Peer Review File

Reviewer A

Comment 1: Applied methods should be more introduced in more detail. For instance, it is hard to understand what authors mean by "emerging research frontier terminology concepts" or "selected 1 year as the screening period for the time slice, and the top 50 per slice in each time slice". In addition, it is not well explained what was the aim of analysing keywords with the minimum spanning tree algorithm. This also undermines results interpretation, how should betweenness centrality results be interpreted?

Reply 1: ①I'm sorry there's a grammar mistake. The sentence "emerging research frontier terminology concepts" means the burst detection algorithm designed by Kleinberg, which is used to identify frontier terminologies emerging in research. We have revised it.

②"selected 1 year as the screening period for the time slice, and the top 50 per slice in each time slice" are parameters of Citespace. As the image shows below, time slicing means separating the data by defined years and the top 50 most cited publications in the period will be selected. This sentence means we selected the top 50 pieces of data each year. We modified the way of expression.
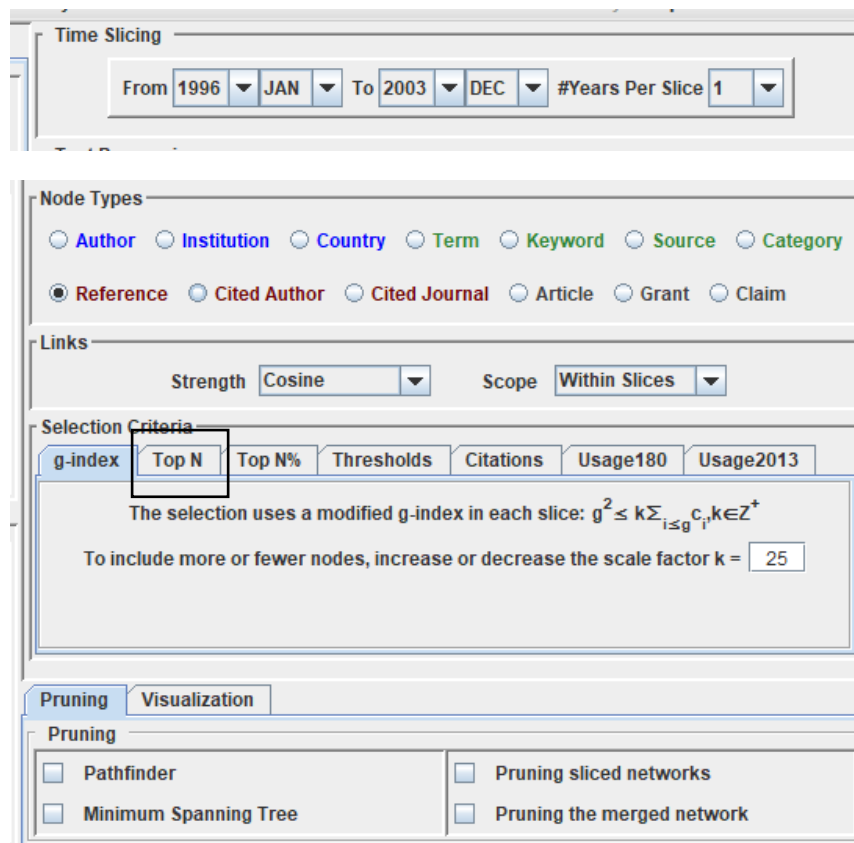
③ We analyzed keywords with the minimum spanning tree algorithm mainly because there were thousands of data to deal with. Every paper has several keywords. If we showed every connection among papers, the calculation quantity would be too large. So it's necessary to simplify the calculation process properly. A common way to achieve it is using the minimum spanning tree algorithm. This method is widely applied in bibliometrics analyses.

④ Thank you for the question about betweenness centrality. Betweenness centrality shows how important a node is within a network. For example, as the image shows below, 'A' connects with 'B' and 'B' connects with 'C', and there can be a connection between 'A' and 'C' because of the existence of 'B'. It appears that 'B' has a high betweenness centrality in this network so 'B' will be an important node for further analyze. It may be hard to understand what a ***"paradigm"*** is. We have revised it to make the definition of betweenness centrality easier to understand.
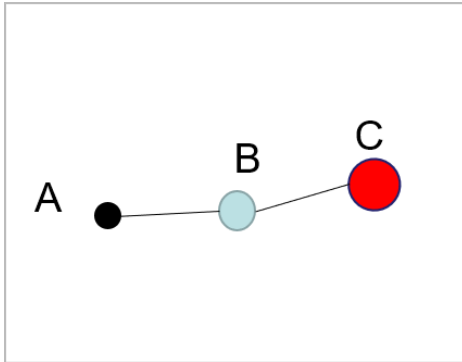
Changes in the text: ① Change "emerging research frontier terminology concepts" to "emerging research frontier.". (Page 4, Row 84)

