

Global Insights and Key Trends in Gut Microbiota Research for Premature Infants: A Bibliometric and Visualization Study

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Background: Premature infants, defined as those born before 37 weeks of gestation, face numerous health challenges due to their underdeveloped systems. One critical aspect of their health is the gut microbiota, which plays a vital role in their immune function and overall development. This study provides a comprehensive bibliometric analysis of research trends, influential contributors, and evolving themes in the study of gut microbiota in premature infants over the past two decades.

Methods: We conducted a bibliometric analysis using the Web of Science Core Collection database, covering publications from January 1, 2004, to June 17, 2024. We employed VOSviewer, the R package “bibliometrix”, and Citespace for data visualization and analysis, focusing on co-authorship, co-citation, and keyword co-occurrence networks.

Results: The temporal analysis revealed a significant increase in research output on gut microbiota in premature infants, particularly in the last decade. Early research primarily focused on characterizing the gut microbiota of premature infants, identifying less diversity and a higher prevalence of pathogenic bacteria compared to full-term infants. Key research themes identified include probiotics, necrotizing enterocolitis (NEC), and breastfeeding. Probiotic studies highlighted the potential of strains like *Bifidobacterium* and *Lactobacillus* in reducing NEC and sepsis incidences. Breastfeeding research consistently showed the benefits of human milk in fostering a healthier gut microbiota profile. Co-authorship and co-citation analyses identified key contributors and influential studies, emphasizing strong international collaborations, particularly among researchers from the United States, China, and European countries.

Conclusion: This bibliometric analysis underscores the growing recognition of the gut microbiota's crucial role in the health of premature infants. The field has seen significant advancements, particularly in understanding how interventions like probiotics and breastfeeding can modulate gut microbiota to improve health outcomes. Continued research and international collaboration are essential to further unravel the complexities of gut microbiota in premature infants and develop effective therapeutic strategies.

Keywords: premature infants, gut microbiota, web of science, bibliometric analysis

Introduction

Premature infants, defined as those born before 37 weeks of gestation, represent a significant public health concern globally due to their high prevalence and associated health complications. The incidence of preterm birth varies widely across different regions, with rates as high as 15% in some areas.^{1,2} These infants are at increased risk for a myriad of short-term and long-term health issues, including respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, and sepsis.³⁻⁵ Long-term complications often extend into childhood and adulthood, manifesting as chronic lung disease, neurodevelopmental impairments, and growth abnormalities.⁶⁻⁸ The early-life challenges faced by premature infants necessitate a comprehensive understanding of their unique physiological and developmental needs to improve survival rates and quality of life.

The gut microbiota plays a crucial role in the health and development of infants, particularly those born prematurely. Premature infants often exhibit a distinct and less diverse gut microbiota compared to full-term infants, characterized by a higher prevalence of pathogenic bacteria and a lower abundance of beneficial microbes such as Bifidobacteria and Lactobacillus species.^{9–12} This dysbiosis is associated with a higher risk of severe complications, including necrotizing enterocolitis (NEC), sepsis, and long-term impacts on immune and metabolic functions.^{13–15} Research into the gut microbiota of premature infants is essential for understanding these associations and developing targeted interventions. Recent studies have highlighted the potential benefits of probiotic supplementation, breastfeeding, and other microbiome-modulating therapies in promoting a healthier gut microbiota composition.^{16–18} For instance, a growing body of evidence suggests that specific probiotics may help prevent NEC and reduce the incidence of sepsis.^{11,19} Advanced sequencing technologies and bioinformatics tools have enabled more detailed and comprehensive analyses of the gut microbiota, uncovering critical insights into the microbial dynamics and their interactions with the host.²⁰ These advancements underscore the necessity of ongoing research to elucidate the precise mechanisms by which gut microbiota influences the health outcomes of premature infants and to identify effective strategies for microbiota-based therapies.

Bibliometrics is a set of methods used to quantitatively analyze scientific literature and measure the impact and development of research in various fields. This analytical approach involves the application of statistical and mathematical techniques to evaluate the quantity and quality of published research, citations, and other academic outputs.²¹ Key features of bibliometrics include citation analysis, co-citation analysis, bibliographic coupling, and the use of various bibliometric indicators such as the impact factor, and citation counts. These tools enable researchers to identify trends, patterns, and the overall influence of specific works, authors, institutions, and journals within a scientific domain.

The importance of bibliometric analysis lies in its ability to provide a comprehensive overview of research activities, highlight influential studies and emerging hotspots, and inform policy and funding decisions. By mapping the intellectual structure of a field, bibliometrics helps to uncover key research themes, collaborations, and knowledge gaps, guiding future research directions. In the context of gut microbiota and premature infants, bibliometric studies can reveal the evolution of research focus, identify leading researchers and institutions, and assess the impact of interventions and new discoveries over time. This systematic evaluation is crucial for advancing our understanding of the role of gut microbiota in premature infant health and for optimizing research strategies to improve clinical outcomes. Given the significant role of gut microbiota in the health of premature infants, it is noteworthy that no previous studies have employed bibliometric analysis to explore this topic comprehensively. Therefore, this study aims to fill this gap by conducting a bibliometric analysis of research on the role of gut microbiota in premature infants. By doing so, we hope to provide valuable insights into the research landscape and identify key trends and future directions in this critical area of study.

Materials and Methods

Data Sources and Literature Search

We selected the Web of Science (WoS) Core Collection as the sole database for this study due to its high-quality indexing and comprehensive coverage of influential, peer-reviewed journals. WoS is known for its robust citation tracking and is widely used in bibliometric research. While other databases like Scopus and Lens offer broader coverage, our focus was to capture the most impactful studies, ensuring the analysis reflects high-quality research outputs. The literature search covered publications from January 1, 2004, to June 17, 2024. The search strategy was designed to capture studies focusing on the role of gut microbiota in preterm or premature infants. The specific search terms used were: (TS= (preterm) OR TS = (premature)) AND (TS = (gut microbiota) OR TS = (Gastrointestinal Microbiome) OR TS = (Gut Microbiome) OR TS= (Gut microbiome) OR TS= (Intestinal Microbiota) OR TS= (Intestinal Microflora) OR TS= (Intestinal Flora)). The search was restricted to articles and reviews to ensure the inclusion of peer-reviewed and substantive research contributions. Additionally, only publications written in English were included in the analysis.

Data Analysis and Visualization

The collected data were analyzed using several bibliometric tools to ensure comprehensive and multifaceted insights. For the analysis and visualization of the bibliometric data, we employed VOSviewer (version 1.6.19),²² the R package

“bibliometrix” (version 4.3.1),²³ and Citespace (version 6.2.R4).²⁴ VOSviewer was used to construct and visualize bibliometric networks, facilitating the creation of maps based on co-authorship, co-citation, and keyword co-occurrence, which allowed us to identify relationships and patterns within the research landscape. The R package “bibliometrix” provided various statistical and graphical tools to evaluate and visualize the scientific literature, including citation analysis, trend analysis, and the identification of prolific authors, institutions, and countries. Citespace was utilized for visualizing and analyzing trends and patterns in scientific literature, aiding in detecting research frontiers, identifying critical turning points, and visualizing the temporal evolution of the research field through co-citation and cluster analysis.

Results

Trends in Publications on Premature Infants and Gut Microbiome

Figure 1A shows the flowchart of the bibliometric analysis process, detailing the steps taken to identify relevant publications from the Web of Science Core Collection. From this search, 1860 publications were initially identified. After refining the criteria to include only articles and reviews published in English from January 2004 to June 2024, a total of 1702 publications were included for the bibliometric analysis. Figure 1B illustrates the annual distribution of these publications. The trend indicates a significant and steady increase in the number of publications over the years. Initially, from 2004 to 2010, there was a gradual rise in publications, with a more noticeable growth starting around 2011.

