Asian Journal of Health Research
Journal Homepage: https://a-jhr.com
Published by Ikatan Dokter Indonesia Wilayah Jawa Timur

OPEN ACCESS

Systematic Review

Vaginal Probiotics as Adjunctive Therapy in Preterm Prelabor Rupture of Membranes: A Qualitative Systematic Review

Mukhammad Nooryanto, Rony Sibuea*

Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Brawijaya/Dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia

ARTICLE HISTORY
Received: 3 May 2026
Revised: 5 June 2026
Accepted: 14 July 2026

CORRESPONDING AUTHOR*
Rony Sibuea
ronysibuea1988@gmail.com
Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Brawijaya/ Dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia

KEYWORDS
Neonatal Outcomes; PPROM; Preterm Birth; Probiotics

This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/)

ABSTRACT

Introduction: Preterm prelabor rupture of membranes contributes substantially to maternal and neonatal morbidity. Because vaginal dysbiosis may promote ascending infection and membrane weakening, probiotics have been proposed as adjunctive therapy. This review evaluated maternal and neonatal outcomes associated with oral or vaginal probiotics in women with, or at risk of, preterm prelabor rupture of membranes.

Methods: PubMed, Scopus, ScienceDirect, and the Cochrane Library were searched through January 2025. Randomized controlled trials of probiotic interventions were eligible. Two reviewers independently screened studies, extracted data, and performed domain-level appraisal using the Joanna Briggs Institute checklist. Owing to clinical and methodological heterogeneity, findings were synthesized qualitatively without meta-analysis.

Results: Four randomized trials involving 306 participants were included. Several trials reported longer latency, higher gestational age at delivery, greater neonatal birth weight, or fewer neonatal intensive care admissions with adjunctive vaginal probiotics. However, one trial showed no significant latency benefit, and results varied by population, formulation, regimen, concomitant antibiotics, and outcome definition. Certainty was low to very low because of small samples, inconsistency, indirectness, and imprecision.

Conclusion: Vaginal probiotics may have potential as adjunctive therapy, but current evidence is preliminary and insufficient to support routine use. Larger multicenter trials using standardized strains, doses, comparators, and outcomes are required.

Cite this as: Nooryanto M, Sibuea R (2026) Vaginal Probiotics as Adjunctive Therapy in Preterm Prelabor Rupture of Membranes: A Qualitative Systematic Review. *Asian J Heal Res.* 5 (2): 213–222. doi: https://doi.org/10.55561/ajhr.v5i2.336

INTRODUCTION

Preterm prelabor rupture of membranes (PPROM) is defined as rupture of the fetal membranes before the onset of labor and before 37 completed weeks of gestation [1,2]. PPROM remains one of the major causes of preterm birth and contributes substantially to maternal and neonatal morbidity worldwide. Complications associated with PPROM include intrauterine infection, placental abruption, neonatal sepsis, respiratory distress, and increased neonatal intensive care unit (NICU) admission [1,2,12,21,46-49].

Emerging evidence suggests that vaginal microbial homeostasis plays an important role in maintaining pregnancy. Lactobacillus-dominant vaginal microbiota contribute to preservation of acidic vaginal pH and suppression of pathogenic microorganisms, whereas disruption of normal vaginal flora may facilitate ascending infection and inflammatory responses associated with membrane weakening and spontaneous preterm birth [4-6,20-33]. Probiotic supplementation has therefore attracted increasing attention as a potential adjunctive therapy because it may help restore microbial balance, suppress pathogenic colonization, and support recovery of vaginal

microbiota following antibiotic exposure [7,8,34-42].

Several studies have investigated probiotics as adjunctive therapy in PPROM management and reported possible benefits, including prolonged latency period and improved neonatal outcomes [9,11,14,16,17]. However, currently available evidence remains limited and heterogeneous with regard to probiotic strains, dosage regimens, intervention duration, and reported outcomes.

Unlike the 2023 meta-analysis, which quantitatively pooled selected vaginal-probiotic trials, this review provides an updated qualitative synthesis that includes a later pilot trial, emphasizes strain- and regimen-level clinical heterogeneity, evaluates methodological domains using the JBI checklist, and interprets the evidence without pooling where direct comparability was considered insufficient [11,13].

Despite increasing interest in probiotic therapy for PPROM, currently available randomized controlled trials remain limited and heterogeneous. Uncertainty persists regarding optimal probiotic strains, routes of administration, dosage regimens, and overall clinical effectiveness. Therefore, this qualitative systematic review aimed to critically evaluate current evidence regarding oral and vaginal probiotics as adjunctive therapy in improving maternal and neonatal outcomes among women with PPROM.

