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Investigating the correlation between gut microbiota and prostate cancer through a two-sample Mendelian randomization analysis

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Abstract

Previous studies in observational epidemiology have suggested a potential correlation between the gastrointestinal tract microbiota and prostate cancer. However, the causal relationship between the 2 remains uncertain, our objective was to thoroughly examine the influence of the gut microbiome on the progression of prostate cancer. In this study, we focused on investigating the gut microbiome as an exposure factor, specifically analyzing data from the MiBioGen consortium, which had a substantial sample size of 18,340 participants. As our disease outcome, we utilized prostate cancer data from the FinnGen genome-wide association study, which involved 13,216 participants. To establish causal relationships, we conducted a comprehensive Mendelian randomization analysis employing multiple methods, including inverse variance-weighted, Mendelian randomization-Egger, maximum likelihood, and weighted median approaches. Additionally, we performed sensitivity analysis to address issues such as heterogeneity and horizontal pleiotropy, ensuring the robustness of our findings. The results obtained through inverse variance-weighted analysis revealed that certain microbial groups exhibited a protective effect on prostate cancer. Specifically, the phylum Verrucomicrobia, particularly the family Rikenellaceae, and the genera Anaerotruncus, Eisenbergiella, Olsenella, and Parabacteroides were found to have a beneficial impact. Conversely, the class Bacilli, class Erysipelotrichia, order Erysipelotrichales, order Lactobacillales, family Erysipelotrichaceae, and the genera Marvinbryantia, Romboutsia, Ruminococcaceae UCG002, and Sutterella had an adverse influence on prostate cancer. The sensitivity analysis did not reveal any such outliers, further strengthening the validity of our results. To summarize, a cause-and-effect connection was discovered between various types and prostate cancer. Nevertheless, additional randomized controlled experiments are required for validation.

Abbreviations: IVs = instrumental variables, IVW = inverse variance weighted, MR = Mendelian randomization, PCa = prostate cancer, SNPs = single nucleotide polymorphisms.

Keywords: genetics, gut microbiota, GWAS study, Mendelian randomization, prostate cancer

1. Introduction

In the United States, prostate cancer (PCa) constituted the second most prevalent cancer in 2020, with approximately 191,930 new cases reported.[1] It also stood as the second leading cause of cancer-related deaths among men. The lifetime risk of being diagnosed with PCa in men is 11.2%.[2] The latest data show that PCa is the leading cause of death from urinary diseases, with an age-standardized mortality rate of 12.63 per 100,000 people.[3] PCa is influenced by various factors, such as advanced age, race, genetic background, and smoking. However, currently, there are no known modifiable factors that can effectively reduce the risk of PCa. To further alleviate the burden of this disease, it is crucial to explore alternative risk factors that have the potential to be modified, and one such factor deserving significant consideration is the gut microbiome. By investigating and understanding its role in PCa, we can potentially identify new avenues for prevention and intervention, ultimately leading to a reduction in PCa incidence and associated morbidity.

Maintaining human health and effectively managing diseases relies heavily on the complex interplay of microorganisms within the gut, collectively known as the gut microbiome. When an individual's gut microbiome experiences metabolic disturbances, it can result in an imbalance and dysfunction in microbial composition, leading to a variety of diseases.[4] The gut microbiome holds great significance in the human body and can be viewed as a distinct entity. Extensive research has

All studies were previously approved by respective institutional review boards. Informed consent has been obtained from all participants and/or their legal guardians in their respective studies. This study only used publicly available data and no additional informed consent is required.

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The datasets generated during and/or analyzed during the current study are publicly available.

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established strong associations between the gut microbiome and various diseases.[5] These include obesity, diabetes, immune disorders, cardiovascular diseases, and neurological conditions. The intricate relationship between the gut microbiome and these diseases highlights the critical role of microbial composition in influencing human health and disease outcomes.

Given the complex nature of the gut microbiota, there may exist intricate regulatory networks linking different types of bacteria. Additionally, the presence of confounding factors poses challenges in establishing a direct causal relationship between the gut microbiota and PCa. To overcome these challenges, Mendelian randomization (MR) utilizes genetic variation to infer causal connections between exposure factors and diseases. MR provides a convenient approach to investigate potential factors that either protect against or increase the risk of diseases. It has been widely employed in numerous research studies to explore the association between the gut microbiota and various diseases. In this analysis, we utilized summary datasets from genome-wide association studies related to the gut microbiota and PCa. By leveraging these datasets, we aimed to uncover potential relationships and shed light on the involvement of the gut microbiota in PCa development.

