Impact of non-pharmaceutical interventions (NPIs) for SARS-CoV-2 on norovirus outbreaks: an analysis of outbreaks reported by 9 US States

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Summary: The incidence of norovirus declined in spring 2020 in the United States, at the same time that non-pharmaceutical interventions for SARS-CoV-2 were introduced. Non-pharmaceutical interventions appear to be an important driver of these patterns.

Abstract

In April 2020, the incidence of norovirus outbreaks reported to the National Outbreak Reporting System (NORS) dramatically declined. We used regression models to determine if this decline was best explained by underreporting, seasonal trends, or reduced exposure due to non-pharmaceutical interventions (NPIs) implemented for SARS-CoV-2 using data from 9 states from July 2012–July 2020. The decline in norovirus outbreaks was significant for all 9 states and underreporting or seasonality are unlikely to be the primary explanations for these findings. These patterns were similar across a variety of settings. NPIs appear to have reduced incidence of norovirus, a non-respiratory pathogen.

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

Keywords: norovirus, social distancing, SARS-CoV-2, non-pharmaceutical interventions

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Background

Since March 2020, non-pharmaceutical interventions (NPIs) such as social distancing, mask wearing, surface disinfection, and increased hand hygiene have become widespread throughout the United States and worldwide in an effort to reduce transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. These changes likely reduced the incidence of influenza in other countries [2, 3], and may also influence the transmission of other pathogens like norovirus. At the same time, healthcare-seeking declined dramatically for acute illnesses, including some illnesses for which incidence would not have been expected to be linked to NPIs [4], suggesting that some decrease in incidence, even for life-threatening diseases, could be related to underreporting. NPIs for SARS-CoV-2 prevention began near the end of the main transmission season for winter-time pathogens, including norovirus [5], so careful analysis is required to separate the effect of responses directed at SARS-CoV-2 from seasonal patterns.

Starting in spring of 2020, there was a large drop in the number of norovirus outbreaks reported to the Centers for Disease Control and Prevention (CDC). We used quasi-Poisson regression models to investigate if this decrease was related to NPIs or could be explained by seasonal changes in incidence and/or underreporting.

Methods

State and local health departments report outbreaks of enteric illness to CDC using the National Outbreak Reporting System (NORS). In August 2012, the Norovirus Sentinel Testing and Tracking network (NoroSTAT) was established to improve timeliness and completeness of norovirus outbreak reporting to CDC. NoroSTAT states are required to report all epidemiologically suspected and laboratoryconfirmed norovirus outbreaks within 7 business days of identification and provide minimum outbreak data elements including the setting and number of cases for each outbreak [6, 7]. NoroSTAT began with 5 states and expanded to 12 states by 2019 (**Appendix Table S1**). Participating states were chosen from those with the highest per capita norovirus outbreak reporting rates and were less likely to be affected by underreporting. Three states participated in NoroSTAT for less than 3 surveillance years prior to 2020 and were therefore not included in our analysis. We used data from the remaining 9 states, beginning the first reporting year of each state's participation in NoroSTAT and concluding in July 2020 (the end of the 2020 reporting year).

To assess how NPIs implemented in response to SARS-CoV-2 might have impacted norovirus outbreak incidence, we compared the number of monthly outbreaks before (August 2012–February 2020) and after NPIs began (April–July 2020). Because incidence data showed evidence of overdispersion even after accounting for seasonality (based on a t-test), we used quasi-Poisson regression models to account for overdispersion. We adjusted for seasonal changes in incidence using cyclic cubic generalized additive model (GAM) smoothing terms for month (with a basis dimension of 12)[8]. As a sensitivity analysis, we re-fitted all GAM models with the same seasonal spline structure but using negative binomial regression and standard Poisson regression.

We also compared the difference in reported outbreaks by month to assess monthly variation in incidence after NPIs began. March 2020 was excluded from the analysis because it was a transition month, during which social distancing measures (e.g., stay at home orders, school and restaurant closures) and recommendations for improved infection prevention strategies (including increased hand hygiene and surface disinfection) were implemented throughout the United States. The same pre/post period was used for all states because reductions in mobility, a proxy for social distancing intensity, [9] started at about the same time, reaching a maximum reduction by April (see **Appendix Figure S1**).

