FOLIA MEDICA CRACOVIENSIA
Vol. LXVI, 1, 2026: 133–144
PL ISSN 0015-5616 eISSN 2957-0557
DOI: 10.24425/ fmc.2026.158992

Positive effects of probiotics in people living with HIV: a narrative review

Wiktoria Sobocińska[1,2], Gabriela Kubicka[2], Łukasz Kołodyński[2]

[1] Student Scientific Group of Pathophysiology, Jagiellonian University Medical College, Kraków, Poland
[2] Jagiellonian University Medical College, Kraków, Poland

Corresponding author: Wiktoria Sobocińska
Student Scientific Group of Pathophysiology, Jagiellonian University Medical College
ul. Brzegi 163, 32-040 Wrząsowice, Poland
Phone: +48 661 565 767; E-mail: wiktoria.sobocinska@student.uj.edu.pl

Abstract: Despite effective antiretroviral therapy (ART), no clear guidelines exist on microbiome-targeted adjuncts for people living with HIV (PLWH). Human immunodeficiency virus (HIV-1) infection damages the gastrointestinal tract by altering the mucosal surface and prompting dysbiosis. Gut microbial imbalance, characterized by the predominance of opportunistic bacteria, leads to increased microbial translocation, which, in turn, results in chronic inflammation, digestive tract symptoms, and reduced quality of life. PLWH have substantial dysbiosis compared to healthy controls. In addition, gastrointestinal complications occur as a side effect of ART treatment. Gut-associated lymphoid tissue (GALT) harbors the majority of $CD4^+$ lymphocytes, and this population is significantly depleted during HIV-1 infection. Antiretroviral therapy does not facilitate $CD4^+$ lymphocyte restoration in GALT tissue. Even if the general $CD4^+$ lymphocyte count increases, the GALT $CD4^+$ count, despite therapy, remains stable and low due to unknown causes. Research assessing probiotics in PLWH on ART has yielded mixed results. Some studies report that probiotics may increase $CD4^+$ T cell counts, improve gut barrier integrity, and reduce the incidence of diarrhea in HIV-positive patients. These benefits may be linked to specific probiotic strains that possibly enhance immune function by promoting regulatory T cell populations, thus decreasing microbial translocation. On the other hand, multiple studies did not show any consistent or significant benefits from probiotic supplementation for PLWH. This article assesses critical clinical trials and systematic reviews on this topic, based on limited existing research data. More data from large clinical trials on this topic is needed to assess whether this is or is not a justified new clinical approach for HIV-1-positive patients.

Keywords: probiotics, HIV infection, CD4, gut barrier, PLWH (People Living with HIV).

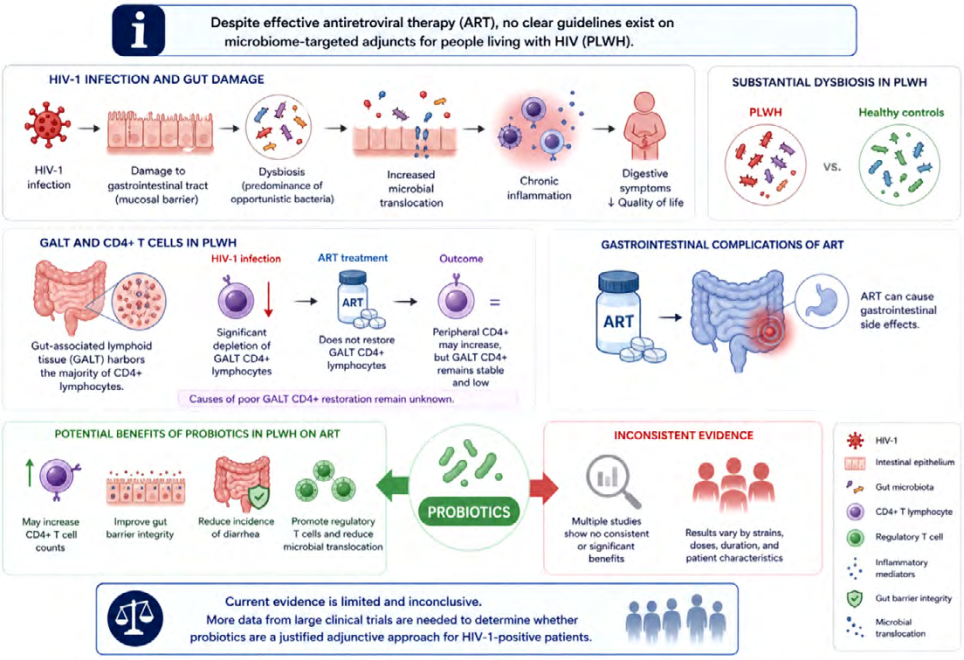
Submitted: 03-Oct-2025; **Accepted in the final form:** 30-Nov-2025; **Published:** 31-Mar-2026.

Introduction

According to the World Health Organization, there are 40 million People Living with HIV (PLWH). In Poland, up to the end of 2024, thirty-five thousand patients have been diagnosed as HIV positive. Gut-associated lymphoid tissues (GALT) contain multifollicular Peyer's patches of the ileum, the vermiform appendix, and the isolated lymphoid follicles (ILF). [1] $CD4^+$ cells,

including different types of T-helper cells, [2] are the population pivotal for adaptive immune response [3] and make up a significant percentage of GALT lymphocytes.

