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ORIGINAL RESEARCH

Causal Associations Between Gut Microbiota and Psoriasis: A Mendelian Randomization Study

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ABSTRACT

Introduction: Previous studies have proposed a possible gut–skin axis, and linked gut microbiota to psoriasis risks. However, there is heterogeneity in existing evidence. Observational research is prone to bias, and it is hard to determine causality. Therefore, this study aims to evaluate possible causal associations between gut microbiota (GM) and psoriasis.

Methods: With published large-scale GWAS (genome-wide association study) summary datasets, two-sample Mendelian randomization (MR) was performed to sort out possible causal roles of GM in psoriasis and arthropathic psoriasis (PsA). The inverse variance weighted (IVW) method was taken as the primary evaluation of causal association. As complements to the IVW method, we also applied MR-Egger, weighted median. Sensitivity analyses were conducted using Cochrane's *Q* test, MR-Egger intercept test, MR-PRESSO (Mendelian Randomization Pleiotropy RESidual Sum and Outlier) global test, and leave-one-out analysis.

Results: By primary IVW analysis, we identified nominal protective roles of Bacteroidetes (odds ratio, OR 0.81, $P = 0.033$) and *Prevotella9* (OR 0.87, $P = 0.045$) in psoriasis risks. Bacteroidia (OR 0.65, $P = 0.03$), Bacteroidales (OR 0.65, $P = 0.03$), and *Ruminococcaceae* UCG002 (OR 0.81, $P = 0.038$) are nominally associated with lower risks for PsA. On

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the other hand, Pasteurellales (OR 1.22, $P = 0.033$), Pasteurellaceae (OR 1.22, $P = 0.033$), *Blautia* (OR 1.46, $P = 0.014$), *Methanobrevibacter* (OR 1.27, $P = 0.026$), and *Eubacterium fissicatena* group (OR 1.21, $P = 0.028$) are nominal risk factors for PsA. Additionally, *E. fissicatena* group is a possible risk factor for psoriasis (OR 1.22, $P = 0.00018$). After false discovery rate (FDR) correction, *E. fissicatena* group remains a risk factor for psoriasis ($P_{FDR} = 0.03798$).

Conclusion: We comprehensively evaluated possible causal associations of GM with psoriasis and arthropathic psoriasis, and identified several nominal associations. *E. fissicatena* group remains a risk factor for psoriasis after FDR correction. Our results offer promising therapeutic targets for psoriasis clinical management.

Keywords: Psoriasis; Gut microbiota; Mendelian randomization; Gut–skin axis; Causal analysis

Key Summary Points

Why carry out this study?

Previous studies have proposed a possible gut–skin axis, and linked gut microbiota to psoriasis risks.

Observational research is prone to bias, and it is hard to determine causality.

We performed a two-sample Mendelian randomization study to evaluate possible causal association between gut microbiota (GM) with psoriasis.

What was learned from the study?

Bacteroidetes and *Prevotella9* are nominally associated with lower risk for psoriasis. Bacteroidia, Bacteroidales, and *Ruminococcaceae* UCG002 are nominally associated with lower risks for arthropathic psoriasis. On the other hand, Pasteurellales, Pasteurellaceae, *Blautia*, *Methanobrevibacter*, and *Eubacterium fissicatena* group are nominal risk factors for arthropathic psoriasis, while *E. fissicatena* group is a risk factor for psoriasis after false discovery rate correction.

Further studies are needed to validate these associations between gut microbiota and psoriasis.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease manifested by red, itchy, and dry skin plaques [1], affecting 0.84% of the population in 2017 [2]. The detailed pathological mechanisms of psoriasis are not fully understood yet. Previously recognized immune dysregulation, hereditary susceptibility, environmental factors, etc. may be associated with psoriasis [1]. Recently, mounting research also reveals an underlying gut–skin axis, where skin and gut are in intimate contact with the immune system and work together to protect from external antigens [3, 4]. As a result of both skin and gut being exposed to a broad range and complicated microbiota, however, there are still large gaps in understanding the associations between gut microbiota and psoriasis.

Gut microbiota refers to the whole microbial population living in the intestinal tract [5]. Gut microbiota play a vital role in physiological activities including protecting from external antigens, providing metabolic activities, and regulating immune system regulation, etc. [4]. Whereas, dysregulation of gut microbiota and gut dysbiosis disrupt immunological tolerance, then subsequently disturb skin immune balance [6]. Growing clinical evidence has linked the alteration of the gut microbiota to psoriasis [7]. For example, *Akkermansia muciniphila* is significantly reduced in patients with psoriasis than in controls [8]. However, the available epidemiological evidence for these associations is occasionally conflicting, possibly because o selective bias, varied measuring methods, etc. For example, Prevotella levels were reported to be higher [9] or lower [10] in patients with psoriasis than in healthy controls. Though clinical evidence elaborates, shared cofounders, selective bias (e.g., age, gender, region), and heterogeneity in clinical research, all may cloud the

understanding of this association between gut microbiota and psoriasis. Studying the mechanism between the gut microbiota and psoriasis, as well as further evaluating a causal association may enhance the understanding of psoriasis mechanisms and offer evidence-based therapeutic targets for clinical management.

