

International Developments in Atherosclerosis Disease Research Using Precision Medicine (1994–2024): A Bibliometric Analysis

Danang Prasetyaning Amukti,¹ Lalu Muhammad Irham,² Sugiyarto Surono,² Wirawan Adikusuma,^{3, 4} Riat El Khair,⁵ Rizky Gustinanda,² Dilpreet Singh,^{6, 7} Rockie Chong,⁸ Ilker Ates,⁹ Daraporn Rungprai¹⁰

Abstract

Cardiovascular disease has risen to the leading cause of global death. Atherosclerosis is an important contributor to the development of cardiovascular disease, which is involved in the formation of atheromatous plaques on the walls of arteries, resulting in arterial stenosis. In the past two decades, the treatment approach has shifted from conventional methods to precision medicine, which aims to tailor medical interventions based on individual patient characteristics, including genetic information, biomarkers and environmental factors. A literature search of precision medicine research on atherosclerosis from 1994 to 2024 was conducted using the Scopus database. VOSViewer v.1.6.16 and Biblioshiny software programs were used to perform bibliometric analysis. Between 1994 and 2024, 482 documents were published from 299 different sources, with an average document age of 3.68 years and an average of 24.52 citations per document. The total number of authors involved was 3.141, with 40 of them writing the documents individually. Collaboration between authors was very prominent, with an average of 7.89 authors per document and 29.46 % of the documents involving international collaboration. The types of documents published were also diverse, including 187 articles, 1 book, 15 book chapters, 11 conference papers, 33 editorials, 1 erratum, 4 letters, 8 notes, 219 reviews and 3 short surveys. Global trends in precision medicine for atherosclerosis research from 1994 to 2024 showed that the field has undergone significant development. Precision medicine has great potential to improve the care of patients with atherosclerosis through a more personalised and data-driven approach. To maximise its benefits globally, international collaboration, investment in technology and education are needed to overcome existing barriers. Thus, precision medicine can bring significant changes to the research and treatment of atherosclerosis in the future.

Key words: Atherosclerosis; Precision medicine; Bibliometrics; *VOSViewer; Biblioshiny; Scopus.*

- Faculty of Health Sciences, Alma Ata University, Yogyakarta, Indonesia
- Faculty of Pharmacy, Ahmad Dahlan University Yogyakarta, Indonesia
- Department of Pharmacy, University of Muhammadiyah Mataram, Mataram, Indonesia.
- Research Centre for Computing, Research Organisation for Electronics and Informatics, National Research and Innovation Agency (BRIN), Cibinong Science Centre, Cibinong, Indonesia.
- 5. Department Medical, Dr Sardjito Central General Hospital, Yogyakarta, Indonesia.
- 6. University Institute of Pharma Sciences, Chandigarh University, Gharuan, Mohali, India.
- University Centre for Research and Development, Chandigarh University, Gharuan, India.
- 8. Department of Chemistry and Biochemistry, University of California, Los Angeles, USA.
- Ankara University, Faculty of Pharmacy, Department of Toxicology, Tandogan, Ankara, Turkey.
- Department of Pharmaceutical Care, Faculty of Pharmacy, Silpakorn University, Nakhon Pathom, Thailand.

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Corresponding author:

LALU MUHAMMAD IRHAM E: lalu.irham@pharm.uad.ac.id

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Introduction

Cardiovascular illnesses are becoming the world's top cause of death due to rising economic growth and improved living conditions.^{1, 2} In

2021, cardiovascular diseases caused approximately 20.5 million deaths, accounting for nearly one-third of all global deaths. In Indonesia, the

prevalence of heart disease based on doctor's diagnosis is approximately 1.5 % of the population.³ The provinces with the highest prevalence are North Kalimantan (2.2 %), Yogyakarta Special Region (2 %) and Gorontalo (2 %).⁴ Deaths from heart disease in Indonesia reached 251.09 per 100,000 population in 2019. Cardiovascular disease is often caused by hyperlipidaemia, atherosclerosis and hypertension. Atherosclerosis is an important contributor to the development of cardiovascular disease, which is involved in the formation of atheromatous plaque on the arterial wall, resulting in arterial stenosis.^{5, 6} The pathogenesis of atherosclerosis shows complexity and diversity. Inflammation, lipid infiltration, oxidative stress and endothelial damage have been proposed as the main causative factors.8,9 Atherosclerosis is a chronic disease characterised by plaque buildup on the arterial wall, which can lead to various cardiovascular complications such as heart attack and stroke.⁵ Although there have been significant advances in the treatment and prevention of atherosclerosis, the disease remains a major cause of morbidity and mortality worldwide.10, 11

