



# OPEN Disease burden of rotavirus related diarrhea in children under 5 years in China: a meta-analysis

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Rotavirus (RV) is a leading cause of severe diarrhea among children under five years of age in China. In this meta-analysis, we assessed the disease burden of RV-related diarrhea by analyzing 73 studies retrieved from the PubMed, Web of Science, China National Knowledge Infrastructure, and Wanfang databases (2013–2023). The incidence of RV-related diarrhea ranged from 0.637/1000 to 31.46/1000 persons. The pooled RV positivity rate for the under-5 age group was 24.7% (95% confidence interval: 22.1–27.4), with higher positivity rates observed among inpatients compared to outpatients (24.1% vs. 22.2%). Notably, the RV positivity rate declined from 27.3 to 21.5% pre- and post- the RotaTeq<sup>®</sup> licensure and 28.8–22.5% following the COVID-19 pandemic. The G9P[8] genotype was predominant, accounting for 71.7% of the RV cases in the under-5 age group. Given the dynamic nature of the incidence rate of RV-related diarrhea and the prevalence of the G9P[8] genotype, it is imperative to enhance surveillance efforts targeting incidence of RV-related diarrhea and the circulating genotypes of rotavirus.

Diarrheal diseases are a major contributor to the Global Burden of Disease (GBD)<sup>1</sup>, with the GBD 2017 study attributing over half a million preventable annual deaths to this condition among children under 5 years of age<sup>2</sup>. Rotavirus (RV), a highly contagious pathogen, is responsible for severe pediatric diarrhea, accounting for approximately 128,500 deaths worldwide in under-5 children in 2016<sup>3,4</sup>. The clinical management of RV infection is further complicated by its high co-infectability with other enteric viruses<sup>5,6</sup>, which may exacerbate disease severity and complicate therapeutic interventions<sup>7</sup>. Current clinical practice for the treatment of RV infections is limited to symptomatic management, due to the lack of targeted antiviral therapies<sup>8</sup>. This therapeutic gap underscores the critical importance of prophylactic measures, like immunization, which demonstrates high efficacy against severe RV gastroenteritis in pediatric populations<sup>8</sup>.

Pursuant to the Infectious Disease Prevention and Control Law of China, hospitals are required to report confirmed cases of rotavirus-related diarrhea to the National Notifiable Infectious Diseases Surveillance System (NNIDSS) within 24 h. The NNIDSS is a legally mandated, multi-tiered framework for infectious disease passive surveillance in China. It collects case information, such as demographics, diagnosis, and laboratory test results, through statutory electronic reporting by all government-funded healthcare facilities. However, RV-related diarrhea is not classified as a distinct notifiable infectious disease. Within the system, cases of RV-related diarrhea are categorized under “Other Infectious Diarrhea” (OID). Besides rotavirus, diarrhea caused by other pathogens, such as norovirus, is similarly reported as OID. Given that etiological test results for OID are not required to be mandatorily reported, it is challenging to accurately estimate the incidence rate of RV-related diarrhea from the NNIDSS.

China’s Marketing Authorization has introduced three vaccines against RV: the Lanzhou Lamb Rotavirus Vaccine (2001)<sup>9</sup>, RotaTeq<sup>®</sup> (2018)<sup>10</sup>, and trivalent reassortant vaccine (2023)<sup>11</sup>. Many international studies have shown that the incidence of RV-related diarrhea has decreased following the use of RotaTeq<sup>®</sup> vaccine<sup>12–14</sup>. However, such research is lacking in China. In addition, there are few studies on the incidence of RV-related diarrhea, making it difficult to fully understand the disease burden of RV-related diarrhea in China. In this study, we aimed to comprehensively evaluate the RV disease burden among children under 5 years of age in China from 2013 to 2023. Additionally, we investigated temporal trends in RV positivity associated with the marketing

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authorization of RotaTeq<sup>®</sup> and the COVID-19 pandemic onset. Lastly, we determined genotype changes of RV in the under-5 age group across the study period.

## Methods

This meta-analysis was prospectively registered in the PROSPERO international registry (CRD42024528658) and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting standards. The PRISMA checklist is provided in Supplementary Appendix 1.

### Search strategy and eligibility criteria

A comprehensive literature search was conducted across PubMed, Web of Science, China National Knowledge Infrastructure, and Wanfang databases to identify Chinese and English language articles on RV-associated diarrhea in children under 5 years of age in China, published between January 2013 and December 2023. For Chinese-language publications, inclusion was restricted to studies indexed in nationally recognized core journal catalogs, namely the Peking University Core Journals, China Science and Technology Paper Citation Database, and China Science Citation Database<sup>15</sup>. The literature search was conducted using the following Boolean operators: (RV OR “Human RV” OR HRV) AND (Infant OR Child OR Baby OR Newborn OR Pediatric OR Toddler OR Preschool OR Kindergarten) AND (Diarrhea OR Epidemiology OR Incidence OR Prevalence OR Mortality OR Severity OR Sequelae OR Etiology OR Complication) (Supplementary Appendix 2). The reference lists of the selected articles were screened manually. The inclusion criteria were as follows: (1) studies reporting laboratory-confirmed RV-associated diarrhea cases in children under 5 years of age; (2) studies reporting more than one clinically relevant outcome parameters (incidence rate, etiological pattern, genotype distribution, RV detection rate, seasonal variation, demographic characteristics [gender/age distribution], clinical manifestations, or long-term sequelae); and (3) studies employing standardized laboratory confirmation methods for RV identification (enzyme-linked immunosorbent assay, reverse transcription-polymerase chain reaction, viral culture, indirect immunofluorescence assay, electron microscopy, latex agglutination testing, immunochromatographic assays, or polyacrylamide gel electrophoresis). The exclusion criteria were as follows: (1) reviews, meta-analyses, case reports, animal studies, and duplicate publications; (2) studies involving non-representative populations, such as patients with low birth weight, chronic illness, atypical gastroenteritis, or HIV/AIDS; and (3) studies conducted in Hong Kong SAR, Macao, or Taiwan (China). Following an initial screening of the titles and abstracts, two researchers independently reviewed the full texts of potentially eligible articles. Any disagreements were resolved through consensus or by discussion with a third researcher.

