Received: 21 March 2023 | Revised: 18 July 2023 | Accepted: 15 August 2023

DOI: 10.1111/apa.16954

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

ORIGINAL ARTICLE

Safety profile of paediatric COVID-19 vaccines: An analysis of the US Vaccine Adverse Event Reporting System

Victoria Nikitina[1] | Greta Santi Laurini[1] | Nicola Montanaro[2] | Domenico Motola[1]

[1]Unit of Pharmacology, Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy

[2]Alma Mater Studiorum University di Bologna, Bologna, Italy

Correspondence
Domenico Motola, Unit of Pharmacology, Department of Medical and Surgical Sciences, University of Bologna, via Irnerio 48, 40126, Bologna, Italy.
Email: domenico.motola@unibo.it

Abstract

Aim: To provide further evidence on the safety profile of COVID-19 vaccines in paediatrics by analysing the spontaneous reports of adverse effects related to these vaccines.

Methods: Reports related to US paediatric population (from 0 to 17 years) vaccinated with authorised COVID-19 vaccines were extracted from Vaccine Adverse Event Reporting System from December 2020 to 17 November 2022. We conducted a descriptive analysis of Adverse Events Following Immunization (AEFI), calculating reporting rate of serious AEFIs and focusing on *myocarditis* and *Guillain-Barré Syndrome* after mRNA COVID-19 vaccines.

Results: Overall, 52 720 reports were retrieved: 77% (40541)-Pfizer-BioNTech, 19% (10083)-Moderna, a small proportion for other vaccines 4% (2096). Most of AEFIs were non-serious and listed in corresponding SPCs. Of serious AEFIs, 96% were related to the Pfizer-BioNTech vaccine. Roughly 91% (47874) were related to people from 6 to 17 years, a small percentage of 9% (4773) to the younger group (0–5 years). In both groups, most of the reports were related to mRNA vaccines and the percentage of AEFIs experienced by females were similar to males.

Conclusions: Data showed that events most frequently reported were non-serious and listed in the corresponding SPCs, extending the evidence of safety of COVID-19 vaccines authorised in the United States in children.

KEYWORDS
children, COVID-19, COVID-19 vaccines, paediatric, pharmacovigilance

1 | INTRODUCTION

Since the start of the pandemic, according to The Johns Hopkins Coronavirus Resource Centre around 98.3 million people have been infected with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and more than 1.1 million people have died from COVID-19 only in the United States, as of 18 November 2022.

The catastrophic consequences of the outbreak of this pandemic made clear the worldwide necessity to contrast the virus spread as soon as possible. This urgent need alongside the identification of

Abbreviations: AEFI, Adverse Event Following Immunisation; CDC, The Centers for Disease Control and Prevention; EAU, Emergency Authorization Use; FDA, Food and Drug Administration; ICSR, Individual Case Safety Report; GBS, Guillain-Barré Syndrome; MedDRA, Medical Dictionary for Regulatory Activities; SARS, CoV-2-Severe Acute Respiratory Syndrome Coronavirus 2; SPC or SmPC, Summary of Product Characteristics; VAERS, Vaccine Adverse Event Reporting System.

the genetic sequence of SARS-CoV-2 led the whole scientific community to an unprecedented collaboration in order to develop vaccines against COVID-19 disease in an extraordinarily short time. COVID-19 vaccines studied to date have undergone rigorous testing in clinical trials, and their favourable safety profile, high efficacy and acceptable risk-to-benefit profile have justified the major regulatory agencies to release the Emergency Authorization Use (EAU).

The priority was to vaccinate vulnerable people or those with underlying medical conditions such as tumour, diabetes, hypertension, cardiac disorder or kidney disease. Later on, the vaccination was gradually expanded to adults of all age groups.[1,2]

However, vaccine safety, efficacy and immunogenicity were evaluated in several ongoing clinical trials involving only adults when in December of 2020, the first COVID-19 vaccine obtained the EAU by the Food and Drug Administration (FDA). In fact, alongside with other vulnerable categories (e.g. pregnant women), children are an exceptional population usually not involved in clinical trials because of ethical and clinical concerns.[3–5] Nevertheless, studies on this group are fundamental to develop the best age-specific medical treatment. It took a year for COVID-19 vaccines to be experimented and authorised for their use in children.

