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Trends in Rotavirus Laboratory Detections and Internet Search Volume Before and After Rotavirus Vaccine Introduction and in the Context of the Coronavirus Disease 2019 Pandemic—United States, 2000–2021

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Background. Since rotavirus vaccines became available in the United States in 2006, there have been reductions in rotavirus hospitalizations, changes in seasonality, and the emergence of a biennial trend of rotavirus activity. Reductions in other pathogens have been associated with coronavirus disease 2019 (COVID-19) mitigation measures. We assessed ongoing rotavirus disease trends during the COVID-19 pandemic.

Methods. We report a 3-week moving average of the number of rotavirus tests, positive tests, and the percent positivity from laboratories reporting to the National Respiratory and Enteric Virus Surveillance System (NREVSS) from July 2000 through June 2021. To complement NREVSS data, we analyzed Google internet search interest in "rotavirus" from July 2004 to June 2021.

Results. Declines in rotavirus activity following vaccine introduction and the biennial trend are evident through the 2018–2019 surveillance year. In 2019–2021, rotavirus test positivity was below the historic ranges during the months of typically high rotavirus activity, and precipitous declines were noted in March 2020.

Conclusions. In the 15 years since rotavirus vaccine was introduced, the number of laboratory-detected rotavirus infections has been consistently lower than during the prevaccine era. During the COVID-19 pandemic, rotavirus activity was suppressed. There may be many rotavirus-susceptible children during the 2021–2022 rotavirus season.

Keywords. rotavirus; rotavirus vaccine; diarrhea.

In 2006, 2 live oral rotavirus vaccines (Rotarix, GlaxoSmithKline Biologicals, Rixensart, Belgium) and RotaTeq (Merck & Co, West Point, Pennsylvania) became available to infants in the United States (US) [1]. Rotavirus vaccines are >80% effective in preventing hospitalizations and emergency department visits due to rotavirus diarrhea among children <5 years old in the US [1]. Population-level reductions in illness and hospitalizations among children age-eligible for rotavirus vaccination have occurred since introduction of the vaccines [1]. Additionally, there have been changes in the seasonality of rotavirus and the emergence of a trend where alternating years have high, sharp peaks in rotavirus activity followed by years of low levels of rotavirus activity [2–4].

In response to the emergence of SARS-CoV-2, the virus that causes COVID-19, many countries implemented nonpharmaceutical prevention measures beginning in early 2020 and continuing into 2021 to minimize the number of COVID-19 illnesses and deaths. Temporally associated reductions in the transmission of pathogens such as influenza, respiratory syncytial virus, and norovirus in countries worldwide may be attributable to physical distancing, mask use, and school closures, among other mitigation measures [5–20].

The rationale for this analysis was 2-fold. First, there are ongoing questions about rotavirus disease trends during the postvaccine era in the US, including changes to seasonality and the long-term stability of the biennial trend. Second, the impact, if any, of COVID-19 and associated mitigation measures on rotavirus disease in the US has not been explored or described. In this evaluation, we assessed rotavirus disease trends in the US before and after the introduction of rotavirus vaccines and in the context of the COVID-19 pandemic.

METHODS

This report includes data from the National Respiratory and Enteric Virus Surveillance System (NREVSS), a national passive laboratory surveillance network that collects the number of weekly aggregate rotavirus tests and rotavirus-positive results by laboratory diagnostic method category. We calculated

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weekly percent positivity from the aggregated number of rotavirus tests and rotavirus-positive tests submitted by participating NREVSS laboratories from July 2000 through June 2021. Enzyme immunoassay (EIA) tests are reported for the entire period; however, polymerase chain reaction (PCR) results are only included beginning in 2012 as PCR test results in NREVSS are limited in earlier years. Additionally, the laboratories reporting PCR tests were limited to pediatric hospital laboratories or laboratories submitting data from a pediatric unit or units as children <5 years old are more likely to have severe rotavirus disease. Because PCR multipathogen panel tests are becoming more common, this requirement was intended to prevent diluting the total number of tests with those not ordered for suspected rotavirus. This surveillance system is unable to provide information about the number of rotavirus-specific tests and multipathogen panel tests ordered. Laboratories could be included in both EIA and PCR analyses during the same surveillance year. Surveillance year was defined as July (epidemiological week 27) to June (epidemiological week 26) of the following year.

