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Potential conflict of interests

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Key message : Influences of the COVID-19 pandemic on severe acute asthma (SAA) requiring pediatric intensive care unit (PICU) admission remains a poorly understood issue. While during the Coronavirus Disease 2019 (COVID-19) lockdown the number of patients with SAA decreased, after lifting of these restrictions, PICU admissions drastically increased again. This increase was higher than in pre-pandemic years and increased susceptibility to viral infections other than SARS-CoV-2 is, most likely, the main cause. In the future, more precaution should be taken for children with SAA in similar situations. Additionally, it is important to be aware of the large variety of (external) triggers SAA might have, and how they may impact trends seen at the PICU.

To the Editor,

Severe acute asthma (SAA) is an asthma exacerbation unresponsive to conventional oral and inhalation therapy and requires a PICU admission for intravenous therapy. It may even lead to the necessity for intubation and can cause serious morbidity and mortality[1]. SAA is usually triggered by a viral infection, but environmental factors such as allergens and air pollution are also common[1]. The Coronavirus Disease 2019 (COVID-19) pandemic is also an external factor which might affect the number of asthma exacerbations, as a result of changes to the environment as well as medical practice and management[2]. While the incidence of asthma exacerbations in children during the COVID-19 pandemic has been evaluated[3], the incidence of SAA requiring PICU admission during the pandemic is, to our knowledge, not known. This is especially of interest as the unique event of the pandemic might teach us about the effect of environmental factors on SAA. Therefore, we evaluated PICU admission trends for SAA before and during the COVID-19 pandemic and its link to the COVID-19 restrictions and other relating environmental triggers.

This study is a single-center, retrospective cohort study conducted at the Amsterdam University Medical Center (UMC), a tertiary hospital in the Netherlands. All patients with a diagnosis of SAA above two years of age admitted to the PICU between 2018 and 2021 were included. Children below the age of two were excluded as they will more likely present with bronchiolitis, and differentiation between bronchiolitis and asthma is difficult. The total number of PICU admissions of the Amsterdam UMC was also extracted. The

diagnosis of SAA was made by a pediatrician and based on the definition: "Severe aggravation of bronchial obstruction not improving after a few doses of bronchodilator inhalation".

The exact dates and levels of governmental COVID-19 restrictions in the Netherlands were obtained from the Oxford COVID response tracker, i.e. school closure, a working from home order or both[4]. Air pollution was represented by hourly concentrations of particulate material with an aerodynamic diameter of less than 2.5 microns (PM2.5), measured at the closest official measuring station to the Amsterdam UMC ("Stadhouderskade" station at 11 km. distance) by the Dutch National Institute for Public Health and the Environment (RIVM)[5]. Pollen exposure was obtained by the pollen index from the monitoring station of the Leiden University Medical Center, located at 35 km. distance[6].

Because of the retrospective design of the study, the Medical Ethics Committee waived the need for informed consent. Statistical analysis was conducted using IBM SPSS Statistics for Windows version 28.0.1.1 (SPSS, Chicago IL, USA). Only descriptive analyses were executed because of the small study population. Graphs were generated using R version 4.2.2.

In total, 168 children were admitted to the PICU of the Amsterdam UMC for SAA between 2018 and 2021. The mean age of the participants was 7.4 years and a minority was female (Table 1). In the pre-pandemic years, admissions tended to increase to the highest rate in April, while in 2021 a peak in admissions was observed in the months August to November (Figure 1). This peak of SAA admissions in the fall of 2021 did not correspond to an overall increased PICU admission rate. Moreover, the annual relative percentage of PICU admissions due to SAA of the total PICU admissions was highest in 2021 (8.0%), followed by 2019 (5.8%), then 2020 (5.4%) and 2018 (4.7%) (Table 1). A relationship between lockdown measures during the pandemic and PICU admissions was observed, with decreased admissions during stricter lockdown measures and increased admission rates after lockdown restrictions were lifted (Figure 2).

The majority of patients (70.2%) showed signs of a viral infection as a trigger; however, not all of these clinical diagnoses were confirmed by a nasal or throat swab, as in only 60.1% a viral test was taken with the highest load of testing in 2020 and 2021. The pandemic led to an increased rate of viral testing at the PICU, as the updated infection control measures required an active SARS-CoV-2 infection to be confirmed or ruled out by a rapid test before admission. Nevertheless, more extensive viral testing for respiratory viruses was limited because of decreased laboratory capacity during the pandemic so the causative viral agent was usually still unknown in our study group. Regarding other environmental triggers, no correlations were observed between the monthly PICU admission numbers and pollen or PM2.5 concentrations (r_s=-0.04 for pollen and r_s=0.23 for PM2.5).

