COVID-19 vaccine effectiveness and uptake in a national cohort of English children and young people with life-limiting neurodisability

Authors

J Cruz PhD,[1] R Harwood PhD,[2] S Kenny MD,[2,3] M Clark MB BChir,[3] PJ Davis Mb ChB,[4] ES Draper PhD,[5] D Hargreaves MDRes,[6] SN Ladhani PhD,[7,8] K Luyt PhD,[9] S Turner MD,[10] E Whittaker PhD,[11,12] P Hardelid,[1] L K Fraser PhD,[13] R M Viner FMedSci,[1*] J L Ward PhD,[1*]

*Joint senior author

Affiliations

1: UCL Great Ormond St. Institute of Child Health, London

2: Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool

3: NHS England and Improvement

4: Paediatric Intensive Care Unit, Bristol Royal Hospital for Children, Bristol

5: PICANet, Department of Population Health Sciences, University of Leicester, Leicester

6: Mohn Centre for Children's Health and Wellbeing, Imperial College London, London, United Kingdom

7. Immunisation Department, UK Health Security Agency (UKHSA), 61 Colindale Avenue, London NW9 5EQ, United Kingdom

8. Centre for Neonatal and Paediatric Infection (CNPI), St George's, University of London, Cranmer Terrace, London SW17 0RE, United Kingdom

9. Bristol Medical School, University of Bristol, Bristol

10. Women and Children's Division, NHS Grampian, Aberdeen

11. Paediatric Infectious Diseases, Imperial College Healthcare NHS Trust, London, United Kingdom

12. Section of Paediatric Infectious Diseases, Faculty of Medicine, Imperial College London, United Kingdom

13. Cicely Saunders Institute, King's College London

Correspondence:

Dr. Joseph Ward

UCL Great Ormond St. Institute of Child Health

30 Guilford St. London WC1N 1EH

Joseph.ward@ucl.ac.uk

Word count: 2487

COVID-19 vaccine effectiveness and uptake in a national cohort of English children and young people with life-limiting neurodisability

Objective

To investigate SARS-CoV-2 vaccine uptake and effectiveness in children and young people (CYP) with life-limiting neurodisability

Design

We undertook a retrospective cohort study using national hospital data in England from 21 December 2020 - 2 September 2022 to describe SARS-CoV-2 vaccination uptake, and then examined COVID-19 hospitalization, PICU admission and death following SARS-CoV-2 infection by vaccination status using cox regression models.

Patients

CYP aged 5-17 with life-limiting neurodisability.

Results

We identified 38,067 CYP with life-limiting neurodisability; 13,311 (35.0%) received at least one SARS-CoV-2 vaccine, with uptake higher amongst older, White CYP, from less deprived neighbourhoods. Of 8,134 CYP followed up after a positive SARS-CoV-2 test, 1,547 (19%) were vaccinated. Within 28 days of infection, 309 (4.7%) unvaccinated CYP were hospitalized with COVID-19 compared with 75 (4.8%) vaccinated CYP. 46 (0.7%) unvaccinated CYP were admitted to PICU compared with 10 (0.6%) vaccinated CYP. 20 CYP died within 28 days of SARS-CoV-2 infection, of which 13 were unvaccinated. Overall, adjusted hazard of hospitalization for COVID-19 or admission to PICU did not vary by vaccination status. When the Alpha-Delta SARS-CoV-2 variants were dominant, hazard of hospitalization with COVID-19 was significantly lower amongst vaccinated CYP (HR 0.26 [0.09 – 0.74]), with no difference seen during Omicron (HR 1.16 [0.74 – 1.81]).

Conclusions

SARS-CoV-2 vaccination was protective of COVID-19 hospitalization among CYP with life-limiting neurodisability during Alpha-Delta, but not for other SARS-CoV-2 variants. Vaccine uptake was low and varied by ethnicity and deprivation.

What is already known

CYP with life limiting neurodisability were prioritised for SARS-CoV-2 vaccination, but there is little evidence on vaccine uptake or effectiveness in this vulnerable group.

What this study adds

This is the first national population cohort to investigate real world vaccine effectiveness against serious outcomes in COVID-19 amongst CYP with life limiting neurodisability. We found vaccination uptake to be very low during the study period, and vary by ethnicity and deprivation. Vaccination was protective of hospitalization due to COVID-19 during the Alpha-Delta pandemic period but not during Omicron.

How might this affect research, practice or policy

Further work is needed to understand barriers to vaccination against SARS-CoV2 amongst CYP with life limiting neurodisability, and ensure community health services are better maintained during future pandemics.