To complement information about medically attended rotavirus infections from NREVSS, we also analyzed monthly internet search volume of the term "rotavirus" from Google (google.com/trends) from July 2004 through June 2021. A previous analysis found that NREVSS and internet search volume are correlated [21]. Monthly internet search volume was measured by internet query shares (IQS), a relative score of 0 to 100, where the month with the highest search interest has an IQS of 100.

Data from both systems were downloaded 2 August 2021. Data subsetting details and analytic methods are described for each analysis and summarized in Supplementary Table 1. All analyses were performed using SAS version 9.4 and R version 3.6.1 software.

Percent Positivity Over Time

We calculated the percent positivity of EIA and PCR rotavirus tests from any participating NREVSS laboratory. We then calculated an unweighted 3-week moving average with the weekly EIA and PCR percent positive from the preceding and following weeks for July 2000–June 2021 for the EIA plot and July 2012–June 2021 for the PCR plot. We also plotted the monthly IQS from July 2004 through June 2021.

To assess the statistical significance of declines in rotavirus from the vaccine period before the pandemic (2007–2019) to the pandemic period (2020–2021), we fit a negative binomial model to the EIA, IQS, and PCR time-series data to predict the expected weekly rotavirus positivity or monthly IQS in the absence of the COVID-19 pandemic. We adjusted for seasonality by including week or calendar month, and secular trends by including year of admission. We assessed model fit with the Pearson χ^2 statistic.

Year-Over-Year Rotavirus Activity

For NREVSS data, we determined the weekly range of the unweighted 3-week moving average of rotavirus EIA percent positivity across surveillance years. For Google Trends data, we calculated the monthly range of rotavirus IQS across surveillance years. We grouped surveillance years into 3 periods to match earlier analyses [2]: before rotavirus vaccine introduction (2000–2001, 2001–2002, 2002–2003, 2003–2004, 2004–2005, 2005–2006), odd peak season surveillance years post–vaccine introduction (2008–2009, 2010–2011, 2012–2013, 2014–2015, 2016–2017, 2018–2019), and even peak season surveillance years post–vaccine introduction (2009–2010, 2011–2012, 2013–2014, 2015–2016, 2017–2018). The 2006–2007 surveillance year was excluded as a transition year. Internet search volume is not available before 2004 so IQS data from the prevaccine introduction surveillance years were limited to 2004–2005 and 2005–2006. For both data sources, the 2019–2020 and 2020–2021 surveillance years are presented individually. PCR tests were not included in the year-over-year analysis because pre–rotavirus vaccine introduction data are not available.

Absolute Number of Rotavirus Tests Over Time

We also present the 3-week moving average of the absolute number of rotavirus tests and positive results by EIA and PCR test type among continuously reporting NREVSS laboratories. For each diagnostic method, we defined continuously reporting laboratories as individual laboratories that reported ≥1 test for ≥26 weeks in every surveillance year during the defined period. For EIA tests, we considered the period for continuous reporting to be July 2015 through June 2020. For PCR tests, we considered the period for continuous reporting to be July 2017 through June 2020. These periods were chosen to maximize the number of laboratories meeting the continuous reporting criteria as few laboratories met the criteria for the full 20-year surveillance period.

RESULTS

Percent Positivity Over Time

Rotavirus-positive EIA tests and internet search volume had a distinct seasonality before and after rotavirus vaccine introduction in 2006, with higher weekly percent positivity in the winter and early spring and lower positivity in the summer and fall (Figure 1). In the prevaccine period, the median annual percent positivity of EIA tests was 25%. From the 2007–2008 surveillance year through 2014–2015, years with high peaks of weekly positivity had a median annual EIA positivity of 11% and alternated with years of lower rotavirus activity that had a median annual EIA positivity of 5% (Table 1). Similarly, tall peaks in the prevaccine era IQS were blunted in the postvaccine period; however, compared to trends in test positivity, there is less distinction between biennial years. Starting in the 2015–2016 surveillance year, the biennial pattern in EIA and PCR positivity

