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ARTICLE

Genetic evidence for associations between food intake and prostatic diseases: a Mendelian randomization study

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Background: *Regional differences in the incidence of prostate cancer (PCa) and prostatitis may be due to different food intake. But which foods affect PCa and prostatitis development or progression remains controversial. This study aims to explore the causal relationship between PCa and prostatitis and 30 different foods using two-sample Mendelian randomization (MR) and multivariable MR (MVMR) analysis.*
Methods: *Data on 30 different foods were screened from the UK Biobank. PCa data came from a large meta-analysis of 140,254 individuals; prostatitis was obtained from the FinnGen consortium. The inverse variance weighted method was the main analysis method. MR-Egger, Cochran's Q, radial MR, and MR-PRESSO tests were used for sensitivity analysis.*
Results: *Our results demonstrated that never eating sugar [odds ratio (OR), 0.30; 95% confidence interval (CI), 0.11–0.80; $p = 0.02$] and never eating eggs (OR, 0.52; 95% CI, 0.28–0.97; $p = 0.04$) reduced the risk of PCa; raw vegetable intake (OR, 2.27; 95% CI, 1.01–5.09; $p < 0.05$) and dried fruit intake (OR, 1.38; 95% CI, 1.02–1.87; $p = 0.04$) increased PCa risk. And a negative correlation existed between processed meat intake and prostatitis (OR, 0.27; 95% CI, 0.08–0.94; $p = 0.04$). After adjusting for smoking and drinking, never eating sugar was negatively correlated with PCa, while the raw vegetable intake was positively correlated with the risk of PCa.*
Conclusion: *Our study found four different foods associated with PCa and one food intake associated with prostatitis. We recommend more high-quality studies to reassess the benefits of individual foods in PCa.*

Key Words: Individual foods, prostate cancer, prostatitis, Mendelian randomization

Introduction

Prostate cancer (PCa) is the most common cancer among men in the United States, with an estimated 288,300 new cases diagnosed in 2023.[1] Prostatitis is the 3rd most common urinary tract disease in men after benign prostatic hyperplasia and PCa.[2] In the United States, the prevalence of prostatitis is up to 16%.[3] Additionally, chronic prostatitis may be implicated in prostate carcinogenesis through specific infections or environmental factors.[4,5] Understanding the specific risk factors associated with the development of PCa and prostatitis is crucial for primary and secondary prevention.

Low dietary quality is a known risk factor for malignancies, particularly in PCa.[6] Nutrition and diet, as modifiable lifestyle factors, have a more significant impact on cancer risk than smoking, and positive behavioral changes can significantly reduce the cancer burden.[7] The World Cancer Research Fund (WCRF) states that a Western-style diet characterized by high consumption of processed food, meat, and meat products with high fat content and a lower intake of fruits and vegetables may contribute to

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a higher PCa risk, whereas a prudent dietary pattern, emphasizing non-starchy vegetables and whole grains, is associated with a lower risk.[8,9] For prostatitis, no formal "Prostatitis Diet" is presently available, and very little is known about the characteristics of food sensitivity in this population. An observational study reported that a high-calorie diet with low fruit and vegetable consumption aggravated the disease.[10] Despite decades of epidemiological studies demonstrating that certain dietary components increase the risk of cancer and inflammation (e.g., alcohol), there are few examples of a single nutrient or component that directly reduces the risk of PCa and prostatitis. This has led to inconsistent or insufficient scientific evidence, and attempts to draw reliable conclusions have been hampered.[7,11]

Mendelian randomization (MR) analysis is a novel and powerful epidemiological tool that uses genetic variants as unconfounded instrumental variables to investigate causal relationships between disease exposure and clinical outcomes.[12] Since genotypes are randomly assigned during gamete formation based on parental genotypes, the MR results are not affected by potential confounders or reverse causality.[13]

Understanding the exact role of food intake in PCa and prostatitis may provide useful information for effective prevention and treatment. In this study, we used two-sample MR (TSMR) and multivariable MR (MVMR) based on the published data of genome-wide association studies (GWASs) to explore the causal effects of different foods on the risk of PCa and prostatitis.

