.227, 0.589) (P<0.001), for each unit increase in serum HDL-C.

Further adjustments were made in the fully adjusted model, which included additional factors including poverty income ratios (PIRs), ethnicity, military enlistment, marriage, education, triglycerides, LDL-C, number of monocytes, number of neutrophils; number of red blood cells, haemoglobin, number of platelets and C-reactive protein. In this model, PSA concentrations rose by 0.400 ng/ml (0.099,0.701) (P<0.009) for each additional unit of serum HDL-C. The results of linear relationship analyses are presented in Table II.

Sensitivity analysis. Sensitivity analyses was performed to confirm the accuracy and robustness of the results of the present study. First, serum HDL-C was converted as a continuous variable to a categorical variable based on quartile values and then the P-value of the trend was calculated (Table II). Surprisingly, the results of the categorical variable were consistent with the effect of serum HDL-C as a continuous variable.

To further investigate the potential linear relationship between serum HDL-C and PSA concentration, a smoothed curve based on a fully adjusted model was constructed. As demonstrated in Fig. 2A, most of the samples clustered at HDL-C concentration to the left of the 2.5 mmol/l vertical line, and the trend of sample distribution was not very clear. The final adjusted smoothed curve fit is shown in fig. 2B. The curve fit demonstrated a positive linear correlation between HDL-C and PSA; for every 1 mmol/l increase in serum HDL-C, the PSA concentration increased by 0.400 ng/ml. These results suggested a positive correlation between serum HDL-C and PSA concentration.

Stratified association between HDL-C and PSA. An analysis was performed to determine the hierarchical relationship between PSA and HDL-C. The findings of the present study revealed a 25.2% reduction in PSA concentrations among individuals with low HDL-C and low household income [hazard ratio (HR=0.748), P<0.001]. Among those with higher household incomes, PSA concentrations were reduced by 58.0% in individuals with low HDL-C (HR=0.420, P=0.011). Additionally, PSA concentrations were reduced by 6.8% among those with lower than secondary education (HR=0.932, P<0.001). The interaction test showed that the effect of household income on PSA concentration was significantly affected by HDL-C levels (P=0.037). These findings suggested a link between low HDL-C levels and lower PSA concentrations, with this association being stronger in individuals with lower household income (Table III).

Results of weighted linear regression modelling of the association between serum HDL-C and PSA after excluding individuals with HDL-C abnormalities (<1.04 mmol/l). First, in the unadjusted model, for every 1 mmol/l increase in HDL-C concentration, PSA concentration increased by 0.53 ng/ml (P<0.001). Second, in the minimum adjustment model which accounted for factors such as PIR, ethnicity, military enlistment, marital status and education, PSA concentration increased by 0.42 ng/ml for every 1 mmol/l increase in HDL-C concentration (P=0.01).

Third, after completely adjusting the poverty-income ratio, ethnicity, joining the army, marital status, education, triglycerides, LDL-C, monocyte count, neutrophil count, red blood cell count, haemoglobin, platelet count and C-reactive protein, PSA concentration increased by 0.50 ng/ml for every 1 mmol/l increase in HDL-C concentration (P=0.009). Even after excluding participants with HDL-C levels <1.04 mmol/l, this positive association remained evident in adult men in USA. These findings suggested that HDL-C is positively correlated with PSA in adult men, even at a reference concentration of >1.04 mmol/l (Table IV).

Discussion

The present study represents one of the most comprehensive cross-sectional studies to determine the association between HDL-C and PSA. It is also the first, to the best of our knowledge, to examine this relationship in men from USA without a history of Pca using the NHANES database. The first analysis relied on checking the stratified connection between HDL-C and PSA. In this analysis, participants were classified based on various factors, such as family income (low group, median group, and high group), education, ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black and other ethnicity), military and marital status (married, single, or living with a partner).

Other researchers suggested a decreased risk of Pca associated with higher HDL-C levels; the weighted median approach indicated the possibility of a different correlation, and the mechanism behind this association remains unclear (16).

However, the positive association between serum HDL-C and PSA concentrations observed in the present study was consistent with the results of previous studies. It was found

Table I. Baseline characteristics of the selected participants.