Mendelian randomization (MR) estimates the potential causal relationship between exposure and outcome via genetic variants as instrumental variables for the exposure factor of interest [11]. Since genetic variants are assigned at random, the MR approach is not susceptible to confounding factors. It can also avoid the reverse causality bias caused by genetic variants being assigned prior to disease development.

In this study, we aim to evaluate an underlying causal association between the gut microbiota and psoriasis via a Mendelian randomization approach. Hopefully, our findings may benefit the understanding of psoriasis pathological mechanisms, as well as offer potential therapeutic targets for psoriasis clinical management.

METHODS

Overall Study Design

Generally, we conducted a two-sample MR study to evaluate the causal effect between gut microbiota and psoriasis. The validity of MR is based on three main assumptions: (i) the genetic variants selected as instrumental variables (IVs) are associated with gut microbiota as exposure of interest; (ii) the used instrumental variable is not associated with common confounders of exposures and outcomes; (iii) instrumental variables should affect the outcome psoriasis only through the exposure (Fig. 1).

GWAS Data Sources

For the exposure gut microbiota, the GWAS dataset from MiBioGen consortium comprising 18,340 participants was applied in this study [12]. This GWAS study examined 211 GM taxa by the 16S rRNA method.

As for the main outcome, psoriasis, the GWAS summary statistics consisting of 339,050 individuals, specifically 8075 patients with psoriasis and 330,975, controls were from FinnGen database R8. The GWAS of arthropathic psoriasis comprised 333,887 individuals, specifically 2912 patients with arthropathic psoriasis and 330,975 controls. Psoriasis and arthropathic psoriasis (PsA) in this GWAS were diagnosed following the International Statistical Classification of Diseases (ICD) (Table 1). This study was conducted on the basis of publicly available data from MiBioGen and FinnGen studies and was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Ethical approval was granted for each of MiBioGen and FinnGen, and informed consent was obtained from all participants prior to participation. Patient personal information in the databases is unidentifiable.

Selection of Genetic Instrument

We selected single-nucleotide polymorphisms (SNPs) associated with gut microbiota with a relatively loose significance level ($P < 1 \times 10^{-5}$). Then, we applied chain disequilibrium $r^2 \leq 0.1$ within the distance of 500 kp, as a cutoff of linkage disequilibrium, for respective independence before being used as primary genetic instruments. Every paired combination was obtained for further analysis after coordinating with responsive outcomes. *F* statistic of IVs were calculated to identify bias from weak instrumental variables. *F* statistic > 10 was considered as no bias from weak instrumental variables.

Statistical Analysis

After harmonizing the SNPs in the data source with the same allele, we performed a two-sample MR analysis. The inverse variance weighting (IVW) method was used as the primary analysis of the causal relationship between gut microbiota and psoriasis. Odds ratios (ORs) of the exponential β for category outcomes and corresponding confidence intervals (CIs) were mainly applied to estimate the effect sizes of causality. *P* value < 0.05 was considered statically significant.

