

Spatial and temporal transmission dynamics of respiratory syncytial virus in New Zealand before and after the COVID-19 pandemic

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Human respiratory syncytial virus (RSV) is a major cause of acute respiratory infection. In 2020, RSV was eliminated from New Zealand due to non-pharmaceutical interventions (NPI) used to control the spread of SARS-CoV-2. However, in 2021, following a brief quarantine-free travel agreement with Australia, there was a large-scale nationwide outbreak of RSV that led to reported cases more than five-times higher than typical seasonal patterns. We generated 1470 viral genomes of both RSV-A and RSV-B sampled between 2015–2022 from across New Zealand. Using a phylodynamics approach, we used these data to better understand RSV transmission patterns in New Zealand prior to 2020, and how RSV became re-established in the community following the relaxation of COVID-19 restrictions. We found that in 2021, there was a large epidemic of RSV due to an increase in importations, leading to several large genomic clusters of both RSV-A ON1 and RSV-B BA9 genotypes. However, while a number of viral importations were detected, there was also a major reduction in RSV genetic diversity compared to pre-pandemic years. These data reveal the impact of NPI used during the COVID-19 pandemic on other respiratory infections and highlight the important insights that can be gained from viral genomes.

Respiratory syncytial virus (RSV) is a major cause of acute respiratory infection (ARI), mainly affecting children, older people, and those with comorbidities, resulting in a considerable hospitalisation burden among children in particular^{1,2}. This RNA virus is part of the *Orthopneumoviruses*, a genus of viruses in the *Pneumoviridae* family, that generally cause upper respiratory tract infections in humans and some other vertebrates³. RSV is known to cause severe disease in children, particularly infants⁴, and in older adults. In 2019, for instance, there

were an estimated 33 million RSV-associated ARIs globally, and over 100,000 deaths in children under 5 years old⁵. While serological studies have found that RSV infection is common in infants⁴, the virus induces poor immunity, and thus, reinfection can be frequent throughout life⁶. RSV infection is less severe in adults, typically causing upper respiratory infections with mild to moderate symptoms⁷. However, in older people, RSV can be more severe and is reported to have morbidity and mortality rates comparable with influenza virus⁸.

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The global circulation of RSV is characterised by distinct seasonality^{9–12}. In New Zealand, a geographically isolated country in the southern hemisphere with a temperate climate, RSV cases usually increase in autumn (i.e., at the end of April) and peak in mid-winter (late June)¹³. However, in 2020, the regular circulation of RSV was disrupted due to the introduction of non-pharmaceutical interventions (NPI) used to curb the spread of SARS-CoV-2, including a stay-at-home order for all non-essential workers and closure of all public venues, non-essential business, and educational facilities¹⁴. The most stringent of these NPI measures was the closure of international borders and the introduction of a 14-day stay in managed quarantine for returning citizens and residents¹⁴. These NPI were effective in eliminating the circulation and re-introduction of SARS-CoV-2 in New Zealand^{15–17}, and consequently, appeared to eliminate the introduction and spread of other respiratory viruses too¹⁵. During the winter of 2020, reported cases of RSV were reduced by 98% when compared to the average annual cases recorded from 2015 to 2019¹⁵. Indeed, compared to annual averages, New Zealand also saw reductions in cases of influenza virus (99.9%), metapneumovirus (92%), enterovirus (82%), adenovirus (81%), parainfluenza virus (80%), and rhinovirus (75%)¹⁵. A decrease in the circulation of RSV during 2020 was also observed in other countries that used NPI including in the USA¹, Australia¹, China¹⁸, Singapore¹⁹, South Africa²⁰, UK and Ireland²¹.

In April 2021, following over a year of restricted travel into New Zealand, a brief quarantine-free travel agreement was initiated between New Zealand, Australia, and other countries in the South Pacific²². This relaxation of travel restrictions coincided with an increase in the circulation of respiratory viruses in New Zealand²³. Specifically, New Zealand reported RSV cases five times higher, and hospitalisations three times higher, than those typically seen in the pre-pandemic phase²⁴. Australia experienced similar epidemic surges of RSV following the relaxation of COVID-19 restrictions leading to extensive off-season outbreaks and hospitalisations during the summer of 2020/2021 from cryptically circulating lineages¹¹. By August 2021, New Zealand had suspended quarantine-free travel and once again closed the border with Australia. New Zealand then entered its second nationwide lockdown in order to control the spread of the highly transmissible SARS-CoV-2 Delta variant²⁵. This, in turn, was met with a sharp decline in the number of reported RSV cases²⁶. Beginning in early 2022, the New Zealand border became unrestricted, and with the increased migration of people into the country there has been widespread community transmission of respiratory viruses once again, including influenza virus, RSV and the SARS-CoV-2 Omicron variant^{26,27}.

Viral genomic data offers valuable insights into the pattern of viral evolution, and, therefore, enhances our understanding of outbreak epidemiology by providing a high level of detail and context to transmission patterns. When combined with geographic and population information, these data can reveal pathways of viral spread that can be used to inform effective national and local interventions^{16,28}. Temporal and geographic information can be integrated into phylodynamic analyses to detect the spread of a pathogen in time and space, develop predictions about an outbreak's trajectory, and identify clusters of similar sequences as an indication of infection sources and superspreading^{28–30}. Herein, we describe the first genome-scale analysis of RSV in New Zealand, spanning eight years from 2015 to 2022. This timeframe incorporates several significant time points, including the New Zealand border closure in early 2020, nationwide lockdowns during the COVID-19 pandemic, the quarantine-free travel period with Australia and the South Pacific in 2021, and later, the easing of travel restrictions as New Zealand reconnected with the rest of the world in 2022. In this study, we investigate the typical patterns and dynamics of RSV transmission in New Zealand prior to 2020, and how RSV became re-established in the community following its elimination.

