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Modulating Psoriasis Microbiome: A Clinical Trial on Mare's Milk Impact

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Research Article

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Abstract

Background: Psoriasis is a chronic inflammatory disease with a complex and multifactorial origin. Previous studies have shown that the gut microbiome can influence immune responses and may play a role in disease development. This study aimed to explore the effect of mare's milk as a dietary prebiotic in patients with psoriasis.

Results: We conducted a non-randomised controlled trial including 50 adults. The intervention group received a daily dose of 60 mg freeze-dried mare's milk for 12 weeks. Stool samples were collected at baseline and at weeks 6 and 12 to evaluate microbiome changes. At baseline, microbial patterns were consistent with the dysbiosis typically described in psoriasis. After mare's milk intake, some of these alterations appeared to improve, with the most notable shift being an increase in Actinobacteriota abundance. Patients in the intervention group also showed reduced psoriasis severity.

Conclusions: Mare's milk supplementation may help support a healthier gut microbiome and could offer therapeutic benefits in psoriasis.

Introduction

Psoriasis is a chronic immune-mediated condition resulting in increased growth of skin cells with red and scaly patches on the skin. It is an immune-mediated disorder, representing one of the most common autoinflammatory diseases. It is a non-contagious disorder that affects up to 8.5% of humans worldwide (2). It impairs quality of life and is related to many comorbidities, often accompanying other autoimmune conditions and cardiovascular diseases. A cohort study found that patients with psoriasis could have a 6-year shorter lifespan than healthy individuals (3). We still do not understand the pathogenesis of the disease. Still, we know that it is related to abnormal crosstalk between the innate and adaptive immune systems, involving many different cytokines and inflammatory signals (4). Autoimmune disorders tend to be chronic because of their dysregulation of the immune system, influenced by many factors that we still do not understand and are not able to control. Chronic diseases typically follow stable periods punctuated with acute episodes, known as flares. Those flares can be triggered by various factors such as stress, infections, or changes in medication. Evidence suggests that *Streptococcus pyogenes* infection may be related to guttate psoriasis, whereas *Staphylococcus aureus, Malassezia* and *Candida albicans* may be linked to psoriasis flares (5). We know that diet plays a fundamental role in the pathogenesis of psoriasis (6). Numerous studies have established an association between gut dysbiosis and various inflammatory disorders (7). It is plausible that dysbiosis contributes to disease pathogenesis, as alterations in bacterial populations may disrupt the integrity of the epithelial barrier, promoting bacterial translocation and initiating an inflammatory response. Moreover, the gut and skin are intricately connected, exerting bidirectional influences on each other, a concept known as the "gut-skin axis" (8), which forms the foundation of our investigation.

In the human gut microbiome, approximately 90% of bacterial species belong to the phyla Bacteroidota (formerly Bacteroidetes) and Bacillota (formerly Firmicutes) (9). These dominant phyla engage in anaerobic fermentation, producing short-chain fatty acids (SCFAs), which are key anti-inflammatory molecules that modulate the gut immune system, particularly through the regulation of T cells (10). In addition to Bacteroidota and Bacillota, the gut microbiome comprises several other important bacterial phyla, including Actinobacteriota (formerly Actinobacteria), Fusobacteria, Verrucomicrobia, and Proteobacteria, alongside diverse communities of fungi, viruses, protozoa, and archaea (11). Despite extensive research, significant variability persists, and a precise definition of a healthy microbiome is yet unclear. Parameters such as the Bacillota/Bacteroidota ratio and the Psoriasis Microbiome Index have been investigated in attempts to differentiate between psoriatic and healthy individuals. However, the most notable findings related to gut physiology appear to be associated with dysbiosis, a reduction in short-chain fatty acids, elevated levels of Trimethylamine N-oxide (TMAO), and imbalances in lymphocyte populations (10). We consider that dysregulation of the microbiome is closely linked to disruptions in overall health, whether as a cause or consequence. Uncovering these microbiome changes will enhance our understanding of disease pathomechanisms in psoriasis, paving the way for novel therapeutic and preventive approaches. Diet plays a pivotal role in shaping the bacterial populations we harbour (13); thus, modifying dietary habits offers a means to influence the microbiome and, in turn, impact health outcomes. One of the most well-known and effective ways to alter our microbiomes is through the ingestion of prebiotics.

Mare's milk consumption began thousands of years ago with nomads in Central Asia and Europe. In contrast, cow's milk consumption emerged later but became widely popular, likely due to its easier production and marketing. However, concerns about its association with digestive disorders and allergies have always accompanied cow milk consumption. These intolerances, along with the recognition of the antimicrobial properties of mare's milk as a prebiotic, have contributed to its resurgence in importance (12).

Hypotheses and Objectives

Researchers from Kazakhstan conducted the clinical trial. The objective was to investigate the changes in the microbiome following the daily intake of 60 mg of freeze-dried mare's milk and to observe whether a clinical improvement followed those changes. In this study, the gut microbiome of patients with psoriasis is analysed and compared to that of healthy individuals to try to understand the potential dysbiosis of the disease. The effects of mare's milk on dysbiosis are also explored. It is believed that mare's milk positively influences the gut microbiome, offering a potential new treatment with fewer side effects in comparison to conventional therapies. Computational analyses are applied to identify patterns and changes, and representation methods are used to interpret complex data.

Materials and Methods

A non-blinded clinical trial was conducted during 2019–2021. The study was run following the Helsinki Declaration, and the protocol received approval from the Ethics Committee of the Medical University of

Astana, Kazakhstan. All patients gave their written informed consent before their inclusion in the study. Patients attending the dermatological outpatient clinic were asked to participate if they met the following criteria: age between 18 and 80 years, diagnosis of psoriasis with mild to moderate clinical manifestation (PASI ≤ 30) and use of standard treatment without systemic drug use, to avoid interference from systemic treatment with the microbiome. Standard treatment was desensitising agents, antihistamines, topical agents, and physiotherapy. The diagnosis was made by a dermatologist based on the medical history, clinical presentation, laboratory results and PASI index. The PASI index is a tool used to measure the severity and extent of psoriasis by assessing the clinical symptoms. It combines the severity (erythema, induration, and desquamation) and the extension of the affected area. Data collection was conducted simultaneously for the cases (patients with psoriasis meeting inclusion criteria) and controls (matched by age and gender). The study included 50 adult patients aged 23 to 80 years, 20 psoriasis cases and 30 controls (20 healthy, 10 with psoriasis). These 20 cases were selected from a total of 60 potential patients (Fig. 1).

