Journal of Multidisciplinary Healthcare Dovepress

Open Access Full Text Article ORIGINAL RESEARCH

Worldwide Research Trends and Regional Differences in the Development of Precision Medicine Under Data-Driven Approach: A Bibliometric Analysis

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Background: Precision medicine is an innovative approach that integrates genomics, clinical informatics, and proteomics to address both genetic and environmental factors in disease prevention and treatment. This bibliometric study analyzes research trends, collaboration patterns, and the unique characteristics of precision medicine across countries to inform future research directions.

Methods: A comprehensive search was conducted in the Web of Science Core Collection (1999–2022) database to identify publications related to precision medicine. The analysis of publication patterns, collaborations, institutions, authors, and research hotspots was performed utilizing Microsoft PowerPoint 2019 in conjunction with the Bibliometrix package in R.

Results: A total of 30,777 publications on precision medicine were identified. The United States and the United Kingdom were recognized as the primary contributors, while European countries exhibited substantial collaborative efforts. Harvard University and the University of California System have played pivotal roles in advancing the field. The keywords analysis showed that in the early 2000s, "gene expression" and "personalized outcomes" were key themes. Since 2015, there's been a significant shift towards advanced technologies like artificial intelligence, machine learning, liquid biopsy, highlighting their growing importance in precision medicine. Research topics across various countries exhibit certain global similarities. However, different nations exhibit distinct thematic research focuses. China emphasizes "Informatics", "Hepatocellular Carcinoma", "Photothermal Therapy", and "Lung Adenocarcinoma", while the United States prioritizes "Informatics", "Treatment Rules", and "Consortium Guidelines". Germany and France share similar interests in particular research domains.

Conclusion: Precision medicine is rapidly globalizing, with significant contributions from multiple countries and emerging technologies acting as catalysts for further development. Greater international cooperation is essential to elevate the quality and impact of research. These advancements hold great potential for transforming personalized healthcare by integrating cutting-edge scientific disciplines.

Keywords: precision medicine, bibliometric analysis, international collaboration, research topic

Introduction

Precision medicine is a medical research and practice model that focuses on the complexity of disease etiologies. It considers individual differences caused by biological characteristics, environmental factors, lifestyle habits, and other relevant parameters to develop effective health intervention plans and strategies.[1] The origin of precision medicine can be traced back to the 1990s, arising from the Human Genome Project led by the National Institutes of Health in the United States.[2] In 2011, the National Academy of Sciences published Towards Precision Medicine: Building a Knowledge

Received: 16 August 2024
Accepted: 21 October 2024
Published: 15 November 2024

Network for Biomedical Research and a New Taxonomy of Disease, which proposed that the achievements in genomics should promote the integration of bioinformatics and clinical informatics, and ushered in the era of precision medicine.[3] In 2015, the National Institutes of Health officially introduced the concept of precision medicine and announced the creation of the Precision Medicine Initiative.[4] The core of precision medicine lies in the deep mining of omics data, such as genomics, transcriptomics, and proteomics, and the integration of cutting-edge technologies, such as modern genetics, molecular imaging, and bioinformatics, in conjunction with patients' personalized lifestyle and environmental background factors to accurately identify the root causes and therapeutic targets of diseases and to thoroughly analyze the various states and evolution processes of diseases.[5]

In recent years, with the advances in technologies such as bioinformatics, medical imaging, regenerative medicine, and artificial intelligence, the concept of precision medicine has had a tremendous impact on medicine, especially in the field of oncology, becoming a new medical model and propelling the development of evidence-based medicine to new heights.[6] Therefore, it is crucial to explore the development trends, accurately understand the global levels of development, and grasp the thematic directions in precision medicine. The present study focused on specific topics associated with precision medicine between 1999 and 2022 using a bibliometric analysis method to fully understand the global trends in precision medicine research. It explores relevant factors, predicts future development trends, compares the development directions in different countries and regions, and conducts a systematic comparative study on the regional trends and differences in precision medicine development. The main goal was to gain insights into development directions, understand the developmental context, and discover the characteristics and advantages of precision medicine in different countries to provide a basis for subsequent research.

Materials and Methods

Data Collection

The bibliographic information for the analysis was exclusively obtained from The Web of Science Core Collection (WoSCC) provided by Clarivate Analytics (https://clarivate.com/), which includes the Science Citation Index Expanded, the Social Science Citation Index, and the Emerging Source Citation Index. The WoSCC is one of the most expansive and all-encompassing electronic repositories of scientific literature worldwide. The documents retrieved from this database can enhance the reliability and authoritative character of the conclusions drawn. In comparison to other research databases such as Scopus and PubMed, WoSCC offers several distinctive advantages. Firstly, it exhibits robust coverage in both the natural and social sciences, particularly excelling in certain high-impact journals within specific fields. Secondly, WoSCC is characterized by its rapid data updates, ensuring the availability of the latest research findings and maintaining the timeliness of analyses. Furthermore, the citation analysis tools provided by WoSCC allow researchers to gain deeper insights into the relationships and influence among the literature.

A structured retrieval strategy was employed in the study (Supplementary Box 1). All electronic searches were performed on 08 October 2023. Using a formatted search query, a total of 41,410 documents were collected. Data were selected from 01 January 1999 to 31 December 2022, resulting in the collection of 37,630 documents. The article type was limited to articles and reviews, and the language was restricted to English. Specifically, editorials (n=3322), meeting abstracts (n=2276), proceedings (n=346), others (n=312), and non-English studies (n=597) were excluded (Supplementary Figure 1). Finally, 30,777 articles (19,055 articles and 11,722 reviews) met the inclusion criteria and were included in this review of precision medicine (Figure 1). The search results were documented in the "Full Record and Cited References" format and presented in "Plain Text".

Data Analysis and Visualization

Preliminary Data Analysis and Processing

This study used Microsoft PowerPoint 2019 and the Bibliometrix package (version 4.1.4) in R software to analyze document types, years, authors, countries, institutions, and keywords to create social network maps. Initially, all complete articles that met the inclusion criteria and citations were imported into the Bibliometrix package and converted to Bibliometrix R data for subsequent analysis. Finally, R was used to perform a descriptive bibliometric analysis and create

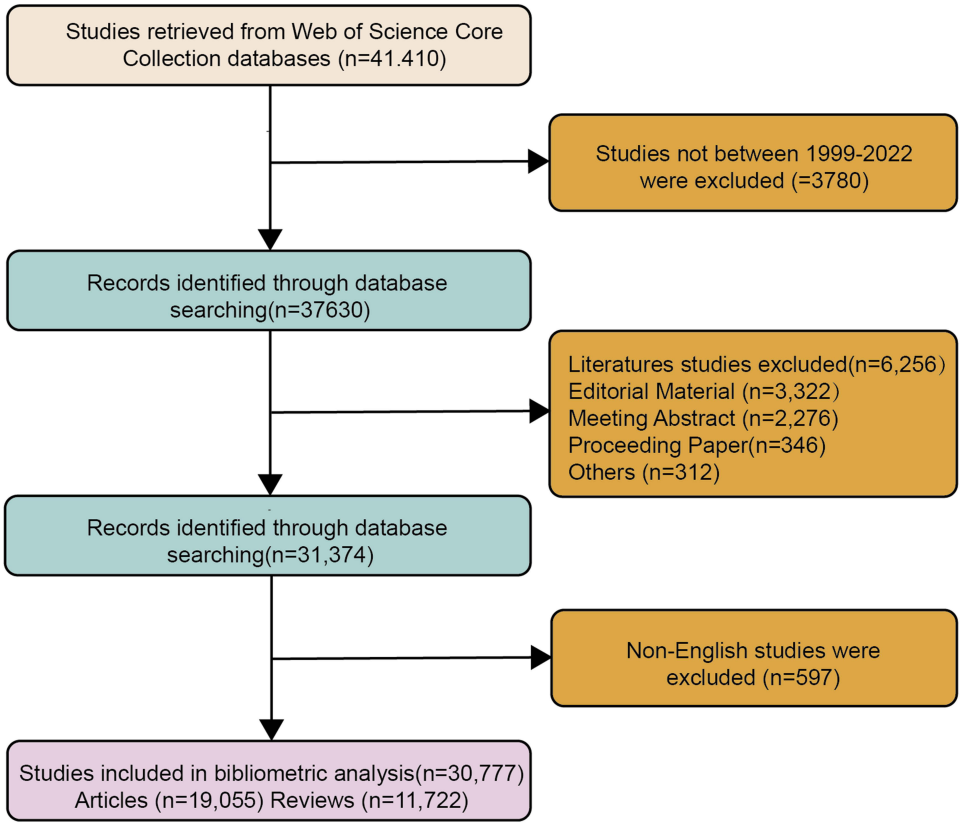

Figure 1 The flowchart of literature selection.

a matrix comprising all documents. In Bibliometrix, the extraction methods were authors from the AU(Author) field, institutions from the AU_UN(Author Institutions) field and countries from the AU_CO(Author Countries) field, year of publication from the PY(Year Published) field, citations from the TC(Times Cited Count) field, abstract from the AB(Abstract) field, keywords from the DE(Author Keywords) field, and research areas from the SC(Research Areas) field. The data were grouped and summarized using the "dplyr" package to calculate annual publications, citation counts, participating countries, and research areas.

