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Temporal associations of the COVID-19 related border restrictions and respiratory viral infections in New Zealand

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Abstract

New Zealand (NZ)'s elimination of community transmission of influenza and respiratory syncytial virus (RSV) infections in May 2020, due to stringent COVID-19 countermeasures, provided a rare opportunity to assess the impact of border restrictions and relaxations on common respiratory viral infections over the subsequent two-years. Using multiple surveillance systems, we observed that border closure to most non-residents, and mandatory government-managed isolation and quarantine on arrival for those allowed to enter, appeared to be effective in keeping influenza and RSV infections out of the NZ community. Partial border relaxations through quarantine free travel with Australia and other countries were associated, within weeks, with importation of RSV and influenza into NZ in 2021 and 2022. Border restrictions did not have effect on community transmission of other respiratory viruses such as rhinovirus and parainfluenza virus type 1. These data can inform future pandemic influenza preparedness as well as provide insights into effective strategies to plan and model the impact of seasonal influenza, RSV, and other respiratory viral infections.

Introduction

COVID-19, declared a public health emergency of international concern by the World Health Organization (WHO) on 30-January-2020, was first identified in the New Zealand (NZ) community on 28-February-2020. From 19-March-2020, NZ responded to the COVID-19 pandemic with stringent public health and social measures (PHSMs) including border restrictions and an Alert Level (AL) system that comprised strict stay-at-home orders.[1,2] These measures were successful in containing the first wave of the COVID-19 outbreak with elimination of community transmission for 101 consecutive days from 1-May to 10-August-2020.[3,4] We previously reported that community transmission of influenza and respiratory syncytial virus (RSV) was also eliminated from May 2020.[5]

The effectiveness of border restrictions was debated throughout the COVID-19 pandemic. Previous experience of border restrictions in the 1918 influenza pandemic showed that screening and quarantine of entering travellers at international borders did not substantially delay introduction except in some island countries,[6] with similar observations made during subsequent influenza pandemics.[7] According to International Health Regulations, border closures and restrictions can only be implemented if a set of criteria are met.[8] Border restrictions were largely discouraged by the WHO during the COVID-19 pandemic, in part due to their potential to be discriminatory and worsen economic and social disruption.

NZ's border restrictions were maintained over two years to 31-July-2022 (see timeline in Fig. 1) with the intention of preventing imported cases of COVID-19 from establishing chains of community transmission in the country. The restrictions included total border closure to most non-residents, and mandatory government-managed isolation and quarantine (MIQ) in designated facilities on arrival for those allowed to enter. After more than 12 months of border closure, partial border relaxation was introduced for a brief period from 19-April to 23-July-2021 allowing quarantine free travel with Australia where community transmission of COVID-19 was also eliminated. In early 2022, after achieving high COVID-19 vaccination

coverage, border restrictions were progressively relaxed. Quarantine free travel was permitted for vaccinated New Zealanders and other eligible travellers from Australia from 28-Feburary-2022,[9] for vaccinated Australians from 13-April-2022, for vaccinated travellers from NZ's list of 60 visa-waiver countries from 2-May-2022, and finally for all travellers irrespective of vaccination status from 31-July-2022.

There are scarce data on the impact of border restrictions on respiratory viral infections in the modern era of extensive international air travel and molecular diagnostic testing. NZ's use of border closure across a period of over two years, interspersed with partial border relaxation, provides a rare opportunity to understand the impact of border restrictions on importations of cases of influenza, RSV, and other respiratory viral infections, and then on their in-country epidemiology in an island nation. Additionally, NZ has invested, over the last 10 years, in comprehensive respiratory virus surveillance platforms including patients admitted acutely to hospitals, those making consultation visits to general practitioners (GPs), and community cohorts with non-medically attended acute respiratory infections. This provided a unique 'real-world' dataset to examine temporal associations of border restrictions and importations of these viral infections with varying disease spectrums. Understanding the effect of border restrictions on these viral infections and associated diseases is critical to informing pandemic influenza preparedness and planning countermeasures for seasonal influenza, RSV, and other respiratory viral infections.

Here we report data from these multiple surveillance systems to describe influenza, RSV, and other respiratory viral infections in NZ during the period when NZ implemented and then eased COVID-19 related border restrictions.

Results

While reported community influenza and RSV cases remained absent during the strictest phase of border restrictions, multiple national surveillance systems consistently showed that re-introduction of RSV and influenza into the NZ community were temporally associated with partial border relaxations in 2021 and 2022, respectively (Fig. 2).

Hospital-based severe acute respiratory infection (SARI) surveillance recorded very low SARI incidence rates in 2020, all below the seasonal threshold defined by the reference period of 2015–2019 (Fig. 2-a). In 2021, RSV-associated SARI hospitalisations (Fig. 2-b) were first reported two weeks following quarantine free travel with Australia from where an inter-seasonal RSV outbreak, very low influenza virus identification, and zero COVID-19 activity were reported.[10,11] In 2022, influenza-associated SARI hospitalisations (Fig. 2-c) were first reported five weeks after the 28th February partial border relaxation. In contrast, rhinovirus-associated SARI hospitalisations (Fig. 2-d) were reported throughout 2019–2022 regardless of border restrictions.

SHIVERS-II, III, IV community cohort surveillance results, consistent with the patterns detected by hospital-based SARI surveillance, showed that ARI incidences (Fig. 2-e) were mainly caused by RSV (Fig. 2-f)

which peaked in late-June-2021, and influenza (Fig. 2-g) which peaked in late-June-2022. Rhinovirus-associated ARI (Fig. 2-h) were reported throughout the surveillance period of 2019–2022.

The HealthStat sentinel general practice (GP) based influenza-like illness (ILI) surveillance data showed that ILI syndromic illness was mostly below the seasonal threshold during 2020 and 2021 and at a low level during 2022 (Fig. 2-i). SHIVERS-V sentinel GP-based ARI surveillance results, like other surveillance streams, indicated that high incidences of RSV (Fig. 2-j), influenza (Fig. 2-k), and rhinovirus (Fig. 2-l) were detected in mid-July-2021, late-June-2022, and throughout the surveillance period, respectively.

The laboratory-based surveillance detected high numbers of RSV virus detections in early-July-2021 (Fig. 2-m) and high numbers of influenza virus detections in mid-June-2022 (Fig. 2-n). The number of rhinovirus detections (Fig. 2-o) were reported throughout 2019–2022 regardless of border restrictions.

SHIVERS-V travellers' ARI surveillance tested 86,295 samples for SARS-CoV-2 from those travellers staying in 29 MIQ facilities. Among those travellers with ARI (2484) who had available left-over samples, 1378 were tested for influenza virus of which 12 were positive, and 1376 were tested for RSV of which 47 were positive (Fig. 3).

