

COVID-19 pandemic: Impact caused by school closure and national lockdown on pediatric visits and admissions for viral and non-viral infections, a time series analysis

François ANGOULVANT, M.D., Ph.D.,^{1,2*} Naïm OULDALI, M.D.,^{3,4,5} David Dawei YANG, M.D.,^{1,2} Mathilde FILSER,⁶ Vincent GAJDOS, M.D., Ph.D.,^{7,8} Alexis RYBAK, M.D.,⁹ Romain GUEDJ, M.D., Ph.D.,^{10,11} Valérie SOUSSAN-BANINI, M.D.,¹² Romain BASMACI, M.D., Ph.D.,^{13,14} Alain LEFEVRE-UTILE, M.D.,^{15,16} Dominique BRUN-NEY, M.D.,^{17,18} Laure BEAUJOUAN,^{17,18} David SKURNIK, M.D., Ph.D.,^{6,19,20}

- 1) Assistance Publique - Hôpitaux de Paris, Pediatric Emergency Department, Necker-Enfants Malades University Hospital, Université de Paris, Paris, France.
- 2) INSERM, Centre de Recherche des Cordeliers, UMRS 1138, Sorbonne Université, Université de Paris, Paris, France.
- 3) Assistance Publique-Hôpitaux de Paris, Department of general pediatrics, pediatric infectious disease and internal medicine, Robert Debré university hospital, Université de Paris, Paris, France.
- 4) Assistance Publique-Hôpitaux de Paris, Clinical epidemiology unit, Robert Debré university hospital, ECEVE INSERM UMR 1123, Université de Paris, Paris, France.
- 5) ACTIV, Association Clinique et Thérapeutique Infantile du Val-de-Marne, Créteil, France
- 6) Assistance Publique-Hôpitaux de Paris, Department of Clinical Microbiology, Necker-Enfants Malades University Hospital, Université de Paris, Paris, France.
- 7) Assistance Publique - Hôpitaux de Paris, Pediatric Department, Antoine Béchère University hospital, Université de Paris Saclay, Clamart, France.
- 8) Centre for Research in Epidemiology and Population Health, INSERM UMR1018, Villejuif, France.
- 9) Assistance Publique - Hôpitaux de Paris, Pediatric Emergency Department, Robert Debré university hospital, Université de Paris, Paris, France.
- 10) Assistance Publique - Hôpitaux de Paris, Pediatric Emergency Department, Armand Trousseau University Hospital, Sorbonne Université, Paris, France.
- 11) Obstetrical, Perinatal and Pediatric Epidemiology Research Team (EPOPé), Centre de Recherche Épidémiologie et Statistique Sorbonne Paris Cité (CRESS), Inserm UMR1153, Université de Paris, Paris, France.
- 12) Assistance Publique - Hôpitaux de Paris, Service de Pédiatrie, Hôpital Ambroise Paré, Boulogne Billancourt, France.
- 13) Assistance Publique - Hôpitaux de Paris, Service de Pédiatrie-Urgences, Hôpital Louis-Mourier, Université de Paris, Colombes, France.
- 14) IAME, INSERM UMR1137, Université de Paris, Paris, France.
- 15) Assistance Publique-Hôpitaux de Paris - General Pediatric and Pediatric Emergency Department, Jean Verdier Hospital, Bondy, France.
- 16) INSERM U976 - Human systems immunology and inflammatory networks, Saint Louis Research Institute, Université de Paris, France
- 17) Assistance Publique-Hôpitaux de Paris, Strategy and Transformation Management Department - Emergencies and Intensive Cares, Paris, France
- 18) Assistance Publique-Hôpitaux de Paris, Patient Quality Medical Organisation Department - Health Crisis Management, Paris France
- 19) INSERM U1151-Equipe 11, Institut Necker-Enfants Malades, Université de Paris, Paris, France
- 20) Division of Infectious Diseases, Harvard Medical School, Boston, Massachusetts, United States of America.