In the past two decades, the treatment approach has shifted from conventional methods to precision medicine, which aims to tailor medical interventions based on individual patient characteristics, including genetic information, biomarkers and environmental factors. 12, 13 Precision medicine offers the potential to improve therapeutic efficacy and reduce side effects by targeting specific molecular mechanisms underlying atherosclerosis.¹⁴ Precision medicine is an emerging medical model that provides personalised medical diagnosis, treatment and care for specific patients after considering genetic information, physiological/pathological information, living environment and many other aspects.¹⁵ Compared with the traditional one-size-fits-all approach, more attention is paid to the influence of individual differences on disease progression.¹⁶

Bibliometrics as an effective and confirmed method for analysing research dynamics and trends in a particular field, has developed rapidly in recent decades.¹⁷ Unlike conventional measurements of scientific documents, bibliometrics is an applicable tool that can comprehensively investigate existing studies in a particular field.¹⁸ It can be easily used with publicly accessible big data, such as *Web of Science, PubMed* and *MEDLINE*. Statistical tools, including *R-bibliometrix, VOSviewer* are

integrated as an automated workflow to perform multi-step bibliometric analysis. In previous studies, bibliometric analysis has been successfully performed in various disciplines, especially in environmental science and medicine.^{19, 20} Bibliometric research is useful for analysing global research trends and identifying fast-growing areas and gaps in scientific literature.²¹

Researchers can more efficiently allocate funds and resources to solve the persistent difficulties in treating atherosclerosis if they have a deeper grasp of worldwide research patterns. By analysing publications related to precision medicine for atherosclerosis from 1994 to 2024, this study aimed to provide a comprehensive overview of the development and direction of research in this field.²² This analysis will also help identify the most influential researchers, institutions and countries in the field, as well as the most frequently cited research topics and emerging trends.^{23, 24} In addition, the results of this research analysis can provide valuable insights for policy makers and healthcare providers in designing more effective and evidence-based treatment strategies.

Methods

This study used bibliometric analysis to explore various studies and scientific literature related to "precision medicine for atherosclerotic disease". In this study, several components were analysed as: document type and language; publication development; most used keywords; citation analysis and number of cited articles, most cited countries related to international developments in atherosclerosis disease research using precision medicine 1994–2024. The research analysis focused on English-language documents, all non-English publications were excluded from the analysis to ensure consistency and clarity in interpreting data findings.

Database

Research related to international developments in atherosclerosis disease research using precision medicine by utilising *Scopus* data published in 1994-2024 (scopus.com/search). *SciVerse Scopus* is one of the databases that can be accessed online to search for publications relevant to this research (accessed on 18 September 2024). *Scopus* was used in this study because it has many

outstanding advantages compared to other online databases. First, this database provides complete and detailed information with various features such as countries, authors, journals and institutions involved. Second, this database also provides a number of citation data for each group of documents per scientific category, which functions as a matrix to determine the reputation of researchers worldwide.

Bibliometric indicators

The criteria for bibliometric analysis used in this study were as follows: (1) document type and language, (2) publication development, (3) keywords most frequently used by researchers, (4) citation analysis and number of cited articles, (5) ten most cited countries, (6) ten most active journals and (7) international collaboration. Data on active, productive and most cited publications were also collected directly from the *Scopus* database by calculating the number of cited documents from each publication. In addition, data on publications with the most citations were obtained from the *Scopus* database by calculating articles and citations for each country each year. Two application programs used to visualise the data included: *VOSViewer* version 1.6 and *Biblioshiny*. The summary of the research methods is visualised in the form of a flow diagram, which can be seen in Figure 1.

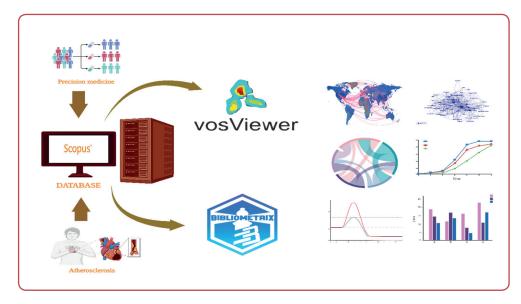


Figure 1: Bibliometric method flowchart created in BioRender.com

Results

Document types and languages

The bibliometric study on "international developments in atherosclerosis disease research using precision medicine 1994–2024". provides a comprehensive overview of the development and direction of research in this field over the past three decades. Between 1994 and 2024, there were 482 documents published from 299 different sources, with an average document age of 3.68 years and an average of 24.52 citations per document, indicating a significant impact of this research. The analysis also recorded 36.226 references, reflecting the breadth of the literature used. In terms of content, there were 5.953 additional

keywords (Keywords Plus) and 1.225 keywords from the author (Author's Keywords), indicating the diverse topics discussed in this research. The total number of authors involved reached 3.141 with 40 of them writing the documents individually. Collaboration between authors was very prominent, with an average of 7.89 authors per document and 29.46 % of the documents involving international collaboration. The types of documents published were also diverse, including 187 articles, 1 book, 15 book chapters, 11 conference papers, 33 editorials, 1 erratum, 4 letters, 8 notes, 219 reviews and 3 short surveys (Table 1). This analysis not only shows trends and patterns

