

R E V I E W

Paediatric vaccinations: A bibliographic analysis on COVID-19 and influenza

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Abstract. *Background and aim:* Vaccinations represent one of the most effective tools for the prevention of disease, as evidenced by the extensive literature on the subject. With COVID-19, this attention has further increased by centralising scientific production. This study aimed to evaluate and compare the literature on the topic of vaccinations for children, with a focus on the differences between the vaccines for influenza and for COVID-19. *Methods:* The literature search was conducted by evaluating English-language articles that studied populations under the age of 18 years and excluding non-full papers or articles that did not provide qualitative data. The full-text analysis was conducted for articles published in the three highest IF journals in paediatrics, general medicine and vaccines. *Results:* The publication timelines show significant diversity with a peak in 2022 for articles concerning the 2019 novel coronavirus (44.6%) and a constant frequency for articles concerning influenza. Concurrently, the populations examined in the studies exhibit minimal divergence, with North America and Europe representing the predominant regions in both groups. *Conclusions:* In light of the multitude of studies examining efficacy and effectiveness, particularly in the context of COVID-19, the scientific community should direct its attention to the underlying factors that shape perceptions of vaccines, whether hesitancy or acceptance. (www.actabiomedica.it)

Key words: COVID-19 vaccine, influenza vaccine, paediatric vaccination

Introduction

Vaccinations are among the most important public health interventions, with the potential to significantly reduce mortality and morbidity associated with numerous infectious diseases. Despite their importance and efficacy, the intrinsic variability of certain pathogens (e.g., orthomyxoviruses and coronaviruses) and the physiological decline in immunoglobulin levels due to aging or disease necessitate periodic vaccine updates and recalls. This ongoing need for adaptation underscores the critical role of vaccination in public health (1). Given their significance, vaccinations have been extensively studied in the scientific literature.

Topics such as vaccine mismatch, efficacy, safety, adherence, and hesitancy have consistently been focal points. This is particularly evident in diseases with seasonal patterns, such as influenza, where antigenic variation diminishes the protective efficacy of prior infections or vaccinations. Such variability contributes to vaccine hesitancy, especially when frequent recalls are required, which can ultimately lower vaccination coverage rates. Since the early 2020s, the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19), has posed a significant global public health challenge. Although COVID-19 primarily manifests as a respiratory illness with a prevalence of

mild symptomatic infections, its widespread transmission and strain on healthcare systems have captured the attention of the scientific community. Within months, global research efforts prioritized two critical objectives: identifying effective therapies and developing preventive measures, particularly focusing on the efficacy and safety of the first mRNA vaccines. The focus on COVID-19 vaccination is also tied to its broader impact on healthcare systems, including the risks of bacterial co-infections and care-related infections from prolonged hospitalizations (2,3). Vaccination has played a central role not only in combating the virus itself but also in significantly reducing hospitalizations and associated complications. However, this intense focus on COVID-19 has inadvertently diminished attention to other non-emergency health issues, including preventive measures such as cancer screening and non-COVID vaccinations. This shift has led to a rise in vaccine-preventable diseases, reigniting interest in vaccinations and their critical role in disease prevention (1). Two notable areas of focus have emerged: the co-administration of COVID-19 vaccines with other vaccines (4), and the emphasis on non-COVID vaccinations for high-risk populations to prevent diseases with high morbidity. Despite the significant attention paid to these issues, there remains a lack of comparative analyses of literature trends on COVID-19 and seasonal influenza vaccinations. This gap poses a challenge for designing future vaccination campaigns and understanding researchers' focus on these high-impact public health topics. The objective of this study is to evaluate trends in the literature on influenza and COVID-19 vaccinations in pediatric populations from 2020 onward. This analysis aims to identify variations over time and provide a comparative understanding of research priorities for these two critical topics.

