Review Article

# Bibliometric Analysis of Clinical Trials on Mouthwashes published in PubMed (1967-2024)

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## ABSTRACT

Mouthwashes have been extensively studied through clinical trials to assess their efficacy in improving oral health. This bibliometric analysis explores research trends, key contributors, collaborative networks, and thematic evolution in this field. The online search was performed in the PubMed database on August 29, 2024, using relevant keyword- string to identify relevant publications. After applying inclusion and exclusion criteria, 1,883 articles published between 1967 and 2024 were selected and analyzed using the bibliometric software VOSviewer and Biblioshiny. The coauthorship analysis identified several key collaborators: Addy M has the highest total link strength (TLS) value of 112. The Journal of Clinical Periodontology emerged as a leading journal, publishing 220 clinical trials on mouthwashes. The USA dominated the research output, followed by Brazil and India. In addition, Brazil showed the highest levels of international collaboration. The thematic analysis suggests that the focus of mouthwash clinical trials shifted from examining basic antibacterial efficacy and formulation to exploring personalized, long-term health effects and incorporating mouthwash into broader oral health and wellness strategies, including psychological aspects. The analysis also revealed that international partnerships are still limited while the field is highly collaborative, with only 5.79% of studies involving cross-border cooperation. This highlights potential areas for growth in advancing global research collaborations. The analysis also suggests that the field has evolved substantially. However, some areas are still underexplored, such as studies on the environmental impact of chronic mouthwash use and its effects on the natural balance of mouth bacteria, which warrant more attention.



## Keywords

Mouthwashes, Clinical Trials, Oral Health, Bibliometrics, Publication Trends, Collaboration, Authorship, Journals, Thematic shifts, Dental Hygiene, Preventive Dentistry, VOSviewer, Biblioshiny, PubMed


## INTRODUCTION

Oral health is a fundamental component of overall well-being, with significant implications for quality of life, systemic health, and socioeconomic factors [1,2]. Mouthwashes have emerged as a popular and widely studied intervention among the various tools and products used to maintain oral hygiene. These oral rinses, containing various active ingredients, complement mechanical plaque removal methods for reducing oral mucositis, gingivitis, and halitosis [3-6]. They may include antimicrobial agents like chlorhexidine, antifungal agents, essential oils, and fluoride, depending upon their intended use [7-10]. Depending on an individual's oral health condition, microbial profile, susceptibility to dental diseases, and even


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genetic markers, different mouthwash formulations can be recommended [11-13].

As the literature on mouthwash clinical trials has grown, comprehensive analysis and synthesis of this research are required. Bibliometric analysis employs statistical and mathematical techniques to analyze publication metadata, providing insights into research trends, collaboration patterns, and areas of focus [14].

Despite the wealth of clinical trials conducted on mouthwashes, there has been no comprehensive bibliometric analysis of this research domain. This gap in the literature presents an opportunity to provide valuable insights to the oral health research community, dental practitioners, and policymakers. This study aims to conduct a thorough bibliometric analysis of clinical trials on mouthwashes, as indexed in the PubMed database. Specifically, we seek to:

i. Analyze publication trends over time to identify periods of increased research activity and potential catalysts for such trends.
ii. Examine the geographical distribution of research output to understand global contributions to the field.
iii. Identify key research themes and their evolution over time through keyword analysis.
iv. Explore collaboration patterns among authors and countries.
v. Highlight influential journals in the dissemination of mouthwash clinical trial research.

By addressing these objectives, this bibliometric analysis aims to provide a comprehensive overview of the mouthwash clinical trial literature, offering valuable insights to guide future research, inform clinical practice, and support evidence-based decision-making in oral health care.

## MATERIALS AND METHODS

### *Data Collection*

A comprehensive search of the PubMed database was conducted on August 29, 2024, to identify relevant publications on clinical trials of mouthwashes. The following search string was used: (“Mouthwashes” OR (mouthwash OR “mouth wash*” OR “oral rinse*” OR “mouth rinse*”).

This search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords related to mouthwashes and clinical trials to ensure comprehensive coverage of the relevant literature. The search results were exported in PubMed formats to text files for further analysis.

### *Inclusion Criteria*

Clinical trials evaluating the effects of mouthwash or mouth rinse.

Studies published in English.

### *Exclusion Criteria*

Articles that are not classified as clinical trials.

Clinical trials in which mouthwashes or mouth rinses were not used to improve oral or dental health, such as those investigating carbohydrate mouth rinses used to enhance physical performance in sports.

### *Study Selection*

The selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15]. Two independent reviewers screened the titles and abstracts of the retrieved articles manually to ensure their eligibility based on predefined inclusion and exclusion criteria. A flow chart depicting the study selection process was created using PRISMA.

### *Data Analysis*

Bibliometric analysis was performed using two specialized software packages:

VOSviewer (version 1.6.20): This tool was utilized to visualize and analyze bibliometric networks, including coauthorship and keyword co-occurrence [16].

Biblioshiny (RStudio 4.3.1): An R-based software package, Biblioshiny was employed for comprehensive bibliometric analysis, including trend analysis, over-time productivity assessment, and thematic evolution [17]. Additional data processing and visualization were conducted using Microsoft Excel.

### *Data Visualization*

Key findings and bibliometric indicators were visualized using a combination of VOSviewer, Biblioshiny, and Microsoft Excel. The BioRender software was used to depict the critical findings of the study [18].

This methodology allows for a comprehensive bibliometric analysis of clinical trials on mouthwashes, providing insights into the structure and dynamics of this research field while accounting for the limitations of PubMed data regarding citation information.

## RESULTS

### *Search Results*

A total of 18,271 articles were initially identified, out of which 3,622 were clinical trials. After filtering for language, 3,457 clinical trials published in English

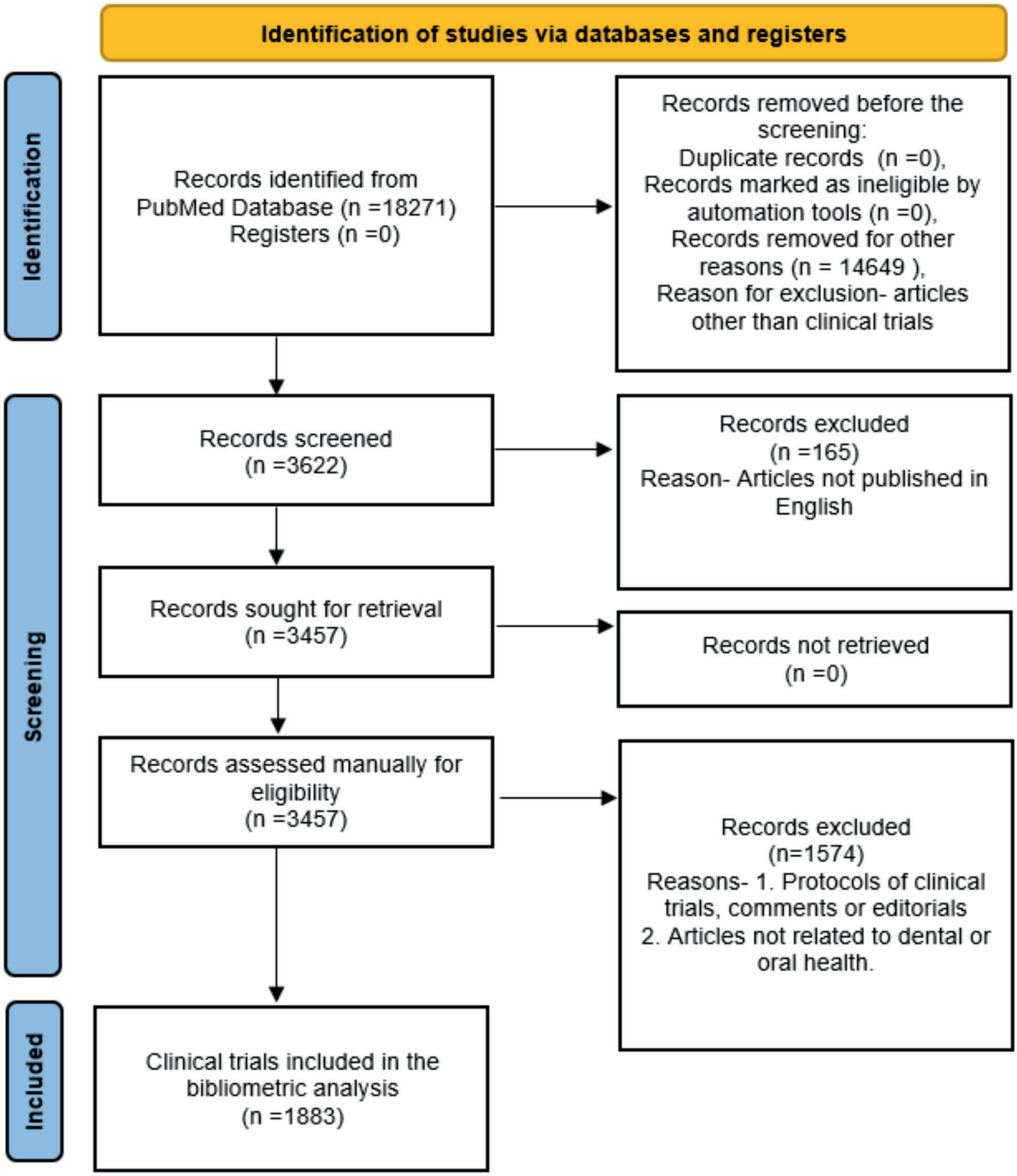


**Figure 1**: The flow chart of the study selection process for bibliometric analysis of clinical trials on mouthwashes
**Image Credit:** Namrata Dagli.

were retained. We then applied the inclusion and exclusion criteria, manually inspecting the articles to remove irrelevant studies. This process led to the exclusion of 9 additional comments, 5 protocols, and studies that focused on forms of chlorhexidine other than mouthwash or non-dental uses of mouthwashes (such as for skin preparation before surgery, surface or instrument disinfection, and carbohydrate rinses for performance enhancement). After this rigorous review, 1,883 articles were selected for bibliometric analysis (Figure 1).

