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COVID-19 vaccine effectiveness in children by age groups. A population-based study in Galicia, Spain

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Abstract

Background: Studies on vaccine effectiveness (VE) against COVID-19 in the pediatric population are outgoing. We aimed to quantify VE against SARS-CoV-2 in two pediatric age groups, 5–11 and 12–17-year-old, while considering vaccine type, SARS-CoV-2 variant, and duration of protection.

Methods: A population-based test-negative control study was undertaken in Galicia, Spain. Children 5–11-year-old received the Comirnaty® (Pfizer, US) vaccine, while those aged 12–17-year-old received the Comirnaty® (Pfizer, US) or SpikeVax® (ModernaTX, Inc) vaccine. Participants were categorized into unvaccinated (0 doses or one dose with <14 days since vaccination), partially vaccinated (only one dose with ≥14 days, or two doses with <14 days after the second dose administration), and fully vaccinated (two doses with ≥14 days after the second injection). Adjusted odds ratios (OR) and their 95% confidence intervals (CI) were estimated using multiple logistic

regression models. VE was calculated as (1-OR) * 100. Stratified and sensitivity analyses were performed.

Results: In the fully vaccinated 5–11-year-old children, VE against the Omicron variant was 44.1% (95% CI: 38.2%–49.4%). In the fully vaccinated 12–17-year-old individuals, VE was 83.4% (95% CI: 81.2%–85.3%) against Delta and 74.8% (95% CI: 58.5%–84.9%) against Omicron. Comirnaty® and SpikeVax® vaccines showed a similar magnitude of VE against Delta [Comirnaty® VE: 81.9% (95% CI: 79.3%–84.1%) and SpikeVax® VE: 85.3% (95% CI: 81.9%–88.1%)]. Comirnaty® (Pfizer, US; VE: 79.7%; 95% CI: 50.7%–92.4%) showed a slightly higher magnitude of protection against Omicron than SpikeVax® (ModernaTX, Inc), yet with an overlapping CI (VE: 74.3%; 95% CI: 56.6%–84.9%). VE was maintained in all age subgroups in both pediatric populations, but it declined over time.

Conclusions: In Galicia, mRNA VE was moderate against SARS-CoV-2 infections in the 5–11-year-old populations, but high in older children. VE declined over time, suggesting a potential need for booster dose schedules.

KEYWORDS
Comirnaty® (Pfizer, US), COVID-19, Delta, mRNA vaccine, Omicron, SARS-CoV-2, Spain, SpikeVax® (ModernaTX, Inc), vaccine effectiveness

1 | INTRODUCTION

The COVID-19 pandemic has presented a major challenge to international public health. According to the World Health Organization (WHO), as of 17 May 2023, there have been 766,440,796 confirmed COVID-19 cases, including 6,932,591 deaths worldwide.[1] Spain registered 13,845,825 COVID-19 cases and 120,964 deaths by that date.[1] As per the epidemiological report of the Spanish Ministry of Health of May 2023, seven COVID-19 pandemic waves have taken place in the country, the most recent wave starting on 28 March 2022.[2] While the elderly population has borne the greatest burden in terms of disease and deaths, the pediatric population has also been affected by the pandemic.[3]

During the surge of the Omicron SARS-CoV-2 variant, COVID-19 cases among children spiked dramatically, coinciding with the relaxation of the nonpharmaceutical preventive measures in many countries.[4] Globally, as of 17 May 2023, children aged 5–14 years accounted for 8.5% of COVID-19 cases.[3] Although COVID-19 is generally less severe in children compared with adults, certain pre-existing conditions such as childhood obesity can exacerbate the disease.[5,6] Worldwide, over 3000 COVID-19-related deaths in children aged 5–14 have been recorded.[3] In Spain, since the beginning of the pandemic, 1977 and 6396 COVID-19-related hospitalizations have been reported in 7–9 and 10–19-year-old children, respectively.[2]

Vaccination against COVID-19 has become an essential tool in combating the pandemic. However, the universal pediatric indication for vaccination has been a subject of controversy and has been less widely implemented.[7] Vaccination not only aims to prevent severe COVID-19 cases but also reduces susceptibility to infection and may influence virus transmissibility.[8] However, evidence suggests that COVID-19 vaccine effectiveness (VE) declines over time and that emerging SARS-CoV-2 variants may evade vaccine-induced immune protection. Ongoing research on COVID-19 VE in the pediatric population, especially in young children aged 5–11 years, has shown variable findings, likely influenced by factors such as vaccine type, settings, baseline immunity, population genetics, and waning vaccine-induced immunity from early follow-up data.[9,10] The heterogeneity among studies makes it challenging to generalize VE across populations.

To the best of our knowledge, COVID-19 VE in the pediatric population in Spain has not been investigated. Accordingly, using population-based real-world data, we aimed to quantify COVID-19 VE in the pediatric population in Galicia, a region in Northwest

Key message

Studies on vaccine effectiveness (VE) against COVID-19 are emerging, especially in younger children. This study showed that in settings like Spain, mRNA-based vaccines are highly effective against the Delta variant of SARS-CoV-2 in children 12–17-year-old, but the effectiveness was moderate against the Omicron variant in 5–11-year-old and 12–17-year-old populations. VE rapidly declined in both age categories, suggesting the need for booster dose schedules.

Spain with a population of nearly three million people. We considered vaccine type, SARS-CoV-2 variant, and duration of protection in our analysis. We present two separate analyses: one among children aged 5–11-year-old, and another among children aged 12–17-year-old.

2 | METHODS

2.1 | Settings and population

This population-based retrospective study was initiated within the framework of a collaboration with the Galician Healthcare Service (Servizo Galego de Saúde, SERGAS), which was established at the beginning of the COVID-19 pandemic to evaluate COVID-19 VE in Galicia.[11,12] Galicia is an autonomous community in Northwest Spain of 2,690,464 inhabitants, 3279,64 (12.2%) of whom are younger than 16 years old.[13]

SERGAS is a public health system that provides universal access to low- or no-cost healthcare. In Galicia, healthcare is organized in seven sanitary areas, with a total of 9818 public hospital beds distributed among 33 hospitals (data for 2022).[14]

In Galicia, the COVID-19 vaccination campaign started on 27 July 2021, for individuals aged 12–17-year-old, and on 13 December 2021, for those aged 5–11 years. mRNA-based vaccines were administered in the pediatric population. Comirnaty® (Pfizer, US) vaccine was administered in 5–11-year-old children, while Comirnaty® (Pfizer, US) and SpikeVax® (ModernaTX, Inc; previously COVID-19 Vaccine Moderna) were authorized for their use in the 12–17-year-old population; however, the administration of the same type of vaccine was recommended during the first and the second dose injection.[15] In our study, we only considered children who received the same vaccine type in the two injections. Data were extracted on 7 October 2022, and our analyses englobed the period of the Omicron variant circulation in the 5–11-year-old population and that of Delta and Omicron in the 12–17-year-old population. Further details on the period of variant circulation are provided in the Outcome section.

