Bibliometric analysis of research on side effects of pharmacological treatments for children with autism spectrum disorder

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Abstract:
This bibliometric analysis investigates the trends and developments in research on the side effects of pharmacological treatments for children with Autism Spectrum Disorder (ASD) from 2010 to 2024. Autism, a neurodevelopmental disorder, often requires pharmacological interventions to manage comorbid symptoms such as aggression and hyperactivity. However, these treatments may induce significant side effects, which this study aims to explore. Using data from the Web of Science database, publications were analysed through temporal, geographical, and thematic lenses. Results revealed a notable increase in publications until 2020, with peaks in 2016 and 2019, followed by a decline post-2020. The United States led in research output, with significant contributions from journals like *Journal of Child and Adolescent Psychopharmacology*. Key themes included the focus on clinical treatments and an emerging interest in the biological foundations of autism. The study highlights the growing need for an integrated research approach, combining clinical and fundamental studies to enhance treatment effectiveness while minimizing adverse effects. Despite challenges, such as a decline in publications in recent years, the analysis underscores the importance of continuing interdisciplinary and global collaborations to advance the understanding of pharmacological interventions for children with ASD.

Keywords
Autism Spectrum Disorder (ASD), Pharmacological treatments, Side effects, Childhood autism, Bibliometric analysis, Scientific trends

Introduction

Childhood autism is a neurodevelopmental disorder characterised by difficulties in communication, social interactions, and behaviour. According to the World Health Organization (WHO), this disorder manifests before the age of three and is marked by abnormal or altered development, as well as a disruption in functioning in these three psychopathological areas [1].
The prevalence of autism has significantly increased in recent years. According to INSERM, approximately 1 in 100 children is born with an autism spectrum disorder (ASD) in France, which accounts for about 8,000 births annually [2].

While behavioural interventions are recognised as effective, particularly in improving social skills and language use, pharmacological treatments provide a complementary approach aimed at reducing certain associated symptoms. These treatments primarily target comorbid disorders such as aggression, hyperactivity, and irritability [1].
Research on potentially effective medications for autism has made significant progress in recent decades. Several therapeutic classes have been studied, including atypical antipsychotics such as risperidone and aripiprazole, which are used to treat aggression and irritability in patients with ASD [1]. However, the use of medication in autistic children raises significant concerns due to potential side effects. These effects can vary considerably from one child to another and may include issues such as weight problems, metabolic disorders, and cardiovascular complications [4].

This literature review aims to describe the trends and developments in research on the side effects of pharmacological treatments in children with autism from 2010 to 2024. By analysing recent data from scientific research and considering the recommendations of health authorities, we aim to provide an informed perspective on the current state of pharmacology in the field of childhood autism, while emphasising the importance of an individualised and informed approach to the care of these young patients.

Materials and Methods

For this study, the Web of Science database was used. We established the following search equation: ("Autis* Spectrum Disorder*") AND children AND "treatment" AND (pharmacological OR drug OR Medicinal) AND (side effects OR Adverse effects OR Secondary effects OR Adverse reactions). The selected publications were those covering the period from 2010 to 2024, providing an overview of recent developments in this field. A data cleaning and transformation process was applied, with a filter to retain only publications that had received at least 11 citations, a threshold corresponding to the median number of citations in the dataset.

The analysis methods included a temporal analysis to observe publication trends over the years, a geographical analysis to identify contributing countries, as well as an examination of research areas, key authors, and influential journals. The data were exported in CSV format, enabling in-depth statistical analysis.

Visualisations were then created to explore the relationships between various variables, providing a deeper understanding of the trends and dynamics of research in this field.

For the data analysis in this bibliometric review, the R software was used due to its advanced capabilities in data manipulation and graphical visualisation. Descriptive statistics were performed using appropriate functions and packages, such as dplyr for data processing. Visualisation of the results was primarily done with the ggplot2 package, allowing for the creation of clear and aesthetically pleasing graphs to explore temporal, geographical, and thematic trends. Additionally, the wordcloud package was used to generate word clouds, providing a visual representation of the most frequently used terms in the selected publications. This approach facilitated the interpretation of the data and allowed for an attractive and accessible presentation of the obtained results.