Results and discussion

The elimination and re-introduction of RSV during the COVID-19 pandemic

In 2021, New Zealand experienced a large epidemic of RSV following a brief period of quarantine-free travel with Australia and other countries in the South Pacific (Fig. 1a). To better understand the transmission dynamics of RSV before, during, and after this outbreak, we generated RSV genomes from patients in New Zealand over eight years. In total, 1,470 viral genomes, including 755 RSV-A and 715 RSV-B sequences, were generated from New Zealand between 2015 and 2022. Both RSV-A and RSV-B co-circulated each year in relatively even prevalence, based on the genomes generated in this study. Genomes were generated from the male and female sexes in equal proportions, and samples were mostly collected from young children with an overall median age of 1 (range 0–99) (Fig. 1e, f, Supplementary Table 3). The severity of RSV infections can be inferred by the surveillance platform from which the sample originated. Among samples from a known origin included in this study, 83% were referred from hospital-based surveillance, including outpatients and ICU, meaning that the vast majority of genomes were most likely generated from more severe infections compared to those seen in the community (Fig. 1d).

Between 2015 and 2019, annual outbreaks of RSV were typically seasonal, with cases peaking in late June, coinciding with mid-winter in New Zealand (Fig. 1a). In 2020, however, reported RSV cases were reduced by 98%, and no community transmission of RSV was reported as a result of NPI used to control the spread of SARS-CoV-2 (see²⁶ for percentage positivity data). Schools and childcare centers were closed during a four-week nationwide lockdown in April 2020, which effectively eliminated SARS-CoV-2 and other respiratory infections from the New Zealand community^{15,26,31}. The following year, in April 2021, and for the first time since restrictions were placed on the New Zealand border due to the COVID-19 pandemic, people could travel to and from Australia without having to enter managed quarantine at the border. Within weeks of lifting border restrictions, there was an exceptionally large RSV epidemic in New Zealand, with a sharp surge in reported cases of both RSV-A and -B (Fig. 1a).

The 2021 RSV surge affected a wider age distribution compared to previous years (Supplementary Fig. 2). Among people who were sampled in this study, we found a 5% increase in infections among 5–18-year-olds and a 15% increase in infections among 19–65-year olds compared to previous years ($p < 0.001$ when comparing all groups to 2021 using a Chi-squared test) (Supplementary Table 3). This surge cannot be explained by weakened immunity due to COVID-19³², as there were fewer than 3000 reported COVID-19 cases (in a population of ~five million) before August 2021. The majority of these COVID-19 cases were associated with returning travellers, which had limited community transmission¹⁶. Rather it was more likely the result of waned immunity due to prolonged lack of viral exposure, as seen in other countries^{33–35}. However, other factors related to sample collection may have also contributed to the apparent surge. One factor was a change in diagnostic viral testing regimes that were implemented during the COVID-19 pandemic, such as the increased use of point-of-care testing with an expanded respiratory viral diagnostic assay that included RSV³⁶, as well as wider testing in hospitals as part of the admission process, in the community as part of the pandemic response, and for returning travellers as part of the new acute respiratory illness surveillance system. These new testing regimens included older children and adults¹⁵. Increased testing not only inflates case counts but can also skew patient age distribution by incorporating less severe cases³⁷. Nevertheless, due to the associated rise in RSV-related hospitalisations²⁶ and the return to normal levels in 2022, it is likely that the 2021 epidemic reflected a period of reduced exposure to RSV and an increase in the immunologically naïve population.

Quarantine-free travel with Australia was brought to an abrupt end in July 2021 due to the uncontrolled spread of the SARS-CoV-2

