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Monovalent rotavirus vaccine effectiveness and long-term impact among children <5 years old in Antananarivo, Madagascar, 2010–2022

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Abstract

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO).

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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.

Background: Monovalent rotavirus vaccine substantially reduced rotavirus disease burden after introduction (May 2014) in Madagascar. We examined the effectiveness and long-term impact on acute watery diarrhea and rotavirus-related hospitalizations among children <5 years old at two hospitals in Antananarivo, Madagascar (2010–2022).

Methods: We used a test-negative case-control design to estimate monovalent rotavirus vaccine effectiveness (VE) against laboratory-confirmed rotavirus hospitalizations among children age 6–23 months with documented vaccination status adjusted for year of symptom onset, rotavirus season, age group, nutritional status, and clinical severity. To evaluate the impact, we expanded to children age 0–59 months with acute watery diarrhea. First, we used admission logbook data to compare the proportion of all hospitalizations attributed to diarrhea in the pre-vaccine (January 2010–December 2013), transition period (January 2014–December 2014), and post-vaccine (January 2015–December 2022) periods. Second, we used active surveillance data (June 2013–May 2022) to describe rotavirus positivity and detected genotypes by vaccine introduction period and surveillance year (1 June–31 May).

Result: Adjusted VE of at least one dose against hospitalization due to rotavirus diarrhea among children age 6–23 months was 61 % (95 % CI: –39 %–89 %). The annual median proportion of hospitalizations attributed to diarrhea declined from 28 % in the pre-vaccine to 10 % in the post-vaccine period. Rotavirus positivity among hospitalized children age 0–59 months with acute watery diarrhea was substantially higher during the pre-vaccine (59 %) than the post-vaccine (23 %) period. In the pre-vaccine period, G3P[8] (76 %) and G2P[4] (12 %) were the dominant genotypes detected. Although genotypes varied by surveillance year, G1P[8] and G2P[4] represented >50 % of the genotypes detected post-introduction.

Conclusions: Rotavirus vaccine has been successfully implemented in Madagascar’s routine childhood immunization program and had a large impact on rotavirus disease burden, supporting continued use of rotavirus vaccines in Madagascar.

Keywords

Rotavirus; Rotavirus vaccine effectiveness; Rotavirus vaccine impact; Rotavirus surveillance; Genotype; Madagascar

1. Introduction

Following the World Health Organization’s 2009 recommendation that all countries introduce rotavirus vaccine [1], Madagascar introduced a two-dose live oral monovalent rotavirus vaccine (Rotarix, GlaxoSmithKline Biologicals, Rixensart, Belgium) into its national childhood immunization program in May 2014 to reduce the substantial diarrheal diseases burden and the financial hardship it imposed on family income [2,3]. An evaluation of the early (2.5 years post-introduction) monovalent rotavirus vaccine impact showed an important reduction in the proportion of hospitalizations due to diarrhea and rotavirus among children <5 years old [3].

A high proportion of low- and middle-income countries including 79 % of countries in Africa have integrated rotavirus vaccines into their national childhood immunization programs [4]. Like other live oral vaccines, rotavirus vaccine performance is lower in

low-income than in wealthier settings [5,6]. Several complex factors including high levels of malnutrition in low-income settings are hypothesized to contribute to this lower performance [6,7]. Madagascar has one of the highest prevalence (40 %) of chronic malnutrition among children <5 years old worldwide [8]. Thus, evaluating rotavirus vaccine effectiveness (VE) and impact in Madagascar will enable us to improve our understanding of rotavirus vaccine performance in settings with high levels of malnutrition.

We estimated the effectiveness of the monovalent rotavirus vaccine on acute diarrhea and rotavirus-associated hospitalizations among children <5 years old of age seeking care at two hospitals in Antananarivo, the capital city of Madagascar, and reexamined its impact with six additional years of post-vaccine introduction data.

2. Methods

2.1. Setting, participants, and data collection

We used data collected at the Centre Hospitalier Universitaire Mère Enfant Tsaralalàna (CHUMET) and Centre Hospitalier Universitaire Joseph Raseta Befelatanana (CHUJRB) to examine the effectiveness of the monovalent rotavirus vaccine introduced in May 2014 and its impact on pediatric rotavirus-associated hospitalizations. CHUMET and CHUJRB are both public pediatric referral hospitals serving patients residing in Antananarivo and throughout the country. CHUMET has conducted rotavirus surveillance as part of the World Health Organization (WHO) Global Rotavirus Surveillance Network since 2013. To ensure a sufficient sample size to assess VE, CHUJRB began active surveillance in 2018.

2.1.1. Active rotavirus surveillance and laboratory methods—At both institutions, we enrolled children age ≤ 59 months admitted with acute watery diarrhea (defined as having ≥ 3 watery stools within 24 h lasting < 7 days) and used a standardized case report form to collect patient demographic, clinical, and socioeconomic information. As part of the VE evaluation, we also collected copies of immunization cards and reviewed vaccine registries to document vaccination status.

To ascertain rotavirus disease status, we collected stool samples within 48 h of admission and tested for rotavirus using a commercial enzyme immunoassay (EIA) (ProSpecT [Thermo Fisher Diagnostics; Oxoid; Basingstoke, UK]). Rotavirus antigen-positive stool samples were stored (-20°C) until they were referred to the rotavirus regional reference laboratory in South Africa (RRL-SA) for confirmation of rotavirus detection and strain characterization. The RRL-SA determined G and P types using a semi-nested multiplex polymerase chain reaction (PCR) method performed with consensus- and genotype-specific primers as described by Gouvea et al. (1990) [9] and Gentsch et al. (1992) [10]. The G and P genotypes were confirmed by sequence analysis, whereby the first-round PCR products (VP4 and VP7 genes) were purified and sequenced using an ABI 3500XL automated sequencer. The sequence data were analyzed with the bioinformatics software packages. The rotavirus 11 genomic segments were separated by polyacrylamide gel electrophoresis (PAGE) with silver staining method to display RNA migration patterns.