*Main information*

The bibliometric data on clinical trials related to mouthwashes published in PubMed between 1967 and 2024, analyzed through Biblioshiny, provides insightful trends and collaboration patterns in this field of research. Over this period, 1,883 documents were published across 429 sources, such as journals and books. The data indicates a steady annual growth rate of 5.61%, which suggests a consistent increase in interest and research output on mouthwashes over time. The average age of the documents is 18.5 years, showing that while the field has long-standing research, there is still ongoing interest and activity. In terms of keywords, both Author's Keywords (DE) and Keywords Plus (ID) list a total of 4,784 unique terms. This shows that a broad spectrum of related concepts has been explored, with keywords capturing specific and broader contexts of the research. These keywords provide insights into the focus areas of studies, including common terms related to mouthwashes, dental health, and related pharmacological or therapeutic agents.

On the authorship front, the data reveals a large pool of contributors, with 7,210 authors involved in the field. Despite this collaborative nature, only 50 authors have published single-authored documents, and the number of single-authored papers is 61, which implies that research on mouthwashes is highly collaborative. On average, each document involves 5.25 co-authors, highlighting the multidisciplinary and cooperative approach often required for clinical trials and healthcare research. International collaborations account for 5.79% of all publications, indicating some level of global cooperation, although most research appears to be conducted within national boundaries.

*Publication Trends*

The overall pattern of scientific publications on clinical trials related to mouthwash has shown a gradual increase since the late 1960s, with some fluctuations along the way. In the early years, from 1967 to the mid-1980s, the number of publications remained quite low, with no more than 18 articles in any given year. However, starting in the late 1980s, there was a significant increase in publications, with 35 articles published in 1989, marking a notable surge in research interest. The maximum number of articles was published in 2023, totaling 73 articles. The most substantial increase occurred between 1988 and 1989, when articles jumped from 12 to 35, likely reflecting a growing interest in using mouthwash in clinical settings. (Figure 2).

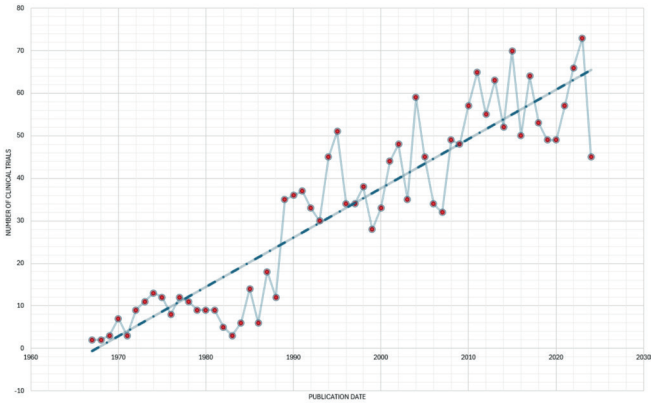


**Figure 2**: Annual Publications of clinical trials on mouthwashes in PubMed.

**Image Credit:** Namrata Dagli.

On the other hand, the maximum decline can be observed in 1983, where the number of articles dropped from 5 in 1982 to just 3 in 1983, signaling a temporary dip in research activity. Other smaller declines occurred sporadically throughout the timeline but were usually followed by recovery or surges in subsequent years. As for future trends, based on the steady growth in recent years, with consistent increases from 2010 to 2023, it is likely that research interest in mouthwash clinical trials will continue to grow or remain stable in the coming years. Contributing factors to this growth might include increased awareness of oral hygiene's importance, advancements in dental and pharmaceutical research, and the rising demand for preventative healthcare measures.

The fluctuations in publication numbers may be influenced by several factors, such as introducing new mouthwash formulations, increasing public health initiatives focused on oral care, and evolving guidelines in clinical research methodologies. The rise in the 1990s and early 2000s could also be attributed to a better understanding of oral biofilms, the role of mouthwash in preventing dental diseases, and its implications in public health settings.

*Most Relevant Authors*

Based on the number of published clinical trials on

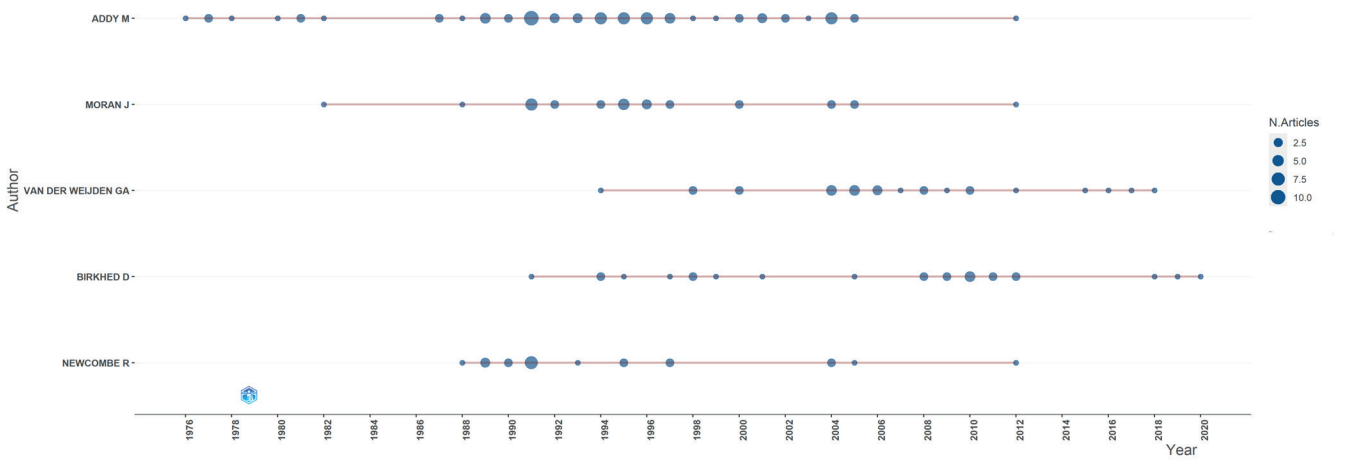


**Figure 3**: The overtime production analysis of the most relevant authors based on the number of published clinical trials on mouthwashes.

**Image Credit:** Namrata Dagli.

mouthwash, the most relevant authors are presented in Table 1.

**Table 1**: Most Relevant authors based on the number of published clinical trials on mouthwashes in PubMed.

| S. No. | Authors | Number of Publications |
|---|---|---|
| 1. | Addy M | 74 |
| 2. | Moran J | 29 |
| 3. | Van Der Weijden GA | 27 |
| 4. | Birkhed D | 25 |
| 5. | Newcombe R | 22 |

The graph (Figure 3) shows the authors' chronological record of publications (Table 1) from 1976 to 2020, focusing on research related to mouthwash clinical trials. The landscape of clinical trials related to mouthwash, as recorded in PubMed, spans several decades and includes numerous contributions from key authors such as Addy M, Moran J, Van der Weijden GA, Birkhed D, and Newcombe R. The early years, particularly the 1970s to the early 1990s, show a steady output from Addy M, who published consistently on the topic, though with a frequency of mostly one to two publications per year. Interestingly, a notable spike was observed in 1991, when Addy M contributed 10 studies, suggesting an intensified research focus or a culmination of several investigations. Similarly, Moran J, who published frequently throughout the 1980s and 1990s, also peaked in 1991, reflecting a parallel trend in clinical interest during this period. Birkhed D's research activity gained momentum in the 1990s and continued through to the 2010s, with regular publications highlighting sustained involvement in mouthwash-related clinical trials every few years. Notably, Birkhed's output shows increased activity in the late 2000s and early 2010s. Van der Weijden GA emerged as a consistent contributor from the mid-1990s onward, with a notable increase in publications between 2004 and 2006. This trend may indicate a growing interest in understanding the efficacy and impact of mouthwash on dental health during this period.

