



Trend of Non-Hodgkin Lymphoma Research Using a Genomics-Based Approach: A Bibliometric Analysis From 1985-2024

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Abstract

Non-Hodgkin lymphoma (NHL) is a group of malignant lymphoproliferative diseases that vary in histology, molecular biology, clinical presentation and prognosis. Genetic mutations and dysregulation play a critical role in its pathogenesis and classification. Understanding the publication landscape of NHL-related genetic studies is essential to map research trends and identify key contributors. This article aimed to conduct a bibliometric analysis of research trends in the field of NHL and related genomic studies. This study used bibliometric analysis using *VOSviewer* 1.6.16 and *Biblioshiny* (R tool) to visualise and interpret global publication trends. Data were collected from the Scopus database using keywords related to "Non-Hodgkin's Lymphoma" and "Genomic", covering publications from 1985 to 2024. The analysis identified that the United States dominates in citation contributions with a total of 7,328 citations, indicating strong research output and impact. The most productive journal was *Blood* with 57 publications, followed by *Leukemia* and the *British Journal of Haematology*. The most cited article was by Gaidano G (1991), published in PNAS, with a total of 906 citations. Co-authorship and keyword analysis revealed active international collaboration and emerging areas of focus such as *BCL2*, *DLBCL* and *MYC*. The trend in publications of NHL-related genetic research showed a significant increase over the years, with the US playing a dominant role in terms of output and citation impact. These findings highlight the growing interest and development in NHL genetic studies, which supports international collaboration and ongoing exploration of molecular targets.

Key words: Lymphoma, non-Hodgkin; Genomics; Bibliometrics.

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Introduction

Non-Hodgkin's Lymphoma (NHL) is a complex and heterogeneous cancer of the lymphatic system, consisting of various subtypes with distinct clinical and molecular characteristics. According to the latest estimates, NHL accounts for approximately 4 % of all cancer cases in the United States,

with around 80,350 new cases (45,140 men and 35,210 women) expected to be diagnosed in 2025. Additionally, 19,390 deaths (11,060 men and 8,330 women) are projected due to NHL in the same year.¹ Globally, the age-standardised incidence and mortality rates for NHL are reported

to be 5.8 and 2.6 per 100,000 individuals, respectively, reflecting the ongoing burden of this malignancy.² These statistics highlight the significant public health impact of NHL and underscore the necessity of continued genomic research to improve diagnostic and therapeutic strategies. One effective way to understand these developments is through bibliometric analysis, which allows us to track research trends, identify key scholarly works and identify research areas that require further attention.³

As technology advances, genomic studies have become an integral part of cancer research. Through this approach, researchers can explore the molecular profiles and genetic mutations that contribute to NHL pathogenesis. Mutations in genes such as *MYC*, *BCL2* and *TP53*, as well as other epigenetic mechanisms, have been identified as important factors in the development of several NHL subtypes.^{4,5} These studies provide a deeper understanding of the heterogeneity of the disease, while paving the way for the development of more precise molecular target-based therapies. Bibliometric analysis in the field of NHL genomic studies can help identify publication trends, international collaborations and topics that are top of mind in the scientific community.^{6,7}

Although research on NHL with a genomic approach continues to grow, there are several gaps that need to be addressed. Firstly, there are not many studies that comprehensively map genomics-based NHL research trends from a bibliometric perspective, especially in the context of technological developments and scientific publications. Second, research contributions are still dominated by developed countries, while the involvement of developing countries, including Indonesia, is relatively low. Third, understanding of the future direction of NHL research that integrates genomic approaches and international collaboration is still limited. In addition, the lack of utilisation of bibliometric data to explore the potential for global collaboration and innovation in precision medicine is a challenge.⁸

This article aimed to conduct a bibliometric analysis of research trends in the field of NHL and related genomic studies, focusing on research developments in the last three decades. This analysis enables us to uncover the progression of research, identify key contributors and highlight major research institutions involved in studies on NHL. Furthermore, it sheds light on how advance-

ments in technology and genomic methodologies have transformed the landscape of NHL research and precision medicine. By mapping these developments, aim was to provide a clearer perspective on the future trajectory of NHL research and identify opportunities for broader collaborations that could enhance treatment strategies and improve clinical outcomes for patients.