2.1.2. Retrospective hospital logbook review—We reviewed hospital admission logbooks from CHUMET for children <5 years of age hospitalized for acute watery diarrhea with or without dehydration from 1 January 2010 to 31 December 2022. Admission logbook data were not available for CHUJRB during the period of the analysis.

2.2. Data analysis

2.2.1. Vaccine effectiveness—We analyzed active surveillance data using a test-negative case-control design to estimate rotavirus VE against laboratory-confirmed rotavirus infections among children age 6–23 months enrolled at CHUMET and CHUJRB from 1 September 2018, when sites began collecting written vaccine records, to 31 December 2022. We included children with rotavirus EIA test results who were age-eligible to receive a rotavirus vaccine (born ≥1 May 2014) and restricted to those with verified vaccination status via a copy of their immunization card or registry or those who were reported never to have received any vaccines. We defined case-patients as children with acute watery diarrhea whose specimens had positive test results for rotavirus and control patients as children with acute watery diarrhea whose specimens had negative test results for rotavirus. We classified children as vaccinated if a dose of rotavirus vaccine was administered at least 14 days before symptom onset. We excluded children who reported being vaccinated against rotavirus but for whom documented vaccination dates were unavailable.

We estimated rotavirus VE as follows: $(1 - \text{adjusted odds ratio of case-patients compared to control-patients for being vaccinated}) \times 100\%$. We used multivariable unconditional logistic regression that modeled the association between rotavirus vaccination status and rotavirus-associated hospitalizations while adjusting for surveillance site, year of symptom onset, rotavirus season (April–July, August–March), age group (6–11 and 12–23 months), nutritional status (stunted and normal height for age), and clinical severity (modified Vesikari Severity Score [MVSS]: 0–10 and 11–20). To examine nutritional status, we used the WHO “anthro” R Package [11] to calculate stunting, an indicator of chronic malnutrition, which is defined as >2 standard deviations below the median height for age [12]. To assess clinical severity of acute watery diarrhea, we used the Vesikari Severity Score [13,14] modified to define levels of dehydration based on symptom information (e.g., lethargy, sunken eyes, and ability to drink properly) according to the World Health Organization’s Integrated Management of Childhood Illnesses dehydration criteria [15]. The other components of MVSS are the maximum number of diarrheal stools and vomiting episodes in 24 h, duration of diarrhea and vomiting in days, maximum recorded temperature, and reception of treatment (oral or intravenous rehydration at the hospital). We categorized the 20 total possible points of the MVSS into two groups: mild (score 0–10) and moderately to very severe (score 11–20) disease. We present overall results and stratified results by age group (6–11 and 12–23 months), nutritional status (stunted and normal height for age), and modified Vesikari score (mild and moderately-very severe).

2.2.2. Impact—To evaluate the impact of the monovalent rotavirus vaccine, we used data collected at CHUMET. First, using the admission logbook data, we compared the number and proportion of all childhood hospitalizations attributable to diarrhea across calendar years and vaccine-introduction periods: pre-vaccine introduction period (1 January 2010–31

December 2013), transition period (1 January 2014–31 December 2014), and post-vaccine introduction period (1 January 2015–31 December 2022). Logbook data were analyzed using calendar years. Second, using active surveillance data, we calculated the proportion of children who tested positive for rotavirus by surveillance year—each surveillance year was defined as 1 June of the earlier calendar year to 31 May of the following calendar year. We referred to the surveillance year by the calendar year in which it started. For example, surveillance year 2013 was from 1 June 2013 through 31 May 2014, and surveillance year 2021 was from 1 June 2021 through 31 May 2022. Additionally, we reported results for all children age <59 months and separately, for those age 0–11, 12–23, and 24–59 months.

2.2.3. Genotypes detected and trends—We described the distribution of genotypes detected over time and by vaccine period among children age 0–59 months enrolled in active rotavirus surveillance (1 June 2013–31 May 2022) at both CHUMET and CHUJRB who tested positive for rotavirus by EIA and their stool samples genotyped at the RLL-SA. We reported the results by vaccine introduction period and surveillance year.

We conducted analyses in R Statistical Software (v4.3.1; R Core Team 2023, Vienna, Austria) [16].

2.3. Ethics statement

The protocol for this evaluation was reviewed and designated as non-research by CHUMET, US Centers for Disease Control and Prevention, and WHO.

3. Results

3.1. Study population: active rotavirus surveillance

We enrolled 2052 children age 0–59 months with AGE through active rotavirus surveillance during 1 June 2013–31 December 2022 (Fig. 1). Of these, 1500 (73 %) had a stool specimen collected within 48 h after hospital admission and were tested for rotavirus using EIA. We show the subset of rotavirus-tested specimens included in the VE, vaccine impact, or genotype distribution analyses in Fig. 1.

3.2. Vaccine effectiveness

Among the 1500 specimens tested for rotavirus from children age 0–59 months with AGE and enrolled at CHUMET and CHUJRB, 401 were from children age 6–23 months who were born on or after vaccine introduction (1 May 2014) and enrolled after sites started documenting vaccination dates (1 September 2018). Of these children, 186 (63 %) were included in the VE analysis because they had documented vaccination dates that were at least 14 days before hospitalization or were unvaccinated. Among the VE analysis eligible children, 34 (18 %) tested positive (case-patients) and 152 (82 %) tested negative (control patients) for rotavirus. Compared to control patients, case-patients were younger (median age: 10 months versus 13 months), had a larger proportion experience severe disease (Vesikari score ≥ 11 : 82 % versus 73 %), and were more likely to be admitted during the April–July months, considered the rotavirus season after vaccine introduction (44 % versus 18 %), but a smaller proportion of case-patients were stunted (32 % versus 48 %) (Table

1). The proportion of case-patients who received at least one dose of rotavirus vaccine was similar to control patients (86 % versus 85 %).