2.2 | Data source and study variables

Population data on sociodemographic characteristics (age, gender, and sanitary area), SARS-CoV-2 test (test date, type, and result), hospitalization (admission date and diagnosis), COVID-19 vaccine administration (vaccine type and date of administration), presence of any comorbidity, and co-medication were extracted from specific databases at SERGAS. The data were pseudonymized by the information technology department at SERGAS. Each individual was assigned a unique code to link data from different registries that correspond to the same individual. The research team did not have access to any personal data of the participants. The study was approved by the Ethics Committee of Galicia (protocol number: 2022-175).

2.3 | Study design

We conducted a test-negative control study design. Individuals were allowed to contribute more than one negative SARS-CoV-2 test to the study, but only one positive SARS-CoV-2 was considered per individual. The unit of analysis in our study is the test rather than the individual.

To be included in the analysis, the following two inclusion criteria were established: (1) age: the test should have been undertaken in an individual whose age falls within the age range of the study population, and (2) previous SARS-CoV-2 infection: the test should not have been preceded by any positive SARS-CoV-2 test result in the past, that is, before the start of the study. The second criterion was applied because the time taken for an antibody response to the vaccine is longer in individuals who have not been previously infected.[16]

We excluded from the study: (1) antigen-based SARS-CoV-2 test results; (2) inconsistent SARS-CoV-2 test results when different findings were available for repeated tests performed in the same day; (3) any SARS-CoV-2 negative test result preceded by a positive SARS-CoV-2 test result; (4) individuals who were vaccinated previous to the official launching of the vaccination campaign such as high-risk individuals who were prioritized during COVID-19 vaccination; (5) 5–11-year-old individuals who were vaccinated with a vaccine other than Comirnaty® (Pfizer, US), and 12–17-year-old individuals who had received any vaccine other than Comirnaty® (Pfizer, US) or SpikeVax® (ModernaTX, Inc); (6) the earlier SARS-CoV-2 test result if more than one negative test result was reported within 15 days in order to avoid an overrepresentation of the negative SARS-CoV-2 test results, especially that individuals could be tested for SARS-CoV-2 infections for non-COVID-19 conditions such as when showing any respiratory disease symptom, getting admitted to emergency departments or hospitalized for a non-COVID condition, or being in contact with a SARS-CoV-2 positive case; (7) negative SARS-CoV-2 tests that occurred within 15 days before or after a positive test to avoid the inclusion of false-negative test results; (8) tests undertaken in subjects whose age does not fall within the 5–11 or 12–17-year-old age criterion; (9) tests undertaken in individuals who had received more than two vaccine doses; (10) tests undertaken in individuals who had received mixed vaccine combinations, that is, the first and second vaccine dose was not from the same brand.

2.4 | Exposure

In our study, exposure is defined as receiving at least one dose of COVID-19 vaccine with 14 days or more from vaccine administration. Exposed individuals could be categorized into partially or fully vaccinated groups depending on the number of received vaccine doses and the time passed since vaccination. Fully vaccinated individuals were defined as those who have completed the primary COVID-19 immunization regimen, that is, received two doses of COVID-19 vaccine and have passed at least 14 days since the administration of the

second vaccine dose.[17] Partially vaccinated subjects were defined as those who received only one dose of COVID-19 vaccine counting 14 days since vaccine administration, or those who received two vaccine doses but have not passed more than 13 days since the administration of the second dose. Unexposed children are those who did not receive any COVID-19 vaccine during the study period or those who received the first vaccine dose but had <14 days since vaccination.

2.5 | Outcome

The main outcomes of the present study are as follows: (1) susceptibility to SARS-CoV-2, defined by a positive SARS-CoV-2 laboratory test result, and (2) COVID-19-related hospitalization, defined as hospital admission within 30 days from SARS-CoV-2 positive laboratory test or within 3 days after hospitalization.[18,19] Positive results of SARS-CoV-2 tests undertaken after 3 days of hospitalization were considered nosocomial infections and were not included in the analysis.

We defined two time periods based on the dominant SARS-CoV-2 variant circulating in Galicia, Delta, and Omicron. A variant is considered predominant when it is present in >90% of the detected SARS-CoV-2 cases.[20,21] Based on data provided by the Galician Ministry of Public Health and on the established 90% threshold, the "Delta period" was set from 27 July 2021 to 16 December 2021; and the "Omicron period" ranged from 1 January 2022, until the date of data extraction (7 October 2022). Cases were assigned to Delta or Omicron variants based on whole genome sequencing. When sequencing information on the SARS-CoV-2 variant was not available, the dominating variant during the period of the SARS-CoV-2 test was attributed.

2.6 | Statistical analysis

We conducted two different analyses for 5–11 and 12–17-year-old children in order to account for the difference in the risk of exposure during the respective age ranges. Odds ratios (OR) were estimated by comparing partially and fully vaccinated children to unvaccinated children. The ORs and their 95% confidence intervals (CIs) were estimated using multiple logistic regression models, which were adjusted for sex and age due to their biological plausibility, the sanitary area as a proxy of the socioeconomic level, as well as the number of undertaken SARS-CoV-2 tests, SARS-CoV-2 positivity rate, and time since vaccine administration as proxies of the evolution of the epidemiological situation.

We stratified the analysis by (1) 2-year age to explore VE in each age group, (2) vaccine type to study the effectiveness of each vaccine for individuals aged 12–17-year-old, (3) SARS-CoV-2 variant in the population aged 12 years or above, (4) and time since the completion of the primary immunization regimen to explore the duration of protection against SARS-CoV-2 infection. For the analysis restricted to the Omicron variant in the 12–17-year-old population, only individuals who were not vaccinated before the Omicron dominance period were included.

2.7 | Robustness analysis

To assess the robustness of our results regarding the inclusion criteria, a sensitivity analysis was performed by including individuals who had a positive SARS-CoV-2 test >90 days before the start of the study. Reinfections were considered if they took place 90 days after the primary infection.[17] ORs and their 95% CIs were re-estimated as in the main multiple logistic regression models, but a previous SARS-CoV-2 infection was added as a covariate.

To examine the impact of the time given for the first vaccine dose to become effective (14 days), the main analysis was repeated using 7 days from the first dose administration as an index to assign individuals to the partially vaccinated group.

All analyses were conducted using R software version 4.0.3.

