What can we learn from our 2021 respiratory syncytial virus experience?

Cameron C Grant, Q Sue Huang, Adrian Trenholme, Susan Taylor, Tim Wood

Respiratory syncytial virus (RSV), named for it causing multinucleated cells (syncytia) to form in cell culture,[1] is the leading cause of acute lower respiratory infections (ALRIs) during early childhood.[2,3] Globally in 2015, among children <5 years old, there were an estimated 33.1 million episodes of RSV-ALRI, with 3.2 million RSV-ALRI hospital admissions and 59,600 RSV-ALRI in-hospital deaths.[2] In 2015, while >80% of RSV-associated ALRIs occurred in children ≥6 months old, 45% of the hospital admissions and in-hospital deaths were in children <6 months old.[2]

In New Zealand, based upon the active surveillance study, SHIVERS (Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance),[4] conducted at Starship Children's, Kidz First Children's, Auckland and Middlemore hospitals in Auckland from 2012 to 2015, the RSV-ALRI hospitalisation rate was 6.1/1,000 children 0–4 years old during the 22-week surveillance periods (May–September inclusive each year). The year-to-year variance in RSV-ALRI hospitalisation rate was 24% (5.5/1,000 children in 2013 to 6.8/1,000 children in 2012).[5] Consistent with global data, 48% of the preschool age group RSV-ALRI hospitalisations were in children <6 months old.[5]

Hospital admissions of young children represent only a proportion of acute respiratory infection (ARI) healthcare visits caused by RSV. Based upon SHIVERS' data collected at Kidz First Children's Hospital, 3,585 (66%) of 5,412 infant ARI emergency department (ED) presentations from May to September 2014–2016 did not result in hospital admission.[6] Of the respiratory viruses tested (RSV, rhinovirus, adenovirus, influenza and human metapneumovirus), RSV was associated with the highest ARI ED-only (34.4/1,000 children) and hospitalisation rates (24.6/1,000 children).[6] The SHIVERS surveillance project also showed the considerable amount of RSV disease resulting in hospital admissions of adults in New Zealand.[7,8]

The year-to-year variability in RSV-ALRI hospitalisation rates among children 0–4 years old that occurs in New Zealand is considerably smaller than the variability between groups of children in New Zealand defined by ethnicity (470% variability) (European/other 2.9/1,000, Asian 2.7/1,000, Māori 9.3/1,000, Pacific 12.8/1,000) or area-level deprivation (290% variability) (least deprived quintile 2.9/1,000 versus most deprived quintile 8.4/1,000).[5]

What happened to respiratory syncytial virus disease burden in New Zealand in 2020?

In association with New Zealand's stringent nonpharmaceutical interventions in response to the coronavirus disease 2019 (COVID-19) pandemic, the circulation in New Zealand during 2020 of RSV and most other respiratory viruses was interrupted.[9] This COVID-19 elimination strategy included a nationwide lockdown from 25 March to 27 April 2020.[9]

In the post-lockdown period (28 April to 27 September 2020), in comparison with the 2015–2019 reference period, large reductions occurred in nation-wide identifications of all tested respiratory viruses. These reductions, from largest to smallest, were in influenza (99.9%), RSV (98.0%), human metapneumovirus (92.2%), enterovirus (82.2%), adenovirus (81.4%), parainfluenza virus (80.1%) and rhinovirus (74.6%).[9]

Community and sentinel general practice influenza-like illness and hospital severe acute respiratory infection surveillance all showed very low rates of disease in comparison with the rates observed in 2018–2019.[9] Early childhood ARI-related hospital admissions decreased dramatically in the post-lockdown period. For example, at Kidz First Children's Hospital, the number of ALRI hospital admissions in children <2 years old from 1 March to 31 August each year from 2015 to 2019 ranged between 1,486 and 2,046, with PCR testing of respiratory samples being positive for RSV in between 252 and 495 samples per year. In comparison, in 2020 there were 159 ALRI hospital admissions from 1 March to 31 August among children <2 years old, with RSV identified from two respiratory samples.[10]

