ORIGINAL RESEARCH

Genome Variability for the Development of Coronary Heart Disease in Type 2 Diabetes Mellitus: A Bibliometric Analysis

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Introduction: Cardiovascular diseases (CVDs) stand as the foremost global cause of mortality, accounting for 32% of total deaths in 2019, with 85% attributed to heart attacks and strokes. Individuals with Type 2 Diabetes Mellitus (T2DM) exhibit an elevated susceptibility to coronary heart disease (CHD). In numerous studies, it has been established that genetic polymorphism of genes influences the onset, progression, and complications of coronary heart disease (CHD) and type 2 diabetes mellitus (T2DM). The aims of this study are to employ bibliometric analysis methods for mapping the array of research on genome variability concerning the development of coronary heart disease in individuals with type 2 diabetes mellitus.

Methods: We derived the data from the Web of Science (WoS) Core Collection database and Scopus on January 6, 2023. All publications from 1987 to 2023 are exported in plain text format for WoS-CC and BibTeX format for Scopus, containing bibliographic information, keywords, and citation information. RStudio v.4.1.2 software (RStudio, PBC, Boston, MA, USA) was used for conducting bibliometric analysis.

Results: Our analysis of 241 articles published between 1987 and 2023 revealed a consistent increase in research output, especially after 2004, highlighting a growing academic focus on genome variability's role in coronary heart disease (CHD) development among Type 2 Diabetes Mellitus (T2DM) patients. Key contributing journals include The Lancet and Nature Genetics, indicating high-impact interest in this domain. The United States leads in research productivity and collaboration, with China also emerging as a notable contributor in recent years. Prominent authors such as S. Humphries have significantly shaped the field, contributing to a cumulative knowledge base that underscores the role of genetic factors in CHD among T2DM patients.

Discussion: Our findings underscore the value of bibliometric studies in guiding future research directions. This increasing scholarly attention to genome variability in CHD and T2DM may encourage deeper investigation into specific genetic polymorphisms and their mechanistic roles in disease progression. Additionally, these insights can help prioritize collaboration across leading research hubs and potentially drive innovation in therapeutic interventions targeting genetic risk factors in CHD and T2DM. Future research could build on these trends by focusing on comparative studies across populations, advancing precision medicine approaches for at-risk individuals with T2DM.

Keywords: Genome Variability, Coronary Heart Disease, Type 2 Diabetes Mellitus, Bibliometric Analysis, Research Hotspots

Introduction

The International Diabetes Federation anticipates a rise in the prevalence of diabetes mellitus, projecting an increase to 643 million individuals by 2030 and a further escalation to 783 million by 2045. In the year 2021 alone, diabetes was

responsible for 6.7 million fatalities.[1] According to the World Health Organization's report, cardiovascular diseases (CVDs) stand as the primary cause of global mortality. Approximately 17.9 million individuals succumbed to cardiovascular diseases in 2019, representing 32% of the total worldwide mortalities. Within this statistical framework, 85% of the fatalities were attributed to incidents of heart attacks and strokes.[2]

Individuals with Type 2 Diabetes Mellitus (T2DM) face an elevated susceptibility to the development of coronary heart disease (CHD). In a meta-analysis conducted by Alshammary et al, the association between Metabolic Syndrome (MS) and its components with the risk of CHD among the adult population was examined.[3] The results revealed a substantial correlation between MS and a risk of CHD. Furthermore, each individual component of MS exhibited a significant association with an increased risk of CHD.[3]

Despite substantial research efforts, the relationship between T2DM and CHD remains complex, with various genetic, metabolic, and environmental factors contributing to disease progression. While numerous investigations have consistently demonstrated that genetic polymorphisms of genes exert a significant influence on the initiation, progression, and complications associated with both CHD and T2DM,[4,5] the exact mechanisms linking these conditions are not fully understood, and a clear causative relationship between specific genetic markers and disease outcomes has yet to be firmly established. In a study conducted by Zheng, J.et al, it was observed that cardiovascular diseases (CVDs) and T2DM share a common genetic basis, underpinned by shared risk factors. This observation was derived from an analysis of 120 features available in the LD-Hub center.[6] Importantly, there exists a positive genetic correlation between CHD and T2DM, signifying the presence of a shared genetic background. Furthermore, genetic variability linked to factors such as increased obesity, fasting insulin levels, glycated hemoglobin, triglycerides, and smoking demonstrates a positive correlation with the occurrence of T2DM, CHD, and ischemic stroke.[7,8]

However, despite these associations, identifying genetic markers with clear predictive or diagnostic utility for both CHD and T2DM has proven challenging. Research has also identified a modulating effect of polymorphisms in certain genetic markers on metabolism and hemodynamics in the context of cardiovascular diseases and T2DM. The findings of numerous studies indicate a higher incidence of CVDs and T2DM, as well as a more severe course of these diseases in the presence of unfavorable genetic polymorphisms.[9–12] Understanding the genetic basis of CHD in the context of T2DM is crucial for advancing personalized medicine approaches and developing targeted interventions.

To address these gaps in the literature, bibliometric analysis methods have proven effective in mapping research trends and identifying influential studies, key authors, and institutions contributing to specific fields of study. The current study applies these methods to examine research trends in genome variability concerning the development of CHD in individuals with T2DM, which, to the best of our knowledge, has not been systematically reviewed before. Previous bibliometric analyses have focused on the Genome-Wide Association Study for Diabetes,[13] or DNA methylation in CVDs,[14] but they did not explore the direct relationship between genetic variability and the combined development of T2DM and CHD.

