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Cohort profile: A population-based record linkage platform to address critical epidemiological evidence gaps in respiratory syncytial virus and other respiratory infections

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Abstract

Introduction
The Western Australia (WA) Respiratory Infections Linked Data Platform is a population-based cohort established to investigate the epidemiology of RSV and other respiratory infections in children aged 0-10 years, incorporating microbiological testing patterns, hospital admissions, emergency department presentations, and socio-demographic data.

Methods
The cohort was formed through individual linkages between datasets from the WA Department of Health including the Birth and Death Registry, Midwives Notification System (MNS), Hospital Morbidity Data Collection, Emergency Department Data Collection, WA Notifiable Diseases Database, WA Register of Developmental Anomalies, WA Cerebral Palsy Register, WA Antenatal Vaccination Database, WA Family Connections, and PathWest Respiratory Virus Surveillance Data. Hospitalisations and emergency department presentations were temporally linked to routine respiratory viral surveillance data.

Results
The cohort consists of 368,830 WA births between 1 January 2010 and 31 December 2020 with accompanying perinatal and demographic data, and with secondary care follow-up to 30 June 2022. Of these births, 24,660 (6.7%) identify as Aboriginal. A total of 4,077 (1.1%) children died from all causes during the study period (2010–2020), and 9.2% (33,818) of children were born preterm (<37 weeks).

Conclusion
The Respiratory Infections Linked Data Platform enables epidemiological investigations, identifying virus-specific risk groups, risk factors, clinical presentation, viral testing patterns, long-term impacts and accurate measures of viral incidence rates in risk and population sub-groups This will not only aid in the calculation of cost-effectiveness estimates of interventions such as immunisations, but also provide guidance for design and implementation of such programs to priority groups. The Respiratory Infections Linked Data Platform will also enable evaluation of the direct and indirect effects of maternal and infant vaccines and new therapeutics. Analyses using this platform will also generate epidemiological data needed for other respiratory viruses on the vaccine pipeline such as parainfluenza virus and human metapneumovirus.

Keywords
respiratory syncytial virus; epidemiology; data linkage; respiratory viruses

Highlights

- The Western Australia (WA) Respiratory Infections Linked Data Platform is a population-based cohort established to investigate the epidemiology of RSV and other respiratory illnesses in children aged 0-10 years. The cohort was formed through individual linkages between datasets from the WA Department of Health including the Birth Registry, Midwives Notification System, Hospital Morbidity Data Collection, Emergency Department Data Collection, WA Notifiable Diseases Database, Death Registry, WA Register of Developmental Anomalies, WA Cerebral Palsy Register, WA Antenatal Vaccination Database, WA Family Connections, and PathWest Respiratory Virus Surveillance Data.
- The cohort consists of 368,830 children born between 01 January 2010 and 31 December 2020, with secondary care follow-up to 30 June 2022.
- Research on the epidemiological characteristics including clinical presentation, risk factors, viral testing patterns, long-term impacts, and accurate measures of incidence rates in risk and population sub-groups through statistical prediction models will improve our understanding of the long-term burden of RSV and other respiratory infections. Statistical prediction models will estimate the under-ascertainment of RSV infections and thus predict more accurate incidence rates. This will aid in the calculation of cost-effectiveness estimates of any interventions and provide guidance for design and implementation of prevention programs to priority groups.
- The platform is a static dataset that can be expanded on in the future.

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Introduction

Respiratory syncytial virus (RSV) is the leading cause of pneumonia in children worldwide [1] and globally responsible for >3.6 million hospitalisations in children aged <5 years with the highest incidence of RSV-associated hospitalisations occurring in young infants [2]. An Australian report published >10 years ago estimated the annual direct cost of RSV in children aged <5 years to be $24–50 million (surpassing that of influenza for this age) [3]. This has recently been updated to $59–121 million [4]. Pathogen-specific incidence rates are needed to accurately determine burden and associated healthcare costs; however, these rates can be impacted by variable microbiological testing patterns. For example, a statistical prediction model developed by our team using RSV-positive hospitalisations and the total number of tests conducted for RSV detection to estimate a 'predicted rate' found previous incidence rates under-estimated the burden in infants by 30–57%, suggesting that 'true' RSV hospitalisation rates in those aged <6 months ranges from 27.9 to 43.7/1000 child-years [5].

In the last 2 years, major changes in both RSV epidemiology and the prevention landscape have occurred. Changes in the typical seasonal patterns of RSV to out-of-season peaks in Australia and other countries following COVID-19 mitigation measures have highlighted the significant burden of RSV and other viruses like human metapneumovirus (hMPV), and resulted in a re-assessment of conventionally accepted thinking regarding seasonality, how immunity is acquired and other transmission dynamics [6, 7]. Additionally, RSV prevention has seen significant advancements, with the development of a single dose long-acting monoclonal antibody (mAb), nirsevimab [8, 9], now given regulatory approval by the European Commission and US Food and Drug Administration for use in newborns and infants for protection against RSV disease [10, 11] and a maternal vaccine [12], now approved for use in the US [13]. Both therapeutics provide passive immunisation to infants, the group experiencing the highest burden. These events have renewed global scientific and public interest in RSV disease and further highlighted gaps in the evidence base related to the country-specific RSV epidemiology [14].

Population sub-groups such as infants born preterm [15], First Nations infants [16], children with comorbidities, and those with congenital anomalies [17] may be suffering from a disproportionate burden of acute lower respiratory infection (ALRI). However, RSV and other respiratory pathogen-specific data in these high-risk groups are limited. In addition, while data exists for infants and young children stratified by age in years or 6-month intervals, data with finer age stratification are needed, particularly to inform the impact of future immunisation measures. Data in older children are also sparse. Epidemiologic research on the clinical presentation, identification of risk factors, viral testing patterns, long-term impacts, and accurate measures of incidence rates through statistical prediction models in risk and population sub-groups will improve our understanding of the long-term burden of RSV and other respiratory infections. This will not only aid in the calculation of cost-effectiveness estimates of any interventions, but also provide guidance for design and implementation of prevention programs to priority groups. Linked population-based datasets also provide a source of real-world data to evaluate the impact of current and future intervention programs.

