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Unforeseen changes in seasonality of pediatric respiratory illnesses during the first COVID-19 pandemic year

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Abstract

Objectives: To investigate whether the three nationwide coronavirus disease 2019 (COVID-19) lockdowns imposed in Israel during the full first pandemic year altered the traditional seasonality of pediatric respiratory healthcare utilization.

Methods: Month by month pediatric emergency department (ED) visits and hospitalizations for respiratory diagnoses during the first full COVID-19 year were compared to those recorded for the six consecutive years preceding the pandemic. Data were collected from the patients' electronic files by utilizing a data extraction platform (MDClone©).

Results: A significant decline of 40% in respiratory ED visits and 54%–73% in respiratory hospitalizations during the first COVID-19 year compared with the pre-COVID-19 years were observed ($p < 0.001$ and $p < 0.001$, respectively). The rate of respiratory ED visits out of the total monthly visits, mostly for asthma, peaked during June 2020, compared with proceeding years (109 [5.9%] versus 88 [3.9%] visits; $p < 0.001$). This peak occurred 2 weeks after the lifting of the first lockdown, resembling the "back-to-school asthma" phenomenon of September.

Conclusions: This study demonstrates important changes in the seasonality of pediatric respiratory illnesses during the first COVID-19 year, including a new "back-from-lockdown" asthma peak. These dramatic changes along with the recent resurgence of respiratory diseases may indicate the beginnings of altered seasonality in pediatric pulmonary pathologies as collateral damage of the pandemic.

KEYWORDS

asthma, bronchiolitis, children, COVID-19, healthcare utilization, lockdown, pneumonia, respiratory illness

1 | INTRODUCTION

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has dramatically changed the lives of people worldwide.[1] One of the most prominent repercussions of its appearance was the drastic measures taken by governments worldwide in an attempt to curb the spread of the virus, such as personal protective measures (e.g., facemasks and hand hygiene), as well as social distancing, isolation, and lockdowns.[2] In Israel, restrictions were gradually applied at the beginning of February 2020, ultimately leading to a closure of all educational institutions on March 15, 2020.[3] This was the first of three periods of lockdown ranging from 4.5 weeks to 9 weeks. During these lockdowns, the educational system was closed, and classes were held solely via virtual systems, while children were instructed to remain at home and avoid social gatherings.

Many short-term studies have described the influence of such protective measures upon the utilization of healthcare systems worldwide and their effect upon patients' health and wellbeing.[4–6] There has been a 51%–78% decrease in health care access for respiratory illness among pediatric populations during lockdown periods compared with pre-coronavirus disease 2019 (COVID-19) periods.[7–9] Several factors may have contributed to this decline, including a decrease in the accessibility to medical services during lockdowns, parental anxiety, and a possible actual decrease in respiratory illnesses.

Pediatric respiratory illnesses had traditionally followed a unique temporal trend. Two examples of such seasonality are viral infections, such as a respiratory syncytial virus (RSV), and asthma exacerbations. RSV bronchiolitis is most prevalent during predictable seasonal outbreaks in the late fall, winter, and early spring in the northern hemisphere.[10,11] Asthma is a chronic respiratory disease with known seasonal flare-ups,[12] with the highest incidence in September[13] and a less dominant peak in the spring.[14] A peak in childhood asthma exacerbations that coincides with the start of the school year in September, known as "back-to-school asthma" (BTS), is well-recognized and accounts for 20%–25% of all exacerbations requiring hospitalization in many northern hemisphere countries.[15,16] The timing of BTS suggests that rhinovirus infections may play a major part in this phenomenon and in the overall annual cycle of asthma morbidity, serving as a trigger for exacerbations.[17] Seasonality of adherence to controller inhalers has also been described, with a peak in adherence among children noted in September–October and a decline in March–April.[18]

Precautions taken during the COVID-19 pandemic are directed against the spread of an airborne virus. It is reasonable to consider that such measures might also have an effect upon other respiratory conditions as well. The aim of this study, therefore, was to investigate whether three consecutive COVID-19 lockdown periods throughout an entire year altered an established timeline of healthcare utilization due to respiratory illnesses in children.

2 | METHODS

2.1 | Study population

This study was conducted at Dana–Dwek Children's Hospital, Tel-Aviv Medical Center between March 1, 2020, and February 28, 2021 (the first COVID-19 year in Israel). The study population included children aged 0–18 years who visited our hospital with respiratory complaints and/or diagnoses during the first COVID-19 year. The control group was comprised of children with the same characteristics who visited the hospital throughout the 6 years before the pandemic (from 2014 to 2020). This study was approved by the local ethics committee (approval number TLV-0609-20), and informed consent was waived since it was retrospective and anonymous.

