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LETTER TO THE EDITOR

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# Reduction of pulmonary exacerbations in young children with cystic fibrosis during the COVID-19 pandemic

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## Abstract

To assess the impact of COVID-19 restrictions on cystic fibrosis (CF) pulmonary exacerbations (PEx) we performed a retrospective review of PEx events at our CF Center and compared the rate of PEx in 2019 versus 2020. Restrictions on social interaction due to the COVID-19 pandemic were associated with a lower number of PEx events at our pediatric CF Center, suggesting that these restrictions also reduced exposure to other respiratory viral infection in children with CF.

**KEYWORDS**
COVID-19, cystic fibrosis, epidemiology, exacerbation

To The Editor,

The COVID-19 pandemic resulted in widespread restrictions on social interactions and lockdowns in many areas of the world.[1] The impact of these measures on cystic fibrosis (CF) pulmonary exacerbations (PEx) has not been described. Respiratory viral infections are a common trigger for PEx,[2,3] and COVID-19 restrictions might lead to fewer PEx by reducing exposure to viruses in general, not just SARS-CoV2. To test the hypothesis that the COVID-19 lockdown would be associated with a lower PEx incidence we compared PEx data at our CF Center from the time with the most stringent restrictions in Indiana to the same time interval in 2019.

We identified PEx events by performing a retrospective chart review of children with CF followed at the CF Center at Riley Hospital for Children. We limited the lower age range to 2 years because differentiating viral upper respiratory infection from PEx can be difficult in this age group,[4] and we set an upper age limit of 11 years to avoid any potential confounding by elexacaftor/tezacaftor/ivacaftor therapy.[5,6] The first COVID-19 case in Indiana was reported on March 1, and the peak incidence of infection during the Spring occurred on April 23. A statewide lockdown was initiated on March 23. With this timeline in mind, we collected data from two time intervals in both 2019 and 2020: January 1–March 15 (which corresponded to the months before the COVID-19 detection in Indiana) and March 16–May 15 (which corresponded with the months of peak COVID-19 incidence in the Spring of 2020). PEx was determined by the treating clinician based on changes in signs, symptoms, and/or lung function that led to oral or intravenous antibiotic therapy. Every PEx event was analyzed during these timeframes, and data collected included demographics, height and weight, lung function, microbiology, location of encounter, and antibiotic treatment. Testing for respiratory viruses is not part of our routine clinical care and data on viral testing was not available for analysis. Data were analyzed using descriptive statistics and generalized linear models where data had repeated measures. This project was reviewed and approved by our local institutional review board before data collection.

The number and location of PEx events during the time intervals studies are shown in the Table 1. The number of PEx events were significantly decreased in both time intervals in 2020 compared to

  

**TABLE 1** Number and location of pulmonary exacerbation events at children ages 2–12 years from January 1 to May 15 in years 2019 and 2020

| | January 1–March 15 | | | March 16–May 15 | | |
|---|---|---|---|---|---|---|
| | 2019 | 2020 | P (2019 vs. 2020) | 2019 | 2020 | P (2019 vs. 2020) |
| Number of PEx event (% of population) | 56 (70%) | 42 (53%) | 0.012 | 35 (44%) | 14 (18%) | <0.001 |
| Location of PEx (N) | | | | | | |
| Hospital | 9 (16.1%) | 7 (16.7%) | .9309 | 4 (11.4%) | 2 (14.3%) | .7637 |
| In person clinic visit | 23 (41.1%) | 11 (26.2%) | .0744 | 15 (42.9%) | 1 (7.1%) | .0066 |
| Telehealth | 0 (0) | 0 (0) | n/a | 0 (0) | 1 (7.1%) | .3135 |
| Phone calls | 24 (42.9%) | 24 (57.1%) | .1313 | 16 (45.7%) | 10 (71.4%) | .0660 |

*Note: p* values are from generalized linear models when data have repeated measures and from Fisher's Exact or the Student *t* tests when not.

2019, although the decline was even greater from March 16 to May 15. The location of patients' PEx events also differed between 2019 and 2020, with a significantly lower percentage of PEx identified through in-person clinic visits and a much larger percentage identified through phone encounters. The number of patients (80 in 2019 and 78 in 2020) and their clinical characteristics, such as sex, genotype, respiratory culture history, baseline lung function, and nutritional indices were similar for both years, suggesting that our observations were not due to an overall improvement in the health of our patients. However, whereas 100% of clinic visits in 2019 and from January 1 to March 16 2020 were in-person, only 16% of visits during the March 16–May 15, 2020 time interval were in-person.

Our analysis shows that COVID-19 restrictions were associated with decreased PEx events and a shift towards PEx diagnosis through phone encounters rather than in-person visits. We speculate that this may have occurred due to reduced exposure to respiratory viral infections in general. Reports have demonstrated sharply decreased influenza and RSV activity associated with lockdowns.[7,8] It is also possible that because our patients and their parents were both at home more, there was improved adherence. Alternatively, it is possible that PEx were missed due to a reduction in measurements of lung function. However, we observed a reduction in PEx reported via phone encounters, which would not have been affected by the reduction in lung function measurements. Furthermore, we also observed a reduction in PEx rate before March 16, which may reflect the fact that patients were already engaging in a degree of self-isolation before the statewide lockdown. The decrease in in-person PEx events reflects the increased use of telehealth at the height of the COVID-19 pandemic in Indiana. Limitations of our analysis include the retrospective study design and the fact that we only analyzed data from a single CF Center. Another limitation is that we did not have a standardized definition of PEx and PEx status was not always explicitly documented in the medical record. We, therefore, inferred PEx status by the patient's clinical signs and symptoms, lung function data (when available), and the clinician's decision to use antibiotic therapy.

In summary, restrictions on social interaction due to the COVID-19 pandemic were associated with a lower rate of PEx at our pediatric CF Center. These results are consistent with other studies demonstrating the importance of respiratory viral infections as a trigger for PEx and will help CF clinicians anticipate the burden of CF lung disease should severe lockdowns due to COVID-19 occur again in their region.

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### AUTHOR CONTRIBUTIONS

Shreya Patel: conceptualization (supporting), data curation (lead), formal analysis (lead), funding acquisition (equal); investigation (equal), writing original draft (supporting). Misty D Thompson: data curation (supporting). Don B Sanders: conceptualization (supporting), formal analysis (supporting), investigation (supporting), writing original draft (supporting), writing review and editing (supporting). Clement L Ren: conceptualization (lead), data curation (supporting), formal analysis (equal), funding acquisition (equal), investigation (equal), methodology (lead), resources (lead), software (lead), supervision (lead), writing original draft (equal), writing review and editing (lead).

### DATA AVAILABILITY STATEMENT

The data are not publicly available due to privacy or ethical restrictions.

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