ORIGINAL RESEARCH ARTICLE

# Exploring A Decade of Research on Down Syndrome: A Bibliometric Analysis

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## ABSTRACT

**Aims:** Trisomy 21, the presence of a supernumerary chromosome 21, results in a collection of clinical features commonly known as Down syndrome (DS). DS is among the most genetically complex of the conditions that are compatible with human survival post-term, and the most frequent survivable autosomal aneuploidy. The research landscape of Down Syndrome is not portrayed clearly by published literature. This study aimed to analyse published literature globally by the medical fraternity in the field of Down syndrome using bibliometric analysis.

**Methodology:** Bibliometric information on literature regarding said topic using specific keywords was searched and collected in the Scopus database. VOSviewer (1.6.18) was applied to conduct bibliometric analysis and visualization.

**Results:** The study highlighted the most significant journals, authors, co-cited authors, institutions, keywords co-occurrence, and most contributed countries in the area of Down syndrome based on bibliometric analysis of studies taken from the database of Scopus for the past ten years (2014–first quarter of 2023).

**Conclusion:** This analysis applied state-of-the-art bibliometric and scientific mapping methods to provide researchers and other stakeholders with a panoramic view of Down syndrome from 2014 –2023. Publications in the field show a stable trend, within developed countries. Funding support is much needed to proceed with such topics as Down syndrome and that may be the reason why underdeveloped countries are still behind in the field.

**Keywords:** Down Syndrome, Chromosome, Bibliometric Analysis

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## INTRODUCTION

Down syndrome (DS) is the prevailing autosomal chromosomal anomaly in humans that is viable after birth, with an estimated prenatal mortality rate of 70-80% and occurs in approximately 1 in 700 live births. The syndrome under consideration is distinguished by a distinct congenital phenotype that encompasses cognitive impairment, reduced muscle tone, and the manifestation of neuropathological features associated with Alzheimer's disease occurring once the individual reaches 35 years of age. The syndrome is referred to as Down syndrome, named in honor of the English physician John Langdon Down, who initially documented its distinctive traits in 1866 (Down, 1866).[1-3] The phenotype of Down syndrome, also known as trisomy 21, is distinguished by anomalies that impact a wide range of organs and organ systems.[1,4] While there is considerable variation in the degree and severity of abnormalities observed among individuals, it is universally acknowledged that all persons with this condition exhibit some type of intellectual disability.[5] This handicap has been linked to certain regions of the brain as well as the impaired execution of certain cognitive activities.[6] Individuals diagnosed with Down syndrome (DS) exhibit a heightened susceptibility to several health disorders, such as hypothyroidism, autoimmune illnesses, obstructive sleep apnea, epilepsy, and auditory and visual impairments.[7] The initial documentation of an association between an additional chromosome 21, known as a supernumerary chromosome 21, and the phenotypic characteristics of Down syndrome (DS) was initially disclosed in 1959.[8] This finding served as a significant milestone in the advancement of genetic medicine.[9] The condition known as Down syndrome (DS) is mostly caused by the presence of an additional copy of chromosome 21, resulting in a full trisomy of this chromosome in around 95% of instances.[10] The other instances can be attributed to either mosaicism for chromosome 21 or the acquisition of a structural rearrangement resulting in partial trisomy of a significant portion of its genetic material. Full trisomy 21 and mosaicism are non-heritable conditions that arise due to abnormalities in cell divisions during the early stages of egg, sperm, or embryo development.[11,12] Despite the substantial knowledge available on Down syndrome (DS), individuals may still encounter challenges in effectively managing and comprehending the condition at times.[13]

Bibliometric analysis (BA) helps to quantify and portray the research landscape of a particular field of interest. BA compares and creates maps to find the networking of research publications across countries, journals, institutions, and so on. BA is having an uptrend in medical research prior to engaging in a systematic review.[14,15] Hence, conducting a BA will reveal the nature of research conducted in the field of Down syndrome which in turn implicates policymakers and stakeholders about the necessity of further research. Therefore, this present study aims to conduct a BA of global publication in the field of Down syndrome over a decade.