2.2 | Data collection and study design

Medical and demographic data were collected from the patients' electronic files by means of MDClone©, a data extraction synthetization platform that provides patient-level data around a reference event.[19] For the purposes of this study, the reference event was a pediatric ED visit or hospitalization due to respiratory complaints or diagnosis that included asthma exacerbation, wheezing, dyspnea, cough, bronchiolitis, or pneumonia according to International Statistical Classification of Diseases and Related Health Problems (ICD) classification systems. Data on demographics (e.g., age and sex) and nasal viral swab test were also retrieved.

The major outcomes of this study were the incidence of ED visits and hospitalizations in hospital wards (e.g., pediatric ward, intensive care unit, etc.) due to respiratory complaints and the timeline of these events. These values were calculated yearly and monthly by dividing the average number of respiratory ED visits and hospitalizations by the average number of total ED visits and hospitalizations during the study (pandemic) period and the control (pre-pandemic) period. The incidence and yearly seasonality of these events during the first COVID-19 year were compared with those of the pre-COVID-19 years. We also performed a subgroup analysis by diagnosis, focusing upon the three major respiratory diagnoses of asthma and/or wheezing, pneumonia, and bronchiolitis.

The Israeli school year routinely starts on September 1 after 2 months of summer vacation. There were three lockdown periods during the COVID-19 year study period, during which all of the educational institutions were closed: the first lockdown took place from March 15 to May 17, 2020 (9 weeks), the second from September 17 to October 18, 2020 (4.5 weeks), and the third from January 8 to February 11, 2021 (5 weeks).

2.3 | Statistical analysis

The preferred method of analysis for continuous variables, such as age in pre-COVID-19 and COVID-19, was parametric using Student's

t test. The non-parametric Mann-Whitney was applied if parametric assumptions could not be satisfied, such as in the case of hospitalization length of stay among pre-COVID-19 and COVID-19 patients, even after attempts at data transformation. Parametric model assumptions were assessed with the normal probability plot or the Shapiro–Wilks statistic for verification of normality and with Levene's test for verification of homogeneity of variances. Categorical variables were tested with Pearson's χ^2 test for contingency tables or Fisher's Exact test, as appropriate. Variable in which this type of analysis was applied to compare pre-COVID-19 and COVID-19 rates include gender, monthly incidence of pneumonia, bronchiolitis, wheezing or asthma, total respiratory cases (both in ED and wards), and positive nasal swabs rates, as well as total ED visits and hospitalizations. All statistical tests and/or confidence intervals were performed at $\alpha = 0.05$ (two-sided). All *p* values were rounded to three decimal places. The data were analyzed with IBM SPSS Statistics software.

3 | RESULTS

There was a total of 20,527 pediatric ED visits, 2545 pediatric ward hospitalizations, and 401 ICU hospitalizations during the first COVID-19 year compared with an annual mean of 28,435 ED visits, 3142 pediatric ward hospitalizations, and 356 ICU hospitalizations in the pre-COVID-19 years ($p < 0.001$, $p < 0.001$ and $p = 0.36$, respectively). There was a 28% reduction in total ED annual visits and a 19% reduction in total annual hospitalizations during the first COVID-19 year compared to pre-COVID-19 years ($p < 0.001$ and $p < 0.001$, respectively). An even greater decrease was observed in respiratory-related presentations, with a 40% reduction in respiratory ED visits and a 54% reduction in respiratory hospitalizations compared with the pre-COVID-19 years ($p < 0.001$ and $p < 0.001$, respectively). A 73% decrease in respiratory ICU hospitalizations was also observed ($p < 0.001$). The characteristics of the study participants are presented in Table 1. There was a significant increase in age of patients with respiratory ED visits and hospitalizations in the COVID-19 year from pre-COVID-19 years (4.44 years vs. 3.16 years for respiratory ED visits, $p < 0.001$; 3.48 years versus 2.64 years for respiratory hospitalizations, $p < 0.001$).