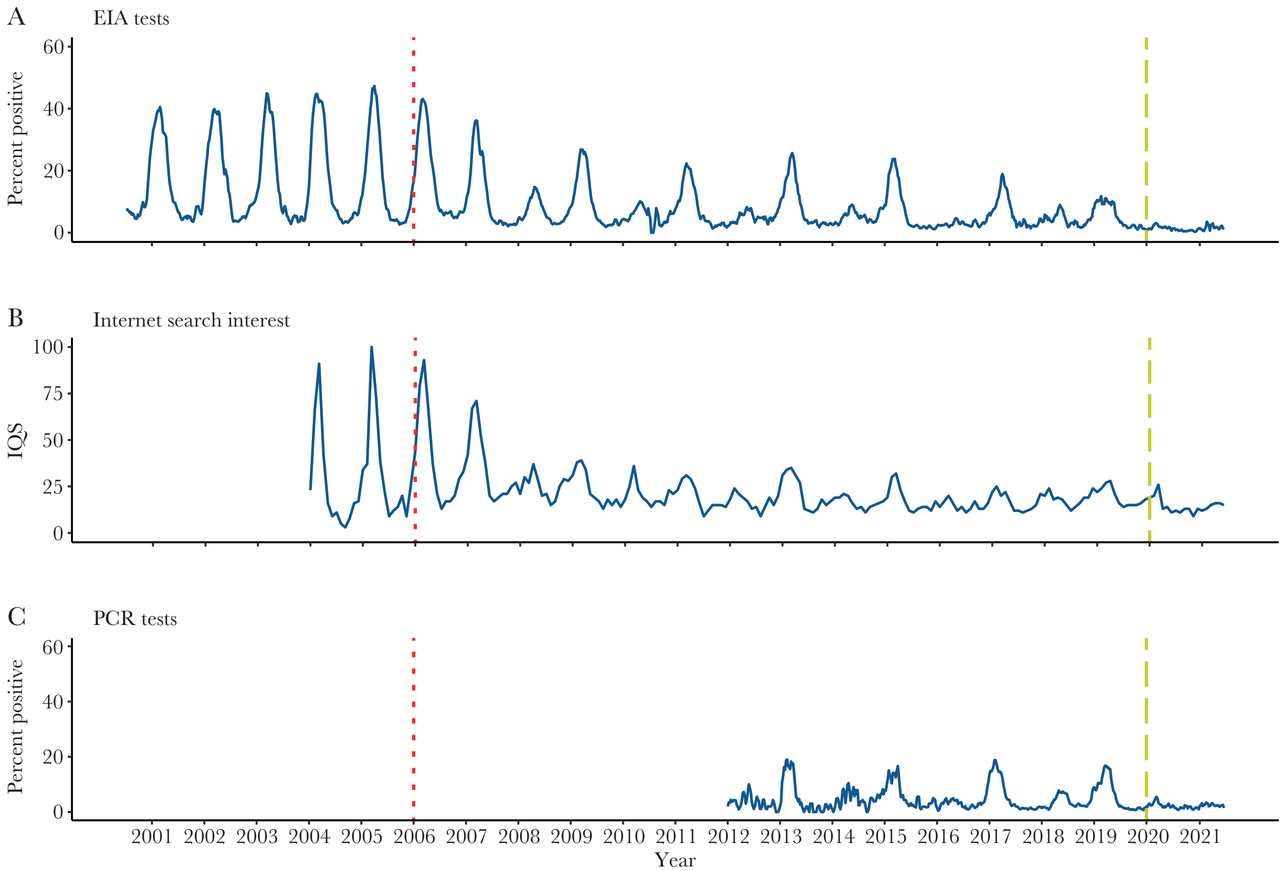

Figure 1. Three-week moving average of rotavirus enzyme immunoassay (EIA) and polymerase chain reaction (PCR) percent positivity among all laboratories reporting to the National Respiratory and Enteric Virus Surveillance System and monthly internet search volume measured as internet query shares (IQS)—United States, July 2000–June 2021. The dotted line shows 2006, when rotavirus vaccines became available, and the dashed line shows 2020, when the coronavirus disease 2019 pandemic began.