Human Immunodeficiency Virus (HIV) is associated with systemic immunological changes, resulting in a decrease in $CD4^+$ lymphocyte count and enteropathy. [4] The gut is an HIV reservoir and is a major virus replication site. [5] Infection leads to inflammatory and immuno-metabolic consequences in the gastrointestinal tract. [6] Weakened gastrointestinal mucosal surface and bacterial translocation play a part in HIV induced immunological activation. [7] The GALT $CD4^+$ cell population is significantly depleted in the HIV-1 positive population. Due to poorly understood reasons, $CD4^+$ GALT compartment reconstruction remains incomplete despite the use of combined antiretroviral therapy (cART). [8, 9] Analysis of gut microbiota in PLWH from multiple studies revealed substantial dysbiosis. [10] Highly active antiretroviral therapy (HAART) has been a major advancement in the treatment of HIV-1 infection; however, knowledge is scarce concerning complementary interventions that restore intestinal structural and functional integrity. Noninfectious diarrhea occurs in 25% of patients on HAART, [11] making it a current and important issue. Individual probiotics, co-infections, and patient age may contribute to the response to treatment and the quality of life of PLWH. Herein, we would like to present data from worldwide scientific research with various endpoints, including gut barrier integrity, $CD4^+$ count, stool consistency, and the effect on diarrhea occurrence. Specific probiotics are not recommended for people with HIV in current guidelines; [12] more data from large clinical trials are needed, and specific strains should be recommended. Zhen Wu *et al.* state that there is a justified recommendation for researchers to explore the potential of probiotics as an adjunctive treatment for HIV. [13]



Graphical abstract. Illustration was made with ChatGPT.

Current status of knowledge: There is not a single HIV guideline that currently recommends routine prebiotic supplementation as part of the standard HIV positive adult and pediatric patient care protocols. The guidelines are primarily focused on early and sustained ART, prevention (PrEP/PEP), and reduction of comorbidity. Probiotic therapies are considered investigational, and more evidence is needed from large clinical trials. Besides general good tolerance and safety of probiotics, practitioners must exercise caution in severely immunocompromised patient groups, as theoretical risks of bloodstream infection have been reported in case reports, clinical trials, and experimental models. [14, 15]

Materials and Methods

A comprehensive narrative review was conducted to analyze evidence from the existing literature on general outcomes of people living with HIV (PLWH) and probiotic therapy, utilizing a PubMed search (probiotics AND HIV). Prospective and experimental studies involving human participants were prioritized for inclusion. The search for reputable publications focused on general probiotic therapy outcomes in PLWH, with various restrictions such as age, ethnicity, clinical status, or other characteristics. Clinical trials were considered essential for evaluating the effects of probiotics. Clinical trial databases were searched; however, many trials were discontinued. The objective is to compare medical studies examining the impact of probiotic use on antiretroviral therapy (ART) and CD4 lymphocyte counts. This review evaluates whether probiotic supplementation benefits HIV-1-positive patients and clarifies the current evidence.

The effect of probiotics supplementation on the gastrointestinal tract of PLWH, immunology, and gut permeability

Research on probiotics demonstrated a reduction in inflammation in antiretroviral-treated individuals. Supplementing combined Antiretroviral Therapy (cART) with probiotics may improve gastrointestinal tract immunity, [16] enhance gut barrier function, and even improve immunity in HIV-infected subjects. [17] Gabriella d'Ettorre *et al.* [18] found benefits from probiotic administration in PLWH on the gut barrier at both gut and immune system levels. Ten patients on ART, aged 18 years or older, with $CD4^+$ T-cell counts above 400 cells/mm^3 and low viral count were included. These patients received probiotics twice daily for 6 months. These probiotics contained: *Lactobacillus plantarum DSM24730, Streptococcus thermophilus DSM24731, Bifidobacterium breve DSM24732, L. paracasei DSM24733, L. delbrueckii subsp. bulgaricus DSM24734, L. acidophilus DSM24735, B. longum DSM24736, B. infantis DSM24737*. The team assessed immune cell activity and T-cell immunophenotype. Following probiotic administration, there was reduced immune activity as indicated by fewer activated T-cells and a higher proportion of Th17 cells in both blood and gut tissues. Tc1 and Tc17 cell levels were not significantly affected, while Th1 cell levels increased in the gut tissue. Stool samples were collected after two and six months. Histopathological assessment of colon samples linked probiotic administration to a healthier gut lining, characterized by fewer immune cells in the lining, a more robust cell structure, and reduced cell death. HIV infection increases gut permeability in PLWH. Schunter *et al.* [19] examined the effect of synbiotics on gut permeability in PLWH in a randomized, placebo-controlled trial with 38 HIV infected women on ART. These patients received a synbiotic product with fibers or fibers alone (placebo). Probiotics were detected in the stool, indicating

bacterial colonization and proliferation. However, there were no changes in inflammation, bacterial invasion into the bloodstream, or immune system activity. Rodney K. Rousseau *et al.* [20] also achieved similar results in their randomized, double-blind, placebo-controlled study using the De Simone Formulation Probiotic (DSFP; Visbiome, with eight bacterial strains). Thirty-six patients with $CD4^+$ T-cell counts under 350/mm^3, despite therapy, were randomly assigned to the probiotic or placebo group in a 2: 1 ratio. $CD4^+$ T-cell activation increased in the probiotic group, while inflammation and immune activation markers remained unchanged. Gut leakage and bacterial migration also remained unchanged. To summarize, studies by Schunter *et al.* and Rodney K. Rousseau *et al.* found successful probiotic colonization but did not observe significant improvements in inflammation, immune activation, or gut permeability markers. On the other hand, Gabriella d'Ettorre *et al.* demonstrated improvement in the gut barrier and immune system. These variations indicate that while some studies report positive effects on gut health and immune activation, others show no consistent or significant benefits for immune or gut permeability markers (Fig. 1).

