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Research article

Association between periodontal disease and coronary heart disease: A bibliometric analysis

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ABSTRACT

Background: Periodontal disease and coronary heart disease are both prevalent diseases worldwide and cause patients physical and mental suffering and a global burden. Recent studies have suggested a link between periodontal disease and coronary heart disease, but there is less research in this field from the perspective of bibliometrics.
Objective: This study aimed to quantitatively analyze the literature on periodontal disease and coronary heart disease to summarize intellectual bases, research hotspots, and emerging trends and pave the way for future research.
Methods: The Science Citation Index Expanded database was used to retrieve study records on periodontal disease and coronary heart disease from 1993 to 2022. After manual screening, the data were used for cooperative network analysis (including countries/regions, institutions and authors), keyword analysis, and reference co-citation analysis by CiteSpace software. Microsoft Excel 2019 was applied for curve fitting of annual trend in publications and citations.
Results: A total of 580 studies were included in the analysis. The number of publications and citations in this field has shown an upward trend over the past 30 years. There was less direct collaboration among authors and institutions in this field but closer collaboration between countries. The United States was the country with the most published articles in this field (169/580, 29.14%). Based on the results of keyword analysis and literature co-citation analysis, C-reactive protein, oral flora, atherosclerosis, infection, and inflammation were previous research hotspots, while global burden and cardiovascular outcomes were considered emerging trends in this field.
Conclusion: Studies on periodontal disease and coronary heart disease, which have attracted the attention of an increasing number of researchers, have been successfully analyzed using bibliometrics and visualization techniques. This paper will help scholars better understand the dynamic evolution of periodontal disease and coronary heart disease and point out the direction for future research.
Clinical significance: This paper presents an overview between periodontal disease and coronary heart disease. Further exploration of the two diseases themselves and the potential causal relationship between the two is necessary and relevant, which may impact basic research, diagnosis,

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and treatment related to both diseases. This will aid the work of researchers and specialist doctors, and ultimately benefit patients with both diseases.

1. Introduction

Periodontal disease (PD) comprises multiple inflammatory conditions that affect the supporting structures of the teeth (gums, alveolar bone, periodontal membrane), which may lead to tooth loosening and loss [1]. It was reported that 50% of the global population suffers from PD, which greatly affects their nutrition, life management, and self-esteem [2]. Moreover, PD is also considered a risk factor for a variety of diseases, including cardiovascular disease, metabolic disease, and neurodegenerative diseases [3–5].

Coronary heart disease (CHD) refers to the aggregation of atherosclerotic plaques in coronary arteries resulting in coronary artery stenosis, which may be associated with diseases such as myocardial ischemia and infarction [6]. CHD stands as one of the foremost global causes of death, contributing to approximately 7 million deaths and 129 million disability-adjusted life years (DALYs) annually [7,8]. In the past decades, the relationship between PD and CHD has also gradually gained the attention of researchers. On the one hand, PD increases the probability of adverse cardiovascular events, including CHD [9,10]. While effective periodontal care can reduce the incidence of cardiac death, myocardial infarction, and heart failure while reducing the concentration of C-reactive protein and fibrinogen [11,12]. On the other hand, the presence of periodontal pathogens and bacterial products significantly increases various inflammatory mediators, including C-reactive protein, prostaglandins, IL-1, IL-6, and certain matrix metalloproteinases, both at oral and systemic levels. This exacerbates atherosclerosis and contributes to a diminished extent of positive atheromatous plaque remodeling [13–16]. In addition, upregulation of miRNA in gingival crevicular fluid associated with cardiovascular disease risk in patients with periodontitis also suggested a link between periodontitis and cardiovascular disease [17,18]. Considering the increasing prevalence of PD and CHD worldwide and their impact on the quality and length of life of patients, further study on PD and CHD is of great clinical importance.

Bibliometrics, defined by Alan Pritchard in 1969, can integrate retrospective information effectively, search correlations of data, and predict future trends for scholars [19,20]. Over the past decades, bibliometric analyses have been widely applied to medical research, such as research on PD [21], cardiovascular and cerebrovascular diseases [22], cancer [23], and metabolic diseases [24]. In the past 30 years, the number of articles related to PD and CHD has been growing rapidly, but bibliometrics have rarely been applied to conduct a systematic analysis. In 2021, Trindade and colleagues [25] examined the molecular associations between PD and CHD by bibliometric methods, but did not further explore the link between the two diseases in other areas. In 2023, Tang et al. [26] conducted a bibliometric analysis of the links between periodontitis and cardiovascular diseases, but this study did not focus its research on the field of coronary artery disease but rather on the entire field of cardiovascular disease.

This study aimed to conduct a bibliometric analysis in this field to summarize intellectual bases, research hotspots, and emerging trends and pave the way for future research. Further identification of the relationship between PD and CHD may impact the future diagnosis and treatment of both diseases. This will help researchers and specialists in their work and ultimately benefit patients suffering from both diseases.

2. Methods

2.1. Data source and search strategy

The Science Citation Index Expanded (SCI-E) database in the Web of Science Core Collection (WOSCC) database (https://www-webofscience-com), considered the optimal database for bibliometric analysis, was selected as the data source in this study [27–29].

The search query was "TS=(Periodontal diseases OR Periodont* OR Gingiv* OR Tooth loss OR Tooth migration OR Tooth mobility) AND TS=(Coronary heart disease OR Coronary artery disease OR Coronary disease OR Myocardial infarction OR Myocardial ischemia OR Coronary thrombo* OR Angina pectoris OR Angina* OR Acute coronary syndrome OR Coronary artery bypass* OR Coronary bypass* OR CABG OR Percutaneous coronary intervention OR PCI)". All retrieved publications were evaluated by two independent reviewers (WPS and XWB) via titles, abstract and keywords to exclude the studies not related to PD and CHD. If disagreement persisted after consultation between two reviewers, the judgment of a third reviewer (HW) was considered final. To avoid bias from database updating, literature retrieval was completed on a single day (2022-11-30).

2.2. Inclusion criteria

Publications that fully met the following conditions were included in the subsequent analysis, and the remaining articles were excluded.

(1) Articles and review articles related to the field of PD and CHD
(2) Articles and review articles written in English;
(3) Articles and review articles published from 1993 to 2022.

2.3. Exclusion criteria

Publications that were clearly unrelated to both PD and CHD, publications that were not written in English, publications of types other than articles and review articles, and publications prior to 1993 were excluded from follow-up bibliometric studies.

2.4. Data collection and data analysis

After performing the literature retrieval, all the study records were exported in plain-text file format including the title, authors, institutions, publication year, countries/regions, keywords, abstract, references.