Several studies suggested that the susceptibility to SARS-CoV-2 infection is lower in children and adolescents and, in general, the illness is milder compared with adults. Nevertheless, COVID-19 disease could still lead them to hospitalisation, as shown by the cumulative rates of laboratory-confirmed COVID-19.[6–10] Furthermore, a current or recent infection or exposure to SARS-CoV-2 virus has been associated with a rare, but serious clinical condition in children and adolescents, known as Paediatric Multisystem Inflammatory Syndrome, temporally associated with SARS-CoV-2 (PIMS-TS).[11–14]

It is also important to consider the role of the young population in the COVID-19 disease transmission, which is still not fully understood due to scarce and conflicting data.[15] Therefore, safe and efficacious vaccines for younger populations are paramount.

The Centers for Disease Control and Prevention (CDC) recommend COVID-19 vaccines for everyone aged 6 months and older, and boosters for everyone aged 5 years and older if eligible. COVID-19 vaccines available under EUA for paediatric population are three: two of them are mRNA vaccines developed by Pfizer-BioNTech and Moderna, and a protein subunit vaccine by Novavax.[16] In particular, the US FDA authorised emergency use of Pfizer-BioNTech and Moderna vaccines in children aged 6 months through 17 years and Novavax in adolescents aged 12 and older.[17] These vaccines had been authorised for use in adults 18 years of age and older.

Despite the proven high efficacy and safe profile of COVID-19 vaccines in the general population,[18–21] the evidence associated with the paediatric population, initially excluded from clinical trials, is limited, although promising.[22,23]

In consideration to the scarce representation of children in studies on COVID-19 vaccines and the exceptionally accelerated approval of these medicines, post-marketing surveillance of their use in children may furnish a crucial contribution to a more solid safety profile of paediatric COVID-19 vaccines. In this context, the aim of this study was to analyse the spontaneous reports of adverse effects of COVID-19 vaccines in children, retrieving data from the Vaccine Adverse Event Reporting System (VAERS).

Key notes

- Considering the scarce representation of children in COVID-19 vaccines studies, post-marketing surveillance of their use in children is crucial in order to furnish a more solid safety profile of these vaccines.
- In this survey, events most frequently reported following vaccination with COVID-19 vaccines among paediatric population were non-serious and listed in the corresponding SPCs.
- Our data extend the evidence of safety of COVID-19 vaccines authorised in the United States in the paediatric population.

2 | METHODS

Data were extracted from the Vaccine Adverse Event Reporting System (VAERS), one of the largest databases of adverse events that occur following immunisation (AEFI) with US-licensed vaccines. It was established in 1990 and it is co-administered by the Centers for Disease Control and Prevention (CDC) and FDA. VAERS is a post-licensure vaccine surveillance system where AEFI is gathered by healthcare professionals, pharmaceutical companies and other reporters including patients. This database is a useful pharmacovigilance tool for detecting possible safety problems (unusual or unexpected patterns of adverse event) with vaccines that provides CDC and FDA with valuable information on the necessity to evaluate and assess a possible safety concern. Furthermore, this system is designed to detect extremely rare events that cannot be identified in clinical trials. In VAERS reports are described information related to patients, adverse events, vaccines characteristics, the date of immunisation, the receipt date, patient characteristics such as age group and sex, and a description of the toxicity, including time of onset and seriousness according to the US Code of Federal Regulations. All adverse events are categorised using the Medical Dictionary for Regulatory Activities (MedDRA), a rich and highly specific standardised medical terminology to facilitate sharing of regulatory information internationally for medical products used by humans. MedDRA terms are arranged in a 5-tiered multi-axial hierarchy, which provides increasing specificity as one descends. One or more symptoms can be reported for each VAERS report (https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/covid-19-vaccine-safety-surveillance). The analysis was conducted using vaccine-reaction pairs, meaning that each individual report may include, for instance, one suspected vaccine and three distinct adverse events, resulting in the generation of three vaccine-event pairs. In the event of two

suspected vaccines, six vaccine-event pairs are generated, and so forth.