The clinical trial consists of 20 cases (1 case lost) and 30 controls (1 control lost, 10 psoriasis patients and 19 healthy controls). Controls undergo stool collection once. Psoriasis cases receive 60 mg daily of mare's milk and are monitored at three distinct time points: Week 1, Week 6, and Week 12. All collected samples are stored and sent together for 16S rRNA gene sequencing.

All psoriasis cases received freeze-dried mare's milk at 60 mg/day for 12 weeks, on top of standard therapy. Criteria for withdrawal were adverse effects observed during the study by the investigators. Due to relocation and withdrawal from the study by some participants, the number of subjects in both cases and the healthy control group decreased by one. During the controlled clinical trial, no side effects were observed in patients taking lyophilised mare's milk. Eighty microbiome samples were obtained for analysis. This included 19 samples from healthy controls. Additionally, there were 10 samples from psoriasis controls and 51 samples from cases. Among those samples, one was degraded, and five had a low concentration and were discharged.

The primary clinical outcome was the PASI score. It helped to monitor clinical improvement after the consumption of mare's milk. It was measured at Week 1, at Week 6 and at Week 12. Body mass index (BMI) measurements were also taken.

The exclusion criteria were the use of antibiotics three months before the study, psoriatic arthritis, any other chronic skin, gastrointestinal, or comorbid condition and pregnancy. Patients were monitored for three months after the study. Clinical assessment of the skin condition was performed using the PASI (Psoriasis Area and Severity Index). We followed the STORMS guideline (Standardised Reporting of Microbiome Studies) checklist, a guideline designed to improve the reporting of microbiome research. This checklist ensures that studies are reported with sufficient detail and transparency, enhancing reproducibility and the validity of results (22).

Microbiome analysis

Stool samples were collected using a Polycool transport package and stored at − 80°C until sequencing. DNA was extracted with the ZymoBIOMICS DNA Miniprep Kit (Zymo Research, D4300), using sterile water as a negative control. The V3–V4 regions of the 16S rRNA gene were amplified with primers 341F (CCTAYGGGRBGCASCAG) and 806R (GGACTACNNGGGTATCTAAT). Libraries were prepared according to Illumina protocols and sequenced on a NovaSeq 6000 platform (2 × 250 bp) by Novogene (Hong Kong, China).

Taxonomic annotation of 16S rRNA gene sequences was carried out with LotuS2 (23) using the SILVA v138.2 database as reference. Two samples with very low read counts were excluded, and the remaining dataset was rarefied to 95% of the lowest sequencing depth using the RTK package in R.

Alpha diversity was quantified with the Shannon index (vegan, ade4) and compared between groups using the Wilcoxon rank sum test (stats). Longitudinal changes were tested with linear mixed-effects models (lme4) and Type III ANOVA (lmtest).

Beta diversity was assessed using Bray–Curtis dissimilarities (vegan), visualised by principal coordinates analysis (vegan, cluster), and tested for group differences with PERMANOVA (adonis, vegan). Associations between community structure and PASI scores were examined by dbRDA (vegan) and linear mixed models (lme4).

Differential abundance was tested at phylum to species levels using the Wilcoxon test (stats), with effect sizes quantified by Cliff's delta (effsize, companion). P-values were adjusted for multiple comparisons with the FDR method (stats).

Plots and data visualisation were generated in R using ggplot2, ggpubr, patchwork, and kableExtra: additional data handling and summaries employed dplyr, reshape2, and tidyverse.

Results

Study Population, Sample Collection, and PASI Score Analysis

The body mass index (BMI) of psoriasis patients was compared to that of healthy controls, and no significant difference was identified using the Wilcoxon test ($p = 0.94$). Changes in disease severity over time were evaluated using a linear mixed-effects model with random intercepts for the donor to account for repeated measures. The analysis revealed a significant overall effect of time on PASI scores (Type III ANOVA: $F(2, 22) = 8.58$, $p = 0.0018$). Estimated marginal means (± 95% CI) showed a decline in PASI from Week 1 (13.1, 9.6–16.6) to Week 6 (11.6, 8.0–15.1) and further to Week 12 (7.0, 3.4–10.5). Pairwise comparisons indicated no significant change between Week 1 and Week 6 ($p = 0.61$), but significant reductions between Week 1 and Week 12 ($\Delta = -6.1$, $p = 0.002$) and between Week 6 and Week 12 ($\Delta = -4.6$, $p = 0.023$). Together, these results demonstrate that clinical severity remained stable between Weeks 1 and 6, but decreased significantly by Week 12 (Fig. 2).

Each violin plot shows the distribution of PASI values, with boxplots indicating the interquartile range and the median. Individual patient trajectories are shown as grey lines. Group medians are marked with white diamonds. A dashed horizontal line represents the overall median across all time points. PASI values were slightly lower at Week 6 compared with Week 1, and a further decrease was observed at Week 12.

A potential dropout bias was analysed by comparing the PASI scores of patients who dropped out of the study with those who remained. The Wilcoxon test did not identify significant differences between the groups (Week 1: $p = 0.41$, Week 6: $p = 0.21$, Week 12: $p = 0.49$). Consequently, we did not consider evidence of a significant bias attributable to dropout in our study.

Alpha and Beta Diversity Changes Following Mare's Milk Intervention

The alpha diversity was assessed using the Shannon index, as it provides a more comprehensive measure of diversity by incorporating evenness. This metric is also sensitive to rare species, widely recognised in the field, and allows for comparisons across studies without being influenced by sample size. The Shannon index was compared between healthy controls and psoriasis cases at Week 1 (baseline). A Wilcoxon rank sum test indicated no significant difference between the two groups ($W = 63$, $p = 0.85$). We evaluated changes in alpha-diversity over time using a linear mixed-effects model with subject as a random factor. A Type III ANOVA with Satterthwaite's approximation indicated a trend toward temporal variation in Shannon diversity, but the effect did not reach statistical significance ($F(2, 25.9) = 2.60$, $p = 0.094$). Post hoc contrasts showed a modest increase in diversity from Week 1 to Week 6 (estimate = − 0.37, SE = 0.17, $t = -2.25$, $p = 0.083$), which did not meet the threshold for significance. Comparisons between Week 1 and Week 12 (estimate = − 0.25, SE = 0.19, $p = 0.41$) and between Week 6 and Week 12 (estimate = 0.13, SE = 0.19, $p = 0.78$) were likewise not significant. Taken together, these analyses suggest a possible upward trend in alpha-diversity between Week 1 and Week 6, which then stabilised by Week 12, although none of the observed changes reached statistical significance (Fig. 3).

Distribution of Shannon alpha-diversity at Weeks 1, 6, and 12 in psoriasis-positive participants. Each violin plot represents the density of observed values at a given time point, with a boxplot embedded to show the interquartile range and median. Individual samples are shown as black dots, and white diamonds indicate group medians. The dashed horizontal line marks the overall median across all samples. The plots illustrate that diversity was slightly lower at Week 1 and tended to increase by Week 6, with values remaining similar at Week 12. However, statistical testing with a linear mixed-effects model and ANOVA did not identify significant differences between time points.