Table 1: Main information of precision medicine for atherosclerosis

Description	Results		
Main information about data			
Timespan	1994:2024		
Sources (journals, books, etc)	299		
Documents	482		
Annual growth rate %	0		
Document average age	3.68		
Average citations per doc	24.52		
References	36226		
Document contents			
Keywords plus (ID)	5953		
Author's keywords (DE)	1225		
Authors	3141		
Authors of single-authored docs	40		
Single-authored docs	44		
Co-authors per doc	7.89		
International co-authorships %	29.46		
Document type			
Article	187		
Book	1		
Book chapter	15		
Conference paper	11		
Editorial	33		
Erratum	1		
Letter	4		
Note	8		
Reviews	219		
Short survey	3		

doc: document;

in precision medicine research for atherosclerosis, but also identifies rapidly growing areas and gaps in the scientific literature. With a better understanding of these global trends, scientific researchers can more effectively direct research resources and efforts to address the challenges that remain in the treatment of atherosclerosis.

Publication trends

Number of scientific articles published each year related to "precision medicine for atherosclerosis" from 1994 to approximately 2024. At the beginning of the period, from 1994 to approximately 2010, research activity was minimal with the number of articles almost close to zero. However, after 2010, there was a gradual increase in article production with some fluctuations. A significant peak occurred around 2018, where the number of articles reached almost 80 before experiencing a sharp decline in the following year. Figure 2 provides a clear visual representation of how scientific interest and attention in "precision medicine"

for atherosclerosis" has evolved over the past two decades. The sharp increase in 2018 may reflect a breakthrough or increased funding and attention to the field. Thus, this graph not only shows research trends but also indicates key periods in the development of science in this field.

The most relevant affiliation

Distribution of research documents related to "precision medicine for atherosclerosis" in various leading journals in the cardiovascular field. From the graph in Figure 3, it can be seen that the journal "Frontiers in Cardiovascular Medicine" had the largest number of documents, followed by "Circulation." Other journals that also contributed significantly were "Journal of Clinical Research," "European Heart Journal," "Atherosclerosis, Thrombosis and Vascular Biology" and "Current Atherosclerosis Reports." This distribution shows that research on "precision medicine for atherosclerosis" is highly focused on journals that have a high reputation in the cardiovascular field, reflecting the importance of this topic in the scientific community. The journal "Frontiers in Cardiovascular Medicine" which leads in the number of documents with 12 documents indicates that this journal may be the main source for researchers looking for the latest and most relevant information in the field of "precision medicine for atherosclerosis". Thus, for anyone interested in exploring "precision medicine for atherosclerosis", these journals are very valuable sources and should be used as primary references.

Author keywords

Figure 4 shows a network visualisation of the most frequently used keywords by authors in "precision medicine for atherosclerosis". Each keyword is represented by a node, with the size of the node reflecting the frequency of use of that keyword. The keyword "precision medicine" was at the centre of the network, indicating that it is a very dominant topic in this research. Other frequently occurring keywords included "atherosclerosis," "myocardial infarction" and "cardiovascular diseases," all of which closely connected to "precision medicine." This visualisation shows that research in this area is heavily focused on precision medicine approaches to cardiovascular disease, with atherosclerosis and myocardial infarction as the primary areas of interest. Keywords such as "biomarkers," "genetics" and "inflammation" also appear frequently, reflecting the importance of molecular and genetic factors

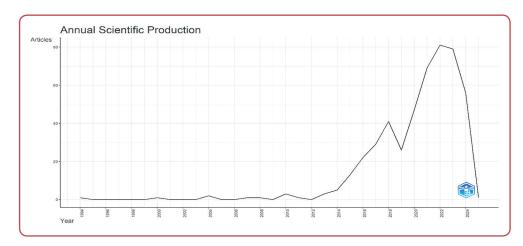


Figure 2: Trend study of precision medicine for atherosclerosis created in Biblioshiny