In this study, we analysed the VAERS reports with COVID-19 vaccines as suspected product from December 2020 (month when the first vaccine received an Emergency Use Authorization for people aged 16 and over) to 17 November 2022 in the paediatric population, from 0 to 17 years, successively divided in two age ranges 0–5 and 6–17 years respectively. Moreover, we arranged the data by different types of COVID-19 vaccines (Pfizer-BioNTech, Moderna, Janssen, Novavax, Pfizer-BioNTech bivalent, Moderna bivalent), focusing on those authorised under EAU in the United States. The analysis was performed on the "United States, Territories and Unknown" group which includes all of the location values, except for "Foreign" locations.

3 | RESULTS

During the study period, a total number of 52 720 individual case safety reports (ICSRs) regarding all COVID-19 vaccines were extracted from the VAERS database for people under 18 years old: 77% (40541)-Pfizer-BioNTech, 19% (10083)-Moderna, a small proportion of 3% (1340) and 1% (576) for Janssen and Pfizer-BioNTech bivalent, respectively, and an irrelevant number 0% (180) for Novavax, Moderna bivalent and reports with unknown vaccine administered. A large percentage of adverse events following the immunisation 94.96% (50063) were non-serious, only 5.04% (2657) were described as serious (Figure 1) and almost all of them are related to Pfizer-BioNTech vaccine 96% (2561). We performed the analysis on 111 883 vaccine-reaction pairs related to the most reported mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna) and Novavax, authorised under emergency use in the United States. The AEFIs most frequently reported were non-serious and listed in corresponding Summaries of Product Characteristics (SPCs): *dizziness* (3614), *pyrexia* (2975) and *headache* (2716) for Pfizer-BioNTech vaccine; *pyrexia* (278), *pain in extremity* (197) and *fatigue* (137) for Moderna vaccine; *headache*, *joint swelling*, *lymphadenopathy*, *pain* and *pyrexia* for Novavax with the same frequency for each AEFI (1) (Tables 1 and 2). We did not consider the events such as incorrect administration, routine laboratory tests or incorrect vaccine storage because it is not pertinent to our discussion of the AEFIs.

We analysed reports with serious events related to the Pfizer-BioNTech vaccine, a total of 23 768 vaccine-reaction pairs: *pyrexia* (33), COVID-*19* (18) and *vomiting* (14) are the most common AEFIs in the youngest group, while *chest pain* (805), *myocarditis* (482) and *pyrexia* (450) in the 6–17 years cohort. Focusing on Pfizer mRNA-based COVID-19, a total of 567 ICSRs of *myocarditis* were submitted into VAERS during the study period in children. The largest proportion of reports 99.5% (564) refers to juveniles aged from 6 to 17 years. Most of the cases with a percentage of 88 (498) regarded males. Roughly 73% (414) of cases occurred after the second dose, 16% (91) and 11% (62) following the first and the third dose, respectively. Approximately, 86% (492) of these events occurred within the 7 days after vaccination.

We also registered a total of 29 cases of Guillain-Barré Syndrome (GBS). All of them related to mRNA COVID-19 vaccines, 28 ICSRs for Pfizer BioNTech and 1 for Moderna. One patient had a previous history of GBS. The majority of the cases 89.7% (26) were related to people from 6 to 17 years and only three cases were reported for children from 3 to 5 years. There is a slightly higher percentage of males who experienced GBS compared to females with 53% (15) and 46% (14) respectively. More than a half of the cases (19) occurred within a month after the vaccination, 48.3% (14) after the second dose, 27.6% (8) after the first dose, 6.9% (2) after the third dose and 17.2% (5) of cases did not contain this information.