We assessed differences in microbial community composition using Bray–Curtis dissimilarities. In the subset analysis, PERMANOVA indicated a significant effect of timepoint ($R^2 = 0.063$, $p = 0.022$, 999 permutations), explaining approximately 6% of the variation in genus-level profiles. To examine whether clinical improvement was linked to microbiome changes, we tested associations between PASI and community composition. Distance-based redundancy analysis (dbRDA) with PASI as a continuous covariate did not show a significant effect. Linear mixed models assessing whether pairwise differences in PASI were related to Bray–Curtis dissimilarities were also not significant (p = 0.20). PCoA plots illustrated partial clustering by time point, but with substantial overlap between groups (Fig. 4). These findings indicate that changes in overall microbial composition did not strongly explain the reduction in PASI scores between Week 1 and Week 12.

Principal coordinates analysis (PCoA) of Bray–Curtis dissimilarities at the genus level. Each point represents a sample, colored by study group and time point. The first two coordinates explain 23.4% and 16.2% of the variance, respectively. Ellipses indicate the 95% confidence intervals for each group. While control groups (Psoriasis – and Psoriasis + at Week 1 (baseline) largely overlap, psoriasis samples show a temporal trend with partial separation between Week 1, Week 6, and Week 12.

Longitudinal Changes of Bacterial Composition Following Mare's Milk Intervention

The microbial community profiles at the phylum level were dominated by Bacillota (formerly Firmicutes) and Bacteroidota across all groups and timepoints. In psoriasis patients at Week 1 (baseline), relative abundances were similar to controls, with Bacillota and Bacteroidota together accounting for more than half of the community. Over the course of treatment, compositional shifts were observed. By Week 12, the proportion of Bacteroidota increased, while Bacillota showed a relative decrease. Minor phyla, including Actinobacteriota, Verrucomicrobiota, and Cyanobacteria, contributed variably but remained below 10% in all groups. Unclassified sequences and taxa labelled as “Unknown” accounted for a small fraction of reads. Overall, psoriasis samples displayed greater variability in low-abundance phyla across timepoints compared with controls, which remained more stable (Fig. 5).

Relative abundance of bacterial phyla across groups and timepoints. Bars represent the mean proportional composition of major phyla in samples from psoriasis patients at Week 1 (baseline), Week 6, and Week 12, compared with healthy controls. Taxa with uncertain classification are shown as Unclassified reads or Unknown.

To explore changes in bacterial composition, Cliff’s Delta non-parametric measure was applied, which ranges from − 1 to 1 to provide information about the magnitude and direction of the difference between Week 1 (baseline) and treatment. Results with a Q-value < 0.1 were filtered to reduce the likelihood of false positive results. Longitudinal analysis of microbial composition revealed significant alterations in several taxonomic groups following the intervention. These changes were most evident at broader taxonomic ranks (Fig. 6).

This cuneiform plot illustrates longitudinal changes in the relative abundance of gut bacterial phyla across three timepoint comparisons: Week 1 vs. Week 6, Week 1 vs. Week 12, and Week 6 vs. Week 12. Each triangle represents a phylum-level taxon. Phyla shown include Actinobacteriota, Bacteroidota, Bacillota (Firmicutes), and Proteobacteria. The intervention is associated with significant enrichment of

Actinobacteriota and Proteobacteria early in the study, and consistent reduction in Bacillota across all timepoints.

At the phylum level, a marked increase in the relative abundance of Actinobacteriota was observed at both Week 6 and Week 12, indicating a sustained enrichment throughout the intervention (Effect Size ≈ + 0.78, $q < 1 \times 10^{-6}$). In contrast, Bacillota showed a consistent decline across all timepoints (Effect Size ≈ − 0.77, $q \approx 1.4 \times 10^{-6}$), suggesting a progressive reduction in taxa associated with fibre fermentation. Bacteroidota displayed a biphasic pattern: a significant decrease from Week 1 to Week 6 ($q \approx 1.2 \times 10^{-8}$), followed by a partial rebound by Week 12 ($q \approx 0.003$). Additionally, Proteobacteria were enriched early in the study, particularly between Week 1 and Week 6 ($q \approx 3.9 \times 10^{-5}$).

The most substantial effects were observed at the class level. Actinobacteria exhibited firm shifts over time, with effect sizes up to ± 1.0 and highly significant q-values. Within this class, Coriobacteriia increased notably by Week 12 ($q < 1 \times 10^{-13}$), consistent with the recovery of taxa linked to mucosal health and immune modulation. Among the orders, only Coriobacteriales showed statistically significant changes, with an increase detected at Week 12 ($q \approx 0.01$–0.02). This finding aligns with the broader enrichment seen in higher-level Actinobacteriota taxa.

At more specific levels—family, genus, and species—no taxa reached statistical significance after adjustment for multiple comparisons. However, several groups (notably within the Coriobacterium genus) exhibited large effect sizes, suggesting potential biological relevance. The lack of statistical significance at these levels may reflect high inter-individual variability in microbial composition.

Study limitations

This is a small, mono-centre study with adult patients, which does not explore the paediatric population, a limitation common to clinical trials and psoriasis studies specifically. Another limitation of our study is that we did not adjust microbiome analyses for age. Age is a recognised covariate that can influence gut microbiome composition. However, our sample size, particularly within subgroups and across longitudinal time points, was too small to allow reliable adjustment without risking model overfitting and loss of statistical power. Besides, it is not a double-blind study, which makes it more susceptible to bias. We collected control samples only once because our primary focus was on changes over time within the supplemented group. The control group served to describe the baseline range of values in a comparable population rather than to track longitudinal trends. Repeated follow-up of controls was not pursued in order to limit participant burden and study costs, and because no intervention was given that might reasonably alter their values across time. A placebo was not provided to the control group. The intention was to compare the biological course under supplementation with the natural course without intervention. Moreover, the supplement had a distinct taste and appearance, which would have made blinding difficult, and developing a matched placebo was beyond the resources of this study. We acknowledge that these choices restrict interpretability. Without repeated control measurements, natural temporal variation or regression to the mean cannot be entirely ruled out. Likewise, in the absence of a placebo, expectancy or behavioural changes cannot be wholly excluded as contributing factors. For these reasons, our findings should be interpreted as preliminary and confirmatory trials with repeated control sampling and placebo arms will be the critical next steps.

