

Impact of public funding for rotavirus vaccines on pediatric emergencies and healthcare workload in a tertiary care hospital

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1. Introduction

Rotavirus is a major pathogen with high environmental stability that causes acute gastroenteritis among infants and young children [1–7]. This stability makes infection prevention extremely difficult, even in developed countries with improved sanitary conditions, and nearly all children worldwide develop rotavirus gastroenteritis by the age of five [2,3,7]. Before the introduction of the vaccine, the disease burden of rotavirus infection in Japan was estimated at 1.2 million children annually, with 1 in 15 hospitalized, and 10–20 deaths per year [2,4,5]. Among severe cases presented with encephalopathy, rotavirus was detected in about 4 % of cases, followed by influenza and HHV-6 in Japan [8]. Yamaguchi University Hospital is the only designated tertiary care hospital in the prefecture. As a large number of pediatric patients hospitalized at our facility have underlying conditions, such as heart disease and blood disorders, strict infection control measures must be implemented when children with rotavirus gastroenteritis are admitted. Furthermore, when emergency admissions occur during off-hours with staff shortages, the burden on healthcare providers increases significantly.

A monovalent vaccine against rotavirus infection has been approved for sale in Japan since November 2011. This vaccination was optional for approximately nine years following approval, only becoming a routine vaccination nationwide in October 2020 [1]. In Ube City, partial public funding for vaccination fees was independently introduced for infants residing in the city from January 2014 to September 30, 2020. This subsidy covered 44.5 % to 46.9 % of the vaccination costs.

Shah et al. previously reported a reduction in emergency department visits for acute gastroenteritis in children under 5 years of age following

the introduction of rotavirus vaccination between 2006 and December 2013. This reduction was particularly pronounced in children under 23 months old [3].

Municipal funding could be expected to be cost-effective, depending on the price of the vaccine [4]. However, its benefit from the perspective of healthcare providers has not yet been documented. Hence, the present study aimed to examine the impact of municipal rotavirus vaccination funding on pediatric emergency care at our tertiary care facility, as well as on the extent of the community-wide reduction in rotavirus incidence by assessing non-subsidized neighboring regions as a control.

2. Methods

2.1. Hospitalization trends

This study enrolled children under 15 years old who resided in Ube City and were admitted to the Division of Pediatrics at Yamaguchi University Hospital with rotavirus gastroenteritis and acute gastroenteritis from January 1, 2010, to December 31, 2020. Rotavirus gastroenteritis was defined as gastrointestinal symptoms, such as vomiting or diarrhea, combined with a positive stool rotavirus rapid antigen test. Acute gastroenteritis was defined as the presence of vomiting and/or diarrhea. The exclusion criteria included cases of inflammatory bowel disease, food protein-induced enterocolitis syndrome, and other negative infections. We retrospectively investigated the number of patients each year from the medical records. The start of the investigation was set to January 1, 2010, the date at which our hospital adopted an electronic medical record system.

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2.2. Trend in after-hours visits

We targeted children under 15 years of age with acute gastroenteritis living in Ube City who visited the Division of Pediatrics of Yamaguchi University Hospital from January 1, 2010, to December 31, 2020. The definitions of rotavirus gastroenteritis and acute gastroenteritis are as described above. Notably, in cases of outpatient visits, a small fraction of patients may not have undergone stool rotavirus antigen testing, but were instead diagnosed from their clinical manifestations. The annual number of patients was obtained from the medical administration records.

2.3. Trends in rotavirus vaccination rates

The target period was set from the start of sales of the rotavirus vaccine in 2011 until this vaccination was adopted as a routine immunization in Japan in October 2020. The number of vaccine recipients in Ube City from 2011 to 2013 was obtained from the shipment record of the manufacturers (GlaxoSmithKline K.K. and MSD K.K.). The number of vaccine recipients from January 1, 2014, to September 30, 2020, during the municipal funding period, was calculated based on the total number of vaccine subsidies provided by Ube City. As the rotavirus vaccine was administered to infants, the vaccination rate was calculated based on the annual number of births in Ube City and the number of recipients. For 2020, we used the number of births from January to September, as routine vaccination was initiated in October in Japan.