3 | RESULTS

3.1 | General population characteristics

Vaccination against COVID-19 was highly accepted in our study population, with 68.9% of the 5–11-year-old and 84.8% of the 12–17-year-old populations fully vaccinated 42 and 64 weeks after the initiation of the vaccination campaigns, respectively (Figure 1). Participating individuals could contribute with more than one SARS-CoV-2 test to the study. The analysis was based on SARS-CoV-2

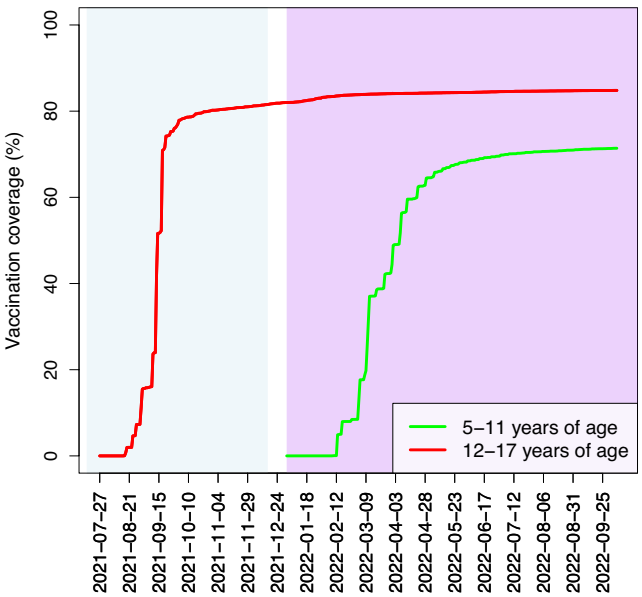

FIGURE 1 Representation of fully vaccinated coverage for the study population.

tests as a unit of analysis. The flow of SARS-CoV-2 test inclusion in the study is represented in Figure 2. Additional information on the number of children who contributed with SARS-CoV-2 test results to the study is available in Figure S1.

3.1.1 | 5–11-year-old population

Table 1 provides a detailed description of the 5–11-year-old population. During the Omicron circulation period, 54,221 [positive:

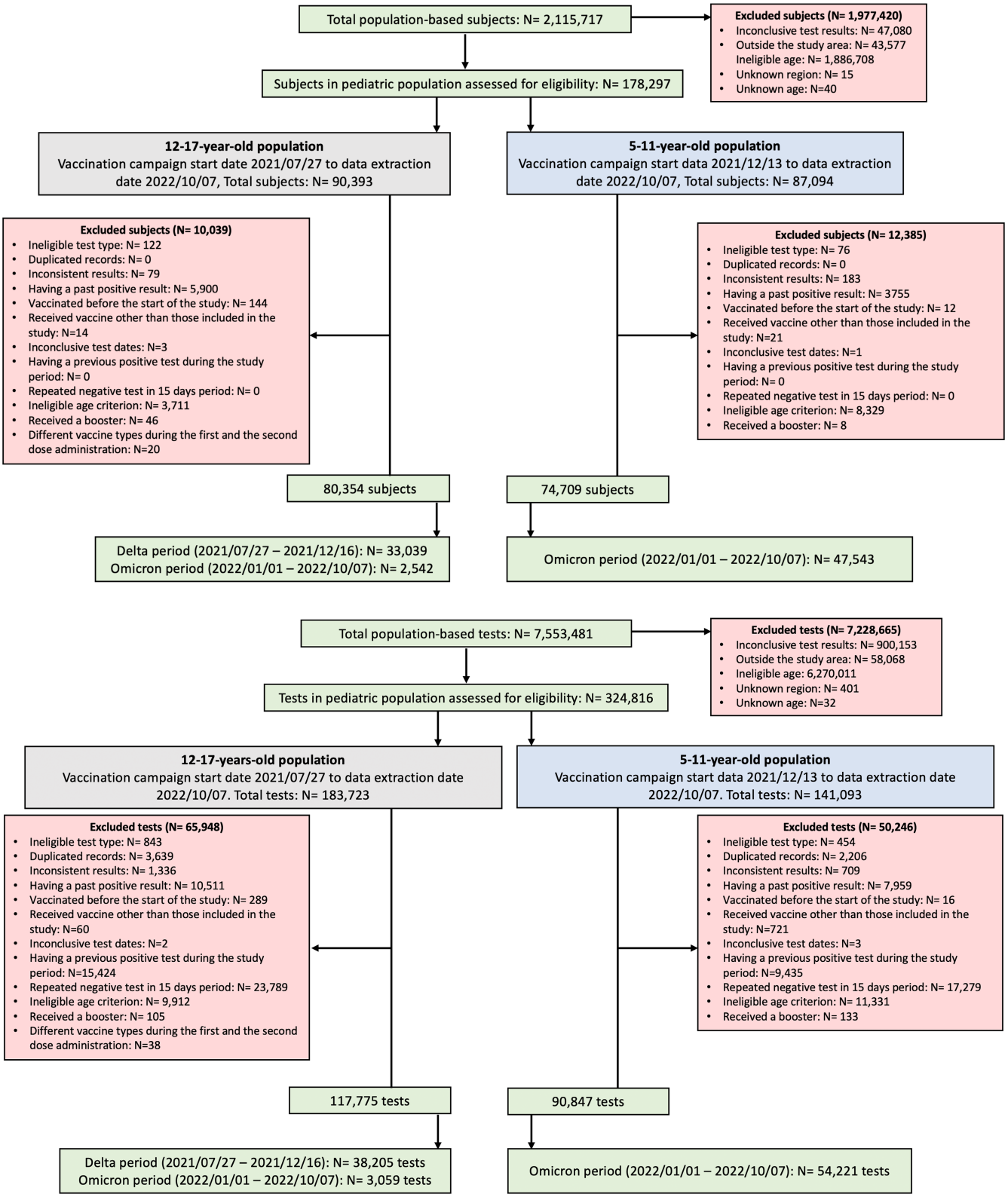

FIGURE 2 Flowchart of SARS-CoV-2 test selection for inclusion in the analysis.

TABLE 1 Characteristics of the 5–11-year-old study population stratified by vaccination status and SARS-CoV-2 test result.

Characteristic	Unvaccinated		Partially vaccinated		Fully vaccinated	
SARS-CoV-2 test result	SARS-CoV-2 Positive *N* (%)	SARS-CoV-2 Negative *N* (%)	SARS-CoV-2 Positive *N* (%)	SARS-CoV-2 Negative *N* (%)	SARS-CoV-2 Positive *N* (%)	SARS-CoV-2 Negative *N* (%)
Overall	10,711 (54.2)	9045 (45.8)	13,235 (48.7)	13,957 (51.3)	3038 (41.8)	4235 (58.2)
Sex						
Male	5525 (53.5)	4797 (46.5)	6918 (48.8)	7270 (51.2)	1539 (40.8)	2232 (59.2)
Female	5186 (55.0)	4248 (45.0)	6317 (48.6)	6687 (51.4)	1499 (42.8)	2003 (57.2)
Age (years)						
5	2918 (51.9)	2704 (48.1)	1458 (37.9)	2390 (62.1)	219 (27.3)	583 (72.7)
6	2474 (55.8)	1956 (44.2)	1787 (42.8)	2385 (57.2)	393 (34.8)	735 (65.2)
7	2053 (54.7)	1701 (45.3)	2399 (49.2)	2480 (50.8)	442 (36.3)	775 (63.7)
8	1674 (55.0)	1367 (45.0)	2778 (52.0)	2566 (48.0)	593 (45.0)	725 (55.0)
9	757 (55.0)	620 (45.0)	3735 (54.1)	3174 (45.9)	835 (47.8)	913 (52.2)
10	479 (56.0)	377 (44.0)	820 (52.2)	752 (47.8)	508 (53.4)	444 (46.6)
11	356 (52.7)	320 (47.3)	258 (55.1)	210 (44.9)	48 (44.4)	60 (55.6)
Age (years) mean (SD)	7 (2)	7 (2)	8 (2)	8 (2)	9 (2)	8 (2)

26,984 (49.8%); negative: 27,237 (50.2%)] test results from children 5–11-year-old and a mean age of 8.1 years (SD: 2.3) fulfilled the inclusion criteria. Twelve unvaccinated, 15 partially vaccinated, and 16 fully vaccinated children had COVID-19-related hospitalization.