* Corresponding author:

Pr François ANGOULVANT
Pediatric Emergency Department,
Hôpital Necker Enfants-Malades,
149, Rue de Sèvres 75015 Paris
E-mail: francois.angoulvant@aphp.fr
Tel : +33 1 71 39 69 68
Fax : +33 1 44 49 42 99

ABSTRACT:

A time series analysis of 871,543 pediatric emergency visits revealed that the COVID-19 lockdown and school closure were associated with a significant decrease in infectious diseases disseminated through airborne or fecal-oral transmissions: common cold, gastroenteritis, bronchiolitis, acute otitis. No change was found for urinary tract infections.

Key Words: covid-19; lockdown; epidemic; pediatric; emergency

Accepted Manuscript

INTRODUCTION:

In late December 2019, patients with viral pneumonia due to an unidentified microbial agent were reported in Wuhan, Hubei province, central China. This disease outbreak, COVID-19, then grew substantially and was declared a pandemic by WHO on March 11, 2020.[1]

In 1995, a major French nationwide strike paralyzed France. For 19 days from November 30, 1995 to December 18, people stayed at home, including children who normally went to day-care centers and a significant decrease of bronchiolitis cases was observed. This decline might have been caused by workplace and school absenteeism, and lower attendance of day-care centers.[2] Likewise, during the 2013-2014 measles epidemic, a reduction in contact rate during school vacations was associated with 4900 averted cases in The Netherlands.[3]

After reaching France on January 24, 2020, a major progression of COVID-19 from February to March led to public health interventions. Partial lockdown and school closure were initiated early March and a national lockdown was officially started on March 17th, 2020.[4, 5] No previous public health intervention can be compared to the extent of the lockdown established for the COVID-19 epidemic. We hypothesized that this unusual situation in France would be associated with a sharp decrease in pediatric infectious diseases that usually disseminate through social contacts, with schools at their center. Being able to prevent these infections, responsible for many pediatric hospitalizations, would be an unwanted direct benefit of the lockdown for children, that seem otherwise significantly more protected than the adult from the SARS-CoV-2 infection.[6] Even more, this could open the road for future guidelines to control future major health issues once the COVID-19 pandemic is under control.

Therefore, the evolution of several major diseases usually correlated with dissemination through contact, such as gastroenteritis, common cold, and acute otitis media, were investigated before and after the start of the national lockdown. Urinary tract infections, which are not reported to be correlated with contacts in children, were used as control outcome.

METHODS:

We conducted a quasi-experimental interrupted time series analysis based on multicenter prospective French surveillance data for pediatric emergency department (PED) visits and related hospital admissions. The Regional Centre of Observation and Action on Emergencies e-CERVEAU, *Agence Régionale de Santé*, is an official network of emergency departments dedicated to public health that automatically transmit a summary of anonymized data from all their visits to the regional database. The database has been approved by the French data protection authority. These data include discharge diagnosis coded by the physicians in

charge of the patient at the end of the PEDs visits according to ICD-10th revision and hospital admission or discharge. This study covers 6 PEDs from academic hospitals being part of Assistance Publique – Hôpitaux de Paris, located in and around Paris, gathering 250,000 annual visits that daily transmitted their from January 1st, 2017 to April 19th, 2020. We used the e-CERVEAU database for this research. Data are anonymous. Patient informed consent is not required according to current dispositions.

Groups of diagnosis extracted were: gastroenteritis, common cold, bronchiolitis, acute otitis media, considered as infectious diseases thriving through social contact, and urinary tract infection (table S1). Visits were grouped by calendar weeks for each year.