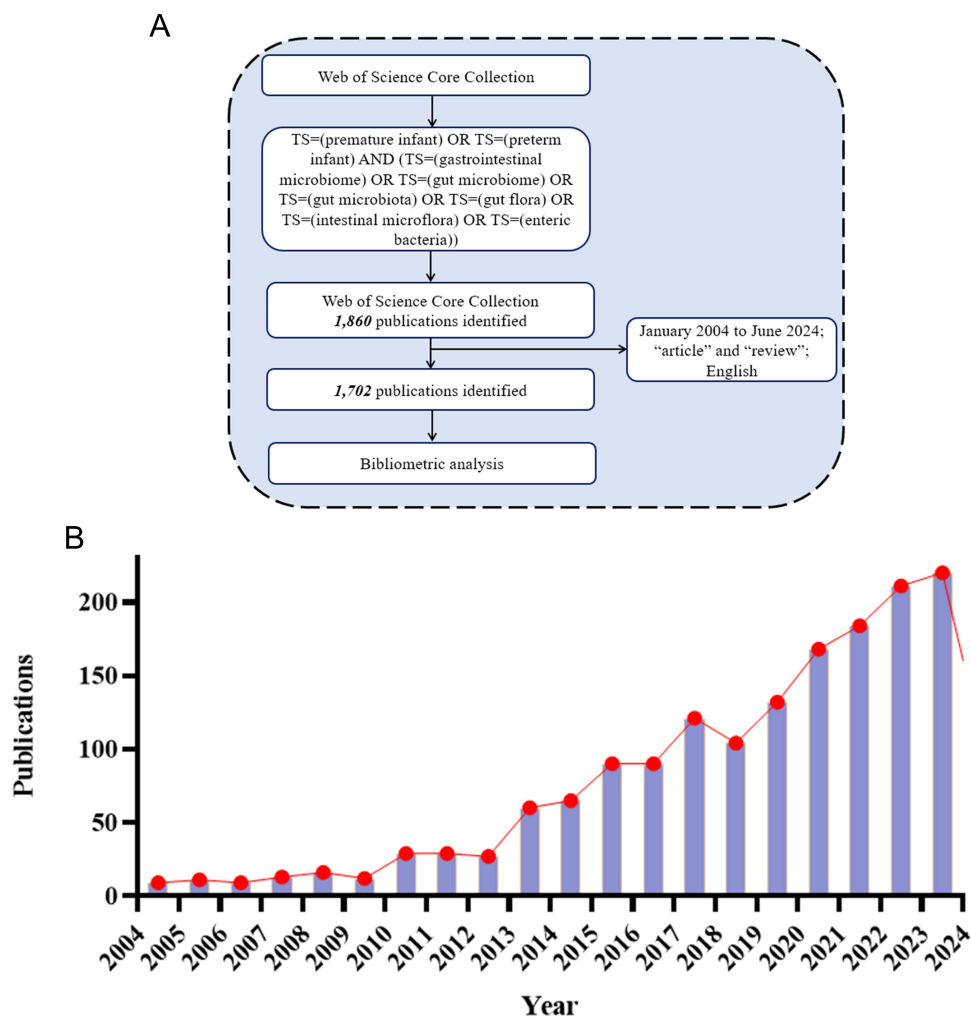


Figure 1 (A) Flowchart of the literature searching and screening in the study. (B) Global trend of publications on gut microbiota in premature infants research.

A marked acceleration can be observed from 2015 onwards, peaking in recent years. The data suggest that research interest in the gut microbiome of premature infants has intensified, particularly in the last decade.

Global Research Collaboration and Productivity in Preterm Infant and Gut Microbiota Studies

Figure 2A illustrates the global collaboration network in research on preterm infants and gut microbiota. The map shows significant collaboration among leading countries, with prominent connections between the United States, China, and European countries including United Kingdom, Spain, Norway, etc. These strong links indicate frequent co-authorship and joint research efforts, highlighting the international nature of research in this field. Figure 2B presents the top 10 countries contributing to research on preterm infants and gut microbiota. The United States leads with the highest number of publications, followed by China, the United Kingdom, Italy, and Germany. Other notable contributors include Canada, Australia, France, Spain, and Japan. This ranking underscores the substantial research output from these countries and their leading roles in advancing the field. Notably, the publication volumes in the United States and China have increased significantly in recent years, reflecting growing research interest and investment in this area. Figure 2C displays the co-occurrence network of countries involved in preterm infant and gut microbiota research. The network highlights the United States as the central node with the highest co-occurrence with other countries, reflecting its pivotal role in global research collaborations. China, the United Kingdom, and Germany also show strong co-occurrence links, indicating their significant collaborative efforts. Figure 2D showcases the institutional co-occurrence network, depicting the relationships and collaborative patterns among different research institutions. The leading institutions with the most extensive collaborative networks include Harvard University, the University of California, and the University of London. Other key institutions include the Chinese Academy of Sciences, Stanford University, and the University of Sydney. Table 1

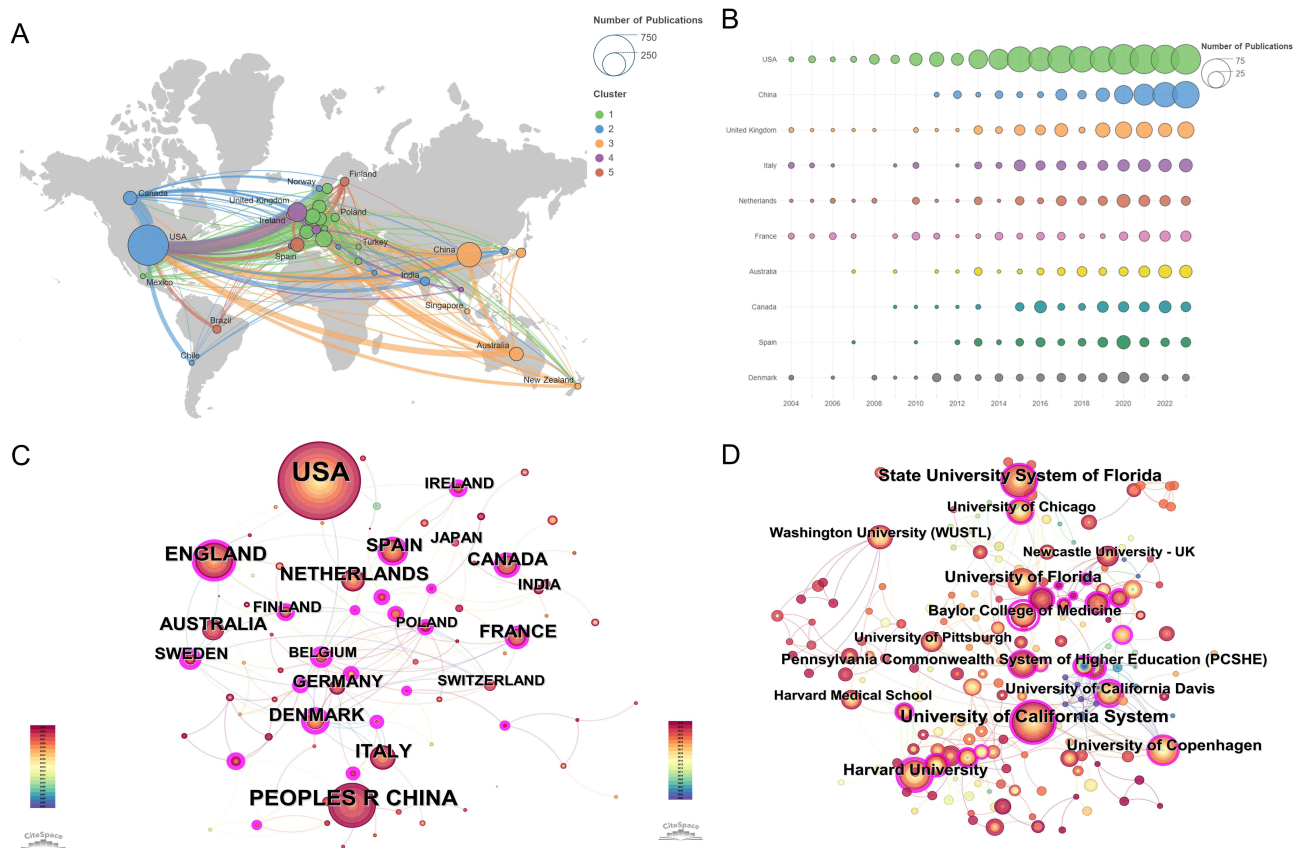


Figure 2 Collaboration networks for gut microbiota in premature infants research. (A) Global collaboration network map. (B) Publication trends of the top ten countries by number of publications. (C) Country/region collaboration. (D) Institution Collaboration.

Table 1 Top 10 Countries and Institutions on Research of Gut Microbiota and Premature Infants

Rank	Country	Count	Institution	Count
1	United States	697 (40.9%)	University of Florida (United States)	65 (3.8%)
2	China	236 (13.8%)	University of Copenhagen (Denmark)	57 (3.3%)
3	United Kingdom	141 (8.2%)	University of Chicago (United States)	47 (2.7%)
4	Italy	114 (6.6%)	University of California, Davis (United States)	47 (2.7%)
5	Netherlands	94 (5.5%)	University of Pittsburgh (United States)	44 (2.5%)
6	France	81 (4.7%)	Baylor College of Medicine (United States)	40 (2.3%)
7	Canada	80 (4.7%)	Washington University (United States)	39 (2.2%)
8	Australia	80 (4.7%)	Newcastle University (United Kingdom)	26 (1.5%)
9	Spain	78 (4.5%)	Harvard Medical School (United States)	25 (1.4%)
10	Denmark	75 (4.4%)	University of Bologna (Italy)	23 (1.3%)

summarized top ten countries and institutions on research of gut microbiota and premature infants. These institutions are central to the research network, driving significant collaborative research and contributing to the field's advancements.