2. Methods

2.1. Data source

This study conducted a comprehensive meta-analysis of gut microbiota composition, incorporating data from the MiBioGen publication, which encompassed 16S rRNA gene sequencing and genotyping information from a substantial cohort of 18,340 participants.[6] In this analysis, we considered all taxa ranging from phyla to genera of bacteria. To ensure a focused and meaningful analysis, we excluded 3 unfamiliar families and genera from consideration. This step was necessary as subsequent MR analysis requires a minimal level of bacterial classification, with genus-level classification being essential. To ensure the reliability and up-to-date nature of the PCa data, we specifically selected the genome-wide association study data released in 2021 by FinnGen.[7]

2.2. Screening instrumental variables

The gut microbiota was considered as the exposure factor, while PCa served as the outcome in this study. Figure 1 provides an illustration of the 3 crucial assumptions that instrumental variables (IVs) must satisfy to ensure validity (Fig. 1). To ensure an adequate number of reliable single nucleotide polymorphisms (SNPs), we set a significance threshold of $<1 * 10^{-5}$ for the *P*-value.[8] Linkage disequilibrium, which refers to the nonrandom association of genes inherited within a population, was addressed by establishing a threshold of $r^2 < 0.001$ for chain imbalance and a distance of 10,000 kb.[9] To maintain consistency and avoid any inconsistencies in orientation between SNPs in the exposure and outcome, we eliminated palindromic SNPs. Additionally, IVs needed to meet the criterion of a *P*-value $>1 * 10^{-5}$ in the outcome, adhering to the exclusivity hypothesis.

2.3. Statistical analysis

The primary analysis method used in this study was the inverse variance-weighted (IVW) approach, which was supplemented by 3 secondary reference methods: MR-Egger regression, weighted median analysis, and weighted mode.[10,11] These additional methods provided further insights and validation to the findings. In the IVW method, when considering exposure factors with each SNP individually, consistent estimations were obtained assuming the authenticity of all SNPs without including an intercept term. The significance and contribution of independent variables were determined using the *F*-statistic. An *F*-statistic >10 for an SNP indicated the absence of a weak instrumental bias, warranting its inclusion. Conversely, if a significant weak instrumental bias was present, the instrumental variable was excluded. To obtain the final estimates in the MR analysis, we re-ran the analysis after excluding any instrumental variables that did not meet the qualification criteria mentioned earlier. This ensured that only robust and reliable IVs were included in the final analysis. The IVW results were considered reliable when there was no heterogeneity and pleiotropy present, as these factors could introduce bias.

2.4. Sensitivity analysis

To assess heterogeneity among the independent variables, Cochran *Q*-test was employed, and a *P*-value <.05 indicated the absence of heterogeneity. The MR-PRESSO method was utilized to evaluate the presence and impact of horizontal pleiotropy, which occurs when an instrumental variable affects the outcome

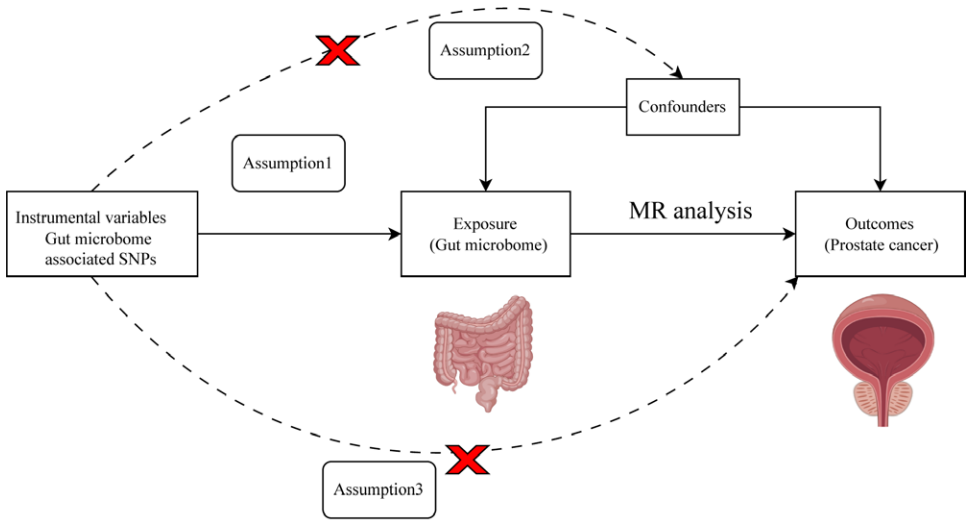

Figure 1. The research methodology employed in the current study, incorporating Mendelian randomization analysis. The MR approach relies on 3 assumptions: assumption 1 asserts that there should be a robust association between the genetic variants and the exposure (in this instance, gut microbiota); assumption 2 stipulates that the genetic variants should not be linked to any confounding factors related to the outcome (in this scenario, prostate cancer); and assumption 3 declares that the genetic variants should solely impact the outcome via exposure factors, excluding alternative pathways. MR = Mendelian randomization.

through pathways independent of the exposure. This analysis helped assess the validity of the instruments used. To evaluate the overall results and identify potential outliers, a leave-one-out analysis was performed. This involved calculating the remaining effects of individual SNPs while excluding each one in turn, allowing for an assessment of the influence of any single outlier. The accuracy of the causal estimates was further examined using the MR Steiger test, which evaluates the directionality and strength of the causal relationship between exposure and outcome.[12] Additionally, an inverse Mendelian randomization analysis was conducted to explore the reverse causality, aiming to investigate whether the outcome variable could causally influence the exposure variable.