Methods

Data collection

To assess causality, we used individual foods as the exposure variable and PCa or prostatitis as the outcome variable. Genetic data of the exposure phenotype in this study were sourced from the Medical Research Council-Integrative Epidemiology Unit (MRC-IEU) from European populations (https://opengwas.io/datasets/). The 30 different foods data using output from the GWAS pipeline using Phenome-wide Scan Analysis Tools (PheSANT)-derived variables from the UK Biobank were summarized in Table 1. The UK Biobank's touchscreen questionnaire included 29 questions about food intake, most of which gathered information on the average frequency of consumption of main foods and food groups over the past year.[14]

Genetic data for the outcome phenotype were sourced from the Prostate Cancer Association Group to Investigate Cancer-Associated Alterations in the Genome (PRACTICAL) consortium, which included 61,106 controls and 79,148 PCa cases, sourced from European populations.[15] Additionally, genetic data for prostatitis were sourced from the FinnGen consortium R5 release data (https://www.finngen.fi/en). Ethical approval was not required for this study because all analyses were conducted using publicly available summary-level data from previously approved studies.

Instrumental variables selection

Three MR assumptions must be met for the selection of single nucleotide polymorphisms (SNPs) as instrumental variables (IVs) to assess the correlation between foods intake and PCa incidence: (1) there is a strong correlation between genetic variations and foods intake, (2) confounding factors have no influence on the IVs selected to affect the relationship between foods intake and PCa (or prostatitis) incidence, and (3) IVs can only affect the incidence of PCa (or prostatitis) incidence through foods intake. Genetic variations related to food intake were gathered from an approximately 500,000-person UK Biobank cohort. SNPs that were associated with food intake were extracted with a genome-wide significance threshold ($p < 5 \times 10^{-8}$). SNPs in linkage disequilibrium (LD) were identified and excluded using the LD clumping method ($R^2 < 0.01$; region size, 10,000 kb). Because bacon intake, milk intake, yogurt intake, salted peanuts intake, unsalted peanuts intake, salted nuts intake, unsalted nuts intake, never eat dairy, never eat wheat, and never eat eggs have fewer that meet the strict threshold ($p < 5 \times 10^{-8}$), for these individual foods, we chose to use a relaxed threshold ($p < 5 \times 10^{-6}$; $R^2 < 0.01$; region size = 10,000 kb) to select SNPs. We also removed palindromic SNPs with intermediate allele frequencies and harmonized the data so that the estimations of SNP exposure and SNP outcome were based on the same allele. In addition, F-tests were used to exclude the possibility that the selected SNPs were affected by weak IVs. To minimize the risk of horizontal pleiotropy and ensure that the selected instrumental variables influenced the outcome primarily through the exposure of interest, all candidate SNPs were further screened for associations with potential confounding lifestyle factors. Using the LDlink (https://ldlink.nih.gov/?tab=home), we excluded SNPs that were previously associated ($p < 5 \times 10^{-8}$) with key behavioral and socioeconomic traits, including smoking status, alcohol consumption, physical activity,

TABLE 1. **Detailed information about the data sources of individual foods, prostatitis, and prostate cancer**