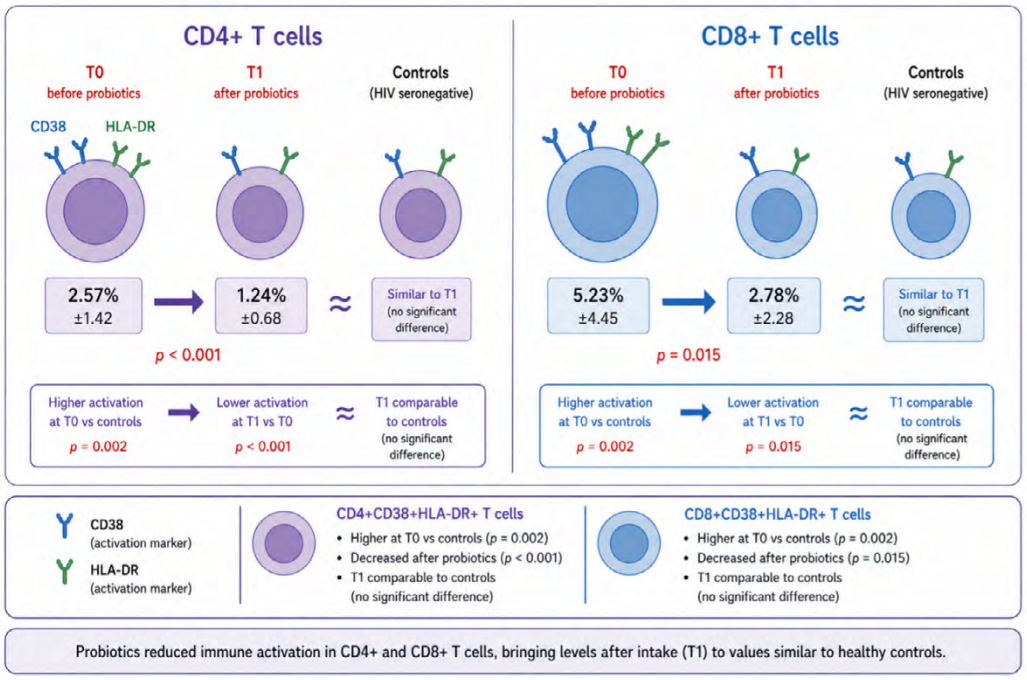


Fig. 1. Immune activation on T-lymphocytes Gabriella d'Ettorre [16]. Assessment of activation markers ($CD38^+HLA\text{-}DR^{+)}$ was performed on $CD4^+$ cells and on $CD8^+$ cells before (T0) and after (T1) probiotic supplementation. Compared with T0, the percentage of activated lymphocytes was significantly lower after probiotic supplementation (T1) in both groups ($CD4^+CD38^+HLA\text{-}DR^+$ T) and ($CD8^+CD38^+HLA\text{-}DR^+$ T). P values <0.05 were considered statistically significant (Fig. 2).
Illustration was made with ChatGPT.

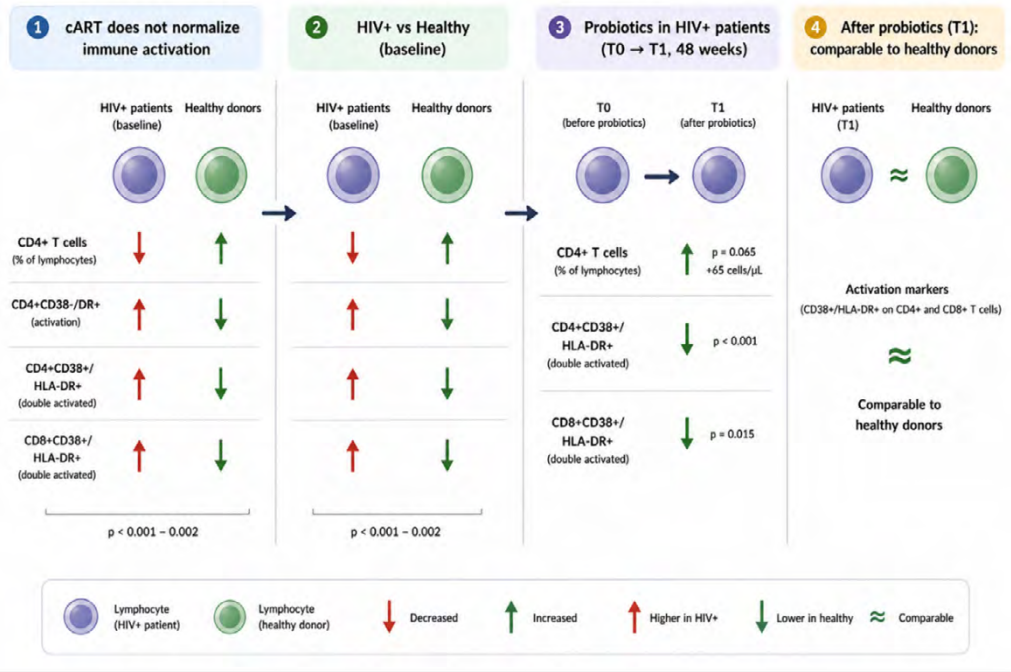


Fig. 2. Summary of Gabriella d'Ettorre's [16] findings.
Illustration was made with ChatGPT.

Clinical evidence on the use of probiotics for HIV-related diarrhea

Non-infectious diarrhea remains a relevant symptom in PLWH, often impairing the quality of life despite highly active antiretroviral therapy (HAART) administration.

While opportunistic diarrhea has become less common in the era of antiviral regimens, functional and treatment-associated gastrointestinal symptoms persist and continue to represent a therapeutic challenge for both patients and clinicians, Rodger D MacArthur. [21] Several interventional studies have investigated the role of probiotics and synbiotics in the treatment of HIV associated diarrhea. Heiser *et al.* [22] presented significant evidence of reduction of diarrhea or complete resolution among HIV positive patients on antiretroviral agents. Enrolled patients were HIV positive males experiencing chronic diarrhea while receiving either lopinavir/ritonavir (8 patients) or nelfinavir (27 patients). The study group consisted of 28 participants randomized to receive dietary supplementation consisting of probiotics and soluble fiber, while the control group consisted of 7 participants who received standard care. Study results showed that supplementation significantly reduced diarrhea. Resolution was found in 36% of patients (10 of 28 participants) in both antiretroviral drug groups. There was no significant change in HIV RNA levels, $CD4^+$ T-cell counts, or weight. Anukam *et al.* [23] have observed diarrhea, flatulence, and nausea resolution within two days after the initiation of probiotic supplementation among HIV patients without antiretroviral therapy. In this study, 24 HIV-positive women were enrolled with moderate diarrhea, $CD4^+$ counts >200 cells/μL without ART. This study