Analysis of National Influences in Precision Medicine Using Specific Indicators

Academic impact is essential for evaluating research achievements, scholars, and organizations.[7] The H-index comprehensively considers authors' research output and impact, and functions as an indicator to showcase the ultimate achievements of researchers in scientific research.[8] The G-index is a derivative of the H-index, defined as follows: for a researcher's first g papers (sorted by citation count), they must have received at least g2 citations, but the (g+1) paper should not have more than (g+1)2 citations.[9] The M-index is a supplement to the H-index, and is calculated as the H-index divided by the span of active publishing years.[10] To assess the academic influence of different countries and institutions in this field, we calculated the H-index of the top 10 countries and analyzed the corresponding G-index, M-index, publication year of first paper (PY_start), total citation count (TC), and number of publications, using the H-index function in the Bibliometrix package to objectively assess the status of different countries in this field.

Analysis of National Collaborations in Precision Medicine

To further understand the cooperative relationships among different countries, we extracted unique country names from the list separated by semicolons in each AU_CO record, ensuring that there were no duplicate country names within the same entry. We also selected the countries with the top 10 h-index values. We then used the "sankeywheel" package to

allocate distinct colors to each country, to enrich the visualization and promote an intuitive grasp of the interconnections in the global research network.

Analysis of the Evolution of Thematic Categories in Precision Medicine

To better understand the current research hotspots and future development directions of precision medicine in various countries, we compared the similarities and differences in the precision medicine themes in different countries. We extracted the thematic categories in the literature list from the DE field. We used the "term extraction" package to extract the theme words in different countries and regions while cleaning and deduplicating the thematic words. Notably, we used the Tau value, a metric in the field of bioinformatics that can assess the tissue-specific expression of genes, for the first time to accurately assess the specificity of the themes in different countries by analyzing specific thematic categories.[11] The formula for calculation of the Tau value is shown below, where n represents the number of countries, i represents different countries, and X_i represents the frequency of specific.

Results

Trends and Evolution in Precision Medicine Research

Based on the WoSCC searches, there was an increasing overall trend in the number of published articles from 1999 to 2022. The number of published articles reached a maximum in 2022, with a total of 5128. The number of cited references showed a year-on-year increasing trend, reaching the highest number in 2017 (Figure 2A). However, because of the time

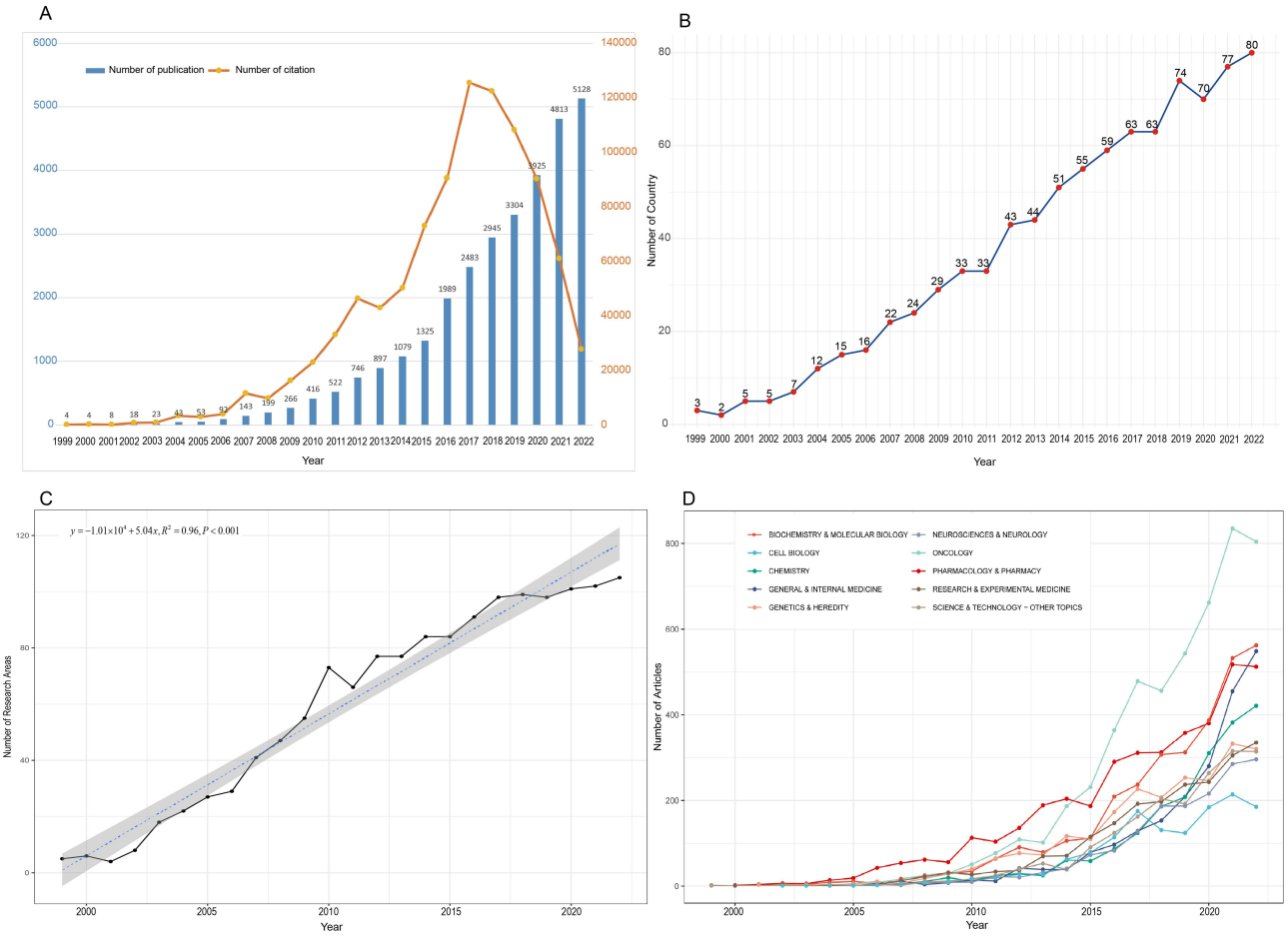

Figure 2 The bibliometric analysis of the annual publication output, total citations (TC), the number of participating countries and research areas on PM between 1999 and 2022. (**A**) Trends in annual publication output and TC of PM research from 1999 to 2022. (**B**) The number of participating countries of PM research from 1999 to 2022. (**C**) Number of WOS research areas covered in PM research from 1999 to 2022. (**D**) Temporal evolution of the top ten most productive WOS research areas in PM research from 1999 to 2022.

accumulation required for citation analysis, excellent research in emerging fields may only partially demonstrate its value in this type of analysis because of the relatively short time frame. Therefore, evaluations based on citation analysis may have a time delay and may not accurately and promptly reflect the impact of emerging research. From the perspective of the number of participating countries, the increase from three countries in 1999 to 80 countries in 2022 indicated that precision medicine research is being valued and attracting widespread global attention (Figure 2B).