2.4. Trends in the total estimated costs

This study included children presented with rotavirus gastroenteritis at our department under 15 years old from January 2010 to December 2020. We classified patients into three groups: 1) hospitalized, 2) Intravenous drip therapy without hospitalization, 3) outpatient care without intravenous therapy. We further calculated the estimates of direct medical costs, direct non-medical costs, and parental productivity losses for each group. Based on the medical administration reports, the direct medical costs for hospitalization and outpatient treatment were estimated at 221,000 and 22,000 JPY (Japanese yen) per person, respectively [2]. The direct non-medical cost per case was estimated at 23,143 JPY for hospitalization, 5207 JPY for outpatient intravenous therapy, and 3534 JPY for outpatient treatment [2]. The estimates for parental productivity losses were 170,407 JPY, 92,290 JPY, and 69,832 JPY per person for hospitalized patients, outpatient intravenous therapy patients, and outpatient non-intravenous therapy patients, respectively [2]. Referring to the report, we investigated the annual trends in the estimated total amount for each year. To enhance international comprehensibility of the cost data, JPY values were converted into U.S. dollars (USD) using a fixed exchange rate of 1 USD = 101.7 JPY. This rate reflects the approximate average exchange rate during the study period (2010–2020). Historical exchange rate data were obtained from the official statistics of the Bank of Japan [9]. USD equivalents are presented in parentheses following the corresponding JPY amounts throughout the manuscript.

2.5. Rotavirus gastroenteritis in adjacent regions

In 2014, rotavirus gastroenteritis was included in the sentinel surveillance system of Yamaguchi Prefecture. We conducted an actual investigation of three health centers: Ube Health Center and the adjacent Shimonoseki Health Center and Yamaguchi Health Center, from January 1, 2014, to December 31, 2020. We subsequently compiled the total number of sentinel reports for the relevant period at each health center. The reported numbers were then obtained from the Yamaguchi Prefecture Infectious Disease Information Center incidence trend survey, and adjusted for a population ratio of 100,000 people. The Ube Health Center oversees Ube City, Sanyo-Onoda City, and Mine City, which is

within the medical service area of our hospital. Shimonoseki Health Center oversees Shimonoseki City, while Yamaguchi Health Center oversees Yamaguchi City. The total number of reports from the three health centers were compared.

2.6. Statistical analysis

The Mann-Whitney *U* test was primarily applied to examine the significance of between periods differences (2010–2013 before the public financial support vs. 2014–2020 after the support) in the number of hospitalized patients, the number of after-hours visits, as well as the estimated total costs related to rotavirus gastroenteritis and acute gastroenteritis in our department. For the detailed assessment of the between-year trends, the number of cases for rotavirus infection or acute gastroenteritis per year were adjusted by the total number of hospitalization or outpatient visits per year, and the Cochran-Armitage trend test was applied. To test for the differences in incidence rates per 100,000 people in the three regions, the Fisher's exact probability test was used. Statistical significance was set at $p < 0.05$.

2.7. Ethics

This study was conducted in accordance with the principles of the Declaration of Helsinki and relevant laws and guidelines, and was approved by the Human Research Ethics Committee of Yamaguchi University Hospital (approval no. 2023–088).

3. Results

In Ube City, hospitalizations due to rotavirus gastroenteritis and acute gastroenteritis (including rotavirus gastroenteritis) showed a decreasing trend after 2014 based on the Cochran-Armitage test (both $p < 0.0001$, Fig. 1). The average (range) of the annual number of hospitalizations due to rotavirus gastroenteritis was 25.0 (22–28) prior to municipal funding (2010–2013) and 2.4 (0–8) after the start of municipal funding (2014–2020), representing a significant decline on the Mann-Whitney test ($p = 0.0097$). Similarly, the annual number of hospitalizations for acute gastroenteritis was 57.0 (46–81) before funding, which decreased to 18.3 (8–28) after funding ($p = 0.011$).