3. Results

A total of 2564 SNPs derived from the gut microbiota were examined as instrumental variables. *F*-statistics were calculated for each instrumental variable to assess their strength as instruments. The outcomes of the MR analysis for instrumental variables are depicted in the forest plot (Fig. 2). Notably, the IVW analysis revealed significant results for 1 phylum, 2 classes, 2 orders, 2 families, and 8 genera.

The significant results from the IVW analysis were as follows: phylum Verrucomicrobia OR = 0.802 (0.69–0.933), *P* = 4.19E-03; class Bacilli OR = 1.132 (1.014–1.264), *P* = 2.78E-02; class Erysipelotrichia OR = 1.226 (1.007–1.492, *P* = 4.19E-02; order Erysipelotrichales OR = 1.226 (1.007–1.492), *P* = 4.19E-02; order Lactobacillales OR = 1.137 (1–1.293), *P* = 4.99E-02; family Erysipelotrichaceae OR = 1.226 (1.007–1.492), *P* = 4.19E-02; family Rikenellaceae OR = 0.872 (0.766–0.992), *P* = 3.71E-02; genus Anaerotruncus OR = 0.862 (0.747–0.994), *P* = 4.14E-02; genus Eisenbergiella OR = 0.904 (0.827–0.988), *P* = 2.63E-02; genus Marvinbryantia OR = 1.18 (1.018–1.368), *P* = 2.81E-02; genus Olsenella OR = 0.919 (0.844–1), *P* = 4.99E-02; genus Parabacteroides OR = 0.817 (0.677–0.987), *P* = 3.61E-02; genus Romboutsia OR = 1.179 (1.003–1.385), *P* = 4.54E-02; genus Ruminococcaceae UCG002 OR = 1.117 (1.006–1.241), *P* = 3.91E-02; and genus Sutterella OR = 1.161 (1.004–1.342), *P* = 4.42E-02.

The findings from the sensitivity analyses are presented in Table 1. Cochran *Q*-test results indicated that none of the gut microbiota variables demonstrated significant heterogeneity, suggesting homogeneity among the IVs. The MR-PRESSO analysis did not identify any outliers, indicating that the data points were not disproportionately influencing the results. The analysis of MR-Egger intercept yielded insignificant findings, suggesting the absence of horizontal pleiotropy (Fig. 3). All the analysis methods employed consistently yielded similar directions of effect, except for the genera Eisenbergiella and Ruminococcaceae UCG002. The MR-Egger technique generated different impact values for these categories compared to the other 3 methods. It is important to note that the MR-Egger method assumes that all IVs are invalid, which may have weakened the statistical power and resulted in less precise outcomes. Therefore, our primary use of this method was to assess horizontal pleiotropy.

Furthermore, all funnel plots displayed symmetry, indicating no evidence of heterogeneity in the findings (Fig. 4). This further supports the robustness of the results. The results from the leave-one-out analysis demonstrated the robustness of the findings, as they remained consistent and unchanged regardless of which SNP was removed from the analysis (Fig. 5).

The reverse MR analysis yielded significant findings for the following taxonomic groups (Fig. 6): class Alphaproteobacteria (OR = 0.866, *P* = .049), order Rhodospirillales (OR = 0.866, *P* = .049), family Rhodospirillaceae (OR = 0.865, *P* = .045), family Veillonellaceae (OR = 0.962, *P* = .011), family Victivallaceae (OR = 0.935, *P* = .043), genus Anaerofilum (OR = 1.080, *P* = .048), genus Anaerostipes (OR = 1.031, *P* = .044), genus Catenibacterium (OR = 0.745, *P* = .016), genus Oxalobacter (OR = 1.208, *P* = .040), genus Paraprevotella (OR = 0.823, *P* = .019), genus RuminococcaceaeUCG002 (OR = 1.038, *P* = .011), genus Ruminococcus2 (OR = 1.128, *P* = .047), and genus Victivallis (OR = 0.895, *P* = .002) (Table 2).

4. Discussion

In recent years, there has been a growing body of research investigating the role of the intestinal microbiota in disease progression. It has been increasingly recognized that the intestinal microbiota is associated with various human diseases, including tumors.[13] The incidence of PCa shows wide regional differences, possibly due to differences in gut microbiota due to dietary habits. Therefore, it is important to understand the impact of gut flora on the onset of prostate cancer.[14] However, studying the regulatory mechanisms of the intestinal flora on tumors poses significant challenges, and observational studies alone cannot establish a clear causal relationship. In this context, our study stands out as the first to utilize Mendelian randomization analysis to establish a causal relationship between the gut microbiota and prostate cancer. By employing this rigorous analytical approach, we provide compelling evidence supporting the notion that the composition and function of the digestive microbiota have a direct impact on the development and progression of prostate cancer.