Traits	GWAS ID	Sample size	SNPs	Year	Pubmed ID (or URL)	*p*-value threshold	F-statistics
Bacon intake	ukb-b-4414	64,949	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	25.6553
Beef intake	ukb-b-2862	461,053	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	41.4728
Beer intake	ukb-b-5174	327,634	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	42.9613
Bread intake	ukb-b-11348	452,236	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	41.6869
Cereal intake	ukb-b-15926	441,640	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	45.0298
Cheese intake	ukb-b-1489	451,486	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	39.0159
Coffee intake	ukb-b-5237	428,860	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	72.7118
Cooked vegetable intake	ukb-b-8089	448,651	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	37.5841
Dried fruit intake	ukb-b-16576	421,764	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	41.8989
Fresh fruit intake	ukb-b-3881	446,462	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	45.9980
Lamb intake	ukb-b-14179	460,006	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	39.5948
Milk intake	ukb-b-2966	64,943	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	22.6053
Non-oily fish intake	ukb-b-17627	460,880	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	44.8023
Oily fish intake	ukb-b-2209	460,443	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	45.2557
Pork intake	ukb-b-5640	460,162	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	37.1075
Poultry intake	ukb-b-8006	461,900	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	32.5385
Processed meat intake	ukb-b-6324	461,981	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	37.7469
Raw vegetable intake	ukb-b-1996	435,435	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	36.9241
Red wine intake	ukb-b-5239	327,026	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	43.6432
Salted nuts intake	ukb-b-15960	64,949	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	23.8541
Salted peanuts intake	ukb-b-1099	64,949	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	23.8392
Tea intake	ukb-b-6066	447,485	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	61.5819
Unsalted nuts intake	ukb-b-12217	64,949	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	22.2847
Unsalted peanuts intake	ukb-b-15555	64,949	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	24.4386
Yogurt intake	ukb-b-7753	64,949	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	22.8277
Never eat eggs, dairy, wheat, sugar: Dairy products	ukb-b-18909	461,046	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	23.7171
Never eat eggs, dairy, wheat, sugar: Eggs or foods containing eggs	ukb-b-17455	461,046	9,851,867	2018	http://app.mrbase.org	5×10^{-6}	22.3510
Never eat eggs, dairy, wheat, sugar: I eat all of the above	ukb-b-2393	461,046	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	40.6375
Never eat eggs, dairy, wheat, sugar: Sugar or foods/drinks containing sugar	ukb-b-5495	461,046	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	36.6491
Never eat eggs, dairy, wheat, sugar: Wheat products	ukb-b-3599	461,046	9,851,867	2018	http://app.mrbase.org	5×10^{-8}	159.3651
Prostate cancer	NA	140,254	20,346,368	2018	http://practical.icr.ac.uk/blog/	NA	NA
Prostatitis	NA	74,658	16,377,460	2021	https://www.finngen.fi/en	NA	NA

Note. NA, Not available; GWAS, genome-wide association study; SNP, single nucleotide polymorphism.

body mass index, and educational attainment. This step was undertaken to enhance the validity of the exclusion restriction assumption. The strength of each SNP instrument was quantified using the F-statistic: $F = \frac{\beta^2}{se^2}$, where β is the SNP-exposure association estimate and se its standard error. An F-statistic > 10 indicated a strong instrument, mitigating weak instrument bias.

MR analysis

Inverse variance weighted (IVW), weighted median (WM), and MR-Egger tests were applied for the two-sample MR analysis. The IVW method is regarded as the most effective MR method when the IVs meet all three assumptions, and can consistently estimate the causal effects of exposure.[16] Meanwhile, to better interpret the results, the beta values obtained in the study were converted to odds ratio (OR), and the 95% confidence interval (CI) were calculated.

The MVMR method adjusts for the effects of other exposures and provides a direct causal estimate of the effect of the exposure on the outcome. We searched the LDlink for SNPs obtained from TSMR analysis. Some of these SNPs were strongly associated with "smoking and alcohol consumption."

Sensitive analysis

Heterogeneity was evaluated using the Cochran's Q test, and when $p > 0.05$, there was no heterogeneity. The random-effects IVW method was applied in cases where heterogeneity was observed. The MR-Egger, radial MR, and MR-PRESSO tests were used to check for horizontal pleiotropy, which can effectively identify outliers of the IVs and provide causal estimates after excluding the outliers. Specifically, the MR-PRESSO outlier test was employed to identify and remove individual SNPs that exhibited significant horizontal pleiotropy, which were defined as variants whose causal estimates were significant outliers ($p < 0.05$) relative to the distribution of estimates from all other instrumental variables. This iterative process ensures that the final causal estimate is not unduly influenced by genetic variants operating through alternative biological pathways. Finally, the stability of the TSMR results was determined by performing a "leave-one-out" analysis of the data, sequentially excluding one SNP to estimate whether a single SNP was driving or biasing the results.

