

# Influence of oral and skin microbiota on multiple sclerosis risk and severity: A mendelian randomization analysis

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## INTRODUCTION

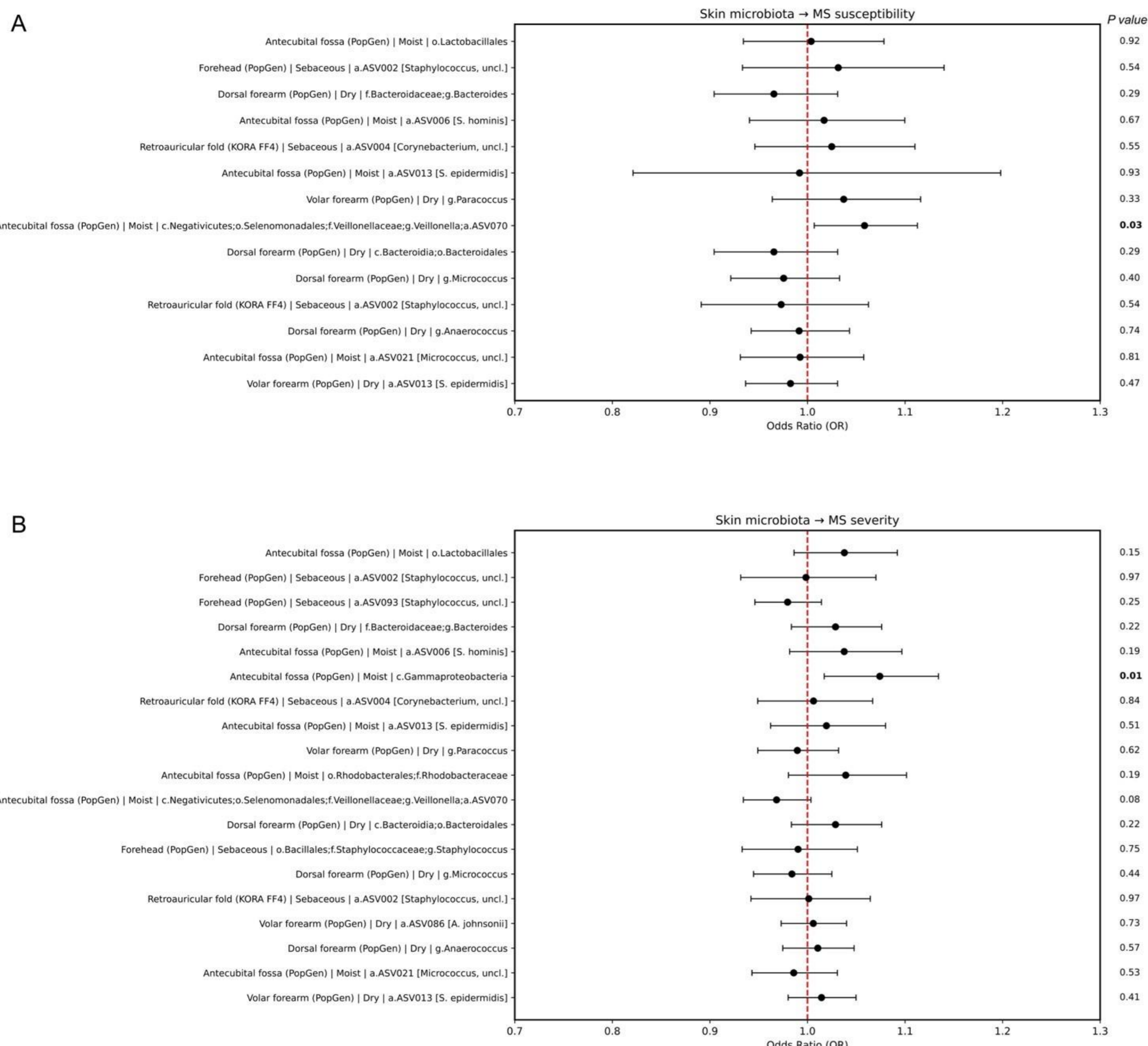
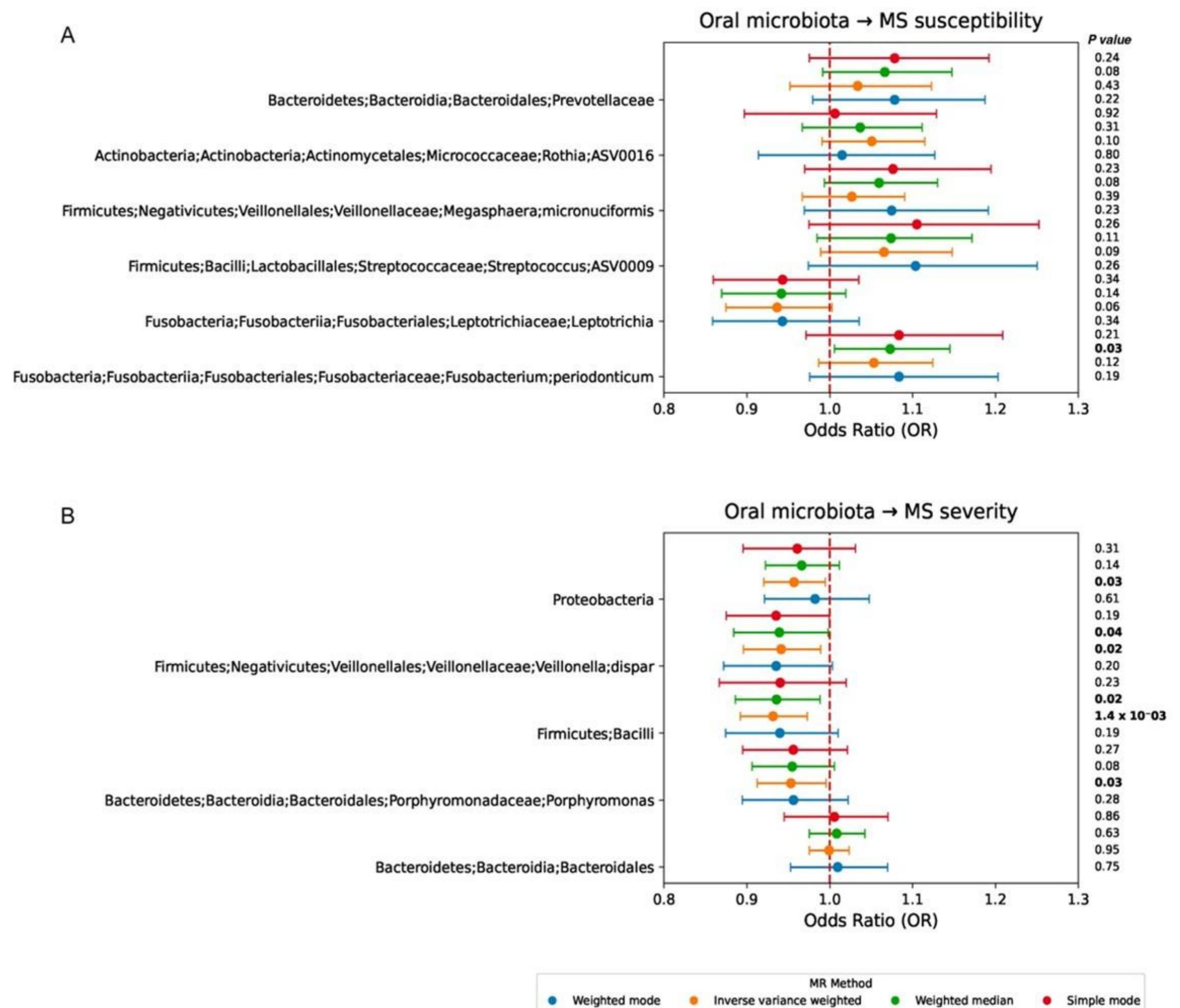
Recent research on the impact of gut microbiota on multiple sclerosis (MS) has been extensive; however, the role of microbial composition across several other key interfaces, such as the mouth and the skin, has received much less attention. In a first step towards addressing this gap, we used Mendelian Randomization (MR) analyses, using genetic variants as proxies for environmental exposures to estimate the causal relationship between a risk factor and an outcome.