Methods

Database

This research method used bibliometric analysis to identify various trends and patterns of research related to NHL with a genomic study approach. In short, it involved quantitative analysis of publication data. Insights, such as productivity, impact and collaborative networks of researchers and institutions. The literature search was conducted in the *Scopus* database. *Scopus* was selected for this bibliometric analysis due to its extensive coverage of high-impact journals, broad indexing of scientific literature and frequent use in bibliometric research.⁹

A thorough search on the *Scopus* database was done using relevant keywords such as “Non-Hodgkin’s AND Lymphoma” and “Genomic”. In this study, some of the components analysed were as follows: Document type and Language, Publication progression, Most frequently used keywords, Citation analysis and Number of cited articles, Most cited countries related to global trends in NHL research with genomic-based approaches from 1985-2024. The analysis of this study focused on English documents; all non-English publications were excluded from the analysis to ensure consistency and clarity in interpreting the data findings. The search yielded 740 scientific articles.

Data analysis

Data were analysed using bibliometric indicators such as the following: (1) document type and language, (2) publication progression, (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. Moreover, data on publications with the highest number of citations were also obtained from the *Scopus* database by counting the number of articles and citations for each

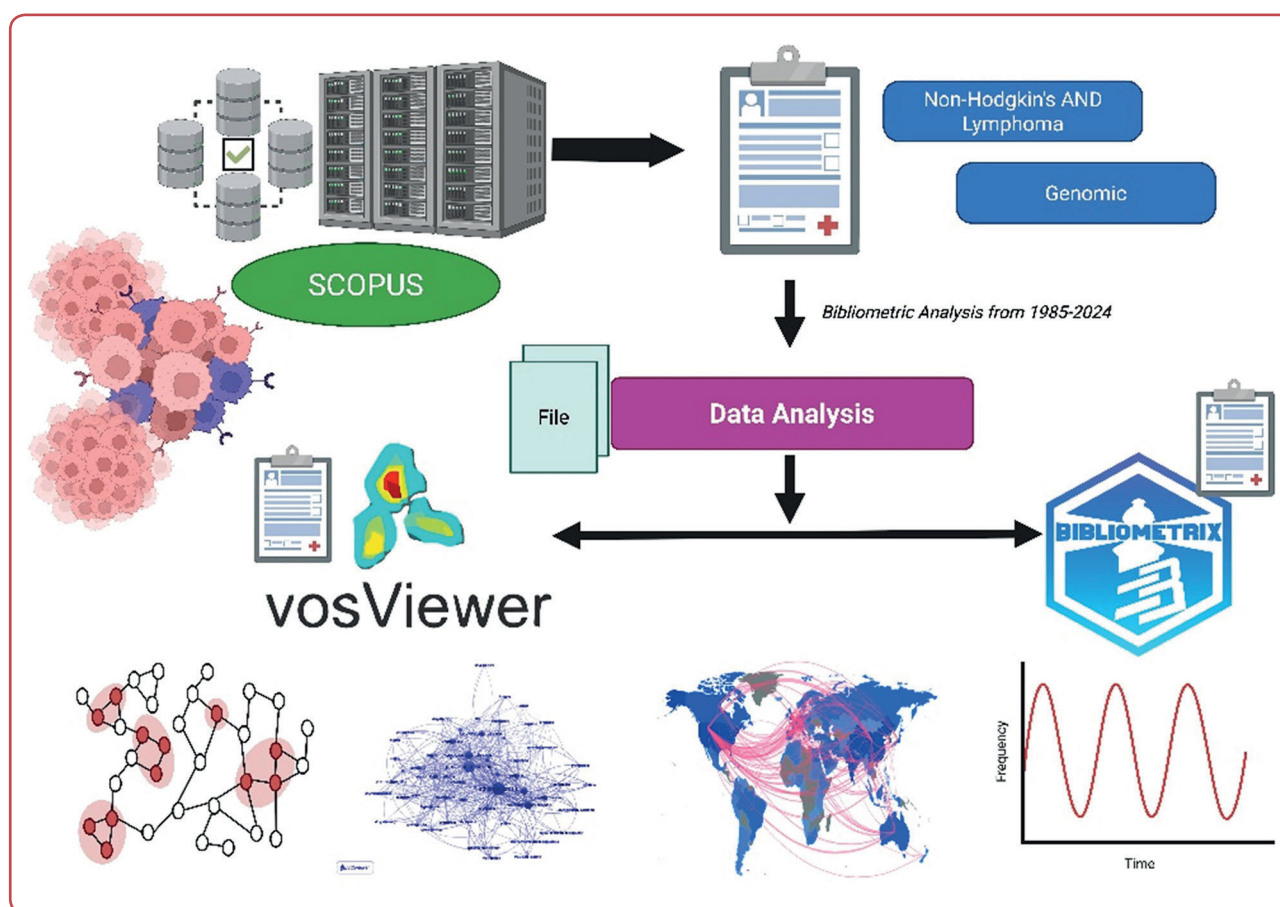


Figure 1: Flowchart of bibliometric study on non-Hodgkin lymphoma research trends using genomic-based models. This image was created at Biorender.com

country in each year. This data was visualised using *VOSviewer* and *Biblioshiny* 1.6.16, with the help of RStudio software (R Foundation for Statistical Computing, Vienna, Austria) (Figure 1).¹⁰