Results

Temporal analysis

Between 2010 and 2022, 155 articles on pharmacological treatments in the context of childhood autism were published. A significant increase in the number of annual publications is observed in 2016, 2019, and 2020, with a peak in 2020, totalling 23 articles. However, after 2020, a significant decline in the number of publications is noted, and no articles receiving at least 11 citations were published after 2022.

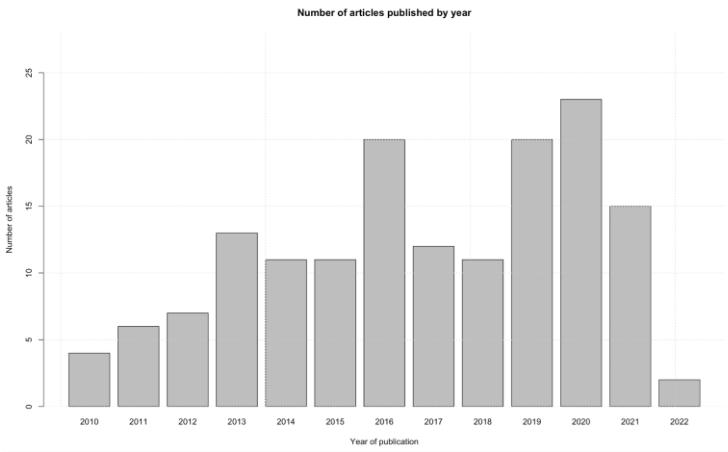

Figure 1 : Number of articles per year

This graph (Figure 2) illustrates the annual evolution of the total number of citations between 01/01/2010 and 01/01/2022, with a total of 8,886 citations. The number of citations fluctuates from year to year, with notable peaks in 2014, 2016, and 2019, followed by a sharp decline in 2020 and 2022.

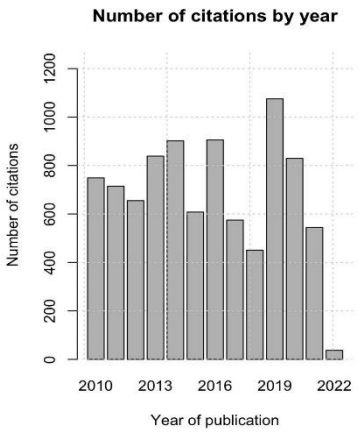

Figure 2 : Number of citations per year

Analysis of scientific output

The representation of the 10 most cited articles (Figure 3) highlights the most influential works in the field of pharmacological treatments for childhood autism. A notable concentration of citations is observed for articles from 2010 and 2011, with the 2010 article "Evaluation, Diagnosis, and Treatment

of Gastrointestinal Disorders in Individuals with ASDs: A Consensus Report" receiving up to 525 citations. This article stands out as a seminal work in the field.

Furthermore, a more recent article from 2020, titled "Safety of 80 antidepressants, antipsychotics, anti-attention-deficit/hyperactivity medications and mood stabilizers in children and adolescents with psychiatric disorders: a large-scale systematic meta-review of 78 adverse effects," ranks 9th with just over 150 citations, indicating that it has already garnered significant attention.