Under normal circumstances, there are at least 500 different kinds of microorganisms in the human gut, the types of intestinal microbiome including bacteria, fungi, viruses, etc.[15] These microorganisms play an extremely important role in our bodies, including: Digestion and absorption of nutrients in food, substance metabolism (toxin metabolism), production of important metabolites such as vitamins and enzymes, immune regulation, such as gut microbes act on the intestinal immune system by regulating the secretion of antibodies from the intestinal mucosa, and further affect innate and acquired immunity.[16,17] When certain factors (such as food additives, indigestion, long-term use of antibiotics, etc) lead to changes in intestinal flora, it will further affect the rest of the human immune system, and once this immune balance is broken, it is easy to lead to various diseases.[18] Recent studies have shown that there is a relationship between gut flora and certain types of cancer. At present, it is generally believed that the mechanism of intestinal flora induced cancer is related to DNA damage induced by enhanced toxin release produced by bacteria, reduction of intestinal beneficial bacteria derived metabolites, intestinal epithelial barrier dysfunction or intestinal flora ecological imbalance.[19] Recent studies have shown that gut microbiota may affect hormone levels, and have been linked to hormone-related cancers such as breast cancer.[20] For prostate cancer, previous studies have shown that prostate cancer is closely related to hormone levels in addition to metabolites and the immune microenvironment.

Previous research has linked gut microbiota to a variety of cancers, including breast and PCa, and they believe genus Ruminococcustorquesgroup can reduce the incidence of PCa.[21] Our study focused on the influence of intestinal flora on PCa. Based on previous studies, we found that other intestinal flora such as family Rikenellaceae could also play a protective role in the incidence of PCa. In addition, we also found that the class Bacilli, class Erysipelotrichia and other intestinal flora can promote the incidence of PCa. The composition of intestinal flora in human body is complex. Our study enriches the understanding of the influence of intestinal flora on the incidence of PCa, and provides a basis for the clinical prevention and treatment of PCa. This study has unveiled a compelling causal association between various gut microbiota and prostate cancer. Specifically, we observed that the presence of certain taxa, such as the phylum Verrucomicrobia, family Rikenellaceae, genus Anaerotruncus, genus Eisenbergiella,

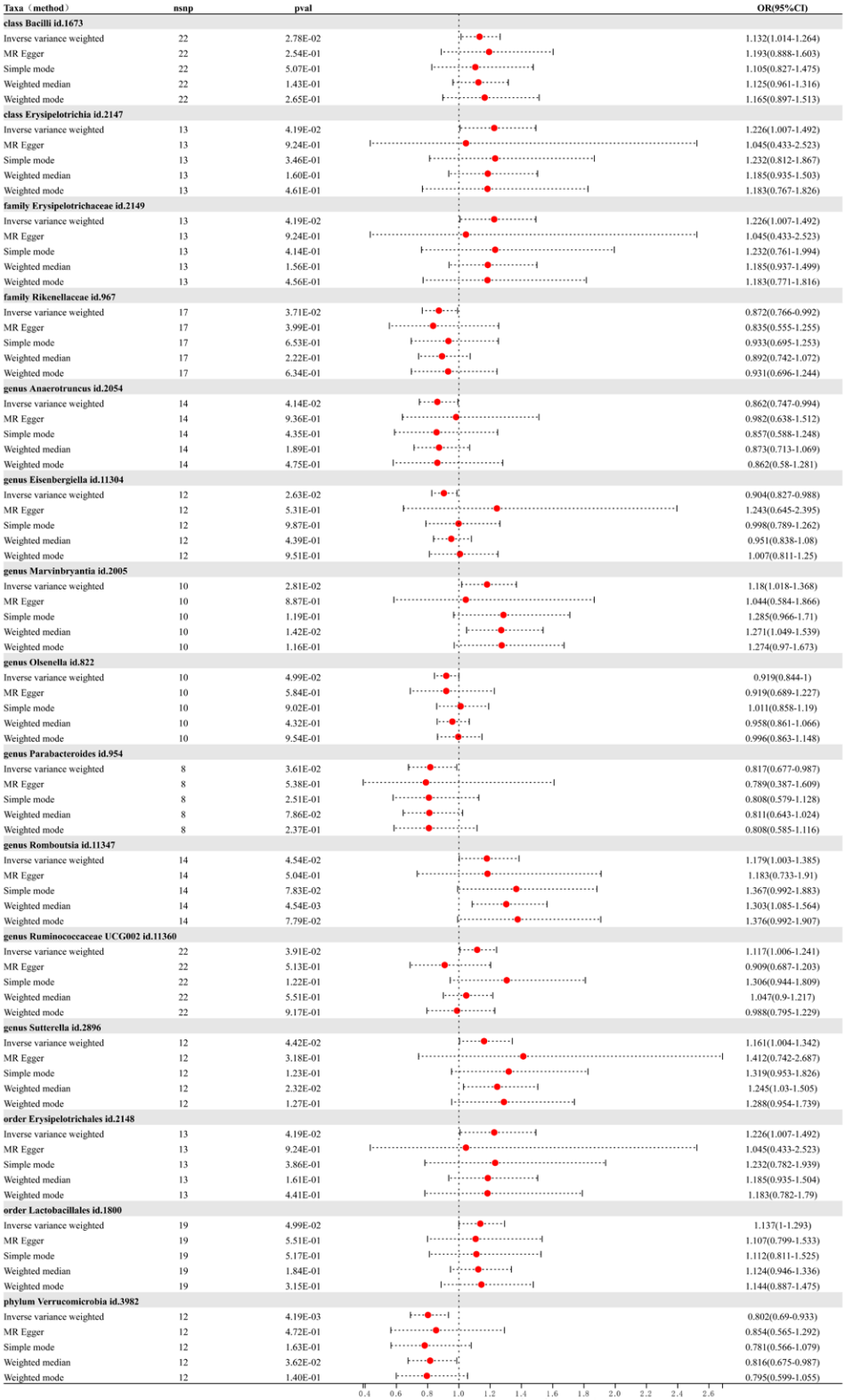

Figure 2. The effects sizes for gut microbiota on prostate cancer were displayed using a forest plot based on MR estimation. MR = Mendelian randomization.