The Analysis and Citation Report in WOS was applied to preliminarily analyze the general information of the publications, including publication year, citations, authors, and journals. The detailed information of journal impact factor (IF) was obtained from the 2020 Journal Citation Reports (http://clarivate.com/products/web-of-science). Curve fitting of annual trend in publications and citations were carried out using Microsoft Excel 2019. The model with the highest correlation coefficient (R^2) value was considered to be the best fitting one. Then, visualization analysis of exported data was conducted with CiteSpace (Version 6.1 R4), a visualization software based on the Java platform [30].

CiteSpace software was used to perform cooperative network analysis and generate a cooperative visualization map. Number of publications and between centrality (BC) of authors, institutions and countries/regions information were calculated through cooperative network analysis. In the cooperative visualization map, the node represents the author, institution, or country, the size of which shows the number of publications. The connections between nodes indicate cooperation. As shown in the legend, various colors represent the year of the first cooperation between nodes. Keywords were applied for co-occurrence and burst analysis. References were selected for co-citation analysis. In addition, discipline and journal analyses were performed using a dual-map overlay. The configuration of CiteSpace is shown in Table 1.

3. Results

3.1. General information

A total of 1904 publications were retrieved from the literature search. Among them, 580 publications were included for follow-up bibliometric analysis after screening, consisting of 500 articles (500/580, 86.207%) and 80 review articles (80/580, 13.793%) (Fig. 1). Between 1993 and 2001, the annual publications in this field remained below 10, but since 2002, there has been a consistent upward trend ($R^2 = 0.9477$), reaching its peak in 2021 with 46 publications, as illustrated in Fig. 2. The annual citation trends mirrored the pattern of publication, displaying an overall upward trajectory ($R^2 = 0.9069$) and reaching a pinnacle in 2021 with 2707 citations (Fig. 3).

3.2. Discipline and journal analyses

A total of 580 studies were disseminated across 245 journals. The three leading journals in terms of the number of articles published were the *Journal of Periodontology* (70/580, 12.07%), the *Journal of Clinical Periodontology* (42/580, 7.24%), and the *Journal of Periodontal Research* (28/580, 4.83%) (Table 2). Most journals (221/245, 90.20%) have published only three or fewer articles in this field in the past 30 years, of which 171 journals have only one publication record (Table 2).

The dual-map overlay (Version 2.0) designed by Chen and Leydesdorff [31] in CiteSpace was applied for discipline and journal analyses in this field, which is able to display citing journals (left side) and cited journals (right side) in the same user interface [32]. The Blondel algorithm was applied to assign journals to a cluster, which provided access to community networks of varying resolutions of community detection [33,34]. In the journal dual-map overlay, the colored curves represent the path of the references, pointing from the citing map on the left to the cited map on the right. The starting and ending positions of these curves indicate how an article builds on previous work because the citing map and cited map are divided into different topic areas and each position on the map belongs to one of the areas [35]. Studies on PD and CHD appeared mainly from three regions' citing maps: molecular/biology/immunology in orange, dentistry/dermatology/surgery in gray, and medicine/medical/clinical in green (Fig. 4). The citation curve from the three main areas on the left points to the three dominating areas of the cited map, labeled molecular/biology/genetics, health/nursing/medicine, and dermatology/dentistry/surgery (Fig. 4). The cited journal provides the knowledge base of the citing journal, and these change tracks indicate the change in the subject center of the journal, such as the change from

Table 1
The configuration of CiteSpace.

Node type	Time slicing	Selection	Pruning
Authors Institution Country	1993–2022; Years per slice: 1	Top 100%	No pruning
Keyword Reference		g-index; k = 25	Pathfinder; Pruning the merged network

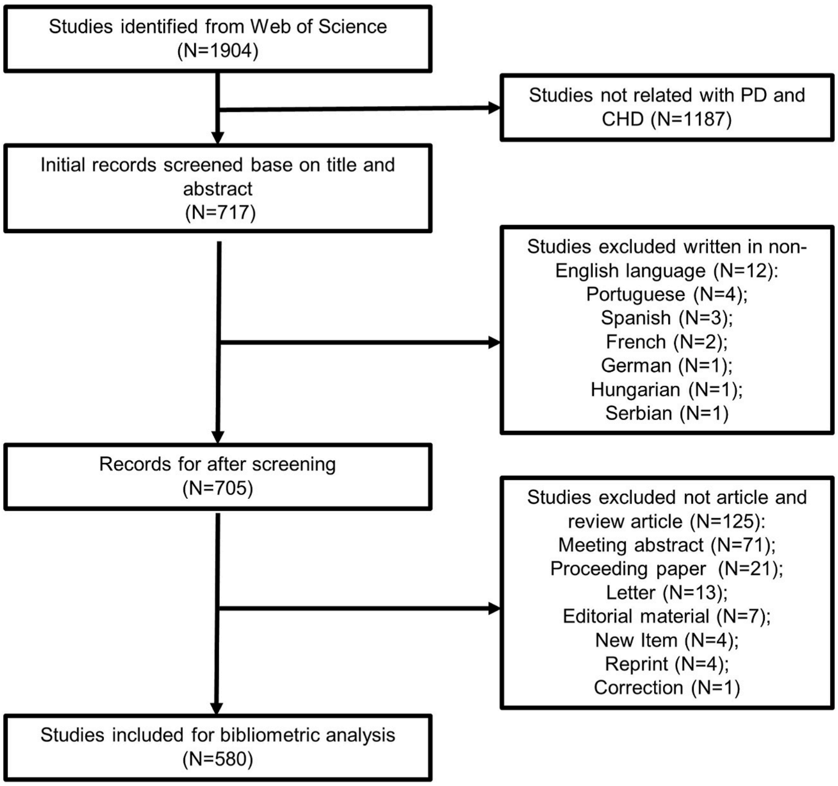

Fig. 1. Flowchart of the search strategy. **Abbreviations: PD**, periodontal disease; **CHD**, coronary heart disease.