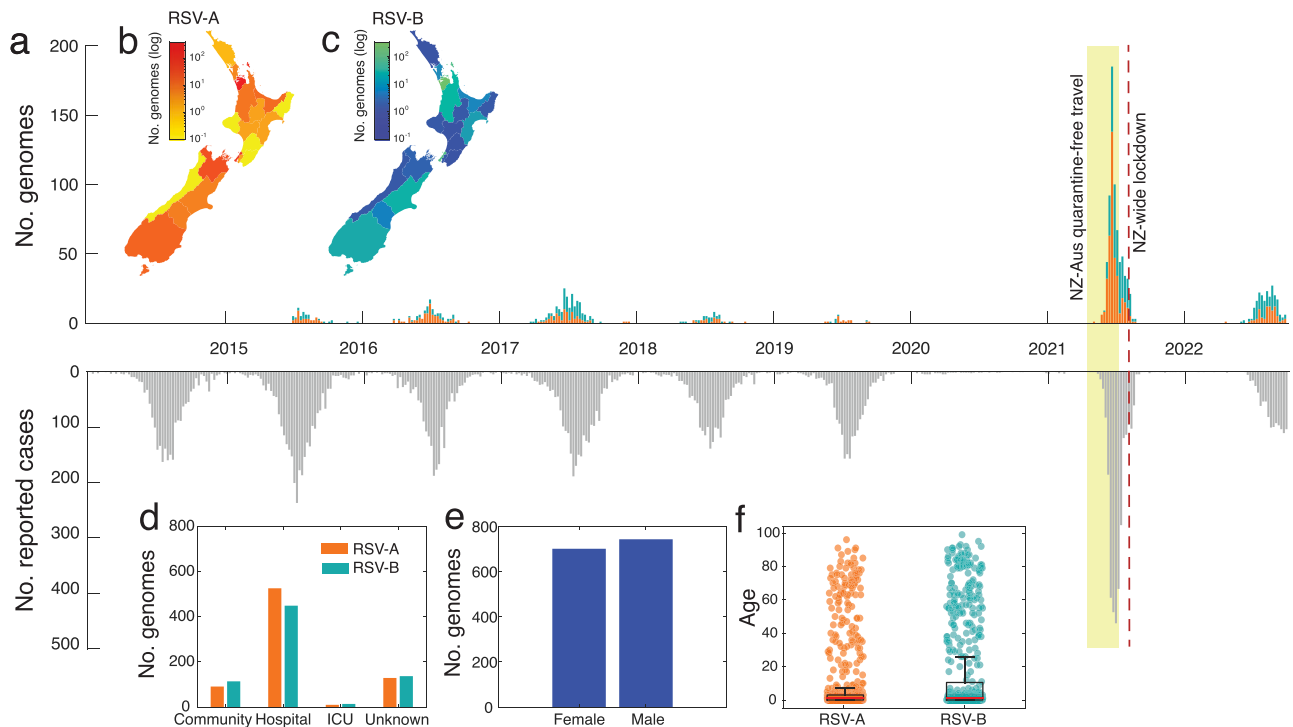


Fig. 1 | Temporal, special, and demographic factors associated with RSV genomes generated. **a** Number of RSV-A (orange) and RSV-B (green) genomes generated over time based on sample collection date. The reflected grey bars below show the number of reported RSV-positive cases in New Zealand over the same timeframe⁶⁸. **b, c** Map of New Zealand, coloured by the number of positive RSV-A and -B cases in each District Health Board. **d** The number of RSV genomes

generated from cases reported in the community, hospital, intensive care unit (ICU), and those from unknown sources. **e** The number of RSV genomes generated from female and male patients. **f** The age distribution of patients from which RSV genomes were generated. A box plot indicates the mean (red), lower and upper quartiles (black), and whiskers (black lines), and the scatter points show the raw data. Source data are provided as a Source Data file.

Delta Variant of Concern in Australia³⁸. Weeks later, New Zealand entered its second nationwide lockdown due to the incursion of Delta SARS-CoV-2, which was genomically linked to cases in Australia²⁵. The lockdown caused the number of reported RSV cases to dramatically reduce (Fig. 1).

Inferring the sources of the 2021 RSV outbreaks using phylodynamics

Phylogenomic analysis of RSV-A and RSV-B genomes, together with genomes sampled from Australia and the rest of the world, showed that in the pre-pandemic phase, genomes sampled from New Zealand were widely distributed among globally sampled genomes, falling among a range of genomic lineages. In 2021, however, genomes sampled from New Zealand formed only a small number of tightly grouped clusters. In particular, RSV-A genomes sampled in 2021 fell into only two distinct lineages with well-supported nodes (Fig. 2d–f). One clade of RSV-A genomes, predominantly sampled from Auckland and surrounding districts, formed a monophyletic clade with no close-in-time sampled genomic ancestors, and unrelated to previously circulating New Zealand lineages (Fig. 2e). Due to stringent testing regimes for all respiratory infections coupled with managed quarantine at the border for all arrivals besides those from Australia and the South Pacific, and that RSV genomes are sparsely sampled at the global scale, this lineage is unlikely to represent undetected transmission in New Zealand. Rather, it is more likely that this lineage is related to unsampled genomes, most probably in Australia.

A second cluster of New Zealand 2021 genomes were grouped with those sampled from Australia during the months prior (Fig. 2f). This 2021 New Zealand cluster was due to multiple introductions, forming several monophyletic clades among Australian samples, and

included genomes from across a wide geographic region including the North and South Islands of New Zealand. Both the highlighted clusters of RSV-A genomes were determined to be the ONI-like genotype based on their G-gene sequences (genomic clade A.3 based on Chen et al.³⁹), which has become globally dominant in recent years^{40,41}. This genotype, which evolved from the previous dominant RSV-A genotype NA-1, has a characteristic 72-nucleotide duplication in the G-gene⁴². All RSV-A genomes sampled in New Zealand conformed to a root-to-tip linear regression reflecting a temporal signal in these data (Pearson correlation coefficient, $r = 0.88$, $p < 10^{-4}$).

Similarly, RSV-B genomes sampled in 2021 were clustered tightly with those sampled in Australia in the months leading up to the outbreak in New Zealand (Fig. 3). These genomes formed several large monophyletic clades among Australian samples and largely clustered according to geographic location in New Zealand. We again found a temporal signal in the New Zealand RSV-B data, illustrated by a root-to-tip linear regression (Pearson correlation coefficient, $r = 0.93$, $p < 10^{-4}$). These genomes were classified as the BA9 genotype based on their G-gene sequences (or the B.5.8 genomic clade³⁹). BA9 is one of 15 genotypes within the BA lineage reported since its emergence circa 1998⁴³. Genotype BA9 was first identified in Japan in 2006⁴⁴ and, like all BA genotypes, is characterised by a 60-nucleotide duplication in the G-gene⁴⁵. Over the last decade, BA9 has become globally dominant and is now found worldwide^{40,41,46–48}. Overall, the RSV-A and RSV-B genomes sampled in 2021 were most likely from new introductions into New Zealand rather than from cryptically circulating lineages that remained undetected in 2020. Indeed, our data support that RSV transmission was eliminated in 2020, and both subtypes were reintroduced in 2021, most likely from Australia following the lifting of border restrictions, including quarantine.