An explanation for the peak in the fall of 2021 could be the COVID-19-related regulations of increased hygienic measures, wearing face masks and social distancing, as these reduced the spread SARS-CoV-2 but also the spread of other viruses[2]. Additionally, the "Hygiene Theory", introduced by Strachan in 1989, further supports this hypothesis, as it states that the trend of allergic diseases may be associated with infectious diseases and unhygienic contact in early childhood could prevent allergic disorders[7]. As during this peak period of 2021, respiratory viruses were the most frequent trigger for SAA, we hypothesize that when restrictions were lifted, children were exposed to these viruses again and admissions peaked. Furthermore, these COVID-19-related regulations may have contributed to an 'immunity debt', which implies the lack of protective immunity caused by prolonged low exposure to a specific pathogen, making children susceptible to viral diseases, especially those whose transient immunity is acquired through physical contact[8].

According to previous studies, declines in the rate of general asthma exacerbations during the pandemic have been attributed to better air quality because of reduced travel and decreased exposure to other asthma triggers[3,9]. Additionally, an increased risk for asthma exacerbations in association with tree pollen has been observed[10]. However, no clear association between pollen, PM2.5 concentration and SAA were found in this study.

Our study was conducted in a single center, making it subject to selection bias. Moreover, given the retrospective nature of this study, we had limited information regarding details of some of the variables.

Also, as we did not have information on the residential addresses of the participants, we used data from one air quality monitoring station as a proxy for personal exposure to PM2.5. Finally, viral testing was not available for all participants.

In conclusion, this study demonstrates that the incidence of SAA at the PICU was lower in the first year of the COVID-19 pandemic with a high-peak incidence in the fall of 2021 after all governmental restrictions had been lifted. This could be due to an increase in exposure to viruses other than SARS-CoV-2. No association between air pollution and pollen index was observed, which could be because of the more prominent role of a viral infection as a trigger for SAA.

Keywords: asthma exacerbation, severe acute asthma, pediatric intensive care unit, children, COVID-19 pandemic, environmental, lockdown

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Impact statement

Severe acute asthma (SAA) is a severe asthma exacerbation usually requiring admission to a pediatric intensive care unit (PICU) and causes serious morbidity and mortality; moreover, over the past few decades the number of PICU admissions for SAA has shown a significant increase. The Coronavirus Disease 19 (COVID-19) pandemic has influenced the medical health care system as a whole including asthma and its exacerbation pattern. In this study, the relationship between number of PICU admissions for SAA and the COVID-19 pandemic lockdown regulations. Additionally, changes to possible environmental factors triggering severe exacerbations, including air pollution and pollen index, are explored. This study took place in a tertiary hospital in Amsterdam, The Netherlands, and included all children over two years of age admitted for SAA to the PICU between 2018 and 2021. It was found that when COVID-19 restrictions were strict, and lockdown was in place, the number of SAA admissions at the PICU drastically decreased. After most restrictions had lifted, especially from August to November of 2021, a large peak in admissions was observed. It is hypothesized that outbreak of viral infections other than COVID-19 might have been the cause for this association, as spread of viruses was decreased during regulations. Finally, no association between air pollution and pollen index and SAA admissions was observed. In the future, it must be known that large societal changes may have an impact on SAA patterns and physicians must be aware of the impact of these changes on the number of children coming to the ED with respiratory symptoms.

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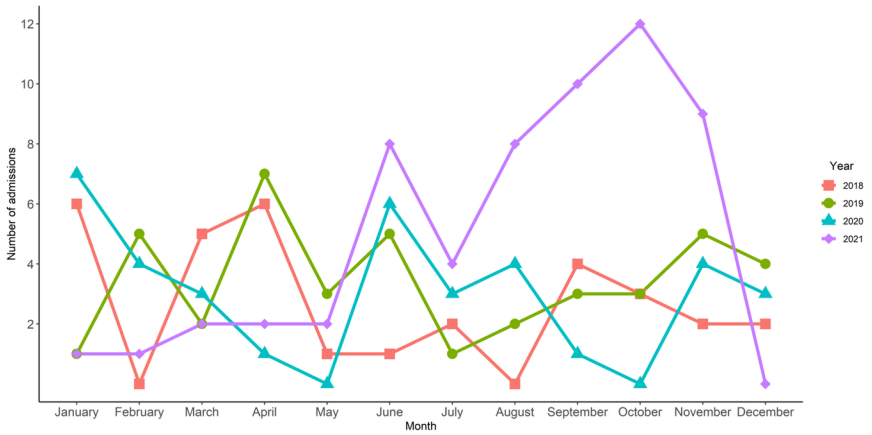
Tables