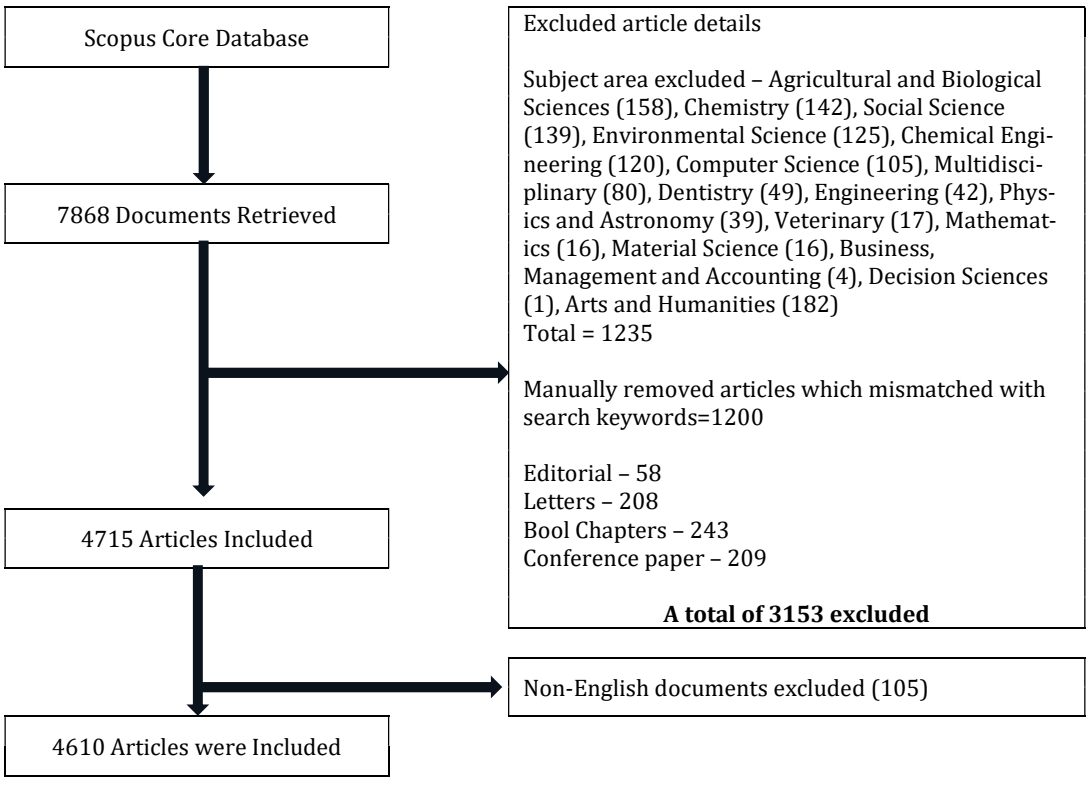


**Figure 1: Flow Chart of Data Collection**

## METHODOLOGY

**Data sources:** This study was conducted in accordance with steps and procedures proposed by a cardinal article, which proposed the crux of bibliometric analysis.[16] Commonly Web of Science, Dimensions, PubMed, Google Scholar, and Scopus are used for research analysis, as these databases show correlations across citation counts and article counts. However, to avoid bias associated with different bibliometric formats of databases we utilized Scopus for literature search. Following the guidelines of BA, the search strategy formulated was based on the review of literature for systematic reviews.[17] Pertinent keywords were identified and MeSH terms were selected before implementing the search in the database.

The phrase "Down's syndrome" OR "trisomy" OR "chromosome" OR "mongolism" OR "genetic" OR "prenatal" AND children OR "child" OR "infant" OR "toddler" OR "preschooler" OR "mother" was used in order to include all publications about research in down syndrome located in Scopus database. The Boolean operator "AND" was used to limit the search to publications that addressed all fields simultaneously. The asterisk was included in order to replace the word endings in order to encompass all possible endings. The time span was from 2014 to the first quarter of 2023, only articles and review articles published in the English language are included for analysis. The procedure of data collection is presented in Figure 1. Initially, the principal investigator conducted a search in the Scopus database using the search terms described above, hitting 7868 records. Subsequently, documents that were not articles or review articles were excluded, and sources almost unrelated to the health and health sciences field were also excluded. 4715 records were obtained. Finally, after excluding 105 documents that were not published in English, 4610 documents were finally included in the analysis.**Data analysis:** Java-based bibliometric tool, VOS viewer (1.6.18) was used to analyze data extracted from the database. VOS viewer was used to conduct citation analysis for authors, countries, and institutions. Bibliometric coupling for journals, keyword occurrences, and co-citation networks of authors were generated. Total link strength was automatically calculated by VOS viewer and percentage using windows Microsoft Excel. The nodes in the figures indicate the number of publications and links that represent collaborations between items, the higher the collaboration thicker the lines across nodes.

