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# The effect of the COVID-19 pandemic on influenza-related hospitalization, intensive care admission and mortality in children in Canada: A population-based study

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## Summary

**Background** The COVID-19 pandemic resulted in unprecedented implementation of wide-ranging public health measures globally. During the pandemic, dramatic decreases in seasonal influenza virus detection have been reported worldwide. Information on the impact on paediatric influenza-related hospitalisations is limited. We describe influenza-related hospitalisation in children in Canada following the onset of the COVID-19 pandemic.

**Methods** Data on influenza-related hospitalisations, intensive care unit (ICU) admissions and in-hospital deaths in children across Canada were obtained from the Canadian Immunisation Monitoring Program, Active (IMPACT). This national active surveillance initiative comprises 90% of all tertiary care paediatric beds in Canada. The study period included eleven influenza seasons, from the 2010/2011 season until the 2020/2021 season inclusive. Time series modelling was used to compare the observed to predicted influenza-related hospitalisations following the COVID-19 pandemic.

**Results** Following the COVID-19 pandemic there was a significant decrease in paediatric influenza-related hospitalisations compared to predicted influenza-related hospitalisations for this time period ( $p < 0.0001$ ). No paediatric influenza-related hospitalisations, ICU admission or deaths were reported for the 2020/2021 influenza season.

**Conclusions** We show complete absence of paediatric influenza infection-related hospitalisation in a Canadian National Surveillance Network during the 2020/2021 influenza season. This significant decrease is likely related in large part to non-pharmacological public health interventions implemented during the COVID-19 pandemic, although the potential role of viral interference is unknown.

**Funding** The Canadian Immunisation Monitoring Program, Active (IMPACT) influenza surveillance is a national surveillance initiative managed by the Canadian Paediatric Society and conducted by the IMPACT network of paediatric investigators on behalf of the Public Health Agency of Canada's Centre for Immunisation and Respiratory Infectious Diseases.

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### Research in Context

#### *Evidence before this study*

We searched PubMed and country-specific public health communications to identify surveillance and epidemiological studies on influenza virus detection during the COVID-19 pandemic. A number of regional and national studies were identified worldwide all of which demonstrated large decreases in circulation of seasonal influenza viruses during the COVID-19 pandemic. Previous studies on the impact of non-pharmaceutical interventions on influenza A and B in Canada included only data on laboratory detections and surveillance at general population level. Studies on the impact of COVID-19 on influenza-related hospitalisation in the paediatric population are lacking.

#### *Added value of this study*

The Canadian Immunisation Monitoring Program, ACTive (IMPACT) conducts active surveillance for influenza-related hospitalisations, intensive care unit (ICU) admissions and in-hospital deaths in children from a network of paediatric academic centres across Canada. IMPACT's paediatric hospital-based active surveillance network provides a rich source of data with rigorous quality control processes and is an integral part of Canada's vaccine safety monitoring and disease reporting surveillance systems. This comprehensive dataset enables the assessment of the impact of the COVID-19 pandemic on seasonal influenza-related hospitalisations and deaths in children across Canada. This is the first country-wide study in the Northern hemisphere to describe the epidemiology and severity of seasonal influenza virus-related hospitalisation in children during the 2020/2021 season.

#### *Implications of all the available evidence*

The absence of the annual seasonal influenza epidemic in Canadian children during the 2020/2021 season has important implications for informing future public health responses to influenza respiratory virus epidemics and pandemics in children, as well as potential implications for the forthcoming influenza season.