HDL-cholesterol (mmol/l)	Q1	Q2	Q3	Q4	P-value
N	1,458	1,682	1,797	1,732	
Total prostate specific antigen (ng/ml)	1.56±2.97	1.64±2.18	1.73±2.78	1.94±3.67	0.002
Age (years)	57.2±11.76	58.43±11.74	58.93±12.09	59.44±11.73	<0.001
Family income	2.62±1.61	2.78±1.59	2.95±1.64	2.91±1.66	<0.001
Military Status					0.285
Yes	467 (32.03%)	583 (34.66%)	613 (34.13%)	608 (35.10%)	
No	991 (67.97%)	1,099 (65.34%)	1,183 (65.87%)	1,124 (64.90%)	
Education					<0.001
Less than high school graduate	505 (34.66%)	503 (29.90%)	541 (30.16%)	500 (28.90%)	
High school graduate	353 (24.23%)	408 (24.26%)	398 (22.19%)	389 (22.49%)	
More than high school graduate	599 (41.11%)	771 (45.84%)	855 (47.66%)	841 (48.61%)	
Marital status					<0.001
Married	1,015 (69.66%)	1,163 (69.27%)	1,287 (71.62%)	1,101 (63.64%)	
Single	361 (24.78%)	439 (26.15%)	429 (23.87%)	535 (30.92%)	
Living with a partner	81 (5.56%)	77 (4.59%)	81 (4.51%)	94 (5.43%)	
Ethnicity					<0.001
Mexican American	305 (20.92%)	332 (19.74%)	338 (18.81%)	238 (13.74%)	
Other Hispanic	116 (7.96%)	90 (5.35%)	111 (6.18%)	99 (5.72%)	
Non-Hispanic White	825 (56.58%)	942 (56.00%)	950 (52.87%)	859 (49.60%)	
Non-Hispanic Black	157 (10.77%)	264 (15.70%)	341 (18.98%)	483 (27.89%)	
Other ethnicity	55 (3.77%)	54 (3.21%)	57 (3.17%)	53 (3.06%)	
Vitamin D (nmol/l)	58.73±19.95	59.66±20.19	61.41±20.90	60.87±23.90	0.002
Triglyceride (mmol/l)	2.96±2.55	1.97±2.08	1.58±1.50	1.15±0.64	<0.001
Low density lipoprotein-cholesterol (mmol/l)	2.87±0.95	3.14±0.90	3.20±0.90	3.12±093	<0.001
Total cholesterol (mmol/l)	5.07±1.23	5.34±1.29	5.33±1.10	5.37±1.01	<0.001
White blood cell count (1,000 cells/μl)	7.78±3.31	7.33±3.03	6.93±2.03	6.69±2.20	<0.001
Lymphocyte number (1,000 cells/μl)	2.25±1.06	2.13±2.28	1.97±0.76	1.92±1.02	<0.001
Monocyte number (1,000 cells/μl)	0.61±0.21	0.58±0.21	0.55±0.18	0.56±0.19	<0.001
Segmented neutrophils number (1,000 cells/μl)	4.62±2.69	4.34±1.58	4.15±1.62	3.96±1.62	<0.001
Red blood cell count (million cells/μl)	4.92±0.48	4.91±0.47	4.90±0.46	4.77±0.48	<0.001
Haemoglobin (g/dl)	15.13±1.38	15.08±1.33	15.04±1.25	14.84±1.32	<0.001
Platelet count (1,000 cells/μl)	242.19±68.64	245.41±66.04	242.26±60.19	239.95±62.17	0.182
C-reactive protein (mg/dl)	0.55±1.17	0.46±0.96	0.37±0.86	0.33±0.82	<0.001

Q1-Q4: Grouped by quartile according to the HDL-cholesterol concentrations. The data of the present study included prostate-specific antigen concentrations, sociodemographic data, and laboratory data for the second analysis. HDL, high-density lipoprotein.

that men with higher serum lipid show increased aggressiveness of Pca (17,18). Additionally, it has been reported that high HDL-C levels were associated with an increased risk of several diseases (19). Moreover, the univariable randomization analysis revealed that the genetic prediction of Lp(a) had a negligible correlation with the overall incidence of Pca (20). One hypothesis suggests that high HDL-C levels may increase androgen hormone production, which can promote Pca cell proliferation, while a recent study proposed that HDL-C might serve as a biomarker for chronic inflammation, which promotes the progression of Pca (21).