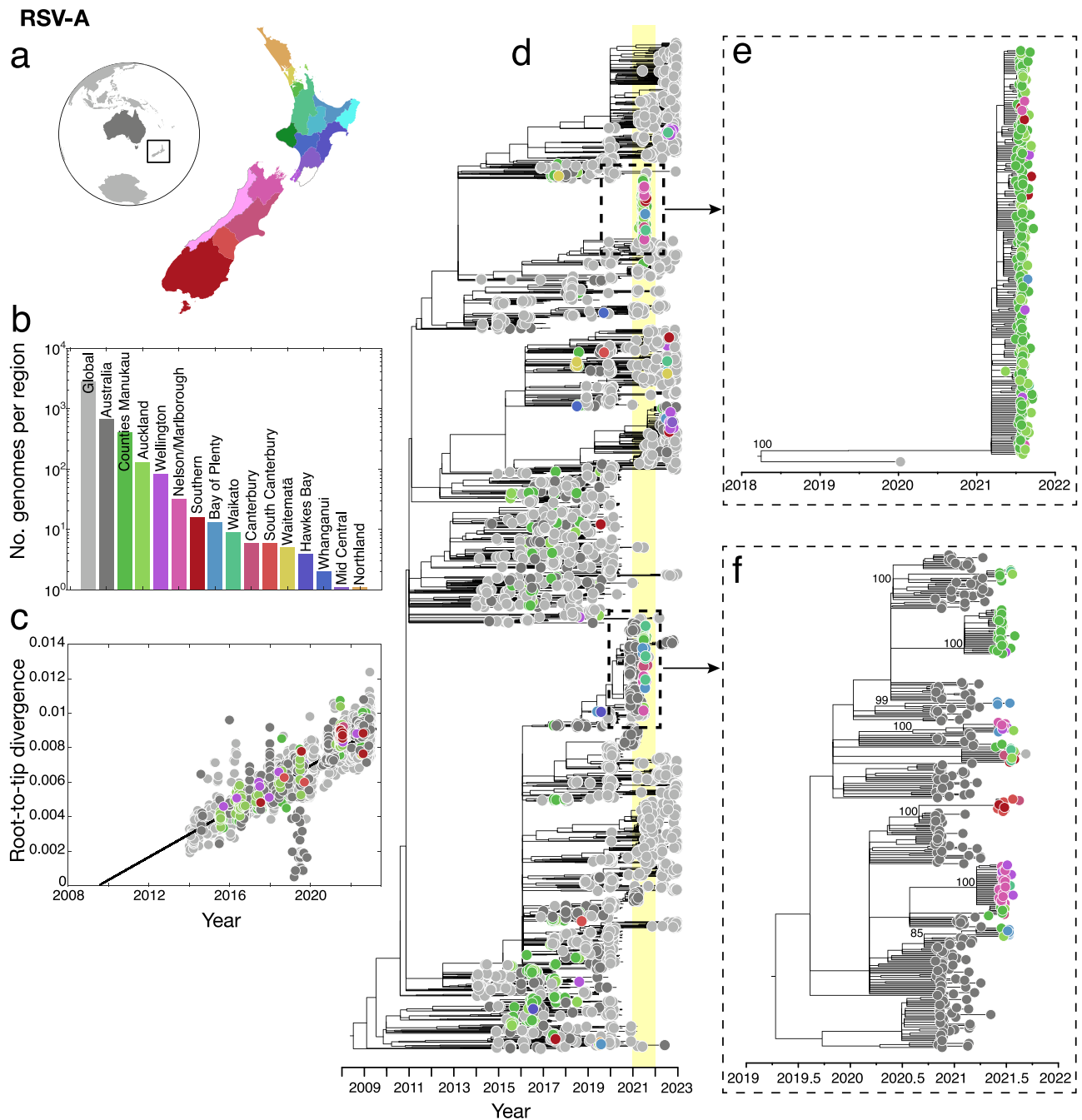


Fig. 2 | Evolutionary history of RSV-A in New Zealand. **a** Map of New Zealand (where regions are categorised by District Health Board (DHB)), Australia (dark grey), and the rest of the world (light grey). **b** Number of RSV-A genomes sampled per region, where colours correspond to those in (a). **c** Root-to-tip regression analysis of RSV-A genomes versus sampling time. **d** Maximum likelihood time-scaled phylogenetic tree showing 755 RSV-A genomes sampled from New Zealand (coloured circles based on DHB region), 662 RSV-A genomes sampled from

Australia (dark grey), and 2913 RSV-A genomes sampled from the rest of the world (light grey). A yellow vertical bar highlights the year 2021 and a dotted box shows the major New Zealand clades sampled. **e**, **f** Maximum likelihood time-scaled phylogenetic trees showing the major clades sampled in New Zealand during 2021 and their closest sampled genetic relatives, showing percentage bootstrap support from 1000 replicates for the nodes of the New Zealand clusters. Source data are provided as a Source Data file.

Examining the spatial transmission dynamics of RSV over time

We estimated the spatial transmission dynamics of RSV over time to elucidate how the number of viral introductions changed as a result of NPI, particularly border restrictions, used during the COVID-19 pandemic. While the number of people arriving in New Zealand peaked in early 2020 following an announcement that the border would be closed, a nationwide lockdown meant that any potential new arrivals of RSV did not lead to onward transmission in the community (Fig. 4). We inferred the number of introductions of both RSV-A and RSV-B into

New Zealand between 2015 and 2022 using genomes sampled from both New Zealand and abroad. Although genomic sequences were too sparse to capture seasonal patterns between 2015 and 2019, introductions of both RSV-A and RSV-B decreased in 2020, resulting in near-zero introductions of either subtype (Fig. 4). In interpreting this analysis, we note that the number of introductions on any given day was approximated by counting the lineages on that day that changed from Global to New Zealand. This approach means that the introduction dates on long branches (such as those that led to the 2021 outbreaks)

