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Bibliometric Analysis of Genetic Variations in Schizophrenia

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Abstract

Schizophrenia is a complex neuropsychiatric disorder with significant genetic variation as an aetiology. This study aimed to explore genetic variation-related research in schizophrenia from a bibliometric perspective. A systematic search was conducted using the Scopus database to identify literature related to schizophrenia and genetic variation published between 2014 and December 17, 2023. The bibliometric data were analyzed using software such as biblioMagika®, Biblioshiny, and VOSviewer. A total of 344 publications were retrieved, showing a growth in the number of publications and citations over time, with the United States (US) having the highest number of publications at 121. Analysis of co-authorship by country also highlighted the US as the leading contributor. Michael Conlon O'Donovan was recognized as the most dominant author in the field. The Schizophrenia Research journal was found to be the most productive. Keyword analysis across different clusters identified significant research directions in schizophrenia, emphasizing treatment efficacy and the interaction of genetic and environmental factors. These findings provide a comprehensive perspective on the broader landscape of this research topic.

Keywords: Schizophrenia; copy number variation; polymorphisms; genetics; bibliometric.

1. INTRODUCTION

Mental illnesses, such as schizophrenia—a severe chronic psychiatric disorder marked by delusions and hallucinations—have been increasing globally [1]. It is estimated that 20 million individuals worldwide struggle with schizophrenia, which has a significant negative impact on patients, families, and society [2]. The complex aetiology of schizophrenia involves a multifaceted

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interplay of genetic, environmental, and neurodevelopmental factors [3-5]. Among these, genetic variation has emerged as a research focus, offering valuable insights into the disorder's underlying mechanisms [6].

Advancements in molecular genetics have significantly improved our understanding of schizophrenia over the past few decades. Two important types of genetic variations, specifically copy number variations (CNVs) and single nucleotide polymorphisms (SNPs), have received significant attention due to their potential roles in disease pathophysiology, susceptibility, and treatment response [7]. Both variations are critical in understanding the genetic architecture of schizophrenia. Stefansson et al. (2008) reported a significant association between large, rare CNVs and the risk of schizophrenia, highlighting the importance of structural genomic alterations [8]. Further studies identified specific CNVs linked to schizophrenia, particularly duplications at 16p11.2 and deletions at 1q21.1 [9, 10].

Genome-wide association studies (GWAS) have identified various SNPs associated with schizophrenia. The Psychiatric Genomics Consortium (PGC) has played a crucial role in gathering GWAS data across multiple cohorts, facilitating the discovery of common genetic variants linked to schizophrenia [11]. SNPs refer to single base pair changes in the DNA sequence [12], and GWAS have highlighted that schizophrenia is a polygenic disorder, with thousands of SNPs collectively contributing to the risk of developing the condition. Moreover, researchers have investigated the relationship between CNVs and SNPs in schizophrenia. A study by Rees et al. (2016) demonstrated that individuals with rare CNVs have a higher burden of common risk alleles identified through GWAS [13], suggesting a potential interplay between rare and common genetic variants in shaping the risk of schizophrenia.

Researchers use bibliometric analysis, a quantitative method to evaluate research productivity, trends, and impact within a specific field [14]. This data analysis provides valuable bibliographic information about authors, institutions, and countries of origin, as well as insights into journal performance and collaboration trends among scholars in the field [15]. It allows researchers to grasp a wide range of topics and predict future directions within specific domains. Bibliographic reviews have investigated the relationship between schizophrenia and various factors, including inflammation [16], gut microbiota [17], oxidative stress [18], magnetic resonance imaging (MRI) [19], COVID-19 [20], scientific productivity [21], dominant entities (articles) [22], and toxoplasmosis [23]. A recent bibliometric analysis by Nour El Huda et al. (2023) highlighted a growing interest in studies focusing on schizophrenia and genetic research over the past decade [24, 25].

Therefore, we conducted a bibliometric analysis of schizophrenia and genetic variation-related research, specifically emphasising CNVs and SNPs. This analysis aimed to identify key research trends, influential publications, and emerging themes, thereby providing a clearer landscape of current research and guiding future scholarly inquiries in this area.

2. MATERIALS AND METHODS

2.1 Research Questions

1. What are the total publications and citations in the field of genetic variations in schizophrenia, and how have they changed over time?
2. Who are the most relevant authors, and which influential institutions contribute

to developing the genetic variations in schizophrenia?
3. Which are the most active countries, and what are the patterns of co-authorship by countries in the field of genetic variations in schizophrenia?
4. What are the most relevant sources of research journals focusing on the genetic variations in schizophrenia?
5. What are the key themes and topics that emerge from the co-occurrence analyses of authors' keywords on genetic variations in schizophrenia?

2.2 Search Strategy

For our study, publications about schizophrenia and genetic variations were downloaded from the Scopus database on December 17, 2023. The search results were confined to publications from January 1, 2014, to December 17, 2023, that were articles written in English. The literature search and screening were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, as shown in **Figure 1**.

2.3 Data Screening and Export

Screening is crucial to ensure that the documents reviewed are relevant to the study topic [27]. Initially, the title and abstract of each document were read to confirm alignment with the topic [27]. After meticulous review, duplicates and unrelated documents were removed. Based on these screening criteria, 457 publications in scientific journals were initially selected, and 113 publications were subsequently removed. In the end, 344 publications were included for bibliometric analysis.

The number of documents initially discovered and subsequently removed and the reasons for removal were documented in the PRISMA flowchart shown in **Figure 1**. The finalized 344 publications represent a comprehensive overview of genetic variation in schizophrenia research within the Scopus database from 2014 to 2023. The publication-related data were exported to a comma-separated value (.csv) file for further cleaning and harmonization.

