A Silver Lining? Fewer non-SARS-CoV-2 Respiratory Viruses during the COVID-19 Pandemic

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Summary: During the COVID-19 pandemic, non-pharmaceutical interventions have substantially reduced transmission of SARS-CoV-2, but have also had an effect on other respiratory viruses. We found that the incidence of non-SARS-CoV-2 respiratory viruses decreased substantially during this time.

Abstract

Non-pharmaceutical interventions (NPIs) have "flattened the curve" of the COVID-19 pandemic, however the effect of these interventions on other respiratory viruses is unknown. We used aggregate level case count data for eight respiratory viruses and compared the institutional and statewide case counts before and during the period that NPIs were active. We observed a 61% (IRR 0.39, 95% CI 0.37 to 0.41, $P < 0.0001$) decrease in non-SARS-CoV-2 respiratory viral infections when NPIs were implemented. This finding, if further verified, should guide future public health initiatives to mitigate viral epidemics.

Keywords: COVID-19, respiratory virus, non-pharmaceutical interventions, seasonal respiratory viruses

Introduction

Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has led to a pandemic with morbidity and mortality not experienced in recent memory. As of December 3, 2020 there are over 64 million confirmed cases and over 1.5 million deaths attributed to COVID-19 worldwide [1]. To reduce transmission of SARS-CoV-2, in addition to rigorous contact tracing and isolation, several non-pharmaceutical interventions (NPI) have been enacted in various geographic regions. These include school closures, shelter-in-place orders, voluntary and mandatory mask wearing policies, and physical distancing. Evidence is mounting that these interventions have led to a "flattened curve" and have effectively reduced transmission of SARS-CoV-2 [2-4].

The NPIs are generic interventions that are not specific for SARS-CoV-2. Hence, their widespread implementation should reduce transmission of other respiratory viruses that disseminate similarly. Reduction in transmission of these respiratory viruses is a long-term public health priority. For instance, seasonal influenza infections cause an average of nearly 40,000 deaths per year in the US [5], and other respiratory viruses are known to cause morbidity in pediatric and immunocompromised patients, along with economic losses from missed school and work [6-8].

While the transmission dynamics of respiratory viruses vary and are not completely elucidated, there is evidence that children in school and day care play an important role in transmission [8, 9]. Several recent studies have highlighted reduced influenza and other respiratory virus incident infections during the COVID-19 pandemic [10-13]. However, the effect of NPIs on non-SARS-CoV-2 viral transmission has not been quantified. We hypothesized that the incidence of non-SARS-CoV-2 respiratory viruses has decreased during the COVID-19 pandemic compared to previous years as a result of the rigorous implementation of NPIs in our community. Our objective was to quantify the magnitude of this effect.

Methods

We conducted an observational ecological comparison of the incidence of respiratory viral infections from January 1, 2014 through February 21, 2021 at one large pediatric health system in Dallas, Texas. The health system serves the North Texas region (population approximately 7.4 million) and provides primary to quaternary care for children in a 490-bed pediatric hospital, an emergency department with approximately 180,000 unique patient encounters per year, and more than 30 primary care and subspecialty clinics. The on-site microbiology laboratory identifies respiratory viral infection with one of two multiplex polymerase chain reaction (PCR) platforms. The BioFire® FilmArray® Respiratory Panel (BioFire Diagnostics, Salt Lake City), which tests for eight viruses (adenovirus, human coronavirus [HKU1, NL63, 229E, or OC43], human metapneumovirus, influenza A [H1N1pdm2009 or H3N2], influenza B, human parainfluenza virus [type 1, 2, 3, or 4], respiratory syncytial virus [RSV], or rhinovirus/enterovirus [which are not distinguished on the panel]), or the Cepheid® Xpert Xpress Flu/RSV PCR performed on the GeneXpert® Dx system (Cepheid, Sunnyvale). Medical providers test patients with the respiratory panels based on clinical judgement. Starting in June 2020, universal screening with the BioFire® FilmArray® Respiratory Panel 2.1 (which includes SARS-CoV-2) was required for all hospital admissions. The laboratory reports the counts of these respiratory viruses to the National Respiratory and Enteric Virus Surveillance System (NREVSS).