was still present, but median annual positivity was reduced, with 2% EIA and 3% PCR annual positivity in 2015–2016. The 2016–2017 surveillance year had a high, sharp season and 7% EIA and 8% PCR annual positivity; and 2017–2018 and 2018–2019 appear to have similar shapes with 4% EIA and 3% PCR annual positivity in 2017–2018 and 6% EIA and 7% PCR annual positivity in 2018–2019. There was no notable period of increased rotavirus activity in 2019–2020 (2% EIA and 2% PCR positivity) or 2020–2021 (1% EIA and 2% PCR positivity). Rotavirus IQS increased to 27 IQS in March 2020 before a precipitous decline to 15 IQS in April 2020, after which IQS remained low.

Time series models showed a 73% (95% confidence interval [CI], 67%–79%) decline between the postvaccine period and the COVID pandemic period in EIA positivity ($P < .001$), a 4% (95% CI, −12% to 19%) decline in IQS ($P = .256$), and an 85% (95% CI, 80%–87%) decline in PCR positivity ($P < .001$).

Year-Over-Year Rotavirus Activity

The declines in rotavirus test positivity following rotavirus vaccine introduction and the subsequent biennial trend are also evident in year-over-year analyses. Compared to the period before rotavirus vaccine introduction, EIA positivity during the rotavirus season and peak week were reduced and delayed in the post–rotavirus vaccine introduction odd season surveillance years while positivity during even season surveillance years was so much lower that the 10% threshold, used as an indicator of the rotavirus season, was surpassed during just 1 week in the NREVSS data (Figure 2A). In the postvaccine era, between January (epidemiological week 1) and April (epidemiological week 17), the minimum and maximum weekly rotavirus percent positive in odd season surveillance years was 6% and 27%, respectively, while the minimum and maximum weekly rotavirus percent positive in even season surveillance years was 2% and 10%, respectively. The rotavirus IQS mirrored these patterns, though there is less distinction between even and odd season surveillance years (Figure 2B). Between January and April, the minimum and maximum monthly IQS during odd season surveillance years was 19 and 39, respectively, while the minimum and maximum monthly IQS during even season surveillance years was 14 and 36, respectively.

The 3-week moving average percent positivity during the 2019–2020 surveillance year (the dotted line in Figure 2A) was within the historic even season surveillance year range for 18 of the 26 weeks from July through December 2019, typically

Table 1. Annual Number of Rotavirus Tests, Number of Positive Tests, and Percent Positivity Among All Laboratories Reporting Enzyme Immunoassay and Polymerase Chain Reaction Tests to the National Respiratory and Enteric Virus Surveillance System—United States, July 2000–June 2021

	Enzyme Immunoassay			Polymerase Chain Reaction		
Surveillance Year	Total Tests	Total Positive	Percent Positivity	Total Tests	Total Positive	Percent Positivity
2000–2001	27 326	6569	24	…	…	…
2001–2002	21 421	5271	25	…	…	…
2002–2003	24 158	5713	24	…	…	…
2003–2004	25 124	6858	27	…	…	…
2004–2005	26 469	6521	25	…	…	…
2005–2006	34 891	8567	25	…	…	…
2006–2007	35 676	6364	18	…	…	…
2007–2008	43 588	3008	7	…	…	…
2008–2009	52 525	6676	13	…	…	…
2009–2010	33 787	1641	5	…	…	…
2010–2011	17 936	1973	11	…	…	…
2011–2012	15 265	612	4	976	41	4
2012–2013	15 235	1734	11	2270	168	7
2013–2014	19 730	866	4	1831	61	3
2014–2015	25 452	2788	11	2773	199	7
2015–2016	20 148	470	2	5612	176	3
2016–2017	17 701	1193	7	12 707	988	8
2017–2018	14 737	577	4	16 767	496	3
2018–2019	12 927	795	6	18 908	1324	7
2019–2020	15 631	281	2	16 712	314	2
2020–2021	10 676	108	1	14 448	304	2

months of limited rotavirus activity. During the second half of the surveillance year from January through June 2020, positivity was within the historic range for 5 of 26 weeks, the week beginning 17 February (epidemiological week 8) through the week beginning 16 March (epidemiological week 12). During the 2020–2021 surveillance year (the dashed line in Figure 2A), the 3-week moving average positivity was outside the historic odd season surveillance year range for 49 weeks; it was within the historic range the week beginning July 6 (epidemiological week 28) through the week beginning July 20 (epidemiological week 30).