genus Olsenella, and genus Parabacteroides, was associated with a decreased risk of prostate cancer (OR < 1). Conversely, the taxa including the class Bacilli, class Erysipelotrichia, order Erysipelotrichales, order Lactobacillales, family Erysipelotrichaceae, genus Marvinbryantia, genus Romboutsia, genus Ruminococcaceae UCG002, and genus Sutterella exhibited the opposite effect, increasing the risk of prostate cancer (OR > 1).

TNFR2, also known as TNFRSF1B and CD120b, is a membrane receptor belonging to the tumor necrosis factor receptor superfamily member 1B. It binds to TNFα, a cytokine involved in various biological processes. In a study conducted by Beli

Table 1

Sensitivity analysis of significant gut microbiota.

Gut microbiota	Cochran *Q*-test pval	MR-Egger interpreter	MR-Egger interpreter pval	MR-PRESSO	Steiger
Bacilli	0.421521953	-0.004388838	0.70839092	0.456	6.94E-84
Erysipelotrichia	0.107037595	0.009976739	0.721783011	0.118	1.80E-48
Erysipelotrichaceae	0.107037595	0.009976739	0.721783011	0.1	1.80E-48
Rikenellaceae	0.787697561	0.00318656	0.830104376	0.805	7.91E-65
Anaerotruncus	0.533769252	-0.009455461	0.540470916	0.506	1.03E-59
Eisenbergiella	0.624052763	-0.034074499	0.359815858	0.634	2.09E-44
Marvinbryantia	0.799103818	0.010906386	0.680226823	0.827	1.25E-43
Olsenella	0.310068663	-7.41E-05	0.997123482	0.345	5.48E-37
Parabacteroides	0.996722944	0.002958598	0.922772051	0.996	4.04E-32
Romboutsia	0.081595112	-0.000314538	0.988056524	0.066	3.81E-50
Ruminococcaceae UCG002	0.450465677	0.016926577	0.135741958	0.435	2.27E-92
Sutterella	0.342837619	-0.013475952	0.553589881	0.33	1.78E-43
Erysipelotrichales	0.107037595	0.009976739	0.721783011	0.11	1.80E-48
Lactobacillales	0.247829346	0.002305525	0.859603686	0.269	9.30E-73
Verrucomicrobia	0.150603926	-0.005968133	0.754850655	0.186	7.33E-44

MR = Mendelian randomization.