## Introduction

The emergence of the coronavirus disease 2019 (COVID-19) outbreak is an unparalleled global health event resulting in unprecedented simultaneous implementation of regional and international public health measures worldwide.<sup>1</sup> In Canada from March 2020, multiple measures for COVID-19 mitigation were introduced and comprised travel restrictions; messaging and mandates regarding handwashing, physical distancing and facemask use; and, targeted lockdowns, including stay-at-home orders and school closures.<sup>2,3</sup> School closures in Canada were implemented in mid-March 2020 and for the majority of jurisdictions, in-person classes

did not resume again until after the summer of 2020, at which time many regions resumed at least part-time in-person instruction, particularly for elementary school children. Ongoing variation in school closures continued thereafter and some regions, such as Ontario, had over 20 weeks of school closures between March 14, 2020 and May 15, 2021.<sup>4</sup>

Seasonal influenza infections in children peak annually during the winter months, resulting in significant hospitalisation and mortality burden in infants and children.<sup>5</sup> Before the 2020/2021 influenza season, significant concerns were raised regarding the potential healthcare utilisation impact of surges in both influenza and COVID-19-related hospitalisations as well as the possible impact of co-infections on patient outcomes.<sup>6–8</sup> Indeed, during the 2019/2020 influenza season, immediately before the WHO declaration of COVID-19 as a global pandemic,<sup>9</sup> the United States Centres for Disease Control and Protection (CDC) reported the highest number of paediatric influenza deaths since reporting began in 2004, except for the H1N1 pandemic in 2009.<sup>10</sup> However, surveillance data from many countries worldwide have shown significant decreases in influenza activity since the onset of the COVID-19 pandemic during 2020 and 2021. During the 2020/2021 season, the CDC reported the lowest influenza-related hospitalisation rates since reporting began and similar historic lows in influenza activity were reported in Australia and New Zealand in the 2020 season.<sup>11–13</sup> These data reports did not specifically examine paediatric hospitalisations and it is known that patterns of respiratory virus infections differ with age between children and adults.<sup>14</sup> To date there is limited information describing the effect of the ongoing pandemic and associated implementation of public health measures on the incidence of severe influenza-disease in the paediatric population. We determine the impact of the COVID-19 pandemic on influenza-related hospitalisation and mortality in children in Canada through a comparison of confirmed paediatric influenza-related hospital admissions, intensive care unit (ICU) admissions, and deaths during the 2020/2021 influenza season to the preceding ten influenza seasons.

## Methods

### Design, setting and data source

This is a prospective active surveillance based observational study using data on influenza-related hospitalisations, ICU admissions and in-hospital deaths in children across Canada. Data were obtained from the Canadian Immunisation Monitoring Program, ACTive (IMPACT). This national surveillance initiative has been collecting influenza data continuously since 2003. Data is collected from 12 participating Canadian paediatric centres.<sup>15</sup> The IMPACT study covers 50% of the paediatric population of Canada based on the catchment

area of each included centre and as participating centres are all tertiary referral centres, the study represents 90% of all tertiary care paediatric beds in Canada. Research ethics and/or hospital approvals for IMPACT data collection were obtained as previously described.<sup>16</sup>

Information on international and provincial travel restrictions and public health measures were obtained from the Government of Canada and Public Health Agency of Canada.<sup>17,18</sup>

### Participants

The study population included all paediatric cases of laboratory-confirmed influenza-related hospitalisation at all IMPACT centres. All participating IMPACT centres remained the same throughout the entire study period. Cases were identified via active surveillance conducted by trained nurse monitors with physician support. Data on case presentation, details of the hospitalisation, and outcome at discharge were collected from patient charts and directly from clinical teams as needed.

### Measures/variables

Influenza-related hospitalisation was defined as any patient aged 16 years or younger admitted to hospital with laboratory-confirmed wild-type influenza virus infection (positive tests confirmed as vaccine strain influenza were excluded). Intensive care admission was defined as admission to a paediatric intensive care unit for any period of time during hospital stay and death was recorded if this occurred during the influenza-related hospitalisation.

The total study period included eleven influenza seasons from the 2010/2011 season until the 2020/2021 season (1st September 2010 to 30th April 2021 inclusive). This study period was chosen to include ten full influenza virus seasons before 2020. The onset of the COVID-19 pandemic was defined as March 2020 as the World Health Organisation (WHO) declared a global pandemic in March 2020.<sup>9</sup> The “pre-pandemic” period included 1st September 2010 until February 29th 2020 inclusive, and the “pandemic” period was defined as beginning 1st March 2020 until 30th April 2021 inclusive.