2.4 Data Cleaning and Harmonisation

Data cleaning and harmonization are crucial for addressing the messiness and incompleteness of Scopus datasets [27]. In our study, we used biblioMagika® 2.5.1 and biblioMagika®Split 1.6, software tools developed by Ahmi, to perform manual data cleaning and harmonization [27]. Issues such as institutional name variations, incorrect naming, multiple languages, spelling errors, and the inclusion of department names instead of full institutional names were identified and rectified. These issues can significantly affect the accuracy of the dataset.

We also used OpenRefine (https://openrefine.org/), a free, open-source tool, to clean and harmonize the data. While manual cleaning has its limitations due to human errors, tools like OpenRefine helped verify the accuracy of our manual cleaning [28]. Keyword cleaning was also conducted using OpenRefine to ensure the precision and reliability of data before further bibliometric analysis using VOSviewer and Biblioshiny.

Data Analysis

In our study on genetic variations in schizophrenia, we conducted bibliometric analyses using three advanced tools: R version 4.3.1 [29], biblioMagika® 2.5.1 [27], and VOSviewer [30]. We employed the Bibliometrix package and its web interface, Biblioshiny, for comprehensive quantitative bibliometric analysis [29, 31]. Using R Studio and the "biblioshiny()" command, metadata was uploaded and analyzed, effectively summarizing publications and citations.

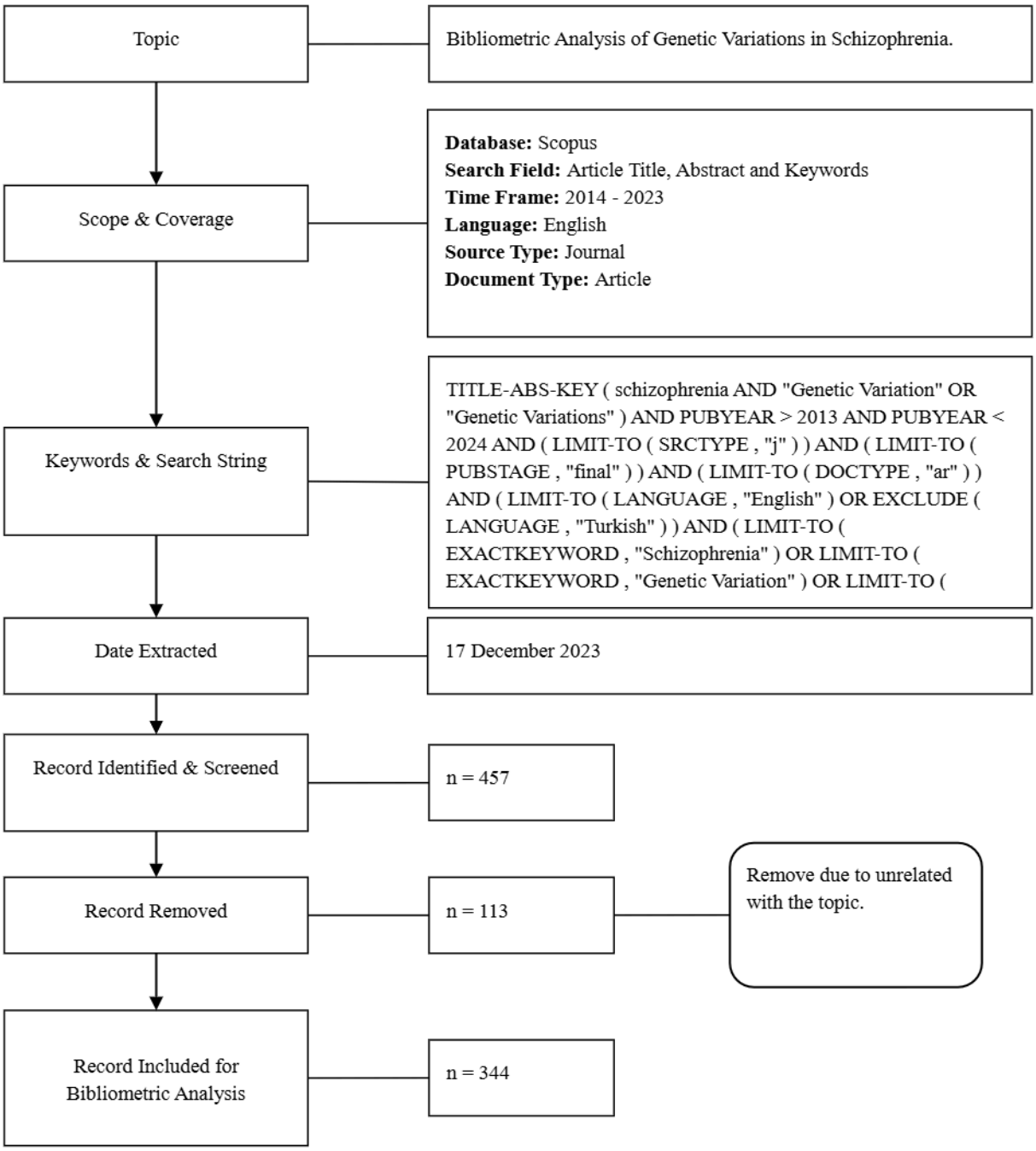

Figure 1. PRISMA Flow diagram of the search strategy [26].