Results

Food intake and PCa

First, we assessed the causal effects of food exposure on PCa. The F-statistics for all exposures were >10, indicating a low risk of weak instrument bias (Table 1).

"Never eat sugar or foods/drinks containing sugar" was found to have a significant protective effect on the risk of PCa (OR, 0.30; 95% CI, 0.11–0.80; $p = 0.02$). And "Never eat eggs or foods containing eggs" has a significant protective effect on the risk of PCa (OR, 0.52; 95% CI, 0.28–0.97; $p = 0.04$). However, a positive correlation existed between "raw vegetable intake" and PCa (OR, 2.27; 95% CI, 1.01–5.09; $p < 0.05$), whereby raw vegetable intake was a risk factor for PCa (**Table S1; Figure 1; Fig. S1**).

In sensitive analysis, horizontal pleiotropy of "coffee intake" was checked with MR-Egger and MR-PRESSO and was deemed existent (p for MR-Egger intercept = 0.024; p for MR-PRESSO < 0.001). Thus, MR results for "coffee intake" were not robust and need to be interpreted with caution. The MR-Egger intercept test for the other 29 different foods showed $p > 0.05$, suggesting that horizontal pleiotropy was absent (**Table S3**). Further MR-PRESSO test detected the pleiotropy in "cereal intake," "tea intake," "raw vegetable intake," "processed meat intake," "poultry intake," "oily fish intake," "non-oily fish intake," "lamb intake," "fresh fruit intake," "dried fruit intake," "cooked vegetable intake," "cheese intake," and "never eat sugar." (**Table S3**). However, there were no significant outliers for "never eat sugar," "bacon intake," "tea intake," "processed meat intake," and "cheese intake". Additionally, excluding outliers did not influence the causal association between "beef intake," "beer intake," "cereal intake," "poultry intake," "oily fish intake," "non-oily fish intake," "lamb intake," "fresh fruit intake," and "cooked vegetable intake" and PCa. And after removing the outlier SNPs identified by MR-PRESSO, "raw vegetable intake" and PCa were no longer causally related (OR, 1.61; 95% CI, 0.93–2.79; $p = 0.09$). The excluded SNPs for raw vegetable intake (rs3095337, rs3129962, rs8130508, rs9427220) are located within or near genes implicated in immune and inflammatory regulation (RERE) and cellular metabolism, suggesting potential pleiotropic effects beyond food intake.[17] Similarly, outliers for dried fruit intake (rs11811826, rs4269101, rs429358, rs62084586) map to loci involved in lipid metabolism (APOC1, APOE), vesicular transport (PICALM),[18] and telomere biology (OBFC1),[19] indicating alternative pathways through which they might influence PCa risk (OR, 1.38; 95% CI, 1.02–1.87;

