Examining the interseasonal resurgence of respiratory syncytial virus in Western Australia

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ABSTRACT

Background Following a relative absence in winter 2020, a large resurgence of respiratory syncytial virus (RSV) detections occurred during the 2020/2021 summer in Western Australia. This seasonal shift was linked to SARS-CoV-2 public health measures. We examine the epidemiology and RSV testing of respiratory-coded admissions, and compare clinical phenotype of RSV-positive admissions between 2019 and 2020.

Method At a single tertiary paediatric centre, International Classification of Diseases, 10th edition Australian Modification-coded respiratory admissions longer than 12 hours were combined with laboratory data from 1 January 2019 to 31 December 2020. Data were grouped into bronchiolitis, other acute lower respiratory infection (OALRI) and wheeze, to assess RSV testing practices. For RSV-positive admissions, demographics and clinical features were compared between 2019 and 2020.

Results RSV-positive admissions peaked in early summer 2020, following an absent winter season. Testing was higher in 2020: bronchiolitis, 94.8% vs 89.2% (p=0.01); OALRI, 88.6% vs 82.6% (p=0.02); and wheeze, 62.8% vs 25.5% (p<0.001). The 2020 peak month, December, contributed almost 75% of RSV-positive admissions, 2.5 times the 2019 peak. The median age in 2020 was twice that observed in 2019 (16.4 vs 8.1 months, p<0.001). The proportion of RSV-positive OALRI admissions was greater in 2020 (32.6% vs 24.9%, p=0.01). There were no clinically meaningful differences in length of stay or disease severity.

Interpretation The 2020 RSV season was in summer, with a larger than expected peak. There was an increase in RSV-positive non-bronchiolitis admissions, consistent with infection in older RSV-naïve children. This resurgence raises concern for regions experiencing longer and more stringent SARS-CoV-2 public health measures.

What is already known on this topic?

- Respiratory syncytial virus (RSV) in temperate climates has predictable seasonality with a mid-winter peak.
- SARS-CoV-2-related public health measures also reduced the circulation of RSV, altering this seasonality.

What this study adds?

- Regions that experienced a reduction in RSV are at risk of an interseasonal resurgence.
- Although the admission rates may be high, the phenotype observed is not clinically more severe.
- The altered in seasonality may bring an increased non-bronchiolitis admissions, consistent with infection in older RSV-naïve children.

INTRODUCTION

Respiratory syncytial virus (RSV) is the most common cause of acute lower respiratory tract infections (ALRIs) in children.[1] RSV-associated ALRIs resulted in an estimated 3 million hospitalisations and almost 60 000 in-hospital deaths in children under the age of 5 years globally.[2] Severe disease can also occur in older adults and those with underlying risk factors, including immunodeficiency and cardiopulmonary dysfunction.[3]

In temperate regions, RSV follows a typical seasonal pattern with peak months in winter at predictable yearly intervals.[4 5] The seasonal RSV peak occurs in July in Perth, the major metropolitan centre in Western Australia (WA).[4]

WA was successful in early eliminating local transmission of SAR-CoV-2, facilitating rapid reduction of public health measures. An initial stay-at-home order was in place for 4 weeks from March 2020 followed by staged reduction of social distancing measures; wearing of masks was not required at any stage in 2020. By July 2020, all schools were open and large sporting events were permitted, limited to 50% capacity.[6] The state border remained closed to interstate and international travellers. Internationally, public health measures targeted at controlling transmission of SARS-CoV-2 have altered the epidemiology and seasonality of other respiratory viruses.[6–9] In WA, the initial SARS-CoV-2-associated public health measures were associated with a 98% reduction in RSV detections through winter 2020.[6] A subsequent interseasonal resurgence with unprecedented RSV detections was observed in WA during the southern hemisphere summer.[10] The increased number of cases was

consistent with modelling predicting larger future outbreaks of endemic respiratory viruses following periods of COVID-19-related non-pharmaceutical interventions.[11] RSV detection numbers in WA peaked in December 2020 and declined in early 2021.[12] A similar late increase in RSV incidence was observed separately in other Australian regions[13] and subsequently in a number of other regions internationally.[14 15]

Our previous report analysed RSV laboratory data from emergency department (ED) and hospitalised patients.[10] These data are potentially influenced by altered sampling secondary to mandated SARS-CoV-2 testing and changes in parental health-seeking behaviours for children with respiratory symptoms. In this study, we aimed to assess the testing pattern and detection rate for RSV in respiratory-coded hospital admissions in 2020, compared with 2019. To further explore the clinical impact of this interseasonal resurgence, we examined the demographic and clinical features of RSV-positive cases.