was conducted in Nigeria, where only a select group of patients are receiving ART during the AIDS sub-Saharan epidemic. The investigated probiotics were either 100 mL/day of conventional yogurt (fermented with Lactobacillus delbrueckii subsp. bulgaricus and Streptococcus thermophilus) supplemented with Lactobacillus rhamnosus GR-1 and L. reuteri RC-14 or unsupplemented yogurt. Hematologic parameters remained unchanged in both groups. Among the participants treated with probiotics, 11 of 12 demonstrated either increased or stable $CD4^+$ counts, compared with 3 of 12 in the control arm. In contrast, S. Guinane [24] stated in her review article that current evidence remains insufficient to recommend or contraindicate the use of probiotics for diarrhea. However, safety and the lack of drug-drug interactions make it a valid option for some patients. Possible evidence of probiotics may improve the immune reconstruction among HIV patients.

Probiotic supplementation and its influence on $CD4^+$ T-cell recovery in HIV-infected adult patients

Several studies have demonstrated that probiotic supplementation may increase $CD4^+$ T-cell levels in the PLVH population. Contrary to these findings, multiple studies have shown no change in $CD4^+$ T-cell counts. Here, we would like to discuss the available findings from clinical trials and secondary studies focused on this issue. Research demonstrating positive outcomes of probiotic intervention on CD4 T cell levels include a notable investigation by Masoud Mortezazadeh *et al.*, [25] a randomized double-blind clinical trial that enrolled 30 patients receiving antiretroviral therapy who exhibited immunologic failure despite sustained viral suppression. The study showed a statistically significant increase in $CD4^+$ T-cell counts in the probiotic group compared with the control group after a seven-month follow-up. However, discontinuation of probiotic supplementation nevertheless showed a subsequent decline in symptoms, and $CD4^+$ T-cell counts at the end of the study remained significantly higher than baseline values. Another study, the 'RECOVER' clinical trial conducted by Blázquez-Bondia *et al.*, [26] investigated the novel probiotic formulation 'i3.1', consisting of two strains of *L. plantarum and one of P. acidilactici.* HIV positive individuals on combination antiretroviral therapy (cART) with $CD4^+$ T-cell counts below 500 cells/mm^3 were enrolled. Subjects were randomized 1: 2: 2 to receive a placebo, a probiotic, or a probiotic plus prebiotic (synbiotic). Only symbiotic (probiotic + prebiotic) supplementation resulted in moderate increases in the CD4/CD8 ratio, as well as minor reductions in soluble CD14 (sCD14). However, the clinical significance of these changes remains unclear. Probiotic supplementation alone did not affect immune parameters or fecal microbiome composition.

The HIV/AIDS epidemic still remains a global health challenge. In 2023, an estimated 25.6 million individuals in sub-Saharan Africa were living with HIV/AIDS and its complications. To address this issue, Jaimie Caitlin Hemsworth [27] and colleagues developed an affordable and tasty nutritional supplement containing probiotics for HIV positive patients. Twenty-one PLWH on HAART were enrolled in a randomized, double-blind, three-period, crossover-controlled trial. The tested formulations were Formulation A (micronutrient plus probiotic), Formulation B (micronutrient alone), and Formulation C (probiotic alone). All the participants received each formulation for 30 days, separated by a 14-day elimination phase. Micronutrient alone (B) was linked to the greatest increase of CD4 lymphocyte count by 41 cells/μL (SD 221). Additionally, micronutrient plus probiotic (A) was associated with a 19 cell/μL increase in CD4 lymphocyte count (SD 142). Unexpectedly exclusive probiotic (C) was linked with a decrease in the CD4

lymphocyte count of 7 cells/μL (SD 154). This study presents the superiority of a combination of micronutrients and probiotics over probiotics alone.

Consistent with these findings González-Hernández *et al.* [28] demonstrated in a randomized, double-blind controlled study a positive effect of probiotic supplementation in the HIV positive AR naive study group. Twenty enrolled patients were divided into three subgroups and assigned to receive a probiotic, a prebiotic, a symbiotic (a combination of probiotics and prebiotics), or a placebo for 16 weeks. In the symbiotic study arm, the $CD4^+$ lymphocyte population increased significantly (median: +102 cells/μL; $p = 0.05$) with a decrease of interleukin-6, the studied inflammation marker. Probiotic supplementation led to a positive bacterial shift in the feces characterized by an increase in Bifidobacterium and a decrease in Clostridium populations. Serrano-Villar *et al.* took a complementary approach [29] when in 2016 they researched the efficiency of a synbiotic-based formulation in a pilot multicenter, randomized, double-blind, placebo-controlled trial. Seventy eight HIV positive, ART-naive patients with a $CD4^+$T count below 350/uL or acquired immunodeficiency syndrome (AIDS) were enrolled. Patients received either PMT25341 (a combination of synbiotics, amino acids, and omega-3/6 fatty acids) or a placebo daily for 48 weeks, either with or without first-line antiretroviral therapy. The mean change in $CD4^+$ T-cell count and the change in CD4/CD8 ratio between treatment groups were not statistically significant. Immunological benefits of ART were not improved by this nutritional intervention targeting the GALT and microbiota. In a subsequent study, Hummelen *et al.* (2011) [30] did not observe any differences in immune markers or diarrhea incidence as a result of supplementing with a probiotic containing Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri for 25 weeks, twice daily, in the study group, with no adverse effects observed. Similarly, Hummelen *et al.* [31] reported in 2014 a good tolerance of probiotics, but without improvement in $CD4^+$ counts. After one month, an average decline in $CD4^+$ count of 70 cells/μL (95% CI: –154 to –15) was observed in the probiotic group compared with a decline of 63 cells/μL (95% CI: –157 to –30) in the control group ($P = 0.9$). One hundred and twelve ART-naive HIV patients were enrolled in this randomized, double-blind, controlled trial. Patients were randomized to receive either micronutrient-fortified yogurt alone or micronutrient-fortified yogurt supplemented with *Lactobacillus rhamnosus* GR-1 for 4 weeks. We need to emphasize the fact that there are some safety concerns regarding the use of probiotics in the PLWH population, such as blood infiltration by a probiotic. [32]

Wolf *et al.* [33] investigated the safety of *Lactobacillus reuteri*, demonstrating no adverse side effects. Supplementation did not affect the safety markers measured and was well-tolerated.