The microbiology laboratory generates reports with the daily aggregate of the number of positive respiratory PCR tests for each of the eight viruses, along with the daily number of total PCR tests run. In addition, weekly counts of test positivity for each respiratory virus were extracted from reports published by the Texas Department of State Health Services (DSHS) weekly influenza activity surveillance system (https://www.dshs.texas.gov/IDCU/disease/influenza/surveillance/). These reports included all participating sites in Texas that were reported to the NREVSS. Of note, the number of participating laboratories varied from week to week.

The primary analysis for the local data modeled the counts of positive PCR tests for each virus per day from January 1, 2014 to February 21, 2021. These counts will be referred to as *incidences* although these are not true incidences due to lack of a denominator for the population at risk. A Poisson regression model was built with the count for all viruses as the response variable, and the time of year and the number of tests collected as explanatory variables. This allowed the model to control for seasonal variation in respiratory viral incidence and the number of tests ordered. Then, an additional explanatory variable was added to the model that took the value of 0 prior to the implementation of NPIs, and the value of 1 from March 15, 2020 to February 21, 2021. This allowed the model to account for a shift in the incidence for all viruses when the NPIs were initiated locally. We labeled the coefficient for this variable the global effect factor. Finally, a model was built removing the global effect factor and instead using pathogen specific effect factors for the eight viruses studied. The methods were the same for the statewide data, except that weekly incidence was used rather than daily incidence (see Supplementary Methods). The quality of each model was measured using the Akaike information criterion (AIC) which accounts for both the goodness of fit to the observed data, and the model's simplicity. A lower AIC indicates a higher quality model. In each model, the exponentiation of the coefficient for the effect factor equals the incidence rate ratio (IRR) for the implementation of NPIs. These were tested against the null hypothesis that the incidence rate ratio equals one and does not change the incidence. Ninety-five percent confidence intervals (95% CI) for the IRR estimates were calculated from the model. A two-sided type I error rate of 0.05 was used for statistical significance with a Holm-Sidak correction for multiple comparisons.

Dallas County, Texas implemented several NPIs throughout the study period beginning with a local health emergency declared on March 12, 2020. All schools in the county were closed on March 17, 2020 and reopened for hybrid learning in the fall. In addition, local health authorities encouraged maintaining a physical distance of at least six feet in public, limiting gathering size, minimizing non-essential travel, and wearing masks in public. A shelter-in-place order was enforced for non-essential workers between March 30, 2020 and April 29, 2020 and a statewide order to wear masks in public went into effect on July 3, 2020 (see Supplemental Figure 1).

This study was determined to be exempt from review by the local Institutional Review Board.

Results

Descriptive Statistics

From January 1, 2014 through March 14, 2020 there were 47,601 PCR tests performed locally and 27,944 were positive (58.7%). From March 15, 2020 to February 21, 2021 there were 12,398 PCR tests performed and 2,829 were positive (22.8%).

Local Incidence

Inclusion of the global effect factor, which accounted for the active NPIs in Dallas County beginning March 15, 2020, improved the parsimony of the regression model (AIC reduced by 2,057). The implementation of NPIs was associated with a reduction in the incidence of all respiratory viral infections by 61% (IRR 0.39, 95% CI 0.37 to 0.41, $P < 0.0001$). Replacing the global effect factor with pathogen specific effects (Figure 1) improved the model parsimony further (AIC reduced by an additional 1,828). Using the pathogen specific model, the period of active NPIs was associated with a significantly reduced incidence of all 8 viruses (Figure 2). The effect was strongest for RSV and influenza, and weakest for rhinovirus/enterovirus and adenovirus (Figure 2, see Supplemental Table 2 and Supplemental Figure 2).

State Incidence

The statewide data followed a similar pattern to the local data. Inclusion of the global effect factor improved the parsimony of the model (AIC reduced by 11,506). The period of active NPIs since CDC week 12 in 2020 was associated with a 68% reduction in the incidence of all respiratory viruses (IRR 0.32, 95% CI 0.31 to 0.33, $P < 0.0001$). Replacing the global effect factor with pathogen specific effects (Figure 1) further improved model parsimony (AIC reduced by an additional 6,938). The predicted counts from the model were much lower for 2020 than for previous years due to fewer tests being performed. Using the pathogen specific model, the period of active NPIs was associated with a significant reduction in the incidence of all eight viruses (Figure 2, see Supplemental Table 3 and Supplemental Figure 2).