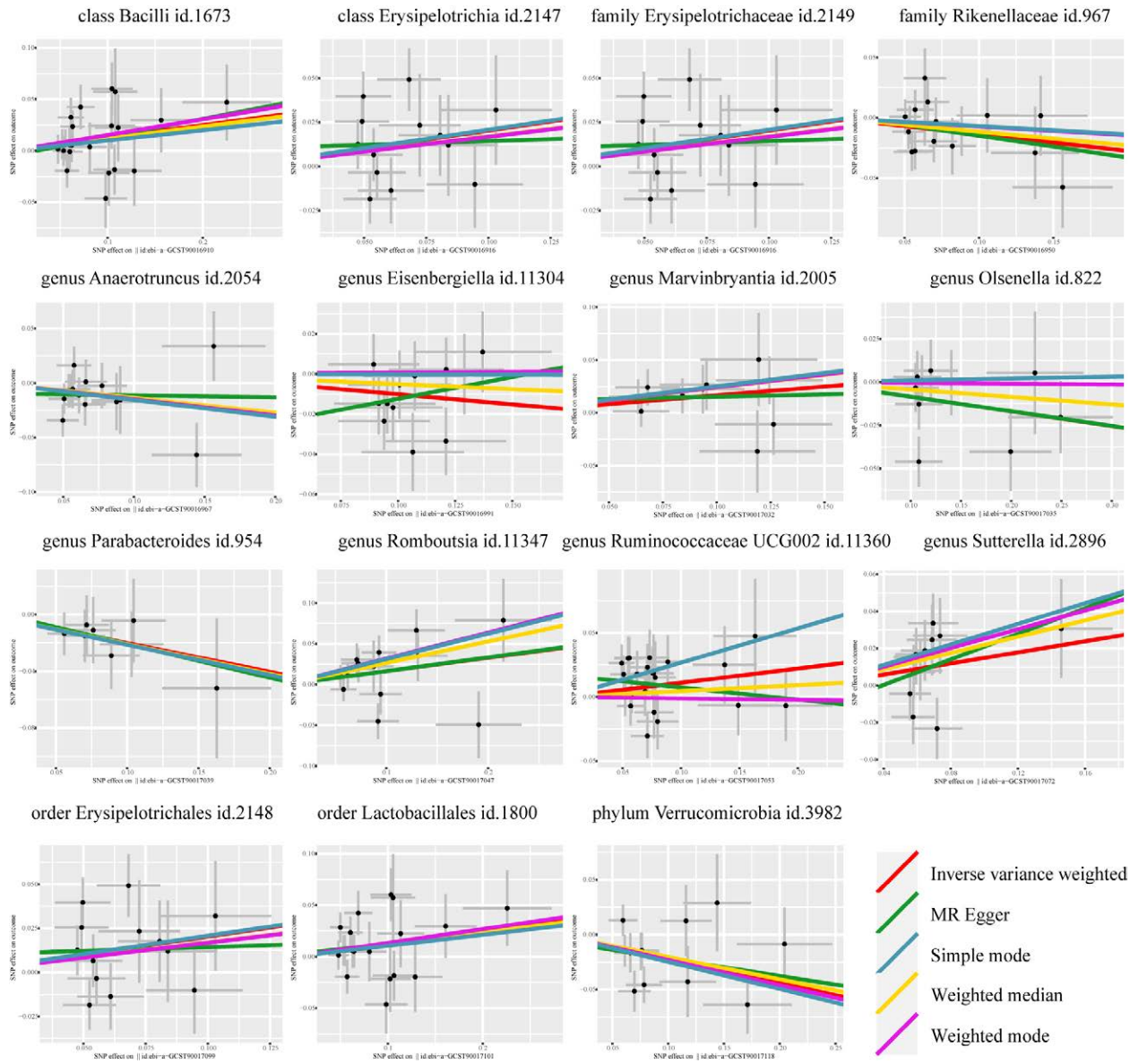

Figure 3. Scatter plots illustrated the impact of intestinal microorganisms on the development of prostate cancer.