## RESULTS

**Global Publications Trends:** A total of 4610 publications were included in the final analysis, which included 4047 articles and 563 review articles. The publications included in this study received a total of 47561 citations, and each publication received an average of 10.3 citations. The annual distribution of publications is shown in **Figure 2**. From 2014 to 2023, there was an increasing publication trend in the field of Down syndrome when it reached the peak of annual publication (646 documents) in 2022. Throughout the period of 10 years, an average of 461 documents were published per year

**Analysis of countries and organizations:** In the field of research related to Down syndrome, a total of 132 countries contributed to at least one publication between 2014 and 2023. As shown in Table 1, the USA had the highest number of publications in the field (592 documents), accounting for 36.05% of the total, followed by the United Kingdom, Australia, Italy, and Canada. The USA had the highest ACI followed by Sweden and the UK which depicts the significant quality of research in the arena of Down syndrome. The top 15 countries that were active in this area of research publications are presented in Table 1; the inclusion criteria set was countries with a minimum of five publications and a minimum of five citations for each document (h index 5), and 60 countries met these criteria.

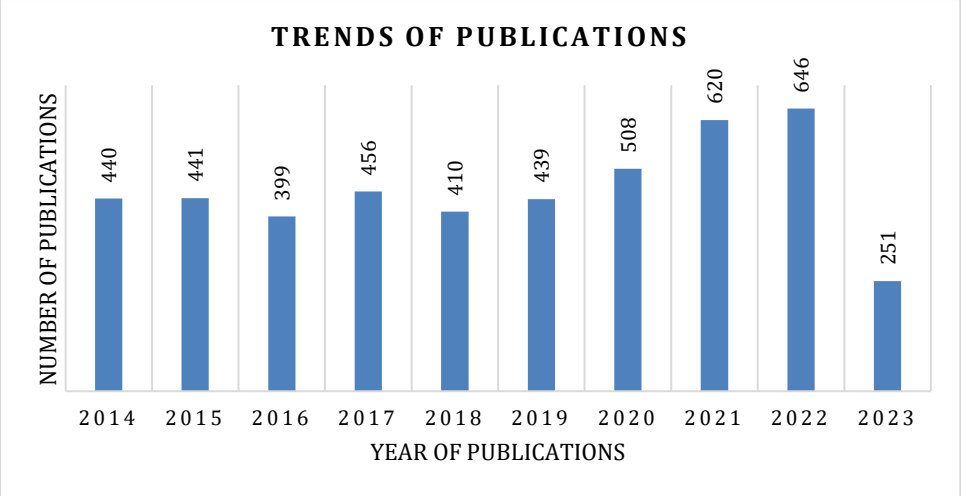


**Figure 2: Graph showing annual publications in the field of Down syndrome**

**Table 1: Top 15 active countries in research related to Down syndrome**

| Sr No | Country | Documents | Percentage | Citations | ACI | TLS |
|---|---|---|---|---|---|---|
| 1 | United States | 592 | 36.05% | 26277 | 44.38 | 164 |
| 2 | United Kingdom | 187 | 11.39% | 6629 | 35.4 | 101 |
| 3 | Australia | 96 | 5.85% | 2384 | 24.83 | 31 |
| 4 | Italy | 95 | 5.79% | 2827 | 29.75 | 57 |
| 5 | Canada | 87 | 5.30% | 4611 | 53 | 55 |
| 6 | India | 81 | 4.93% | 781 | 9.64 | 17 |
| 7 | Brazil | 74 | 4.51% | 1029 | 13.9 | 13 |
| 8 | France | 55 | 3.35% | 1710 | 31.09 | 48 |
| 9 | China | 52 | 3.17% | 560 | 10.7 | 19 |
| 10 | Germany | 46 | 2.80% | 1285 | 27.93 | 49 |
| 11 | Japan | 43 | 2.62% | 761 | 8.39 | 14 |
| 12 | Sweden | 40 | 2.44% | 1456 | 36.4 | 22 |
| 13 | Turkey | 36 | 2.19% | 321 | 8.9 | 06 |
| 14 | Netherlands | 35 | 2.13% | 905 | 25.85 | 31 |
| 15 | Denmark | 34 | 2.07% | 981 | 28.85 | 34 |

