# Understanding the environmental factors related to the decrease in Pediatric Emergency Department referrals for acute asthma during the SARS-CoV-2 pandemic

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## Abstract

Background: Asthma exacerbations, a common reason for Pediatric Emergency Department (PED) referral, can be triggered by multiple factors, including infections, air pollution and allergens. Lockdown measures and other public health interventions during the SARS-CoV-2 pandemic determined radical changes to behavioral and social habits, that were reflected by a reduction in the transmission of all respiratory pathogens and in the emissions of relevant air pollution anthropogenic sources. Objective: This study aims to describe how restrictions during SARS-CoV-2 pandemic impacted the PED referral for asthma exacerbations and their potentially associated environmental triggers in densely populated urban areas. Methods: PED referrals for acute asthma from 2015 to 2020 were compared to air pollution and pollen data. To this purpose, historical daily concentration records of PM2.5, PM10 (including specific chemical tracers), as well as NO2, C6H6, tree, grass and weed pollen were analyzed. Results: In 2020, asthma-related PED referrals decreased up to 85%, compared to the average referral rate of the previous 5 years ($P<0.01$). The drastic drop in PED referrals was associated with a reduction of high-priority cases by 50-60%, unlike PED referrals for overall diagnoses, showing a larger contribution for severe outcomes. A concomitant diminished contribution of traffic-related air pollution was shown. Conclusions: The lower rate of asthma exacerbations in childhood can be related to synergic interactions of the multiple effects of lockdown measures which induced lower viral infection rates and decreased exposure to outdoor allergens. The reduction of traffic-related air pollution determined a weakening of inflammatory properties of urban PM.

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**Key words: asthma exacerbations; allergens; traffic-related air pollution; oxidative stress**

**(Short title: Acute childhood asthma during SARS-CoV-2 pandemic)**

**Abstract**

**Background:** Asthma exacerbations, a common reason for Pediatric Emergency Department (PED) referral, can be triggered by multiple factors, including infections, air pollution and allergens. Lockdown measures and other public health interventions during the SARS-CoV-2 pandemic determined radical changes to behavioral and social habits, that were reflected by a reduction in the transmission of all respiratory pathogens and in the emissions of relevant air pollution anthropogenic sources.

**Objective:** This study aims to describe how restrictions during SARS-CoV-2 pandemic impacted the PED referral for asthma exacerbations and their potentially associated environmental triggers in densely populated urban areas.

**Methods:** PED referrals for acute asthma from 2015 to 2020 were compared to air pollution and pollen data. To this purpose, historical daily concentration records of $PM_{2.5}$, $PM_{10}$ (including specific chemical tracers), as well as $NO_2$, $C_6H_6$, tree, grass and weed pollen were analyzed.

**Results:** In 2020, asthma-related PED referrals decreased up to 85%, compared to the average referral rate of the previous 5 years ($P$ <0.01). The drastic drop in PED referrals was associated with a reduction of high-priority cases by 50-60%, unlike PED referrals for overall diagnoses, showing a larger contribution for severe outcomes. A concomitant diminished contribution of traffic-related air pollution was shown.

**Conclusions:** The lower rate of asthma exacerbations in childhood can be related to synergic interactions of the multiple effects of lockdown measures which induced lower viral infection rates and decreased exposure to outdoor allergens. The reduction of traffic-related air pollution determined a weakening of inflammatory properties of urban PM.

**List of abbreviations:**

**Arpae** : Agency for Prevention, Environmental and Energy of Emilia-Romagna (Italy)

**BC** : Black carbon (PM chemical component)

**$C_6H_6$** : Benzene (gaseous air pollutant)

**COVID-19** : Coronavirus disease-2019

**IOP** : Intensive observation periods

**Lockdown-1** : The first lockdown period in Italy from March $9^{th}$ to May $3^{rd}$ in 2020 and continued with less restrictions until the end of May

**Lockdown-2** : The second (moderate) lockdown period in Italy from October $13^{th}$ to the end of 2020 and continued in 2021 with restrictive measures varying according to the local trend of infections

**$NO_2$** : Nitrogen oxide (gaseous air pollutant)

**$O_3$** : Ozone (gas air pollutant)

**PED** : Pediatric Emergency Department

**PM** : Particulate matter

**$PM_{10}$** : Particulate matter smaller than 10 microns

**$PM_{2.5}$** : Particulate matter smaller than 2.5 microns

**SARS-CoV-2** : Severe acute respiratory syndrome-coronavirus-2

**SSOU** : Short-stay clinical observation unit

**TRAP** : Traffic-related air pollution

**TRAP contribution tracer:** It represents the relative abundance of the mass fragment at m/z 57 over the total organic $PM_1$ mass spectrum as measured by HR-ToF-AMS

**WHO** : World Health Organization

## 1. Introduction

Several studies reported an overall decrease in the number of Pediatric Emergency Department (PED) admissions in 2020 during lockdown periods related to social measures adopted to limit spreading of SARS-CoV-2 pandemic, including a marked reduction of asthma referrals[1,2]. This led to a growing interest in determining to what extent these life-style changes might have influenced asthma triggers[3–5].