Therefore, the aims of this study were: a) to employ bibliometric analysis methods for mapping the array of research on genome variability concerning the development of coronary heart disease in individuals with type 2 diabetes mellitus; and b) to examine the characteristics and development of research related to genome variability concerning the development of coronary heart disease in individuals with type 2 diabetes mellitus, including identifying influential publications and productive institutions, as well as analyzing highly effective keywords and topic trends.

Materials and Methods
Data Collection
We derived the data from the Web of Sciences (WOS) Core Collection database and Scopus on January 6, 2023, using the key words. All publications from 1987 to 2023, are exported in plain text format for WOS-CC and BiBTeX format for Scopus, which contains bibliographic information, keywords information and citation information, etc. The research articles were included in this bibliometric analysis and the language was restricted to English. Both datasets were merged using code in RStudio, and the combined data was exported in xlsx format. The manual removal of unrelated articles were performed (Supplementary excel file). The detailed search process illustrated in Figure 1. The search formula was listed in Table 1.
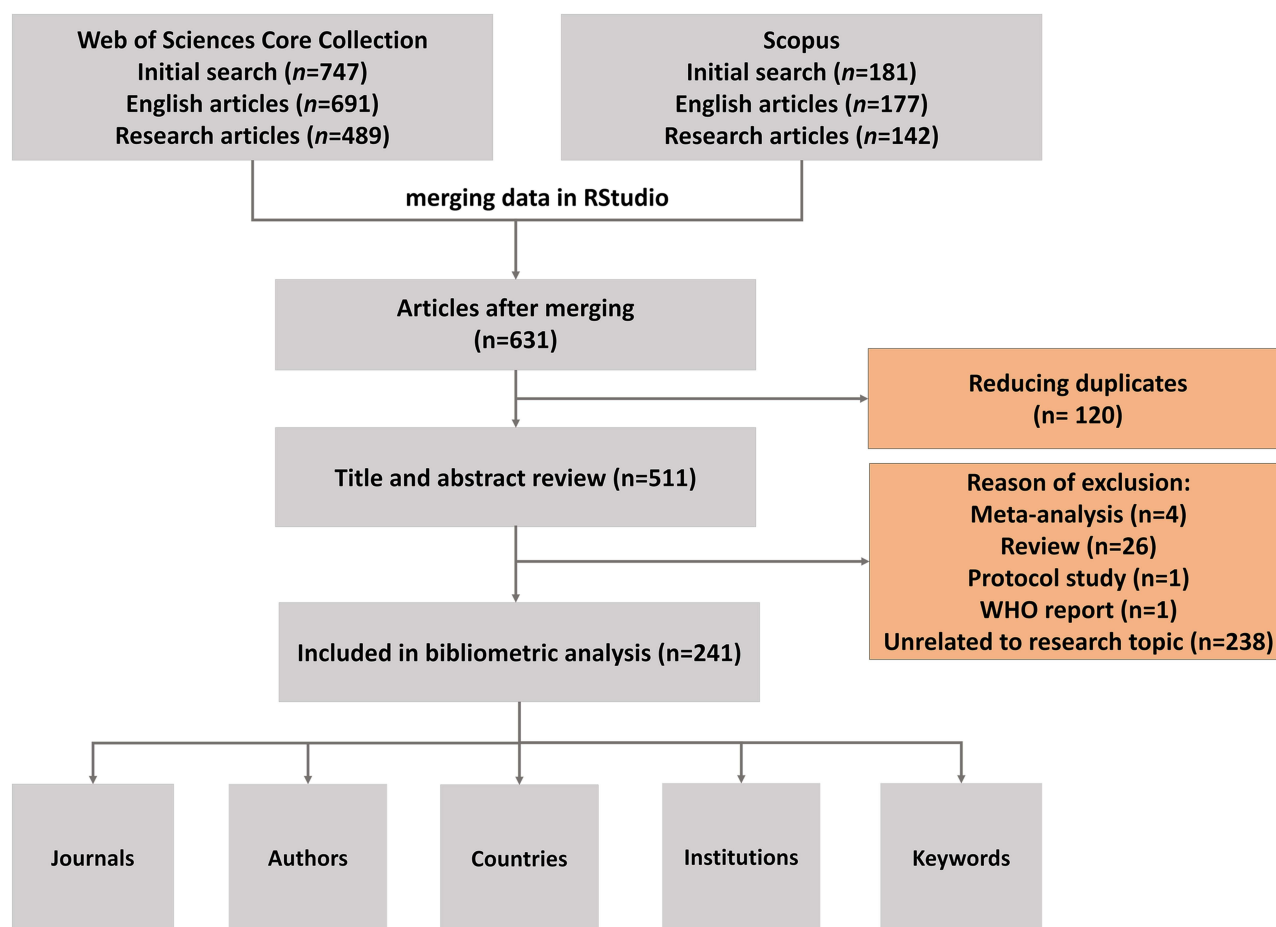
Figure 1 Flowchart for bibliometric analysis of genome variability for the development of coronary heart disease in type 2 diabetes mellitus.