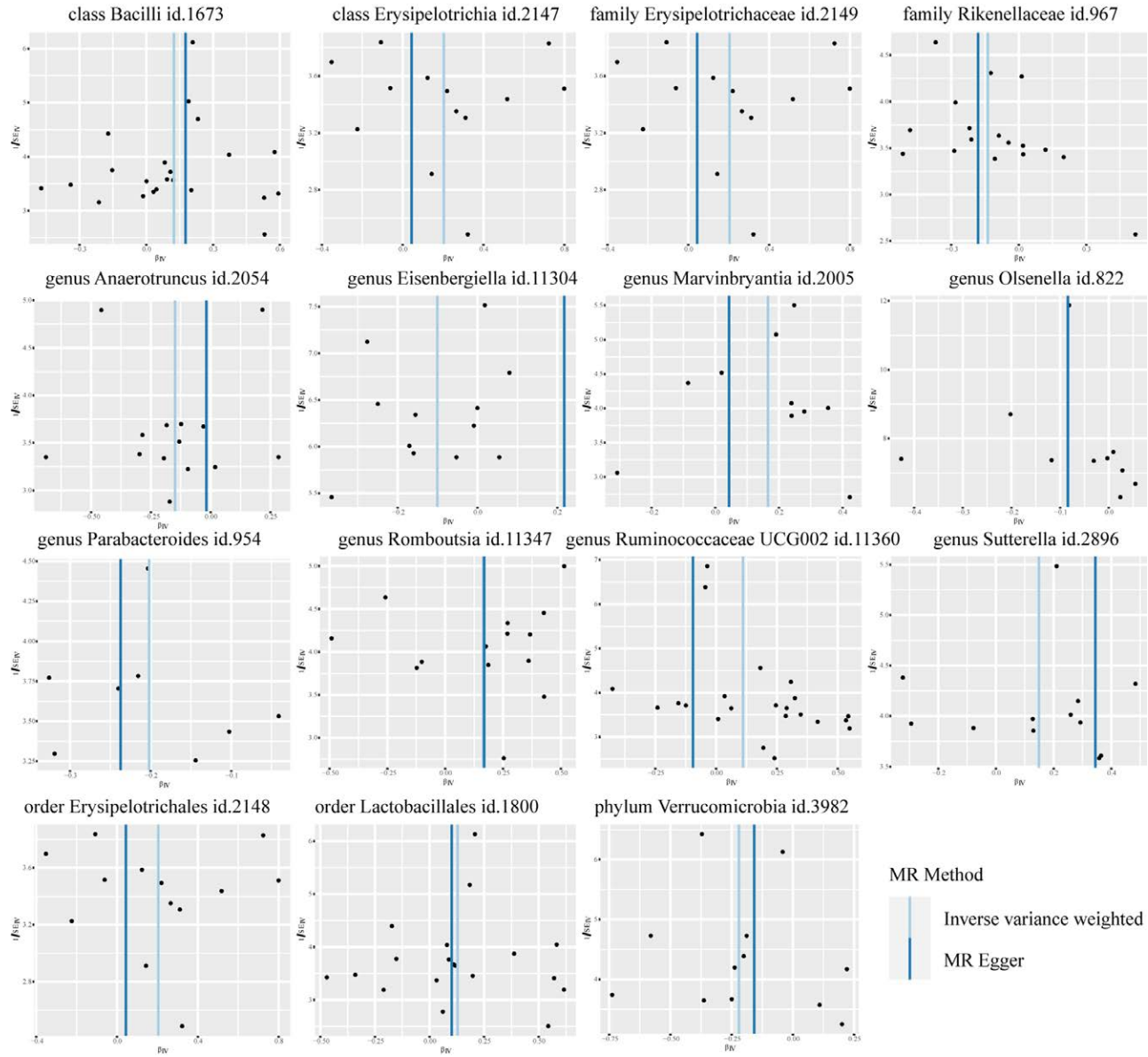

Figure 4. Funnel plots show symmetrical distribution of individual variant estimates around the point estimate.

et al, they explored the effects of intermittent fasting on diabetic retinopathy. The researchers observed that intermittent fasting resulted in a decrease in Verrucomicrobia microorganisms in the gut, and it also led to a reduction in retinal TNF-α expression compared to mice fed freely.[22] These findings raise an interesting possibility to investigate the potential role of the Verrucomicrobia phylum in modulating TNF-α and its membrane receptor TNFR2, providing a fresh perspective on the relationship between Verrucomicrobia and TNFR2. Research has revealed that a combination of orally administered antibiotics (Abx) in mice with prostate cancer, along with a high-fat diet, can induce significant alterations in the composition of Rikenellaceae, a bacterial family found in the intestines. This treatment approach has been shown to impede the growth of prostate cancer cells, decrease the expression of insulin-like growth factor-1 in the prostate, and reduce circulating levels of insulin-like growth factor-1.[23] Furthermore, Loke et al conducted a study that identified the genus Anaerotruncus. In their research involving 17 Asian colorectal cancer patients, the investigators explored the differences in intestinal microbial composition and metabolites between tumor tissue and normal tissue. They observed that the levels of Anaerotruncus genus had an impact on the biosynthesis of steroids and terpenes, as well as bile metabolism. Consequently, this led to an increase in tumor-associated metabolites such as S-adenosylmethionine and S-adenosyl-homocysteine.[24]

The presence of Eisenbergiella has been found to be associated with an increased likelihood of experiencing moderate to severe asthma, potentially due to its role in regulating the immune function of the body.[25] Regarding Olsenella, a study conducted by Zhong et al demonstrated that the consumption of blueberry juice fermented with probiotics resulted in a significant decrease in levels of low-density lipoprotein cholesterol and fat buildup. Furthermore, it improved insulin resistance and enhanced the abundance and diversity of microbial communities in the intestines of mice fed a high-fat diet.[26] Preliminary studies suggest that the presence of the genus Parabacteroides in colorectal cancer and early hepatocellular carcinoma compared to cirrhosis could potentially serve as a biomarker. Additionally, a separate investigation revealed a negative association between PD-L1 and the genus Parabacteroides.[27] According to certain studies, the presence of Bacilli has been found to be higher in patients

Figure 5. There are plots that demonstrate the connection between gut microbiota and the probability of prostate cancer development using the leave-one-out method.

with encephalitis and Graves' disease compared to individuals in good health.[28] Pindjakova et al discovered that Erysipelotrichia was more abundant in overweight mice that were fed a high-fat obesogenic diet, which was not inflammatory.[29] Additionally, patients with autoimmune liver disease, atopic dermatitis, type 1 diabetes, and Graves' disease exhibited an increase in the abundance of Lactobacillales.[30] In a clinical trial investigating the correlation between gut microbiota, chemotherapy toxicity, and treatment response in postmenopausal individuals diagnosed with estrogen receptor-positive breast cancer, researchers observed significant fluctuations in the levels of Marvinbryantia throughout the study period.[31] Furthermore, a previous investigation revealed that the presence of Ruminococcaceae in the family led to an increase in the production of short-chain fatty acids, enhanced infiltration of CD8 T-cells into the tumor microenvironment, and improved efficacy of anti-PD-L1 therapy in combating colon cancer in mice.[32] Previous studies have found that genus Ruminococcaceae UCG005 is associated with prostate cancer and may promote the incidence of PCa.[33] In this study, we found that Ruminococcaceae UCG002 from the same family may also promote the incidence of PCa. This may suggest that it could be a potential target for PCa prevention and control. The authors Zhang and colleagues made an important discovery that Romboutsia showed significant abundance within the gastrointestinal tracts of individuals diagnosed with gastric intraepithelial neoplasia.[34] Furthermore, an analysis of 16S rRNA gene sequencing in 18 surgical specimens from individuals with colorectal cancer revealed a notable enrichment of Sutterella in the