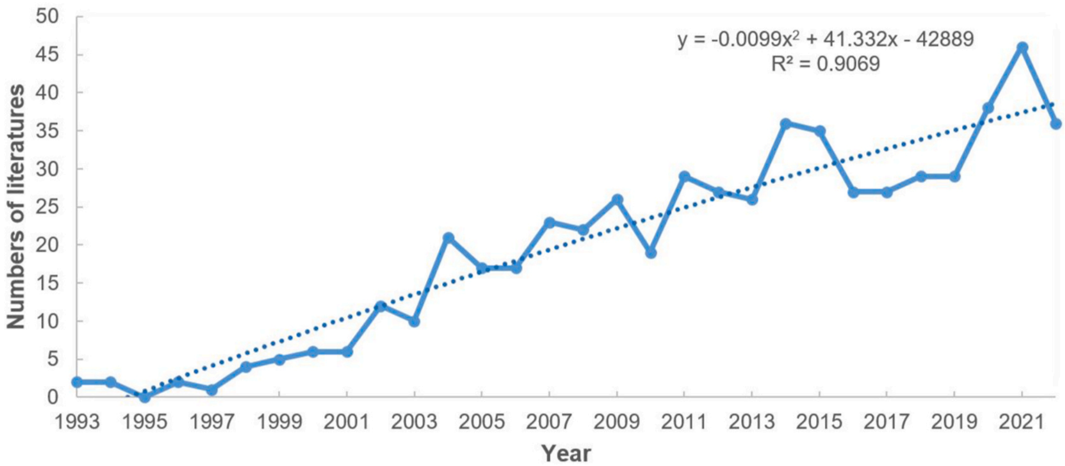

Fig. 2. The number of published studies over time.

molecular/biology/genetics to dentistry/dermatology/surgery.

4. Cooperation network analysis

4.1. Distribution of countries/regions

The 580 publications were from 61 countries, among which the United States contributed more than a quarter of the publications (169/580, 29.14%), followed by Sweden and Finland (**Supplemental Table S1**). Moreover, the United States also peaked at the BC of cooperation (0.56), which indicated that the cooperation degree between the United States and other countries was at a relatively high

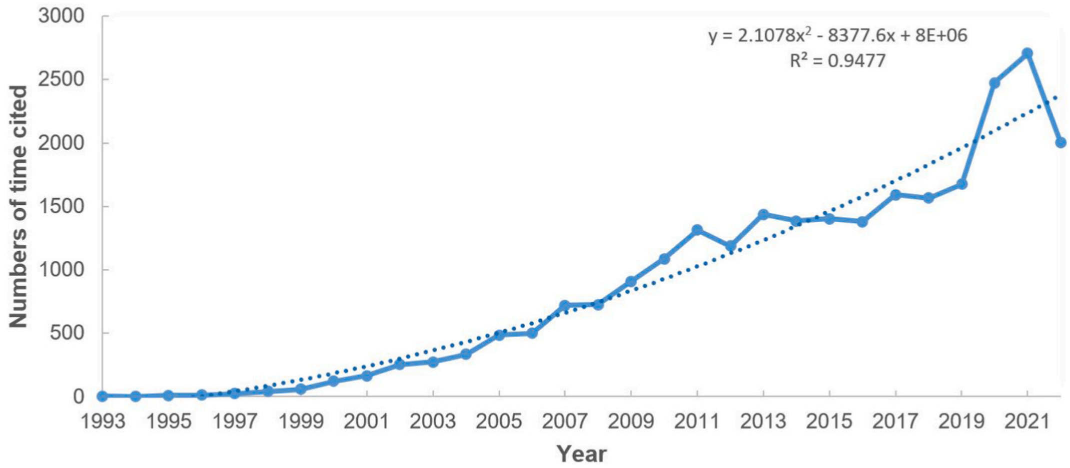

Fig. 3. The annual trends in citations.

Table 2
Top 10 journals with the largest number of published studies.

No.	Journals	Counts	% of 580	Categories	2022 IF
1	*Journal of Periodontology*	70	12.069%	Dentistry, Oral Surgery & Medicine	4.3
2	*Journal of Clinical Periodontology*	42	7.241%	Dentistry, Oral Surgery & Medicine	6.7
3	*Journal of Periodontal Research*	28	4.828%	Dentistry, Oral Surgery & Medicine	3.5
4	*Journal of Dental Research*	21	3.621%	Dentistry, Oral Surgery & Medicine	7.6
5	*Atherosclerosis*	17	2.931%	Peripheral Vascular Disease; Cardiac & Cardiovascular Systems	5.3
6	*PLOS ONE*	16	2.759%	Multidisciplinary Sciences	3.7
7	*BMC Oral Health*	8	1.379%	Dentistry, Oral Surgery & Medicine	2.9
8	*Journal of Clinical Medicine*	8	1.379%	Medicine, General & Internal	3.9
9	*Oral Diseases*	8	1.379%	Dentistry, Oral Surgery & Medicine	3.8
10	*Scientific Reports*	7	1.207%	Multidisciplinary Sciences	4.6

level (**Supplemental Table S2**). As shown in the countries/region cooperation visualization map, the countries/regions that cooperated closely with the United States were mainly distributed in developed countries/regions, including Australia, South Korea, Chinese Taiwan, and Canada (Fig. 5).

4.1.1. Distribution of institutions

Authors at 906 institutions published studies in this field. The institution with the highest number of published articles was the University of Helsinki (47/580, 8.10%), which was also the only institution with a BC exceeding 0.1 (0.16) (**Supplemental Tables S3 and S4**). As shown in Fig. 6, the institution cooperation visualization map was relatively sparse, as was the case for high-publication institutions. For example, there was only a small amount of direct collaboration between the top two most published institutions (the University of Helsinki and Karolinska Institute), while the third most published institution (the University of North Carolina) had no direct collaboration with the two.

5. Distribution of authors

A total of 2659 authors participated in the publications related to PD and CHD. Pussinen PJ (15/580, 2.59%) ranked first in terms of publications, followed by Offenbacher S and Buhlin K (**Supplemental Table S5**). The cooperation visualization map of authors shows a certain degree of cooperation between authors (Fig. 7). However, author cooperation was relatively scattered, which was consistent with the low BC of all authors ($\leq$0.02) (**Supplemental Table S6**).

6. Keywordanalysis

Keywords are concise summaries of articles, the analysis of which can ascertain hotspots and emerging trends in research [36]. After preliminary extraction and manual sorting, 1653 keywords were filtered out from 580 articles. The top 10 frequent and BC keywords are listed in Supplemental Tables S7 and S8. C-reactive protein and infection were the keywords that appeared most frequently except for two diseases and related words. Moreover, C-reactive protein, Porphyromonas gingivalis (P. gingivalis), Actinobacillus actinomycetemcomitans (A. actinomycetemcomitans), infection, and inflammation were associated with a higher BC.