3.1.2 | 12–17-year-old population

In the 12–17-year-old population, a total of 41,264 SARS-CoV-2 test results with a mean age of 15.3 (SD: 1.7) years were eligible for the analysis. 38,205 tests (92.6%) corresponded to the Delta circulation period, of which 3856 (10.1%) were positive. The remaining 3059 (7.4%) test results were undertaken during the Omicron circulation period, of which 1300 (42.5%) were positive.

Of the 3856 Delta infections, 455 (11.8%), 148 (3.8%), and 3253 (84.4%) were, respectively, registered in fully vaccinated, partially vaccinated, and unvaccinated populations. Among the Omicron infections, 55 (4.2%) were observed in the fully vaccinated group, 99 (7.6%) in the partially vaccinated and 1146 (88.2%) in the unvaccinated populations. Seventeen hospitalizations were registered during the Delta (unvaccinated: 15; vaccinated: 2). No hospitalizations were observed when the analysis was restricted to the Omicron circulation period. Table 2 summarizes the main characteristics of the 12–17-year-old population.

3.2 | COVID-19 vaccine effectiveness in 5–11-year-old population

In children 5–11-year-old, partial vaccination with Comirnaty® (Pfizer, US) against SARS-CoV-2 is associated with 30.3% (95% CI: 26.3%–34.1%) less odds of infection with the Omicron variant of SARS-CoV-2 compared with unvaccinated individuals (Table 3). A higher overall magnitude of VE was observed in fully Comirnaty® (Pfizer, US) vaccinated children (VE: 44.1%, 95% CI: 38.2%–49.4%; *p*-Value <.0001) than that in partially vaccinated.

In fully vaccinated children, Comirnaty® (Pfizer, US) VE reached its peak in the first 6 weeks after 14 days from the second dose administration (VE: 62.7%; 95% CI: 58.1%–66.8%), and then, it started waning after that period (>6 and ≤9 weeks VE: 48.3%; 95% CI: 40.5%–55.0%; >9 and ≤12 weeks VE: 45.0%; 95% CI: 35.7%–53.0%; >12 and ≤15 weeks VE: 47.2%; 95% CI: 37.9%–55.1%; and >15 weeks VE: 18.0%; 95% CI: 4.8%–29.4%; Table 3).

Stratifying the analysis by 2-year age showed that Comirnaty® (Pfizer, US) VE against Omicron was maintained in all age categories, but was more pronounced in fully vaccinated children of 5–6 (VE: 57.8%; 95% CI: 51.1%–63.7%) and 7–8 (VE: 54.7%; 95% CI: 46.6%–61.6%) years of age than in older fully vaccinated children (9–10 years VE: 30.7%; 95% CI: 18.5%–41.1%; Table 4). No significant association between vaccination and Omicron infection was in observed 5–11-year-old, probably due to sample size limitations in this age category (Table 4).

3.3 | COVID-19 vaccine effectiveness in 12–17-year-old population

In children 12–17-year-old, partial vaccination with mRNA-based vaccines is associated with 62.4% (95% CI: 54.5%–69.1%) and 73.0% (95% CI: 59.2%–82.3%) less odds of infection with Delta and Omicron variants of SARS-CoV-2, respectively (Table 3). In fully vaccinated individuals, the protection increased up to 82.9% (95% CI: 80.7%–84.9%) against Delta infections and to 74.8% (95% CI: 58.5%–84.9%) against Omicron.

VE against Delta infections was the highest in the first 6 weeks from completing the two doses of the primary vaccination regimen

TABLE 2 Characteristics of 12–17-year-old study population stratified according to SARS-CoV-2 variant and vaccination status and disaggregated by SARS-CoV-2 test results.

SARS-CoV-2 variant	Delta						Omicron					
Characteristic	Unvaccinated		Partially vaccinated		Fully vaccinated		Unvaccinated		Partially vaccinated		Fully vaccinated	
SARS-CoV-2 test result	Positive *N* (%)	Negative *N* (%)	Positive *N* (%)	Negative *N* (%)	Positive *N* (%)	Negative *N* (%)	Positive *N* (%)	Negative *N* (%)	Positive *N* (%)	Negative *N* (%)	Positive *N* (%)	Negative *N* (%)
Overall	3253 (18.2)	14,631 (81.8)	148 (3.7)	3831 (96.3)	455 (2.8)	15,887 (97.2)	1146 (43.9)	1466 (56.1)	99 (36.8)	170 (63.2)	55 (30.9)	123 (69.1)
Sex												
Male	1584 (18.0)	7217 (82.0)	63 (3.3)	1828 (96.7)	225 (2.8)	7937 (97.2)	614 (43.0)	815 (57.0)	52 (36.1)	92 (63.9)	28 (31.8)	60 (68.2)
Female	1669 (18.4)	7414 (81.6)	85 (4.1)	2003 (95.9)	230 (2.8)	7950 (97.2)	532 (45.0)	651 (55.0)	47 (37.6)	78 (62.4)	27 (30.0)	63 (70.0)
Age (years)												
12	414 (17.7)	1923 (82.3)	8 (1.2)	648 (98.8)	60 (3.1)	1901 (96.9)	253 (50.9)	244 (49.1)	70 (46.1)	82 (53.9)	39 (36.8)	67 (63.2)
13	426 (16.9)	2095 (83.1)	8 (1.4)	556 (98.6)	56 (2.5)	2224 (97.5)	198 (41.1)	284 (58.9)	10 (31.2)	22 (68.8)	1 (9.1)	10 (90.9)
14	452 (17.9)	2067 (82.1)	8 (1.7)	472 (98.3)	80 (3.6)	2164 (96.4)	195 (46.9)	221 (53.1)	5 (23.8)	16 (76.2)	4 (44.4)	5 (55.6)
15	548 (18.6)	2401 (81.4)	16 (2.9)	533 (97.1)	85 (2.8)	2972 (97.2)	197 (44.9)	242 (55.1)	3 (14.3)	18 (85.7)	4 (26.7)	11 (73.3)
16	652 (18.0)	2964 (82.0)	41 (5.3)	729 (94.7)	87 (2.7)	3167 (97.3)	161 (40.6)	236 (59.4)	5 (17.2)	24 (82.8)	3 (14.3)	18 (85.7)
17	761 (19.3)	3181 (80.7)	67 (7.0)	893 (93.0)	87 (2.5)	3459 (97.5)	142 (37.3)	239 (62.7)	6 (42.9)	8 (57.1)	4 (25.0)	12 (75.0)
Mean (standard deviation)	16 (2)	16 (2)	17 (2)	15 (2)	15 (2)	16 (2)	15 (2)	15 (2)	12 (2)	13 (2)	12 (2)	13 (2)

TABLE 3 COVID-19 vaccine effectiveness (VE) against SARS-CoV-2 infections in 5–11 and 12–17-year-old study populations stratified by SARS-CoV-2 variant and time since vaccination.