### Statistical methods

Data analysis was performed using GraphPad Prism 9.1.0 (GraphPad Software) and Excel 2016 (Microsoft). The pre-pandemic period was compared to the pandemic period using multiplicative model time series analysis.<sup>19</sup> Briefly, 12-month centralised moving averages were calculated and data decomposed into seasonal (normalised) and time trend components (trend determined by regression analysis). Predicted values were calculated by the multiplication of seasonal and trend

components. All time points (including influenza season and inter-season months) during the pre-pandemic period were included in the time-series analysis to model the predicted number of admissions for the entire pandemic period (1st March 2020 to 30th April 2021 inclusive). The Mann-Whitney test was used to compare predicted versus actual values for the monthly number of influenza-related hospitalisations during the pandemic period. A *p*-value of <0.05 was regarded as statistically significant.

For comparison of the number of influenza-related hospitalisations and ICU admissions during the 2020/2021 influenza season to previous seasons, the 2020/2021 influenza season was defined as beginning 1st September 2020 to 30th April, 2021. To permit direct comparison with pre-pandemic seasons we calculated average influenza-related hospitalisations for the influenza seasons included in the pre-pandemic period. Influenza seasons in the pre-pandemic period were defined as beginning 1st September until 30th April the following year and data from 1st May until 31st August were excluded from the calculation of these average values.

### Role of the funding source

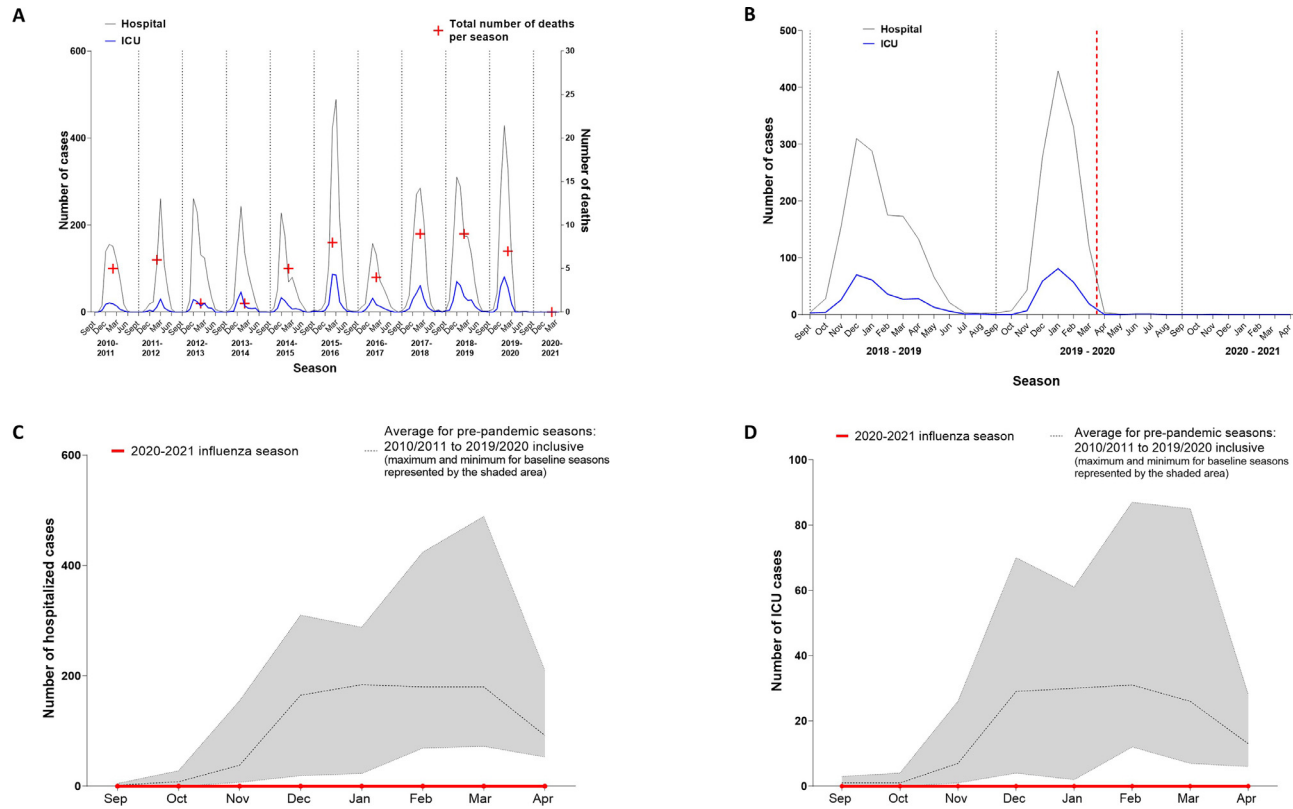
The study funding source did not have any involvement in study design, data collection, analysis or interpretation of data; in the writing of the report or in the decision to submit the paper for publication.

