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National Trends in Paediatric Acute Gastroenteritis Following Universal Rotavirus Vaccination in Thailand: A Nationwide Database Study

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Abstract

Background

Rotavirus is a major cause of acute gastroenteritis (AGE) in young children. Thailand introduced rotavirus vaccination into its National Immunization Program (NIP) in fiscal year (FY) 2020. Longer-term, nationwide health-system impacts of this programme remain incompletely characterized. This study evaluated national trends in AGE-related healthcare utilisation, mortality, seasonality, healthcare expenditure, and vaccine coverage among children under 5 years following rotavirus vaccine introduction in Thailand.

Methods

We conducted a nationwide population-based ecological study using administrative healthcare data from Thailand's National Health Security Office (NHSO), FY2017–FY2024. AGE was identified using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Thai Modification (ICD-10-TM). FY2020 was excluded as a transition year; pre-NIP (FY2017–FY2019) and post-NIP (FY2021–FY2024) periods were compared. Outcomes included outpatient visit and hospitalization rates, mortality, monthly seasonal case distribution, vaccine coverage, and healthcare expenditure.

Results

The study included a total of 2,116,494 outpatient visits, 621,437 hospitalizations, and 188 AGE-related deaths. First-dose rotavirus vaccine coverage increased from 84.0% in FY2020 to 97.2% to FY2024. After expanding the NIP, outpatient visits declined from 12.84 to 8.29 per 100 person-years (IRR 0.646, 95% CI 0.644–0.647; −35.4%), and hospitalizations declined from 3.37 to 2.79 per 1,000 person-years (IRR 0.828, 95% CI 0.824–0.832; −17.2%). Mortality decreased from 1.08 to 0.79 per 100,000 person-years (IRR 0.75, 95% CI 0.54–0.98; −27%). A cool-season peak persisted post-NIP but with markedly attenuated case volumes. Mean annual inpatient expenditure decreased by THB 53.3 million (USD 1.61 million), with an estimated 37,160 admissions averted and total cost savings of THB 295.6 million (USD 8.91 million) post-NIP.

Conclusions

Rotavirus vaccine introduction into Thailand's NIP was temporally associated with sustained reductions in AGE-related outpatient visits, hospitalizations, and mortality, alongside attenuated seasonal peaks and substantial cost savings. Given the ecological design, these findings may reflect population-level health-

system impact. Sustaining high vaccination coverage should be promoted to maximize long-term benefits.

Background

Acute gastroenteritis (AGE) remains a major cause of morbidity and healthcare utilisation among children younger than 5 years of age, contributing substantially to outpatient visits, hospitalizations, and mortality worldwide. In Thailand, acute diarrhoeal disease has likewise represented an important burden on the national healthcare system, particularly among young children [1,2]. Rotavirus is a major cause of severe gastroenteritis during early childhood and has been an important target of childhood vaccination programmes. Rotavirus has also accounted for a substantial proportion of diarrhoeal morbidity and mortality among children younger than 5 years globally, providing an important epidemiological rationale for routine vaccination[3]

The introduction of rotavirus vaccines into national immunization programmes has therefore provided an opportunity not only to reduce rotavirus-specific disease but also to reduce the broader healthcare burden associated with childhood gastroenteritis. Accumulating post-licensure evidence has demonstrated substantial population-level benefits following rotavirus vaccine introduction. A global review of 105 studies from 49 countries reported median reductions of 59% in rotavirus hospitalizations, 36% in acute gastroenteritis hospitalizations, and 36% in AGE mortality among children younger than 5 years after vaccine introduction, with larger reductions generally observed among younger children and in settings with higher vaccine coverage[4]. A separate systematic review and meta-analysis of observational studies likewise found substantial population-level effectiveness of both monovalent and pentavalent rotavirus vaccines against healthcare attendances for rotavirus gastroenteritis and acute gastroenteritis, supporting the consistency of post-licensure effects across healthcare settings[5] In addition, data from the WHO-coordinated Global Rotavirus Surveillance Network demonstrated sustained reductions in rotavirus detection among children hospitalized with acute diarrhoea following vaccine introduction, supporting the broader population-level effect of vaccination on severe gastroenteritis[6]. These findings indicate that the impact of rotavirus vaccination may extend beyond prevention of laboratory-confirmed rotavirus infection to reductions in healthcare utilisation for AGE at the population level.

Thailand incorporated rotavirus vaccination into the National Immunization Program (NIP) in fiscal year (FY) 2020.Our previous nationwide analysis using National Health Security Office (NHSO) data demonstrated a reduction in acute diarrhoeal healthcare utilisation during the first year of universal implementation of rotavirus vaccination[7]. However, that study primarily evaluated the early period following programme introduction and therefore could not determine whether the observed changes were sustained over subsequent years or characterize the broader health-system consequences of vaccination. More recent national studies have provided further evidence regarding the burden and

epidemiology of childhood diarrhoeal disease in Thailand following the introduction of rotavirus vaccination[8,9].

Despite increasing evidence of the benefits of rotavirus vaccination, the longer-term health-system consequences of national implementation in Thailand remain incompletely characterized. Previous studies have largely focused on disease incidence, diarrhoeal episodes, or hospitalization. Less is known about how the introduction of rotavirus vaccination has affected the distribution of healthcare utilisation between outpatient and inpatient settings, seasonal patterns of AGE, hospitalization duration, mortality, and healthcare expenditure within a common national healthcare database. In particular, the admission-to-outpatient ratio may provide complementary information on changes in the composition of healthcare utilisation when outpatient and inpatient encounters do not decline proportionally, although this measure should be interpreted as a population-level healthcare-utilisation indicator rather than a direct measure of clinical severity. The economic consequences are also relevant to national immunization policy. Previous modelling studies in Thailand have suggested that rotavirus vaccination can reduce government healthcare expenditure and may be economically favourable under specified assumptions[10].However, model-based estimates do not directly describe the expenditure changes observed after implementation of a national programme.

Routinely collected NHSO reimbursement data provide an opportunity to quantify real-world changes in inpatient healthcare expenditure and to estimate direct medical costs associated with hospitalizations potentially averted following vaccine introduction. Such information may complement conventional measures of vaccine impact by demonstrating consequences for healthcare resource utilisation. Unfortunately, rotavirus infection cannot be reliably identified from routine administrative healthcare data alone. Although International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Thai Modification (ICD-10-TM) contains codes for rotavirus gastroenteritis, laboratory confirmation is not routinely available across all healthcare settings in the NHSO database. Therefore, the present study is designed to evaluate population-level changes in AGE-related healthcare utilisation temporally associated with rotavirus vaccine introduction, rather than to estimate individual-level rotavirus vaccine effectiveness. We aimed to provide a comprehensive assessment of the longer-term population-level changes in AGE-related healthcare burden and healthcare-resource utilisation following national rotavirus vaccine implementation in Thailand.