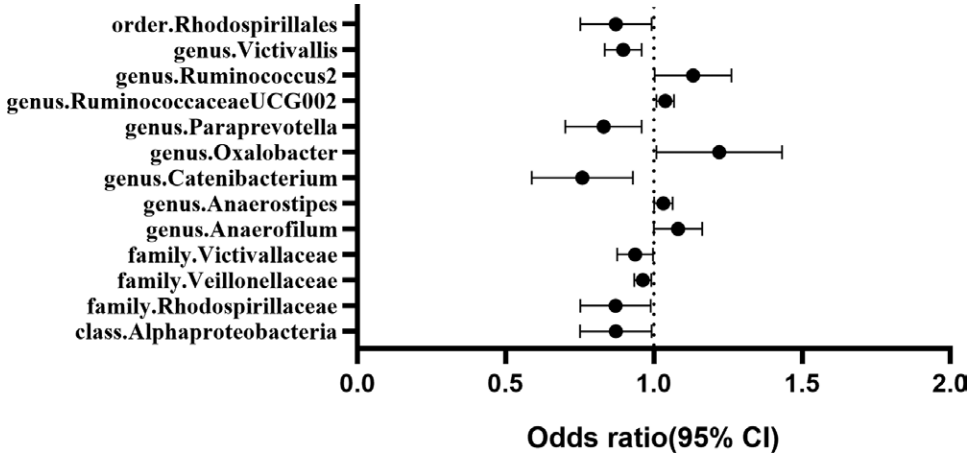

Figure 6. Forest plot of bi-directional MR results. MR = Mendelian randomization.

Table 2

Bi-directional MR results of the causal effects between gut microbiome and cancer risk.

Gut microbiota (outcome)	Method	nsnp	OR	OR lci95	OR uci95	*P*
class.Alphaproteobacteria.id.2379	MR Egger	41	0.865799393	0.753570756	0.994742144	0.048748693
family.Rhodospirillaceae.id.2717	MR Egger	41	0.865474581	0.755036302	0.992066537	0.044692887
family.Veillonellaceae.id.2172	Inverse variance weighted	41	0.962152707	0.93386625	0.99129595	0.01126988
family.Victivallaceae.id.2255	Inverse variance weighted	41	0.935335572	0.876818779	0.997757636	0.042549465
genus.Anaerofilum.id.2053	Weighted median	41	1.079045095	1.000746368	1.163469939	0.047769606
genus.Anaerostipes.id.1991	Inverse variance weighted	41	1.03147173	1.00082357	1.063058426	0.044062785
genus.Catenibacterium.id.2153	MR Egger	36	0.74529073	0.594238184	0.934740122	0.015672443
genus.Oxalobacter.id.2978	MR Egger	41	1.207906135	1.01473916	1.437844609	0.040015014
genus.Paraprevotella.id.962	MR Egger	41	0.823257329	0.704563408	0.961946961	0.018949672
genus.RuminococcaceaeUCG002.id.11360	Inverse variance weighted	41	1.038048791	1.00856497	1.068394525	0.01108132
genus.Ruminococcus2.id.11374	MR Egger	41	1.12763812	1.005613986	1.264469018	0.046538803
genus.Victivallis.id.2256	Inverse variance weighted	36	0.895142127	0.835112074	0.959487298	0.001761762
order.Rhodospirillales.id.2667	MR Egger	41	0.866353018	0.754595939	0.99466153	0.048586708

MR = Mendelian randomization.

mucus layer compared to the underlying mucosa.[35] These findings suggest that these specific microbiotas may contribute to the promotion of inflammation in the colorectal region.

The reverse analysis of the microbiome revealed that several gut microbiota species exhibited a tendency to inhabit the gastrointestinal tract of individuals diagnosed with prostate cancer. This observation suggests a potential connection between the patients' dietary habits, treatment regimens, and the composition of their gut microbiota.

This study explored the relationship between intestinal flora and PCa through Mendelian randomization, providing new ideas for the prevention of PCa. The results of this study indicated that some specific intestinal flora played a role in the pathogenesis of PCa, and could provide a new intervention target for the prevention of PCa. By modulating specific gut microbiota, it may help reduce the risk of developing PCa and thus become a potential prevention strategy. The diverse and individualized nature of the gut microbiota makes it a key component of precision medicine. If certain gut flora is closely related to the development of PCa, then in the diagnosis, prognosis assessment or treatment of PCa, gut flora analysis can be used as an important tool for personalized treatment, helping to develop more targeted treatment plans.

This study has several limitations that warrant consideration. Firstly, our analysis was conducted exclusively within a European population, which may limit the generalizability of the results to other ethnicities and geographical regions, as gut microbiota composition can vary significantly across diverse populations. Additionally, due to taxonomic limitations, our research was restricted to genus-level classifications, preventing a more granular investigation into specific microbial species that could have unique associations with prostate cancer. Species-level analysis might yield deeper insights into the specific bacterial contributions to PCa risk. Finally, it is important to acknowledge that this study primarily identifies correlations between gut microbiota and PCa without exploring the underlying biological mechanisms. Further research is necessary to clarify how gut microbiota might influence PCa development and progression at a mechanistic level.

5. Conclusion

MR analysis established a causal link between the gut microbiota and prostate cancer. New biomarkers may emerge from these strains, offering potential guidance for the prevention and treatment of prostate cancer.

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Author contributions

Data curation: Lingyu Guo.

Formal analysis: Lingyu Guo.
Methodology: Lingyu Guo.
Resources: Tian An.
Software: Tian An.
Writing – review & editing: Tian An.

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