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Original Article

Changes in infection-related hospitalizations in children following pandemic restrictions: an interrupted time-series analysis of total population data

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Abstract

Background: Infectious diseases are a leading cause of hospitalization during childhood. The various mitigation strategies implemented to control the coronavirus disease (COVID-19) pandemic could have additional, unintended benefits for limiting the spread of other infectious diseases and their associated burden on the health care system.

Methods: We conducted an interrupted time-series analysis using population-wide hospitalization data for the state of Victoria, Australia. Infection-related hospitalizations for children and adolescents (aged <18 years, total source population ∼1.4 million) were extracted using pre-defined *International Classification of Diseases 10th Revision Australian Modification* (ICD-10-AM) codes. The change in weekly hospitalization rates (incidence rate ratio, IRR) for all infections following the introduction of pandemic-related restrictions from 15 March 2020 was estimated.

Results: Over 2015–19, the mean annual incidence of hospitalization with infection among children less than 18 years was 37 per 1000 population. There was an estimated 65% (95% CI 62-67%) reduction in the incidence of overall infection-related hospitalizations associated with the introduction of pandemic restrictions. The reduction was most marked in younger children (at least 66% in those less than 5 years of age) and for lower respiratory tract infections (relative reduction 85%, 95% CI 85-86%).

Conclusions: The wider impacts of pandemic mitigation strategies on non-COVID-19 infection-related hospitalizations are poorly understood. We observed marked and rapid decreases in hospitalized childhood infection. In tandem with broader consequences, sustainable measures, such as improved hand hygiene, could reduce the burden of severe childhood infection post-pandemic and the social and economic costs of hospitalization.

Key words: Infectious disease, paediatric epidemiology, hospitalization, COVID-19, restrictions

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Key Messages

- Pandemic-related restrictions, introduced in many countries to limit the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, may have unintended benefits on non-SARS-CoV-2 infections.
- In an interrupted time-series analysis, we identified a rapid and dramatic 65% reduction in infection-related paediatric hospitalizations in the 7 months following the introduction of pandemic mitigation strategies, compared with the previous 5 years.
- Hospitalizations declined by around two-thirds for children aged <5 years, but also dropped by at least 40% for children aged 10–17 years.
- The greatest reductions were seen for lower respiratory infections, which reduced by 85%. Infections that spread via person-to-person contact were markedly reduced, underscoring the role of non-pharmaceutical interventions for reducing the spread of these infections.

Introduction

Public health measures to limit the coronavirus (COVID-19) pandemic have included enhanced hand hygiene, physical distancing, school and business closures, face masks and restrictions to travel and social gatherings. In addition to limiting transmission of the severe acute respiratory syndrome coronavirus-2 virus (SARS-CoV-2), these measures have had broad, non-specific impacts on health-seeking behaviour, access to health care and the epidemiology of non-COVID-19 illnesses.[1,2] Changes to the incidence of non-SARS-CoV-2 infections might be expected to be largest in children, who disproportionately contribute to the transmission of many infections[3] and bear the largest morbidity burden.[4] Single and multicentre studies have reported marked reductions in non-COVID-19 hospital presentations and admissions[5–9] and respiratory pathogen detections in children.[10] These studies may be limited by selection bias and incomplete hospitalization data. A recent study covering 210 hospitals in Japan, examining the 4 months following school closure, found reductions in paediatric hospitalization for infectious disease ranging from 41% at the end of March to 74% at the end of May 2020.[9] The population-level impact of pandemic-related restrictions on childhood hospitalizations with infections, the leading cause of childhood admission,[11] is unknown.