The stratified analysis of the present revealed a stronger inverse correlation between lower HDL-C levels and reduced PSA concentrations, particularly among individuals with higher family incomes. This suggests socioeconomic factors, such as lifestyle habits and healthcare access, may contribute to this observed relationship. Another study identified a significant association between obesity and high-grade Pca on biopsy, and highlighted the role of metabolic health factors, including HDL-C and obesity, influencing Pca risk and progression (22). Aligned with the findings of the present study, previous research by Jamnagerwalla *et al* (23) reported that low HDL-C levels were associated with increased Pca risk in men with lower educational attainment.

The findings of the present study contrast with a previous study on HDL-C and PSA, which report varying associations between lipids and Pca risk, with some indicating a favourable link and others suggesting a negative relationship

Table II. Univariate and multivariate analyses by the weighted linear model.

Exposure	Non-adjusted model	Minimally adjusted model	Fully adjusted model
HDL-cholesterol	0.470 (0.281,0.659) <0.001	0.408 (0.227,0.589) <0.001	0.400 (0.099,0.701) 0.009
HDL-cholesterol			
Q1	Ref	Ref	Ref
Q2	0.077 (-0.130,0.284) 0.467	0.108 (-0.086,0.303) 0.275	-0.001 (-0.312.0.310) 0.995
Q3	0.166 (-0.038,0.370) 0.109	0.196 (0.004,0.389) 0.045	0.064 (-0.249,0.377) 0.689
Q4	0.377 (0.172,0.583) 0.001	0.351 (0.156,0.546) 0.001	0.228 (-0.112.0.568) 0.189
P for trend	<0.001	<0.001	0.026

The non-adjusted model adjusts for none. The minimally adjusted model adjusts for family income, ethnicity, military status, marital status and education. The fully adjusted model adjusts for family income, ethnicity, military status, marital status, education, mononuclear count, triglyceride, LDL-cholesterol, monocyte number, segmented neutrophils number, red blood cell count, haemoglobin, platelet count and C-reactive protein. HDL, high-density lipoprotein.