METHODS

Study population

This study was conducted at Perth Children's Hospital (PCH), a 298-bed tertiary paediatric hospital.[16] Diagnosis coding using International Classification of Diseases, 10th edition Australian Modification (ICD-10-AM[17]) in primary and secondary fields was used to identify respiratory-related admissions of children <16 years (J00–06, J9–18, J20–22, J30–39, J40–47, J60–70, J80–J99, R06.2) between 1 January 2019 and 31 December 2020. Admissions <12 hours were excluded to minimise the influence of changes in health-seeking behaviours and SARS-CoV-2 testing practices by excluding the ED short-stay unit. RSV-negative admissions with ICD-10-AM codes, associated with chronic, non-infective conditions and bacterial infections (J30–39, J40–44, J60–70 and J80–99), were also excluded.

Laboratory data

Associated RSV nucleic acid amplification testing results were identified using the PathWest Laboratory Medicine database, the sole pathology provider to PCH. Results were included if specimen collection occurred within 7 days of admission. Additional RSV-positive result from testing at an external provider was ascertained through review of the ICD-10-AM codes (J12.1, J20.5, J21.0 and J22) and confirmed by manual clinical record review.

Part A: respiratory-coded admissions

For analysis of RSV testing, admissions were grouped into bronchiolitis (J21), other ALRI (OALRI) (J9–J18, J20 and J22), and wheeze (R06.2, J45–46). These groupings were chosen due to their strong association with RSV and high incidence.

Part B: RSV-positive admissions

To ascertain clinical features of RSV-positive admissions, ICD-10-AM codes, the electronic discharge summary and laboratory result manager were reviewed. Data included: date of birth, sex at birth, reported ethnicity, postcode, clinical presentation, respiratory support (if required) at admission and peak, antibiotic use, indication and if continued at discharge, investigations, intensive care unit (ICU) admission, discharge diagnosis, length of stay (LOS) and readmission within 1 week. For clinical features, data not detailed were considered negative.

RSV-positive admissions were grouped by the clinical diagnosis in the discharge summary as bronchiolitis, OALRI, wheeze responsive to salbutamol and other.

Definitions

Postcode was used to identify children from an area in the lowest quintile (most deprived) on Index Relative Socio-Economic Advantage and Disadvantage (IRSAD).[18] Respiratory support included low-flow oxygen, humidified high-flow nasal oxygen (HHFNO), continuous positive airway pressure (CPAP) and mechanical ventilation. HHFNO and CPAP were grouped, defined as pressure support. Prematurity was defined as birth gestational age <37 weeks.[19] Significant congenital heart disease was defined as previously described.[20] Neurological and neuromuscular conditions (eg, hypotonia, seizure disorders, cerebral palsy) and syndromes (eg, trisomy-21) were grouped together.[21]

Statistical analysis

Incidence rates were calculated using metropolitan Perth population (postcodes 6000–6199) as the denominator.[22] As data were not available for 2020, 2019 denominators were used.[22] The average epidemic curve of RSV detections in <16 years in metropolitan Perth from 2012 to 2019 was compiled as previously described.[6] Data analyses were performed using Stata/IC, V.11.2 statistical software (Stata Corp, College Station, Texas, USA). X^2 was used to compare proportions of groups and Mann-Whitney U test to compare non-normally distributed continuous variables.

RESULTS

A total of 5467 respiratory-coded admissions were identified during the study period (figure 1). Of these, 2757 (50.4%) underwent RSV testing at PathWest. A further 67 (1.2%) admissions were identified as RSV detected, with testing performed by an external pathology provider. Patients admitted for <12 hours (1687) and admissions with ICD-10-AM codes consistent with chronic respiratory conditions that were RSV negative (107) were excluded. Of the remaining 3780 (69.1%) ICD-10-AM respiratory-coded admissions, a positive RSV result was identified in 917 (24.3%).