The onset of AEFIs ranged from day 0 (i.e. vaccination day) in 35 785 cases, up to over 120 days after the vaccination. As shown in the Figure 2 (see also Table S1 in the Supplementary Appendix), dividing the study population in two groups by age, roughly 91% (47874) of AEFIs are related to people from 6 to 17 years and only a small percentage of 9% (4773) to the younger group from 0

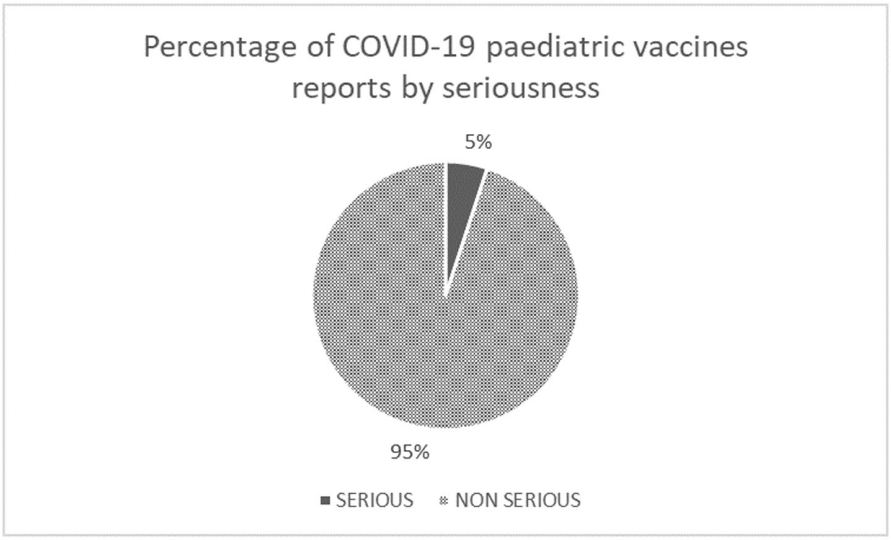

FIGURE 1 Percentage of reports referred to COVID-19 vaccines in paediatric population by seriousness.

TABLE 1 Most reported adverse events for the *Pfizer-BioNTech* and *Pfizer-BioNTech bivalent* vaccines in VAERS.

Events	*N*	%	Events	*N*	%
Pfizer-BioNTech			**Pfizer-BioNTech bivalent**		
Dizziness	3614	2.96	Dizziness	43	3.20
Pyrexia	2975	2.43	Syncope	32	2.38
Headache	2716	2.22	Pyrexia	28	2.09
Syncope	2476	2.03	Fatigue	21	1.56
Nausea	2254	1.84	Loss of consciousness	20	1.49
Vomiting	2195	1.80	Headache	19	1.42
Fatigue	2058	1.68	Nausea	18	1.34
Chest pain	1861	1.52	Vomiting	18	1.34
Loss of consciousness	1369	1.12	Pallor	17	1.27
Pallor	1330	1.09	Hyperhidrosis	15	1.12
Pain	1327	1.09	Unresponsive to stimuli	15	1.12
Dyspnoea	1270	1.04	Fall	13	0.97
Rash	1265	1.03	Pain in extremity	12	0.89
Pain in extremity	1219	1.00	Asthenia	11	0.82
Hyperhidrosis	1193	0.98	Malaise	11	0.82
Chills	1062	0.87	Chest pain	9	0.67
Urticaria	979	0.80	Tremor	9	0.67
Covid-19	860	0.70	Chills	8	0.60
Unresponsive to stimuli	711	0.58	Dyspnoea	7	0.52
Fall	708	0.58	Injection site swelling	7	0.52
Troponin increased	662	0.54	Erythema	6	0.45
Asthenia	645	0.53	Feeling hot	6	0.45
Malaise	628	0.51	Flushing	6	0.45
Sars-cov-2 test positive	606	0.50	Hypotension	6	0.45
Seizure	594	0.49	Injection site pain	6	0.45
Cough	592	0.48	Rash	6	0.45
Pruritus	592	0.48	Seizure	6	0.45
Oropharyngeal pain	575	0.47	Abdominal pain	5	0.37
Sars-cov-2 test negative	567	0.46	Head injury	5	0.37
Myocarditis	566	0.46	Injection site erythema	5	0.37
Tremor	557	0.46	Presyncope	5	0.37
Injection site pain	556	0.45	Tinnitus	5	0.37
Electrocardiogram	543	0.44	Urticaria	5	0.37
Lymphadenopathy	523	0.43	Condition aggravated	4	0.30

to 5 years. In both age ranges, almost all the reports are related to mRNA vaccines: 97.2% (46555) for 6–17 years and 99.5% (4747) in the younger group. Moreover, in both age cohorts, the percentage of AEFIs experienced by female are similar to those reported for males: 49% (2329) and 48% (2295) in the group from 0 to 5 years, 39% (24418) and 37% (223,79) for 6–17 years, respectively. In these last analyses, we did not consider the ICSRs referred to unknown COVID-19 vaccines.