### *Coauthorship Analysis of Authors*

Coauthorship analysis of authors by VOSviewer (1.6.20 version) identified 7677 authors, out of which 124 authors published at least 5 clinical trials on mouthwashes. All of these 124 authors were included in the analysis, and the total strength of coauthorship links was calculated for each. Addy M has been identified with the highest total link strength (TLS) value of 112 and 73 publications. The other authors with relatively higher TLS values are Moran J, with a TLS value of 59, Van Der Weijden GA, with a TLS value of 54, and Newcombe R, with a TLS value of 47. Some of the 124 authors in the network are not connected. The most extensive set of connected authors consisting of 54 authors is spread across 6 clusters with 124 links and 414 TLS (Figure 4).

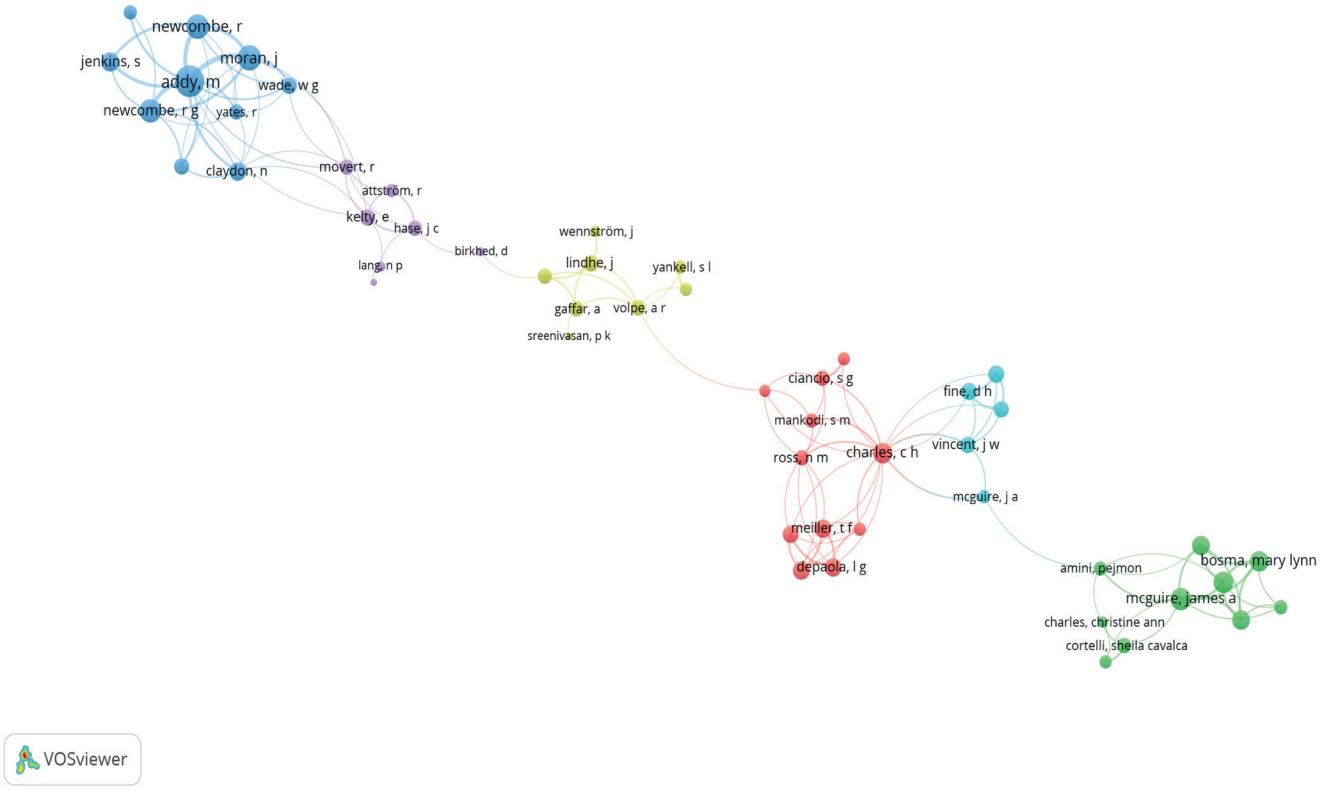


**Figure 4** The most extensive set of connected authors identified in coauthorship analysis by VOSviewer. (Weight: Total Link Strength)

**Notes:** The nodes represent the total link strength values, and the connecting line represents the links between the authors. For clarity, the size of the nodes has been increased in this figure. As a result, some names may not be visible.

**Image Credit:** Namrata Dagli.

### *Most Relevant Journals*

Table 2 summarizes the number of publications related to clinical trials on mouthwashes across the most relevant journals based on the number of publications on the topic. The graph (Figure 5) presents an overview of the publications over time across the journals. The Journal of Periodontology was one of the early contributors, beginning in 1969 and steadily increasing its output through the 1970s and 1980s. By the mid-1990s, the Journal of Clinical Periodontology emerged as a leading journal for clinical trials on mouthwash, and it continued to publish a growing number of articles, reaching 220 publications by 2024. Other journals, such as Caries Research and the Journal of Dental Research, have also contributed to the body of research, particularly from the 1980s onward. The Journal of Clinical Dentistry and the International Journal of Dental Hygiene have consistently published trials since the 1980s and 1990s, respectively. More recently, journals like Clinical Oral Investigations, Oral Health & Preventive Dentistry, and BMC Oral Health have seen increasing publications, particularly from the 2000s. From 2010 onwards, journals such as the Journal of Clinical Periodontology and Journal of Periodontology continued to publish the most trials, with others like the American Journal of Dentistry and the International Journal of Dental Hygiene also contributing to the research landscape.

**Table 2**: Most Relevant Journals based on the number of published clinical trials on mouthwashes.

| Serial No. | Journals | Number of publications |
|---|---|---|
| 1. | Journal Of Clinical Periodontology | 220 |
| 2. | Journal Of Periodontology | 102 |
| 3. | The Journal of Clinical Dentistry | 56 |
| 4. | Caries Research | 54 |
| 5. | International Journal of Dental Hygiene | 52 |
| 6. | American Journal of Dentistry | 51 |
| 7. | Clinical Oral Investigations | 50 |
| 8. | BMC oral health | 35 |
| 9. | Oral Health and Preventive Dentistry | 32 |
| 10. | Journal of Dental Research | 31 |

*Analysis of Corresponding Authors' Countries*

Figure 6 depicts clinical trial publications related to mouthwashes, highlighting the collaboration of research activity across corresponding authors' countries. Most of the publications are single-country publications (SCP). The collaboration patterns in clinical trials on mouthwash vary considerably among countries, especially those with the most relevant corresponding authors based on the number of publications. The USA leads in total publications, but the level of international collaboration is low, as evidenced by its MCP ratio. Brazil also prominently showcased considerable international engagements, followed by China and Italy. Countries like Iran, India, and Germany exhibit moderate collaboration levels, with their research involving some level of international input. On the other hand, the Netherlands and Norway show the lowest MCP ratio, indicating a preference for conducting research within their borders. Turkey and Japan stand