Part A: respiratory-coded admissions

Testing rates and RSV positivity differed over the 2-year period (figure 2). Admissions with a positive RSV test in 2019 approximated the average epidemic curve. RSV testing rates were higher in 2020 (figure 2B); bronchiolitis, 94.8% vs 89.2% (p=0.01); OALRI, 88.6% vs 82.6% (p=0.02); and wheeze, 62.8% vs 25.5% (p<0.001). Between May and September 2020, 80% (307 of 382) of these admissions underwent RSV testing, with RSV positivity <1% (2 of 307). In November and December 2020, 94% of admissions underwent RSV testing, with RSV positivity reaching 81.7% (379 of 464). All were also tested for SARS-CoV-2 with no positive detections.

Part B: RSV-positive admissions

Of 917 RSV-positive admissions, 3 admissions were excluded as there was no electronic discharge summary and 15 (6 from 2019) as RSV detection was a non-significant contributor (eg, prolonged admission for induction chemotherapy for acute leukaemia). For 28 admissions, the ICD-10-AM code differed from the clinical diagnosis (see online supplemental table 1).

Of the remaining 899 RSV-positive admissions, 445 (49%) were from 2020, with 417 (93.7%) occurring in November and December 2020 (figure 3). Comparing 2019 and 2020, there was no significant difference in gender (57.7% vs 51.9% male, p=0.08), proportion identifying as Aboriginal and/or Torres

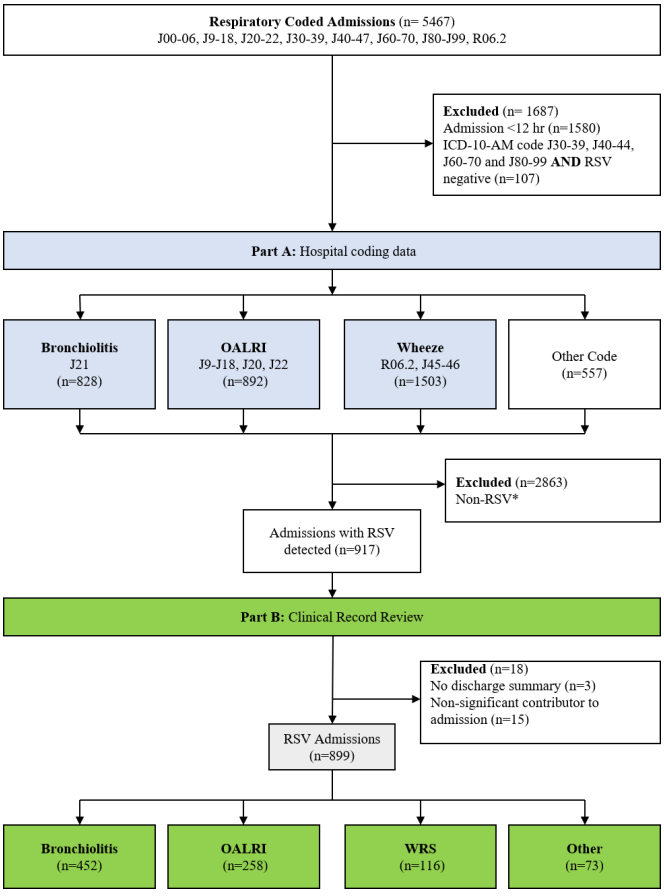


Figure 1 Flow chart of identified ICD-10 respiratory-coded hospital admissions into parts A and B of the study. Figure created using study data by Foley DA and permission to use granted. ICD-10-AM, International Classification of Diseases, 10th edition Australian Modification; n, number; OALRI, other acute lower respiratory tract infection; RSV, respiratory syncytial virus; WRS, wheeze responsive to salbutamol.

Strait Islander (9.3% vs 7.2%, p=0.25) or the proportion in the lowest IRSAD quintile (7.5% vs 9.7%, p=0.24).