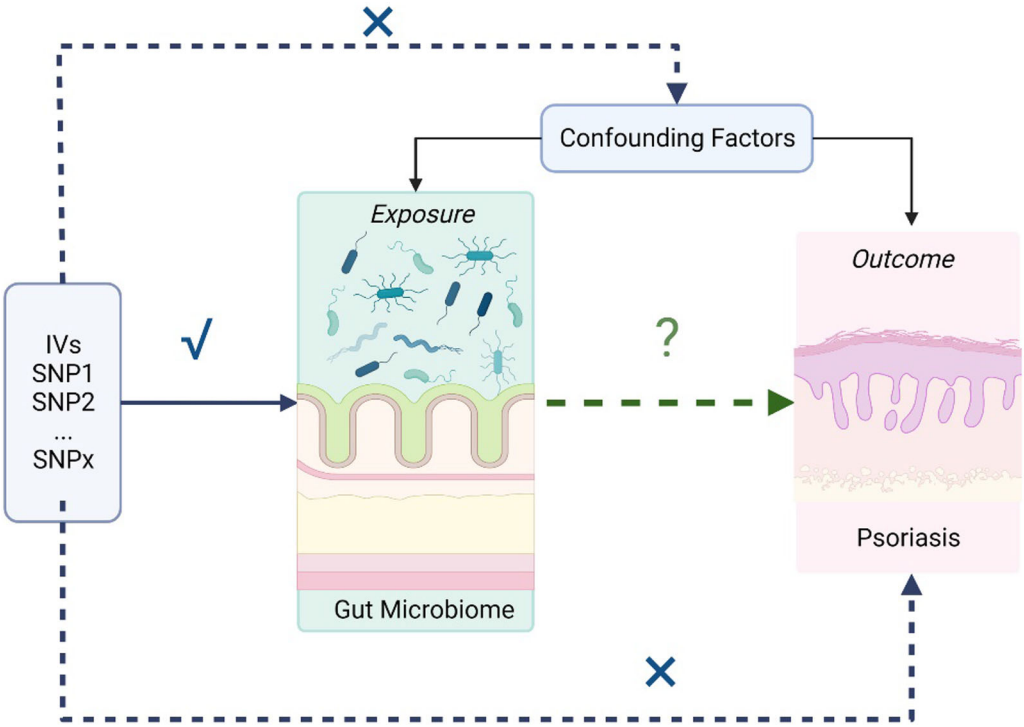

Fig. 1 Mendelian randomization to assess the causal association between gut microbiota and psoriasis. *SNPs* single-nucleotide polymorphism, *IVs* instrumental variables

Table 1 Summary of genome-wide association studies (GWAS) datasets included in our study

Trait	Year	Population	Sources	Sample sizes	Cases	Controls
Exposure						
211 GM taxa	2021	72.3% European	MiBioGen	18,340	–	–
Outcome						
Psoriasis	2022	European	FinnGen (R8)	339,050	8075	330,975
Arthropathic psoriasis	2022	European	FinnGen (R8)	333,887	2912	330,975

GM gut microbiota

Then, to verify the consistency of our results and analyze sensitivity, MR-Egger, weighted median, MR-PRESSO (Mendelian Ran- 29 domization Pleiotropy RESidual Sum and Out- 30 lier), and leave-one-out analysis were performed. Potential pleiotropy was evaluated and corrected by MR-Egger intercept test and MR-PRESSO global test. Heterogeneity was assessed by Cochrane's *Q* test calculated in the IVW method and MR-Egger method. Once potential pleiotropy or heterogeneity was identified, we would try to identify and remove outliers using MR-PRESSO; then the above analysis would be repeated. Finally, FDR correction was applied to reduce the possibility of false positives.

RESULTS

Details of Selected Instrument Variables

As shown in Supplementary Material Table S1, after screening at a relatively loose threshold ($P < 1 \times 10^{-5}$) and LD clumping, SNPs of gut

microbiota ranging from phylum to genus levels were applied. All the *F* statistics of the instrumental variables were over 10.

Causal Impact of Gut Microbiota on Psoriasis

An overview of the causal effect of 211 gut microbiota taxa on psoriasis and PsA is shown in Fig. 2. More specifically, original statistical results are available in Supplementary Material Tables S2 and S3. The effect of each single SNP on psoriasis and arthropathic psoriasis is available in Supplementary Material Fig. S1.

At the phylum level, we observed that Bacteroidetes has a nominally protective role in psoriasis (OR 0.81, 95% CI 0.67–0.98, $P = 0.033$) by the primary IVW method. Then at the genus level, *Prevotella9* also showed a nominally protective impact on psoriasis (OR 0.87, 95% CI 0.76–1.00, $P = 0.045$). On the other hand, *Eubacterium fissicatena* group is associated with an increased risk of developing psoriasis (OR 1.22, 95% CI 1.10–1.35, $P = 0.00018$) (Fig. 3). Then after multiple-testing correction was performed (false discover rate [FDR] < 0.05, Supplementary Material Table S4), *E. fissicatena* group remains a significant risk factor for psoriasis ($P_{FDR} = 0.03798$).

Causal Impact of Gut Microbiota on PsA

Then, we focused on the PsA subgroup. According to primary IVW analysis, class Bacteroidia (OR 0.65, 95% CI 0.44–0.96, $P = 0.03$), order Bacteroidales (OR 0.65, 95% CI 0.44–0.96, $P = 0.03$), genus *Ruminococcaceae* UCG002 (OR 0.81, 95% CI 0.66–0.99, $P = 0.038$) are associated with a nominal lower risk for PsA (Fig. 3). Although genus *Butyricicoccus* also showed an association by IVW method (OR 0.66, 95% CI 0.47–0.94, $P = 0.022$), there is horizontal pleiotropy in IVs (Table 3, MR-Egger intercept, $P = 0.048$). MR-Egger method, which provides pleiotropy-corrected causal estimates [13], showed no causal association between *Butyricicoccus* and PsA (Table 2, OR 1.30, 95% CI 0.70–2.41, $P = 0.44$).