METHODS

Literature Search

Preparation and reporting of this review followed PRISMA 2020 guidance [18]. A comprehensive literature search was conducted using four electronic databases: PubMed, Scopus, ScienceDirect, and the Cochrane Library through January 2025. The search strategy combined Boolean operators and Medical Subject Headings (MeSH)-related terms, including: ("PPROM" OR "preterm prelabor rupture of membranes" OR "preterm premature rupture of membranes") AND ("probiotics" OR "Lactobacillus" OR "vaginal probiotics" OR "oral probiotics") AND ("neonatal outcomes" OR "preterm birth" OR "latency period" OR "birth weight" OR "NICU admission"). Database-specific search strategies were adapted according to the indexing system of each database. Additional relevant studies were identified through manual screening of reference lists. Detailed electronic search strategies are presented in Appendix 1.

Detailed database-specific electronic search strategies, including Boolean operators, MeSH-related terms, filters, and eligibility restrictions, are presented in Appendix 1 to improve reproducibility.

Protocol Registration

This review was not prospectively registered in PROSPERO. The absence of prospective protocol registration is acknowledged as a limitation because it may increase the risk of reporting bias.

Eligibility Criteria

Study selection was based on the PICOS framework. Eligible studies included randomized controlled trials involving pregnant women diagnosed with PPROM or considered at risk of PPROM. Interventions included oral or vaginal probiotic administration, while comparison groups received placebo, antibiotics alone, standard therapy, or no probiotic treatment. Studies reporting maternal or neonatal outcomes, including gestational age at delivery, neonatal birth weight, latency period, neonatal sepsis, and NICU admission, were considered eligible.

Review articles, conference abstracts, editorials, case reports, non-randomized studies, and studies without sufficient outcome data were excluded.

Data Extraction and Risk of Bias Assessment

Two reviewers independently screened titles and abstracts, assessed potentially eligible full texts, and extracted data using a standardized form. Extracted data included study characteristics, participant demographics, probiotic strains and formulations, dose and route, treatment duration, follow-up period, comparator protocols, and reported clinical outcomes. Disagreements were resolved by discussion and consensus.

Two reviewers independently assessed methodological quality using the Joanna Briggs Institute Critical Appraisal Checklist for Randomized Controlled Trials [19]. Judgments

were interpreted by individual methodological domains rather than by total score alone. Disagreements were resolved through discussion and consensus.

Statistical Analysis

Considerable clinical and methodological heterogeneity was identified among included studies regarding probiotic strains, treatment duration, dosing regimens, gestational age at enrollment, adjunctive antibiotic protocols, and outcome definitions. Therefore, formal meta-analysis was not considered methodologically appropriate. A descriptive qualitative synthesis was conducted, and comparative outcome visualization was used to summarize differences in gestational age at delivery and neonatal birth weight between intervention and control groups.

No pooled effect size, confidence interval, weighting analysis, or heterogeneity statistic was calculated because quantitative meta-analysis was not performed. The graphical outcome comparisons presented in this review are intended solely for descriptive visualization and should not be interpreted as formal quantitative meta-analytic results.

Experimental Protocol

The review process included literature identification, duplicate removal, title and abstract screening, full-text eligibility assessment, and qualitative synthesis.

Ethics Approval

Not required. This study was a systematic review of previously published studies and did not involve direct participation of human subjects.

RESULTS

Study Selection

Database searches initially identified 1351 records from PubMed, Scopus, ScienceDirect, and the Cochrane Library. After duplicate removal and preliminary eligibility screening, 37 articles underwent title and abstract evaluation. A total of 1314 records were excluded because they were review articles, conference abstracts, editorials, non-randomized studies, unrelated topics, animal studies, or did not evaluate probiotic interventions in PPROM.

Six full-text articles were subsequently assessed for eligibility. Two studies were excluded because of insufficient outcome reporting or ineligible study design. Ultimately, four randomized controlled trials fulfilled the inclusion criteria for qualitative synthesis. The process of literature screening and study inclusion is illustrated in Figure 1.

Characteristics of Included Studies

A total of four randomized controlled trials involving 306 participants were included in this review [13,14,16,17]. All four studies evaluated vaginal probiotics in women with PROM or PPROM. The trial by Moraes et al. was a small pilot study and included women with PROM between 24 and 36 weeks of gestation [13]. All studies compared probiotic interventions with control or standard therapy groups. Detailed study characteristics are presented in Table 1.

Study Quality

Overall, most studies fulfilled key methodological criteria, including randomization and blinding procedures. Nevertheless, several limitations remained, particularly small sample sizes, incomplete reporting of allocation procedures, and potential reporting bias due to unavailable study protocols [19]. Detailed quality assessment results are presented in Appendix 2.