Table 1 shows the cumulative number of respiratory viruses detected across all the surveillance systems and the proportional reduction for each virus during 2020–2022, versus the reference period of 2015–2019, before, during and after the border restrictions. In a period of border restrictions from week 18 of 2020 to week 8 of 2022, in comparison with the reference period, dramatic reductions (> 99%) were observed for influenza virus with only 21 influenza virus detections. Of these, 17 were from travellers who stayed in MIQ facilities from 21-Dec-2020 to 27-Feb-2022, and 4 were detected from 11-May-2020 to 26-July-2020 with unknown travel information. When border restrictions were relaxed (weeks 9–30 of 2022), a nearly four-fold increase in the number of influenza virus detections was reported. Like influenza, marked reductions were also evident for RSV detections (> 97%) during a period of border closure (week 18 of 2020 to week 15 of 2021). This was followed by a two-fold increase in RSV detections soon after quarantine free travel with Australia was implemented. Interestingly, some of the other respiratory viruses were less affected by border restrictions. For example, rhinovirus detections were reduced (82%) after strict lockdown and implementation of other countermeasures and then re-bounded quickly and increased (18%) during the period of border closure (from week 18 of 2020 to week 15 of 2021). The temporal distributions of parainfluenza virus type 1 (PIV1) showed a peak of PIV1 community transmission in the spring-summer time from November 2020 to January 2021 when border closure was implemented (Fig. 4).

We generated 237 and 230 whole RSV-A and RSV-B genomes, respectively, identified from June to August 2021 during NZ's winter period and post-border opening with Australia. Together, these genomes represent 40% of the 1168 RSV positive samples reported across NZ during this period. They were referred from nine diagnostic laboratories to the Institute of Environmental Science and Research (ESR). Phylogenetic analysis of these genomes indicates that there were only a limited number of introductions of RSV into NZ in 2021, likely due to partial border opening with Australia during that time. These few

introductions led to subsequent large community transmission in NZ as represented in Fig. 5. NZ clades were most often linked to Australian sampled ancestors, although such genomes were perhaps oversampled compared with the rest of the world (Fig. 5).

Discussion

New Zealand, a southern hemisphere country with a temperate climate, has a well-established pattern of influenza and RSV circulation with peak incidences usually in the winter months from June to September annually.[12] NZ's elimination of influenza, RSV and the first wave of COVID-19 in May 2020,[5] provides a unique opportunity to describe and understand the impact of border restrictions on infections caused by these viruses for the subsequent two years, because travellers from overseas countries became the only reservoir for these viruses to be re-introduced. Comprehensive surveillance of hospitalisations, GP visits and non-medically attended ARI showed that the border restrictions were effective at keeping influenza and RSV out of the NZ community. Re-introduction of RSV and influenza into NZ were temporally associated with partial border relaxations in 2021 and 2022, respectively. RSV viruses detected in NZ after the introduction of quarantine free travel with Australia were phylogenetically closely related to those from Australia and not to those circulated in NZ before the pandemic. Tight border controls appeared to be effective in preventing importations of influenza and RSV into the NZ community. However, border restrictions did not have much impact on non-enveloped viruses such as rhinovirus and some of the enveloped viruses such as PIV1, probably due to their suppressed (but not eliminated) transmission within NZ during the most stringent PHSMs.

The WHO's pandemic influenza intervention guidance does not recommend border restrictions when pandemic influenza emerges in human populations because these measures have been considered ineffective and impractical.[13] However, the knowledge base used in developing WHO guidance for influenza pandemic prevention consists primarily of historical observations and modelling studies with the overall quality of evidence for the effectiveness of border closure being very low.[6,14,15] In contrast, NZ's real-world data, utilising multiple surveillance systems, showing the effectiveness of border restrictions in preventing influenza transmission during the COVID-19 pandemic, is consistent with that reported from other countries including Australia,[16-19] Hong Kong,[20] Chile,[21] and South Africa,[22] as well as from Hong Kong during the 2003 SARS epidemic.[23] Therefore, we suggest it is important to re-evaluate the role of border restrictions (when used in conjunction with PHSMs) in mitigating or even potentially eliminating severe pandemic influenza in the framework of international health regulations. Although such measures are associated with significant negative impacts on society, the potential beneficial effects of delaying respiratory viral transmission can provide the time needed for developing, producing, and distributing vaccines and therapeutics that can prevent death and disease. New knowledge from this assessment may inform better preparedness for future influenza pandemics and other severe respiratory viral threats. Additionally, it would be worthwhile to conduct detailed analysis to identify which components of border restrictions (total versus partial closure, screening, quarantine,

isolation, testing etc) were most effective in preventing importation of influenza and other respiratory virus infection including COVID-19.[24,25]

Influenza virus is characterised by a marked seasonality in temperate regions, where the virus exhibits a distinct annual peak in epidemic activity during the winter months.[26] Viruses that seed new influenza epidemics may arise from two possible sources: 1) virus may continue to be transmitted at low levels during the inter-epidemic period but go undetected by commonly used hospital-based surveillance methods; or 2) local virus may disappear from the local population, creating an absolute requirement for new virus introduction from an outside population. However, the origin of seed viruses for new influenza epidemics remains enigmatic. Our findings showed that NZ's local influenza virus transmission disappeared during 2020 and 2021 and sporadic influenza cases detected during this period were mostly from travellers while staying in MIQ facilities. Our data support the current understanding that the origin of seed virus is generally from an influenza virus importation from a locality either in those countries or the hemisphere in which the influenza season is current,[27] or from the tropics where low levels of virus may circulate year-round.[28,29]

Border restrictions and stringent PHSMs appear to have led to the elimination of the annual RSV epidemic in NZ in 2020. Following border relaxation with Australia in April 2021, community transmission of RSV returned to NZ. The NZ pattern is different from Australia where a peak of RSV cases was observed from September 2020 followed easing of restrictions on gatherings and school re-openings but preceding the relaxation of border restrictions, suggesting within-country low circulation of RSV or incomplete border closure.[30] One important difference between Australia and NZ's pandemic restrictions (relevant for RSV) is that Australia allowed childcare centres to mostly remain open during pandemic restriction periods, providing an opportunity for maintaining community transmission.[10] Indeed, during the 2020/21 RSV season in Europe, where overall RSV activity was very low, the only countries with major RSV outbreaks were those with policies to keep primary school and childcare centres open.[31] Examination of the effects of individual measures, when possible, can help determine efficacy in a local and regional context, help to improve understanding of disease transmission and allow better modelling for resource allocation and healthcare policies, including timing and effectiveness of public health interventions.[32] The COVID-19 pandemic provided a rare moment when public health interventions were adopted on a massive scale for a limited time period. A detailed regional analysis of temporal trends in RSV infections around the time of implementation and lifting of specific interventions, such as mask mandates, school closures, and travel restrictions, can provide valuable insight into the most effective strategies to prevent/mitigate future epidemics of RSV in each local context.