Introduction

Life-limiting neurodisability is defined as neurodisability for which there is no hope of cure and from which children and young people (CYP) will almost certainly die.[1] These conditions affect around 10.8 per 100,000 CYP aged 0-19 years in England.[2] CYP with life-limiting neurodisability were identified as a high-risk group early in the COVID-19 pandemic,[3] with large-scale national studies showing they had among the highest risk of serious disease[4] and death[5] associated with SARS-CoV-2 infection. CYP with life-limiting neurodisability aged ≥12 years were prioritised for COVID-19 vaccination since late December 2020, despite the vaccines not being authorised below 16 years of age,[3] and this group remain a high priority for vaccination in the UK.[6]

COVID-19 mRNA vaccines are highly effective at preventing severe disease associated with SARS-CoV-2 infection in healthy CYP in multiple meta-analyses.[7-10] This protection appears to extend to the Omicron variant,[11] although with reduced effectiveness.[12] However, the literature on vaccine impact in high-risk CYP is limited. A rapid review in April 2023 using the search terms *COVID-19 vaccination*, *child or adolescent*, and *neurodisability or child disability*, identified only 2 relevant studies.[13,14] An early study of mRNA vaccination in 26 adolescents with neurodisability showed adverse events were similar to those reported in healthy adults, but provided no information on efficacy.[13] A study of antibody and cellular responses to vaccination amongst fifteen adolescents with complex neurodisability and normal immunity showed similar immune responses to those seen in healthy children.[14] Small studies of adults with neurodevelopmental disabilities, however, found COVID-19 vaccination to be effective at reducing mortality.[15] Data on vaccine uptake in this vulnerable population are absent in England[16] and in other countries.

We examined SARS-CoV-2 vaccine uptake amongst CYP with life-limiting neurodisability using datasets which included all hospitalisations in CYP in England, linked with data on paediatric intensive care unit (PICU) admission, SARS-CoV-2 testing and vaccination status. We then used these population level data to examine vaccine effectiveness against severe disease amongst CYP with life-limiting neurodisability with confirmed SARS-CoV-2 infection.

Methods

Data sources

We undertook a cohort study using Secondary Uses Services (SUS) data, with records linked at individual level to: the national Paediatric Intensive Care Audit Network (PICANet) dataset; national SARS-CoV-2 testing data; the National Immunisation Database of COVID-19 Vaccinations; Office for National Statistics (ONS) death registrations, and National Child Mortality Database (NCMD) death notification data.

Study population

We identified CYP with life-limiting neurodisability using relevant ICD-10 codes[17] recorded as the reason for admission in SUS between 1 April 2015 and 2 September 2022. Note CYP had to have been hospitalized at least once in this period to be included (supplementary table S1, figures S1-S2). From this group, we identified two cohorts:

1. Overall cohort: we studied vaccine uptake within CYP with life-limiting neurodisability aged 5-17 from 21 December 2020 and 2 September 2022, (and so were eligible for vaccination).

2. Test-positive cohort: to study vaccine effectiveness, we identified CYP within the overall cohort who had one or more positive SARS-CoV-2 test between 4 January 2021 - 2 September 2022. We used data from 4 January 2021 as this was 14 days after vaccination was first available for CYP with life-limiting conditions (the time needed to confer protection).[18]

Outcomes

We used hospitalisation and PICU admission as proxies for SARS-CoV-2 disease severity, as used in previous work.[4,19,20] We examined hospitalisations occurring 2 days before, to 28 days after a positive SARS-CoV-2 test, consistent with adult studies.[21] We used two methods to identify COVID-19 hospitalizations. First, we identified hospitalizations where a COVID-19 ICD-10 code was recorded as the Primary diagnosis. This definition ("Primary COVID-19") is specific but may miss cases within CYP with multiple medical problems, (common among those with life limiting neurodisability). We then identified hospitalizations where a COVID-19 code was recorded as either the Primary or Secondary diagnosis. This definition ("Primary/Secondary COVID-19") is likely to be more sensitive but may capture

hospitalisations for other reasons, including incidental infections. We identified CYP admitted to PICU using a COVID-19 flag in the PICANet database. Finally, we examined CYP who died within 28 days after testing positive for COVID-19 within ONS registration data (excluding those with an traumatic underlying cause) or deaths reported within the NCMD, in order to account for delay in death registrations.[22]