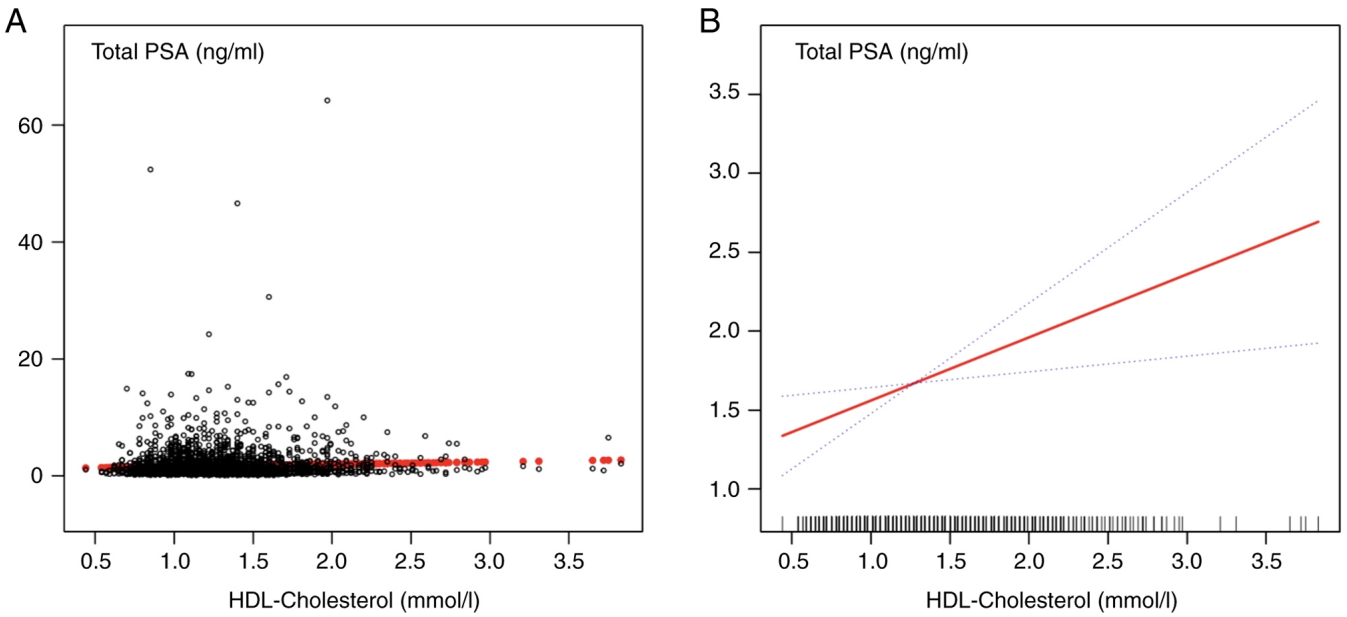

Figure 2. Representation of the fully adjusted smooth curve fitting model. (A) Each black dot represents a sample. (B) The red line represents the smooth curve fit between the variables. The blue line represents the 95% confidence interval for the fit, adjusted for poverty-income ratio, ethnicity, military service, marriage, education, triglycerides, low-density lipoprotein cholesterol, monocyte count, neutrophil count, red blood cell count and haemoglobin. HDL, high-density lipoprotein cholesterol.

between the two factors (24). The aforementioned study was used to select 13 relevant publications for an epidemiological investigation exploring the association between HDL-C and Pca. Out of these, three publications established a direct connection between HDL-C levels and the occurrence of cancer, whereas five articles indicated a marginal correlation between HDL-C and cancer (25). While these studies are consistent with the findings of the present study, it is important to not dismiss those that suggest a negative or no correlation between HDL-C and PSA. Hence, it is necessary to conduct more data analysis to verify this association and to determine if other risk factors are closely related to the occurrence and development of Pca.

Overall, the present study supports the conception that HDL positively correlates with PSA (26), indicating that higher HDL-C levels lead to increased PSA concentrations, thereby raising the probability of diagnosing Pca. These findings suggest that this relationship could be employed as a viable cancer screening approach, potentially improving PSA test specificity in men with high triglycerides. Therefore, implementation of this Pca detection mechanism, could help early treatment and prevent cancer from spreading. In most cases, identifying cancer earlier means there will be a reduced need for aggressive treatment which can help the patients save their lives (27).

Furthermore, the benefits of the present study outweigh those of earlier research on the same topic. First, the present study comprises 6,669 male participants, resulting in more accurate and convincing results than other small sample studies, as well as more objective research findings. Second, the present study is the first large-scale cross-sectional study, which found a poor relationship between serum HDL-C and

Table III. Effect size of HDL-cholesterol on prostate-specific antigen in the prespecified and exploratory subgroup.

HDL-cholesterol	N	B	95% CI low	95% CI high	P-value	P for interaction
Stratified by age, years						0.190
<60	3,630	0.266	0.020	0.511	0.034	
60-80	2,796	0.618	0.329	0.907	<0.001	
>80	243	0.399	-0.626	1.424	0.446	
Stratified by ratio of family income						0.037
Low group	2,075	0.748	0.453	1.043	<0.001	
Median group	2,082	0.194	-0.116	0.504	0.220	
High group	2,079	0.420	0.094	0.746	0.011	
Stratified by ethnicity						0.663
Mexican American	1,213	0.268	-0.217	0.753	0.278	
Other Hispanic	416	0.429	-0.411	1.268	0.317	
Non-Hispanic White	3,576	0.314	0.038	0.590	0.025	
Non-Hispanic Black	1,245	0.646	0.279	1.013	0.001	
Other ethnicity	219	0.447	-0.663	1.557	0.430	
Stratified by military status						0.249
Yes	2,271	0.305	-0.026	0.635	0.071	
No	4,397	0.541	0.311	0.771	<0.001	
Stratified by marital status						0.310
Married	4,566	0.345	0.100	0.590	0.005	
Single	1,764	0.662	0.333	0.991	<0.001	
Living with a partner	333	0.380	-0.348	1.108	0.306	
Stratified by education						0.006
Less than 9th grade	2,049	0.932	0.599	1.264	<0.001	
High school graduate	1,548	0.264	-0.117	0.645	0.174	
More than 9th grade	3,066	0.279	-0.009	0.567	0.057	