Outcome measure

The main outcome was the evolution of the number of hospital admissions following the French decision to close schools and start a lockdown for the whole country.[5] The secondary outcomes were the number of PEDs visits for gastroenteritis, bronchiolitis, common cold, acute otitis media. As recommended to prevent potential confusion,[7, 8] urinary tract infections were analyzed as a control outcome, given that this common pediatric infectious disease is not expected to be impacted by social distancing, although indirect effect such as stress or diet change cannot be excluded. This outcome was already used as a control concerning previous acute respiratory tract infections studies.[9]

Statistical analysis

Outcomes were analyzed by quasi-poisson regression, accounting for seasonality, secular trend before and after lockdown, and overdispersion of data.[7, 8, 10, 11] Seasonality was taken into account by including harmonic terms (sines and cosines) with 12-months and 6-months periods to adjust for the seasonal pattern.[11] The time unit chosen was one week to provide optimal precision to the model.[8]

We hypothesized that the intervention would have an immediate impact, meaning after one time unit, considering the incubation time of most viral diseases. Thus, intervention assessment involved a dummy variable in the model estimating the immediate post-intervention change.[8, 10] Pre-intervention period was from January 1st, 2017 to March 17th, 2020 and post-intervention period was from March 18th, 2020 to April 19th, 2020. Intervention impact was estimated by comparing estimates in the post-intervention period to expected estimates if the lockdown did not occur, based on quasi-poisson regression modeling. Validity of the quasi-poisson regression model was assessed by visual inspection of the

correlograms (Auto Correlation and Partial Auto Correlation Functions) and residuals analysis. Analysis of acute gastroenteritis was performed on data from four hospitals combining 81% of the visits during the study period. All statistical tests were two-sided, and we considered a result as “significant” when the p-value was <0.05. All statistical analysis involved using R v3.6.1 (<http://www.R-project.org>).

RESULTS:

A total of 871,543 PEDs visits in the six participating centers from January 1st, 2017 to April 19th, 2020 were included. Data collected in 2017, 2018, and 2019 were used to generate a model fitting the observed values of the PEDs visit allowing us to project the number of PEDs visit that could have been expected without lockdown.

As presented in Figure 1a, sharp discrepancy was found between expected and observed values after lockdown, reflecting the significant decrease of PEDs visit (-68.0% 95 CI [-81.2 ; -55.8]) and hospital admission following PEDs visits (-45.0% [-57.0 ; -32.4]) in the lockdown period (Table S2, Figure 1 and Figure S1).

We found a significant decrease of acute gastro-enteritis, common cold and acute otitis media (Table S2, Table S3) with a sharp decrease over 70% compared to the expected values (Figures 1b-d). Decrease of bronchiolitis was also significant (-63.5% 95CI [-101.8 ; -25.9]) (Table S2).

Consistent both with our hypothesis and the incubation time of these different diseases, a dramatic decrease of overall PEDs visits (-68.5%) and hospitalization (-44.7%) was observed as soon as one week after the start of the lockdown (Figure S1). By contrast, urinary tract infections were not impacted by the lockdown both regarding overall PEDs visits (-16.4% [-40.8 ; +6.4]) and hospital admissions (+20.7% [-27.0 ; +58.5]) (Table S2, Figure 1e, and Figure S1).

DISCUSSION:

In this time series analysis of 871,543 PEDs visits, the number of PEDs visits and admission after the lockdown decreased by -68% and -45%, respectively. We found a significant decrease over 70% of acute gastro-enteritis, common cold, bronchiolitis and acute otitis media compared to the expected values. Unprecedented public health interventions were ordered to reduce the risk of SARS-CoV-2 transmission.[4] Our data suggest that these measures have also a critical impact on the transmission of numerous infectious diseases, more specifically on viral or viral-induced pediatric diseases. This major achievement may also play a critical role in making more health resources with adults admitted in ICU and health care workers available to fight COVID-19 pandemic.[12] In Paris area, children with acute illness could be seen not only in PED but also in private office (general practitioners or pediatrician), general practitioner house calls, and communities' center. However most of these sites of care do not work 24/7 and rarely perform additional tests especially for the younger children.