An Excel-based tool, biblioMagika®, enabled insightful analysis of Scopus data, focusing on key authors, influential journals, and country-wise publication trends [27]. VOSviewer was used to reveal collaboration patterns and thematic concentrations within the scholarly community, as well as to create visual networks of co-authorship and keyword co-occurrence [30, 32, 33]. These methodologies provided a multifaceted view of the research landscape, highlighting both historical contributions and emerging trends in the field.

3. RESULTS

3.1 Analysis of Total Publications and Citations by Year

The trend of total publications and citations by year on genetic variation and schizophrenia research from 2014 to 2023 is illustrated in **Figure 2**. The total number of publications per year, represented by blue bars, experienced a steady increase starting from 2014, peaking in 2017 with 47 publications. Subsequently, there was a slight decrease, stabilizing around 30 to 35 publications per year.

Meanwhile, the orange line represents the total citations per year, which peaked in 2017 at 3,462 citations. However, it showed a noticeable downtrend, reaching 31 citations in 2023. This pattern suggests an early surge in interest and groundbreaking research on the genetic variation of schizophrenia, followed by a phase of consolidation in the number of publications. The decline in citation frequency could indicate a maturation of previous research themes or the natural citation lifecycle of foundational works published during the peak period.

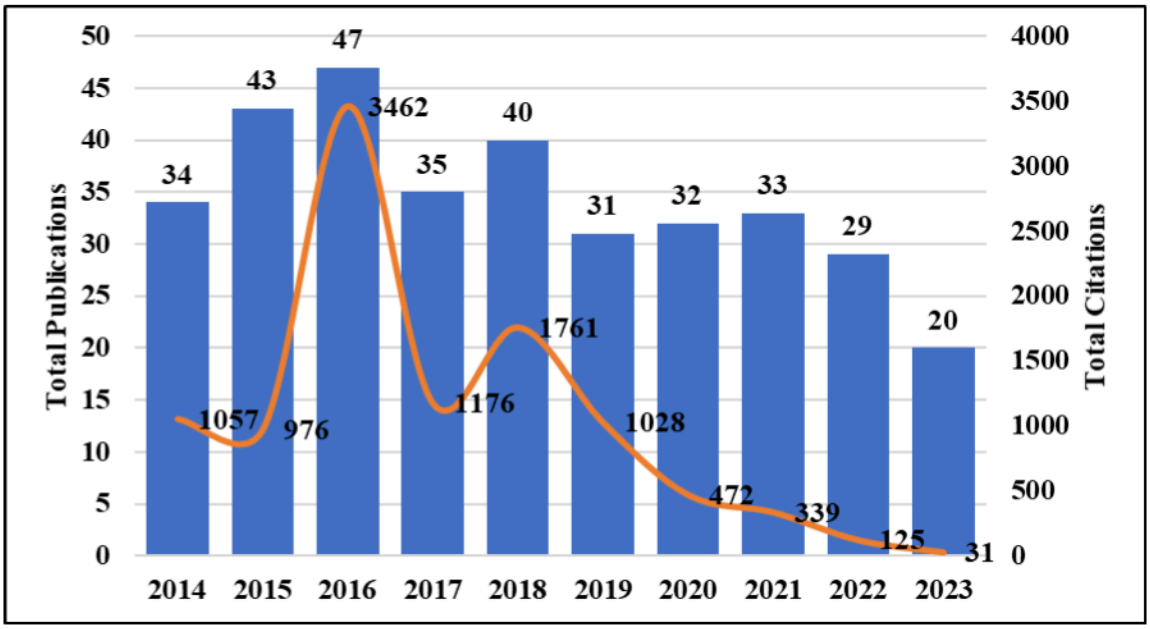

Figure 2. Total publications and citations published by year from 2014 to 2023 in genetic variation and schizophrenia-related studies retrieved from the Scopus database.

3.2 Analysis of Most Relevant Authors

In total, research papers on schizophrenia and genetic variations involved 3,414 authors. Among them, 3,370 authors published fewer than five papers, 34 published 6 to 9 papers, and 10 published more than 10 papers. **Table 1** presents the analysis of the top 10 most relevant authors in the field of genetic variation in schizophrenia, ranked by their scholarly output and impact.

Michael Conlon O'Donovan is ranked as the most influential author in the field, with 15 articles and the highest total citations of 2,194. O'Donovan has an h-index of 13, indicating that he has at least 13 papers cited 13 or more times, and a g-index of 15, suggesting that his most cited works have collectively garnered a substantial number of citations.

The geographic distribution of these top authors spans the United Kingdom, Germany, Australia, Canada, and Switzerland, indicating a global interest and collaborative effort in schizophrenia research. Notably, O'Donovan and Owen are both affiliated with Cardiff University in the United Kingdom.

Table 1. Top 10 Most Relevant Authors

Author's Name	Affiliation	Country	TP	NCP	TC	C/P	C/CP	*h*	*g*
O'Donovan, Michael Conlon	Cardiff University	United Kingdom	15	15	2194	146.27	146.27	13	15
Sullivan, Patrick F.	Charité – Berlin University Medicine	Germany	14	13	2084	148.86	160.31	11	14
Owen, Michael John	Cardiff University	United Kingdom	13	13	2036	156.62	156.62	11	13
Bousman, Chad A.	The University of Melbourne	Australia	12	11	172	14.33	15.64	8	12
Kennedy, James Lowery	Centre for Addiction and Mental Health (CAMH)	Canada	11	11	1384	125.82	125.82	9	11
Rietschel, Marcella	Heidelberg University	Germany	11	11	1068	97.09	97.09	9	11
Pantelis, Christos	The University of Melbourne	Australia	11	10	352	32.00	35.20	8	11
Rujescu, Dan	Ludwig Maximilian University of Munich	Germany	10	10	1523	152.30	152.30	8	10
Cichon, Sven	University of Basel	Switzerland	10	10	678	67.80	67.80	9	10
Nöthen, Markus Maria	University of Bonn	Germany	10	10	1037	103.70	103.70	8	10

Notes: TP=total number of publications; NCP=number of cited publications; TC=total citations; C/P=average citations per publication; C/CP=average citations per cited publication; h=h-index; and g=g-index.