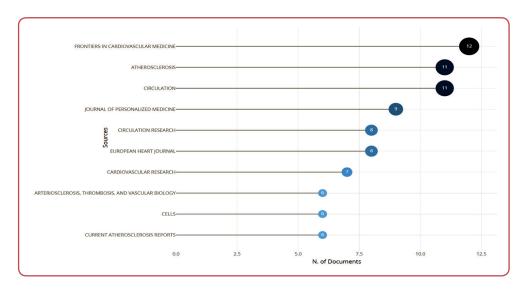


Figure 3: Most relevant source of documents of precision medicine for atherosclerosis created in Biblioshiny

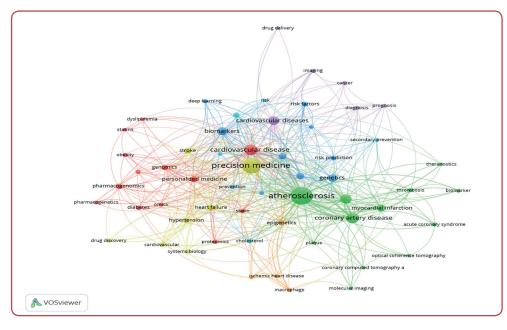


Figure 4: Most frequently used author keywords created in VOSViewer v.1.6

in understanding and treating atherosclerosis. This network provides insight into how the various topics in this research relate to each other and indicates emerging research trends. Thus, this visualisation not only depicts the frequency of keyword usage but also shows the relationships and interrelationships between different aspects of research in "precision medicine for atherosclerosis", providing a comprehensive overview of the focus and direction of research in this field.²⁵

Collaboration among authors from multiple continents

Collaboration between authors from different continents plays a vital role in scientific research. including in the field of "precision medicine for atherosclerosis". This collaborative research allows researchers from different cultural backgrounds, disciplines and institutions to work together, combining their expertise and resources to achieve the common goal of generating new scientific knowledge.26 These international collaborations often strengthen the reliability of studies, allow access to complementary skills and resources and expand the number of projects that can be worked on simultaneously. In the context of global research, these collaborations also help to address complex challenges that cannot be solved by a single researcher or institution. Figure 5 shows a horizontal bar graph titled "Corresponding author's countries," which displays the number of papers published by authors from different countries. The bars were color-coded to represent two categories: single country publication (SCP) in red and multiple country publication (MCP) in blue. The graph indicates collaboration between authors from different continents by showing the proportion of publications from a single country versus publications from multiple countries for each country listed. The United States leads the way with the largest number of papers, followed by China, Germany, the United Kingdom and Australia. This graph is interesting because it visually represents international collaboration in authorship, with several countries having a significant number of publications involving collaboration between countries.

Most cited documents

Table 2 shows the most frequently cited documents in "precision medicine for atherosclerosis" research. These documents cover a wide range of important and innovative topics in the field, which have made significant contributions to the understanding and development of precision therapies for atherosclerosis. One of the most frequently cited documents was an article discussing the application of single-cell profiling in precision medicine for atherosclerosis. This article in the journal "Nature Reviews Drug Discovery" highlights emerging single-cell sequencing techniques and how they provide new insights into the phenotypic characteristics of atherosclerotic plaques, blood, liver and intestinal tract.²⁷ This document is very important because it offers significant prospects for earlier diagnosis and more accurate medical interventions. Another frequently cited document was a review of new therapeutic mechanisms and targets in atherosclerosis, emphasising the importance

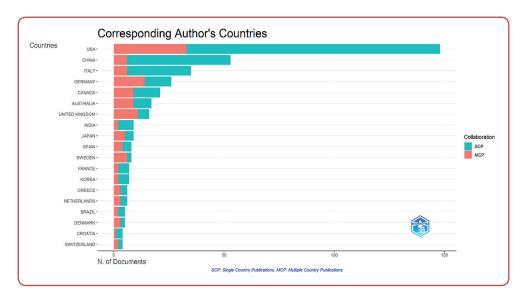


Figure 5: Research collaboration among countries of precision medicine for atherosclerosis created in Biblioshiny

Table 2: Top 10 most globally cited documents in publications

Paper	Year	Journal	DOI	Total citations	TC per year	Normalised TC
Wishart DS	2016	Nat Rev Drug Discovery	10.1038/nrd.2016.32	1013	112.56	15.23
Crea F	2017	Circulation	10.1161/CIRCULATIONAHA.117.029870	355	44.38	7.28
Folkersen L	2020	Nature Meta	10.1038/s42255-020-00287-2	319	63.80	6.21
Poller W	2018	Eur Heart J	10.1093/eurheartj/ehx165	318	45.43	9.18
Libby P	2019	Circ Res	10.1161/CIRCRESAHA.118.311098	317	52.83	7.00
Dorsheimer L	2019	Jama Cardiol	10.1001/jamacardio.2018.3965	306	51.00	6.76
Jensen Ab	2014	Nat Commun	10.1038/ncomms5022	278	25.27	4.10
Erdmann J	2018	Cardiovasc Res	10.1093/cvr/cvy084	247	35.29	7.13
Kazemian N	2020	Microbiome	10.1186/s40168-020-00821-0	226	45.20	4.40
Sookoian S	2015	World J Gastroenterol	10.3748/wjg.v21.i3.711	213	21.30	3.95

