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Low uptake rotavirus vaccine: A study of vaccine effectiveness against rotavirus-related hospitalization based on electronic health records, Slovenia, 2019–2023

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ABSTRACT

Background: In Slovenia, coverage of rotavirus vaccines (Rotarix (RV1) and RotaTeq (RV5)) remains low, and the vaccines are not included in the National Vaccination Programme (NVP). We aimed to estimate vaccine effectiveness (VE) against rotavirus-related hospitalization among children aged 6 weeks to 5 years to inform national vaccination policy.

Methods: We linked Slovenian population registry with vaccination, surveillance, and hospitalization databases for 2019–2023 birth cohorts. We defined fully vaccinated as those receiving all recommended doses with the last dose ≥14 days before the end date (disease onset or hospitalization date, death, or study end) and partially vaccinated those receiving ≥1 dose ≥14 days before the end date. We estimated VE using quasi-Poisson regression, adjusting for age, healthcare access, socioeconomic status, and calendar time, with person-time at risk included as an offset. We also examined the relationship between full vaccination coverage and hospitalization rates across municipalities using Pearson's correlation coefficient.

Results: Among 89,994 children, 4% were partially, and 25% fully vaccinated. A total of 1272 rotavirus hospitalizations occurred, 94% among unvaccinated children. VE against hospitalization was 84% (95% CI: 73%–91%) for full and 81% (95% CI: 42%–94%) for partial vaccination. VE was 85% (95% CI: 74%–91%) for RV1 and 78% (95% CI: −29%–96%) for RV5. VE was 73% (95% CI: 30%–89%) among children aged <11 months and 88% (95% CI: 76%–94%) among those aged 11 to 23 months, with sustained high effectiveness through 5 years of age (84%, 95% CI: 63%–93%). We observed a negative correlation between full vaccination coverage and hospitalization rates across municipalities ($r = -0.155$, $p = 0.024$).

Conclusion: Both full and partial rotavirus vaccination significantly reduced rotavirus-related hospitalizations among children in Slovenia. These findings support efforts to improve vaccine uptake and consideration of rotavirus vaccination inclusion in the NVP to reduce disease burden.

1. Introduction

Globally, rotavirus infection remains a leading cause of diarrhoea-related morbidity and mortality among children under five years of age [1], with the most common cause of gastroenteritis in young children being rotavirus alphagastroenteritidis (group A) [2]. Although substantial progress has been made in reducing the burden of rotavirus disease, mostly with rotavirus vaccines, hospitalizations due to rotavirus gastroenteritis remain a major public health concern, particularly in settings with low vaccine uptake or where access to vaccination remains limited [3]. Prior to vaccine introduction, the median age of children with a rotavirus-related hospitalization was approximately 16 months, with 38% of cases occurring by one year and 96% by five years of age [4]. Four globally available rotavirus vaccines for prevention of group A rotavirus infection are Rotarix (RV1; GlaxoSmithKline), RotaTeq (RV5; Merck), Rotasiil (Serum Institute of India Ltd.), and Rotavac (Bharat Biotech Ltd.) [5]. RV1 and RV5 are oral live vaccines for active immunisation of infants. Both schedules begin at 6 weeks of age; RV1 is administered in two doses completed by 24 weeks, and RV5 in three doses completed by 32 weeks, with a minimum interval of four weeks between doses [3]. A 2019 meta-analysis of randomized controlled trials indicated high efficacy of rotavirus vaccines against severe disease in

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infants shortly after the final dose. Specifically, in low-mortality settings, vaccine efficacy has been reported at 98% two weeks after last dose in the recommended schedules of each version of the vaccine [6]. Real world studies in these settings have indicated an estimated 76%–100% vaccine effectiveness (VE) of a full vaccination series of rotavirus vaccines against disease requiring hospitalization [7–14]. While full vaccination with RV1 and/or RV5 provides a high degree of protection, partial protection may also be achieved following an incomplete vaccination series [1,7,13,15,16]. Interchangeability between the RV1 and RV5 has also been evaluated, and mixed schedules proved to be safe and induce comparable immune responses when administered in a 3-dose schedule [3].

In Slovenia, a confirmed case of rotavirus disease is defined as a patient with at least one clinical symptom (vomiting or diarrhoea), and a laboratory confirmation of rotavirus infection, which includes detection of rotavirus antigen, visualization of the virus by electron microscopy, or identification of the viral genome in faeces or vomit [17]. Despite the availability of effective oral rotavirus vaccines in Slovenia since 2008 (RV1) and 2010 (RV5), rotavirus vaccination is not included in the National vaccination programme (NVP), and is therefore not publicly funded but widely available through primary care paediatric services on a self-pay basis. During the study period, the approximate cost per dose ranged from €68–€78 for RV1 and €55–€61 for RV5. Vaccine uptake remains relatively low, with only 31% of infants from the 2021 birth cohort receiving the second dose of RV1 or RV5 [18]. Although global and regional studies provide strong evidence of the impact of rotavirus vaccination on reduction of rotavirus-related hospitalization, no such study has been performed in Slovenia to date.

