nature portfolio

Peer Review File

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

Corresponding Author: Professor Jemma Geoghegan

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
Jelley et al. conduct a phylodynamic analysis of RSV genomes collected in New Zealand (NZ) from 2015 to 2022 to better understand the impact of COVID-19 non-pharmaceutical interventions (NPIs) on RSV transmission patterns. Leveraging a multi-center cohort across NZ hospital and community-based settings, the authors identified a reduction of RSV genetic diversity after the easing of COVID-19 NPIs in 2021. Phylodynamic analyses suggest RSV-A and RSV-B were introduced from Australia during a period when international travel in the region was permitted. By linking case count to basic demographic information such as age and sex, the authors also identified a shift in age distribution after 2020 in support of the theory of an increased naïve population due to decreased RSV exposure.

While the study does a fair job describing the dynamics of RSV spread in NZ over the time frame, it remains largely descriptive and largely echoes the findings of similar studies, though admittedly in a different geographical region. These are largely based on a small set of phylodynamic analyses, which make some technical assumptions that could greatly influence the results (i.e., allowing up to 50% ambiguity in sequences). While the conclusions are consistent with the data presented, oftentimes more information would need to be included to make the inferences drawn. For example, case count alone is rarely sufficient for prevalence in the absence of diagnostic testing and/or percent positivity data. Overall, there are several limitations that the study would need to address to be suitable for publication.

Major Concerns:

1) Methods in Sequence Analysis: “Consensus viral genomes were generated, and subject to quality testing, and those with fewer than 50% ambiguities were selected for further analysis” (Lines 150 -159). The manuscript does not specify the type of quality testing performed on the generated RSV genomes. Furthermore, the broad range of coverage (50 – 100%) among the sequences raises concern for the accuracy of groupings identified in the phylogenetic analysis. It is difficult to infer a reliable phylogeny without knowing the distribution of genome coverage and whether low-coverage sequences drive clustering due to trends in sequencing missingness.

2) Cluster Definition: The lineage classifications and definitions for the tightly defined clusters are never mentioned in the results or methods section. The use of statistical methods to indicate strong support of the clusters across subtypes is needed (Lines 269 – 270).

3) Specimen Description: Several key descriptors of specimens (i.e., specimen type) are missing. A demographics table summarizing critical elements of specimens by year would be massively helpful in identifying potential biases of the dataset (i.e., sex, age, subtype, source, region, etc.).

4) Inferences about Epidemiological Patterns: The authors repeatedly claim that RSV was essentially eliminated from NZ based on case counts and sequence analysis alone (i.e., line 238). Several changes to the paper would need to be made to support this claim:
a. The authors discuss point-of-care testing shifts, but show no data on testing or percent positivity, which would be required

to interpret case count data effectively. There is furthermore no data or background references to discuss the existing testing practices in New Zealand before the COVID-19-associated non-pharmaceutical interventions (Lines 251 – 255).
b. No other data is provided on the other NPIs in place in NZ with the exception of border closings. Much more context for which NPIs were enforced when would be needed to assess the likelihood that all RSV transmission was halted in the country.
c. The emergence of an RSV-A cluster of unknown origin seems most consistent with continued transmission in the country and lack of sufficient surveillance due to relative undersampling in 2018 and 2019 and lack of any positive specimens sequenced in 2020. More sequence data from the timeframe preceding the shutdown would be needed to better assess this claim.

5) Diversity section: “Nevertheless, this reduced genetic diversity was seemingly short-lived with more widespread lineages reappearing by 2022…” This section in general lacks support and figure call outs. The text does not describe the widespread lineages that reappear in Figures 2 and 3. Since the central theme of the manuscript ties increased migration to increased genetic diversity, these lineages should be described in more depth (Lines 368 – 370).

6) Manuscript Structure: The manuscript has no clear distinction between results and discussion, which makes it very hard to discern findings from speculation and interpretation. The Figures are referred to in general with no figure panel call outs. There is no Limitations section.

7) Takeaway Message: The findings of this study largely parallel reports of other groups, though in a distinct geographical region. The authors should do more to emphasize the novelty of their findings and how their data specifically and uniquely contributes to the field and what is known about RSV spread over the pandemic.

Minor Concerns:

1) Data Accessibility: Although the author provides GISAID sequence accession numbers, GISAID accessibility is oftentimes limited. Providing NCBI accession numbers in addition to the GISAID IDs can improve accessibility and transparency when searching for global genomes. (Lines 150 – 159 & Supplementary Table 2).