To address these evidence gaps and needs, we have constructed the Western Australian (WA) Respiratory Infections Linked Data Platform, established through individual-level linkage of population-based state administrative databases and registers via probabilistic matching. The Data Platform is a static platform that will be expanded on in the future. While our current focus is on RSV and the platform was built with RSV in mind, the Respiratory Infections Linked Data Platform will provide a valuable resource for wider epidemiological research on other respiratory viruses and infections in the future. Members of our team have long-standing expertise using linked population data in previous analyses, including the evaluation of maternal influenza and pertussis vaccine safety and effectiveness [18, 19], and direct and indirect effects of maternal [20–22] and childhood [16, 23] vaccines, which has aided the design of this platform and will assist with investigations of all respiratory infections. The Respiratory Infections data platform will enable evaluation of the direct and indirect effects of maternal RSV vaccines and/or monoclonal antibodies on RSV and non-RSV hospitalisations. Subsequent to these research outcomes for RSV, robust data will be needed for other respiratory pathogens on the vaccine pipeline such as parainfluenza virus and hMPV.

Methods

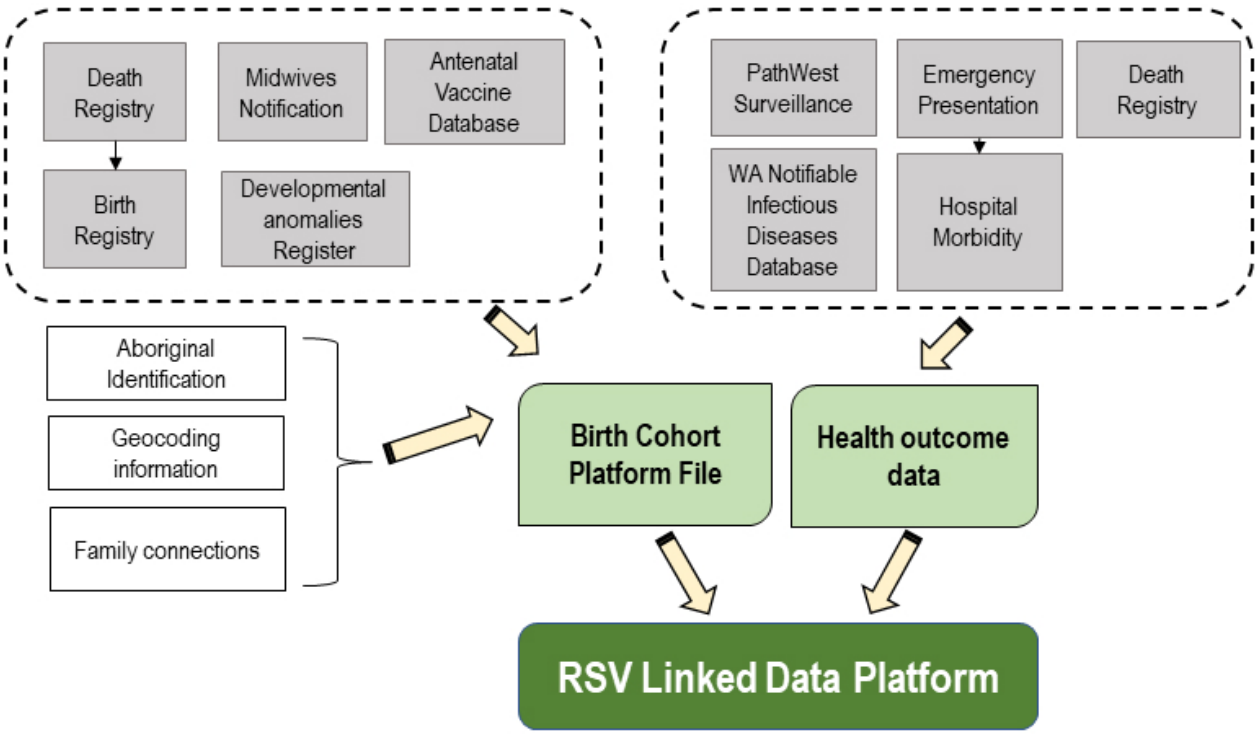
Setting and population

WA is the largest state, covering the western third of Australia, and has a population of 2.7 million, of which Aboriginal and/or Torres Strait Islander people (hereafter respectfully referred to as Aboriginal as the accepted term in WA) comprise 6.4% of the population [24]. The majority of the State's population live in the metropolitan areas of the capital city, Perth, and its surrounds (2.1 million people, 78%) [24]. Climate ranges from tropical in the northern regions to temperate in the metropolitan and southern regions. The winter respiratory virus season typically spans from May to September inclusive.

Data sources and linkage

The WA Respiratory Infections Linked Data Platform comprises a static population-based cohort of births between 2010 and 2020 across WA (Figure 1). The Platform was formed through individual-level linkage of a number of administrative health databases and registries, described in Table 1. Data extraction and linkage of individual records was performed by Data Services at the WA Department of Health. In the absence of a unique national personal identifier in Australia, the Data Services team uses probabilistic linkage processes in a 'best practice protocol' to link the same individual in a number of different health databases and registers [25]. Best practice protocol involves the separation of personal demographic data from clinical or service information; linkage of records; removal of personal identifiers; and the assignment of unique encrypted linkage keys, to allow researchers to link individuals between different datasets.