Discussion

Using aggregated data from respiratory viral testing in a large Children's Hospital and statewide in Texas, we found that the observed number of respiratory viral infections decreased while several NPIs were in place during the COVID-19 pandemic. The reduced incidence was most notable for RSV, influenza A and B, parainfluenza virus, and seasonal human coronaviruses.

It is not clear why the effect of the NPIs on rhinovirus/enterovirus and adenovirus infections was weaker. These viruses have little if any seasonality and are always endemic in the population. Both of these viruses saw reduced incidence early after the initial NPIs were implemented but they returned to normal levels by the summer. This could be due to virus-specific differences in effective transmission contact that respond differently to specific NPIs. For instance, rhinovirus/enterovirus and adenovirus may have been more sensitive to school closure and reopening. Human metapneumovirus counts were strongly affected by a local outbreak in March 2020 that started prior to the implementation of NPIs.

A strength of this study is that we used a large dataset in a particular geographic region to evaluate the incidence of viral infections during the period of NPIs. Therefore, we reduced the effect of variable geographic implementation of NPIs over time. When expanding our analysis to data from the entire state that included both children and adults, we found a similar effect size, which supports the robustness of this finding. In addition, our results are concordant with dramatic decreases in influenza infection incidence rates associated with the implementation of NPIs reported by other investigators [10-12].

However, this study has several weaknesses. Not all positive PCR tests represent acute infections. We only had access to aggregate data which limited the comparisons we could make and this type of ecological analysis cannot show causation. There are alternate explanations (such as viral interference [14] with SARS-CoV-2 or random chance) but none are as plausible as an effect of NPIs. Changes in the indication for PCR testing over time may have contributed to the reduction in percent positivity observed locally. However, the state (which saw a reduction in PCR testing) and the local hospital (which saw an increase in PCR testing) had similar estimates for the effect size, so it is unlikely that changes in testing strategy substantially confounded the results. Finally, in this observational study we could not isolate the impact of any specific NPIs or other factors. For instance, we cannot say whether school closure, mask wearing, or increased lay awareness of viral transmission dynamics played a role.

These results suggest that the children in Dallas and the population of Texas had far fewer respiratory viral infections in 2020 compared to usual years. This study helps to quantify the potential protective effect of enacting NPIs during other, non-SARS-CoV-2, respiratory virus epidemics. This could help public health and governmental planning to strategize future implementation of NPIs during high incidence epidemics for respiratory viruses.

In conclusion, we have identified a large decrease in the incidence of non-SARS-CoV-2 respiratory viral infections during the COVID-19 pandemic that may be due to the implementation of NPIs. This information should be used by local and national health authorities for resource preparation for upcoming viral epidemics. Additional surveillance of respiratory viral infections will be crucial to understanding the short- and long-term effects of this period.

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Footnotes

The authors declare no conflicts of interest.

The authors received no financial support for this project.