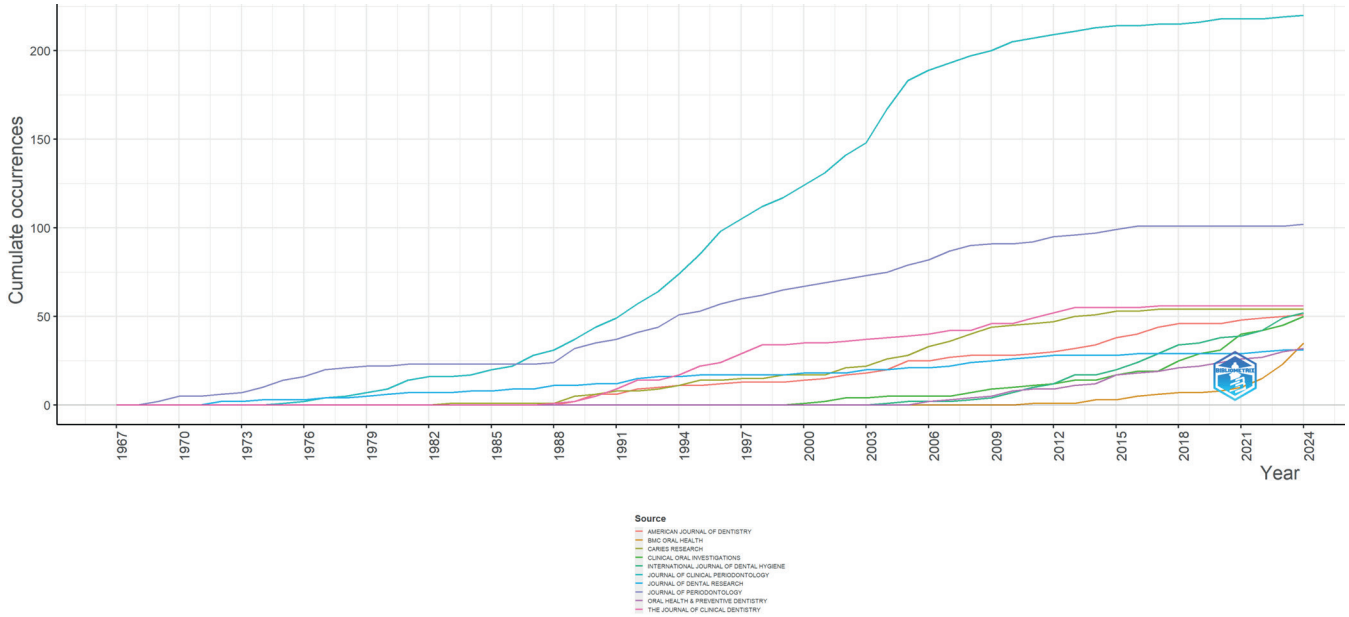


**Figure 5**: Temporal analysis of the published clinical trials on mouthwashes in the most relevant journals.

**Image Credit:** Namrata Dagli.

out as countries with no international collaborations, focusing solely on domestic research endeavors.

*Country's production over time*

The analysis of clinical trials on mouthwashes across different countries highlights the USA as having the highest number of publications, indicating its active role in oral health research. Brazil follows, showing a solid contribution to the field from South America. Iran and India also make notable contributions, reflecting ongoing research efforts in oral hygiene in these regions. Europe, Spain, Italy, and Germany all feature prominently, with Spain leading in publications. China and Japan demonstrate significant engagement in the

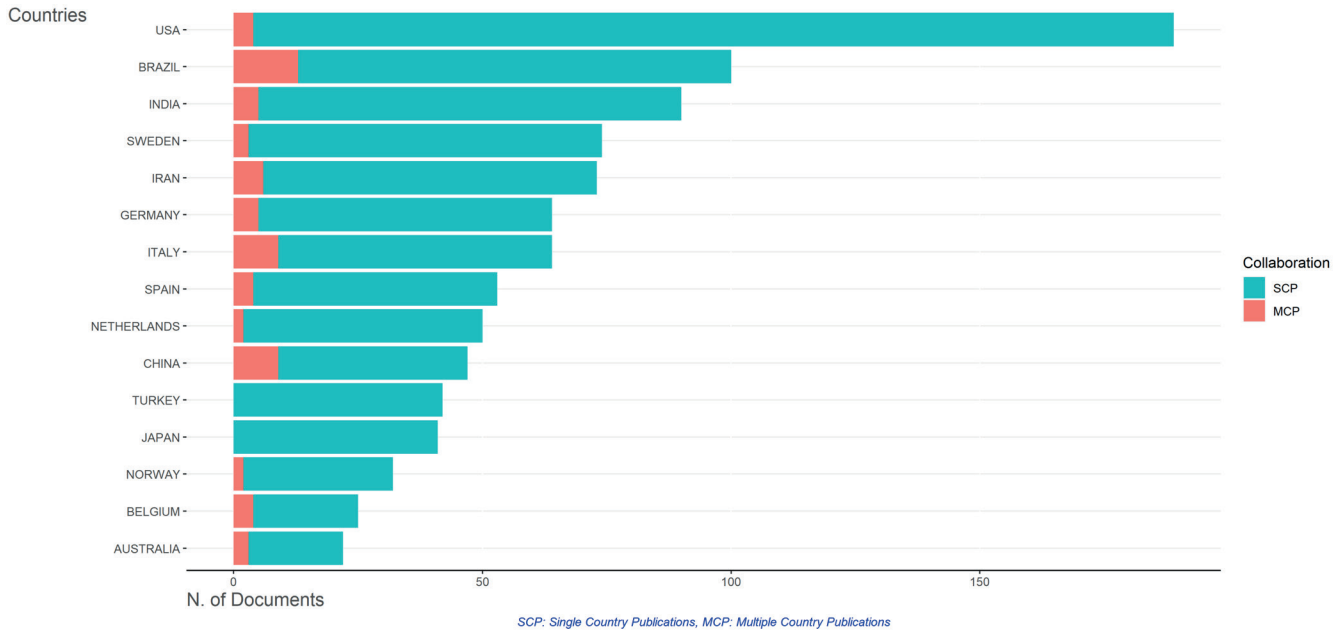


**Figure 6**: Collaboration of Corresponding Author's Countries in publishing clinical trials on mouthwashes

**Image Credit:** Namrata Dagli.

research from Asia, while Australia contributes to the growing body of research on oral health interventions.

Figure 7 shows a gradual increase in the scientific production of clinical trial articles on mouthwashes from various countries. Japan's contribution to research in this field began in the early 1990s with modest numbers and has seen a steady rise, reaching its highest levels in the 2020s. Italy, starting slightly later, also demonstrated consistent growth in its research output, with a notable increase in clinical trials in the 2010s and 2020s.

In the USA, the growth of mouthwash-related clinical trials accelerated in the mid-1990s, maintaining a steady increase over the decades, making it one of the leading countries in this field by the 2020s. Brazil began contributing to this research in the 1990s, showing a substantial rise in publications by the 2010s, and it continues to contribute to a significant number of clinical trials in recent years. Spain's involvement started in the late 1990s and saw moderate growth, with an accelerated increase in publications around the mid-2010s. China's contributions began slowly but have expanded significantly since the mid-2010s. Similarly, India and Iran have shown marked increases in research output since the 2000s, with both countries demonstrating a robust upward trend in the number of clinical trials published in recent years. Germany and Australia, starting with fewer publications in the early years, have also seen consistent growth in research, with notable increases in their contributions to the field since the 2010s. These trends collectively highlight a growing global interest in studying mouthwashes and their clinical applications.

### *Co-occurrence Analysis of MeSH keywords*

Co-occurrence Analysis of MeSH keywords by VOSviewer identified a total of 2099 keywords, of which 302 repeated a minimum of 10 times were included in the analysis, and the TLS was calculated for each. All the items were connected and included in the network visualization generation (Figure 8). The keywords spread across the 6 clusters with 16564 links and 168761 TLS values. The keywords with the highest TLS are humans, mouthwashes, male, female, and adults, while the subject-specific keywords with the highest TLS are- dental plaque, chlorhexidine, local anti-infective agents, dental plaque index, and gingivitis. The keywords in each cluster are presented in Table 3.