Most included studies demonstrated low risk of performance and detection bias because appropriate blinding procedures were generally implemented. However, several studies showed unclear risk of selection bias due to incomplete reporting of allocation concealment and baseline comparability. In addition, potential reporting bias could not be completely excluded because study protocols and prespecified outcome reporting were not consistently available.

Synthesis of Outcomes

Across the included studies, probiotic supplementation was associated with favorable maternal and neonatal outcomes, including prolonged latency period, increased gestational age at delivery, higher neonatal birth weight, lower

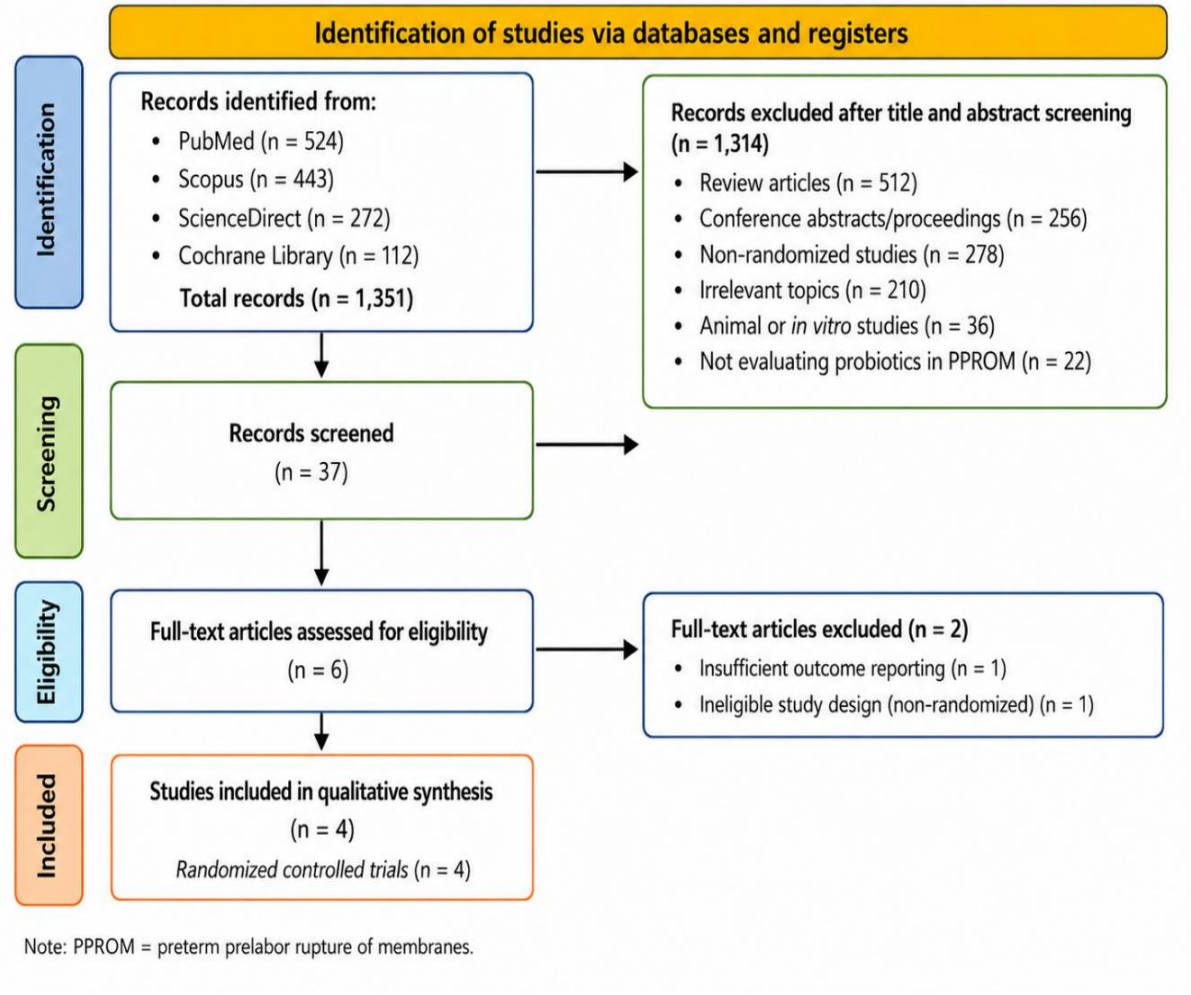


Figure 1. Flowchart describing literature screening and study inclusion process

NICU admission rates, and shorter NICU stay duration [9,11,14,16,17].