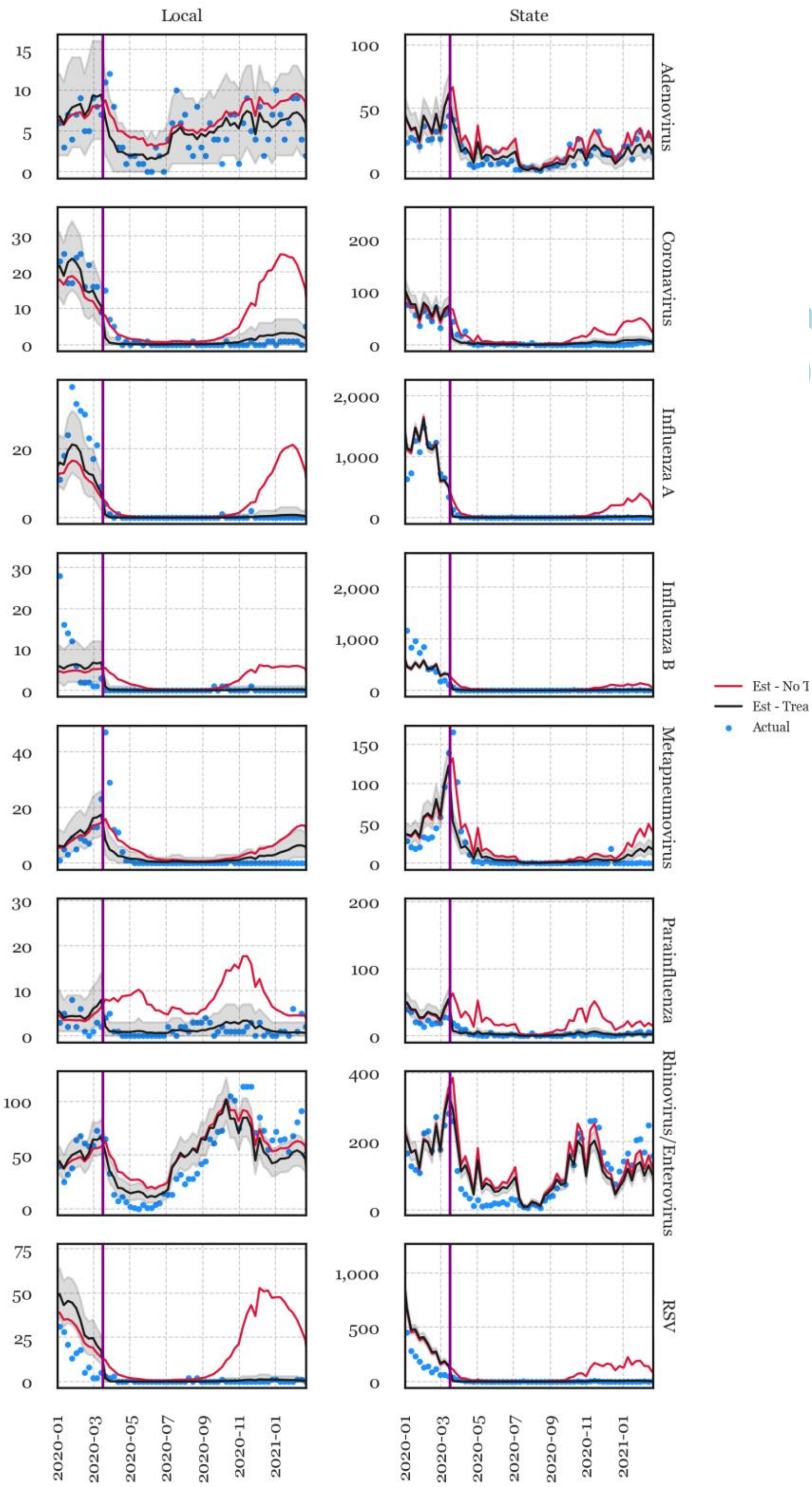
The results of this study have not been shared at any conferences or meetings.

Figure Legends

Figure 1. Number of positive tests for each respiratory virus before (left of the purple line) and during (right) the implementation of non-pharmaceutical interventions (NPI) during the COVID-19 pandemic from January 1, 2020 to February 21, 2021. ‘Local’ refers to the institutional case counts at one large pediatric health system in Dallas County, Texas and ‘State’ refers to case counts covering the entire state of Texas. The blue dots are the actual observed incidence, the black line is the predicted incidence using a Poisson regression model dependent on the time of year, the number of tests collected, and a pathogen specific effect for the implementation of NPIs, and the red line is the predicted incidence using the same Poisson model but only dependent on time of year and number of tests collected. The gray area surrounding the black line is the 95% prediction interval. RSV – respiratory syncytial virus