② Change "selected 1 year as the screening period for the time slice, and the top 50 per slice in each time slice" to "and selected the top 50 most cited publications each year". (Page 5, Row 98)

③ Change "potential paradigm changes" to "connecting other points like a bridge". (Page 4, Row 86)

Comment 2: Results: first sentence, I would not call search query an algorithm, could be "search strategy"

Reply 2: Thanks for your suggestion and we have corrected it in the new version of manuscript.

Changes in the text: Delete "algorithm". (Page 5, Row105)

Comment 3: row 117, "high-quality research" how is that determined?

Reply 3: High-quality research are articles indexed by influencing journals[1]. It depends on the influencing factor of journals as well as the citation number of the article itself. In our study, we gave priority to articles from influencing journals closely related to diabetes-associated periodontal diseases, such as *Journal of Periodontology, Journal of Clinical Periodontology*, *Periodontology 2000*, and *Journal of Diabetes[2]*. We added several related references to support.

Changes in the text: We added several references. (Page 6, Row124)

Comment 4: about "Characteristics of publications": It is hard to understand why and how described examples of studies were selected from the sample.

Reply 4: We chose the time period according to the number of annual publications. We illustrated the publication characteristics of each period and the described examples of studies were selected according to the citations and the content. The chart below shows part of the publications from 1929 to 1990. We reviewed the title and abstract of top cited publications and summarize the characteristics of them. We selected the examples which had close relationship with diabetes-associated periodontal disease[3-5].

Changes in the text: We added more references to support the popular topic of each period. (Page

5-6, Row 111-112, 116-117,118-120)

Authors	Article Title	DOI	Publication Year	Times Cited, WoS Core
ZAMBON, JJ; CHRISTERSSON, LA; SLOTS, J	ACTINOBACILLUS-ACTINOMYCETEMCOMITANS IN HUMAN PERIODONTAL-DISEASE - PREVALENCE IN PATIENT GROUPS AND DISTRIBUTION OF BIOTYPES AND SEROTYPES WITHIN FAMILIES	10.1902 /jop.198 3.54.12. 707	1983	378
GOLUB, LM; LEE, HM; LEHRER, G; NEMIROFF, A; MCNAMARA, TF; KAPLAN, R; RAMAMURTHY, NS	MINOCYCLINE REDUCES GINGIVAL COLLAGENOLYTIC ACTIVITY DURING DIABETES - PRELIMINARY-OBSERVATIONS AND A PROPOSED NEW MECHANISM OF ACTION	10.1111 /j.1600- 0765.19 83.tb00 388.x	1983	355
ZAMBON, JJ; SLOTS, J; GENCO, RJ	SEROLOGY OF ORAL ACTINOBACILLUS-ACTINOMYCETEMCOMITANS AND SEROTYPE DISTRIBUTION IN HUMAN PERIODONTAL-DISEASE	10.1128 /IAI.41. 1.19-27.1983	1983	293
GOLUB, LM; MCNAMARA, TF; DANGELO, G; GREENWALD, RA; RAMAMURTHY, NS	A NON-ANTIBACTERIAL CHEMICALLY-MODIFIED TETRACYCLINE INHIBITS MAMMALIAN COLLAGENASE ACTIVITY	10.1177 /002203 458706 600804 01	1987	232
GOLUB, LM; WOLFF, M; LEE, HM; MCNAMARA, TF; RAMAMURTHY, NS; ZAMBON, J; CIANCIO, S	FURTHER EVIDENCE THAT TETRACYCLINES INHIBIT COLLAGENASE ACTIVITY IN HUMAN CREVICULAR FLUID AND FROM OTHER MAMMALIAN SOURCES	10.1111 /j.1600- 0765.19 85.tb00 405.x	1985	176
HUGOSON, A; THORSTENSSON, H; FALK, H; KUYLENSTIERNA, J	PERIODONTAL CONDITIONS IN INSULIN-DEPENDENT DIABETICS	10.1111 /j.1600- 051X.1 989.tb0 1644.x	1989	139
ZAMBON, JJ; REYNOLDS, H; FISHER, JG; SHLOSSMAN, M; DUNFORD, R; GENCO, RJ	MICROBIOLOGICAL AND IMMUNOLOGICAL STUDIES OF ADULT PERIODONTITIS IN PATIENTS WITH NONINSULIN-DEPENDENT DIABETES-MELLITUS	10.1902 /jop.198 8.59.1.2 3	1988	136
MASHIMO, PA; YAMAMOTO, Y; SLOTS, J; PARK, BH; GENCO, RJ	THE PERIODONTAL MICROFLORA OF JUVENILE DIABETICS - CULTURE, IMMUNOFLUORESCENCE, AND SERUM ANTIBODY STUDIES	10.1902 /jop.198 3.54.7.4 20	1983	120
COHEN, D W; FRIEDMAN, L A; SHAPIRO, J; KYLE, G C; FRANKLIN, S	DIABETES MELLITUS AND PERIODONTAL DISEASE: TWO-YEAR LONGITUDINAL OBSERVATIONS. I.		1970	109

