



# Global status and trends in type 2 diabetes remission from 2002 to 2022

### A bibliometric and visual analysis

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#### **Abstract**

Type 2 diabetes mellitus (T2DM) is estimated to impact 693 million individuals globally by 2045. Diabetes remission has the potential to slow disease progression, alleviate psychological burdens, minimize complications, and improve quality of life. We aimed to perform a bibliometric analysis of research on T2DM remission. We searched the Web of Science (WoS) database to identify relevant publications on T2DM remission during 2002 to 2022. Research trends and hotspots in T2DM remission were analyzed using Bibliometrix R and CiteSpace. The analysis considered various factors such as publication year, authors, journal, institution, country/region, themes, thematic evolution, keywords, and keyword bursts. The WoS search yielded 2254 articles. The annual scientific output has consistently increased. Lee was the most prolific author (48 papers). Obesity surgery was the leading journal (296 publications), while diabetes care had the highest h\_index (43). The University of Copenhagen was the most active institution (116 papers). The most productive countries were the US (476), China (347), the UK (180), Italy (121), and Japan (90). The top 3 keywords were "bariatric surgery," "weight loss," and "remission." From 2013 to 2015, the usage of the term "medical therapy" significantly surged, lasting for 3 years. The term "GLP-I receptor agonists" also had a lasting burst. In the past 5 years, "weight loss" and "low-calorie diets" have emerged as prominent areas of research. This study analyzed the research trends and key factors in the field of type 2 diabetes mitigation through bibliometrics, providing important data support and a basis for decision-making for future research and public health policies.

**Abbreviations:** GLP-I = glucagon-like peptide-I, HbA1c = glycosylated hemoglobin, MCP = multiple country publications, MCP/Articles = MCP ratio, NP = total number of publications, PY\_start = the year for the first publication, Q value = the module value, RCTs = randomized controlled trials, S value = the average profile value, SCI-E = science citation index expanded, SCP = single country publications, SGLT2 = sodium-glucose co-transporter 2, T2DM = type 2 diabetes mellitus, TC = total number of citation, VLCD = very-low-calorie diet, WoS = Web of Science, WoSCC = Web of Science core collection.

Keywords: bibliometrics, diabetes mellitus, emerging trends, remission, spontaneous, type 2

#### 1. Introduction

The International Diabetes Federation Diabetes Atlas (10th edition) reports that the prevalence of diabetes is increasing worldwide, significantly affecting the health and well-being of individuals, families, and societies. The atlas offers detailed insights into the projected prevalence of diabetes in different countries and regions for the years 2021, 2030, and 2045.

Diabetes mellitus is responsible for a wide spectrum of ill-effects on human well-being, ranging from the immediate peril of severe hypoglycemia to the harm caused by severe hyperglycemic hyperosmolar syndrome and metabolic disarray resulting from ketoacidosis as well as enduring complications from damage to major and minor arterial vessels,<sup>[1]</sup> and the nervous system.<sup>[2]</sup> The condition diminishes the overall quality of life, causes a multitude of psychosocial concerns, and persists throughout the patient's lifespan.<sup>[3,4]</sup> In the past, type 2 diabetes mellitus (T2DM) was deemed incurable; however, recent research has explored various methods, such as diet, surgery, behavior modification, weight loss, and medication, that offer the potential for remission and the elimination of glucose-lowering drugs. Diabetes remission aims to reduce

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

All data utilized in this study were sourced from publicly accessible WOS databases and approved by their respective institutional review boards. Consequently, no additional ethical approval was required for this research.

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the psychological burden on patients, enhance their quality of life, slow disease progression, and minimize the risk of complications. [5] Despite the increasing number of studies on T2DM remission, which mainly focus on case reports, clinical trials, and cohort studies, relatively little research is available on the overall trends, research hotspots, key authors and institutions, and the geographical distribution of research fields in T2DM remission studies. This study aims to conduct a systematic quantitative analysis of the literature in the field of T2DM alleviation through bibliometric methods, in order to reveal the current research status and development trends in this area.

Bibliometric analysis is a quantitative approach that tracks the progress of a research domain over time. [6] It is a highly effective tool for examining detailed trends in a given field of study.[7] In this technique, statistical analysis is employed to objectively present the research contributions and collaborations of authors, journals, institutions, and countries in a specific scientific domain. The technique has been widely utilized in scientific publications to anticipate future directions or areas of interest, [8] highlighting emerging issues in a particular field that necessitate solutions and generate considerable interest among the global academic community. The ability to predict future research directions enables the identification of urgently needed research that will have a profound impact on the future. Although a large number of studies have focused on the field of diabetes remission, the quantitative analysis of its research trends and influencing factors is still insufficient. The purpose of this study is to solve this gap by carrying out bibliometric research on diabetes remission to systematically analyze the status quo of type 2 diabetes remission research through bibliometric methods, reveal the research hotspots and development trends, and provide direction for future research. The research results will not only help researchers identify research priorities and provide a basis for decision-making for policy makers, but also promote interdisciplinary and cross-regional research cooperation and knowledge dissemination, which are of great significance for improving patients' quality of life, and promoting scientific research and technological progress in this field.