These data have immediate relevance as the pandemic unfolds and would also inform post-pandemic interventions. In Australia, pandemic-related restrictions were progressively introduced from 15 March 2020 and eased in May 2020.[12] The state of Victoria experienced a second epidemic of SARS-CoV-2 infections and introduced further restrictions in July and August, including re-closing schools (Figure 1A). By the beginning of October, Victoria had recorded 20 200 confirmed cases of COVID-19 (incidence proportion 0.3%) of which 2621 were in children less than 18 years of age (incidence proportion 0.2%). The hospitalized proportion for children has been low, with just 47 (1.8%) cases hospitalized during their illness. We aimed to investigate whether non-SARS-CoV-2 paediatric infection-related hospitalizations declined following the introduction of COVID-19-related restrictions in Victoria. We examined whether the extent of change varied by type of infection and/or age group, using population-level data.

Methods

Data in this study were collected, used and reported under the Public Health and Wellbeing Act of Victoria. Nevertheless, approval to conduct the study was granted
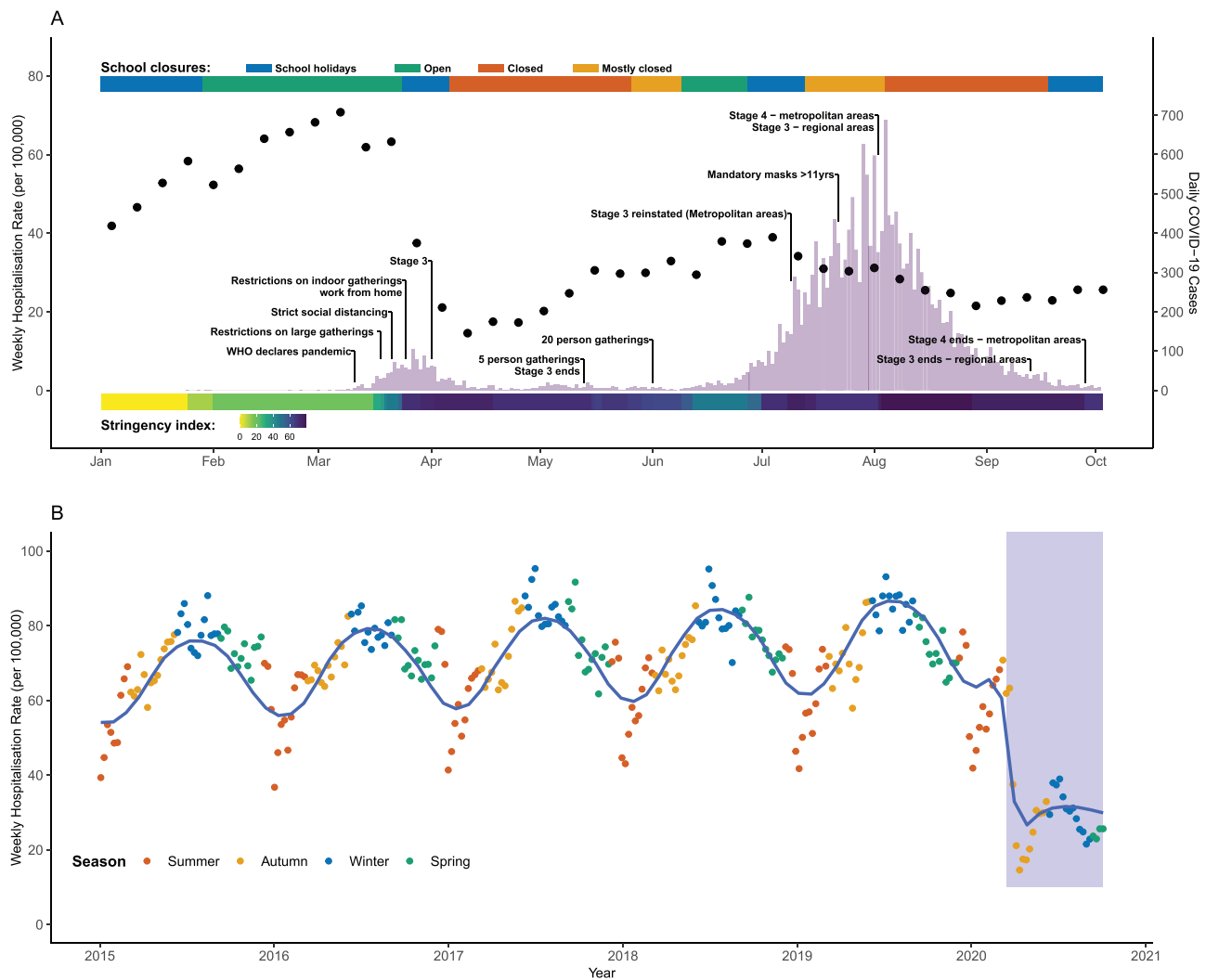
Figure 1 Overview of the data. Panel A shows total daily COVID-19 notifications (all laboratory confirmed cases) in all ages for the state of Victoria,[19] Australia (purple bars; right y-axis), with significant pandemic mitigation strategies marked. School closures are indicated at the top of the plot, with the Oxford Stringency Index[20] shown at the bottom to indicate the severity of restrictions. Black dots indicate the weekly hospitalization rate in children (left y-axis). Panel B provides weekly hospitalization rates for 2015–20 in children. Dots are coloured by season, noting that the usual respiratory infection period falls between autumn and spring, inclusive. The blue panel indicates the pandemic period specified in the interrupted time-series model. Source: *Victorian Admitted Episodes Dataset*.[13] Stage 3—four reasons to leave home: (i) essential work; (ii) shopping for supplies; (iii) to provide or receive care; (iv) exercise. Stage 4 included all Stage 3 restrictions as well as: (a) curfew from 8 pm to 5am; (b) limit of 1 h outside exercise per day; (c) 5 km travel limit; (d) one person can leave house to shop per day