ERVASTI, T; KNUUTTILA, M; POHJAMO, L; HAUKIPURO, K	RELATION BETWEEN CONTROL OF DIABETES AND GINGIVAL BLEEDING	10.1902 /jop.198 5.56.3.1 54	1985	105
BACIC, M; PLANCAK, D; GRANIC, M	CPITN ASSESSMENT OF PERIODONTAL-DISEASE IN DIABETIC-PATIENTS		1988	97
TERVONEN, T; KNUUTTILA, M	RELATION OF DIABETES CONTROL TO PERIODONTAL POCKETING AND ALVEOLAR BONE LEVEL	10.1016 /0030-4220(86)90417-2	1986	97
RYLANDER, H; RAMBERG, P; BLOHME, G; LINDHE, J	PREVALENCE OF PERIODONTAL-DISEASE IN YOUNG DIABETICS	10.1111 /j.1600-051X.1 987.tb0 1511.x	1987	93
LARKIN, JG; FRIER, BM; IRELAND, JT	DIABETES-MELLITUS AND INFECTION	10.1136 /pgmj.6 1.713.2 33	1985	86
FINESTONE, AJ; BOORUJY, SR	DIABETES MELLITUS AND PERIODONTAL DISEASE	10.2337 /diab.16 .5.336	1967	84
ZAMBON, JJ; DELUCA, C; SLOTS, J; GENCO, RJ	STUDIES OF LEUKOTOXIN FROM ACTINOBACILLUS-ACTINOMYCETEMCOMITANS USING THE PROMYELOCYTIC HL-60 CELL-LINE	10.1128 /IAI.40. 1.205-212.198 3	1983	80
WILTON, JMA; GRIFFITHS, GS; CURTIS, MA; MAIDEN, MFJ; GILLETT, IR; WILSON, DT; STERNE, JAC; JOHNSON, NW	DETECTION OF HIGH-RISK GROUPS AND INDIVIDUALS FOR PERIODONTAL-DISEASES - SYSTEMIC PREDISPOSITION AND MARKERS OF GENERAL HEALTH	10.1111 /j.1600-051X.1 988.tb0 1009.x	1988	73
SASTROWIJOTO, SH; HILLEMANS, P; VANSTEENBERGEN, TJM; ABRAHAMINPIJN, L; DEGRAAFF, J	PERIODONTAL CONDITION AND MICROBIOLOGY OF HEALTHY AND DISEASED PERIODONTAL POCKETS IN TYPE-1 DIABETES-MELLITUS PATIENTS	10.1111 /j.1600-051X.1 989.tb0 1662.x	1989	72
GUSBERTI, FA; SYED, SA; BACON, G; GROSSMAN, N; LOESCHE, WJ	PUBERTY GINGIVITIS IN INSULIN-DEPENDENT DIABETIC CHILDREN .1. CROSS-SECTIONAL OBSERVATIONS	10.1902 /jop.198 3.54.12. 714	1983	72
MURRAH, VA	DIABETES-MELLITUS AND ASSOCIATED ORAL MANIFESTATIONS - A REVIEW	10.1111 /j.1600-	1985	71

BARNETT, ML; BAKER, RL; YANCEY, JM; MACMILLAN, DR; KOTOYAN, M	ABSENCE OF PERIODONTITIS IN A POPULATION OF INSULIN-DEPENDENT DIABETES-MELLITUS (IDDM) PATIENTS	0714.1985.tb00494.x 10.1902/jop.1984.55.7.402	1984	71

Comment 5: row 148: "huge amount", these kind of comments not needed in the results section

Reply 5: Thanks for your suggestion. we have removed these subjective words in the results.