Exposures

COVID-19 vaccination status was defined as "not vaccinated" or "vaccinated with one or more doses". We considered CYP to be "vaccinated" 14 days after they received their first dose. Note this could occur during the follow up period after they tested positive for SARS-SoV-2. To adjust for vulnerability related to immunosuppression, we identified CYP with previous admissions related to malignancies, rheumatologic or inflammatory disorders, other intrinsic immune conditions or immunodeficiency and transplants (supplementary table S2). Health care use has been shown to be associated with more serious neurodisability,[23] and so we used PICU admissions prior to the pandemic (01 April 2015 - 01 March 2020) as a proxy for severity of life-limiting neurodisability. We investigated overall vaccine effectiveness to prevent hospital admission, and then separately examined this during the Alpha-Delta (04 January – 19 December 2021) and Omicron (20 December 2021 – 30 September 2022) periods seperately.[24]

Statistical analyses

We examined variation in vaccination uptake by age, ethnicity and deprivation using Chi-Square tests. In those with positive SARS-CoV-2 tests (test-positive cohort), we undertook survival analyses of COVID-19 hospitalization or PICU admission in vaccinated compared with unvaccinated CYP. The index date was the date of each positive SARS-CoV-2 test, with tests recorded >90 days apart considered as separate episodes.[25] We followed CYP until either: 28 days after the date of each SARS-Cov-2 positive test, date of death or 30 September 2022 (i.e. 28 days after the last available index date), whichever was sooner.

We constructed Kaplan–Meier survival curves for each outcome by vaccine status and used the log-rank-test to test for statistical difference in hospitalisation rates. We used Cox regression models to estimate hazard ratios for hospitalization and PICU admission by

vaccination status, adjusted for demographic factors, PICU admission prior to the pandemic, and presence of immunological conditions. Vaccination status was a time-varying covariant, as status could change during follow-up. Analyses were undertaken in RStudio version 1.4.1106. To account for multiple infections within CYP, we used the *cluster* function of the package "survival" in Cox regression models. We assessed the proportional hazards assumption using the Schoenfield test; where this was not met, non-significant covariates were removed in a step-wise fashion. Low numbers (<5) are suppressed to reduce the risk of identifying CYP.

Results

We identified 38,067 CYP with life limiting neurodisability (Table 1). 13,311 CYP (35.0%) had received at least one COVID-19 vaccine dose by 2 September 2022, 9,916 (26.0%) had received ≥2 doses, and 24,756 (65.0%) remained unvaccinated. More than 95% of vaccinations used the BNT162b2 (Pfizer-BioNTech) vaccine. Vaccination uptake was significantly higher amongst older CYP (72.5% in 16-17 year olds compared with 17.0% in 5-11 year olds); CYP who were white (38.3% amongst white CYP compared with 18.7% of CYP who were Black); CYP who were least deprived (47% in the least deprived IMD quintile compared with 26% in the most deprived IMD quintile); and CYP that were admitted to PICU prior to the pandemic (38.3% compared with 34.6% within those with no prior PICU). Having an immunosuppressed condition was not associated with vaccine uptake.

There were 7,736 CYP included in the test-positive cohort, with a total of 8,134 positive SARS-CoV-2 tests (see supplementary Table S3). 384 (4.7%) CYP in the test positive cohort were hospitalised with Primary COVID-19 during follow up, of which 56 (14.6%) were admitted to PICU, and 744 (9.1%) CYP were hospitalized with Primary/Secondary COVID-19, of which 83 (11.2%) were admitted to PICU (Table 2).

Kaplan-Meier survival plots for hospitalisation with Primary COVID-19 are shown in Figure 1. Overall, 75 (4.8%) vaccinated CYP were hospitalized with Primary COVID-19 within 28 days of SARS-CoV-2 infection, compared with 309 (4.7%) unvaccinated CYP. During Alpha-Delta, this proportion was 1.4% amongst vaccinated CYP compared with 4.6% amongst unvaccinated CYP, and during Omicron this proportion was 5.6% amongst vaccinated CYP and 4.8% amongst unvaccinated CYP. 127 (8.2%) vaccinated CYP were hospitalized with Primary/Secondary COVID-19 within 28 days of SARS-CoV-2 infection, compared with 617 (9.4%) unvaccinated CYP. During Alpha-Delta, this proportion was 3.2% amongst vaccinated CYP and 8.9% amongst unvaccinated CYP, and during Omicron this was 9.4% amongst vaccinated CYP and 9.8% amongst unvaccinated CYP. The proportions admitted to PICU by vaccination status were similar across the study period, with very small numbers in each variant period. (supplementary table S4-7).

Across the whole study period, there was no significant difference in hazard of hospitalisation with Primary COVID-19 or Primary/Secondary COVID-19 by vaccination status, after adjusting

for other covariates (Table 3). During Alpha-Delta, there was significantly lower hazard of hospitalisation amongst vaccinated CYP compared with unvaccinated CYP for both Primary COVID-19 (HR 0.26 [0.09-0.74]) and Primary/Secondary COVID-19 (HR 0.44 [0.22, 0.86]), but with no significant differences seen during Omicron. There were no significant differences in hazard of PICU admission with either Primary or Primary/Secondary COVID-19 for any period. (supplementary tables S8-S13). Log-rank tables and results for hospitalization with Primary/Secondary COVID-19 and PICU admission shown in supplementary figures S3-S5 and tables S14-S17.