TC: total citations;

of the inflammatory component in this disease. This review introduced new strategies to limit side effects and improve therapeutic efficacy by targeting the IL-1\u03b3-IL6 inflammatory axis and the CD40L-CD40 co-stimulatory molecule interaction.²⁸ In addition, a global bibliometric study of atherosclerosis research trends is also one of the frequently cited documents. This study identified the journal "Atherosclerosis" as the most productive journal and "Circulation" as the journal with the most citations. These documents not only provide in-depth insights into the molecular mechanisms and novel therapeutic strategies for atherosclerosis, but also demonstrate the importance of international collaboration and the use of advanced technologies in this research.^{1, 29} Thus, they serve as a key reference for researchers who want to explore and develop precision medicine for atherosclerosis.

Discussion

In the past two decades, research on atherosclerosis has undergone a significant transformation thanks to advances in precision medicine. Precision medicine, which combines an individual's genetic, environmental and lifestyle data, has paved the way for a more personalised approach to the diagnosis and treatment of the disease. ^{30, 31} Technologies such as next-generation sequencing have enabled researchers to identify genetic variations that contribute to atherosclerosis, reveal cellular heterogeneity in affected tissues and provide new insights into the pathogenesis of the disease. ^{32, 33} One of the main advantages of precision medicine is its ability to offer more individualised treatments. By taking into account each

patient's unique factors, therapies can be tailored to increase efficacy and reduce side effects. Additionally, advances in single-cell profiling techniques and big data analysis have accelerated earlier diagnosis and the development of more precise therapies. However, despite its many benefits, precision medicine also faces several challenges. Implementing these technologies requires significant investment in infrastructure and specialised expertise, which can be prohibitive for countries with limited resources. Complex genetic and clinical data analysis also requires sophisticated software and specialised expertise that are not always available at all research centres.34 Moreover, despite much promising research, the clinical application of these findings is still limited and often uneven, with developed countries benefiting more than developing countries.

Overall, precision medicine has revolutionised the research and treatment of atherosclerosis. This more personalised, data-driven approach has great potential to improve patient care. However, to maximise its benefits globally, challenges such as cost, data complexity and limited clinical application need to be overcome. International collaboration and investment in technology and education can help overcome these barriers and bring precision medicine to more patients around the world.

Conclusion

A bibliometric analysis of global trends in precision medicine for atherosclerosis research from 1994 to 2024 shows that the field has undergone significant development. Precision

medicine has enabled a deeper understanding of genetic variations that contribute to atherosclerosis, as well as more personalised and effective treatment approaches. Advanced technologies such as next-generation sequencing and big data analysis have accelerated earlier diagnosis and the development of more precise therapies. Overall, precision medicine has great potential to improve the care of patients with atherosclerosis through a more personalised and data-driven approach. To maximise its benefits globally, international collaboration, investment in technology and education are needed to overcome existing barriers. Thus, precision medicine could bring significant changes to atherosclerosis research and treatment in the future.

Ethics

This study was a secondary analysis based on the currently existing data and did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

Author ORCID numbers

Danang Prasetyaning Amukti (DPA): 0000-0002-4256-6534 Lalu Muhammad Irham (LMI): 0000-0002-0091-4887 Sugiyarto Surono (SS): 0000-0001-6210-7258 Wirawan Adikusuma (WA): 0000-0001-9165-690X Riat El Khair (REK): 0000-0002-1775-1041 Rizky Gustinanda (RG): 0009-0004-7767-9979 Dilpreet Singh (DS): 0000-0001-8286-3800 Rockie Chong (RC): 0000-0001-6736-9687 Ilker Ates (IA): 0000-0001-5791-7694 Daraporn Rungprai (DR): 0000-0003-1814-8663

Author contributions

Conceptualisation: DPA, LMI Methodology: DPA, LMI Software: LMI, SS, WA Formal analysis: LMI, SS, WA Data curation: LMI, SS, WA

Writing - original draft: DPA, LMI, SS

Writing - review and editing: DPA, REK, RG, DS, RC, IA

Funding acquisition: LMI

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