The number of after-hour visits to our department for rotavirus gastroenteritis and acute gastroenteritis (including rotavirus infection), also showed a decreasing trend from 2010 to 2020 ($p < 0.0001$, Cochran-Armitage test) as shown in Fig. 2. The annual number of after-hours visits for acute gastroenteritis on average (range) was 30.8 (25–38) before the funding, decreasing to 9.1 (3–14) after funding, representing a significant decrease ($p = 0.013$). The average (range) annual number of hospitalizations due to rotavirus gastroenteritis also decreased from 13.8 (6–18) before municipal funding to 2.4 (0–6) after funding ($p = 0.011$).

The rotavirus vaccination rate for infants under 1 year old in Ube City was 1.9 % in 2011, when the rotavirus vaccine was first introduced in Japan. Subsequently, the vaccination rate gradually increased even during this period of voluntary vaccination. The vaccination rate in 2014, after the subsidy, was estimated to be 72.7 %, and it continued to increase, reaching a high level of 95.1 % in 2020 (Fig. 3).

The total estimated amount of direct medical costs, direct non-medical costs, and productivity loss of guardians for cases that visited our department with rotavirus gastroenteritis before availability of the public subsidy ranged from 9,454,010–12,180,304 JPY (92,960–119,767 USD) between 2010 and 2013. Conversely, the total estimated costs after the public subsidies (2014–2020) were abruptly decreased to a level between 0 and 1,043,513 JPY (10,261 USD) per year ($p = 0.011$) (Fig. 4, Table 1; for detailed USD conversions of the itemized cost data, please refer to supplementary Table 1). After the initiation of public funding, the total number of sentinel reports for rotavirus gastroenteritis in the adjacent regions showed that the Ube

Health Center had significantly fewer reports than the neighboring Shimonoseki ($p = 0.0070$) and Yamaguchi ($p < 0.0001$) Health Centers (Fig. 5).

4. Discussion

In Japan, the “Work Style Reform-related Law” has been gradually implemented since April 1, 2019, while new regulations regarding physicians' work schedule have been enforced since April 2024. Yamaguchi Prefecture is currently facing severe population decline due to declining birth rates and an aging population, making it increasingly difficult to hire medical personnel. Consequently, securing healthcare workers and addressing the uneven distribution of physicians have both arisen as pressing issues.

Ube City, located in Yamaguchi Prefecture, southwestern Honshu, has a population of approximately 150,000 and an area of 286.7 km². A notable regional characteristic of this region is the absence of secondary emergency hospitals with pediatric capabilities. Despite being the only tertiary care facility, our hospital provides pediatric care even for mild cases visiting outside of regular hours. Additionally, our department accepts patients with infectious diseases originally treated at secondary emergency hospitals, as requested. These regional characteristics can increase staff physicians' workload. After-hour consultations and telephone responses for mild pediatric cases tend to hinder optimal hospital functioning and the provision of adequate care. To alleviate physicians' excessive workload resulting from these clinical practices, our hospital has made various proposals in collaboration with the local governments and medical associations. These include: (1) providing partial or full subsidies for voluntary vaccinations, (2) offering public assistance for two-week and one-month health check-ups and establishing pediatric family doctors from early postnatal stages, and (3) setting up emergency outpatient services during holidays and overnight to promote preventive healthcare throughout the community.

In Japan, the rotavirus vaccine was introduced as a routine vaccination in October 2020 [10]. Since the start of public funding for the rotavirus vaccine in Ube City in January 2014, the number of hospitalizations and after-hours visits due to rotavirus gastroenteritis have significantly decreased. According to Korematsu et al. [2], the median number of hospitalizations for rotavirus gastroenteritis among children under three years of age per 2500 patients was 33 from 2007 to 2013, decreasing to 12 during 2014–2018 after partial public funding began. Additionally, Zlamy et al. [11] reported that hospitalizations for rotavirus gastroenteritis among infants decreased by 87.8 %, while hospitalizations among patients under 18 years decreased by 73.9 % after the introduction of routine rotavirus vaccination. In this study, we confirmed the efficacy of rotavirus vaccination revealed in these reports.