by the University of Melbourne Human Research Ethics Committee (reference number: 2020–14642-12880–3).

Data source

Hospitalization data were obtained from the Victorian Admitted Episodes Dataset which records all admissions to public and private hospitals in Victoria.[13] Each hospitalization record includes a primary and up to 39 additional diagnoses using the *International Classification of Diseases, Tenth Revision, Australian Modification* (ICD-10-AM).

We categorized records for the period 1 January 2015 to 3 October 2020 into pre-defined infection-related

discharge diagnoses: (i) all infections; (ii) upper respiratory (URI) (respiratory tract proximal to the vocal chords, external, middle and inner ear, mastoid and sinuses); (iii) lower respiratory (LRI) (microbiologically, clinically or radiologically diagnosed airway infection in and distal to the bronchi, including influenza with predominantly respiratory features); (iv) gastrointestinal (bacterial, viral or protozoal gastroenteritis or clinical diagnosis of infective gastroenteritis); (v) skin and soft tissue (skin and adnexa, including cellulitis and myositis); (vi) invasive bacterial (bacterial isolation from a normally sterile deep site); (vii) viral (viral causes not otherwise categorized); and (viii) urinary tract or sexually transmitted infections (UTI and STI)

(urinary or genital tract, including sexually transmitted diseases) (see Supplementary data at *IJE* online).[14] Records with more than one infection-related diagnosis contributed a single count to each respective category. We conducted a sensitivity analysis using only the primary diagnosis. Six age groups were considered: 8 days-<6 months, 6 months-<1 year, 1-<2 years, 2-<5 years, 5-<10 years and 10-<18 years.

Statistical analysis

We calculated the weekly hospitalization rate of all infections with the estimated resident population as the denominator.[15] Interrupted time-series (ITS) regression was used to estimate the change in weekly hospitalization rates for all infections following the introduction of local restrictions from 15 March 2020. We modelled the weekly hospitalization count using a quasi-Poisson model to allow for over-dispersion. This model included: an offset for the estimated resident population[15]; a covariate for time (weeks) to account for secular trend; a dummy variable indicating the pre-pandemic and pandemic periods; and a harmonic term for month to adjust for seasonality. The estimated co-efficient for the dummy variable described the overall relative change in infection-related hospitalizations between the pre-pandemic and pandemic time periods. In addition, we compared differences across age and diagnostic groups,

using incidence rate ratios (IRR) comparing the hospitalization rate for the period 15 March to 3 October 2020 with the mean hospitalization rate for the equivalent calendar periods in 2015 to 2019 (Table 1). The relative reduction in hospitalizations was calculated as 1-IRR*100%. Finally, to investigate the potential for a shift in the severity of illness among children presenting to hospital, we compared length of stay between the two time periods. Analyses were conducted in the R statistical package version 3.6.1.[16]