	SARS-CoV-2 test result					
Time since full vaccination	Positive *N* (%)	Negative *N* (%)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)	VE (95% CI)	*p*-Value
Omicron infection						
5–11 years						
Unvaccinated	10,711 (54.2)	9045 (45.8)	1	1		
Partially vaccinated	13,235 (48.7)	13,957 (51.3)	0.80 (0.77; 0.83)	0.70 (0.66; 0.74)	30.3% (26.3%; 34.1%)	<.0001
Fully vaccinated 0–6 weeks	1152 (37.7)	1904 (62.3)	0.51 (0.47; 0.55)	0.37 (0.33; 0.42)	62.7% (58.1%; 66.8%)	<.0001
Fully vaccinated 7–9 weeks	595 (48.0)	645 (52.0)	0.78 (0.69; 0.87)	0.52 (0.45; 0.59)	48.3% (40.5%; 55.0%)	<.0001
Fully vaccinated 10–12 weeks	400 (46.9)	452 (53.1)	0.75 (0.65; 0.86)	0.55 (0.47; 0.64)	45.0% (35.7%; 53.0%)	<.0001
Fully vaccinated 12–15 weeks	447 (53.1)	395 (46.9)	0.96 (0.83; 1.10)	0.53 (0.45; 0.62)	47.2% (37.9%; 55.1%)	<.0001
Fully vaccinated >15 weeks	444 (34.6)	839 (65.4)	0.45 (0.40; 0.50)	0.82 (0.71; 0.95)	18.0% (4.8%; 29.4%)	.0092
12–17 years						
Unvaccinated	1146 (43.9)	1466 (56.1)	1	1		
Partially vaccinated	99 (36.8)	170 (63.2)	0.74 (0.57; 0.96)	0.27 (0.18; 0.41)	73.0% (59.2%; 82.3%)	<.0001
Fully vaccinated 0–6 weeks	19 (21.6)	69 (78.4)	0.35 (0.21; 0.58)	0.15 (0.08; 0.29)	84.7% (71.3%; 92.1%)	<.0001
Fully vaccinated >6 weeks	36 (40.0)	54 (60.0)	0.85 (0.55; 1.30)	0.42 (0.24; 0.73)	58.1% (26.5%; 76.4%)	.0027
Delta infection						
≥12 years						
Unvaccinated	3253 (18.2)	14,631 (81.8)	1	1	1	
Partially vaccinated	148 (3.7)	3831 (96.3)	0.17 (0.15; 0.20)	0.38 (0.31; 0.46)	62.4% (54.5%; 69.1%)	<.0001
Fully vaccinated 0–6 weeks	45 (0.7)	6803 (99.3)	0.03 (0.02; 0.04)	0.09 (0.06; 0.12)	91.0% (87.7%; 93.5%)	<.0001
Fully vaccinated 7–9 weeks	118 (2.5)	4530 (97.5)	0.12 (0.10; 0.14)	0.17 (0.14; 0.20)	83.4% (79.8%; 86.4%)	<.0001
Fully vaccinated 10–12 weeks	234 (5.5)	4031 (94.5)	0.26 (0.23; 0.30)	0.21 (0.18; 0.25)	78.8% (74.7%; 82.3%)	<.0001
Fully vaccinated >12 weeks	58 (10.0)	523 (90.0)	0.50 (0.38; 0.65)	0.33 (0.24; 0.46)	66.7% (54.4%; 75.9%)	<.0001

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]Adjusted for sex, age, healthcare area, time in vaccination status (days) and the number of tests realized on the present date, and SARS-CoV-2 positivity rate.

TABLE 4 COVID-19 vaccine effectiveness (VE) against Delta and Omicron SARS-CoV-2 infections stratified by age in years within the 5–11 and 12–17-year-old study populations, respectively.

	SARS-CoV-2 test result					
Age (years)	Positive *N* (%)	Negative *N* (%)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)	VE (95% CI)	*p*-Value
Omicron						
5–6						
Not vaccinated	5392 (53.6)	4660 (46.4)	1	1		
Partially vaccinated	3245 (40.5)	4775 (59.5)	0.59 (0.55; 0.62)	0.74 (0.67; 0.80)	26.5% (19.8%; 32.5%)	<.0001
Fully vaccinated	612 (31.7)	1318 (68.3)	0.40 (0.36; 0.44)	0.42 (0.36; 0.49)	57.8% (51.1%; 63.7%)	<.0001
7–8						
Not vaccinated	3727 (54.8)	3068 (45.2)	1	1		
Partially vaccinated	5177 (50.6)	5046 (49.4)	0.84 (0.79; 0.90)	0.81 (0.74; 0.89)	19.2% (11.2%; 26.5%)	<.0001
Fully vaccinated	1035 (40.8)	1500 (59.2)	0.57 (0.52; 0.62)	0.45 (0.38; 0.53)	54.7% (46.6%; 61.6%)	<.0001
9–10						
No vaccinated	1236 (55.4)	997 (44.6)	1	1		
Partially vaccinated	4555 (53.7)	3926 (46.3)	0.94 (0.85; 1.03)	0.81 (0.73; 0.90)	19.1% (9.8%; 27.4%)	.0001
Fully vaccinated	1343 (49.7)	1357 (50.3)	0.80 (0.71; 0.89)	0.69 (0.59; 0.81)	30.7% (18.5%; 41.1%)	<.0001
11						
Not vaccinated	356 (52.7)	320 (47.3)	1	1		
Partially vaccinated	258 (55.1)	210 (44.9)	1.10 (0.87; 1.40)	0.94 (0.68; 1.30)	5.5% (−29.8%; 31.5%)	.7272
Fully vaccinated	48 (44.4)	60 (55.6)	0.72 (0.48; 1.08)	0.62 (0.34; 1.10)	38.5% (−10.4%; 66.4%)	.1093
Delta						
12–13						
Not vaccinated	821 (17.2)	3954 (82.8)	1	1		
Partially vaccinated	16 (1.3)	1171 (98.7)	0.07 (0.04; 0.10)	0.18 (0.10; 0.31)	81.6% (69.4%; 89.6%)	<.0001
Fully vaccinated	72 (2.1)	3394 (97.9)	0.10 (0.08; 0.13)	0.15 (0.11; 0.19)	85.4% (81.0%; 88.9%)	<.0001
14–15						
Not vaccinated	997 (18.3)	4449 (81.7)	1	1		
Partially vaccinated	24 (2.3)	998 (97.7)	0.11 (0.07; 0.16)	0.37 (0.23; 0.57)	63.1% (43.0%; 77.1%)	<.0001
Fully vaccinated	107 (2.4)	4433 (97.6)	0.11 (0.09; 0.13)	0.16 (0.13; 0.21)	83.6% (79.2%; 87.1%)	<.0001
16–17						
Not vaccinated	1410 (18.7)	6120 (81.3)	1	1		
Partially vaccinated	106 (6.2)	1614 (93.8)	0.29 (0.23; 0.35)	0.55 (0.43; 0.69)	45.3% (31.0%; 56.9%)	<.0001
Fully vaccinated	106 (1.8)	5862 (98.2)	0.08 (0.06; 0.10)	0.14 (0.11; 0.17)	86.5% (82.9%; 89.4%)	<.0001

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]Adjusted for sex, healthcare area, time in vaccination status (days) and the number of tests realized on the present date, and SARS-CoV-2 positivity rate.