2) Sequence Selection Criteria: Selection criteria (time range, genome length, search terms of global RSV genomes for genomic diversity inferences are not included) (Line 173). Please additionally elaborate on the uniform sampling method and splitting methods for RSV phylogenetic and phylodynamic analysis, as they are only briefly mentioned in the text (Lines 175 – 176, 186 – 187).

3) Missing Statistics: There are no statistical analyses performed to verify whether there are statistically significant changes across age distribution per year in RSV-A and RSV-B (Supplementary Figure 1).

4) Specimen Description: The sample collection section does not specify the kind of viral samples (swabs, bronchoalveolar lavages, nasal scrapings) used for RSV sequencing (Lines 121 – 136).

5) Inference on Severity: “Severity of RSV infections can be inferred by the surveillance platform from which the sample originated…vast majority of genomes were most likely generated from severe infections.” (Line 217 – 218 | 256 -257). Patients served in hospital settings vary widely, therefore broad sample origin classifications are not sufficient to make claims about disease severity. The author even acknowledges later that changes in testing practices have broadened age distribution and may have lead to the inclusion of less severe cases.

6) Subtype Circulation: “Both RSV-A and RSV-B co-circulated each year in relatively even prevalence” (Line 215 | Figure 1). It is unclear whether the text is referring to the generated genomes or if it is referring to the total number of reported cases on the bottom panel of 1A. If referring to the latter, subtyping information prevalence should be depicted more clearly somewhere in the figure.

7) Missing Data Source: The source of data used to generate Figure 4a is not provided in the figure nor the methods section.

8) Missing Scale Bars: There are no scale bars provided for the maximum likelihood of time-scaled phylogenetic trees.

9) Histogram: The histogram in Figure 1f is hard to see and interpret.

Reviewer #2

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

Reviewer #3

(Remarks to the Author)
Jelly et al conducted a phylodynamic study to characterise RSV transmission patterns in New Zealand prior to and after the

COVID-19 pandemic, by collecting 1,471 viral genomes of RSV-A and RSV-B from 2015 and 2022 from across New Zealand and using global genomes from GISAID. Using phylodynamic analysis, they found that several large genomic clusters of RSV-A and B genomes in the large epidemics of RSV in 2021, which were temporally associated with the increase of migration due to quarantine-free travel from Australia. They also found that the closest genetic relatives to the New Zealand RSV genomes were viral genomes sampled in a large, off-season summer outbreak earlier occurring in Australia. They also found a major reduction in RSV genetic diversity compared to pre-pandemic seasonal outbreaks. These RSV genomic data offer important insights into the transmission patterns and trajectories of RSV after NPIs were eased, and the impact of international travel-related interventions on RSV transmission. Several questions remain to be addressed and clarified to improve the paper.

1. L189-191: This sentence regarding sampling the global genomes is not clear. Do you mean that “to ensure geographical representativeness of subsamples” instead of “to correct for geographical biases on GISAID”? Not sure if the inherent biases in the original data could be addressed by sampling. How many iterations of sampling were done? Do you sample the country with replacement? Please clarify in the text.
2. Figure 4: what is the unit of the migration rates of RSV-A and B into NZ over time? per arrival per day, or per day? Please clarify. One would expect the introductions would peak after the travel restrictions were eased, yet they peaked at the very beginning of the lift of travel restrictions, and gradually reduced during the period. Please add details to clarify or discuss this.
3. Figure 4: From what sources were the arrival and departure data obtained? from data or from model? Please clarify in the text.
4. L252-257, L337-338: Although it is not a primary aim of this study, it would still be helpful to provide information on changing testing regimes in the text or supplementary files, such as number of specimens that were tested, preferably stratified by age groups and time (stratified by year or timing of NPIs).
5. L342-344: The spatial transmission dynamics of RSV over time from abroad to New Zealand show that easing travel restrictions led to a rise in RSV importations and increased local RSV transmission. Assuming that not all the infections were due to the importations, would it be feasible to estimate the contribution of the importations and subsequent generations of infections in the epidemic?
6. Note that the genome data were collected from across different regions across New Zealand. Would it be feasible to further examine the transmission trajectories of RSV within New Zealand using temporal and spatial information?
7. L367-368: Could the travel restrictions be a factor for the little genomic diversity in circulating RSV viruses? The travel restriction policy could influence the sources of importations, by taking different policies for arrivals from Australia versus other countries.