Analysis of the monthly respiratory ED visits and hospitalization rates revealed a significant decrease throughout the first COVID-19 year compared with pre-COVID-19 years, except for the months of March and June (Figure 1, Supporting Information Appendix Table S1). For example, the number of respiratory-driven ED visits during the month of March of first COVID-19 year was similar to that of previous years (109 [7.4%] vs. 150 [6.4%] visits; $p = 0.14$), while those visits during the month of June of first COVID-19 year displayed a reversed trend, with a significant increase having been recorded in ED visits compared with previous years (110 [6%] vs. 87

TABLE 1 General characteristics of patients

		The first COVID-19 year (March 2020–February 2021	The pre-COVID-19 years (2014–2020)	*p* Value
ED visits	Annual mean visits due to any diagnoses, mean	20,527	28,435	**<0.001**
	ED visits due to respiratory diagnoses			
	n[a]	770 (3.8%)	1787 (6.3%)	**<0.001**
	Age, mean (*SD*), year	4.44 (4.68)	3.16 (3.65)	**<0.001**
	Sex, male, *n*	470 (61%)	6317 (58.9%)	0.25
Hospitalizations	Annual hospitalizations for any diagnoses, mean	2545	3142	**<0.001**
	Hospitalizations due to respiratory diagnoses			
	n[a]	230 (9%)	612 (19.5%)	**<0.001**
	Age, mean (*SD*), year	3.48 (3.97)	2.64 (3.42)	**<0.001**
	Sex, male, *n*	151 (65.7%)	2138 (58.3%)	**0.03**
ICU	Annual hospitalizations for any diagnoses, mean	401	356	0.36
	ICU hospitalizations due to respiratory diagnoses			
	n[a]	30 (7.4%)	98 (27.5%)	**<0.001**
	Age, mean (*SD*), year	6.97 (6.1)	3.78 (4.56)	**0.008**
	Sex, male, *n*	21 (70%)	335 (56.9%)	0.15

Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; ICU, intensive care unit; *SD* standard deviation.

[a]Out of total visits/hospitalizations.

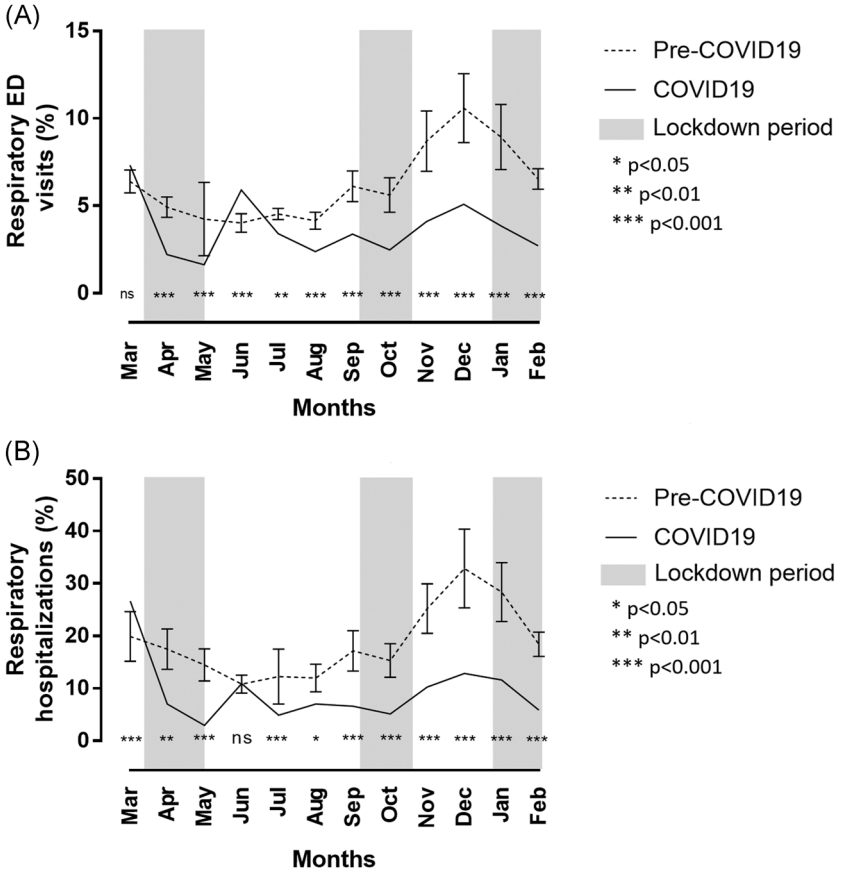

FIGURE 1 Incidence of respiratory ED visits and hospitalizations by month The incidence of respiratory ED visits (A) and respiratory hospitalizations (B) by month in the COVID-19 year (black) compared with pre-COVID-19 mean annual visits and hospitalizations (red). The incidence was calculated by dividing the respiratory ED respiratory visits or respiratory hospitalizations by the total visits or hospitalizations during that month. COVID-19, coronavirus disease 2019; ED, emergency department, ns, nonsignificant

[4%] visits; $p < 0.001$). There was no significant difference in respiratory-driven hospitalizations in the month of June (24 [10.9%] vs. 26 [10.8%] hospitalizations; $p = 0.97$).