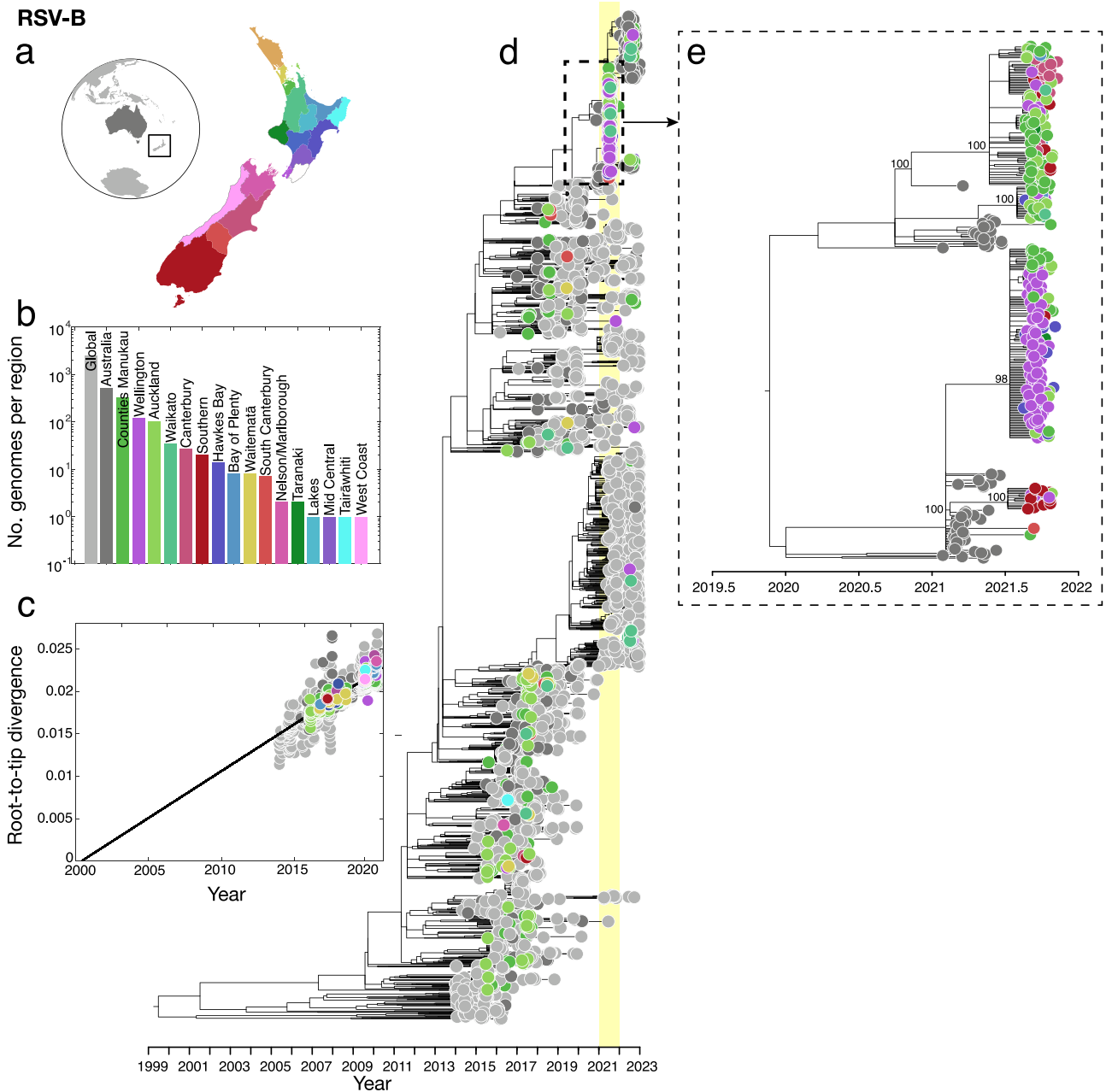


Fig. 3 | Evolutionary history of RSV-B in New Zealand. **a** Map of New Zealand (where regions are categorised by District Health Board (DHB)), Australia (dark grey), and the rest of the world (light grey). **b** Number of RSV-B genomes sampled per region, where colours correspond to those in **a**. **c** Root-to-tip regression analysis of RSV-B genomes versus sampling time. **d** Maximum likelihood time-scaled phylogenetic tree showing 715 RSV-B genomes sampled from New Zealand (coloured circles based on DHB region), 518 RSV-B genomes sampled from

Australia (dark grey), and 2577 RSV-B genomes sampled from the rest of the world (light grey). A yellow vertical bar highlights the year 2021 and a dotted box shows the major New Zealand clade sampled. **e** Maximum likelihood time-scaled phylogenetic tree showing the major clades sampled in New Zealand during 2021 and their closest sampled genetic relatives, showing percentage bootstrap support from 1000 replicates for the nodes of the New Zealand clusters. Source data are provided as a Source Data file.

are likely to be underestimated. With this limitation noted, these results corroborate that the number of introductions dramatically increased the following year in 2021, particularly for RSV-A, coinciding with quarantine-free travel to and from Australia.

In 2022, RSV-B showed a larger number of introductions, which is consistent with the multiple different lineages that were circulating in 2022. Although both subtypes were introduced many times throughout the eight years (around 80 for RSV-A and 100 for RSV-B), only a small number of these introductions eventuated in large, detected outbreaks in 2021 (Figs. 2 and 3). We estimate that the 689 genomes and 2818 cases in 2021 were linked to just 10 (95% credible

interval, CI: 6.6, 14) introductions of RSV-A and 6.7 (CI: 3.8, 10) for RSV-B. This means that each introduction in 2021 produced an average of 41 genomes and 169 cases. In contrast, the 63 (51, 76) RSV-A introductions and 76 (61, 92) B introductions between 2014 and 2019 each resulted in an average of three genomes and 90 cases. This reflects the immunologically naive population of 2021 combined with the highly stochastic nature of disease transmission, which often occurs through superspreader events^{49,50}. In contrast, very few export events were identified. Our analysis showed that RSV-B mutated slightly faster than RSV-A (Table 1) and at a comparable rate with previous studies⁵¹. These experiments proved