Effect estimates varied across studies. Descriptive comparisons suggested possible differences in gestational age at delivery and neonatal birth weight, but inconsistent findings, small samples, and clinical heterogeneity preclude inference of an overall treatment effect [9,11,14,16,17].

Descriptive Comparative Analysis

Descriptive comparison plots for gestational age at delivery and neonatal birth weight are presented in Figures 2 and 3. No pooled statistical analysis, weighting analysis, or heterogeneity calculation was performed because of substantial clinical heterogeneity and limited sample size across included studies. The direction and magnitude of effects were not consistent across studies; therefore, the descriptive plots should not be interpreted as demonstrating an overall treatment effect [9,11,14,16,17].

DISCUSSION

Current evidence suggests that adjunctive probiotic supplementation may potentially improve maternal and neonatal outcomes in women with PPROM. Several included studies demonstrated improvements in gestational age at delivery, neonatal birth weight, and NICU admission rates among women receiving probiotics [9,11,14,16,17].

Clinical heterogeneity was substantial. Trials differed in gestational age at enrollment, PROM

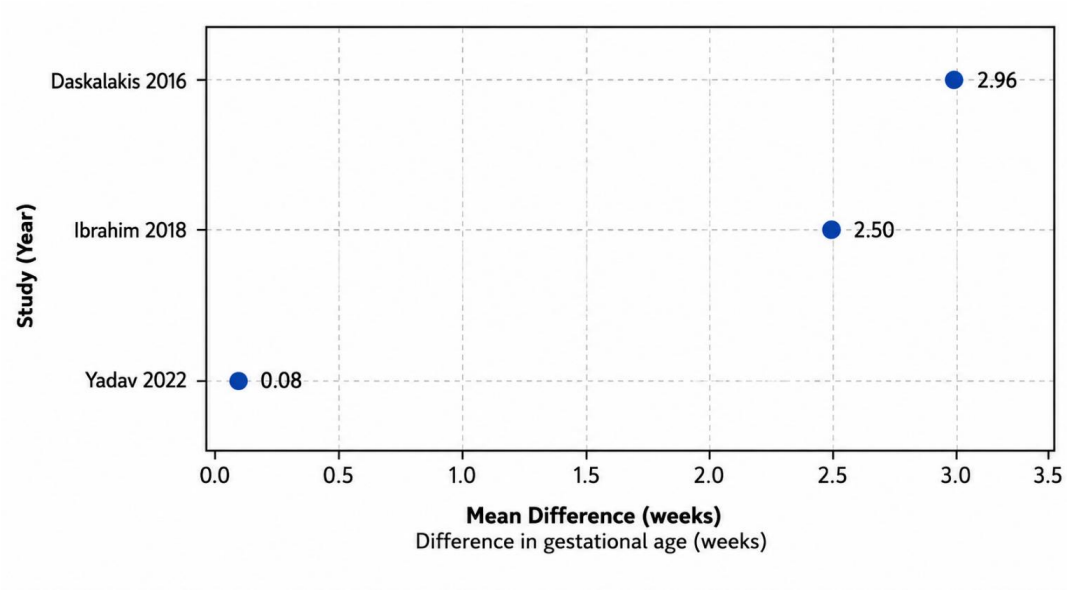


Figure 2. Gestational Age at Delivery
Graphs are presented for descriptive visualization only and do not represent formal meta-analytic forest plots.