### Data extraction and literature quality assessment

Bibliographic management was conducted using EndNote. Data extraction and quality assessment were performed independently by two researchers. The following information was collected from the eligible studies: number of positive RV cases, RV positivity rate, RV incidence, age category, gender characteristics, seasonal patterns, genotypes, hospitalization status, study design and complexity, and diagnostic or genotyping methods. Literature quality was assessed according to the Strengthening the Reporting of Observational Studies in Epidemiology checklist<sup>16</sup>, as well as the methodological insights provided by Sanderson et al.<sup>17</sup> and Fowkes et al.<sup>18</sup>. Participant selection methods, exposure and outcome variable measurement, and confounding factor control were selected as the primary criteria, while study design-specific bias sources and statistical approaches were selected as the secondary criteria. The overall risk of bias was quantified using a customized algorithm (Supplementary Appendix 3) implemented in Microsoft Excel. The algorithm independently evaluated each criterion based on a four-tier risk of bias classification: high, medium, low, or unclear. Ultimately, each study was assessed and classified as having a high, medium, or low risk of bias. A study was considered to have a high risk of bias if it contained at least one criterion that clearly indicated bias or at least two primary criteria suggesting potential bias or uncertainty. A medium risk of bias was assigned if two or more criteria indicated possible bias or uncertainty. Conversely, a study was classified as having a low risk of bias if no major criteria suggested bias and only minor criteria indicated possible bias or uncertainty.

### Data classification and integration

China is divided into seven distinct geographical regions, namely Northeast China, North China, East China, Central China, South China, Northwest China, and Southwest China<sup>19</sup>. The provinces were categorized into high-income, middle-income, and low-income groups based on their gross regional product (GRP) per capita relative to the national average<sup>20</sup>. The GRP per capita of the high-, middle-, and low-income groups were > 120%, 80–120%, and < 80% of the national average (\$15,133.11), respectively.

### Statistical analysis

RV prevalence was calculated as the number of RV-positive cases divided by the total number of tested cases. A meta-analysis of the pooled proportions was conducted using the Metafor package in the R (v4.3.1) software, with pooled estimates derived using the Mantel–Haenszel method. Heterogeneity was assessed by calculating the  $I^2$  statistic. Substantial heterogeneity ( $I^2 \geq 50\%$ ,  $p < 0.05$ ) was addressed by a random-effects model applied using the DerSimonian–Laird method<sup>17</sup>. Publication bias was evaluated using Egger’s test and visualized using a funnel plot<sup>21</sup>.

## Results

### Literature selection

A total of 9,281 articles were initially identified from online databases, along with 24 additional articles retrieved through manual searches of references and citations. After removing 1,026 duplicate records and excluding 227 articles that were published in minor journals, we selected 8,052 articles for title and abstract screening. Following this, 7,507 articles were excluded, leaving 545 for full-text review. Ultimately, 73 articles that met the inclusion criteria were selected for meta-analysis. Among these, 69 reported only on RV positivity rates, 3 exclusively reported on RV incidence, and 1 provided data on both RV positivity rate and incidence. Additionally, we included four articles on RV-related diarrhea incidence for qualitative description (Fig. 1). Of the 73 included articles, 19 were published in English, while 54 were in Chinese. A detailed description of the search strategy is provided in Supplementary Appendix 2, while details about the authors, publication year, study location (province), participant age, specimen type, diagnostic methods, sample size, and research outcomes are presented in Supplementary Appendices 4 and 5. The quality assessment of articles reporting RV positivity rates is presented in Supplementary Appendix 3.

### Basic characteristics of included articles

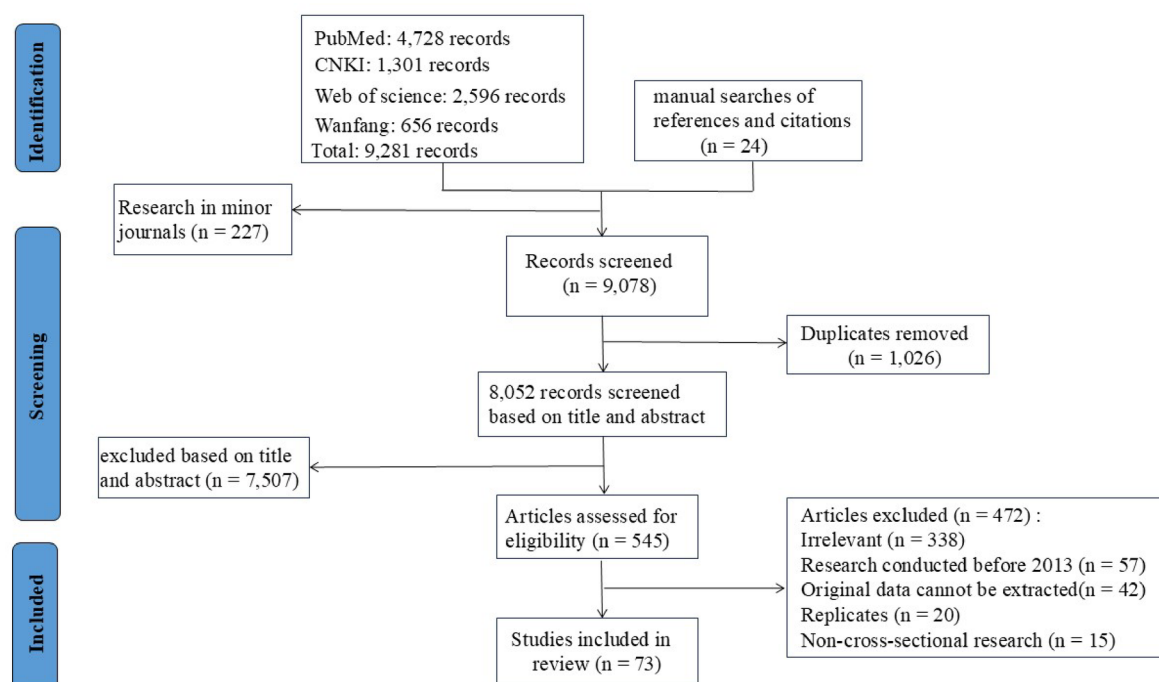
The majority of RV infections were reported from hospitals. Of the included studies, 60 (82.2%) were hospital-based, while 13 (17.8%) used data from NNIDSS. A total of 34 (46.5%) articles reported only on RV testing, while 36 (49.3%) articles reported on testing for multiple pathogens, including RV, norovirus, and enteric adenovirus. Additionally, 66 (94%) articles reported on the clinical diagnostic criteria for RV-related diarrhea. In terms of the healthcare settings, 33 (47%) articles considered outpatients, 19 (27%) considered inpatients, 7 (10%) considered both outpatients and inpatients, and 11 (16%) had unspecified study population. Further details about the selected articles are available in Supplementary Appendix 4.