On the other hand, order Pasteurellales (OR 1.22, 95% CI 1.02–1.46, $P = 0.033$), family Pasteurellaceae (OR 1.22, 95% CI 1.02–1.46, $P = 0.033$), genus *Blautia* (OR 1.46, 95% CI 1.08–1.98, $P = 0.014$), genus *Methanobrevibacter* (OR 1.27, 95% CI 1.03–1.56, $P = 0.026$), and genus *E. fissicatena* group (OR 1.21, 95% CI 1.02–1.43, $P = 0.028$) are nominally associated with increased risks of developing PsA (Fig. 3). After FDR correction (Supplementary Material Table S5), none of gut microbes showed any significant causal associations with PsA.

Sensitivity Analysis

In validating these causal associations identified by the IVW method, we observed inconsistent direction by the MR-Egger method of *E. fissicatena* group and *Butyricicoccus* (Table 2, Supplementary Material Fig. S4). This would theoretically be refined by either removing outliers or narrowing the genome-wide significance threshold, then selecting IVs more strictly for reanalysis [14]. But this process was not practical here with such a limited number of SNPs left, and there were no outliers identified by MR-PRESSO or funnel plot (Supplementary Material Fig. S2). With no horizontal pleiotropy or outliers observed, the IVW method should still be considered the primary result for evaluating the causal association of *E. fissicatena*.

All possible causal associations identified by the IVW method showed no significant heterogeneity by Cochrane's *Q* test. Leave-one-out analysis confirmed the results were not driven by a single SNP (Supplementary Material Fig. S3). Most IVs for gut microbiota showed no horizontal pleiotropy except for *Butyricicoccus* (Table 3). Pleiotropy-corrected MR-Egger method was therefore considered the more appropriate method for estimating the causal association [13] between *Butyricicoccus* and PsA. Hopefully, when GWAS datasets of the gut microbiota with more participants and SNPs are made publicly available in the future, we can further validate these associations.