Materials and methods

The structured search was conducted in PubMed using a combination of Medical Subject Headings (MeSH) and free-text terms. The literature analysis examined articles addressing vaccines as both a medical intervention and a component of health organization for the prevention of COVID-19 or influenza. The

analysis focused on literature published between 2020 and May 6, 2024. To ensure fair weighting in terms of Impact Factor (IF), only articles published in the three highest-impact journals in pediatrics, vaccination, and general medicine (as per Journal Citation Reports [JCR]) were included. Boolean operators (AND and OR) were appropriately and logically combined to construct the search strategy. No filters were applied. Keywords included terms related to influenza, COVID-19, vaccines, pediatrics, and similar topics. The strategy searches were for COVID19 and Influenza respectively ("COVID19"[Title/Abstract] OR "Sarscov2"[Title/Abstract] OR "sars cov2"[Title/Abstract] OR "2019 ncov infection"[Title/Abstract] OR "severe acute respiratory syndrome coronavirus 2 infection"[Title/Abstract] OR "2019 novel corona-virus disease"[Title/Abstract] OR "coronavirus disease 19"[Title/Abstract] OR "covid 19 virus infection"[Title/Abstract]) AND ("vaccination"[Title/Abstract] OR "vaccine"[Title/Abstract] OR "immunization"[Title/Abstract]) AND ("pediatric"[Title/Abstract] OR "child"[Title/Abstract] OR "pediatricians"[Title/Abstract] OR "children"[Title/Abstract]) AND ("NPJ vaccines"[Journal] OR "lancet london england"[Journal] OR "The New England journal of medicine"[Journal] OR "BMJ open"[Journal] OR "nature reviews immunology"[Journal] OR "Pediatrics"[Journal] OR "The Lancet Child Adolescent Health"[Journal] OR "JAMA pediatri"[Journal] OR "Immunity" [Journal]) ((("Influenza"[Title/Abstract] OR "human influenzas"[Title/Abstract] OR "human flu"[Title/Abstract] OR "Grippe"[Title/Abstract] OR "human influenza"[Title/Abstract]) AND ("vaccination"[Title/Abstract] OR "vaccine"[Title/Abstract] OR "immunization"[Title/Abstract]) AND ("pediatric"[Title/Abstract] OR "child"[Title/Abstract] OR "pediatricians"[Title/Abstract] OR "children"[Title/Abstract]) AND ("NPJ vaccines"[Journal] OR "lancet london england"[Journal] OR "The New England journal of medicine"[Journal] OR "BMJ open"[Journal] OR "nature reviews immunology"[Journal] OR "Pediatrics"[Journal] OR "The Lancet Child Adolescent Health"[Journal] OR "JAMA pediatri"[Journal] OR "Immunity" [Journal]) AND (2020:2024[mdat]))

We included only articles that met the following criteria: (i) written in English; (ii) population: pediatric (≤ 18 years, both female and male); (iii) interventions

or exposures: vaccination for COVID-19 or influenza. Additionally, any type of original study (both observational and trial-based) was considered eligible, with no restrictions on geographical settings. Exclusion criteria were: (i) articles not published in English; (ii) populations over the age of 18; (iii) interventions or exposures involving vaccinations other than those for COVID-19 or influenza. Furthermore, articles lacking quantitative information or details, non-full-text papers (e.g., letters to the editor, conference papers, commentary notes, expert opinions, abstracts), and articles not published as peer-reviewed in international journals were excluded from the assessment. Data on year of publication, topic of the study and geographical area where the study was conducted were extracted. For statistical analysis, categorical variables were described as frequencies and percentages. Inferential analyses were conducted using either Fisher's exact test or the chi-squared test, as appropriate. All analyses were performed using R software (version 4.3.2), and a p -value < 0.05 was considered statistically significant.

Results

The literature search yielded 127 and 60 records for COVID-19 and influenza, respectively. Of the 127 COVID-19-related records, 35 were excluded after reviewing the abstracts and full texts because they did not pertain to COVID-19 vaccinations, focusing instead on hospitalization or symptoms of patients infected with SARS-CoV-2. Similarly, 8 of the 60 influenza-related records were excluded as they addressed other vaccinations or described clinical manifestations of influenza. Table 1 presents data comparing the COVID-19 and influenza literature. Regarding the type of journal, the majority of articles were published in pediatric specialty journals: 55.4% for COVID-19 and 73% for influenza. General medical journals ranked second, with 39.1% of COVID-19 articles and 21.2% of influenza articles. Immunology journals accounted for approximately 5% of the publications in both cases: 5.4% for COVID-19 and 5.8% for influenza. In terms of topics investigated, COVID-19 literature demonstrated a stronger focus on efficacy/effectiveness, parental perceptions, and side

effects, accounting for 54.3%, 22.8%, and 21.7% of publications, respectively. Conversely, influenza literature prioritized efficacy/effectiveness, vaccination policies, and parental perceptions, with 48.1%, 30.8%, and 26.9% of publications, respectively. Side effects related to influenza vaccination were the least studied topic, comprising only 13.5% of articles. While efficacy/effectiveness was the predominant topic for both groups, the variations in focus highlight significant differences in research priorities.