Results

Article type

This study used documents related to NHL cancer research trends with a genomic approach with the criteria of English-language documents that have been published in the *Scopus* database in the period 1985-2024 (Table 1). Seven hundred forty relevant studies related to NHL cancer with a genomic approach were found, including 557 original articles, 140 review articles and 43 other documents. The data presented that the majority of articles were research articles. This indicates that the urgency of lymphoma cancer research is still very important to do research through a genomic approach, this is relevant to cancer is still one of the world's health issues with a high mor-

tality rate and an increasing incidence rate.¹¹ In addition, the basic reasons related to the sources associated with this disease are still very minimal, meaning that there is still a need to continue to develop research related to NHL cancer using a genomic approach.

Author keywords

Analysis of the keywords used by the researchers revealed a total of 1441 keywords from all publications. After visual mapping with a minimum occurrence threshold (≥ 5 times), several keywords were identified that met the inclusion criteria. The most frequently occurring keywords indicated the central themes in research on NHL. The dominant keywords included "non-Hodgkin lymphoma," "diffuse large B-cell lymphoma," "prognosis," "DLBCL," "targeted therapy," "follicular lymphoma" and "gene expression," reflecting the primary research focus on lymphoma subtypes, molecular mechanisms and therapeutic strategies (Figure 2).

This visual mapping provides valuable insight

Table 1: Main information of non-Hodgkin lymphoma and genomic study

Description	Results
Main information about data	
Timespan (years)	1985:2024
Sources (journals, books, etc) (n)	331
Documents (n)	740
Annual growth rate (%)	6.9
Document average age (year)	13.6
Average citations per doc (n)	40.16
References (n)	34,955
Document contents	
Keywords plus (ID)	5826
Author's keywords (DE)	1441
Authors	
Authors (n)	4870
Authors of single-authored docs (n)	35
Authors collaboration	
Single-authored docs	37
Co-authors per doc	8.42
International co-authorships (%)	26.62
Document types	
Article	557
Book	2
Book chapter	12
Conference paper	4
Editorial	4
Letter	14
Note	4
Review	140
Short survey	3

into how terminology is distributed across research areas related to NHL. The clustering pattern shows distinct groupings, such as those related to genetic profiling (eg “gene expression,” “sequencing,” “mutation”), disease classification (eg “DLBCL,” “follicular lymphoma,” “mantle cell lymphoma”) and treatment approaches (eg “targeted therapy,” “chemotherapy,” “rituximab”).

Furthermore, the presence of keywords such as “Epstein-Barr virus,” “HIV” and “immune response” suggests a notable interest in the etiological factors contributing to lymphoma development. The visualisation also reveals how closely connected the research topics are, indicating a multidisciplinary approach involving genomics, immunology and clinical outcomes. This mapping helps identify trending areas in lymphoma research and reveals opportunities for future exploration, particularly in precision medicine, biomarkers and immunogenetics (Figure 2).

Most relevant source of documents of NHL and genomic study

In the period 1995–2023, a total of 557 documents focusing on NHL and genomic studies were collected. The earliest publications appeared in 1995 and demonstrated a slow but steady increase throughout the late 1990s and early 2000s. A significant growth trend began to emerge after 2007, followed by notable peaks in the years 2011, 2015, 2019 and reaching the highest productivity in 2021, with over 40 articles published. These surges may be associated with key advancements in genomic technologies, such as next-generation sequencing and the increasing adoption of personalised medicine approaches in oncology. The graph presented in (Figure 3) clearly reflects this pattern of exponential growth, underlining a growing scientific interest in the genetic underpinnings of NHL.

In addition to the scientific momentum, this rise in publication output suggests expanded collaboration across institutions and countries, driven by the global burden of lymphoma and the potential of genomic tools to improve outcomes. The downward trend in 2023 may be attributed to delayed indexing or shifts in research focus, yet overall, the long-term trajectory remains strongly positive. Given the ongoing innovations in cancer genomics, bioinformatics and immunotherapy, it is anticipated that research activity in this field will continue to grow. This trend highlights the importance of integrating genomic insights into both the understanding and clinical management of NHL.

There were 10 leading journals with the most relevant research related to genomic studies in NHL. The journal *Blood* contributed the highest number of publications with 57 documents, followed by *Leukemia* with 27 publications and *British Journal of Haematology* and *Leukemia and Lymphoma*, both with 26 publications each. Other prominent sources include *Genes Chromosomes and Cancer* and *Haematologica* (n = 16), *Oncogene* (n = 12), *Cancer Genetics and Cytogenetics* (n = 11), *Cancers* (n = 10) and *Oncotarget* (n = 8) (Figure 4).