Not all respiratory viruses were impacted by border restrictions, especially those non-enveloped respiratory viruses (rhinovirus, enterovirus, and adenovirus). For example, although rhinovirus infections decreased (but not eliminated) during the most stringent PHSMs such as lockdown, it was less influenced by other PHSMs such as border closure and was the first virus to cause non-COVID ARI peaks in many countries including NZ.[5,33-35] Rhinovirus persisted in NZ throughout the two-year period of border

restrictions. Rhinovirus infections, responsible for more than one-half of cold-like illnesses, normally circulate year-around. Children are a major reservoir for rhinovirus infection and a key driver of transmission to adults.[36] Additionally, rhinoviruses are non-enveloped viruses so might be inherently less susceptible to inactivation by soap-and-water handwashing.[37] Moreover, rhinovirus exhibits stability with good survival on many environmental surfaces for hours after contamination.[38] Rhinovirus' non-enveloped nature, persistence in environment as well as high prevalence in population, may account for it being less affected by border restrictions.

Interestingly, PIV1 (an enveloped virus) was also less affected by border restrictions. PIV1 was probably suppressed (but not eliminated) within NZ during the most stringent PHSMs. This might lead to local transmission with a rapid increase in the spring-summer time from November 2020 to January 2021 when NZ was under border closure but PHSMs were relaxed. Unlike influenza and RSV, prolonged shedding of low levels of PIV has been documented in normal asymptomatic healthy adults[39], children[40], and immunocompromised persons.[41] Two PIV outbreaks (PIV1 & PIV3) occurred in healthy young adults 10 and 29 weeks after complete social isolation at the South Pole and were likely due to persistent low level shedding in some individuals.[39] Infants and young children have been shown to shed PIV3 for as long as 3 to 4 weeks.[40] Prolonged asymptomatic parainfluenza virus infections among hematopoietic cell transplant patients,[41] were also reported with implications for enhanced (symptomatic and asymptomatic) infection control measures, rather than symptom-based infection control strategies which have been successful in curtailing RSV and influenza outbreaks. Additionally, young children can excrete large quantities of PIV which may be viable on porous surfaces for up to 10 hours.[42,43] Evidence from studies in adult volunteers shows that the infectious dose of PIV1 is small.[44] The highly infectious nature of PIV with capability of persistent low level shedding may account for PIV1 being not eliminated by the short period (5 weeks) of the most stringent PHSMs implemented in 2020 in NZ.

In the upcoming northern hemisphere autumn and winter of 2022-2023, many temperate countries will have continuing COVID-19 circulation overlapping with the influenza/RSV season, resulting in increased burden on already stretched health systems. NZ's natural experiment showed larger-than-usual influenza/RSV outbreaks due to the preceding time interval of absent circulation and a likely resultant immunity gap (i.e. a group of susceptible individuals who avoided infection and therefore lacked recent virus-specific immunity boosting).[45] Of note, the influx of RSV cases into NZ was observed prior to widespread circulation of COVID-19 providing more evidence that the increase was due to the preceding period of limited RSV circulation rather than other COVID-19 mediated factors. Both international and domestic air travel have been suggested as important drivers of influenza introduction and subsequent spread,[46] although the significant role of international travel in RSV diffusion is still under debate.[30,47] The NZ experience provides early warnings to northern hemisphere countries that they may experience high influenza and RSV activity during their incoming winter as a result of population immunity gaps due to low virus circulation during preceding years,[48] more seeding events through increased air travel, and more social contacts with ease of COVID-19 related restrictions. Real-time pathogen and syndromic

surveillance are crucial for northern hemisphere countries to inform timely preparations by health-care systems for potential high intensity influenza/RSV epidemics.

Our study has several limitations. Firstly, all our surveillance systems were triggered when patients/participants experience acute respiratory illnesses with the subsequent collection of swab samples from them and then tested for respiratory viruses. In addition, we had no real time routine surveillance protocols for swabbing asymptomatic individuals who may have influenza/RSV infections. We plan to conduct an influenza serosurvey during 2023 for SHIVERS community cohort participants which will provide additional data on whether NZ had silent transmission of influenza during border restrictions. Secondly, the number of laboratory detections of influenza/RSV/other respiratory viruses is influenced by testing technology, instruments, reagents, priorities, demands, and human resources as was very apparent during the COVID-19 laboratory response. Additionally, those samples ordered by clinicians for hospital inpatients and outpatients during routine clinical practices were based on the clinician's judgement, rather than a systematic sampling approach. This results in selection bias. Thirdly, the NZ government set up several community-based testing centres around the country to provide access to safe and free sampling and testing for COVID-19 infections. This interrupted the usual flow and processes established for sentinel general practice-based ILI surveillance as many patients with ILI would visit these centres instead of sentinel GP clinics. This probably resulted in lower consultation and under-reporting for HealthStat's ILI syndromic rates during 2020-2022. However, specifically established SHIVERS-V GP ARI surveillance with virological testing showed that the influenza and RSV circulation pattern resembled the findings from SARI and SHIVERS-II, III, IV surveillance systems.

In conclusion, NZ's rare setting of influenza and RSV elimination in May 2020, due to stringent COVID-19 pandemic controls, allowed us to examine the impact of border restrictions and relaxations over the subsequent two-year period on influenza, RSV, and other respiratory viral infections. Our findings showed that total border closure to most non-residents, and mandatory government-managed isolation and quarantine on arrival for those allowed to enter appeared to be effective in preventing influenza and RSV spread into the NZ community. Border relaxation through quarantine free travel was quickly followed by importation of influenza and RSV into NZ. Border restrictions did not have much impact on other respiratory viruses such as rhinovirus and parainfluenza virus type 1, probably due to their suppressed (but not eliminated) transmission within NZ during stringent pandemic measures. Our data provide important insights into the role of border restrictions in managing future pandemic threats against influenza and other severe respiratory viruses, and into the global circulation and epidemiology of human respiratory pathogens. These 'real-world' data can also facilitate future modelling studies by providing the precision and accuracy of predictions for the timing and severity of seasonal influenza, RSV, and other respiratory viral outbreaks.

Online content

Any methods, additional references, supplementary information, acknowledgements, details of author contributions, competing interests, and disclaimer are available online.

Methods

Hospital-based severe acute respiratory infection (SARI) surveillance

The population-based hospital SARI surveillance among residents (catchment population of one million people across the central, east, and south of the Auckland region) was established in 2012 as the first iteration of the Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance (SHIVERS-I) study.[49,50] Active surveillance period for ICU was all-year-around and for general medical wards usually during May to September of each year but started early from 7-February-2022 due to COVID-19 community transmission. Research nurses working in secondary and tertiary care hospital settings usually reviewed daily records of all overnight general medical wards and ICU admitted acute inpatients to identify any inpatient with a suspected acute respiratory illness. The research nurses enrolled those patients with cough and history of fever (subjective fever or measured temperature ≥38°C) and onset within the past 10 days, defined by the WHO as SARI. A respiratory specimen (nasopharyngeal or nasal or throat swab) was collected and tested simultaneously by nucleic acid amplification tests (NAAT) specifically for:[50] influenza virus, RSV, rhinovirus, parainfluenza virus types 1-3, enterovirus, adenovirus, human metapneumovirus.

