

# Mapping global research trends in diabetes and COVID-19 outbreak in the past year: a bibliometric analysis

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**Background:** Diabetes is an independent risk factor for COVID-19 patients, and SARS-CoV-2 infection may in turn induce hyperglycemia. In this work, we will map the trends of global research of COVID-19 and diabetes by using the method of bibliometric analysis, help researchers quickly understand the research hotspots and find meaningful research directions.

**Methods:** Documents related to COVID-19 and diabetes were obtained from the database of Science Citation Index Expanded of Web of Science. We then analysed the data by country/organization coauthorship analysis, sources/documents citation analysis, and keywords co-occurrence analysis. VOSviewer was applied to map the global research trends and hotspots in this field.

**Results:** A total of 1,206 articles were retrieved, including a total of 101 countries, 2,595 organizations, 526 journals, and 3,405 keywords. China had the highest total citations, followed by the United States, while these two countries were reversed in terms of the number of documents. Half of the top 10 highly cited organizations were from China, including Capital Medical University, which had the highest citations, and Huazhong University of Science and Technology, which had the largest number of documents. *Diahetes Research and Clinical Practice* was the most productive journal. *Journal of Medical Virology* was the most highly cited journal. Zhou *et al.*'s article (*The Lancet*, 2020) was the most representative and widely cited. The keywords mainly focused on 3 categories, namely risk factors & clinical outcomes, receptor ACE2 & cytokine storm, as well as clinical characteristics & epidemiology. Among them, hyperglycemia, obesity, outcomes, and cytokine storm are the hotspots of recent concern.

**Conclusions:** This research mapped the global research trends in COVID-19 and diabetes, which may help researchers identify relevant collaborators and discover current hotspots and potential research directions.

Keywords: COVID-19; SARS-CoV-2; diabetes; bibliometrics; VOSviewer

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## Introduction

Coronavirus disease 2019 (COVID-19) is a new acute respiratory infectious disease, induced by a new type of coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2), which has the characteristics of fast transmission, wide range, and strong infectivity. It has been widely spread worldwide and caused serious adverse effects on social and economic development. It is currently believed that elderly patients infected with COVID-19 are more likely to develop severe illness (1-3), and the age of infected patients is positively correlated with the viral load in the body (4). Diabetes represents one of the most prevalent chronic conditions worldwide. Studies have shown that infected patients with diabetes have a higher incidence of serious diseases and mortality than those without diabetes (5-8). COVID-19 patients with newly diagnosed diabetes may be more likely to experience poor outcomes than those with existing diabetes (9). Due to the high prevalence of diabetes among the elderly in the world, it is necessary to pay more attention to these infected patients with diabetes. In order to prevent and control the COVID-19 pandemic as soon as possible, researchers around the world are actively conducting extensive research. With the deepening of research, a series of studies on the role of COVID-19 and diabetes are gradually increasing. However, there is still a lack of a global comprehensive analysis to help researchers quickly understand the overview and find meaningful research directions.

Bibliometric analysis is defined as the statistical analysis of publications, which can summarize the current research status and predict future trends qualitatively and quantitatively (10). At present, this method has been widely used in hot spot analysis of various diseases, providing a reference for further research on disease prevention and treatment (11,12). However, there are few bibliometric literatures on COVID-19 and diabetes (13). In view of this, we conducted a comprehensive analysis of the content and external characteristics of COVID-19 and diabetes research based on bibliometrics methods, using the visualization technology to summarized past research, and predicted future research hotspots. This study is expected to provide a reference for further in-depth research on COVID-19 and diabetes by revealing research hotspots and trends.

## **Methods**

## Data collection

The Web of Science (WOS) SCI-Expanded database was used to identify all literature related to COVID-19 and diabetes published in English from 2020-01-01 to 2021-01-07. The data retrieval strategy was presented as follows: TS = ((Diabetes) AND ("coronavirus disease 2019" or "coronavirus 2019" or "COVID 2019" or "COVID-19" or "COVID19" or "COVID 19" or "nCoV-2019" or "nCoV2019" or "nCoV 2019" or "Severe acute respiratory syndrome coronavirus 2" or "2019 novel coronavirus" or "2019-novel CoV" or "2019-ncov" or "2019 ncov" or "SARS-CoV-2")). The database search was done on a single day, January 7, 2021, so as to avoid significant fluctuations in citations, as well as numbers of studies; 1,471 studies were acquired through this step.