We carried out a subgroup analysis of the cohort focusing on three major respiratory diagnoses: asthma and/or wheezing, bronchiolitis, and pneumonia (Figure 2, Supporting Information Appendix Tables S2 and S3). The number of ED visits of children with the diagnosis of asthma and/or wheezing was significantly lower throughout most of the first COVID-19 year compared with previous years, except for the months of March, July, and August. There was a significant reversal of this trend in June, with a higher rate of asthma ED visits in the first COVID-19 year compared with the pre-COVID years (50 [2.8%] vs. 194 [1.4%] visits; $p < 0.001$). The asthma-related hospitalization rate was not significantly different from the pre-COVID years during most of the first COVID-19 year, except for the lockdown months of April, May, September, and January, when the rates were significantly lower in the first COVID-19 year compared with previous years.

The bronchiolitis ED visits and hospitalization rates were significantly lower during the bronchiolitis high season (from October to February) for the first COVID-19 year compared with previous years. Moreover, there was a reversal of the traditional trend in March and June when the rates of ED visits and hospitalizations were higher during the first COVID-19 year compared with the pre-COVID years (March: 17 [1.2%) vs. 90 [0.6%] visits; $p = 0.03$, and 17 [10.1%] vs. 63 [4.2%] hospitalizations; $p < 0.001$, respectively; June: 6 [0.3%] vs. 8 [0.1%] visits $p = 0.004$, and 3 [1.4%] vs. 4 [0.3%] hospitalizations; $p = 0.05$, respectively).

The prevalence of positive nasal swab test for respiratory viruses among children hospitalized for respiratory reasons was significantly lower for RSV (only 4.3% during the first COVID-19 year compared with 21.6% in the pre-COVID-19 years; $p < 0.001$) and for Influenza A (0% during the first COVID-19 year compared with 2% in the pre-COVID-19 years; $p = 0.02$). The prevalence of positive test for other viruses like Para-influenza and Influenza B was not significantly different. Finally, pneumonia was significantly less prevalent throughout most of the first COVID-19 year, both for ED visits and for hospitalizations. The exceptions were March for the ED visits and April and June for the pediatric department hospitalizations when the rates were lower but without statistical significance.

4 | DISCUSSION

In this study, we calculated the numbers of pediatric respiratory events in a real-world setting during an entire pandemic year and compared them to pre-pandemic values. Our results revealed a significant decrease in ED visits and pediatric hospitalizations for common pediatric respiratory diseases, following new seasonality. Specifically, we showed changes in the traditional seasonality of pulmonary diseases as well as lower rates of respiratory diseases, especially asthma, pneumonia, and bronchiolitis, during the first pandemic year in