Broadly, the monthly IQS followed a similar pattern. During the 2019–2020 surveillance year (the dotted line in Figure 2B), it was within or above the historic even season surveillance year range during all 6 months during the first half of the surveillance year and outside the historic range during April and June. During the 2020–2021 surveillance year (the dashed line in Figure 2B), it was outside the historic odd season surveillance year range during 8 months; it was within the historic range in July, August, October, and June.

Absolute Number of Rotavirus Tests Over Time

The annual number of EIA rotavirus tests among 30 continuously reporting laboratories declined from 12 382 in the 2014–2015 surveillance year to 8054 EIA tests in 2019–2020 (Figure 3A). The biennial trend is evident in the number of rotavirus-positive EIA tests, with sharp peaks of positive tests noted in 2014–2015, 2016–2017, and 2018–2019, when the peaks in the 3-week moving average in the number of positive tests were 76, 41, and 26, respectively. Including the period before 2014–2015, there is a clear biennial trend in total rotavirus tests through the 2015–2016 surveillance year, although the annual number of laboratories reporting any rotavirus tests ranged from 13 to 30 (Supplementary Table 2). The annual number of PCR tests among 9 continuously reporting laboratories increased from 16 750 in 2017–2018 to 18 912 in 2018–2019 and then declined slightly to 16 168 in 2019–2020 (Figure 3B). Even prior to the continuous reporting period, the biennial trend in number of rotavirus-positive PCR tests is evident. There are clear sharp peaks of rotavirus-positive tests in 2016–2017 and 2018–2019, when the peak in the 3-week moving average in the number of positive tests was 62 and 71, respectively. In the 2018–2019 surveillance year, the only odd season surveillance year in the continuous reporting periods for both tests, 11 March 2019 (epidemiological week 11) and 25 March 2019 (epidemiological week 13) were the weeks with the highest 3-week moving average of number of rotavirus-positive EIA and PCR tests, respectively.

There was a precipitous decline in EIA and PCR test volume in March 2020, when many places first began to implement COVID-19 mitigation measures. The first quarter of 2020 (epidemiological weeks 1–13) saw a median of 172 EIA and 345 PCR weekly tests. The second quarter of 2020 (epidemiological weeks 14–26) saw a median of 87 EIA and 191 PCR weekly tests, a 51% and 55% decline compared to the first quarter, respectively. The number of weekly PCR tests recovered in the beginning of 2021;