Articles and reviews that reflect original scientific output were included in the analysis, while other types of publications such as editorials, letters, meeting abstracts, news and corrections were excluded. After that, 1,206 articles were left in the next bibliometric analysis. The retrieved documents were downloaded in Win UTF8 format files with full records and references, containing the title, author names, abstract, key words, and more.

#### Bibliometric analysis with VOSviewer

The files containing these 1,206 articles on COVID-19 and diabetes were imported into the VOSviewer (version 1.6.15) software to perform bibliometric analysis, including country/organization coauthorship, sources/documents citation and keywords co-occurrence analysis. The overlay/ network visualization map was drawn step by step according to the setting parameters by VOSviewer.

## Country/organization coauthorship analysis

Coauthorship analysis refers to the collaboration of different analysis objects (countries/regions, organizations) to publish one or more articles. The total link strength can usually be used to quantitatively evaluate the relationship between two objects. The greater the total link strength, the greater the correlation. In this study, country/ organization coauthorship was performed by VOSviewer in coauthorship analysis in the unit of countries/organizations. In the overlay visualization map, the nodes represented the country/organization elements, and the more total documents, the larger the nodes. Different colors of the nodes indicated the average citations of the documents. The distance and thickness of the connecting curve lines between nodes represented the relatedness and strength of their coauthor link, respectively.

#### Sources/documents citation analysis

Citation analysis refers to the citation of different analysis objects (source, document). The more citations, the greater the impact. Sources citation and documents citation were performed by VOSviewer in citation analysis in the unit of sources and documents, respectively. In the network visualization map of sources/documents citation analysis, the size of the node was determined by total documents/ citations. Different colors of the nodes indicated different cluster categories. The distance between nodes indicated their relatedness.

## Keywords co-occurrence analysis

Co-occurrence analysis is a quantitative study of the included keywords, which can visually display the basic characteristics such as the frequency of the keywords and the law of development and evolution, so as to understand the research status and development trends of related fields. In this study, we uniformed "coronavirus disease 2019, coronavirus 2019, COVID 2019, COVID-19, COVID19, COVID 19, nCoV-2019, nCoV2019, nCoV 2019, Severe acute respiratory syndrome coronavirus 2, 2019 novel coronavirus, 2019-novel CoV, 2019-ncov, 2019 ncov, sarscov-2" to "covid-19". In addition, "diabetes-mellitus, diabetes mellitus" were uniformed to "diabetes". "Sars" was uniformed to "sars coronavirus". "Risk" was uniformed to "risk factors". "Functional receptor" was uniformed to "receptor". Then the txt file was imported into VOSviewer to perform co-occurrence analysis in the unit of all keywords. In the map, the size of the node was determined by occurrences of each keyword. The distance between nodes indicated their relatedness. Different colors of the nodes indicated different cluster categories in the network visualization map and the average publication year of the keyword occurrences in the overlay visualization map, respectively.

## Results

#### Country/organization coauthorship analysis

The 1,206 articles on COVID-19 and diabetes, included authors from 101 countries in total. With the minimum number of documents of a country was set to 5, and the minimum number of citations of a country was set to 0; 48 countries (47.52%) finally met the threshold. The overlay visualization map of country coauthorship analysis was conducted by VOSviewer, including the cooperation among countries, the total citations of each country, and the average year of their publications. In the map, it showed the varying degrees of close cooperation among these 48 countries (Figure 1A). China had the highest total citations, and the United States had the largest number of documents. The scientific collaboration between these two countries was very close. Additionally, most of the top 20 citations countries were from Europe (Table 1). The map also revealed that the England was in a leading position both in terms of citations and documents among these European countries.