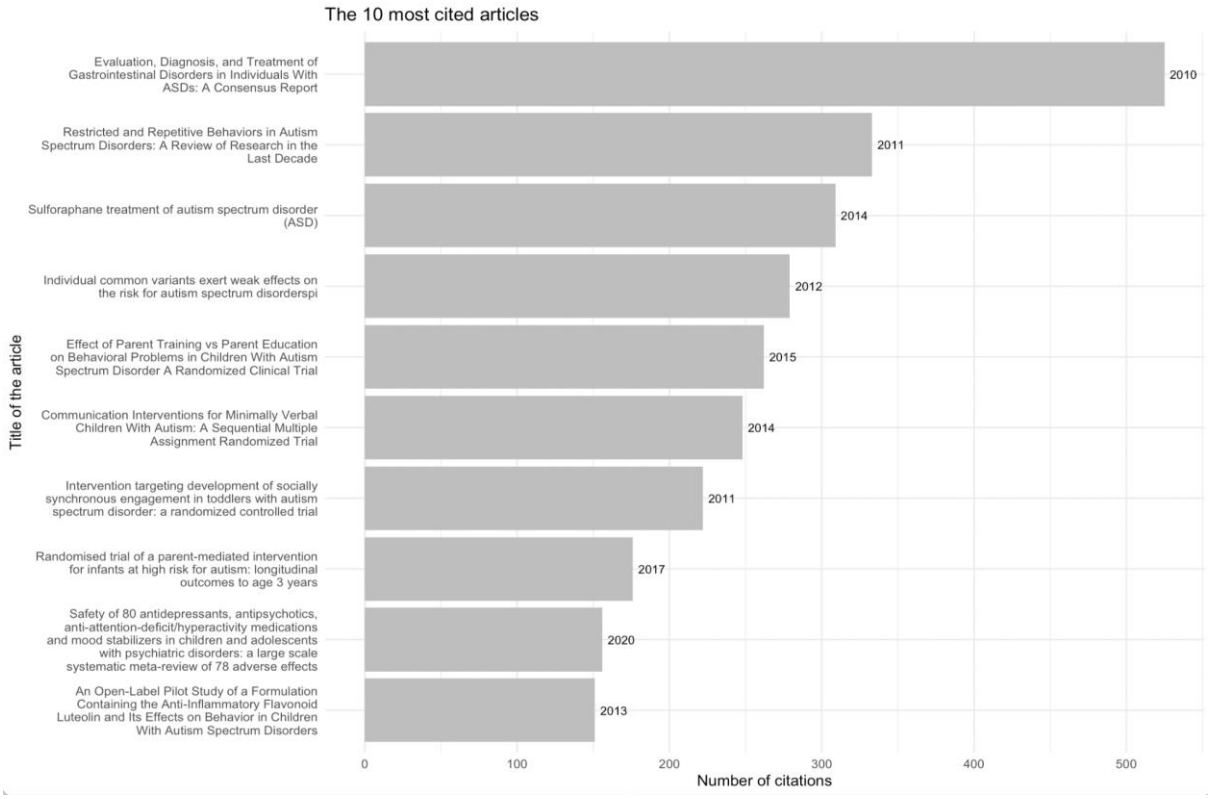

Figure 3 : Most cited articles

The analysis of journals publishing on pharmacological treatments for childhood autism between 2010 and 2024 reveals distinct trends in terms of scientific output (number of publications) and impact (average citations per publication). The *Journal of Child and Adolescent Psychopharmacology* leads in terms of publications, followed by specialised journals such as *Journal of Autism and Developmental Disorders* and *Molecular Autism*. However, when evaluating impact through the average number of citations per publication, multidisciplinary journals like *Psychological Bulletin* and *Proceedings of the National Academy of Sciences of the USA* surpass the others, indicating a high academic impact for their work. Journals marked in red, such as *Pediatrics* and *Journal of Child Psychology and Psychiatry*, appear in both rankings, highlighting their dual role as key contributors and sources of highly cited articles.