(VE: 91.0%; 95% CI: 87.7%–93.5%) and then it started to wan after that period, reaching 66.7% (95% CI: 54.4%–75.9%) in the period of >12-week postprimary vaccination regimen completion (Table 3). As for VE against Omicron, it was substantial during the first 6 weeks 14 days after the second dose administration (VE: 84.7%, 95% CI: 71.3%–92.1%) and then it declined after that period to 58.1% (95% CI: 26.5%–76.4%; Table 3).

Stratifying VE against Delta infections by 2-year-age showed that substantial VE was maintained in all groups (fully vaccinated, 12–13 years VE: 85.4%, 95% CI: 81.0%–88.9%; 14–15 years VE: 83.6%; 95% CI: 79.2%–87.1%; 16–17 years VE: 86.5%; 95% CI: 82.9%–89.4%; Table 4). Due to sample size limitations in the Omicron strata, VE against this variant was not stratified by age within 12–17-year-old population.

Of the 16,520 tests that corresponded to fully vaccinated 12–17-year-old children, 12,149 and 4371 had received Comirnaty® (Pfizer, US) and SpikeVax® (ModernaTX, Inc) vaccines, respectively. Both vaccines showed high effectiveness with a similar magnitude of protection against the Delta variant [Comirnaty® (Pfizer, US) VE: 81.9%; 95% CI: 79.3%–84.2% and SpikeVax® (ModernaTX, Inc) VE: 85.3%; 95% CI: 81.9%–88.1%]. Likewise, substantial protection was observed against Omicron infections among fully vaccinated individuals with Comirnaty® (Pfizer, US) or SpikeVax® (ModernaTX, Inc) vaccines; nonetheless, the former showed a slightly higher magnitude

TABLE 5 COVID-19 vaccine effectiveness (VE) against SARS-CoV-2 infections in the 12–17-year-old study population stratified by SARS-CoV-2 variants and vaccine type.

	SARS-CoV-2 test result					
	Positive *N* (%)	Negative *N* (%)	Crude OR (95% CI)	Adjusted OR[a] (95% CI)	VE (95% CI)	*p*-Value
Delta						
Comirnaty® (Pfizer, US)						
No vaccinated	3253 (18.2)	14,631 (81.8)	1	1		
Fully vaccinated	348 (2.9)	11,769 (97.1)	0.13 (0.12; 0.15)	0.18 (0.16; 0.21)	81.9% (79.3%; 84.2%)	<.0001
SpikeVax® (ModernaTX, Inc)						
No vaccinated	3253 (18.2)	14,631 (81.8)	1	1		
Fully vaccinated	107 (2.5)	4118 (97.5)	0.12 (0.10; 0.14)	0.15 (0.12; 0.18)	85.3% (81.9%; 88.1%)	<.0001
Omicron						
Comirnaty® (Pfizer, US)						
No vaccinated	1146 (43.9)	1466 (56.1)	1	1		
Fully vaccinated	8 (25.0)	24 (75.0)	0.43 (0.18; 0.91)	0.21 (0.08; 0.49)	79.7% (50.7%; 92.4%)	.0007
SpikeVax® (ModernaTX, Inc)						
No vaccinated	1146 (43.9)	1466 (56.1)	1	1		
Fully vaccinated	47 (32.2)	99 (67.8)	0.61 (0.42; 0.86)	0.26 (0.15; 0.43)	74.3% (56.6%; 84.9%)	<.0001

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]Adjusted for sex, age, healthcare area, time in vaccination status (days) and the number of tests realized on the present date, and SARS-CoV-2 positivity rate.

of protection against Omicron than SpikeVax® (ModernaTX, Inc), yet with an overlapped CI [Comirnaty® (Pfizer, US) VE: 79.7%; 95% CI: 50.7%–92.4% and SpikeVax® (ModernaTX, Inc) VE: 74.3%; 95% CI: 56.6%–84.9%] (Table 5).

4 | DISCUSSION

This population-based study in Galicia, Spain, demonstrated that vaccination with Comirnaty® (Pfizer, US) against SARS-CoV-2 offers moderate protection (VE = 44.1%) against susceptibility to infection with the Omicron variant in children 5–11-year-old. Additionally, the study revealed significant protection against Delta (VE = 82.9%) and Omicron (VE = 74.8%) infections in the pediatric population aged 12–17-year-old who had received two doses of the mRNA vaccines, either Comirnaty® (Pfizer, US) or SpikeVax® (ModernaTX, Inc).

The findings of this study are aligned with two meta-analyses of VE against Omicron infections in 5–11-year-old population, which reported pooled VE estimates of 41.6%,[9] and 45.18%,[10] after two doses of the COVID-19 vaccine. The study also revealed that the highest magnitude of VE against Omicron infection (62.7%) in children aged 5–11 years was observed in the first 6 weeks after full vaccination, with a subsequent decline in VE. This observation was consistent with the meta-analysis conducted by Piechotta and colleagues, which concluded that all studies included in their meta-analysis reported at least a 15% decline in VE since the first time point estimate.[9]

Regarding the VE against Omicron in children aged 12–17-year-old, the findings of this study are in line with the pooled VE from the meta-analysis by Li et al. (73%).[10] Similarly, Sabu and colleagues reported a higher VE against Delta compared with Omicron in their meta-analysis.[22] The VE estimate of 82.9% against the Delta variant in this study aligns with a previous meta-analysis (85%).[23] Notably, a decline in VE against Delta and Omicron was observed in our study, highlighting the expected waning immunity in mRNA-based vaccines, as outlined in several studies on the duration of VE.[24,25] These findings underscore the need for a booster dose schedule to maintain effectiveness against SARS-CoV-2.

Due to the rarity of COVID-19 hospitalization in the pediatric age group, the study observed a very small number of children (5–11 or 12–17 years) admitted for COVID-19, making it unfeasible to estimate VE against hospitalization. Thus, larger studies are warranted to evaluate this outcome.

To control for bias from the effect of past infections on the immunity response, the analysis included infection-naïve test results exclusively. However, a sensitivity analysis was conducted by including positive SARS-CoV-2 test results that occurred more than 90 days before the study initiation. The sensitivity analysis yielded similar findings, indicating that attrition bias due to the exclusion of previously infected individuals is unlikely to have occurred.