Asthma is a multi-factorial airways disease: in predisposed people, exposure to respiratory infections, air pollution and allergens may trigger asthma exacerbations[6,7]. Infections are the main triggers of acute bronchospasm in children of any age, especially in the preschoolers[8,9]. Sensitization to environmental allergens, such as pollen, is reported as a further important risk factor for the development of asthma exacerbations[10].

Regarding the role of air pollution, most studies reported how particulate matter smaller than 2.5 microns and 10 microns ($PM_{2.5}$, $PM_{10}$) and the co-emitted gaseous pollutants (NO, $NO_2$, $O_3$) can induce airway inflammation, hyper-responsiveness and oxidative injury to the airways, which can lead to asthma[11]. However, even if the international air quality standards for atmospheric particulate matter (PM) are based on total mass concentrations, the World Health Organization (WHO) acknowledges that not every PM chemical component is equally important in causing airways disease[12]. Research on this issue is mostly focused on traffic-related air pollution (TRAP) and has provided evidence of the links between adverse health effects and PM chemical composition[11,13–15]. Urban anthropogenic PM presents a three-fold higher oxidative potential per unit of PM mass concentration than rural PM[16].

In this observational retrospective cross-sectional study, we aimed to identify how asthma-related referrals in children were affected by the restrictive measures during the entire 2020, in relation to the main features of potentially associated environmental triggers, i.e. air pollution and pollen. The selected urban area of Bologna, in Northern Italy, represents an important population basin of about 400000 inhabitants and can be considered an ideal setting for this study as it is one of the areas more dramatically hit by the pandemic, and also well-known for a high prevalence of respiratory disease and for being one of the main air quality European hotspot, characterized by PM levels well above the limit set by the European Air Quality Directive and by the WHO.

## 2. Methods

### 2.1 Air pollution

Daily ground level mass concentrations of $PM_{10}$ and $PM_{2.5}$ and gaseous pollutants ($NO_2$, $C_6H_6$), as routinely measured by the air quality monitoring program of the Agency for Prevention, Environmental and Energy (Arpae) network, are considered. Measurements cover the time period from January 1$^{st}$, 2015 to December 31$^{st}$, 2020 and were recorded at the urban background site and the urban traffic site. The choice of the urban background site is aimed at maximizing the representativeness of population exposure at the urban scale. On the contrary, the traffic site is useful to better highlight changes in emission rates of local traffic-related sources.

Two independent additional measurements, not available for routine air quality monitoring are used as ancillary data to highlight specific chemical features of PM composition, tracing the contribution of combustion PM sources and TRAP, associated with asthma disease in other studies[13,15]. The first one is f57, deriving from data analysis of the mass spectra of non-refractory submicron particle and representing the relative abundance of the mass fragment at m/z 57 over the total organic $PM_1$ particles (PM less than 1 micron: fine and ultrafine particles) mass spectrum. f57 is commonly used as a spectral tracer for the contribution of PM emitted from fossil fuel combustion and it is mostly attributed to traffic-related sources in urban environment[17,18]. For this reason it is indicated from hereafter as the TRAP contribution tracer. Data were obtained online by a High-Resolution Time-of-Flight Aerosol Mass Spectrometer[19] and refer to measurements during the lockdown period in 2020 and from eight intensive observation periods carried out from November 2011 to May 2014, representative of a wide spectrum of seasonal conditions[20]. The second additional measurement is the black carbon (BC) fraction of PM, sometimes defined as soot, a major component of PM, emitted through incomplete combustion of fossil fuels and biomass, representing a known tracer of the main anthropogenic sources concentrated in urban areas, including heating and transport. Hourly concentrations are used as quantified from a MetOne (single-wavelength at 880nm) run during the time period January-May in 2019 and 2020.

### 2.2 Pollen data

Daily concentrations of *Compositae* : mugwort (*Artemisia* ) and *Urticaceae* (*Parietaria* ), tree (birch) and grass pollen were analyzed for the time period January 1$^{st}$, 2015 to December 31$^{st}$, 2020. These four species were selected as the most relevant allergens for the study area (Central-Southern Europe).