3.3 Analysis of Publication and Co-authorship by Countries

Considering the authors' countries, the selected documents originated from 57 countries worldwide. The countries contributing to the productivity of scientific publications in the schizophrenia and genetic variations research area are shown in **Figure 3**. The top country was the United States, with a total of 121 publications, followed by

China and the United Kingdom, with 63 and 54 publications, respectively. Two of the top 10 countries are in Asia: China (63 publications) and Japan (22 publications). This information is vital in determining the influence and importance of countries in the research area of schizophrenia and genetic variations.

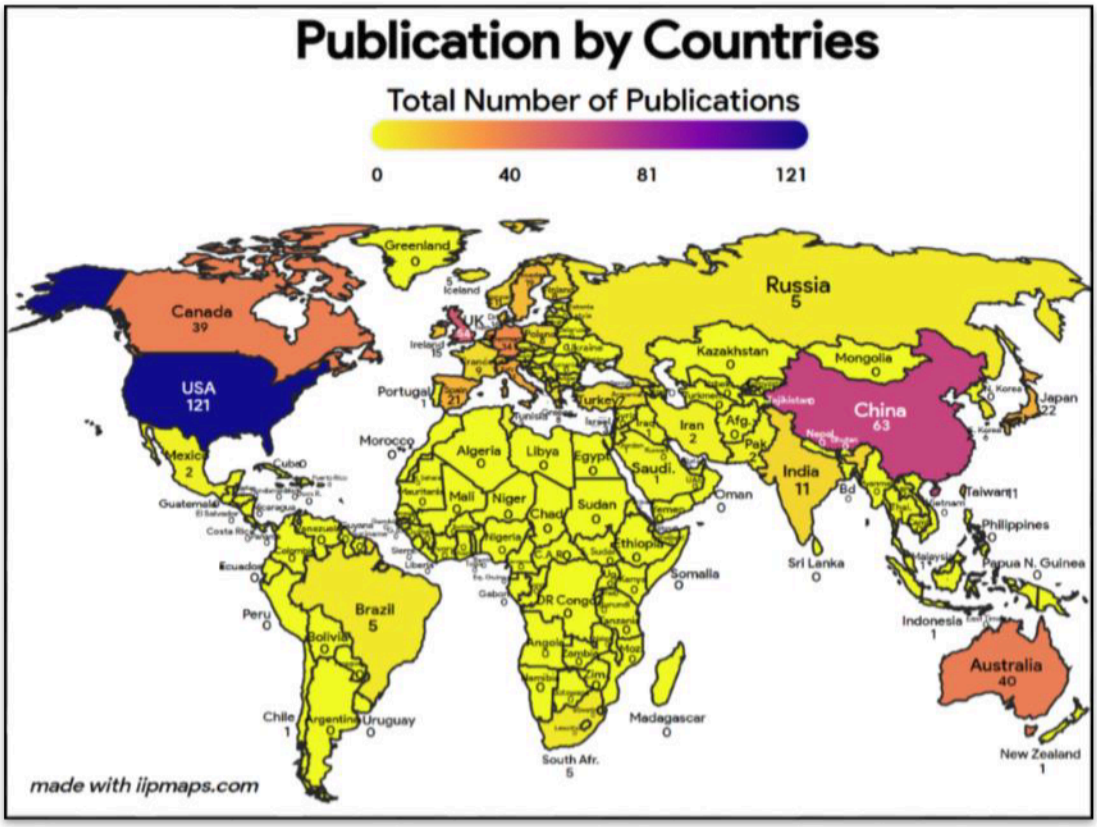

Figure 3. Publication by Countries

(Image generated from https://iipmaps.com/)

Figure 4 illustrates the network visualization map showing co-authorship of research related to schizophrenia and genetic variations among different countries, generated using VOSviewer software. In this map, circles or nodes represent individual entities, and lines or edges represent connections between those entities, indicating collaborative efforts in the research field [34]. The size of a node typically indicates its importance or prominence within the network [34].

The United States (US) appears to be the most prominent country in the network, based on the larger size of its node. This suggests that the US has contributed the most publications in this field. Other relatively large nodes include China, Germany, Japan, Australia, and the United Kingdom, indicating significant contributions from these countries.

The colors in the map likely represent clusters of countries that have co-authored research papers together more frequently. For instance, the United States appears to be in a cluster with China and Singapore, all highlighted in purple. This might suggest stronger research collaborations between

these countries. Similarly, Australia, Brazil, and India form another cluster, highlighted in yellow, possibly indicating frequent co-authorship among these countries.