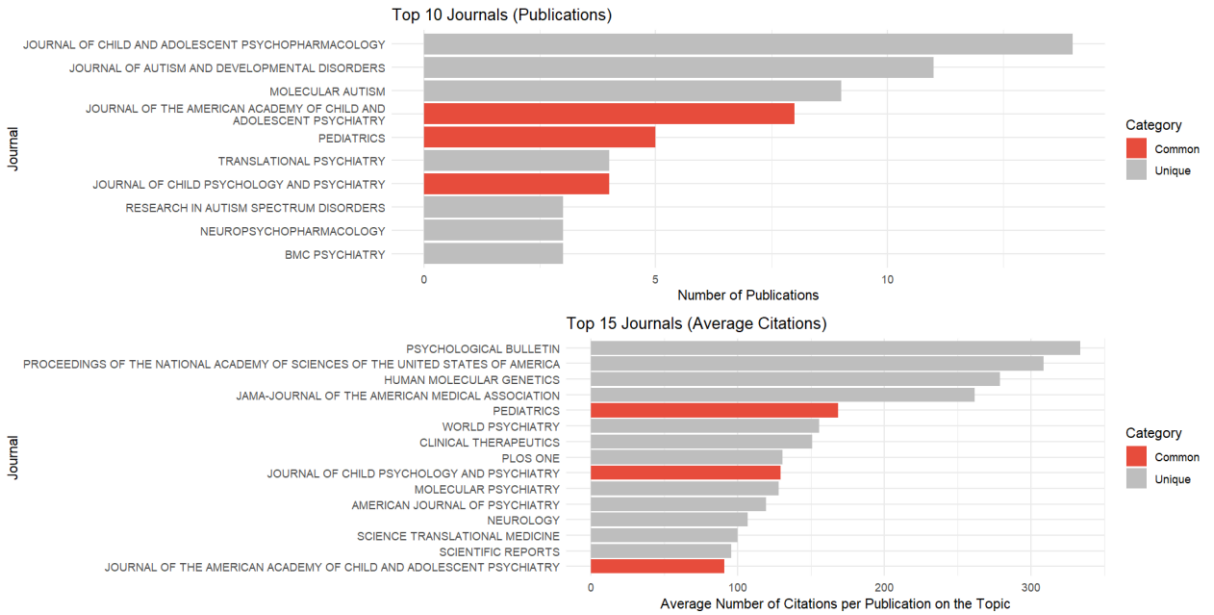

Figure 4 : Comparison of top journals

The most prolific authors identified in the analysed corpus, each author is ranked based on their number of publications. The Figure 5 highlights the engagement of key contributors.

The data collected shows that certain researchers have particularly distinguished themselves with a high number of publications. Dr. Richard E. Frye is the most prolific author in our corpus, with 8 publications, alongside Dr. Christopher J. McDougle. These two researchers are major figures in the development of pharmacological treatments for autism, having made significant contributions to the understanding of therapeutic approaches.

Other researchers, such as Dr. Eric Pedapati (7 articles) and Dr. James SJ (6 articles), are also among the most active and influential in the field. Although their publication count is slightly lower, researchers like Dr. McCracken JT, Dr. Hoekstra PJ, and Dr. Dziura J remain essential for progress in pharmacological treatments for childhood autism. These authors play a key role in the search for innovative solutions and in deepening knowledge in this area.

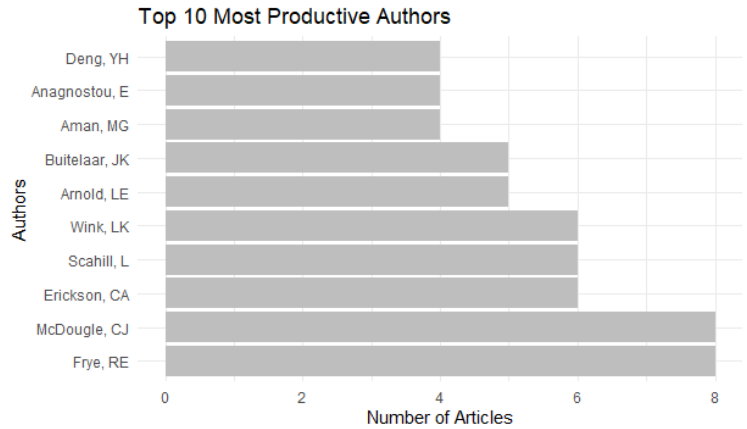

Figure 5 : Most productive authors

In addition to the number of publications, the analysis of collaborations between these authors is crucial for understanding the interactions that drive research progress. The cooperation among these researchers highlights how knowledge and expertise intersect to tackle the complex challenges related to autism treatment.

Figure 6 presents the 15 most frequent collaborations between authors. One of the most notable collaborations is between Link, LK and Erickson, CA, who have worked together on several important papers, ranking among the most frequent co-author pairs. Other notable collaborations include those between McCracken, JT and Deng, YH, as well as between Frye, RE and James, SJ. These recurrent collaborations demonstrate the synergy between these researchers, enhancing the understanding and treatment of autism through pharmaceutical approaches.

The numerous collaborations observed in this field highlight the importance of interdisciplinarity in addressing complex scientific challenges. These teams, combining clinical and methodological expertise, are actively contributing to improving treatments and understanding the mechanisms of autism.