Table 1. Summary of secondary research on the effect of probiotic intervention on $CD4^+$ lymphocyte population.

Author	Type of research	Outcome
Fu *et al.* 2020 [34]	systematic review and meta-analysis	Evidence of a positive outcome on the CD4 count is insufficient.
Zhang *et al.* 2021 [35]	systematic review and meta-analysis	Probiotics had no effect on CD4 cell counts in HIV/AIDS patients.
Kazemi *et al.* 2018 [36]	systematic review and meta-analysis	Supplementation with probiotics may not change CD4 counts. A significant increase in CD4 counts was observed in females following synbiotic treatment compared with pro- or prebiotic treatment alone.

Table 1. Cont.

Author	Type of research	Outcome
Oyadiran *et al.* 2024 [37]	Systematic review and meta-analysis	Meta-analysis reported no consistent effect on CD4; evidence for other outcomes was also inconsistent.
Wen *et al.* 2025 [38]	Meta-analysis	The results of this meta-analysis suggested that probiotics supplementation may have no effect on $CD4^+$ T cell counts. The adverse events reported appeared to have no correlation with the probiotic treatment.

Taken together, evidence from randomized trials and systematic reviews suggests that probiotic supplementation in PLWH is generally safe and well-tolerated, although its effects on $CD4^+$ T-cell counts remain inconsistent. Synbiotic formulations may show greater potential in specific subgroups, such as women, though further large-scale and long-term studies are required to establish their clinical significance.

Studies on pediatric HIV-1 positive population

Every year, around 120,000 new cases of pediatric HIV-1 infection are reported. Vertical infection and infant infection result in the initiation of antiretroviral therapy from the first days of life. We lack data on the influence of HIV-1-related dysbiosis and enteropathy on the development and maturation of the microbiota. [39] Infection in children living with HIV (CLWH) results in bacterial translocation, loss of gut epithelial integrity, $CD4^+$ T lymphocyte cell depletion, systemic immune activation, and viral reservoir establishment; these are identical consequences as in the adult population. Herein, we would like to present a few clinical trials that have been conducted on the effect of probiotics in the pediatric population.

Firstly, we would like to mention the Sachdeva *et al.* [40] systematic review and meta-analysis of randomized control trials (RCTs) of the HIV positive pediatric population. Data from those RCTs showed that in children, probiotic use is associated with improved $CD4^+$ cell counts with no adverse side effects. The study emphasizes the need for future research on this topic on a large scale as well as through international clinical trials. Patients had increased CD4 cell counts in both the ART-treated population and the ART-naive arm, as observed in the subgroup population analysis. A mean difference of 123.92 $CD4^+$ T-cell counts (95% CI: 104.36-143.48) was shown in the pooled analysis of the included trials, $p < 0.0001$, with no heterogeneity ($I2 = 0$). The Cochrane risk of bias tool and Egger's test for publication bias were used for evaluation. In 2014, Gautam *et al.* [41] conducted an open-label randomized control study in Agra (India). Enrollment criteria included HIV infection and age below 15 years. One hundred and twenty-seven pediatric patients were randomized to receive either probiotics for 3 months or micronutrients for 6 months. In children aged 5 years or older receiving probiotic supplementation, CD4 counts increased significantly compared with the control group ($p = 0.0022$). After 6 months in the micronutrient supplementation group (without ART), a statistically significant improvement in WHO clinical staging ($p = 0.049$) was observed. To summarize, this study suggests that probiotic supplementation can be beneficial in the pediatric population, and micronutrient supplementation (including vitamins B, C, E, and folic acid) may slow the progression of disease. However, according to the author, because of the lack of objective data on HIV mortality or progression, these data must be expanded with a larger randomized controlled

trial. New combinations of probiotic strains are an interesting topic. [42] Lívia Trois Trois *et al.* investigated whether the formula containing *Bifidobacterium bifidum* and *Streptococcus thermophilus* (2.5×10^{10} CFU) would be beneficial in comparison with the standard formula (control group). A randomized, double-blind, controlled trial was conducted, enrolling 77 pediatric patients aged 2–12 years. Children were randomized to receive either a studied probiotic formula or a standard formula (control group) for 2 months. The study group demonstrated a significant increase in mean $CD4^+$ T-cell counts (+118 cells/mm^3), whereas the control group exhibited a decline (−42 cells/mm^3; $p = 0.049$) at the end of intervention. Both groups showed a significant improvement in stool consistency ($p < 0.01$), and the occurrence of loose or soft stools decreased slightly in both groups ($p = 0.955$). Similarly, Ishizaki *et al.* [43] assessed the beneficial properties of probiotic strain *Lactobacillus casei Shirota* (LcS) in a 2017 study conducted in Vietnam. Sixty HIV-1 positive children were enrolled, 29 receiving ART for a median of 3.5 years, and 31 without antiretroviral therapy. Twenty HIV-1-negative children were in the control group. Participants consumed fermented milk containing probiotics for 8 weeks. After intervention, there were significant increases in peripheral $CD4^+$ lymphocyte counts and in the Th2 ($CXCR3^-CCR6^-CD4^+$) subset in both HIV-positive arms. Notably, Th17 lymphocyte ($CXCR3^-CCR6^+CD4^+$) rates increased across all groups. On the contrary, regulatory T-cell ($CD25highCD4^+$) counts decreased in the HIV positive ART group and the control group. Bacterial translocation was not detected, and no significant differences in bacterial 16S/23S rRNA were found in patient plasma. The intervention did not lead to any serious adverse events, confirming the safety of LcS supplementation. On the other hand, in Iran, Alpha Fardah Athiyyah *et al.* [44] studied the effect of *L. plantarum* IS-10506 supplementation, and the intervention did not show any beneficial effect on lymphocyte count. Twenty-one pediatric patients aged from 2 to 18 years treated with ART for more than 6 months were enrolled and completed the study. Participants were randomly assigned to two groups: a study group and a placebo group. The study group received 2.86 × 10^10 cfu/day of probiotic L. plantarum IS-10506 for 6 weeks. Results revealed no difference in the absolute $CD4^+$ T cell count, percent $CD4^+$ cells, absolute $CD8^+$ T cell count, $CD4^+/CD8^+$ T cell ratio, and faecal sIgA. However, the bacterial translocation marker, blood lipopolysaccharide (LPS) level, was statistically significantly decreased in the study group ($p = 0.001$).Together, these findings demonstrate that probiotic supplementation in HIV-infected children is well tolerated and may enhance $CD4^+$ T-cell recovery, exert an immunostimulatory effect, and improve stool consistency. While clinical outcomes varied between studies, the evidence supports a potential adjunctive role for probiotics in pediatric HIV care. Larger, long-term randomized trials are needed to validate these findings and determine their clinical relevance in relation to disease progression and quality of life.