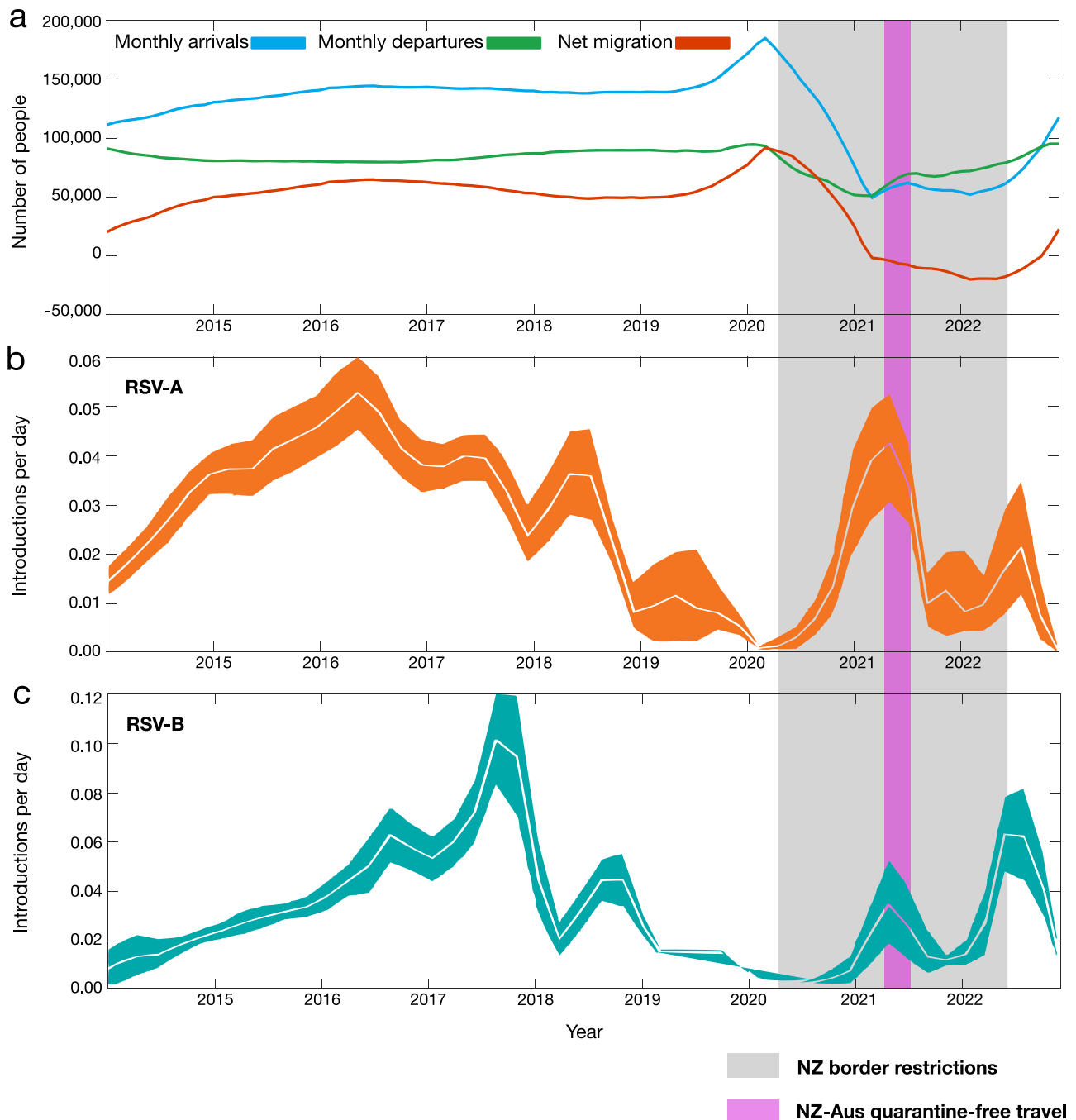


Fig. 4 | RSV importations into New Zealand over time. **a** Number of people arriving into New Zealand (blue), number of people departing New Zealand (green), and the overall net migration of people into New Zealand (red)⁶⁹. **b, c** Estimated migration rates of RSV-A and B into New Zealand over time (mean estimates are

shown in white, and 95% credible intervals are coloured). A grey-shaded area shows the period in which New Zealand underwent border restrictions during the COVID-19 pandemic. A purple-shaded area shows the quarantine-free travel period with Australia. Source data are provided as a Source Data file.

robust to genome subsampling, with each replicate yielding similar clock rates and migration counts.

Genomic diversity of RSV before and after the COVID-19 pandemic

Despite the border-opening associated increase in both viral introductions and genomic surveillance in New Zealand, the surge of RSV introductions in 2021 had very little genomic diversity compared to the pre-pandemic phase, as shown by the limited number of New Zealand genomic clusters in our phylogenetic analysis. Indeed, a Bayesian coalescent skyline analysis estimating the effective population size of New Zealand RSV-A and RSV-B genomes over time

illustrated that the diversity in genomes decreased in 2020 and 2021 (Supplementary Fig. 3). Similar genomic bottlenecks have been reported in Europe⁵² and Australia¹¹, where major lineages of RSV were collapsed following NPI during the COVID-19 pandemic. The resurgence of RSV in 2021 led to very little genomic diversity in circulating lineages, with only two major clades of RSV-A and one clade of RSV-B being reintroduced into New Zealand. Nevertheless, this reduced genetic diversity was seemingly short-lived lived with more widespread lineages reappearing by 2022 when border restrictions were removed (Figs. 2 and 3). Overall, the extensive NPI used to control SARS-CoV-2 in New Zealand significantly impacted the epidemiology of other respiratory viral infections, including the

Table 1 | Summary of estimated clock rates and RSV migration events between New Zealand and the rest of the world (BEAST2)