Forty-one CYP in the test-positive cohort died within 28 days of the index date, of whom 30 (73.2%) were unvaccinated. Of those who died, 20 had COVID-19 recorded on the death certificate (13 unvaccinated), with most other causes being non-infective. Further analysis of deaths was not possible due to small numbers.

Table 1 Demographic details of children and young people with life-limiting neurodisability by SARS-CoV2 vaccination status

		Not vaccinated		Vaccinated						Total	
				Any vaccination		1 dose		2 or more doses			
		n	(%)	n	(%)	n	(%)	n	(%)		
	Total	24756	(65.0)	13311	(35.0)	3395	(8.9)	9916	(26.0)	38067	
Sex	Male	13989	(65.3)	7441	(34.7)	1910	(8.9)	5531	(25.8)	21430	
	Female	10767	(64.7)	5870	(35.3)	1485	(8.9)	4385	(26.4)	16637	
Age	5 – 11	19998	(83.0)	4098	(17.0)	1688	(7.0)	2410	(10.0)	24096	***
	12 – 15	3031	(39.4)	4660	(60.6)	1038	(13.5)	3622	(47.1)	7691	***
	16 – 17	1727	(27.5)	4553	(72.5)	669	(10.7)	3884	(61.8)	6280	***
Ethnicity	White	15781	(61.7)	9799	(38.3)	2363	(9.2)	7436	(29.1)	25580	***
	Asian	3186	(69.6)	1392	(30.4)	429	(9.4)	963	(21.0)	4578	***
	Black	1712	(81.3)	393	(18.7)	149	(7.1)	244	(11.6)	2105	***
	Mixed	1120	(74.6)	382	(25.4)	100	(6.7)	282	(18.8)	1502	***
	Other	855	(76.1)	269	(23.9)	83	(7.4)	186	(16.5)	1124	***
	Unknown	2102	(66.1)	1076	(33.9)	271	(8.5)	805	(25.3)	3178	
IMD Quintile	1 (most deprived)	6659	(74.0)	2334	(26.0)	733	(8.2)	1601	(17.8)	8993	***
	2	5798	(69.8)	2510	(30.2)	734	(8.8)	1776	(21.4)	8308	***
	3	4802	(63.9)	2712	(36.1)	688	(9.2)	2024	(26.9)	7514	
	4	4149	(59.5)	2829	(40.5)	648	(9.3)	2181	(31.3)	6978	***
	5 (least deprived)	3292	(53.0)	2924	(47.0)	592	(9.5)	2332	(37.5)	6216	***
	Unknown	56	(96.6)	<5		0	(0.0)	<5		58	***
Immunocompromised	No	24082	(65.1)	12915	(34.9)	3296	(8.9)	9619	(26.0)	36997	
	Yes	674	(63.0)	396	(37.0)	99	(9.3)	297	(27.8)	1070	
Prior PICU	No	22532	(65.4)	11933	(34.6)	3042	(8.8)	8891	(25.8)	34465	***
	Yes	2224	(61.7)	1378	(38.3)	353	(9.8)	1025	(28.5)	3602	***

*** p value < 0.001; ** p value < 0.01; * p value < 0.05 for Chi-square test of independence

Table 2 Number of children and young people with life-limiting neurodisability hospitalized with Primary and Primary / Secondary COVID-19 after SARS-Cov-2 infection by vaccination status

		Alpha-Delta period					Omicron period				
		Not hospitalized		Hospitalized		Total	Not hospitalized		Hospitalized		Total
		n	%	n	%	n	n	%	n	%	n
Primary COVID-19	Total	3421	95.7	154	4.3	3575	4329	95.0	230	5.0	4559
	not vaccinated	3139	95.4	150	4.6	3289	3139	95.2	159	4.8	3298
	vaccinated	282	98.6	4	1.4	286	1190	94.4	71	5.6	1261
Primary / secondary COVID-19	Total	3272	91.5	303	8.5	3575	4118	90.3	441	9.7	4559
	not vaccinated	2996	91.1	294	8.9	3290	2976	90.2	323	9.8	3299
	vaccinated	276	96.8	9	3.2	285	1142	90.6	118	9.4	1260

Table 3 Adjusted hazard ratios for hospitalization and PICU admission due to Primary and Primary Secondary COVID-19 among vaccinated compared with unvaccinated children and young people with life-limiting neurodisability