### Results

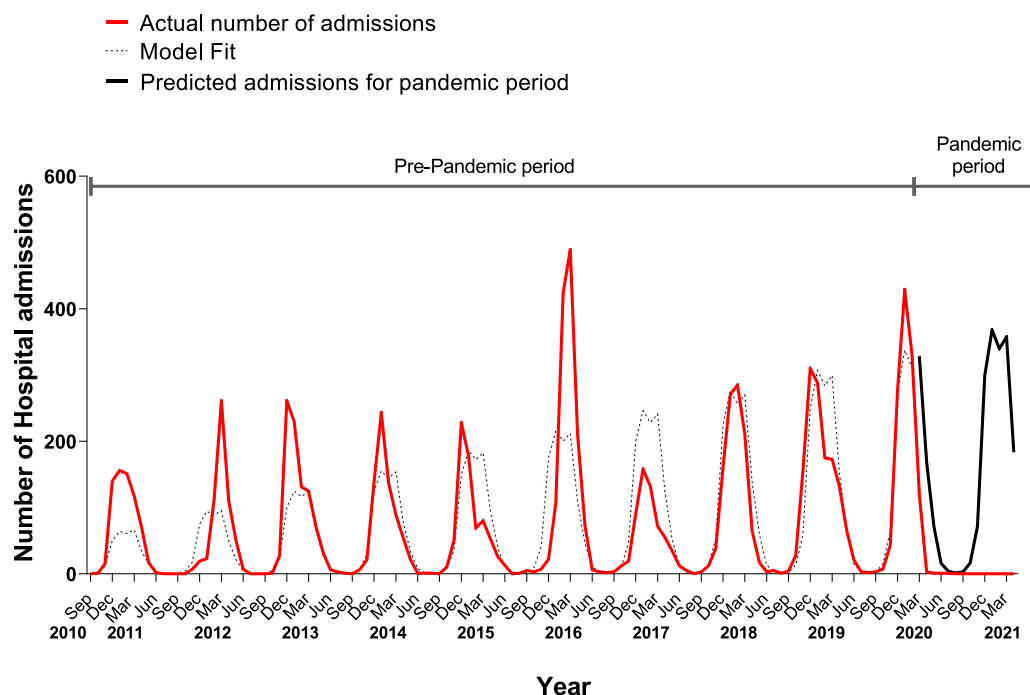
During the pre-pandemic period, the total number of paediatric influenza-related hospitalisations was 9036, of which, 8598 (95.2%) occurred between September and April. In the pandemic period, following the declaration of the COVID-19 pandemic in March 2020, only three paediatric influenza-related hospitalisations were reported in April 2020 (Fig. 1a,b). By comparison, 120 paediatric influenza-related hospitalisations occurred in March 2020 and the average for the month of April in the preceding pre-pandemic period (2010/2011 to 2019/2020 inclusive) was 92 cases (range 53–210) (Fig. 1c). In total, 126 paediatric influenza-related admissions were reported during the entire pandemic period. This is significantly lower than the predicted influenza-related hospitalisations for this period which totalled 2227, (*p* < 0.0001).