#### 2. Materials and methods

#### 2.1. Data sources and search methods

The statistical analysis in this study was mainly conducted through descriptive bibliometric analysis. Bibliometric analysis is a method of quantitatively studying the distribution characteristics, trends, and correlations of academic literature by using statistical methods. The highly influential scientific literature database known as the Web of Science (WoS) was accessed through the Jilin University Library website. The WoS database is the largest database of its kind, containing over 12,000 influential high-quality academic journals from around the world, covering a wide range of influential research fields. Considered the world's largest, most commonly used, authoritative, and comprehensive collection of information resources, the WoS database is particularly suitable for bibliometric analysis due to its standardized data structure and rich citation information. The WoS Core Collection (WoSCC) database has a complete citation index and a large number of bibliometric indicators, and is widely used in bibliometric research in different fields.[9-11] We retrieved relevant studies published between January 1, 2002 and December 31, 2022, by using the science citation index expanded (SCI-E) within the web of science core collection (WoSCC). We excluded data from 2023 due to its incomplete nature. Our search strategy focused on specific terms related to the remission and type of diabetes. The search strategy was as follows: (TS = [remission, spontaneous OR remissions, spontaneous OR spontaneous remission OR spontaneous remissions OR remission OR remissions]) AND TS = (diabetes

mellitus, type 2 OR diabetes mellitus, noninsulin-dependent OR diabetes mellitus, ketosis-resistant OR diabetes mellitus, ketosisresistant OR ketosis-resistant diabetes mellitus OR diabetes mellitus, noninsulin dependent OR diabetes mellitus, noninsulindependent OR noninsulin-dependent diabetes mellitus OR diabetes mellitus, stable OR stable diabetes mellitus OR diabetes mellitus, type II OR NIDDM OR diabetes mellitus, noninsulindependent OR diabetes mellitus, maturity-onset OR diabetes mellitus, maturity-onset OR maturity-onset diabetes mellitus OR maturity-onset diabetes mellitus OR MODY OR diabetes mellitus, slow-onset OR diabetes mellitus, slow-onset OR slow-onset diabetes mellitus OR type 2 diabetes mellitus OR noninsulin-dependent diabetes mellitus OR noninsulindependent diabetes mellitus OR maturity-onset diabetes OR diabetes, maturity-onset OR maturity-onset diabetes OR type 2 diabetes OR diabetes, type 2 OR diabetes mellitus, adult-onset OR adult-onset diabetes mellitus OR diabetes mellitus, adultonset). Only articles and reviews were considered, and non-English publications were excluded. On April 20, 2023, we downloaded all the data, with titles, authors, keywords, abstracts, references, and journals from the WoS database. A total of 2254 documents were generated from the query and subsequently analyzed for this study. The specific search process is illustrated in Figure 1. We exported the online literature. including cited references and complete texts, in plain text format and imported it into R for analysis.

#### 2.2. Bibliometric and visualization analyses

Three tools were used for bibliometric analysis in this study: the "Bibliometrix" R software package, the bibliometric online analysis tool (https://bibliometric.com/), and CiteSpace 6.2.R2. These widely utilized bibliometric tools provided an impartial and extensive comprehension of research related to the remission of T2DM. R software is a powerful statistical programming tool equipped with extensive data processing and visualization capabilities.[12] It has a large number of scalable software packages, such as bibliometrix and biblioshiny, which provide comprehensive functionality for bibliometric analysis.[13] The R-bibliometrix tool was developed by Massimo Aria and Corrado Cuccurullo to conduct thorough science mapping analyses.[14] It is a comprehensive bibliometric software package that can collect and analyze publication and citation counts of countries, institutions, journals, and authors. The bibliometric online analysis tool (www.bibliometric.com) is used to visualize national cooperation networks, analyze the total number of publications in each country, and evaluate international cooperation patterns. CiteSpace, an open-source Java application developed by Prof Chao-Mei Chen, enables the visualization and analysis of trends and patterns in scientific literature. This tool has proved to be highly valuable in identifying the progress of domains and visually representing the advancement of knowledge domains. [6,15,16] In the analysis of type 2 diabetes remission research, we constructed a visual knowledge map according to the key procedure steps of CiteSpace, including time slicing, thresholding, modeling, trimming, merging, and mapping. [6] This analytical method helps to reveal research trends, emerging themes, and key turning points in the field, providing valuable insights for researchers and guiding future research directions.

#### 3. Results

The bibliometrix R package was used to analyze the literature on type 2 diabetes in remission, focusing on the number of different authors, journals, institutions, and countries. Through keyword analysis and theme exploration, the primary research areas within the retrieved articles were revealed. Moreover, citation analysis was employed to investigate the logical connections in the literature and establish a collaborative network that

highlights the cooperation between institutions, countries, and authors within this field.

#### 3.1. Amount of yearly literature and its projected increase

A total of 2254 publications were chosen for analysis based on the specified criteria. These publications, consisting of 1903 articles and 351 reviews, focus on research related to the remission of type 2 diabetes, and cover the period from 2002 to 2022. Figure 2 shows the distribution of these publications across the 20-year span. The cumulative citations for these publications, as determined from the WoSCC, amounted to 73,584, with an average of 32.65 citations per paper. Figure 2 demonstrates a consistent and huge increase in the number of annual publications, starting from 16 in 2002 and peaking at 269 in 2021. This upward trend indicates the growing importance and attention given to type 2 diabetes remission research in recent years. Furthermore, the number of citations has also experienced remarkable growth, rising from 26 in 2002 to a noteworthy peak of 9947 in 2021. This trend underscores the profound interest of researchers in this field.

#### 3.2. Literature distribution across different categories

Our analysis focused on the distribution of the literature across authors, journals, institutions, and countries. A total of 9956 authors were involved in the 2254 studies on type 2 diabetes remission that were published in WoS during the 20-year study period. Among the top 20 most prolific authors, Lee had the highest publication count (48), followed by Roy Taylor with 37 articles and Carel W. Le Roux with 35 articles (Fig. 3).

Each author was rated based on the number of publications and their h\_index to determine the leading authority in the area of diabetes type 2 remission during the last 20 years. The h\_index, created in 2005 in the United States by the Hershey Group, is a combined measure of the significance and breadth of a researcher's total contributions. [17,18] Table 1 shows the 10 best authors with the most publications and their h\_indices. With 48 publications and an h\_index of 25, Lee was the most productive author, followed by Philip R. Schauer and S.C. Chen, who had h\_indices of 22 and 18, respectively.