The overall and stratified VE estimates were imprecise (not statistically significant) due to the small sample size (Fig. 2). VE of at least one dose against hospitalization due to rotavirus diarrhea of any severity among children age 6–23 months was 61 % (95 % CI: –39 %–89 %), adjusted for age group, year of admission, rotavirus season, chronic-malnutrition status, and clinical severity. Adjusted VE was 52 % (95 % CI: –271 %–94 %) among children age 6–11 months and 30 % (95 % CI: –249 %–86 %) among children age 12–23 months. Stratified by chronic malnutrition status, adjusted VE was 40 % (95 % CI: –372 %–92 %) among stunted children and 71 % (95 % CI: –55 %–95 %) among children with a normal height-for-age. Adjusted VE was 52 % (95 % CI: –271 %–94 %) and 61 % (95 % CI: –90 %–92 %) among children experiencing mild and moderately-very severe disease, respectively. VE estimates comparing receipt of two doses (complete dose course) and zero doses yielded similar estimates and did not improve precision (95 % CI width).

3.3. Impact

The logbook review identified 35,487 all-cause hospitalizations at CHUMET among children age 0–59 months from 1 January 2010–31 December 2022 and the median number of annual all-cause hospitalizations was 2739 (interquartile range [IQR]:2464–3125) (Fig. 3). The large decreases in all-cause hospitalizations occurred due to closures for renovations in January 2017 and changes in healthcare-seeking behaviors during the COVID-19 pandemic in April–September 2020. In the pre-vaccine period (1 January 2010–31 December 2014), diarrhea hospitalizations represented an annual median of 28 % (IQR: 21–33) of all-cause hospitalizations (Table 2) with two discernable increases in counts each year during April–June and October–November. After rotavirus vaccine introduction, the proportion of diarrhea-associated hospitalizations declined incrementally and remained stable. During the post-vaccine period (1 January 2015–31 December 2022), diarrhea-associated hospitalizations represented an annual median of 10 % (IQR: 8–16) of all-cause hospitalizations. The two annual peaks in diarrhea-associated hospitalizations attenuate overtime.

Among the 1324 children age 0–59 months enrolled in active surveillance at CHUMET with rotavirus results available, 238 (18 %) were enrolled during the pre-vaccine period (1 June 2013–31 May 2014) and 1086 (82 %) during post-vaccine period (1 June 2014–31 May 2022) (Fig. 4). Overall, rotavirus positivity was substantially higher during the pre-vaccine (59 %) than the post-vaccine (23 %) period. After the first full year of rotavirus vaccine implementation, rotavirus positivity decreased from 59 % to 12 % in 2015. Rotavirus positivity remained stable during 2016–2022 (range: 18 %–23 %), but the total number of children enrolled decreased, which paralleled the decrease in the number of all-cause diarrhea-associated hospitalizations observed from the logbook data. Additionally, the percentage of all rotavirus-positive children that were age 0–11 months enrolled in active surveillance was lower in the post-vaccine (51 %) than in the pre-vaccine (66 %) period (Fig. 5B), which also paralleled the shift in the age distribution towards older ages among children hospitalized with all-cause diarrhea (Fig. 5A).

3.4. Genotype distribution

Among the 1500 stools samples tested for rotavirus from children age 0–59 months with AGE and enrolled at CHUMET and CHUJRB, 411 (27 %) were rotavirus positive (Fig. 1). Of these, 293 (71 %) were successfully genotyped. In the pre-vaccine introduction period, G3P[8] (76 %) was the dominant genotype detected followed by G2P[4] (12 %) (Fig. 6). Although the distribution of genotypes detected varied by surveillance year, G1P[8] and G2P[4] accounted for >50 % of the genotypes detected starting in the 2015 surveillance year with a greater and sustained increase in the share of G2P[4]. Most (61 %) genotypes in the ‘Other’ classification group ($n = 59$) were mixed or untypeable.

4. Discussion

The monovalent rotavirus vaccine was 61 % effective against hospitalization due to rotavirus diarrhea among children 6–23 months in the capital of Madagascar. The overall VE and subpopulation VE estimates were similar to those from other African countries and countries with high <5 years old child mortality worldwide [5]. The reasons for lower rotavirus VE in high than low child mortality settings are not well understood, but malnutrition has been found to decrease oral rotavirus vaccine performance in some evaluations [7], which is consistent with our findings. Chronic malnutrition affects nearly half of children both in the Antananarivo region and in our VE study population [8]. The interaction of chronic malnutrition with rotavirus vaccine in such a large proportion of the population may reduce the population-level benefits of rotavirus vaccines.

Despite the lower VE, there was a substantial and sustained impact of the rotavirus vaccine on severe diarrhea over the first eight years after introduction. Diarrhea seasonality was noticeably attenuated after vaccine introduction, though most years had two periods of increased activity around May and October like in the pre-vaccine period. From 2013 to 2019, the proportion of all-cause diarrhea hospitalizations declined from 22 % to 9 %, and rotavirus positivity among hospitalized children age 0–59 months with acute watery diarrhea declined from 59 % to 31 %. These pre-pandemic findings are comparable to other published reports, though published reports from African countries with more than four years of post-vaccine introduction data are limited [17].