In 2019, most RSV-positive admissions were bronchiolitis (271 of 454, 59.7%) followed by OALRI (113 of 454, 24.9%). There was no statically significant difference in the proportion in each age category and clinical phenotype, when comparing the first and second 6 months of 2019 (p>0.05). In 2020, bronchiolitis (181 of 445, 40.7%) and OALRI (145 of 445, 32.6%) contributed to similar proportions of cases. The median age for RSV-positive admissions doubled from 2019 (8.1 months, IQR 2.3–20.7) to 2020 (16.4 months, IQR 5.42–25.8), p<0.001 (table 1).

The peak months for 2019 (July) and 2020 (December) were compared (table 2). The total number of RSV-positive admissions in December 2020 was more than 2.5-fold that of July 2019. The age-specific incidence was higher in 2020 compared with 2019 across all age groups, most marked in those 12–24 months (6.2-fold).

When comparing 2019 and 2020 RSV-positive bronchiolitis admissions (online supplemental table 2), there were no significant differences in demographics, although premature infants represented a smaller proportion of admissions in 2020. While the proportion requiring any respiratory support did not differ between years, infants in 2020 were more likely to receive low-flow oxygen and less likely to receive pressure support at admission; there was no significant difference in proportion of infants receiving pressure support at peak (27.6% vs 32.5% peak respiratory support). LOS for RSV-positive bronchiolitis was significantly shorter in 2020 (2.1 days, IQR 1.2–3.7, vs 2.7 days, IQR 1.5–4, p=0.04).

For RSV-positive OALRI (online supplemental table 3), incidence was higher in 2020 in both the groups 12–24 months (3.1 (IQR 2.44–3.86) vs 1.6 (IQR 1.14–2.15) per 1000 in 2019) and 24–48 months (0.84 (IQR 0.61–1.12) vs 0.52 (IQR 0.35–0.75) per 1000 in 2019). A smaller proportion of patients with RSV-positive OALRI had a history of prematurity in 2020. Clinical features and requirement for any respiratory support were similar between years, although patients with RSV-positive OALRI in 2020 were less likely to receive pressure support at admission and at peak of illness. LOS for RSV-positive OALRI admissions was shorter in 2020 compared with 2019 (1.8 days, IQR 1–2.9 vs 2 days, IQR 1.5–4.1, p=0.02).