### Incidence of RV-related diarrhea

Four population-based studies reported on the incidence of RV-related diarrhea in children under 5 years of age. Luo<sup>22</sup> reported an average annual national incidence of 0.637 /1000 persons between 2005 and 2018. Ding et al.<sup>23</sup> reported an incidence of 12.7 per 1,000 person-years in Zhongshan (Guangdong, China) from 2015 to 2021; Zhou et al.<sup>24</sup> reported an incidence of 21.8 per 1000 person-years in Sanjiang (Guangxi, China) in 2013; and Chen et al.<sup>25</sup> reported an incidence of 31.46 per 1000 person-years in Yuhuan (Zhejiang, China) from December 2016 to April 2017. Further details about these population-based studies are provided in Supplementary Appendix 5.

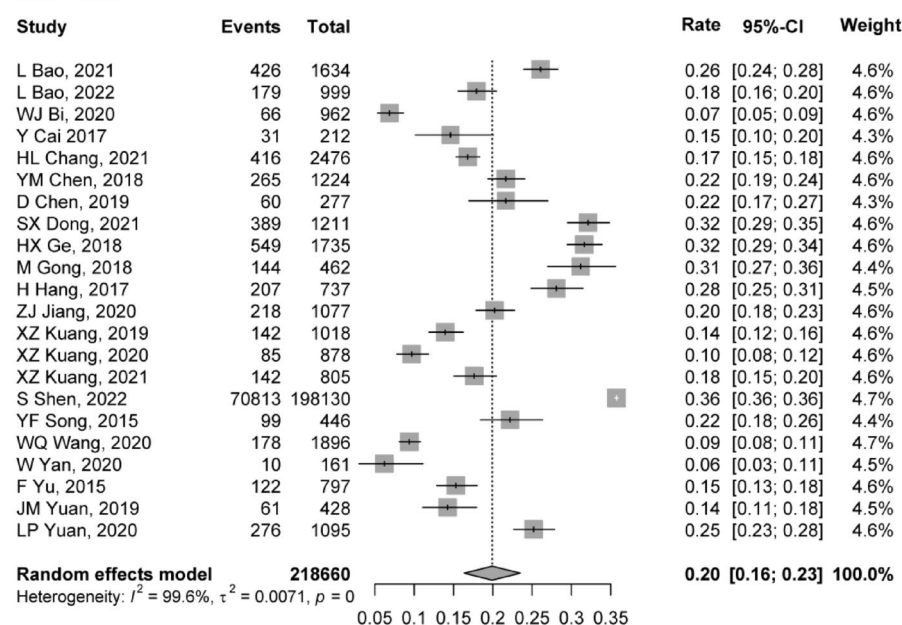
### RV positivity rates

This meta-analysis involved a total 70 studies, which investigated the RV positivity rate, encompassing 605,466 pediatric diarrhea cases in China. The pooled RV detection rate for the under-5 age group was 24.7%. The highest RV prevalence occurred in children aged 1–2 y (36 studies,  $n = 101,419$ ), with 36.4% (95% CI 31.5–41.3) RV positivity rate. RV positive rate showed a gradual decline among the older pediatric age groups, being 28.4% in 2–3 y-olds (27 studies), 21.4% (95% CI 15.8–27.1) in 3–4 y-olds, and 16.4% (95% CI 12.4–20.5) in 4–5 y-olds.



**Fig. 1.** Flow diagram of literature search and selection.

## East China



## South, Southwest and Central China

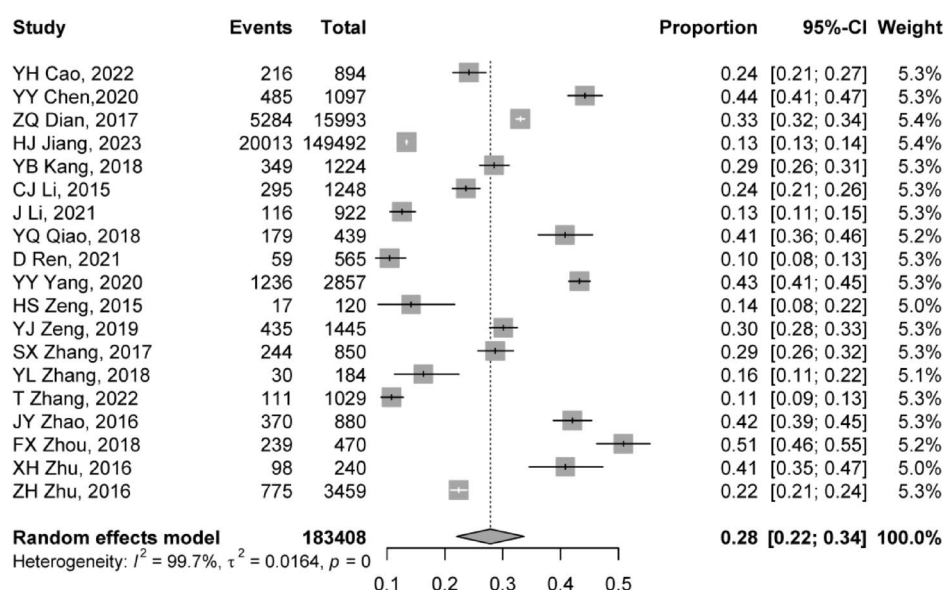


Fig. 2. Forest plots of RV infections in different geographical regions of China.