SHIVERS-II, III, IV community cohort acute respiratory infection (ARI) surveillance

SHIVERS-II (the second iteration of SHIVERS) is a prospective adult cohort study in the Wellington region, NZ.[5] The aim is to understand how adult's prior influenza exposure influences their subsequent influenza infections or vaccinations. The cohort study has been in operation since 2018 enrolling individuals aged 20-69 years, randomly selected from those healthy individuals listed in the management systems of selected primary care general practices. The study staff followed up SHIVERS-II adult participants (approximately 1400 in 2020, 1100 in 2021, and 900 in 2022) and monitored them for their ILI and ARI episodes.

SHIVERS-III is a prospective infant cohort study for seven years (2019-2026) situated in Wellington, NZ.[5] The study aims to understand how a child's first influenza exposure shapes their immune responses to subsequent influenza exposures. The study staff followed up infant participants (approximately 80 in 2020, 300 in 2021, and 600 in 2022) and monitored them for their ILI and ARI episodes.

SHIVERS-IV is a prospective household cohort study which follows approximately 500 Wellington families (approximately 1800 participants) for up to seven years (2021-2028), aiming to understand transmission of and susceptibility to influenza virus. The study staff followed up household participants (approximately 1000 in 2021 and 1700 in 2022) and monitored them for their ILI and ARI episodes.

The active surveillance period for each of these community studies occurs usually May to September of each year. In 2022, surveillance started early from 7-February due to COVID-19 community transmission. During active surveillance, the study staff sent weekly surveys to participants regarding their ARI. Research nurses reviewed participant's symptom reports and identified those met ARI case definition: "an

acute respiratory illness with fever or feverishness and/or one of following symptoms (cough, running nose, wheezing, sore throat, shortness of breath, loss of sense of smell/taste) with onset in the past 10 days". Research nurses guided the participant with ARI to take a nasopharyngeal or nasal swab to test by NAAT for influenza, RSV, rhinovirus, parainfluenza virus types 1-3, enterovirus, adenovirus, human metapneumovirus, and SARS-CoV-2.[51]

HealthStat's sentinel general practice (GP)-based influenza like-illness (ILI) surveillance and SHIVERS-V sentinel GP-based ARI surveillance

HealthStat general practice (GP) based ILI surveillance is based on a nationally representative random sample of approximately 300 general practices that use ILI Read codes.[5,52] The case definition used for ILI by HealthStat is "an acute upper respiratory tract infection, with abrupt onset of two or more symptoms from chills, fever, headache and myalgia". This surveillance system monitors the number of people who consult GPs with an ILI. HealthStat is based on automated extracts from practice management computer systems. ESR received the data during 2019-2022 from CBG Health Research Ltd and published the weekly data on ESR's website.[53] HealthStat ILI surveillance did not include virological surveillance.

SHIVERS-V sentinel GP-based ARI surveillance (from eight sentinel general practices in Auckland, Wellington, and Dunedin) was established in the middle of June 2021. The participating general practitioners and practice nurses assessed all consultation seeking patients. If a patient met the ARI case definition (the same as SHIVERS-II, III, IV ARI). A respiratory specimen (nasopharyngeal or nasal swab) was collected to test by NAAT for SARS-CoV-2, influenza, RSV, rhinovirus, and other respiratory viruses.

SHIVERS-V traveller ARI surveillance

SHIVERS-V traveller ARI surveillance was established on 10-May-2021 and was operational until 27-Feb-2022. All travellers staying in 32 mandatory government-managed isolation and quarantine (MIQ) facilities were required to test for COVID-19. SHIVERS-V traveller ARI surveillance included five hospital-based laboratories covering 29 MIQ facilities. A daily electronic extract from the COVID-19 éclair (https://www.sysmex-ap.com/product/eclair/) database was generated for each participating hospital laboratory to identify any traveller with a suspected acute respiratory infection who may meet the ARI case definition (the same as SHIVERS-V GP ARI). If there was any left-over specimen after the SARS-CoV-2 testing, the specimen was tested by NAAT for influenza, RSV, rhinovirus, and other respiratory viruses.

Laboratory-based surveillance

The laboratory-based surveillance for influenza, RSV and other common respiratory viruses is carried out all-year-around by the NZ virus laboratory network consisting of the WHO National Influenza Centre (NIC) at ESR and six hospital-based laboratories in Auckland (2), Waikato, Wellington, Christchurch, and Dunedin. This laboratory network tests specimens ordered by clinicians for hospital inpatients and outpatients during normal clinical practice (serving approximately 70% of the NZ population). Sample

collection is based on clinician's judgement, rather than a systematic sampling approach. This may introduce selection bias. In addition, this laboratory network conducts testing for public health surveillance including SARI, ILI/ARI, and SHIVERS-II, III, IV cohort surveillance.

Genome sequencing and assembly

RSV genomes were sequenced using the Illumina (USA) Respiratory Virus Oligo Panel V2 from total RNA purified using the MagMax™ Viral/Pathogen Nucleic Acid Isolation Kit from ThermoFisher Scientific (cat #A48310). Consensus based assembly was performed using Seattle Flu Assembly Pipeline modified to use with the ESR compute infrastructure (https://github.com/seattleflu/assembly). Two additional references were used for consensus calling. These are GISAID assemblies EPI_ISL_2543807 and EPI_ISL_2543850. Both were recent genomes from samples isolated in Australia. For each sample the consensus genome with fewest number of ambiguities were used for downstream analysis.

Phylogenetic analysis of RSV

RSV sequences from NZ were analyzed together with all global RSV full genomes sampled between January 2012 and September 2022, which were obtained from GISAID[54] (September 2022; see Supplementary Data for accession numbers). This resulted in 1,359 RSV-A global genomes and 1,259 RSV-B global genomes, including 428 and 242 Australian sampled genomes, respectively. Genomes for each subtype were aligned using MAFFT(v 7),[55] using the FFT-NS-2 algorithm. A maximum likelihood phylogenetic tree was estimated using IQ-TREE (v 2.0.3),[56] utilising the Hasegawa-Kishino-Yano (HKY+Γ)[57] nucleotide substitution model with a gamma distributed rate variation among sites. The best fit model was determined by ModelFinder,[58] and branch support assessment using the ultrafast bootstrap method.[59] To depict virus evolution in time, we used Least Squares Dating implemented within IQ-TREE to estimate a time-scaled phylogenetic tree using the day of sampling.

Data analyses

Study data were captured using REDCap 10.0.19 electronic data capture tools.[60] Analyses were performed in Stata 16.1 (StataCorp LLC).