Methods

We conducted a nationwide population-based ecological study using routinely collected administrative healthcare data to evaluate changes in healthcare utilisation following the introduction of rotavirus vaccine into Thailand's NIP. The study evaluated outpatient visits, hospitalizations, mortality, age distribution, healthcare severity, length of stay (LOS), healthcare expenditure, estimated direct medical cost savings, and rotavirus vaccine coverage among children younger than 5 years.

Data were obtained from the NHSO, Thailand's largest administrative healthcare database, which includes nationwide outpatient claims, inpatient discharge records, mortality data, healthcare reimbursement information, and childhood immunization records[1].The database is derived from the Universal Coverage Scheme (UCS), the largest public health insurance scheme in Thailand, which provides healthcare coverage to more than 47 million people, representing approximately three-quarters of the Thai population[11]. Administrative data from FY 2017–2024 were analyzed.

Rotavirus vaccine was introduced into the Thai National Immunization Program in FY2020. Because FY2020 represented both the initial phase of nationwide vaccine implementation, it was considered a transition year and excluded from comparative analyses evaluating vaccine-associated changes. Accordingly, healthcare outcomes during the pre-NIP period (FY2017–FY2019) were compared with those during the post-NIP period (FY2021–FY2024). Vaccine coverage analyses included FY2020 because it represented the first year of nationwide implementation.

AGE was identified using the ICD-10-TM codes A08 (viral and other specified intestinal infections) and A09 (other gastroenteritis and colitis of infectious and unspecified origin). Although ICD-10-TM includes a specific diagnostic code for rotavirus gastroenteritis, rotavirus-specific coding and laboratory confirmation are not routinely available across all healthcare settings in the NHSO database. Consequently, a syndromic case definition based on ICD-10-TM codes A08 and A09 was adopted to evaluate population-level changes in AGE following rotavirus vaccine introduction. This approach was supported by our previous nationwide burden-of-disease study, which demonstrated that these two diagnostic categories accounted for more than 90% of diarrheal-related hospitalizations and deaths among Thai children younger than five years[2]. To improve specificity, diarrheal diseases with distinct etiologies, including cholera (A00), typhoid and paratyphoid fever (A01), Salmonella infections (A02), shigellosis (A03), other bacterial intestinal infections (A04), bacterial foodborne intoxications (A05), amoebiasis (A06), and other protozoal intestinal diseases (A07), were excluded from the primary analyses.

The primary outcomes were outpatient visit rates, hospitalization rates, and mortality rates attributable to AGE. Outpatient visit rates were expressed per 100 person-years, hospitalization rates per 1,000 person-years, and mortality rates per 100,000 person-years. Secondary outcomes included age-specific healthcare utilisation, median age at hospital admission, seasonal variation, admission-to-outpatient (IPD/OPD) ratio, prolonged hospitalization, healthcare expenditure, estimated direct medical cost savings, and rotavirus vaccine coverage. The admission-to-outpatient ratio was calculated by dividing the annual number of AGE hospital admissions by the corresponding number of AGE outpatient visits and was used as a population-level indicator of healthcare utilisation patterns across inpatient and outpatient settings. LOS was calculated as the interval between hospital admission and discharge. Prolonged hospitalization was defined a priori as LOS > 3 days, and the proportion of prolonged admissions was compared between the pre- and post-NIP periods.

Economic outcomes included annual inpatient healthcare expenditure, estimated direct medical cost savings attributable to reduced hospital admissions following vaccine introduction, and cost savings per averted admission. Healthcare expenditure was obtained from inpatient reimbursement records in the NHSO database. Mean annual inpatient expenditure was calculated separately for the pre-NIP and post-NIP periods. The number of averted admissions was estimated as the difference between the expected number of admissions, based on the mean annual admissions during the pre-NIP period, and the observed number during the post-NIP period. Estimated direct medical cost savings were calculated by multiplying the number of averted admissions by the mean inpatient reimbursement per admission. Healthcare expenditure and cost savings are presented in Thai baht (THB) and United States dollars (USD), using the average exchange rate during manuscript preparation (1 USD = 33.16 THB).

Age-specific analyses were performed for five predefined age groups: 0–12 months, > 1–2 years, > 2–3 years, > 3–4 years, and > 4–5 years. Seasonal variation was assessed descriptively using monthly outpatient visits, hospitalizations, and mortality aggregated by calendar month. Seasonal patterns before and after vaccine introduction were compared by examining changes in peak magnitude, timing, and overall seasonal distribution, excluding FY2020. Rotavirus vaccine coverage was assessed using the NHSO immunization database.

Vaccine uptake was estimated using infants receiving the first dose of diphtheria–tetanus–whole-cell pertussis–hepatitis B–*Haemophilus influenzae* type b (DTwP-HB-Hib) vaccine as the denominator because rotavirus vaccine is administered during the same routine immunization visits. In routine practice, Rotarix (RV1) was administered concomitantly with DTwP-HB-Hib at 2 and 4 months of age, whereas RotaTeq (RV5) was administered at 2, 4, and 6 months. The first dose of rotavirus vaccine was required to be administered before 15 weeks of age, with completion of the vaccination schedule before 8 months of age. Uptake was defined as receipt of the first dose of either RV1 or RV5 among infants receiving the first DTwP-HB-Hib dose. Completion of the vaccination schedule was assessed separately for RV1 (second dose) and RV5 (third dose) using the corresponding scheduled DTwP-HB-Hib visits as denominators. Completed dose of vaccination was defined as completion of the recommended schedule for either vaccine. Vaccine dropout was defined as the proportion of children who received the first dose but did not complete the recommended vaccine schedule. Because individual-level linkage between vaccine doses was unavailable, these estimates represent repeated cross-sectional administrative coverage rather than true longitudinal cohort-based coverage.

Comparisons between the pre-NIP and post-NIP periods were performed using incidence rate ratios (IRRs) with corresponding 95% confidence intervals (CIs). Vaccine-associated reductions were calculated as (1 − IRR) × 100%. Temporal trends in outpatient visit rates, hospitalization rates, and mortality rates were evaluated using Poisson, negative binomial, or joinpoint regression as appropriate. They were summarized as Average Annual Percent Change (AAPC) with corresponding 95% CIs. All analyses were performed using the Stata version 15.1 (StataCorp LLC, College Station, TX, USA) or Joinpoint Regression Program (National Cancer Institute, Bethesda, MD, USA)[12]. All statistical tests were two-sided, and p values < 0.05 were considered statistically significant.

The study was approved by the Center for Ethics in Human Research, Khon Kaen University (approval no. HE681223). The requirement for informed consent was waived by the ethics committee because the study used routinely collected, de-identified administrative data and involved no direct contact with participants.

Results

Overall healthcare utilisation

A total of 2,116,494 outpatient visits, 621,437 hospital admissions, and 188 diarrheal-related deaths with a primary diagnosis of acute gastroenteritis (ICD-10-TM A08–A09) among children aged < 5 years were identified during FY2017–FY2024. Overall healthcare utilisation declined following introduction of rotavirus vaccine into Thailand's NIP, while the characteristic seasonal pattern of AGE remained evident throughout the study period.