Visualization and Statistical Tools

Bibliometric and scientometric research was conducted by Bibliometrix R-package (http://www.bibliometrix.org) provides tools. It runs on RStudio v.4.1.2 software (RStudio, PBC, Boston, MA, USA). It can produce a descriptive analysis of a bibliographic data frame, as well as build a network for analyzing bibliographic coupling, co-citation, collaboration,

Table 1 Search Queries for Bibliometric Analysis of Genome Variability for the Development of Coronary Heart Disease in Type 2 Diabetes Mellitus

Number	Queries
#1	"Genes" or "Genomics" or "Genome" or "Genetic Code" or "Genetic variations" or "Genetic Predisposition to Disease"
#2	"Coronary Diseases" or "Disease Coronary" or "Diseases Coronary" or "Coronary Heart Disease" or "Coronary Heart Diseases" or "Disease, Coronary Heart" or "Diseases, Coronary Heart" or "Heart Disease, Coronary" or "Heart Diseases, Coronary"
#3	"Diabetes Mellitus, Type 2 " or "Diabetes Mellitus, Noninsulin-Dependent" or "Ketosis-Resistant Diabetes Mellitus" or "Diabetes Mellitus, Non-Insulin Dependent" or "Diabetes Mellitus, Non-Insulin-Dependent" or "Non-Insulin-Dependent Diabetes Mellitus" or "Diabetes Mellitus, Stable" or "Stable Diabetes Mellitus" or "Diabetes Mellitus, Type II" or "NIDDM" or "Diabetes Mellitus, Noninsulin Dependent" 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 "Type 2 Diabetes Mellitus" or "Noninsulin-Dependent Diabetes Mellitus" or "Noninsulin Dependent 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, Adult Onset"
#4	#1AND #2AND #3

and co-occurrence. We used it to extract the Corresponding author's countries, Most relevant affiliations, Most relevant sources, Most local cited sources as tables. RStudio was also used to conduct the figure of Core sources by Bradford's law, Authors' production over time, Treemap, Author's production over time. Flourish (Kiln Enterprises Ltd, UK) was used to draw the bar charts, chord diagram of Country collaboration and of streamgraph (area chart) of Country production over time.

Results

## Characteristic of Publication

This study aimed to investigate characteristics of publications in genome variability concerning the development of coronary heart disease in individuals with type 2 diabetes mellitus. We analyzed 241 publications from 146 different sources spanning 1987 to 2023, involving the collaboration of 2421 authors. These authors collectively achieved an impressive average citation rate of 40.3 per document.

Annual Analysis of Publication

Figure 2 gives the number the number of publications in the journals. Publication-year distribution shows an increasing trend. The annual publication was less than seven in the first seventeen years from 1987. Since 2004, the number of publications has been increasing steadily, and the annual publications are greater than 16 from 2021 to 2023. The number of publications increased significantly in 2021, which shows that more and more researchers have paid attention to the genome variability concerning the development of coronary heart disease in individuals with type 2 diabetes mellitus.

Journals

Bradford's Law describes the distribution of scientific articles across various journals. In Figure 3, we have identified 12 core journals that researchers commonly consider as their primary outlets. Table 2 shows the information of top 10 most relevant journals and most cited journals including number of articles, impact factor of the journal (IF) and JCR category (quartile). The Journal of Diabetes contributed the highest number of publications (n=13). Among the top ten relevant journals, the Journal of Nature Genetics ranked first in terms of citations (n = 495) and has an impressive impact factor (IF = 30.8). In the list of most cited sources, The Lancet had the highest impact factor (IF = 168.9), followed by the New England Journal of Medicine (IF = 158.5) and the Journal of the American Medical Association (IF = 120.7). Notably, three journals—Diabetes, Diabetes Care, and Diabetologia—appear in both the most relevant and most cited lists.
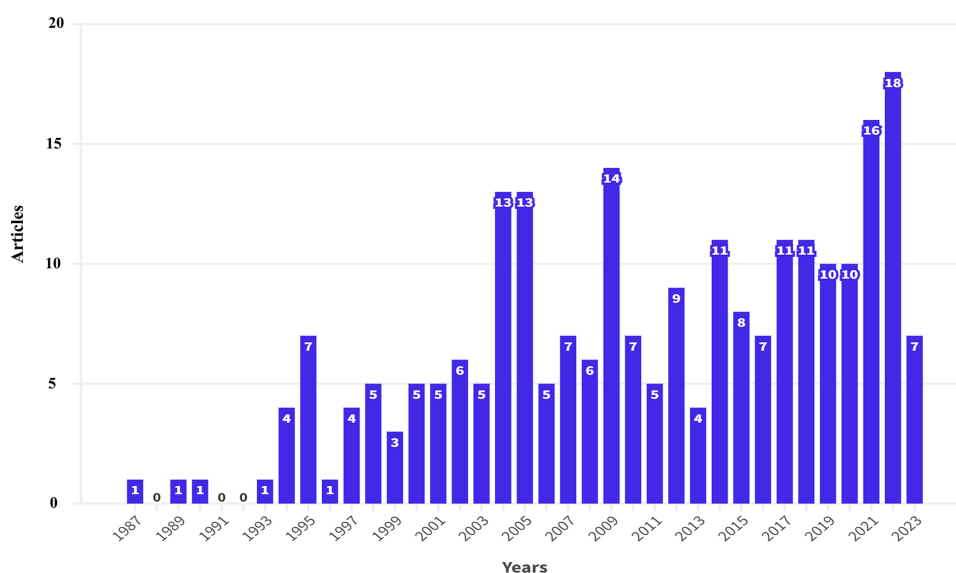
Figure 2 Number of published papers from 2005 to 2023 for bibliometric analysis of genome variability for the development of coronary heart disease in type 2 diabetes mellitus.