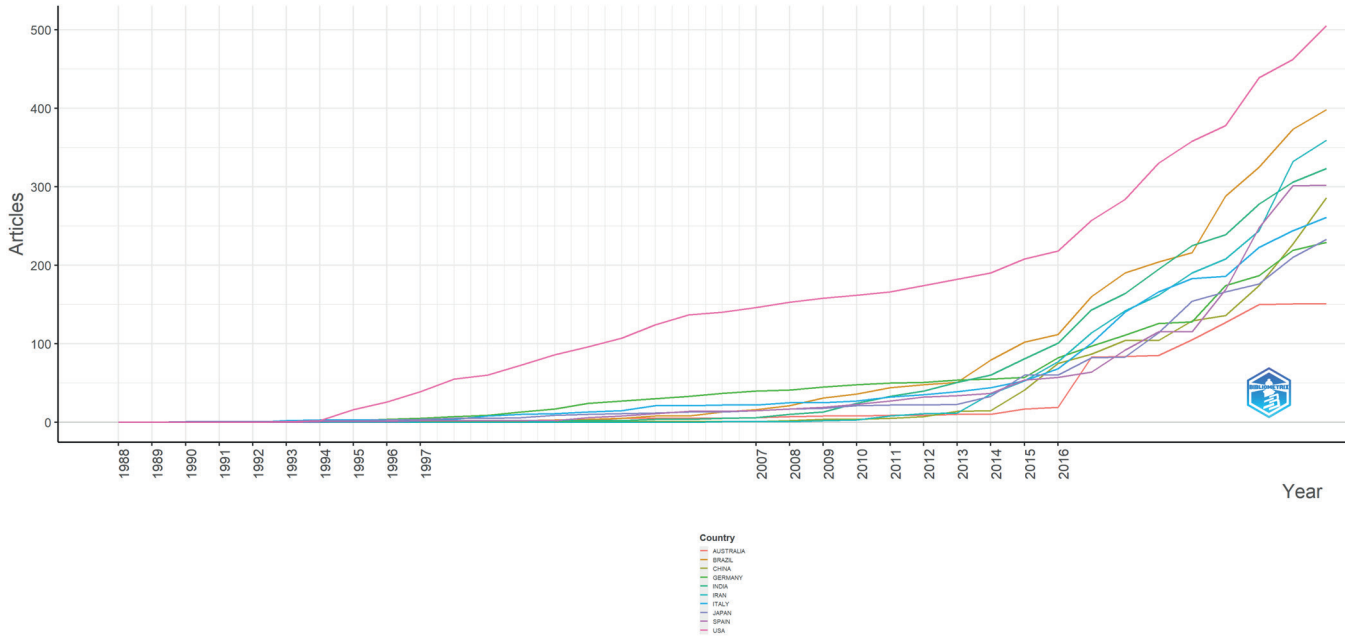


**Figure 7**: Temporal analysis of the published clinical trials on mouthwashes in the most

**Image Credit:** Namrata Dagli.

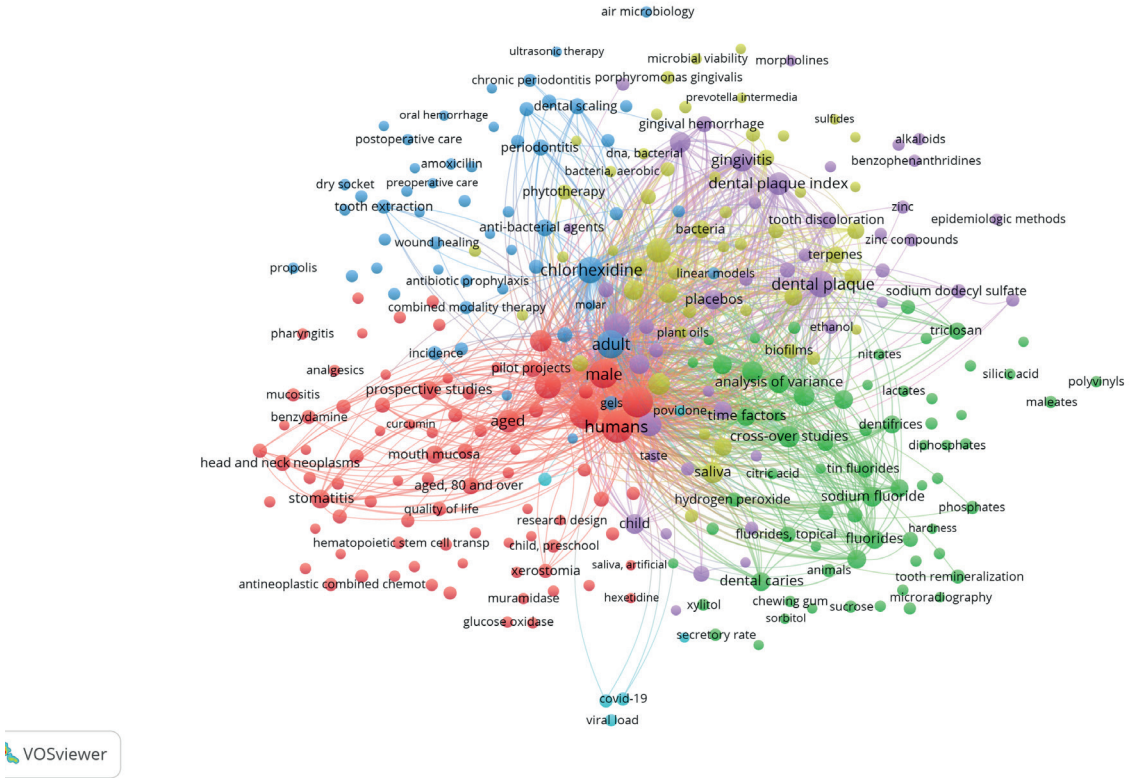


**Figure 8**: Co-occurrence analysis of MeSH keywords by VOSviewer. The nodes represent the number of occurrences (Weight: Occurrences).

**Notes:** The nodes represent the number of occurrences of MeSH keywords, and the connecting line represents the strength of the link. For clarity, the size of the nodes has been increased in this figure. As a result, some names may not be visible.

**Image Credit:** Namrata Dagli.

**Table 3**: The MeSH keywords in clusters identified in keyword co-occurrence analysis.

| Serial No. | Clusters | Keywords |
|---|---|---|
| 1. | Cluster 1 (82 items) | Administration oral, administration topical, aged, aged 80 and over, aloe, analgesics, anti-inflammatory agents, non-steroidal anti-inflammatory agents, antifungal agents, antineoplastic agents, antineoplastic combined chemotherapy protocols, benzydamine, bone marrow transplantation, breast neoplasms, burning mouth syndrome, candida, candida albicans, candidiasis oral, carcinoma squamous cell, chemotherapy, child preschool, chitosan, chronic disease, clinical protocols, cohort studies, curcumin, dental care for aged, dental implants, dexamethasone, drug administration schedule, combination drug therapy, female, fluorouracil, glucose oxidase, head and neck neoplasms, hematopoietic stem cell transplantation, hexetidine, humans, infant, inflammation, lactoperoxidase, lichen planus oral, logistic models, male, middle aged, mouth diseases, mouth mucosa, mouth neoplasms, mouthwashes, mucositis, muramidase, neoplasms, nursing homes, nystatin, oral health, pain, pain measurement, patient compliance, patient satisfaction, peri-implantitis, pharyngitis, photochemotherapy, pilot projects, pregnancy, probiotics, prospective studies, quality of life, radiation injuries, radiotherapy, recurrence, research design, saliva artificial, severity of illness index, sodium bicarbonate, sodium chloride, stomatitis, stomatitis aphthous, denture stomatitis, surveys and questionnaires, tablets, treatment outcome, xerostomia |
| 2. | Cluster 2 (67 items) | amines, analysis of variance, animals, area under curve, biological availability, calcium, calcium phosphates, cariostatic agents, cattle, chewing gum, citric acid, color, coloring agents, complex mixtures, composite resins, cross-over studies, dental caries, dental caries susceptibility, dental devices home care, dental enamel, dentifrices, dentin, dentin sensitivity, diphosphates, drug combinations, drug delivery systems, durapatite, fluorides, fluorides topical, hardness, hydrogen peroxide, hydrogen-ion concentration, image processing computer-assisted, lactates, lactic acid, maleates, materials testing, microradiography, microscopy electron scanning, nitrates, orthodontic brackets, phosphates, polyvinyls, reference value, secretory rate, silicic acid, single-blind method, sodium fluoride, sorbitol, statistics as topic, statistics nonparametric, sucrose, surface properties, sweetening agents, time factors, tin fluorides, tooth, tooth bleaching, , tooth demineralization, tooth erosion, tooth remineralization, toothbrushing, triclosan, water, xylitol |
| 3. | Cluster 3 (53 items) | adult, aerosols, air microbiology, alveolar bone loss, ampicillin, antibacterial agents, antibiotic prophylaxis, bacteria, chi-square distribution, chlorhexidine, chronic periodontitis, combined modality therapy, dental scaling, diabetes mellitus type 2, disinfectants, dry socket, feasibility studies, gels, gingiva, hyaluronic acid, incidence, intensive care units, linear models, mandible, metronidazole, molar, molar third, oral hemorrhage, oral surgical procedures, pain postoperative, periodontal attachment loss, periodontal diseases, periodontal pocket, periodontitis, pneumonia ventilator-associated, postoperative care, postoperative complications, preoperative care, prevalence, propolis, reproducibility of results, risk factors, root planing, smoking, staphylococcus aureus, surgical flaps, surgical wound infection, therapeutic irrigation, tooth extraction, tooth impacted, tranexamic acid, ultrasonic therapy, wound healing |
| 4. | Cluster 4 (50 items) | aggregatibacter actinomycetemcomitans, anti-infective agents local, bacteria aerobic, bacteria anaerobic, bacterial adhesion, bacterial load, bacteroides, biofilms, breath tests, case-control studies, cetylpyridinium, chemistry pharmaceutical, colony count microbial, dna bacterial, fluorescent dyes, follow-up studies, fusobacterium nucleatum, gram-negative bacteria, halitosis, hydrogen sulfide, in vitro techniques, India, lactobacillus, microbial sensitivity tests, microbial viability, microbiota, microscopy fluorescence, mouth, oils volatile, oxides, phytotherapy, plant extracts, plant oils, plant preparations, plaque index, *Porphyromonas gingivalis*, *Prevotella Intermedia*, salicylates, saliva, *Streptococcus*, *Streptococcus mutans*, sulfides, sulfur compounds, tea, terminalia, terpenes, tongue, young adult |
| 5. | Cluster 5 (44 items) | adolescent, alkaloids, anti-infective agents, benzoates, benzophenanthridines, biguanides, child, chlorides, clinical trials as topic, dental calculus, dental health surveys, dental plaque index, dental prophylaxis, dmf index, dose-response relationship, double-blind method, drug evaluation, epidemiologic methods, ethanol, evaluation studies as topic, gingival hemorrhage, gingivitis, isoquinolines, longitudinal studies, mouthwashes, oral hygiene, oral hygiene index, periodontal index, phenols, placebos, quaternary ammonium compounds, random allocation, regression analysis, school dentistry, sodium, sodium dodecyl sulfate, surface-active agents, taste, taste disorders, tooth discoloration, zinc, zinc compounds |
| 6. | Cluster 6 (6 items) | brazil, covid-19, povidone, povidone-iodine, sars-cov-2, viral load |

The keywords in these 6 clusters suggest a broad spectrum of research on mouthwashes and oral health, as might be found in clinical trials published on PubMed.