Outpatient visits

The outpatient visit rate decreased from 12.84 per 100 person-years during the pre-NIP period to 8.29 per 100 person-years during the post-NIP period, corresponding to an IRR of 0.646 (95% CI 0.644–0.647; $p < 0.001$), representing a 35.4% reduction in outpatient healthcare utilisation following vaccine introduction (Table 1 and Fig. 1).

Table 1
Comparison of rotavirus-associated healthcare utilisation and outcomes before and after National Immunization Programme (NIP) introduction

Type of impact	Pre-NIP (FY2017–2019)	Post-NIP (FY2021–2024)	Statistical values
OPD visit rate (per 1,000 population)	12.84	8.29	IRR 0.646 (95% CI 0.644–0.647; p < 0.001)
Hospitalization rate (per 1,000 population)	3.37	2.79	IRR 0.828 (95% CI 0.824–0.832; p < 0.001)
Mortality rate (per 100,000 person-years)	1.08	0.79	IRR 0.75 (95% CI 0.54–0.98; p = 0.029)
IPD/ OPD ratio (mean (SD))	0.27 (0.017)	0.33 (0.036)	Mean difference − 0.0627 (95% CI − 0.0641 to − 0.0613; p < 0.001)
LOS > 3 days (%)	*38.0*	*37.6*	Risk difference − 0.5% (95% CI − 0.7% to − 0.2%; p < 0.001)
Age distribution; (years); median (IQR)	1.06 (0.78, 1.34)	1.02 (0.75, 1.32)	Median difference 0.033 years, 95% CI 0.028–0.037; p < 0.001
Healthcare expenditure (million USD)	7.01	5.40	-

NIP = National Immunization Programme; IPD/OPD = inpatient department/outpatient department; IQR = interquartile range; IRR = incidence rate ratio; LOS = length of stay; SD = standard deviation; USD = United States dollar.

There was no statistically significant long-term secular trend (AAPC − 2.29%, 95% CI − 14.31 to 6.13; p = 0.432). Monthly outpatient visits demonstrated a persistent bimodal seasonal pattern, characterized by a major peak during the cooler months and a smaller peak later in the year. Following vaccine introduction, both seasonal peaks were attenuated, with the later annual peak occurring approximately 1–2 months later than during the pre-vaccination period. During FY2020, seasonal variation became markedly flattened, consistent with the concurrent effects of the COVID-19 pandemic (Fig. 2).

Outpatient visit rates declined across all age groups. The largest proportional reduction occurred among children aged > 2–3 years (IRR 0.621, 95% CI 0.617–0.625), whereas the smallest reduction was observed among those aged > 4–5 years (IRR 0.728, 95% CI 0.722–0.734). Infants and young toddlers continued to experience the highest outpatient visit rates throughout the study period (Fig. 1).

Hospitalizations

The hospitalization rate decreased from 3.37 to 2.79 admissions per 1,000 person-years, corresponding to an IRR of 0.828 (95% CI 0.824–0.832; p < 0.001), representing a 17.2% reduction following implementation of the NIP (Table 1 and Fig. 3). No significant long-term temporal trend was detected (AAPC 2.83%, 95% CI − 12.01 to 15.85; p = 0.761). Hospital admissions also exhibited a bimodal

seasonal distribution before vaccine introduction. Following implementation of the vaccination program, both seasonal peaks declined substantially, particularly the later annual peak, which became smaller and occurred approximately 1–2 months later (Fig. 2). Seasonal variation was similarly attenuated during FY2020. Hospitalization rates remained highest among infants. Although point estimates suggested reductions in children younger than two years, age-specific comparisons did not reach statistical significance because of wide confidence intervals. No statistically significant differences were observed among older age groups (Fig. 3).

Healthcare severity

The admission-to-outpatient (IPD/OPD) ratio increased progressively from 0.25 in FY2017 to 0.35 in FY2024. When study periods were compared, the mean (standard deviation (SD)) admission-to-outpatient ratio increased from 0.27 (0.017) during FY2017–FY2019 to 0.33 (0.036) during FY2021–FY2024 (difference − 0.0627, 95%CI -0.0641 to -0.0613; $p < 0.001$) (Table 1). This finding indicates that outpatient visits declined proportionally more than hospitalizations, resulting in a greater proportion of children requiring inpatient care among all healthcare encounters for AGE.

Length of stay

The proportion of prolonged hospitalizations (LOS > 3 days) remained similar between the pre-NIP and post-NIP periods (38.0% vs 37.6%). Although the difference was statistically significant because of the large sample size (risk difference − 0.5%, 95% CI − 0.7% to − 0.2%; $p < 0.001$), the absolute difference was small (Table 1).

Age distribution

The age distribution of hospitalized children remained stable throughout the study period. The pooled median age at admission was 1.04 years (interquartile range (IQR) 0.78–1.34). Median age decreased slightly from 1.06 years (IQR 0.78–1.34) during FY2017–FY2019 to 1.02 years (IQR 0.75–1.32) during FY2021–FY2024 (median difference 0.033 years, 95% CI 0.028–0.037; $p < 0.001$) (Table 1). Although the difference reached statistical significance, the absolute change was minimal (0.033 years) and is unlikely to represent a clinically meaningful shift in the age distribution of hospitalized children.

Mortality

Mortality rates declined from 1.08 to 0.79 deaths per 100,000 person-years between the pre- and post-NIP periods, representing an overall reduction of approximately 27% (IRR 0.75, 95% CI 0.54–0.98; p 0.029) (Table 1 and Fig. 4). The overall trend was downward (AAPC − 4.45%, 95% CI − 16.51 to 7.02), although annual changes were not statistically significant. Age-specific mortality was concentrated among infants aged 0–12 months, whereas deaths in older age groups were uncommon throughout the study period (Fig. 4).

Rotavirus vaccine coverage

Administrative immunization data demonstrated progressive improvement in rotavirus vaccine uptake following introduction into the NIP. First-dose uptake increased from 84.0% in FY2020 to 97.2% in FY2024. Completion of the two-dose RV1 schedule improved from 61.2% to 92.9%, whereas completion of the three-dose RV5 schedule remained lower and more variable, ranging from 5.5% in FY2020 to 9.5% in FY2024, with a transient increase observed in FY2022. RV1 dropout declined substantially following vaccine introduction, whereas RV5 dropout showed greater year-to-year variability. Overall, the findings indicate progressive improvement in rotavirus vaccine uptake and completion following implementation of the NIP.

Economic outcomes (Supplementary Table 1).

Mean annual inpatient healthcare expenditure decreased from THB 232.5 million (USD 7.01 million) during the pre-NIP period to THB 179.2 million (USD 5.40 million) during the post-NIP period, representing a mean annual reduction of THB 53.3 million (USD 1.61 million) (Table 1). Compared with the expected number of hospital admissions based on the pre-NIP period, an estimated 37,160 admissions were averted during FY2021–FY2024, corresponding to total direct medical cost savings of THB 295.6 million (USD 8.91 million). The estimated direct medical cost saving per averted admission was THB 2,088 (USD 62.97).