This literature study provided a thorough grasp of the 5 outstanding authors, who were distinguished by the amount of

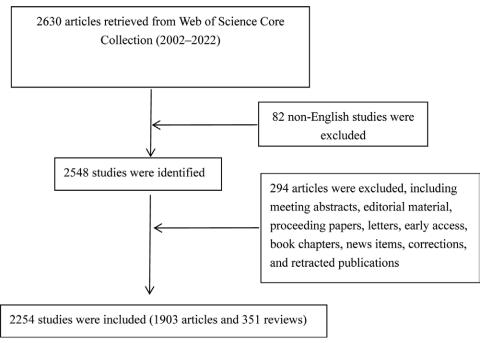


Figure 1. Literature search process.

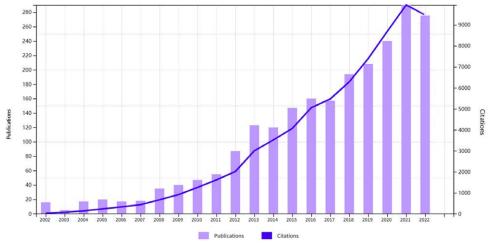


Figure 2. Annual scientific production and citations.

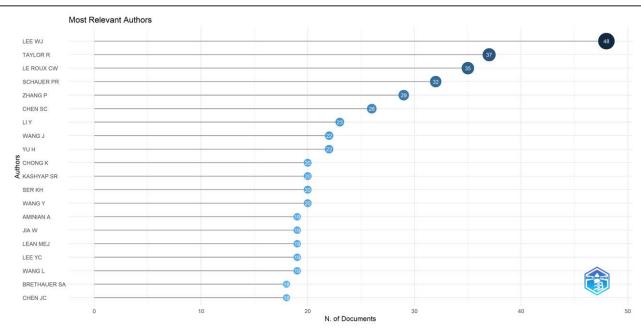


Figure 3. Most relevant authors.

Table 1
Top 10 most productive authors and their h\_indices.

Element	h_index	g_index	m_index	TC	NP	PY_start
Lee	25	47	1.786	2289	48	2010
Schauer	22	32	1.571	4668	32	2010
Chen	18	26	1.5	1068	26	2012
Chong	18	20	1.286	1677	20	2010
Taylor	18	37	1.636	1992	37	2013
Le Roux	17	35	1.214	1359	35	2010
Ser	17	20	1.214	1133	20	2010
Rubino	16	18	0.727	3934	18	2002
Cummings	14	15	0.933	2132	15	2009
Jia	14	19	0.933	598	19	2009

 $NP = total\ number\ of\ publications,\ PY\_start = the\ year\ for\ the\ first\ publication,\ TC = total\ number\ of\ citation.$ 

publications and h\_index value. Prof Lee, affiliated with Min-Sheng Gen. Hosp., focuses on the link between bariatric surgery and type 2 diabetes. Their highly cited paper titled "Roux-en-Y Gastric Bypass versus Intensive Medical Management for the Control of Type 2 Diabetes, Hypertension, and Hyperlipidemia: The Diabetes Surgery Study randomized clinical trial," was published in the Journal of the American Medical Association (JAMA) in 2013. [19] Professor Le Roux, from University College Dublin, published "Weight loss to disrupt type 2 diabetes" on April 15, 2023. [20] Through ongoing research, Le Roux continues to focus on obesity and weight-based therapeutic goals to alleviate type 2 diabetes. Philip R. Schauer, associated with the Louisiana State University System, concentrates on studying the long-term effects of bariatric surgery and intensive drug therapy in obese patients with type 2 diabetes. They have published various articles on this topic, including "bariatric surgery versus intensive medical therapy for diabetes – 3-year outcomes" and "bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes" in the New England Journal of Medicine. [21,22] Roy Taylor, affiliated with Newcastle University, developed the well-known twin cycle hypothesis, which provides a pathological basis for the remission of type 2 diabetes. Pin Zhang, from Shanghai Jiao Tong University, China, also focuses on type 2 diabetes remission. They presented a publication titled "Visceral Fat Area as a New Predictor of Short-term

Diabetes Remission After Roux-en-Y Gastric Bypass Surgery in Chinese Patients with a Body Mass Index <35 kg/m².[23] which has generated interest among various researchers. Zhang also investigates the effects of bariatric surgery on kidney function in obese patients.

The present study provided insights into the characteristics of journals that published research on type 2 diabetes remission. The characteristics analyzed included the journal name, total publications, total citations, and h\_index. A total of 608 journals published studies in this field of research. Table 2 displays the top 10 most active journals, which collectively accounted for 769 publications or 34.11% of the total publications. The journal Obesity Surgery had the highest number of articles, with 296 publications or 13.13% of all articles. It also had 2126 citations, averaging 7.26 citations per article. Surgery for Obesity and Related Diseases had 178 articles; Diabetes Care had 93 articles; diabetic medicine had 39 articles; and frontiers in endocrinology had 30 articles. The journals obesity surgery, surgery for obesity and related diseases, and diabetes care were the top 3 journals in terms of both the total number of published articles and the total number of articles cited in national journals. The h\_index[17] was used to evaluate journal impact, and among the top 5 journals ranked according to their h\_indices, Diabetes Care had the highest h\_index at 43 (Table 3). The other 4 journals, obesity surgery,

surgery for obesity and related diseases, diabetes, and annals of surgery, also had significant h\_indices. these journals dominate the research in the field of type 2 diabetes remission, and their articles are considered of high quality and deserving of further analysis.

The WoS database search results showed that 67 countries/ territories published research on type 2 diabetes remission between 2002 and 2022. Table 4 presents the top 10 countries based on the number of articles contributed. China ranks second with 347 articles, preceded by the United States with 476 articles. The United Kingdom has published 180 articles; Italy has published 121 articles; and Japan has published 90 articles. Notably, there has been a substantial increase in the literature on type 2 diabetes remission in China over the past 20 years.