WOS research areas, assigned by Clarivate Analytics, were used to classify the research papers. Each paper is classified into at least one research area in the WOS database.[12] In the present study, the number of research areas covered by the precision medicine literature increased from 4 in 1985 to 68 in 2022 (Figure 2C). Figure 2D shows the annual evolution of the 10 most productive areas in precision medicine research, illustrating the changes in the focus areas over time. It is worth noting that oncology has been a primary focus in precision medicine, with the implementation of genomics into clinical practice aiming to enhance personalized healthcare delivery. Since the United States proposed the Precision Medicine Initiative in 2015, researchers have increasingly focused on changes in the oncology field, explaining the explosive growth in the number of publications in this area. As the genetic factors influencing drug responses typically include polymorphisms in drug-metabolizing enzymes that affect drug exposure, and genotype-based dose adjustment can alter treatment outcomes by regulating or regularizing drug exposure, the pharmacology and pharmacy field is also the subject of increasing attention. With the continuous emergence of new technologies in omics, research in precision medicine has accelerated in the directions of quantification and high throughput. Integration analysis of multi-omics data has become a new direction for scientists to explore the mechanisms of life.

Analysis of National Publication Volumes and Citations in Precision Medicine

Research evaluation serves as a crucial tool for institutions and journals to manage research and assess performance, and has significant roles in optimizing research resource allocation, enhancing research management levels, and promoting sustainable and healthy development in research institutions.[13] To clarify the publication volume status for precision medicine in different regions, we analyzed the continent distribution of the authors' countries. The results showed that America (37.86%), Europe (37.53%), and Asia (21.29%) contributed the most significant volumes of publications (Supplementary Figure 2). Table 1 lists the top 10 countries with their G-index, M-index, publication year of first paper (PY_start), total citation count (TC), and number of publications sorted by the H-index. Notably, the United States had the highest H-index (520), followed by the United Kingdom (256), Germany (210), France (198), and China (196). The numbers of published papers and citations in each country over time are shown in Figure 3A. The United States and Germany were the earliest to start research in precision medicine, with the first relevant literature published in 1999. The United Kingdom started its research in 2000, Canada started in 2002, and China, France, and Switzerland started the latest, publishing their first relevant literature in 2004. It is worth noting that the importance of literature vents also influenced the growth of the literature.

Based on this concept, the present study grouped documents based on the number of citations, defining those with >100 citations as "highly cited articles", those with <1 citation (articles that have not been cited) as "lowly cited articles",

Table 1 The Top 10 Countries/Regions Contributing to Publications of Precision Medicine

Rank	Country	h_Index	g_Index	m_Index	PY_Start	TC	NP
1	USA	520	801	20.8	1999	2,262,521	47,227
2	United Kingdom	256	424	10.67	2000	362,463	7265
3	Germany	210	346	8.40	1999	299,144	8322
4	France	198	323	9.90	2004	239,211	6093
5	China	196	292	9.33	2003	332,217	14,241
6	Netherlands	193	318	9.65	2004	183,814	3882
7	Italy	172	298	7.48	2001	259,234	10,994
8	Canada	171	285	7.77	2002	196,551	5590
9	Australia	151	229	7.95	2005	128,055	3897
10	Switzerland	143	262	6.22	2001	102,540	2252

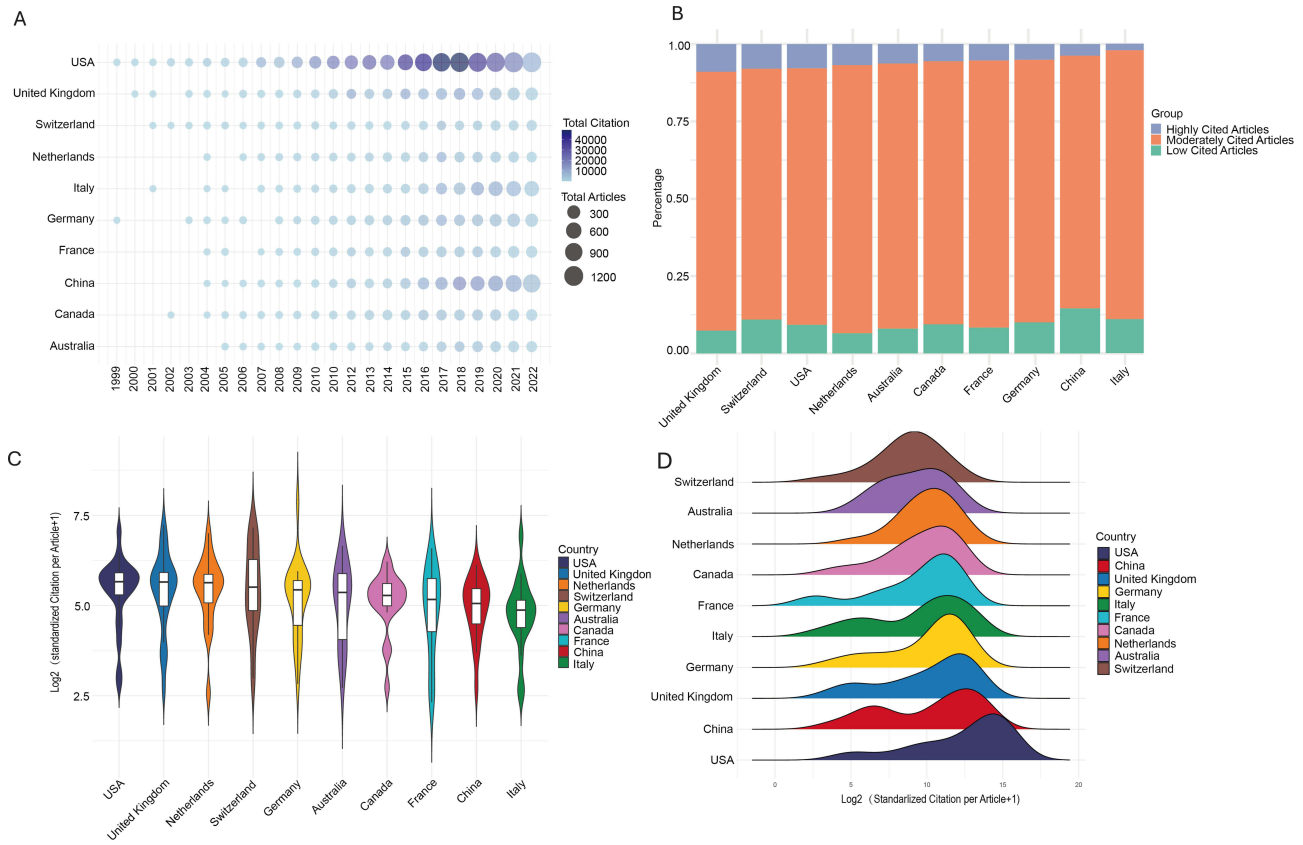

Figure 3 The bibliometric analysis of the national publication volume and citation of Precision Medicine. (**A**) The collaboration relationship for countries with collaboration frequency more significant than 10 times. (**B**) Publication volume and citation frequency of the top 10 countries of PM research from 1999 to 2022. (**C**) Violin plot of standardized citation counts across countries in PM research from 1999 to 2022. (**D**) Density plot of standardized citation counts across countries in PM research from 1999 to 2022.

and those in between as "moderately cited articles".[14] Interestingly, the top five countries with the highest proportions of highly cited articles were the United Kingdom (0.089), Switzerland (0.079), the United States (0.078), the Netherlands (0.068), and Australia (0.063). Meanwhile, China (0.146), Italy (0.110), Switzerland (0.110), Germany (0.101), and Canada (0.094) had higher proportions of lowly cited articles (Figure 3B). As described above, the United States has taken a leadership position in precision medicine, and represents the global frontier level. Besides its strong economy, its substantial investment in healthcare has contributed to its achievements. National economic support and international cooperation will further promote the overall development in this field.