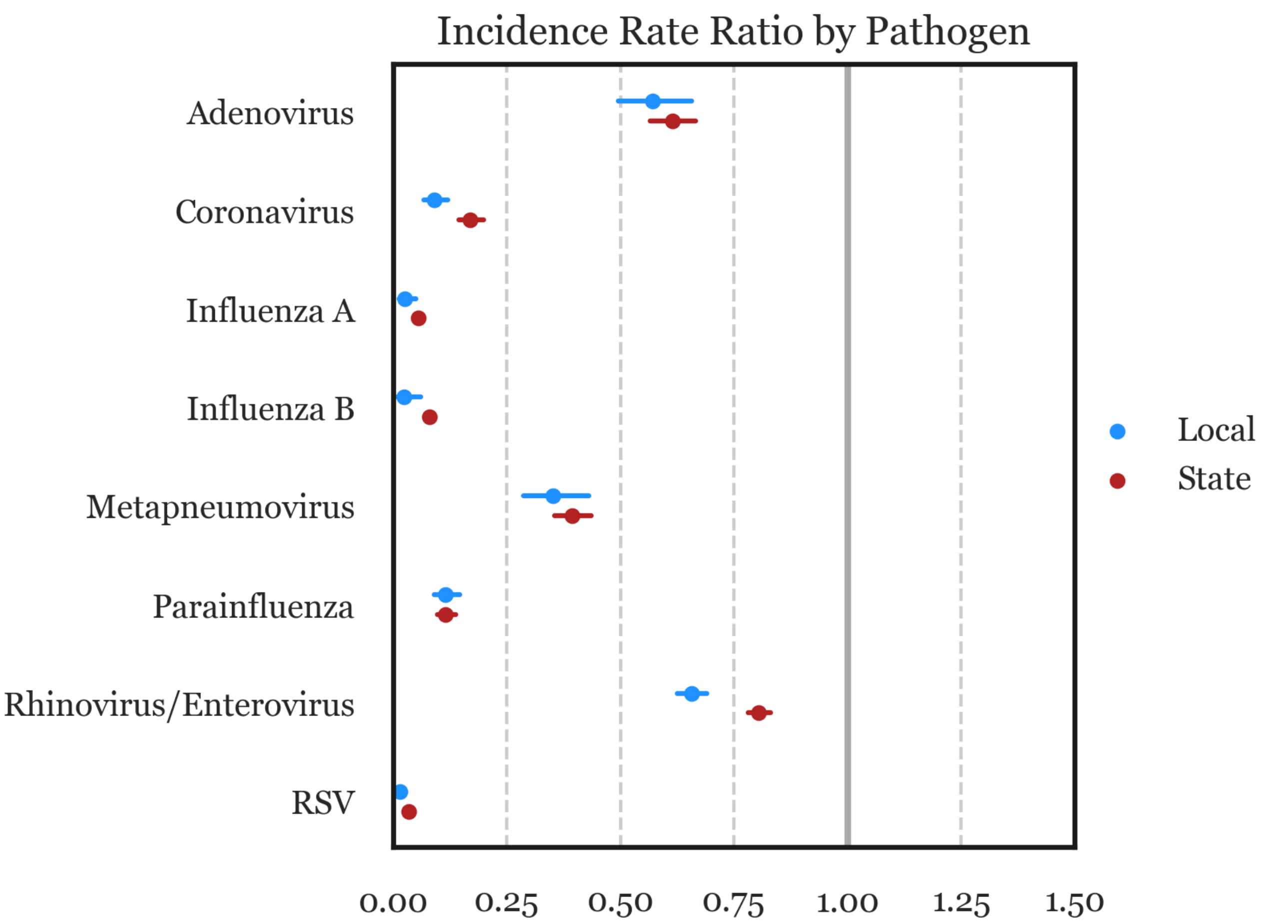
Figure 2. Incidence rate ratio for infections with each virus comparing the counts of positive tests before and after March 15, 2020 (CDC week 12 in 2020 for the state data). ‘Local’ refers to the incidence at one large pediatric hospital in Dallas County, Texas and ‘State’ refers to the statewide incidence collected from the Texas Department of State Health Services. To the left of the black vertical line favors a decreased incidence during the time period of active NPIs during the COVID-19 pandemic compared to before. The dots represent the point estimate and the bars represent the 95% confidence intervals. RSV – respiratory syncytial virus.

Figure 1



Local
State
Adenovirus
Coronavirus
Influenza A
Influenza B
Metapneumovirus
Parainfluenza
Rhinovirus/Enterovirus
RSV
Est - No T
Est - Trea
Actual
2020-01
2020-03
2020-05
2020-07
2020-09
2020-11
2021-01

Figure 2



Incidence Rate Ratio by Pathogen
Adenovirus
Coronavirus
Influenza A
Influenza B
Metapneumovirus
Parainfluenza
Rhinovirus/Enterovirus
RSV
0.00
0.25
0.50
0.75
1.00
1.25
1.50
Local
State