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
We appreciate the authors’ revisions, especially the addition of bootstrapping values to lend statistical support to their findings, the addition of other diversity metrics, the inclusion of a specimen characteristics table, the improved contextualization of their finding, and their deposition of data in a BioProject. While a majority of initial concerns were addressed, there are a couple of outstanding issues that must be addressed prior to publication.

1) Lines 170-179: “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).” We appreciate the clarification of this point, which is bolstered by the addition of the bootstrapping values. While I would advocate for the removal of specimens with less than 90% coverage, I know that repeating these analyses can be computationally burdensome. As a compromise, and to ensure that readers can visualize this directly, please add a supplementary figure that shows a distribution of sequence coverage among the samples included in this study.

2) Lines 340-346: “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 (Figure 2). Due to the increased testing regimes coupled with managed quarantine at the border for all arrivals besides those from Australia and the South Pacific, 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.” It is fine that we disagree with the interpretation of these data. Given the limited sequencing information included in this study from 2018 and 2019 and the lack of a nearest common ancestor from Australia or another region of the South Pacific, I still believe that the origin of the emergent RSV-A strain in 2021 cannot be inferred. Without a clear discussion section, it is important that this point is thoroughly discussed and identifiable as speculation. Please expand on this in the text to include the points raised in your rebuttal.

3) Lines 293-295: “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).” We appreciate the addition of this table, but its usability for cross-comparisons would be greatly enhanced by adding percentages to each category [i.e., #(%)] and by adding a total

column at the far right. Also not that the cited statistic seems exclusive to this one comparison. Broader statistical comparisons are still lacking in Supplementary Figure 1 and Supplementary Table 3.

4) Although the text now provides more detail on the specific NPIs deployed in New Zealand in the introduction (Lines 75 – 81), no timeframe of these strategies was provided. Elaborating on whether these employed mitigation strategies were sustained throughout the pandemic or if there were breaks in between measures (such as the description of quarantine-free travel [Lines 90 – 103]) would provide more context for international readers.

5) Line 253-256: “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 (Figure 1).” To further corroborate the study’s conclusions and aforementioned inferences, the composition of hospital-based surveillance isolates should be stratified by the different listed categories (i.e., outpatient, inpatient, ICU, etc.). Since hospital systems may reinforce testing requisites/standards that do not directly correlate to the patient’s clinical severity, additional stratification and caveat is needed.

6) Manuscript Structure: The authors do a better job at differentiating between results and speculation and I will defer to the editors if it is sufficient. Similarly, they have added some discussion of their limitations. However, I would again ask that the authors please call out each figure panel in the text to help the reader follow along with their argument and to direct their attention to specific analyses.

Reviewer #2

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

Reviewer #3

(Remarks to the Author)
The authors have addressed my comments, and I have no further comments.

Response to Reviewers' Comments

Reviewer 1

Jelley et al. conduct a phylodynamic analysis of RSV genomes collected in New Zealand (NZ) from 2015 to 2022 to better understand the impact of COVID-19 non-pharmaceutical interventions (NPIs) on RSV transmission patterns. Leveraging a multi-center cohort across NZ hospital and community-based settings, the authors identified a reduction of RSV genetic diversity after the easing of COVID-19 NPIs in 2021. Phylodynamic analyses suggest RSV-A and RSV-B were introduced from Australia during a period when international travel in the region was permitted. By linking case count to basic demographic information such as age and sex, the authors also identified a shift in age distribution after 2020 in support of the theory of an increased naïve population due to decreased RSV exposure.

While the study does a fair job describing the dynamics of RSV spread in NZ over the time frame, it remains largely descriptive and largely echoes the findings of similar studies, though admittedly in a different geographical region. These are largely based on a small set of phylodynamic analyses, which make some technical assumptions that could greatly influence the results (i.e., allowing up to 50% ambiguity in sequences). While the conclusions are consistent with the data presented, oftentimes more information would need to be included to make the inferences drawn. For example, case count alone is rarely sufficient for prevalence in the absence of diagnostic testing and/or percent positivity data. Overall, there are several limitations that the study would need to address to be suitable for publication.