In order to eliminate the effect of the number of publications on the number of citations, this study standardized the number of citations by the number of publications to infer each country's objective influence in precision medicine. It is worth noting that American countries, such as the United States, and European countries, such as the United Kingdom, the Netherlands, Switzerland, and Germany, have achieved a series of accomplishments in promoting the continuous development of precision medicine. Countries like Australia, Canada, France, and China have achieved good results in the numbers of published articles in precision medicine (Figure 3C). The density plot in Figure 3D depicts the distribution of standardized citations for various countries, highlighting both concentration and dispersion patterns. Switzerland exhibits the highest density of articles with substantial citations, followed closely by Australia and the Netherlands, indicating a strong and consistent citation impact in these countries. Canada, France, and Italy also show a notable concentration of higher citation counts, though less pronounced. In contrast, countries like the United States, China, and the United Kingdom present more spread-out distributions, with a considerable number of articles receiving lower citation counts, indicating greater variability in their academic impact. Germany's distribution falls somewhere in between, with a moderate concentration of articles in the mid-range of citations. This suggests that while certain

countries maintain high citation consistency, others experience a wider range of citation impact, reflecting varying levels of academic influence across different regions.

Analysis of National Collaborations in Precision Medicine

To better understand the global landscape of precision medicine research, we analyzed the international collaboration patterns between countries. Thus, we drew a collaboration relationship graph for countries with collaboration frequencies that were more significant than ten times. The results showed that, as a leader in the development of precision medicine, the United States occupies a leading position in terms of publication volume and collaboration breadth. European countries such as the United Kingdom, Germany, France, the Netherlands, Italy, and Switzerland also have high achievements in precision medicine. Furthermore, there is close collaboration and communication between European countries. Regarding Asian countries, China, Japan, and South Korea are showing good development in precision medicine, but the collaboration among the countries is poor (Figure 4A). Many countries are gradually strengthening international cooperation and exchanges. The top 10 countries selected according to the H-index were analyzed in this study. The United States is dominant in the field, with the most significant output of publications and an important position in international collaborations. China takes the lead among its collaborating countries, followed by the United

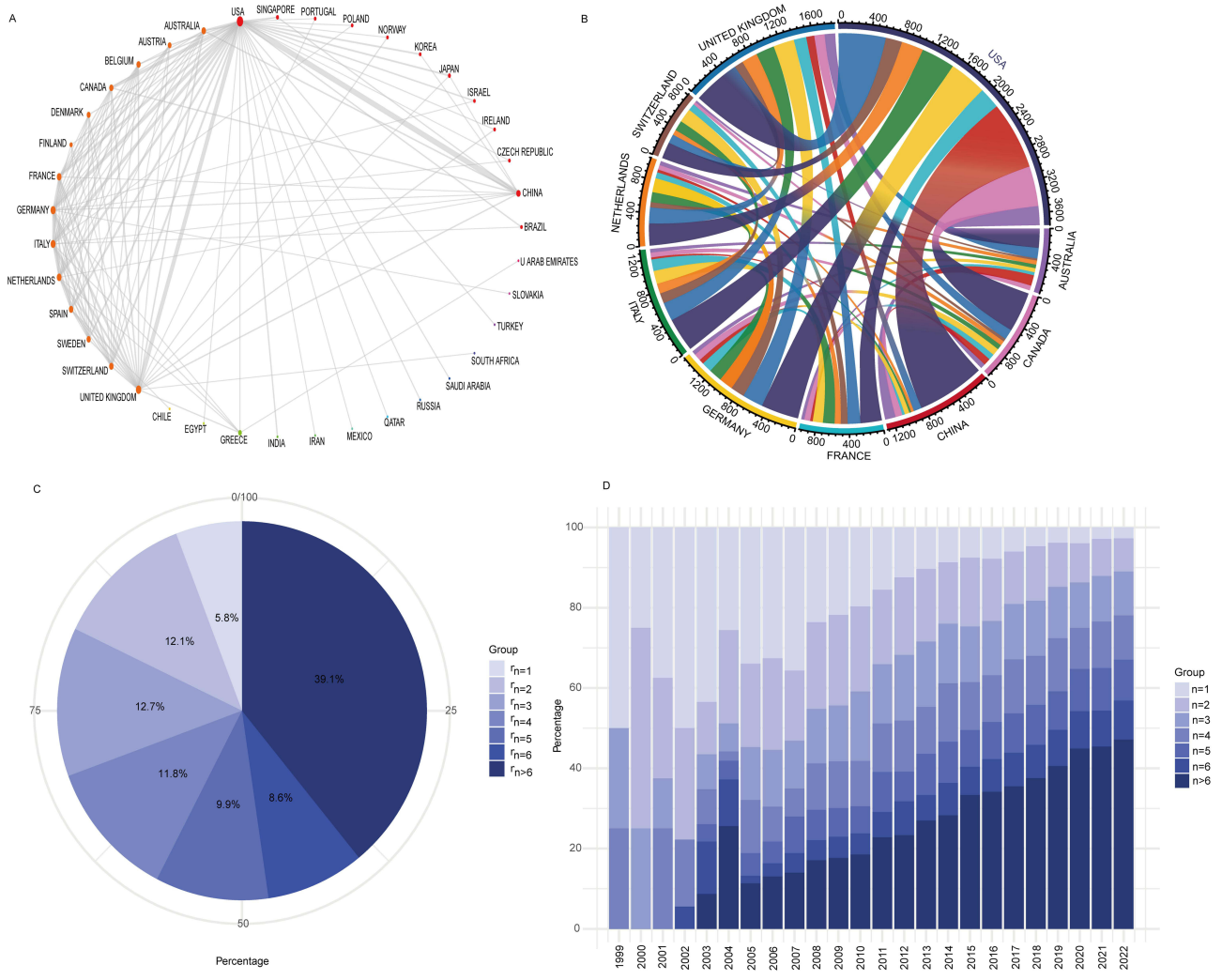

Figure 4 Analysis of national collaboration of Precision Medicine. (**A**) The collaboration relationship for top 10 countries selected based on the H-index. (**B**) Different citations for the top 10 countries based on the H-index. (**C**) The proportion of the number of authors in different literatures in PM research from 1999 to 2022. (**D**) Bar chart of the number of authors of different literatures over time.

Kingdom, Canada, Germany, and Italy. At the same time, the United Kingdom, although ranked second in national collaborations, continuously strengthens its cooperation with other countries such as the United States and Germany. In contrast, Asian countries like China are achieving good results in the number of publications, but need to further strengthen international cooperation to increase their academic influence in this field (Figure 4B).

To explore the trends in collaborative development, we collected information for all authors on articles. As shown in Figure 4C, the proportion of articles with more than one author was close to 90%. Among studies completed through collaboration, articles with six or more authors comprised the highest portion. As depicted in Figure 4D, the proportion of single-author publications has markedly declined over the observed period, while the share of articles involving multiple authors has demonstrated a consistent upward trend. This shift underscores an increasing emphasis on collaborative efforts and interdisciplinary research within the field of precision medicine. The rise in multi-author publications reflects the growing necessity for collective expertise and the integration of diverse perspectives, particularly as the field evolves from isolated, nation-specific endeavors toward more comprehensive international collaborations. Consequently, the trend toward internationalization in precision medicine research has become increasingly evident, highlighting the critical importance of global collaboration in advancing the field.

Analysis of Institutions and Impacts of Authors in Precision Medicine

A total of 8017 institutions were involved in the publication of the 30,777 articles evaluated in this study. Table 2 lists the top 10 institutions together with their country, G-index, M-index, publication year of first paper (PY_start), total citation count (TC), and number of publications, sorted by the H-index. Harvard University, University of California System, Harvard Medical School, and University of Texas System in the United States and Udice French Research Universities in France have made significant contributions to this field. Interestingly, seven of the ten institutions are based in the United States, reinforcing the leading position of the United States in this field.