4 | DISCUSSION

This pharmacoepidemiological study provides an updated picture of the safety profile of vaccines in paediatrics. Although the data are from the US population, the results can be extended to a general level.

From the start of the vaccination programme in young people to the beginning of November 2022, more than 57 million doses

TABLE 2 Most reported adverse events for the *Moderna* and *Moderna bivalent* vaccines in VAERS.

Events	N	%	Events	N	%
Moderna			**Moderna bivalent**		
Pyrexia	278	2.04	Pyrexia	9	4.31
Pain in extremity	197	1.45	Fatigue	6	2.87
Fatigue	137	1.01	Headache	4	1.91
Headache	110	0.81	Pain	4	1.91
Vomiting	86	0.63	Myalgia	3	1.44
Off label use	79	0.58	Nausea	3	1.44
Pain	79	0.58	Pain in extremity	3	1.44
Rash	69	0.51	Syncope	3	1.44
Urticaria	65	0.48	Vomiting	3	1.44
Injection site pain	63	0.46	Arthralgia	2	0.96
Cough	57	0.42	Chills	2	0.96
Decreased appetite	54	0.40	Dizziness	2	0.96
Diarrhoea	53	0.39	Erythema	2	0.96
Chills	51	0.37	Fall	2	0.96
Dizziness	50	0.37	Immunisation reaction	2	0.96
Myalgia	49	0.36	Loss of personal independence in daily activities	2	0.96
Sars-cov-2 test negative	49	0.36	Pallor	2	0.96
Vaccination site pain	48	0.35	Rash	2	0.96
Covid-19	44	0.32	Swelling	2	0.96
Irritability	44	0.32	Abdominal discomfort	1	0.48
Injection site erythema	42	0.31	Blindness transient	1	0.48
Rhinorrhoea	38	0.28	Dehydration	1	0.48
Rash erythematous	35	0.26	Educational problem	1	0.48
Nausea	34	0.25	Gait disturbance	1	0.48
Erythema	33	0.24	Gait inability	1	0.48
Lethargy	33	0.24	Influenza like illness	1	0.48
Sars-cov-2 test positive	32	0.24	Injection site pain	1	0.48
Injection site swelling	31	0.23	Injury associated with device	1	0.48
Chest pain	30	0.22	Irritability	1	0.48
Dyspnoea	30	0.22	Joint swelling	1	0.48

were administered to people under 18 years old (https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends), corresponding to a rate of roughly four reports per 100 000 doses of the serious AEFIs. The first COVID-19 vaccine to obtain EAU was Pfizer-BioNTech, which is also the most reported vaccine, followed by the second mRNA COVID-19 vaccine Moderna and lately by Novavax. The most frequently reported adverse events in the paediatric population were *dizziness*, *pyrexia*, *headache*, *pain in extremity* and *fatigue*, which are in line with the safety profile of Pfizer-BioNTech, Moderna and Novavax vaccines.

Myocarditis is a rare, but serious AEFI associated with mRNA-based COVID-19 vaccines.[25] It typically occurs more frequently among adolescents and young adults of male sex, with a higher incidence among males aged 12–17 years, which agrees with our findings.[26]

Our study showed that most of the cases of myocarditis occurred in males, which is in line with a previous study conducted by Oster et al. showed that 82% of the cases regarded males. In addition, comparing our findings with those of Oster et al., we can reiterate that the risk of myocarditis after receiving mRNA-based COVID-19 vaccines was highest after the second vaccination dose in adolescent males.[24]

Guillain-Barré Syndrome (GBS), a rare neurological disease where the body immune system damages nerves, has been reported