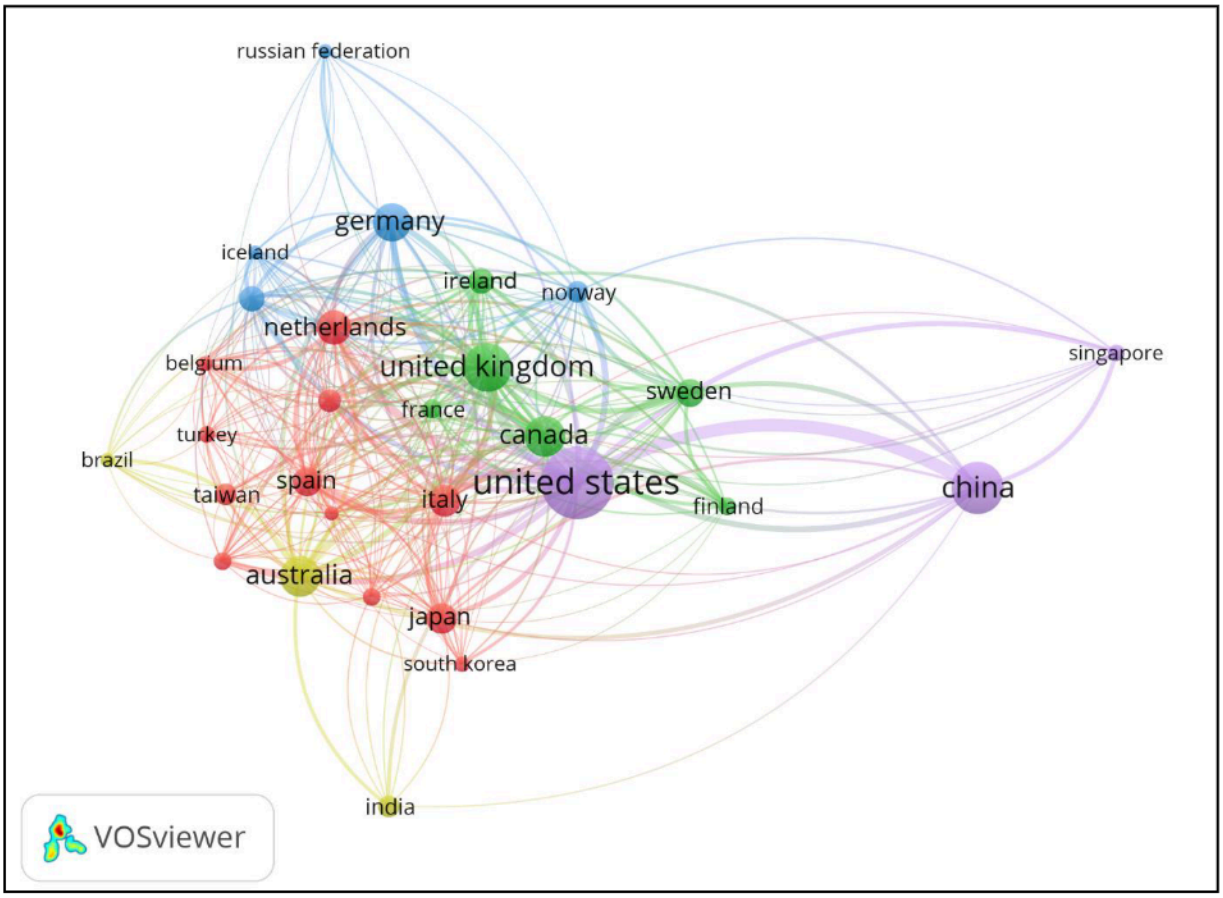

Figure 4. Network visualisation map of the co-authorship by countries.

3.4 Analysis of Most Relevant Sources

The articles on schizophrenia and genetic variations have been published in 149 different journals. **Figure 5** shows the top 10 most productive scientific journals in this field. The most productive journals, with more than 10 publications, are Schizophrenia Research, Translational Psychiatry, Psychiatry Research, American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, Schizophrenia Bulletin, Molecular Psychiatry, and Scientific Reports. These journals reflect the subject areas of psychiatry and genetics.

The figure includes journals specifically focused on schizophrenia research (Schizophrenia Research, Schizophrenia Bulletin) as well as more general psychiatry journals (American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, Psychiatric Genetics). Additionally, Molecular Psychiatry and Schizophrenia Bulletin have the most citations (545 and 535, respectively) among the journals listed for schizophrenia and genetic variations research. This indicates that these journals publish influential research in the field.

Regarding top publishers, Elsevier and Springer Nature are the most prominent, with three (Schizophrenia Research, Psychiatry

Research, Biological Psychiatry) and two (Translational Psychiatry, Molecular Psychiatry, Scientific Reports) journals on the list, respectively.