While the proportions of hospitalizations due to diarrhea and rotavirus positive specimens during the COVID-19 pandemic (2020–2022) were similar to those immediately before the COVID-19 pandemic, the absolute number of diarrhea hospitalizations was markedly lower in 2020. This suggests non-pharmaceutical interventions (e.g., mandatory use of facemasks, increased emphasis on hand-washing, social distancing, and lockdowns in major cities) against SARS-CoV-2 may have reduced enteric infections in Madagascar, which has been documented for rotavirus and norovirus in other settings [18–22]. However, during the COVID-19 pandemic, rotavirus vaccination coverage decreased from 70 % in 2018 to 53 % in 2022 in Madagascar [23]. Suboptimal rotavirus vaccination may give rise to rotavirus outbreaks as was observed in Botswana or a trend of higher rotavirus activity in alternating years as seen in some countries [22,24,25]. Importantly, this lower vaccine coverage could translate to more severe rotavirus-associated hospitalizations and reduced the population-level benefit of the vaccine. Ongoing rotavirus sentinel surveillance is warranted

to assess the impact of rotavirus vaccine coverage on rotavirus-associated hospitalizations after the COVID-19 pandemic.

We observed changes in the distribution of circulating genotypes in the context of a mature monovalent rotavirus vaccine program. Homotypic and heterotypic strains declined after the introduction of G1P[8] monovalent rotavirus vaccine, suggesting cross protection of the vaccine. G1P[8] remained relatively common after rotavirus vaccine introduction, unlike what has been reported elsewhere [26,27]. This may be due to low vaccine coverage in Madagascar. The G2P[4] genotype was predominant post-vaccine introduction, similar to findings from Europe, Africa, and Australia [26]. In the pre-vaccine introduction period, the G3P[8] was identified as the most prevalent genotype but it disappeared between 2015 and 2022; a similar pattern was observed in the Africa, South East Asia and Western Pacific Regions [26,27]. It is also notable that the proportion of mixed and untypeable genotypes has increased in recent years, although the number of specimens was small; this trend has not been found more widely [28]. These results contribute the global understanding of secular trends in rotavirus genotypes in the post-rotavirus vaccine era.

These estimates of the effectiveness and impact of rotavirus vaccine in Madagascar should be considered alongside several limitations. First, children in this evaluation were enrolled at 2 hospitals in Antananarivo, the capital of Madagascar, and these results may not be generalizable. However, our results are consistent with other countries which is reassuring. Second, vaccine cards were not available for all enrolled children and 39 % were excluded from the VE analysis for lack of vaccine documentation. If the children without cards were significantly different than children with cards, this may have biased our VE results. Similarities between included and excluded children suggest any bias would be minimal, for example the percent of children who tested positive for rotavirus among included (18 %) and exclude (20 %) children was similar. Finally, our sample size for the VE analysis was small, and thus the VE results were imprecise. However, the point estimates were consistent with those found in high childhood mortality settings.

Rotavirus vaccines have been successfully implemented as part of the routine childhood immunization program in Madagascar since 2014. During the first 8 years of use, rotavirus vaccines have had a tremendous impact on rotavirus diarrhea hospitalizations, which are costly and burdensome to families and the healthcare system. Our findings demonstrate these vaccines are effective and highlight several areas for continued monitoring, including genotype composition and rotavirus vaccine performance in a setting with high chronic malnutrition. Finally, rotavirus coverage is suboptimal in Madagascar and increasing coverage is crucial to maximize the population-level benefit from rotavirus vaccines.

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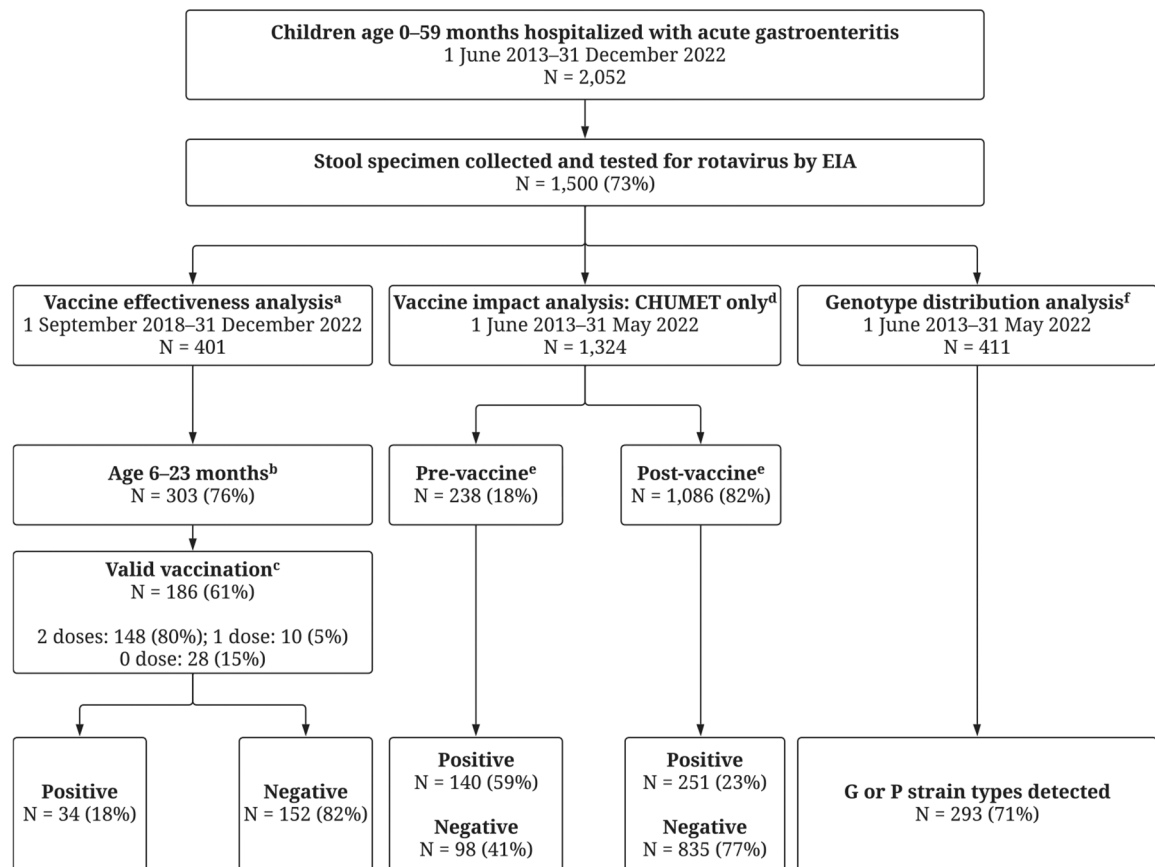
Data availability