In the present study, the average annual number of hospitalizations for rotavirus gastroenteritis was 25.0 before municipal funding,

decreasing significantly by 92.0 % to 2.4 after the start of municipal funding. Similarly, the analysis of hospitalization numbers for acute gastroenteritis also showed a significant drop, indicating that rotavirus played a major role in hospitalizations for acute gastroenteritis. One report [3] from the United States indicated that there was a decrease in emergency room visits for acute gastroenteritis in children under 5 years old after the introduction of the rotavirus vaccine. In the present study, we focused on after-hours emergency room visits for acute gastroenteritis in children under 15 years old, which differs in definition from the previous reports. In the present study, the annual number of after-hours visits for acute gastroenteritis and rotavirus gastroenteritis was decreased drastically.

Although infection control was not investigated in this study, our hospital requires contact precautions in addition to standard preventive measures for hospitalized rotavirus gastroenteritis patients [12]. Consequently, decreasing the burden caused by hospitalizations for rotavirus gastroenteritis may have reduced the burden of preventive measures on hospital staff. Additionally, as previously reported [3,7], the number of after-hour visits for acute gastroenteritis in children decreased, reducing the burden of after-hour care for our on-call physicians. This reduction in emergency visits and hospitalizations seems to have contributed to a reduction in physician workload. Future studies should directly investigate healthcare workers' workload to confirm this effect, perhaps using surveys or interviews.

In Japan, a vaccination rate of over 70 % is desirable to keep maintain hospitalization rate for rotavirus infection low [4]. According to Korematsu et al., municipal funding of 63.0 % of the cost of rotavirus vaccination resulted in an immunization coverage of 68.5–73.9 %. In another study by Hashiguchi et al. [13], the vaccination rate reached 91.2–93.9 % with 100 % municipal funding. In this study, when the subsidy rate in Ube City was 44.5–46.9 %, the vaccination rate was 72.7–95.1 %. Ube City has established a pediatric primary care system starting in early infancy, providing one-, three-, and six-month health check-ups conducted by pediatricians since 2010. This may explain why the vaccination rate exceeded 70 %, despite the relatively low subsidy rate. Additionally, even before public funding, the number of hospitalizations for rotavirus gastroenteritis in Ube City was lower than in previous reports from Japan [2,4,5]. As voluntary vaccination started in 2011–2012, the proactive promotion of vaccination in the region may have contributed to this outcome. Although intussusception, a serious side effect of the rotavirus vaccine, was previously reported during the voluntary vaccination period in Japan [14], it was not observed during our study period.

There is still debate as to whether to include productivity losses of guardians in reports on the cost-effectiveness of vaccines. Some reports have further indicated that cost-effectiveness cannot be expected, particularly in developed countries [15]. However, reports that included productivity losses of guardians showed cost-effectiveness [2,4]. If

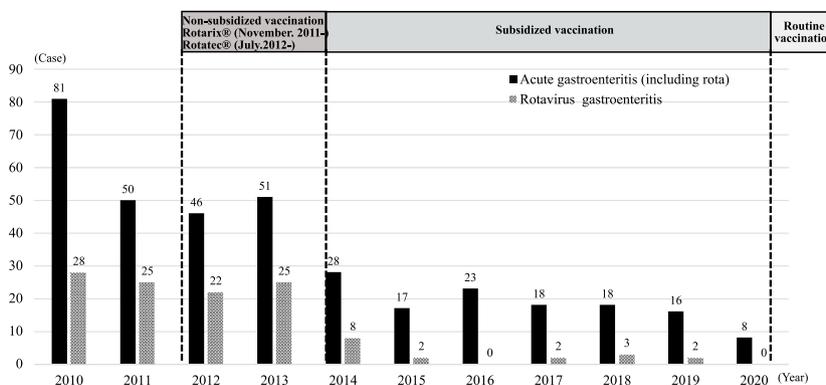


Fig. 1. Trends in hospitalizations due to acute gastroenteritis (including rotavirus gastroenteritis cases) from January 2010 to December 2020.