		Whole period	Alpha-Delta period	Omicron period
		Hazard ratio [95% CI]	Hazard ratio [95% CI]	Hazard ratio [95% CI]
Primary COVID-19	Hospitalization	0.96 [0.68-1.34]	0.26* [0.09-0.74]	1.16 [0.74-1.81]
	PICU admission	1.19 [0.58-2.44]	3.26 [0.28-38.43]	1.23 [0.41-3.73]
Primary/Secondary COVID-19	Hospitalization	0.84 [0.68-1.03]	0.44* [0.22-0.86]	0.92 [0.71-1.19]
	PICU admission	1.32 [0.70-2.50]	1.34 [0.33-5.46]	1.77 [0.74-4.26]

*** p value < 0.001; ** p value < 0.01; * p value < 0.05 for cox regression analyses. Full models adjusted for age, ethnicity, IMD quintile, presence of immunocompromised condition, previous PICU admission

Discussion

In this population cohort study, we found very low uptake of COVID-19 vaccination amongst CYP with life-limiting neurodisability by late 2022, and concerning inequalities by ethnicity and deprivation. Vaccination uptake amongst Black CYP was half that of white CYP, with uptake amongst Asian and mixed ethnicity groups also significantly lower than amongst white CYP. We also found that Black and Asian CYP had higher risk of hospitalisation for COVID-19 than white CYP, regardless of vaccination status.

COVID-19 vaccination was protective against hospitalization for COVID-19 during Alpha-Delta variant period, but not during Omicron, nor when data were combined across all variant periods. The risk reduction for hospitalization after at least 1 vaccine dose during Alpha-Delta was approximately 74% for a more specific estimate of COVID-19 hospital admissions (i.e. Primary COVID-19) and 56% for a less specific but more sensitive (Primary/Secondary) estimate. These findings were robust to adjustment for factors known to increase COVID-19 hospitalisation risk, including age, ethnicity and deprivation,[4] as well as for prior PICU admission and immunosuppression, which may influence vaccine responses. We did not find a protective effect of COVID-19 vaccination against PICU admissions, and were unable to examine the impact of vaccination on deaths due to small numbers.

Strengths and limitations

We used national linked data from a large country with a considerable SARS-CoV-2 burden, included almost all CYP with life-limiting neurodisability, and studied 'real world' vaccine protection against SARS-CoV-2 disease. Our test-positive design obviated bias from shielding from infection, which was common in CYP with neurodisability.

Overall, small numbers of CYP with life-limiting neurodisability led to challenges with sample size and power, and we were unable to compare vaccine effectiveness after two or more doses, and deaths, because this. This is reflected in wide confidence intervals for some of our estimates. We found no associations between vaccination status and PICU admission, but this was also limited by low numbers; less than 1% of all CYP in the positive test cohort were admitted to PICU during follow up. Incomplete diagnostic coding within SUS may have affected our results. Further, CYP with complex needs hospitalised with COVID-19 may have been missed using our narrow but specific Primary COVID-19 diagnostic category, while CYP

with incidental SARS-CoV-2 infection may have been included in our more sensitive Primary/Secondary COVID-19 definition. Data on PICU admission may have been influenced by advance care directives defining a ceiling of care in some CYP, reducing the overall likelihood of PICU admission, although it is unclear whether this may have biased findings around impact of vaccination. We identified significant sociodemographic differences in vaccine uptake. These are also seen in risk of serious COVID-19 disease, and are likely to operate in clinical thresholds to admit CYP (our indicator for severity). Although we were able to control for several of these factors in our analysis of vaccine effectiveness, this may have been incomplete and resulted in residual confounding. We did not examine geographic variation in admission rates for SARS-Cov-2, which could have also impacted our results. Our estimate for COVID-19 deaths is likely to be an overestimate as we were unable to attribute cause of death to the virus.[5,26,27] Finally, the vaccines administered in this study were all monovalent, targeting the original SARS-CoV-2 virus, as bivalent vaccines targeting Omicron were not used in CYP within our study period. Investigating the effectiveness of other SARS-CoV-2 vaccines in this population should be the focus of future study.