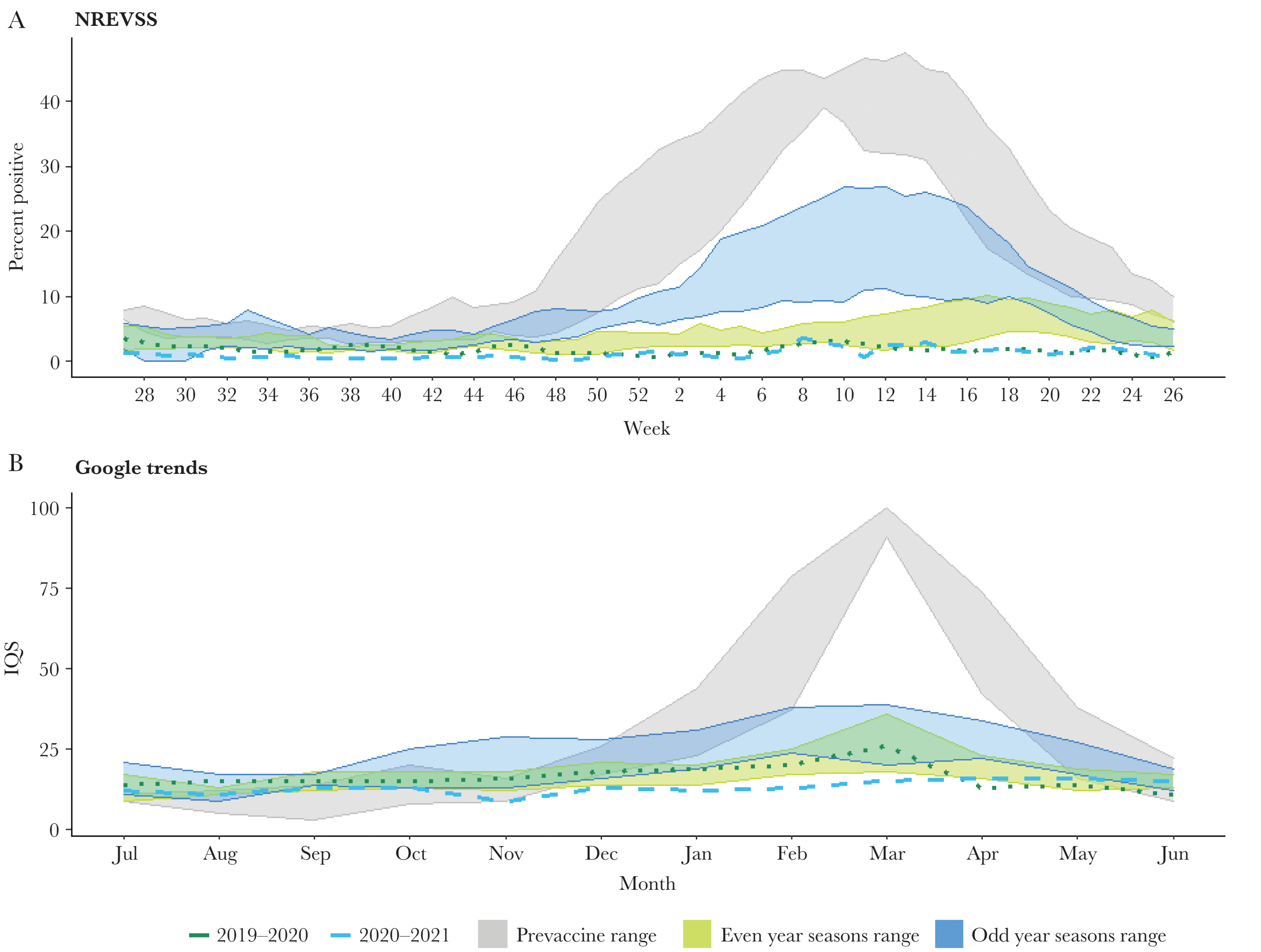

Figure 2. Pre–rotavirus vaccine, even season surveillance year and odd season surveillance year ranges, United States, July 2000–June 2021. *A*, Three-week moving average of rotavirus enzyme immunoassay percent positivity among all laboratories reporting to the National Respiratory and Enteric Virus Surveillance System (NREVSS). *B*, Internet search volume measured in internet query shares (IQS).

however, the number of weekly EIA tests had not reached pre-March 2020 levels by the end of June 2021. The second quarter of 2021 (epidemiological weeks 14–26) saw a median of 65 EIA and 389 PCR tests weekly. In the 2020–2021 surveillance year, 18 of 30 EIA laboratories and 8 of 9 PCR laboratories met the continuous reporting criteria (Supplementary Table 2).

DISCUSSION

In the 15 years since rotavirus vaccine was introduced in the US, the number of laboratory-detected rotavirus infections and the proportion of rotavirus-positive laboratory tests has been consistently lower than during the prevaccine era. These trends are mirrored in internet search patterns, which likely include rotavirus infections not requiring medical attention. In the first decade after rotavirus vaccine implementation, there was a distinct biennial trend of alternating high and low years, likely due to suboptimal rotavirus vaccine coverage [2–4]. This biennial trend has been found in a few other countries (eg, Haiti and Poland [18, 22]), although the high- and low-activity years are not the same across countries. Even prior to the pandemic, the percentage of children 12–23 months old who have received a full course of rotavirus vaccine in the US has remained substantially below that of other infant vaccines; among children born 2016–2017, coverage was estimated to be 75% for rotavirus vaccine and 93% for DTaP (diphtheria, tetanus, acellular pertussis) vaccine [23]. Suboptimal coverage leads to an accumulation of susceptible children over the 2-year period, resulting in a season of increased rotavirus activity. Additional years of total test and positivity data as well as the lack of biennial trend starting in 2017 in the IQS data indicate this pattern may have been evolving or deteriorating prior to the COVID-19 pandemic; however, we are unable to speculate further.