ACI- Average Citations per Item, TLS – Total Link Strength

**Table 2: Top 10 active organizations in research related to Down syndrome**

| No. | Organizations | Country | Documents | % | Citations | TLS |
|---|---|---|---|---|---|---|
| 1 | National center on birth defects and developmental disabilities, centers for disease control and prevention, Atlanta, ga, united states | United States | 10 | 63.5 | 635 | 9 |
| 2 | Department of Epidemiology, University of North Carolina, chapel hill, NC, united states | United States | 7 | 1.7 | 12 | 15 |
| 3 | Department of Pathology, Ohio state university, Columbus, oh, united states | United States | 5 | 112 | 560 | 12 |
| 4 | Division of pediatric epidemiology and clinical research, department of pediatrics, university of Minnesota, Minneapolis, mn, united states | United States | 5 | 27 | 135 | 13 |
| 5 | New jersey department of health and senior services, Trenton, NJ, united states | United States | 5 | 3.4 | 17 | 19 |
| 6 | University of Minnesota cancer center, Minneapolis, mn, united states | United States | 5 | 25.8 | 129 | 12 |
| 7 | Department of Pediatrics, college of medicine, university of Arkansas for medical sciences, little rock, ar, united states | United States | 4 | 14.25 | 57 | 16 |
| 8 | Department of epidemiology, college of public health, university of Iowa, Iowa city, ia, united states | United States | 4 | 8.75 | 35 | 16 |
| 9 | New York state department of health, troy, ny, united states | United States | 3 | .03 | 01 | 19 |
| 10 | Department of human genetics, emory university, Atlanta, ga, united states | United States | 3 | 17.6 | 53 | 09 |

TLS- Total Link Strength

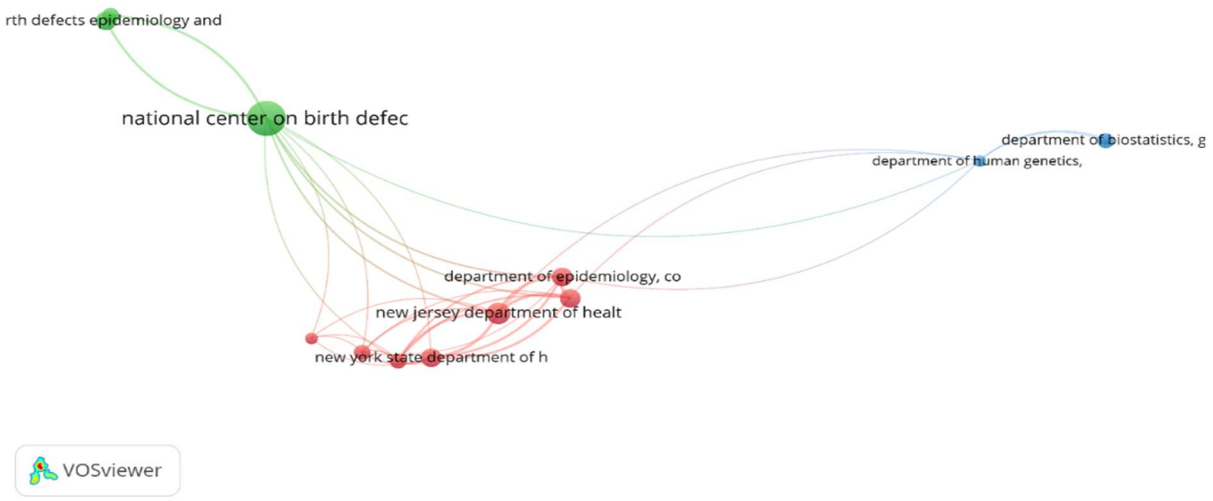


**Figure 3: Active organizations and linkages between them**

The top ten organizations involved in extensive research on the field are presented in Table 2, organizations with h index 3 were sorted and 35 organizations with 5 clusters met the threshold, which reveals National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, United States followed by Department of epidemiology, university of north Carolina, chapel hill, NC, united states have a significant number of publications and citations for their publications. All the top contributed organizations belonged to the United States, Fig 3 illustrates the further explanation of clusters and the linkages between the organizations.

### Analysis of Journals

**ACI- Average Citations per Item, IF-Impact Factor:** **Table 3** highlights the sources of publications and the total number of publications over the same time frame. We set inclusion criteria of h index 2 for journals and 635 journals met the criteria American Journal of Medical Genetics and Journal of intellectual disability research stood first and second.