Several factors contributed to these dramatic reductions in RSV infections and acute illnesses. The international border controls, including mandatory 14-day isolation of arriving international travellers, will have limited the normal seasonal introduction of RSV into New Zealand.[10] Physical distancing and hygiene measures are also likely to have contributed. Handwashing damages the lipid layer that surrounds RSV, thus reducing its capacity for person-to-person transmission and infection.[11] Rhinovirus, which is a non-enveloped virus that may therefore be less susceptible to the effects of handwashing,[11] continued to be isolated from respiratory samples collected from children admitted to Kidz First Children's Hospital with ALRI during 2020 in similar numbers to preceding years.[10]

Similar RSV-related observations were reported in Australia following the closure of their international border to non-residents on 20 March 2020.[12] In Western Australia, where the border with other states was also closed on 6 April 2020, RSV detections from April to August 2020 were 98% lower than annual average RSV detections during these same winter months from 2012 to 2019.[12] In the Sydney Children's Hospitals Network, RSV detections (94% decrease), ARI emergency department attendances (70% decrease) and hospital admissions for bronchiolitis (86% decrease) were lower during April–June in 2020 than during these same months in the five preceding years.[11]

Then, during the latter part of 2020, an increase in RSV detections occurred in Australia. For example, in Western Australia, RSV detections increased from late September 2020.[13] By November, the weekly number of detections exceeded the median seasonal peak from 2012–2019, with this high number of weekly detections continuing into summer.[13] The median age of children in whom RSV was detected in 2020 was higher than the annual upper range from 2012–2019 (18.4 months versus 7.3–12.5 months).[13]

What happened to respiratory syncytial virus disease burden in New Zealand in 2021?

Following the opening of the trans-Tasman travel bubble between Australia and New Zealand in April 2021, an increase in RSV identifications has occurred in New Zealand. This surveillance is laboratory based and consists of the World Health Organization National Influenza Centre at the Institute of Environmental Science & Research Limited (ESR) and six hospital laboratories in Auckland (two hospital laboratories), Waikato, Wellington, Christchurch and Dunedin. This reporting is based upon testing of specimens ordered by clinicians working in normal clinical practice in hospital inpatient and outpatient settings that serve approximately 70% of the New Zealand population.

During 2021, the weekly number of RSV detections nation-wide first exceeded five during week 21 (week ending 30 May 2021).[14] The weekly number of RSV detections increased rapidly from week 21, with the detections in successive weeks being 37, 110, 258, 590, 774 and 892, peaking in week 28 at 951 and being 787 in week 29 and 542 in the most recently reported week (week 30, ending 1 August 2021).[15] When expressed as a rate per million population, the peak weekly RSV detection rates in 2021 were at least five-fold higher than those observed in 2015–2019.

In addition to the number of RSV detections being greater during 2021 compared with 2019, the age distribution also differed. As shown in data reported from Laboratory Services at Middlemore Hospital (which includes Kidz First Children's Hospital), the number of RSV detections among children

0–<12 months were two-fold higher in 2021 versus 2019, whereas the number of RSV detections among children 12–<48 months were at least five-fold higher (Figure 1). These findings are consistent with older preschool-aged children presenting with ALRIs, presumably because of increased susceptibility to more severe disease following their first exposure to RSV during 2021 rather than 2020.

What does this mean for the respiratory infection disease burden in New Zealand in the future?

PHARMAC-approved funding, initiated this year, for the prophylactic use of the monoclonal antibody palivizumab for infants aged <6 months with extreme prematurity and chronic lung disease, or with severe congenital heart disease,[16] will help to protect those most at risk of life-threatening RSV disease.[17,18]