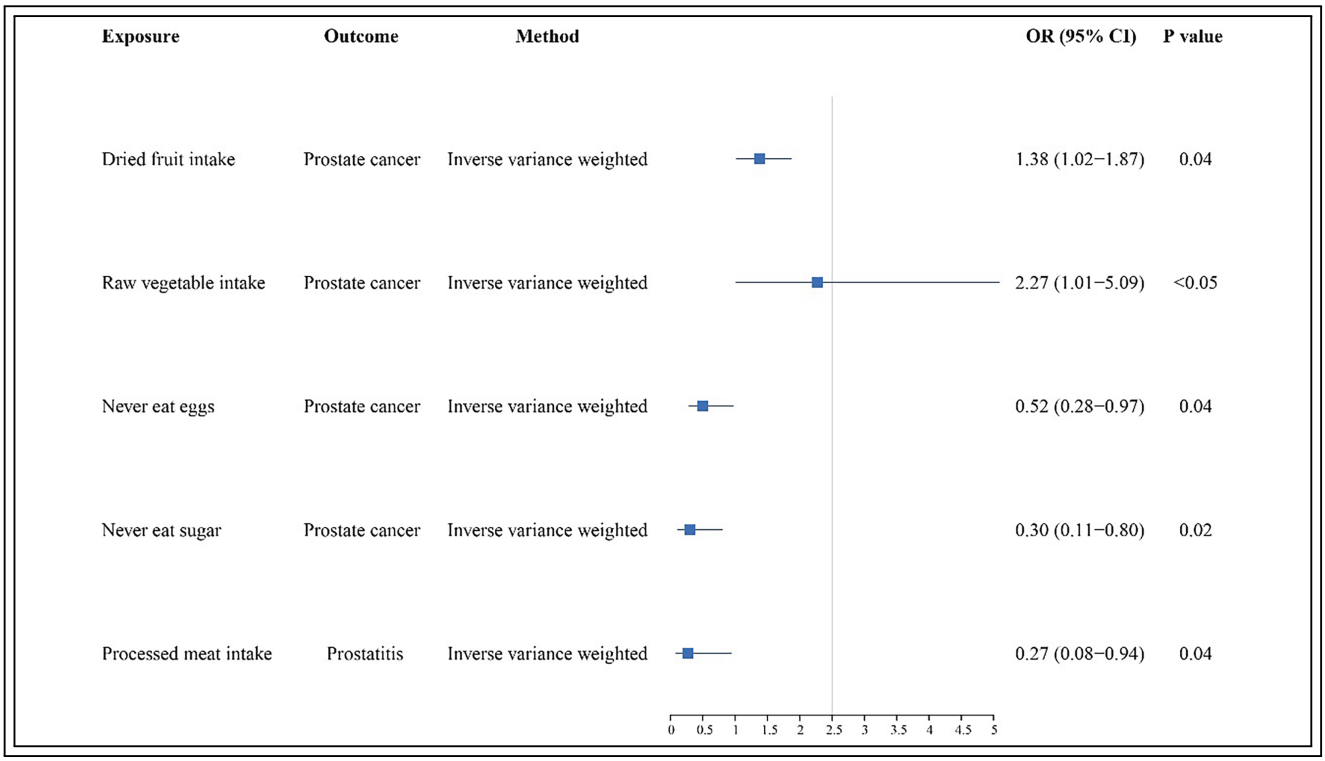

FIGURE 1. Forest plot of the causal associations between "dried fruit intake", "raw vegetable intake", "never eat eggs", and "never eat sugar" and prostate cancer, and "processed meat intake" and prostatitis

$p = 0.04$) (**Table 2**; **Figure 2**). The "leave-one-out" analysis was performed on all data, and after testing by individual removal, no single SNP had a significant effect on the robustness of the results; hence, this study was stable (Fig. S2).

Food intake and prostatitis

First, we assessed the causal effects of exposure to various types of food on prostatitis. The F-statistics for all exposures were >10, indicating a low risk of weak instrument bias (**Table 1**).

"Processed meat intake" was found to have a significant protective effect against the risk of prostatitis (OR, 0.27; 95% CI, 0.08–0.94; $p = 0.04$) (**Table S2**; **Figure 1**).

In the sensitivity analysis, the MR-Egger intercept test yielded a p value of > 0.05, suggesting the absence of horizontal pleiotropy in all results. Moreover, the MR-PRESSO test found no evidence of pleiotropy, confirming the accuracy of all results (**Table S4**). The "leave-one-out" analysis was performed on all data, and after testing individual removal, no single SNP exhibited a significant effect on the robustness of the results, ensuring the stability of this study (Fig. S3).

MVMR analysis

MVMR analysis revealed that, after adjusting for smoking and alcohol consumption, never eating sugar was associated with a significantly lower odds of prostate cancer (OR, 0.35; 95% CI, 0.13–0.92; $p = 0.03$), while higher raw vegetable intake was associated with an increased odds (OR, 2.55; 95% CI, 1.13–5.78; $p = 0.03$). No other exposures, including never eating eggs, dried fruit intake, or processed meat intake (for prostatitis), showed statistically significant direct effects on the outcomes. Furthermore, smoking exhibited a significant positive association with prostate cancer in two models, whereas alcohol consumption showed no significant association in any model (**Table S5**).