To clarify the most prolific authors, we reviewed the researcher profiles in the WOCSS and ranked them according to the total numbers of articles. In total, 129,538 authors produced the 30,777 articles selected for this study. As shown in Table 3, Golubnitschaja Olga from University Bonn Hospital was the most productive author, with 71 articles published and an H-index of 35. Following closely behind were Giovanni Scambia from Fondazione Policlinico Universitario Agostino Gemelli IRCCS (62 articles; H-index: 79), Patrinos, George P from University of Patras (25 articles; H-index: 28), and Stephan Ripke from Charite Medical University of Berlin (58 articles; H-index: 75). Among the top ten authors, eight are affiliated with institutions in European countries, highlighting Europe's prominent leadership in the domain of precision medicine.

Analysis of the Evolution of Thematic Categories in Precision Medicine

This study detected 27,664 author keywords in the 30,777 papers published on precision medicine research during 1999–2022. To further analyze the relationship between themes and time evolution, the results show an increasing focus on cutting-edge technologies such as artificial intelligence, machine learning, liquid biopsy, Nanoparticles, and next-generation sequencing,

Table 2 The Top 10 Institution Contributing to Publications of Precision Medicine

Rank	Institution	Country	h_Index	g_Index	PY_Start	TC	NP	m_Index
1	Harvard University	USA	218	369	2003	230,236	3268	10.38
2	University of California system	USA	156	291	2002	134,454	2255	7.09
3	Udice-French research universities	French	145	251	2004	112,905	2536	7.25
4	Harvard medical school	USA	135	250	2003	88,638	1455	6.43
5	University of texas system	USA	124	253	2004	77,669	1191	6.20
6	University of London	UK	122	241	2008	72,060	1108	7.63
7	Brigham & women's hospital	USA	117	217	2003	59,257	827	5.57
8	University of Toronto	UK	116	221	2006	75,885	1558	6.44
9	Stanford University	USA	111	205	2006	54,712	880	6.17
10	Dana-Farber cancer institute	USA	108	186	2008	40,308	491	6.75

Table 3 The Top 10 Authors Contributing to Publications of Precision Medicine

Rank	Researcher	Articles	H-Index	Country	Institution
1	Golubnitschaja, Olga	71	35	Germany	University Bonn Hospital
2	Giovanni Scambia	62	79	Roma	Fondazione Policlinico Universitario Agostino Gemelli IRCCS
3	Patrinos, George P.	25	28	Greece	University of Patras
4	Stephan Ripke	58	75	Germany	Charite Medical University of Berlin
5	Dan Roden	54	128	USA	Vanderbilt University
6	Filippo Crea	54	88	Italy	Gemelli Isola Hosp
7	Vidhya Jagannathan	48	28	Switzerland	University of Bern
8	Tosso Leeb	48	44	Switzerland	University of Bern
9	Jerome Rotter	46	140	Korea	Korea National Institute of Health
10	Antonio Gasbarrini	44	94	Roma	Università Cattolica del Sacro Cuore Roma

particularly after 2015, reflecting their growing importance in the field. In contrast, "Gene-Expression", "Personalized Outcomes" and "Pharmacogene Expression" were more frequently studied in the early 2000s (Figure 5A). The map underscores a significant shift in research priorities towards advanced computational and molecular techniques, marking a transformation in precision medicine over the past two decades. The findings presented in Figure 5B indicate that the

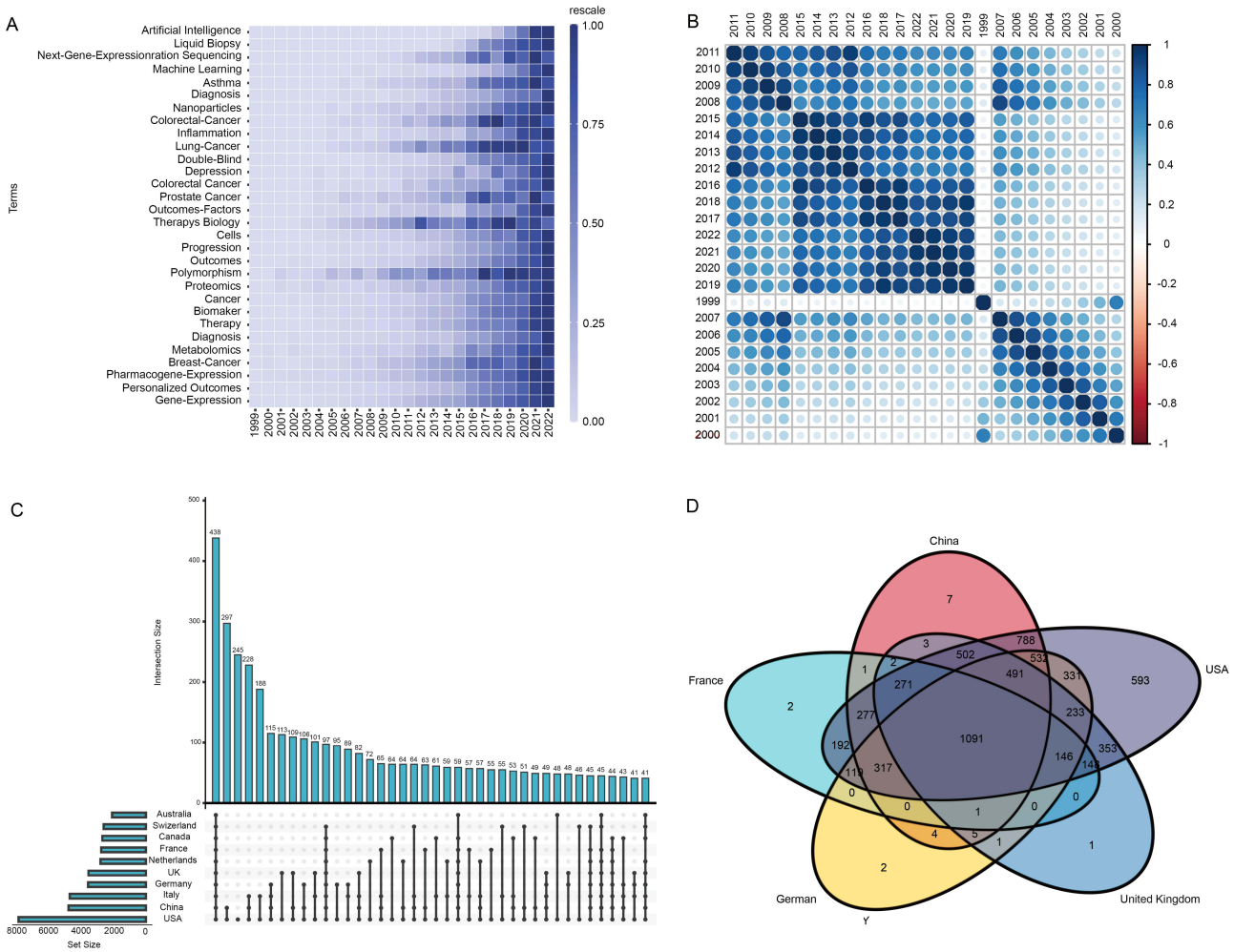

Figure 5 Analysis of the themes evolution of Precision Medicine. (**A**) Upset map of overlap of theme categories in different countries for top 10 countries selected based on the H-index. (**B**) Venn Diagrams of the coincidence of theme categories for top 5 countries selected based on the H-index. (**C**) Heat maps of trends in different topics over time. (**D**) Correlation matrix for different theme categories over time.

correlation among research topics was relatively low from 2000 to 2007. This phenomenon may be attributed to the nascent stage of precision medicine during this period, characterized by limited technological capabilities and a fragmented research landscape. Conversely, the notable increase in the relevance of research topics observed between 2008 and 2012 may be closely associated with the advancements and widespread adoption of Next-Generation Sequencing(NGS). Advancements in technology have significantly accelerated genomic analysis, rendering it more cost-effective and facilitating the swift advancement of precision medicine. Notably, around 2008, next-generation sequencing (NGS) technology gained widespread adoption in cancer research, personalized therapy, and other domains, leading to a more concentrated focus on research topics that reflect the shared interests of scholars within the precision medicine application field. The correlation among these topics has markedly intensified since 2013, particularly between 2015 and 2020, during which the alignment of research themes reached its zenith. This phenomenon is closely related to the application of key technologies such as gene editing technology, liquid biopsy, and artificial intelligence technology. These technologies have greatly promoted the development of cancer treatment, personalized diagnosis and gene therapy, making the research hotspot in the field of precision medicine gradually focus on the application and clinical transformation of these technologies.