The observed incidence rates of influenza-PCR-confirmed SARI or ARI or ILI were corrected each week to account for missed swabs from ARI cases by applying the influenza positivity rate of those tested to those not tested (corrected number of influenza-PCR-confirmed SARI or ILI or ARI events = Number of SARI or ILI or ARI x Actual number of influenza-PCR-confirmed SARI or ILI or ARI /Actual number of SARI or ILI or ARI swabs).

Based on SARI and ARI surveillance data from 2015-2019, the start of the annual influenza season and intensity level of the influenza epidemics was defined by using the Moving Epidemic Method (MEM).[52,61,62] Briefly, MEM has three main steps: Step 1: for each season separately, the length of the epidemic period is estimated as the minimum number of consecutive weeks with the maximum

accumulated percentage rates, splitting the season into three periods: a pre-epidemic, an epidemic, and a post-epidemic period; Step 2: MEM calculates the epidemic threshold as the upper limit of the 95% one-sided confidence interval of 30 highest pre-epidemic weekly rates, the n highest for each season taking the whole training period, where n = 30/number of seasons; Step 3: medium, high, and extra-ordinary intensity thresholds were estimated as the upper limits of the 40%, 90%, and 97.5% one-sided confidence intervals of the geometric mean of 30 highest epidemic weekly rates, the n highest for each season taking the whole training period, where n = 30/number of seasons. Five categories are used to set thresholds and define intensity level as no activity or below epidemic threshold, low (0-40%), moderate (40-90%), high (90-97.5%) and extra-ordinary (>97.5%) one sided confidence interval of the geometric mean.

Laboratory-based surveillance data used the median of the annual total of the specified week period over the years 2015-2019 to represent the reference period for that week period. Median and interquartile ranges were calculated for the number of viruses reported during 2015-2019; Percentage of reduction = {1 - [No. virus/median no. virus (2015-2019)]} x100.

Declarations

Data availability

Anonymised raw data and Stata syntax were used to produce all the analyses, figures, and tables. Source data are provided with this manuscript. All requests for raw and analysed data will be reviewed by the corresponding authors to verify whether the request is subject to any intellectual property or funder or confidentiality obligations. Genomic data generated in this study is available under NCBI accession numbers pending. Global genomes accession numbers are provided in Supplementary Data.

Ethical approval

Ethical approval was obtained for the SHIVERS (including SARI and ILI/ARI surveillance), SHIVERS-II, III, IV cohort studies and SHIVERS-V surveillance from the NZ Northern A Health and Disability Ethics Committee (NTX/11/11/102). The laboratory-based respiratory virus surveillance data are part of public health surveillance in NZ. This surveillance is conducted in accordance with the Public Health Act and thus ethics committee approval was not needed for collection or use of these data.

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resource has no role in study design, collection, analysis, or interpretation of data; writing of reports; nor decision to submit papers for publication.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US National Institute of Allergy and Infectious Diseases, the Institute of Environmental Science and Research (ESR), the University of Auckland or any other collaborating organisations.

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Authors' contributions:

All authors meet the International Committee of Medical Journal Editors criteria for authorship. QSH, NT, PM, NA, SJ, TD, AT, CB, MB, CM, CCG, AN, HCD, PCS, KD, SR, CM, CW, MGB, PT, MAW, RW designed and operationalised the SARI, and/or SHIVERS-I, II&III&IV&V platforms; JDL, LJ, CET, UR, KB, MO, KVDW, GM, HA, MD, JF, AW, JE, JG, MA, NZ, CM provided the testing and reporting; RS, TJ, MR, JC, EC, JJ, EP, NA, CY, MM, AA did the clinical data and samples collection, weekly data management and analysis, reporting and operations; TW, JG, QSH did the data analysis for this manuscript; QSH wrote the first draft of the manuscript. All authors contributed to the interpretation of the results, revision of the manuscript critically for intellectual content and have given final approval of the version to be published.