It is also the first clinical trial on the effect of mare's milk on psoriasis, and therefore, there are no other studies to compare with. In this study, we use the Psoriasis Area and Severity Index (PASI), which is widely utilised. However, we did not include the Dermatology Life Quality Index (DLQI), which is used in many other studies and would provide more extrapolatable data. The gut microbiome refers to all the microorganisms living in our intestines, but most studies focus only on bacteria. This supposes a limitation in understanding those ecosystems. Still, it may be related to the fact that studying bacteria is relatively more straightforward because of developed techniques like 16S rRNA gene sequencing, which may not be available for viruses. In the analysis, the number of reads in the psoriasis controls was significantly lower than in the psoriasis intervention group. This might have been due to batch contamination or different laboratory treatments, even if all the samples of the study were frozen and sent to the laboratory at the same time point. Since the laboratory analysis was conducted in 2021, before the pandemic, this limitation could not be further researched. Nonetheless, we decided to include this group in the analysis to avoid selection bias. With the aid of visualisation, we can mitigate the risk of drawing false conclusions.

Discussion

To date, several publications and clinical trials have investigated the effects of prebiotics on psoriasis. One clinical trial examined changes in the microbiome of patients with atopic dermatitis after mare's milk administration (14), and a pilot study suggested beneficial effects of mare's milk consumption on microbiome recovery after antibiotic treatment (24). No clinical trials have yet examined mare's milk in psoriasis, making this the first to address the subject. Dysbiosis has been reported in the skin and gut of psoriasis patients (15). A systematic review summarised findings from ten studies on the gut microbiome in psoriasis (16). Eight of these assessed alpha diversity and found no significant differences; similarly, in our study no significant differences were observed, although we noted a trend toward increased diversity between Week 1 and Week 6 that stabilised by Week 12. All included studies reported significant differences in beta diversity between psoriasis patients and healthy individuals, which was also observed in our data. We further identified a correction of these differences after prebiotic intake, suggesting that dysbiosis may be reversible. At least two studies have reported a lower relative abundance of Bacteroidota and a higher abundance of Bacillota in psoriasis patients, consistent with our findings (7, 16). These observations have led to the proposal of a “psoriasis-core microbiome” (17). Bacteroidota play an important immunomodulatory role in the gut through the regulation of T cells (18), and their reduction may alter immune responses to the gut microbiota and aggravate dysbiosis.

In our data, Actinobacteriota showed a marked and sustained increase by Weeks 6 and 12, driven in part by enrichment of Coriobacteriia and Coriobacteriales. This suggests a recovery of taxa linked to mucosal health and immune regulation. Bacillota declined consistently across all timepoints, particularly fibrefermenting groups, which may reflect changes in metabolic activity induced by the intervention. Bacteroidota followed a biphasic pattern, decreasing between Weeks 1 and 6 and partially rebounding at Week 12, consistent with previous studies. Proteobacteria were transiently enriched during the early phase of the intervention. At lower taxonomic levels, no differences remained statistically significant after correction for multiple testing, though several taxa, including Coriobacterium and Eggerthellaceae, showed large effect sizes suggestive of biological relevance. These findings provide further evidence that prebiotic intake can partially restore microbial imbalances characteristic of psoriasis-associated dysbiosis (17, 19).

The improvement in PASI scores between Weeks 6 and 12 coincided with the restoration of Actinobacteriota populations. Mare's milk may restore depleted Actinobacteriota through several bioactive mechanisms. Its oligosaccharide profile provides selective substrates for Coriobacteriaceae, which possess specialised utilisation pathways. The higher whey-to-casein ratio promotes the formation of bioactive peptides that support the growth of immunoregulatory bacteria (25). Restoration of Actinobacteriota may reduce systemic inflammation through mechanisms including increased production of short-chain fatty acids that promote regulatory T-cell development and enhancement of intestinal barrier function.

The intervention dose of 60 mg/day of freeze-dried mare's milk was chosen based on the compositional profile of the product batch used in this trial. Two analytical reports from an accredited laboratory (Supplementary Files 1 and 2) confirmed the presence of peptides, oligosaccharides, and enzymes with antimicrobial and immunomodulatory activity, providing a biochemical justification for the intervention dose. Mare's milk contains a distinctive set of bioactive compounds, including lysozyme with several hundred-fold higher activity than bovine milk, lactoferrin, specific oligosaccharides, and short-chain fatty acids (25). These compounds may target psoriatic pathogenesis through complementary mechanisms. Lysozyme acts through peptidoglycan hydrolysis and membrane disruption, particularly effective against antibiotic-resistant Mollicutes (26). Lactoferrin disrupts LPS outer membranes and blocks LPS-induced NF-κB activation by binding directly to LPS and inhibiting TLR4 signalling (27, 28). Mare's milk oligosaccharides selectively stimulate butyrate-producing Firmicutes (Faecalibacterium, Roseburia) and restore Coriobacteriales that metabolise bile acids into immunomodulatory secondary metabolites (29). Butyrate inhibits the NLRP3 inflammasome, activates GPR43/GPR109A receptors, and enhances Treg populations through HDAC inhibition and Foxp3 upregulation (30). Secondary bile acids activate FXR/TGR5 receptors, further suppressing IL-17A and promoting tolerance. These mechanisms may underlie the clinical improvements observed, supporting the concept of microbiome-targeted therapy that avoids the risks associated with immunosuppression.

Dysbiosis has also been reported in other skin diseases, including atopic dermatitis, hidradenitis suppurativa, dandruff, acne, rosacea, and lichen sclerosus (20). Beyond dermatology, altered microbial composition at the phylum level has been linked to inflammatory bowel disease, type 2 diabetes, psoriasis, Parkinson's disease, and reflux oesophagitis (21). Whether the features observed in our study represent part of a broader risk profile remains unclear. Identifying common microbial changes across conditions could support collaborative research and help uncover mechanisms and therapeutic targets. More work is needed to clarify how the microbiome interacts with the immune system, and how these interactions influence disease. Synthesising existing evidence will also be important as research questions in this field continue to grow in complexity.

In conclusion, psoriasis is associated with gut dysbiosis, consistent with previous findings in other inflammatory conditions. In this first clinical trial of mare's milk in psoriasis, we observed partial restoration of microbial balance, particularly involving Actinobacteriota, coinciding with clinical improvement. Mare's milk may represent a safe adjunctive therapy for psoriasis. Larger and longer studies are required to confirm efficacy, elucidate mechanisms, and assess long-term safety.

Declarations

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Disclosure statement

The authors report there are no competing interests to declare.