	Rep	Clock rate (subs/site/year)	Total number of introductions	Total number of exports
RSV-A	1*	8.79×10^{-4} (8.40×10^{-4} , 9.13×10^{-4})	85.3 [83, 88]	2.94 [1, 5]
	2	8.31×10^{-4} (7.95×10^{-4} , 8.66×10^{-4})	81.9 [80, 84]	3.93 [3, 5]
	3	8.25×10^{-4} (7.90×10^{-4} , 8.59×10^{-4})	89.4 [84, 93]	2.15 [1, 5]
	4	8.68×10^{-4} (8.29×10^{-4} , 9.04×10^{-4})	83.4 [82, 85]	3.11 [2, 4]
	5	8.52×10^{-4} (8.19×10^{-4} , 8.87×10^{-4})	84.6 [82, 87]	3.71 [2, 6]
	6	8.68×10^{-4} (8.32×10^{-4} , 9.04×10^{-4})	80.2 [78, 82]	4.16 [3, 6]
RSV-B	1*	1.04×10^{-3} (1.00×10^{-3} , 1.09×10^{-3})	100 [97, 104]	0.86 [0, 3]
	2	1.00×10^{-3} (9.64×10^{-4} , 1.05×10^{-3})	101 [97, 104]	0.57 [0, 1]

Each replicate contains a different subsample of genomes. Mean estimates (and 95% credible intervals) are rounded to three significant figures. MCMC chains that did not converge (replicates RSV-B 306) are omitted from the table. *These replicates are shown in Fig. 4.

near-elimination and diminished genetic diversity of typically seasonal viruses.

Methods

Ethics

The New Zealand Northern A Health and Disability Ethics Committee approved the Southern Hemisphere Influenza Vaccine Effectiveness Research and Surveillance (SHIVERS) study (NTX/11/11/102). Ethics approval was not required for the primary care, laboratory, or hospital-based surveillance platforms as they were conducted in accordance with the Public Health Act 1956.

Sample collection

Respiratory samples (nasal, throat or nasopharyngeal swabs) were obtained from several surveillance and research platforms, each serving a different purpose. Community-based samples were obtained from general practitioners (GPs) across New Zealand from patients with influenza-like illness (ILI), for which the surveillance period typically began in late April and ended in late September. Hospital-based samples were obtained from patients with severe acute respiratory infection (SARI) from two major Auckland-based hospitals year-round. Laboratory-based surveillance samples were referred to the Institute for Environmental Science and Research (ESR) from both community and hospital diagnostic laboratories throughout the year in several major centres: Auckland, Bay of Plenty, Waikato, Hawkes Bay, Wellington, Nelson, Christchurch and Dunedin. Samples were also collected and tested at ESR for the Southern Hemisphere Influenza Vaccine Effectiveness Research and Surveillance (SHIVERS) study. This study included three Wellington-based community cohorts, where samples were obtained from participants who experienced ARI. The surveillance period for these cohorts matched that of the community-based surveillance. In 2021, a fifth iteration of SHIVERS commenced in which samples from diagnostic and hospital laboratories throughout New Zealand referred positive RSV samples to ESR for further testing and analysis. Collection dates of the genomes used in this study were collected from July 2015 up to and including October 2022.

Viral RNA extraction and qRT-PCR

Samples were received by the Clinical Virology Department at ESR from 2015 to 2022. Viral RNA was extracted using the Thermo Fisher Scientific™ MagMax Viral/Pathogen Nucleic Acid Isolation Kit (A48310) as per manufacturer's instructions on either the Zixpress or the Kingfisher Flex automated extraction instruments. An RSV singleplex qRT-PCR was performed on RNA using primer and probes synthesised by biosearch using sequences published by Kim et al.⁵³, coupled with the AgPath-ID™ One step RT-PCR buffer and enzyme (4387424). Positive RSV RNA was genotyped (RSV-A, RSV-B) using primers and probes synthesised by biosearch using sequences published by Hu et al.⁵⁴, coupled with the AgPath-ID™ One step RT-PCR buffer and enzyme

(4387424). Samples collected between 2015 and 2021 with a cycle threshold (Ct.) below 25, as well as samples from 2022 with a Ct. below 30, were referred to the genomic sequencing department at ESR.

Generating viral genomes from RSV samples

In brief, sequencing was performed on the Illumina Nextseq platform using the respiratory virus oligo panel v2 (20044311), RNA prep enrichment kit (20040537), and the 500/550 midoutput kit (20024905) and used as per the manufacturer's instructions. Consensus-based assembly was performed using a standardised pipeline, based on the Seattle Flu assembly pipeline, and modified for use by ESR, (<https://github.com/seattleflu/assembly>). Two additional references were used for consensus calling: EPI_ISL_2543807 and EPI_ISL_2543850, available from GISAID⁵⁵. Consensus viral genomes were generated, and subject to quality testing, and those with fewer than 50% ambiguities were selected for further analysis (median coverage was 99.95% of the assembled genomes, with 80% of all samples having >99% or more of the genome covered, meaning that the vast majority of genomes were of high quality, see Supplementary Fig. 1). The genomes generated are available on GISAID under two blocks of consecutive accession numbers (EPI_ISL_16959469 - EPI_ISL_16960152 and EPI_ISL_19206151 - EPI_ISL_19207488) and on NCBI's GenBank database under BioProject PRJNA939717.

Genotyping RSV genomes

Reference G glycoprotein gene (G-gene) sequences for each known genotype for both RSV-A and RSV-B were obtained from GenBank (see Supplementary Table 1 for a list of accession numbers and their genotypes). G-gene sequences were first annotated and extracted from the New Zealand genomes using Geneious Prime 2022.1.1 (<https://www.geneious.com>) and aligned with the reference sequences using MAFFT (v7)⁵⁶ using the FFT-NS-2 algorithm. A maximum likelihood phylogenetic tree for each of RSV-A and RSV-B was estimated using IQ-TREE (v 1.6.8)⁵⁷, using the Hasegawa-Kishino-Yano nucleotide substitution model with a gamma-distributed rate variation among sites (HKY + Γ)⁵⁸ (determined to be the best-fit model by ModelFinder)⁵⁹. Using the topology of the reference sequences, the genotypes of the New Zealand RSV G-genes were determined. Genotyping across whole genome sequences was also performed using LABEL⁶⁰ based on genotypes proposed by Chen et al.³⁹ following alignment with MAFFT (v7)⁵⁶.