**Collaborative Network of Countries in Research:** Research collaboration of countries in the arena of DS was done with the mapping of a minimum of two documents and five citations as the threshold. Out of 131 countries 82 met the criteria and a network map was created as **Figure 4**. The network was spread out in 16 clusters with a total LS 0f 485 United States led as the top country with maximum collaborations followed by the United Kingdom, Italy, Germany, and China. These can be correlated with the number of documents and total link strength of each country mentioned in **Table 1**.

**Citation and co-citation network of authors:** Of the 201720 authors, only 1969 authors met the threshold of h index 25; among them, Skotko B G received a maximum citation of 395 followed by Marcus L with 360 citations and Fidler D J with 352 citations stood in the third position. there were links associated with some authors. **Figure 5:** depicts the co-citation network of authors globally;

**Table 3: Top ten active journals in the domain of research in Down syndrome**

| Journal | Documents | % | Citations | ACI | IF | Quartile |
|---|---|---|---|---|---|---|
| American journal of medical genetics | 163 | 25.00 | 1651 | 22.03 | 2.58 | Q2 |
| Journal of intellectual disability research | 106 | 16.26 | 1550 | 20.68 | 3.64 | Q2 |
| International journal of pediatric otorhinolaryngology | 80 | 12.27 | 749 | 9.99 | 1.62 | Q2 |
| Journal of pediatrics | 74 | 11.35 | 1070 | 14.28 | 5.1 | Q1 |
| Pediatric blood and cancer | 48 | 7.36 | 388 | 5.18 | 3.83 | Q1 |
| International journal of environmental research and public health | 38 | 5.83 | 148 | 1.97 | 4.61 | Q2 |
| Journal of pediatric surgery | 38 | 5.83 | 471 | 6.28 | 2.6 | Q1 |
| American journal on intellectual and developmental disabilities | 36 | 5.52 | 377 | 5.03 | 2.29 | Q1 |
| Pediatric Cardiology | 35 | 5.37 | 265 | 3.54 | 1.83 | Q2 |
| Otolaryngology - head and neck surgery | 34 | 5.21 | 826 | 11.02 | 1.62 | Q1 |

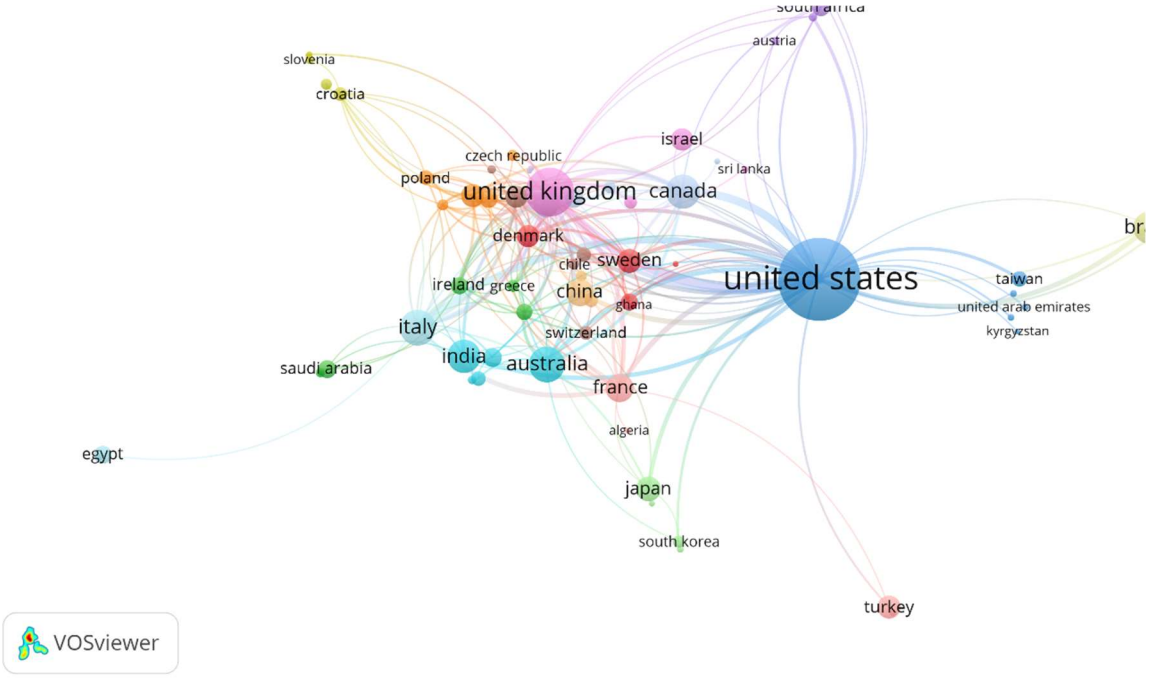


**Figure 4: Bibliometric Coupling of countries with the most research collaborations**

Note: The figure was generated using a Java-based bibliometric tool, VOS viewer (1.6.18)