In 2013, the World Health Organisation recommended the inclusion of rotavirus vaccination in NVPs [1]. As of 2024, rotavirus vaccination was included in the nation-wide schedule in 17 EU countries, while Portugal offered it only to specific risk groups [19]. Eight other EU countries besides Slovenia (Croatia, Cyprus, Czechia, Denmark, Hungary, Malta, Romania, and Slovakia) had not introduced rotavirus vaccination in theirs NVPs. Among EU countries that reported rotavirus vaccine coverage, the median uptake in 2024 for the full vaccination series was 76% (interquartile range (IQR): 63%–86%) [19]. This uneven vaccination policy and uptake across EU countries highlights the need for national data to guide decision makers, while also contributing to the broader evidence base relevant for other countries that have not yet included rotavirus vaccination in their NVPs.

Our study aimed to estimate the real-world rotavirus VE against rotavirus-related hospitalization among children aged 6 weeks to 5 years in Slovenia, to provide country-specific estimates relevant to national immunisation policy.

2. Methods

2.1. Study design and data sources

We conducted a retrospective cohort study using routinely collected data from electronic national registries in Slovenia. We identified the study population through the Central registry of patient data (CRPD), which included all children in Slovenia with date of birth between 1 January 2019 and 31 December 2023. We included children with Slovenian residency verified by a valid unique personal identification number or national health insurance number, a registered address in Slovenia, and eligibility for rotavirus vaccination, defined as reaching the age of six weeks. We excluded children with a recorded rotavirus episode before six weeks of age, identified through national surveillance or hospital database, to ensure that early natural infection did not influence VE estimates (Fig. 1).

For the study population, we extracted data from three electronic health databases. We obtained demographic and vaccination data from the Electronic register of vaccinated persons and adverse effects following immunisation (eRCO), which also includes data from the CRPD. We retrieved date of disease onset from the Communicable disease registry (NIJZ48) and hospitalization data from the National hospital health care statistics database (SBO). We linked the data using a combination of deterministic and probabilistic data linkage methods: data from CRPD and eRCO were already linked, the SBO data were deterministically linked to eRCO using national identifiers, and NIJZ48 data were linked using a combination of deterministic and probabilistic methods based on first and last name, date of birth, sex, and place of residence [20,21].

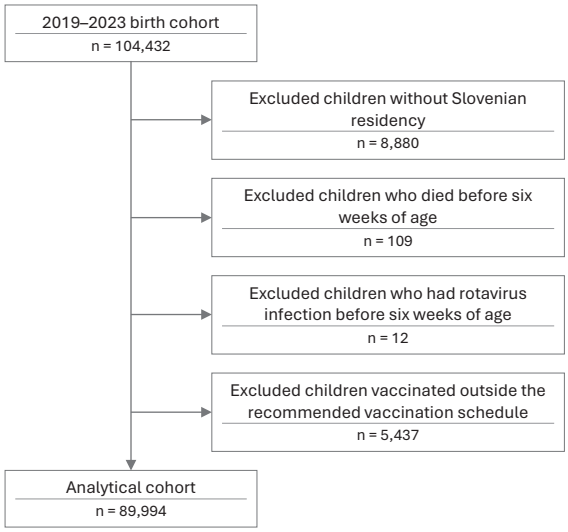

Fig. 1. Flowchart outlining exclusion criteria to generate cohort for analysis.