### 2.3 Study population

Files of children evaluated for "acute asthma", "bronchospasm", or "wheezing bronchitis" from January 1$^{st}$, 2015 to December 31$^{st}$, 2020, in the PED of Sant'Orsola University Hospital of Bologna were retrospectively revised. The triage acuity, defined by a 4-colour scale and divided into low-priority (white and green) and high-priority (yellow and red) codes, and the outcome (discharge, admission to the Short Stay Observation Unit, SSOU, or to the ward) were also considered.

### 2.4 Statistical data analysis

Normality of data distributions were examined with the Kolmogorov-Smirnov test. Continuous variables are expressed as mean ± SD or median with interquartile range as appropriate, and categorical variables are expressed as a percentage. For the continuous variables, comparisons between two groups were made using t-tests while for 3 or more groups with ANOVA and Bonferroni test for multiple comparisons. All the analyses were conducted in SPSS version23 [SPSS Inc., Chicago, IL, USA], Microsoft Windows version, and *P* [?] 0.05 from 2-sided tests was considered statistically significant.

**Ethical Statement**

This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the local Ethical Committee (protocol number 177/2021/Oss/AOUBo).

## 3. Results

### 3.1 Air pollution

In Figure 1 and 2, the timeseries observed in 2020 is compared to the multiannual timeseries of daily mass loading for $PM_{2.5}$and $PM_{10}$ and for the gaseous pollutants $NO_2$ and $C_6H_6$, measured at the urban background site and the urban traffic site identified above.

Air pollutants behavior reflects seasonal and interannual fluctuation in emission rates and climatological drivers. A detailed analysis of all these factors is beyond the scope of this work. For the purpose of this paper, we limited to exemplify changes in specific air pollution patterns that might have affected population exposure at the urban scale of Bologna.

Focusing on the first period of lockdown, March-May 2020 (lockdown-1), gaseous pollutants were strikingly reduced: $NO_2$concentrations in 2020 decreased on average by 43% and 46% ($P$ <0.01) at the urban background and urban traffic sites, respectively; and $C_6H_6$, only measured at the urban traffic site, decreased by 53% ($P$ <0.01). When compared to historical levels, the differences of both gaseous pollutants gradually attenuated in late spring and summer, partially reflecting the slow, although not complete, return to regular activities that occurred in late-spring and summer. With the second outbreak, these divergences reappeared as a consequence of the new measures during the second (moderate) lockdown period from mid-October to December 2020 (lockdown-2), although those measures were less restricting than during lockdown-1.

In contrast, no significant impact of the lockdown measures is evidenced on the mass loading of $PM_{10}$ and $PM_{2.5}$, both at the urban background and traffic sites, consistently with other European cities[21].

Despite the lack of evidence of reduction of the mass loading of $PM_{10}$ and $PM_{2.5}$, considering PM chemical composition, clear signals of reduced TRAP are observed. Figure 3A shows the contribution of BC mass to $PM_{2.5}$ mass in 2019 vs 2020 (March to May). The average relative contribution of BC to $PM_{2.5}$ significantly decreased from 11% to 6% ($P$ <0.01). This is in line with a recent study reporting, for Europe, a more pronounced reduction of BC concentrations in the range of 20-40% during lockdown events in those countries that suffered more dramatically from the pandemic (e.g. Italy)[22].

Accordingly, Figure 3B shows the TRAP contribution tracer, by comparing the measurements carried out during lockdown-1 with those one corresponding to intensive observation periods (IOPs) during previous years, covering a wide spectrum of seasonal conditions. The TRAP contribution tracer evidenced a marked decline up to 50% in 2020 with respect to previous IOPs ($P$ <0.01).

### 3.2 Pollen

The main pollen plumes in 2020 were compared to the previous years to detect any significant variation. No remarkable variation beyond their interannual fluctuation was observed during lockdown periods (data not shown).

### 3.3 Asthma

Given non-significant variations within the selected reference period 2015-2019 by comparing, month by month, every year to each other, daily PED referrals for asthma in 2020 were compared to the previous 5 years grouped together. Table 1 shows the average daily acute asthma referrals to our PED on a monthly basis.

During lockdown-1, the total acute asthma referrals decreased abruptly by 85% compared to the same period in the previous 5 years (total referrals were 16, compared to a mean of 108 +- 11 in the years 2015-2019, $P<0.01$ ). In the following months (from May 4$^{th}$ to the end of July) asthma-related PED referrals showed a similar decrease by 80% (20 vs 98 +- 15, $P<0.01$ ), followed by a reduction by 44%, and 51% in concomitance with the peak usually reported at the end of summer and early autumn, and later on during lockdown-2, respectively.