Results

Victoria has a current total population of 6.6 million of whom 1.4 million are less than 18 years of age.[15] A total of 277 792 infection-related hospitalizations in children less than 18 years of age were analysed in our ITS analysis, of which 265 833 occurred in the pre-pandemic period (1 January 2015 to 14 March 2020) and 11 959 occurred in the pandemic period (15 March 2020 to 3 October 2020). In the 5 years preceding the pandemic in 2020, the mean annual infection-related hospitalization rate in those less than 18 years ranged from 36 to 38 per 1000 population per year. The pandemic-related restrictions were introduced from 15 March 2020 and were associated with an immediate drop in the overall infection-related hospitalization rate in children (Figure 1B), corresponding to an

Table 1 Incidence rate ratio calculations for infection types and age groups. The number of hospitalizations and person-years (py) are for the calendar dates 15 March to 3 October of each relevant year. These date ranges corresponded to 3 824 152 py for 2015 to 2019 and 800 743 py for 2020 for all age groups combined. Age group results are for all infections. Relevant py for each age group are enclosed in parentheses following the number of hospitalizations in the bottom half of the table

Infection type	Hospitalizations 15 Mar-3 Oct, 2015–19 *n*	Hospitalizations 15 Mar-3 Oct, 2020 *n*	Incidence rate 15 Mar-3 Oct, 2015–19 (per 1000 py)	Incidence rate 15 Mar-3 Oct 2020 (per 1000 py)	Incidence rate ratio (95% CI)
All infections	154 312	11 959	40.4	14.9	0.37 (0.36-0.38)
Upper respiratory	53 949	3925	14.1	4.9	0.35 (0.34-0.36)
Lower respiratory	42 033	1280	11.0	1.6	0.15 (0.14-0.15)
Viral	30 779	2493	8.0	3.1	0.39 (0.37-0.40)
Gastrointestinal	13 491	1221	3.5	1.5	0.43 (0.41-0.46)
UTI and STI	6188	1071	1.6	1.3	0.83 (0.77-0.88)
Bacterial	4423	542	1.2	0.7	0.59 (0.54-0.64)
Skin and soft tissue	2630	317	0.7	0.4	0.58 (0.51-0.65)
Age group	*n* (person-years)	*n* (person-years)			
8 days-<6 months	20 221 (109 634)	1353 (21 557)	184.4	62.8	0.34 (0.32-0.36)
6 months-<1 year	14 359 (109 634)	861 (21 557)	131.0	39.9	0.30 (0.28-0.33)
1-<2 years	27 906 (222 046)	1789 (43 567)	125.7	41.1	0.33 (0.31-0.34)
2-<5 years	39 120 (675 835)	2642 (137 956)	57.9	19.2	0.33 (0.32-0.34)
5-<10 years	27 759 (1 098 084)	2250 (232 616)	25.3	9.7	0.38 (0.37-0.40)
10-<18 years	24 947 (1 608 919)	3064 (343 492)	15.5	8.9	0.58 (0.55-0.60)

py: person-years; CI: confidence interval; UTI: urinary tract infections; STI: sexually transmitted infections.

estimated 65% (95% CI 62-67%) reduction. This estimated reduction was similar (67%, 95% CI 64-70%) if only the primary discharge diagnosis was used (see Supplementary data at *IJE* online).