The publications from the United States had the highest number of references (24,562) with an average reference count of 51.6 (Table 5). The United Kingdom ranked second, with 8059 citations and an average citation count of 44.8. China had 6125 citations with an average count of 17.7, while Italy had 5702 citations and an average count of 47.1. Denmark had 2525 citations and an average citation count of 44.30. Of the top 10 most prolific countries, 7 were in Europe, 1 was in North America, 1 was in Oceania, and 1 was in Asia. Additionally, 8 of the top 10 producers were developed countries, while the remaining 2 were developing countries. It should be noted that China is currently experiencing rapid economic growth. Furthermore, epidemiological research suggests that the frequent consumption of high-calorie meals contributes to the increased prevalence of type 2 diabetes. [24] This implies a potential correlation between positive financial relationships and type 2 diabetes remission.

We found that 3172 organizations were involved in research on type 2 diabetes remission (Table 6). Leading the pack is the University of Copenhagen, which has published a total of 116 papers. Close at its heels is Shanghai Jiao Tong University with

114 papers, followed by Newcastle University (UK) with 101 papers, Min-Sheng Gen. Hosp. with 96 papers, the University of Washington with 91 papers, the University of Glasgow with 77 papers, Columbia University with 74 papers, the University of Sao Paulo with 69 papers, Cent South Univ. with 63 papers, and Schauer Hospital with 60 papers. Among all the organizations in this analysis, Shanghai Jiao Tong University stood out as the top contributor in China and secured the second position globally in terms of number of research papers on type 2 diabetes remission.

#### 3.3. Keywords analysis

The keywords used for indexing and categorizing articles offer a precise and succinct overview of the subject matter.<sup>[25]</sup> They also reflect current trends and pioneering areas in a particular field. Analyzing keywords allows us to gain a broad comprehension of the topics and traits found in published works. Co-occurrence analysis reveals that terms used together in a document are closely connected to the conceptual framework of the research field. Additionally, by clustering the keyword co-occurrence network, we can identify sub-domains within the research domain.

The frequency and centrality of keywords can be used to identify potential research areas. Figure 4 displays the keywords that were most commonly used in research on T2DM remission. The term "bariatric surgery" appeared the most frequently in the literature, followed by the terms "weight loss," "remission," "diabetes," "gastric bypass," " $\beta$ -cell function," "obesity," "obese patients," "treatment," and "outcome."

A comprehensive analysis of the keywords was performed to uncover the most rapidly changing trends in recent times. As indicated by Figure 5, the intensity of bursts for the top 25 keywords varied from 5.59 to 25.21. The phrase "medical therapy" demonstrated the highest burst intensity and lasted for a period of 3 years, while its associated drug, glucagon-like

Table 2

#### Top 10 active journals ranked by total citations.

Journals	Total number of articles	Total number of citations	Average citation count
Obesity Surgery	293	2126	7.26
Surgery for Obesity and Related Diseases	177	1414	7.99
Diabetes Care	92	1387	15.08
JAMA-Journal of the American Medical Association	9	808	89.78
Annals of Surgery	27	741	27.44
New England Journal of Medicine	9	696	77.33
Lancet Diabetes and Endocrinology	17	542	31.88
Lancet	6	456	76.00
Diabetes	28	348	12.43
Diabetologia	27	342	12.67

#### Table 3

#### Top 10 active journals ranked by h\_index.

Element	h_index	g_index	m_index	TC	NP	PY_start
Diabetes Care	43	76	1.955	5879	93	2002
Obesity Surgery	39	64		6169	296	
Surgery for Obesity and Related Diseases	36	60	2.250	4667	178	2008
Diabetes	23	28	1.150	3283	28	2004
Annals of Surgery	21	27	0.955	2361	27	2002
Diabetologia	18	27	0.947	1099	27	2005
Diabetes Medicine	17	27	0.773	758	39	2002
Journal of Clinical Endocrinology and Metabolism	16	29		1246	29	
Lancet Diabetes and Endocrinology	16	17	1.455	1965	17	2013
Diabetes Obesity and Metabolism	13	21	0.929	464	26	2010

Table 4

Top 10 active countries ranked by number of articles.

Country	Articles	SCP	MCP	Freq	MCP_ratio
USA	476	389	87	0.211	0.183
China	347	297	50	0.154	0.144
United kingdom	180	119	61	0.080	0.339
Italy	121	92	29	0.054	0.240
Japan	90	82	8	0.040	0.089
Spain	83	70	13	0.037	0.157
Germany	74	46	28	0.033	0.378
Brazil	64	41	23	0.028	0.359
Canada	64	53	11	0.028	0.172
Denmark	57	48	9	0.025	0.158

MCP = multiple country publications, SCP = single country publications.

Table 5

Top 10 active countries ranked by total citations.

Country	TC	Average article citation
USA	24,562	51.60
United Kingdom	8059	44.80
China	6125	17.70
Italy	5702	47.10
Denmark	2525	44.30
Australia	2260	57.90
Spain	2184	26.30
France	1974	35.20
Germany	1949	26.30
Sweden	1895	37.20

TC = total number of citation.

peptide-I (GLP-I) receptor agonists, has remained a prominent keyword for 5 years. Over the past 5 years, "weight loss" and "low-calorie diets" have emerged as the newest and most concentrated area of research focus, indicating an ongoing interest in this field.

The R-bibliometrix tool was used to analyze the trend topics in keywords in the past 20 years. Figure 6 visually presents the results of this analysis, with the year and primary keyword graphed on the horizontal and vertical axes, respectively. Each keyword is represented by a node, and its size corresponds to how frequently it appears. The horizontal line represents the duration of keyword occurrence. Notably, the keyword "bariatric surgery" had the highest frequency from 2016 to 2018, in the context of type 2 diabetes remission. The most recent trend topic identified was an "intensive lifestyle."

#### 3.4. Keywords cluster analysis: co-occurrence

The co-occurrence network of the most frequent keywords, such as "metabolic surgery," "obesity," "glucose metabolism," "adipose tissue," "prevention," "intervention," and "remission," is shown in Figure 7.

