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Asthma-related outcomes during the SARS-CoV2 pandemic: A single-center observational study

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Clinical Implications

- During the SARS-CoV2 pandemic, there was a significant decrease in pediatric emergency department visits and steroid prescriptions for asthma exacerbations, as well as rhinovirus infections. Further study regarding whether this is a causative or correlative finding is warranted.

Asthma is a common chronic disease affecting approximately 7.5% of children and adults in the United States.[1] Respiratory viral infections are a frequent cause of asthma exacerbations, triggering up to 85% of exacerbations in children, of which rhinovirus (RV) consistently accounts for approximately 60% to 70%.[2,3] Rhinovirus infections are common throughout the year; most do not produce exacerbations.[4] However, studies examining emergency department (ED) visits consistently demonstrate spikes in asthma exacerbations in the spring and fall, which correspond to allergy seasons in the northern hemisphere where the studies were conducted.[5] Subsequent studies demonstrated a clear link between RV-induced asthma exacerbations and aeroallergen exposure, resulting in a spring asthma "epidemic."

In 2019, a novel virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), appeared, leading to the coronavirus disease 2019 (COVID-19) pandemic. COVID-19 was first detected in Virginia on March 7, 2020, resulting in a call for social distancing and a stay-at-home order that was implemented from March 30 to June 8, 2020. We hypothesized that the implementation of these social distancing measures would lead to a decrease in RV infections and thus asthma exacerbations, particularly in the spring and fall. In this study, we examined whether measures of asthma exacerbation, including ED visits, outpatient steroid prescriptions, and documented RV infections, decreased among children and adults at the University of Virginia (UVA) from March to December 2020.

Data were abstracted for patients aged 0 to 40 years, who were receiving care at the UVA Health System from January 1, 2016 until December 31, 2020. The UVA Medical Center Enterprise Data Warehouse system, which contains data sourced from UVA's Electronic Medical Record System, was used to identify patients with a diagnosis of asthma with acute exacerbation using International Classification of Diseases, 10th Revision (ICD-10) codes J45.21, J45.31, J45.41, J45.51, and J45.901. Outpatient oral steroid use was defined as a prescription for systemic steroid preparations (prednisolone, prednisone, methylprednisolone, or dexamethasone) associated with any ICD-10 code for asthma (J45.2-J45.5 and J45.9) as an outpatient, which includes outpatient or telemedicine visits, telephone calls, and orders placed at the end of ED or inpatient visits for outpatient use. An ED visit for an asthma exacerbation was defined as an ICD-10 code for asthma with acute exacerbation seen in the ED. Rhinovirus infections were defined as a positive polymerase chain reaction (PCR) detected on the outpatient or inpatient respiratory pathogens panel, which is distinct from the SARS-CoV2 assay at UVA. Data on race and ethnicity were extracted from the medical record based on patient self-report.

The number of cases per month were collected for each outcome. Monthly RV infections were defined as the percentage of RV-positive tests among all RV PCR tests performed. For each outcome, segmented autocorrelation time series regression was conducted to determine whether the trend in monthly numbers for each outcome from January 2016 to March 2020 was different in April to December 2020. The transition point for these models was identified as April 1, 2020, because the Virginia stay-at-home order went into effect on March 30. For the outpatient steroid prescription, ED visits, and the percentage of RV-positive tests, the time series models were stratified a priori by age (0-5, 6-18, and 19-40 years), because the prevalence of RV-associated asthma exacerbations is lower in adults than in children.[6] Interaction terms were included in the models to assess for effect modification by age or, in the outpatient steroid prescription model only, race or ethnicity. All segmented autocorrelation time series regression analyses were performed using the PROC AUTOREG software of SAS (version 9.4, Cary, NC). This study was approved by the UVA Institutional Review Board.