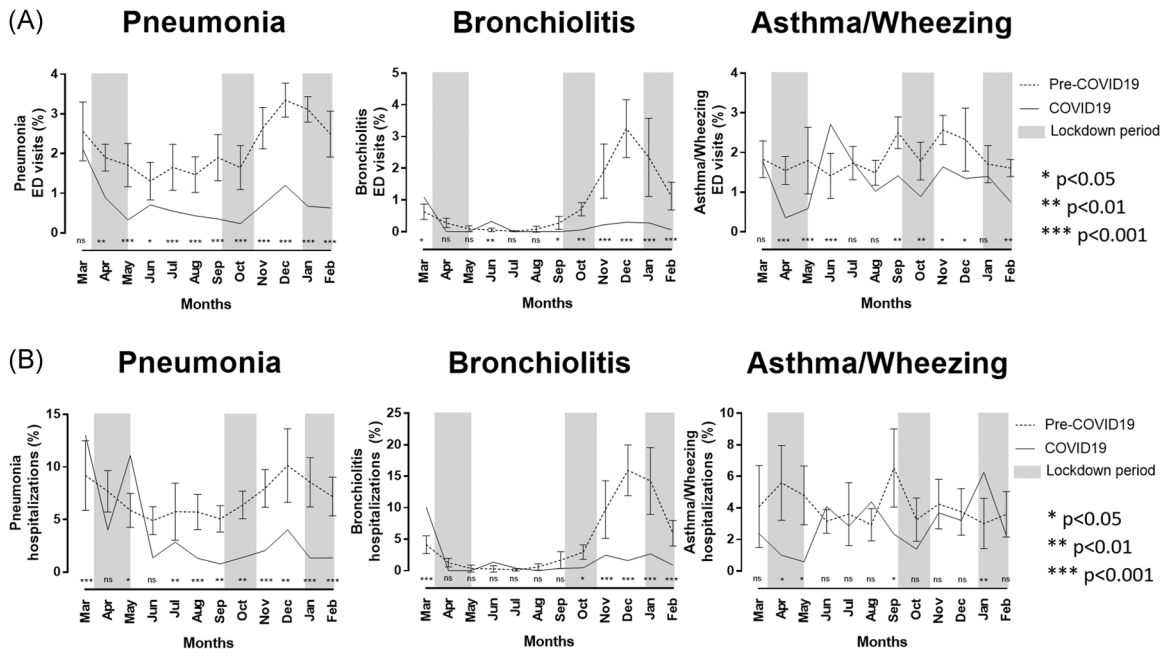

FIGURE 2 Incidence of specific respiratory diagnoses by month The number of respiratory ED visits (A) and respiratory hospitalizations (B) by month throughout the COVID-19 year (black) compared to pre-COVID-19 mean annual visits and hospitalizations (red). The incidence was calculated by dividing the respiratory ED respiratory visits or respiratory hospitalizations by the total visits or hospitalizations during that month. COVID-19, coronavirus disease 2019; ED, emergency department, ns, nonsignificant.

comparison to the six consecutive pre-pandemic years. We examined the specific impact of three lockdown periods and showed a significant reduction in healthcare utilization throughout most of the year and more so during those lockdowns. Previous studies have also shown lower healthcare utilization in general and specifically due to respiratory complaints during the COVID-19 pandemic compared with previous periods in the short term.[20] Bover-Bauza et al.[21] demonstrated significant decreases in pediatric ED visits and admissions for asthma exacerbation during the first lockdown in Spain compared with the same period in the previous year. Our findings stand in agreement with these findings and expand them even further. In our study, we have demonstrated a decrease in each of the three lockdowns, regardless of the season, the time of the school year, and the established local seasonality of the respiratory illnesses.

Short-term decreases in healthcare utilization due to respiratory illnesses during the COVID-19 year have been investigated by others and several reasons were suggested. First, there was an actual decrease in pediatric respiratory illnesses secondary to changes in behavior, including social distancing, adherence to hand hygiene practices, and the use of facemasks—to decrease person-to-person transmission of respiratory viruses[22,23]; decrease in air pollution mostly during lockdowns when traffic was most restricted,[23,24] and limited exposure to outdoor pollution and aeroallergens.[23] There was also greater adherence to preventive treatment of respiratory illnesses[25,26] as the result of parents spending more time with their children during lockdowns and providing better supervision and a higher level of vigilance.[27] Second, except for the actual decrease in pediatric respiratory illnesses, fear of contracting COVID-19 during hospitalization was a major factor in the reduced healthcare utilization during lockdown.[5,28] However, as shown by our current findings, not only was the rate of ED visits lower, but the rate of hospitalizations was lower as well, suggesting that the decrease in utilization was not solely due to hospital avoidance or related anxiety but due to a decrease in morbidity as well.[8]

W observed a dramatic change in the timing of respiratory illness occurring during the first COVID-19 year compared to previous years. These findings are in line with the work of Pelletier et al. who showed a seasonal variation of major pediatric diagnoses in the first half of 2020, including premature termination of winter-predominant conditions, such as bronchiolitis and pneumonia, and a reduction in admissions for asthma in 2020 compared with previous years.[29] Interestingly, bronchiolitis seemed to follow normal seasonality trends e.g. no differences in spring and summer, while both asthma and pneumonia did not follow, or did but to a lesser degree. This supports the notion of multiple triggers for asthma/pneumonia (allergies, stress, more exercise in warmer months, and bacterial pathogens) versus the single trigger of bronchiolitis, being viral, which was lessened by the lockdowns. Moreover, there was a significant increase in the age of patients with respiratory ED visits and hospitalizations in the COVID-19 year from pre-COVID-19 years. This could be explained by several factors, including the younger age children who are more prone to viral respiratory illnesses compared to the older children whose respiratory illnesses are more influenced by variable triggers. Another possible explanation might be parental anxiety regarding sending infants to daycares even after a lockdown was lifted.[27]