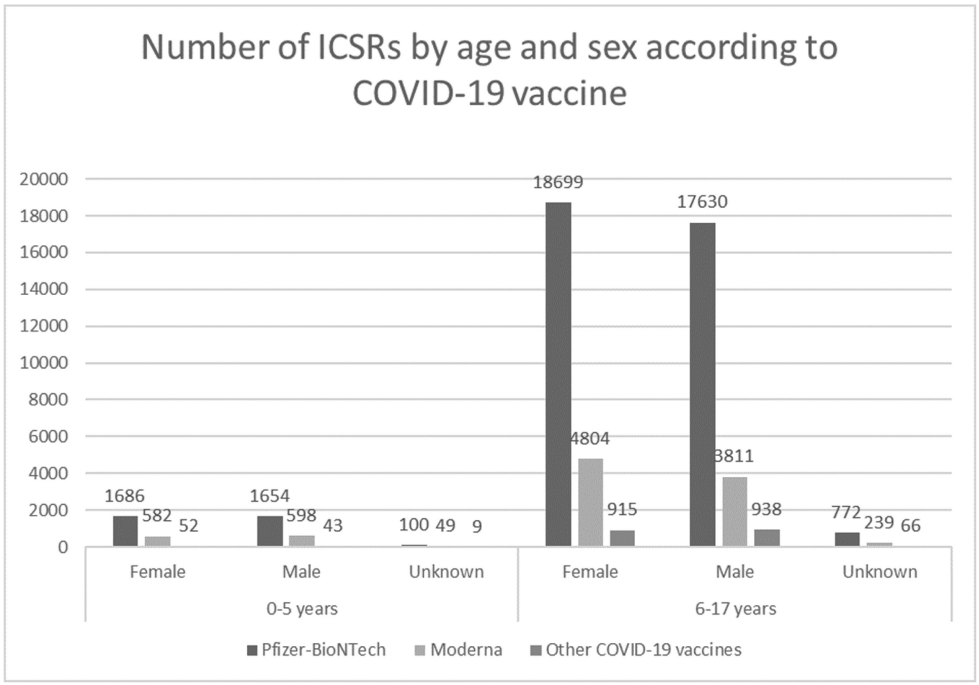

FIGURE 2 Number of ICSRs by age and sex according to COVID-19 vaccines. *Other COVID-19 vaccines: *Pfizer-BioNTech bivalent*, *Moderna bivalent*, *Novavax* and *Janssen*.

worldwide in association with vaccination against COVID-19. The first case of GBS following immunisation with mRNA vaccine (Pfizer-BioNTech) was described by Waheed et al. in February 2021.[26] According to the systematic review conducted by Abolmaali et al. most of the cases occurred after a vaccination with a vector-based vaccine, while the Pfizer BioNTech vaccine ranked second for COVID-19 vaccine–associated GBS in their study.[27] However, no neurological adverse events were described in the phase III study.[18] Our results in children have shown that the majority of GBS cases occurred after the second dose, which is in line with what was reported for adults in Abolmaali's study, but in contrast to other observations.[27,28] There is no adequate evidence to support a causal relationship between the Pfizer COVID-19 vaccine and GBS in children. Nevertheless, all the COVID-19 vaccines should be monitored for this syndrome and all cases evaluated closely.

Overall, our analysis depicts that the data on safety of these vaccines are in line with those reported in the SPCs of the vaccines and with other studies available in the literature.[22–29]

4.1 | Strengths and limitations

Surveillance systems based on spontaneous reports provide continuously essential information of clinical importance thanks to real-life data collected on a large scale of patients in a cost-effective way, allowing to discover serious and/or rare adverse events not detected during clinical trials. Post-marketing research can be very useful for the evaluation of drug safety, especially in the special cohorts that are usually excluded from the clinical trials, such as the paediatric population, as in our survey. However, pharmacovigilance studies based on spontaneous reporting systems present several limitations. First, reporting quality: since everyone, healthcare professionals or not, can voluntarily file a VAERS report, this may result in providing scarce or wrong information. Secondly, VAERS contains all reports without the previous assessment of causality between the AEFIs and related vaccines. Moreover, spontaneously reported data can be affected by several biases such as the length of time that the vaccine has been on the market, the country, the availability of the vaccine and the development of reporting systems. Among the above limitations, underreporting remains one of the main limitations of passive surveillance systems, including VAERS, where only a small fraction of the actual AEFIs is reported. The degree of underreporting varies widely, and it is difficult to estimate. For instance, more serious and unexpected medical events are more likely to be reported than minor ones, especially when they occur soon after vaccination, even if they may be coincidental and related to other causes. Another limitation is the lack of a denominator, that is, the number of patients exposed to the medical product and thus at risk for the adverse event of interest, that is important to make incidence rates.[30]