Cluster 1 focuses on trials of the clinical approach to oral care, targeting the elderly, cancer patients undergoing chemotherapy or radiotherapy, and conditions such as burning mouth syndrome, candidiasis, and oral mucositis. The mouthwash with therapeutic agents benzydamine, dexamethasone, and probiotics was used for palliative treatment to manage pain, inflammation, and oral health during intensive cancer treatments, along with improving patient compliance, quality of life, and addressing conditions like xerostomia, fungal infections, and peri-implantitis.

Cluster 2 delves into basic oral health research focusing on preventive measures for conditions such as dental

caries, dentin sensitivity, and tooth demineralization. Trials here likely assess the biological availability of mouthwash components, such as fluorides, hydrogen peroxide, and calcium phosphates, and their role in tooth remineralization. This cluster suggests a focus on the efficacy of fluoridated and cariostatic agents, sweeteners like xylitol, and the impact of chemical compositions on dental hard tissue, implying that mouthwash could be evaluated as part of preventive care or for its remineralization properties.

Cluster 3 focuses on periodontal diseases and post-surgical care, particularly in managing chronic periodontitis, alveolar bone loss, and dry sockets. Keywords such as chlorhexidine, antibiotic prophylaxis, root planing, and gingival care suggest clinical trials could evaluate mouthwashes as adjunctive therapies for improving postoperative healing, preventing infections, and reducing periodontal attachment loss. The focus on pain management, surgical complications, and periodontal interventions indicates a strong emphasis on therapeutic mouthwash trials.

Cluster 4 targets microbial factors associated with oral diseases. It includes research on biofilms, bacterial adhesion, and specific oral pathogens, such as *Porphyromonas gingivalis* and *Streptococcus mutans*, implicated in dental plaque formation and periodontal diseases. Trials could focus on the antimicrobial effects of mouthwash, particularly anti-infective agents like cetylpyridinium chloride and plant extracts, testing their role in reducing oral bacterial load, halitosis, and improving plaque control.

Cluster 5 highlights studies on oral hygiene, particularly in adolescents and children. This cluster includes clinical trials, double-blind methods, random allocation, and placebo-controlled studies, suggesting a focus on evaluating the effectiveness of mouthwash formulations in reducing dental plaque, improving gingivitis outcomes, and preventing tooth discoloration. It also reflects trials assessing the public health impact of mouthwash in school-based dentistry and longitudinal oral hygiene studies.

Cluster 6 introduces COVID-19-related research, reflecting trials on mouthwash's potential to reduce patient viral load, with keywords such as povidone-iodine and SARS-CoV-2. This cluster suggests that mouthwash trials could explore its role in managing oral transmission or viral load reduction in the context of the pandemic.

These clusters suggest a broad spectrum of research, from therapeutic use in cancer care and periodontal disease management to preventive dental care and evaluating antimicrobial properties in clinical settings. The keywords reflect a variety of methodologies, including cohort studies, randomized trials, and cross-over designs, indicating rigorous approaches in investigating the effectiveness of mouthwash products in oral health.

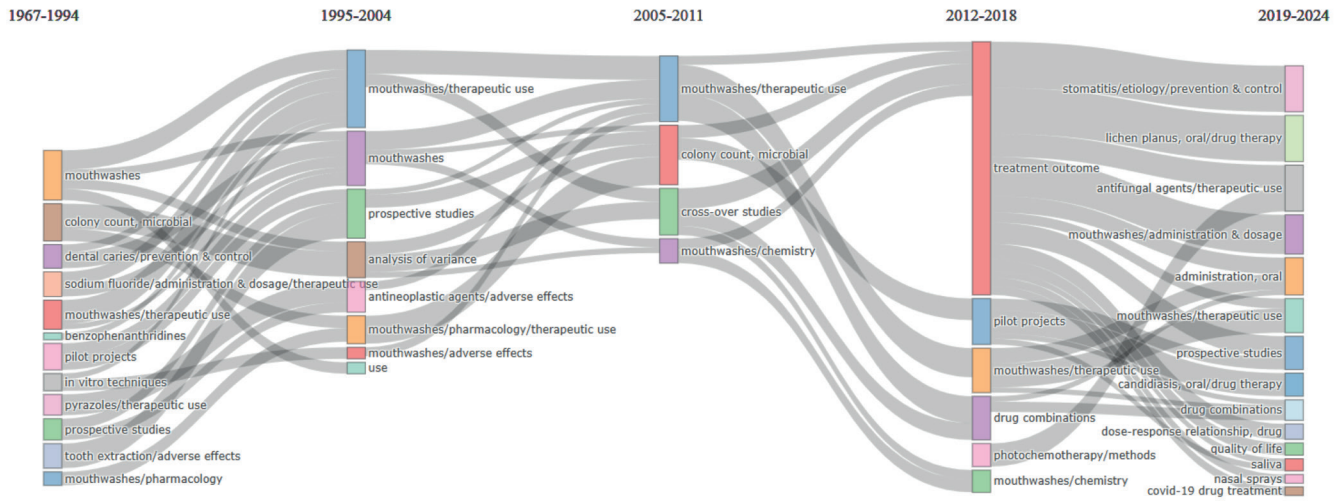


**Figure 9**: Thematic evolution (by Biblioshiny) based on the keywords used in the clinical trials on mouthwash published in PubMed. (Minimum cluster frequency- 4 per thousand documents, weight- occurrences)

**Image Credit:** Namrata Dagli.

*Thematic Evolution*

The thematic evolution of keywords in published clinical trials on mouthwashes in PubMed over various periods demonstrates how research trends have shifted across decades (Figure 9). Between 1967 and 1994, keywords such as "benzophenanthridines" and "colony count, microbial" were more common, focusing on the microbiological aspects of dental health. From 1995 to 2004, themes shifted toward practical applications and clinical uses of mouthwashes, with keywords like "mouthwashes/therapeutic use" and "anti-infective agents/therapeutic use," reflecting a growing interest in therapeutic outcomes and pharmacological effects. During this period, the inclusion index for terms related to therapeutic agents and microbial control, like "chlorhexidine" and "streptococcus mutans," increased significantly.

From 2005 to 2011, there was a more refined focus on the efficacy and safety of mouthwashes, as indicated by keywords such as "mouthwashes/adverse effects" and "anti-infective agents/administration & dosage." This shows a shift toward assessing mouthwash use's benefits and potential risks. Themes like "dental plaque prevention & control" and "gingivitis prevention & control" were prevalent, emphasizing preventive dental care.

From 2012 to 2018, the focus broadened, incorporating terms such as "phytotherapy" and "biofilms/drug effects," indicating an interest in alternative and more sophisticated approaches to managing oral biofilms. There was also an increase in studies exploring patient-centric outcomes such as "treatment outcome" and "patient compliance," highlighting the importance of patient experience and satisfaction in clinical settings.

In the most recent period from 2019 to 2024, themes continue to evolve, with increasing attention given to "probiotic mouthwashes," "halitosis/drug therapy," and "biofilm disruption," reflecting advancements in understanding and addressing oral health from both a microbial and patient-quality-of-life perspective. The term "antimicrobial resistance" also emerged, signaling growing concern over the long-term effectiveness of traditional therapeutic agents in mouthwashes. This thematic evolution underscores the dynamic nature of clinical research in oral health, moving from basic microbiological studies to complex, patient-focused interventions.

## DISCUSSION

The bibliometric analysis of clinical trials on mouthwashes from 1967 to 2024 offers valuable insights into the development and collaboration patterns within this area of research. Consistent publication growth, with an annual increase of 5.61%, reflects a sustained interest in mouthwash studies. The fluctuations in publication output over the years seem linked to innovations in mouthwash formulations, heightened public health initiatives, and advancements in understanding oral biofilms and dental diseases. The high average document age (18.5 years) indicates this is a well-established field, yet the steady rise in output suggests that new research continues to build on this foundational work. The range of 4,784 unique keywords highlights the diverse research areas and evolving focus of studies, from essential oral health to pharmacological interventions.