Research collaboration among countries related to NHL and genomic study

In the world of science, collaboration between researchers in each country is very important. Scientists agree that collaboration between countries can reduce the scientific gap. This

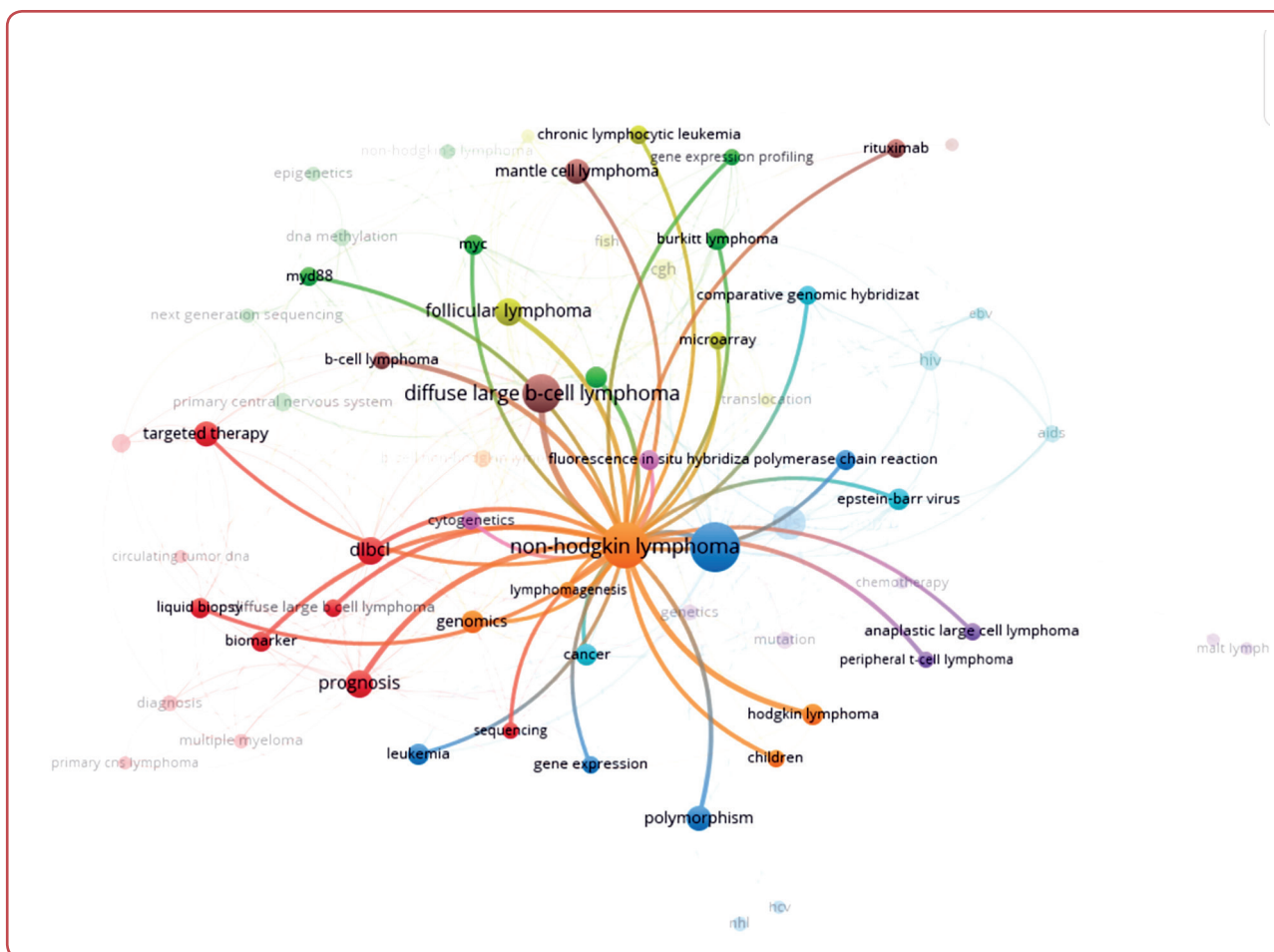


Figure 2: Visualisation of authors' most frequent keywords related to non-Hodgkin lymphoma (NHL) trends using a genomics-based approach: 1985-2024