Core Sources by Bradford's Law
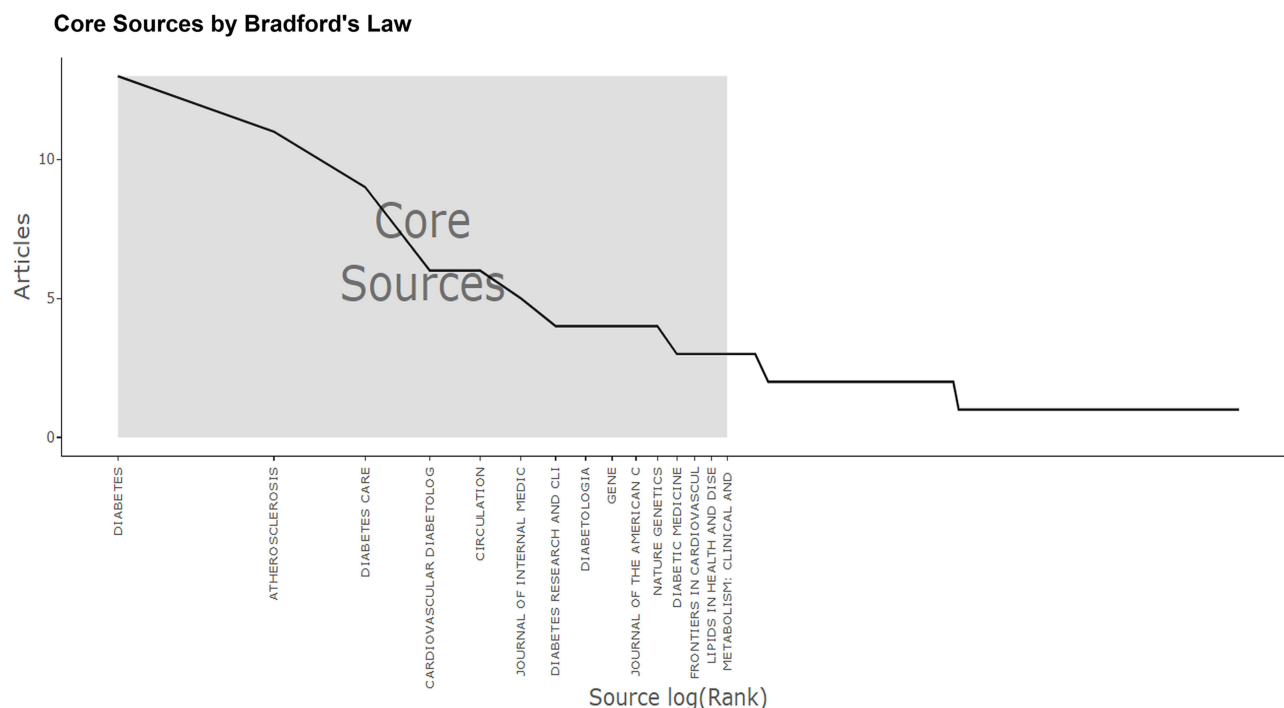
Figure 3 Core journals by Bradford's Law (2005–2023) for bibliometric analysis of genome variability for the development of coronary heart disease in type 2 diabetes mellitus.

Contributions of Authors

The author with the highest scientific production regarding competitiveness in the international context was Humphries S., with twelve documents. Affiliated with University College London, he has a prolific record of more than 200 publications, reaching an h-Index of 126. Over the preceding year, in 2023, his research has focused on the following topics: hypercholesterolemia, atherosclerosis, and type 2 diabetes mellitus. Figure 4A shows the 10 most productive

Table 2 Most Relevant Journals and Most Cited Journals in the Field of Oral Health Related Quality of Life and Children with Caries (2005–2023)

Sources	Articles	IF	Journal Citation Reports (JCR) category [quartile]*
Most relevant sources			
Diabetes	13	7.7	Endocrinology & Metabolism- Science Citation Index-Expanded (SCIE) [Q1]
Atherosclerosis	11	5.3	Cardiac & Cardiovascular systems- SCIE [Q2]
			Peripheral vascular disease- SCIE [Q2]
Diabetes Care	9	7.7	Endocrinology & Metabolism- SCIE [Q1]
Cardiovascular Diabetology	6	9.3	Cardiac & Cardiovascular systems- SCIE [Q1]
			Endocrinology & Metabolism- SCIE [Q1]
Circulation	6	37.8	Cardiac & Cardiovascular systems- SCIE [Q1]
			Peripheral vascular disease-SCIE [Q1]
Journal of Internal Medicine	5	11.1	Medicine, general and Internal-SCIE [Q1]
Diabetes Research and Clinical Practice	4	5.1	Endocrinology & Metabolism-SCIE [Q2]
Diabetologia	4	8.2	Endocrinology & Metabolism-SCIE [Q1]
Gene	4	3.5	Genetics & Heredity-SCIE [Q1]
			Biochemistry & Molecular Biology-SCIE [NA]
Journal of The American College of Cardiology	4	24.4	Cardiac & Cardiovascular systems-SCIE [Q1]

(Continued)

Table 2 (Continued).