The main analysis considered a time window of 14 days after the administration of the first vaccine dose to classify a test as partially vaccinated. However, given the suggestion that a primary cellular immune response may start as early as Day 7 after the first vaccine dose administration,[26] a sensitivity analysis using a 7-day time window was conducted. Re-estimating VE using this new classification did not significantly alter the finding against Delta infections in children aged 12 years and above (82.9% vs. 81.8%). However, a

slightly higher VE estimate was observed against Omicron in both the 5–11-year-old (44.1% vs. 51.7%) and 12–17-year-old (74.8% vs. 84.5%) populations.

It should be noted that the VE against SARS-CoV-2 infections, but not against hospitalization, in this study could be overestimated for two main reasons. First, in Spain, like in many other countries, SARS-CoV-2 rapid tests are available at pharmacies without a medical prescription and at low cost. Consequently, SARS-CoV-2 infections detected in nonlaboratory settings may not be reported, leading to a lower number of registered infections in public health databases. Second, young children often have mild symptoms or are asymptomatic, making them less likely to be tested for SARS-CoV-2 and resulting in underreported cases. However, the underreporting of SARS-CoV-2 infections is unlikely to significantly affect the number of registered COVID-19-related hospitalizations since all hospitalizations in the study setting are automatically registered upon patient admission.

In a fast-evolving pandemic, especially with the appearance of new variants of SARS-CoV-2, the findings on VE may not be generalizable. Additionally, other factors such as the socioeconomic level or the implementation of nonpharmaceutical measures in the study location might affect VE estimates. However, the findings of this study are valuable for meta-analysis on VE against SARS-CoV-2, particularly because: (1) the analysis relied on population-based data, (2) undertook a comprehensive analysis by age subgroup (2-year-age categories), SARS-CoV-2 variant, vaccine type and duration of protection, and (3) provide estimates on VE in two pediatric populations from Europe. Previous meta-analyses highlighted the need for studies undertaken in different geographic regions and for findings on the effectiveness of different vaccine types.

COVID-19 disproportionately affects older adults and individuals with underlying comorbidities, irrespective of age. Current Strategic Advisory Group of Experts (SAGE) on Immunization recommendations for COVID-19 vaccine booster administration establish the highest priority group in older adults; younger adults with significant comorbidities (e.g., diabetes and heart disease); people with immunocompromising conditions (e.g., people living with HIV and transplant recipients), including children aged 6 months and older; pregnant women; and frontline health workers.[27] Healthy children and adolescents aged 6 months to 17 years belong to the low-priority group despite the safety and effectiveness of COVID-19 vaccines in this age group. The decision to vaccinate this age group should be based on the disease burden, cost-effectiveness, and other health or programmatic priorities and opportunity costs.[27] A similar approach has been adopted by several supranational and national recommending bodies.[28,29] Our data reassure the effectiveness of COVID-19 vaccination in healthy children and also confirm the current limited burden of the disease as well as the limited duration of the VE, impacting any cost-effectiveness analysis of further doses in this group. For these reasons, other traditional essential vaccines like rotavirus, pneumococcal conjugate, or measles vaccines should be prioritized over COVID-19 vaccines in the healthy child population.

5 | CONCLUSIONS

In our settings, Pfizer's mRNA vaccine [Comirnaty® (Pfizer, US)] demonstrated moderate effectiveness against the Omicron variant of SARS-CoV-2 in the 5–11-year-old population. Vaccination with Pfizer's or Modern's mRNA vaccines resulted in higher VE against Omicron and Delta in older children. However, a significant decline in effectiveness after 6 weeks was observed over time in both the pediatric populations aged 5–11 and 12 years and above, indicating the eventual need for a booster dose schedule.

It is worth noting that SARS-CoV-2 infections have a limited impact on healthy children, as evidenced by the small number of COVID-19-related hospitalizations. Therefore, our findings are crucial for relevant public health authorities when making decisions regarding universal vaccination against COVID-19 in healthy children.

AUTHOR CONTRIBUTIONS

Narmeen Mallah: Investigation; writing – original draft; methodology; validation; visualization; writing – review and editing; formal analysis; conceptualization. **Jacobo Pardo-Seco:** Writing – review and editing; methodology; formal analysis; data curation. **Sonia Ares-Gómez:** Writing – review and editing; methodology; formal analysis. **Luis-Ricardo López-Pérez:** Writing – review and editing; project administration; resources. **Juan-Manuel González-Pérez:** Writing – review and editing; project administration; resources. **Benigno Rosón:** Writing – review and editing; project administration; resources. **María-Teresa Otero-Barrós:** Writing – review and editing; project administration; resources. **Carmen Durán-Parrondo:** Conceptualization; writing – review and editing; project administration; supervision; resources. **Victoria Nartallo-Penas:** Writing – review and editing; project administration; resources. **Susana Mirás-Carballal:** Writing – review and editing; project administration; resources. **Carmen Rodríguez-Tenreiro-Sánchez:** Writing – review and editing; project administration; resources. **Irene Rivero-Calle:** Investigation; writing – review and editing. **Alberto Gómez-Carballa:** Writing – review and editing; investigation; resources. **Antonio Salas:** Writing – review and editing; funding acquisition; investigation; resources. **Federico Martinón-Torres:** Conceptualization; investigation; funding acquisition; writing – review and editing; methodology; project administration; resources; supervision.

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CONFLICT OF INTEREST STATEMENT

Irene Rivero-Calle reports a relationship with GSK, Pfizer Inc, Sanofi Pasteur Inc, and MSD Vaccines that includes speaking and lecture fees. Federico Martinón-Torres reports a relationship with GSK Vaccines SRL, Pfizer Inc, Sanofi Pasteur Inc, Janssen Pharmaceuticals Inc, MSD, and Seqirus Pty Ltd that includes consulting or advisory. Federico Martinón-Torres has received support for the present work from the Instituto de Salud Carlos III (Proyecto de Investigación en Salud, Acción Estratégica en Salud): Fondo de Investigación Sanitaria (FIS; PI070069/PI1000540/PI1601569/PI1901090) del plan nacional de I+D+I and "fondos FEDER" and Proyectos GaIN Rescata-Covid_IN845D 2020/23 (GAIN, Xunta de Galicia). Federico Martinón-Torres has acted as principal investigator and Irene Rivero-Calle has acted as subinvestigator in randomized controlled trials of Ablynx, Abbot, Seqirus, Sanofi Pasteur MSD, Sanofi Pasteur, Cubist, Wyeth, Merck, Pfizer, Roche, Regeneron, Jansen, Medimmune, Novavax, Novartis, and GSK. The remaining authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