The clarity of the keyword clustering results was evaluated based on the average profile value (S value) and the module value (Q value). A Q value above 0.3 indicates a distinct and significant clustering structure, while an S value exceeding 0.5 suggests a reasonable clustering outcome. Keyword clustering was accomplished using the LLR algorithm in CiteSpace. Using this algorithm, we obtained the CiteSpace keyword clustering network knowledge map, which revealed a clustering module (Q) value of 0.7955 and an average profile (S) value of 0.9214, indicating a highly significant clustering structure and compelling clustering effect (Fig. 8). The top 5 keyword clusters identified were "Roux-en-Y gastric bypass," "resistance," "diabetes mellitus," "type 2 diabetes," and "secretion."

Table 6

Top 10 active affiliations ranked by the number of articles published.

Affiliation	Articles	
University of Copenhagen	116	
Shanghai Jiao Tong University	114	
Newcastle University	101	
Min Sheng General Hospital	96	
University of Washington	91	
University of Glasgow	77	
Columbia University	74	
University of Sao Paulo	69	
Central South University	63	
Schauer	60	

#### 3.5. Themes and their evolution

The R-bibliographic matrix allows for the analysis of topic progression by assessing density and centrality. Various aspects such as titles, keywords, abstracts, and the standardization and conceptualization of features were investigated. Using centrality and density, we used a strategic graph to analyze changes in the dynamics of research subjects over time. Density signifies the level of cohesion within a cluster, while centrality represents the degree of interconnectedness between clusters. The research themes were categorized into 4 groups and visually depicted in the 4 quadrants of the strategic diagram (Fig. 9):

- (a) Motor topics in the top-right quadrant are thoroughly developed and pertinent to the subject, and include the topics "metabolic surgery," "weight loss," and "remission."
- (b) Primary and cross-cutting themes in the lower right-hand quadrant are relevant to the area but still in the process of development, such as "insulin resistance" and "GLP-1 receptor agonists."
- (c) Themes that are either emerging or declining and inadequately developed can be found in the lower left quadrant, encompassing "insulin secretion," "resistance," and "sensitivity."
- (d) Isolated topics are found in the upper left quadrant, and are not particularly relevant to the research field.

The size of each cluster is determined by the number of keywords, with the label cluster representing the most commonly utilized word within that cluster. The Walk Trap algorithm was employed to cluster the data in this study.

#### 3.6. Collaboration network

Enhanced knowledge exchange and expanded research scope are commonly observed outcomes of academic cooperation within different regions, authors, and institutions. In this study, we examined the academic collaborations in type 2 diabetes



Figure 4. Most common keywords.

Top 25 Keywords with the Strongest Citation Bursts

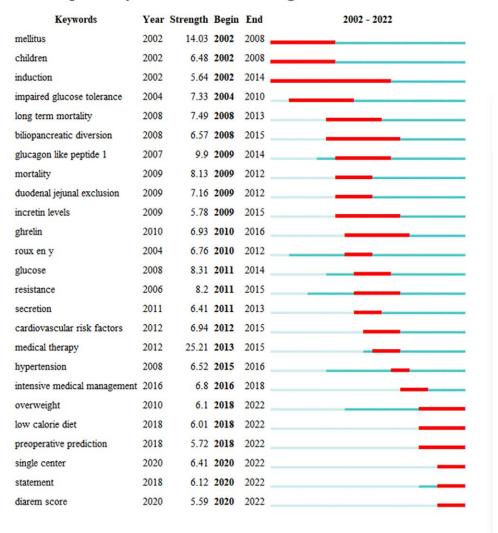


Figure 5. Top 25 keywords with the strongest citation bursts.

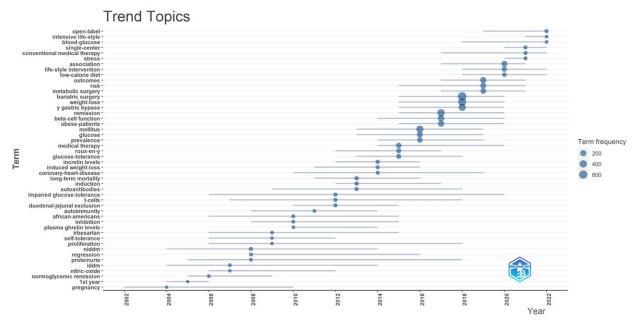


Figure 6. Map of trend topics in keywords from 2002 to 2022.

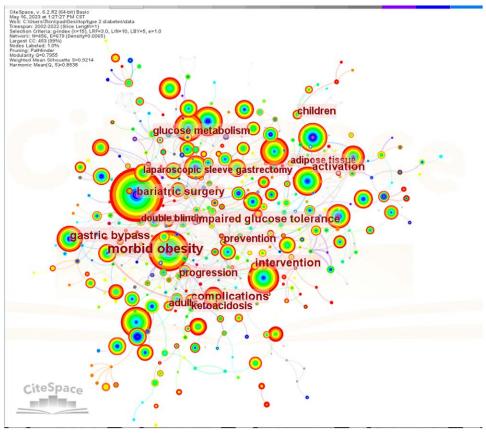


Figure 7. Co-occurrence analysis of keywords.

remission research by employing Bibliometrix. We classified authors and countries based on their collaboration network, where nodes represented the countries or authors and links depicted co-authorship.

In Figure 10, the map shows extensive collaboration among different countries, with the intensity of cooperation represented by varying shades of blue. The red line highlights partnerships

between countries, emphasizing the significant involvement of the United States in international cooperation. Figure 11 offers a more detailed view of the collaborations between the United States, China, the UK, Italy, Germany, and other nations. Notably, the United States leads in internationalization, engaging with numerous regions in this field. The UK, China, Italy, and Germany also exhibit substantial cross-border cooperation.

The top 10 most productive countries all demonstrate a strong tendency to collaborate with other nations. It is interesting to note that although Germany ranks seventh in the number of papers, it ranks fifth within international cooperation, actively participating in collaborations to expand its knowledge and expertise in diabetes remission research.