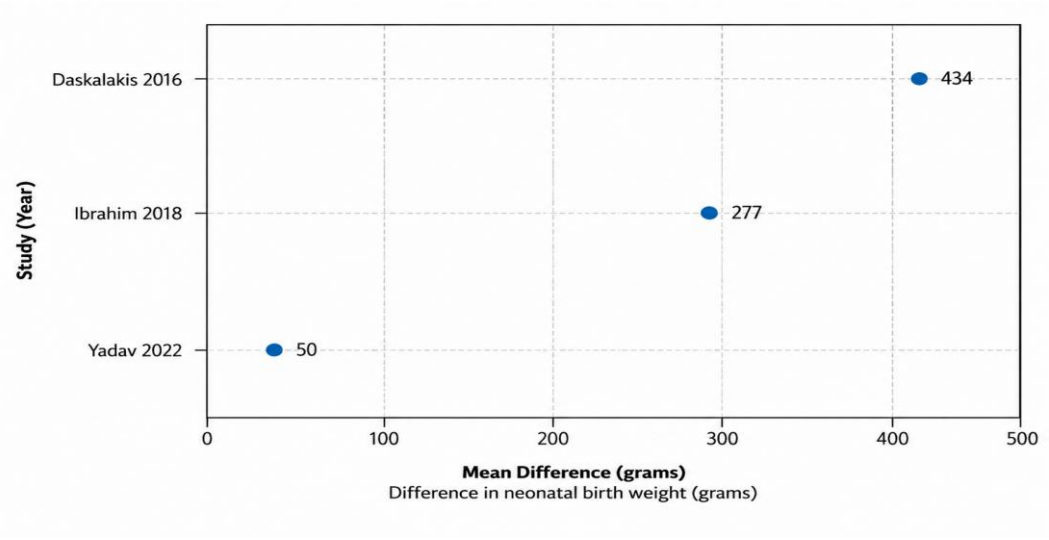


Figure 3. Neonatal Birth Weight
Graphs are presented for descriptive visualization only and do not represent formal meta-analytic forest plots

versus PPROM case definitions, baseline infection risk, probiotic species and formulation, frequency and duration of administration, concomitant antibiotic regimens, and definitions of latency and neonatal morbidity. These differences limit direct cross-trial comparison and were the principal reason a pooled estimate was not calculated.

Interestingly, not all included studies demonstrated consistent benefit. Yadav et al. reported minimal differences in latency period and neonatal outcomes between probiotic and control groups [17]. These discrepancies may reflect differences in probiotic strains, baseline maternal characteristics, concomitant antibiotic protocols,

and gestational age at enrollment [11,17]. Therefore, interpretation of the currently available evidence should remain cautious. The relatively small sample sizes and inconsistent findings across studies prevent definitive conclusions regarding probiotic efficacy in PPROM management [3,14,16,17].

The observed benefits may be associated with restoration of vaginal microbial homeostasis and reduction of inflammatory pathways related to membrane weakening. Lactobacillus-dominant vaginal microbiota contribute to maintenance of acidic vaginal pH and suppression of pathogenic microorganisms [24-37]. Disturbance of this microbial environment has been associated with ascending infection and inflammatory activation, both recognized contributors to spontaneous preterm birth [21,24-33].

The inconsistent findings across included studies may reflect strain-specific probiotic effects. Different Lactobacillus strains possess distinct antimicrobial, immunomodulatory, and anti-inflammatory properties, potentially resulting in variable clinical outcomes [7,8,34-42]. In addition, differences in gestational age at enrollment, concomitant antibiotic therapy, treatment duration, and outcome definitions further complicate direct comparison between studies and limit external validity [11,14,16,17].

Potential biological mechanisms underlying probiotic benefit may include restoration of Lactobacillus-dominant vaginal microbiota, maintenance of acidic vaginal pH, suppression of pathogenic colonization, and modulation of inflammatory cytokine pathways associated with membrane weakening and spontaneous preterm birth [6-8,24-37].

Conventional management of PPROM commonly includes antibiotic therapy aimed at reducing infectious morbidity and prolonging pregnancy duration [44,45]. Nevertheless, antibiotic exposure may disrupt normal vaginal flora and contribute to microbial imbalance. Adjunctive probiotic therapy may therefore help restore microbial equilibrium and limit recolonization by pathogenic microorganisms [7,8].

Among the included studies, vaginal probiotic administration appeared to demonstrate more favorable outcomes than oral supplementation, possibly because of its direct local interaction with vaginal microbiota [13,14]. However, interpretation of current evidence should remain cautious because substantial heterogeneity existed regarding probiotic strains, dosage regimens, intervention duration, and reported outcome measures.

These observations are in line with previous reports describing improved neonatal outcomes associated with adjunctive probiotic therapy in PPROM [11]. However, the relatively limited number of randomized controlled trials and methodological variability continue to restrict definitive recommendations regarding optimal probiotic protocols in clinical practice.

At present, available evidence remains insufficient to recommend routine probiotic administration in all patients with PPROM [11,44,45]. Nevertheless, probiotics may represent a promising adjunctive therapeutic strategy that warrants further investigation through larger multicenter randomized controlled trials with standardized intervention protocols. Further randomized controlled trials with larger sample sizes are required to clarify the clinical role of probiotics in PPROM management. Taken together, currently available evidence should be considered preliminary rather than definitive because of methodological heterogeneity and limited randomized evidence [3,11,14,16,17].

CONCLUSION

Current evidence suggests that vaginal probiotics may represent a promising adjunctive strategy in PPROM management because several included studies demonstrated potential improvements in maternal and neonatal outcomes. However, the certainty of evidence remains limited because of substantial heterogeneity, relatively small sample sizes, and methodological variability across studies. Additional large-scale randomized controlled trials are required to establish optimal probiotic strains, dosage regimens, routes of administration, and duration of therapy before routine clinical implementation can be recommended.