Similarly, we next conducted an organization coauthorship analysis on a total of 2,595 organizations. With the minimum number of documents of an organization was set to 10, 32 organizations met the threshold, of which 2 organizations did not cooperate with any other organizations. The remaining 30 organizations were shown in the map (Figure 1B). The analysis results showed that half of the top 10 highly cited organizations were from China, including Capital Medical University, which had the highest citations, and Huazhong University of Science and Technology, which had the largest number of documents. Four organizations received more than 1,000 citations, among which the highest citation was 5,135. In addition, among organizations from other countries, University of Oxford had the highest citations and most collaborations, and Harvard Medical School had the largest number of documents.

#### Sources citation analysis

Recently, a total of 526 sources/journals have appeared in the field of COVID-19 and diabetes research. With the minimum number of documents of a source was set at 10, and 16 sources (3.04%) reached this threshold.



Figure 1 Country/organization coauthorship analysis. In the overlay visualization map of country (A)/organization (B) coauthorship analysis, the nodes represented the country/organization elements, and the more total documents, the larger the nodes. Different colors of the nodes indicated the average citations of the documents according to the color bar on the lower right corner. The distance and thickness of the connecting curve lines between nodes represented the relatedness and strength of their coauthor link, respectively.

These sources published 264 of all 1,206 pieces (21.89%) of documents on COVID-19 and diabetes in this study (*Figure 2*). Of these, the top 5 highly cited journals were Journal of Medical Virology, Diabetes Care, Journal of Clinical Medicine, Diabetes Research and Clinical Practice, Aging-US (Table 2). In particular, the 3 journals Diabetes Research and Clinical Practice, Diabetes Care, Journal of Medical Virology also ranked among the top 5 in terms of total link strength. Diabetes Research and Clinical Practice had the largest number of documents. Overall, it can be seen that the journals of Journal of Medical Virology, Diabetes Care, and Diabetes Research and Clinical Practice occupied a vital position in the research field of COVID-19 and diabetes, which can

provide an important reference for further research in related fields in the future.

#### Documents citation analysis

With the minimum number of citations of a document was set at 60, 58 documents met the threshold among the 1,206 documents (4.81%) in total. Eleven items of them had no linkage with others. The remaining 47 documents were shown in the map (*Figure 3*). The network visualization map of documents citation analysis indicated the cooperation among sources of documents, as well as the total citations corresponding to each source. The results showed that the

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	Country				Organization			
ID	Name	Citations	Documents	Total link strength	Name	Citations	Documents	Total link strength
1	China	12,507	234	179	Capital Med Univ	5,135	10	2
2	USA	6,635	338	297	Wuhan Univ	1,775	36	15
3	England	2,050	129	220	20 Huazhong Univ Sci & Technol		52	19
4	Italy	1,461	161	210	Fudan Univ	1,312	10	1
5	Switzerland	1,067	28	94	Univ Oxford	771	15	20
6	Germany	852	56	154	Harvard Med Sch	762	37	23
7	France	778	55	108	Univ Washington	754	14	8
8	Scotland	636	20	41	Zhejiang Univ	746	11	2
9	India	576	73	96	Imperial Coll London	442	14	16
10	Spain	521	58	132	Columbia Univ	383	12	3
11	Canada	444	32	52	Univ Birmingham	285	10	7
12	Brazil	431	51	69	Queen Mary Univ London	227	10	14
13	Australia	399	40	80	Cent South Univ	217	10	8
14	The Netherlands	385	28	127	Univ Manchester	189	10	10
15	Ireland	370	11	57	Univ Penn	188	11	7
16	Belgium	344	27	96	Univ Campania Luigi Vanvitelli	161	11	2
17	Poland	236	16	69	Kings Coll London	160	20	13
18	Israel	209	11	41	Albert Einstein Coll Med 158		10	2
19	Norway	192	7	19	Brigham & Womens Hosp	146	11	12
20	Sweden	165	17	59	Univ Sao Paulo	123	17	1

Table 1 Top 20 country/organization coauthorship analysis for COVID-19 and diabetes

article "Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study" published by Zhou et al. in The Lancet in 2020 had been cited the most, reaching 4,877 times (Table 3).