On the other hand, some studies emphasize that antiretroviral therapy alone can mildly improve Inflammation and Gut Permeability and microbial translocation induced by HIV infection. [45, 46]

Conclusions

In summary, collectively, these studies suggest that probiotic interventions are safe and may alleviate gastrointestinal symptoms, particularly diarrhea, in HIV-positive populations. While improvements in immune activation and $CD4^+$ T-cell counts have been inconsistent, evidence supports symptomatic relief and enhanced quality of life, highlighting the potential of probiotic-based nutritional therapies as adjunctive strategies in HIV guidelines. Larger, longer-term, and international randomized controlled trials are needed to confirm these benefits and clarify their immunological and clinical significance.

Author's contribution

W.S. — conception of work, formal analysis, writing — original draft, project administration. G.K. — formal analysis, writing — original draft. Ł.K. — formal analysis, writing — original draft.

Conflict of interest

None declared.

References

1. *Mörbe U.M., Jørgensen P.B., Fenton T.M., von Burg N., Riis L.B., Spencer J., Agace W.W.*: Human gut-associated lymphoid tissues (GALT); diversity, structure, and function. Mucosal Immunol. 2021 Jul; 14 (4): 793–802. doi: 10.1038/s41385-021-00389-4.
2. *Luckheeram R.V., Zhou R., Verma A.D., Xia B.*: CD4+T Cells: Differentiation and Functions. Clin Dev Immunol: 2012: 2012: 925135. doi: 10.1155/2012/925135.
3. *Brucklacher-Waldert V., Carr E.J., Linterman M.A., et al.*: Cellular plasticity of $CD4^+$ T cells in the intestine. Front Immunol. 2014 Oct 7: 5: 488. doi: 10.3389/fimmu.2014.00488.
4. *Guadalupe M., Reay E., Sankaran S., Prindiville T., Flamm J., McNeil A., Dandekar S.*: Severe $CD4^+$ T-Cell Depletion in Gut Lymphoid Tissue during Primary Human Immunodeficiency Virus Type 1 Infection and Substantial Delay in Restoration following Highly Active Antiretroviral Therapy. J Virol. 2003 Nov; 77 (21): 11708–11717. doi: 10.1128/jvi.77.21.11708-11717.2003.
5. *Yoder A.C., Guo K., Dillon S.M., Lee P.T., Harper M.S., Helm K., et al.*: The transcriptome of HIV-1 infected intestinal $CD4^+$ T cells exposed to enteric bacteria. PloS Pathog. 2017 Feb 27; 13 (2): e1006226. doi: 10.1371/journal.ppat.1006226.
6. *Alzahrani J., Hussain T., Simar D., Palchaudhuri R., Abdel-Mohsen M., Crowe S.M., et al.*: Inflammatory and immunometabolic consequences of gut dysfunction in HIV: Parallels with IBD and implications for reservoir persistence and non-AIDS comorbidities. EBioMedicine. 2019 Aug: 46: 522–531. doi: 10.1016/j.ebiom.2019.07.027.
7. *Brenchley J.M., Price D.A., Schacker T.W., Asher T.E., Silvestri G., Rao S., et al.*: Microbial translocation is a cause of systemic immune activation in chronic HIV infection. Nat Med. 2006 Dec; 12 (12): 1365–1371. doi: 10.1038/nm1511.
8. *Mavigner M., Cazabat M., Dubois M., L'Faqihi F.-E., Requena M., Pasquier C., et al.*: Altered $CD4^+$ T cell homing to the gut impairs mucosal immune reconstitution in treated HIV-infected individuals. J Ciln Invest. 2012 Jan; 122 (1): 62–69. doi: 10.1172/JCI59011.
9. *Mehandru S., Poles M.A., Tenner-Racz K., Jean-Pierre P., Manuelli V., Lopez P., et al.*: Lack of mucosal immune reconstitution during prolonged treatment of acute and early HIV-1 infection. Infect Dis Ther. 2022 Aug; 11 (4): 1541–1557. doi: 10.1371/journal.pmed.0030484.
10. *Dolo O., Coulibaly F., Somboro A.M., Sun S., Diarra M., Maiga A., et al.*: The human gut microbiome and its metabolic pathway dynamics before and during HIV antiretroviral therapy Microbiol.Spect. 2025 Aug 5; 13 (8): e0220524. doi: 10.1128/spectrum.02205-24.
11. *Macarthur R.D.*: Management of noninfectious diarrhea associated with HIV and highly active antiretroviral therapy. Am J Mang Care. 2013 Sep; 19 (12 Suppl): s238–245.
12. Global HIV Programme (WHO World Health Organization).
13. *Wu Z., Xie Z.-P., Cui X.-X., Sun X.-B., Zhao F.-Y., Wang N., et al.*: HIV and the gut microbiome: future research hotspots and trends. Front Microbiol. 2025 Feb 7: 16: 1466419. doi: 10.3389/fmicb.2025.1466419.
14. *Carter G.M., Esmaeili A., Shah H., Indyk D., Johnson M., Andreae M., Sacks H.S.*: Probiotics in Human Immunodeficiency Virus Infection: A Systematic Review and Evidence Synthesis of Benefits and Risks. Open Forum Infect Dis. 2016 Jul 29; 3 (4): ofw164. doi: 10.1093/ofid/ofw164.