Sources	Articles	IF	Journal Citation Reports (JCR) category [quartile]*
Most cited sources			
Nature Genetics	495	30.8	Genetics & Heredity- SCIE [Q1]
American Journal of Human Genetics	238	9.8	Genetics & Heredity- SCIE [Q1]
Nature	224	64.8	Multidisciplinary sciences- SCIE [Q1]
Diabetes	213	7.7	Endocrinology & Metabolism- SCIE [Q1]
New England Journal of Medicine	190	158.5	Medicine, General & Internal- SCIE [Q1]
Circulation	169	37.8	Cardiac & Cardiovascular systems- SCIE [Q1]
			Peripheral vascular disease- SCIE [Q1]
Lancet	150	168.9	Medicine, General & Internal- SCIE [Q1]
Diabetes care	148	16.2	Endocrinology & Metabolism-SCIE [Q1]
Diabetologia	131	8.2	Endocrinology & Metabolism-SCIE [Q1]
Journal of the American Medical Association	109	120.7	Medicine, General & Internal- SCIE [Q1]

Note: * Journals indexed in Arts and Humanities Citation Index (AHCI) and Emerging Sources Citation Index (ESCI) are receiving a journal impact factor (JIF) for the first time in June 2023, they will not receive ranks, quartiles, or percentiles until the release of 2023 data in June 2024.

authors in competitiveness research from 1987 to 2023. The most locally cited author is Dorria A. with nine citations, followed by Rotter G. with eight citations (Figure 4B). It is necessary to note that Dorria A., Kathiresan S., and Oi L. were presented in both lists as the most relevant and most locally cited authors. This suggests that they are recognized and cited not only broadly but also within a specific local context, reinforcing their significance in the field. Figure 4C presents the top 10 authors' production over time. Kesaneiemi Y. and Ukkola O. were the first authors to publish articles in this field in 1993, followed by Froguel P. in 1994 and Humphries S. in 1995. This indicates the far-reaching impact of
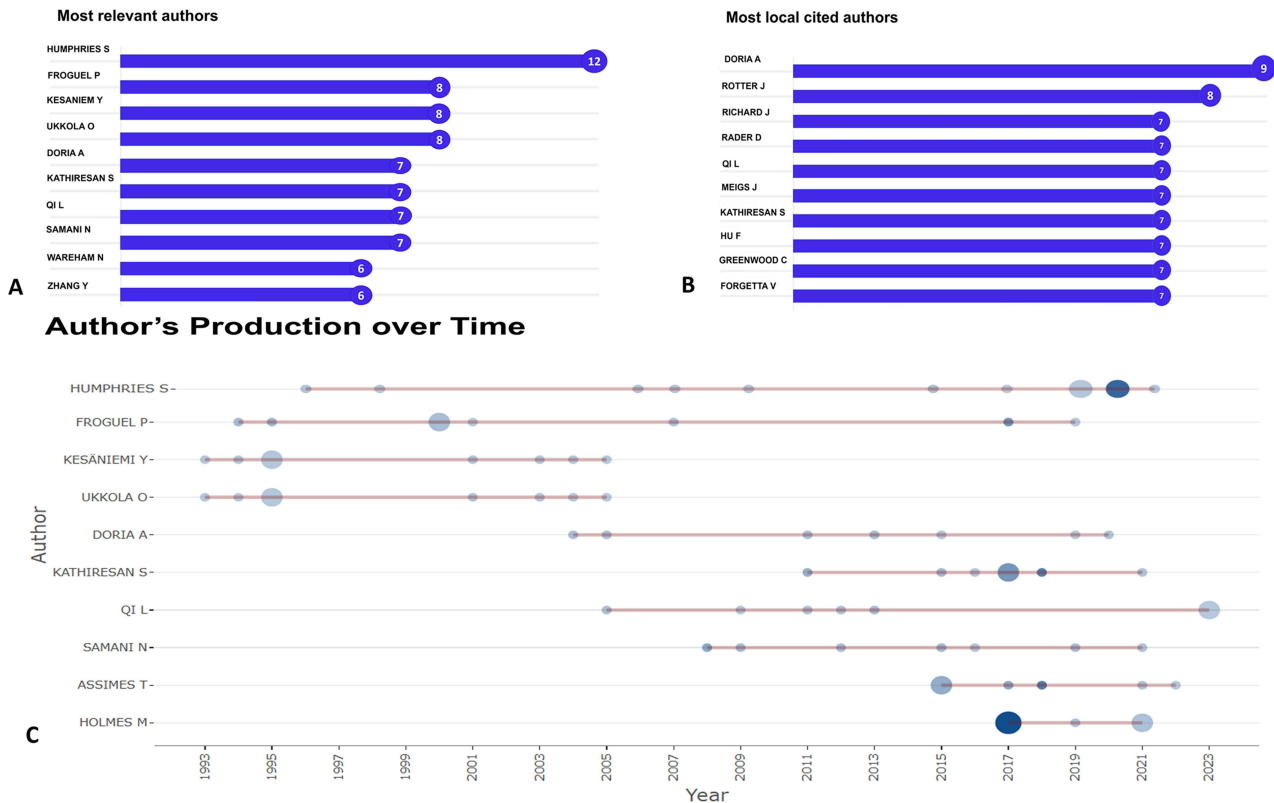

Figure 4 Most relevant authors (**A**). Most locally cited authors (**B**). Authors' production over time (**C**).

their work. Other authors published their first article between 2004 and 2015. Humphries S. maintained publishing activity until 2018. Furthermore, Humphries S. published two articles in 2017, accumulating a total of 67 citations per year.