Discussion

It is now widely recognized that individual foods play a crucial role in both the prevention and development of PCa, although the underlying mechanisms are unclear.[20,21] The consumption of sugar is detrimentally associated with various risk factors, including

TABLE 2. **Radial MR method to test for heterogeneity and horizontal pleiotropy in IVW and MR Egger**

Exposure and outcome	Methods	Estimate	SE	*t* value	*p* value
Raw vegetable intake and prostate cancer	Radial IVW				
	Effect (1st)	0.8189	0.4368	1.8747	0.0608
	Iterative	0.8197	0.4369	1.8762	0.0606
	Exact (FE)	0.8960	0.2367	3.7845	0.0001
	Exact (RE)	0.8400	0.4434	1.8944	0.0763
	Q-Statistic for heterogeneity	NA	NA	55.7351	2.6913e−06
	Radial MR-Egger				
	(Intercept)	−1.7797	3.4703	−0.5128	0.6155
	Wj	2.5208	3.3487	0.7527	0.4632
	Q-Statistic for heterogeneity	NA	NA	54.7747	1.9483e−06
Dried fruit intake and prostate cancer	Radial IVW				
	Effect (1st)	0.1349	0.2147	0.6285	0.5296
	Iterative	0.1349	0.2147	0.6285	0.5296
	Exact (FE)	0.1463	0.1176	1.2433	0.2137
	Exact (RE)	0.1381	0.2297	0.6013	0.5510
	Q-Statistic for heterogeneity	NA	NA	133.2746	5.8567e−12
	Radial MR-Egger				
	(Intercept)	3.0242	1.6960	1.7831	0.0823
	Wj	−2.1121	1.2774	−1.6534	0.1062
	Q-Statistic for heterogeneity	NA	NA	123.2283	1.1443e−10

Note. NA, Not available; MR, Mendelian randomization; IVW, inverse variance weighted; SE, standard error; FE, fixed-effect (model); RE, random-effect (model); Q, Cochran's Q statistic; Wj, weight (for the jth variant).

obesity, diabetes, cardiovascular disease, and cancer.[22–25] High dietary sugar intake usually causes more harm than good, and there is a direct relationship between increased dietary sugar intake and an increased risk of developing symptomatic PCa.[26] Our study also demonstrated that never eating sugar reduces the risk of PCa. According to the latest summary of evidence, it is recommended to limit the intake of free or added sugars to less than 25 g/day (approximately 6 teaspoons/day) and limit the intake of sugary beverages to less than one serving per week.[27] Eggs are rich in proteins, amino acids, cholesterol, and choline. A dose-response meta-analysis showed a positive association between consuming five eggs per week and fatal PCa (relative risk (RR), 1.47; 95% CI, 1.01–2.14).[28] In another prospective study, no association was observed between egg protein intake and PCa mortality in one-fifth of the population. However, there was suggestive evidence of a positive association in each standard deviation increment of the analysis, implying that the risk of dying from PCa may be higher in men who consume more protein from eggs.[29] Some evidence indicates that dietary protein may be associated with higher circulating concentrations of insulin growth factor-I (IGF-I) and elevated IGF-I levels are recognized as risk factors for PCa.[30,31] In addition, cholesterol serves as a precursor for the biosynthesis of sex hormones such as androgens and estrogens, which promote cell proliferation, thereby contributing to the carcinogenesis of PCa.[32,33] Limiting egg intake to lower blood cholesterol levels appears to be a healthy strategy for preventing the onset of PCa. This may also aid in the early detection of PCa, potentially leading to a better prognosis.[34]