*The most relevant contributors and collaborators*

The collaborative nature of research in this field is evident, with many authors contributing to the literature. However, despite this, the relatively low number of single-author papers suggests that most studies are produced by research teams, emphasizing the cooperative approach required for clinical trials and healthcare research. Fluctuations in publication trends over the decades likely correspond to the introduction of new mouthwash formulations, advancements in dental research, and heightened public awareness of oral hygiene. The sharp increase in publications during the late 1980s and 1990s may reflect growing interest in oral biofilms and the role of mouthwash in preventing dental diseases. Key contributing authors have shaped the field with sustained contributions. Meanwhile, journals such as the Journal of Clinical Periodontology and the Journal of Periodontology have played pivotal roles in disseminating this research.

The analysis reveals that the USA leads in mouthwash clinical trial publications, followed by Brazil, with notable contributions from Iran, India, Spain, Italy, Germany, China, Japan, and Australia. This may reflect differences in research priorities, funding, or institutional focus. Overall, the global interest in clinical trials on mouthwashes continues to grow, particularly in regions like Asia, Europe, and South America, signaling the importance of this field in advancing oral health research and clinical practices. Notably, age and gender-related words were excluded from this analysis for better visibility of subject-specific relevant words.

*Keyword co-occurrence analysis*

Research on mouthwash has covered many areas, mainly focusing on its therapeutic uses in managing oral complications from diseases and treatments such as cancer therapy and its role in daily oral hygiene practices. Studies have examined how mouthwash

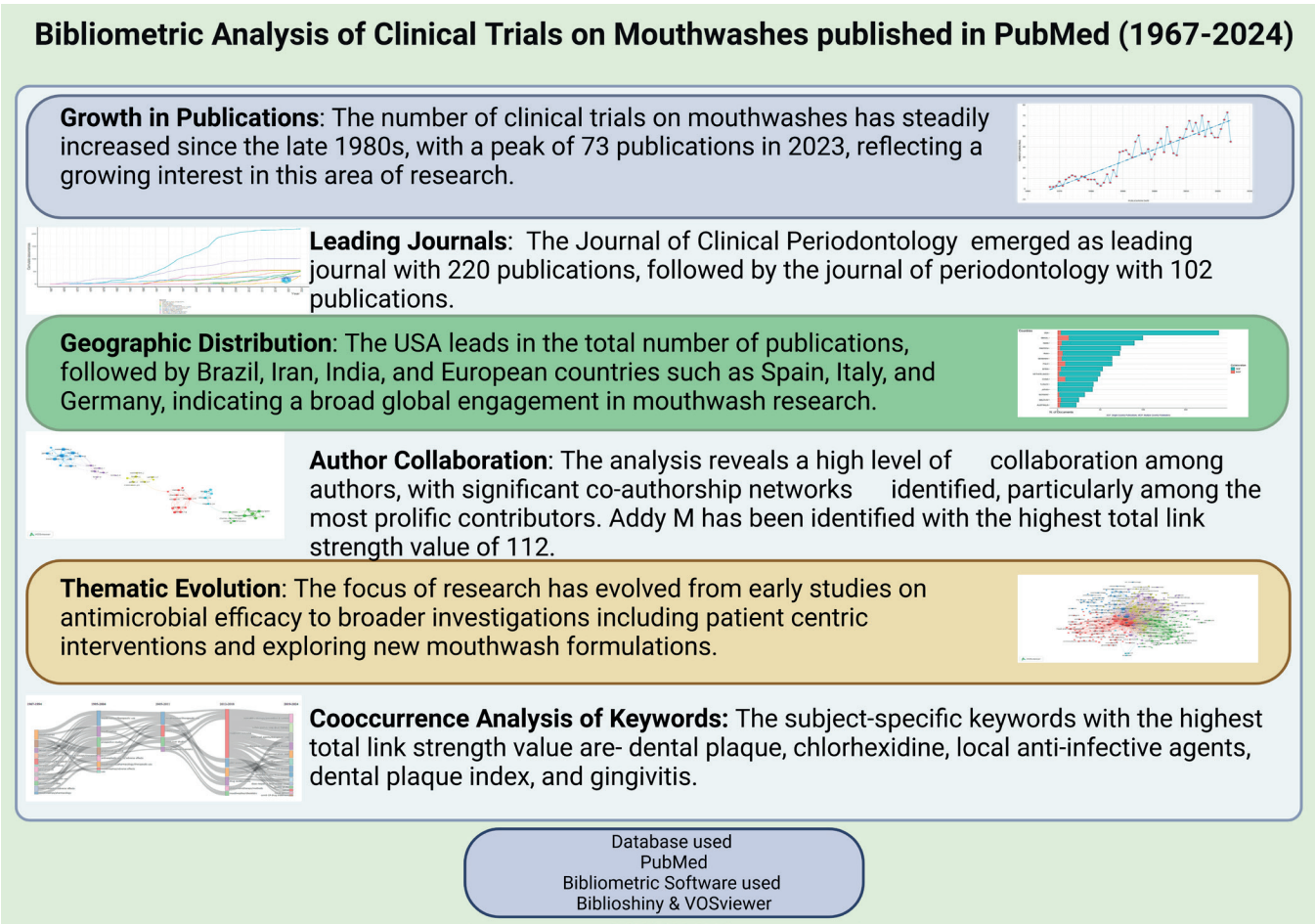


**Figure 10**: Key findings of the bibliometric analysis of clinical trials on mouthwashes. The figure is produced using the premium version of the Biorender App (https://www.biorender.com/) with publishing agreement license number XN27BU57HJ, dated September 20, 2024.

**Image Credit:** Namrata Dagli.

can help ease pain, reduce infections, and improve patient outcomes during and after treatments like chemotherapy. Additionally, considerable attention has been paid to how different mouthwash ingredients prevent tooth decay and protect tooth enamel. The research also explores mouthwash's antibacterial and antifungal properties, aiming to understand its effect on harmful oral bacteria and biofilm.

### *Thematic Evolution*

The progression of clinical trials on mouthwash research reflects a notable shift in focus and priorities over time. Early studies concentrated on assessing basic properties, particularly antibacterial efficacy, laying the groundwork for understanding mouthwash's role in maintaining oral hygiene. Over time, research expanded to include comparisons between different formulations and an interest in patient comfort, indicating a broader consideration of user experience alongside effectiveness. As the years passed, attention shifted to specific oral health conditions, highlighting the potential of mouthwash as a complementary tool in oral care routines. More recent investigations have taken a personalized approach, examining the role of mouthwash in diverse populations and its long-term implications. This evolution points to an increasingly holistic approach to oral health, exploring localized benefits and broader impacts on overall well-being.

## Strengths and Limitations

The study benefits from a comprehensive search strategy and careful manual inspection while study

selection, ensuring the inclusion of relevant clinical trials related to mouthwashes. This approach minimizes the likelihood of overlooking relevant studies and provides a broad perspective on the research landscape. The study selection process is further strengthened by adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, which reduce selection bias and enhance the reliability of the results. Another major strength is advanced bibliometric tools such as VOSviewer and Biblioshiny, which allow for detailed visualization and analysis of research trends, key contributors, and collaboration networks. These tools provide insights into thematic shifts in research focus. The longitudinal nature of the study, spanning nearly six decades from 1967 to 2024, adds further value by highlighting the evolution of research in the field, making it possible to trace how the focus has shifted over time from antimicrobial efficacy to more psychological aspects like quality of life.

Additionally, the thematic analyses complement the quantitative analysis to provide a complete picture of the research landscape. We have summarized the key findings in Figure 10. Moreover, to our knowledge, no other bibliometric analysis has been done on the topic. Only a few similar studies were identified [19, 20].

Despite a valuable contribution to the current literature, the study is not free from limitations. One of the study's main limitations is its reliance on PubMed as the sole data source, which may result in the exclusion of relevant studies indexed in other databases such as Scopus or Web of Science. This could lead to an incomplete representation of the global mouthwash research landscape. Another limitation is the inclusion of only English-language publications, which may introduce geographic and linguistic bias by excluding valuable research conducted in non-English speaking regions. The absence of citation data due to PubMed's lack of citation metrics is another drawback, as it prevents an assessment of the impact of individual studies and authors, limiting the ability to gauge the influence of key contributors in the field.

Furthermore, the focus on clinical trials exclusively narrows the scope of the analysis, potentially overlooking observational or in vitro studies that could complement the understanding of mouthwash efficacy. Lastly, although each title and abstract was reviewed, the full text of the articles was not analyzed, limiting the research evaluation's depth and quality. Thus, the quantitative contribution was preferred over the qualitative contribution when assessing the relevancy.

## FUTURE STUDY RECOMMENDATIONS

The thematic analysis based on keywords helps identify several underexplored areas in clinical trials on mouthwashes that could benefit from further research. One area is the long-term effects of mouthwash use, particularly regarding their impact on the oral microbiome and overall oral health. Another important aspect is the potential for personalized medicine approaches, where research could investigate how mouthwash efficacy varies based on individual factors such as genetics, diet, or oral microbiome composition. The ecological impact of mouthwashes on the oral microbial community, not just targeting specific pathogens, warrants more exploration. There is a need for more emphasis on the connections between mouthwash use and systemic health, such as potential links to cardiovascular health or diabetes management.