Study Limitations

This study has several limitations, including the relatively small number of included randomized controlled trials and substantial heterogeneity regarding probiotic strains, routes of administration, dosage regimens, gestational age at enrollment, adjunctive antibiotic protocols, and outcome definitions. These differences substantially limit comparability and external validity. Although four major databases and reference lists were searched, Embase and Web of Science were not available for this review; eligible non-English reports may also have been missed because the search was restricted to English-language publications.

In addition, formal quantitative meta-analysis was not performed because of methodological heterogeneity and incomplete statistical reporting across studies. Consequently, pooled effect estimates and heterogeneity statistics could not be calculated. Potential publication bias could not be formally assessed because of the limited number of included studies and absence of quantitative meta-analysis. This review was also not prospectively registered in PROSPERO, which may increase the risk of reporting bias.

Using GRADE principles, certainty was judged low to very low across the principal outcomes because of risk-of-bias concerns, inconsistency between trials, indirectness arising from different populations and probiotic regimens, and serious imprecision from small sample sizes. Publication bias could not be evaluated reliably with fewer than 10 studies. These judgments are narrative because no pooled outcome-specific estimates were generated.

ACKNOWLEDGMENT

The authors would like to acknowledge all individuals who contributed to manuscript preparation and language refinement.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

Availability of Data and Materials

All data underlying the results are available as part of the article and no additional source data are required.

REFERENCES

1. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Preterm birth. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY, editors. Williams obstetrics. 23rd ed. New York: McGraw-Hill; 2010. p. 804-21.
2. Dayal S, Jenkins SM, Hong PL. Preterm and term prelabor rupture of membranes (PPROM and PROM). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 May 2]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532888/
3. Vaduva CC, Petrescu AM, Dira LM, Ruican D, Pana RC. Probiotics in the prophylaxis of premature rupture of membranes and cervical incompetence. Nutrients. 2024;16(23):4230.
4. Xu L, Yang T, Wen M, Wen D, Jin C, An M, et al. Frontiers in the etiology and treatment of preterm premature rupture of membrane: from molecular mechanisms to innovative therapeutic strategies. Reprod Sci. 2024;31(4):917-31.
5. Mohammed HA, Heraiz A. Contribution of vaginal infection to preterm premature rupture of membrane and adverse pregnancy outcome. Microbes Infect Dis. 2022;3(1):101-11.
6. Brown RG, Marchesi JR, Lee YS, Smith A, Lehne B, Kindinger LM, et al. Vaginal dysbiosis increases risk of preterm fetal membrane rupture, neonatal sepsis and is exacerbated by erythromycin. BMC Med. 2018;16:1-5.
7. Liu P, Lu Y, Li R, Chen X. Use of probiotic lactobacilli in the treatment of vaginal infections: in vitro and in vivo investigations. Front Cell Infect Microbiol. 2023;13:1153894.
8. Gorczyca K, Koziol MM, Kimber-Trojnar Z, Kepa J, Satora M, Rekowska AK, et al. Premature rupture of membranes and