As compared to the 2015-2019 reference years, in 2020 an overall 40% decrease of asthma-related PED referrals was observed. Remarkably, the decrease in overall asthma referrals was associated with the concomitant reduction in high-priority codes, being more evident during lockdown-1 (Figure 4).

Outcomes of asthma-related PED referrals are displayed in Figure 5. Hospital admissions in 2020 were higher in the pre-pandemic period and remarkably dropped during lockdown-1 and the following months; none was registered in April, May, June and August. A reduction in the use of SSOU was observed during the pandemic, except for August, presenting an increase in the total referrals and SSOU utilization.

## 4. Discussion

Our findings show that in 2020, during the first and second outbreak of SARS-CoV-2 across Northern Italy, overall childhood asthma exacerbations were inhibited, as compared to the same calendar period of the previous 5 years: during lockdown-1, PED referrals incurred a significant decline by 85%, and in the following months by 80%, reflecting the slow, although incomplete return to almost regular activities during summer. An increase in PED referrals for acute asthma re-started in August, continued in September, with a peak in October, anticipating the so-called "September asthma epidemics", the common burst of exacerbations generally observed with the start of the school year and due to a combination of infectious, allergic, environmental, and climatic triggers[23]. The peak in October was less pronounced than the previous years and this decreasing trend continued in November and December, when only 8 asthma referrals were registered, likely reflecting the strict hygiene measures and social distancing adopted as a consequence of lockdown-2. We also observed a prevalent reduction trend of hospital admissions and short-stay observations during the pandemic.

Our PED and many others, reported a substantial activity decrease by ca. 70-80% during lockdown-1, with drastic reductions in referrals for a wide spectrum of diagnoses[1,2]. In other studies, this was attributed to the introduction of new guidance for primary care (e.g. phone selection triage procedure, more telehealth) and fear of exposure to SARS-CoV-2 infection, leading to higher risk of severe illness from delayed diagnosis[1,2,24]. In contrast, the reduction of PED referrals for asthma exacerbations was associated with a significant reduction by 50-60% of high-priority cases, thus, the reluctance to seek hospital care cannot be the only explanation. A major role is likely played by a combination of factors.

As reported in other studies, social distancing and stepped-up hygiene measures determined a concomitant reduction in the diffusion of respiratory pathogens, leading to decreased respiratory tract infections[3,25–27]. Moreover, the feeling of the emergency period might have enhanced adherence to controller medications among asthmatic population[27,28].

In addition, the reduced exposure to environmental factors – i.e. air pollution and pollen - may have played a role in the "anomalous" pattern of asthma exacerbations in 2020. With regard to changes in air quality during the pandemic, the gaseous pollutants $NO_2$and $C_6H_6$, generally associated with fossil fuel combustion and directly correlated with vehicular traffic in urban context, showed substantially decreased concentrations during lockdown periods. In densely populated areas, this clearly mirrored a reduction of traffic-related sources in concomitance with the restrictive measures, consistent with observations at a larger scale in Italy and mobility drop of 75%[29].

Unlike $NO_2$ and $C_6H_6$, PM mass concentration was not significantly affected by lockdown measures. This can be explained by the complex emission patterns of PM in urbanized environment, encompassing both natural and anthropogenic, primary and secondary sources, thus leading to mass concentrations driven to a large extent by non-urban and non-traffic sources[20]. By contrast, a substantial reduction in the contribution of specific chemical components of traffic-related PM was clearly shown during lockdown-1, i.e. black carbon (BC) and the TRAP contribution tracer.

It is worth noting that traffic-related PM may gain relevance per unit mass of PM because of its higher oxidative potential and smaller size, leading to deposition in the deepest tracts of respiratory system[16]. Thus, these observations point to PM less enriched in ultrafine particles and those co-emitted components and micropollutants (e.g. BC, heavy metals and polycyclic aromatic hydrocarbons), which are recognized as specific asthma triggers, able to drive a cascade of pro-inflammatory and oxidative responses that increase the risks of acute pulmonary diseases[30]. This effect was likely amplified by less time spent outdoor and less movements during traffic rush-hours, reducing risk associated with proximity of children to strong local sources (exhaust and non-exhaust vehicular traffic). Moreover, a higher impact is expected in inner-city urban areas, where vehicular traffic presents a higher share of emissions. This evidence would suggest the recommendation for adopting more specific chemical tracers as air quality indicators, to elucidate associations between air pollution and respiratory diseases, despite the commonly used PM mass concentration.