Mobility data was only used to determine the appropriate pre/post period for each state and was not included formally in the regression models. By April 2020, all 9 of the included states had implemented their initial NPIs. Because norovirus seasonality varied by both state and setting, we ran separate models (1) for each state (combining all settings) and (2) for each setting (combining all states). Setting-specific models were adjusted for state using indicator variables and adjusted for season intrinsically by using only data from April–July of each year.

For state-specific models, we considered two alternative ways of adjusting for seasonality in the pooled effect estimate across states: (1) we combined all states into a single meta-regression model, where seasonally-adjusted state-specific estimates were weighted by inverse variance with a random effect for state (our primary analysis) and (2) we subset the data to only include April–July of each year, just like the setting-specific models (since the reporting year begins in August, this gave us one fewer year of surveillance data for each state and only used a subset of the available reference period data) and used standard quasi-Poisson models to estimate the impact of NPIs. The meta-regression approach (our primary analysis) allows the timing and degree of seasonality to vary by state, which should minimize residual confounding by season due to state-level differences and makes use of the full reference period, including data from August 2012–February 2020. For the meta-regression approach, a linear model was used, where ln(IRR) was modeled as the outcome and state-level estimates were weighted by inverse variance. To account for state-level differences, a random effect was included for each state.

To test whether the decline in norovirus outbreaks was due to changes in reporting, particularly preferential reporting of only the largest outbreaks, we compared the size of outbreaks reported to NoroSTAT during the spring and summer months prior to the start of the SARS-CoV-2 pandemic (April–July 2013–2019) with outbreak size after the pandemic began (April–July 2020) using quasi-Poisson regression models (to account for overdispersion in outbreak size). This analysis makes use of a subset reference period, including only certain months of the year. Because these models were stratified to compare the same times of year, they were not adjusted for month. We also assessed whether changes in outbreak size varied by setting, comparing outbreaks in nursing homes, child daycares, schools/colleges/universities, healthcare facilities, and other locations (see **Appendix Table S2** for detailed setting information).

All code used in the analysis is available on github at https://github.com/Noro-COVID-Rollins/NPI-Noro-COVID. All statistical analysis was conducted in R version 4.0.2. We used the 'mgcv' R package for GAM regression models and the 'metafor' package to obtain the pooled estimate across states.

Results

Across all states, there was a monthly mean of 6.19 [range: 0–34] reported outbreaks in April–July during the subset reference period for each state (range: 3–7 years) compared to 0.78 (range 0–4) reported outbreaks during April–July 2020 (**Appendix Table S1**). Because there were no outbreaks in Tennessee during April–July 2020, the variance for this state was infinite and its confidence interval was undefined. We therefore excluded this state from the meta-regression point estimate (because of the need to weight individual estimates by 1/variance). We included Tennessee in the two alternative approaches (pooled GAM model and season-stratified model) because these approaches did not require use of the stratified variance estimate for Tennessee.

In our primary analysis (using the full GAM model, accounting for seasonal trends, including data from the full reference period, August 2012–February 2020, and combining state level estimates using meta-regression) the incidence of reported norovirus outbreaks was significantly reduced for all states April–July 2020 compared with the reference period for each state (pooled monthly incidence rate ratio

(IRR)=0.14, 95% CI: 0.08, 0.25) (**Figure 1A**). The point estimate was similar when states were combined, without using meta-regression (IRR=0.12, 95% CI: 0.07, 0.22) and was also similar for the model that included only April–July of each year (using the subset reference period) (IRR=0.13, 95% CI: 0.06, 0.27). We also re-ran the pooled GAM model and season-stratified model without Tennessee included and the results were similar (IRR=0.13, 95% CI: 0.07, 0.24 for the pooled GAM model and IRR=0.13, 95% CI: 0.06, 0.29 for the season-stratified subset reference period model). Point estimates for all states were strong and effect sizes were similar, with IRR values ranging from 0 (95% CI: 0, Inf) for Tennessee to 0.22 (95% CI: 0.06, 0.80) for Wisconsin. Likewise, the reduction in outbreak incidence was apparent in all settings but was least dramatic in long-term care and other healthcare facilities (**Figure 1B**).