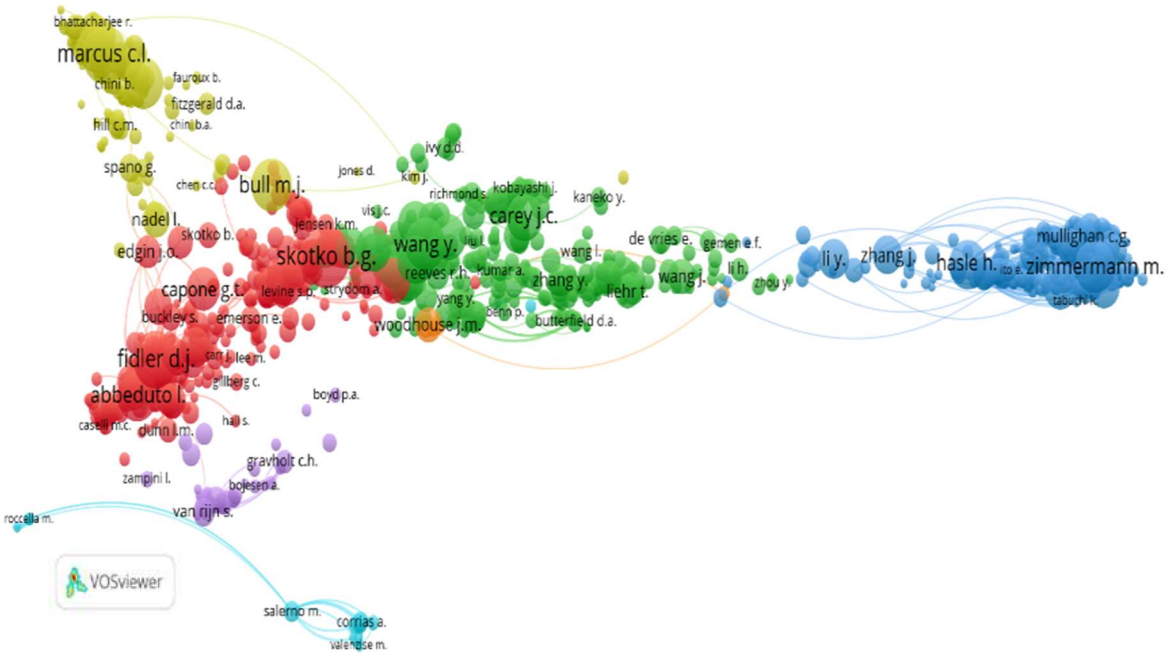


**Figure 5: Co-citation network of authors**

Note: figure 5 was generated using a Java-based bibliometric tool, VOS viewer (1.6.18)