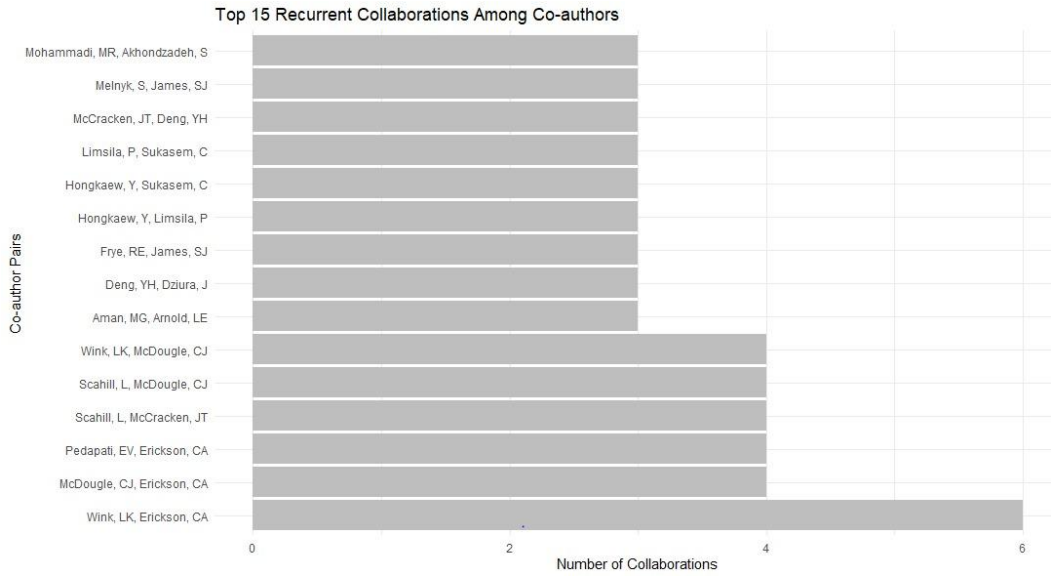

Figure 6 : Most frequent collaborations

Thematic Analysis

The word cloud (Figure 7) illustrates the most prominent research areas within the analysed corpus of articles. The most represented fields are clearly linked to psychiatry, psychology, and paediatrics, three major disciplines in the study of autism spectrum disorders and their treatments. Other areas, such as genetics and heredity, as well as experimental research in medicine, also stand out, highlighting the focus on the biological and methodological foundations of pharmacological interventions.

Figure 7 : Word cloud of research domains

Figure 8 : Most common terms in the titles

The word cloud (Figure 8) based on the article titles highlights the major themes and methodologies in research on pharmacological treatments for autism. A strong concentration is observed around rigorous clinical trials, with terms such as *randomized*, *placebo*, *double*, and *blind*, underscoring the emphasis on controlled studies to evaluate treatment efficacy. The main themes, represented by words like *symptoms*, *efficacy*, and *therapy*, indicate a focus on symptom improvement and the effectiveness of interventions.

Geographical Analysis

The distribution of publications by country shows a clear dominance of the United States, with 74 publications, confirming its central role in research on pharmacological treatments for childhood autism. The Netherlands follows with 12 publications, highlighting their significant contribution within Europe. Other notable countries, such as Iran, Australia, and England, record 7, 6, and 5 publications respectively, indicating geographical diversity in scientific output. Countries like Canada, Japan, Israel, and Germany fall within a similar range (5 to 4 publications each), demonstrating occasional but meaningful contributions. Finally, several countries such as France, Italy, and Sweden exhibit lower participation with 3 publications, while nations like China, Turkey, and others produce 2 or fewer, indicating a more limited role in the field.