The number of asthma-related outpatient steroid prescriptions and ED visits from January 2016 to December 2020, stratified by age, is displayed in Figure 1 and Figure E1 (in this article's Online Repository at www.jaci-inpractice.org), respectively. Based on trends before social distancing, the geometric mean number of asthma-related outpatient steroid prescriptions in April 2020 was 24% of that forecasted (95% confidence interval [CI]: [12-48]; $P < .001$) among children aged 0 to 5 years (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). This was also seen for children aged 6 to 18 years (38%; 95% CI: [22-64]; $P < .001$), but not adults (67%; 95% CI [38-119]; $P = .18$). The test for interaction was significant for age ($P = .005$), but not race or ethnicity ($P = .11$). Similarly, the geometric mean number of asthma-related ED visits in April 2020 was 15% (95% CI: [8-26]; $P < .001$) of that forecasted based on trends before the SARS-CoV2 pandemic (Table E1). This was also seen for children aged 6 to 18 years (17%; 95% CI: [6-43]; $P < .001$), but not adults (71%; 95% CI, 40-125; $P = .23$; age interaction, $P = .024$).

The percent positivity for monthly RV testing from January 2018 to December 2020 is shown in Figure 2. Similar to the other asthma-related outcomes, the odds ratio (OR) for a positive RV PCR test in April 2020 was 0.23 (95% CI, 0.08-0.86; $P = .009$) of that forecasted among children aged 0 to 5 years (Table E1). This was also seen for children aged 6 to 18 years (OR = 0.22; 95% CI, 0.05-0.99; $P = .048$), but not adults (OR = 0.37; 95% CI, 0.02-5.68; $P = .47$; age interaction, $P = .61$). These differences persisted in all asthma-related outcomes from April to December 2020, except for ED visits and RV infections among