Major Concerns:

1) Methods in Sequence Analysis: "Consensus viral genomes were generated, and subject to quality testing, and those with fewer than 50% ambiguities were selected for further analysis" (Lines 150 -159). The manuscript does not specify the type of quality testing performed on the generated RSV genomes. Furthermore, the broad range of coverage (50 – 100%) among the sequences raises concern for the accuracy of groupings identified in the phylogenetic analysis. It is difficult to infer a reliable phylogeny without knowing the distribution of genome coverage and whether low-coverage sequences drive clustering due to trends in sequencing missingness.

Response: *We thank the reviewer for their helpful comment. While the criteria for either accepting or rejecting genomes has a maximum limit of 50% ambiguities, in reality, this percentage is much lower. Among the genomes that were selected for further analysis, the median coverage was 99.95%, 80% of these genomes had <1% ambiguities, meaning that most were of very high quality. The high bootstrap supports now displayed in Figures 2 and 3 further corroborate the notion that there is a strong signal in the data, despite such using a lenient threshold for sequence ambiguity.*

2) Cluster Definition: The lineage classifications and definitions for the tightly defined clusters are never mentioned in the results or methods section. The use of statistical methods to indicate strong support of the clusters across subtypes is needed (Lines 269 – 270).

Response: *We have amended Figures 2 and 3 to show the bootstrap support values to illustrate the node support for the 2021 clusters. The Methods includes details on bootstrapping with 1000 replicates and Results has now been revised to include how these clades were defined. Indeed, these were the only clusters of New Zealand samples in 2021 and all had very high bootstrap node support. The lineage classifications (i.e. RSV genotypes) were defined in the previous version.*

3) Specimen Description: Several key descriptors of specimens (i.e., specimen type) are missing. A demographics table summarizing critical elements of specimens by year would be massively helpful in

identifying potential biases of the dataset (i.e., sex, age, subtype, source, region, etc.).

Response: *We have amended Supplementary Table 3 with additional demographic information of the specimens used in this study. The specimen type has now been included in the Methods.*

4) Inferences about Epidemiological Patterns: The authors repeatedly claim that RSV was essentially eliminated from NZ based on case counts and sequence analysis alone (i.e., line 238). Several changes to the paper would need to be made to support this claim:

a. The authors discuss point-of-care testing shifts, but show no data on testing or percent positivity, which would be required to interpret case count data effectively. There is furthermore no data or background references to discuss the existing testing practices in New Zealand before the COVID-19-associated non-pharmaceutical interventions (Lines 251 – 255).

Response: *We have included references to support changes in testing regimes during the COVID-19 pandemic. We agree with the Reviewer that such data would be helpful. In fact, we have published such data on the testing for RSV such as number of specimens that were tested and % positive each week during 2019-2022 stratified by the timing of lockdown and border restrictions (see reference: Huang et al. 2024; doi: 10.1111/irv.13247). We have now elaborated on this point in the manuscript.*

b. No other data is provided on the other NPIs in place in NZ with the exception of border closings. Much more context for which NPIs were enforced when would be needed to assess the likelihood that all RSV transmission was halted in the country.

Response: *We have now included more details of the NPIs that New Zealand put in place to stop SARS-CoV-2 transmission in the Introduction.*

c. The emergence of an RSV-A cluster of unknown origin seems most consistent with continued transmission in the country and lack of sufficient surveillance due to relative undersampling in 2018 and 2019 and lack of any positive specimens sequenced in 2020. More sequence data from the timeframe preceding the shutdown would be needed to better assess this claim.

Response: *We respectfully, but strongly, disagree with this comment. First, there were multiple, robust, surveillance systems that were either active prior to 2020 or initiated in early 2020 (see reference 15, Huang et al. 2021) and we are confident these systems would have detected RSV if it were circulating in 2020. As RSV has no known animal reservoir, RSV transmission would have needed to be sustained in the New Zealand human population for more than a year and remain undetected during a time of stringent testing for respiratory infections. Second, the basic reproductive number of RSV is estimated to be, on average, similar to SARS-CoV-2. Since the NPIs used in New Zealand successfully eliminated SARS-CoV-2, it is highly likely these NPIs would have eliminated RSV too. Finally, genome sequencing of RSV is extremely sparse on a global scale, representing only a fraction of actual cases. It is therefore much more likely that the genomes sampled in New Zealand were new introductions and that the closest genetic relatives from one of the clades were unsampled.*

5) Diversity section: "Nevertheless, this reduced genetic diversity was seemingly short-lived with more widespread lineages reappearing by 2022…" This section in general lacks support and figure call outs. The text does not describe the widespread lineages that reappear in Figures 2 and 3. Since the central theme of the manuscript ties increased migration to increased genetic diversity, these lineages should be described in more depth (Lines 368 – 370).