Collaboration in research can be effectively evaluated through the analysis of institutional partnerships. According to Figure 11A, the top 5 institutions with the most extensive collaborations in diabetes remission research are the Cleveland Clinic Foundation, Harvard University, the University of London, Imperial College London, and the University of Copenhagen. It is important to note that the University of Copenhagen, from Denmark, not only stands out as the most productive and prolific university but also ranks among the top

5 institutions for extensive collaborations in diabetes remission research. Shanghai Jiao Tong University ranks first in China and second globally in terms of the number of research papers on type 2 diabetes remission, and ranks 14th in international interinstitutional collaboration.

The collaborative network of authors consisted of 6 clusters, each represented by a different color (Fig. 11B). It is evident from Figure 10 that the majority of collaborators in the network share the same region or country. The collaborative studies primarily focus on diabetes remission, and mainly include cohort studies, large clinical trials, and randomized controlled trials (RCTs). To effectively conduct these studies, it is crucial to encourage collaboration between research organizations. It is worth mentioning that the top 10 most productive authors in the area of type 2 diabetes remission demonstrate a high level

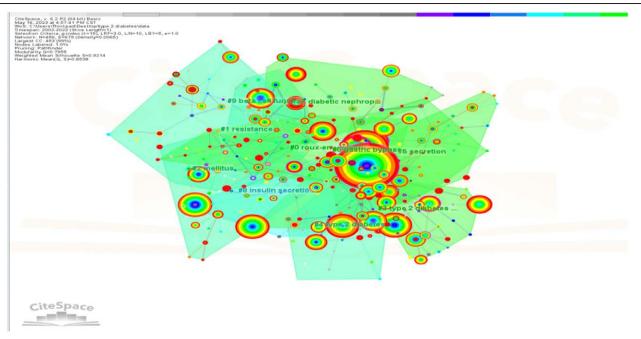


Figure 8. Top 5 keyword clusters.

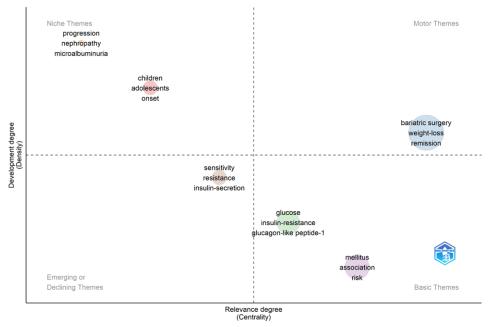


Figure 9. Thematic map of type 2 diabetes remission research.

of cooperation. Additionally, the significant contribution of Prof Lee to research on type 2 diabetes remission is highlighted through their emergence as a critical node in the collaborative network.

#### 4. Discussion

Type 2 diabetes is a chronic metabolic condition that currently lacks a definitive cure. However, research has demonstrated that some individuals with diabetes can achieve normal blood glucose levels through natural means or via medical intervention. In certain cases, this improvement can be sustained even after discontinuing the medication. Recent advancements in treatment have made long-term improvement more common. In the early 1930s, Bouchardat et al conducted a study on dietary restriction as a treatment for diabetes mellitus, and found that some patients were able to achieve normal glucose tolerance and remain free of urine glucose for several years while following a regular diet. In 1939, Newburgh and Conn reported that obese individuals with diabetes could restore normal glucose tolerance through weight loss. The concept of diabetic remission gained attention in 1959. [26] In 1960, Barr[27] documented 2 cases of diabetes remission, one of which lasted for 17 years after reducing carbohydrate intake and losing weight through diet alone. The formal recognition of type 2

diabetes remission as the "honeymoon period" of the disease occurred in 1997. [28] In 2002, the World Health Organization and the American Diabetes Association (ADA) reached a consensus on the definition of diabetes remission. The ADA revisited and redefined diabetes remission in 2009. [29] In 2019, the Association of British Clinical Diabetologists/Primary Care Diabetes Society stated in regards to type 2 diabetes remission that in order to alleviate type 2 diabetes, the clinical pathway is changing to provide support and appropriate follow-up.[30] In 2021, an international panel of experts convened by the ADA proposed "remission" as the most suitable term to describe this situation. The ADA definition and interpretation of type 2 diabetes remission, published in 2021, has become the standard for defining type 2 diabetes remission.[31] The diagnostic criterion for remission is a glycosylated hemoglobin (HbA1c) level below 6.5% after at least 3 months of discontinuing glucoselowering medications. Alternatively, a fasting glucose concentration lower than 7.0 mmoL/L or an estimated HbA1c level below 6.5% calculated through ambulatory glucose monitoring can be used as an alternative diagnostic criterion for type 2 diabetes remission.

Bibliometrics, introduced as a scientific approach by Alan Pritchard in 1969,<sup>[32]</sup> has proven to be a valuable tool for exploring research within a specific field. By using bibliometric analysis, researchers can effectively identify significant aspects

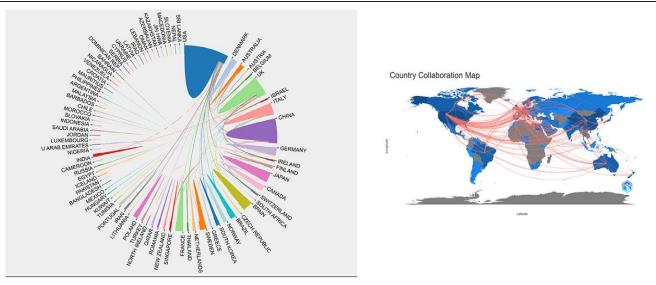
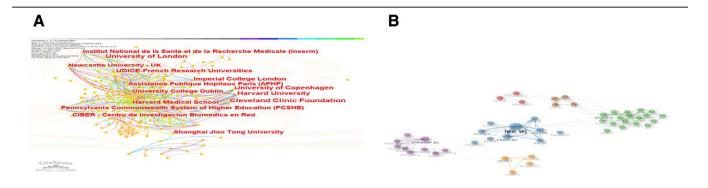


Figure 10. Country collaboration map.