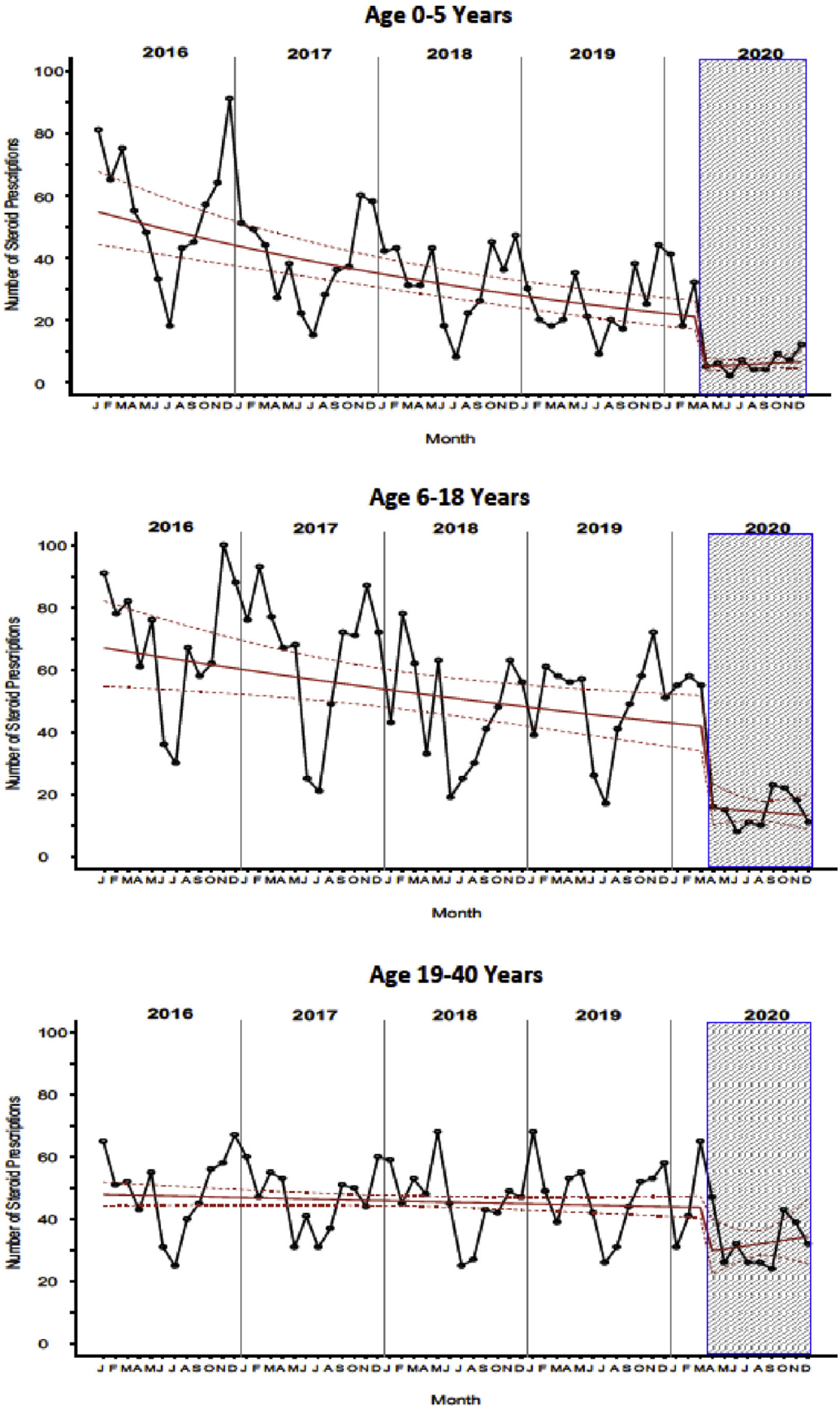

FIGURE 1. Segmented autocorrelation time series trends for number of asthma-related steroid prescriptions stratified by age. Open circles identify monthly number of prescriptions; solid red line identifies maximum likelihood prediction for geometric mean trajectory of time series. Dashed red lines identify corresponding 95% confidence interval. Shaded region identifies monthly number of steroid prescriptions after implementing social distancing measures.