The change in the infection-related hospitalization rate decreased with age, with estimated reductions of at least 62% in those aged less than 10 years, compared with an estimated reduction of 42% in those aged 10 years and over (Figure 2, Table 1). The hospitalization rate for all clinical infection groups reduced by at least 17% (Figure 3, Table 1). The greatest reductions were for lower respiratory (85%, 95% CI 85-86%), upper respiratory (65%, 95% CI 64-66%), viral (61%, 95% CI 60-63%) and gastrointestinal (57%, 95% CI 54-59%) infections.

The median length of stay during the pandemic period was slightly longer than the median length of stay for the preceding 5 years (see Supplementary Table S2, available as Supplementary data at *IJE* online). Most hospitalizations were short and the differences in median length of stay were less than 1 day.

Discussion

This total population analysis shows the considerable impact of COVID-19-related restrictions on hospitalizations for non-SARS-CoV-2 infections in children in Victoria, Australia. The overall estimated reduction in the hospitalization rate was almost two-thirds and reductions were observed in all age groups. These findings are consistent with data from other centres and microbiological notifications of both hospitalized and non-hospitalized children.[5–10] The data are likely to be broadly generalizable to other high-income settings that imposed similar restrictions in response to the pandemic and where paediatric health care is free.

Reductions in hospitalization rates were most evident for upper and lower respiratory infections (LRI), for which the hospitalization burden in children is significant. Globally, LRI hospitalizations among children less than 5 years, attributable to respiratory syncytial virus, were estimated at 3.2 million (2.7–3.8) in 2015,[17] and those attributable to influenza numbered 870 000 (543 000–1 415 000) in 2018.[18] If the dramatic reduction we observed in LRI hospitalizations is widely replicated, this would have a major impact on the global burden of severe paediatric infections in 2020.

In addition to respiratory infections, gastrointestinal and viral infections were also markedly reduced; these are all infections where person-to-person spread (droplet, faecal-oral or aerosol) is necessary for infection. More modest reductions in hospitalizations were observed for infections where person-to-person spread is less important than

infection by endogenous flora (such as urinary tract infections) or where microbial colonization may occur weeks or months before clinical infection (such as some invasive bacterial infections). Reductions in hospitalizations were observed in all age groups but were more marked in children less than 10 years of age. This may reflect differing impacts of pandemic restrictions on both the infection types and the relative extent to which they impact on each age group, as well as behavioural factors that differ with age.

Strengths and limitations of study

Our study has a number of strengths, particularly the analysis of total population data, which reduces the potential for selection bias from single centre or incomplete population data on hospitalization. By comparing hospitalization rates in 2020 with those from the preceding 5 years, we accounted for annual variations in the incidence and severity of seasonal epidemics, such as influenza and respiratory syncytial virus (RSV).[10] However, given that COVID-19-related restrictions coincided with Victoria's winter, the observed reductions in infection-attributable hospitalization may attenuate with non-pandemic seasonal variation in infection-related hospitalizations. Ongoing surveillance of the incidence of hospitalizations with childhood infections will be important as the pandemic unfolds and levels of restrictions vary.

We included all discharge diagnoses as this is considered a more robust measure of total infection burden than primary diagnosis alone[14]; if the hospitalization record has more than one diagnosis, the primary reason for admission may be unclear. To ensure that infection-related hospitalizations were not overestimated, we also performed a sensitivity analysis using only the primary diagnosis, and the findings were essentially unchanged. Additionally, in contrast to other settings, virological testing was encouraged and freely available throughout the pandemic in Victoria, so the incidence of SARS-CoV-2 infections is unlikely to be biased by limitations in testing availability.