Figure 1: Establishment of the Respiratory Infections Linked Data Platform, Western Australia 2010–2020



Probabilistic linkage compares groups of records using complex non-unique identifiers or field matching algorithms [26]. These algorithms compare common demographic fields (e.g., given name, surname, date of birth, and other relevant fields dependent on the contents and context of the dataset [25]), and provide a similarity weighting index which is positively associated with the likelihood that two or more records belong to the same individual [26]. Clerical review is required to assess potential non-matched records; this process has been shown to reduce the error rate of matching to less than 0.1% [27]. Individuals in the resulting linked datasets are identified through a 16-digit unique alpha numeric code (unique child ID, or "root") which is included in each dataset provided and allows the same child to be identified in more than one dataset. Similarly, Mother ID allows mothers to be identified in perinatal data, the antenatal vaccine register, and in mapping files linking mother to child.

The birth cohort was formed by merging all registered births (live and stillbirths) from Birth Register data with a date of birth from 1 January 2010 to 27 June 2022, with perinatal records from the MNS from 1 January 2010 to 31 December 2020, based on the unique child ID. Together, the overall coverage of the birth cohort comprised 371,387 children born in WA (all live and stillbirths) and spanned from 1 January 2010 to 31 December 2020 with complete perinatal data (Figure 2). As data are refreshed, perinatal data for the subsequent years will be provided. Antenatal vaccination data recorded in Western Australia Antenatal Vaccines Database (WAAVD) were linked for each mother and child in the birth cohort by date of vaccination using the conception date (calculated from gestational age at birth and the child's date of birth recorded in the perinatal data collection) and the date of birth. Gestational age at vaccination in weeks and trimesters were re-calculated from the date of vaccination for vaccinations between March 2012 and September 2016.

The Platform provides several health outcome related outputs to enable a wide range of research. Healthcare utilisation data includes all records, regardless of diagnosis, relating to emergency department (ED) presentations, hospital separations, deaths and associated healthcare measures such as hospital length of stay, in-hospital procedures, intensive care unit (ICU) attendance and length of stay. Respiratory pathogen detections, including notifiable infectious diseases, are also identified. Separate PathWest respiratory pathogen testing records were combined if they related to the same child with the same day of specimen collection. Specimens collected on or after the date of death were considered to be post-mortem specimens. From a combined dataset of all hospital admissions and ED presentations (herein, termed as secondary care episodes), we temporally linked laboratory testing records using the unique child ID and dates of hospital admission and/or presentation and date of specimen collection. These health outcomes are available from birth up to the most recent date at the time of data extraction and linkage for all individuals in the cohort. Longitudinal data over successive years also allows assessment of repeat infections and Family Connections data enable studies assessing risk across siblings within families.

Due to the wealth of data items available on the MNS and additional indicators available through Data Services (e.g., Aboriginal identification and geocoding information), the cohort can be comprehensively described. This includes demographic structure (number and place of births over time; levels of socio-economic deprivation) and important covariate factors (e.g., gestational age, maternal comorbidities, maternal smoking status, maternal antenatal vaccination status, birth defects, other perinatal factors) that are often used in

Table 1: Data sources incorporated into the WA respiratory infections data linkage platform

Database	Description	Data within the respiratory infections data linkage platform		
		Roots[a] N	Records N	Time period
Birth Cohort Platform File				
Birth Registrations	Administered by the Registry of Births, Deaths and Marriages and includes all children born and subsequently registered in Western Australia.	417,563	417,563	1 Jan 2010–27 June 2022
Midwives Notification System (MNS) [42]	State perinatal data collection includes demographic maternal and newborn data, maternal medical and obstetric history, information on labour, delivery and birth on 99% of births [28] with gestational age $\geq$20 weeks and birthweight $\geq$400 g (where gestational age is unknown) in WA. From July 2016, MNS also records trimester of antenatal influenza and pertussis vaccinations.	371,387	371,387	1 Jan 2010–31 Dec 2020
WA Register of Developmental Anomalies (WARDA) [43]	Legally mandated register compiling records of up to 10 major and minor birth defects per individual diagnosed in utero, at, and following birth, and up to the age of 6 years using active and passive case ascertainment to provide accurate information in a timely manner. The quality of data in WARDA has been evaluated and is estimated to be high, with only 1.5% of missing data of the 20 essential variables collected by WARDA [44]	20,982	20,998	1 Jan 2010–30 Jun 2022
WA Cerebral Palsy Register [45]	Sub-section of the WARDA also contains a clinical register on cerebral palsy (CP) and associated impairments. The CP Register data may be delayed as diagnosis of CP, particularly for milder forms of CP, may not be rendered until the brain is fully developed at 3–5 years of age.	554	554	12 Jan 2010–25 Apr 2020
Family Connections data	WA Family Connections system contains links between individuals who are related using data stored in the Birth Register and MNS. It is a unique dataset to WA and allows investigations of disease within families. Family connections data contained within the WA Respiratory Pathogens Data Linkage Platform allow the identification of full and half siblings with a date of birth that falls both within and outside of the birth cohort. Mapping files link the child's ID to mother ID and father ID. Siblings will have the same mother ID. The relationship of half siblings are stated in the mapping files.	474,315	474,315	1 Jan 1990–31 Dec 2020
WA Antenatal Vaccinations Database (WAAVD) [46]	State-wide registry of healthcare provider-reported vaccines administered during pregnancy between March 2012 and September 2016, including vaccine brand, batch number, and date of vaccination. Previous validation of WAAVD has demonstrated specificity and positive predictive values exceeding 95% [46] The database was archived in 2016 and from 2016 onwards antenatal vaccinations are recorded in the perinatal record in the MNS.	35,428	41,244	16 Mar 2012–30 Sep 2016