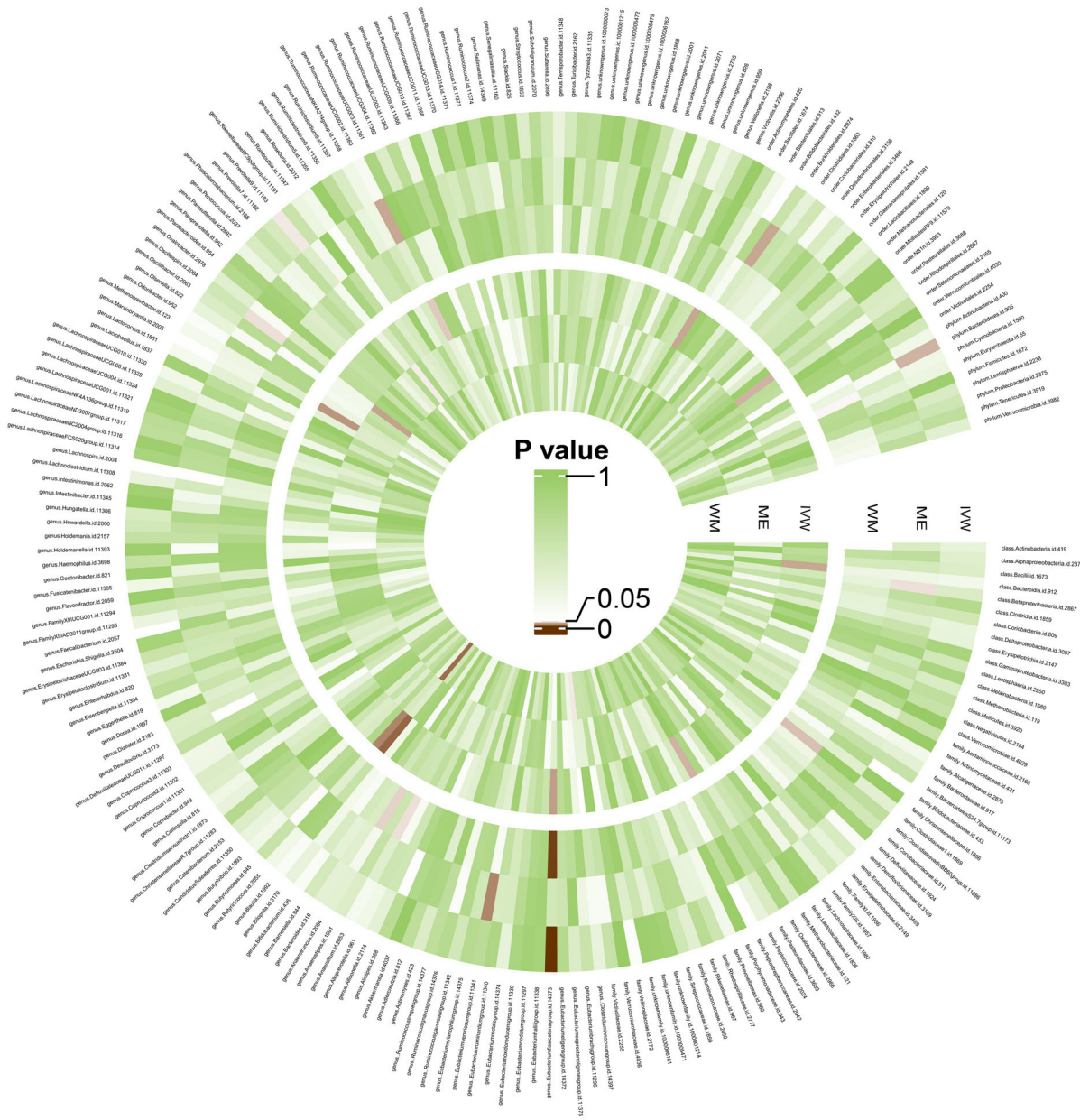

Fig. 2 Overview of the causal role of gut microbiota in psoriasis (outer section) and arthropathic psoriasis (inner section). The brown color indicates statistical significance ($P < 0.05$). *IVW* inverse variance weighted method, *ME* MR-Egger method, *WM* weighted median method

DISCUSSION

In this study, we comprehensively evaluated the causal effect of 211 GM taxa (from phylum to genus level) on psoriasis and PsA, with the merit of large-scale GWAS summary statistics. Generally, we identified several gut microbes nominally associated with psoriasis and arthropathic psoriasis. After FDR correction, *E. fissicatena* group remains a risk factor for psoriasis. Hopefully, these identified gut microbiota biomarkers may be of benefit to the understanding of psoriasis pathology and offer promising therapeutic recommendations.

