

LETTER TO THE EDITOR

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# Clinical trial landscape for periodontitis treatment: Trend analysis and future perspectives

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Dear editor,

Periodontitis, particularly chronic periodontitis, is a common chronic inflammatory disease affecting both oral and systemic health, often leading to alveolar bone resorption and loss of periodontal attachment [1, 2]. Recent studies have demonstrated a close relationship between periodontitis and the onset and progression of systemic diseases, making the prevention and treatment of periodontitis crucial for overall health [4]. Currently, periodontal treatment mainly relies on ultrasonic scaling and periodontal debridement [5]. However, with the development of stem cells, traditional Chinese medicine, and other biomedical approaches, many new interventions have emerged in recent years, challenging conventional invasive treatment methods [3].

The clinical trial landscape of periodontitis reflects the recent development and evaluation of clinical interventions, providing deep insights into the latest treatment strategies, research trends, and future directions. On September 1, 2024, we conducted a database search using the keyword “periodontitis,” excluding non-interventional clinical trials, and identified 248 clinical trials. These trials were categorized based on their phase,

status, and treatment type to evaluate their development trends (Supplementary Table 1).

In recent years, the number of clinical trials has remained relatively stable, reaching a peak in 2024, although the decline over the past two years may be attributed to the impact of the COVID-19 pandemic. These clinical trials cover different research phases, particularly Phase II and beyond (Fig. 1A), with Phase IV trials dominating, comprising 69 studies focused on post-market surveillance and safety. Phase III trials include 66 studies (17.5%) validating efficacy, while Phase II trials also represent a significant proportion (50 studies, 20.1%). The lower proportion of early-phase trials may indicate market saturation or the challenges of early research. The proportions of Phase I and Phase 0 trials are 9.6% (24 studies) and 7.2% (18 studies), respectively. Currently, most clinical trials have been completed and will soon enter clinical application, indicating a new breakthrough in periodontitis treatment (Fig. 1B). The number of trials related to supplements (including dietary supplements) and natural products (81 trials, 32.66%) suggests an increasing interest in non-invasive or dietary interventions (Fig. 1C). Meanwhile, traditional local treatment methods remain the mainstay of periodontitis treatment, accounting for 16.13% (47 trials) of the studies. Research on other categories is less common, reflecting a diverse yet non-dominant research landscape. Among all trials related to supplements and natural products, natural products continue to dominate (Fig. 1D), particularly products such as curcumin, resveratrol, aloe vera, and so on. As research on oral microbiota deepens, studies on prebiotics, probiotics, and related products are gradually