Key Authors in the Research Field

The co-authorship analysis reveals several key contributors who have significantly impacted the research field of preterm infants and gut microbiota (Figure 3A). Josef Neu emerges as a central figure, actively contributing significant research efforts. Michael J. Morowitz follows closely, reflecting his consistent contributions and collaborations. Janet E. Berrington and Mark A. Underwood have been actively involved, highlighting their collaborative efforts in advancing the field. Nicholas D. Embleton also stands out for his significant collaborative research. These authors represent the core network driving the research forward through their extensive collaborations and shared expertise. The co-citation analysis identifies influential authors whose works are frequently cited together, signifying their foundational role in the field (Figure 3B). HARMSEN HJM is particularly prominent, indicating the substantial and sustained impact of their research. DE LACOCHEIÈREMF also plays a critical role, demonstrating widespread influence in the literature. DIGIULIO DB has widespread influence and is frequently cited. Additionally, DANI C and KUNZ C, though less frequent, still hold significant contextual importance. Table 2 displays the top ten authors and co-cited authors on research of gut microbiota and premature infants. These co-citation patterns highlight the foundational and frequently referenced contributions of these authors, underscoring their critical role in shaping current understanding and guiding future research in the field.

Journal Co-Citation and Overlay Analysis

The co-citation network of journals, as illustrated in Figure 4A, highlights the primary journals contributing to the research field. The figure reveals a dense network of co-cited journals, indicating a well-connected body of literature. Prominent journals such as the Journal of Pediatrics, Pediatric Research, and Journal of Clinical Investigation appear frequently, showcasing their significant influence in this research area. This interconnectedness suggests a strong collaborative network among researchers, emphasizing the integral role these journals play in disseminating research findings related to premature infants and gut microbiota. Figure 4B presents a dual-map overlay of journals, illustrating the citation relationships between different disciplines. The overlay map shows that research related to premature infants and gut microbiota spans across multiple fields, including medicine, microbiology, and nutrition. The citing journals are predominantly from the fields of health, medicine, and clinical sciences, while the cited journals span broader categories such as molecular biology, immunology, and genetics. Table 3 displays the top 10 journals and co-cited journals on research of gut microbiota and premature infants. This distribution underscores the multidisciplinary nature of this research area, highlighting how advancements in understanding premature infant health and gut microbiota are informed by a wide range of scientific disciplines.

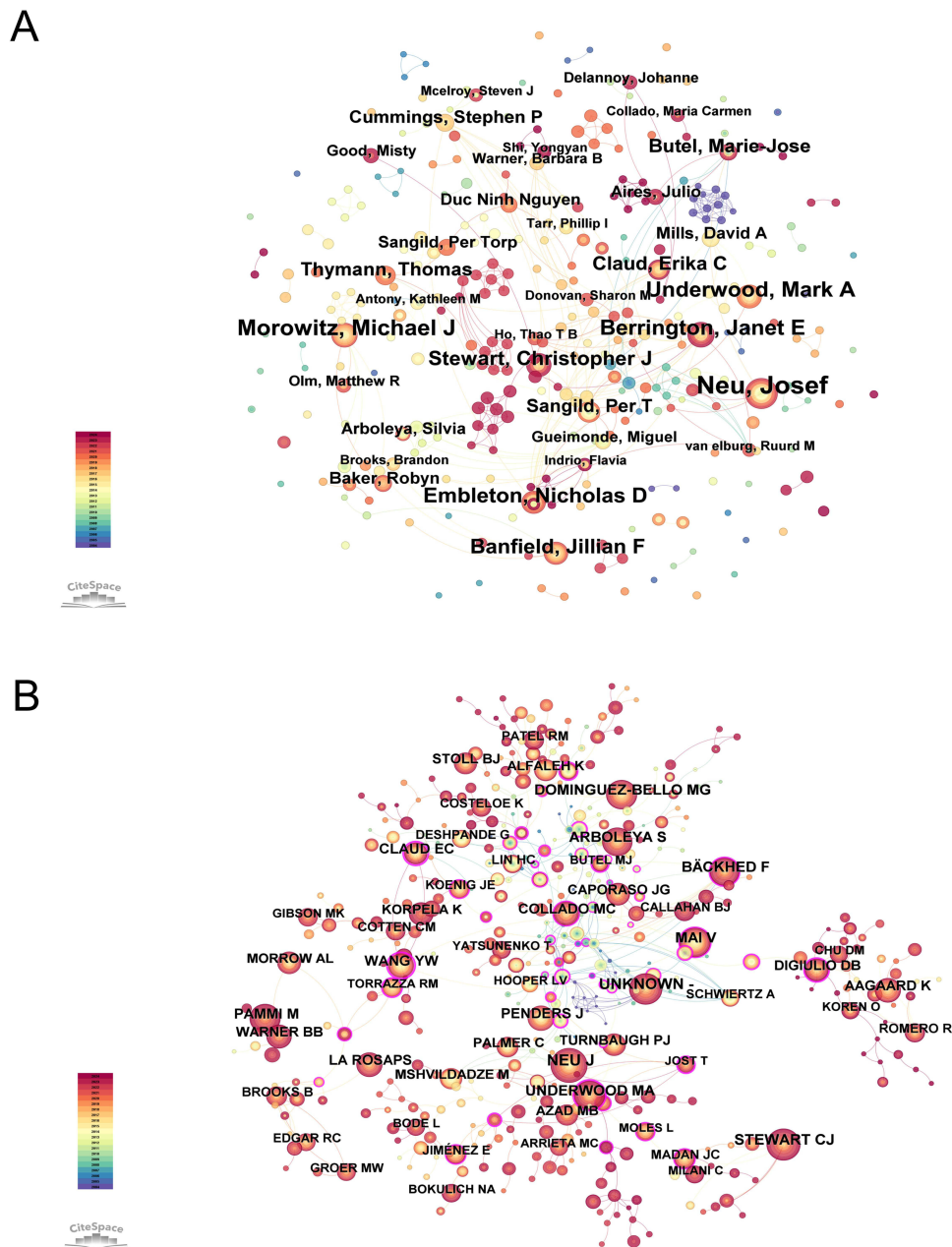


Figure 3 Visualiaztion of authors and co-cited authors. **(A)** Visual representation of authors on the research of gut microbiota in premature infants. **(B)** Visual presentation of co-cited authors on the research of gut microbiota in premature infants.

Analysis of Article Citations and Co-Citations

Figure 5A illustrates the article citation network within the field of neonatal gut microbiota research. Prominent works such as those by Aagaard K. (2014), Warner BB. (2016), and Stewart CJ. (2018) are highly cited, indicating their substantial influence on subsequent research. The visualization showcases dense clusters of citations, reflecting the foundational impact these studies have had in shaping current understanding and ongoing investigations. Figure 5B depicts the co-citation network, highlighting key articles frequently cited together. Influential studies by authors such as Warner BB. (2016), Stewart CJ. (2018), and Aagaard K. (2014) appear prominently, underscoring their integral roles in the field. The network reveals strong co-citation clusters, indicating the interconnectedness of these pivotal works. Table 4 displays the top 10 co-cited references on research of gut microbiota and premature infants.

Table 2 Top 10 Authors and Co-Cited Authors on Research of Gut Microbiota and Premature Infants

Rank	Authors	Count	Co-cited authors	Citations
1	Josef Neu	44	Josef Neu	545
2	Mark A Underwood	32	Christopher J Stewart	482
3	Michael J Morowitz	30	Silvia Arboleya	401
4	Christopher J Stewart	25	Mark A Underwood	368
5	Thomas Thymann	25	Maria Gloria Dominguez Bello	315
6	Erika C Claud	24	Rene Romero	303
7	Nicholas D Embleton	24	Fredrik Bäckhed	295
8	Janet E Berrington	23	Volker Mai	292
9	Jillian F Banfield	20	Mohan Pammi	282
10	Per Torp Sangild	19	John Penders	277

Keyword Analysis

Figure 6A illustrates the keyword co-occurrence network, highlighting key terms frequently used together in the research field of premature infants and gut microbiota. Prominent keywords include “preterm infants”, “probiotics”, “intestinal microbiota”, “necrotizing enterocolitis”, and “bacterial colonization”. These keywords reflect major research themes and focus areas, such as the role of gut microbiota in the health and disease states of premature infants, the use of probiotics, and the study of specific conditions like necrotizing enterocolitis. The network also shows connections between various terms, indicating the interdisciplinary nature and integration of multiple research aspects within this field. Figure 6B presents the keyword cluster network map, identifying nine major clusters that represent distinct research topics. The largest cluster, labeled “#0 intensive care unit”, encompasses studies related to the care and management of preterm infants in intensive care settings. Cluster “#1 birth weight infants” focuses on issues related to birth weight and its implications. Other significant clusters include “#2 human milk”, which highlights the importance of breast milk in the development of gut microbiota, “#3 bronchopulmonary dysplasia”, and “#4 necrotizing enterocolitis”, both addressing critical conditions affecting preterm infants. Additional clusters such as “#5 gut microbiota”, “#6 supplementation”, “#7 double blind”, “#8 risk”, and “#9 preterm infant” further emphasize the diverse range of research areas, from clinical interventions and dietary supplements to methodological approaches and risk assessments.