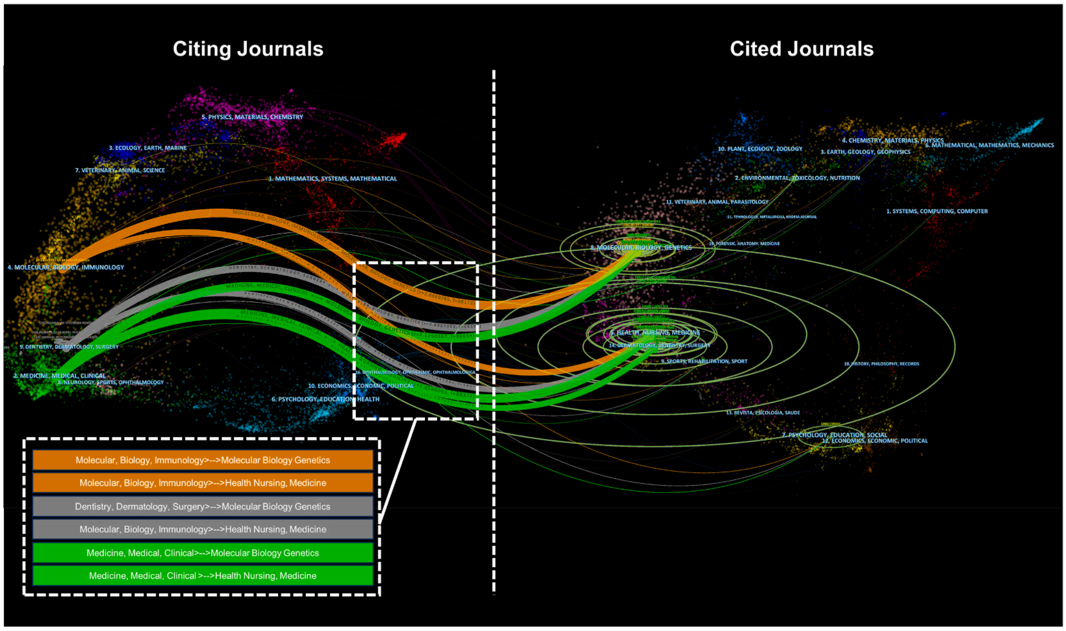

Fig. 4. The dual-map overlay of journals related to periodontal disease and coronary heart disease generated by CiteSpace. The clusters on the left side and right side respectively displayed citing journals and cited journals. The colored curves represented the pathway from citing map to cited map, the size of which showed the frequency of citation.

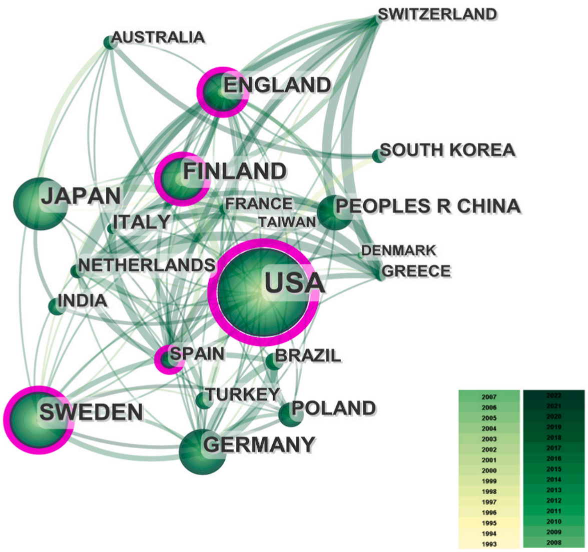

Fig. 5. Cooperation network map of countries/regions. The size of the nodes indicated the number of publications and the connections between them showed cooperation. Various colors represent the year of cooperation. The outermost purple ring represents the centrality level, and the nodes with high centrality are considered to be the key points in the research field. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

To better reflect the research hotspots and trends in this field, high-frequency keywords were used for further analysis [21]. The top 15 levels of the most cited or occurring keywords from each slice were selected for the generation of a high-frequency keyword co-occurrence network and cluster network mapping (Fig. 8). The high-frequency keywords had a better clustering effect, and the average modularity and silhouette of clustering were 0.7657 and 0.9153, respectively. High-frequency keywords produced 8 clusters, including C-reactive protein (#2) and risk factor (#3).

Burst keyword analysis detects the keywords with high-frequency change rates and fast growth rates by investigating the time distribution of keywords and then analyzing the frontier fields and development trends of the subject. As shown in Fig. 9, the keyword

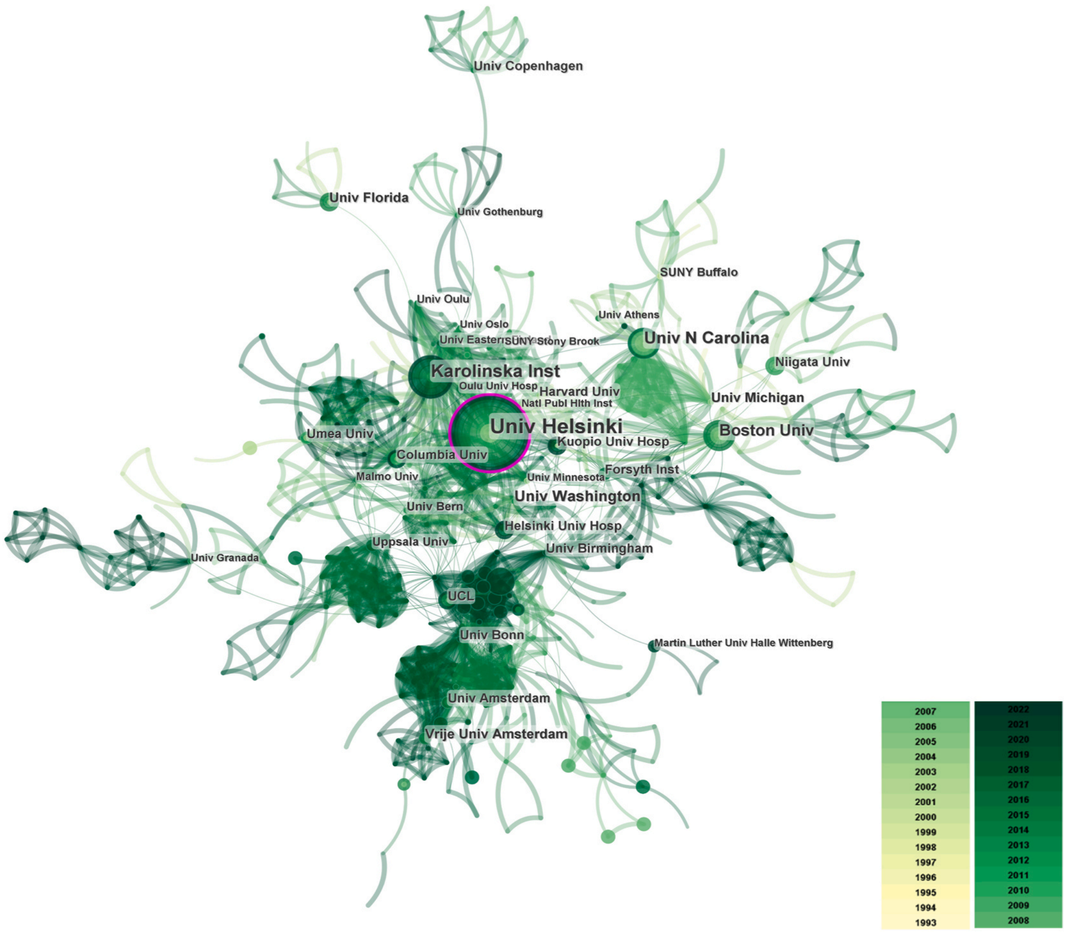

Fig. 6. Cooperation network map of institutions. The size of the nodes indicated the number of publications and the connections between them showed cooperation. Various colors represent the year of cooperation. The outermost purple ring represents the centrality level, and the nodes with high centrality are considered to be the key points in the research field. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

C-reactive protein burst for the longest period, and A. actinomycetemcomitans had the highest burst strength. Moreover, event, disease, and global burden were the latest burst keywords since 2020.