We acknowledge some limitations. First, health-seeking behaviour will have changed during the pandemic.[1,2] Families may have delayed or avoided seeking health care through fear of exposure to SARS-CoV-2. For example, we observed a reduction by 17% in hospitalizations for the category that included urinary tract infections, which are not typically associated with person-to-person transmission in children. This may be indicative of a change in health-seeking behaviour, but we were unable to investigate this directly as non-hospital data were not available. It is also possible that physicians modified their clinical threshold for hospitalization with infection during the
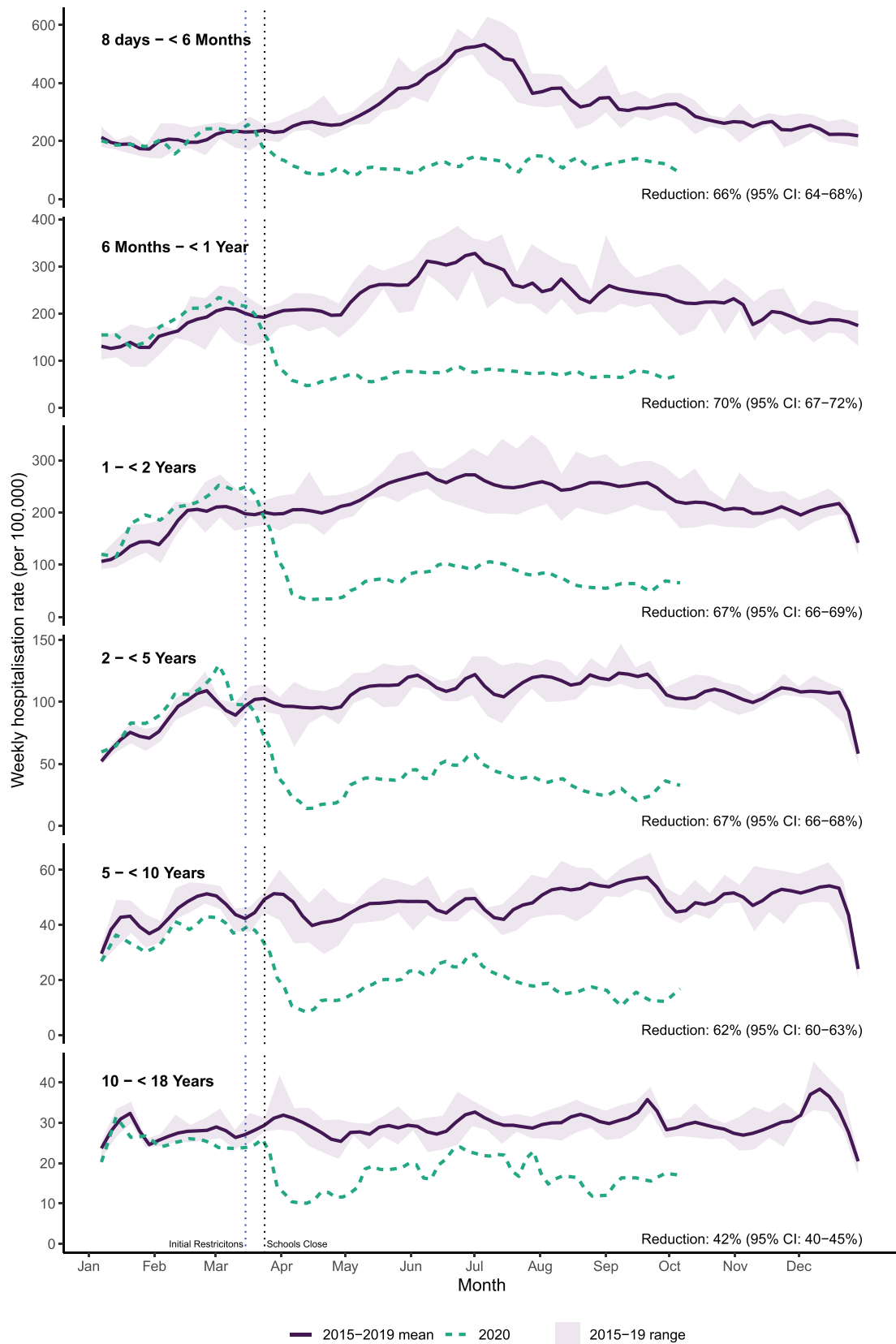
Figure 2 Weekly hospitalization rates for all infection-related causes by age group. The average weekly rate for 2015–19 is plotted in the solid purple line, with shaded regions indicating the range for 2015–19. The 2020 rate is shown in the dashed green line. Weekly rates are smoothed using the LOESS method. The vertical dotted blue line indicates 