On the contrary, pollen emissions are not impacted by changes in human behaviors and social restrictions, deriving from known natural sources. Indeed, during lockdown periods, pollen emissions did not present substantial variations beyond their interannual variability. However, the restrictive measures likely influenced exposure profiles of children in other ways, such as by reducing exposure to outdoor seasonal allergens.

In conclusion, several factors may explain the substantial decrease in the number of acute asthma PED referrals during the SARS-CoV-2 pandemic in 2020, with the concomitant reduction of high-priority codes. The restrictive measures adopted to limit the pandemic entailed a reduced exposure to viruses, outdoor environmental allergens, and air pollution, the latter notably exhibiting weakened inflammatory/oxidative properties.

Further investigations are needed to clarify in a more quantitative manner the role of each confounding trigger, driving synergistically variation in the clinical course of asthma. However, due to the peculiarity of the lockdown periods, which acted as a big experiment of anthropogenic air pollution cleansing and radical changes of human lifestyle, this study represented a unique opportunity to observe these hypotheses using real data from a severely SARS-CoV-2 affected urban area, reflecting what occurred in many densely populated areas around the world.

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**Conflict of interest**

The authors do not declare any conflict of interest.

**Author contributions**

Ar.D and M.L. conceptualization and full responsibility over the manuscript; L.B., C.C., Ar.D. drafted the initial manuscript; L.B. and C.C. data analysis and preparation of tables and figures; Ad.D. statistical analysis; M.P., M.R. analysis of HR-ToF-AMS data; F.S. and V.P. analysis of MetOne data and responsible for Arpae Air Quality measurements; Ar.D., L.B., C.C., Ad.D, M.P., M.R., M.G., F.S., V.P., M.F., M.L., equal contribution to overview/editing of the manuscript.

**Data sharing**

Air Quality and pollen data that support the findings of this study are available in the Arpae public repository. These data were derived from the following resources available in the public domain: https://apps.arpae.it/qualita-aria/bollettino-qa-provinciale/bo;

https://www.arpae.it/index.asp?idlivello=117. Asthma outcomes, HR-ToF-AMS and MetOne data are available from the corresponding author upon reasonable request.

**References**


1. Masetti R, Corsini I, Leardini D, Lanari M, Pession A. Presentations to the emergency department in Bologna, Italy, during COVID-19 outbreak.*BMJ Paediatr Open* . 2020;4(1):1-3. doi:10.1136/bmjpo-2020-000748

2. Matera L, Nenna R, Rizzo V, et al. SARS-CoV-2 pandemic impact on pediatric emergency rooms: A multicenter study. *Int J Environ Res Public Health* . 2020;17(23):1-12. doi:10.3390/ijerph17238753

3. Taquechel K, Diwadkar AR, Sayed S, et al. Pediatric Asthma Health Care Utilization, Viral Testing, and Air Pollution Changes During the COVID-19 Pandemic. *J Allergy Clin Immunol Pract* . 2020;8(10):3378-3387.e11. doi:10.1016/j.jaip.2020.07.057

4. Papadopoulos NG, Custovic A, Deschildre A, et al. Impact of COVID-19 on Pediatric Asthma: Practice Adjustments and Disease Burden. *J Allergy Clin Immunol Pract* . 2020;8(8):2592-2599.e3. doi:10.1016/j.jaip.2020.06.001

5. Tregony S, Kimberly F. G, Adam H, Kyle N, Jonathan M. G. Impact of the COVID-19 Pandemic on Pediatric Emergency Department Utilization for Asthma. *Ann Am Thorac Soc* . Published online 2020. doi:doi: 10.1513/AnnalsATS.202007-765RL

6. Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. *Lancet* . 2018;391(10122):783-800. doi:10.1016/S0140-6736(17)33311-1

7. Murrison LB, Brandt EB, Myers JB, Khurana Hershey GK. Environmental exposures and mechanisms in allergy and asthma development. *J Clin Invest* . 2019;129(4):1504-1515. doi:10.1172/JCI124612

8. Dondi A, Calamelli E, Piccinno V, et al. Acute asthma in the pediatric emergency department: Infections are the main triggers of exacerbations. *Biomed Res Int* . 2017;2017. doi:10.1155/2017/9687061