Data availability statement

- The 16S rRNA Gene Sequencing Data is available in the NCBI SRA repository. The data can be accessed using the following DOI or accession ID: https://www.ncbi.nlm.nih.gov/bioproject/PRJNA1312266
- The Clinical Trial Outcome Data is newly generated. These data are openly available in Figshare at DOI: 10.6084/m9.figshare.29149838.
- The Mare's Milk Composition Data can be found in Supplementary Files 1 and 2.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. The protocol was reviewed and approved by the Ethics Committee of the Medical University of Astana, Kazakhstan. All participants provided written informed consent prior to enrollment. The trial was registered at ClinicalTrials.gov (Identifier: NCT03594877) on 25 June 2018. Available at: https://clinicaltrials.gov/study/NCT03594877. The manuscript adheres to the CONSORT guidelines and reports the date of trial registration.

Consent for publication

Not applicable. This manuscript does not contain any individual person's data in any form (including individual details, images, or videos).

Health and Safety

We confirm that all mandatory laboratory health and safety procedures have been followed during the experimental work reported in this paper.

CRedit

- Silvia González Colino: Conceptualisation, Formal analysis, Writing – original draft and Visualisation.
- Ulrike Löber: Data curation and Supervision
- Sofia Kirke Forslund-Startceva: Supervision
- Bakytgul Yermekbayeva: Conceptualisation and Methodology (designed the experiments)
- Samat Kozhakhmetov: Methodology and Investigation (designed the experiments, primary sample analysis)
- Togzhan Algazina: Investigation (recruiting, clinical and laboratory tests, human samples collection)
- Gulnaz Touir: Investigation (recruiting, clinical and laboratory tests, human samples collection)
- Gulnar Batpenova: Investigation (recruiting, clinical and laboratory tests, human samples collection)
- Almagul Kushugulova: Investigation and Funding Acquisition

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Figures

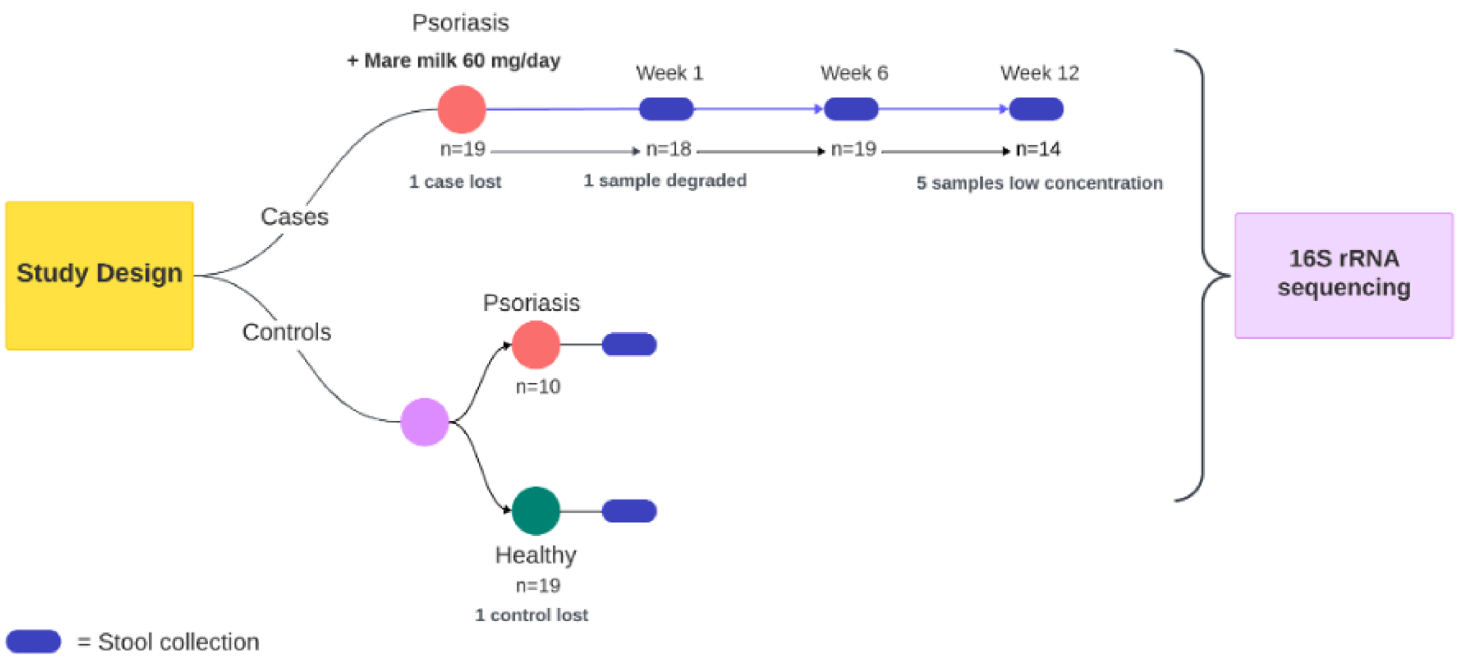

Figure 1

Study design scheme

The clinical trial consists of 20 cases (1 case lost) and 30 controls (1 control lost, 10 psoriasis patients and 19 healthy controls). Controls undergo stool collection once. Psoriasis cases receive 60 mg daily of mare's milk and are monitored at three distinct time points: Week 1, Week 6, and Week 12. All collected samples are stored and sent together for 16S rRNA gene sequencing.