This image illustrates the relationships between various concepts related to NHL based on scientific research. The node colours represent different categories: blue for the main concept (NHL), brown for major subtypes (diffuse large B-cell lymphoma), green for other subtypes (follicular lymphoma, mantle cell lymphoma), red for prognosis and therapy-related factors (targeted therapy, biomarker), orange for genetic and molecular factors (polymorphism, gene expression) and purple for environmental factors and additional therapies (chemotherapy, HIV). The connecting lines indicate the strength of relationships between concepts: thicker lines represent stronger and more frequently studied connections, while thinner lines indicate weaker or less commonly researched links. The opacity of the text reflects the relevance of concepts in the literature: clear text represents well-researched topics, while faded text indicates concepts with weaker associations in scientific studies.

collaboration will certainly help significantly in spreading science and also provide access to funding for countries or organisations that cannot afford sophisticated technology. Single country publication or SCP is the name of a type of article written by several authors from the same country which is an example of collaboration within a country. Then multi-country publication or MCP which means all authors come from various countries or even corners of the world who work together to collaborate in research. MCP is certainly very useful because it is more often cited than one country publication. The largest collaboration of authors related to NHL cancer with a genomic approach is the United States with a total publication of 40 MCP articles and 166 SCP articles, followed by China with 45 MCP article

publications and 117 SCP articles and Brazil had the least collaboration. Although Indonesia does not yet have a collaboration on genomic study research with NHL, Indonesia has the potential to collaborate because NHL cases are quite high (Figure 5).

The most productive country publication related to NHL and genomic study

From the most productive countries in the publication of research articles related to NHL cancer with a genomic-based approach, the United States was ranked first with the highest number of publications, namely 7328 articles, followed by Germany with 1683 articles. Spain occupied the third position with the number of publications

that have been published as much as 1031. The data illustrates that countries have contributed very important and significant in research, the development of science about NHL cancer based on a genomic approach (Figure 6).

Top 10 most cited papers related to NHL and genomic study

In the journal *Proceedings of the National Academy of Sciences* an article¹² entitled “p53 mutations in

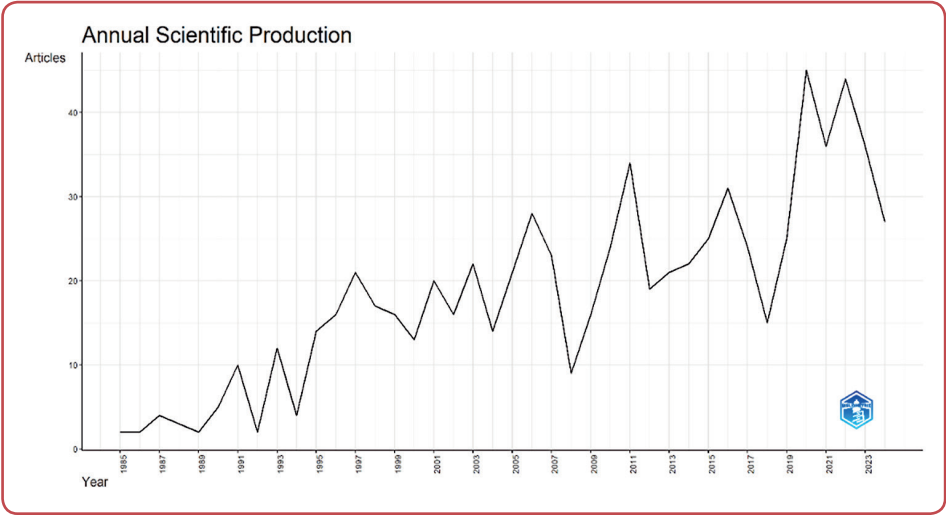


Figure 3: Trends in scientific publications on non-Hodgkin lymphoma (NHL) using a genomics-based approach: 1983-2024

The figure presents the annual trend of publications related to genomic studies in NHL from 1985 to 2024. The majority of these studies focused on understanding the genetic and molecular heterogeneity of NHL, identifying key genomic alterations that contribute to disease progression, prognosis and classification. While these insights have significantly contributed to the advancement of precision medicine and molecular target-based therapies, the primary role of genomics in these publications has been to characterise disease complexity rather than being directly applied as a therapeutic intervention.