Exposure and outcome definitions We categorized children into three groups according to their vaccination status. We considered children as fully vaccinated if they received two doses of RV1, or three doses of RV5 or combination of RV1 and RV5 in accordance with the recommended dosing schedule and intervals between doses [3], and the final dose administered at least 14 days before the end date. The end date was defined as the date of disease onset or hospitalization date, death, or the end of the study, whichever occurred first. We considered children partially vaccinated if they received only one dose (RV1 or RV5), or two doses of RV5 or a combination of RV1 and RV5, with the last dose given at least 14 days before the end date, or they received all recommended doses less than 14 days before the end date. Children were considered unvaccinated if there was no record of vaccination in eRCO or if the first dose was administered less than 14 days before the end date. We excluded children vaccinated outside the recommended vaccination schedule. Only the first rotavirus infection or a hospitalization coded with ICD-10 A08.0 per child was included because reinfections were rare and prior infection offers substantial protection against subsequent moderate-to-severe disease [1]. We identified rotavirus-related hospitalizations in the SBO database by extracting all admissions with International Classification of Diseases 10th Revision (ICD-10) code A08.0 (rotaviral enteritis) recorded in any diagnostic position (admission, primary discharge, or secondary discharge diagnosis). We automatically classified hospitalizations with A08.0 as the primary discharge diagnosis as rotavirus-related. For admissions where A08.0 appeared only as an admission or secondary discharge diagnosis, individual records were independently reviewed by two authors to determine whether rotavirus infection was the main reason for hospitalization; additional eligible cases were included based on this review. We linked hospitalization records with rotavirus cases from the NIJZ48. As reporting to NIJZ48 requires separate notification, not all hospitalized cases were recorded in this database. We assessed concordance between cases with assigned ICD-10 A08.0 code as the primary discharge diagnosis from SBO database and rotavirus cases recorded in the national surveillance registry. For time-to-event analyses, we used the date of disease onset recorded in

NIJZ48 when available. For hospitalizations identified only in SBO database without a corresponding NIJZ48 record, we used hospital admission date as the end date.

Follow-up and person-time For each child in the study population, we calculated person-time at risk in days. The follow-up period began at six weeks of age and was split into successive intervals according to vaccination dates, age groups, and calendar months and years. Vaccination status was treated as a time-varying exposure: children contributed person-time as unvaccinated until 14 days after the first dose, as partially vaccinated until 14 days after completion of the full schedule, and as fully vaccinated thereafter. Follow-up ended at the end date (disease onset or hospitalization date, death, or at the end of the study). We divided follow-up by calendar month so each interval belonged to a single calendar month-year, to account for seasonal variation and the reduction in rotavirus hospitalizations during the COVID-19 pandemic restrictions.

2.2. Covariates

We used the information on having a chosen or personal paediatrician as a proxy for children's access to primary healthcare and their availability of primary health services. We used the municipal development coefficient [22] of the municipality of child's residence as a proxy for their socio-economic status. This coefficient is a governmental indicator that reflects the overall development level of Slovenian municipalities [23]; it combines economic, social, cultural, and environmental factors and captures broader contextual influences on population health.

Statistical analysis For estimating rotavirus VE against rotavirus-related hospitalization, we used quasi-Poisson regression calculating incidence risk ratios (IRR) among fully and partially vaccinated children compared with unvaccinated, and corresponding 95% confidence intervals. We computed VE as (1 − IRR) * 100. To account for differences in follow-up time, we included person-time at risk as an offset. We adjusted models for age (categorical variable), having a chosen paediatrician (binary variable), the municipal development coefficient (continuous variable), and calendar time (month-year; categorical variable). To assess potential effect modification by socioeconomic context at the individual level, we included an interaction term between vaccination status and municipal development coefficient in the adjusted quasi-Poisson model. We additionally stratified VE estimates by age group (6 weeks to 10 months, 11 to 23 months, and 24 to 59 months) and by vaccine product (RV1 and RV5). We calculated Pearson's correlation coefficient to examine the correlation between the full vaccination coverage and rotavirus hospitalization rate across municipalities in Slovenia. Given the country's low full vaccination coverage and that 95% of rotavirus-related hospitalizations occur before the age of five [4], only the 2019 birth cohort was eligible for complete 60-month follow-up by the study end and was included in the spatial analysis. To ensure reliable estimates, we excluded 18 out of 212 municipalities that had fewer than 50 children in the 2019 birth cohort. Municipalities were categorized into three groups (low, medium, high) for each indicator (full vaccination coverage and rotavirus hospitalization rate) using the Jenks natural breaks classification method, which minimizes within-group variance and maximizes between-group variance, producing groups that best fit the observed data distribution [24]. The resulting cut-offs were: low (≤17%), medium (18%–30%), and high (≥31%) full vaccination coverage; and low (≤2.6%), medium (2.7%–10%), and high (≥11%) hospitalization rates. This classification resulted in nine possible combinations (e.g., low vaccination coverage and high hospitalization rate). To visualize these patterns, we plotted municipalities on a bivariate map, with darker purple indicating areas with both low vaccination coverage and high hospitalization rates, and teal shades indicating higher vaccination coverage and lower hospitalization rates. We performed all analyses in R Statistical Software (v4.4.2) [25].

2.3. Ethical considerations

All procedures were performed in compliance with relevant laws and institutional guidelines. Ethical approval was not required, as all surveillance data were mandatorily collected in accordance with the law (Communicable Diseases Act [26] and Healthcare Databases Act [27]). Although personal identifiers were available during data merging, the analytical dataset was anonymised and no individual could be identified in the analysis or in the reported results.