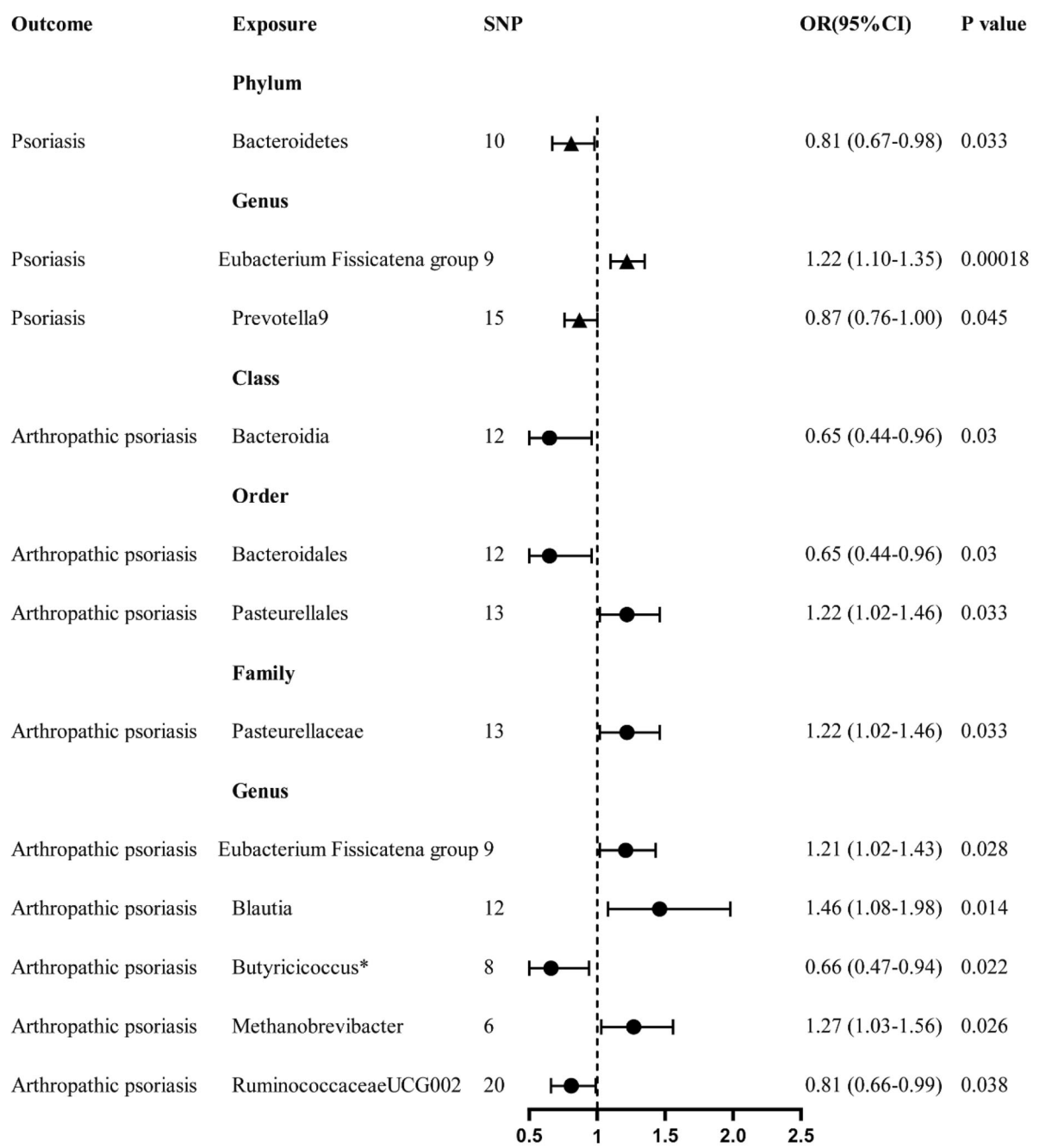

Fig. 3 Forest plot of gut microbiota taxa associated with psoriasis or arthropathic psoriasis identified by the inverse variance weighted method. *SNP* single-nucleotide polymorphism, *OR* odds ratio, *CI* confidence interval. *Pleiotropy-corrected MR-Egger method showed no causal association between *Butyricicoccus* and arthropathic psoriasis

Firstly, we identified the nominal protective role of Bacteroidetes and *Prevotella9* in psoriasis risks, as well as Bacteroidia, Bacteroidales, and *Ruminococcaceae* UCG002 which are nominally associated with lower risks for PsA. Notably, four out of these six protective GMs identified

Table 2 Results of MR analyses in nominal significance level (IVW $P < 0.05$)

Exposure	Outcome	Method	SNPs	OR (95% CI)	*P* value
Phylum					
Bacteroidetes	Psoriasis	IVW	10	0.81 (0.67–0.98)	0.033
		MR-Egger	10	0.70 (0.45–1.07)	0.13
		Weighted median	10	0.86 (0.66–1.11)	0.24
Genus					
Eubacterium fissicatena group	Psoriasis	IVW	9	1.22 (1.10–1.35)	0.00018
		MR-Egger	9	0.82 (0.48–1.40)	0.48
		Weighted median	9	1.23 (1.07–1.42)	0.0036
Prevotella9	Psoriasis	IVW	15	0.87 (0.76–1.00)	0.045
		MR-Egger	15	0.83 (0.55–1.24)	0.38
		Weighted median	15	0.89 (0.75–1.05)	0.15
Class					
Bacteroidia	Arthropathic psoriasis	IVW	12	0.65 (0.44–0.96)	0.03
		MR-Egger	12	0.98 (0.40–2.39)	0.97
		Weighted median	12	0.79 (0.51–1.22)	0.29
Order					
Bacteroidales	Arthropathic psoriasis	IVW	12	0.65 (0.44–0.96)	0.03
		MR-Egger	12	0.98 (0.40–2.39)	0.97
		Weighted median	12	0.79 (0.51–1.23)	0.29
Pasteurellales	Arthropathic psoriasis	IVW	13	1.22 (1.02–1.46)	0.033
		MR-Egger	13	1.00 (0.68–1.47)	0.99
		Weighted median	13	1.07 (0.83–1.38)	0.59
Family					
Pasteurellaceae	Arthropathic psoriasis	IVW	13	1.22 (1.02–1.46)	0.033
		MR-Egger	13	1.00 (0.68–1.47)	0.99
		Weighted median	13	1.07 (0.83–1.38)	0.59
Genus					
Eubacterium fissicatena group	Arthropathic psoriasis	IVW	9	1.21 (1.02–1.43)	0.028
		MR-Egger	9	0.63 (0.26–1.53)	0.34
		Weighted median	9	1.22 (0.97–1.54)	0.09
Blautia	Arthropathic psoriasis	IVW	12	1.46 (1.08–1.98)	0.014
		MR-Egger	12	1.45 (0.66–3.15)	0.37
		Weighted median	12	1.64 (1.10–2.46)	0.016