Discussion

In this nationwide population-based ecological study, introduction of rotavirus vaccination into Thailand's NIP was temporally associated with a substantial reduction in healthcare utilisation for AGE among children younger than 5 years. Our findings demonstrate that rotavirus vaccine introduction was associated with substantial reductions in inpatient healthcare utilisation and generated meaningful cost savings for Thailand's publicly funded healthcare system, despite relatively modest reductions in hospitalization rates.

Our earlier NHSO analysis demonstrated an early reduction in diarrhoeal healthcare utilisation following the introduction of rotavirus vaccination, whereas the present study extends the observation period to four complete post-NIP fiscal years and evaluates a broader range of health-system outcomes[7].Two recently published national studies also provide similar perspective. Sailuenarm et al. reported a substantial reduction in acute diarrhoeal disease using Thailand's Health Data Centre (HDC), whereas Srisaeng et al. characterized the national burden and temporal trends of diarrhoeal hospitalizations using the NHSO inpatient claims database[8,9]. Together, these studies provide complementary national evidence of changes in childhood diarrhoeal disease and healthcare utilisation following the introduction of rotavirus vaccination in Thailand. The present findings should, however, be interpreted according to the clinical outcomes and case definitions used by each study. In the present study, A08–A09 was used to identify AGE as a syndromic outcome in the absence of laboratory-confirmed rotavirus testing. In contrast, Sailuenarm et al. used a broader case definition of acute diarrhoeal disease based on ICD-10-TM codes A00–A09 and K56.1, thereby encompassing a wider spectrum of intestinal infectious

diseases and related gastrointestinal conditions[8]. The two studies therefore address related but non-identical disease outcomes. Because the present study did not require laboratory confirmation of rotavirus infection, the observed reductions should be interpreted as population-level changes in AGE-related healthcare utilisation following vaccine introduction, rather than as estimates of individual-level rotavirus vaccine effectiveness. This distinction is important when comparing effect estimates across studies with different case definitions and levels of diagnostic specificity. The WHO Global Rotavirus Surveillance Network similarly relies on laboratory confirmation to identify rotavirus infection among children hospitalized with acute gastroenteritis, because clinical presentation alone cannot reliably establish rotavirus aetiology[6]. Within Thailand, the magnitude of the reduction observed in the present NHSO analysis should be interpreted alongside, rather than directly compared with, estimates derived from the HDC. Differences between the estimates may reflect differences in case definitions, population coverage, healthcare settings, data-generation processes, and denominators, as well as differences in the populations and healthcare systems captured by these databases. Accordingly, some variation in the magnitude of estimates between the two data sources would be expected. Rather than requiring numerical agreement, the broadly consistent direction of change across these independent national data systems provides complementary evidence of a population-level reduction in childhood diarrhoeal disease and healthcare utilisation following vaccine introduction.[8,9].

The overall pattern is also compatible with international post-licensure evidence. A global review of 105 studies from 49 countries reported median reductions of 59% in rotavirus hospitalizations, 36% in AGE hospitalizations, and 36% in AGE mortality following vaccine introduction, with larger reductions generally observed among younger children and in settings with higher vaccine coverage[4]. These findings are also consistent with earlier post-licensure systematic evidence showing substantial effectiveness of rotavirus vaccination against healthcare utilisation for rotavirus gastroenteritis and AGE[5]. A systematic review and meta-analysis similarly demonstrated substantial protection against rotavirus gastroenteritis following vaccination[13]. Importantly, these studies primarily evaluated laboratory-confirmed or clinically defined rotavirus-associated outcomes, whereas the present study evaluates a broader syndromic AGE outcome. Therefore, these international estimates provide epidemiological and biological context for our findings rather than direct benchmarks against which the magnitude of the present effect should be compared.

The consistency in the overall direction of effect across different settings and study designs nevertheless supports the biological plausibility of the population-level changes observed in Thailand. Population-level benefits may also include indirect protection arising from reduced transmission within the community, although the present ecological design cannot distinguish direct from indirect effects[14]. Taken together, the findings indicate that the introduction of rotavirus vaccination was accompanied by a broad reduction in AGE-related healthcare burden in Thailand. Although the ecological design and syndromic outcome definition preclude inference of individual-level vaccine effectiveness or attribution of all observed changes specifically to rotavirus prevention, the convergence of evidence across healthcare outcomes and independent national data systems supports a meaningful population-level

association. These findings support continued rotavirus vaccination and efforts to sustain high and timely vaccine coverage to maximize reductions in childhood gastroenteritis and associated healthcare utilisation.

The largest relative reduction observed in the present study occurred in outpatient healthcare utilisation. This finding is clinically plausible because rotavirus vaccination can prevent medically attended illness across the spectrum of disease severity, including mild and moderate disease that does not require hospitalization. In the Medically Attended Acute Gastroenteritis (MAAGE) study, rotavirus vaccination demonstrated approximately 70% effectiveness against laboratory-confirmed medically attended rotavirus gastroenteritis, and most children in the vaccine-effectiveness analysis had illness managed in ambulatory settings. Thus, the effect of rotavirus vaccination is not restricted to prevention of severe disease requiring admission[15].

The magnitude of the outpatient reduction in the present study should nevertheless not be interpreted as rotavirus-specific vaccine effectiveness. Outpatient AGE represents a heterogeneous clinical syndrome caused by multiple pathogens, while the vaccine targets rotavirus infection. The observed population-level reduction therefore reflects the combined effects of rotavirus prevention and the epidemiological consequences of vaccination at the population level, rather than prevention of every outpatient AGE episode.

The outpatient findings also provide an important extension of previous Thai evidence. Our earlier NHSO study demonstrated a reduction in diarrhoeal outpatient utilisation during the first year of nationwide implementation[7]. The present analysis demonstrates that the reduction was sustained over a longer post-implementation period and occurred alongside reductions in hospitalization and other health-system outcomes. The recently reported HDC analysis provides a complementary national observation, although its broader acute diarrhoeal disease definition and different data infrastructure mean that its numerical estimates should not be directly compared with those of the present study[8].

The greater relative reduction in outpatient utilisation than hospitalization is also clinically plausible. Outpatient healthcare encompasses a large number of less severe episodes, whereas hospitalization represents a selected subgroup influenced by dehydration, comorbidity, pathogen characteristics, referral practices, and admission thresholds. Consequently, population-level vaccination may produce a larger proportional effect on ambulatory healthcare demand than on the residual pool of children who require inpatient management.

Consequently, the substantial reduction in outpatient utilisation suggests that rotavirus vaccination may reduce the volume of AGE-related ambulatory care, with potential implications for primary-care workload and healthcare resource allocation.

The reduction in hospitalization observed after implementation of the NIP provides complementary evidence that the population-level impact of rotavirus vaccination extends beyond ambulatory disease. Global post-licensure evidence has consistently demonstrated reductions in both rotavirus-specific and

broader AGE hospitalizations after vaccine introduction. Burnett et al. reported a median 36% reduction in AGE hospitalization among children younger than 5 years across 49 countries, while reductions were greater for rotavirus-specific hospitalization[4].