3. Results

3.1. Study population characteristics

In our study population of five birth cohorts ($N = 89{,}994$), 71% ($n = 64{,}052$) of children were unvaccinated, 4% ($n = 3578$) were partially vaccinated and 25% ($n = 22{,}364$) were fully vaccinated with rotavirus vaccines (Table 1). Of children vaccinated with at least one dose, 94% were vaccinated with RV1, 5.5% with RV5 and 0.3% with a combination of RV1 and RV5. The median age of all children was 31 months (IQR: 16–45), and was highest in the unvaccinated group (median = 31, IQR: 16–46 months) and lowest in partially vaccinated group (median = 26, IQR: 9–41 months) ($p < 0.001$) (Table 2). Of all children, 7% did not have a chosen paediatrician; this percentage was highest among the unvaccinated (8.6%), and significantly lower among partially and fully vaccinated (2.5% and 3.1%, respectively ($p < 0.001$)). Overall, 1272 rotavirus-related hospitalizations were reported; 1.9% of the unvaccinated, 0.4% of partially vaccinated and 0.3% of fully vaccinated children ($p < 0.001$) were hospitalized (Table 1).

3.2. Case ascertainment and concordance analysis

Among 1272 hospitalizations in the SBO database, 1184 (93.1%) were coded as A08.0 in the primary discharge diagnosis field. Of the 1272 hospitalizations, 788 (62.0%) were also present in the national surveillance database, while 484 (38.0%) were identified only in the SBO database. Among cases present in both databases, 780 (99.0%) were laboratory confirmed and 730 (92.6%) were coded as A08.0 as the primary discharge diagnosis. In the SBO-only group, 454 of 484 cases (93.8%) were coded as A08.0. This indicates that the use of ICD-10 code A08.0 as the primary discharge diagnosis was closely aligned with laboratory-confirmed rotavirus surveillance data.

3.3. Characteristics of hospitalized children

Among children hospitalized due to rotavirus, 94% ($n = 1195$) were unvaccinated, 1% ($n = 13$) partially vaccinated, and 5% ($n = 64$) fully vaccinated. Among fully vaccinated hospitalized children, 92% received RV1, while 7.8% received RV5. The shortest duration of hospitalization was among partially vaccinated children (1 day, IQR: 1–2). There were no significant differences in the age and sex distributions, the municipal development coefficient, or the proportion of children with a chosen paediatrician across different vaccination groups of hospitalized children (Table 1 and Table 2).

3.4. Vaccine effectiveness estimates

Compared with unvaccinated children, the adjusted VE against rotavirus-related hospitalization for fully vaccinated children was 84% (95%CI: 73%—91%) and for partially vaccinated 81% (95%CI: 42%—94%) (Table 3; Supplementary Tables S1-S12). We observed no evidence of interaction between vaccination status and municipal development coefficient (p-interaction = 0.81), suggesting similar individual-level VE across socioeconomic levels. When we stratified by age group, among children aged 6 weeks to 10 months, VE for fully vaccinated was 73% (95%CI: 30%–89%), while VE for partially vaccinated was not

Table 1
Study population characteristics by rotavirus vaccination status, n and %, Slovenia, birth cohorts 2019–2023.

			Overall		Unvaccinated		Partially vaccinated		Fully vaccinated		p-value[1]
			n	%	n	%	n	%	n	%	
All children	**Vaccine product**	Unvaccinated	64,052	71%	64,052	100%	/	/	/	/	/
		RV1	24,441	27%	/	/	3274	92%	21,167	95%	
		RV5	1435	1.6%	/	/	256	7.2%	1179	5.3%	
		Mixed	66	<0.1%	/	/	48	1.3%	18	<0.1%	
	Sex	Male	46,284	51%	32,905	51%	1871	52%	11,508	51%	0.6
		Female	43,710	49%	31,147	49%	1707	48%	10,856	49%	
	Age groups	6 weeks to 10 months	13,796	15%	10,246	16%	940	26%	2610	12%	<0.001
		11 to 23 months	19,327	21%	13,154	21%	703	20%	5470	24%	
		24 to 59 months	56,871	63%	40,652	63%	1935	54%	14,284	64%	
	Child has a chosen	No	6283	7,0%	5493	8.6%	91	2.5%	699	3.1%	<0.001
	paediatrician	Yes	83,711	93%	58,559	91%	3487	97%	21,665	97%	
	RVGE hospitalization	No	88,722	99%	62,857	98%	3565	100%	22,300	100%	<0.001
		Yes	1272	1.4%	1195	1.9%	13	0.4%	64	0.3%	
Hospitalized children	**Vaccine product**	Unvaccinated	1195	94%	1195	100%	/	/	/	/	/
		RV1	70	5.5%	/	/	11	85%	59	92%	
		RV5	7	0.6%	/	/	2	15%	5	7.8%	
	Sex	Male	690	54%	653	55%	8	36%	29	45%	0.3
		Female	582	46%	542	45%	5	35%	35	55%	
	Age group	6 weeks to 10 months	242	19%	222	19%	6	46%	14	22%	0.2
		11 to 23 months	550	43%	522	44%	3	23%	25	39%	
		24 to 59 months	480	38%	451	38%	4	31%	25	39%	
	Child has a chosen	No	43	3.4%	43	3.6%	0	0%	0	0%	0.3
	paediatrician	Yes	1229	97%	1152	96%	13	100%	64	100%	