Our study have limitations; we cannot exclude a change in clinical management such as avoidance of ENT examination because of COVID-19 fear which could have influenced diagnosis coding; we did not collect data regarding severity and so we cannot exclude that reduction in presentations was associated with children presenting later in their illness. While the dramatic decrease in PEDs could be partially due to transportation limitations and a fear of going to the hospital and increase of telemedicine, the stability in the number of urinary tract infections cases that we used as control outcome and the significant decrease in hospital admissions do not favor this hypothesis. Moreover visits to private doctors' offices decrease by 40%.[13] While the role of the children in the dissemination of SARS-CoV-2 is still being discussed, finding that school closure and national lockdown were linked to a dramatic decrease in pediatric emergency visits concerning gastroenteritis, acute otitis media, bronchiolitis, and other viral diseases could be not only an unexpected benefit for the children but could also raise the question of the impact on the health care system of starting lifting the French national lockdown by reopening the schools.[14] Complementary studies using more granular data such as severity could be useful to better understand lockdown's impact on children's health.

This nation-level quasi-experiment is unprecedented in the modern era. It provides unique evidence which could be key in the post COVID-19 era, to implement new guidelines and new routines in our way of life, and in order to fight past but also potential future infectious diseases threats reaching both children and adults.

Funding: none

All authors declare no potential conflict of interest relevant to this article.

Accepted Manuscript

REFERENCES

1. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Available at: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>. Accessed 23 April 2020.
2. Thelot B, Bourrillon A. Coincidence of public transport strike with bronchiolitis epidemic. *Lancet* **1996** Dec 21-28;348(9043):1743-4.
3. Klinkenberg D, Hahne SJM, Woudenberg T, Wallinga J. The Reduction of Measles Transmission During School Vacations. *Epidemiology* **2018** Jul;29(4):562-70.
4. Ghanchi A. Adaptation of the National Plan for the Prevention and Fight Against Pandemic Influenza to the 2020 COVID-19 Epidemic in France. *Disaster medicine and public health preparedness* **2020** Apr 7:1-3.
5. French Government. Décret n° 2020-260 du 16 mars 2020 portant réglementation des déplacements dans le cadre de la lutte contre la propagation du virus covid-19. Available at: <https://www.legifrance.gouv.fr/eli/decret/2020/3/16/PRMX2007858D/jo/texte>. Accessed May 26, 2020.
6. Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020. *MMWR Morbidity and mortality weekly report* **2020** Apr 10;69(14):422-6.
7. Jandoc R, Burden AM, Mamdani M, Levesque LE, Cadarette SM. Interrupted time series analysis in drug utilization research is increasing: systematic review and recommendations. *Journal of clinical epidemiology* **2015** Aug;68(8):950-6.
8. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *Journal of clinical pharmacy and therapeutics* **2002** Aug;27(4):299-309.
9. Ouldali N, Bellettre X, Milcent K, et al. Impact of Implementing National Guidelines on Antibiotic Prescriptions for Acute Respiratory Tract Infections in Pediatric Emergency Departments: An Interrupted Time Series Analysis. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* **2017** Oct 16;65(9):1469-76.
10. Kontopantelis E, Doran T, Springate DA, Buchan I, Reeves D. Regression based quasi-experimental approach when randomisation is not an option: interrupted time series analysis. *BMJ* **2015** Jun 9;350:h2750.
11. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *International journal of epidemiology* **2017** Feb 1;46(1):348-55.
12. Paediatric Intensive Care Society. PICS and ICS Joint Position Statement (12 Mar 2020). Available at: <https://picsociety.uk/news/pics-and-ics-joint-position-statement-12-mar-2020/>. Accessed 23 April 2020.
13. French Senat. Minutes of the social affairs committee. Available at: <http://www.senat.fr/compte-rendu-commissions/20200413/soc.html>. Accessed May 26, 2020.
14. French Government. French Government measures. Available at: <https://www.gouvernement.fr/en/coronavirus-covid-19>. Accessed 24 April 2020.

FIGURE LEGENDS

Figure 1

Impact of lockdown on weekly pediatric emergency department visits and major pediatric infectious diseases, from January 1st, 2017 to April 19th, 2020.