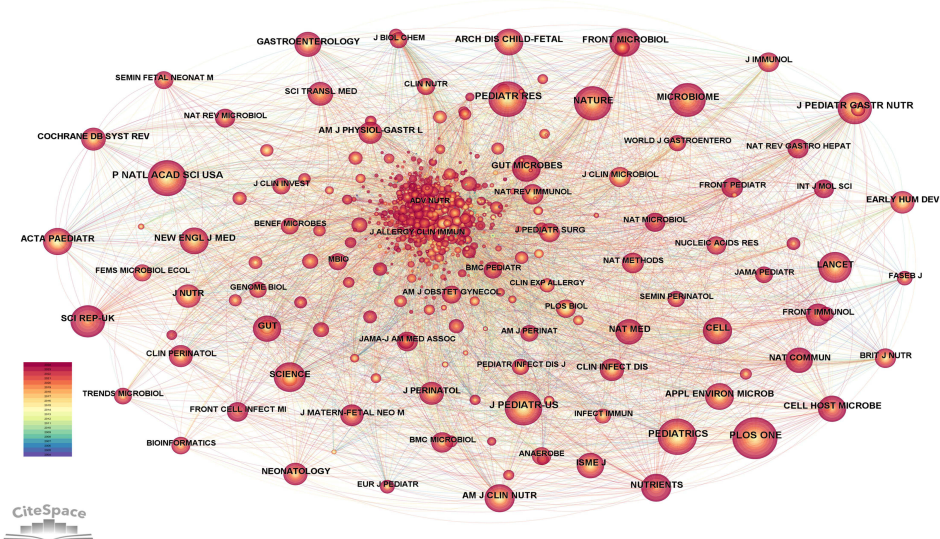
The cluster timeline view network of keywords illustrates the temporal evolution of research topics related to gut microbiota in premature infants (Figure 7A). Key clusters identified include “intensive care unit”, “birth weight infants”, “human milk”, “bronchopulmonary dysplasia”, and “gut microbiota”. Over the years, the focus has shifted from general topics like “premature infants” and “probiotics” to more specific areas such as “oxidative stress”, “donor human milk”, and “vaginal microbiota”. This demonstrates a growing diversification and specialization in research topics over time. The timezone chart maps the progression and emergence of various keywords over the specified timeline (Figure 7B). Early research concentrated on foundational topics like “bacteria”, “probiotics”, and “intestinal flora”. Recent years have seen an increased emphasis on clinical and applied aspects such as “oxidative stress”, “gestational age”, “human breast milk”, and “neonatal sepsis”. This shift indicates an expanding interest in understanding specific factors influencing gut microbiota in premature infants and their clinical implications.

Figure 8 illustrates the top 15 keywords with the most substantial citation bursts in the study of gut microbiota in premature infants. The blue bars represent periods when the keywords were rarely cited, while the red bars indicate times of frequent citation. Keywords such as “gut microbiota”, “probiotics”, and “preterm infants” show significant bursts, reflecting their increasing importance and interest in recent research.

Discussion

This study provides a comprehensive bibliometric analysis of research on gut microbiota in premature infants, demonstrating significant trends, influential contributors, and evolving research themes over the past two decades. The results

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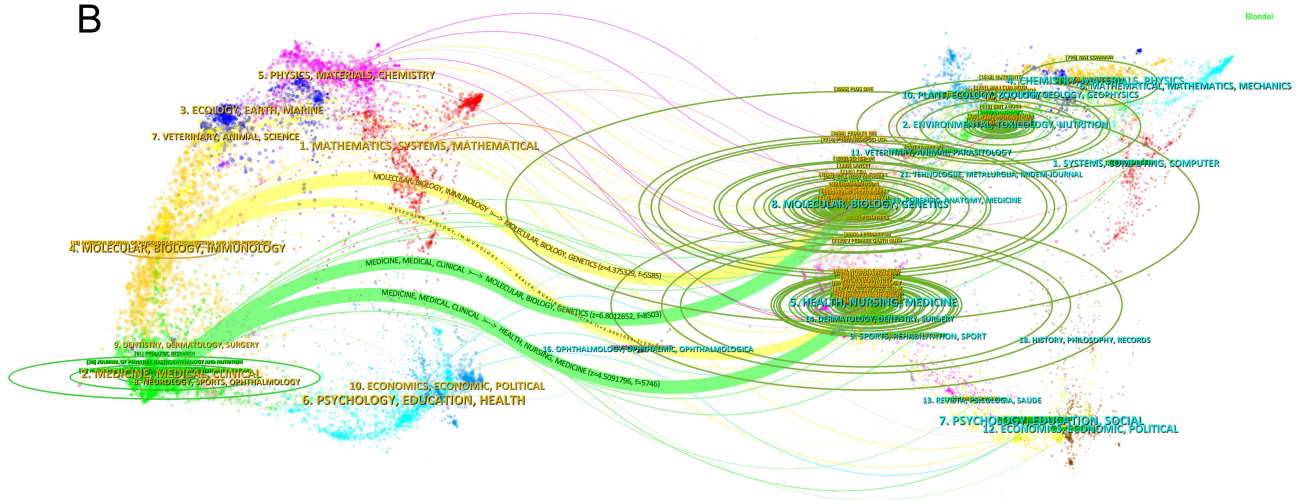


Figure 4 Visualization of co-journals involvement. **(A)** Visual presentation of co-citations among journals on the research of gut microbiota in premature infants. **(B)** The dual-map overlay of journals on the research of gut microbiota in premature infants.

illustrate a marked increase in research activity, particularly in the last decade, highlighting the growing recognition of the gut microbiota’s critical role in the health and development of preterm infants.

The temporal analysis of publications revealed a substantial increase in research output on gut microbiota in premature infants. Early studies focused on identifying the differences in gut microbiota between premature and full-

Table 3 Top 10 Journals and Co-Cited Journals on Research of Gut Microbiota and Premature Infants

Rank	Journal	Count	IF	Q	Co-cited Journal	Co-citation	IF	Q
1	Nutrients	78 (4.5%)	5.9	Q1	PLoS One	3962	3.7	Q1
2	Pediatric Research	61 (3.5%)	3.6	Q1	Pediatrics	2913	8.0	Q1
3	PLoS One	48 (2.8%)	3.7	Q2	Pediatric Research	2438	3.6	Q1
4	Frontiers in Microbiology	46 (2.7%)	5.2	Q2	Journal of Pediatrics	2332	5.1	Q1
5	Frontiers in Pediatrics	46 (2.7%)	2.6	Q2	Nature	2303	64.8	Q1

(Continued)

Table 3 (Continued).

Rank	Journal	Count	IF	Q	Co-cited Journal	Co-citation	IF	Q
6	Journal of Pediatric Gastroenterology and Nutrition	36 (2.1%)	2.9	Q2	Proceedings of the National Academy of Sciences (PNAS)	2214	11.1	Q1
7	Microorganisms	33 (1.9%)	4.5	Q2	Journal of Pediatric Gastroenterology and Nutrition	2120	2.9	Q2
8	Frontiers in Immunology	33 (1.9%)	7.3	Q1	Microbiome	2047	15.5	Q1
9	Scientific Reports	32 (1.8%)	4.6	Q2	Nutrients	1619	5.9	Q1
10	Microbiome	28 (1.6%)	15.5	Q1	Scientific Reports	1578	4.6	Q2

term infants, finding that premature infants often have less diverse gut microbiota and a higher prevalence of pathogenic bacteria.^{35–37} These initial findings spurred further research into interventions aimed at modulating the gut microbiota to improve health outcomes.^{38,39} The keyword analysis identified major research themes, including probiotics, NEC, and