Response: *We thank the reviewer for their comment and we have now included a measure of genetic diversity through time with the addition of the Bayesian skyline analysis, Supplementary Figure 2, and have updated the methods section to include this analysis..*

6) Manuscript Structure: The manuscript has no clear distinction between results and discussion, which makes it very hard to discern findings from speculation and interpretation. The Figures are referred to in general with no figure panel call outs. There is no Limitations section.

Response: *We thank the reviewer for this comment, and as such we have added limitations and caveats throughout the manuscript where appropriate. Many articles in the Springer Nature-family of journals are structured in this way, indeed we have done this many times in the past, and we feel that this structure works well for the current study.*

7) Takeaway Message: The findings of this study largely parallel reports of other groups, though in a distinct geographical region. The authors should do more to emphasize the novelty of their findings and how their data specifically and uniquely contributes to the field and what is known about RSV spread over the pandemic.

Response: *We appreciate the Reviewer's opinion and therefore have added further analysis and discussion of the New Zealand context, which was unique given the elimination and reintroduction scenarios.*

Minor Concerns:

1) Data Accessibility: Although the author provides GISAID sequence accession numbers, GISAID accessibility is oftentimes limited. Providing NCBI accession numbers in addition to the GISAID IDs can improve accessibility and transparency when searching for global genomes. (Lines 150 – 159 & Supplementary Table 2).

Response: *These genomes have also been uploaded to NCBI, under Bioproject PRJNA939717.*

2) Sequence Selection Criteria: Selection criteria (time range, genome length, search terms of global RSV genomes for genomic diversity inferences are not included) (Line 173). Please additionally elaborate on the uniform sampling method and splitting methods for RSV phylogenetic and phylodynamic analysis, as they are only briefly mentioned in the text (Lines 175 – 176, 186 – 187).

Response: *We have elaborated on the random sampling methods used to clarify that this was without replacement. There were no search terms as genomes were obtained from the GISAID RSV database as stated.*

3) Missing Statistics: There are no statistical analyses performed to verify whether there are statistically significant changes across age distribution per year in RSV-A and RSV-B (Supplementary Figure 1).

Response: *We have now included a statistical test.*

4) Specimen Description: The sample collection section does not specify the kind of viral samples (swabs, bronchoalveolar lavages, nasal scrapings) used for RSV sequencing (Lines 121 – 136).

Response: *We have updated the Methods section with the information regarding sample type.*

5) Inference on Severity: "Severity of RSV infections can be inferred by the surveillance platform from

which the sample originated…vast majority of genomes were most likely generated from severe infections." (Line 217 – 218 | 256 -257). Patients served in hospital settings vary widely, therefore broad sample origin classifications are not sufficient to make claims about disease severity. The author even acknowledges later that changes in testing practices have broadened age distribution and may have lead to the inclusion of less severe cases.

Response: *While we agree that patients' severity is very broad in hospital settings, there are indeed general inferences that can be made based on hospitalisations and this is a common measure in epidemiological studies. We do not use these data in any analysis but it is important to state the major sources of genomes generated. We have included a caveat with this statement in the revised manuscript.*

6) Subtype Circulation: "Both RSV-A and RSV-B co-circulated each year in relatively even prevalence" (Line 215 | Figure 1). It is unclear whether the text is referring to the generated genomes or if it is referring to the total number of reported cases on the bottom panel of 1A. If referring to the latter, subtyping information prevalence should be depicted more clearly somewhere in the figure.

Response: *We are referring to genomes sequenced and have edited the text to clarify this point.*

7) Missing Data Source: The source of data used to generate Figure 4a is not provided in the figure nor the methods section.

Response: *We have now referenced the data source in the revised manuscript.*

8) Missing Scale Bars: There are no scale bars provided for the maximum likelihood of time-scaled phylogenetic trees.

Response: *The Reviewer is mistaken. The time scale on the x-axis is the scale, given that the branches are scaled by time.*

9) Histogram: The histogram in Figure 1f is hard to see and interpret.