[1] Pearson's Chi-squared test.

Table 2
Study population characteristics by rotavirus vaccination status, median and interquartile range (IQR), Slovenia, birth cohorts 2019–2023.

		Overall		Unvaccinated		Partially vaccinated		Fully vaccinated		p-value[1]
		Median	IQR	Median	IQR	Median	IQR	Median	IQR	
All children	**Age in months**	31	16, 45	31	16, 46	26	9, 41	30	17, 45	<0.001
	Municipal development coefficient	1.09	1.00, 1.19	1.09	1.00, 1.18	1.10	1.00, 1.21	1.09	1.01, 1.21	<0.001
Hospitalized children	**Age in months**	20	12, 28	20	12, 28	22	4, 25	21	12, 29	0.5
	Days hospitalized	2	1, 3	2	1, 3	1	1, 2	2	1, 2	0.041
	Municipal development coefficient	1.08	1.00, 1.15	1.09	1.00, 1.15	1.01	0.94, 1.14	1.07	0.98, 1.15	0.5

[1] Kruskal-Wallis rank sum test.

significant. Among children aged 11 to 23 months, VE for fully vaccinated was 88% (95%CI: 76%–94%), and 89% (95%CI: 29%–98%) for partially vaccinated. Among children aged 24 to 59 months, VE for fully vaccinated was 84% (95%CI: 63%–93%) and VE for partially vaccinated was not significant. When we stratified VE estimates by vaccine type, among children vaccinated with only RV1 compared with unvaccinated children, VE for fully vaccinated was 85% (95%CI: 74%–91%), and 83% (95%CI: 41%—95%) for partially vaccinated (Table 3). Among children vaccinated with only RV5, VE was not significant. The small number of RV5-vaccinated children and hospitalization events in this group resulted in limited precision of these estimates.

3.5. Spatial analysis

In the spatial analysis of 194 Slovenian municipalities, Pearson's correlation coefficient between the full vaccination coverage and the rotavirus hospitalization rate was −0.155 ($p = 0.024$); municipalities with higher full vaccination coverage had lower hospitalization rates (Fig. 2). No municipality had both high full vaccination coverage and high rotavirus-related hospitalization rate (Table 4). Of 194 municipalities, 29% had medium and 17% had high vaccination coverage combined with low hospitalization rate, 19% had both low vaccination coverage and low hospitalization rate, and 14% had a combination of low vaccination and moderate-to-high hospitalization rate.

4. Discussion

4.1. Principal findings and comparison with previous studies

This retrospective, population-based study of five birth cohorts indicated that both full and partial rotavirus vaccination schemes were effective in preventing rotavirus-related hospitalizations among young children. VE among fully vaccinated children was 84% compared with unvaccinated, while partial vaccination also provided strong protection with a VE of 81%. These findings are consistent with previous studies in low-mortality settings (e.g. high-income countries such as the United States, Canada, Australia, and EU), where VE against rotavirus-related hospitalization typically ranges from 76% to 100% for full vaccination and 70% to 93% for partial vaccination [7–16,28]. Our slightly lower VE compared with the upper range of previous studies may be influenced by local factors such as vaccine coverage, circulating rotavirus strains, or health system characteristics that determine hospitalization criteria. For example, during the study period in Slovenia, the predominant genotypes were G3P [8] (46%) and G9P [8] (38%), with smaller proportions of G1P [8] and G2P [4] [29]. Both RV1 and RV5 contain P [8] components. The sustained high VE observed in our study is consistent with evidence that both vaccines provide strong protection against these commonly circulating strains [1].

4.2. Product-specific and age-stratified VE

We observed high VE among fully vaccinated children who received

Table 3
Unadjusted and adjusted vaccine effectiveness estimates and stratified analysis according to age group and vaccine brand, Slovenia, birth cohorts 2019–2023.