Hospitalized patients demonstrated a 24.1% RV positivity rate and the outpatient cohorts exhibited a 22.2% (95% CI 17.5–27.0) RV positivity rate. Studies encompassing both inpatients and outpatient settings recorded the highest pooled RV prevalence of 28.5%. A pooled analysis of 56 studies ( $n = 115,330$  cases) demonstrated a pooled RV positivity rate of 27.3% (95% CI 24.2–30.3) before the marketing authorization of the RotaTeq<sup>®</sup> vaccine in 2018. In contrast, pooled analysis of 25 studies ( $n = 803,286$  cases) revealed a significant reduction in the RV positivity rate (21.5%) (95% CI 17.0–25.9) following RotaTeq<sup>®</sup> licensure. A pooled analysis of 46 pre-COVID 19 studies ( $n = 316,968$  cases) revealed an RV positivity rate of 28.8%. In contrast, analysis of 5 post-pandemic studies ( $n = 33,936$  cases) showed a marked reduction in the RV positivity rate (22.5%, 95% CI 12.7–32.2). A total of 18 studies conducted in winter showing the highest pooled positivity rates of 39.3%. Spring and autumn exhibited comparable RV positivity rates (25.1% and 24.2%), while summer (17 studies) recorded the lowest point at 12.9% (95% CI 7.9–18.0). The RV prevalence for east, north, south and central part of China were shown in Fig. 2. Geographical stratification showed that Northeast China (3 studies) had the highest RV positivity rates (29.7%, 95% CI 4.8–54.5), followed by Central China (27.9%, 95% CI 15.8–39.9), South China (27.5%, 95% CI 10.1–44.8), and Southwest China (27.4%, 95% CI 19.4–35.4), which demonstrated similar prevalence patterns



## North, Northeast, and Northwest China

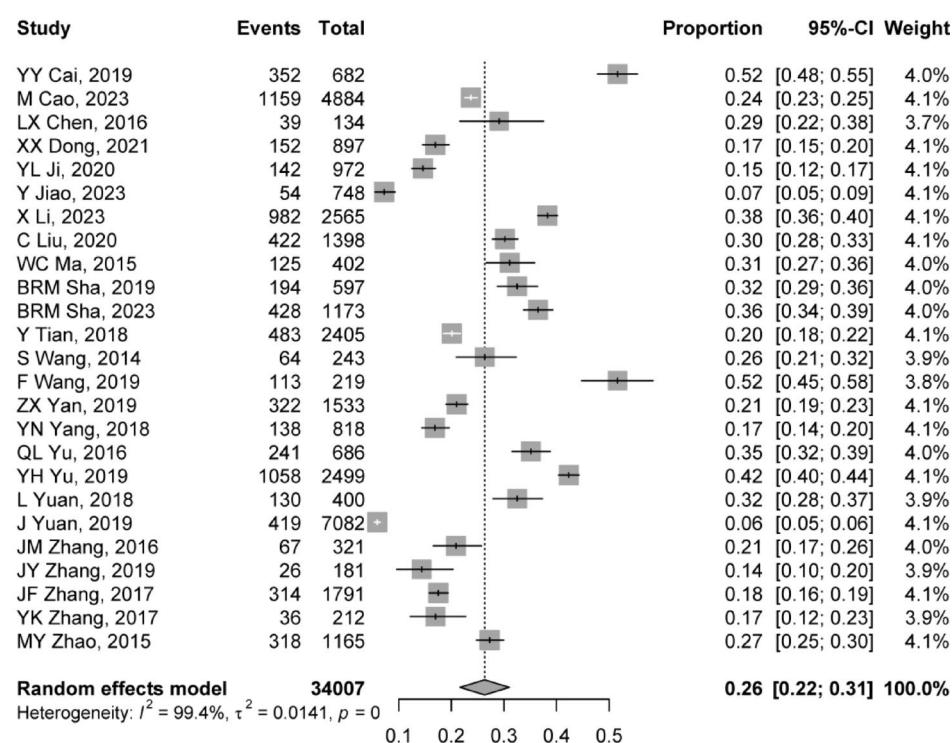


Figure 2. (continued)

( $I^2 \geq 98.6\%$ ,  $p < 0.0001$ ). Notably, East China (22 studies) showed the lowest regional RV prevalence (19.9%, 95% CI 16.4–23.5) despite contributing the largest sample ( $n = 218,660$ ). Low-income regions exhibited the highest RV detection rate (32.2%, 95% CI 26.7–37.7), followed by the middle-income (24.4%, 95% CI 19.0–29.8) and high-income (20.5%, 95% CI 17.3–23.6) regions (Tables 1 and 2).

## Prevalence of different RV genotypes

The prevalence of RV G9 genotype (24 studies) was estimated to be 69.6% (95% CI 60.6–78.5), while that of the RV G3 and G1 genotype was 10.7% and 7.0% respectively. The prevalence of the RV P8 genotype (24 studies) was 82.1% (95% CI 74.5–89.7). Among the G-P genotypes, G9P[8] (22 studies) exhibited the highest prevalence, at 71.7% (95% CI 64.9–78.6). The G3P[8] and G1P[8] genotypes exhibited prevalence at 9.5% and 6.2% respectively (Table 3). The prevalence of G9P[8] rose from 50.3% (95% CI 26.8–73.8) in 2013 to 93.6% (95% CI 87.4–99.9) in 2020, emerging as the dominant circulating genotype in China (Supplementary Appendix 6).