15. *Xu R., Yu Y., Chen T.*: Exploring the dark side of probiotics to pursue light: Intrinsic and extrinsic risks to be opportunistic pathogens. Curr Res Food Sci. 2025; 10: 101044. doi: 10.1016/j.crfs.2025.101044.
16. *d'Ettorre G., Ceccarelli G., Giustini N., Serafino S., Calantone N., De Girolamo G., et al.*: Probiotics Reduce Inflammation in Antiretroviral Treated, HIV-Infected Individuals: Results of the "Probio-HIV" Clinical Trial-Clinical Trial. PLoS One. 2015 Sep 16; 10 (9): e0137200. doi: 10.1371/journal.pone.0137200.
17. *Monachese M., Cunningham-Rundles S., Diaz M.A., Guerrant R., Hummelen R., Kemperman R., et al.*: Probiotics and prebiotics to combat enteric infections and HIV in the developing world: a consensus report. Gut Microbes. 2011 May–Jun; 2 (3): 198-207. doi: 10.4161/gmic.2.3.16106.
18. *d'Ettorre G., Rossi G., Scagnolari C., Andreotti M., Giustini N., Serafino S., et al.*: Probiotic supplementation promotes a reduction in T-cell activation, an increase in Th17 frequencies, and a recovery of intestinal epithelium integrity and mitochondrial morphology in ART-treated HIV-1-positive patients. Immun Inflamm Dis. 2017 Sep; 5 (3): 244–260. doi: 10.1002/iid3.160.
19. *Schunter M., Chu H., Hayes T.L., McConnell D., Crawford S.S., Luciw P.A., et al.*: Randomized pilot trial of a synbiotic dietary supplement in chronic HIV-1 infection. BMC Complement Altern Med. 2012 Jun 29; 12: 84. doi: 10.1186/1472-6882-12-84.
20. *Rousseau R.K., Walmsley S.L., Lee T., Rosenes R., Reinhard R.J., Malazogu F., et al.*: Randomized, Blinded, Placebo-Controlled Trial of De Simone Formulation Probiotic During HIV-Associated Suboptimal CD4+ T Cell Recovery. J Acquir Immune Defic Syndr. 2022 Feb 1; 89 (2): 199–207. doi: 10.1097/QAI.0000000000002840.
21. *MacArthur R.D., DuPont H.L.*: Etiology and pharmacologic management of noninfectious diarrhea in HIV-infected individuals in the highly active antiretroviral therapy era. Clin Infect Dis. 2012 Sep; 55 (6): 860–867. doi: 10.1093/cid/cis544.
22. *Heiser C.R., Ernst J.A., Barrett J.T., French N., Schutz M., Dube M.P.*: Probiotics, soluble fiber, and L-Glutamine (GLN) reduce nelfinavir (NFV)- or lopinavir/ritonavir (LPV/r)-related diarrhea. J Int Assoc Physicians AIDS Care (Chic). 2004 Oct–Dec; 3 (4): 121–129. doi: 10.1177/154510970400300403.
23. *Anukam K.C., Osazuwa E.O., Osadolor H.B., Bruce A.W., Reid G.*: Yogurt containing probiotic Lactobacillus rhamnosus GR-1 and L. reuteri RC-14 helps resolve moderate diarrhea and increases CD4 count in HIV/AIDS patients. J Clin Gastroenterol. 2008 Mar; 42 (3): 239–243. doi: 10.1097/MCG.0b013e31802c7465.
24. *Guinane S.*: The effectiveness of probiotics for managing diarrhoea in people with HIV infection: a critically appraised topic. HIV Med. 2013 Mar; 14 (3): 187–190. doi: 10.1111/j.1468-1293.2012.01042.
25. *Mortezazadeh M., Kalantari S., Abolghasemi N., Ranjbar M., Ebrahimi S., Mofidi A., et al.*: The effect of oral probiotics on CD4 count in patients with HIV infection undergoing treatment with ART who have had an immunological failure. Immun Inflamm Dis. 2023 Jun; 11 (6): e913. doi: 10.1002/iid3.913.
26. *Blázquez-Bondia C., Parera M., Català-Moll F., Casadellà M., Elizalde-Torrent A., Aguiló M., et al.*; Probiotic effects on immunity and microbiome in HIV-1 discordant patients. Front Immunol. 2022 Dec 8; 13: 1066036. doi: 10.3389/fimmu.2022.1066036.
27. *Hemsworth J.C., Hekmat S., Reid G.*: Micronutrient supplemented probiotic yogurt for HIV-infected adults taking HAART in London, Canada. Gut Microbes. 2012 Sep–Oct; 3 (5): 414–419. doi: 10.4161/gmic.21248.
28. *González-Hernández L.A., Jave-Suarez L.F., Fafutis-Morris M., Montes-Salcedo K.E., Valle-Gutierrez L.G., Campos-Loza A.E., et al.*: Synbiotic therapy decreases microbial translocation and inflammation and improves immunological status in HIV-infected patients: a double-blind randomized controlled pilot trial. Nutr J. 2012 Oct 29: 11: 90. doi: 10.1186/1475-2891-11-90.
29. *Serrano-Villar S., de Lagarde M., Vázquez-Castellanos J., Vallejo A., Bernadino J.I., Madrid N., Matarranz M.*: Effects of Immunonutrition in Advanced Human Immunodeficiency Virus Disease: A Randomized Placebo-controlled Clinical Trial (Promaltia Study). Clin Infect Dis. 2019 Jan 1; 68 (1): 120–130. doi: 10.1093/cid/ciy414.
30. *Hummelen R., Changalucha J., Butamanya N.L., Koyama T.E., Cook A., Habbema J.D.F., Reid G.*: Effect of 25 weeks probiotic supplementation on immune function of HIV patients. Gut Microbes. 2011 Mar–Apr; 2 (2): 80–85. doi: 10.4161/gmic.2.2.15787.