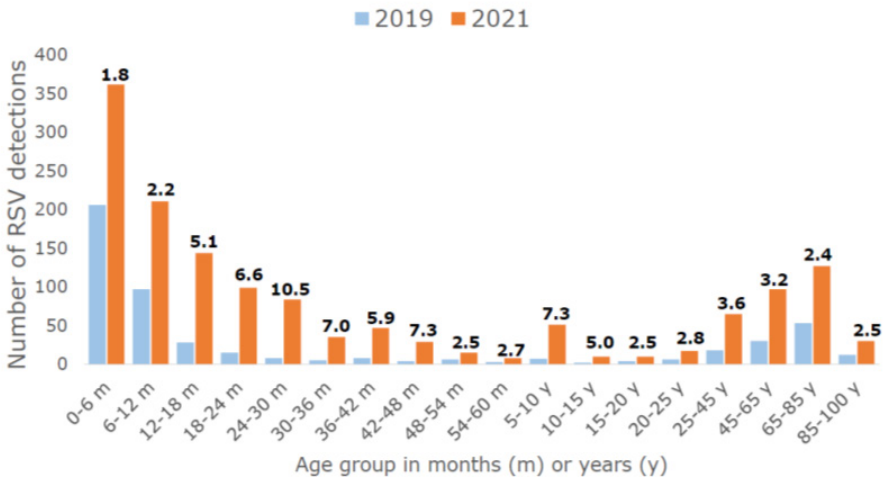
From a more general respiratory virus perspective, what we have seen happen with RSV in 2021 may just be the first of several variances resulting from the impact of COVID-19 on the relationships established between humans and respiratory pathogens. In addition to the current adult COVID-19 vaccination programme, the vaccine protection of children in New Zealand against other respiratory pathogens needs urgent attention.

We should anticipate and plan for influenza epidemics to differ in size and age distribution similarly to the increase in proportion of the New Zealand population that is susceptible to more severe disease following exposure to RSV.[19] There is the potential that children will be more vulnerable to future influenza epidemics.[20] Influenza vaccine should be added to the schedule of vaccines for all children in New Zealand.[21]

New Zealand should also anticipate an increase in incidence in bacterial respiratory pathogen disease. Reports of reductions in invasive pneumococcal disease,[22,23] and invasive group A streptococcal disease incidence,[23] in association with the public health measures instituted to control the COVID-19 pandemic, and with the reductions that occurred in influenza circulation,[24] will likely be reversed with the return of RSV, and particularly so if influenza infection becomes re-established in New Zealand.[25]

Urgent attention is required to address the critical current failure of our childhood immunisation programme if we are to prevent children in New Zealand from experiencing epidemics of pertussis and measles

Figure 1: Number of respiratory syncytial virus (RSV) detections by age group in 2021* compared with 2019.



* 2021 compared with 2019 in each age group, with the number above each 2021 bar indicating the ratio of 2021 to 2019 RSV detections in each age group.

† Data from Laboratory Services, Middlemore Hospital, Counties Manukau District Health Board. 2021 data limited to weeks 0–30 (1 January–1 August 2021).

following their, at times horrific, 2021 RSV experience, and to protect them against influenza and invasive pneumococcal disease.

The New Zealand childhood immunisation schedule begins in pregnancy.[21] Receipt during pregnancy of influenza and pertussis vaccine protects young infants against illnesses caused by these infections and requiring hospital admission.[26–28] In New Zealand, coverage during pregnancy for women giving birth in 2018 was 31% for influenza vaccine and 44% for pertussis vaccine.[29] From 2013 to 2018, the odds of Māori and Pacific women receiving either of these vaccines were lower than women living in New Zealand of non-Māori and non-Pacific ethnic groups, and were lower for women living in households in more versus less deprived areas.[29]

For the three months 1 April–30 June 2021, only 75.3% of New Zealand children aged six months were fully immunised.[30] At age six months, coverage for the six-week, three-month and five-month scheduled vaccines among NZ European was 80.1%, among Māori 54.9%, among Pacific 68.7%, among Asian 93.0% and among children of other ethnic groups 78.8%.[30] Coverage for children living in the most deprived quintile of households was 64% and in the least deprived quintile it was 83%.[30]

The 470% variance in early childhood RSV-ALRI hospitalisation rates by ethnicity, and the 290% variance by household deprivation in New Zealand, are both simply unacceptable and indefensible. As New Zealand has now entered an important phase of health reform, RSV provides us with insight into what to expect. From a health perspective we should expect and plan for the unexpected. The worst-case scenarios are likely to be worse than what we have come to expect. We must use the opportunity present now to eliminate inequities in vaccine access based upon ethnicity, socioeconomic status and age. Influenza, measles, pertussis and invasive pneumococcal disease all have the potential to make our 2021 RSV experience appear relatively trivial in retrospect.

ISSN 1175-8716

Competing interests:
Nil.

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