## Publication bias

Egger's test revealed no significant publication bias among the 70 included studies (0.21; 95% CI 0.15–0.26,  $p = 0.067$ ). Funnel plots illustrating the RV positivity distribution are provided in Supplementary Appendix 7.

## Discussion

Our study found that only four studies have investigated the incidence RV-related diarrhea, with the incidence ranging from 0.637 per 100,000 to 31.6 per 100,000 persons. The substantial disparities in the findings may be attributed to the distinct surveillance methods employed across the studies. Our study also revealed a 24.7% RV positivity rate among children under 5 years of age in China. The RV positivity rates decreased from 27.3 to 21.5% pre- and post- the RotaTeq<sup>®</sup> approval and declined from 28.8 to 22.5% before and after the COVID-19 pandemic. The prevalence of G9P[8] rose from 50.3% in 2013 to 93.6% in 2020.

Our analysis identified peak RV positivity in children aged 1–2 y. The age-dependent factors (waning maternal immunity; exploratory behaviors; and sanitation disparities) may drive the high RV positive rate in this age group<sup>26–28</sup>. Considering the high prevalence of RV infections within the 0–3 age group, our findings corroborate WHO recommendations for prioritizing RV vaccination within the first 24 months, optimally initiated at 6–12 months, to bridge critical immunity gaps<sup>29</sup>. In addition, our study revealed a higher RV positivity rate among hospitalized patients (24.1%) compared to outpatients (22.2%). This could be attributed to the fact that the clinical severity of inpatients is higher than that of outpatients. This finding corroborates African epidemiological data (2009–2022)<sup>30</sup>, where RV prevalence was estimated to be 25.0% (95% CI 17.8–33.0%) in ambulatory gastroenteritis cases and 33.2% (95% CI 31.1–35.4%) in hospitalized patients.

Our study showed peak positivity rates during winter (39.3%) and spring (25.1%). Under low-temperature conditions, rotavirus has a longer survival time in the environment, thereby increasing the opportunity for

	Total patients	RV-positive patients	RV positive rate (%; 95% CI)	I <sup>2</sup> (%)	P-value	Number of included articles
Age groups						
0–1 y	177,651	49,728	25.5 (21.0–29.9)	99.5	< 0.0001	35
0–6 m	87,029	21,799	17.4 (13.5–21.3)	99.6	< 0.0001	34
6–12 m	88,289	27,432	32.4 (27.3–37.6)	98.0	< 0.0001	31
1–2 y	101,419	37,630	36.4 (31.5–41.3)	99.0	0	36
2–3 y	42,385	15,241	28.4 (22.1–34.7)	98.9	0	27
3–4 y	17,213	4629	21.4 (15.8–27.1)	97.0	< 0.0001	15
4–5 y	13,546	2808	16.4 (12.4–20.5)	94.6	< 0.0001	15
Healthcare setting						
Hospitalized patients	193,970	30,692	24.1 (19.7–28.4)	99.6	0	19
Outpatients	26,170	5698	22.2 (17.5–27.0)	98.4	< 0.0001	33
Inpatients and outpatients	352,143	110,947	28.5 (22.0–35.0)	99.9	0	7
Unspecified	23,591	6875	22.6 (14.9–30.3)	99.3	< 0.0001	11
Marketing authorization of RotaTeq <sup>®</sup>						
Pre-licensure	115,330	32,565	27.3 (24.2–30.3)	99.4	0	56
Post-licensure	803,286	163,522	21.5 (17.0–25.9)	99.8	0	25
COVID-19						
Pre-pandemic	316,968	104,165	28.8 (25.8–31.8)	99.6	0	46
Post-pandemic	33,936	6393	22.5 (12.7–32.2)	97.6	< 0.0001	5

**Table 1.** Stratified analysis on RV positivity in children under the age of 5 years in China. COVID-19, Coronavirus disease 2019; CI, confidence interval; and RV, rotavirus.

	RV-positive patients	Total patients	RV Positive rate (%; 95% CI)	I <sup>2</sup> (%)	P-value	Number of included articles
Seasonal distribution <sup>a</sup>						
Spring	17,957	60,005	25.1 (18.3–31.9)	99.6	0	19
Summer	13,878	61,333	12.9 (7.9–18.0)	99.7	0	17
Autumn	21,081	69,684	24.2 (18.0–30.5)	99.6	0	17
Winter	32,677	67,259	39.3 (30.5–48.1)	99.8	0	18
Regional distribution						
Northeast China	2192	5961	29.7 (4.8–54.5)	99.6	< 0.0001	3
North China	2785	11,946	24.4 (18.5–30.2)	98.1	< 0.0001	7
Northwest China	2801	16,100	27.4 (17.9–36.9)	99.5	0	3
Central China	1739	7184	27.9 (15.8–39.9)	98.9	< 0.0001	8
Southwest China	22,731	157,766	27.4 (19.4–35.4)	99.6	0	8
South China	797	2465	27.5 (10.1–44.8)	98.6	< 0.0001	14
East China	74,878	218,660	19.9 (16.4–23.5)	99.6	0	22
Economic distribution <sup>b</sup>						
High-income regions	76,545	225,903	20.5 (17.3–23.6)	99.6	0	30
Middle-income regions	32,498	137,646	24.4 (19.0–29.8)	99.6	0	20
Low-income regions	31,401	183,596	32.2 (26.7–37.7)	99.7	0	17

**Table 2.** Seasonal, regional, and economic distribution of RV infections. <sup>a</sup>Spring: 1 March to 31 May; Summer: 1 June to 31 August; Autumn: 1 September to 30 November; and Winter: 1 December to 28/29 February.

<sup>b</sup>High-income regions: GRP pc > 20%; middle-income regions: GRP pc between 80 and 120%; and low-income regions GRP pc < 80% of the national average (\$15133.11).

transmission<sup>31–33</sup>. Northeast China demonstrated the highest RV prevalence (29.7%), while East China exhibited lower RV prevalence rates (19.9%). This discrepancy may be attributed to a combination of temperature factors and differences in RV vaccination coverage rates<sup>34</sup>.