The findings presented in Figure 5C and D demonstrate that the overarching thematic categories of precision medicine are consistent across various countries. This consistency is shaped by international collaboration, as evidenced by the similar research trajectories observed in China and the United States. This suggests that while precision medicine themes exhibit regional characteristics, they are also significantly influenced by regional cooperation. Furthermore, the scope of medical research is progressively broadening, indicating an emerging trend towards globalization. Notably, the United States, due to its pioneering role in precision medicine, exhibits a distinct thematic evolution.

To further investigate the distribution of specific subject terms across various countries, we classified the thematic areas of precision medicine-related literature published by the top ten countries ranked by H-index, utilizing their Tau values. The findings indicate substantial disparities in the emphasis placed on particular topics among these nations. For example, China and the United States exhibit greater intensities for certain subject terms, suggesting a higher degree of specialization in these research domains within these countries. Furthermore, cluster analysis indicates that Germany and France exhibit comparable emphasis on particular subject terms, which may reflect shared research interests and trajectories within this field (Figure 6A). As a highly developed economy, the United States concentrates its precision medicine efforts on areas such as “Informatics”, “Treatment Rules”, “Consortium Guidelines”, “Health Equity”, and “Molecular Pathological Epidemiology” (Figure 6B). These domains are intricately linked to the nation’s sophisticated bioinformatics technologies and precision medicine infrastructure. In the United Kingdom, research within the field of precision medicine primarily focuses on “Pharmaceuticals Regulation”, “Pharmacometabonomics”, “Stratified Medicine”, “Abacavir Hypersensitivity”, and “Phenotype Standardization” (Figure 6C). As a nation with an advanced healthcare infrastructure, these areas underscore the significant emphasis placed on drug safety regulation and personalized medicine. Furthermore, the United Kingdom possesses a robust practical foundation in clinical medical research and pharmacotherapy, which positions pharmacogenomics and phenotypic standardization as key areas of scholarly interest.

Germany and France exhibit distinct research themes within the field of precision medicine. In Germany, the research focuses on areas such as “SLC Transporter”, “Inflammatory Bowel Disease”, “Neoadjuvant Chemoradiation”, “Molecular Tumor Board”, and “Therapy Monitoring” (Figure 6D). As a country that highly values medical technology and research innovation, Germany has significant research strengths in cancer treatment and therapeutic monitoring.[15] In contrast, the research themes in France are centered around “Pheochromocytoma”, “High-Dose Chemotherapy”, “Inborn Errors of Metabolism”, “Chronotherapy”, and “Molecular Screening”, reflecting a specialized focus on oncological studies and genetic metabolic disease research (Figure 6E).

In China, the primary research themes in the field of precision medicine include “Informatics”, “Hepatocellular Carcinoma”, “Photothermal Therapy”, and “Lung Adenocarcinoma” (Figure 6F). These themes are closely aligned with the nation’s domestic disease burden and healthcare requirements, reflecting the implications of its large population. Furthermore, advancements in information technology and biomedicine within China have substantially propelled research and applications in precision medicine.

In the Netherlands, the research themes are diverse and encompass areas such as “Health−Status”, “Learning Healthcare”, “Ecological Momentary Assessment”, “Intensive Care Unit”, and “Intestinal Organoids” (Supplementary Figure 3A). Similarly,

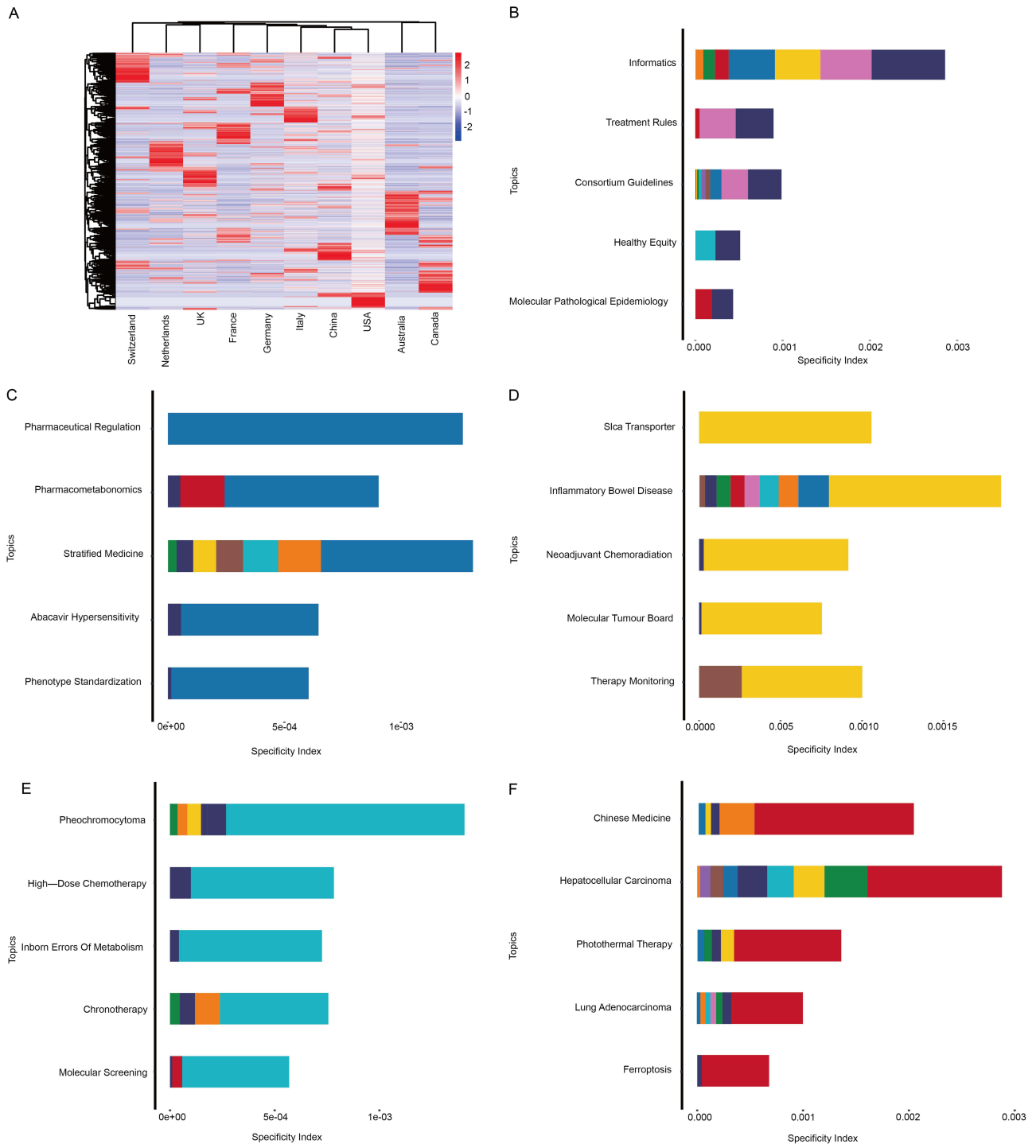

Figure 6 Analysis of the themes categories evolution of Precision Medicine. (**A**) Heat maps of different country-specific theme categories. (**B**) Top 5 country-specific theme categories in the United States. (**C**) Top 5 country-specific theme categories in the United Kingdom. (**D**) Top 5 country-specific theme categories in Germany. (**E**) Top 5 country-specific themes categories in France. (**F**) Top 5 country-specific themes categories in China.