Changes in the text: Change "5672 authors have published papers related to diabetes-associated periodontal disease, which is a huge amount." to "A total of 5672 authors have published papers related to diabetes-associated periodontal disease." (Page 8, Row158)

Comment 6: row 154: "have 8 papers co-occurrence" so they had published 8 papers together?

Reply 6: Yes, we intended to present cooperation within the articles that authors published together. As the **image below** (as well as **Figure 6** in the manuscript) shows, every node presents an author. The size of the node presents the number of authors in the published articles. The line between two nodes presents the same articles that both authors have published. Thank you for your question that let us know about the missing details. We will make it more clear in the sentence and also clarify the definition of co-occurrence in the section of **Material and methods.**

Changes in the text: ①We added the definition of co-occurrence: Every publication was described with characteristic information mentioned above. Co-occurrence refers to the cooperation within the articles that authors published together. (Page 5, Row 92-94)

②We revised the sentence to make it clear to read. (Page 8, Row 164)
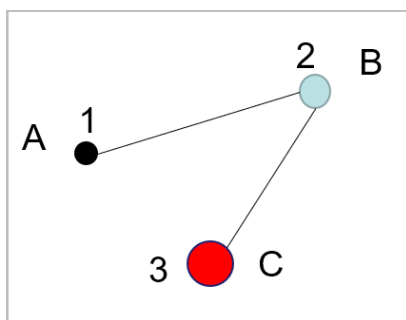
Comment 7: "Association means diabetes and periodontal disease affect each other" is very vague. Association is statistical phenomena.

Reply 7: We intended to summarize the content of keyword *"association"*-related papers but it may be too vague and general. We revised the sentence to summarize the paragraph more precisely.

Changes in the text: We revised the sentence. (Page 9, Row194)

Comment 8: row 217, what is "keyword impact"?

Reply 8: Sorry to make you confused. It is supposed to be the keyword "impact". We revised it and modified the format of several keywords.

Changes in the text: We modified the format of several keywords. (Page 8 Row 174, Row 176; Page 9, Row 179, Row 189; Page 10, Row210, Row 213, Row220; Page 11, Row228, Row232)

Comment 9: row 228 has -> have
Reply 9: Thanks for your correction and we have revised it.
Changes in the text: Change "has" to "have". (See Page 12, Row 244)

Comment 10: row 240: "Especially the mechanism of RAGE influencing inflammatory response is still unclear." needs reference(s) / explanation
Reply 10: It's reported that AGEs improve the expression of IL-6 and ICAM-1 by activating RAGE, MAPK and NF-κB pathways[6]. The AGE-RAGE axis is one of the key pathogenic mechanisms involved in the periodontal destruction associated with diabetes. But there are several forms of RAGE. Soluble RAGE, particularly cleaved RAGE, may serve as biomarkers for the presence and severity of periodontitis and may be involved in its pathogenesis.On the other hand, the molecular mechanism of inflammation-enhanced AGE formation remains unknown[7]. To sum up, the AGE-RAGE axis is important in diabetes-associated periodontitis but the mechanism is unclear.
Changes in the text: We added two references and revised "RAGE" to "AGE-RAGE axis".(See Page 12, Row 256)

Comment 11: row 251, please revise using causal language. see for instance https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5888052/
Reply 11: The latest study didn't support a bidirectional causal association between periodontitis and type 2 diabetes through two-sample Mendelian randomization (MR) [8]. However, this finding had its limitation because only five SNPs were related with periodontitis. Considering methodological bias, it is difficult to determine in conventional observational studies whether these correlations are causal. Diabetes increases the risk of periodontitis and periodontitis also increases the risk of diabetes. So we didn't use causal language. Thanks for your suggestion. We simplified the part of association and indicated that it's difficult to determine whether the association between diabetes and periodontitis is causal.
Changes in the text: We added "Since the methodological bias, it is difficult to determine in conventional observational studies whether the correlations between diabetes and periodontitis are causal" and deleted the paragraph of "The association between diabetes and periodontal disease is controversial". (See Page 12, row267-275)

Comment 12: paragraphs starting rows 251 and 274, please indicate how this discussion relates to your findings.
Reply 12: The paragraph from row 251 to row 263 illustrated the relationship between diabetes and periodontitis according to the hotspot *"risk"* and *"association"*. There is a concern about whether diabetes lead to periodontitis and whether periodontitis promote diabetes. What's more important is what we can achieve by knowing the association? Periodontitis can be a detective item of other chronic diseases related to immune disorders, and we tried to explain the complex association between diabetes and periodontitis. We also proposed the viewpoint that it's reasonable to distinguish diabetes-associated periodontitis from other types of periodontitis because the mechanism was quite different. We summarized the theme of burst words from row 264 to row 273

and proposed the viewpoint that *"early prevention"* could present the four burst words (*peri-implantitis, global burden, susceptibility, impact*). In this section, we cited several articles to support our viewpoint to emphasize the importance of early prevention. And in the next paragraph, we introduce SNPs which may predict individual morbidity of disease because it's a proof that early prevention especially individual prevention is the frontier research part. We simplified these paragraphs in the discussion.