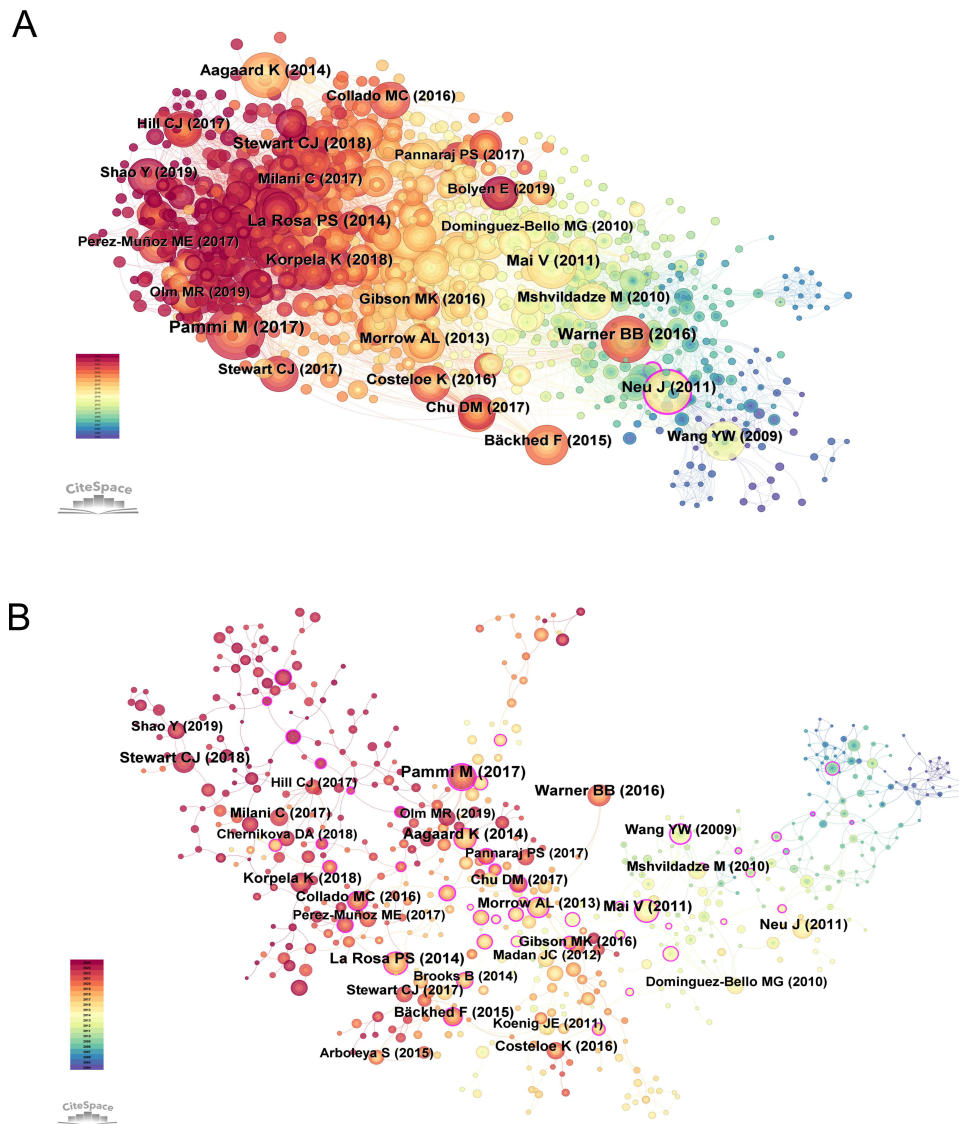


Figure 5 The visualization of references and co-cited references. (A) Visual representation of references on the research of gut microbiota in premature infants. (B) Visual presentation of co-cited references on the research of gut microbiota in premature infants.

Table 4 Top 10 Co-Cited References on Research of Gut Microbiota and Premature Infants

Rank	Co-cited reference	Citations
1	Dominguez-Bello MG, 2010, P Natl Acad Sci USA, v107, p11971 ²⁵	236
2	Neu J, 2011, New Engl J Med, v364, p255 ²⁶	229
3	Wang YW, 2009, ISME J, v3, p944 ²⁷	216
4	Penders J, 2006, Pediatrics, v118, p511 ²⁸	203
5	La Rosa Ps, 2014, P Natl Acad Sci USA, v111, p12522 ²⁹	200
6	Mai V, 2011, PLoS One, v6 ³⁰	188
7	Pammi M, 2017, Microbiome, v5 ³¹	181
8	Bäckhed F, 2015, Cell Host Microbe, v17, p690 ³²	179
9	Palmer C, 2007, PLoS Biol, v5, p1556 ³³	165
10	Aagaard K, 2014, Sci Transl Med, v6 ³⁴	164

breastfeeding. Studies on probiotics have shown that specific strains, such as *Bifidobacterium* and *Lactobacillus*, can reduce the incidence of NEC and sepsis, highlighting the potential of probiotic supplementation as a preventive strategy. A landmark study by Underwood et al demonstrated that the administration of *Bifidobacterium longum* subsp. *infantis* in preterm infants led to significant colonization and subsequent reduction in the incidence of NEC and sepsis.⁴⁰ Research on breastfeeding has consistently shown that human milk is beneficial for the gut microbiota development in premature infants, promoting a more favorable microbial profile compared to formula feeding. For example, Patel et al found that human milk feeding is associated with a lower incidence of NEC and promotes the colonization of beneficial bacteria like *Bifidobacteria* and *Lactobacillus*.⁴¹

The co-authorship analysis identified key contributors, such as Josef Neu and Michael J. Morowitz, who have significantly impacted the field through extensive research and collaborations. Neu's work has been pivotal in advancing the understanding of the developmental biology of the preterm gut and its microbial colonization. Morowitz's research has focused on the dynamics of gut microbiota in relation to neonatal sepsis and NEC, providing critical insights into the prevention and treatment of these conditions. The co-citation network highlighted influential studies that are foundational to the current understanding of gut microbiota in preterm infants. For instance, the work of Arboleya et al on the microbial succession in the neonatal gut has been frequently cited, underscoring its importance in the field.⁴²

International collaboration networks showed strong research connections between the United States, China, and European countries, emphasizing the global effort to advance this field. Collaborative studies across these regions have been instrumental in sharing knowledge, standardizing methodologies, and conducting large-scale clinical trials. These international efforts have accelerated the pace of discovery and facilitated the translation of research findings into clinical practice, ultimately improving outcomes for premature infants globally.

Recent studies have provided deeper insights into the mechanisms by which gut microbiota influences the health of premature infants. The role of gut microbiota in modulating the immune system and its impact on inflammatory responses has been a critical area of research. For instance, Warner et al highlighted that preterm infants often exhibit delayed colonization with commensal bacteria and a higher prevalence of potentially pathogenic microorganisms. This dysbiosis is linked to life-threatening conditions such as NEC and late-onset sepsis, emphasizing the importance of understanding microbial dynamics in this vulnerable population.⁴³ Advanced sequencing technologies have allowed researchers to characterize the gut microbiota more accurately, uncovering critical insights into microbial composition and interactions. For example, studies by Stewart et al and Hill et al utilized 16S rRNA gene sequencing to identify significant differences in gut microbial communities between preterm infants and full-term controls. Their findings revealed a higher abundance of Proteobacteria in preterm infants, which is associated with increased inflammation and infection risks.^{44,45} Another significant finding from these studies was the impact of feeding type on gut microbiota development. Research by Morrow et al demonstrated that preterm infants fed with mother's own breast milk (MBM) had a more beneficial microbiota composition compared to those fed with donor milk or formula. Specifically, MBM-fed