Data will be made available on request.

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**Fig. 1.**

Vaccine effectiveness, vaccine impact, and genotype distribution analyses flowchart using active rotavirus surveillance data, Madagascar, 1 June 2013–31 December 2022.

Abbreviations: G, glycoprotein (VP7); P, protease-cleaved protein (VP4).

^a We restricted the vaccine effectiveness (VE) analysis children enrolled at the Centre Hospitalier Universitaire Mère Enfant Tsaralalàna (CHUMET) and Centre Hospitalier Universitaire Joseph Raseta Befelatanana (CHUJRB) from 1 September 2018 (when sites began collecting written vaccine records) to 31 December 2022.

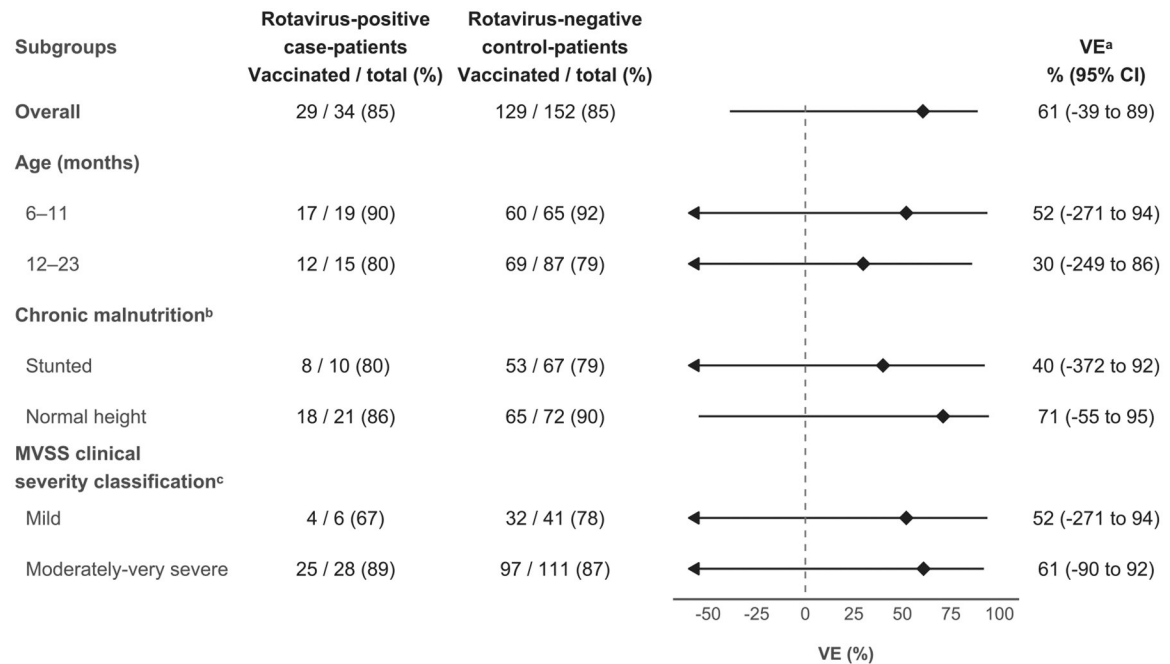
^b We restricted the VE analysis further to children age 6–23 month because rotavirus burden was highest in this age group.

^c We included children who were age-eligible to receive a rotavirus vaccine (born ≥ 1 May 2014) with verified vaccination status via a copy of their immunization card or registry or those who were reported to never have received any vaccines. We classified children as vaccinated if a dose of rotavirus vaccine was administered at least 14 days before symptom onset.

^d We restricted the vaccine impact analysis to data collected at CHUMET, where active surveillance data were available from pre-vaccine and post-vaccine periods.

^e Pre-vaccine introduction period: 1 June 2013–31 May 2014 period; post-vaccine introduction period: 1 June 2014–31 May 2022.

^f The genotype distribution analysis was restricted to rotavirus positive stool specimens with G or P strain detected.

**Fig. 2.**

Monovalent rotavirus vaccine effectiveness (at least one dose) for the prevention of rotavirus-associated hospitalizations among children age 6–23 months, 1 September 2018–31 December 2022.

Abbreviations: AGE, acute gastroenteritis; VE, vaccine effectiveness.

^a VE adjusted for age group (6–11 and 12–23 months), year of admission, rotavirus season (April–July and August–March), Vesikari score (<11 and ≥11) and chronic-malnutrition status (stunting and normal height for age). If the models stratified by one of the adjustment variables, then this variable was excluded from the model. For example, in the age stratified model, we included hospital admission year, rotavirus season, Vesikari score, and chronic-malnutrition status as adjustment variables.