Our study demonstrated a decline in the RV positivity rates from 27.3 to 21.5% following the marketing authorization of RotaTeq<sup>®</sup> in 2018. Several countries with high RV vaccine coverage have documented the substantial reductions in the incidence of rotavirus gastroenteritis (RVGE). A study conducted in the United States found that RotaTeq<sup>®</sup> administration is associated with a 66% reduction in RVGE-related hospitalizations and a 74% decrease in associated healthcare costs<sup>13</sup>. Similarly, in Finland, the integration of RotaTeq<sup>®</sup> into

Genotypes	RV-positive patients	Total patients	RV prevalence (%; 95% CI)	I <sup>2</sup> (%)	P-value	Number of included articles
RV	157,217	605,466	24.7 (22.1–27.4)	99.8	<0.0001	70
G9	6472	9250	69.6 (60.6–78.5)	99.8	0	24
G3	753	8446	10.7 (6.0–15.4)	95.8	<0.0001	23
G1	684	8044	7.0 (4.1–9.9)	96.8	<0.0001	20
G2	434	7305	6.7 (4.1–9.2)	90.0	<0.0001	18
G4	54	5437	1.0 (0.5–1.5)	77.4	<0.0001	10
G8	70	3297	2.5 (0.03–4.91)	91.5	<0.0001	6
P8	7181	9247	82.1 (74.5–89.7)	99.9	0	24
P4	746	8298	7.6 (4.7–10.5)	95.5	<0.0001	18
P6	136	5742	2.3 (0.5–4.0)	93.1	<0.0001	10
P9	31	2491	1.14 (0.29–1.98)	80.0	0.0018	4
P11	13	1369	3.3 (0–9.8)	77.9	0.0333	2
P5	1	142	0.7 (0.02–3.7)	/	/	1
G9P[8]	6378	9022	71.7 (64.9–78.6)	97.8	<0.0001	22
G3P[8]	594	7555	9.5 (5.7–13.3)	94.7	<0.0001	21
G1P[8]	407	5881	6.2 (3.2–9.2)	95.6	<0.0001	16
G2P[4]	326	6561	5.3 (3.3–7.3)	88.6	<0.0001	15
G9P[4]	65	5585	1.1 (0.5–1.7)	72.3	0.0002	10
G2P[8]	42	3453	1.3 (0.2–2.3)	74.7	0.0006	7
G8P[8]	57	1849	5.7 (0.03–11.4)	92.2	<0.0001	3

**Table 3.** Meta-analyses of P, G, and PG genotypes of RV (2013–2023).

the National Immunization Program resulted in a 90% reduction in both RVGE-related hospitalizations and outpatient clinic visits<sup>35</sup>. Similar results have been reported among children in South Australia<sup>14</sup>, Northeast Poland<sup>36</sup>, and Taiwan, China<sup>37</sup>.

From a genotypic perspective, G9P[8] exhibited the highest RV positivity rate (71.7%) among the under-5 age group in China. A meta-analysis of 361 studies<sup>38</sup> from 2005 to 2023 conducted in 204 countries found that following the introduction of RotaTeq<sup>®</sup> or Rotarix<sup>®</sup>, the prevalence of the G9P[8] genotype decreased from 17 to 7.6% globally, indicating that the vaccine may influence the circulation of G9P[8] genotype. However, China showed the opposite trends in the G9P[8] genotype prevalence. The discrepancy could be attributed to insufficient rotavirus vaccination in China.

Following the COVID-19 pandemic, RV prevalence declined from 28.8 to 22.5%, consistent with the a nationwide, retrospective, case registry-based surveillance study conducted in Finland<sup>39</sup>, which reported that compared with the pre-pandemic period (2018–2019), the incidence of gastroenteritis-related healthcare visits among under-5 children decreased by 46% in 2020 (from 703 to 381 per 100,000). Similar trends have also been observed in Germany<sup>40</sup>, Japan<sup>41</sup>, and Australia<sup>42</sup>. These findings suggest that the non-pharmaceutical interventions to control COVID-19 may have inadvertently contributed to reducing the transmission of various viruses, including RV<sup>43,44</sup>.

## Limitations

Notwithstanding these insights, several constraints in our study warrant acknowledgment. First, significant heterogeneity was evident across included studies, manifesting as marked variability in the reported effect sizes. This inconsistency likely stems from inter-study differences in demographic sampling frameworks, geographic representativeness, and RV ascertainment methodologies. Second, our strict inclusion criteria for Chinese publications may inadvertently exclude regionally relevant data, potentially introducing underrepresentation biases. Lastly, while our analysis identified a temporal correlation between RotaTeq<sup>®</sup> authorization and reduced RV positivity rates, establishing causality requires further evidence from controlled prospective studies.

## Conclusions

Despite the aforementioned limitations, this investigation establishes critical baseline data for assessing the rotavirus-associated diarrheal disease burden in China. Our analysis identified a concerning paucity of high-quality epidemiological studies quantifying rotavirus incidence, compounded by data source variations across existing studies. There is an urgent need for more standardized and rigorous studies focusing on incidence rates to accurately assess the disease burden of RV-related diarrhea. Our analysis also revealed slight shifts in the epidemiological profile of rotavirus infections pre- and post- RotaTeq<sup>®</sup> licensure. These findings suggest that the RotaTeq<sup>®</sup> vaccination may precipitate dynamic alterations in circulating viral genotypes. Accordingly, it is crucial to strengthen surveillance initiatives aimed at monitoring the incidence RV-related diarrhea and RV genotypes and boost rotavirus vaccination to curb the disease burden of RV-related diarrhea.

## Data availability

The datasets used and analyzed during the current study available from the corresponding author (Yaming Zheng) on reasonable request.