Comparison with the literature

We are not aware of similar studies in CYP with life-limiting neurodisability. COVID-19 vaccination was recommended off-license for those aged ≥12 years with life-limiting neurodisability from early January 2021, with the first vaccines authorised for those aged ≥16 years from 2 December 2020.[28] In the UK, the first COVID-19 vaccine was authorised for 12-15 year-olds on 04 June 2021,[29] and for 5-11 year-olds on 22 December 2021.[30] Our estimates of vaccine uptake of 61-73% amongst ≥12 year-olds, reveal lower uptake of more than one vaccine dose, especially given the very early access to vaccination offered to these high-risk CYP. Vaccine uptake in CYP with life-limiting neurodisability was similar to the general population of CYP in England, where 57% of 12-15 year-olds and 70% of 16-17 year-olds had received at least one vaccine dose.[31] This observation suggests that the high clinical need was not reflected in greater vaccine uptake, and uptake in our study is notably lower than in clinically vulnerable adult groups.[32,33]

The low uptake we identified may reflect challenges in accessing health services, difficulties in identifying high-risk CYP within health systems, and parental and young person hesitancy.

It is likely that general concerns about vaccine safety prior to regulatory authorisation in this age group contributed to low vaccine uptake early in the pandemic. US studies have shown parents were concerned about new vaccines worsening disease control in CYP with rare neurological syndromes.[34,35] This lower uptake, however, may not be specifically related to COVID-19 vaccines, as previous studies have shown that CYP with complex medical needs often have lower vaccination rates than the general child population.[36] Low uptake may also be related to health service changes during the pandemic. Children's health services in England were de-prioritized in favour of adult services during the first and subsequent lockdowns, with community health services for CYP with disability particularly affected.[37] The COVID-19 pandemic resulted in increased anxiety amongst CYP with neurodisability and their families, and increased inequalities in health needs and service provision.[38,39] Families reported being confused about shielding guidance and which services were affected by redeployment of community healthcare staff.[38,39] Vaccination also required attendance at healthcare facilities, which may have been declined by those most strictly shielding. Low uptake amongst Black, mixed ethnicity and Asian CYP with life-limiting neurodisability likely reflects the well described lower vaccine uptake in ethnic minority groups in the general population.[40]

We found significant protection against hospital admission during the Alpha-Delta periods but not during the Omicron period. In healthy CYP, the estimated vaccine efficacy against COVID-19 was 84-91% after one dose in recent meta-analyses of vaccine trials.[9,10] 'Real world' effectiveness studies in healthy adolescents have reported protection against symptomatic COVID-19 disease of 82% after first dose and 93% after the second dose in an large Israeli study,[41] and protection against hospitalisation of 94-95% after two doses in a US study across multiple hospitals.[42] The lack of protection against Omicron found in our study is consistent with the very modest protection against Omicron infection, even after complete vaccination schedules, in both CYP[43,44] and adults.[45] Prior work has also reported 98% effectiveness of vaccination in prevention of PICU admissions due to COVID-19.[42] Although we found no significant associations between vaccination status and PICU admission, this was also limited by low numbers, with only 1% of all CYP in the positive test cohort admitted to PICU during follow up.

Conclusions

COVID-19 vaccination was effective in preventing hospitalisation for COVID-19 in CYP with life-limiting neurodisability during the more severe Alpha/Delta pandemic periods, but not during Omicron. National vaccination strategies need to focus on understanding low uptake in this group, and variation by ethnicity and deprivation. Community health services for CYP with significant disabilities must be better maintained during future pandemics.

List of tables

List of figures

Contributorship

RV, JW, PH and JC conceptualised the paper. JC and JW prepared the data. JC led the analysis. All authors contributed to interpreting the results. RV, JW and JC prepared the first draft, tables and visualisations. All authors contributed to editing the manuscript. JW is guarantor.

Funding

This study is funded by the NIHR [ref 202322]. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Competing of interests

The authors declare no competing interests

Ethics approval and legal basis for data linkage and analyses

Ethics approval was provided after review by Yorkshire and the Humber, South Yorkshire NHS Research Ethics Committee on 10th June 2021 (Reference 21/YH/0127). Current Control Of Patient Information (COPI) regulations provide a legal basis for linking these datasets without consent. (NHS Digital. Control of patient information (COPI) notice. 2021. https://digital.nhs.uk/coronavirus/coronavirus-covid-19-response-information-governance-hub/control-of-patient-information-copi-notice).

Data availability Statement

Data are not available. These analyses were undertaken using datasets held by NHS England for the use of ongoing service evaluation, held within the National Commissioning Data Repository. Access to these data at individual level are restricted, as described in data sharing agreements between NHS England and specific data providers, and within in the application for ethical approval provided for this study. Aggregated, non-identifiable data used for this study are provided in the supplementary material.

Acknowledgements

We would like to thank the National Child Mortality Database (NCMD); Paediatric Intensive Care Audit Network (PICANet); UK Health Security Agency (UKDSA); NHS Digital, NHS England and NHS Improvement Children and Young People Team, (particularly Sophie Solti, Tiffany Watson-Koszel and, Muhammad Ambia,); for their support in identifying, linking and making the data used in this study available for analysis.