Inferring genomic diversity of RSV using phylodynamic analysis

Newly acquired New Zealand RSV genomes were aligned with globally sourced RSV genomes with MAFFT (v7)⁵⁶ using the FFT-NS-2 algorithm (see Supplementary Table 2 for global genome accession numbers, or GISAID Epi set ID: EPI_SET_241014ew or <https://doi.org/10.55876/gis8.241014ew>). These global genomes (3487 RSV-A and 3002 RSV-B) were sampled uniformly at random without replacement from ~50,000 international sequences on GISAID⁵⁵ between 2015 and 2022 (as of

March 2024). A maximum likelihood phylogenetic tree was estimated using IQ-TREE (v 1.6.8)⁵⁷ using the HKY + Γ^{58} nucleotide substitution model. We integrated the in-built Least Squares Dating method to estimate a time-scaled phylogenetic tree using the day of sampling. Phylogenetic branch support was assessed using the ultrafast bootstrap⁶¹ approximation. We used TempEst (v 1.5.3)⁶² to analyse the root-to-tip genetic regression against sampling dates to investigate the temporal signal of RSV-A and RSV-B genomes.

To measure relative genetic diversity over time (inferred through the effective population size), up to 50 New Zealand RSV genomes for each year (2015–2022) were uniformly selected at random without replacement and aligned using MAFFT (v7)⁵⁶. These genomes were subject to Bayesian phylodynamic analysis using BEAST2 (v2.7)⁶³ with the Bayesian Integrated Coalescent Epoch Plot using a structured coalescent tree prior⁶⁴ and a strict clock rate estimated. We repeated this analysis three times for each RSV-A and RSV-B. We sampled the posterior distribution using Markov chain Monte Carlo (MCMC), running each analysis for 20 million steps, sampling states every 20,000 steps, and discarding the first 10% as burn-in. Convergence was assessed in Tracer v 1.6⁶⁵, ensuring that all analyses had over 200 effective samples for all reported parameters.

Estimating introductions of RSV using Bayesian phylodynamic analysis

To infer the migration dynamics of RSV into New Zealand over time, we treated geographic location as a discrete trait with two demes where genomes were either sampled as being ‘local’ (i.e., sampled from New Zealand) or ‘global’ (i.e., sampled from the rest of the world). Due to the size of the dataset, local and global RSV-A and RSV-B genomes were randomly split into six subsamples, making sure that near equal numbers of genomes were selected for each deme for each year. For each of RSV-A and RSV-B, each subsample comprised approximately 400 local and 400 global genomes. To ensure the geographical representativeness of subsamples, global genomes were subsampled by iteratively sampling a country and then a genome from that country. Each subsample was aligned using MAFFT (v7)⁵⁶ and subject to Bayesian phylodynamic analysis using BEAST2 (v2.7)⁶³ with the MAS-COT structured coalescent tree prior⁶⁶. We again used the HKY + Γ^{58} nucleotide substitution and a strict clock LogNormal(mean = 0.001, sigma = 0.1) clock rate prior (units: substitutions per site per year). Introduction (i.e., the transition from global to local) and export (local to global) events were assumed to be rare occurrences, and introductions were assumed much more common than exports, reflecting prior knowledge about epidemics originating overseas and then coming to New Zealand. The prior introductions were Exponential (mean = 0.1) migrations per year and Exponential (mean = 0.001) for exports. The (constant) effective population sizes of the two demes had independent LogNormal(mean = 0.2, sigma = 0.4) priors. We sampled the posterior distribution using MCMC running each analysis for 100 million steps, sampling states every 10,000 steps, and discarding the first 10% as burn-in. Convergence was assessed in Tracer v 1.6⁶⁵, ensuring that all analyses had over 200 effective samples for all reported parameters. All 6/6 RSV-A analyses and 2/6 RSV-B analyses were completed to this standard (the failed analyses are not reported here). The number of introductions of RSV-A and RSV-B over time was estimated using the Babel package in BEAST2, and the results were summarised in R⁶⁷.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The genomes generated are available on GISAID under two blocks of consecutive accession numbers (EPI_ISL_16959469 - EPI_ISL_16960152

and EPI_ISL_19206151 - EPI_ISL_19207488) and on NCBI's GenBank database under BioProject PRJNA939717. GISAID accession numbers of global genomes used in the analysis are available in Supplementary Table 2, accessed via GISAID Epi set ID: EPI_SET_241014ew or <https://doi.org/10.55876/gis8.241014ew>. Metadata included with the genomes comprises sampling date and location. Patient age and sample source data (e.g. hospital, ICU, etc.) are subject to controlled access due to privacy and ethical reasons. Data can be requested via the Institute of ESR and maybe subject to ethics approvals, and thus a timeframe for response cannot be provided. Source data are provided in this paper.

Code availability

All code used in this study is from open-source software described in the Methods.

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J.L.G., J.D., L.J., N.F., Q.S.H. and D.W. conceived the ideas for the study and designed the analysis. L.J., M.O., K.B., A.C., J.W., S.U., H.J., J.B., M.A., J.d.L., C.E.T., R.S., T.W., N.A., T.J., N.T., P.M., T.D., A.T., C.B. and D.W. collected data and generated RSV genomes. J.L.G., J.D., L.J., D.W., R.W., N.F., Q.S.H. and D.W. participated in the scientific discussion and data analysis. L.J., J.D. and J.G. wrote the manuscript. All authors have discussed and approved the final manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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