15 March 2020 when restrictions began to be introduced, and the vertical dotted black line indicates 24 March 2020 when schools were first closed. Note the different y-axes for each age group. Source: *Victorian Admitted Episodes Dataset*[13]
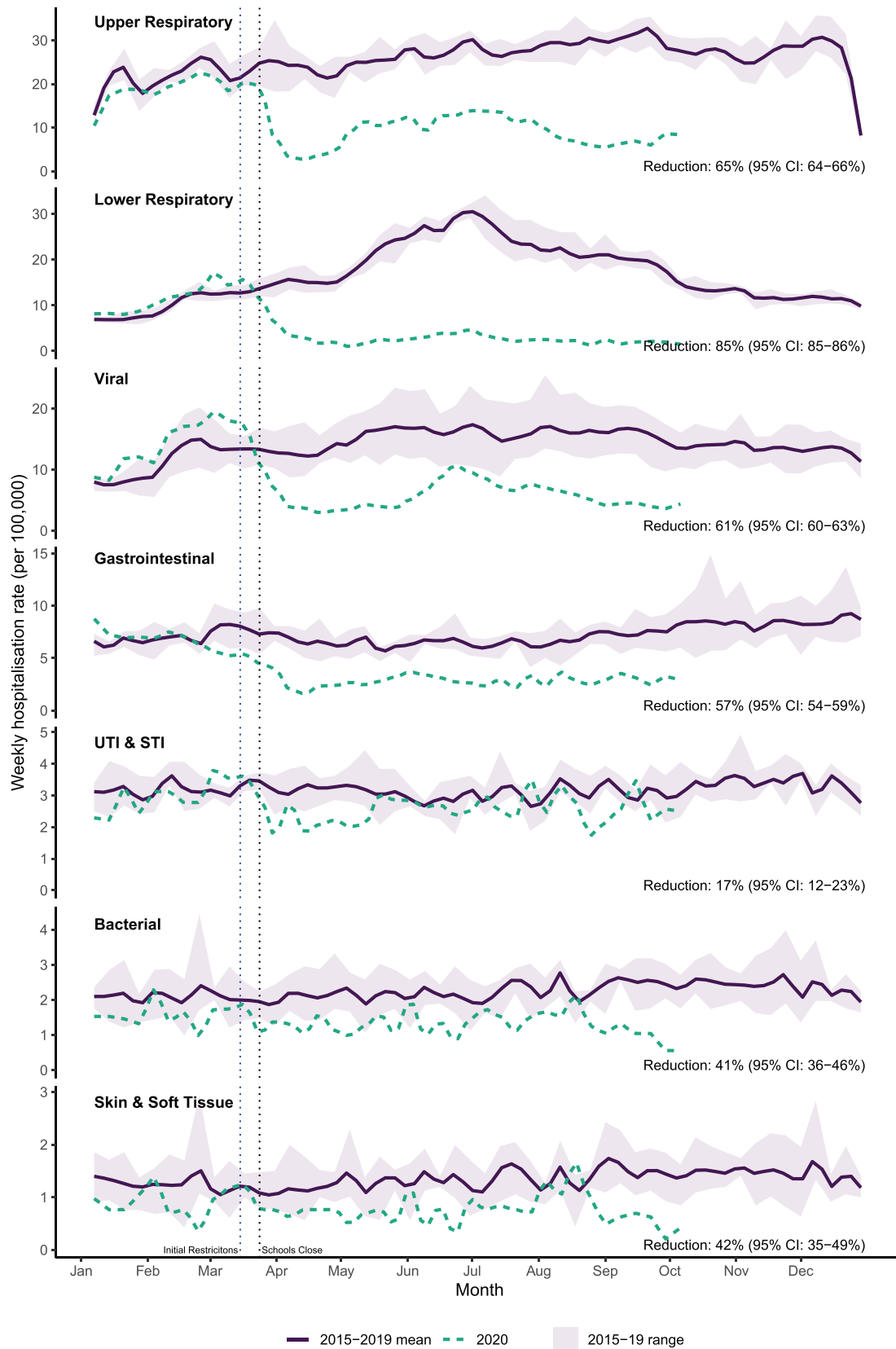
Figure 3 Weekly hospitalization rates by seven infection groups. The average weekly rate for 2015–19 is plotted in the purple solid line, with shaded regions indicating the range for 2015–19. The 2020 rate is shown in the dashed green line. Weekly rates are smoothed using LOESS method. The vertical dotted blue line indicates 15 March 2020 when restrictions began to be introduced, and the verticaldotted black line indicates 24 March 2020 when schools were first closed. Note the different y-axes for each infection group. Weekly hospitalizations for 2020 are shown in green. The greatest reduction in hospitalizations was seen in the lower respiratory infection group, in which the estimated reduction in hospitalizations was 85%. Source: *Victorian Admitted Episodes Dataset*.[13]