The Most Productive Country and Institutions

Figure 5A shows the top 5 productive countries in publications on genome variability concerning the development of coronary heart disease in individuals with type 2 diabetes mellitus. The USA published the most articles, with 2138 (47.9%), followed by the United Kingdom with 974 (21.39%), Finland with 439 (9.6%), China with 693 (15.2%), and Canada with 308 (6.7%) between 1990 and 2023. As demonstrated in Figure 5B, extensive collaboration was observed among productive countries. For instance, the USA collaborated closely with the United Kingdom, Canada, and the Netherlands. Table 3 shows the most relevant countries by corresponding authors, single-country publications (SCPs), multiple-country publications (MCPs), and MCP ratio (MCP/articles). China has surpassed the USA in the number of publications by corresponding authors. Canada and the United Kingdom are the countries with the highest MCP ratio, 0.857 and 0.263, respectively, while Germany, Finland, Japan, and France are the countries with the lowest ratio (0.000) in the top 10 list.

The top 10 most prolific institutions are illustrated in Table 4. These institutions were mostly represented by the USA and European countries, including seven from the USA, two from the United Kingdom, and one from Finland. Among them, Harvard University had the largest number of publications, with 50, followed by the University of Oxford with 24, Harvard Medical School, the University of Cambridge, and the University of Washington, each with 22.

Key Words

Figure 6A presents the ten most frequently occurring author's keywords from available 431. The analysis includes common terms such as "coronary heart disease", "type 2 diabetes", "type 2 diabetes mellitus", "polymorphism", "genetics", "diabetes", "coronary artery disease", "diabetes mellitus", "atherosclerosis", and "myocardial infarction." "Coronary heart disease" had the highest frequency at 52 time in 2023 year. It has been consistently used as a keyword since 1994 and remains a frequently used term among authors. The second most frequently used keyword is "type 2 diabetes", and the third is "genetics" (Figure 6B).
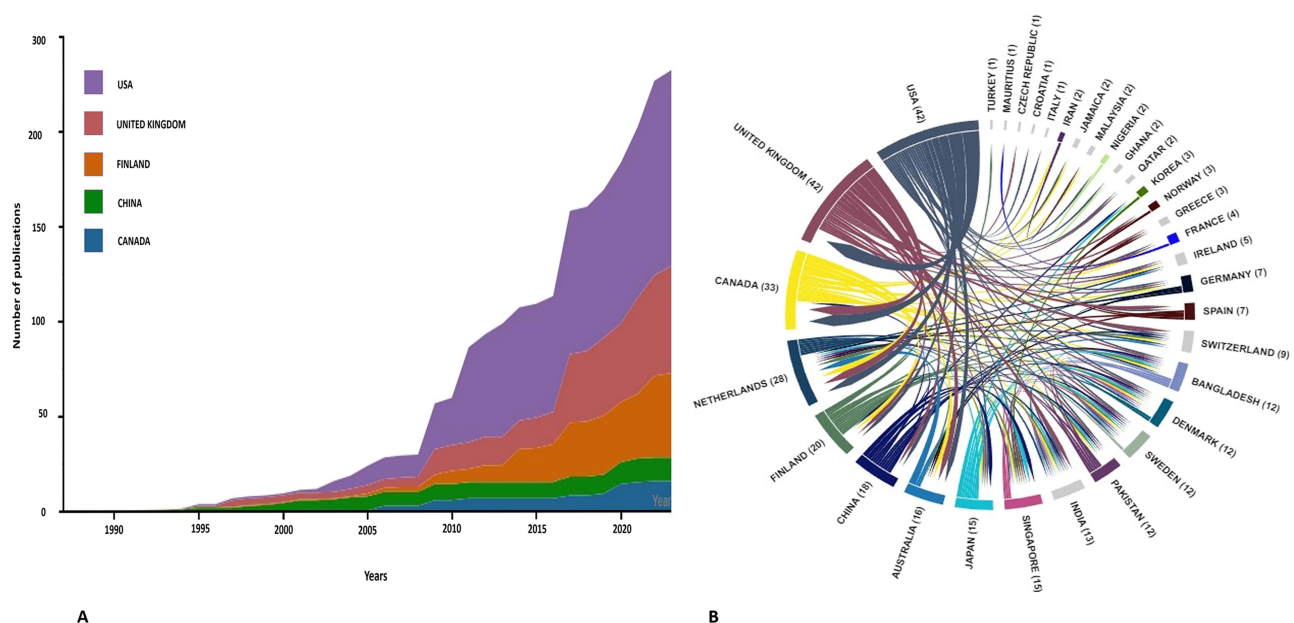
Figure 5 The annual number of publications in the top five prolific countries from 1987–2023. The area occupied per country is proportional to the number of documents (**A**). International collaboration of countries in this domain. Line thickness reflects the closeness between countries, and a thicker line represents a stronger collaboration (**B**).