Time of admission (year)
Number of general PICU admissions (n)
Number of admissions for SAA (n)
Relative percentage of PICU admissions for SAA (%)
Demographics of the study population
Girls (n (%))
Age in years (mean (SD))
Divorced parents (n (%))
Living with a single parent (n (%))
Clinical characteristics of the study population
Clinical diagnosis of viral infection ++ (n (%))
Conducting virology laboratory tests § (n (%))
Allergy history (n (%))
Previously diagnosed with asthma (n (%))
Days between symptom onset and admission (median (25^{th}-75^{th} percentiles))

Time of admission (year)	
Duration of hospitalization in days (median (25^{th}-75^{th} percentiles))	
Environmental factors	
Ambient PM2.5 concentration (micrograms per cubic meter of air) (median (25^{th}-75^{th} percentiles))	
Pollen (grains per cubic meter of air) (median (25th-75th percentiles))	

Abbreviations: $PM_{2.5}$ = fine particulate matter; SAA = severe acute asthma Footnotes: + Peak 2021 was the time period f

Table 1 . Characteristics of the study population and number of general PICU admissions.



Figures

Figure 1 | The number of PICU admissions for SAA in 2018-2021. The monthly pediatric intensive care unit (PICU) admissions for severe acute asthma (SAA) are shown for the years 2018-2021.

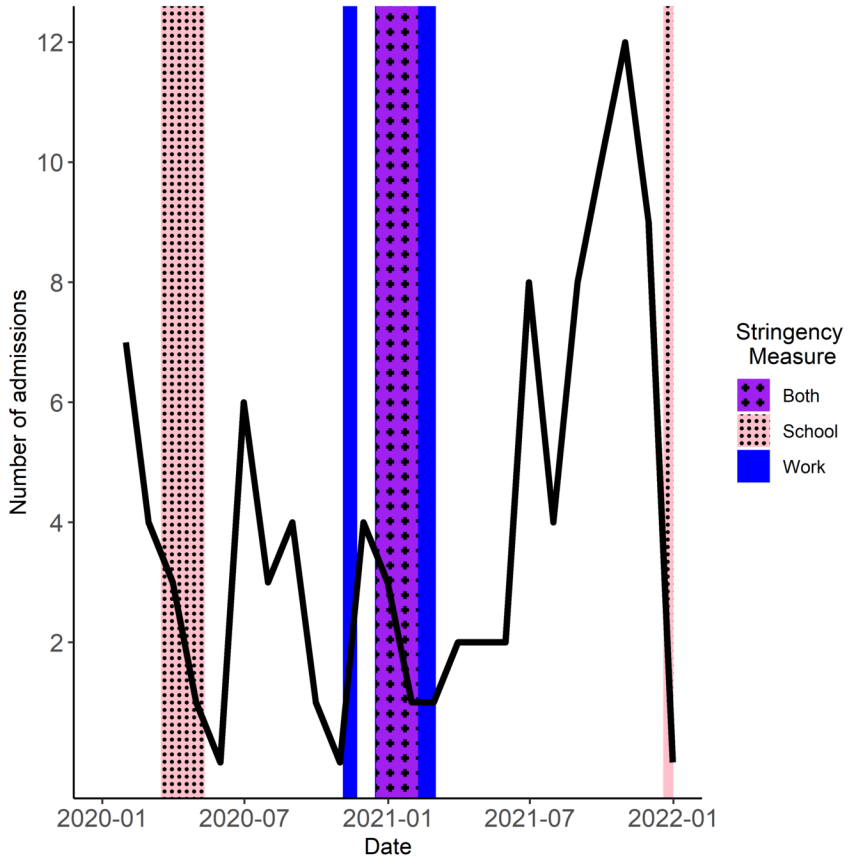


Figure 2 | The number of PICU admissions for SAA in 2020 and 2021 and the stringency measures. The monthly pediatric intensive care unit (PICU) admissions for severe acute asthma (SAA) are shown for the years 2020 and 2021 of the COVID-19 pandemic. Additionally, the stringency lockdown measures that were applicable in that time period (i.e. closure of schools, only allowing to work from home or both) in the Netherlands are also shown as colored bars.