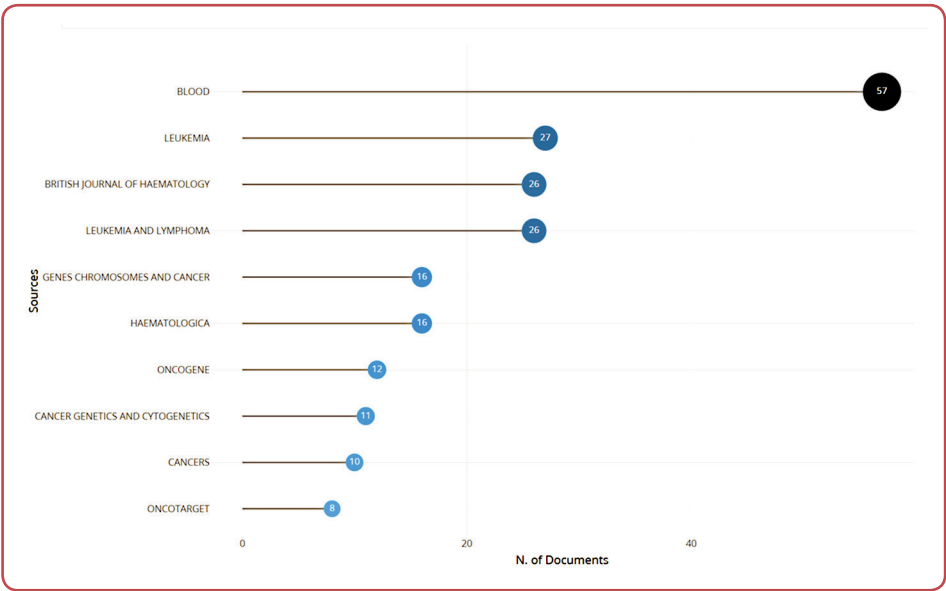


Figure 4: Source of documents related to non-Hodgkin lymphoma (NHL) using genomic information

This figure presents the distribution of research publications on NHL that incorporate genomic approaches, categorised by source journals. While these studies contribute to the development of precision medicine, their primary focus has been on understanding the genetic and molecular heterogeneity of NHL. The genomic research in these publications has largely been used to identify molecular markers, classify NHL subtypes and explore genetic pathways associated with disease progression. This foundational knowledge has paved the way for precision medicine rather than being directly implemented in therapeutic applications.

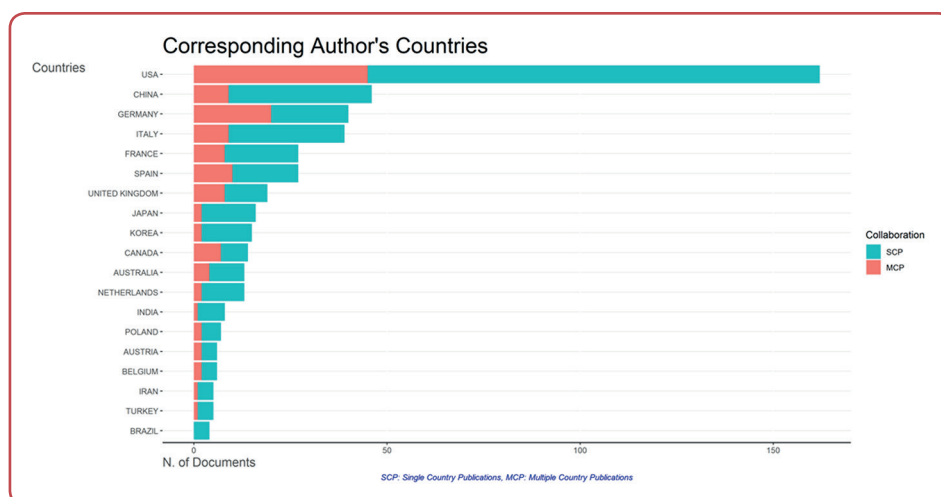


Figure 5: Collaboration among authors from multiple continents in publications non-Hodgkin lymphoma (NHL) using genomic-based approach 1983-2024

SCP (single country publication): Articles written by authors from the same country. MCP (multi-country publication): Articles co-authored by researchers from multiple countries, indicating international collaboration.