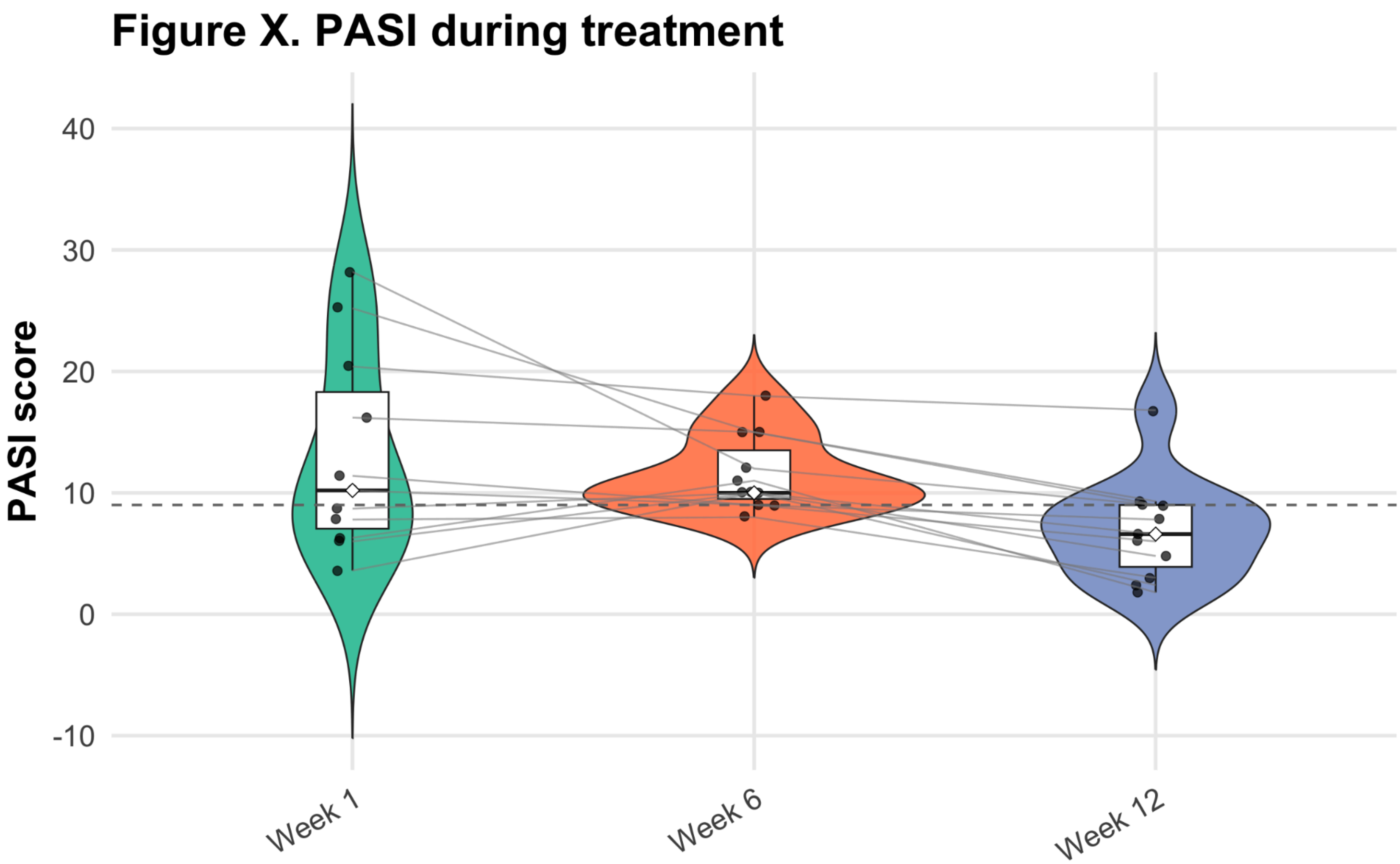

Figure 2

PASI evolution during the intervention

Each violin plot shows the distribution of PASI values, with boxplots indicating the interquartile range and the median. Individual patient trajectories are shown as grey lines. Group medians are marked with white diamonds. A dashed horizontal line represents the overall median across all time points. PASI values were slightly lower at Week 6 compared with Week 1, and a further decrease was observed at Week 12.

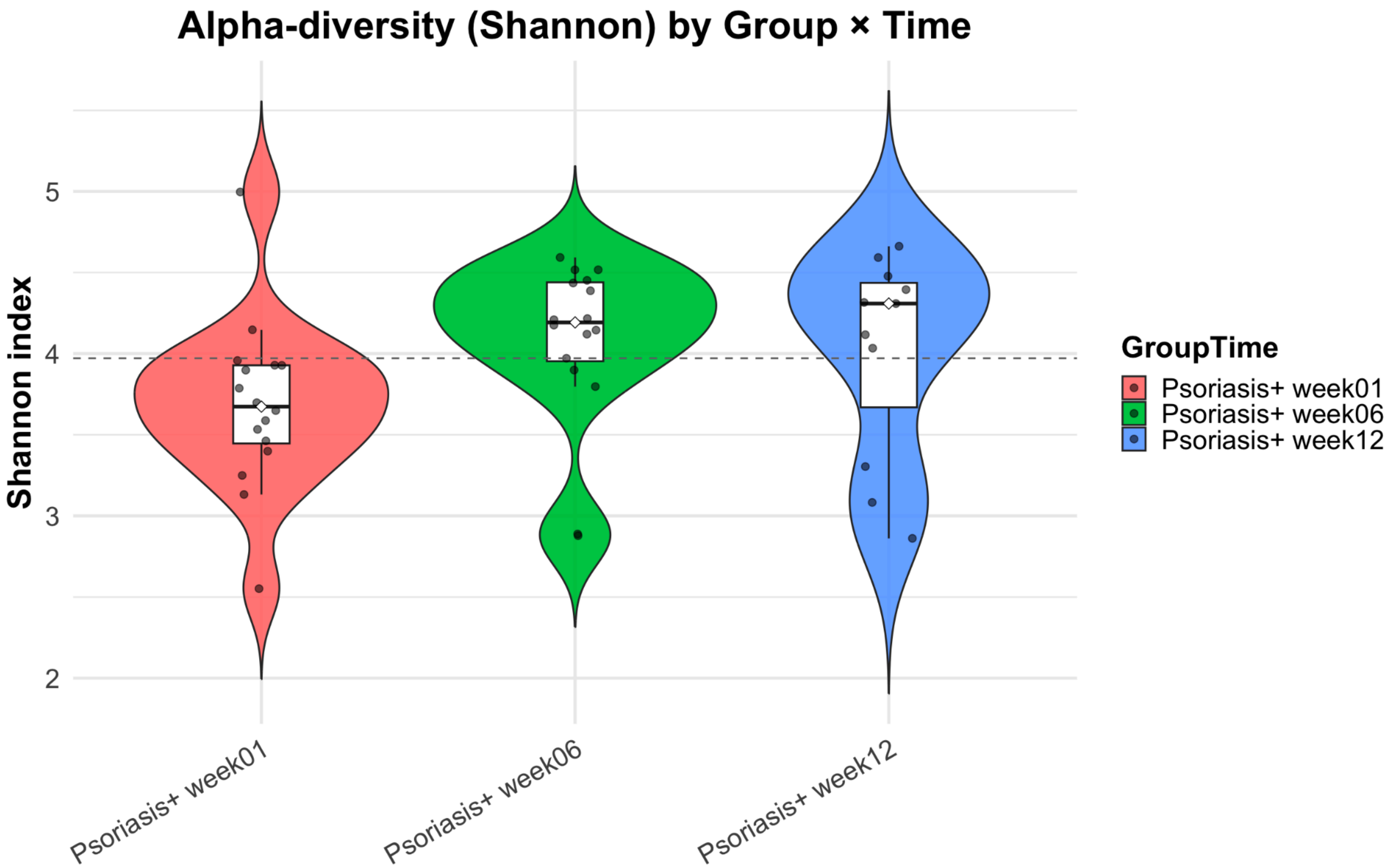

Figure 3

Evolution of Diversity (Shannon) during treatment

Distribution of Shannon alpha-diversity at Weeks 1, 6, and 12 in psoriasis-positive participants. Each violin plot represents the density of observed values at a given time point, with a boxplot embedded to show the interquartile range and median. Individual samples are shown as black dots, and white diamonds indicate group medians. The dashed horizontal line marks the overall median across all samples. The plots illustrate that diversity was slightly lower at Week 1 and tended to increase by Week 6, with values remaining similar at Week 12. However, statistical testing with a linear mixed-effects model and ANOVA did not identify significant differences between time points.