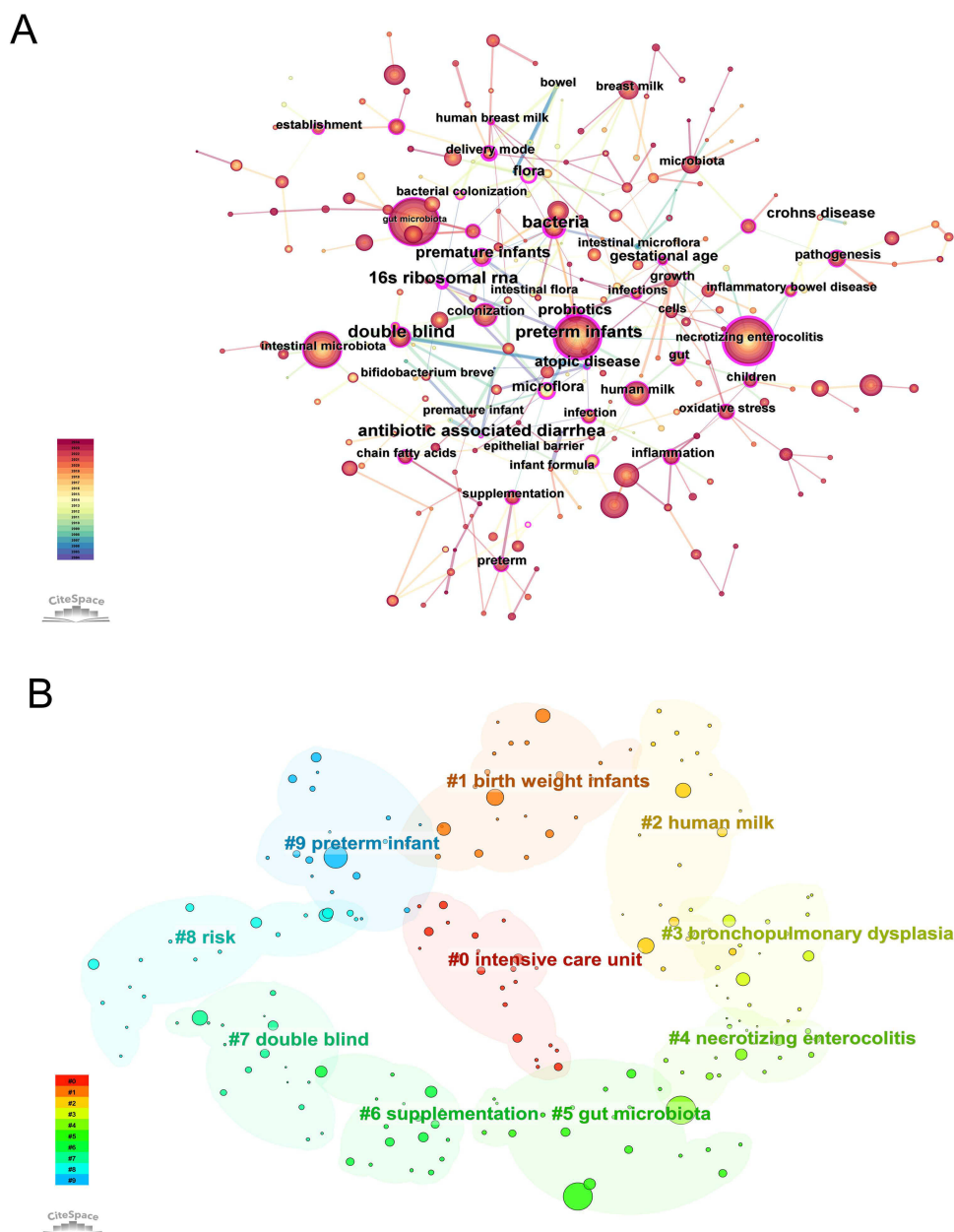
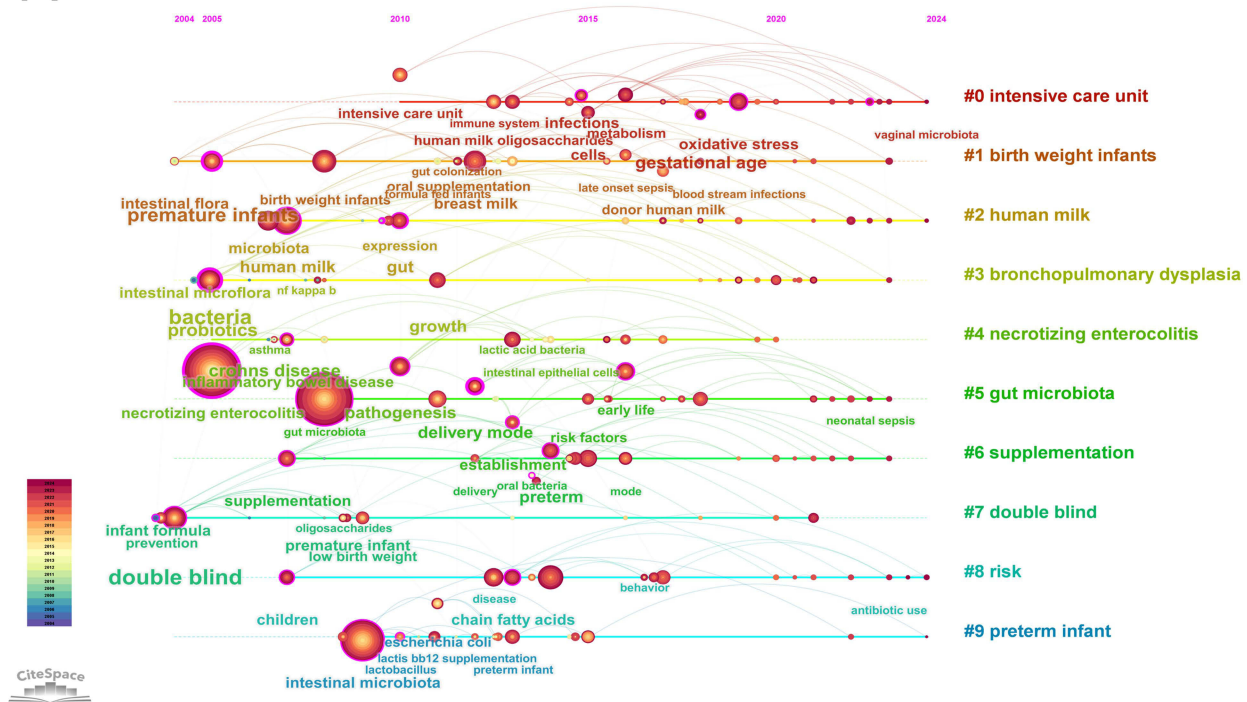


Figure 6 Keyword (A) co-occurring network map and (B) cluster network map.

infants showed higher levels of Bifidobacteria and Lactobacillus, which are crucial for healthy gut development and immune function.⁴⁶ Further, the research by Collado et al underscored the importance of early microbial colonization. They found that infants who received probiotics exhibited a more diverse and stable gut microbiota, reducing the risk of NEC and sepsis. This suggests that probiotic supplementation could be a viable strategy for enhancing gut health in preterm infants.⁴⁷ In addition to probiotic interventions, studies have explored the role of specific microbial metabolites in influencing host health. For example, the production of short-chain fatty acids (SCFAs) by beneficial gut bacteria has been shown to play a critical role in maintaining intestinal barrier function and modulating inflammatory responses. This highlights the potential therapeutic avenues for modulating the gut microbiota to improve health outcomes in preterm infants.⁴⁸ The advancements in gut microbiota research underscore the multifaceted interactions between microbial communities and host health. Understanding these relationships is crucial for developing targeted interventions to mitigate the health risks associated with preterm birth. For instance, research by Neu and Walker emphasizes the

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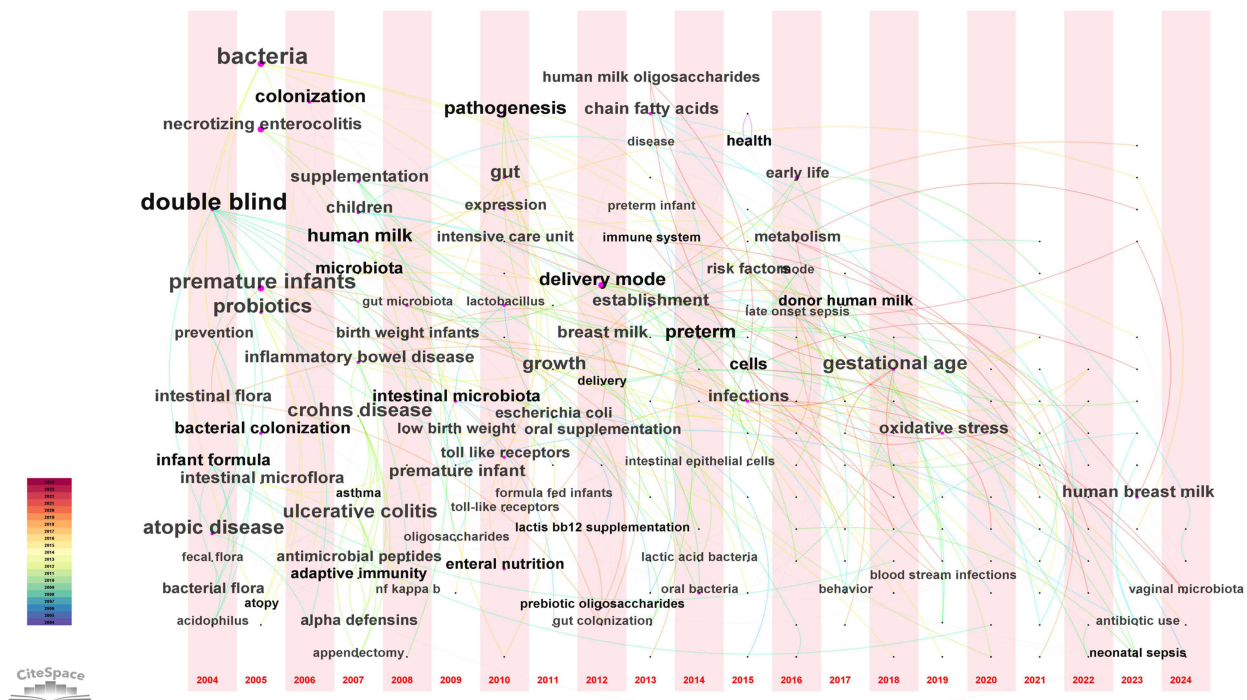


Figure 7 (A) The cluster timeline view network of keywords related to gut microbiota in premature infants. (B) The timezone chart of keywords related to gut microbiota in premature infants.