The smaller reduction in hospitalization compared with outpatient utilisation is epidemiologically plausible. Hospitalized children represent a clinically selected population in whom disease severity is influenced by factors beyond rotavirus infection, including other enteric pathogens, dehydration, nutritional status, comorbidities, and healthcare referral patterns. Because the present study evaluates AGE as a clinical syndrome rather than laboratory-confirmed rotavirus disease, the population-level effect is expected to be attenuated by illnesses that are not directly preventable by rotavirus vaccination.

WHO surveillance provides important context for this interpretation. The WHO-coordinated Global Rotavirus Surveillance Network has demonstrated sustained reductions in the proportion of hospitalized AGE attributable to rotavirus following vaccine introduction. In a global analysis covering 69 countries, rotavirus detection among children hospitalized with AGE declined substantially after vaccine introduction, with effects sustained over several years[6].These findings demonstrate that vaccination can substantially alter the aetiological composition of hospitalized gastroenteritis, even when gastrointestinal hospitalization as a broader syndrome remains.

The seasonal pattern of AGE persisted after introduction of rotavirus vaccination but became less pronounced, particularly during the later annual peak. This finding is consistent with an attenuation of epidemic intensity rather than elimination of seasonal transmission. Rotavirus epidemiology varies geographically, with year-round transmission and seasonal peaks occurring in different settings. Global analyses have demonstrated substantial geographic variation in rotavirus seasonality, with patterns ranging from relatively year-round transmission in tropical settings to more pronounced seasonal peaks in temperate regions[16]. WHO notes that tropical and low-income settings may experience intense transmission against a background of more continuous circulation, whereas more pronounced seasonal patterns are typically observed in temperate settings[17].[8] Seasonal variation in childhood diarrhoeal disease is also influenced by the circulation of multiple enteric pathogens, and the magnitude and timing of seasonal peaks may differ between pathogens and geographic settings[18]. The attenuation of seasonal activity is biologically plausible because vaccination reduces the susceptible population and can decrease the intensity of transmission within successive birth cohorts. Global surveillance has demonstrated substantial reductions in rotavirus-associated hospitalized AGE following vaccine introduction, supporting the potential for vaccination to modify the epidemiological pattern of disease at the population level[6].

However, the seasonal pattern observed in this study represents AGE rather than rotavirus-specific transmission. Other viral and bacterial enteric pathogens contribute to the seasonal burden of gastroenteritis, and therefore persistence of seasonal activity after vaccination is expected. The absence of complete elimination of seasonality should not be interpreted as evidence of limited vaccine impact.

Interpretation of the transition period also requires caution because the COVID-19 pandemic substantially altered patterns of infectious disease transmission and healthcare utilisation. Excluding FY2020 from the primary pre–post analysis reduces the influence of the most disruptive transition year, although residual changes in healthcare-seeking behaviour and infectious disease epidemiology may have persisted into subsequent years. From a public-health perspective, attenuation of seasonal AGE peaks may reduce periodic surges in pediatric healthcare demand and facilitate more predictable allocation of outpatient and inpatient resources.

However, the increase in the admission-to-outpatient ratio requires careful interpretation. In the present study, this ratio should be regarded as a healthcare-utilisation indicator rather than a direct measure of clinical severity. A higher ratio can occur even when both outpatient visits and hospitalizations decline if outpatient utilisation decreases more rapidly. This pattern is consistent with preferential prevention of milder medically attended disease. As vaccination reduces a proportion of less severe rotavirus-associated illness, the remaining population seeking inpatient care may represent a progressively more clinically selected group. Hospitalization is influenced by dehydration, comorbidities, age, pathogen, nutritional status, and healthcare access, and therefore does not represent a homogeneous measure of disease severity. The increasing ratio therefore should not be interpreted as evidence that AGE became clinically more severe after vaccine introduction. Rather, it may indicate a change in the composition of healthcare utilisation, with a greater proportion of the remaining healthcare encounters occurring at the inpatient level. This interpretation is also consistent with global evidence showing that rotavirus vaccination has a particularly substantial effect on severe disease and hospitalization[4,13]. The residual inpatient population after vaccine introduction may consequently contain a greater relative contribution from non-rotavirus pathogens and host-related determinants of hospitalization. Therefore, the absolute hospitalization rates remain the more appropriate indicator of inpatient disease burden, whereas the admission-to-outpatient ratio provides complementary information on how healthcare utilisation is distributed across levels of care.

For LOS, the minimal change in median LOS and in the proportion of prolonged hospitalization suggests that the principal effect of rotavirus vaccination may occur before hospitalization rather than during the inpatient episode. Vaccination prevents infection and clinically significant disease; among children who nevertheless develop illness severe enough to require admission, the subsequent duration of hospitalization is determined by multiple clinical and system-level factors. The LOS is influenced by dehydration, electrolyte disturbances, nutritional status, comorbidities, complications, pathogen aetiology, response to treatment, discharge practices, and access to follow-up care. These determinants may not be substantially modified by whether rotavirus vaccination was received. Therefore, the combination of fewer hospital admissions with relatively stable length of stay is clinically plausible. The major inpatient resource benefit would be expected to arise from avoided admissions and associated bed-days, rather than from shortening the hospitalization of children who remain sufficiently ill to require inpatient care. The stable length of stay suggests that the economic and capacity benefits of vaccination are likely to arise primarily through prevention of hospitalization rather than through shortening inpatient treatment among admitted children.

The age distribution provides additional information regarding the population-level epidemiology of AGE following vaccine introduction. Rotavirus disease disproportionately affects young children, particularly during infancy and early childhood, and routine vaccination is therefore targeted to the first months of life. WHO recommends rotavirus vaccination as part of routine childhood immunization programmes because of its substantial potential to prevent severe disease and hospitalization[17]. Global evidence suggests that vaccine impact may be particularly pronounced among younger children. Burnett et al. reported larger reductions among younger age groups following vaccine introduction[4].[4] In addition, WHO-coordinated surveillance has documented changes in the age distribution of rotavirus-positive hospitalized children following vaccine introduction, with a relative shift toward older children in some settings[6].The relatively stable median age observed in the present study should therefore be interpreted cautiously. Because the study evaluates the broader AGE syndrome rather than laboratory-confirmed rotavirus infection, changes in the age distribution of other gastrointestinal pathogens may obscure an age shift that would be detectable in rotavirus-specific surveillance. Moreover, median age is a summary measure and may remain stable despite heterogeneous changes across individual age groups. Age-specific incidence rates are therefore more informative for evaluating whether vaccination changes the epidemiological distribution of disease. From a public-health perspective, the findings reinforce the importance of timely infant immunization while highlighting the value of age-specific and pathogen-specific surveillance for detecting longer-term changes in disease epidemiology.