During the 2020/2021 influenza season there were zero paediatric influenza-related hospitalisations (Fig. 1a,b,c) which is significantly lower than the predicted influenza-related hospitalisations for this period (*p* < 0.001). The total number of predicted influenza-related hospitalisations for September 2020 to April 2021 inclusive was 1638 (Fig. 2).

In total, 1495 paediatric influenza-related ICU admissions occurred during the pre-pandemic period,



**Figure 1. Seasonal variation in influenza-related paediatric hospitalisation, ICU admissions and deaths before and during the COVID-19 pandemic.** Panels (A) and (B) show monthly totals for influenza-related hospitalisation and intensive care unit (ICU) admissions; beginning 1st September 2010 to 30th April 2021 inclusive for panel A (representing total study period 2010/2011 to 2020/2021 influenza seasons) and beginning 1st September 2018 to 30th April 2021 inclusive for panel B. Deaths per influenza season are shown in panel A (red cross). Canadian provincial and territorial governments declared emergencies with international travel restrictions initiated and school closures across Canada from mid-March 2020<sup>33</sup> (red dotted line). Panels (C) and (D) show the temporal distribution of influenza-related hospitalisations (C) and ICU admissions (D) in children from 1st September 2020 to 30th April 2021 inclusive compared with the average for pre-pandemic influenza seasons (black dotted line). The shaded area represents the maximum and minimum for the pre-pandemic seasons (from 2010/2011 to 2019/2020 influenza seasons inclusive).



**Figure 2.** Time series analysis of influenza-related hospitalisations for children in Canada for the period of 1st September 2010 to 30th April 2021 inclusive. Graph represents the monthly actual (crude) number of influenza-related hospital admissions and modelled numbers for each season with predicted numbers of admissions for the pandemic period (1st March 2020 to 30th April 2021 inclusive). (Spearman correlation of model fit,  $R = 0.93$ ).

of which, 1411 (94.4%) were between September and April. In the pandemic period, a total of 21 influenza-related ICU admissions were reported, of which 19 occurred in March 2020 (Fig. 1a,b).

The average total number of paediatric influenza-related ICU admissions during each influenza season in the pre-pandemic period was 141 (range 59–255) (Fig. 1d). The average rate of ICU admission per 100 paediatric influenza-related hospitalisations was 15.8 (range from 11.1 to 20.1) for influenza seasons during the pre-pandemic period. During the 2020/2021 season, there were zero paediatric influenza-related ICU admissions.

For the pre-pandemic period, the average number of paediatric deaths per influenza season was 5.5 (range 1–9) (Fig. 1a) The average death rate per 1000 paediatric influenza-related hospitalisations was 6.5 (range 1–11) for influenza seasons during the pre-pandemic period. During the 2020/2021 influenza season, no influenza-related paediatric ICU deaths were reported (Fig. 1a).

## Discussion

This is the first, nationwide study to examine the impact of the COVID-19 pandemic on influenza-related hospitalisation and mortality in children for the 2020/2021 influenza season. We show a complete absence of

influenza-related hospitalisations during the 2020/2021 season, with no ICU admissions or deaths. Significant decreases in the detection of circulating influenza cases have been reported globally during the COVID-19 pandemic.<sup>20</sup> Our findings in the paediatric population are consistent with United States CDC influenza surveillance data showing only one influenza-associated paediatric death for the 2020/2021 season compared to a range of 144 to 198 in three preceding seasons.<sup>11</sup> Decreases in other respiratory viral illnesses in children have also been described worldwide, including decreased circulation of respiratory syncytial virus (RSV) in New South Wales, Australia and dramatic decreases in bronchiolitis-related paediatric admissions to intensive care units in Paris, France.<sup>21,22</sup>