In general, the decline in monthly outbreaks began in April, after NPIs had been more fully implemented. Beginning in April, the number of reported monthly outbreaks dropped to nearly zero for all states and remained at low levels through the end of July (see **Appendix Figure S2**). In terms of size, outbreaks were on average 61.2% smaller in April–July 2020 (95% CI: 19.2%, 81.4%) compared with the same period in prior years, with similar patterns across all settings (**Figure 2**). The exception was in settings classified as "other", for which the single outbreak that occurred between April and July was similar to the average outbreak size in prior years.

These results were also robust to the modeling approach used, and conclusions were similar when models were fitted using negative-binomial or standard Poisson regression (**Appendix Table S3** and **Appendix Table S4**). The one exception was Massachusetts, for which confidence intervals overlapped the null using quasi-Poisson regression but not for the other two approaches. The quasi-Poisson regression had the widest confidence intervals and also tended to have slightly higher R^2 values than the other two approaches. We emphasize the quasi-Poisson results here so that our findings will be conservative.

Discussion

We found a decline of >80% in incidence of reported norovirus outbreaks during April– July 2020 compared to the same time period in previous years, likely in part due to the implementation of NPIs for COVID-19 in spring and summer 2020. This decline was consistent across states and settings and could not be explained solely by seasonality. Given that this decline coincided with a decrease in average outbreak size, underreporting is also unlikely to be the primary explanation for these findings. Moreover, based on ongoing dialogue with state public health departments participating in NoroSTAT, all known norovirus outbreaks continue to be reported to NORS.

While smaller and fewer outbreaks were reported across all settings, the difference was least dramatic in nursing homes and healthcare facilities. Stringent SARS-CoV-2 prevention measures have been implemented in nursing homes and healthcare facilities throughout the United States in response to the COVID-19 pandemic [10, 11], yet unlike schools and daycares, these facilities could not completely close. Our results cannot exclude the possibility that reduced testing priority for norovirus symptoms could have led to some outbreaks being undetected. However, reduced health-seeking behavior is less likely to explain patterns in outbreak size for long-term care and healthcare facilities, where outbreak detection may be more closely linked to staff monitoring than patient health-seeking behaviors.

While uncertain, differences in effect sizes suggest that these patterns may initially have been driven by widespread closures of locations like schools where norovirus outbreaks commonly occur. As the 2020–2021 norovirus season begins and locations such as schools and restaurants continue to reopen, ongoing patterns of norovirus incidence based on outbreak surveillance might provide more clarity on the reasons behind these trends. For example, as schools, daycares, and restaurants begin to reopen, incidence may increase again [12]. However, sustained social distancing, more frequent surface disinfection, and enhanced hand hygiene might continue to reduce the number of norovirus outbreaks. Conversely, population immunity may be lower at the start of the norovirus season, which could lead more frequent or larger norovirus outbreaks.

Our findings are similar to reported declines in norovirus incidence in the England and Wales during March and April 2020 [13]. While most initial studies showing declining infectious disease trends have focused on influenza, we show that these declines in incidence were observed for norovirus, a non-respiratory pathogen. Unlike SARS-CoV-2 and other respiratory pathogens, which are commonly spread by droplets [14], norovirus is primarily transmitted by the fecal-oral route [15]. Therefore, the unanticipated benefits of NPIs for SARS-CoV-2 might also be present for other pathogens transmitted person-to-person.

Figure 1. Incidence rate ratio and 95% confidence intervals of norovirus outbreaks for April–July 2020 compared with prior years (ref) by A) state and B) outbreak setting. Note that there were no outbreaks reported in Tennessee in April–July 2020, making its variance infinite and the confidence interval undefined. For this reason, Tennessee was not included in the meta-regression pooled effect estimate calculation (primary analysis, shown in Figure 1A).