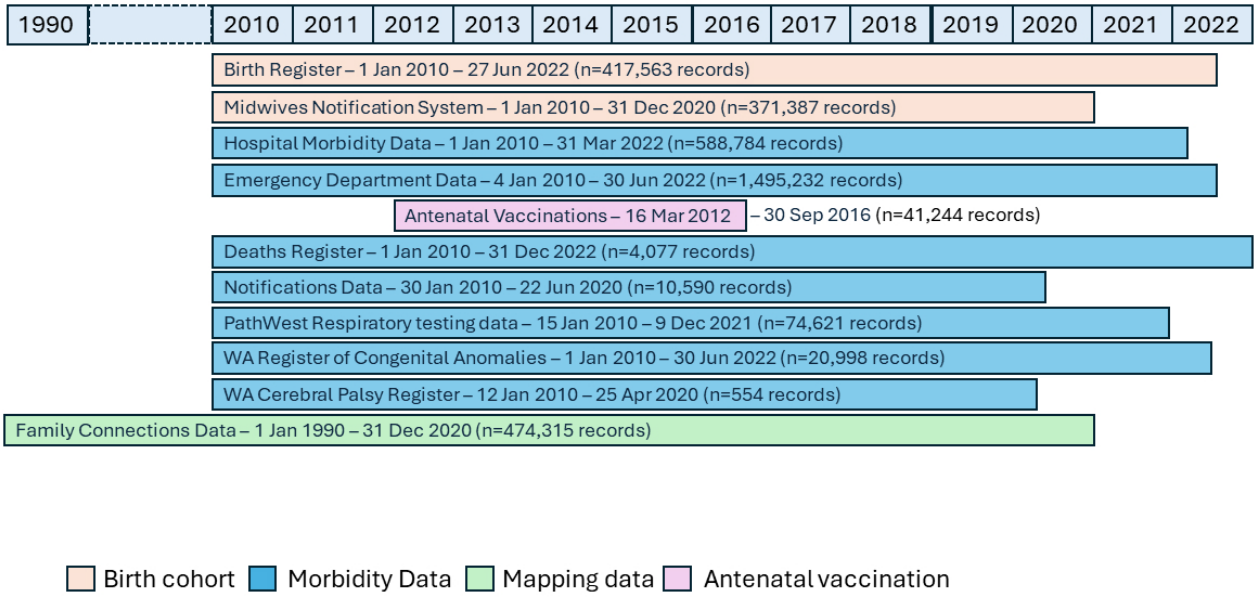
Continued

Table 1: Continued

Database	Description	Data within the respiratory infections data linkage platform		
		Roots[a] N	Records N	Time period
Health Outcome Data[b]				
Hospital Morbidity Data collection [47]	Hospitalisation admissions (inpatient) data covered all inpatient separations (discharges, transfers and deaths) from all free-standing hospitals across the state. Data includes dates of admission and separation, the primary diagnosis code (first-listed diagnosis) and 20 secondary diagnosis codes (coded using the ICD-10-AM[c] coding system), ACHI[d] codes for procedures performed during the stay, intensive care unit attendance and associated length of stay.	241,512	588,784	1 Jan 2010–31 Mar 2022
Emergency Department Data Collection [48]	Emergency department data contain date of ED presentation and a combination of diagnostic information to describe the presenting complaint. This includes coded diagnosis (using ICD-10-AM codes), symptoms (using the Systematised Nomenclature of Medicine Clinical Terms) or free text. ED activity in all public hospitals and private hospitals under contract with the WA government is captured in this dataset.	319,107	1,495,232	4 Jan 2010-30 Jun 2022
WA Notifiable Infectious Diseases Database (WANIDD)[e]	Collates data on all public health notifications of notifiable infections. Recorded information includes disease, date of onset, diagnosis method and organism serotype. For the WA Respiratory Infections Data Linkage Platform, notifications include influenza virus, pertussis, invasive pneumococcal disease and COVID-19.	10,197	10,590	30 Jan 2010–22 Jun 2020[e]
Death Registrations and cause of death[f]	Death registration data (from the National Death Index) includes demographic information, date and cause of death (including contributing causes) on all deaths in WA coded using ICD-10-AM coding	4,077	4,077	1 Jan 2010–31 Dec 2022
PathWest respiratory virus surveillance data	Routine respiratory microbiological test results (positive and negative) performed at all government funded PathWest laboratory services, WA's sole public pathology provider. Data include the date of specimen collection, specimen type, test, and result. All respiratory specimens were tested using PCR other than the inclusion of cases based on a clinical case definition for pertussis. For the WA RSV Data Linkage Platform, respiratory viruses include RSV, influenza, parainfluenza viruses 1-3, human metapneumovirus, adenovirus, enterovirus, rhinovirus, pre-COVID-19 seasonal coronaviruses, SARS-CoV-2, *Chlamydia pneumoniae*, *Legionella pneumophila* and *longbeachae*, *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Pneumocystis jirovecii*. Influenza and RSV subtyping is also available.	48,823	74,621	15 Jan 2010–9 Dec 2021

[a]Unique child ID.
[b]Health outcome data in the Respiratory Infections Data Linkage Platform include data for the birth cohort only.
[c]ICD-10-AM, International Statistical Classification of Diseases and Related Health Problems, 10^{th} Revision, Australian Modification.
[d]Australian Classification of Health Interventions.
[e]There were no respiratory virus notifications for influenza, pertussis, or RSV for the remainder of 2020.
[f]Cause of death coded by the National Coronial Information System and the Victorian Department of Justice and Community Safety (Home | National Coronial Information System Victoria (ncis.org.au)).

Figure 2: Time period of data provided for individual datasets and number of records in the Respiratory Infections Linked Data Platform, Western Australia



infectious disease epidemiology research. The MNS has been validated and is estimated to capture 99% of births [28] (live and stillborn) with a gestational age of $\geq$20 weeks. Furthermore, it is mandated and provides data into national data collections at the Australian Institute of Health and Welfare, and thus, the quality of data is high.