9. Papadopoulos NG, Christodoulou I, Rohde G, et al. Viruses and bacteria in acute asthma exacerbations - A GA 2LEN-DARE* systematic review. *Allergy Eur J Allergy Clin Immunol* . 2011;66(4):458-468. doi:10.1111/j.1398-9995.2010.02505.x

10. Taylor PE, Jacobson KW, House JM, Glovsky MM. Links between pollen, atopy and the asthma epidemic. *Int Arch Allergy Immunol* . 2007;144(2):162-170. doi:10.1159/000103230

11. Guarnieri M, Balmes JR. Outdoor air pollution and asthma.*Lancet* . 2014;383(9928):1581-1592. doi:10.1016/S0140-6736(14)60617-6

12. Dye C, Reeder JC, Terry RF. Research for universal health coverage.*Sci Transl Med* . 2013;5(199). doi:10.1126/scitranslmed.3006971

13. Khreis H, Kelly C, Tate J, Parslow R, Lucas K, Nieuwenhuijsen M. Exposure to traffic-related air pollution and risk of development of childhood asthma: A systematic review and meta-analysis. *Environ Int* . 2017;100:1-31. doi:10.1016/j.envint.2016.11.012

14. Bates JT, Weber RJ, Abrams J, et al. Reactive Oxygen Species Generation Linked to Sources of Atmospheric Particulate Matter and Cardiorespiratory Effects. *Environ Sci Technol* . 2015;49(22):13605-13612. doi:10.1021/acs.est.5b02967

15. Bowatte G, Lodge C, Lowe AJ, et al. The influence of childhood traffic-related air pollution exposure on asthma, allergy and sensitization: A systematic review and a meta-analysis of birth cohort studies. *Allergy Eur J Allergy Clin Immunol* . 2015;70(3):245-256. doi:10.1111/all.12561

16. Daellenbach KR, Uzu G, Jiang J, et al. Sources of particulate-matter air pollution and its oxidative potential in Europe. *Nature* . 2020;587(November). doi:10.1038/s41586-020-2902-8

17. Zhang Q, Alfarra MR, Worsnop DR, Allan JD, Coe H, Canagaratna MR. Deconvolution and Quantification of Hydrocarbon-like and Oxygenated Organic Aerosols Based on Aerosol Mass Spectrometry. *Environ Sci Technol* . 2005;39(13):4938-4952. doi:10.1021/es048568l

18. Ge X, Setyan A, Sun Y, Zhang Q. Primary and secondary organic aerosols in Fresno , California during wintertime : Results from high resolution aerosol mass spectrometry. *J Geophys Res* . 2012;117:1-15. doi:10.1029/2012JD018026

19. Canagaratna MR, Jayne JT, Jimenez JL, et al. Chemical and microphysical characterization of ambient aerosols with the aerodyne aerosol mass spectrometer. *Mass Spectrom Rev* . 2007;26(2):185-222. doi:10.1002/mas.20115

20. Paglione M, Gilardoni S, Rinaldi M, et al. The impact of biomass burning and aqueous-phase processing on air quality: A multi-year source apportionment study in the Po Valley, Italy. *Atmos Chem Phys* . 2020;20(3):1233-1254. doi:10.5194/acp-20-1233-2020

21. European Environmental Agency. *Air Quality and COVID-19* . https://www.eea.europa.eu/themes/air/air-quality-and-covid19/air-quality-and-covid19

22. Evangeliou N, Platt S, Eckhardt S, et al. Changes in black carbon emissions over Europe due to COVID-19 lockdowns. *Atmos Chem Phys Discuss* . 2020;(October):1-33. doi:10.5194/acp-2020-1005

23. Cohen HA, Blau H, Hoshen M, Batat E, Balicer RD. Seasonality of asthma: A retrospective population study. *Pediatrics* . 2014;133(4). doi:10.1542/peds.2013-2022

24. Lazzerini M, Barbi E, Apicella A, Marchetti F, Cardinale F, Trobia G. Delayed access or provision of care in Italy resulting from fear of COVID-19. *Lancet Child Adolesc Heal* . 2020;4(5):e10-e11. doi:10.1016/S2352-4642(20)30108-5

25. Chan K, Liang F, Tang H, Siong H, Yu W. Collateral benefits on other respiratory infections during fighting COVID-19. *Med Clin (Barc)* . 2020;155 (6)(January):249-253. https://doi.org/10.1016/j.medcli.2020.05.026