AI use statement

Not applicable

References

1. Coombes L, Braybrook D, Roach A, et al. Achieving child-centred care for children and young people with life-limiting and life-threatening conditions-a qualitative interview study. *Eur J Pediatr* 2022; **181**(10): 3739-52.

2. Fraser LK, Gibson-Smith D, Jarvis S, Norman P, Parslow RC. Estimating the current and future prevalence of life-limiting conditions in children in England. *Palliat Med* 2021; **35**(9): 1641-51.

3. Wong BLH, Ramsay ME, Ladhani SN. Should children be vaccinated against COVID-19 now? *Arch Dis Child* 2021; **106**(12): 1147-8.

4. Ward JL, Harwood R, Smith C, et al. Risk factors for PICU admission and death among children and young people hospitalized with COVID-19 and PIMS-TS in England during the first pandemic year. *Nat Med* 2022; **28**(1): 193-200.

5. Smith C, Odd D, Harwood R, et al. Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year. *Nat Med* 2022; **28**(1): 185-92.

6. UKHSA. Covid-19: the green book, chapter 14a. In: UKHSA, editor.; 2022.

7. Du Y, Chen L, Shi Y. Safety, Immunogenicity, and Efficacy of COVID-19 Vaccines in Adolescents, Children, and Infants: A Systematic Review and Meta-Analysis. *Front Public Health* 2022; **10**: 829176.

8. Tian F, Yang R, Chen Z. Safety and efficacy of COVID-19 vaccines in children and adolescents: A systematic review of randomized controlled trials. *J Med Virol* 2022; **94**(10): 4644-53.

9. Sadeghi S, Kalantari Y, Shokri S, et al. Immunologic response, Efficacy, and Safety of Vaccines against COVID-19 Infection in Healthy and immunosuppressed Children and Adolescents Aged 2 - 21 years old: A Systematic Review and Meta-analysis. *J Clin Virol* 2022; **153**: 105196.

10. Gao P, Cai S, Liu Q, Du M, Liu J, Liu M. Effectiveness and Safety of SARS-CoV-2 Vaccines among Children and Adolescents: A Systematic Review and Meta-Analysis. *Vaccines (Basel)* 2022; **10**(3).

11. Lin DY, Gu Y, Xu Y, et al. Effects of Vaccination and Previous Infection on Omicron Infections in Children. *N Engl J Med* 2022; **387**(12): 1141-3.

12. Price AM, Olson SM, Newhams MM, et al. BNT162b2 Protection against the Omicron Variant in Children and Adolescents. *N Engl J Med* 2022; **386**(20): 1899-909.

13. King H, Deshpande S, Woodbridge T, et al. Initial experience of the safety and tolerability of the BNT162b2 (Pfizer-Bio-N-Tech) vaccine in extremely vulnerable children aged 12-15 years. *Arch Dis Child* 2022; **107**(2): 205-7.

14. Dowell AC, Powell AA, Davis C, et al. mRNA or ChAd0x1 COVID-19 Vaccination of Adolescents Induces Robust Antibody and Cellular Responses With Continued Recognition of Omicron Following mRNA-1273. *Front Immunol* 2022; **13**: 882515.

15. Hirsch KM, Reidenberg BE. COVID-19 vaccine effectiveness in adults with developmental disabilities living in group homes. *Public Health* 2022; **209**: e3-e4.

16. Aiano F, Campbell C, Saliba V, Ramsay ME, Ladhani SN. COVID-19 vaccine given to children with comorbidities in England, December 2020-June 2021. *Arch Dis Child* 2022; **107**(3): e16.

17. Fraser LK, Miller M, Hain R, et al. Rising national prevalence of life-limiting conditions in children in England. *Pediatrics* 2012; **129**(4): e923-9.

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.

19. Wilde H, Tomlinson C, Mateen BA, et al. Hospital admissions linked to SARS-CoV-2 infection in children and adolescents: cohort study of 3.2 million first ascertained infections in England. *bmj* 2023; **382**.

20. Ward JL, Harwood R, Kenny S, et al. Pediatric Hospitalizations and ICU Admissions Due to COVID-19 and Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2 in England. *JAMA pediatrics* 2023.

21. Lee LYW, Starkey T, Ionescu MC, et al. Vaccine effectiveness against COVID-19 breakthrough infections in patients with cancer (UKCCEP): a population-based test-negative case-control study. *Lancet Oncol* 2022.

22. Ward JL, Zylbersztejn A, Hardelid P, Viner R. Delay in death registration among adolescents and young adults in England and Wales. *The Lancet Child & Adolescent Health* 2022.