The mortality also declined during the post-NIP period, although the temporal trend did not reach statistical significance. This finding should be interpreted in the context of the relatively low frequency of AGE-related deaths in Thailand, which limits statistical power to detect modest changes over time. The direction of the observed mortality trend is nevertheless compatible with international evidence. Burnett et al. reported a median 36% reduction in AGE mortality among children younger than 5 years following rotavirus vaccine introduction across countries with available pre- and post-introduction data[4].Their analysis also found greater reductions among younger children and in settings with higher vaccine coverage. The WHO position paper emphasizes the substantial contribution of rotavirus to severe childhood diarrhoeal disease and supports routine rotavirus vaccination as an important public-health intervention[17].However, because mortality in the present study was based on administrative healthcare data and the outcome encompasses broader AGE, the observed mortality trend cannot be attributed specifically to rotavirus prevention. The absence of statistical significance should therefore not be interpreted as evidence that vaccination has no effect on mortality. Rather, mortality represents a relatively rare endpoint for which national ecological analyses may have insufficient statistical power to detect modest changes, particularly when the underlying outcome includes multiple infectious and non-infectious determinants. From these findings, the favourable direction of mortality together with reductions in outpatient utilisation and hospitalization supports continued vaccination, while pathogen-specific surveillance is needed to quantify the contribution of rotavirus vaccination to mortality prevention.

Rotavirus vaccine coverage increased progressively during the post-NIP period, reaching more than three-quarters of eligible children by the end of the study period. This temporal increase provides important context for interpreting the progressive reduction in AGE-related healthcare utilisation. High and timely vaccine coverage is essential to maximize population-level benefit. WHO recommends rotavirus vaccination as part of national immunization programmes and emphasizes achieving high coverage to maximize protection[17].Global surveillance has also demonstrated lower rotavirus positivity among hospitalized children in countries that have introduced rotavirus vaccination compared with countries without routine vaccination[19]. The rotavirus coverage observed in Thailand remained below that of some established infant vaccines. One important programmatic consideration is that rotavirus vaccination has a restricted age window. Centers for Disease Control and Prevention (CDC) recommendations specify that the first dose should be administered before 15 weeks of age and the final dose should be completed before 8 months of age. In the United States, Rotarix is administered as a 2-dose series at 2 and 4 months, whereas RotaTeq is administered as a 3-dose series at 2, 4, and 6 months[20]. This narrow eligibility window creates a particular challenge for programme implementation. Unlike vaccines for which delayed vaccination can generally be addressed through catch-up schedules, delayed rotavirus vaccination may result in a permanently missed opportunity once the infant exceeds the recommended age limit. Consequently, improving attendance at routine infant immunization visits may be particularly important for maximizing rotavirus vaccine coverage. For international comparison, WHO/UNICEF estimates of national immunization coverage provide an independent framework for assessing routine vaccine programme performance. WHO/UNICEF estimates include rotavirus vaccine completion as a standard national immunization indicator, although the methodology differs from the administrative estimates used in the present study[21]. The progressive increase in coverage observed in the present study is also consistent with the expectation that population-level benefits accumulate as vaccinated birth cohorts progressively replace incompletely vaccinated cohorts. Burnett et al. observed larger reductions in AGE hospitalization in settings with higher vaccine coverage[4].Because individual-level linkage between vaccine doses was unavailable, however, the coverage estimates in the present study should be interpreted as administrative population-level estimates rather than longitudinal cohort-based coverage. In terms of public health, improving timely completion of the rotavirus vaccine schedule and minimizing missed opportunities during routine infant visits represent important strategies for increasing the population-level impact of the national programme.

Finally, the reduction in inpatient healthcare expenditure provides an important additional dimension of the impact of rotavirus vaccination. Preventing hospitalization can reduce direct medical expenditure even when the analysis is not designed as a formal economic evaluation.

The present study estimated changes in inpatient expenditure using real-world NHSO reimbursement data. This approach provides a healthcare-payer perspective based on observed healthcare utilisation, rather than a modelled estimate of the full economic value of vaccination.

This distinction is important when comparing our findings with previous Thai economic evaluations. Luangasanatip et al. modelled the cost-effectiveness and budget impact of rotavirus vaccination in Thailand and found that implementation of WHO-prequalified rotavirus vaccines could reduce government healthcare expenditure while generating health gains[10]. Their analysis incorporated vaccination costs and projected healthcare outcomes using a transmission-dynamic model, whereas the present study evaluates observed changes in inpatient expenditure after national programme implementation.

The two approaches therefore address complementary questions. Economic modelling estimates the expected value of introducing vaccination under specified assumptions, whereas the present study provides real-world evidence of changes in healthcare expenditure associated with the observed reduction in inpatient utilisation.

The economic findings should consequently not be described as demonstrating that the rotavirus vaccination programme itself was definitively cost-saving. A formal cost-saving or cost-effectiveness conclusion would require incorporation of vaccine acquisition and delivery costs, outpatient expenditure, and potentially indirect societal costs such as caregiver productivity losses and transportation costs.

Nevertheless, the observed reduction in inpatient expenditure is clinically and economically relevant because hospitalization represents a resource-intensive component of AGE management. When considered alongside reductions in outpatient utilisation and hospitalization, the findings suggest that the benefits of rotavirus vaccination extend beyond disease prevention to healthcare-resource conservation.

From a public-health concrn, the observed reduction in inpatient expenditure provides real-world evidence that rotavirus vaccination may reduce healthcare resource use and supports continued investment in a sustained national immunization programme.

This study has several important strengths. First, it uses a nationwide administrative healthcare database covering children within the Universal Coverage Scheme, allowing assessment of population-level changes across multiple dimensions of healthcare utilisation. Second, the analysis extends beyond the initial implementation period and includes four complete post-NIP fiscal years. Third, the study evaluates several complementary outcomes—including outpatient utilisation, hospitalization, seasonality, mortality, vaccine coverage, length of stay, and expenditure—within a common national framework. Fourth, the findings can be interpreted alongside recent independent Thai analyses using HDC and NHSO data, providing an opportunity for cross-database triangulation.

Several limitations should also be considered. Most importantly, the ecological design precludes individual-level causal inference. The temporal association between vaccine introduction and reductions in AGE healthcare utilisation cannot establish that vaccination was solely responsible for the observed changes. Secular trends, healthcare-seeking behaviour, pathogen circulation, healthcare delivery, and other public-health interventions may have contributed. Second, the clinical outcome was based on

administrative diagnosis rather than laboratory-confirmed rotavirus infection. Consequently, the study estimates population-level changes in AGE healthcare utilisation rather than rotavirus-specific vaccine effectiveness. This distinction is important because rotavirus represents only one component of the broader aetiological spectrum of childhood gastroenteritis. WHO surveillance specifically uses laboratory confirmation to monitor rotavirus disease and vaccine impact[6]. Third, comparison with other Thai databases should be interpreted cautiously because the underlying populations, case definitions, healthcare settings, and data-generation processes differ. The HDC study by Sailuenarm et al. evaluated a broader acute diarrhoeal disease outcome[8], whereas the present study focused on AGE. Therefore, concordance in direction is more informative than numerical equivalence between estimates. Fourth, vaccine coverage was estimated from routinely collected administrative immunization data without individual-level linkage between vaccine doses. These estimates should therefore not be interpreted as longitudinal cohort coverage. Finally, the economic analysis quantifies observed inpatient expenditure rather than performing a full cost-effectiveness analysis. Vaccine costs and broader societal costs were not incorporated. Accordingly, the economic findings should be interpreted as evidence of healthcare expenditure reduction associated with reduced inpatient utilisation, rather than definitive evidence of net programme savings. These limitations define the appropriate level of inference: the study provides real-world population-level evidence of changes in AGE-related healthcare burden following national rotavirus vaccine introduction, rather than an individual-level estimate of vaccine effectiveness.