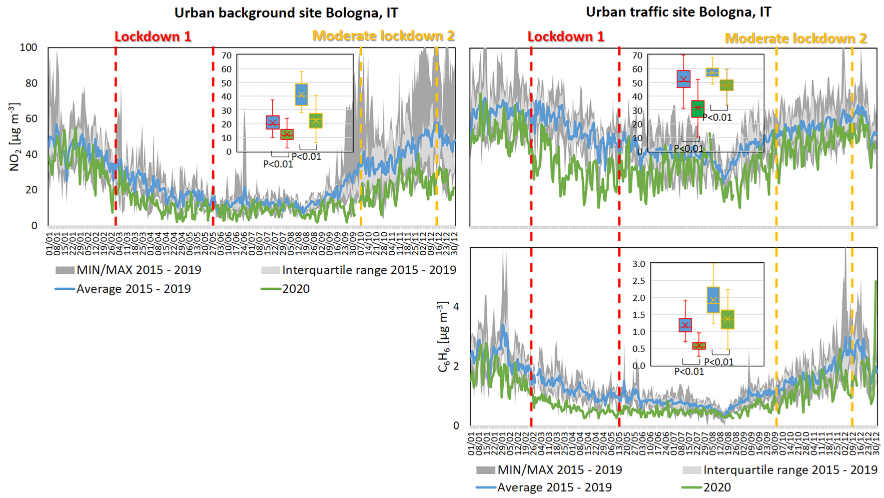
26. Pelletier JH, Rakkar J, Au AK, Fuhrman D, Clark RSB, Horvat CM. Trends in US Pediatric Hospital Admissions in 2020 Compared With the Decade Before the COVID-19 Pandemic. *JAMA Netw Open* . 2021;4(2):1-13. doi:10.1001/jamanetworkopen.2020.37227

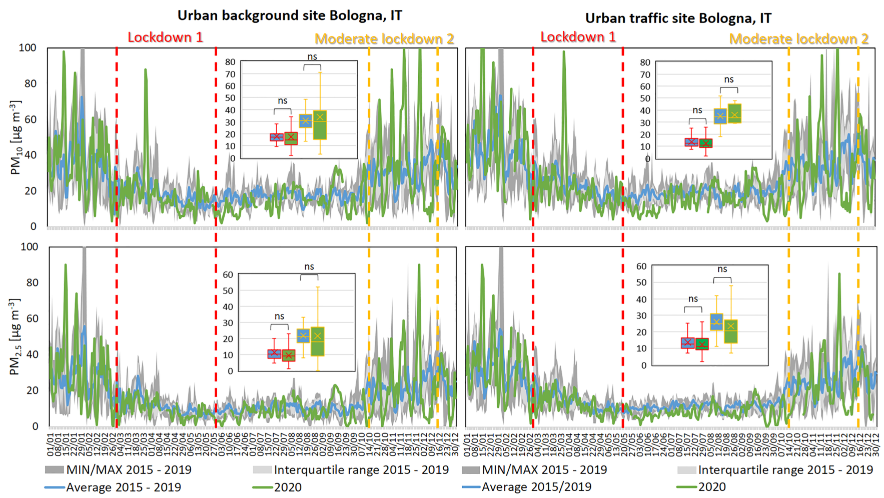
27. Papadopoulos NG, Deschildre A, Wong GW, et al. Childhood asthma outcomes during the COVID-19 pandemic: Findings from the PeARL multi-national cohort. *Allergy* . Published online 2021. doi:10.1111/ALL.14787

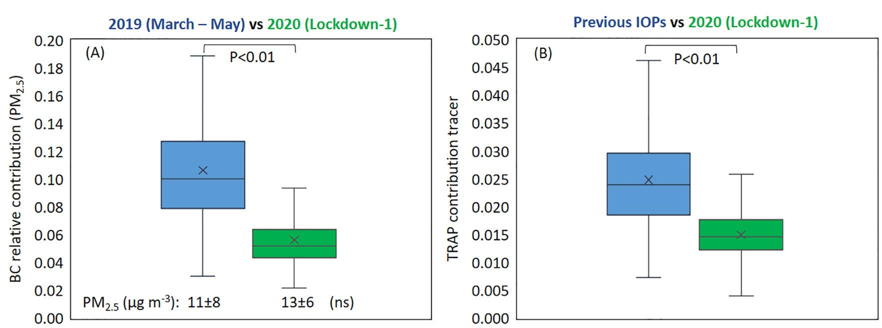
28. Kaye L, Theye B, Smeenk I, Gondalia R, Barrett MA, Stempel DA. Changes in medication adherence among patients with asthma and COPD during the COVID-19 pandemic. *J Allergy Clin Immunol Pract* . 2020;8 (7)(January). https://doi.org/10.1016/j.jaip.2020.04.053