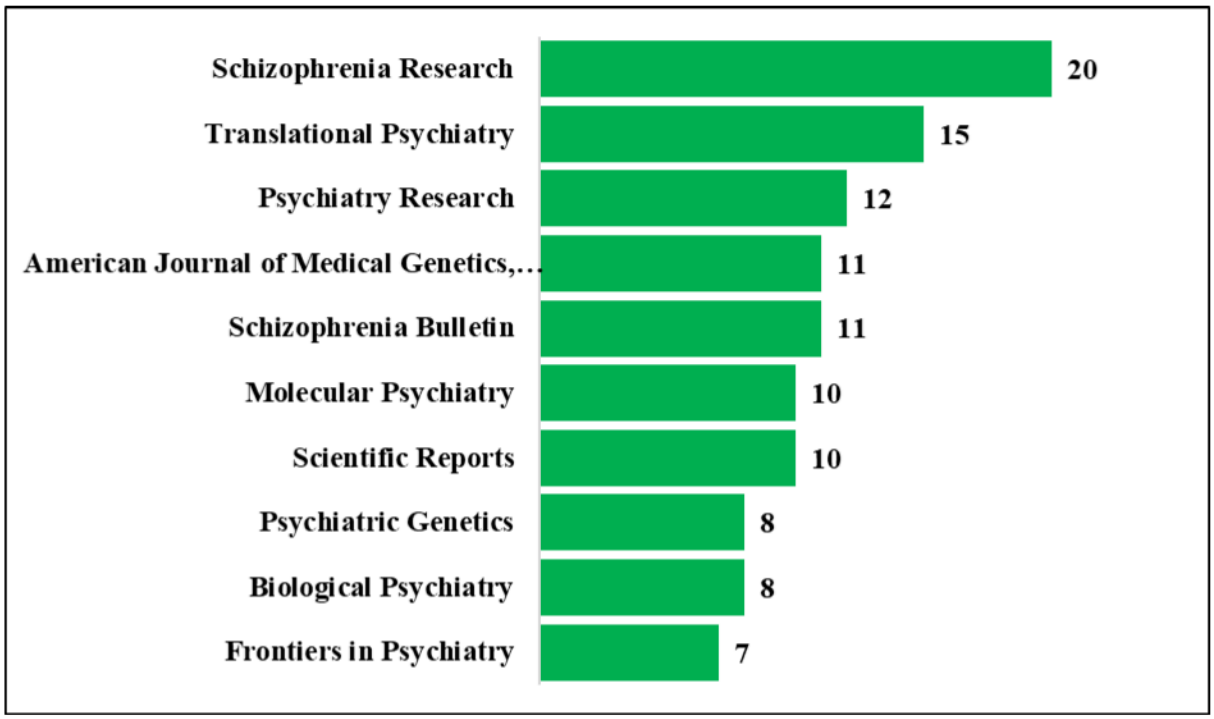

Figure 5. Top 10 most productive scientific journals in schizophrenia and genetic variations-related studies.

3.5 Analysis of Co-occurrence of Authors' Keywords

A network visualization map constructed using VOSviewer software shows the co-occurrence of author keywords related to genetic variation studies in schizophrenia (**Figure 6**). This figure also highlights the leading keywords used by authors, representing the content of their research. In this visualization, circles or nodes represent keywords, and lines or edges represent the co-occurrence of these keywords in the same article. The size of a node indicates its frequency of occurrence, and the thickness of an edge indicates the strength of the co-occurrence relationship between keywords [35].

The larger nodes in the network represent keywords that appear more frequently across the schizophrenia and genetic variation research articles analyzed. The most prominent keywords include schizophrenia, SNP, CNV, gene, expression, brain, antipsychotic, and development. This suggests that these are the most common areas of focus within the research, likely investigating how genetic variations (SNPs and CNVs) influence gene expression in the brain, potentially affecting development and contributing to schizophrenia.