At the beginning of the COVID-19 pandemic, an earlier than expected end to the 2019/2020 influenza season was observed, with a 30-fold decrease in influenza-related hospitalisations during April 2020 compared to the pre-pandemic season average. The COVID-19 pandemic resulted in unprecedented implementation of stringent public health measures across Canada. It is likely non-pharmaceutical public health measures contributed in large part to the rapid decrease in numbers of paediatric influenza cases from April 2020 and the subsequent absence of influenza-related hospitalisations in children in Canada during the 2020/2021



season. Within Canada, there was significant variation in the timing of implementation of public health measures between provinces and territories (Supplemental Table 1) as well as variation in the subsequent relaxation and re-introduction of these non-pharmaceutical interventions (NPIs) over time. In addition, multiple measures such as mask mandates and school closures were typically employed simultaneously and as such, it is not possible to estimate the impact of individual NPIs on the observed decrease in paediatric influenza cases.

Notably, significant ongoing detection of SARS-CoV-2 was observed throughout the 2020/2021 influenza season in Canada,<sup>23</sup> with detection of co-infection by influenza and SARS-CoV-2 reported infrequently.<sup>24</sup> Viral interference between influenza and other respiratory viruses, such as rhinoviruses, has been postulated in epidemiological modelling studies to occur at both individual and population levels.<sup>14,25</sup> Upregulation of interferon-stimulated gene expression following rhinovirus infection has been shown to occur in *in vitro* work in differentiated airway epithelial cultures, with resulting significant inhibition of subsequent influenza A virus infection.<sup>25</sup> Accordingly, the possibility remains that viral interference by SARS-CoV-2 may have decreased influenza viral infections at individual and population level and thus played a role in the decrease in paediatric influenza virus infections seen in the pandemic period. However, it is unlikely that viral interference alone could account for the very large decrease in influenza-related hospitalisation observed in this study.

As COVID-19 public health measures are relaxed worldwide, inter-seasonal resurgences of paediatric respiratory virus infections are being observed.<sup>26,27</sup> In the United States, for example, increases in seasonal human coronaviruses, parainfluenza viruses, and respiratory adenoviruses were noted from January 2021, RSV activity increased from April 2021 and rhino/enteroviruses were noted to increase from June 2020.<sup>28</sup> Previous experience during the 2009 H1N1 influenza pandemic, such as the resurgence of influenza cases in children in China on re-opening of schools after summer vacation, suggests the potential for influenza resurgence in children as pandemic control measures related to schools are relaxed and this may be compounded by easing of other COVID-19 mitigation practises.<sup>29</sup> Indeed, the concept of an “immunity deficit” amongst children with low exposures to respiratory viruses due to the non-pharmaceutical measures introduced during COVID-19 has been highlighted and mathematical models predict this may lead to larger influenza epidemics in the coming years.<sup>30,31</sup> Accordingly, understanding the reasons for the dramatic decrease in paediatric influenza-related hospitalisation and mortality during the 2020/2021 influenza season is important for informing responses to forthcoming seasonal influenza epidemics as well as future influenza pandemics.

## Limitations

As detailed above, data collection from participating centres includes 90% of all tertiary care paediatric beds in Canada, however, it is possible that influenza-related paediatric hospitalisation in smaller community centres may have occurred. It is not possible in this study to determine whether changes in health-seeking behaviours during the pandemic, such as decreased hospital attendance due to concerns regarding the risk of SARS-CoV-2 exposure, may have resulted in decreased hospital attendances with influenza infection. However, it is unlikely behaviour changes would significantly impact the need for hospitalisation due to an influenza-related illness and the subsequent need for tertiary level or intensive care admission is also unlikely to be influenced by changes in health-seeking behaviours. A further limitation of the current study is that it does not enable a review of trends in all-cause paediatric acute respiratory illness (ARI)-related hospitalisation or in patterns of diagnostic testing for paediatric influenza at each included paediatric centre over the study period. In addition, it is beyond the scope of this study to determine if variation in the viral diagnostic protocols and type of testing platform used for both influenza and non-influenza respiratory viruses in paediatric ARI-related hospitalisation occurred between centres over the study period. Concerning testing practices for influenza, previously published data from the Canadian Respiratory Virus Detections Surveillance System showed laboratory reporting for all hospitals across Canada remained consistent throughout the pandemic with no significant change in practice during the pandemic compared to pre-pandemic years.<sup>23</sup> While this data is not specific to paediatric admissions, the lack of a decrease in laboratory testing in general during the COVID-19 pandemic suggests that changes in influenza testing practices at participating centres during the COVID-19 pandemic are unlikely to explain the observed significant reduction in detected paediatric influenza cases.