31. *Hummelen R., Hemsworth J., Changalucha J., Butamanya N.L., Hekmat S., Habbema J.D.F., Reid G.*: Effect of micronutrient and probiotic fortified yogurt on immune-function of anti-retroviral therapy naive HIV patients. Nutrients. 2011 Oct; 3 (10): 897–909. doi: 10.3390/nu3100897.
32. *Doron S., Snydman D.R.*: Risk and Safety of Probiotics. Clin Infect Dis. 2015 May 15; 60 (Suppl 2): S129–134. doi: 10.1093/cid/civ085.
33. *Wolf B.W., Wheeler KB., Ataya D.G., Garleb K.A.*: Safety and tolerance of Lactobacillus reuteri supplementation to a population infected with the human immunodeficiency virus. Food Chem Toxicol. 1998 Dec; 36 (12): 1085–1094. doi: 10.1016/s0278-6915(98)00090-8.
34. *Fu Y.-S., Chu Q.-S., Ashuro A.A., Di D.-S., Zhang Q., Liu X.-M., Fan Y.-G.*: The Effect of Probiotics, Prebiotics, and Synbiotics on CD4 Counts in HIV-Infected Patients: A Systematic Review and Meta-Analysis. Biomed Res Int. 2020 Nov 26: 2020: 7947342. doi: 10.1155/2020/7947342.
35. *Zhang X.-L., Chen M.-H., Geng S.-T., Yu J., Kuang Y.-Q., Luo H.-Y., Wang K.-H.*: Effects of Probiotics on Diarrhea and CD4 Cell Count in People Living With HIV: A Systematic Review and Meta-analysis. Front Pharmacol. 2021 Jul 19: 12: 570520. doi: 10.3389/fphar.2021.570520.
36. *Kazemi A., Djafarian K., Speakman J.R., Sabour P., Soltani S., Shab-Bidar S.*: Effect of Probiotic Supplementation on CD4 Cell Count in HIV-Infected Patients: A Systematic Review and Meta-analysis. J Diet Suppl. 2018 Sep 3; 15 (5): 776–788. doi: 10.1080/19390211.2017.1380103.
37. *Oyadiran O.T., Ogunlade S.B., Okusanya T.R., Okoka E.M., Kuyebi M.A., Omotayo M.O., Abioye A.I.*: Effect of intake of probiotics and probiotic fermented foods on clinical outcomes among people living with HIV: A systematic review and meta-analysis. Trop Med Int Health. 2024 Feb; 29 (2): 113–127. doi: 10.1111/tmi.13955.
38. *Wen M., Yang G., Yang L., Chang Y.Y.D.*: Effect of probiotics supplementation on $CD4^+$T cell counts and inflammation in adults living with HIV: A systematic review and meta-analysis. Eur J Integr Med. 2025 Aug; 77: 102453. doi.org/10.1016/j.eujim.2025.102453.
39. *Soo N., Farinre O., Chahroudi A., Boliar S., Goswami R.*: A gut check: understanding the interplay of the gastrointestinal microbiome and the developing immune system towards the goal of pediatric HIV remission. Retrovirology. 2024 Oct 18; 21 (1): 15. doi: 10.1186/s12977-024-00648-9.
40. *Sachdeva M., Sra H.K., Agarwal A., Chauhan A., Pradhan P., Singh M., Singh M.*: Effect of Probiotics on the Frequency of $CD4^+$ T-Cells in HIV-Infected Children and Adolescents: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Trop Pediatr. 2022 Feb 3; 68 (2): fmac006. doi: 10.1093/tropej/fmac006.
41. *Gautam N., Dayal R., Agarwal D., Kumar R., Singh T.P., Hussain T., Singh S.P.*: Role of multivitamins, micronutrients and probiotics supplementation in management of HIV infected children. Indian J Pediatr. 2014 Dec; 81 (12): 1315–1320. doi: 10.1007/s12098-014-1407-6.
42. *Trois L., Cardoso E.M., Miura E.*: Use of probiotics in HIV-infected children: a randomized double-blind controlled study. J Trop Pediatr. 2008 Feb; 54 (1): 19–24. doi: 10.1093/tropej/fmm066.
43. *Ishizaki A., Bi X., Van Nguyen L., Matsuda K., Pham H.V., Phan C.T.T., et al.*: Effects of Short-Term Probiotic Ingestion on Immune Profiles and Microbial Translocation among HIV-1-Infected Vietnamese Children. Int J Mol Sci. 2017 Oct 19; 18 (10): 2185. doi: 10.3390/ijms18102185.
44. *Athiyyah A.F., Brahmantya H., Dwiastuti S., Darma A., Puspitasari D., Husada D., et al.*: Effect of *Lactobacillus plantarum* IS-10506 on blood lipopolysaccharide level and immune response in HIV-infected children. Iran J Microbiol. 2019 Apr; 11 (2): 137–144.
45. *Brenchley J.M., Douek D.C.*: HIV infection and the gastrointestinal immune system. Mucosal Immunol. 2008 Jan; 1 (1): 23–30. doi: 10.1038/mi.2007.1.
46. *Villoslada-Blanco P., Pérez-Matute P., Íñiguez M., Recio-Fernández E., Blanco-Navarrete P., Metola L., et al.*: Integrase Inhibitors Partially Restore Bacterial Translocation, Inflammation and Gut Permeability Induced by HIV Infection: Impact on Gut Microbiota Infect Dis Ther. 2022 Aug; 11 (4): 1541–1557. doi: 10.1007/s40121-022-00654-4.