The partnership between institutions

Figure 11. (A) The partnership between institutions; (B) collaborative network of authors.

and attributes of the literature related to a particular topic, thereby offering valuable insights for clinical policies.<sup>[33]</sup> In this study, we conducted an extensive bibliometric analysis of 2254 articles regarding the remission of type 2 diabetes within the WoSCC, spanning the period from 2002 to 2022. Our analysis contributes to the advancement of future research and clinical care.

## 4.1. General trends, and influential countries, journals, authors, and academic collaborations in research on type 2 diabetes remission

The number of citations and publications over time can serve as an indicator of productivity and trends in a specific field of study.[34] In English, the WoSCC has published a total of 2254 articles on type 2 diabetes remission in the last 20 years. Initially, the number of articles was low during the exploratory phase, but it has steadily increased since 2009. This demonstrates a positive development trend in the field, emphasizing the importance for clinicians to continue paying attention to it. It is worth noting that there was a peak in publications in 2021, which coincided with the year when an international panel of experts was convened by the ADA. During this meeting, the term "remission" was proposed and evaluated as the most appropriate term, and defined as HbA1c < 6.5% (48 mmoL/moL) at least 3 months after discontinuing pharmacological glucose-lowering treatment. The researchers also explored other questions and unmet requirements regarding the influencing factors and consequences of diabetes remission, proposing the active monitoring of individuals who achieve remission.[31] This underscores the importance of healthcare providers worldwide paying closer attention to type 2 diabetes remission. European and American countries notably rank among the top 10 nations in terms of publication count, demonstrating extensive collaboration and solidifying their position as global leaders in this field.

The level of research by a country, institution, or author can be measured by the number of publications in a specific field. According to this measure, the leading countries in the field of type 2 diabetes remission are the United States, China, and the United Kingdom. Among journals, surgery for obesity, obesity surgery and related diseases, and diabetes care have not only the highest number of publications but also the highest number of citations. Therefore, researchers interested in type 2 diabetes remission should give priority to these journals. The most prolific authors in this field are Lee, Taylor, and Le Roux. Their respective h\_indexes of 25, 18, and 17 indicate their high academic output and scholarly impact in this field. For instance, Lee focuses on bariatric surgery related to metabolic syndrome at the Department of Surgery, Min-Sheng General Hospital. Roy Taylor, affiliated with the Institute of Cellular Medicine, Newcastle Magnetic Resonance Centre, Newcastle University, has made significant contributions to reversing type 2 diabetes through his twin cycle hypothesis, which explores the pathophysiological mechanisms of remission. [35,36] His hypothesis suggests the involvement of factors such as the hepatic production of triglyceride-rich very-low-density lipoproteins, hepatic fat deposition, overweight/obesity, insulin resistance, and β-cell dysfunction.[37] Later on, Prof Taylor conducted a series of studies to further validate his proposed hypothesis. The findings from the counterpoint study suggest that reducing caloric intake can reverse β-cell dysfunction and insulin resistance in patients with type 2 diabetes, particularly in some obese individuals.[38] Specifically, the counterpoint study<sup>[39]</sup> included 30 patients who had T2DM and followed a very-low-calorie diet (VLCD) for 8 weeks. Compared to those who did not achieve remission, patients who achieved diabetes remission in the counterpoint study had a shorter duration of disease, were younger, and exhibited better islet function. The Diabetes REmission Clinical Trial (DiRECT) built upon the findings of the above 2 studies. [40]

The results revealed that approximately 33% of the patients achieved remission after 2 years of follow-up. Furthermore, of those who were in remission after 1 year, approximately 75% maintained the remission at 2 years. The remission rate was found to be higher among patients with greater weight loss, with a remarkable 86% reversal rate for individuals who lost more than 15 kg. Additionally, Prof Le Roux from University College Dublin concentrates on the impact of bariatric surgery on glycemic control in obese individuals with diabetes<sup>[41]</sup> as well as on the use of GLP-1 agonists for weight management and reducing the risk of progression to type 2 diabetes in obese individuals with prediabetes.<sup>[42]</sup>

The main objective of academic collaboration is to improve innovation and find better solutions for unresolved challenges, especially on a global level. Through this study, many collaborations among different countries, institutions, and authors were identified. Among these partnerships, the ones in the United States have emerged as the most prominent worldwide. Notably, the Cleveland Clinic Foundation, Harvard University, and the University of London have played a vital role in this collaborative network, highlighting their significant contributions to type 2 diabetes remission research over the past 2 decades.

#### 4.2. Hot trends in research on type 2 diabetes remission

This study analyzed the evolution and future potential of research on type 2 diabetes remission from various perspectives. The keyword burst analysis indicated that "weight loss" and "low-calorie diets" have gained significant attention in the past 5 years, with a notable surge in interest (Fig. 5). Furthermore, an examination of keyword trends revealed that "intensive lifestyle" ranks first among recent inquiries related to type 2 diabetes remission research (Fig. 5). The above analyses emphasized 3 key trends.

4.2.1. Reversing T2DM through dietary interventions. The potential of achieving the remission of type 2 diabetes lies in calorie-restricted diets, especially when combined with a comprehensive lifestyle modification program.<sup>[43]</sup> In 2008, Taylor proposed a hypothesis that substantial calorie restriction could lead to a rapid decrease in liver fat, normalization of hepatic insulin sensitivity, and a return to normal levels of hepatic glucose production.[37] A clinical trial conducted by Lim et al[38] has demonstrated that dietary calorie restriction alone effectively normalizes both hepatic insulin sensitivity and β-cell function in individuals with type 2 diabetes. This was associated with reduced levels of triacylglycerol reserves in the liver and pancreas. Thus, by consuming fewer calories, it is possible to reverse the irregularities associated with type 2 diabetes.[38] Furthermore, Steven et al found that a sustainable weight-loss program resulted in continued diabetes remission for at least 6 months in 40% of respondents who were able to lower their fasting plasma glucose level to below 7 mmol/L through a VLCD.[39] Lean et al conducted an RCT[40] that found that more than one-third of individuals with type 2 diabetes who participated in the DiRECT study maintained their remission for 24 months. There was a correlation between the extent of long-term weight loss and sustained remission. Taheri et al<sup>[44]</sup> conducted an RCT that compared the results of a VLCD with those of medical intervention at the 12-month mark. They found that an intensive lifestyle intervention resulted in a significant reduction in body weight and was associated with diabetes remission in over 60% of patients. Additionally, the intervention successfully achieved normoglycemia in more than 30% of individuals.[44] Another study concluded that dietary intervention can yield similar outcomes to metabolic surgery. [45]