Additionally, research on combination therapies could examine how mouthwashes interact with other oral care products or treatments to achieve synergistic effects. Environmental considerations are notably absent in the current research landscape, highlighting the importance of studying the ecological impact of mouthwash use and disposal. Furthermore, cost-effectiveness studies comparing mouthwash interventions in various clinical scenarios could provide valuable economic insights. Finally, behavioral aspects such as patient compliance are other areas where more in-depth research could help improve long-term adherence to mouthwash regimens.

## CONCLUSION

The bibliometric analysis of clinical trials on mouthwashes between 1967 and 2024 reveals a robust and steadily growing field of research. With an annual growth rate of 5.61%, it is clear that interest in the therapeutic and preventative applications of mouthwash has increased consistently over time. Despite the field's long-established presence, ongoing publications and the broad range of explored keywords indicate that research continues to evolve, encompassing various aspects of oral health and hygiene. The thematic analysis suggests that the focus of mouthwash clinical trials shifted from studying basic antibacterial efficacy and composition to exploring personalized, long-term health impacts and the integration of mouthwash into broader wellness strategies. Authorship data highlights the highly collaborative nature of this research, with few single-authored studies and a substantial number of co-authors per publication. However, the relatively low level of international collaboration, especially in leading countries like the USA and the Netherlands, suggests that most research is conducted within national borders.

Key authors and journals have significantly contributed to the field, shaping the mouthwash research trajectory. The field has experienced steady advancement, supported by collaborative efforts, although more outstanding international partnerships could further enhance its global impact.

## CONSENT FOR PUBLICATION

The author reviewed and approved the final version and has agreed to be accountable for all aspects of the work, including any accuracy or integrity issues.

## DISCLOSURE

The author declares that they do not have any financial involvement or affiliations with any organization, association, or entity directly or indirectly related to the subject matter or materials presented in this editorial. This includes honoraria, expert testimony, employment, ownership of stocks or options, patents, or grants received or pending royalties.

## DATA AVAILABILITY

Information is taken from freely available sources for this bibliometric analysis.

## AUTHORSHIP CONTRIBUTION

All authors contributed significantly to the work, whether in the conception, design, utilization, collection, analysis, and interpretation of data or all these areas. They also participated in the paper's drafting, revision, or critical review, gave their final approval for the version that would be published, decided on the journal to which the article would be submitted, and made the responsible decision to be held accountable for all aspects of the work.

## REFERENCES


1. Meurman JH, Bascones-Martinez A. Oral Infections and Systemic Health - More than Just Links to Cardiovascular Diseases. *Oral Health Prev Dent*. 2021;**19**:441-448. doi: 10.3290/j.ohpd.b1993965.
2. Knorst JK, Sfreddo CS, de F Meira G, Zanatta FB, Vettore MV, Ardenghi TM. Socioeconomic status and oral health-related quality of life: A systematic review and meta-analysis. *Community Dent Oral Epidemiol*. 2021;**49**(2):95-102. doi: 10.1111/cdoe.12616.
3. Halboub E, Al-Maweri SA, Al-Wesabi M, Al-Kamel A, Shamala A, Al-Sharani A, Koppolu P. Efficacy of propolis-based mouthwashes on dental plaque and gingival inflammation: a systematic review. *BMC Oral Health*. 2020;**20**(1):198. doi: 10.1186/s12903-020-01185-5.
4. Eid Alroudhan I, Gamal M, Ganji KK, Khan AM, Alsharari KN, Alruwaili MK, Al Waqdani NH. The Effectiveness of Mouthwashes With Various Ingredients in Plaque Control: A Systematic Review and Meta-Analysis. *Altern Ther Health Med*. 2021 Sep;27(5):52-57. http://www.alternative-therapies.com/oa/6823.html
5. Szalai E, Tajti P, Szabó B, Hegyi P, Czumbel LM, Shojazadeh S, Varga G, Németh O, Keremi B. Daily use of chlorine dioxide effectively treats halitosis: A meta-analysis of randomized controlled trials. *PLoS One*. 2023;**18**(1):e0280377. doi: 10.1371/journal.pone.0280377.
6. Katebi K, Hassanpour S, Eslami H, Salehnia F, Hosseinifard H. Effect of Pilocarpine Mouthwash on Salivary Flow Rate in Patients with Xerostomia: A Systematic Review and Meta-Analysis. *J Dent (Shiraz)*. 2023;**24**(1 Suppl):76-83. doi: 10.30476/dentjods.2022.94335.1778.
7. Karamani I, Kalimeri E, Seremidi K, Gkourtsogianni S, Kloukos D. Chlorhexidine Mouthwash for Gingivitis Control in Orthodontic Patients: A Systematic Review and Meta-Analysis. *Oral Health Prev Dent*. 2022;**20**:279-294. doi: 10.3290/j.ohpd.b3170043.
8. Potting CM, Uitterhoeve R, Op Reimer WS, Van Achterberg T. The effectiveness of commonly used mouthwashes for the prevention of chemotherapy-induced oral mucositis: a systematic review. *Eur J Cancer Care (Engl)*. 2006;**15**(5):431-9. doi: 10.1111/j.1365-2354.2006.00684.x.
9. Twetman S, Petersson L, Axelsson S, Dahlgren H, Holm AK, Källestål C, Lagerlöf F, Lingström P, Mejàre I, Nordenram G, Norlund A, Söder B. Caries-preventive effect of sodium fluoride mouthrinses: a systematic review of controlled clinical trials. *Acta Odontol Scand*. 2004; **62** (4): 223-30. doi: 10.1080/00016350410001658.
10. van Swaaij BWM, Van der Weijden GA, Smith RJ, Timmerman MF, Slot DE. Essential oils mouthwash with or without alcohol in relation to effect on parameters of plaque and gingivitis: A systematic review and meta-analysis. *Int J Dent Hyg*. 2024. doi: 10.1111/idh.12843.
11. Brookes ZLS, Belfield LA, Ashworth A, Casas-Agustench P, Raja M, Pollard AJ, Bescos R. Effects of chlorhexidine mouthwash on the oral microbiome. *J Dent*. 2021;**113**:103768.

doi: 10.1016/j.jdent.2021.103768.

12. Watanabe Y, Seto Y, Oikawa R, Nakazawa T, Furuya H, Matsui H, Hosono S, Noike M, Inoue A, Yamamoto H, Itoh F, Wada K. Mouthwash-Based Highly Sensitive Pyro-Genotyping for Nine Sexually Transmitted Human Papilloma Virus Genotypes. *Int J Mol Sci*. 2020; **21**(10): 3697. doi: 10.3390/ijms21103697.
13. Khobragade VR, Vishwakarma P, Dodamani AS, Kshirsagar MM, Raut SN, Deokar RN. Herbal Mouthwash for the Management of Oral Diseases: A Review on the Current Literature. *J Oral Health Community Dent*. 2021; **15** (2): 71. doi: 10.5005/jp-journals-10062-0085
14. Donthu N, Kumar S, Mukherjee D, Pandey N, Lim WM. How to conduct a bibliometric analysis: An overview and guidelines. *J Bus Res*. 2021;**133**:285-96. https://doi.org/10.1016/j.jbusres.2021.04.070
15. 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. doi: https://doi.org/10.1136/bmj.n71
16. Van Eck NJ, Waltman L. VOSviewer Manual. Leiden, Netherlands: Leiden University; 2023. [Cited 2024 April 14]. Available from: http://ttps://www.VOSviewer.com/documentation/Manual_VOSviewer_1.6.20.pdf.
17. Aria M, Cuccurullo C: bibliometrix: An R-tool for comprehensive science mapping analysis. *J Inform*. 2017, **11**:959-75. doi:10.1016/j.joi.2017.08.007
18. BioRender. 2024. Available at https://biorender.com [Accessed September 20, 2024]
19. Zhou F, Mu X, Li Z, Guo M, Wang J, Long P, Wan Y, Yuan T, Lv Y. Characteristics of Chinese herbal medicine mouthwash clinical studies: A bibliometric and content analysis. *J Ethnopharmacol*. 2023; **307**:116210. doi: 10.1016/j.jep.2023.116210.
20. Mauricio F, Mauricio-Vilchez C, Galarza-Valencia D, Alvitez-Temoche D, Vilchez L, Espinoza-Carhuancho F, Mayta-Tovalino F. Scientometric Analysis of Activated Carbon or Probiotics in Mouthwashes or Toothpastes: Dynamicity, Spatiotemporal Evolution and Trends. *Odovtos-Int J Dent Sc*. 2024, **26** (4): 247-58. https://doi.org/10.15517/ijds.2024.60813