Table 2 continued

Exposure	Outcome	Method	SNPs	OR (95% CI)	*P* value
Butyricicoccus[a]	Arthropathic psoriasis	IVW	8	0.66 (0.47–0.94)	0.022
		MR-Egger	8	1.30 (0.70–2.41)	0.44
		Weighted median	8	0.77 (0.49–1.20)	0.25
Methanobrevibacter	Arthropathic psoriasis	IVW	6	1.27 (1.03–1.56)	0.026
		MR-Egger	6	1.47 (0.68–3.20)	0.38
		Weighted median	6	1.29 (0.99–1.67)	0.06
Ruminococcaceae UCG002	Arthropathic psoriasis	IVW	20	0.81 (0.66–0.99)	0.038
		MR-Egger	20	0.74 (0.43–1.25)	0.27
		Weighted median	20	0.89 (0.67–1.18)	0.4

SNPs single-nucleotide polymorphism, *OR* odds ratio, *IVW* inverse-variance weighted, *CI* confidence interval, *MR* Mendelian randomization

[a]With pleiotropy present, the MR-Egger method, which provides pleiotropy-corrected causal estimates, should be considered as the primary estimate of the causal association between *Butyricicoccus* and PsA (arthropathic psoriasis)

are from Bacteroidetes phylum (including Bacteroidetes, Bacteroidia, Bacteroidales, *Prevotella9*); these four gut microbes could produce short-chain fatty acids (SCFAs). Consistent with our results, previous clinical research has also reported that patients with psoriasis and PsA showed a decrease in SCFAs [15] and SCFA-producing bacteria, such as Bacteroidetes [16] and Prevotella [16].

SCFAs, including butyrate, propionate, etc., are the main metabolites from gut microbial fermentation of dietary fiber [17]. SCFAs show anti-inflammatory characteristics [7] by reducing the proliferation of various immune cells, and pro-inflammatory cytokine production, such as Th17, Treg, and DCs [18]. Additionally, SCFAs also upregulate T_{reg} cells, transforming growth factor (TGF)-β, etc. [19], which are responsible for keeping inflammatory and immune reactions in line. Considering the inflammatory nature of psoriasis, these immune regulation SCFAs are critical for controlling psoriasiform inflammation [20]. More specifically, butyrate is an inhibitor of histone deacetylase (HDAC) and induces Foxp3 enhancer. Then with the expression of Foxp3, naïve $CD4^+$ T cells are induced to differentiate into peripheral-derived T_{reg} (pT_{reg}) cells, protecting the host from inflammation [19, 21]. Further, in patients with psoriasis, SCFA metabolism genes are significantly downregulated [22]. In consideration of these pathways, SCFAs and SCFAs-producing microbes should be further studied as therapeutic targets for psoriasis. On the other hand, other bacterial metabolites such as trimethylamine N-oxide (TMAO) have been widely recognized for their pro-inflammatory effect. TMAO could cause M1 polarization and Th1 and Th17 differentiation [23]. TMAO was also reported to be elevated in patients with psoriasis [24]. However, considering the complexity of gut microbiota, there is indeed inconsistency between our results and existing evidence. For instance, previous research reported the Ruminococcaceae family, *Coprococcus_1* genus [25], was decreased with psoriasis improvement. Prevotella was reported to be higher in those with psoriasis compared to the control group [26] and may be associated with psoriasis improvements in mice. Therefore, with these potential therapeutic targets provided in this study, future studies are also in need to develop personalized, evidence-based treatment protocols for patients with psoriasis.

On the other hand, Pasteurellales, Pasteurellaceae, *Blautia*, *Methanobrevibacter*, and

Table 3 Sensitivity analysis of 12 taxa associated with psoriasis or arthropathic psoriasis