Definitions

Pregnancy trimesters were defined as first trimester (0–13 completed weeks of gestation), second trimester (14–26 completed weeks), and third trimester (27 or more completed weeks). Gestational age in weeks at birth was used to derive preterm birth categories, defined as extremely preterm ($<$28 weeks), very preterm (28-31 weeks), moderate to late preterm (32–36 weeks), and term (37 weeks or more) births. Small for gestational age births were defined as birthweight lower than the 10^{th} percentile for liveborn, singleton infants and based on the Australian national birthweight percentiles by sex and gestational age [29]. Low birthweight was defined as a live birth with birthweight less than 2,500g irrespective of gestational age. Proportion optimal birthweight was calculated by WA Data Services [30] and provides a method of assessing appropriateness of intrauterine growth that is less dependent on the health of the reference population or the quality of their morphometric data than is percentile position on a birth weight distribution. Major birth defects were identified and include those known to increase susceptibility to respiratory infection morbidity including congenital heart, lung and neurological diseases and Trisomy 21.

Aboriginal children were identified using a derived flag for Aboriginal status from a combination of routine data sources using a pre-validated algorithm [31]. Geocoding data provided by the WA Data Services included the Socio-Economic Indices for Areas (SEIFA) scores to measure socioeconomic status [32]. SEIFA scores are derived from the Australian Bureau of Statistics and were calculated at the Statistical Areas Level 1, based on the boundaries used at the child's year of birth, for population-based epidemiological and statistical research [32]. Statistical Areas Level 1 are geographic areas built from whole Mesh Blocks and generally have an average population of approximately 400 people. Of the four different SEIFA scores available, we chose to use the Index of Relative Socio-Economic Advantage and Disadvantage, which is derived from 17 different variables including education, occupation, income, housing, disability and family measures collected from the Census of Population and Housing [32]. SEIFA scores are grouped into five decile categories with the lowest scores representing the most socioeconomically deprived. Remoteness is determined through the Accessibility and Remoteness Index of Australia [33] which uses postcode of residence to categorise all individuals to major cities, inner regional, outer regional, remote, and very remote areas.

The identified exposures and outcomes of interest will differ according to each specified analysis using the Data Linkage Platform. Pathogen specific outcomes measured in the cohort include respiratory viral tests (including positive and negative results) from routine microbiological tests conducted through PathWest and disease notifications from Western Australian Notifiable Diseases Database (WANIDD), including influenza, pertussis, invasive pneumococcal disease and COVID-19. Hospital admissions and separations and ED presentations of interest will be identified using International Classification of Diseases diagnosis codes, version 10, Australian modification (ICD-10-AM). Principal and up to 20 additional diagnosis fields are used to classify outcomes of interest. For ED presentations, a hierarchy of coding was applied whereby the single principal diagnosis ICD code was used in preference over other free-text diagnosis and symptom codes in the following order: a) an ICD code; b) a symptom code; c) diagnosis at discharge text field; d) presenting complaint (symptom) text field; and e) a major diagnostic category ('diseases and disorders of the respiratory system') as previously published [34]. Importantly,

our datasets include hospital and ED presentations for all causes, enabling the identification of non-specific outcomes (e.g. skin infections, all-cause injuries and trauma) that temporally link to a respiratory viral testing record, notifiable disease or conditions that can be used as negative controls. Procedure codes were based on the Australian Classification of Health Interventions codes, 11^{th} edition. Common diagnoses and procedures relating to respiratory infections and the associated ICD-10-AM codes are shown in Supplementary Table 1.

Results

From the complete cohort of 371,387 births, we removed 2,557 (0.7%) children born in WA but residing elsewhere, as we had no follow up secondary care data on these children. Of the remaining 368,830 births, 24,660 (6.7%) identify as Aboriginal (Table 2). A total of 4,077 (1.1%) children died during the study period (2010–2020), and 33,818 (9.2%) children were born preterm (<37 weeks). Other perinatal factors and cohort descriptors by Aboriginal status are shown in Table 2. Aboriginal mothers were younger, more likely to smoke, and less likely to be maternally vaccinated. They were also more likely to live in rural and remote locations and be in the lower socioeconomic quintiles.

Respiratory virus testing data over this time period was conducted for 48,823 children. Approximately 66% of specimens were tested for RSV, of which 15% of tests were positive. Based on an analysis of the proportion of pathology records linking to secondary care episodes up to 8 days either side of the date of specimen collection for the same child, we calculated the proportion of included PathWest records that linked, shown in Figure 3. Just over a half 39,725 (53.2%) laboratory records linked to a secondary care episode on the same day, with 56,059 (75.1%) linking within a 48-hour window either side. If the linkage rule was extended to 4 days either side of the date of secondary care admission/presentation, 57,836 (77.5%) laboratory records linked. We will use the 4-day inclusion rule to identify secondary care episodes with linked laboratory records for our planned analysis, over a previously used 2-day rule due to recent analyses showing a longer duration of RSV viral shedding [35].

Hospital separations related to birth admissions were removed. Inter-hospital transfers were defined as multiple adjacent hospital admission records of the same person where either a) the admission date was identical to the discharge date of the prior record; or b) the admission date occurred before the discharge date of the prior record; or c) both admission and discharge dates fell within the time span of the prior record. These records were collapsed and considered a single admission. From 588,784 admissions, 24,590 (4.1%) were part of a transfer set of records.