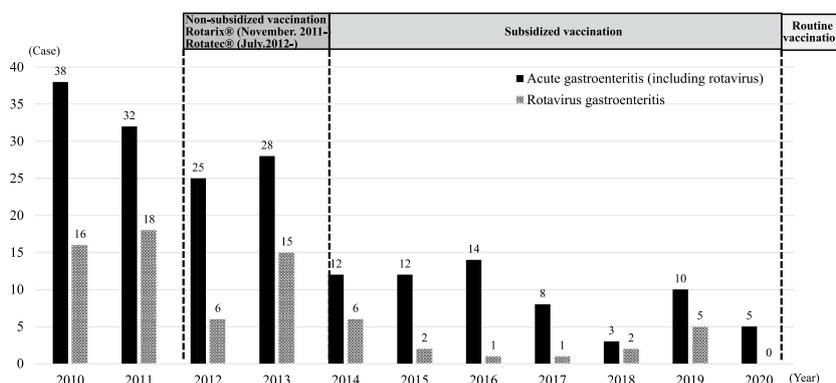


Fig. 2. Trends in after-hours visits due to acute gastroenteritis (including rotavirus gastroenteritis cases) from January 2010 to December 2020.

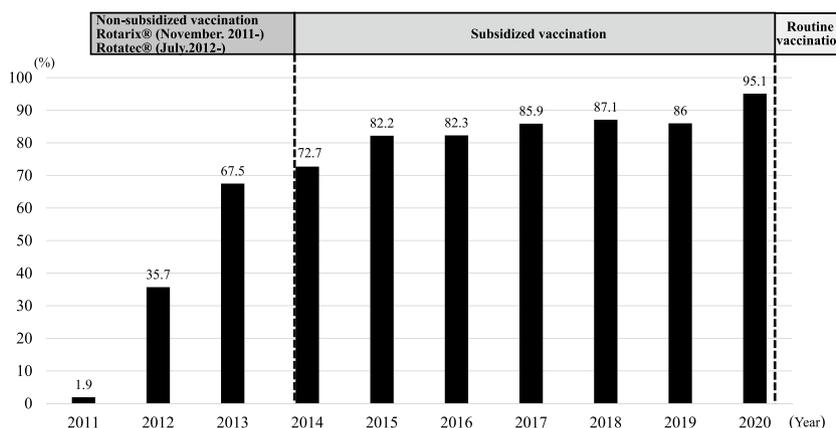


Fig. 3. Trends in rotavirus vaccination rates in infants under 1 year old in Ube City from January 2010 to September 2020.

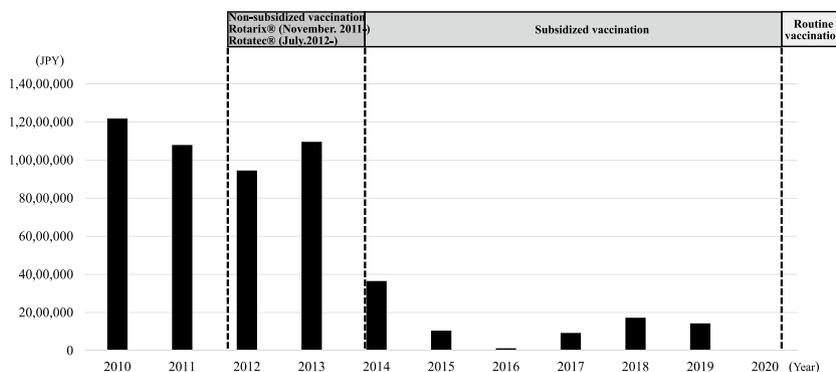


Fig. 4. Trends in the estimated annual cost of treating rotavirus gastroenteritis. The total cost was estimated as the sum of the annual direct medical expenses, direct non-medical expenses, and productivity losses incurred by guardians for rotavirus gastroenteritis cases treated at our hospital. Please refer to Table 1 for details. For detailed U.S. dollar (USD) conversions of the itemized cost data, please refer to supplementary Table 1. JPY: Japanese yen.