5 | CONCLUSION

After more than 2 years, COVID-19 pandemic continues to be a relevant public health threat worldwide. COVID-19 vaccines remain the most important intervention aimed to contain the virus and the extension of the mass vaccination programme to younger age groups is paramount. Vaccination of children could not only protect

them from the disease but also might improve their mental health and well-being by facilitating a return to normalcy, assuring a continual school education and social interactions important for child development.

The AEFIs analysis showed that the events most frequently reported were non-serious and listed in the corresponding summary of product characteristics. The results from this study involving paediatric populations extend the evidence of safety of COVID-19 vaccines authorised in the United States.

AUTHOR CONTRIBUTIONS

Substantial contributions to conception or design of the work (D.M., V.N., G.S.L., NM), or the acquisition (V.N.), analysis (V.N., D.M.) or interpretation of data for the work (V.N., G.S.L., D.M., N.M.). Drafting of the work (V.N, D.M.) or revising it critically for important intellectual content (N.M., G.S.L.). All authors approved the submitted final version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

FUNDING INFORMATION

No external funding source, and no editorial or manuscript support.

CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL AND PATIENT CONSENT

The manuscript does not contain clinical studies or patient data. For this type of study, ethics committee approval and formal consent are not required.

ORCID

Victoria Nikitina https://orcid.org/0000-0002-0089-3043
Greta Santi Laurini https://orcid.org/0000-0002-7897-2956
Nicola Montanaro https://orcid.org/0000-0002-5710-8077
Domenico Motola https://orcid.org/0000-0001-6253-4014