pandemic, although clinical guidelines regarding hospitalization were unchanged. We restricted our study to hospitalization data to limit the impact of changed health-seeking behaviour, as it seems likely that children with severe infection would eventually be hospitalized. Indeed, lower hospitalization rates were sustained throughout April to October, suggesting a true reduction in infection. Furthermore, hospital care is free in Australia and access or financial concerns are unlikely to have strongly influenced health-seeking behaviour. Overall, it is difficult to disentangle changed health-care-seeking from reductions in pathogen transmission given there is no routine surveillance of the incidence of infectious disease in non-hospitalized Victorian children. Whereas mortality data might provide a more sensitive estimate of changed rates of disease, they would not be expected to be useful in Australian paediatric populations where mortality rates are extremely low. Our observation of marginally increased length of stay during the pandemic periods may reflect increased severity of disease, but could also reflect changes in staffing, patient flow and discharge practices rather than changes in infection severity.

Second, given the observational nature of the study, the heterogeneity in different stages of pandemic restrictions and the potential lag between the introduction of restrictions and changing hospitalization rates, it was not possible to quantify the effects of specific pandemic control measures. Further analyses across different settings could possibly address this important issue, but is beyond the scope of this analysis. In addition, the indirect effects of restrictions, such as reduced air pollution, may have also affected hospitalization rates and warrants further study. Last, current population estimates may overestimate the true population denominator due to dramatic reductions in immigration in 2020. However, application of the 2019 population denominators continued to show similar reductions in rates as those observed using our 2020 population estimates.

In conclusion, these findings underscore the considerable indirect effects of the public health responses to the COVID-19 pandemic on infection-related hospitalizations in children. Several public health measures were introduced contemporaneously, making it difficult to ascertain which had the greatest impact. Individual-level measures could be readily implemented after the pandemic, such as attention to cough etiquette and hand hygiene, and supporting parents of children with symptomatic infection to exclude them from school or day care. In tandem with population-level interventions, such as increasing immunization rates for seasonal influenza and reducing air pollution, these measures could considerably reduce the human and economic burden of infection-associated hospitalizations in children.

The data used in this study were from the Victorian Admitted Episodes Dataset. These data are available for request from the Victorian Department of Health, [https://www2.health.vic.gov.au/hospitals-and-health-services/data-reporting/health-data-standards-systems/data-collections/vaed].

Supplementary Data

Supplementary data are available at *IJE* online.

Author Contributions

I.M.F.T., J.E.M., S.L.R., D.P.B. and S.G.S. designed the study. Data were collected before the study. I.M.F.T. did the statistical analysis and S.G.S. reviewed. I.M.F.T., J.E.M., D.P.B. and S.G.S. interpreted the data. I.M.F.T., D.P.B. and S.G.S. drafted the manuscript. I.M.F.T., J.E.M., S.L.R., D.P.B. and S.G.S. critically revised the manuscript for intellectual content.

Conflict of Interest

None declared.

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