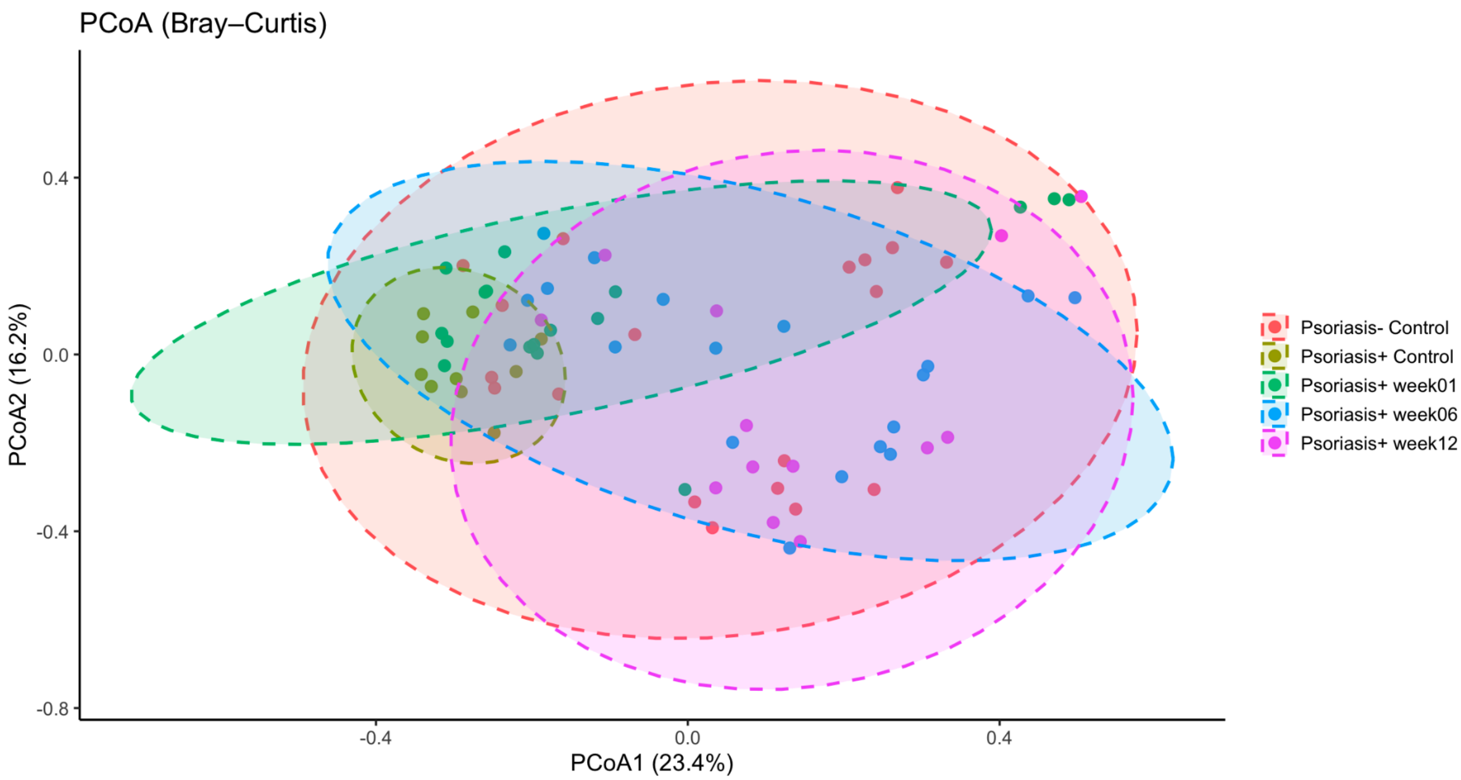

Figure 4

Principal Component Analysis of Beta Diversity (Bray–Curtis)

Principal coordinates analysis (PCoA) of Bray–Curtis dissimilarities at the genus level. Each point represents a sample, colored by study group and time point. The first two coordinates explain 23.4% and 16.2% of the variance, respectively. Ellipses indicate the 95% confidence intervals for each group. While control groups (Psoriasis– and Psoriasis+ at Week 1 (baseline) largely overlap, psoriasis samples show a temporal trend with partial separation between Week 1, Week 6, and Week 12.