Regarding the geographical origin of study populations, most studies in both groups originated in North America: 64.1% for COVID-19 and 92.3% for influenza. The populations studied were predominantly European and North American for influenza, while COVID-19 studies had a more global representation. However, this geographical distribution did not show statistically significant differences between the groups. Finally, the temporal distribution of research output revealed distinct patterns between COVID-19 and influenza. COVID-19 research exhibited a symmetrical distribution, peaking in 2022 with 41 articles (44.6% of the total). In contrast, influenza research showed a consistent annual output from 2020 to 2023, with approximately 13 articles (25.0%) published each year.

Figure 1 illustrates the time trends in literary production between 2020 and 2024, considering both articles published in the highest-impact-factor (IF) journals and the broader body of literature. For the highest IF journals, the temporal trend for influenza-related vaccination papers shows relative stability, with publication rates ranging from 15.4% to 26.9% between 2020 and 2023, followed by a decrease to 7.7% in 2024. In contrast, COVID-19-related publications display greater variability, with rates ranging from 1.1% in 2020 to a peak of 44.9% in 2022. When considering the overall body of literature, a different trend emerges. For influenza-related publications, there is a steady increase in literary production, rising from 12.9% in 2020 to 31.6% in 2023. Conversely, the trend for COVID-19-related publications parallels the pattern observed in high-IF journals but exhibits a narrower range, increasing from 4.0% in 2020 to 35.5% in 2022. In both groups, a decline in literary production is observed during the first half of 2024 compared to previous years.

Table 1. Data for COVID-19 (N=92) and Influenza (N=52) literature.

	<i>COVID-19</i>	<i>Influenza</i>	<i>P-value</i>
Journal			
<i>General Medicine</i>			
The Lancet	4 (4.3%)	0 (0.0%)	
New England Medical Journal	18 (19.6%)	4 (7.7%)	
British Medical Journal	14 (15.2%)	7 (13.5%)	
<i>Immunology</i>			
Nature Reviews Immunology	1 (1.1%)	0 (0,0%)	
Immunity	0 (0.0%)	0 (0,0%)	
NPJ Vaccine	4 (4.3%)	3 (5,8%)	
<i>Pediatrics</i>			
JAMA Pediatrics	13 (14.1%)	5 (9.6%)	
Lancet Child Adolescence Health	5 (5.4%)	2 (3.8%)	
Pediatrics	33 (35.9%)	31 (59.6%)	
Year of Publication			
2020	1 (1.1%)	13 (25,0%)	< 0.001
2021	13 (14.1%)	8 (15,4%)	
2022	41 (44.6%)	13 (25,0%)	
2023	25 (27.2%)	14 (26,9%)	
2024	12 (13.0%)	4 (7,7%)	
Topic			
Side Effects	<i>20 (21.7%)</i>	7 (13.5%)	0.03552
Efficacy and effectiveness	<i>50 (54.3%)</i>	25 (48.1%)	
Vaccination Policy	<i>9 (9.8%)</i>	16 (30.8%)	
Healthcare workers perception	<i>8 (8.7%)</i>	8 (15.4%)	
Parents perception	<i>21 (22.8%)</i>	14 (26.9%)	
Geographic area*			
Europa	11(12.0%)	11 (21.2%)	0.1294
North America	59 (64.1%)	48 (92.3%)	
South America	2 (2.2%)	0 (0.0%)	
East Asia	9 (9.8%)	6 (11.5%)	
South Asia	4 (4.3%)	0 (0.0%)	
Middle East	8 (8.7%)	1 (1.9%)	
Africa	3 (3.3%)	1 (1.9%)	
Oceania	4 (4.3%)	7 (13.5%)	

*Since some multicenter studies were conducted in centers across different continents, the sum of the numbers (and percentages) exceeds the total number of studies (and 100%) for both COVID-19 and influenza.