Changes in the text: We deleted the paragraph of "The association between diabetes and periodontal disease is controversial" and added" What can we learn from the inflammatory mechanism? With the deepening analysis of the interaction mechanism between periodontitis and diabetes, some scholars tried to investigate the association between periodontitis and other systemic diseases, such as cardiovascular disease and obesity, through the host inflammatory response mechanism. It reminds us the possibility of regarding periodontitis as a detective item of other chronic diseases related to immune disorders."(Page 13, row 270-274) We added " Since the methodological bias, it is difficult to determine   whether the correlations between diabetes and periodontitis are causal in conventional observational studies"(Page 14, row 271-286).

Comment 13: A limitations section/paragraph is missing from the discussion and it should be added and discuss for instance are the used methods and data valid? How accurate are the metrics, e.g. citations? Could we get different results from another database?

Reply 13: Thanks for your advice and we added a paragraph about the limitations. Over the past few years, bibliometric and visualization-based analyses have been applied in biomedical fields[9]. WoSCC is an important database and there're many bibliometric analyses based on WoSCC[2, 10, 11], including Science Citation Index (CI) Expanded, Emerging Sources CI (ESCI), Conference Proceedings CI-Science (CPCI-S), and Conference Proceedings CI-Social Science & Humanities (CPCI-SSH). Compared with other databases such as Scopus and Medline, it has comprehensive up-to-date information and source files since 1940. Thus, the data in WoSCC covers the majority of publications in this field. However, we haven't found articles comparing the reliability and validity of different databases, and it's a topic worthwhile considering. Thank you for your suggestion, and in the next study, we'll try to use more databases.

Changes in the text: We added a paragraph of limitation (Page 14-15, Row 307-311)

Reviewer B

Comment: I reviewed this manuscript from Hua et al, entitled: Visualized analysis of hotspots and frontiers in diabetes-associated periodontal disease research: A bibliometric study. This study analyzes 3572 articles on diabetes-associated periodontal disease with bibliometrics analysis software Citespace5. The objective of the study was to provide references for researchers in relevant fields with hotspots and frontiers in diabetes-associated periodontal disease research. Data were analyzed from the Web of Science core collection (WOSCC) based on Java Developed by Professor Chaomei Chen, a professor at Drexel University in the United States. All electronic searches were performed on Aug. 20th 2021. The search period was from January 1st 1929 to January 1st 2021. You discovered that inflammatory pathways are the hotspots and early prevention is the frontier of the research on the diabetes-associated periodontal disease through bibliometric research results. It was interesting to know the information on diabetes-associated periodontal disease including related subject categories, leading authors, influencing countries, constitutions, and so on. I agree that it

helps scholars refresh the research direction and ultimately helps the patients with diabetes-associated periodontal disease get better prevention and treatment. Indeed, on a translational perspective, it would be interesting that primary care network work closer with dentistry in order to prevention inflammatory pathways on patients with diabetes.

Your manuscript is well-written, easy to read and the tables are very well presented.

Reply: Thank you for your comment and encouragement! We have added more details in the supplement and revised some grammar mistakes. Thanks for your appreciation again!

Re-review comments

Reviewer A:

Comment 1: I am satisfied with most of changes authors made. However, I am still unsure how your discussion on rows 443-455 relates to or is justified by YOUR findings. You didn't conduct a review on these topics, you made a bibliographical investigation.

Reply: Thank you for your comment. According to the analysis about research hotspots, we found that *"inflammation"* was the most popular keyword. The keywords *"risk"* and *"association"* also had high level of occurrence frequency. We tried to explain the clinical significance of investigating the inflammatory mechanism (rows 443-447) and further explain the meaning of *"risk"* and *"association"* (rows 448-455). However, as you suggest, the content of rows 448-455 was not necessary. Thank you for your advice and we deleted the rows 448-455. If there's any other problems, please don't hesitate to contact us. We'll be pleasure to receive your advice.

Changes in the text: We deleted the rows 448-455.