Exposure	Outcome	SNPs	MR-Egger intercept		Cochrane's *Q* IVW		Cochrane's *Q* Egger		Presso Gable *P*
			Intercept value	*P* value	*Q* value	*P* value	*Q* value	*P* value	
Phylum									
Bacteroidetes	Psoriasis	10	0.012494926	0.4560901	7.892532	0.545012	7.279194075	0.506831161	0.6
Genus									
Eubacterium fissicatena group	Psoriasis	9	0.052530524	0.1803491	6.172651	0.627899	3.958467739	0.784548513	0.71
Prevotella9	Psoriasis	15	0.005113565	0.8050901	19.94096	0.132014	19.84413741	0.099165384	0.12
Class									
Bacteroidia	Psoriasis	12	− 0.031146761	0.3438256	18.08594	0.079608	16.46069013	0.087182309	0.11
Order									
Bacteroidales	PsA	12	− 0.031146761	0.3438256	18.08594	0.079608	16.46069013	0.087182309	0.15
Pasteurellales	PsA	13	0.026874918	0.2730482	12.2673	0.424458	10.93611813	0.448630555	0.46
Family									
Pasteurellaceae	PsA	13	0.026874918	0.2730482	12.2673	0.424458	10.93611813	0.448630555	0.45
Genus									
Eubacterium fissicatena group	PsA	9	0.085266114	0.1864937	6.318046	0.611653	4.173526271	0.759587767	0.63
Blautia	PsA	12	0.00083935	0.9764953	8.588019	0.659861	8.587106829	0.571684409	0.68
Butyricicoccus[a]	PsA	8	− 0.067010589	0.0481149	8.641218	0.279451	2.514420145	0.866850344	0.27
Methanobrevibacter	PsA	6	− 0.022446721	0.7121411	1.925832	0.859309	1.768808465	0.778183813	0.86
Ruminococcaceae UCG002	PsA	20	0.007469164	0.7246516	17.2654	0.571893	17.13737163	0.513680071	0.54

SNPs single-nucleotide polymorphism, *IVW* inverse-variance weighted, *PsA* arthropathic psoriasis, *MR* Mendelian randomization

[a]With pleiotropy present, the MR-Egger method, which provides pleiotropy-corrected causal estimates, should be considered as primary estimate of the causal association between *Butyricicoccus* and PsA

E. fissicatena group are nominal risk factors for PsA, while *E. fissicatena* group is a risk factor for psoriasis after FDR correction. Consistent with our results, several clinical research studies reported that *Blautia* genus increased in psoriasis [25, 27, 28], and decreased as psoriasis improved [25]. Whereas, to the best of our knowledge, there has not been previous research on the association between *E. fissicatena* group and psoriasis. Although the detailed mechanism of GMs on psoriasis is not fully understood yet, there are a few theories. Firstly, the interleukin (IL)-23/Th17 axis, tumor necrosis factor (TNFα), etc. [29] have been recognized as significant biomarkers in the mechanism of irregular upregulation of inflammation in psoriasis. While gut microbiota plays a critical role in immune response, gut microbiota alterations were reported to be associated with alteration in Th17 cells [29, 30]. Additionally, as mentioned previously, gut microbiota-related metabolites, especially SCFAs, are essential for regulating immune hemostasis [31]. Whereas, gut dysbiosis and inflammatory gut may lead to lower production of SCFAs [32], and therefore increase psoriasis risks.

This study is the first of its kind, comprehensively analyzing the causal association of 211 GM taxa and psoriasis via Mendelian randomization approach. This method could significantly mitigate the potential effects of reverse causation and residual confounding factors. However, there are several limitations in this present study that should be disclosed. Firstly, in screening IVs for gut microbiota, we noticed extremely minimal IVs fulfilled $P < 5 \times 10^{-8}$, thus we finally applied a relatively loose threshold ($P < 1 \times 10^{-5}$). In addition, this study included individuals mainly of European ancestry, which may undermine the applicability of our results to citizens from other regions. Meanwhile, the GWAS dataset for gut microbiota applied in this study was confined from phylum to genus level, with several microbes without specific names. Future analysis based on large-scale studies is needed to evaluate the species level. Further, with an extremely limited number of SNPs left, and no specific outliers identified by MR-PRESSO, we were unable to address inconsistent direction by the MR-Egger method. There could be also a number of known or unidentified factors influencing both microbiota on the host and possible psoriasis risk. These limitations all make it difficult to determine the causal relationship between gut microbiota and psoriasis at this time. Hopefully, when GWAS dataset of gut microbes with more participants and SNPs is made publicly available in the future, further studies can validate these associations.

CONCLUSION

Several gut microbes are nominally associated with psoriasis and arthropathic psoriasis. Our results offer promising therapeutic targets for psoriasis clinical management. Further studies are needed to validate these associations between gut microbiota and psoriasis.

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Data Availability. Publicly available datasets were analyzed in this study. This data is publicly available at https://mibiogen.gcc.rug.

nl/, https://r8.finngen.fi/. The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Ethical Approval. This study was conducted on the basis of publicly available data from MiBioGen and FinnGen studies and was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.. Ethical approval was granted for each of MiBioGen and FinnGen, and informed consent was obtained from all participants prior to participation. Patient personal information in the databases is unidentifiable.

Conflict of Interest. Chenyang Zang, Jie Liu, Manyun Mao, Wu Zhu, Wangqing Chen, Baojian Wei declare no conflict of interest.

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