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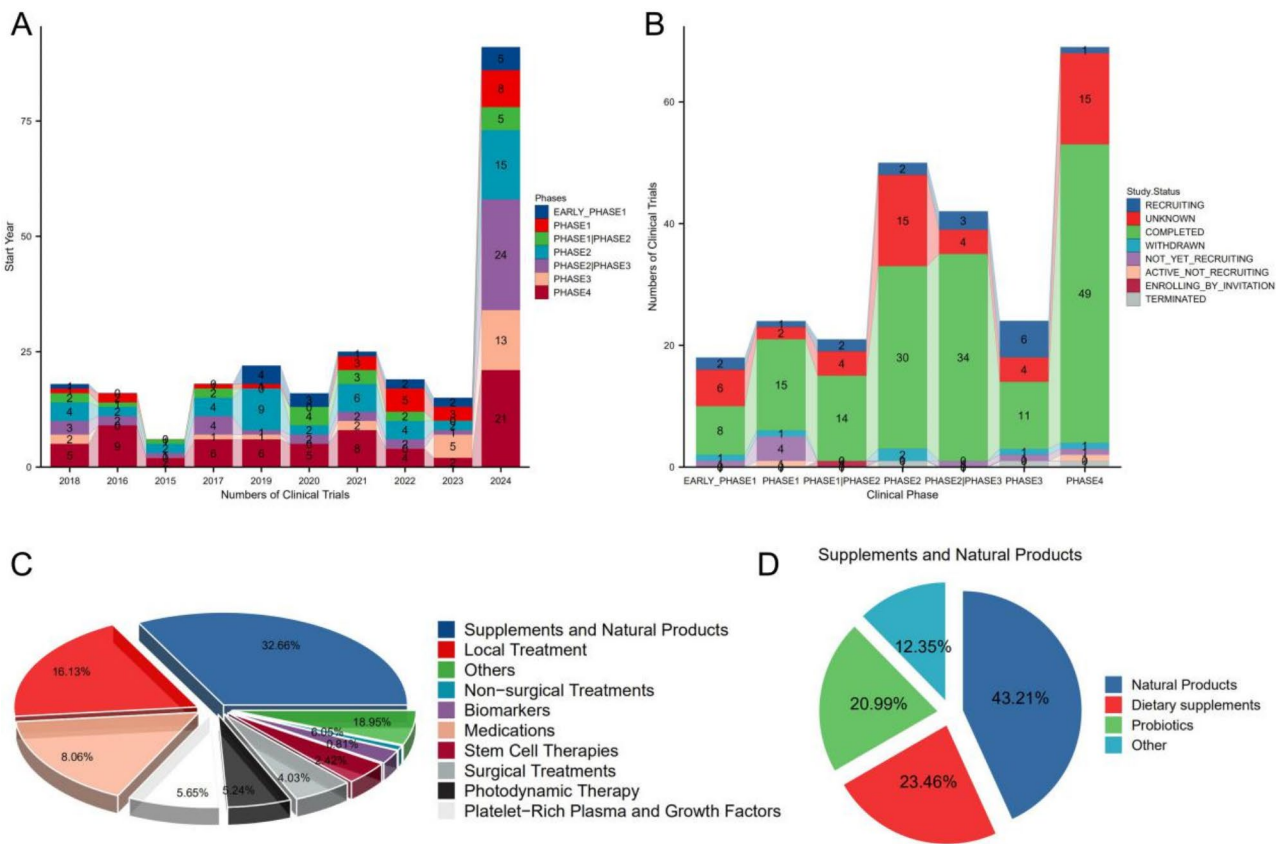


**Fig. 1** The Clinical Trial Landscape for Periodontitis. **(A)** Distribution and status of clinical trials across different phases (A significant increase in clinical trials began after 2018). **(B)** Distribution and status of clinical trials across different phases from 2018 to 2024. **(C)** Interventional clinical trials for periodontitis categorized by treatment type. **(D)** Main components within the supplements and natural products category

emerging, further highlighting their role in inflammation management.

However, this analysis has certain limitations, primarily due to incomplete and biased data in clinical trial databases, as not all trials are registered or detailed. To mitigate this issue, we also searched government databases. Nevertheless, the lack of start dates hindered the analysis of annual trends. Additionally, the challenge of separating drug effects in multi-drug trials complicates classification and data interpretation. In future research, advanced statistical methods and subgroup analysis can help clarify the contribution of each drug in combination therapies.

This evaluation reveals that the clinical trial landscape for periodontitis treatment is undergoing significant changes. Although traditional invasive local treatment methods still hold an important position, increasing research is focusing on non-invasive or natural product interventions, indicating that clinical practice is gradually shifting towards safer and more patient-friendly approaches. This trend challenges existing periodontitis treatment theories, necessitating a reassessment of current treatment models and consideration of how to

integrate these emerging non-invasive interventions into standard care.

Although the number of studies on supplements and natural products is increasing, large-scale, long-term clinical trials are still needed to verify their efficacy and safety. These studies should focus on understanding the mechanisms of these interventions to better grasp how they affect the progression of periodontitis. Since the etiology and progression of periodontitis may be influenced by factors such as race, diet, and environment, multi-center and international clinical trials will help evaluate the treatment effects on different populations and determine the best treatment strategies worldwide. As combination therapies rise, future research should aim to optimize the combination of different drugs and interventions to maximize therapeutic effects while minimizing side effects. This may require the application of advanced statistical and machine learning methods to analyze complex datasets and determine the optimal treatment regimen.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12967-024-05697-4>.

Supplementary Material 1

### Author contributions

Zhegnrui: Conceptualization; methodology; software; validation; formal analysis; investigation; data curation; writing – original draft; project administration. Jing Li: Conceptualization; methodology; software; validation; formal analysis; investigation; data curation; writing – original draft. Xufeng Huang: Funding acquisition; methodology; resources; writing – review and editing; supervision. All authors read and approved the final manuscript.

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### Data availability

All data used and/or analyzed in this manuscript are publicly available in the clinical trial database (<https://clinicaltrials.gov/>).

### Declarations

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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