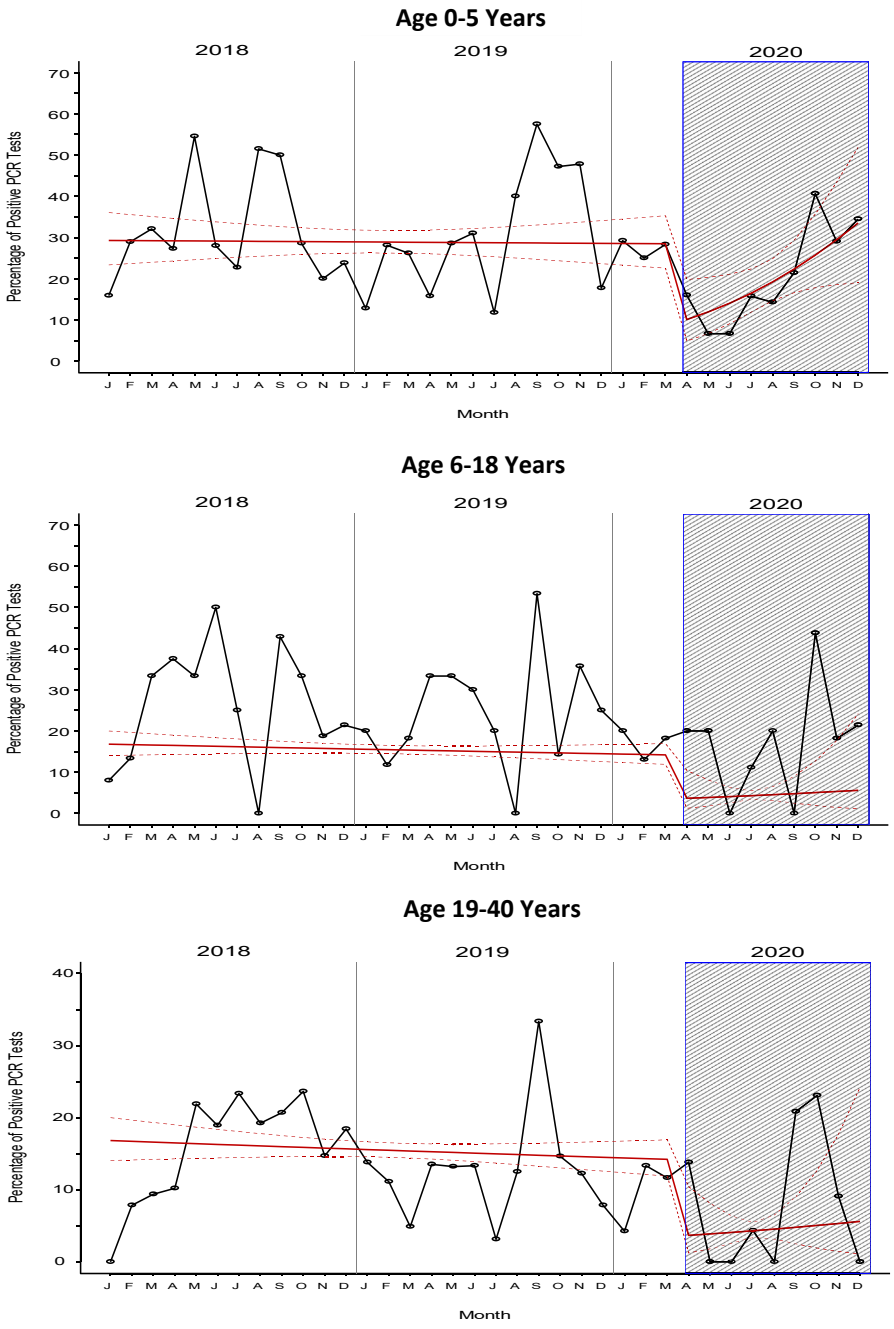

FIGURE 2. Segmented autocorrelation time series trends in percentage of positive rhinovirus polymerase chain reaction (PCR) tests stratified by age. Open circles identify monthly percentage of positive PCR tests. Red solid line identifies maximum likelihood prediction for mean trajectory of the time series. Dashed red lines identify corresponding 95% confidence interval. Shaded region identifies percentages of positive PCR tests after implementing social distancing measures.

children aged 0 to 5 years, for which there was a significant increase in the geometric mean number of ED visits ($P = .001$) and a significant increase in the OR for RV infection ($P = .029$) (Table E1).

In this study, we investigated the incidence of asthma-related outcomes in the 4 years before the SARS-CoV2 pandemic and compared this with that observed in 2020. Our data demonstrate that fewer patients cared for at UVA presented with asthma exacerbations in 2020, and the spring asthma epidemic that typically occurs coincident with the grass pollen season[5] did not occur (Figure 1). This reduction was demonstrated as reduced ED visits and fewer patients (or their parents) requesting oral corticosteroid prescriptions. These results are consistent with the decrease in asthma-related outcomes reported in Pennsylvania,[7] Japan,[8] and Slovenia[9] during the SARS-CoV2 pandemic. These data suggest an improvement in asthma control with the

adoption of public health interventions to limit the spread of SARS-CoV2.

We further found that this decrease in asthma-related outcomes was particularly evident among children aged 18 years or less, and this occurred with a concomitant decrease in the incidence of RV infections during the SARS-CoV2 pandemic. Because most asthma exacerbations in children are triggered by viral infections, especially RV, it is possible that this association is not merely correlative. Public health interventions in 2020 included social distancing, the wearing of personal protective equipment such as face masks, and frequent hand washing. Although these measures were encouraged to prevent the spread of SARS-CoV2, these interventions are equally effective in preventing the spread of other respiratory viruses. In addition, the closing of schools and day care facilities led to the mitigation of environments associated with the spread of other pathogens. This hypothesis is further supported by the upward trend in RV infections and ED visits for asthma, which appeared to occur after the stay-at-home order was lifted in June 2020. These findings suggest that mitigation techniques designed to decrease the spread of respiratory viruses and other pathogens may be an effective prevention strategy for asthma exacerbations, even after the SARS-CoV2 pandemic.