In our study, we demonstrated that raw vegetable intake and dried fruit intake could potentially be risk factors for PCa. However, it is essential to approach the causal relationship cautiously. First, the precise quantity of vegetable and dried fruit consumption remained unknown, and evidence indicates that the amount of vegetable intake can affect the risk of both cardiovascular disease and cancer.[35] The associations in our study might be related to excessive food intake. A balanced dietary approach, avoiding both excessive and inadequate intake, is considered a healthy diet, and moderation has become a consensus across all dietary patterns.[36] Furthermore, an increased risk of PCa may be associated with unhealthy plant-based diet (PD), including potatoes and fiberless juice. Two

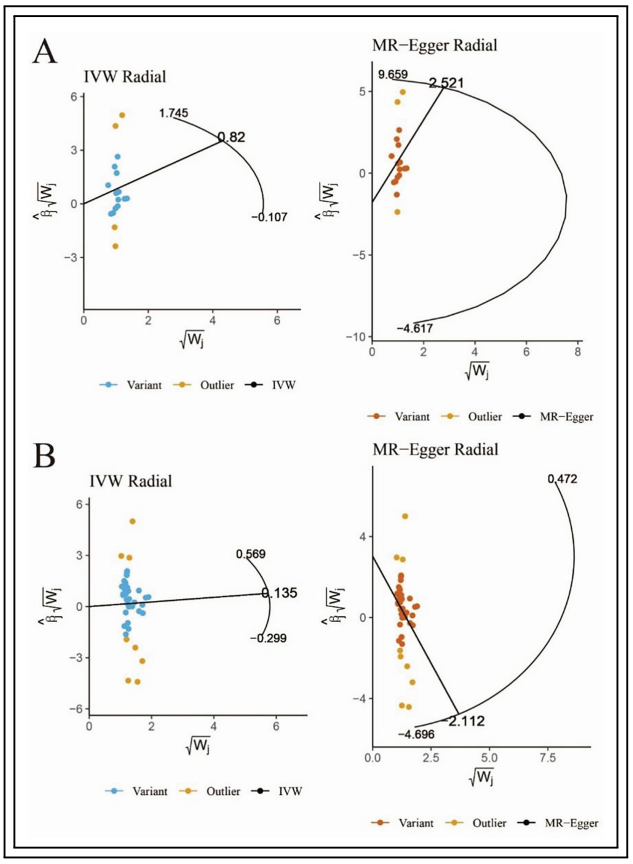

FIGURE 2. Radial MR analyses for food intake and PCa. **A.** Radial MR analysis of the causal relationship between "raw vegetable intake" and PCa. **B.** Radial MR analysis of the causal relationship between "dried fruit intake" and PCa. The Y-axis represents the strength of the association between each genetic variant and the exposure. The X-axis represents the causal effect estimate (Wald ratio) of the exposure on the outcome derived from each individual genetic variant. The slope of the fitted line represents the overall causal effect estimate pooled by the IVW model. This plot is used to visualize the causal effect estimates and their heterogeneity, and to help identify potential outlier variants. IVW, inverse variance weighted; MR, Mendelian randomization; PCa, prostate cancer

prospective cohort studies noted that unhealthy PD was associated with increased coronary heart disease and type 2 diabetes, both recognized as high-risk factors for cancer.[37] Finally, there exists an age-dependent relationship for PCa risk. Compared with other cancers, the risk of developing PCa increases dramatically with age. Only 0.6% of patients aged 35–44 years are diagnosed with PCa, but the prevalence of the cancer among patients aged 65–74 years is 35%. The number of cancer cases in men over 80 years of age is about 40 times higher than in men under 50 years of age.[38–40] The GWAS data for food intake in this study were not stratified by age, and age rather than food may be a more significant risk factor for PCa in older men. Furthermore, raw vegetables were no longer associated with PCa after removing the outlier SNPs.

In the quest for healthier processed meats, more reformulated low-fat healthy meat products are being developed to improve the fatty acid profile and reduce total fat and cholesterol by replacing animal fats with vegetable oils.[41,42] Physical activity effectively reduces the negative effects of processed meat intake.[43] In our study, processed meat was a protective factor against prostatitis, suggesting potential benefits from reformulation strategies and physical activity. However, despite the Nutritional Recommendations Consortium advising adults to maintain their current consumption of processed meat, caution is advisable due to its carcinogenicity.