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Competing interests

The authors declare that they have no competing interests

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Table

Table 1 is available in the Supplementary Files section

Figures

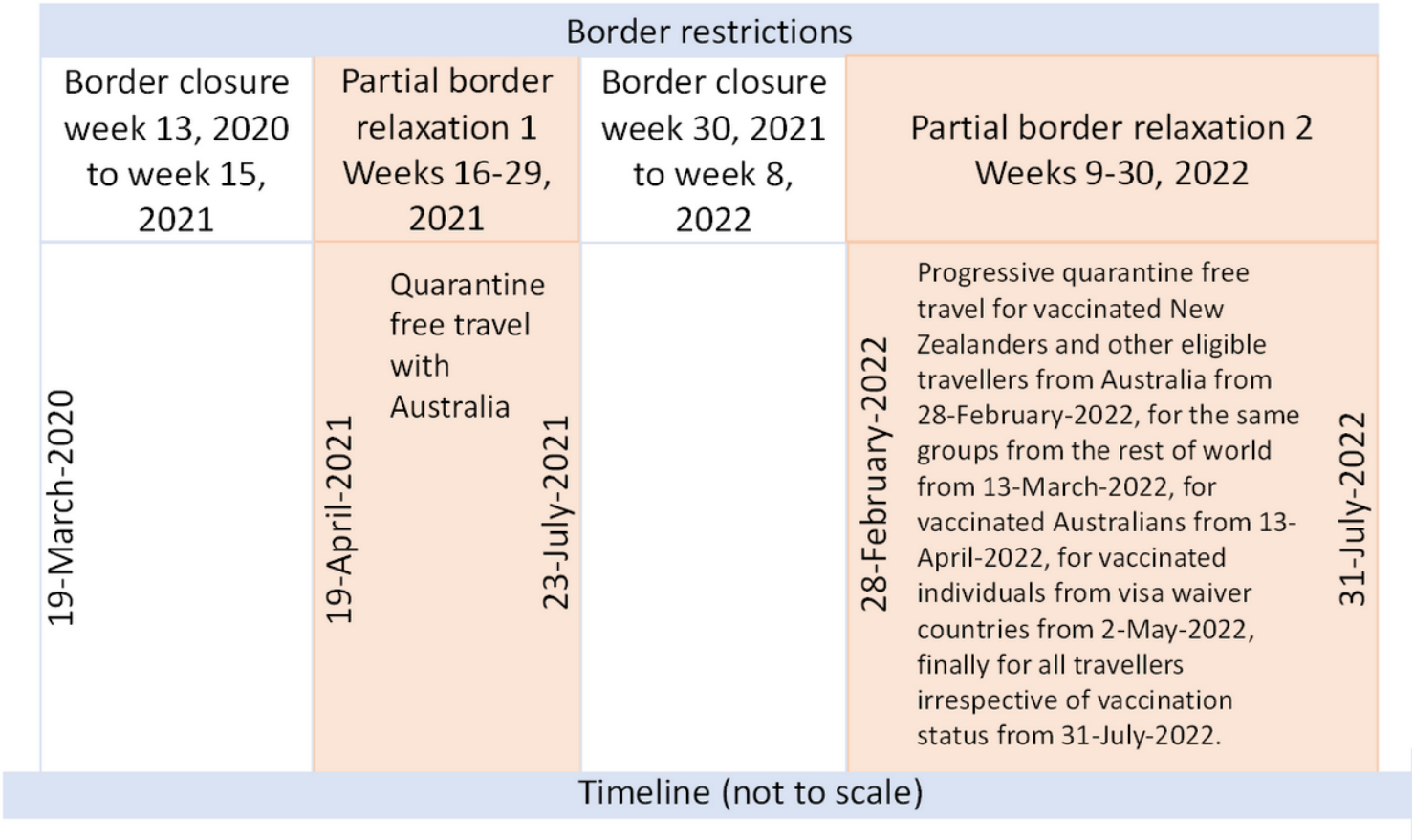

Figure 1

Timeline of New Zealand's border restrictions

*Footnote for 'Border closure'= borders close to all but New Zealand citizens and permanent residents. For those allowed to enter, they are required to comply with mandatory government-managed isolation and quarantine (MIQ) in designated facilities on arrival.

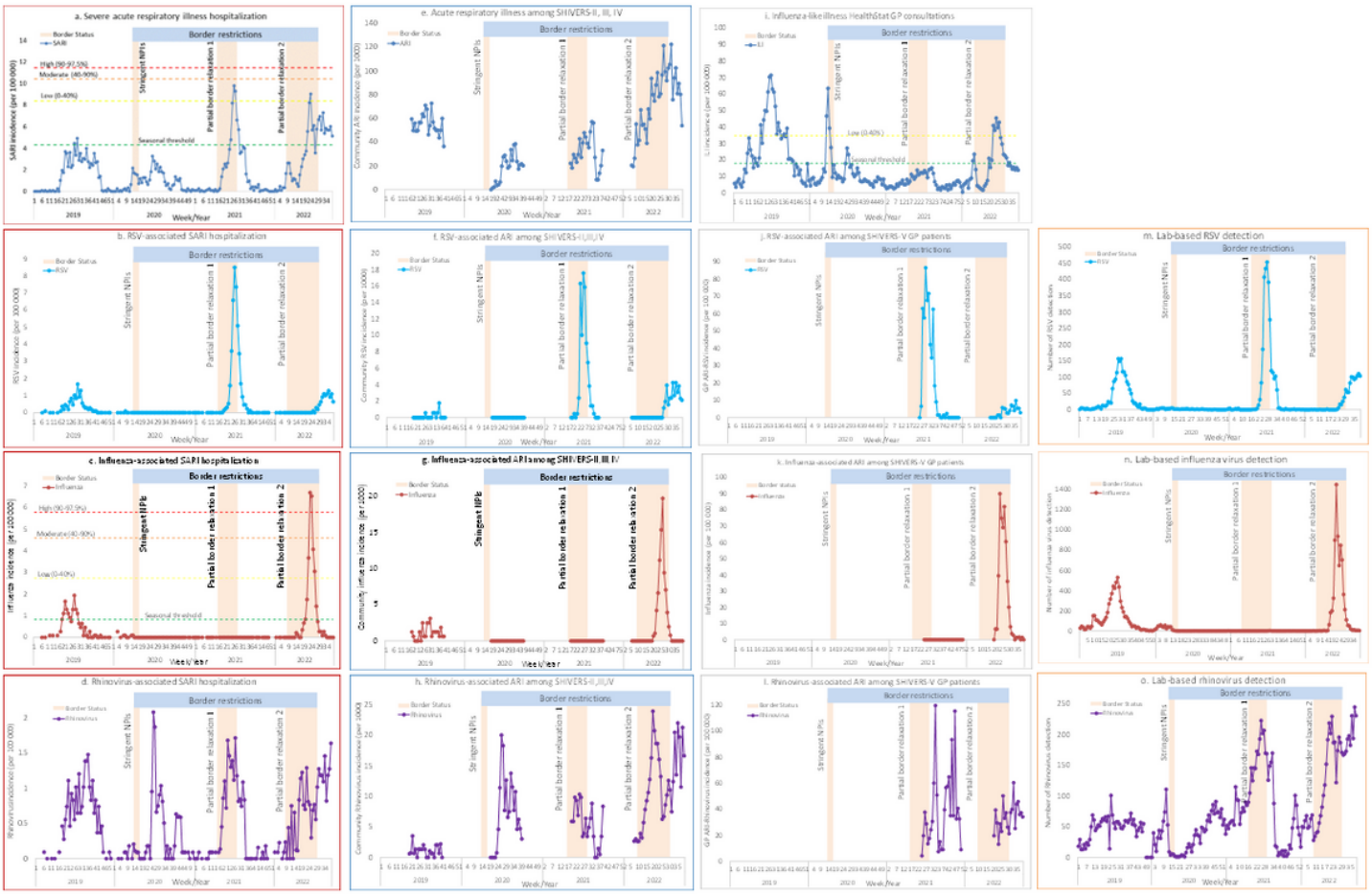

Figure 2

Temporal distribution of acute respiratory infections (ARI) and associated influenza, RSV, and rhinovirus detections with (2020-2022) and without (2019) border restrictions. a,b,c,d Hospital-based severe acute respiratory infection (SARI) incidence rate, RSV (respiratory syncytial virus)-associated SARI, influenza-associated SARI, and rhinovirus-associated SARI. **e,f,g,h** SHIVERS-II&III&IV cohort-based ARI incidence rate, RSV-associated ARI, influenza-associated ARI, and rhinovirus-associated ARI. **i,j,k,l** ILI consultations among HealthStat GP patients, RSV-associated ARI, influenza-associated ARI, and rhinovirus-associated ARI among SHIVERS-V GP patients. **m,n,o** Laboratory-based RSV, influenza, rhinovirus detection. SARI severe acute respiratory infection, GP general practice, ILI influenza-like illness, ARI acute respiratory infection, SHIVERS-II&III&IV&V-the 2nd, 3rd, 4th, 5th iterations of the Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance programme. The calculation for epidemic threshold and influenza activity are described in the Methods. A patient with cough and history of fever (subjective fever or measured temperature ≥38°C) and onset within the past 10 days meets the SARI case definition if hospitalised. The ARI case definition among SHIVERS-II&III&IV&V participants refers to an “acute respiratory illness with fever or feverishness and/or one of following symptoms (cough, runny nose, wheezing, sore throat, shortness of breath, loss of sense of smell/taste) with onset in the past 10 days.” Partial border relaxation 1 refers to brief introduction of quarantine free travel with Australia during 19-April-2021 to 23-July-2021. Partial border relaxation 2 refers to progressive border relaxation between 28-

Feburary-2022 to 31-July-2022. Introduction of quarantine free travel initially for vaccinated New Zealanders from Australia on 28-Feburary-2022 and for the same groups from the rest of the world on 13-March-2022, then for vaccinated Australians from 13-April-2022 and vaccinated travellers from NZ's visa-waiver countries from 2-May-2022 onwards.