The aforementioned adjusts for family income, ethnicity, military status, marital status, education, mononuclear count, triglyceride, LDL-cholesterol, monocyte number, segmented neutrophils number, red blood cell count, haemoglobin, platelet count and C-reactive protein. In each case, the model was not adjusted for the stratification variable itself. HDL, high-density lipoprotein; CI, confidence interval.

Table IV. Results of weighted linear regression modelling for associations of the HDL-cholesterol with prostate-specific antigen after excluding individual blood HDL-cholesterol concentrations <1.04 mmol/l.

Exposure	Non-adjusted model	Minimally adjusted model	Fully adjusted model
HDL-cholesterol	0.53 (0.27,0.79) <0.001	0.42 (0.16,0.67) 0.001	0.50 (0.12,0.87) 0.009
HDL-cholesterol			
Q1	Ref	Ref	Ref
Q2	0.00 (-0.25,0.26) 0.9777	0.04 (-0.21,0.28) 0.7748	-0.06 (-0.39,0.28) 0.7381
Q3	0.21 (-0.05,0.47) 0.1078	0.22 (-0.03,0.47) 0.0910	0.20 (-0.15,0.54) 0.2601
Q4	0.39 (0.14,0.65) 0.0027	0.31 (0.06,0.56) 0.0163	0.35 (-0.01,0.72) 0.0568
P for trend	0.003	0.010	0.046

Non-adjusted model adjusts for none. Minimally adjusted model adjusts for family income, ethnicity, military status, marital status and education. Fully adjusted model adjusts for family income, ethnicity, military status, marital status, education, mononuclear count, triglyceride, LDL-cholesterol, monocyte number, segmented neutrophils number, red blood cell count, haemoglobin, platelet count and C-reactive protein. HDL, high-density lipoprotein.

PSA in men from USA with no history of Pca. This establishes a basis for further extensive research on this topic to achieve more definitive results. Third, the sample in the present study is a multi-level random sample, representing the general population in USA, and has highly reliable and standardized data. Simultaneously, multi-layer random sampling technology

provides researchers with more freedom and flexibility in selecting samples, which is also conducive to the data collection of geographically dispersed populations. Fourth, the present study has made certain contributions to the existing knowledge base. Researchers have established a connection between elevated levels of HDL and an increased risk of Pca. Using this detection method can improve early cancer detection, allowing patients to start treatment sooner and prevent the cancer from spreading. Finally, the relationship between serum HDL-C and PSA using both linear and non-linear methods was analyzed, considering other factors that might affect the results. By applying generalized estimation equation analysis, reliable findings were able to be obtained that support these hypotheses. However, the present study had certain limitations including the cross-sectional design, which limits the ability to establish causality, and the use of a single PSA measurement, which may not accurately reflect long-term PSA levels. Thus, prospective cohort studies are needed to confirm the causality. Moreover, the study population is mostly non-Hispanic white, which may limit how well the findings of the present study apply to other ethnic groups. Additionally, the present study was based on the NHANES database, which is restricted to the population of USA. Thus, generalizability is geographically restricted. To address these issues, further research is needed in the future.

While the present study provided valuable insights, further research is needed to clarify and extend these results, particularly in relation to patients with Pca. Future studies should aim to include a cohort of patients with Pca to determine whether the observed effects are consistent across different cancer types. In conclusion, the present study found a positive association between serum HDL-C and PSA concentrations in adult men in USA without a Pca diagnosis.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

MMA conceptualized the study and wrote the original draft. BH, SMH and MMA acquired and analysed the data. YD, MY and MMA interpreted the data. MMA and SMH confirm the authenticity of all the raw data. GL and SMH reviewed and edited the manuscript. YD, GL and BH reviewed, edited and critically analysed the results. GL and YD supervised the present study. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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