## Keywords co-occurrence analysis

Keywords co-occurrence analysis visually displayed hotspots related to COVID-19 and diabetes by studying highfrequency keywords. In this study, there were a total of 3,405 keywords, of which 29 keywords with a frequency of more than 30 times were selected (*Table 4*). The overlay visualization map scaled by occurrences indicated the hotspots in the field of COVID-19 and diabetes. The result of cluster analysis of keywords showed that these 29 keywords can be divided into 4 categories, mainly focusing on 3 categories, namely risk factors & clinical outcomes, receptor ACE2 & cytokine storm, as well as clinical characteristics & epidemiology of Wuhan COVID-19 (*Figure 4A*). According to the evolution of time trend, hyperglycemia, obesity, outcomes, and cytokine storm are the hotspots of recent concern (*Figure 4B*).

#### Discussion

COVID-19 is a newly emerging disease with formidable infectivity and high mortality. Studies suggested that diabetes was one of the most prevalent comorbidities



Figure 2 Sources citation analysis. In the network visualization map of sources citation analysis, the nodes represented the source elements, and the size of the node was determined by total documents. Different colors of the nodes indicated different cluster categories. The distance between nodes indicated their relatedness.

ID	Journal	Citations	Documents	Total link strength
1	Journal of Medical Virology	544	21	22
2	Diabetes Care	313	20	41
3	Journal of Clinical Medicine	260	20	16
4	Diabetes Research and Clinical Practice	221	44	51
5	Aging-US	221	12	13
6	Diabetes Obesity & Metabolism	171	10	31
7	Acta Diabetologica	108	14	28
8	Diabetes Technology & Therapeutics	89	12	15
9	PLoS One	71	30	18
10	Medical Hypotheses	71	11	6

Table 2 Top 10 high-cited sources for COVID-19 and diabetes

among COVID-19 patients (14,15). The patients with diabetes had a higher risk of hospitalization and death than those without diabetes (16-18). There were also studies that suggested that diabetes mellitus may be an immediate and long-term complication of COVID-19 (19,20). The causal relationship between COVID-19 and diabetes is intricate and complicated. Although related researches are carried out in full swing, there is no good analysis of current and future research hotspots. In this work, we mapped the current status and trends of global researches of COVID-19 and diabetes by using the method of bibliometric analysis.

The results showed that China and the US were hotspots of publications and citation on this topic. Capital Medical University had the highest citations and Huazhong University of Science and Technology had the largest number of documents. *Diabetes Research and Clinical Practice* was the most productive journal. *Journal of Medical Virology* was the most highly cited journal. Zhou *et al.*'s article (*The Lancet*, 2020) was the most representative and widely cited. The keywords mainly focused on 3 categories, namely risk factors & clinical outcomes, receptor ACE2 & cytokine storm, as well as clinical characteristics & epidemiology.



Figure 3 Documents citation analysis. In the network visualization map of documents citation analysis, the nodes represented the document elements, and the size of the node was determined by total citations. Different colors of the nodes indicated different cluster categories. The distance between nodes indicated their relatedness.

Among them, hyperglycemia, obesity, outcomes, and cytokine storm are the hotspots of recent concern.

Regarding the contributions of countries and organizations, China occupied a major position in the field of COVID-19 research. Wuhan, China was the epicenter of the disease outbreak. In the face of the unknown and terrifying disease, major forces such as medical and health institutions and science and technology departments were making every effort to carry out related research on pandemic prevention and control, while also promoting the global exchange and sharing of scientific research results in a comprehensive, multi-level and timely manner. Several universities from China, including Capital Medical University, Wuhan University, Huazhong University of Science and Technology, and Fudan University, had made tremendous research progress in COVID-19 related research.

However, with the spread of the pandemic, the United States had become the country with the largest cumulative number of confirmed cases of COVID-19 in the world. At the same time, it was also the country with the largest number of related research articles, although the number of citations of Chinese articles far exceeded it, which was consistent with the results described by Corrales-Reyes *et al.* (13). The United States has unique advantages in basic and clinical medical research, including sufficient funds, advanced equipment and professional researchers. Among its outstanding institutions, such as Harvard Medical School, University of Washington, and Columbia University had published many high-level research results. COVID-19 is a disease with a certain degree of complexity and novelty, and it urgently needs global collaboration and teamwork. This is of particular practical significance to the lives of people in all countries in the context of the current pandemic.