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## References

1. GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: A systematic analysis for the global burden of disease study 2017. *Lancet* **392**, 1736–1788. [https://doi.org/10.1016/S0140-6736\(18\)32203-7](https://doi.org/10.1016/S0140-6736(18)32203-7) (2018).
2. GBD 2017 Diarrhoeal Disease Collaborators. Quantifying risks and interventions that have affected the burden of diarrhoea among children younger than 5 years: An analysis of the global burden of disease study 2017. *Lancet Infect. Dis.* **20**, 3759. [https://doi.org/10.1016/S1473-3099\(19\)30401-3](https://doi.org/10.1016/S1473-3099(19)30401-3) (2020).
3. GBD 2016 Diarrhoeal Disease Collaborators. Estimates of the global, regional, and National morbidity, mortality, and aetiologies of diarrhoea in 195 countries: A systematic analysis for the global burden of disease study 2016. *Lancet Infect. Dis.* **18**, 1211–1228. [https://doi.org/10.1016/S1473-3099\(18\)30362-1](https://doi.org/10.1016/S1473-3099(18)30362-1) (2018).
4. Troeger, C. et al. Rotavirus vaccination and the global burden of rotavirus diarrhoea among children younger than 5 years. *JAMA Pediatr.* **172**, 958–965. <https://doi.org/10.1001/jamapediatrics.2018.1960> (2018).
5. Montasser, K. A., Youssef, M. I., Ghandour, A. A. & Kamal, M. Infection with adenovirus, rotavirus, and coinfection among hospitalized children with gastroenteritis in an Egyptian university hospital. *J. Med. Virol.* **94**, 4950–4958. <https://doi.org/10.1002/jmv.27935> (2022).
6. Makimaa, H., Ingle, H. & Baldrige, M. T. Enteric viral co-infections: Pathogenesis and perspective. *Viruses* **12**, 904. <https://doi.org/10.3390/v12080904> (2020).
7. Zhang, S. et al. Synergistic Effects of Rotavirus and Co-Infecting Viral Enteric Pathogens on Diarrheal Disease - Guangzhou City, Guangdong Province, China, 2019. *China CDC Wkly.* **5**, 725–730. <https://doi.org/10.46234/ccdcw2023.138> (2023).
8. Ma, W. et al. Effectiveness of pentavalent rotavirus vaccine in Shanghai, China: A test-negative design study. *J. Pediatr.* **259**, 113461. <https://doi.org/10.1016/j.jpeds.2023.113461> (2023).
9. Fu, C., Tate, J. E. & Jiang, B. Effectiveness of Lanzhou lamb rotavirus vaccine against hospitalized gastroenteritis: Further analysis and update. *Hum. Vaccin.* **6**, 953. <https://doi.org/10.4161/hv.6.11.12847> (2010).
10. Kirkwood, C. D. & Steele, A. D. Rotavirus vaccines in China: Improvement still required. *JAMA Netw. Open.* **1**, e181579. <https://doi.org/10.1001/jamanetworkopen.2018.1579> (2018).
11. Writing Group for Expert Consensus on Rotavirus Gastroenteritis. Expert consensus on immunoprophylaxis of childhood rotavirus gastroenteritis (2024 version). *Chin. J. Prev. Med.* **58**, 421–453 (2024).
12. Plosker, G. L. Pentavalent rotavirus vaccine (RotaTeq): a review of its use in the prevention of rotavirus gastroenteritis in Europe. *Drugs* **70**, 1165–1188. <https://doi.org/10.2165/11205030-000000000-00000> (2010).
13. Wang, F. T., Mast, T. C., Glass, R. J., Loughlin, J. & Seeger, J. D. Effectiveness of the pentavalent rotavirus vaccine in preventing gastroenteritis in the United States. *Pediatrics* **125**, e208–e213. <https://doi.org/10.1542/peds.2009-1246> (2010).
14. Clarke, M. F., Davidson, G. P., Gold, M. S. & Marshall, H. S. Direct and indirect impact on rotavirus positive and all-cause gastroenteritis hospitalisations in South Australian children following the introduction of rotavirus vaccination. *Vaccine*, **29**, 4663–4667. <https://doi.org/10.1016/j.vaccine.2011.04.109> (2011).
15. Peking University Library. Chinese core journals. (2020). <https://www.zzqklm.com/w/hxml/28462.html> (2024).
16. Von Elm, E. et al. The strengthening of reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Lancet* **370**, 1453–1457. [https://doi.org/10.1016/S0140-6736\(07\)61602-X](https://doi.org/10.1016/S0140-6736(07)61602-X) (2007).
17. Sanderson, S., Tatt, I. D. & Higgins, J. P. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: A systematic review and annotated bibliography. *Int. J. Epidemiol.* **36**, 666–676. <https://doi.org/10.1093/ije/dym018> (2007).
18. Fowkes, F. G. & Fulton, P. M. Critical appraisal of published research: Introductory guidelines. *BMJ* **302**, 1136–1140. <https://doi.org/10.1136/bmj.302.6785.1136> (1991).
19. Yu, J. et al. Prevalence of rotavirus and rapid changes in circulating rotavirus strains among children with acute diarrhea in China, 2009–2015. *J. Infect.* **78**, 66–74. <https://doi.org/10.1016/j.jinf.2018.07.004> (2019).
20. National Bureau of Statistics of China. Gross Regional Product (GRP) per capita by province, 2013–2023. in *National Bureau of Statistics of China* (2024). <http://data.stats.gov.cn/easyquery.htm?cn=E0103>.
21. Baek, M. H. et al. Secondary cytoreductive surgery in Platinum-Sensitive recurrent ovarian cancer: A meta-analysis. *J. Clin. Oncol.* **40**, 1659–1670. <https://doi.org/10.1200/JCO.21.02085> (2022).
22. Luo, H. et al. Analysis of epidemiological characteristics of report cases of rotavirus diarrhea in children under 5 years old in China, 2005–2018. *Chin. J. Prev. Med.* **54**, 181–186 (2020).
23. Ding, J. et al. Epidemiological characteristics of rotavirus diarrhea in Zhongshan City from 2015 to 2021. *Mod. Prev. Med.* **50**, 1316–1320 (2023).
24. Zhou, H. L. et al. Burden and etiology of moderate and severe diarrhea in children less than 5 years of age living in North and South of China: prospective, population-based surveillance. *Gut Pathog* **13**, 33. <https://doi.org/10.1186/s13099-021-00428-2>.
25. Chen, D. et al. Investigation on rotavirus diarrhea in infants aged two years and below in Yuhuan. *Prev. Med.* **31**, 628–630 (2019). (in Chinese).
26. Petri, W. A. Jr et al. Enteric infections, diarrhea, and their impact on function and development. *J. Clin. Invest.* **118**, 1277–1290. <https://doi.org/10.1172/JCI34005> (2008).
27. Ethelberg, S. et al. Risk factors for diarrhea among children in an industrialized country. *Epidemiology* **17**, 24–30. <https://doi.org/10.1097/01.ede.0000187621.41373.0a> (2006).
28. Baker, K. K. et al. Sanitation and hygiene-specific risk factors for moderate-to-severe diarrhea in young children in the global enteric multicenter study, 2007–2011: Case-control study. *PLoS Med.* **13**, e1002010. <https://doi.org/10.1371/journal.pmed.1002010> (2016).
29. Rotavirus vaccines. WHO position paper-January. *Wkly. Epidemiol. Rec.* **88**, 49–64 (2013).
30. Njifon, H. L. M. et al. Epidemiology of rotavirus in humans, animals, and the environment in Africa: A systematic review and meta-analysis. *J. Infect. Dis.* **229**, 1470–1480. <https://doi.org/10.1093/infdis/jiad500> (2024).
31. Patel, M. M. et al. Global seasonality of rotavirus disease. *Pediatr. Infect. Dis. J.* **32**, e134–e147. <https://doi.org/10.1097/INF.0b013e31827d3b68> (2013).
32. Kraay, A. N. M. et al. Modeling environmentally mediated rotavirus transmission: the role of temperature and hydrologic factors. *Proc. Natl. Acad. Sci. U S A* **115**, E2782–E2790. <https://doi.org/10.1073/pnas.1719579115> (2018).
33. Romero-Maraccini, O. C., Shisler, J. L. & Nguyen, T. H. Solar and temperature treatments affect the ability of human rotavirus Wa to bind to host cells and synthesize viral RNA. *Appl. Environ. Microbiol.* **81**, 4090–4097. <https://doi.org/10.1128/AEM.00027-15> (2015).