changes in the vaginal microbiome-probiotics. Reprod Biol. 2024;24(3):100899.
9. Kahvazi F, Rahimi K, Soufizadeh N, Zare S, Seyedoshohadaei F, Rahmani K. The effects of vaginal probiotic administration on perinatal outcomes in patients with premature preterm rupture of membrane. Arch Obstet Gynaecol. 2022;3:59-63.
10. Othman M, Alfirevic Z, Neilson JP. Probiotics for preventing preterm labour. Cochrane Database Syst Rev. 2007;(1):CD005941.
11. Baradwan S, AlSghan R, Sabban H, Khadawardi K, Ali ZA, Felemban LH, et al. Vaginal probiotics as an adjunct to antibiotic prophylaxis in the management of preterm premature rupture of membranes: a systematic review and meta-analysis of randomized controlled trials. Eur J Obstet Gynecol Reprod Biol. 2023;287:100-1.
12. Singh M, Alsaleem M, Gray CP. Neonatal sepsis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 May 2]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK531478/
13. Moraes DV, Queiroz DB, Eleutério J Jr. Vaginal probiotics on the outcomes of premature rupture of membranes: a pilot randomised clinical trial. J Obstet Gynaecol. 2022;42(8):3527-30. doi:10.1080/01443615.2022.2151349.
14. Daskalakis GJ, Karambelas AK. Vaginal probiotic administration in the management of preterm premature rupture of membranes. Fetal Diagn Ther. 2017;42(2):92-8.
15. Sowmya B, Kar D, Panigrahy R, Pati B. A comparative observational study on effectiveness of probiotics and antibiotics in bacterial vaginosis. Indones J Public Health. 2023;18(3):409.
16. Ibrahim FA, Mostafa MK, Farahat MM. Vaginal probiotic administration in the management of preterm premature rupture of membranes. Egypt J Hosp Med. 2018;73(10):7672-82.
17. Yadav J, Das V, Kumar N, Agrawal S, Pandey A, Agrawal A. Vaginal probiotics as an adjunct to antibiotic prophylaxis in the management of preterm premature rupture of the membranes. J Obstet Gynaecol. 2022;42(5):1037-42.
18. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
19. Aromataris E, Munn Z, editors. JBI manual for evidence synthesis [Internet]. Adelaide: JBI; 2020 [cited 2026 May 2]. Available from: https://synthesismanual.jbi.global/
20. Romero R, Miranda J, Chaiworapongsa T, Korzeniewski SJ, Chaemsaithong P, Gotsch F, et al. Prevalence and clinical significance of sterile intra-amniotic inflammation in patients with preterm labor and intact membranes. Am J Reprod Immunol. 2014;72(5):458-74.
21. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet. 2008;371(9606):75-84.
22. DiGiulio DB, Romero R, Amogan HP, Kusanovic JP, Bik EM, Gotsch F, et al. Microbial prevalence, diversity and abundance in amniotic fluid during preterm labor. PLoS One. 2008;3(8):e3056.
23. Mendz GL, Kaakoush NO, Quinlivan JA. Bacterial aetiological agents of intra-amniotic infections and preterm birth in pregnant women. Front Cell Infect Microbiol. 2013;3:58.
24. Freitas AC, Bocking A, Hill JE, Money DM. Increased richness and diversity of the vaginal microbiota and spontaneous preterm birth. Microbiome. 2018;6(1):117.
25. Kindinger LM, Bennett PR, Lee YS, Marchesi JR, Smith A, Cacciatore S, et al. The interaction between vaginal microbiota, cervical length, and vaginal progesterone treatment for preterm birth risk. Microbiome. 2017;5(1):6.
26. Fettweis JM, Serrano MG, Brooks JP, Edwards DJ, Girerd PH, Parikh HI, et al. The vaginal microbiome and preterm birth. Nat Med. 2019;25(6):1012-21.
27. Callahan BJ, DiGiulio DB, Goltsman DSA, Sun CL, Costello EK, Jeganathan P, et al. Replication and refinement of a vaginal microbial signature of preterm birth in two racially distinct cohorts. Proc Natl Acad Sci U S A. 2017;114(37):9966-71.