Figure 2 illustrates the percentage of articles addressing pediatricians' perceptions of COVID-19 vaccination. The analysis highlights a shift in focus over time: initially, there was a greater emphasis on the need for studies evaluating vaccine efficacy and safety. Over the four years, however, the focus has transitioned toward studies on vaccination policies and caregiver perceptions. This shift aligns with the trends observed in influenza vaccine literature, which emphasize strategies

to increase vaccine coverage rates (VCR), such as policy development and understanding perceptions.

Discussion

Vaccination is one of the most effective and cost-efficient tools for disease prevention, offering high efficacy at a low delivery cost. Its importance was

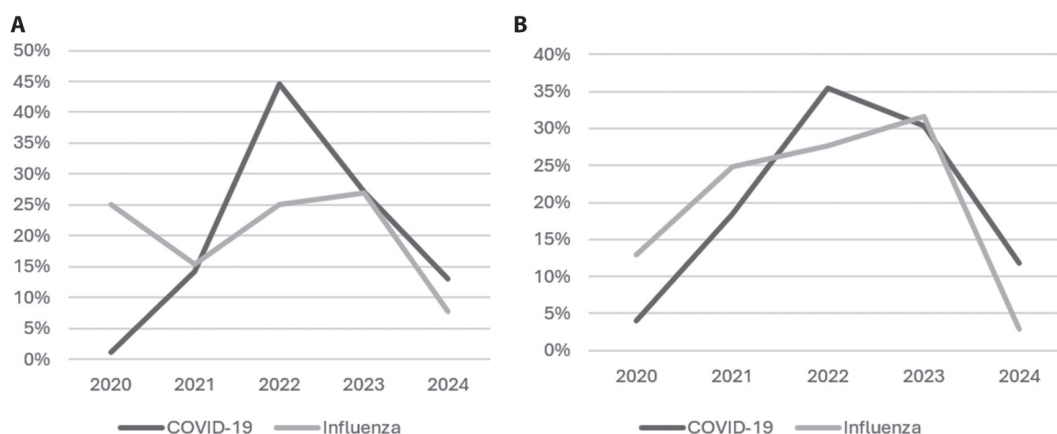


Figure 1. Time trend of COVID-19 and influenza vaccine publications between 2020 and 2024. (A) Literature production from the 9 highest IF journals in the 3 areas of interest: NPJ Vaccine, The Lancet, New England Medical Journal, British Medical Journal, Nature Reviews Immunology, Immunity, Pediatrics, JAMA Pediatrics, Lancet Child Adolescence Health, Pediatrics. (B) Entire literary production according to stated inclusion and exclusion criteria.

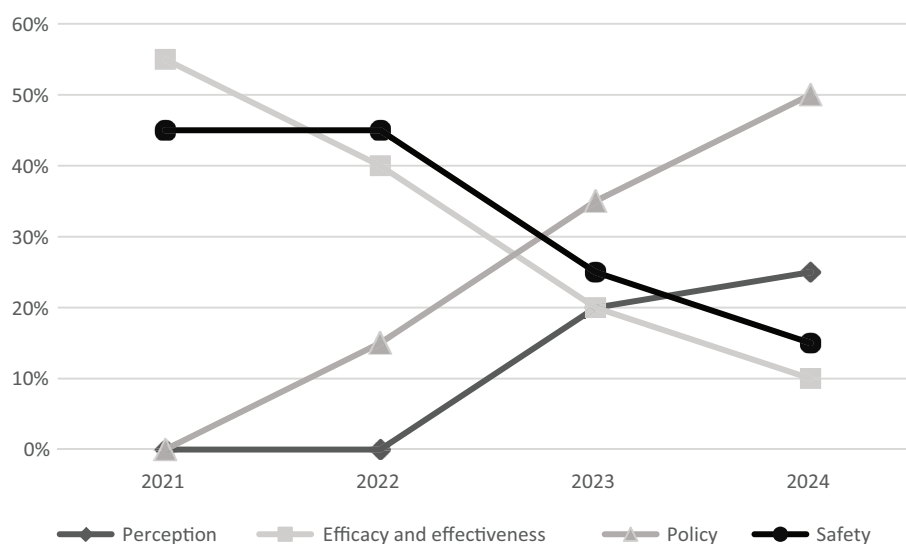


Figure 2. Figure 2 illustrates the alterations in the primary subjects encompassed in publications concerning the novel strain of coronaviruses from 2021 to 2024. The data are expressed as percentages of the total number of publications in the individual year.