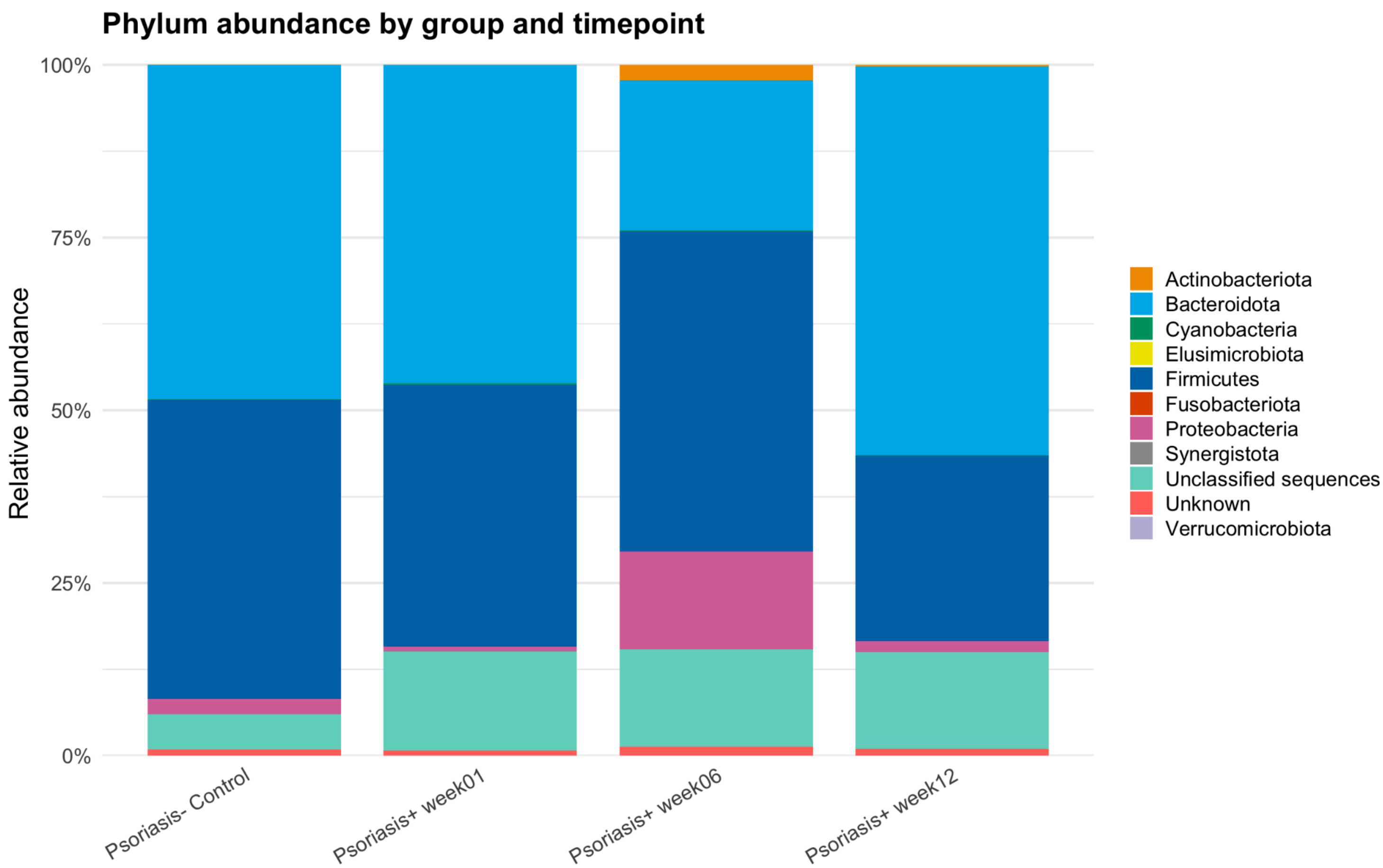

Figure 5

Phylum-level composition

Relative abundance of bacterial phyla across groups and timepoints. Bars represent the mean proportional composition of major phyla in samples from psoriasis patients at Week 1 (baseline), Week 6, and Week 12, compared with healthy controls. Taxa with uncertain classification are shown as Unclassified reads or Unknown.

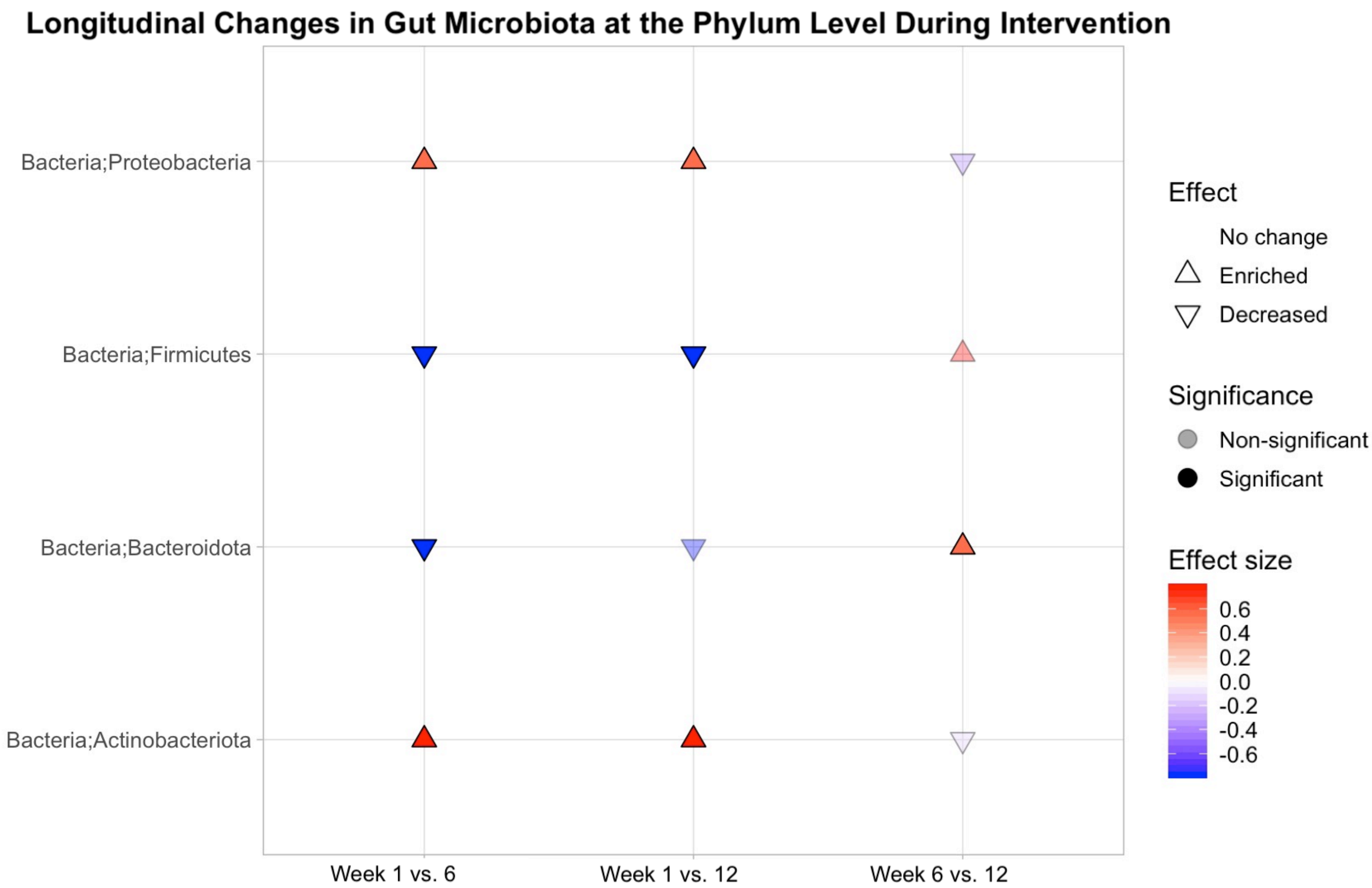

Figure 6

Longitudinal Changes in Gut Microbiota at the Phylum Level

This cuneiform plot illustrates longitudinal changes in the relative abundance of gut bacterial phyla across three timepoint comparisons: Week 1 vs. Week 6, Week 1 vs. Week 12, and Week 6 vs. Week 12. Each triangle represents a phylum-level taxon. Phyla shown include Actinobacteriota, Bacteroidota, Bacillota (Firmicutes), and Proteobacteria. The intervention is associated with significant enrichment of Actinobacteriota and Proteobacteria early in the study, and consistent reduction in Bacillota across all timepoints.