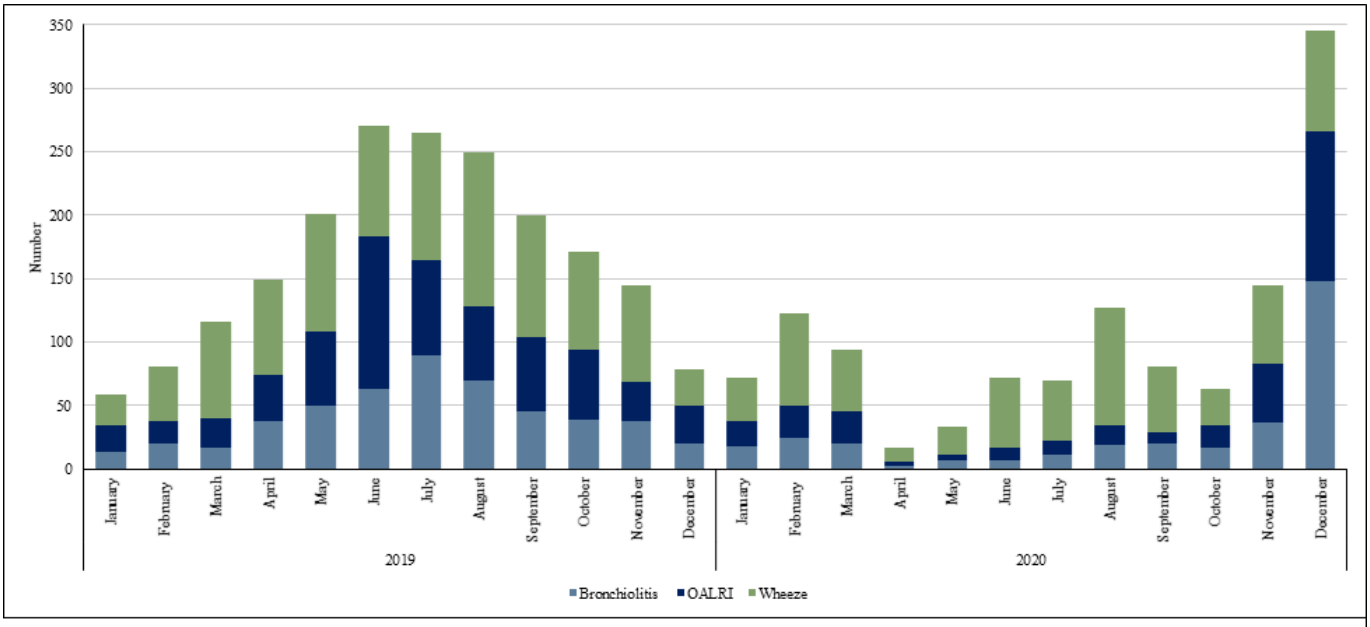
DISCUSSION

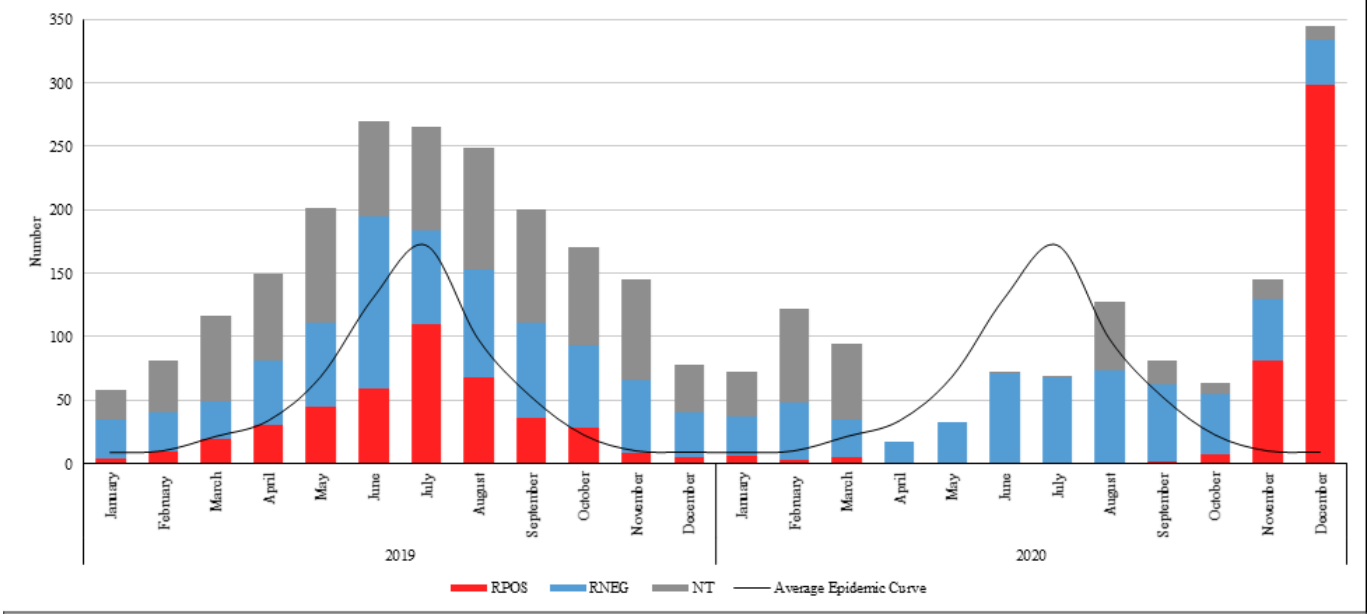
SARS-CoV-2 public health measures contributed to a significant shift in transmission of respiratory viruses in WA, including a delay in the expected RSV season.[10] Examining hospital admissions data, we found an unprecedented summer peak of RSV-positive admissions, 2.5-fold the magnitude of the previous mid-winter peak, not fully explained by changes in RSV testing practices. This comprised an older cohort of children, consistent with our previous report.[10] Examining the clinical phenotype, we found an increase in the proportion of non-bronchiolitis admissions, with increased OALRI and wheeze admissions.