Conclusion

In this nationwide population-based ecological study, introduction of rotavirus vaccination into Thailand's NIP was temporally associated with a substantial reduction in outpatient AGE healthcare utilisation, accompanied by a smaller reduction in hospitalization, attenuation of seasonal activity, and a favourable direction in mortality. The admission-to-outpatient ratio increased despite declining absolute healthcare utilisation, whereas median age at hospitalization and prolonged hospitalization changed minimally. Rotavirus vaccine coverage increased progressively throughout the post-NIP period and was accompanied by reductions in inpatient healthcare expenditure.

The findings complement previous Thai national evidence from both NHSO and HDC and are broadly consistent with international post-licensure evidence demonstrating reductions in rotavirus and AGE healthcare burden following vaccine introduction. Importantly, differences in disease definitions and database characteristics should be considered when interpreting effect estimates across studies. Because the present study evaluates AGE using routinely collected administrative healthcare data and uses an ecological pre–post design, the findings should be interpreted as population-level health-system impact associated temporally with rotavirus vaccine introduction rather than individual-level rotavirus vaccine effectiveness.

Continued efforts to achieve high and timely vaccine coverage, minimize missed opportunities during routine infant immunization, and maintain integrated clinical, laboratory, and administrative surveillance will be important to maximize and accurately quantify the long-term

Abbreviations

AAPC
Average Annual Percent Change
AGE
Acute gastroenteritis
CDC
Centers for Disease Control and Prevention
CI
Confidence Interval
DTwP-HB-Hib
Diphtheria – Tetanus – Pertussis (whole cell) – Hepatitis B – Haemophilus influenzae type b
FY
Fiscal Year
HDC
Health Data Centre
ICD-10-TM
International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Thai Modification
IPD/OPD
Inpatient Department/Outpatient Department
IQR
interquartile range
IRR
Incidence Rate Ratio
LOS
Length of Stay
MAAGE
Medically Attended Acute Gastroenteritis
NHSO
National Health Security Office
NIP
National Immunization Program
RV1
Monovalent rotavirus vaccine (Rotarix)
RV5
Pentavalent rotavirus vaccine (RotaTeq)
SD
standard deviation
THB

Thai Baht
UCS
Universal Coverage Scheme
UNICEF
United Nations Children's Fund
USD
United States Dollar
WHO
World Health Organization
WUENIC
WHO/UNICEF Estimates of National Immunization Coverage

Declarations

Ethics approval and consent to participate

The present study was approved by the international review board, Center for Ethics in Human Research, Khon Kaen University, Human Research Ethics Committee (HE681223). Consent was waived by Center for Ethics in Human Research, Khon Kaen University because of no personally identifiable data. The authors confirm that all methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

BC and SG (as an essentially intellectual contributor) conceptualized and designed the study, performed the computations, discussed the results, drafted the initial manuscript, and contributed to the final manuscript. KS performed the computations, was involved in data acquisition, discussed the results, drafted the initial manuscript, and contributed to the final manuscript. WP performed the computations, discussed the results, and contributed to the final manuscript. SS performed the computations, was involved in data acquisition, discussed the results, and contributed to the final manuscript. KT performed the computations, was involved in data acquisition, was responsible for the analysis and interpretation of the data, designed the figures and tables, and contributed to the final manuscript. Sirirattanakul S and Supasai S performed the computations, was involved in data acquisition, was responsible for the analysis and interpretation of the data, discussed the results, and contributed to the final manuscript. OP performed the economic burden analysis, contributed to the analysis and interpretation of the economic data, discussed the results, and contributed to the final manuscript. Generative AI (ChatGPT, OpenAI, GPT-4) was used to improve language clarity and manuscript structure. It was not used for data analysis, interpretation, or generation of scientific conclusions. All outputs were reviewed and approved by the authors, who take full responsibility for the content.

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Availability of data and materials

The data that support the findings of this study are available from Thailand National Health Coverage but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Thailand National Health Coverage

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Figures

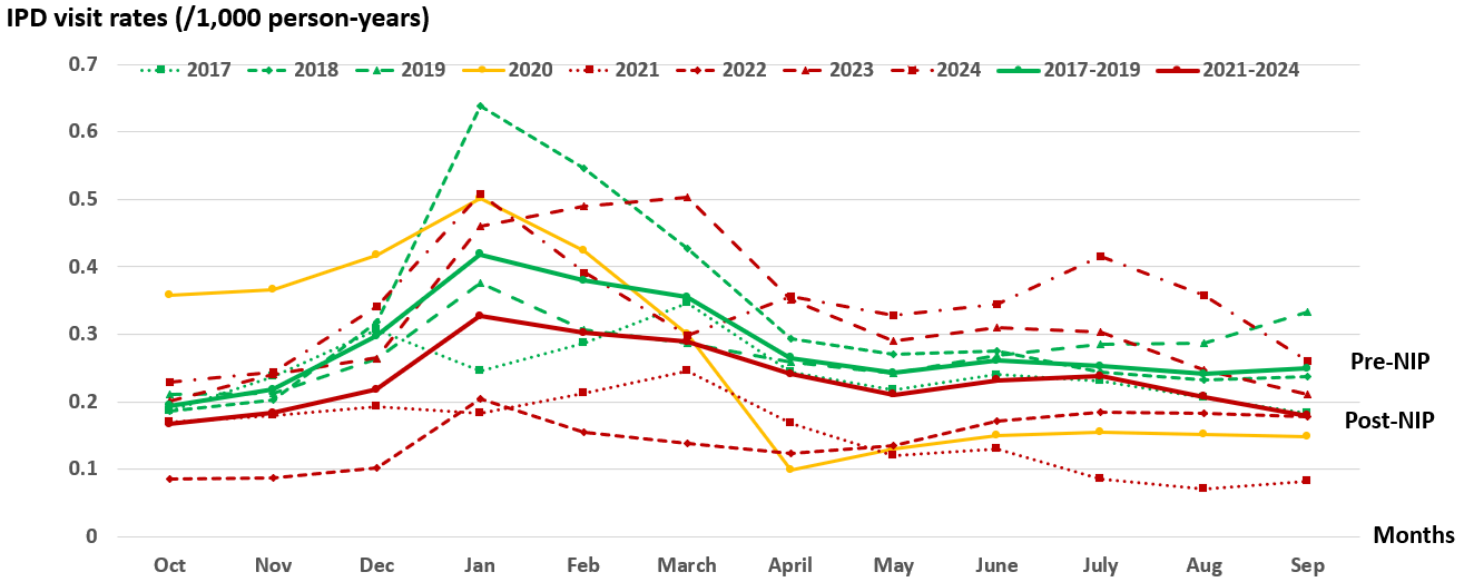


Figure 4

Fig. 2. Monthly trends in healthcare utilization for acute gastroenteritis among Thai children under 5 years of age before and after rotavirus vaccine introduction