especially evident during the SARS-CoV-2 pandemic, where both COVID-19 and influenza vaccinations significantly contributed to reducing disease severity and hospitalization rates. The pandemic heightened public awareness not only of COVID-19 vaccination but also of other respiratory disease vaccines, such as influenza. Studies have shown a marked increase in

vaccination rates against these pathogens during the first year of the pandemic, supporting the hypothesis that the pandemic positively influenced vaccination uptake. This heightened attention to vaccines, however, also reflects a broader shift in biomedical research priorities. The emergence of SARS-CoV-2 catalyzed an unprecedented focus on its epidemiological, clinical,

and preventive aspects, leading to a rapid surge in publications, particularly those addressing vaccine efficacy and effectiveness. Two key trends emerge: first, the initial focus was predominantly clinical, assessing the vaccine's impact on mitigating the pandemic, rather than its acceptance by healthcare workers or the public. This can be attributed to the novelty of the vaccine. Second, interest in COVID-19 vaccines declined as the pandemic's clinical, social, and organizational impact lessened. In contrast, influenza-related literature demonstrates a more stable temporal pattern, reflecting its longstanding history and well-established scientific knowledge. The focus on influenza vaccines often extends beyond efficacy to include public perceptions, policies, and tools for increasing vaccination coverage rates (VCR). This contrast highlights the differing research dynamics between a novel vaccine for an emergent pathogen and a longstanding vaccine with established data. The geographical distribution of studies further underscores these differences. Influenza studies are predominantly conducted in North America and Europe, with a strong emphasis on non-clinical factors such as vaccine perception and policy. COVID-19 studies, however, involve a broader range of populations and focus primarily on efficacy and effectiveness to evaluate the vaccine's role in controlling the pandemic across diverse settings. A critical area of investigation is the evolving perceptions of pediatricians regarding COVID-19 vaccination. While mandatory vaccination practices have somewhat reduced the emphasis on vaccine hesitancy compared to other vaccines, pediatricians' perceptions of necessity, safety, and efficacy remain crucial. Early literature, such as Del Duca's study (21), highlighted knowledge gaps as a key issue among pediatricians. However, more recent studies (from 2023 onward) reveal a shift toward evaluating healthcare providers' perceptions of vaccine safety and risk of side effects. This shift mirrors broader trends in pediatric vaccinology, where emphasis moves from understanding efficacy to addressing public perceptions and policy. The shift in focus is particularly evident in studies analyzing pediatricians' views on COVID-19 vaccines. Initially centered on efficacy and knowledge gaps, recent research increasingly emphasizes caregivers' perceptions of the vaccine. This trend suggests that COVID-19 vaccination

is becoming part of routine pediatric practice, resembling the approach taken with influenza vaccination. The focus on caregiver perceptions highlights the need for more inclusive strategies to improve VCR by engaging both pediatricians and caregivers. This study has several limitations. First, we searched only one database. Second, we did not analyze the quality of the included studies. Third, we relied on the publication dates of the studies, which may not correspond to when the studies were conducted. Lastly, we could not account for ongoing studies.

Conclusions

The pandemic has highlighted the critical role of vaccination in public health, driving unprecedented research and discussion. However, greater attention is needed on underexplored areas such as vaccine perception and safety, including the perspectives of both the public and healthcare providers, which significantly influence vaccine acceptance.

Future research should focus on developing effective communication strategies to address hesitancy and improve adherence, tailored to the underlying factors driving vaccine acceptance. While the pandemic catalyzed vaccine-related research, the predominant focus on clinical aspects has limited scope. Addressing gaps in understanding vaccine acceptance and hesitancy is essential for enhancing vaccination coverage and advancing public health initiatives.

Ethic Approval: Due to the absence of clinical or demographical data Ethic approval is Not applicable.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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G.P.M. and S.C.; supervision, S.C. and G.P.M.; project administration, S.C.; funding acquisition, S.C. All authors have read and agreed to the published version of the manuscript.

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