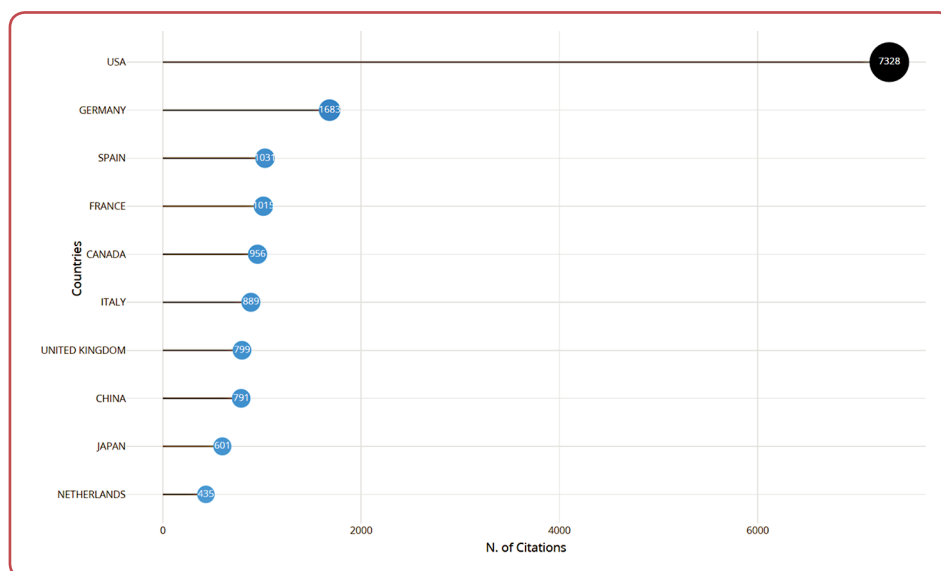


Figure 6: Most productive countries in non-Hodgkin lymphoma publications using genomics-based approaches 1985-2024

Table 2: Top 10 most cited articles on non-Hodgkin lymphoma (NHL)

Author	Year	Journal	PMID	Total citations	TC per year	Normalised TC
Gaidano G	1991	Proc Natl Acad Sci Usa	2052620	906	26.65	6.42
Naor D	1997	Adv Cancer Res	9111868	892	31.86	8.24
Pasqualucci L	2011	Nature	21390126	757	54.07	12.48
Moore PS	1996	J Virol	8523568	526	18.14	4.63
Yunis JJ	1987	New Engl J Med	3537802	503	13.24	3.49
Yokota S	1997	Leukemia	9324277	406	14.50	3.75
Pérez-Galán P	2011	Blood	20940415	344	24.57	5.67
Choi J	2015	Nat Genet	26192916	343	34.30	8.50
Silvestri F	1996	Blood	-	337	11.62	2.97
Ferri C	1993	Blood	8260706	328	10.25	2.84

human lymphoid malignancies: association with Burkitt lymphoma and chronic lymphocytic leukemia” received the highest number of citations at 906 citations, with an annual average of 26.65 citations. In addition, the article¹³ published in the journal *Advances in Cancer Research* had the second highest number of citations at 892, with an average of 31.86 citations (Table 2).

Discussion

NHL is a group of malignancies with diverse genetic backgrounds, so genomic approaches are very important to understand the pathogenesis and improve therapeutic strategies for this disease. In this bibliometric analysis, literature data were collected from the period 1985 to 2024, with a total of 740 documents sourced from 331 publications, including scientific journals, books and conference proceedings. The aim of this study is to provide a comprehensive overview of the global research trends related to NHL with a genomic-based approach. Over the past two decades, there has been a significant increase in the number of publications in this field, indicating the increasing attention to the role of genetics in the diagnosis, classification and treatment of NHL.

NHL is a cancer that has many differentiations with a varied genetic background. As shown in Figure 7 the B cell differentiation pathway in the germinal centre and how this pathway is related to the emergence of various types of NHL based

on the genetic mutations that occur. B cells originate from the bone marrow, then migrate to secondary lymphoid organs such as lymph nodes.^{19,20} After being exposed to antigen, activated B cells enter the germinal centre and undergo an important evolutionary process consisting of two zones, namely the dark zone and the light zone. In the dark zone, B cells (called centroblasts) undergo proliferation and somatic hypermutation (SHM) to increase affinity for antigens. After that, cells move to the light zone as centrocytes, where selection occurs based on affinity and class switch recombination (CSR). Cells that fail selection will undergo apoptosis, while those that pass will continue to differentiate into various forms of effector B cells, including memory cells and plasma cells.^{21, 22}

In this process, various types of NHL can arise due to disruption or mutations in certain genes that occur in the stages of B cell development. For example, mantle cell lymphoma originates from the mantle zone and is characterised by the genetic translocation t(11;14) which causes overexpression of *CCND1* (Cyclin D1).²³ Follicular lymphoma originates from the light zone and generally has the *BCL2* mutation t(14;18) which prevents apoptosis of abnormal cells.²⁴ Burkitt lymphoma, which is very aggressive, develops from the dark zone and is characterised by the *MYC* translocation t(8;14) which triggers rapid cell proliferation.²⁵ Meanwhile, GCB-DLBCL (germinal centre B-cell-like diffuse large B-cell lymphoma) and ABC-DLBCL (activated B-cell-like DLBCL) are two subtypes of DLBCL that develop in