^b Chronic malnutrition was based on stunting defined as >2 standard deviations below the median height for age.

^c Clinical severity classification was based on total modified Vesikari Severity Score (MVSS): mild disease (0–10) and moderately-very severe disease (11–20).

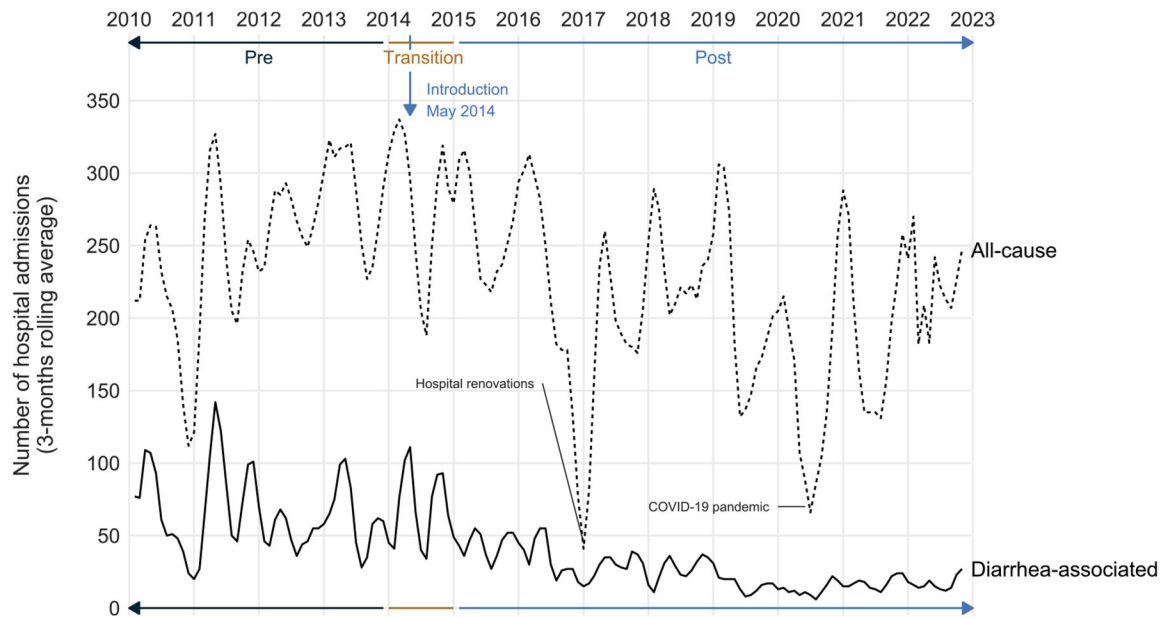


Fig. 3.

Three-month rolling average of the number of all-cause and diarrhea-associated hospitalizations at CHUMET among children age 0–59 months, 1 January 2010–31 December 2022.

Abbreviations: CHUMET, Centre Hospitalier Universitaire Mère Enfant Tsaralalàna.

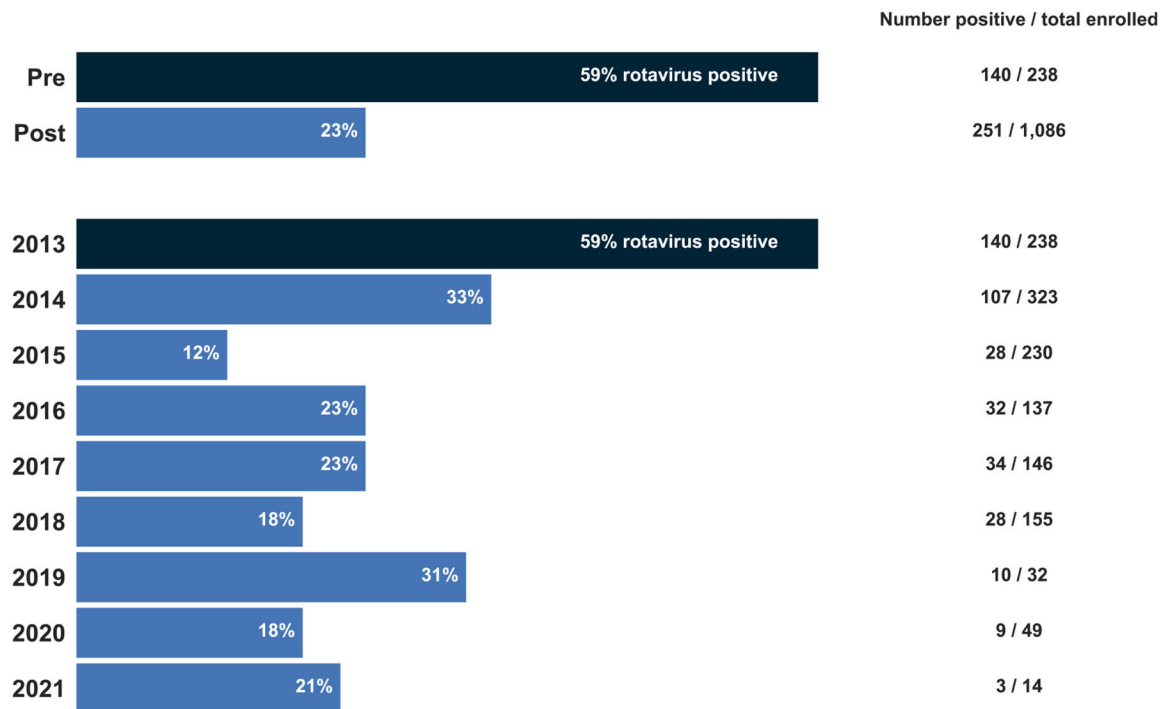


Fig. 4.