6.1. Reference co-citation analysis

Two articles cited by later studies at the same time are called reference co-citations, which are often applied to reflect the relationship and structure of references in an academic field [37,38]. Reference co-citation analysis is used to explore co-citation correlations between articles and summarize the data to create major clusters.

The cited references with the highest frequency and highest BC are listed in Supplemental Tables S9 and S10, respectively. The study "Periodontal disease and atherosclerotic vascular disease: Does the evidence support an independent association?: A scientific statement from the American Heart Association" published in 2012 in Circulation received the most citations [39]. This review from the American Heart Association evaluated the association between PD and atherosclerotic vascular disease (ASVD) and introduced the mechanistic details of PD and ASVD related to this topic [39]. The reference with the highest BC was the epidemiological study on periodontal microbiota and carotid intima-media thickness published by Desvarieux et al. in Circulation in 2005 [40]. In general, the references with high numbers of citations were mainly summative and critical papers, while the references with high BC values were mostly original studies.

As shown in Fig. 10, the work by Lockhart PB et al. [39] reviewing the association between PD and atherosclerotic vascular disease had the strongest burst strength of reference co-citations. The reference co-citation burst of Ryden L et al. [10] and Park SY et al. [12] continued until 2022 (Fig. 10). The timeline cluster graph of the cited references is shown in Fig. 11. The largest cluster (#0) is labeled dental status by the log-likelihood ratio (LLR), in which the top 3 cited members in this cluster are the works of Lockhart PB et al. [39], Tonetti MS et al. [41], and Schenkein Harvey A et al. [13]. The latest 3 clusters were cardiovascular outcome (#3), cardiovascular

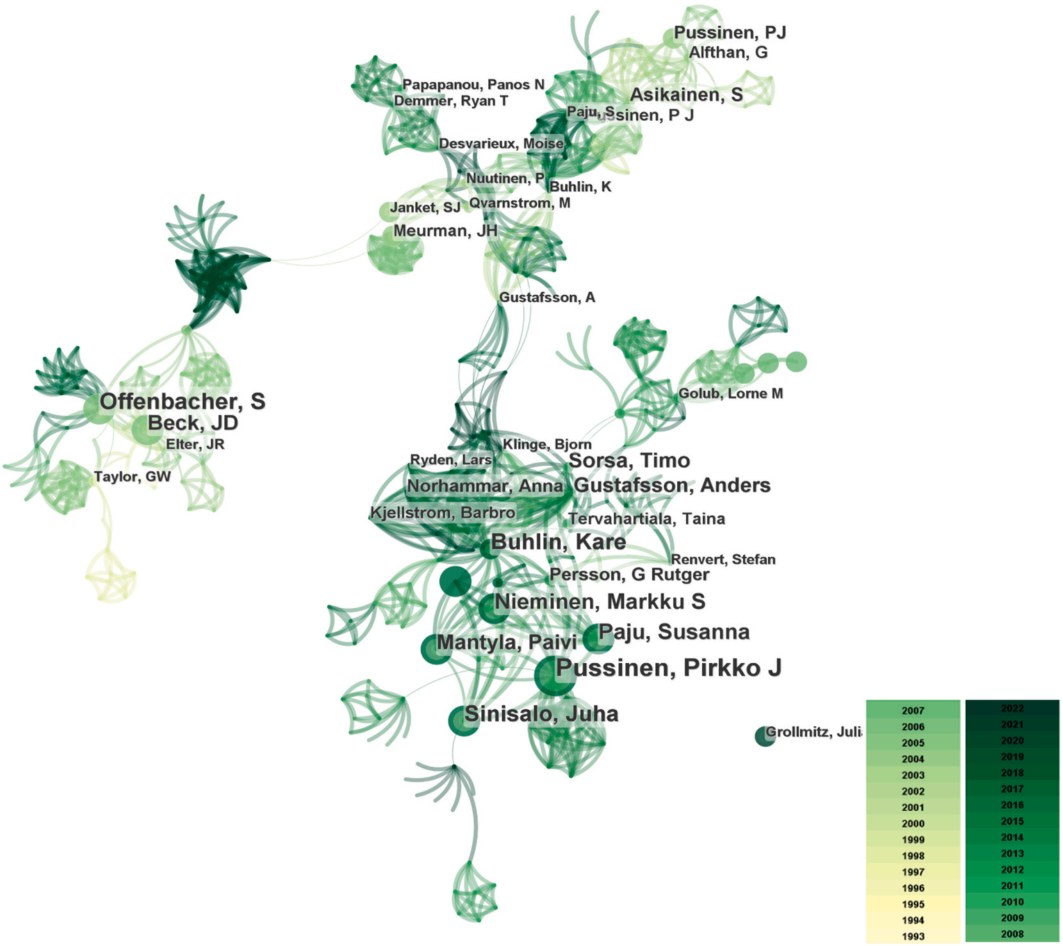

Fig. 7. Cooperation network map of authors. The size of the nodes indicated the number of publications and the connections between them showed cooperation. Various colors represent the year of cooperation. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

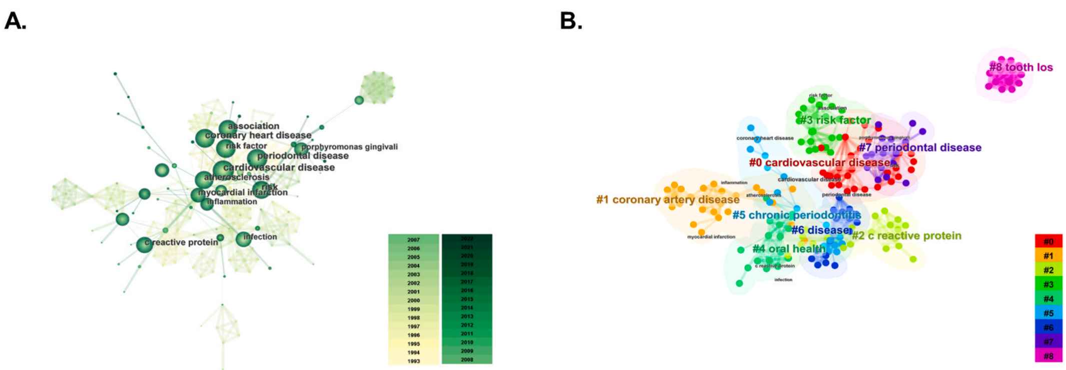

Fig. 8. Visualization map of high-frequency keyword analysis. A. Co-occurrence network map; B. Cluster network map.