REFERENCES

1. Centers for Disease Control. Accessed November 18, 2022. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html
2. Ge E, Li Y, Wu S, Candido E, Wei X. Association of pre-existing comorbidities with mortality and disease severity among 167,500 individuals with COVID-19 in Canada: a population-based cohort study. PLoS One. 2021;16(10):e0258154. doi:10.1371/journal.pone.0258154
3. Edwards SD, McNamee MJ. Ethical concerns regarding guidelines for the conduct of clinical research on children. J Med Ethics. 2005;31(6):351-4. doi:10.1136/jme.2004.009555
4. Nicholson RH. Medical Research with Children: Ethics, Law, and Practice: the Report of an Institute of Medical Ethics Working Group on the Ethics of Clinical Research Investigations on Children. Oxford University Press; 1986: at 25.
5. Kopelman LM. Children as research subjects: a dilemma. J Med Philos. 2000;25(6):745-64. doi:10.1076/jmep.25.6.723.6129
6. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics. 2020;145(6):e20200702. doi:10.1542/peds.2020-0702
7. Garg S, Kim L, Whitaker M, et al. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 – COVID-NET, 14 states, march 1–30, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(15):458-64. doi:10.15585/mmwr.mm6915e3
8. Viner RM, Mytton OT, Bonell C, et al. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. JAMA Pediatr. 2021;175(2):143-56. doi:10.1001/jamapediatrics.2020.4573. Erratum in: *JAMA Pediatr*. 2021 Feb 1;175(2):212.
9. Havers FP, Whitaker M, Self JL, et al. Hospitalization of adolescents aged 12-17 years with laboratory-confirmed COVID-19 – COVID-NET, 14 states, March 1, 2020-April 24, 2021. MMWR Morb Mortal Wkly Rep. 2021;70(23):851-7. doi:10.15585/mmwr.mm7023e1
10. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-62. doi:10.1016/S0140-6736(20)30566-3
11. Dufort EM, Koumans EH, Chow EJ, et al. Multisystem inflammatory syndrome in children in New York state. N Engl J Med. 2020;383(4):347-58. doi:10.1056/NEJMoa2021756
12. Jones VG, Mills M, Suarez D, et al. COVID-19 and Kawasaki disease: novel virus and novel case. Hosp Pediatr. 2020;10(6):537-40. doi:10.1542/hpeds.2020-0123
13. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet. 2020;395(10239):1771-8. doi:10.1016/S0140-6736(20)31103-X
14. Abrams JY, Godfred-Cato SE, Oster ME, et al. Multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2: a systematic review. J Pediatr. 2020;226:45-54.e1. doi:10.1016/j.jpeds.2020.08.003
15. The Lancet Infectious Diseases. Should we vaccinate children against SARS-CoV-2? Lancet Infect Dis. 2021;1(7):889. doi:10.1016/S1473-3099(21)00339-X
16. Centers for Disease Control and Prevention (CDC). COVID-19 Vaccination for Children. Public Dashboard. Accessed November 18, 2022. https://www.cdc.gov/vaccines/covid-19
17. Food and Drug Administration. Coronavirus (COVID-19) Update: FDA Authorizes Moderna and Pfizer-BioNTech COVID-19 Vaccines for Children Down to 6 Months of Age. Accessed November 18, 2022. https://www.fda.gov/news-events/covid-19-vaccines-children
18. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. N Engl J Med. 2020;383(27):2603-15. doi:10.1056/NEJMoa2034577
19. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384:403-16. doi:10.1056/NEJMoa2035389
20. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARSCoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2021;397(10269):99-111. doi:10.1016/S0140-6736(20)32661-1. Erratum in: *Lancet*. 2021 Jan 9;397(10269):98.
21. Anderson EJ, Rouphael NG, Widge AT, et al. Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. N Engl J Med. 2020;383:2427-38. doi:10.1056/NEJMoa2028436
22. Walter EB, Talaat KR, Sabharwal C, et al. Evaluation of the BNT162b2 covid-19 vaccine in children 5 to 11 years of age. N Engl J Med. 2022;386:35-46. doi:10.1056/NEJMoa2116298

23. Frenck RW Jr, Klein NP, Kitchin N, et al. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. N Engl J Med. 2021;385(3):239-50. doi:10.1056/NEJMoa2107456
24. Oster ME, Shay DK, Su JR, et al. Myocarditis cases reported after mRNA-based COVID-19 vaccination in the US from December 2020 to August 2021. JAMA. 2022;327(4):331-40. doi:10.1001/jama.2021.24110
25. Kytö V, Sipilä J, Rautava P. The effects of gender and age on occurrence of clinically suspected myocarditis in adulthood. Heart. 2013;99(22):1681-4. doi:10.1136/heartjnl-2013-304449
26. Waheed S, Bayas A, Hindi F, Rizvi Z, Espinosa PS, et al. Neurological complications of COVID 19: Guillain-Barre syndrome following Pfizer COVID-19 vaccine. Cureus. 2021;13:e13426.
27. Abolmaali M, Rezania F, Behnagh AK, Hamidabad NM, Gorji A, Mirzaasgari Z. GuillainBarré syndrome in association with COVID19 vaccination: a systematic review. Immunol Res. 2022;70:752-64.
28. Finsterer J, Scorza FA, Scorza CA. Post SARS-CoV-2 vaccination Guillain-Barre syndrome in 19 patients. Clinics. 2021;76:e3286. doi:10.6061/clinics/2021/e3286
29. Hause AM, Marquez P, Zhang B, et al. Parker C, COVID-19 mRNA vaccine safety among children aged 6 months-5 years – United States, June 18, 2022-August 21, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(35):1115-20. doi:10.15585/mmwr.mm7135a3
30. Goldman SA. Limitations and strengths of spontaneous reports data. Clin Ther. 1998;20(Suppl C):C40-4. doi:10.1016/s0149-2918(98)80007-6

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Nikitina V, Santi Laurini G, Montanaro N, Motola D. Safety profile of paediatric COVID-19 vaccines: An analysis of the US Vaccine Adverse Event Reporting System. Acta Paediatr. 2023;112:2426–2433. https://doi.org/10.1111/apa.16954