Top 15 Keywords with the Strongest Citation Bursts

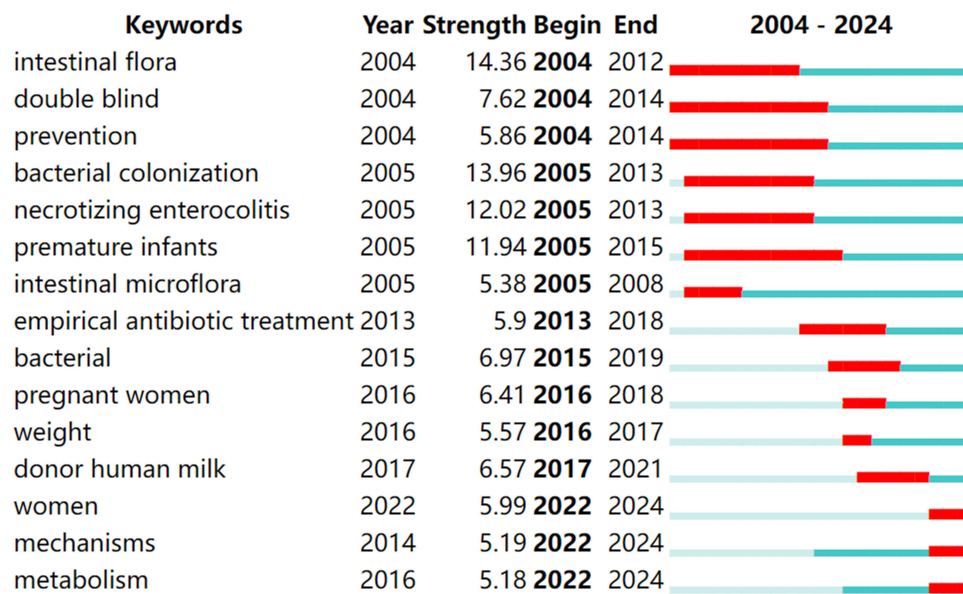


Figure 8 Top 15 keywords with the strongest citation bursts. The blue bar showed that the keyword was rarely cited, and the red bar indicated frequent citation.

significance of gut microbiota in the development of the immune system and its long-term health implications.²⁶ Future research should continue to explore the longitudinal development of the gut microbiota, the impact of various clinical practices, and the potential of personalized microbiota-based therapies to improve the health and development of premature infants. Moreover, studies have identified key periods during which interventions may be most effective. For example, La Rosa et al noted that the first few weeks of life represent a critical window for microbiota establishment, suggesting that early interventions could have lasting impacts on health outcomes.²⁹ This underscores the potential for early, targeted interventions to foster beneficial microbiota development and prevent adverse outcomes in preterm infants.

The bibliometric analysis underscores the need for continued research, particularly longitudinal studies that follow preterm infants into later childhood to understand the long-term impacts of early gut microbiota interventions. There is also a need for research focusing on personalized microbiota-based therapies, which take into account the unique microbial and health profiles of individual infants. Future studies should aim to elucidate the specific microbial strains and their metabolites that confer health benefits, paving the way for targeted therapeutic approaches.

This study has several limitations that should be considered when interpreting the results. First, the analysis was restricted to publications indexed in the Web of Science Core Collection, potentially excluding relevant studies published in other databases such as Scopus, Lens, or in non-English languages. This choice may have introduced a selection bias, as WoS tends to index high-impact, peer-reviewed journals, which could skew the findings towards more established and frequently cited studies. As a result, our analysis may not fully capture the broader research landscape, including emerging studies from less frequently indexed journals or those published in languages other than English. This limitation could affect the overall comprehensiveness and generalizability of the bibliometric analysis, as important contributions from diverse and non-elite sources may be underrepresented. Second, while bibliometric tools like VOSviewer, bibliometrix, and Citespace provide valuable insights into publication trends and research networks, they have inherent limitations in terms of data accuracy and completeness, particularly regarding author affiliations and citation counts. Third, the study period was limited to publications from 2004 to 2024, which may not capture earlier foundational research that could influence the current understanding of gut microbiota in premature infants. Finally, bibliometric analysis, by nature, focuses on quantitative aspects of research output and may not fully capture the qualitative impact and clinical relevance of individual studies. Future research should consider integrating bibliometric data with clinical outcomes to provide a more holistic view of the field.

Conclusions

This bibliometric analysis highlights the significant increase in research on gut microbiota in premature infants over the past two decades, reflecting the growing recognition of the microbiota's critical role in preterm infant health. Key research themes identified include probiotics, NEC, and breastfeeding, with notable contributions from leading researchers such as Josef Neu and Michael J. Morowitz. The analysis underscores the importance of international collaborations, particularly among researchers from the United States, China, and European countries, which have been instrumental in driving advancements in this field.

However, this study had limitations that the analysis was restricted to English-language publications indexed in the WoS, potentially excluding relevant research published in other languages and databases such as Scopus and Lens. This limitation may have introduced a bias toward high-impact, elite journals, potentially underrepresenting important contributions from less frequently indexed sources.

Despite these limitations, our findings have important implications for future research. The evolving landscape of gut microbiota research in premature infants suggests a growing need for more inclusive, multilingual, and cross-database analyses to capture a broader spectrum of scientific contributions. Additionally, ongoing global cooperation and large-scale studies are essential to further explore the complex interactions between gut microbiota and preterm infant health. We recommend that future research also consider integrating clinical data to validate findings from bibliometric analyses, which will help translate these insights into tangible health outcomes.

In conclusion, continued research and global cooperation are critical to advancing our understanding of gut microbiota in premature infants, ultimately improving clinical practices and health outcomes for this vulnerable population.

Data Sharing Statement

The data used in this study are derived from the Web of Science Core Collection, a publicly accessible database. The bibliometric analysis conducted utilized data on publications from January 1, 2004, to June 17, 2024, focusing on research related to gut microbiota in premature infants. The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request. Any additional information or data supporting the findings of this study are also available from the corresponding author on request.

Ethics Approval and Consent to Participate

This study did not involve the collection of new data from human participants or animals. All data used in this bibliometric analysis were obtained from the Web of Science Core Collection. Therefore, ethics approval and consent to participate were not required for this study. The research complies with all relevant ethical guidelines and regulations for studies involving publicly available data. Any further research based on the findings of this study should seek appropriate ethical approvals if it involves direct interactions with human participants or animals.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