Fig. 9. Top 20 keywords with the strongest citation bursts. The red line represents years when keywords burst, and the green line indicates years when keywords were used less frequently. Burst strength reflects the occurrence times of keywords in a certain period. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

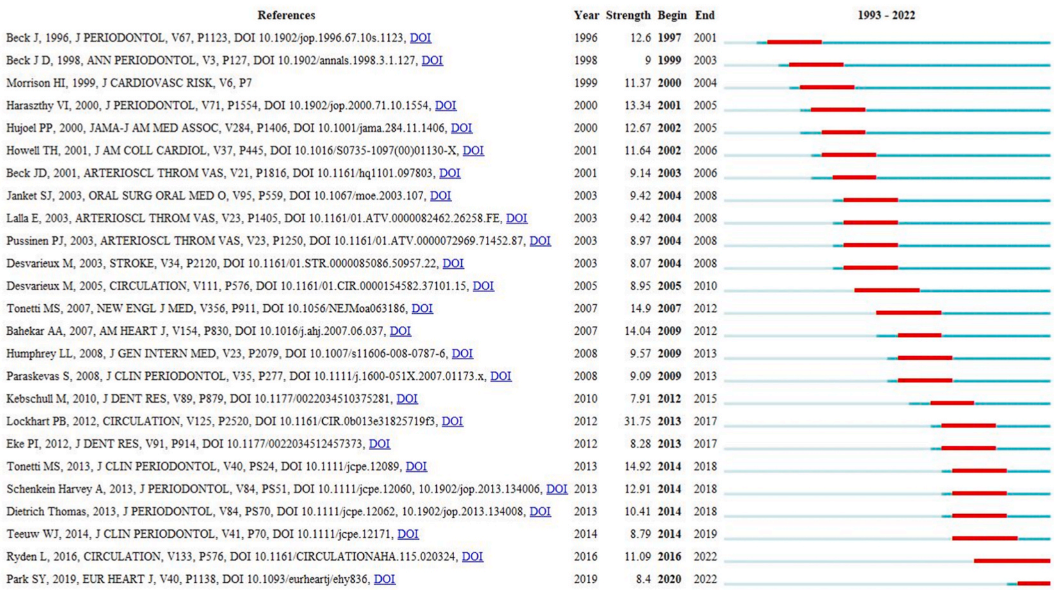

Fig. 10. Top 25 cited references with the strongest citation bursts. The red line represents years when keywords burst, and the green line indicates years when keywords were used less frequently. Burst strength reflects the occurrence times of citations in a certain period. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

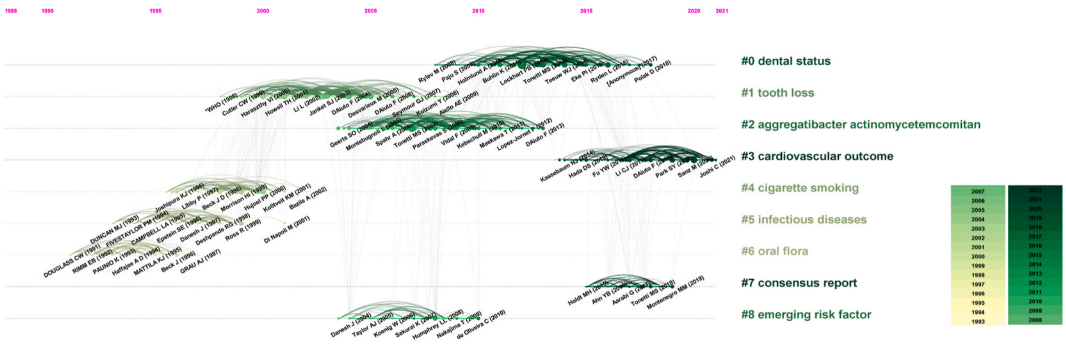

Fig. 11. Timeline cluster map of co-citations.

outcome (#7), and cardiovascular outcome (#0). The most representative keywords under different labels of each cluster are shown in Supplemental Table S11.

7. Discussion

7.1. Intellectual bases of the studies between PD and CHD

Based on bibliometrics, CiteSpace software was used to visualize and analyze the literature in the field of periodontitis and CHD, and the research hotspots and emerging trends in this field were also summarized. After searching and screening, 580 articles and review articles were included for the follow-up bibliometric analysis. Since 1993, the number of annual publications and citations in this field has shown a continuous upward trend and peaked in 2021. This suggests that the association between PD and CHD is receiving continued and increasing attention.

The analysis of disciplines and journals can help researchers study the distribution of disciplines in the field, track research progression, and select more appropriate journals for submission. Four journals in the category of dentistry, oral surgery and medicine occupied the top four places in terms of journal publication volume (161/580, 27.8%), suggesting that journals in the category of that may have higher attention to this field. Moreover, journals with the labels molecular/biology/immunology, dentistry/dermatology/surgery, and medicine/medical/clinical were the dominant areas on the left side of the journal dual-map overlay, which indicated that the journals with these labels were highly active in publishing articles in the field.

Scientific cooperation is defined as researchers collaborating with the shared purpose of producing new scientific knowledge [42]. Scientific cooperation is divided into different levels, including interindividual, interinstitutional, and international collaboration. Sociality is as important as academic output in assessing the importance of nodes in a collaborative network, and BC is an important evaluation index of sociality. If the BC of a node exceeds 0.1, this indicates that the node is the central node and is relatively important and has a great influence on the research [21]. As shown in the cooperation network map, direct collaborations between authors and institutions in this field are loose, which is also shown by the low BC of author and institution nodes. This may be related to the ability of institutions and authors to independently complete such research. The United States is the leading country in this field, with authors from the United States publishing the most articles (169 studies) and obtaining the highest BC (0.56) in the country collaboration analysis. These values are much higher than those of second-ranked Sweden with 62 publications and a BC of 0.15. Authors from the United States are more likely to partner with researchers from developed countries. Although CHD has been shown to be one of the leading causes of death in both developed and developing countries and has received attention in both types of countries [43], the low priority of oral health care in developing countries hampers data collection on PD in developing countries [44], which hinders research into the link between the two diseases. The population aging problem in developed countries increases the risk of these two diseases [45,46], which also increases the research motivation of researchers in developed countries in this field. In addition, more research funding and better infrastructural facilities for researchers in developed countries compared to developing countries may also be to blame [47].