With heightened SARS-CoV-2-related awareness of respiratory illness, it was expected that viral testing patterns and parental health-seeking behaviours may have changed in 2020. Our study used data from admissions as a more stable benchmark and compared data with the preceding year, to mitigate the impact of these potential differences. We found a large interseasonal peak in RSV-positive admissions in late 2020. Although there was a statistically significant increase in RSV testing in bronchiolitis, OALRI and wheeze in 2020, this change in testing practices preceded the summer surge in RSV detections.

There was a notable increase in testing for RSV in wheeze admissions, with the rates of positivity also increasing, reflecting a greater disease burden. This finding suggests that RSV may be a greater contributor to wheeze than previously recognised. The introduction of routine respiratory virus testing in wheeze presentations will help establish the burden of RSV disease and its relationship with wheeze and later asthma, critical information that is needed to inform future vaccination programmes.[23]

Children admitted with RSV during the summer resurgence in 2020 had an older median age, almost twice that of 2019. This may, in part, be due to increased testing of older children during wheeze-coded admissions, although less than 20% of RSV-positive admissions had wheeze as the clinical diagnosis, with bronchiolitis and OALRI comprising almost 75%. Although age was not significantly different between 2019 and 2020 in the bronchiolitis and OALRI admissions, the increase in absolute number and proportion of OALRI in 2020 contributed markedly to the increase in age. In addition, comparing age-stratified incidence in peak months in 2019 and 2020, the greatest increase was seen in the group 12–24 months (6.2-fold) followed by the group 24–48 months (3.4-fold). These findings support the hypothesis that the increase in RSV-positive admissions was due to infection occurring in the expanded older RSV-naïve cohort.





	Bronchiolitis			OALRI			Wheeze		
Year	2019	2020		2019	2020		2019	2020	
Total	499	329	P-value	586	306	P-value	898	605	P-value
N tested (% of total)	445 (89.2)	312 (94.8%)	0.01	484 (82.6)	271 (88.6)	0.02	229 (25.5)	380 (62.8)	<0.001
RSV positive (% of total)	274 (54.9)	182 (55.3)	0.9	117 (20)	140 (45.8)	<0.001	30 (3.3)	81 (13.4)	<0.001
RSV test positivity	61.6	58.3	0.36	24.2	51.7	<0.001	13.1	21.3	0.01

Figure 2 (A) Bronchiolitis, OALRI and wheeze hospital-coded admissions per month, between 2019 and 2020, inclusive. (B) RSV detection rate for hospital-coded admissions for bronchiolitis, OALRI and wheeze (identified in (A)). The average epidemic curve is based on all RSV detections for children aged <16 years, residents in the metropolitan area between 2012 and 2019, inclusive. Figure created using study data by Foley DA and permission to use granted. N, number; NT, not tested; OALRI, other acute lower respiratory tract infection; RNEG, tested and RSV negative; RPOS, tested and RSV positive; RSV, respiratory syncytial virus.

The RSV season was delayed by approximately 6 months, resulting in a novel, and significantly expanded cohort of RSV-naïve infants in the age range 6–18 months, as well as a smaller increased number of RSV-naïve older children who had avoided infection in previous seasons. In addition, as immunity post-RSV infection is incomplete, the delayed season may have resulted in waning of protection in older children, leading to more severe disease with reinfection.[24]

Regarding management and illness severity, clinical features of RSV-positive bronchiolitis and OALRI and requirement for ICU care were not significantly different between years. There was a change in respiratory support used. This change may be due in part to infection prevention guidance for the SARS-CoV-2 pandemic, to restrict pressure support secondary to the associated generation of small respiratory particles.[25] In OALRI, the proportion that received antibiotics at admission was lower