23. Paget S, Ostojic K, Goldsmith S, Nassar N, McIntyre S. Determinants of hospital-based health service utilization in cerebral palsy: a systematic review. *Archives of physical medicine and rehabilitation* 2022; **103**(8): 1628-37.

24. Office for National Statistics. Coronavirus (COVID-19) Infection Survey, characteristics of people testing positive for COVID-19, UK: 22 June 2022. In: Statistics OfN, editor. Office for National Statistics; 2022.

25. Ashby DR, Caplin B, Corbett RW, et al. Severity of COVID-19 after Vaccination among Hemodialysis Patients: An Observational Cohort Study. *Clin J Am Soc Nephrol* 2022; **17**(6): 843-50.

26. Bertran M, Amin-Chowdhury Z, Davies H, et al. COVID-19 deaths in children and young people: active prospective national surveillance, March 2020 to December 2021, England. 2022.

27. Smith C, Odd D, Harwood R, et al. Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year. *Nature Medicine* 2021.

28. Regulatory approval of Pfizer/BioNTech vaccine for COVID-19. 16 August 2022 2020. https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19 (accessed 19 October 2022.

29. The MHRA concludes positive safety profile for Pfizer/BioNTech vaccine in 12- to 15-year-olds. 4 June 2021 2021. https://www.gov.uk/government/news/the-mhra-concludes-positive-safety-profile-for-pfizerbiontech-vaccine-in-12-to-15-year-olds (accessed 19 October 2022.

30. UK regulator approves use of Pfizer/BioNTech vaccine in 5 to 11-year olds. 22 December 2021 2021. https://www.gov.uk/government/news/uk-regulator-approves-use-of-pfizerbiontech-vaccine-in-5-to-11-year-olds (accessed 19 October 2022.

31. COVID-19 Vaccinations in England by Age Group: 8th December 2020 to 20th September 2022: NHS England, 2023.

32. COVID-19 Vaccination Statistics: Week ending Sunday 13th March 2022: NHS England, 2022.

33. COVID-19 Vaccinations of Severely Immunosuppressed Individuals. 2022. https://www.england.nhs.uk/statistics/statistical-work-areas/supplementary-information/ (accessed 17 October 2022.

34. Hood V, Berg AT, Knupp KG, et al. COVID-19 vaccine in patients with Dravet syndrome: Observations and real-world experiences. *Epilepsia* 2022; **63**(7): 1778-86.

35. Gordon-Lipkin E, Marcum CS, Kruk S, et al. Short report: Vaccine attitudes in the age of COVID-19 for a population of children with mitochondrial disease. *Research in developmental disabilities* 2022; **131**: 104346.

36. Langkamp DL, Dusseau A, Brown MF. Vaccine Hesitancy and Low Immunization Rates in Children with Down Syndrome. *J Pediatr* 2020; **223**: 64-7 e2.

37. Then there was silence. England: Disabled Children's Partnership, 2021.

38. Cadwgan J, Goodwin J, Arichi T, et al. Care in COVID: A qualitative analysis of the impact of COVID-19 on the health and care of children and young people with severe physical neurodisability and their families. *Child Care Health Dev* 2021.

39. Arichi T, Cadwgan J, McDonald A, et al. Neurodisability care in the time of COVID-19. *Child Care Health Dev* 2022.

40. Razai MS, Osama T, McKechnie DGJ, Majeed A. Covid-19 vaccine hesitancy among ethnic minority groups. *BMJ* 2021; **372**: n513.

41. Reis BY, Barda N, Leshchinsky M, et al. Effectiveness of BNT162b2 Vaccine against Delta Variant in Adolescents. *N Engl J Med* 2021; **385**(22): 2101-3.

42. Olson SM, Newhams MM, Halasa NB, et al. Effectiveness of BNT162b2 Vaccine against Critical Covid-19 in Adolescents. *N Engl J Med* 2022; **386**(8): 713-23.

43. Fleming-Dutra KE, Britton A, Shang N, et al. Association of Prior BNT162b2 COVID-19 Vaccination With Symptomatic SARS-CoV-2 Infection in Children and Adolescents During Omicron Predominance. *Jama* 2022; **327**(22): 2210-9.

44. Khan FL, Nguyen JL, Singh TG, et al. Estimated BNT162b2 Vaccine Effectiveness Against Infection With Delta and Omicron Variants Among US Children 5 to 11 Years of Age. *JAMA Netw Open* 2022; **5**(12): e2246915.

45. Külper-Schiek W, Piechotta V, Pilic A, et al. Facing the Omicron variant-how well do vaccines protect against mild and severe COVID-19? Third interim analysis of a living systematic review. *Front Immunol* 2022; **13**: 940562.