8. Research hotspots between PD and CHD

Based on the results of keyword analysis and reference co-citation analysis, we summarized the research hotspots of the association between PD and CHD, including CRP, oral flora (including *P. gingivalis* and *A. actinomycetemcomitans*), atherosclerosis, infection, and inflammation.

8.1. CRP

Human CRP was identified as a kind of acute-phase plasma protein that could be primarily expressed and secreted by the liver [48, 49]. The concentrations of CRP can increase in response to tissue injury, infection, and chronic inflammation [48]. There is increasing evidence that CRP plays an important role in inflammation and the host response to infection, including the complement pathway, apoptosis, phagocytosis, nitric oxide release, and the release of inflammatory factors (especially interleukin-6 and tumor necrosis factor-α) [50]. A systematic review and meta-analysis published in 2021 indicated that patients with periodontitis had consistently higher levels of CRP than systemically healthy individuals, and periodontitis treatment could result in a temporary increase in CRP levels that gradually decreases over time [51]. Moreover, numerous studies have reported an association between elevated CRP levels and an increased risk of CHD events [52,53]. CRP has also been shown to upregulate thrombosis, inflammation, and atherosclerosis, which are likely to lead to or aggravate CHD events [53–56]. As an inflammatory disease, PD may be associated with CHD events through CRP, a major risk factor for CHD [57].

8.2. Atherosclerosis and inflammation

Atherosclerosis is the most common underlying pathology of CHD and is now considered a chronic inflammatory disease [58]. The chronic accumulation of obstructive plaques in the intima of large and medium arteries (e.g., coronary arteries) can lead to significant stenosis of blood vessels, thereby restricting blood flow and leading to severe tissue hypoxia (e.g., myocardial ischemia) [59–61]. At the same time, atherosclerotic plaque rupture can also lead to a variety of acute events, including myocardial infarction [62]. In recent years, inflammation and atherosclerosis have attracted increasing attention. Pro-inflammatory activation of endothelial cells, the release of inflammatory cytokines (e.g., interleukin-8, E-selectin, P-selectin) and chemokines, and inflammatory cell (e.g., monocytes and macrophages) infiltration have been shown to be involved in almost all processes of atherosclerosis [63–65]. Inflammation can drive atherosclerosis and may ultimately lead to the occurrence of CHD [65].

It is worth noting that there is increasing evidence that PD can lead to bacteria or their products entering the bloodstream and activating host inflammatory responses through multiple mechanisms, thereby favoring the formation, maturation, and exacerbation of atherosclerotic lesions [62]. Periodontal pathogen invasion, inflammation, and atherosclerosis may be one of the axes of the association between PD and CHD.

8.2.1. Oral flora and infection

PD comprises multiple infectious conditions dominated by oral flora [66,67]. Periodontal pathogens, including *P. gingivalis* and *A. actinomycetemcomitans*, play an important role in the development of PD by inducing gingival damage and accelerating alveolar bone resorption [68].

Periodontal pathogens have been shown to promote the formation of atherosclerosis in a variety of animal models, including mice, rabbits, and pigs [13]. The oral flora can be associated with PD and CHD through multiple pathways. First, evidence suggests that oral bacteria could enter the circulation, cause bacteremia, and reach systemic vascular tissues [4,69,70]. Researchers have successfully isolated a variety of oral bacterial species, including *P. gingivalis* and *A. actinomycetemcomitans,* from atherosclerotic tissues [71,72], which had a higher expression probability in patients with PD [73,74]. It has been reported that periodontal pathogens can cause or aggravate atherosclerosis by mediating the apoptosis of vascular endothelial cells, inducing the proliferation of vascular cells, interacting with monocytes/macrophages, promoting thrombosis and coagulation, accelerating atheromatic plaque disruption, reducing regulatory T cells (Tregs) and activating mast cells, which is consequently associated with CHD [75,76]. Activation of Toll-like receptors and other pattern recognition receptors in vascular endothelial cells, increased autoimmune responses, and oxidative stress induced by periodontal pathogens may be involved in these processes [76–78]. Second, serum antibody levels in patients with PD are elevated and can cross-react with antigens in cardiovascular tissues. There is evidence that heat shock proteins (HSPs) from periodontal pathogens (e.g.*, P. gingivalis and A. actinomycetemcomitans*) are able to trigger antibodies that could cross-react with human HSPs. These antibodies have been shown to increase cytokine production and activate monocytes and endothelial cells [4, 79–81]. The antibody cross-reactivity between periodontal pathogen HSPs and malondialdehyde-humanized-modified LDL (MAA-LDL)/oxidized LDL (OxLDL) also suggest an association between periodontitis and atherosclerosis [82]. Several studies have found that elevated levels of cardiolipin antibodies caused by periodontal pathogens are associated with an increased risk of atherosclerosis and CHD [83–87]. A systematic review and meta-analysis published in 2021 by Joshi et al. [88] indicated that higher anti-*P. gingivalis* or anti-*A. actinomycetemcomitans* IgG antibody levels resulted in a modest increase in the risk of CHD.

8.3. Emerging trends of PD and CHD

Based on keyword burst analysis, event, disease, and global burden were the burst keywords that persisted until 2022. The word event often appeared together with CHD to form the phrase CHD event. The word disease appeared in both PD and CHD. Therefore, the words event and disease were not analyzed as emerging trends. After exclusion of both diseases, a transition of the keyword bursts from the earlier dental infection, c-reactive protein, A actinomycetemcomitans and periodontal pathogen to the latest global burden can be observed. This may be related to the fact that early studies mainly focused on exploring the association between PD and CHD and the mechanisms involved. As this association has become clearer, the global burden caused by the link between PD and CHD as two global public health problems has received increasing attention.

In terms of reference burst analysis, the citation burst of two references continued until 2022 and were related to cardiovascular outcomes. One of these two studies was published by Rydén et al. [10] in Circulation in 2016. This publication was a study report based on the Periodontal Disease and the Relation to Myocardial Infarction (PAROKRANK) study to reveal the risk of PD and first myocardial infarction [10]. After the inclusion of 805 patients with first-time myocardial infarction and 805 controls, the study found that PD patients had a significantly increased risk of first-time myocardial infarction, which strengthened the possibility of an independent relationship between PD and myocardial infarction [10]. Another study by Park et al. [12] published in the European Heart Journal investigated the association between oral hygiene care and cardiovascular disease risk. The results based on the Korean population showed that oral hygiene care (e.g., frequent toothbrushing and regular professional dental cleaning) could decrease the risk of future cardiovascular events in healthy adults, and improved oral hygiene behavior might modify the association between cardiovascular diseases and oral health [12]. As shown in Fig. 11, cardiovascular outcomes (#3) was the latest cluster in the timeline cluster map of citations. Therefore, global burden and cardiovascular outcomes were the emerging trends for subsequent discussion.