**4.2.2.** Role of metabolic surgery in achieving T2DM remission. More than 75% of people with T2DM are overweight, obese, or have an increased waist circumference,

which is considered a trustworthy sign of metabolic and cardiovascular risk. [46] Convincing evidence derived from both non-RCTs, RCTs, and meta-analyses has revealed that obesity-metabolic surgery stands as the most efficacious approach for managing patients with T2DM. [22,47-50] Metabolic surgery has the potential to promote diabetes remission in obese patients with type 2 diabetes. Nevertheless, the precise mechanism behind diabetes remission following metabolic surgery remains poorly understood. Pertinent studies have highlighted that diabetes remission post-surgery is attributed to enhancements in  $\beta$ -cell function and insulin secretion, [51] adjustments in insulin sensitivity, [52] as well as alterations within the gastrointestinal tract and adipose tissue, among various other factors.

4.2.3. Intensive glucose-lowering therapy initiates diabetes remission. A 2008 RCT by Weng et al<sup>[53]</sup> showed that shortterm intensive insulin therapy resulted in remission in 50% of participants in the intervention group, as compared to 10% in the control group. In a study titled "Remission of Type 2 Diabetes Mellitus Following a Short-term Intervention with Insulin Glargine, Metformin, and Dapagliflozin" by McInnes et al, [54] it was found that after 24 weeks, 24.7% of participants in the intervention group and 16.9% in the control group achieved remission. In a subsequent study, McInnes et al<sup>[55]</sup> used lifestyle approaches and treatment with metformin, acarbose, and insulin glargine to optimize combination therapy. Their findings indicated that after 8 weeks, 50.0% of the intervention group and only 3.6% of the control group achieved normoglycemia. At 16 weeks, this percentage increased to 70.4% in the intervention group, while remaining 3.6% in the control group. Sugiyama et al<sup>[56]</sup> examined the efficacy of a combined treatment approach involving sodium-glucose co-transporter 2 (SGLT2) inhibitors and metformin in terms of weight reduction and remission of recently diagnosed T2DM in a real-world clinical context. Another study<sup>[57]</sup> suggested that insulin sensitizers like pioglitazone and metformin have the potential to offer sustained glycemic control in individuals with type 2 diabetes. Further studies should focus on optimizing different combinations of hypoglycemic agents to achieve the remission of type 2 diabetes.

#### 4.3. Strengths of this study

This study used bibliometric methods to conduct a comprehensive and systematic analysis of a large body of relevant literature, ensuring the representativeness and reliability of the research results. Through visualization tools, this study depicted the complex relationship of type 2 diabetes mitigation research in the form of charts and graphs, making the research trends and hot spots more intuitive, understandable, and innovative. By identifying key institutions and researchers within the field, it helps promote scientific collaboration and encourages communication and resource sharing among different research teams. It can provide valuable teaching materials for researchers in medicine, public health, and related disciplines, helping them understand bibliometric methods and their applications in scientific research. It can provide decision-making support for policy makers and medical institutions on the status and trends of T2DM mitigation research, help guide future research directions and resource allocation, and is of great significance for promoting scientific research and social health in the field of type 2 diabetes mitigation.

#### 4.4. Limitations of this research

This study presents an extensive analysis of the worldwide situation, research hotspots, and trends in type 2 diabetes remission research over the past 2 decades. We performed a comprehensive bibliometric analysis of the WoS database. Nevertheless, some limitations should be recognized. First, the scope of this

study was limited to English-language publications, and the study only considered literature in the WoSCC. Therefore, research conducted in other languages and literature not included in the WoSCC may have been overlooked, potentially excluding important studies. Second, the software used for analysis was unable to merge different manifestations of the same author or institution, such as variations in names and abbreviations. Consequently, the study findings may contain some discrepancies.

#### 5. Conclusions

In this study, CiteSpace was used to analyze the research hotspots and frontier issues of type 2 diabetes remission. Although weight loss surgery to reverse diabetes has been fully developed and widely studied, and intensive lifestyle intervention and diet therapy to reverse diabetes have become the latest and most concentrated research focus, there remain some research gaps, such as the evaluation of the long-term effects of weight loss surgery and intensive lifestyle intervention as well as personalized treatment programs for different patient groups. Future research needs to focus on in-depth exploration in these fields. In addition, the drug GLP-1 receptor agonist, which has the effect of weight reduction and glucose reduction, is a prominent keyword and is still in the process of development. Future research directions in this field should involve innovative research design, such as comparing the efficacy of GLP-1 receptor agonists and premixed insulin intensified therapy in inducing clinical remission in overweight or obese T2DM patients, which would provide new insights and breakthroughs in the field of diabetes remission. Interdisciplinary collaboration plays an important role in the study of T2DM remission, and future research can further promote collaboration in multiple fields such as medicine, public health, nutrition, and psychology, to form more comprehensive treatment and remission strategies. Future research should also aim at promoting global cooperation and resource sharing to narrow the gap in research capacity between developed and developing countries, and ensure a more equitable distribution of knowledge and progress in diabetes care.

#### **Author contributions**

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Supervision: Gui-Xia Wang. Writing – original draft: Yang Liu.

Writing - review & editing: Yang Liu, Xiao-Kun Gang, Yuan

Gao, Ying-Xuan Wang, Gui-Xia Wang.

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