productivity losses and other guardian losses are not included, cost-effectiveness depends largely on the vaccination fee [16,17]. In the present study, we found that the total estimated medical costs and losses in caregiver productivity for our department's patients significantly decreased after the start of municipal funding; however, the cost-effectiveness could not be examined. One reason for this is that our department is a designated advanced medical institution, which could indicate a higher threshold for outpatient visits and hospitalizations due to rotavirus gastroenteritis. In particular, for mild gastroenteritis, patients are more likely to visit nearby clinics to undergo outpatient care. As such, the data may not accurately represent the actual number of

patients with rotavirus gastroenteritis. Nevertheless, despite this limitation, the observed trend of a complete reduction in hospitalizations is still meaningful. Although these findings should be interpreted with caution, they nevertheless indicate that the subsidy may have had a positive impact by reducing the incidence of rotavirus gastroenteritis, hospitalizations and healthcare costs, as well as alleviating healthcare workers' workload.

The jurisdiction of the Ube Health Center includes not only Ube City, but also the surrounding cities (Sanyo-Onoda and Mine Cities). Since the start of sentinel reporting for rotavirus infection in Yamaguchi Prefecture in 2014, the number of patients reported during the period of

Table 1
Annual trends in the itemized costs of treating rotavirus gastroenteritis in Yamaguchi University Hospital.

(Year)	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Number of Hospitalized Patients (cases)	28	25	22	25	8	2	0	2	3	2	0
Direct Medical Expenses (a)	6,188,000	5,525,000	4,862,000	5,525,000	1,768,000	442,000	0	442,000	663,000	442,000	0
Direct Non-Medical Expenses (b)	648,004	578,575	509,146	578,575	185,144	46,286	0	46,286	69,429	46,286	0
Loss of Productivity of Guardians (c)	4,771,396	4,260,175	3,748,954	4,260,175	1,363,256	340,814	0	340,814	511,221	340,814	0
Number of Outpatients with Intravenous Drip (cases)	4	2	2	1	2	1	1	0	4	5	0
Direct Medical Expenses (d)	88,000	44,000	44,000	22,000	44,000	22,000	22,000	0	88,000	110,000	0
Direct Non-Medical Expenses (e)	20,828	10,414	10,414	5207	10,414	5207	5207	0	20,828	26,020	0
Loss of Productivity of Guardians (f)	369,160	184,580	184,580	92,290	184,580	92,290	92,290	0	369,160	461,450	0
Number of Outpatients without Intravenous Drip (cases)	1	2	1	5	1	1	0	1	0	0	0
Direct Medical Expenses (g)	22,000	44,000	22,000	110,000	22,000	22,000	0	22,000	0	0	0
Direct Non-Medical Expenses (h)	3534	7068	3534	17,670	3534	3534	0	3534	0	0	0
Loss of Productivity of Guardians (i)	69,382	138,764	69,382	346,910	69,382	69,382	0	69,382	0	0	0
Total Amount (a + b + c + d + e + f + g + h + i) (JPY)	12,180,304	10,792,576	9,454,010	10,957,827	3,650,310	1,043,513	119,497	924,016	1,721,638	1,426,570	0

JPY: Japanese yen. Direct medical costs per case: Inpatient 221,000 JPY per person, Outpatient 22,000 JPY per person. Direct non-medical costs per case: Inpatient 23,143 JPY per person, Outpatient intravenous therapy 5207 JPY, Outpatient treatment 3534 JPY. Losses related to caregiver productivity per case: Inpatient 170,407 JPY per person, Outpatient intravenous therapy 92,290 JPY per person, Outpatient visit 69,382 JPY per person.

municipal funding was significantly lower in Ube Health Center compared to that in the adjacent areas (Shimonoseki Health Center and Yamaguchi Health Center), where such a subsidy was not provided. Consequently, the impact of the subsidy is evident from the uneven difference in rotavirus incidence. Of note, one important original aspect of this study was that we were able to use adjacent regions as controls to assess the impact of vaccination subsidies.