Switzerland engages in comprehensive research themes that address critical topics, including "Primary Vascular Dysregulation", "Genodermatosis", "Nanobiotechnology", "Whole Genome Sequencing", and "Oncoproteomics" (Supplementary Figure 3B). The emphasis on these research topics highlights Switzerland's exceptional capabilities in nanotechnology, biomedical engineering, and genetics, while also illustrating its advanced exploration within these fields (Supplementary Figure 3C). In contrast, the

research themes in Italy are characterized by distinct areas of focus, including "Innovative Biotechnologies", "Rehabilitation", "Targeted Therapy", "Primary Biliary Cholangitis", and "Autoinflammation" (Supplementary Figure 3D). In Canada, the research themes encompass "Adaptive Treatment Strategies", "Dynamic Treatment Regimes", "Quantitative Ultrasound", "Energy Metabolism", and "Research Ethics", thereby illustrating a diverse array of topics. Conversely, Australia demonstrates a robust foundation in the research areas of "Sleep Medicine", "Neuroscience", and "Patient Care", highlighting its emphasis on sleep medicine and neuroscience research (Supplementary Figure 3E).

In conclusion, the precision medicine themes in different countries are shaped by their economic and environmental factors, dietary and lifestyle habits, and disease spectrums. Gaining a deeper insight into these variations will enhance global precision medicine research guidance, propel the progress and application of precision medicine, and offer more effective solutions for global health challenges.

Discussion

In this study, we conducted a comprehensive and systematic analysis of the publication trends, the contribution intensities of countries, institutions, and authors, the cooperation network, and the research hotspots in various countries, with the aim of deepening the understanding of precision medicine research and potentially enlightening scholars and policy-makers for proper decision-making.

Increasing Global Attention and Publication Trends in Precision Medicine

This study revealed a significant upward trend in precision medicine research publications from 1999 to 2022. The first article, published in 1999, reviewed the potential of pharmacogenomics to improve healthcare, reduce treatment-related morbidity and mortality, and accelerate the development of therapeutic compounds.[16] The growth rate in publication was gradual before 2005, but following advancements in next-generation sequencing technology, the volume of literature began to grow exponentially. In 2022, the number of publications peaked at 5128, underscoring the rapidly increasing interest and investment in this field. The number of participating countries grew from just 3 in 1999 to 80 in 2022, reflecting a broader geographic engagement and deepening commitments worldwide to precision medicine research. This expansion highlights the growing collaborative nature of precision medicine, with an increasing number of countries contributing to its development. Furthermore, this expansion can be attributed to growing international collaborations, which have helped to disseminate knowledge and share technical expertise. The remarkable growth in publication volume and diversity of research topics also points to increasing investments in this field. Governments and private entities are recognizing the potential impact of precision medicine on public health outcomes, which is driving funding initiatives and fostering an environment conducive to innovation. This funding has supported infrastructure development, such as biobanks and genomic databases, which are critical for enabling large-scale precision medicine studies.

Global Efforts by National, Institutional, and Author Contributions

Essential Science Indicators serve as vital evaluation tools for assessing the international academic standing and influence of universities, institutions, countries, and regions.[17] One key measure of an article's impact on the scientific community is the number of citations it receives, which reflects its significance and relevance.[18] In the realm of precision medicine, the United States has emerged as a leader, demonstrating both high publication volumes and extensive international collaborations. This preeminence can be largely attributed to the country's robust economic foundation and significant investments in healthcare, which create a fertile environment for research and innovation. Moreover, supportive government initiatives—including funding for research projects, policy development, and the expansion of medical insurance—have provided essential resources that facilitate the advancement and application of precision medicine. Collectively, these factors underscore the United States' pivotal role in shaping the future of precision medicine research and practice.

Countries are increasingly strengthening their cooperation. Notably, the United States and European countries like the United Kingdom, Canada, Germany, and Italy play pivotal roles in international collaborations. European countries, in particular, have demonstrated strong cooperation, helping the region achieve growth in this field. For instance, the European Union's Innovative Medicines Initiative 2, launched in 2014, aimed at providing individualized treatment to

patients at the right time, was one of the critical steps guided by precision medicine concepts.[19] Furthermore, the Horizon Europe Implementation Plan (2021–2027) also identifies precision medicine as a key focus area. France has been proactive as well, launching the France Genomic Medicine 2025 Project, focusing on genomics and personalized medicine.[19] Meanwhile, France initiated the France Genomic Medicine 2025 Project in 2016, which focuses on genomics and personalized medicine, and aims to develop the national genomic healthcare industry[20] (Figure 7). Although China entered this field later, its government has provided significant support and participated in international collaborations that have substantially advanced human genome research. China has undertaken important national projects that contributed to the global progress of precision medicine, notably through collaborations and technology exchanges.

A total of 8017 institutions were involved in the publication of the 30,777 articles evaluated in this study. The top institutions listed in Table 2 indicate that Harvard University, University of California System, Harvard Medical School, and University of Texas System in the United States, along with Udice French Research Universities in France, have made significant contributions to this field. Interestingly, seven of the ten institutions are based in the United States, reinforcing its leading position in precision medicine. In addition, the analysis of authors highlighted the prolific contributions of researchers. With 129,538 authors producing the 30,777 articles, Golubnitschaja Olga from University Bonn Hospital emerged as the most productive author, followed by Giovanni Scambia, Patrinos George P, and Stephan Ripke. Notably, eight of the ten most prolific authors are based in Europe, indicating that Europe is also a leader in this field. This underscores the collaborative efforts and shared expertise that are shaping the future of precision medicine research globally.

Comparative Analysis of Precision Medicine Themes Across Regions

As shown in Figure 7, with the occurrence of important historical events, the attention to PM has continuously increased. China joined the International Human Genome Project in 1999.[21] In 2003, the leaders of the six member states announced that the human genome had been completely sequenced. Specifically, on 14 April 2003, they issued a historic declaration indicating that the goals of the Human Genome Project had been achieved, prompting clinicians to anticipate a data-driven transformation in healthcare.[22] High-throughput sequencing is a revolutionary change to traditional Sanger sequencing technology that can simultaneously sequence hundreds of thousands to millions of nucleic acid molecules. Consequently, it is also known as next-generation sequencing. The emergence of high-throughput sequencing technology has made it possible to conduct detailed analyses of the transcriptomes and genomes of individual species.[23] With the concept of precision medicine, the modern medical model is transitioning from 4P medicine to 5P medicine, referring to Preventive, Predictive, Personalized, Participatory, and Precision medicine.[24] In 2015, the United States launched the Precision Medicine Initiative, marking the first time that precision medicine had been prioritized as a critical national research and development project, with the aim of providing personalized treatment plans for patients by integrating technologies such as genomics, bioinformatics, and extensive data analysis.[25] European countries such as France and Germany subsequently enacted similar precision medicine policies.[26] The term "2021 Precision Medicine" was mentioned as a critical development area in the 2021–2025 fiscal year strategic plan of the United States National Institutes of Health, indicating that the precision medicine field will remain active in the coming years.[26] An underlying reason for this may be the increasing numbers of people who are benefiting from personalized medicine. The establishment of systems and policies has also promoted the rapid development of precision medicine.

To gain a deeper understanding of the similarities and differences in the themes of precision medicine in individual countries and regions, this study extracted specific thematic categories from precision medicine literature, and compared the differences and specificities between the theme words in various countries. In the United States, the government's continuous support and development promotion of precision medicine, including investment in research projects, formulation of relevant policies and regulations, and expansion of medical insurance coverage, have provided a vital policy environment and resource guarantees for research and application of precision medicine.[27] The United States also has numerous top medical schools, research institutions, and biotechnology companies with rich experience and technological advantages in primary medicine, clinical research, bioinformatics, and molecular pathology. Furthermore, it is worth noting that the United States has made many efforts in terms of health equity, with the goal of eliminating disparities and improving the overall health status of affected populations.[28]