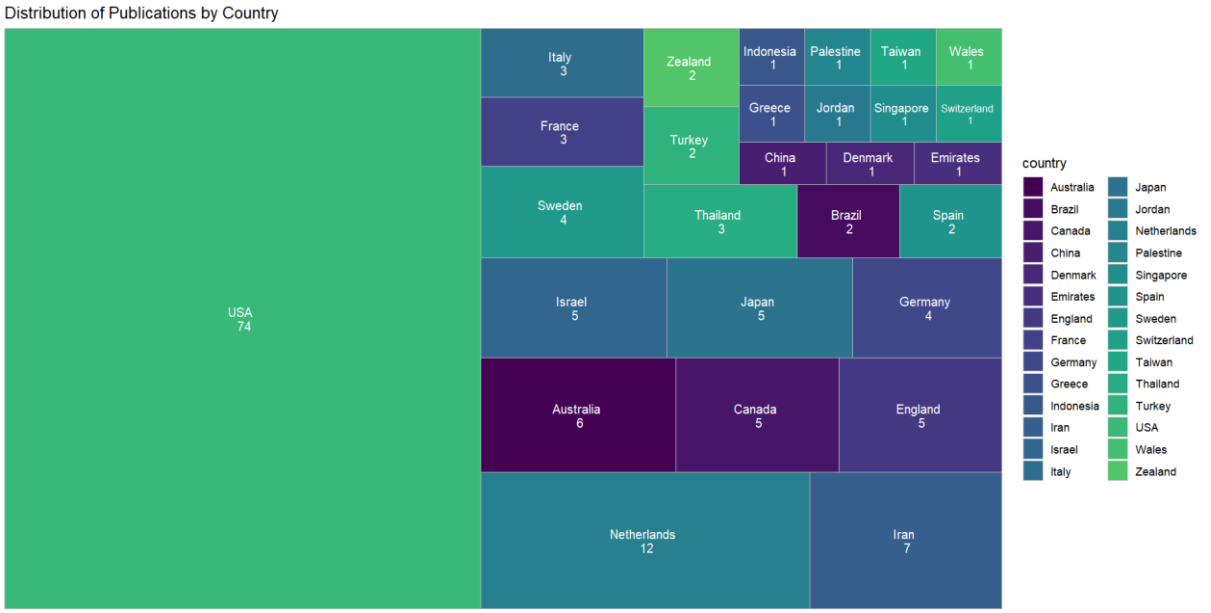

Figure 9 : Most productive countries

Discussion

Interpretation of results

- **Temporal analysis**

The evolution of the number of articles and citations reveals a notable correlation, with both reaching significant peaks in 2016 and 2019. These years may correspond to particularly influential publications or major advances in the field, leading to increased interest and contributing to significant impact. The large citation peaks in 2014, 2016, and 2019, with a maximum of 1,075, likely reflect the relevance or impact of the published studies, reinforcing the attention given to the topic. Conversely, the observed decline after 2020 in both publications and citations may reflect a shift in research priorities, a decrease in interest in this field, or external constraints such as changes in funding or resources. Additionally, the drastic decline in citations in 2022 could be linked to the proximity to the year of analysis, with recent articles not yet having time to accumulate a significant number of references. This decrease could also reflect a temporary decline in interest in the subject or a redirection of efforts toward other priorities, such as those related to the COVID-19 pandemic. Thus, the joint evolution of publications and citations reflects a complex interaction between the impact of published studies, academic interest, and external dynamics influencing scientific production.

- **Analysis of Scientific Production**

The analysis of scientific production on infantile autism reveals several key dynamics, each contributing to a broader understanding of trends and developments in this field. The lasting impact of older articles, such as the one from 2010, illustrates their continued relevance in autism research, having fuelled many studies over the years. On the other hand, more recent articles, particularly those published after 2020, seem to be less cited, which may indicate either a reduced interest from the scientific community in these publications or a delay in gaining visibility. The decrease in the total number of publications after 2020, combined with the low number of citations received by these works, could also reflect a shift in research priorities or a reallocation of funding in the field. These observations highlight the importance of examining the temporal dynamics of citations to better understand the trends and future directions of research in this area. This evolution in citations and publications is also related to how research is disseminated and received by academic networks.

A clear distinction emerges between research output and its academic impact. Specialized journals, such as the *Journal of Child and Adolescent Psychopharmacology*, play a crucial role in disseminating autism-focused studies, while multidisciplinary journals like the *Psychological Bulletin* generate a larger number of citations due to their broad audience and academic influence. Journals that are both prolific and highly cited reflect a strategic balance between high publication frequency and significant scientific impact. These results not only highlight the role of journals in amplifying scientific impact but also emphasize the importance of authors and collaborations in the production and dissemination of knowledge.

The author analysis highlights the contributions of major researchers such as Dr. Richard E. Frye and Dr. Christopher J. McDougle, whose productivity reflects recognized expertise in the field. Frequent collaborations, such as those between Mohammadi, MR, and Akhoondzadeh, S, underscore the central role of interdisciplinarity in addressing complex issues like autism, combining clinical and theoretical approaches to innovate in pharmacological treatments. However, some limitations emerge: the number of publications does not always reflect the quality or impact of the work, and while international collaborations are growing, they are often concentrated in certain regions, indicating untapped potential

elsewhere. These findings highlight the need to strengthen tools and platforms that promote collaboration among researchers from diverse regions and disciplines.
In summary, these analyses converge to underscore the importance of multiple dynamics – influential articles, strategic journals, and interdisciplinary collaborations – in understanding scientific trends and advancing research on infantile autism.