The primary limitation of this study is that the threshold to allow hospitalization for rotavirus gastroenteritis may have been high due to the high risk of nosocomial infection in critically ill patients, as our hospital is a specialty hospital. This situation may have led to an underestimation of the number of hospitalizations. Moreover, the impact of the COVID-19 pandemic on the reduced incidence in acute gastroenteritis in 2020 cannot be denied.

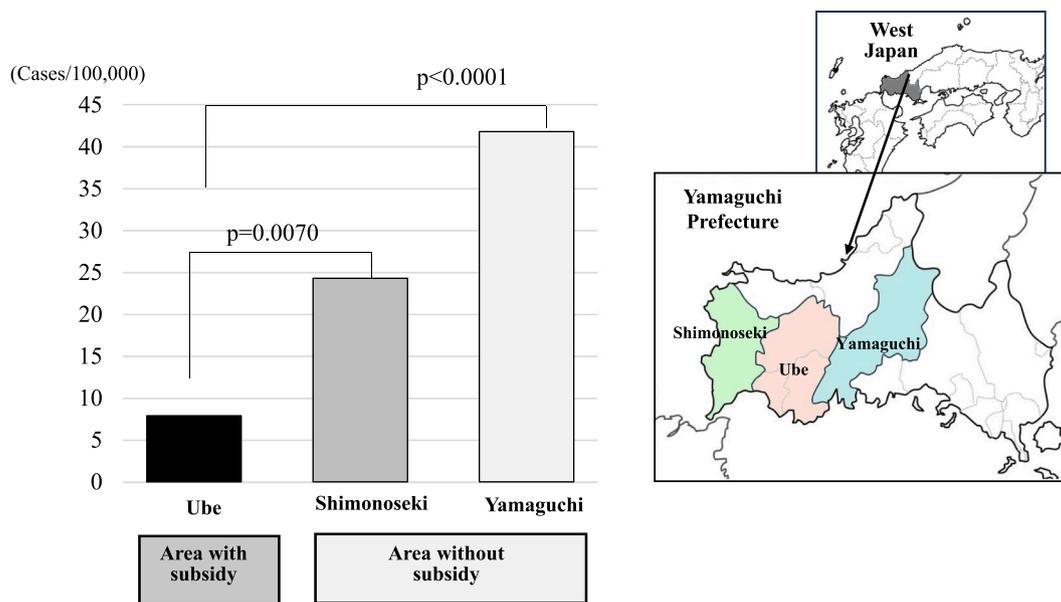


Fig. 5. Rotavirus sentinel reports in three areas (Ube, Shimonoseki, and Yamaguchi) during the vaccination funding period in Ube City, from January 2010 to December 2020. Data were adjusted to a population of 100,000. The Ube Health Center oversees Ube City, Sanyo-Onoda City, and Mine City, whereas the Shimonoseki Health Center oversees Shimonoseki City, and the Yamaguchi Health Center oversees Yamaguchi City.

Overall, this study revealed that public funding for rotavirus vaccines reduced the incidence of rotavirus gastroenteritis, and prevented severe cases. Additionally, these results indicate that this vaccination program may allow a reduction in the burden on healthcare providers. Japanese healthcare has created a society in which medical care is accessible when needed, but requires support by the long working hours of some healthcare workers. To continue providing the necessary medical care, it is essential for hospital administration and the medical community to work together to create a more sustainable healthcare system. This requires role-sharing depending the severity of the condition. From an administrative perspective, it is important to retrospectively review the effects of public funding and connect them to future policy plans.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: MH is affiliated with Ube City, which has a financial interest in the topics or materials discussed in this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jvaxc.2025.100677>.

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