(2b) Monthly hospitalization rates (/1,000 person-years)

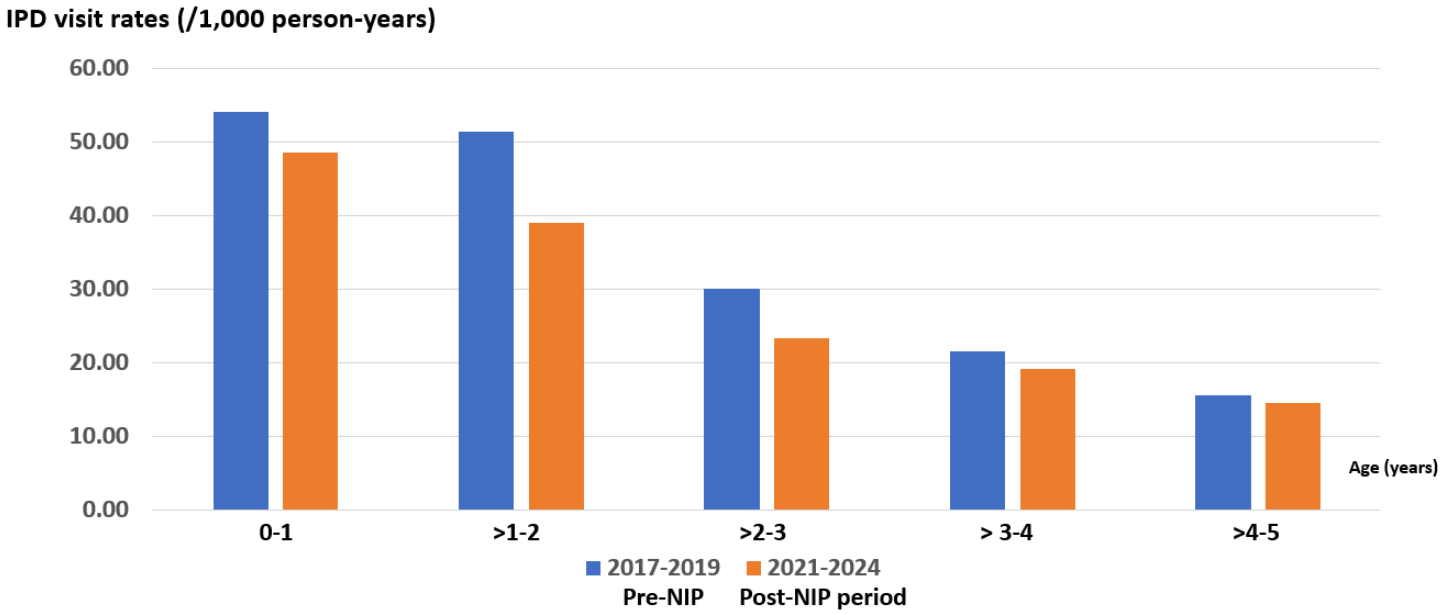


Figure 6

Fig 3. Trends in hospitalization rates for acute gastroenteritis among Thai children under 5 years of age before and after rotavirus vaccine introduction.

(3b) Hospitalization rates (/1,000 person-years) by age group

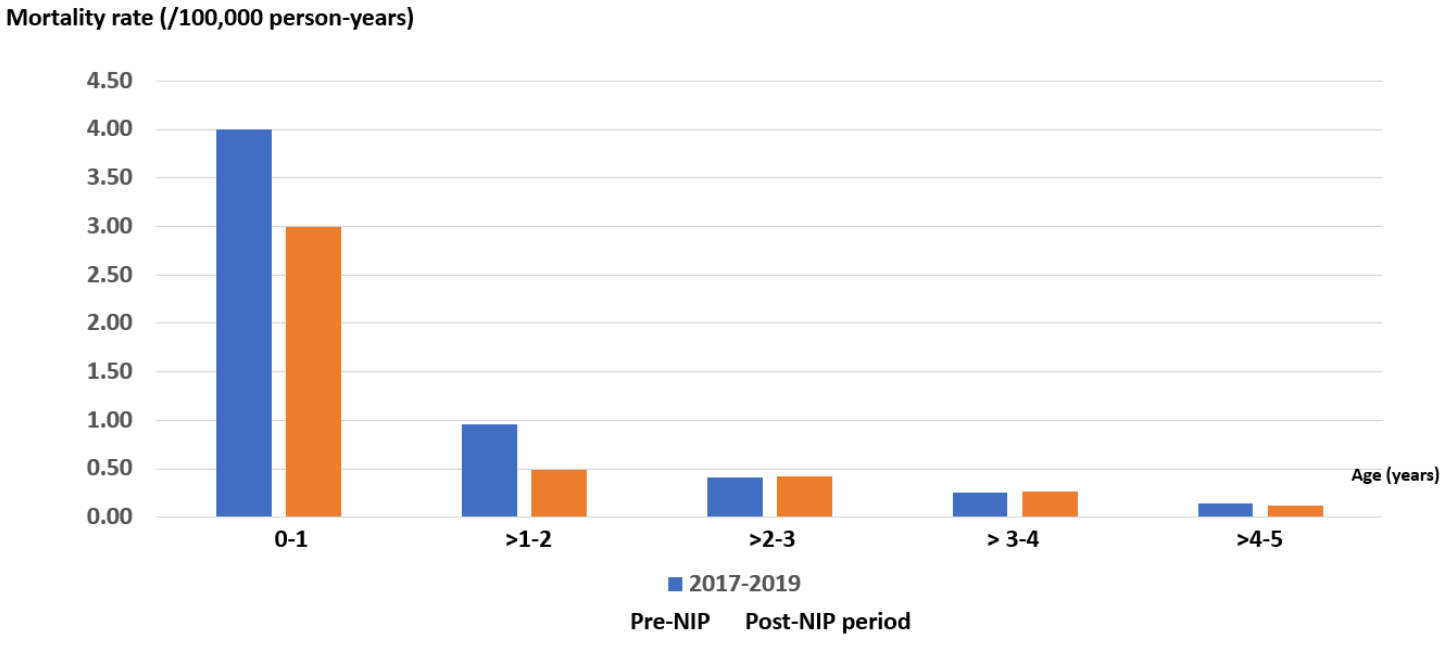


Figure 8

Fig 4. Trends in mortality rates (/100,000 person-years) among Thai children under 5 years of age before and after rotavirus vaccine introduction

(4b) Mortality rates (/100,000 person-years) by age group

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable1.docx