References

1. Mercer EM, Arrieta MC. Probiotics to improve the gut microbiome in premature infants: are we there yet? *Gut Microbes*. 2023;15(1):2201160. doi:10.1080/19490976.2023.2201160
2. de Almeida VO, Pereira RA, Amantea SL, Rhoden CR, Colvero MO, de Almeida VO. Neonatal diseases and oxidative stress in premature infants: an integrative review. *J Pediatr*. 98(5):455–462. doi:10.1016/j.jpeds.2021.11.008
3. Vohr BR. Neurodevelopmental Outcomes of Premature Infants with Intraventricular Hemorrhage Across a Lifespan. 1558–075X.
4. Beligere N, Perumalswamy V, Tandon M, et al. Retinopathy of Prematurity and Neurodevelopmental Disabilities in Premature Infants. 1878–1946.
5. Sampath V, Martinez M, Caplan M, Underwood MA, Cuna A. Necrotizing enterocolitis in premature infants-A defect in the brakes? Evidence from clinical and animal studies. *Mucosal Immunol*. 1935–3456.
6. Cannavò LA-O, Perrone SA-O, Viola V, Marseglia LA-O, Di Rosa G, Gitto E. Oxidative Stress and Respiratory Diseases in Preterm Newborns. *Int J Mol Sci*. 12504.
7. Rogers EE, Hintz SR Early neurodevelopmental outcomes of extremely preterm infants. (1558–075X.)
8. Ream MA, Lehwald L. Neurologic Consequences of Preterm Birth. *Curr Neurol Neurosci Rep*. 18. doi:10.1007/s11910-018-0862-2
9. Stuijvenberg GA-O, Burton JA-O, Bron PA, Reid GA-O. Why Are Bifidobacteria Important for Infants? *Microorganisms*.
10. Westerbeek EA, van den Berg A, Fau - Lafeber HN, et al. The intestinal bacterial colonisation in preterm infants: a review of the literature. *Clin Nutr*.
11. Sharif S, Meader N, Oddie SJ, Rojas-Reyes MX, McGuire W. Probiotics to prevent necrotising enterocolitis in very preterm or very low birth weight infants. *Cochrane Database Syst Rev*.
12. Ang JA-O, Athalye-Jape GA-O, Rao S, Bulsara M, Patole S. Limosilactobacillus reuteri DSM 17938 as a probiotic in preterm infants: an updated systematic review with meta-analysis and trial sequential analysis. *J Parenteral Enteral Nutr*.
13. Duess JW, Sampah ME, Lopez CM, et al. Necrotizing enterocolitis, gut microbes, and sepsis. *Gut Microbes*. 1949–1984.
14. Kaplina AA-O, Kononova SA-O, Zaikova EA-O, Pervunina T, Petrova N, Sitkin SA-O. Necrotizing Enterocolitis: the Role of Hypoxia, Gut Microbiome, and Microbial Metabolites. *Int J Mol Sci*. doi:10.3390/ijms24032471
15. Masi AA-O, Embleton NA-O, Lamb CA-O, et al. Human milk oligosaccharide DSLNT and gut microbiome in preterm infants predicts necrotising enterocolitis. *Gut*. 1468–3288.
16. Rao SC, Athalye-Jape GK, Deshpande GC, Simmer KN, Patole SK. Probiotic Supplementation and Late-Onset Sepsis in Preterm Infants: a Meta-analysis. *Pediatrics*. 1098–4275.
17. Villamor-Martínez EA-O, Pierrro MA-O, Cavallaro GA-O, Mosca F, Kramer B, Villamor EA-O. Probiotic Supplementation in Preterm Infants Does Not Affect the Risk of Bronchopulmonary Dysplasia: a Meta-Analysis of Randomized Controlled Trials. *Nutrients*. 1197.
18. Nolan LA-O, Rimer JM, Good MA-O. The Role of Human Milk Oligosaccharides and Probiotics on the Neonatal Microbiome and Risk of Necrotizing Enterocolitis: a Narrative Review. *Nutrients*.
19. Thomas D, Sharma A, Sankar MJ. Probiotics for the Prevention of Mortality and Sepsis in Preterm Very Low Birth Weight Neonates from Low- and Middle-Income Countries: A Bayesian Network Meta-Analysis. 2296–861X.
20. Wensel CR, Pluznick JL, Salzberg SL, Sears CL. Next-generation sequencing: insights to advance clinical investigations of the microbiome. *J Clin Invest*. e154944.
21. Lazarides MA-O, Lazaridou IA-OX, Papanas NA-OX. Bibliometric Analysis: bridging Informatics With Science. *Interl j Lower Extremity Wounds*. 1552–6941.
22. van Eck Nj Fau - Waltman L, Waltman L. Software Survey: Vosviewer, a Computer Program for Bibliometric Mapping: 0138–9130.
23. Aria M, Cuccurullo C. An R-tool for comprehensive science mapping analysis. *J Informetr*. 2017;11(4):959–975. doi:10.1016/j.joi.2017.08.007
24. Chen CM, Ibekwe-SanJuan F, Hou JH. The Structure and Dynamics of Cocitation Clusters: a Multiple-Perspective Cocitation Analysis. *J Am Soc Inf Sci Tec*. 2010;61(7):1386–1409. doi:10.1002/asi.21309
25. Dominguez-Bello MG, Costello EK, Contreras M, et al. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proc Natl Acad Sci U S A*. 2010;107(26):11971–11975. doi:10.1073/pnas.1002601107
26. Neu J, Walker WA. Necrotizing enterocolitis. *N Engl J Med*. 2011;364(3):255–264. doi:10.1056/NEJMr1005408
27. Wang Y, Hoenig JD, Malin KJ, et al. 16S rRNA gene-based analysis of fecal microbiota from preterm infants with and without necrotizing enterocolitis. *ISME J*. 2009;3(8):944–954. doi:10.1038/ismej.2009.37
28. Penders J, Thijs C, Vink C, et al. Factors influencing the composition of the intestinal microbiota in early infancy. *Pediatrics*. 2006;118(2):511–521. doi:10.1542/peds.2005-2824
29. La Rosa PS, Warner BB, Zhou YJ, et al. Patterned progression of bacterial populations in the premature infant gut (vol 111, pg 12522, 2014). *Proc Natl Acad Sci U S A*. 2014;111(48):17336. doi:10.1073/pnas.1409497111
30. Mai V, Young CM, Ukhanova M, et al. Fecal microbiota in premature infants prior to necrotizing enterocolitis. *PLoS One*. 2011;6(6):e20647. doi:10.1371/journal.pone.0020647
31. Pammi M, Cope J, Tarr PI, et al. Intestinal dysbiosis in preterm infants preceding necrotizing enterocolitis: a systematic review and meta-analysis. *Microbiome*. 2017;5(1):31. doi:10.1186/s40168-017-0248-8
32. Backhed F, Roswall J, Peng Y, et al. Dynamics and Stabilization of the Human Gut Microbiome during the First Year of Life. *Cell Host Microbe*. 2015;17(5):690–703. doi:10.1016/j.chom.2015.04.004
33. Palmer C, Bik EM, DiGiulio DB, Relman DA, Brown PO, Ruan Y. Development of the human infant intestinal microbiota. *PLoS Biol*. 2007;5(7):e177. doi:10.1371/journal.pbio.0050177
34. Aagaard K, Ma J, Antony KM, Ganu R, Petrosino J, Versalovic J. The placenta harbors a unique microbiome. *Sci Transl Med*. 2014;6(237):237ra65. doi:10.1126/scitranslmed.3008599
35. Bresesti IA-O, Salvatore S, Valetti G, Baj AA-O, Giaroni CA-O, Agosti M. The Microbiota-Gut Axis in Premature Infants: physio-Pathological Implications. *Cells*.
36. Healy DA-O, Ryan CA-O, Ross RP, Stanton C, Dempsey EM. Clinical implications of preterm infant gut microbiome development. *Nature microb*. 2058–5276.
37. Xiang Q, Yan X, Shi W, Li H, Zhou K. Early gut microbiota intervention in premature infants. *Appli Persp*. 2090.

38. Lu J, Martin CR, Claud EC. Neurodevelopmental outcome of infants who develop necrotizing enterocolitis. *The Gut-Brain Axis*. 1558–075X.
39. JA-O L, Claud EC, Gabrielle N, Capitanio JP, Higley JD. Connection between gut microbiome and brain development in preterm infants. *Develop Psych*. 2021;1098–2302. doi:10.1002/dev.22098
40. Underwood MA, German JB, Lebrilla CB, Mills DA. Bifidobacterium longum subspecies infantis: champion colonizer of the infant gut. *Pediatr Res*. 2015;77(1–2):229–235. doi:10.1038/pr.2014.156
41. Patel AL, Johnson TJ, Engstrom JL, et al. Impact of early human milk on sepsis and health-care costs in very low birth weight infants. *J Perinatol*. 2013;33(7):514–519. doi:10.1038/jp.2013.2
42. Arboleya S, Binetti A, Salazar N, et al. Establishment and development of intestinal microbiota in preterm neonates. *FEMS Microbiol Ecol*. 2012;79(3):763–772. doi:10.1111/j.1574-6941.2011.01261.x
43. Warner BB, Deych E, Zhou Y, et al. Gut bacteria dysbiosis and necrotizing enterocolitis in very low birthweight infants: a prospective case-control study. *Lancet*. 2016;387(10031):1928–1936. doi:10.1016/S0140-6736(16)00081-7
44. Stewart CJ, Embleton ND, Marrs EC, et al. Temporal bacterial and metabolic development of the preterm gut reveals specific signatures in health and disease. *Microbiome*. 2016;4(1):67. doi:10.1186/s40168-016-0216-8
45. Hill CJ, Lynch DB, Murphy K, et al. Evolution of gut microbiota composition from birth to 24 weeks in the INFANTMET Cohort. *Microbiome*. 2017;5(1):4. doi:10.1186/s40168-016-0213-y
46. Morrow AL, Lagomarcino AJ, Schibler KR, et al. Early microbial and metabolomic signatures predict later onset of necrotizing enterocolitis in preterm infants. *Microbiome*. 2013;1(1):13. doi:10.1186/2049-2618-1-13
47. Collado MC, Cernada M, Bäuerl C, Vento M, Pérez-Martínez G. Microbial ecology and host-microbiota interactions during early life stages. *Gut Microbes*. 2012;3(4):352–365. doi:10.4161/gmic.21215
48. Tan J, McKenzie C, Potamitis M, Thorburn AN, Mackay CR, Macia L. The role of short-chain fatty acids in health and disease. *Adv Immunol*. 2014;121:91–119. doi:10.1016/B978-0-12-800100-4.00003-9

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