An important limitation of our studies is the well-recognized comprehensive decline in patients making ED visits because of fears of exposure to SARS-CoV2; therefore, the decreases in ED visits for asthma may have reflected this confounding influence. However, this is less likely to have influenced patients contacting their physicians in the setting of severe shortness of breath related to asthma. As such, we posit that the decreased numbers of requests for prescriptions for oral steroid prescriptions are particularly compelling. Our study was further limited by the lack of individual-level data on potential confounders that may have influenced our results, such as socioeconomic status and medication adherence. Although we speculate that the decrease in RV infection explains the decrease seen in asthma exacerbations, it is also possible that other factors such as decreased exposure to pollution or increased medication adherence during the pandemic could explain our findings. Finally, UVA is a tertiary care academic center, so these results may not be generalizable to other populations.

During the SARS-CoV2 pandemic, we found a significant decrease in ED visits and outpatient steroid prescriptions for asthma exacerbations among children aged 0 to 18 years at UVA, which paralleled the decreasing trend in RV infections. Further study on whether this is a causative or correlative finding is warranted.

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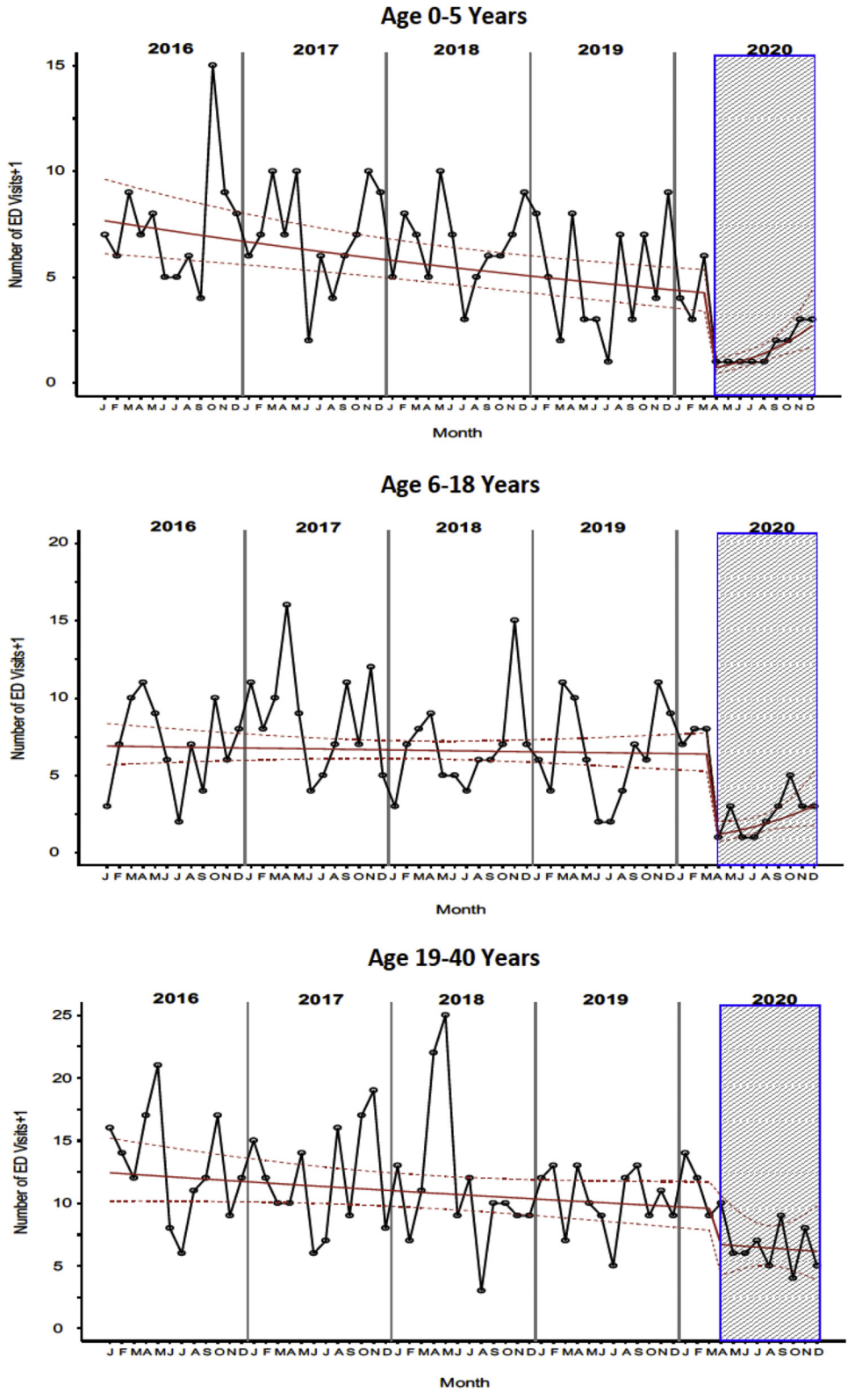