Distribution of rotavirus positivity among children age 0–59 months enrolled in active surveillance stratified by vaccine introduction period, CHUMET, 1 June 2013–31 May 2022.^a

Abbreviations: CHUMET, Centre Hospitalier Universitaire Mère Enfant Tsaralalàna.

^a Pre-vaccine introduction period: 1 June 2013–31 May 2014 period; post-vaccine introduction period: 1 June 2014–31 May 2022. Surveillance year: each year ranged 12 months starting on 1 June of an earlier calendar year and ending on 31 May of the following calendar year later year. For example, surveillance year 2013 ranged from 1 June 2013 through 31 May 2014, and surveillance year 2021 ranged from 1 June 2021 through 31 May 2022.

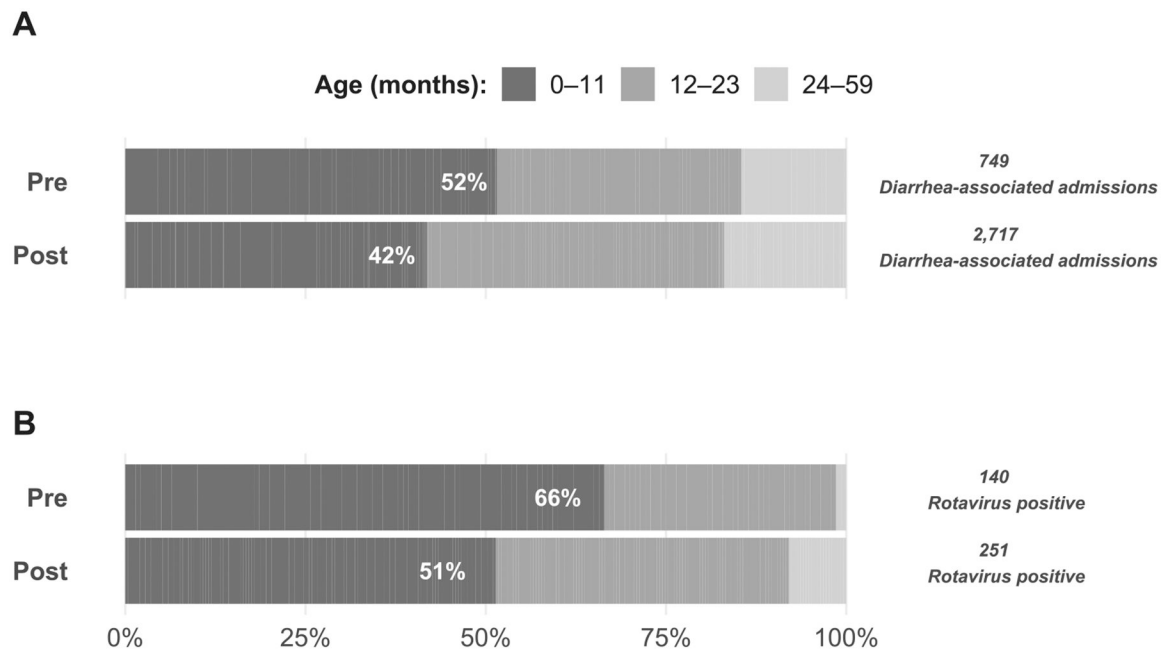
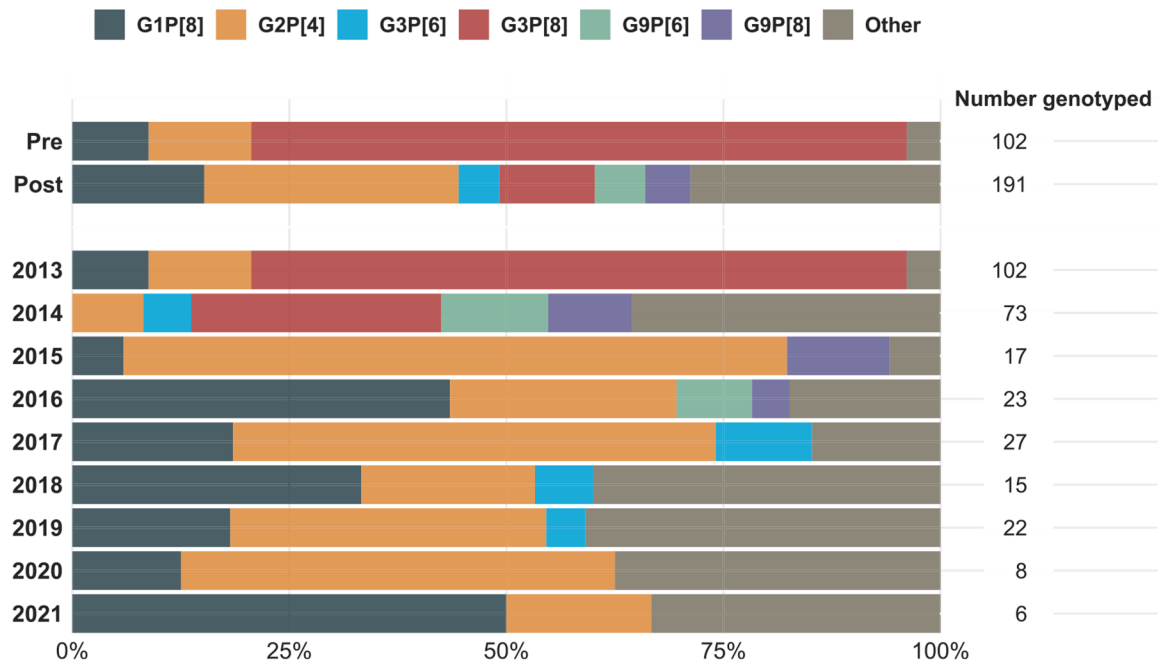


Fig. 5. Age distribution of children age 0–59 months hospitalized with all-cause diarrhea based on logbook data (Panel A) and children enrolled in active surveillance and tested positive for rotavirus (Panel B) stratified by vaccine introduction period, CHUMET, 1 June 2013–31 May 2022^a.