To the best of our knowledge, this is the first description of rotavirus surveillance data in the US during the COVID-19 pandemic. The 2 surveillance years during the pandemic included in this report statistically significantly less rotavirus activity. US rotavirus test positivity was below the usual weekly range in December 2019 and January 2020, before COVID-19 mitigation measures were widely adopted in the US. The 2020–2021 surveillance

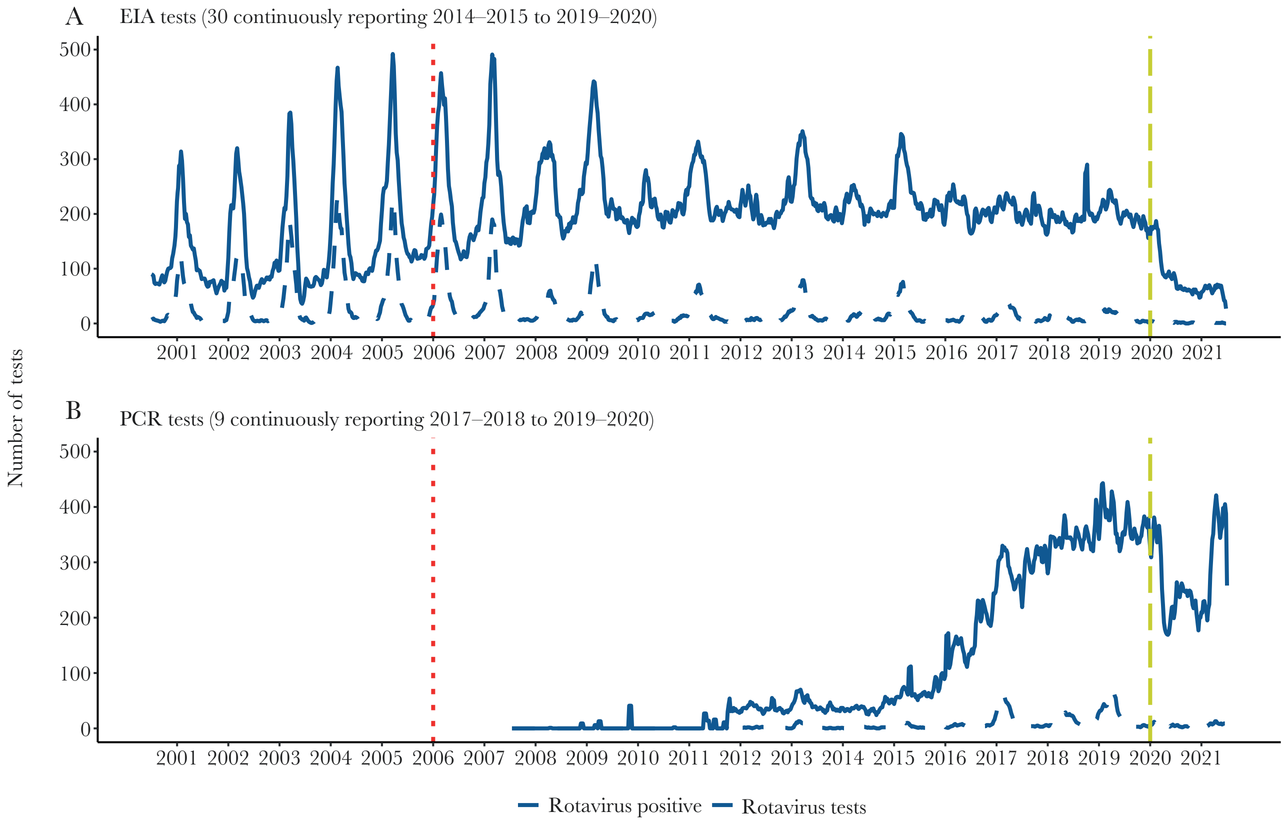

Figure 3. Three-week moving average of the number of rotavirus-positive and total rotavirus enzyme immunoassay (EIA; *A*) and polymerase chain reaction (PCR; *B*) tests among continuous reporting laboratories to the National Respiratory and Enteric Virus Surveillance System—United States, June 2000–July 2021. Non-shaded area indicates period of required continuous reporting for inclusion. The dotted line shows 2006, when rotavirus vaccines became available, and the dashed line shows 2020, when the coronavirus disease 2019 pandemic began.