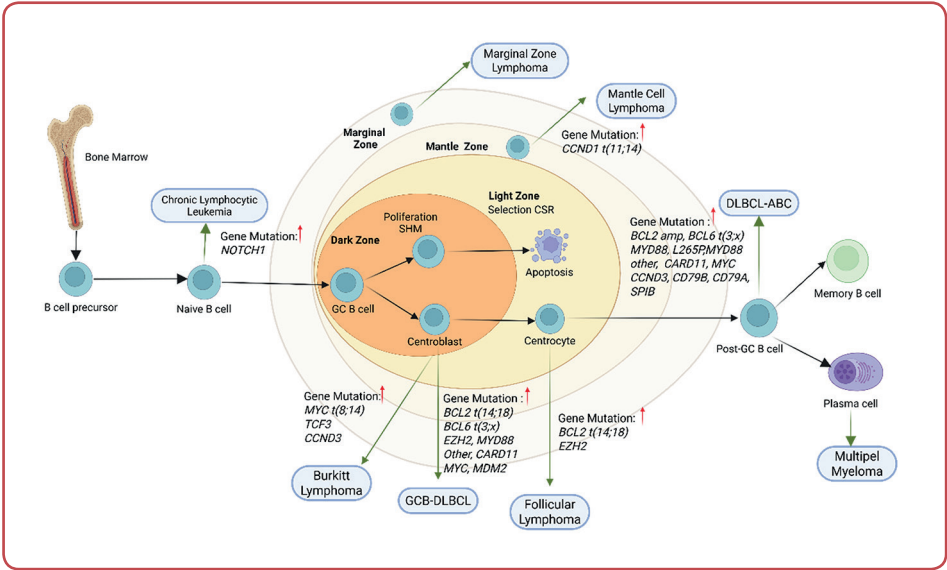


Figure 7: Overview of development and genetic mutations in non-Hodgkin lymphoma (NHL). Subtypes based on the location of B cell differentiation in the germinal centre¹⁴⁻¹⁸

different pathways. GCB-DLBCL usually originates from cells in the germinal centre with mutations in *BCL2*, *BCL6*, *EZH2*, *MYD88*, *CARD11* *MYC* and *MDM2*, while ABC-DLBCL arises after B cells exit the germinal centre with more complex mutations such as *BCL2* amplification, *BCL6*, *MYD88*, *CARD11*, *MALT1*, *CCND3*, *CD79A*, *CD79B* and *SP1B*.^{26,27}

In addition, other types of lymphoma such as marginal zone lymphoma develop from B cells in the marginal zone, which are generally triggered by chronic antigen stimulation and are usually found to have mutations in *KMT2D*, *PTPRD*, *NOTCH2* and *KLF2*.¹⁸ Chronic lymphocytic leukaemia (CLL) originates from naïve B cells that have not undergone the selection process in the germinal center, mutations in the *NOTCH1* gene play an important role. This gene is part of the *NOTCH* signalling pathway that plays a role in regulating cell proliferation, differentiation and apoptosis.²⁸ Multiple myeloma is not NHL, but originates from plasma cells which are the final stage of B cell differentiation. By understanding this pathway, we can recognise how disruptions at certain stages in the B cell maturation process can lead to different types of lymphoma, as well as the importance of certain genetic mutations in determining the biological and clinical characteristics of each disease.

Based on the data in (Figure 3), there are 10 countries that dominate the number of citations related to genetic research on NHL. The United States (USA) is the country with the highest number of citations reaching 7,328, showing a major role in the development and dissemination of knowledge in this field. The high number of citations is inseparable from the active contribution of researchers in the United States in publishing their research results in reputable international journals. This also reflects the trend that USA is becoming the main centre of publication and scientific references in NHL genetic studies. This trend is reinforced by the dominance of the journal *Blood*, published by the American Society of Hematology and is the most dominant source of publications with 57 documents. In other words, America is not only the country with the highest citations, but also the most active country in producing and disseminating scientific research through leading journals, making it an important barometer of the progress of NHL genetic research in the world.

Specifically, this bibliometric study on NHL provides significant value by providing compre-

hensive general information about publications, journals that have a significant impact and global contribution to NHL research from 1985 to 2024. However, this study also has limitations related to data collection methods, potential bias in citation metrics and the lack of qualitative insight that should be considered when evaluating the results. As a result of this, bibliometric analysis will be improved over time and contribute to more effective strategies for treating NHL through the targeted research objectives.

Conclusion

This study demonstrates a significant upward trend in publications related to the genetics of NHL over the years, with the USA emerging as the leading contributor in both publication volume and citation impact. This reflects the high global interest and attention toward NHL genetic research. *Blood* was identified as the most prolific journal, while the article by Gaidano G (1991) ranked as the most cited, highlighting its major influence in the field. Additionally, international collaboration and keyword analysis revealed evolving research focuses, particularly on genes and proteins such as *BCL2*, *MYC* and *DLBCL*. These findings emphasise the value of bibliometric approaches in mapping research directions and development in NHL genetics and support the continued growth of cross-country collaborations 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.

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