An interesting finding in our study was a peak of incidence in ED respiratory visits and respiratory hospitalizations in the month of June 2020. This peak took place two weeks after the end of the first lockdown, which was the most stringent and longest of all lockdowns in Israel. That peak was most prominent for asthma, and it resembled the phenomenon of BTS asthma with its well-known peak incidence in September after the beginning of the school year.[13,30] The BTS asthma phenomenon is generally explained by universal seasonality or the return to school per se.[13,15,17] Our finding, which we termed *back-from-lockdown* (BFL) asthma, resembles BTS in many aspects. First, children returning to school after 2 months of social distancing, are re-exposed to viral respiratory infections.[13,16,17] Rhinovirus infections, which are the strongest trigger for asthma exacerbations, especially as part of BTS asthma, are known to be most common in early autumn after the summer vacation.[13,16,17,31] Since the examined peak of BFL asthma was in June, the seasonality of the virus would not be expected to have been a contributing factor.[31] Nevertheless, some data suggest that a new pattern of viral seasonality was created due to the newly introduced SARS-CoV-2,[32] as seen, for example, from our data on RSV.

Other factors that may explain both BFL and BTS asthma include high stress associated with school return, which can worsen asthmatic symptoms in children,[33,34] and re-exposure to high levels of sensitizing allergens in the school environment.[13,17] All of the above factors may also play a role in the BFL asthma phenomenon observed in June 2020. Moreover, it can be argued that these factors are even more prevalent during a lockdown in comparison to a regular school break because of the extreme measures taken (e.g., masks, social distancing, travel restrictions, and pandemic-related stress). However, allergic exposures likely play a much smaller role in respiratory diseases than we had previously imagined. During the lockdown, children were more likely to be exposed to pets, environmental tobacco smoke, and potentially the outside environment rather than sitting in a classroom all day. This may explain, in part, why aggressive allergen mitigation efforts appear to have a negligible impact on asthma exacerbations.[35]

The new BFL asthma and the changes observed in time patterns of respiratory illnesses during the first COVID-19 year raise the question of whether the term "seasonality" is adequate when discussing respiratory morbidity, especially with viral etiology. Rather than discussing seasonality, it is time to accept that when viruses are readily transmitted among children it is then we will see an increase in respiratory illnesses, and this is most probably unrelated to a season.

Some limitations to our study bear mention. First, the data were from a single center in Israel, therefore it is not clear whether these results would be generalizable to like institutions in other countries. Second, only hospital data and not primary care or telemedicine services were included. Regarding remote medicine, our medical center utilized remote medicine services only for ambulatory care and not as urgent care. Therefore, remote medicine probably did not affect the rate of ED visits or hospitalizations. Moreover, telemedicine services were more accessible at the community clinics, and were likely more accessible in the second and third lockdown periods. Therefore, one may have expected an even larger drop in ED visits in place of online visits, which did not seem to occur, thus making the telemedicine role less likely as the principal reason for decreased ED visits.

In conclusion, this study demonstrates important changes in the seasonality of pediatric respiratory illnesses during the first COVID-19 year, including a new "back-from-lockdown" asthma peak. These dramatic changes along with the recent resurgence of respiratory diseases suggest that the last word has not yet been said and may imply a global change in pediatric respiratory medicine as we know it.

AUTHOR CONTRIBUTIONS

Moria Be'er: Data curation (lead); investigation (lead); methodology (lead); visualization (lead); writing—original draft (lead); writing—review & editing (lead). **Israel Amirav**: Conceptualization (equal); supervision (equal); writing—original draft (equal); writing—review & editing (equal). **Michal Cahal**: Data curation (equal); investigation (equal); writing—review & editing (equal). **Mika Rochman**: Data curation (equal); investigation (equal); writing—review & editing (equal). **Yotam Lior**: Formal analysis (lead); investigation (supporting); validation (equal); writing—review & editing (equal). **Ayelet Rimon**: Data curation (equal); writing—review & editing (supporting). **Roni Gur Lavy**: Data curation (equal); writing—review & editing (supporting). **Moran Lavie**: Conceptualization (equal); investigation (equal); methodology (equal); supervision (lead); writing—original draft (equal); writing—review & editing (equal).

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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