Figure 2. Average norovirus outbreak size by setting for April–July 2013–2019 (black) and for April–July 2020 (gray). An asterisk (*) indicates a significant difference between time periods using quasi-Poisson regression. The number of outbreaks (n) used to calculate the size for each period is shown above each colored bar.

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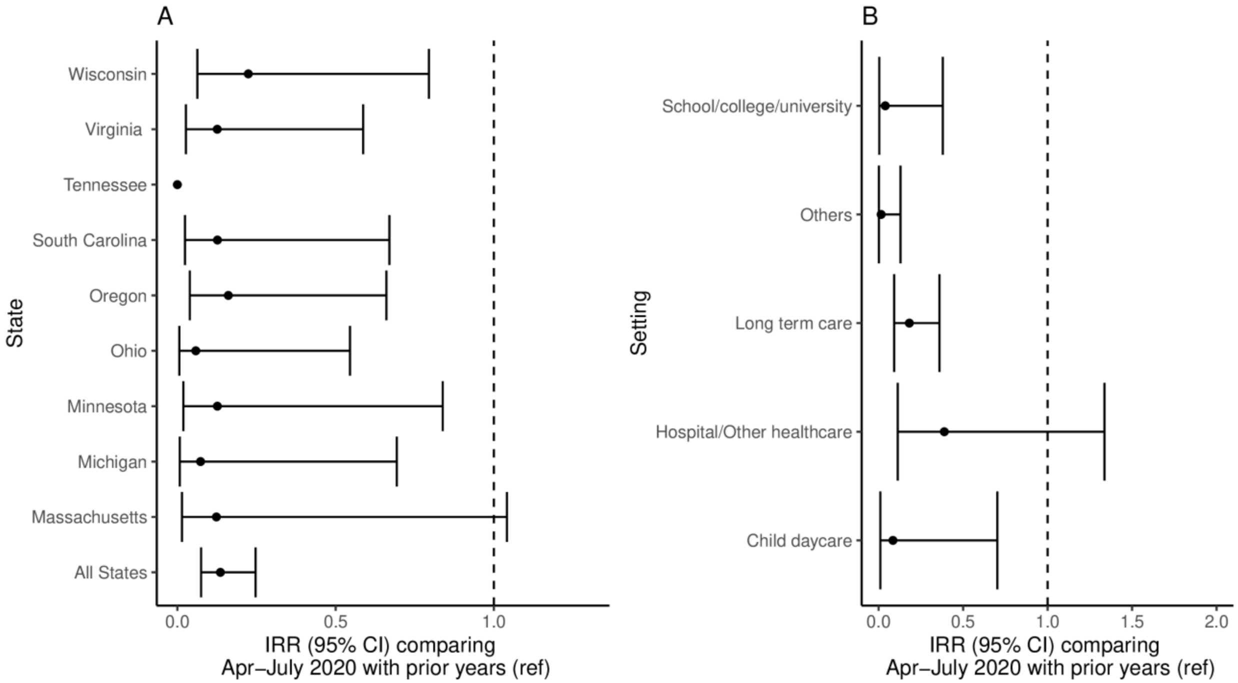
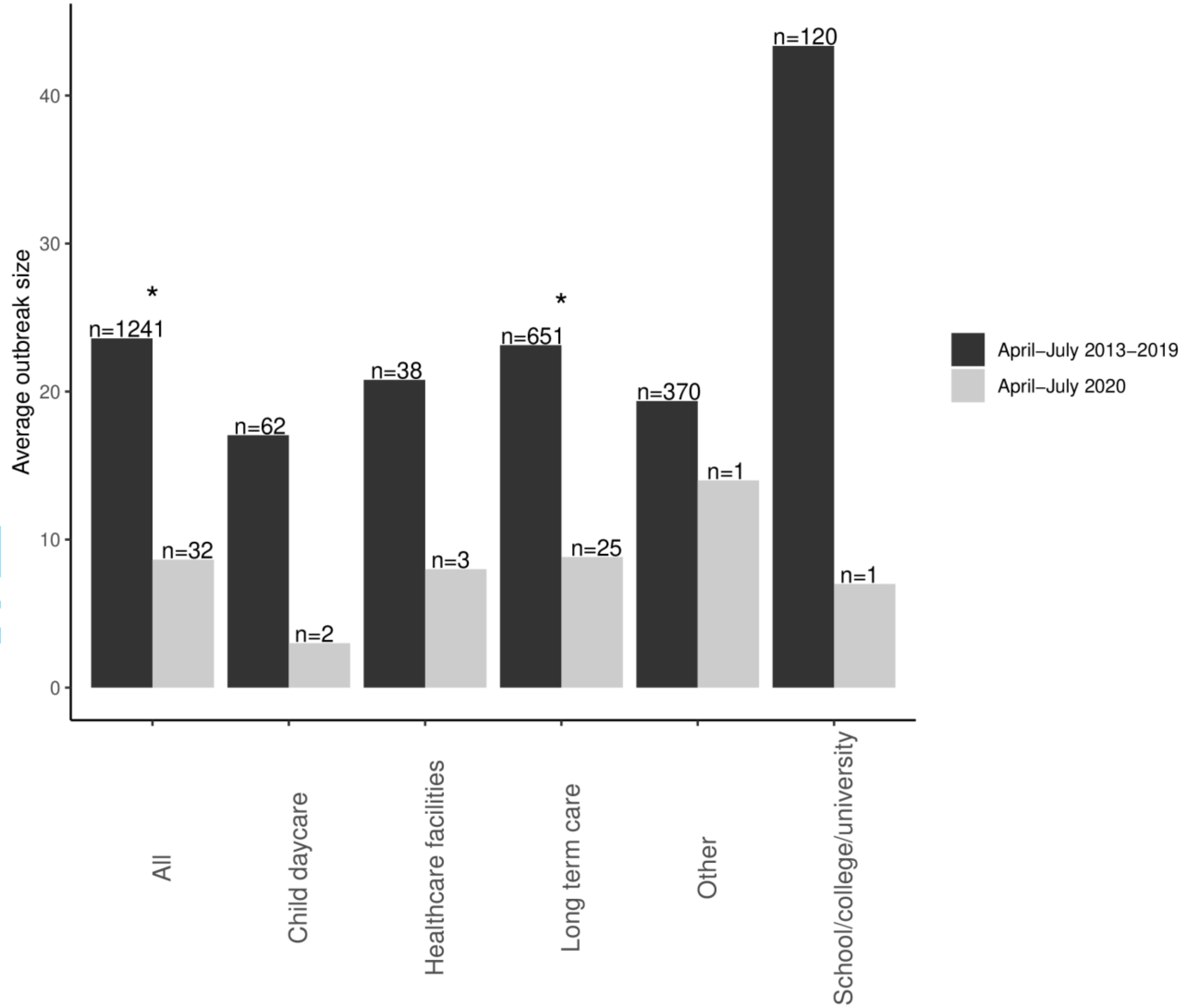
Figure 1



A
Wisconsin
Virginia
Tennessee
South Carolina
Oregon
Ohio
Minnesota
Michigan
Massachusetts
All States
State
0.0
0.5
1.0
IRR (95% CI) comparing
Apr–July 2020 with prior years (ref)
B
School/college/university
Others
Long term care
Hospital/Other healthcare
Child daycare
Setting
0.0
0.5
1.0
1.5
2.0
IRR (95% CI) comparing
Apr–July 2020 with prior years (ref)

Figure 2


Average outbreak size
0
10
20
30
40
n=1241
n=32
n=62
n=2
n=38
n=3
n=651
n=25
n=370
n=1
n=120
n=1
*
*
All
Child daycare
Healthcare facilities
Long term care
Other
School/college/university
April–July 2013–2019
April–July 2020