Discussion

The Respiratory Infections Linked Data Platform takes advantage of data linkage capacity in WA, and the availability of State and Commonwealth data sources, to capture population-level RSV and other respiratory virus epidemiology in an Australian setting, focusing on the paediatric population. It will assess the public health impact of current RSV immunisation strategies, future RSV and other respiratory virus prevention strategies, and provide enduring utility to guide ongoing public health policy decisions.

Future updates and planned work

The current iteration of the Respiratory Infections Linked Data platform contains predominantly pre-pandemic data. As RSV became notifiable nationally in 2021/22 (in WA, from 1 August 2021) [36], we envisage a data refresh of the Data Platform in future years with the addition of all-age RSV notifications, during and post COVID-19 periods when RSV seasonality was disrupted (2021-25). This will complement laboratory surveillance data, providing valuable insights on community RSV incidence outside secondary care in all age groups and critical inputs for dynamic models informing RSV population dynamics.

We are also in the process of requesting approval to link Commonwealth datasets, including the Australian Immunisation Register (data on infant and child vaccinations), Medicare Benefits Scheme data (family physician encounters) and Pharmaceutical Benefits Scheme data (data on medication and prescriptions, including antimicrobial agents). The addition of these datasets will allow studies on direct, indirect, and non-specific maternal and childhood vaccine effects on a range of outcomes.

The use of polymerase chain reaction testing by diagnostic pathology laboratories surged in 2010 following the influenza pandemic of 2009. In WA, in-house tests were commonly used, which allowed discrimination of subtypes of influenza, RSV and parainfluenza viruses. Steadily over the period covered by this dataset that coverage has diminished, and that trend is likely to continue. Furthermore, we are now in the era of rapid antigen testing (RAT) which is available for influenza and RSV as well as SARS-CoV-2. As the uptake of RATs increases, it will replace PCR as the primary diagnostic tool for community infections, which will not be notified. The timing of this primarily pre-pandemic linked data set is therefore unique with respiratory viruses identified with unprecedented granularity and represents a truer snapshot of respiratory pathogen testing and positivity. It also comprises baseline data with which to compare future data updates as testing practices change.

Strengths and limitations

We have constructed a population-based linked dataset comprising administrative and registry data from 14 databases to provide a longitudinal analysis of RSV and other respiratory virus pre-COVID-19 activity. However, our established platform does have some notable limitations. Our study only includes children born and resident in WA from 2010 to the most recent date at the time of request, as we were unlikely to have outcome data on children non-resident in WA but born here. Similarly, we did not include children born elsewhere in Australia and residing in WA as we did not have perinatal data on these children (the primary source of risk factor data for our planned analyses). With respect to immigration, the latest Australian census (2016) estimates that in 2020, 0.3%

Table 2: Demographic characteristics of key variables of the study cohort, including proportion of missing data for key variables

Characteristic	Total N = 368,830	Non-aboriginal N = 344,170 (93.3%)	Aboriginal N = 24,660 (6.7%)
Maternal and socio-demographic factors			
Maternal age at birth			
<20 years	11,154 (3.0%)	7,104 (2.1%)	4,050 (16.4%)
20–24 years	47,723 (12.9%)	39,902 (11.6%)	7,821 (31.7%)
25–29 years	102,086 (27.7%)	95,574 (27.8%)	6,512 (26.4%)
30–34 years	126,729 (34.4%)	122,698 (35.7%)	4,031 (16.3%)
35 or more years	81,138 (22.0%)	78,892 (23.0%)	2,246 (9.1%)
Smoking during pregnancy			
No	332,512 (90.2%)	318,269 (92.5%)	14,243 (57.8%)
Yes	36,318 (9.8%)	25,901 (7.5%)	10,417 (42.2%)
Maternal history of asthma			
No	336,566 (91.3%)	314,301 (91.3%)	22,265 (90.3%)
Yes	32,264 (8.7%)	29,869 (8.7%)	2,395 (9.7%)
Maternal aboriginal status[a]			
Non-Aboriginal	346,266 (93.9%)	342,915 (99.6%)	3,351 (13.6%)
Aboriginal	22,564 (6.1%)	1,255 (0.4%)	21,309 (86.4%)
Maternal antenatal vaccinated			
Influenza	90,316 (24.5%)	84,962 (24.7%)	5,354 (21.7%)
Pertussis	118,159 (32.0%)	112,115 (32.6%)	6,044 (24.5%)
Socio-economic disadvantage			
0–20% (most disadvantaged)	73,009 (19.8%)	60,455 (17.6%)	12,554 (51.3%)
21–40%	77,460 (21.0%)	71,953 (20.9%)	5,507 (22.5%)
41–60%	78,817 (21.4%)	75,044 (21.8%)	3,773 (15.4%)
61–80%	75,602 (20.5%)	73,716 (21.4%)	1,886 (7.7%)
81–100% (least disadvantaged)	63,276 (17.2%)	62,548 (18.2%)	728 (3.0%)
Missing	666 (0.2%)	454 (0.1%)	212 (0.9%)
Remoteness index			
Major city	287,103 (77.9%)	276,935 (80.5%)	10,168 (41.5%)
Inner regional	29,097 (7.9%)	27,447 (8.0%)	1,650 (6.7%)
Outer regional	26,896 (7.3%)	23,031 (6.7%)	3,865 (15.8%)
Remote	16,626 (4.5%)	12,354 (3.6%)	4,272 (17.4%)
Very remote	8,612 (2.3%)	4,044 (1.2%)	4,568 (18.6%)
Missing	496 (0.1%)	359 (0.1%)	137 (0.6%)
Child factors			
Delivery mode			
Vaginal/instrumental	234,830 (63.7%)	217,024 (63.1%)	17,806 (72.2%)
Caesarean	134,000 (36.3%)	127,146 (36.9%)	6,864 (27.8%)
Infant sex			
Female	189,728 (51.4%)	176,909 (51.4%)	12,819 (52.0%)
Male	179,036 (48.5%)	167,208 (48.6%)	11,828 (48.0%)
Indeterminate	66 (0.0%)	53 (0.0%)	13 (0.1%)
Gestational age			
≥ 37 weeks	335,012 (90.8%)	314,159 (91.3%)	20,853 (84.6%)
32–36 weeks	28,108 (7.6%)	25,089 (7.3%)	3,019 (12.2%)
28–31 weeks	2,791 (0.8%)	2,412 (0.7%)	379 (1.5%)
<28 weeks	2,919 (0.8%)	2,510 (0.7%)	409 (1.7%)
Season of birth			
Spring (Sept-Nov)	92,132 (25.0%)	86,196 (25.0%)	5,936 (24.1%)
Summer (Dec-Feb)	90,351 (24.5%)	84,217 (24.5%)	6,134 (24.9%)
Autumn (Mar-May)	94,760 (25.7%)	88,315 (25.7%)	6,445 (26.1%)
Winter (Jun-Aug)	91,587 (24.8%)	85,442 (24.8%)	6,154 (24.9%)
Number of other siblings			
0	99,013 (26.8%)	93,348 (27.1%)	5,665 (23.0%)
1	113,305 (30.7%)	107,711 (31.3%)	5,594 (22.7%)
2 or more	156,512 (42.4%)	143,111 (41.6%)	13,401 (54.3%)