Table 3 Top 10 Most Relevant Countries by Corresponding Authors

Country	Articles	SCP[a]	MCP[b]	Frequency	MCP_Ratio[c]
China	38	36	2	0.158	0.053
USA	37	33	4	0.154	0.108
United Kingdom	19	14	5	0.079	0.263
Germany	10	10	0	0.041	0
Finland	8	8	0	0.033	0
Canada	7	1	6	0.029	0.857
Japan	7	7	0	0.029	0
Turkey	7	6	1	0.029	0.143
France	6	6	0	0.025	0
Spain	6	5	1	0.025	0.167

Notes: [a]Single-country publication, indicating that the authors of the publication from the same country. [b]Multiple-country publications, indicating that the authors of the publication are from multiple countries, which means the cooperation between countries. [c]MCP/articles, indicating the ratio of co-authored articles in the country's published articles.

Table 4 The Top 10 Institutions That Contributed to the Publications

Rank	Affiliation	Country	Articles
1	Harvard University	USA	50
2	University of Oxford	USA	24
3	Harvard medical school	USA	22
4	University of Cambridge	USA	22
5	University of Washington	USA	22
6	University of London	United Kingdom	21
7	University of Pennsylvania	USA	20
8	Massachusetts general hospital	USA	16
9	University of Bristol	United Kingdom	16
10	University of Oulu	Finland	16

Discussion

Our paper conducted a bibliometric analysis of genome variability for the development of coronary heart disease in type 2 diabetes mellitus, spanning from 1987 to 2023. The full record and cited references of 241 articles were included in our study from the WOS-CC and Scopus databases. The significance of such analyses lies in their ability to provide a panoramic view of the scientific output, collaborations, and trends in a particular research domain. The steady increase in annual publications indicates the growing interest and recognition of the impact of dental caries on genome variability for the development of coronary heart disease in type 2 diabetes mellitus.

Bradford's Law is employed to characterize the distribution of scientific articles across different journals. The Journal of Diabetes stands out by contributing the highest number of publications (n=13) among the top ten relevant journals. However, in terms of citations, the Journal of Nature Genetics takes the lead with an impressive count of 495 citations, coupled with a noteworthy impact factor of 30.8. Delving into the list of the most cited sources, The Lancet emerges as the journal with the highest impact factor (IF = 168.9), followed closely by the New England Journal of Medicine (IF = 158.5) and the Journal of the American Medical Association (IF = 120.7). These journals reflect a remarkable influence within the field. A noteworthy observation is the overlap between the most relevant and most cited lists, where three journals—Diabetes, Diabetes Care, and Diabetologia—demonstrate dual prominence. This suggests not only the significance of these journals as primary outlets for researchers but also their substantial impact on the scholarly landscape, being among the most cited sources in the field. This intersection underscores the pivotal role these journals play in disseminating and shaping diabetes-related research.

Tree Map

Words' Frequency over Time
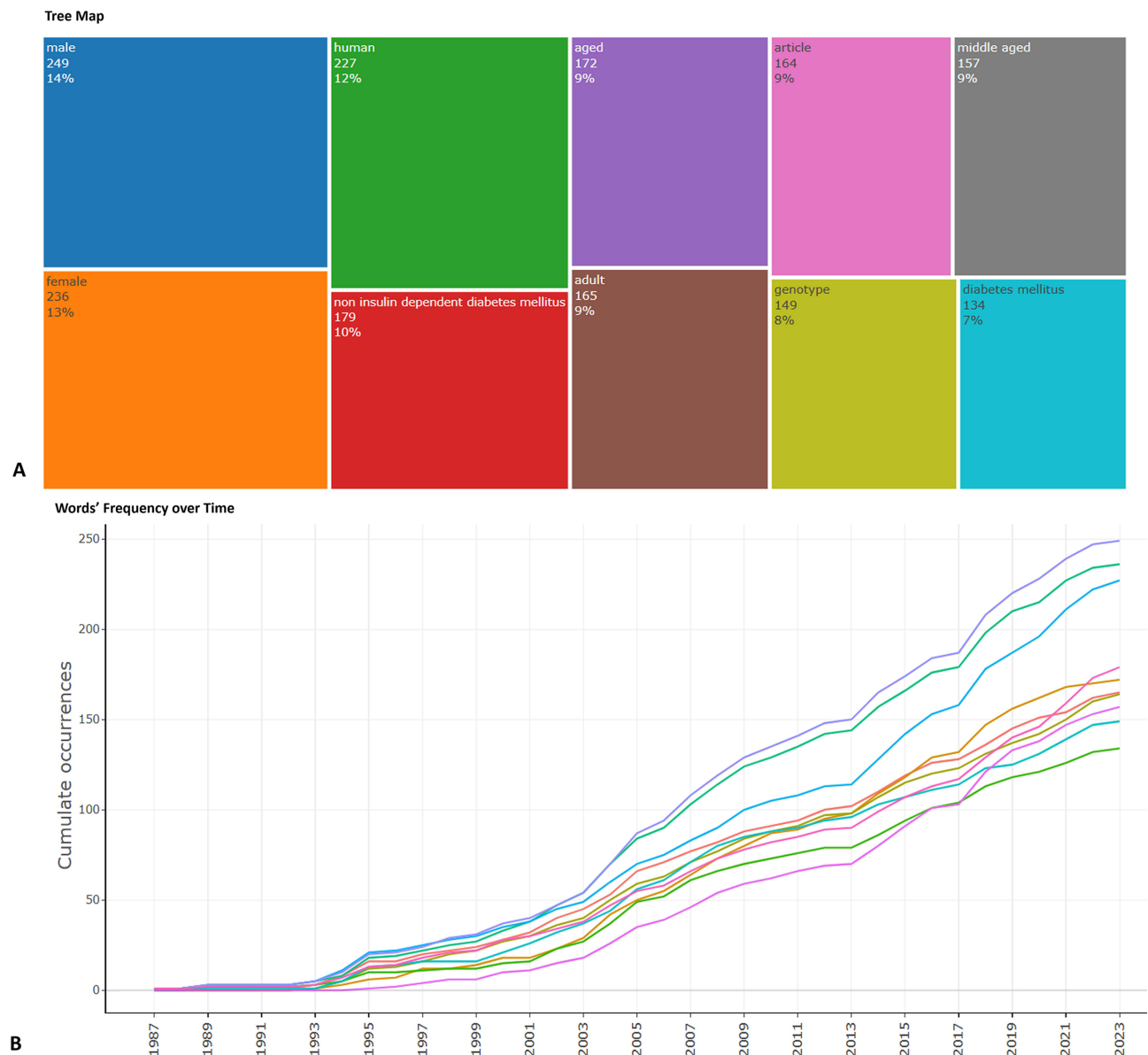
Figure 6 TreeMap (**A**) and scatter plot (**B**) illustrating the top ten author keywords between 1989 and 2023.