In the face of this pandemic, the academic community has joined the "battlefield" without gunpowder at the fastest speed. Thus, the treatment strategy can be continuously updated, and the vaccine development progress can be rapidly advanced. Demonstrating the ability of COVID-19 patients to mount a neutralizing antibody responses to SARS-CoV-2 in the presence of diabetes is critical for vaccine development (21). The publication of research results on COVID-19 has been strongly supported by many journals, such as the *New England Journal of Medicine*,

ID	Journal	IF2020	Citations	Article title	Year	Author
1	Lancet	79.321	4,877	Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study	2020	Zhou F, <i>et al.</i>
2	JAMA Intern Med	21.873	1,297	Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China	2020	Wu CM, <i>et al.</i>
3	JAMA	56.272	1,283	Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area	2020	Richardson S, <i>et al.</i>
4	Allergy	13.146	758	Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China	2020	Zhang JJ, et al.
5	N Engl J Med	91.245	580	Covid-19 in Critically III Patients in the Seattle Region-Case Series	2020	Bhatraju PK, <i>et al.</i>
6	Obesity	5.002	379	High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation	2020	Simonnet A, <i>et al</i> .
7	Diabetes Metab Res Rev	4.876	273	Diabetes is a risk factor for the progression and prognosis of COVID-19	2020	Guo WN, <i>et al.</i>
8	BMJ	39.890	261	Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study	2020	Docherty AB, et al.
9	JAMA	56.272	224	Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State	2020	Rosenberg ES, et al.
10	Nature	49.962	215	Factors associated with COVID-19-related death using OpenSAFELY	2020	Williamson EJ, <i>et al.</i>

Table 3 Top 10 high-cited documents for COVID-19 and diabetes

*JAMA*, and other world-class medical journals that have specially opened columns for COVID-19 and accelerated the publishing process. Therefore, we can see that many highly cited articles have been published in the abovementioned authoritative journals. A retrospective cohort study published by Zhou *et al.* in *The Lancet* in March 2020 summarized the clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China (16), and has been cited up to 4,877 times. In addition, the clinical characteristics, risk factors and outcomes of COVID-19 patients were also the focus of other highly cited documents.

The results of documents citation analysis showed that half of the top 10 high-cited sources are top journals in the field of diabetes research, which may provide more professional research references for exploring the interaction mechanism between COVID-19 and diabetes. Diabetes Care was the leader of authoritative journals, while the journal Diabetes Research and Clinical Practice seemed to be more closely related to other journals, and the number of published studies was also far ahead of other journals. These articles have contributed greatly to the research on COVID-19 and diabetes. Interestingly, the journal Medical Hypotheses has also entered the ranks of the top 10 highly cited journals, which prompts us to actively explore unknown diseases and put forward our own opinions on the basis of scientific hypotheses.

Keyword co-occurrence analysis can reflect the development trend and hot spots of related research to a certain extent, and reveal potentially valuable research. The results of this study showed that ACE2 receptor of SARS-CoV-2 and cytokine storm have become another eyecatching hotspot in addition to clinical features and risk factors of COVID-19. Many studies have shown that factors

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Table 4 Keywords co-occurrence analysis for COVID-19 and diabetes