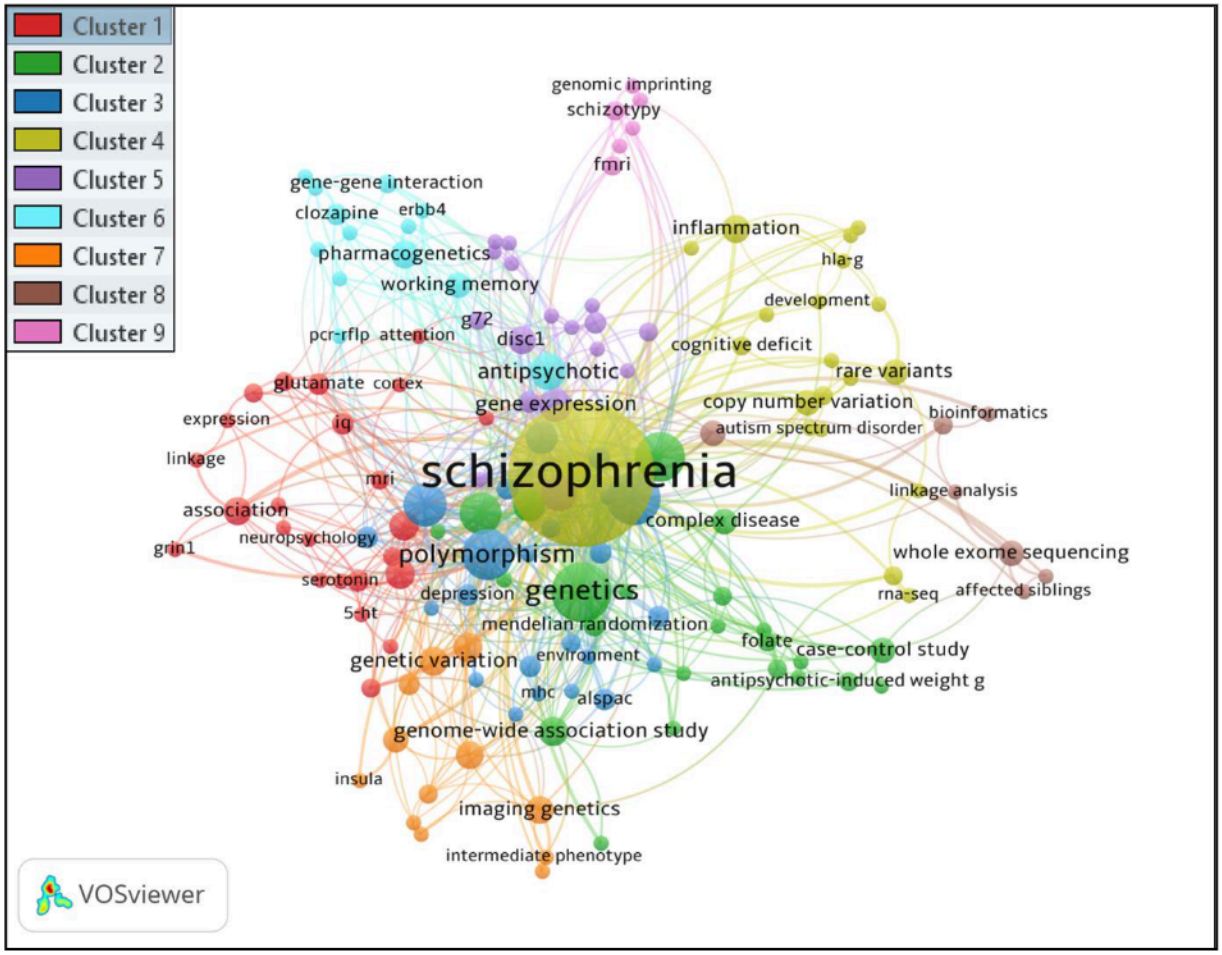

Figure 6. Network visualisation map of the co-occurrence of the author's keywords in schizophrenia and genetic variations-related studies.

The edges connecting the keywords represent thematic relationships between different research areas. For instance, the keyword "schizophrenia" is connected to keywords like "SNP," "CNV," "gene," and "expression," reflecting a focus on how genetic variations influence genes and their expression in the brain. Similarly, "gene" connects to "expression" and "pathway," suggesting a focus on how gene expression is involved in disease pathways.

The different colors in the map represent clusters of keywords that co-occur more frequently together. There are nine clusters highlighted in this analysis. Cluster 1 (red) contains keywords like "schizophrenia," "antipsychotic agents," and "antipsychotic treatment." Cluster 2 (green) includes keywords related to "genome-wide association study" and "GWAS." Cluster 3 (blue) features keywords like "polymorphism," "environment," and "gene-environment interaction." Cluster 4 (yellow) comprises "rare variants," "copy number variation," and "CNV."

Cluster 5 (purple) includes keywords such as "gene expression," "functional genomics," and "pathway analysis." Cluster 6 (light blue) consists of keywords like "gene-gene interaction," "erbb4," and "chrm1." Cluster 7 (orange) groups keywords such as "imaging genetics," "magnetic resonance imaging

(MRI)," "voxel-based morphometry (VBM)," and "insula." Cluster 8 (brown) includes "bioinformatics," "whole genome sequencing," and "whole exon sequencing." Lastly, Cluster 9 (pink) comprises keywords like "genetic risk," "schizotypy," and "genomic imprinting." By analyzing these clusters, we can identify thematic areas within the broader field of schizophrenia and genetic variation research.

DISCUSSION

This bibliometric analysis study examined the development of research on schizophrenia and genetic variation over the past decade. The analysis found that the number of published articles and citations related to schizophrenia and genetic variations increased from 2014 to 2017 and then stabilized around 30 to 35 publications per year in subsequent years. A previous bibliometric study on global scientific publications on schizophrenia from 1975 to 2022 found that the number of publications grew substantially starting in 2011 [36]. This research trend can be attributed to the increasing recognition of the role of genetic variation in the development of schizophrenia [37] and, consequently, increased research funding in this field.

The study identified 3,414 authors who have contributed to research on schizophrenia and genetic variations. While most authors have published fewer than five papers, a few have been highly productive. The top three authors, based on total publications, are Michael Conlon O'Donovan (15 articles), Patrick F. Sullivan (14 articles), and Michael John Owen (13 articles). Michael Conlon O'Donovan stands out with the highest h-index (13) and g-index (15), indicating impactful publications.

Institutional affiliation reveals a concentration of expertise. Both Michael Conlon O'Donovan and Michael John Owen are affiliated with Cardiff University, UK, indicating that this institution has actively contributed to the field. Cardiff University has become the most prominent institution in contributing to the development of schizophrenia studies, attributable to the initiation of the Centre for Neuropsychiatric Genetics and Genomics (CNGG) in 2009, which brings together world-leading researchers to investigate the major causes of mental health problems.

Patrick F. Sullivan is affiliated with Charité-Berlin University Medicine in Germany, highlighting the multinational nature of research efforts in studies of genetic variations in schizophrenia. Michael Conlon O'Donovan has the highest total citations (2,194), owing to his career as a world-leading academic researcher known for his work on schizophrenia, psychiatry, bipolar disorder, genome-wide association studies, and clinical psychology. His outstanding citation count is followed by Patrick F. Sullivan (2,084) and Michael John Owen (2,036).

O'Donovan's schizophrenia research spans a wide range of disciplines, including genetics, psychosis, and depression. His genetics association studies often draw connections to other fields, solidifying his position as the top author in schizophrenia and genetic variations research, with the highest total citations.

The analysis of publications by country revealed that the United States is the most active country in schizophrenia genetic variation research, with 121 publications, followed by China (63) and the United Kingdom (54). Notably, two Asian countries, China (63) and Japan (22), are in the top 10, highlighting the global nature of research

efforts in this field, with both established and emerging players contributing significantly.

The network visualization map revealed collaboration patterns among countries in schizophrenia genetic variation research, with the United States being the most prominent contributor. Other nations like China, Germany, Japan, Australia and the UK also play significant roles. The map further suggests potential regional research clusters, with the US collaborating more frequently with China and Singapore, while Australia, Brazil and India form another collaborative group. This data indicates strong individual country contributions and the emergence of regional research partnerships.