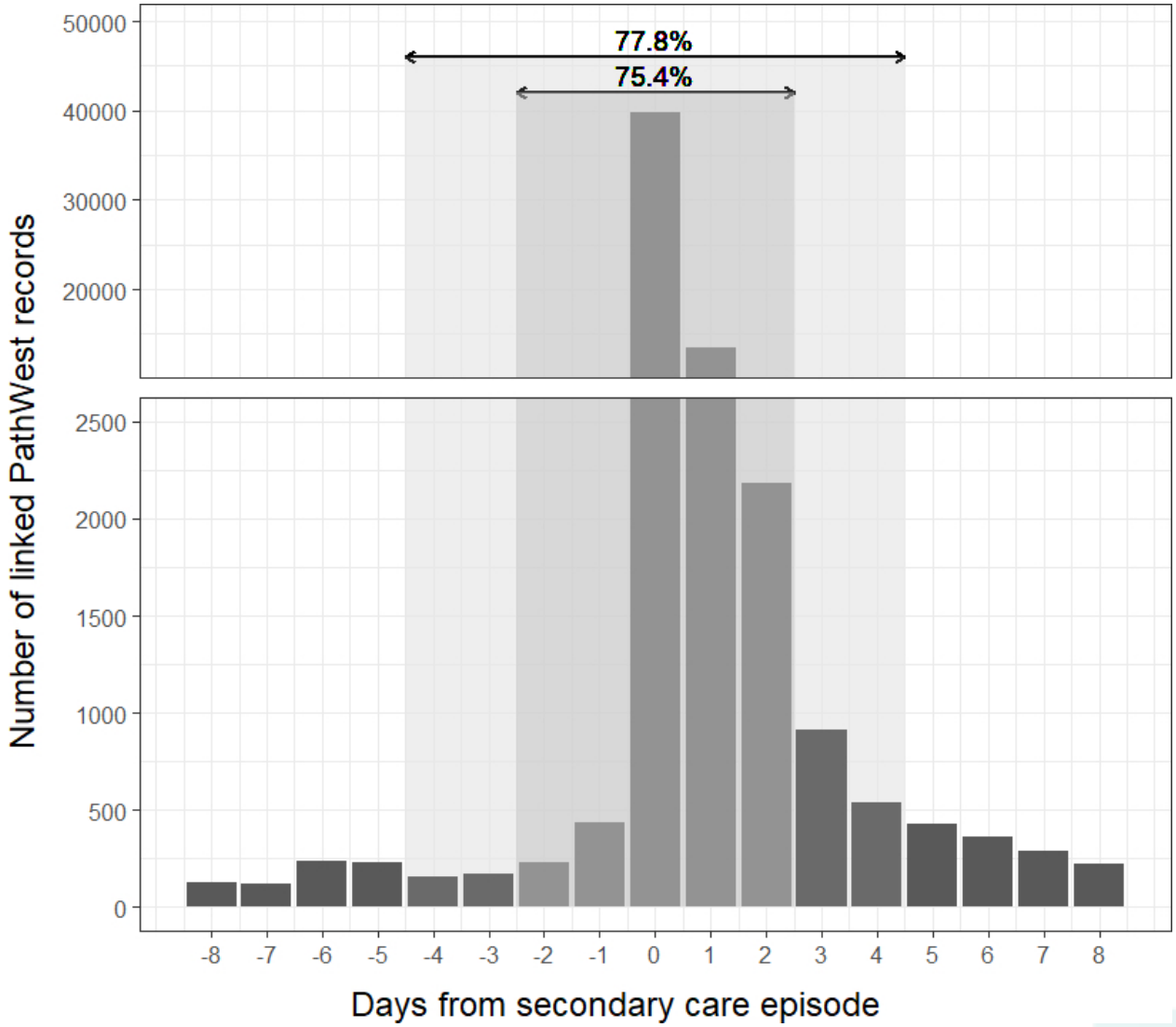
Continued

Table 2: Continued

Characteristic	Total N = 368,830	Non-aboriginal N = 344,170 (93.3%)	Aboriginal N = 24,660 (6.7%)
Multiple births			
Singleton birth	358,383 (97.2%)	334,434 (97.2%)	23,949 (97.1%)
Multiple birth	10,447 (2.8%)	9,736 (2.8%)	711 (2.9%)

[a]based on the algorithm by Christensen et al. [31].
[b]Australian Bureau of Statistics Socio-economic indexes for areas [32].
[c]Accessibility/Remoteness index of Australia.