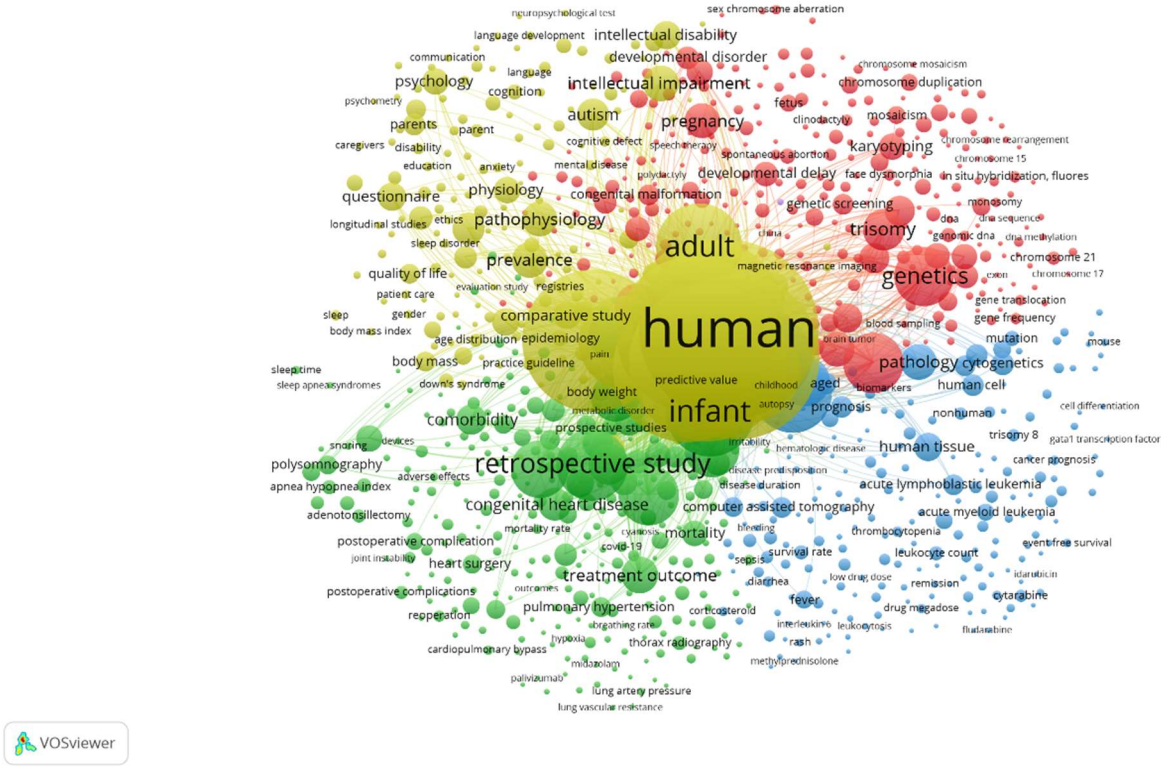


**Figure 6: Keyword network analysis**

## Keyword analysis and co-occurrence

**Table 4** reflects the most frequently used keywords in the research works related to Down syndrome. Keywords with a minimum of 10 occurrences were included, 20 keywords out of a total of 1001 that meet the threshold were analyzed for occurrences and ranked up to 20. Words with TLS such as human (115187), article (3877), female (3554), and child (3624). Other prominent keywords include; humans. male, down syndrome, preschool child, adolescent, major clinical study, infant, controlled study, adult, priority journal, child, preschool, clinical article, retrospective study, complication, case report, genetics

Fig 6: highlights the co-occurrence of keywords. These keywords may be helpful for academicians and authors to delve into the evolving literature on

Down syndrome and the research associated with it. Keyword clustering with clusters contributes to the explorations and current hot spots of research in Down syndrome depicted in Figure 6.

**Analysis of funding agencies:** Among all publications in the field of Down syndrome from 2014–2023, a total of 3818 research received at least one grant. Table 5 presents the top ten funding agencies that provided the largest number of grants, with seven from the USA and one each from China, Japan, and the United Kingdom. The National Institutes of Health (USA) 643 studies and the National Natural Science Foundation of China 524- studies stood first and second position in promoting grants.

**Table 4: Top twenty high-frequency keywords in the domain of Down syndrome**

| Rank | Keyword | Occurrences | Rank | Keyword | Occurrences |
|---|---|---|---|---|---|
| 1 | Human | 4353 | 11 | Infant | 1579 |
| 2 | Article | 3877 | 12 | Controlled Study | 1497 |
| 3 | Child | 3624 | 13 | Adult | 1493 |
| 4 | Female | 3554 | 14 | Priority Journal | 1492 |
| 5 | Humans | 3424 | 15 | Child, Preschool | 1460 |
| 6 | Male | 3264 | 16 | Clinical Article | 1317 |
| 7 | Down Syndrome | 3119 | 17 | Retrospective Study | 1169 |
| 8 | Preschool Child | 1916 | 18 | Complication | 909 |
| 9 | Adolescent | 1711 | 19 | Case Report | 900 |
| 10 | Major Clinical Study | 1708 | 20 | Genetics | 879 |

**Table 5: Top 10 funding agencies in the field of Down syndrome**

| Sr no | Agency | Quantity | Country |
|---|---|---|---|
| 1 | National Institutes of Health | 643 | USA |
| 2 | National Natural Science Foundation of China | 524 | China |
| 3 | Eunice Kennedy Shriver National Institute of Child Health and Human Development | 256 | USA |
| 4 | National Institute of Child Health and Human Development | 206 | USA |
| 5 | National Cancer Institute | 171 | USA |
| 6 | Japan Society for the Promotion of Science | 166 | Japan |
| 7 | National Centre for Advancing Translational Sciences | 161 | USA |
| 8 | National Heart, Lung, and Blood Institute | 154 | USA |
| 9 | Medical Research Council | 104 | UK |
| 10 | National Institute of Mental Health | 94 | USA |