## OBJECTIVES

Here we performed a two-sample MR analysis to assess the causal link between oral and skin microbiome composition and both MS risk and severity.

## METHODS

Exposure data were extracted from summary statistics of two large genome-wide association studies (GWAS) assessing the influence of host genetics on the microbiome composition of the oral cavity and skin. Outcome data derived from the largest GWAS on MS susceptibility and the recent GWAS on MS severity. After stringent instrumental variant selection, we applied inverse-variance-weighted (IVW) and Wald's ratio as primary MR methods, MR EGGER to control for horizontal pleiotropy, and checked directionality through Steiger's test.



## RESULTS

We found that the relative abundance of *Veillonella* genus in the skin may enhance MS risk, while no significant association between oral composition and MS susceptibility emerged. Furthermore, we found the *Gammaproteobacteria* class in the skin is associated with MS severity. We also identified suggestive, protective signals from different oral microbial strains (*Bacilli* class, *Porphyromonas* genus, *Proteobacteria* phylum, and *Veillonella dispar* species).

See Figure 1 (above) for results of MR analysis of oral microbiota strain abundance and MS susceptibility (A) and severity (B). See Figure 2 (left) for results of MR analysis of skin microbiota strain abundance and MS susceptibility (A) and severity (B).

## CONCLUSIONS

Our findings provide preliminary evidence supporting the hypothesis that skin microbiota might contribute to MS risk, and both oral and skin microbial composition could affect disease severity, reinforcing the relevance of dysbiosis in disease etiopathogenesis and broadening our insights beyond the gut. Exploring the influence of host-environmental interactions on susceptibility and disease course may inform the development of novel preventive and therapeutic strategies.

## Disclosures

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