34. Zhang, H. et al. Coverage and equity of childhood vaccines in China. *JAMA Netw. Open.* **5**, e2246005. <https://doi.org/10.1001/jamanetworkopen.2022.46005> (2022).
35. Hemming-Harlow, M., Markkula, J., Huhti, L., Salminen, M. & Vesikari, T. Decrease of rotavirus gastroenteritis to a low level without resurgence for five years after universal RotaTeq vaccination in Finland. *Pediatr. Infect. Dis. J.* **35**, 1304–1308. <https://doi.org/10.1097/INF.0000000000001305> (2016).
36. Toczyłowski, K. et al. Rotavirus gastroenteritis in children hospitalized in Northeastern Poland in 2006–2020: severity, seasonal trends, and impact of immunization. *Int. J. Infect. Dis.* **108**, 550–556. <https://doi.org/10.1016/j.ijid.2021.05.070>.
37. Chang, W. C. et al. Effectiveness of 2 rotavirus vaccines against rotavirus disease in Taiwanese infants. *Pediatr. Infect. Dis. J.* **33**, e81–e86. <https://doi.org/10.1097/INF.000000000000105> (2014).
38. Amin, A. B. et al. Rotavirus genotypes in the postvaccine era: A systematic review and Meta-analysis of global, regional, and Temporal trends by rotavirus vaccine introduction. *J. Infect. Dis.* **229**(5), 1460–1469. <https://doi.org/10.1093/infdis/jiad403> (2024).
39. Kuitunen, I., Artama, M., Haapanen, M. & Renko, M. Noro- and rotavirus detections in children during COVID-19 pandemic—a nationwide register study in Finland. *Acta Paediatr.* **111**, 1978–1980. <https://doi.org/10.1111/apa.16446> (2022).
40. Van de Berg, S. et al. Epidemiology of common infectious diseases before and during the COVID-19 pandemic in Bavaria, Germany, 2016 to 2021: an analysis of routine surveillance data. *Euro. Surveill.* **28**, 2300030. <https://doi.org/10.2807/1560-7917.ES.2023.28.41.2300030> (2023).
41. Okitsu, S. et al. Changing distribution of rotavirus A genotypes Circulating in Japanese children with acute gastroenteritis in outpatient clinic, 2014–2020. *J. Infect. Public. Health* **15**, 816–825. <https://doi.org/10.1016/j.jiph.2022.06.009> (2022).
42. Roczo-Farkas, S. et al. Annual Report. *Commun. Dis. Intell.* **46**. <https://doi.org/10.33321/cdi.2022.46.75> (2021).
43. Chan, M. C. Return of norovirus and rotavirus activity in winter 2020–21 in city with strict COVID-19 control strategy, China. *Emerg. Infect. Dis.* **28**, 713–716. <https://doi.org/10.3201/eid2803.212117> (2022).
44. Sawakami, T., Karako, K., Song, P., Sugiura, W. & Kokudo, N. Infectious disease activity during the COVID-19 epidemic in Japan: Lessons learned from prevention and control measures. *Biosci. Trends* **15**, 257–261. <https://doi.org/10.5582/bst.2021.01269> (2021).

## Author contributions

Y.M.Z. and L.W. conceived the original study concept. Y.M.Z. designed the search strategy. L.C. conducted the literature search and data extraction, supervised by B.T. and F.K. Z.C. and, Y.P.Z. conducted quality assessment of studies. L.C. conducted the statistical analysis. Y.M.Z. and L.C. wrote the first draft of the manuscript. All authors participated in the interpretation of data, have critically reviewed the manuscript and provided edits and comments, and approved its final submission.

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## Declarations

## Competing interests

The authors declare no competing interests.

## Additional information

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