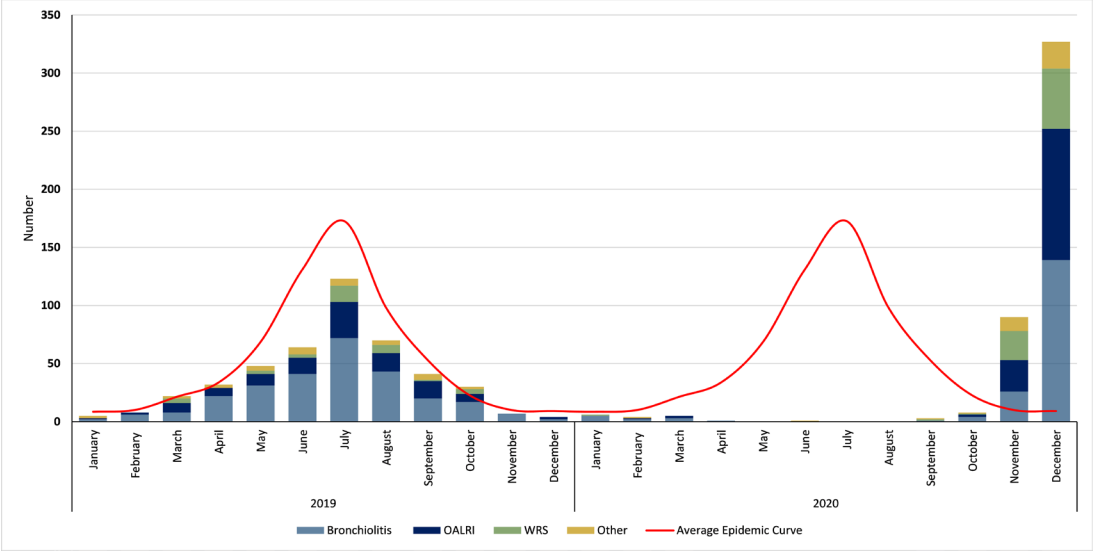


Figure 3 Clinical phenotype of RSV-positive admissions per month. The average epidemic curve is based on all RSV detections for children aged <16 years, residents in the metropolitan area between 2012 and 2019, inclusive. Figure created using study data by Foley DA and permission to use granted. OALRI, other acute lower respiratory tract infection; RSV, respiratory syncytial virus; WRS, wheeze.

in 2020, possibly linked to the clustering of similar presentations. The use of antibiotics remained high in both years representing the ongoing diagnostic challenge of distinguishing viral from bacterial pneumonia, with over 50% continuing antibiotics on discharge. Although secondary bacterial infection can complicate RSV lower respiratory tract infection, epidemiological data based on systematic testing suggest that coinfection is uncommon.[26] The high proportion of children receiving antibiotics highlights an ongoing challenge for paediatric antimicrobial stewardship services to better target use of antibiotics in children with pneumonia.

Table 1 Comparison of RSV presentations in Western Australia (WA) in 2019 and 2020 by clinical phenotype and rates per age group in WA Metropolitan region

Year		2019	2020	P value
Total		454	445	
Clinical phenotype		N (% total)	N (% total)	
Bronchiolitis		271 (59.7)	181 (40.7)	<0.001
OALRI		113 (24.9)	145 (32.6)	0.01
Wheeze responsive to salbutamol		36 (7.9)	80 (18)	<0.001
Other		34 (7.5)	39 (8.7)	0.51
Median age in months (IQR)		8.1 (2.3–20.7)	16.4 (5.4–25.8)	<0.001
WA Metropolitan region	N (% total)	382 (84.1)	408 (91.6)	<0.001
Under 12 months	N	220	145	
	Rate per 1000	8.72	5.75	<0.001
	95% CI	7.61 to 10	4.9 to 6.8	
Between 12 and 24 months	N	87	141	
	Rate per 1000	3.36	5.59	<0.001
	95% CI	2.7 to 4.1	4.7 to 6.6	
Between 24 and 48 months	N	51	91	
	Rate per 1000	0.9	1.7	<0.001
	95% CI	0.7 to 1.2	1.4 to 2.1	

N, number; OALRI, other acute lower respiratory tract infection; RSV, respiratory syncytial virus.