ID	Keyword	Cluster	Total link strength	Occurrences	Average publication year
1	COVID-19	1	1,650	783	2020.0117
2	Diabetes	1	806	255	2020.0135
3	Mortality	1	505	158	2020.0219
4	Risk factors	1	335	104	2020.022
5	Outcomes	1	287	81	2020.0548
6	Obesity	1	274	81	2020.0294
7	Hypertension	1	254	69	2020
8	Association	1	227	58	2020
9	Cardiovascular disease	1	158	38	2020
10	Hyperglycemia	1	120	37	2020.0323
11	Management	1	132	37	2020
12	Severity	1	159	35	2020
13	Prevalence	1	132	35	2020
14	Coronavirus	2	737	240	2020.0138
15	Infection	2	516	168	2020
16	Sars coronavirus	2	370	109	2020.01
17	Receptor	2	408	107	2020
18	Ace2	2	372	105	2020.011
19	Expression	2	155	48	2020
20	Disease	2	150	45	2020
21	Cytokine storm	2	99	35	2020.0312
22	Acute respiratory syndrome	2	90	30	2020
23	Pneumonia	3	442	116	2020.0183
24	Clinical characteristics	3	216	57	2020.0196
25	Wuhan	3	205	56	2020.0377
26	China	3	213	54	2020.02
27	Epidemiology	3	108	39	2020
28	Meta-analysis	3	120	30	2020
29	Pandemic	4	86	34	2020

such as the proinflammatory state, the compromised innate immune response, and possibly elevated ACE2 of diabetic patients levels may lead to increased susceptibility to SARS-CoV-2 infection and worsening prognosis (15,22,23). The activation of pro-inflammatory cytokines or chemokines leads to apoptosis or necrosis of infected cells and triggers an inflammatory response. It is well known that the most severe form of COVID-19 is acute respiratory distress syndrome, which is characterized by the highest levels of inflammatory cytokines, known as "cytokine storm". Cytokine storm is one of the important drivers of disease progression and death in COVID-19 patients. The study



**Figure 4** Keywords co-occurrence analysis. In the map, the size of the node was determined by occurrences of each keyword. The distance between nodes indicated their relatedness. (A) In the overlay visualization map of keywords co-occurrence analysis, colors of the nodes indicated the average year of the keyword occurrences. (B) In the network visualization map of keywords co-occurrence analysis, different colors of the nodes represented different clusters divided by keywords co-occurrence.

of cytokine storm may provide a new direction for the treatment of COVID-19. On the other hand, SARS-CoV-2 infection may result in the occurrence of new-onset diabetes or less well-controlled diabetes. ACE2 is a key enzyme in the renin-angiotensin system. Activation of the reninangiotensin system resulting in unopposed deleterious actions of angiotensin II may partially explain the underlying mechanisms of the occurrence of new-onset diabetes with SARS-CoV-2 infection during the acute phase (24). In addition to viral invasion in islets can cause  $\beta$ -cell damage, over-activated inflammation may also contribute to insulin resistance and the elevated level of blood glucose (20). One of the interesting hotspots is new-onset diabetes in long-COVID. Recent and emerging evidence suggested that COVID-19 patients with new-onset diabetes may confer a greater risk for poor prognosis than those with pre-existing diabetes (9). In general, the relationship between diabetes and COVID-19 is still elusive.

However, this study still has some limitations. The existence of publication bias was common to all bibliometric analysis. First, we only analyzed the documents that were included in the WOS SCI-Expanded database before the search date, and the documents published and included in the database after that were not included in the analysis. Secondly, some preprint platforms (such as BioRxiv, and MedRxiv) are becoming more and more popular, especially many of the latest studies on COVID-19 will be published on the preprint website first. Our study failed to include the data of these platforms into the analysis, and there may be some biases. In addition, language type may also be a factor of bias. Therefore, our bibliometric analysis will inevitably be different from the actual published situation to a certain extent.

#### Conclusions

In this study, we used bibliometric analysis to map global research trends of COVID-19 and diabetes, including country/organization coauthorship analysis, sources/ documents citation analysis, and keywords co-occurrence analysis. Then we analyzed the research hotspots in the field of COVID-19 and diabetes on the basis of these studies. In addition to the clinical features and risk factors of COVID-19, the ACE2 receptor of SARS-CoV-2 and cytokine storm have gradually become another eye-catching hotspot. Further exploration of the relationship between COVID-19 and diabetes will bring new hope for patients' diagnosis and treatment. In summary, we believe that our research can help researchers understand the current status and hotspots of COVID-19 and diabetes research from a macro perspective, which will help achieve major scientific breakthroughs in the future.

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## Footnote

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://apm. amegroups.com/article/view/10.21037/apm-21-2636/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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