## DISCUSSION

Research progress in the field of Down syndrome can be estimated based on the quantity and trend of annual publications and citations. In general, the number of publications in this field has always maintained a decent number of publications and increased in the past two years significantly, publications in this field have entered a period of rapid growth during the COVID-19 pandemic times, indicating that research on Down syndrome has received increasing attention in recent years. The probable association of this context could be that patients with Down syndrome have immunological dysregulation linked to heightened interferon activity, which may result in a more intense cytokine storm and a greater probability of severe COVID-19 symptoms.[18-21]

The USA contributed the largest quantity of publications and had the strongest collaborative network followed by the United Kingdom and Australia. In contrast to other active developed countries in this field developing countries had a smaller number of publications. The lifetime prevalence of Down syndrome is significantly rising in correlation with the expanding worldwide population. In the USA, the population prevalence of Down syndrome surged from roughly 50,000 in 1950 (3.3 per 10,000 individuals) to over 212,000 in 2013 (6.7 per 10,000 individuals), mostly because of developments in the survival rates of children with Down syndrome.[22-24]

Among the institutions, the National Center on Birth Defects and developmental disabilities and Centers for Disease Control and Prevention, Atlanta, United States published the largest number of documents, and the majority of the other institutions were also those from the USA. In terms of institutional collaboration, only the USA institutions had strong collaborative networks. The rate of elective pregnancy terminations is affected by the accessibility and precision of screening tests in each country, the proportion of individuals opting for prenatal screening and then prenatal testing, and parental choices following a prenatal diagnosis of Down syndrome. 3,400 elective terminations due to Down syndrome were performed in the USA in 2013, leading to a 33% decrease in the number of newborns with DS born that year.[25,26] Overall, apart from the USA, cooperation between countries and institutions was weak, thus strengthening international and institutional cooperation, especially in developing countries, is a priority in this field.

The journal with the largest number of publications American Journal of Medical Genetics with 163 publications and citations 1651stood at the topmost position, in addition to this journal like Journal of intellectual disability research, the International Journal of Pediatric Otorhinolaryngology, and the Journal of Pediatrics also actively contributed and are all quartile 1 or quartile 2 journals. The scientists with the largest number of citations, led by Skotko B. G. received a maximum citation of 395 followed by Marcus L. with 360 citations, and Fidler D. J. with 352 citations stood in the third position. Recent advancements in medical care have raised life expectancy and enhanced the quality of life for those with Down syndrome (DS). These advancements stem from both pre-clinical and clinical research, although there is still a lack of understanding regarding DS. In 2020, the NIH announced its intention to revise its DS research plan and sought feedback from the scientific and advocacy community.[27]

Studying DS in several areas such as clinical, pathological, genetic, cellular, and molecular fields is crucial for creating effective interventions to enhance health and well-being throughout one's life. Research in this field has thrived due to technical advancements, growing multinational partnerships, higher financing, and global advocacy campaigns.[28,29]

## Limitations

This study is embraced with certain limitations; first, the studies included for analysis are only of English language, and omissions for studies published in other languages. Secondly, to avoid differences in bibliometric data structure from distinct databases we gathered data from only one electronic database. Furthermore, only original articles and review articles were included in the analysis. Manual exclusion of articles can also lead to minor glitches in analysis and interpretation; however, the aggregated results will yield an overall research landscape.

## Conclusion

This study reveals yearly publication trends, influential articles, the geographical distribution of research, notable authors and journals, and important areas of concentrated research activity by analyzing co-authorship, citation patterns, co-occurrence, and co-citation relationships applying bibliometric analysis and scientific mapping methods to provide researchers, policymakers, and stakeholders with a panoramic view of the field of Down syndrome. Publications in the field revealed an excellent contribution from developed countries, led by the United States; they maintained high quality and a significant number of publications as well. Only a small number of papers originated from developing countries this might be due to the expensive nature of research concerning Down syndrome. Finally, National and international health organizations should encourage and fund researchers to do continuous assessment and research on Down syndrome, especially in low-income countries.

### Abbreviations used

DS – Down Syndrome
BA - Bibliometric analysis
TLS- Total Link Strength
ACI- Average Citations per Item,
IF-Impact Factor

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