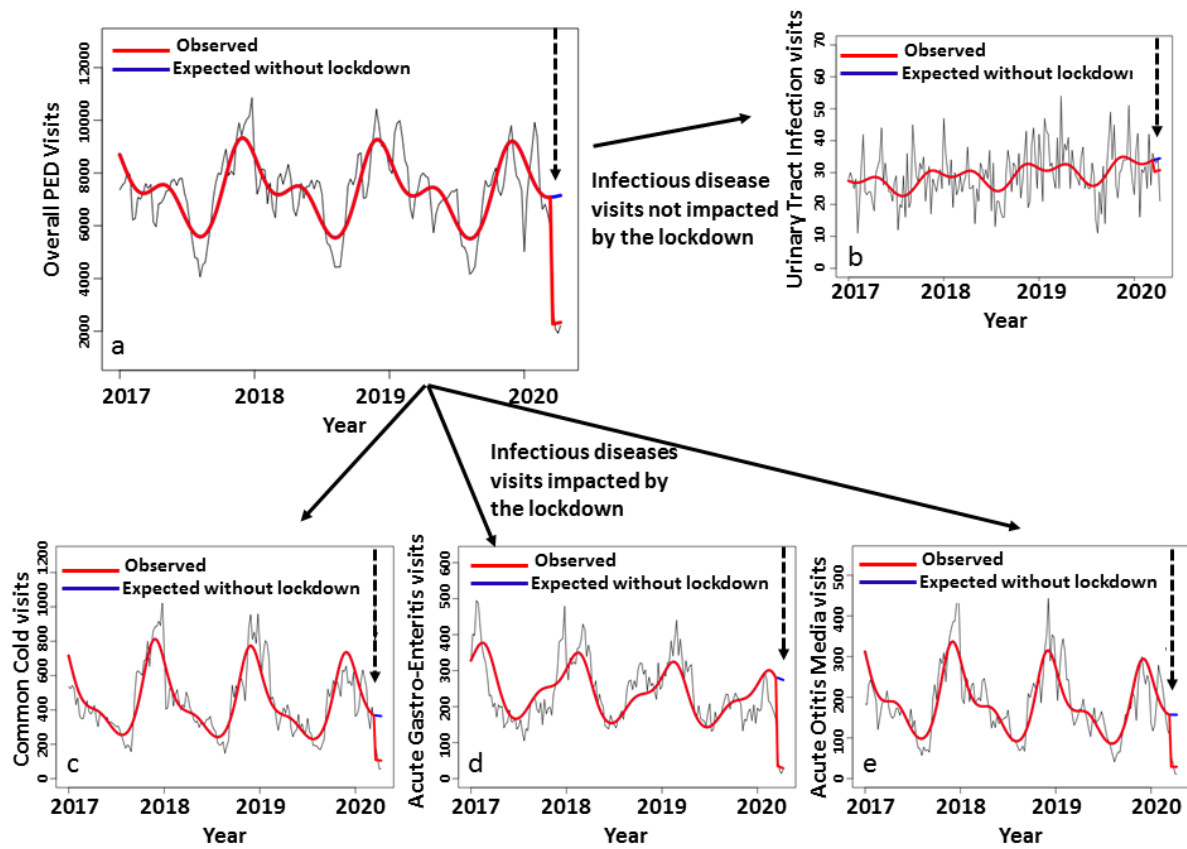
- a: Overall PEDs visit (n=871,543).
- b: PEDs visits for Urinary Tract Infections (n= 5,001).
- c, d, e: PEDs visits for common cold (n= 67,210), acute gastroenteritis (n= 35,025), and acute otitis media (n= 27,810) respectively.

The black line shows the observed data. The bold red slope shows the model estimates based on observed data (quasi-poisson regression modeling). The bold blue slope shows the expected values without lockdown in the post-intervention period (quasi-poisson regression modeling). The start of the lockdown is indicated by the vertical black arrow.

Abbreviations: PEDs: Pediatric Emergency Departments

Accepted Manuscript

Figure 1



Accepted