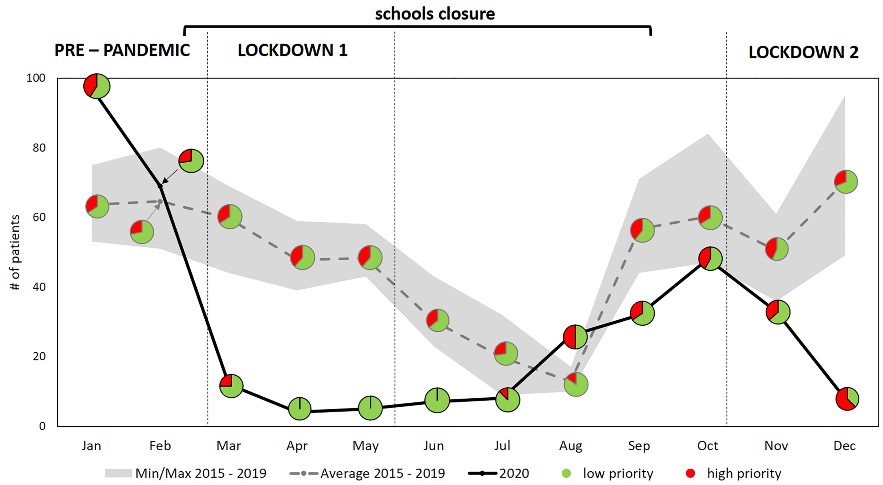
29. Putaud J-P, Pozzoli L, Pisoni E, et al. Impacts of the COVID-19 lockdown on air pollution at regional and urban background sites in northern Italy. *Acpd* . 2020;(2):1-18. https://doi.org/10.5194/acp-2020-755

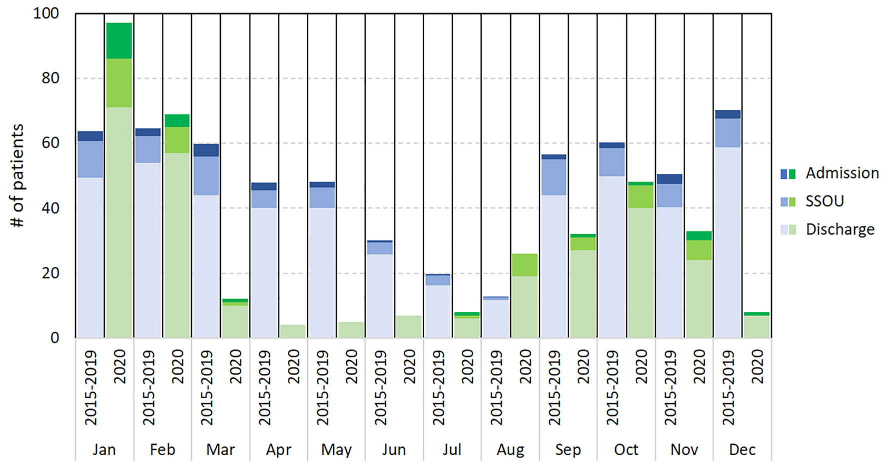
30. Costabile F, Gualtieri M, Ancona C, Canepari S, Decesari S. Ultrafine particle features associated with pro-inflammatory and oxidative responses: Implications for health studies. *Atmosphere (Basel)* . 2020;11(4). doi:10.3390/ATMOS11040414


Urban background site Bologna, IT
Urban traffic site Bologna, IT
Lockdown 1
Moderate lockdown 2
NO2 [µg m-3]
C6H6 [µg m-3]
P<0.01
MIN/MAX 2015 - 2019
Interquartile range 2015 - 2019
Average 2015 - 2019
2020


Urban background site Bologna, IT
Urban traffic site Bologna, IT
Lockdown 1
Moderate lockdown 2
PM10 [µg m-3]
PM2.5 [µg m-3]
ns
MIN/MAX 2015 - 2019
Interquartile range 2015 - 2019
Average 2015 - 2019
Average 2015/2019
2020


2019 (March – May) vs 2020 (Lockdown-1)
Previous IOPs vs 2020 (Lockdown-1)
(A)
(B)
P<0.01
BC relative contribution (PM2.5)
TRAP contribution tracer
PM2.5 (µg m-3): 11±8
13±6 (ns)

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`Table 1.pdf` available at https://authorea.com/users/409045/articles/518814-understanding-the-environmental-factors-related-to-the-decrease-in-pediatric-emergency-department-referrals-for-acute-asthma-during-the-sars-cov-2-pandemic