- **Thematic Analysis**

The analysis of the results shows that the fields of psychiatry, psychology, and pediatrics clearly dominate, highlighting the importance of these disciplines in understanding autism spectrum disorders and developing appropriate pharmacological treatments. This dominance of clinical approaches directly reflects the need for treatment and care of autistic children. However, the notable influence of genetics and heredity, as well as experimental medical research, indicates a growing trend to explore the biological foundations of autism. This evolution suggests a convergence between clinical and fundamental research, aiming to offer more comprehensive and effective therapeutic solutions. In summary, this word cloud highlights the complementarity between these two approaches, revealing an essential multidisciplinary dynamic for advancing knowledge and treatment of infantile autism.
At the same time, the thematic analysis of titles highlights key elements of current research. The presence of the term "risperidone" shows that this drug is central to the research, while words like "psychiatric" and "risk" reflect particular attention to comorbidities and the potential risks of treatments. Additionally, terms like "adolescent" and "adult" suggest a diversification of studied populations, extending research beyond autistic children to include other age groups. Finally, terms like "transcranial" and "meta" indicate an interest in alternative approaches and a willingness to synthesize existing knowledge, thus representing a diverse and methodologically rigorous research agenda. These elements illustrate the depth and diversity of the themes explored in autism research.

- **Geographical Analysis**

The results show a concentration of autism research in a limited number of countries, with a significant dominance of the United States, likely linked to substantial investments and well-established academic networks. The Netherlands stands out for its involvement, probably related to specialized centres or international collaborations. The involvement of countries such as Iran and Australia illustrate the extension of research beyond major powers, although their production remains moderate. Finally, the weak contributions from developing countries highlight global disparities in funding and infrastructure, emphasizing the importance of international collaborations for more inclusive research.

Strengths and Limitations

The study stands out for several key strengths. It adopts a multidimensional approach, integrating temporal analyses to identify publication trends, geographical analyses to highlight country contributions, and an evaluation of the most influential journals and authors. The use of word clouds to explore the themes addressed also provides valuable qualitative insight into the topics. Additionally, the study benefits from the use of advanced analytical tools, including R software and powerful packages like dplyr, ggplot2, and wordcloud, allowing for rigorous data manipulation, aesthetic visualizations, and in-depth analysis of statistical and thematic trends. Temporal relevance is another strength, as the period studied (2010-2024) provides a perspective on contemporary dynamics and recent developments in a constantly evolving field.
However, notable limitations must be considered. The exclusive use of the Web of Science database potentially limits the scope of the bibliometric review, as certain relevant publications may not be

included if they are not indexed in this database. Combining with other databases, such as Scopus or PubMed, could have enriched the results. Furthermore, the restrictive search criteria, while precise, may exclude relevant articles containing synonyms or expressions not included in the search equation, introducing bias into the analysis. Finally, the citation-based filter set at a threshold of 11 favours older or high-impact articles, which may limit the inclusion of recent or emerging works that are still accumulating citations.

Conclusion

This bibliometric review has analysed the evolution of research on pharmacological treatments and side effects in children with autism spectrum disorders (ASD) between 2010 and 2024. The results show a notable increase in scientific publications up to 2020, with peaks of interest in 2016 and 2019. However, the marked decline in publications and citations after 2020 could reflect a shift in research priorities or a decrease in interest in this specific field, possibly influenced by external factors such as the COVID-19 pandemic. The journal analysis revealed that the most influential publications were concentrated in journals specializing in psychiatry and pediatrics, such as the *Journal of Child and Adolescent Psychopharmacology*, as well as in multidisciplinary journals like the *Psychological Bulletin*, which also recorded a high average of citations per publication. The geographical mapping indicated that the United States and the United Kingdom dominate scientific production, although some European countries also show significant contributions. Finally, the results of the thematic and geographical analyses highlighted a strong focus on psychiatry, psychology, and pediatrics, while emphasizing a growing interest in the biological and genetic aspects of the disorder. These findings underscore the need to continue exploring the biological foundations of ASD and to consider the importance of an integrated approach combining clinical and fundamental research to improve pharmacological treatments and their effectiveness while minimizing side effects. Overall, this study provides a comprehensive perspective on the evolution of research on pharmacological treatments for infantile autism, while highlighting ongoing challenges and opportunities for the future.

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