Unadjusted		n of hospitalizations	IRR[1]	Lower 95% CI[1]	Upper 95% CI[1]	VE[1]	Lower 95% CI[1]	Upper 95% CI[1]	p-value
Whole cohort	**Unvaccinated**	1195	–						
	Partially vaccinated	13	0.18	0.05	0.45	82%	55%	95%	0.002
	Fully vaccinated	64	0.17	0.10	0.28	83%	72%	90%	<0.001
6 weeks to 10 months	**Unvaccinated**	222	–						
	Partially vaccinated	6	0.29	0.03	1.09	71%	−9%	97%	0.14
	Fully vaccinated	14	0.28	0.07	0.72	72%	28%	93%	0.023
11 to 23 months	**Unvaccinated**	522	–						
	Partially vaccinated	3	0.12	0.00	0.60	88%	40%	100%	0.056
	Fully vaccinated	25	0.13	0.06	0.27	87%	73%	94%	<0.001
24 to 59 months	**Unvaccinated**	451	–						
	Partially vaccinated	4	0.20	0.01	0.89	80%	11%	99%	0.11
	Fully vaccinated	25	0.17	0.07	0.34	83%	66%	93%	<0.001
RV1	**Unvaccinated**	1195	–						
	Partially vaccinated	11	0.17	0.04	0.45	83%	55%	96%	0.003
	Fully vaccinated	59	0.17	0.10	0.27	83%	73%	90%	<0.001
RV5	**Unvaccinated**	1195	–						
	Partially vaccinated	2	0.33	0.00	2.21	67%	−121%	100%	0.4
	Fully vaccinated	5	0.25	0.02	0.99	75%	1%	98%	0.12
Adjusted									
Whole cohort*	**Unvaccinated**	1195	–						
	Partially vaccinated	13	0.19	0.06	0.58	81%	42%	94%	0.004
	Fully vaccinated	64	0.16	0.09	0.27	84%	73%	91%	<0.001
6 weeks to 10 months**	**Unvaccinated**	222	–						
	Partially vaccinated	6	0.28	0.07	1.15	72%	−15%	93%	0.077
	Fully vaccinated	14	0.27	0.11	0.70	73%	30%	89%	0.007
11 to 23 months **	**Unvaccinated**	522	–						
	Partially vaccinated	3	0.11	0.02	0.71	89%	29%	98%	0.02
	Fully vaccinated	25	0.12	0.06	0.24	88%	76%	94%	<0.001
24 to 59 months **	**Unvaccinated**	451	–						
	Partially vaccinated	4	0.20	0.03	1.46	80%	−46%	97%	0.11
	Fully vaccinated	25	0.16	0.07	0.37	84%	63%	93%	<0.001
RV1***	**Unvaccinated**	1195	–						
	Partially vaccinated	11	0.17	0.05	0.59	83%	41%	95%	0.005
	Fully vaccinated	59	0.15	0.09	0.26	85%	74%	91%	<0.001
RV5***	**Unvaccinated**	1195	–						
	Partially vaccinated	2	0.37	0.02	6.18	63%	−518%	98%	0.5
	Fully vaccinated	5	0.22	0.04	1.29	78%	−29%	96%	0.092

Models adjusted for:
[1] IRR = Incidence Rate Ratio, CI = Confidence Interval, VE = Vaccine Effectiveness.
* age group, child has a chosen paediatrician, municipal development coefficient, year-month.
** child has a chosen paediatrician, municipal development coefficient, year-month.
*** age group, child has a chosen paediatrician, municipal development coefficient, year-month.

RV1 (85%). The VE estimate for RV5 (78%) was imprecise and not statistically significant, reflecting the small number of RV5-vaccinated children and hospitalizations in this group. Therefore, our data do not allow reliable assessment of potential differences in effectiveness between vaccine products. Previous studies from other settings have reported comparable effectiveness of RV1 and RV5, with some observing slightly higher point estimates for RV5 [10,28,30]. Stratified analyses by age group indicated meaningful variation in VEs. Effectiveness was lowest among children aged 6 weeks to 10 months (73% for full vaccination, non-significant for partial), higher in the 11 to 23-month group (88% for full, 89% for partial), and remained high through 24 to 59 months (84% for full, non-significant for partial). These findings are consistent with a 2017 meta-analysis [30], which reported higher VE in children over 12 months of age up to 2 years in low-mortality settings, especially for RV1. While that meta-analysis included only children up to 24 months of age, our study extends this evidence by indicating sustained high VE through 5 years of age. Post-licensure studies in high-income settings have also described shifts in the age distribution of rotavirus hospitalizations in the vaccine era [7,8,28]. In our study, hospitalized children had a median age of approximately 20 months, indicating that severe cases occurred predominantly beyond infancy. Similar changes in age distribution have been described in multi-country analyses in the vaccine era [31]. The sustained VE observed in our cohort supports continued protection beyond infancy. Together, these findings suggest minimal waning of protection during early childhood, an important finding given that most children are infected with rotavirus by this age [4]. Some studies report narrower infant age strata (e.g., 6 weeks–5 months and 6–11 months); however, due to limited numbers of vaccinated events in these subgroups, we used broader age categories. Therefore, direct comparison with studies using narrower