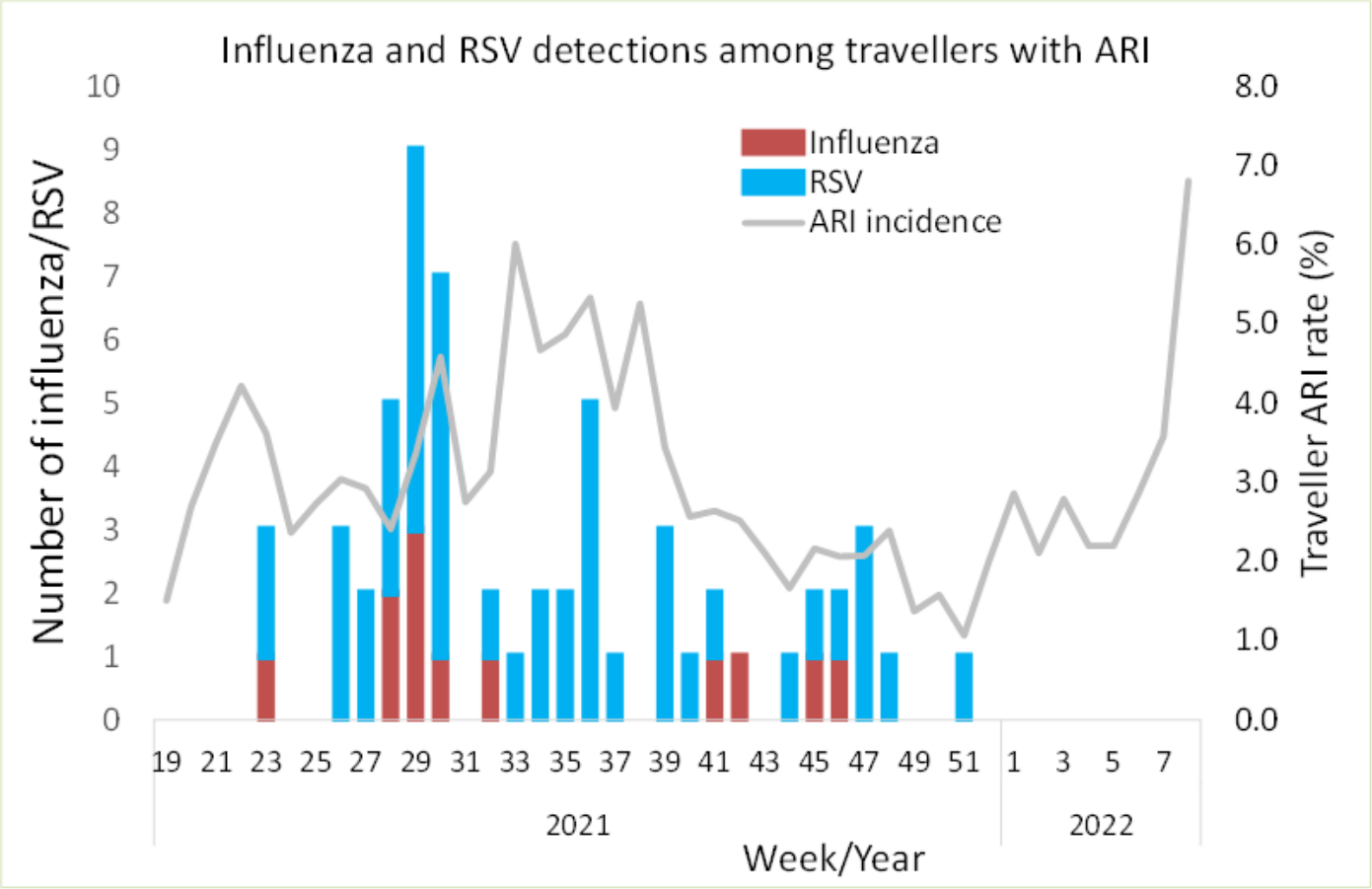

Figure 3

Temporal distribution of influenza and respiratory syncytial virus (RSV) associated acute respiratory infections (ARI) among travellers during 2021-2022. The ARI case definition among travelers refers to an "acute respiratory illness with fever or feverishness and/or one of following symptoms (cough, running nose, wheezing, sore throat, shortness of breath, loss of sense of smell/taste) with onset in the past 10 days."