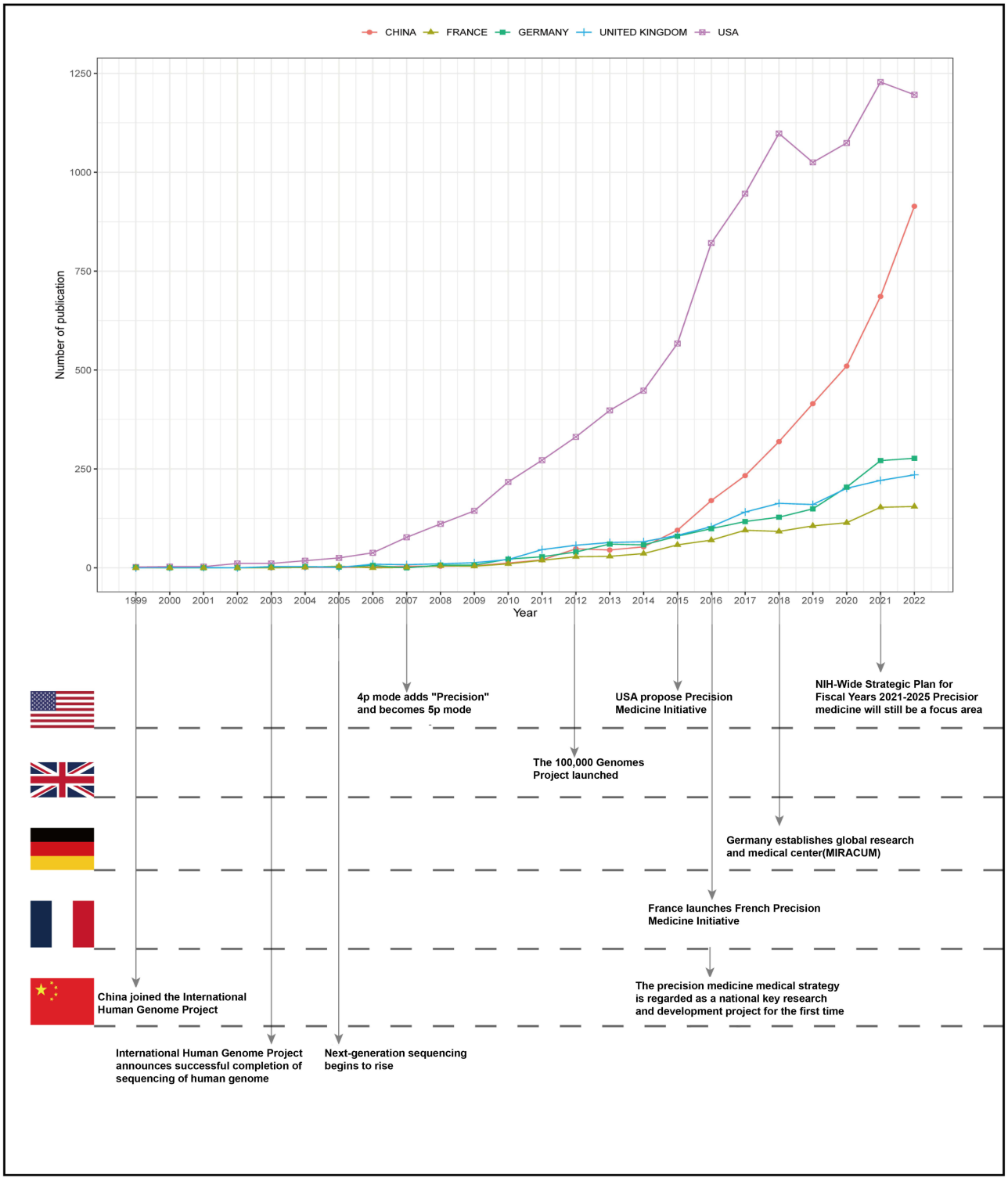

Figure 7 Important historical events of PM research.

In Europe, the Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom has played a vital role in establishing regulatory pathways for new drug evaluations, particularly in advanced therapeutic areas such as cell and gene therapies.[29,30] In this approach, drug doses are adjusted based on an individual's genomic makeup to optimize treatment effectiveness and reduce adverse effects.[31] The MHRA has issued guidelines for new drug approval

and regulatory pathways to expedite the evaluation of new drugs, particularly in advanced therapy areas such as cell and gene therapy.[32] In 2014, the UK launched the Early Access to Medicines Scheme, which aimed to provide early treatment to critically ill patients before obtaining market approval, emphasizing rapid responses to urgent medical needs.[33]

With rapid technological advances, the underlying concepts and technical frameworks of precision medicine continue to evolve, transforming disease classification, diagnostic approaches, and drug development strategies.[26] The implementation of relevant technologies into clinical practice is improving disease prevention, diagnosis, and treatment. As for future development, Francis Collins, the former Director of the US National Institutes of Health, outlined a vision for precision medicine by 2030, focusing on key areas such as large-scale population cohorts, routine genomic technologies in clinical care, phenomics, environmental exposure research, big data integration, artificial intelligence, and participant diversity with associated privacy concerns.[1]

In China, the focus on precision medicine research themes such as "Informatics", "Hepatocellular Carcinoma", "Photothermal Therapy", and "Lung Adenocarcinoma" reflects a strategic response to the country's specific healthcare challenges and disease burdens. Recent statistics indicate that lung cancer and liver cancer are the primary causes of death from malignant tumors in China, highlighting a critical public health challenge.[34] In response, there has been a notable increase in research focused on these cancers within the framework of precision medicine. This trend reflects a proactive approach to address the specific needs of the population, emphasizing personalized treatment strategies that consider individual genetic and environmental factors. By prioritizing liver and lung cancer research, Chinese researchers aim to enhance early detection, improve therapeutic outcomes, and ultimately reduce mortality rates associated with these prevalent diseases. This alignment of research efforts with the burden of disease underscores the importance of tailoring precision medicine initiatives to effectively tackle the most pressing health issues facing the population.

In comparison to other similar studies in the field, this research provides a focused analysis of academic development trends in precision medicine across various countries. By utilizing bibliometric analysis, this study identifies key research hotspots and themes, offering insights into the evolving landscape of precision medicine research. Future directions based on the presented data could include a more comprehensive analysis that integrates findings from multiple databases to capture a broader spectrum of research outputs. Additionally, researchers may explore the thematic evolution within precision medicine by examining emerging trends and patterns over time. This approach could facilitate the identification of underexplored areas and inform future research initiatives, ultimately contributing to a deeper understanding of the field and its potential trajectories.

The present study has some limitations that require consideration. First, it is essential to note that the data were exclusively derived from the WoSCC database, which could lead to the omission of noteworthy discoveries published in alternative databases. Nonetheless, it is worth noting that the WoSCC has a reputable status as a comprehensive database within the medical domain, encompassing a substantial portion of relevant information. Second, the study only includes articles written in English and recorded in the WoSCC database, which affects the overall number and influence of papers published in different countries. Third, recently published high-quality studies may not yet have received the attention they deserve because of citation delays and require further evaluation in follow-up studies. Despite these limitations, the findings in the present study will help researchers to understand the academic development trends, especially the hot topics and research directions, in precision medicine research in various countries.

Conclusions

This study aimed to comprehensively analyze the current global research status of precision medicine through systematic bibliometric analysis and visualization from various perspectives, including nations, institutions, authors, and differences in research themes among countries. Over the past few decades, the extensive collaboration among researchers and institutions from China and the United States and the close cooperation among European countries have led to the emergence of many outstanding researchers in this field. Based on regional characteristics and differences in their populations, economies, environments, diets, lifestyles, and disease spectrums, the focuses in precision medicine vary among countries with distinct regional research themes. Countries need to clarify the factors influencing precision medicine, grasp the development trajectory, embrace diversity while seeking common ground, strategize swiftly, and optimize medical resource allocation to diversify global health research and collaboratively establish a precision

medicine model for health maintenance and disease control. Although our study is not exhaustive, it provides a practical foundation for the critical areas of global precision medicine, offers valuable insights, and furnishes important clues for subsequent studies.

Data Sharing Statement

The data in this study is not sensitive and is accessible in the public domain. Therefore, this dataset is readily accessible and devoid of any confidential attributes. All the data employed in this study has been integrated into the article and Supplementary Material.

Acknowledgments

The authors thank Alison Sherwin, PhD, from Liwen Bianji (Edanz) (www.liwenbianji.cn/) for editing the English text of a draft of this manuscript.

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.

Funding

Funded by Tianjin Key Medical Discipline (Specialty) Construction Project (TJYXZDXK-005A).

Disclosure

The authors affirm that the research was conducted without any apparent commercial or financial affiliations that could be construed as potential conflicts of interest.

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