Figure 3: Linkage of PathWest respiratory virus testing data with hospital admissions and emergency department data (n = 74,621 laboratory, n = 588,784 hospital and n = 1,495,232 emergency department records)



of WA children less than 10 years of age were born overseas [37]. Therefore, our study cohort may not be generalisable to immigrant children. We were also unable to capture hospital encounters for our cohort that occurred outside of WA. However, a study linking hospitalisations across four Australian states found that only 0.2% of hospitalisations in WA residents occurred in the other states [38]. RSV was made a notifiable disease in August 2021 in WA, after ethics approvals for the Platform were gained and data were extracted for linkage. Hence, our Platform lacks RSV notifications. Importantly and uniquely in Australia, the PathWest data provide the only source of laboratory-confirmed RSV infections for the years prior to 2021 when RSV became notifiable. Over the period 2010-2020, PathWest laboratories consistently covered all public hospital testing (>80% of all hospitalised patients; close to 100% for all children). Coverage of community tests

decreased between 2010 and 2020, with private pathology providers increasing their scope of testing, particularly in metropolitan and southern WA. Private pathology data are not currently available for research due to client privacy and confidentiality concerns; however, this is an area of ongoing investigation with our research team. PathWest is often the sole provider in remote WA and has maintained good representation of collection centres in rural locations [39, 40]. Finally, our study includes primarily secondary care data and lacks primary care data to provide community burden. However, we currently have a program of research in early childcare to alleviate this gap.

Collaboration

The data within the Respiratory Infections Data Linkage Platform cannot be shared publicly. Access to the data is subject to approval by data custodians and provided by Data Services at the WA Department of Health (https://www.datalinkage-wa.org.au/contact-us/). Use of the data is restricted to named researchers only on the approved ethics protocols. Further details on the data platform can be accessed through lead investigators (Hannah.Moore@telethonkids.org.au), while access to the raw data can be requested via Data Services at the WA Department of Health (DataServ@health.wa.gov.au).

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Ethics statement

Ethical approval was granted by the WA Department of Health Human Research Ethics Committee [Project ID: RGS4675] and the Western Australian Aboriginal Health Ethics Committee [Project ID: 1138]. Obtaining individual consent for population-level data is impractical. Therefore, a waiver of consent was approved by the WA Department of Health Human Research Ethics Committee in accordance with state and national privacy legislation. This allowed the use of administrative data containing personal information for approved health research (NHMRC guidelines, section 95, Privacy Act 1988) [41]. As per our approved data application, all research outputs will be approved by the WA Data Services prior to publication, no raw data will be presented and all cell sizes of less than 5 will be suppressed.

Conflicts of interest

HCM has received institutional honoraria from advisory committees sponsored by Merck Sharpe & Dohme (Australia) Pty. Ltd, Pfizer and Sanofi for other work unrelated to this analysis. HCM, BT, PR have received funding from Sanofi-Aventis in the form of an externally sponsored collaboration agreement. PR has received institutional honoraria from advisory committees sponsored by GSK, Pfizer, Merck, AstraZeneca, and Novavax. PR also receives funding from Merck Sharpe & Dohme (Australia) Pty. Ltd, GSK. HCM and MS have received travel funding from Seqirus.

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Abbreviations

CP:	Cerebral Palsy
ED:	Emergency Department
hMPV:	Human Metapneumovirus
ICD:	International Classification of Diseases
ICU:	Intensive Care Unit
mAb:	Monoclonal Antibody
MNS:	Midwives Notification System
RSV:	Respiratory Syncytial Virus
SEIFA:	Socio-economic Index for Areas
WA:	Western Australia
WAAVD:	West Australian Antenatal Vaccines Database
WANIDD:	West Australian Notifiable Infectious Diseases Database
WARDA:	West Australian Register of Developmental Anomalies

Supplementary Table 1: Common diagnosis and procedure codes used

Condition	**ICD-10-AM[a]**	**Symptom code[b]**
All-cause acute respiratory infection		
Viral infection of unspecified site	B34	STJ00
Croup	J05	SND00
Unspecified respiratory infection	–	SQ000, SEF00
Unspecified upper respiratory infection	J06.9	ADK
Influenza	J09–J11	–
Pneumonia	J12–J18	SQJ00
Pertussis	A37	SNJ00
Bronchitis	J20, J40	SQC00
Bronchiolitis	J21	SNB00
Unspecified lower respiratory infection	J22	–
Abnormal breathing	R06	–
Apnoeic episodes	R06.81	CA000, SNA00
Flu-like symptoms	–	AAV
Asthma	J45, J46	SQA00, SQAA0, ADO
Exacerbation chronic airways limitation		SQE00
Convulsions (incl febrile)	R56, P90	AAT, AEA, SNG00
Cough	R05	AAN, CC000, CCA00, CCB00, CCC00
Febrile and other viral illnesses	–	PG000
Fever (incl pyrexia unknown origin)	R50	VD000, AAU, SNU00
Stridor	R06.1	CG000, ADI
Wheeze	R06.2, R05	ADH, CH000, ADJ
Procedures		**ACHI codes[c]**
Management of non-invasive ventilatory support		92209-XX
Management of continuous ventilatory support		13882-XX
Management of combined ventilatory support (for neonates who receive both)		92211-00

Abbreviations: ALRI: acute lower respiratory infection; "-XX" denotes all sub-codes within a particular block.
[a]International Classification of Diseases, Australian Modification, 10^{th} edition. In hospital principal and all co-diagnoses, as principal diagnosis in Emergency Department data.
[b]Symptom codes using the Systematised Nomenclature of Medicine (SNOMED) Clinical Terms in Emergency Department data only.
[c]Australian Classification of Health Interventions codes, 11^{th} edition.