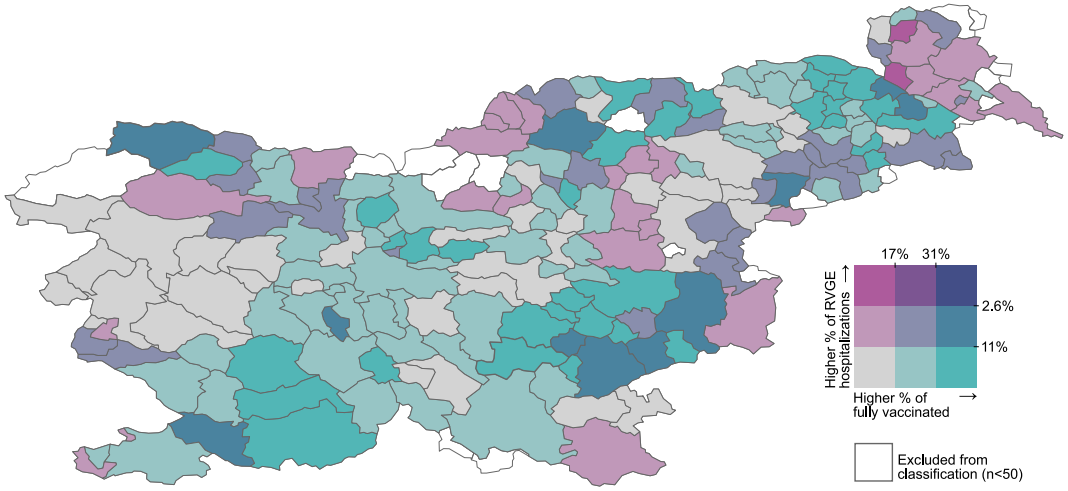

Fig. 2. Correlation between full vaccination coverage and rotavirus-related hospitalization rates, by municipalities, Slovenia, birth cohort 2019. *As shown in the matrix above, darker purple indicates areas with both low vaccination coverage and high hospitalization rate, and teal shades indicate higher vaccination coverage and lower hospitalization rate. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 4
Characteristics of classified municipalities groups on the percentage of fully vaccinated children and the percentage of children hospitalized due to RVGE, median and interquartile range (IQR), Slovenia, birth cohort 2019.

V – H category[1]	n of municipalities ($n = 194$)	% of municipalities	% of fully vaccinated		% hospitalized due to RVGE	
			Median	IQR	Median	IQR
Low V – Low H	37	19%	13	7.5, 15	0.00	0.00, 1.6
Low V – Medium H	26	13%	12	8.0, 14	4.2	3.7, 5.9
Low V – High H	2	1.0%	12	6.7, 17	17	13, 20
Medium V – Low H	56	29%	25	22, 29	0.00	0.00, 1.3
Medium V – Medium H	28	14%	23	21, 25	4.2	3.3, 6.1
High V – Low H	34	17%	37	33, 42	0.00	0.00, 0.54
High V – Medium H	11	5.7%	38	34, 43	4.5	3.1, 5.9
Low V	65	34%	13	7.5, 15		
Medium V	84	43%	24	22, 28		
High V	45	23%	38	33, 42		
Low H	127	65%			0.00	0.00, 1.3
Medium H	65	34%			4.2	3.5, 5.9
High H	2	1.0%			17	13, 20

[1] V = % of fully vaccinated children, H = % of children hospitalized due to rotavirus disease.

infant age strata may be limited.

Partial rotavirus vaccination provides substantial protection against hospitalization, especially in middle age group (11 to 23 months old), aligning with other studies reporting meaningful protection from a single dose or partial vaccination scheme for rotavirus vaccines [10,30,32] in low-mortality settings. This is particularly relevant for sub-populations with lower vaccine acceptance or adherence full vaccination scheme, and highlights the value of initiating vaccination even if full completion is uncertain.