The study identified 149 journals publishing research on schizophrenia and genetic variations. Among these, several stand out for their publication volume. Journals such as Schizophrenia Research, Translational Psychiatry, Psychiatry Research, and the American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics focus specifically on this research area. They are joined by broader psychiatry journals, highlighting the field's interdisciplinary nature. Furthermore, citation counts reveal the influence of specific journals. Molecular Psychiatry and Schizophrenia Bulletin lead with 545 and 535 citations, respectively, suggesting they publish highly impactful research. Interestingly, both Elsevier and Springer Nature emerge as prominent publishers, with several top journals under their wing. This data provides valuable insight into the publication landscape for schizophrenia genetics research.

A co-occurrence analysis of author keywords unveils central themes in schizophrenia genetics research. Thematic relationships are further revealed by emerging keyword clusters with distinct research directions in schizophrenia. Nine thematic areas were identified in our study. These areas include the genetic basis of schizophrenia (red), the application of GWAS in gene identification (green), the interplay of genetic variations with environmental influences (blue), the influence of rare variants on disease mechanisms (yellow), gene co-expression and pathway analysis (purple), treatment outcomes and antipsychotic effectiveness (light blue), imaging genetics (orange), the use of advanced genomic technologies and computational approaches to uncover the genetic basis of schizophrenia (brown), and understanding genetic predispositions underlying schizophrenia susceptibility, related personality traits, and the role of epigenetic mechanisms in gene expression regulation (pink). These thematic area analyses provide valuable insights into the core research questions and directions within the field of schizophrenia genetics, which could ultimately lead to improved treatments for this complex disorder.

This study has several limitations. Firstly, the data were retrieved solely from Scopus, which, although considered the most reliable and trustworthy database for bibliometric studies [38], may have missed some articles. Secondly, only English publications were included in this study, which may lead to selection bias in terms of publication language. Lastly, the literature produced before 2014 was not fully assessed due to the study cutoff time. Studies investigating the relationship between genetic variation and schizophrenia are limited, despite the potential significant role that genetic variations may play in the pathogenesis and treatment of schizophrenia. Most existing

studies are of cross-sectional design, making it challenging to establish causality. Therefore, future research should focus on the role of genetic variations in the pathogenesis of schizophrenia and effective treatments using data analysis approaches that better avoid confounding factors.

CONCLUSION

This study significantly advances our understanding of the bibliometric landscape surrounding schizophrenia and genetic variations. By collecting and analyzing an extensive dataset of 344 documents from Scopus, our research provides a detailed overview of the bibliography in this field from 2014 to 2023. Using tools such as Biblioshiny, biblioMagika®, and VOSviewer, we identified the most influential authors, notably Michael Conlon O'Donovan, Patrick F. Sullivan, and Michael John Owen. The global distribution of research activity, with the US, China, and the UK leading, signifies a worldwide commitment to unraveling the complexities of schizophrenia. Schizophrenia Research was highlighted as the top publication venue.

The recurrent themes identified through keyword analysis reflect the field's current state and provide insights into future research pathways. These findings are crucial as they offer a comprehensive perspective on the broader landscape of this research topic, guiding novice researchers in their future work. These insights create a knowledge bridge, helping new researchers build on a solid foundation of existing literature, inspiring new areas of study, and contributing to a future where the interplay between genetics and schizophrenia is comprehensively understood.

Our findings serve as a history of scientific endeavor and a guide for the next generation of researchers toward opportunities for discovery and innovation in mental health science. This article demonstrates the power of bibliometric analysis in shaping the future directions of scientific inquiry and enriching the collective quest for knowledge.

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التحليل الببليومتري للاختلافات الجينية في الفصام

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الملخص

الحلفية والاهداف : الفصام هو اضطراب نفسي وعصبي معقد، تحدث فيه فيه تباينات تغيرات جينية ملحوظة مهمة والتي تعتبر المُسبّب للمرض. وهدفت هذه الدراسة إلى استكشاف الأبحاث ذات الصلة بالاختلاف الجيني لدى مرضى في الفصام من منظور ببليومتري.

منهجية الدراسة : تم اجراء بحث منهجي في قاعدة البيانات سكوبس لتحديد الأدبيات ذات الصلة بالفصام، والتنوع الجيني المنشورة بين عام 2014 و17 ديسمبر عام 2023 .تم تحليل البيانات الببليومترية باستخدام برامج مثل، ®biblioMagika، وBiblioshiny، وVOSviewer. بلغ العدد الإجمالي للأبحاث التي تم استرجاعها 344 منشورًا، الأمر الذي يدل على ازدياد في أعداد المنشورات والاستشهادات بمرور الوقت، مع وجود العدد الأكبر من المنشورات في الولايات المتحدة بعدد 121.

الاستنتاجات أظهر تحليل التأليف المشترك حسب الدولة أنَّ الولايات المتحدة هي المساهم الرئيسي. واعتُرِف بالمؤلف مايكل كونلون أودونوفان على أنَّه المؤلف صاحب أعلى مساهمة في المجال. تم ايجاد مجلة بحث الفصام هي الأكثر إنتاجية. حدَّدَ تحليل الكلمات الرئيسية عبر المجموعات المختلفة اتجاهات بحثية مهمة في مرض الفصام، مع التركيز على فاعلية العلاج، وتفاعل العوامل الوراثية والبيئية. توفر هذه النتائج منظورًا شاملاً على نطاق واسع لهذا الموضوع البحثي.

الكلمات الدالة: الفصام، اختلاف عدد النسخ، تعدد الأشكال، علم الوراثة، الببليومترية.