PEER REVIEW

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REFERENCES

1. World Health Organization. WHO coronavirus (COVID-19) dashboard. 2023. https://covid19.who.int/. Accessed May 23, 2023.
2. Spanish Ministry of Health. Informe n° 177. Situación de COVID-19 en España. [Report no. 177. COVID-19 situation in Spain]. 2023. https://www.sanidad.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/situacionActual.htm. Accessed May 23, 2023.
3. World Health Organization. Confirmed and probable COVID-19 cases by age. 2023. https://app.powerbi.com/view?r=eyJrIjoiYWRiZWVkNWUtNmM0Ni00MDAwLTljYWMtN2EwNTM3YjQzYmRmIiwidCI6ImY2MTBjMGI3LWJkMjQtNGIzOS04MTBiLTNkYzI4MGFmYjU5MCIsImMiOjh9. Accessed May 23, 2023.
4. World Health Organization. Interim statement on COVID-19 vaccination for children. 2022. https://www.who.int/news/item/11-08-2022-interim-statement-on-covid-19-vaccination-for-children. Accessed May 23, 2023.
5. World Health Organization. COVID-19 disease in children and adolescents: scientific brief. 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci_Brief-Children_and_adolescents-2021.1. Accessed May 23, 2023.
6. Tsankov BK, Allaire JM, Irvine MA, et al. Severe COVID-19 infection and pediatric comorbidities: a systematic review and meta-analysis. *Int J Infect Dis*. 2021;103:246-256.
7. Martinon-Torres F. Pediatric vaccination against COVID-19 and despite COVID-19. *An Pediatr (Engl ed)*. 2022;96(1):4-7.
8. Lyngse FP, Molbak K, Denwood M, et al. Effect of vaccination on household transmission of SARS-CoV-2 Delta variant of concern. *Nat Commun*. 2022;13(1):3764.
9. Piechotta V, Siemens W, Thielemann I, et al. Safety and effectiveness of vaccines against COVID-19 in children aged 5-11 years: a systematic review and meta-analysis. *Lancet Child Adolesc Health*. 2023;7(6):379-391.
10. Li Y, Liang H, Ding X, Cao Y, Yang D, Duan Y. Effectiveness of COVID-19 vaccine in children and adolescents with the omicron variant: a systematic review and meta-analysis. *J Infect*. 2023;86(3):e64-e66.
11. Pardo-Seco J, Mallah N, Lopez-Perez LR, et al. Evaluation of BNT162b2 vaccine effectiveness in Galicia, Northwest Spain. *Int J Environ Res Public Health*. 2022;19(7):4039.
12. Mallah N, Pardo-Seco J, Lopez-Perez LR, et al. Effectiveness of COVID-19 vaccine booster in the general population and in subjects with comorbidities. A population-based study in Spain. *Environ Res*. 2022;215(Pt 2):114252.
13. Instituto Galego de Estatistica [Galician Statistics Institute]. Población [Population]. 2022. https://www.ige.gal/web/index.jsp?paxina=001&idioma=gl. Accessed May 02, 2023.
14. Instituto Galego de Estatistica [Galician Statistics Institute]. Hospitais [Hospitals]. 2022. https://www.ige.gal/web/mostrar_actividade_estatistica.jsp?idioma=gl&codigo=0202001. Accessed May 2, 2023.
15. Servizo Galego de Saúde [Galician Health Service]. Plan gallego de vacunación frente al SARS-CoV-2 [Galician vaccination plan against SARS-CoV-2]. https://coronavirus.sergas.gal/Contidos/Plan-galego-vacinacion-COVID. Accessed June 24, 2023.
16. Tut G, Lancaster T, Krutikov M, et al. Profile of humoral and cellular immune responses to single doses of BNT162b2 or ChAdOx1 nCoV-19 vaccines in residents and staff within residential care homes (VIVALDI): an observational study. *Lancet Healthy Longev*. 2021;2(9):e544-e553.
17. Sacco C, Del Manso M, Mateo-Urdiales A, et al. Effectiveness of BNT162b2 vaccine against SARS-CoV-2 infection and severe COVID-19 in children aged 5-11 years in Italy: a retrospective analysis of January-April, 2022. *Lancet*. 2022;400(10346):97-103.
18. Yeo I, Baek S, Kim J, et al. Assessment of thirty-day readmission rate, timing, causes and predictors after hospitalization with COVID-19. *J Intern Med*. 2021;290(1):157-165.
19. Mehta HB, Li S, Goodwin JS. Risk factors associated with SARS-CoV-2 infections, hospitalization, and mortality among US nursing home residents. *JAMA Netw Open*. 2021;4(3):e216315.

20. Monge S, Rojas-Benedicto A, Olmedo C, et al. Effectiveness of mRNA vaccine boosters against infection with the SARS-CoV-2 omicron (B.1.1.529) variant in Spain: a nationwide cohort study. *Lancet Infect Dis*. 2022;22(9):1313-1320.
21. Carcereny A, Martinez-Velazquez A, Bosch A, et al. Monitoring emergence of the SARS-CoV-2 B.1.1.7 variant through the Spanish national SARS-CoV-2 wastewater surveillance system (VATar COVID-19). *Environ Sci Technol*. 2021;55(17):11756-11766.
22. Sabu JM, Zahid I, Jacob N, Alele FO, Malau-Aduli BS. Effectiveness of the BNT162b2 (Pfizer-BioNTech) vaccine in children and adolescents: a systematic review and meta-analysis. *Vaccines (Basel)*. 2022;10(11):1880.
23. Mahumud RA, Ali MA, Kundu S, Rahman MA, Kamara JK, Renzaho AMN. Effectiveness of COVID-19 vaccines against Delta variant (B.1.617.2): a meta-analysis. *Vaccines (Basel)*. 2022;10(2):277.
24. Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-dose and 3-dose effectiveness of mRNA vaccines against COVID-19-associated emergency department and urgent care encounters and hospitalizations among adults during periods of Delta and omicron variant predominance – VISION network, 10 states, August 2021–January 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(7):255-263.
25. Ferdinands JM, Rao S, Dixon BE, et al. Waning of vaccine effectiveness against moderate and severe covid-19 among adults in the US from the VISION network: test negative, case-control study. *BMJ*. 2022;379:e072141.
26. Zaffina S, Alteri C, Ruggiero A, et al. Induction of immune response after SARS-CoV-2 mRNA BNT162b2 vaccination in healthcare workers. *J Virus Erad*. 2021;7(2):100046.
27. World Health Organization. Meeting of the strategic advisory group of experts on immunization, March 2023: conclusions and recommendations. Weekly epidemiological record. 2023. https://www.who.int/publications/i/item/who-wer9822-239-256. Accessed 14 September, 2023.
28. European Centre for Disease Prevention and Control. ECDC-EMA statement on updating COVID-19 vaccines composition for new SARS-CoV-2 virus variants. 2023. https://www.ecdc.europa.eu/en/news-events/ecdc-ema-statement-updating-covid-19-vaccines-composition-new-sars-cov-2-virus-variants. Accessed 14 September, 2023.
29. Royal College of Pediatrics and Child Health. COVID-19 vaccination for children and young people. 2023. https://www.rcpch.ac.uk/resources/covid-19-vaccination-children-young-people. Accessed 14 September, 2023.

SUPPORTING INFORMATION

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

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