year was expected to have high rotavirus activity based on pre–COVID-19 pandemic trends and, through June 2021, there was not been an increase in rotavirus laboratory detections in the US. These findings are consistent with other reported declines in viral gastroenteritis [14–20]. Though the decline in IQS was not statistically significant, this is likely because increased queries, comparable with the prepandemic period, had begun through March 2020 and the consistency across data sources suggests a true reduction in rotavirus transmission during this time. In the post–rotavirus vaccine era, outbreaks have frequently been attributed to person-to-person transmission and primarily occur in daycares and congregate living settings [24, 25]. It has been hypothesized that airborne droplets may also contribute to rotavirus transmission [26]. This surveillance system does not allow us to evaluate if mitigation measures specifically targeting airborne transmission, such as masking and improved ventilation, contributed to reduced rotavirus transmission. However, reduced person-to-person contact, improved hand hygiene, and school and daycare closures likely did impact rotavirus disease transmission during the 2019–2020 and 2020–2021 surveillance years. Adherence to individual nonpharmaceutical COVID-19 mitigation measures was relatively consistent in the US during this analysis period [27]. However, Hong Kong reported a return of rotavirus activity with mitigation measures still in place [28]. This is an area that warrants further study, as some of these measures may be useful tools in preventing rotavirus diarrhea in the future.

Changing patterns in testing may have impacted these findings. For example, the low volume of EIA rotavirus tests in the 2020–2021 surveillance year may be at least partially due to a decline in continuously reporting laboratories, whereas PCR tests during the same period had returned to their prepandemic levels. Additionally, over time the number of EIA tests has declined while PCR tests have increased. This makes it challenging to determine if, for example, the lack of biennial high numbers of EIA rotavirus tests in recent years are due to changing epidemiology or testing practices. Similarly, it is not possible to compare current PCR testing with the prevaccine period. In this analysis, we did compare EIA and PCR testing and positivity during the same, limited period and concluded that they broadly follow similar patterns in peak seasonality. Diagnostic methods and changing testing practices will continue to be an important consideration in evaluating the long-term impact of rotavirus vaccine implementation.

NREVSS is a near real-time, national surveillance system, which has been a significant strength for monitoring rotavirus during the unpredictability of the COVID-19 pandemic. Because the data are aggregated and do not include information about the ages of individuals or reasons for testing, there are also important limitations to our findings. In this report, we tried to minimize these limitations by supplementing the main findings with internet search data and by limiting laboratories included in analyses of PCR tests to pediatric sites. The longevity of this surveillance system is another strength; however, the limited number of laboratories that have continuously reported data and changing testing practices limit our ability to compare across the full duration of surveillance. Finally, because these data are ecological, it is challenging to differentiate true reductions in disease prevalence during the 2019–2020 and 2020–2021 surveillance years from avoidance of the healthcare system, disruptions to surveillance systems, and other challenges. However, both rotavirus positivity and IQS for rotavirus continue to be below the historical range, suggesting a real reduction in rotavirus disease.

Substantial declines in laboratory detections of rotavirus have been sustained for 15 years since the introduction of rotavirus vaccine in the US, though trends in seasonality that emerged during the early post–rotavirus vaccine era may be evolving. This is the first description of rotavirus disease during the COVID-19 pandemic in the US and the first analysis of PCR and EIA data from this surveillance system. The coming 2021–2022 surveillance year may be especially active for rotavirus because of an unusually large number of rotavirus-susceptible children, as some children missed routine infant vaccinations due to the pandemic [29] and may not have caught up on rotavirus vaccination due to age restrictions and because less circulating rotavirus in the community offered fewer opportunities for natural immunity. Rotavirus disease surveillance and rotavirus vaccination will continue to be important in the 2021–2022 surveillance year and beyond.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Disclaimer. The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Potential conflicts of interest. All authors: No reported conflicts of interest.

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