Our study has several limitations. First, as rightly noted, the GWAS data for individual foods were based on questionnaire assessments of intake over the preceding year. Although MR leverages genetic proxies for lifelong exposure, significant non-genetic changes in foods over the life course could introduce measurement error and potentially bias the causal estimates if those changes are associated with the outcome. The development of GWAS for long-term food intake patterns, when available, will be valuable for future replication of our findings. Second, the GWAS data used in this study were obtained from a European population, limiting the generalizability of the findings to other ethnic groups. Further studies on other populations and regions are required. Third, TSMR analysis did not incorporate age stratification, thus preventing the exploration of potential age-related differences in PCa risk. Fourth, while the MR design offers considerable robustness against unmeasured confounding by leveraging random genetic assignment, and despite our efforts to exclude pleiotropic variants via LDlink and to employ MVMR techniques, a limitation inherent to the method remains. We cannot definitively rule out the possibility that some genetic instruments exerted effects on prostatic diseases through pathways unrelated to the individual food exposures, such as via other unmeasured or imperfectly measured lifestyle factors. Although our sensitivity analyses did not detect widespread pleiotropy, this residual uncertainty underscores the importance of interpreting our findings as the effect of a genetic predisposition to certain food intake, which may be intertwined with

broader lifestyle profiles. Finally, it is important to acknowledge the challenge of multiple statistical testing in our study, which examined associations across a range of food intake. While the MR framework reduces certain forms of bias, the possibility that some findings may be due to chance cannot be entirely excluded. These results, particularly those that differ from previous observational studies, should therefore be interpreted as preliminary and require further validation in future independent analyses. However, this study has several strengths. First, MR studies can enhance causal estimation while minimizing the risk of confounding bias and reverse causation. Additionally, they effectively reduce the risk of overfitting and false-positive results. Second, the sample sizes of the 30 different foods and PCa were much larger than those of previous observational studies, which could provide sufficient statistical power to assess causality. In addition, the correlation between several different MR methods was examined in a sensitivity analysis, and the consistency of the results confirmed the robustness of our findings.

In conclusion, specific food interventions for cancer prevention and treatment are exciting areas of research. In conjunction with the results of our study, particularly the relationship between PCa and 'never eat eggs', 'raw vegetable intake', and 'dried fruit intake', we suggest that the possible benefits of PD for PCa should be reconsidered and evaluated. Moving forward, greater attention should be directed toward exploring the cancer-preventive role of single foods rich in vegetables, complex carbohydrates, lean meat and antioxidants, as well as single foods containing more soy and green tea.

Conclusion

Our MR study investigated the associations between genetically predicted food intake and prostatic diseases. The analysis suggested potential protective effects of "never eat sugar" and "never eat eggs" on PCa risk, while also indicating potential risk associations with dried fruit and raw vegetable intake. A negative correlation was additionally observed between processed meat intake and prostatitis risk. Although every effort was made to ensure methodological rigor through sensitivity analyses and instrumental variable selection, the possibility of chance findings due to multiple testing should be considered. These results highlight potentially novel relationships and underscore the value of further replication in future studies.

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Author Contributions

Xiangyu Chen and Congzhe Ren designed the study and analyzed the data. Lijun Xie revised the images. Xiangyu Chen and Congzhe Ren performed the literature search and collected data for the manuscript. Xiaoqiang Liu revised the manuscript. All authors reviewed the results and approved the final version of the manuscript.

Availability of Data and Materials

All data to support the conclusions have been either provided or are otherwise publicly available.

Ethics Approval

Ethical approval was not required for this study because all analyses were conducted using publicly available summary-level data from previously approved studies.

Conflicts of Interest

The authors declare no conflicts of interest to report regarding the present study.

Supplementary Materials

The supplementary material is available online at https://www.techscience.com/doi/10.32604/cju.2025.069578/s1.

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