At this time the potential role of variation in influenza vaccination on paediatric influenza-related hospitalisation during the study period is unclear. Across Canada, influenza vaccination implementation varies by province and data on pan-Canadian paediatric age-specific influenza vaccination coverage is not available to enable comparison of influenza vaccination coverage in the 2020/2021 influenza season to previous seasons. On review of data for influenza vaccine coverage in adults during the 2020/2021 influenza season, this is reported to have been similar to the 2019/2020 season.<sup>32</sup> We cannot exclude the possibility of an increase in paediatric influenza vaccination uptake during the COVID-19 pandemic compared to pre-pandemic levels, which could have contributed, in part, to the observed decrease in paediatric influenza-related hospitalisations.

However, it is unlikely that even very high uptake of influenza vaccination amongst the paediatric population during the 2020/2021 influenza season could explain the dramatic decrease in observed influenza-related hospitalisation during the pandemic period.

## Conclusion

In conclusion, we report a dramatic decrease in paediatric influenza-related hospitalisation following the onset of the COVID-19 pandemic with a total absence of influenza-related hospitalisation and mortality in the Canadian paediatric active surveillance program during the 2020/2021 influenza season. While the cause of this dramatic decrease is not fully understood, public health measures introduced to mitigate the impact of the COVID-19 pandemic are likely to have been a major factor. With the potential for a rebound in seasonal influenza infections amongst children on relaxation of pandemic control measures, ongoing surveillance and increased understanding of the reasons underlying the observed decreases in paediatric influenza-related hospitalisation are of utmost importance. The question remains whether practices such as face-masks, distancing, hand-washing and symptomatic isolation might be beneficial for influenza control and the mitigation of future seasonal influenza epidemics in children.

## Contributors

HEG: conceptualisation, data collection and verification of underlying data, formal data analysis, methodology, visualisation, writing – original draft

KM: data collection/curation and verification of underlying data, writing – review & editing

JP, JAB, MS, SAH: conceptualisation, writing – review & editing

SKM: conceptualisation, overall supervision, writing – review & editing

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## Data sharing statement

Due to the nature of ethics approval and data collection which occurs without consent at the individual subject

level, data is unable to be shared directly from the IMPACT team. However, influenza hospitalisation data reported by the Immunisation Monitoring Program Active (IMPACT) network is publicly available from the Government of Canada website (via link; <https://www.canada.ca/en/public-health/services/diseases/flu-influenza/influenza-surveillance.html>). Details of the conditions for use of this open dataset are available on the Government of Canada website.

## Declaration of Interests

HEG: received personal fees from Abbvie unrelated to the submitted work; JP: Received grants from MedImmune and Sanofi Pasteur, and grants and personal fees from Seegene and AbbVie, all unrelated to the submitted work; MS received grants from GlaxoSmithKline, Seqirus, Merck, Pfizer, VBI, Vaccines, Sanofi Pasteur, SYmvivo. All payments made to the institution. No personal payments received; SKM: Received an investigator-led grant and served on an advisory board with Pfizer, and personal fees from GlaxoSmithKline, all unrelated to the submitted work. KM, JAB, SAH: none declared.

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#### Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2021.100132.

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