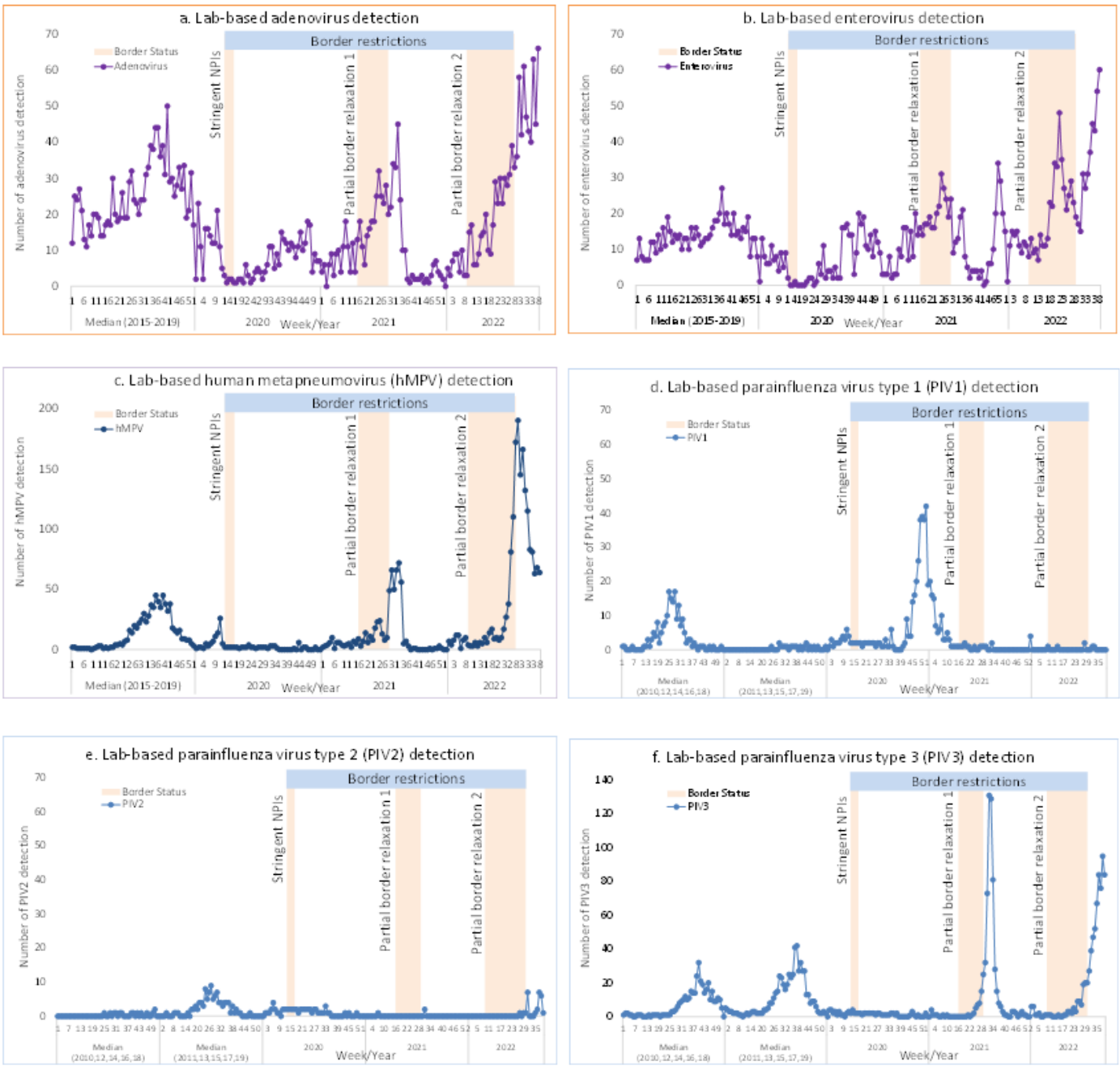

Figure 4

Temporal distribution of other respiratory viral detections during 2020-2022 compared with the reference period of 2015-2019 for adenovirus, enterovirus, and human metapneumovirus (hMPV) or the reference period of even-numbered* years (2010, 12, 14, 16, 18) or odd-numbered* years (2011, 13, 15, 17, 19) for parainfluenza virus types 1-3. **a** Lab-based adenovirus detection. **b** Lab-based enterovirus detection. **c** Lab-based human metapneumovirus (hMPV) detection. **d** Lab-based parainfluenza virus type 1 (PIV1) detection. **e** Lab-based parainfluenza virus type 2 (PIV2) detection. **f** Lab-based parainfluenza virus type 3 (PIV3) detection.

(*Note: In NZ, PIV1 activity occurred during even-numbered years while PIV2 activity in odd-numbered years and PIV3 activity annually. For laboratory-based PIV1-3 detections during 2003-2022, see Supplementary Figure)

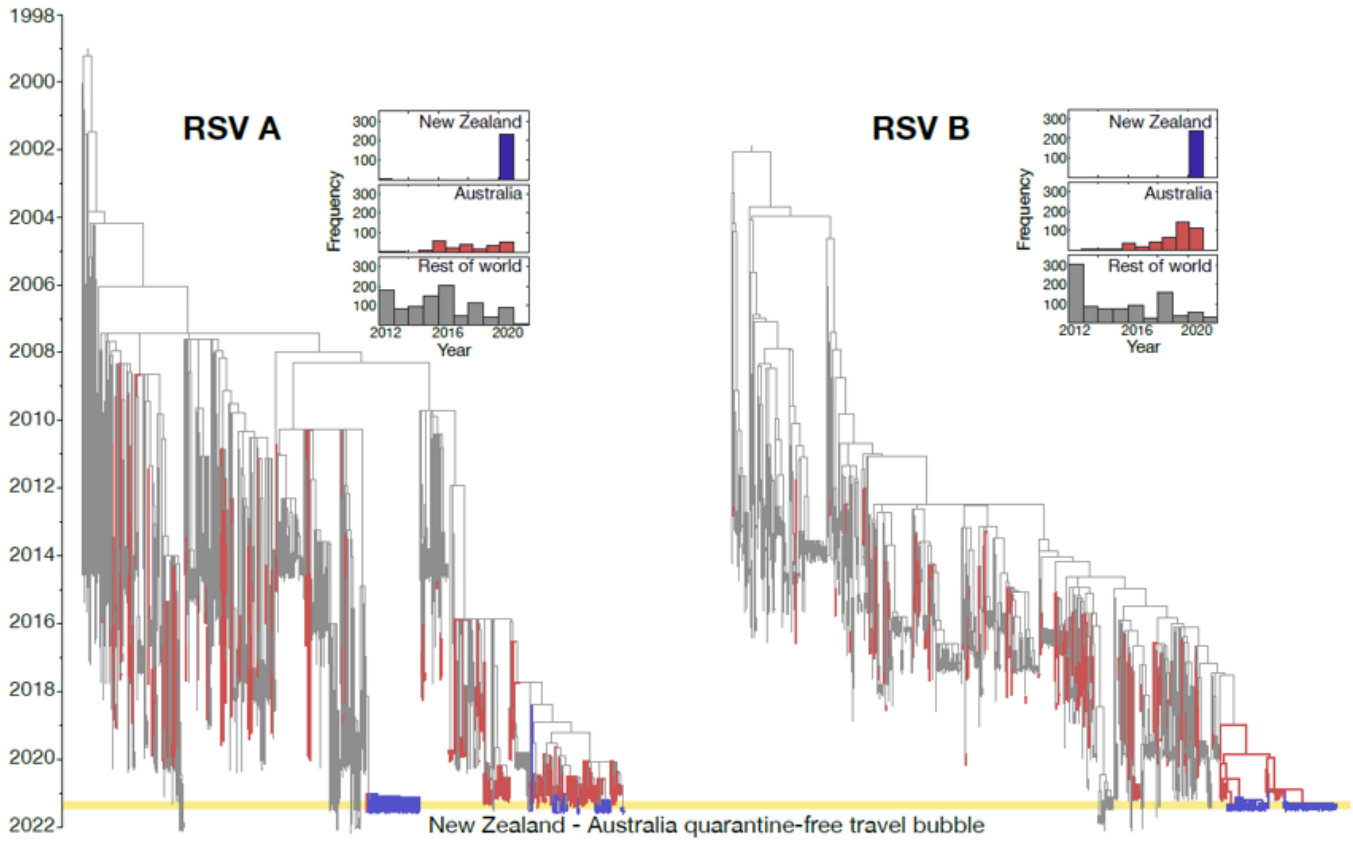

Figure 5

Maximum-likelihood time-scaled phylogenetic analysis of 237 and 230 RSV-A and RSV-B genomes, respectively, sampled from New Zealand (blue lines) on a background of globally available data sampled from Australia (red lines) and the rest of the world (grey lines). The 2021 quarantine-free travel 'bubble' with Australia is indicated as well as the frequency of genomes sampled from New Zealand, Australia, and the rest of the world over time

Supplementary Files

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