8.4. Global burden

PD is a global public health problem with a global prevalence of up to 50%, with 1.1 billion patients suffering from severe periodontitis according to data in 2019 [2]. Patients with PD are at increased risk for dental defects, loss of dentition, and chewing dysfunction, which negatively affect their nutrition, quality of life, and self-esteem. It has been reported that the prevalence and severity of periodontitis vary greatly in different regions, which may be related to oral health behavior, sociodemographic status, availability of health services, socioeconomic structure, and political environment [89,90]. Individuals living in poor countries are more susceptible to periodontitis due to a lack of access to and affordability of oral health instruction and interventions [44,91]. The aging population, as a global issue of increasing importance, has also been implicated as another reason for the high burden of periodontitis, as older populations are more susceptible to PD [2,92,93]. In brief, the cost of treating PD places a tremendous financial burden on families and health care systems [90].

The total prevalence of CHD is approximately 6.3%, which is not related to the national Human Development Index (HDI) but is on the rise in developing countries and on the decline in developed countries [94]. Although the incidence is lower than that of PD, CHD is responsible for nearly 7 million deaths and 129 million DALYs annually and is a huge global economic burden [95]. At present, with the improvement in medical technology and medical services, the mortality of CHD is decreasing [96–99]. As the survival rate of CHD increases and the population ages, the humanistic (CHD-related disability and quality of life changes) and economic burden of CHD will further increase. The outbreak of COVID-19 at the end of 2019 has now infected more than 600 million people (data from Johns Hopkins University School of Medicine on December 16, 2022, https://coronavirus.jhu.edu/map.html) and has caused economic growth to slow down or even decline in most economies around the world [100,101]. This may further increase the global economic burden of PD and CHD.

8.5. Cardiovascular outcomes

To evaluate cardiovascular risk, researchers should investigate cardiovascular outcomes, including cardiovascular mortality, myocardial infarction, and stroke [102]. As mentioned earlier, PD can increase the probability of cardiovascular diseases, especially CHD (e.g., myocardial infarction and myocardial ischemia) [4,10,103,104]. Dental care was also proven to decrease the risk of cardiovascular outcomes. A study involving 11,869 participants found that self-dental care (toothbrushing behavior) could decrease the risk of cardiovascular events and downregulate concentrations of C-reactive protein and fibrinogen, which are markers of inflammation and coagulation [11]. In another study, frequent toothbrushing and regular professional dental cleaning also reduced the occurrence of cardiac death, myocardial infarction, stroke, and heart failure [12]. This is also largely consistent with the findings of several other studies [105–107]. Those who do not respond well to periodontal treatment have a higher risk of developing cardiovascular disease (the composite endpoint of myocardial infarction, stroke, and heart failure) in the future [108].

8.6. Limitations

Consistent with other bibliometric analyses, this study also had some limitations: (I) In this study, several retrieval strategies were used. Only studies written in English published in the past 30 years (1993–2022) were included in the follow-up analysis. This may result in some key studies not being included. (II) Although different selection criteria and pruning were used for different node types, the study records involved in the bibliometric analysis and visualization were still determined by the size of the threshold. It is necessary to compare the results of visualization analysis under different thresholds. (III) In this study, the researchers manually merged synonyms or similar words for authors and keywords in their analysis. However, the researchers could not guarantee that they had eliminated the bias associated with synonyms and similar words. (IV) This study included two study types, articles and review articles, but did not group the specific study types (such as in vivo/in vitro studies). The results of this study do not apply to the analysis of specific study types. (V) The literature retrieval was performed on November 30, 2022, and the number of publications and citations in 2022 was not accurate, which may influence the results of the subsequent analysis. (VI) Some recently published high-quality research may have been excluded because they had not been cited enough, which may affect research hotspots and emerging trends in this study. (VII) Although the SCI-E database is a reliable global citation database and the most commonly used database in bibliometric research, the literature and citation information it contains may not be sufficient to cover all publications in this field.

Despite the aforementioned limitations, we maintain the view that this study effectively captures the research hotspots and emerging trends in the study of PD and CHD. Based on this study, researchers in the future could quickly understand the research situation in this field and choose their research direction according to the research hotspots and emerging trends.

9. Conclusion

The association between PD and CHD is supported by a growing body of basic research and clinical practice findings. The bibliometric analysis provides an objective and quantitative method for evaluating trends and frontiers of the field of PD and CHD. The upward trend in publications and citations in this field over the past three decades suggests that the field is attracting the attention and research enthusiasm of a growing number of scholars. Globally, the United States is the leading country in this research. In the future, it is necessary to strengthen cooperation and exchanges among institutions and authors. Several research hotspots in this field were identified, including CRP, oral flora, atherosclerosis, infection, and inflammation. Moreover, global burden and cardiovascular outcomes were the emerging trends of PD and CHD. This study summarized intellectual bases in this field, revealed the current research hotspots and emerging trends, and provided valuable guidance for future researchers to choose an appropriate research direction.

Data availability statement

Data associated with this study has not been deposited into a publicly available repository. Data included in article/supplemental materials/referenced in the article.

Ethics approval and consent to participate

Ethical approval was waived since this article does not contain any studies with human participants or animals.

Consent for publication

Not applicable.

Declaration of generative AI in scientific writing

During the preparation of this work the authors used [ChatGPT 3.5] in order to improve readability and language. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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CRediT authorship contribution statement

Wen-peng Song: Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis. **Xiao-wen Bo:** Writing – original draft, Methodology, Investigation, Formal analysis. **Hui-xin Dou:** Writing – review & editing, Writing – original draft, Methodology. **Qian Fan:** Writing – review & editing, Supervision, Resources, Funding acquisition, Conceptualization. **Hao Wang:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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List of abbreviations

PD Periodontal disease
CHD Coronary heart disease
DALYs Disability-adjusted life years
SCI-E Science Citation Index Expanded
WOSCC Web of Science Core Collection
IF Impact factor
BC Between centrality
P. gingivalis Porphyromonas gingivalis
A. actinomycetemcomitans Actinobacillus actinomycetemcomitans
ASVD Atherosclerotic vascular disease

LLR log-likelihood ratio
Tregs Regulatory T cells
HSPs Heat shock proteins
MAA-LDL Malondialdehyde-humanized-modified LDL
OxLDL Oxidized LDL
PAROKRANK Periodontal Disease and the Relation to Myocardial Infarction
HDI Human Development Index

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e28325.

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