Finally, the LOS for RSV-positive OALRI and bronchiolitis admissions was significantly shorter in 2020; this difference was diminished when premature infants were excluded. For bronchiolitis, the shorter LOS may be due to the older age at the time of acquisition of RSV.[27] The mechanism in OALRI for a shorter LOS is less clear, with lower pre-existing conditions an important factor. However, resource limitations may have driven earlier discharge in 2020, supported by a suggestion of increased bronchiolitis readmission rate (8 of 271 (3%) in 2019 and 12 of 181 (6.6%) in 2020, p=0.07).

Another notable difference was the smaller proportion of children with a history of prematurity in 2020, a group more vulnerable to complicated respiratory infections.[28] The reason this group was impacted less by RSV in 2020 is unclear. Contributing factors may include an increased vigilance, related to the SARS-CoV-2 pandemic, regarding respiratory etiquette and physical distancing. A similar increase in protective behaviours may have contributed to the under-representation of all infants

Table 2 Comparison of RSV presentations in peak months for 2019 and 2020 and rates per age group in Western Australia (WA) Metropolitan region

Peak month		July 2019	December 2020	P value
Total (percentage of yearly total)		123 (27.1)	327 (73.5)	<0.001
WA Metropolitan region	N (% total)	99 (80.5)	310 (94.8)	<0.001
Under 12 months	N	54	115	
	Rate per 1000	2.14	4.56	<0.001
	95% CI	1.6 to 2.8	3.8 to 5.5	
Between 12 and 24 months	N	17	104	
	Rate per 1000	0.7	4.1	<0.001
	95% CI	0.4 to 1.1	3.4 to 5	
Between 24 and 48 months	N	20	67	
	Rate per 1000	0.4	1.3	<0.001
	95% CI	0.2 to 0.6	1 to 1.6	

N, number; RSV, respiratory syncytial virus.

less than 3 months of age. In addition, there may have been a smaller cohort of premature infants due to a reduction in the frequency of preterm births locally, as has been observed in other high-income countries.[29] Alternatively, as only a partial RSV season was captured, it may be too early to assess the impact of these altered chains of transmission.[30 31]

It remains unclear how epidemiology of RSV transmission will evolve in the immediate future. Locally, ongoing laboratory data indicate a return to usual interseasonal levels of RSV transmission by April 2021.[12] With winter approaching in Australia, and a presumed reduction in the cohort of RSV-naïve children, the usual winter season may be delayed again. National notification of RSV to continue to monitor these changes in preparation for vaccine implementation is urgently needed. More broadly, close surveillance may be indicated in other countries where the usual RSV winter season was attenuated in the setting of SARS-CoV-2 pandemic-related public health measures. As demonstrated by the surge in RSV-positive admissions in our data, rapid spread of RSV in the setting of reduction of restrictions and reduced population immunity has potential to place large strain on health services. Appropriate service provision planning, public health messaging and, where available, timely initiation of RSV passive immunisation programmes may lessen the overall impact.[23]

Limitations

The RSV season in WA remained ongoing at the time of completion of this analysis, thus clinical data were not captured for the entire delayed season. Notably, the distribution of clinical phenotype and age did not differ between the first and second halves of 2019 and a similar stable distribution is expected in 2020/2021. Although parental health-seeking behaviours are expected to have altered between the two periods, with risk of case ascertainment bias, a strength of this study was the combination of restricted analysis to admissions and specific hospital-coding groupings and high baseline testing rates. RSV testing results at other providers, especially negative results, were not captured unless ICD-10-AM RSV-related code used; testing rates and negatives are therefore expected to be higher than reported.

CONCLUSION

We report a rapid resurgence of RSV admissions in late 2020, during the southern hemisphere summer, with more than 2.5 times the admissions compared with the winter peak. There was a notable increase in non-bronchiolitis RSV admissions, consistent with older RSV-naïve children acquiring infections. There were no clinically meaningful differences in disease severity. However, the unanticipated timing and patient numbers are a point of concern, especially those who have experienced longer and more stringent public health measures to control SARS-CoV-2. It is expected that for each diminished or delayed RSV season, there will be greater numbers of RSV-naïve children which, coupled with waning community immunity, may facilitate and strengthen chains of transmission, resulting in a substantial resurgence and significant pressure on healthcare resources.

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