In the realm of competitiveness research in the international context, Humphries S. stands out as the author with the highest scientific production, contributing twelve documents to the field. Affiliated with University College London, Humphries S. boasts a prolific record comprising more than 200 publications and attaining an impressive h-Index of 126. Notably, his research focus in the year 2023 encompassed hypercholesterolemia, atherosclerosis, and type 2 diabetes mellitus. Additionally, he was among the most productive authors in competitiveness research from 1987 to 2023. It becomes evident that Humphries S. is a key figure in the landscape. Furthermore, the most locally cited author is identified as Dorria A., accumulating nine citations, closely followed by Rotter G. with eight citations. An intriguing observation is the recurrence of Dorria A., Kathiresan S., and Oi L. in both the lists of the most relevant and most locally cited authors. This dual recognition implies that these authors are not only broadly acknowledged but also hold significant influence within a specific local context, underscoring their importance in the field. Comprehensive analysis of authors in competitiveness research highlights the significant contributions of Humphries S. and other key figures, emphasizing the enduring impact of their work and the recognition they have garnered both globally and locally.

The USA was the most published country (n=2138), with about two times as many publications as United Kingdom (n = 974) and about five times more than Finland (n = 439). While by the most relevant countries by corresponding authors is China with 38 articles, following by USA, United Kingdom and Germany. Moreover, seven of the top 10 active institutions were from the USA, the following two institutions were from the United Kingdom and one from Finland. As we can observe, the distribution of institutions was extremely unbalanced, and the USA dominated in this field. Among the countries and institutions the mostly countries are high-income developing economies, while Turkey is middle-income developing economies.[15] Developed countries typically have more significant financial resources and well-established infrastructures for scientific research. This allows them to allocate more funds to genetic research, ensuring better access to modern technologies and equipment.[16]

The keyword analysis provides a snapshot of prevalent themes, with "coronary heart disease", "type 2 diabetes", "type 2 diabetes mellitus", "polymorphism", "genetics", "diabetes", "coronary artery disease", "diabetes mellitus", "atherosclerosis", and "myocardial infarction." The first three keywords reflect the direction of the topic and capture the attention of researchers. Their increasing usage indicates a growing interest among researchers in this field. Despite numerous studies confirming the connection between genetics and the development of heart diseases in diabetes, there are studies asserting the absence of such correlation. An assessment of genetic overlap between Coronary Artery Disease (CAD) and type 2 diabetes (T2D) was conducted on 66,643 subjects to evaluate the differentiated genetic influence on the risk of ischemic heart disease in individuals with T2D. The results of this study indicated that none of the previously characterized CAD loci had a specific impact on CAD in individuals with T2D. Additionally, a genome-wide interaction analysis revealed no new variants for CAD that could be considered specific to T2D.[17]

While our bibliometric analysis provides valuable insights into the landscape of genome variability for the development of coronary heart disease in type 2 diabetes mellitus, spanning from 1987 to 2023. Our study is confined to publications in the English language, potentially introducing a language bias. Relevant contributions in other languages may exist, especially considering that dental research is conducted globally. This limitation might result in an incomplete representation of the entire body of literature on the subject. Our search was based on the Web of Science Core Collection (WOS-CC) and Scopus databases, which, while comprehensive, might not include all relevant sources. Some regional or specialized databases may not be covered, leading to potential omissions in our analysis.

Conclusions

Overall, our study provides a bibliometric analysis of genome variability for the development of coronary heart disease in type 2 diabetes mellitus from 1987 to 2023. The findings underscore the importance of ongoing research in understanding the role of genome variability for the development of coronary heart disease in type 2 diabetes mellitus. Our study can provide an overview and research hotspots in this field for future studies.

Data Sharing Statement

Data are contained within the article. Datasets related to this project can be obtained from corresponding author based on a reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Nazira B Bekenova and Tamara A Vochshenkova are co-first authors for this study. Amin Tamadon was employed by PerciaVista R&D Co. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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