4.3. Spatial patterns and public health implications

Our spatial analysis extends our individual-level findings. Although the negative correlation between the municipal-level vaccination coverage and hospitalization rates was weak ($r = -0.155$), it was statistically significant. There were no municipalities with both high vaccination coverage and high hospitalization rate, which supports the protective effect of vaccination at the population level. Municipalities with low vaccination coverage and moderate-to-high hospitalization rates represent clear targets for strengthened public health vaccination efforts. While a range of factors likely contribute to these patterns, some of the municipalities with low vaccination coverage and higher hospitalization rates also rank lower on the municipal development coefficient and are known to include a higher proportion of vaccine-hesitant populations, such as Roma communities. These contextual differences may partially explain spatial disparities in vaccine uptake and disease outcomes. Together with the individual-level VE results, these findings provide supporting evidence for the inclusion of rotavirus vaccination in the NVP in Slovenia, and highlight the need for locally tailored immunisation strategies that address diverse community needs and barriers. Other factors such as costs-effectiveness and healthcare-related factors should be taken into account before a final decision. We did not observe difference in individual-level VE by municipal development coefficient, indicating consistent vaccine performance across socioeconomic contexts within Slovenia. Although lower rotavirus VE has been reported in low-income compared with high-income countries [30], no such variation was evident within this high-income setting. This may reflect relatively uniform access to healthcare and vaccination services across municipalities in Slovenia.

4.4. Strengths and limitations

The strengths of our study include the use of a national population-based dataset, analysis across multiple age strata, and estimating VE for partially vaccinated children. However, several limitations should be acknowledged. During 2020 and 2021, Slovenia implemented extensive public health and social measures to control SARS-CoV-2 transmission, including temporary closure of childcare facilities and restrictions on

social contacts. These measures also reduced transmission of other communicable diseases, including rotavirus, as reported in several other high-income countries [29]. Most of these restrictions were gradually lifted during 2022 and largely removed by early 2023. Although these interventions altered overall incidence and disrupted typical seasonal patterns, evidence from other settings indicates that rotavirus VE remained stable during the COVID-19 pandemic years [16]. Pandemic-related changes in transmission are therefore unlikely to have substantially biased our VE estimates. Our cohort included five birth cohorts and was weighted toward older children, particularly those aged ≥24 months, which should be considered when interpreting age-specific estimates. Although assignment to a chosen paediatrician is expected for all children within the Slovenian healthcare system, a small proportion in our dataset did not have one recorded. However, because the majority of children had a chosen paediatrician, variability in this proxy measure of healthcare access was limited. As our analysis was based on national registries, not all potential confounding factors could be fully accounted for. Some important variables known from previous studies to be associated with both vaccination uptake and risk of rotavirus disease, such as the number of siblings, daycare attendance, low birth weight, and comorbidities, were not available in our data and could not be controlled for. Our outcome definition was based on hospital discharge coding (ICD-10 A08.0) rather than direct linkage of individual laboratory results. Although concordance with the national surveillance registry was high, differences in outcome definitions across studies, including the use of laboratory-confirmed cases or broader acute gastroenteritis definitions in other studies, may partly explain variation in reported VE estimates. The high agreement between discharge diagnoses and surveillance cases suggests that outcome misclassification in our setting was likely limited. Socioeconomic status and healthcare access were assessed using proxy indicators, which might not accurately capture individual-level circumstances. Information on comorbidities was available only for hospitalized children, however since just one child in our dataset had a recorded comorbidity, this variable was not included in the analysis. Because of this, we were also not able to address the healthy vaccinee effect, where vaccinated children might have been generally healthier than the unvaccinated ones. Additionally, data on rotavirus genotypes were not available, limiting our ability to assess potential strain-specific differences in VE. Lastly, small sample sizes in some subgroups, particularly children vaccinated with RV5 and those partially vaccinated, limited the statistical power and precision of those estimates; therefore, these results should be interpreted with caution.

5. Conclusions

Our study provides real-world evidence that both full and partial rotavirus vaccination substantially reduce rotavirus-related hospitalizations among children in Slovenia. VE remained high across most age groups, with the strongest protection observed during the second year of life and sustained protection up to five years of age, although some subgroup estimates did not reach statistical significance due to limited number of hospitalizations. Although vaccine uptake in Slovenia remains low, our findings indicate that the currently available rotavirus vaccines (RV1 and RV5) are highly effective in preventing severe disease, consistent with evidence from other low-mortality settings. These results support efforts to increase vaccine coverage and, together with country-specific cost-effectiveness analyses, can inform inclusion of rotavirus vaccination in the NVP to reduce disease burden. Beyond national relevance, this study contributes to the broader evidence base on rotavirus vaccine impact, and highlights the importance of closing immunisation gaps to achieve more consistent protection of children worldwide.

CRediT authorship contribution statement

Maja Mrzel: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Conceptualization. **Kostas Danis:** Writing – review & editing, Methodology, Conceptualization. **Veronika Učakar:** Writing – review & editing, Conceptualization.

Disclaimer

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Declaration of competing interest

The 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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2026.128440.

Data availability

The authors do not have permission to share data.

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