28. Elovitz MA, Gajer P, Riis V, Brown AG, Humphrys MS, Holm JB, et al. Cervicovaginal microbiota and local immune response modulate the risk of spontaneous preterm delivery. Nat Commun. 2019;10(1):1305.
29. Payne MS, Bayatibojakhi S. Exploring preterm birth as a polymicrobial disease: an overview of the uterine microbiome. Front Immunol. 2014;5:595.
30. Lamont RF, Sobel JD, Akins RA, Hassan SS, Chaiworapongsa T, Kusanovic JP, et al. The vaginal microbiome: new information about genital tract flora using molecular based techniques. BJOG. 2011;118(5):533-49.
31. Hillier SL, Nugent RP, Eschenbach DA, Krohn MA, Gibbs RS, Martin DH, et al. Association between bacterial vaginosis and preterm delivery of a low-birth-weight infant. N Engl J Med. 1995;333(26):1737-42.
32. Leitich H, Bodner-Adler B, Brunbauer M, Kaider A, Egarter C, Husslein P. Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. Am J Obstet Gynecol. 2003;189(1):139-47.
33. McDonald HM, O'Loughlin JA, Jolley P, Vigneswaran R, McDonald PJ. Vaginal infection and preterm labour. Br J Obstet Gynaecol. 1991;98(5):427-35.
34. Reid G, Younes JA, Van der Mei HC, Gloor GB, Knight R, Busscher HJ. Microbiota restoration: natural and supplemented recovery of human microbial communities. Nat Rev Microbiol. 2011;9(1):27-38.
35. Petrova MI, Reid G, Vaneechoutte M, Lebeer S. Lactobacillus iners: friend or foe? Trends Microbiol. 2017;25(3):182-91.
36. O'Hanlon DE, Moench TR, Cone RA. Vaginal pH and microbicidal lactic acid when lactobacilli dominate the microbiota. PLoS One. 2013;8(11):e80074.
37. Borges S, Silva J, Teixeira P. The role of lactobacilli and probiotics in maintaining vaginal health. Arch Gynecol Obstet. 2014;289(3):479-89.
38. Reid G. Probiotic lactobacilli for urogenital health in women. J Clin Gastroenterol. 2008;42 Suppl 3 Pt 2:S234-6.
39. Homayouni A, Bastani P, Ziyadi S, Mohammad-Alizadeh-Charandabi S, Ghalibaf M, Mortazavian AM, et al. Effects of probiotics on the recurrence of bacterial vaginosis: a review. J Low Genit Tract Dis. 2014;18(1):79-86.
40. Huang H, Song L, Zhao W. Effects of probiotics for the treatment of bacterial vaginosis in adult women: a meta-analysis of randomized clinical trials. Arch Gynecol Obstet. 2014;289(6):1225-34.
41. Senok AC, Verstraelen H, Temmerman M, Botta GA. Probiotics for the treatment of bacterial vaginosis. Cochrane Database Syst Rev. 2009;(4):CD006289.
42. Van de Wijgert JHHM, Jespers V. The global health impact of vaginal dysbiosis. Res Microbiol. 2017;168(9-10):859-64.
43. Peebles K, Velloza J, Balkus JE, McClelland RS, Barnabas RV. High global burden and costs of bacterial vaginosis: a systematic review and meta-analysis. Sex Transm Dis. 2019;46(5):304-11.
44. National Institute for Health and Care Excellence. Preterm labour and birth. London: NICE; 2022.
45. American College of Obstetricians and Gynecologists. Prelabor rupture of membranes: ACOG Practice Bulletin No. 217. Obstet Gynecol. 2020;135(3):e80-e97.
46. Mercer BM. Preterm premature rupture of the membranes. Obstet Gynecol. 2003;101(1):178-93.
47. Waters TP, Mercer B. Preterm PROM: prediction, prevention, principles. Clin Obstet Gynecol. 2011;54(2):307-12.
48. Menon R, Richardson LS. Preterm prelabor rupture of the membranes: a disease of the fetal membranes. Semin Perinatol. 2017;41(7):409-19.
49. Caughey AB, Robinson JN, Norwitz ER. Contemporary diagnosis and management of preterm premature rupture of membranes. Rev Obstet Gynecol. 2008;1(1):11-22.
50. Lee SE, Romero R, Park CW, Jun JK, Yoon BH. The frequency and significance of intra-amniotic inflammation in patients with cervical insufficiency. Am J Obstet Gynecol. 2008;198(6):633.e1-633.

Table 1. Characteristics of included randomized controlled trials.

Study	Population	Sample size (I vs C)	Probiotic regimen	Treatment/follow-up	Key outcomes (I vs C)	Interpretation
Daskalakis et al., 2017 [14]	PPROM, 24–34 weeks	49 vs 57	EcoVag Balance vaginal capsules: L. rhamnosus DSM 14870 and L. gasseri DSM 14869 (1×10^8 CFU); adjunct to standard antibiotics	Three vaginal doses daily for 10 days; maternal and neonatal outcomes assessed through delivery and neonatal hospitalization	GA at delivery: 35.49 vs 32.53 weeks; birth weight: 2439.1 vs 2004.8 g; NICU/special care admission: 27.1% vs 56.1%	Longer latency and improved selected neonatal outcomes; small single-center trial
Ibrahim et al., 2018 [16]	PPROM	33 vs 34	Vaginal probiotic plus standard antibiotic prophylaxis; exact strain/CFU should be checked against the full trial report	Administered during expectant management; follow-up through delivery and neonatal admission	GA at delivery: 34.5 vs 32.0 weeks; birth weight: 2224 vs 1947 g; NICU admission: 24.3% vs 55.8%	Potential neonatal benefit; reporting of allocation and regimen details was incomplete
Yadav et al., 2022 [17]	PPROM, 24–34 weeks	52 vs 54	Vaginal probiotic adjunctive to standard antibiotic prophylaxis; formulation details as reported by the trial authors	Treatment during expectant management; follow-up through delivery and neonatal hospitalization	GA at delivery: 31.58 vs 31.50 weeks; birth weight: 1555.3 vs 1605.7 g; NICU admission: 42.3% vs 42.6%	No significant latency or gestational-age benefit; selected neonatal outcomes were reported as better
Moraes et al., 2022 [13]	PROM, 24–36 weeks	16 vs 11	Vaginal L. rhamnosus plus L. gasseri with standard treatment versus placebo with standard treatment	Pilot triple-blind trial; treatment and follow-up continued during the latency period through delivery	Latency period and GA at delivery were higher in the probiotic group; most other outcomes showed little variation	Very small pilot trial; estimates are imprecise and not directly comparable with PPROM-only trials