Abbreviations: CHUMET, Centre Hospitalier Universitaire Mère Enfant Tsaralalàna.

^a Pre-vaccine introduction period: 1 January 2010–31 May 2014 period; post-vaccine introduction period: 1 June 2014–31 May 2022.

**Fig. 6.**

Distribution of common rotavirus genotypes among children age 0–59 months enrolled in active surveillance by vaccine introduction period and surveillance year, CHUMET and CHUJRB, 1 June 2013–31 May 2022^a.

Abbreviations: CHUMET, Centre Hospitalier Universitaire Mère Enfant Tsaralalàna.

^a Pre-vaccine introduction period: 1 June 2013–31 May 2014 period; post-vaccine introduction period: 1 June 2014–31 May 2022. Surveillance year: each year ranged 12 months starting on 1 June of an earlier calendar year and ending on 31 May of the following calendar year later year. For example, surveillance year 2013 ranged from 1 June 2013 through 31 May 2014, and surveillance year 2021 ranged from 1 June 2021 through 31 May 2022.

Table 1

Description of participants age 6–23 months included in the rotavirus vaccine effectiveness analysis, 1 September 2018–31 December 2022.

Characteristics ^a	Overall N = 186	Rotavirus-positive case-patients N = 34	Rotavirus-negative control-patients N = 152
Age, months, median (IQR)	12 (8–16)	10 (8–14)	13 (9–16)
Male sex	120 (65)	20 (59)	100 (66)
Chronic malnutrition (stunted) ^b	77 (45)	10 (32)	67 (48)
MVSS moderately-very severe disease ^c	139 (75)	28 (82)	111 (73)
Chronic conditions	11 (6)	3 (9)	8 (5)
Died	8 (4)	0 (0)	8 (5)
Vaccination status			
2 doses	148 (80)	26 (77)	122 (80)
1 dose	10 (5)	3 (9)	7 (5)
0 doses	28 (15)	5 (15)	23 (15)
Maternal age, years, median (IQR)	27 (22–32)	25 (21–32)	27 (23–32)
Maternal education (formal schooling)			
None	8 (4)	2 (3)	6 (4)
Primary	46 (25)	8 (24)	38 (25)
Secondary	65 (35)	9 (27)	56 (37)
Post-secondary	39 (21)	9 (27)	30 (20)
University or above	26 (14)	6 (18)	20 (13)
No. of persons in home, median (IQR)	4 (3–5)	4 (4–5)	4 (3–5)
Socioeconomic parameters			
Electricity in home	164 (88)	31 (91)	133 (88)
Mattress	164 (88)	28 (82)	136 (90)
Car in home	14 (8)	1 (3)	13 (9)
Computer in home	38 (20)	4 (12)	34 (22)
Enrollment hospital			
CHUMET	128 (69)	25 (74)	103 (68)
CHUJRB	58 (31)	9 (27)	49 (32)
Year			
2018	38 (20)	4 (12)	34 (22)
2019	54 (29)	14 (41)	40 (26)
2020	35 (19)	8 (24)	27 (18)
2021	29 (16)	4 (12)	25 (16)
2022	30 (16)	4 (12)	26 (17)
Rotavirus season			
April–July	43 (23)	15 (44)	28 (18)
August–March	143 (77)	19 (56)	124 (82)

Abbreviations: CHUJRB, Centre Hospitalier Universitaire Joseph Raseta Befelatanana; CHUMET, Centre Hospitalier Universitaire Mère Enfant Tsaralalàna; IQR, interquartile range; MVSS, modified Vesikari Severity Score; No., number.

^a N (%) reported unless otherwise noted.

^b Stunted is an indicator of chronic malnutrition, which is defined as >2 standard deviations below the median height for age.

^c Based on the total MVSS: mild disease (0–10) and moderately-very severe disease (11–20).

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Table 2

Number of all-cause hospitalizations and diarrhea-associated hospitalizations by vaccine introduction period and calendar year at CHUMET among children age 0–59 months, 1 January 2010–31 December 2022.

Vaccine Introduction Period ^a	Calendar Year	All-cause hospitalizations	Diarrhea-associated hospitalizations ^b
		N	N (%)
Pre-vaccine	2010	2494	817 (33)
	2011	2925	953 (33)
	2012	3149	614 (19)
Transition	2013	3458	774 (22)
	2014	3395	836 (25)
	2015	3125	534 (17)
Post-vaccine	2016	2696	424 (16)
	2017	2118	352 (17)
	2018	2834	318 (11)
	2019	2464	201 (8)
	2020	1800	152 (8)
	2021	2290	205 (9)
	2022	2739	221 (8)

Abbreviations: CHUMET, Centre Hospitalier Universitaire Mère Enfant Tsaralalàna

^aPre-vaccine introduction period: 1 January 2010–31 December 2013; Transition period: 1 January 2014–31 December 2014, which includes months before and after rotavirus implementation; post-vaccine introduction period: 1 January 2015–31 December 2022.

^bThe percent refers to the proportion of all-cause hospitalizations that were associated with diarrhea multiplied by 100.