FIGURE E1. Trends in emergency room asthma-related visits from 2016 to 2020. *ED*, emergency department.

TABLE E1. Segmented time series autoregression model parameter estimates for asthma-related outcomes from January 2016 to December 2020

Group	Time frame	Regression parameter	Estimate (95% confidence interval)	*P*
0-5 y	Outpatient steroid prescriptions			
	Overall transition point*	δ1	0.24 (0.12-0.48)	<.001
	Post-COVID-19 social distancing†	β2	1.05 (0.90-1.24)	.53
	ED asthma visits			
	Transition point‡	δ1	0.15 (0.08-0.26)	<.001
	Post-COVID-19 social distancing§	β2	1.19 (1.08-1.32)	.001
	RV infections			
	Transition point‖	δ1	0.23 (0.08-0.86)	.009
	Post-COVID-19 social distancing¶	β2	1.21 (1.02-1.43)	.03
6-18 y	Outpatient steroid prescriptions			
	Overall transition point*	δ1	0.38 (0.22-0.64)	<.001
	Post-COVID-19 social distancing†	β2	0.99 (0.91-1.08)	.82
	ED asthma visits			
	Transition point‡	δ1	0.17 (0.06-0.43)	<.001
	Post-COVID-19 social distancing§	β2	1.13 (0.86-1.47)	.38
	RV infections			
	Transition point‖	δ1	0.22 (0.05-0.99)	.048
	Post-COVID-19 social distancing¶	β2	1.06 (0.76-1.47)	.70
19-40 y	Outpatient steroid prescriptions			
	Overall transition point*	δ1	0.67 (0.38-1.19)	.18
	Post-COVID-19 social distancing†	β2	1.02 (0.88-1.19)	.79
	ED asthma visits			
	Transition point‡	δ1	0.71 (0.40-1.25)	.23
	Post-COVID-19 social distancing§	β2	1.00 (0.90-1.10)	.92
	RV infections			
	Transition point‖	δ1	0.37 (0.02-5.68)	.47
	Post-COVID-19 social distancing¶	β2	0.86 (0.38-1.98)	.72

ED, emergency department; *RV*, rhinovirus.

*Factor by which the April 2020 geometric mean number of steroid prescriptions differed from the predicted number based on pre-social distancing trends (ie, January 2016 to March 2020). The geometric mean is less influenced by extreme values than the arithmetic mean when the data distribution is positively skewed, as is generally case for count data.

†Ratio of the geometric mean number of steroid prescriptions at month $m+1$ relative to month m (April to December 2020).

‡Factor by which the April 2020 geometric mean number of ED asthma exacerbation visits (+1) differed from the predicted number based on pre-social distancing trends (ie, January 2016 to March 2020).

§Ratio of the geometric mean number of ED asthma exacerbation visits (+1) at month $m+1$ relative to month m (April to December 2020).

‖Odds ratio for positive RV polymerase chain reaction test relative to predicted number based on pre-social distancing trends (ie, January 2016 to March 2020).

¶Odds ratio for positive RV polymerase chain reaction test in month $m+1$ relative to month m (April to December 2020).