Response: *We agree with this comment and have removed the vertical histogram that shows frequency leaving the box plot in place.*

Reviewer 3

Jelley et al conducted a phylodynamic study to characterise RSV transmission patterns in New Zealand prior to and after the COVID-19 pandemic, by collecting 1,471 viral genomes of RSV-A and RSV-B from 2015 and 2022 from across New Zealand and using global genomes from GISAID. Using phylodynamic analysis, they found that several large genomic clusters of RSV-A and B genomes in the large epidemics of RSV in 2021, which were temporally associated with the increase of migration due to quarantine-free travel from Australia. They also found that the closest genetic relatives to the New Zealand RSV genomes were viral genomes sampled in a large, off-season summer outbreak earlier occurring in Australia. They also found a major reduction in RSV genetic diversity compared to pre-pandemic seasonal outbreaks. These RSV genomic data offer important insights into the transmission patterns and trajectories of RSV after NPIs were eased, and the impact of international travel-related interventions on RSV transmission. Several questions remain to be addressed and clarified to improve the paper.

Response: *We thank the Reviewer for their comments.*

1. L189-191: This sentence regarding sampling the global genomes is not clear. Do you mean that "to ensure geographical representativeness of subsamples" instead of "to correct for geographical biases on GISAID"? Not sure if the inherent biases in the original data could be addressed by sampling. How many iterations of sampling were done? Do you sample the country with replacement? Please clarify in the text.

Response: *We thank the Reviewer for this suggestion and have edited the text as suggested and clarified the methodology used. As stated, we subsampled six times for both RSV-A and RSV-B.*

2. Figure 4: what is the unit of the migration rates of RSV-A and B into NZ over time? per arrival per day, or per day? Please clarify. One would expect the introductions would peak after the travel restrictions were eased, yet they peaked at the very beginning of the lift of travel restrictions, and gradually reduced during the period. Please add details to clarify or discuss this.

Response: *These units are migrations per day (not migrations per arrival per day), as displayed on the y-axes. We concur that one would expect the introductions to peak after the travel restrictions ended, rather than 1 month before. This apparent mismatch stems from a limitation in the phylogenetic method. The exact time of arrival is not estimated as part of the phylogenetic model, and instead the introduction time is plotted here as occurring anywhere along the branch that lead to the introduction. We have clarified this in the discussion.*

3. Figure 4: From what sources were the arrival and departure data obtained? from data or from model? Please clarify in the text.

Response: *We have now cited the data source and thank the Reviewer for pointing this out.*

4. L252-257, L337-338: Although it is not a primary aim of this study, it would still be helpful to provide information on changing testing regimes in the text or supplementary files, such as number of specimens that were tested, preferably stratified by age groups and time (stratified by year or timing of NPIs).

Response: *We agree with the Reviewer that such data would be helpful. In fact, we have published such data on the testing for RSV such as number of specimens that were tested and % positive each week during 2019-2022 stratified by the timing of lockdown and border restrictions (see reference: Huang et al. 2024; doi: 10.1111/irv.13247). We have now elaborated on this point in the manuscript.*

5. L342-344: The spatial transmission dynamics of RSV over time from abroad to New Zealand show that easing travel restrictions led to a rise in RSV importations and increased local RSV transmission. Assuming that not all the infections were due to the importations, would it be feasible to estimate the contribution of the importations and subsequent generations of infections in the epidemic?

Response: *We agree with the Reviewer's helpful comment and have provided an estimate of secondary cases based on the estimated number of introductions and the total number of reported cases and genomes sampled in 2021. It must be noted however that due to the nation-wide lockdown due to Delta SARS-CoV-2, the RSV epidemic was also cut short.*

6. Note that the genome data were collected from across different regions across New Zealand. Would it be feasible to further examine the transmission trajectories of RSV within New Zealand using temporal and spatial information?

Response: *While we agree that this would be useful, although the nationwide surveillance would have picked up community RSV circulation, we are not confident that the temporal and spatial nature of the sampling is conducive to such analyses. Due to this we would be very uneasy about presenting transmission trajectories.*

7. L367-368: Could the travel restrictions be a factor for the little genomic diversity in circulating RSV viruses? The travel restriction policy could influence the sources of importations, by taking different policies for arrivals from Australia versus other countries.

Response: *We agree with the Reviewer that the low genomic diversity in RSV in 2021 is due to NPIs used during the COVID-19 pandemic, not just in New Zealand but elsewhere too. We have edited the manuscript to reflect this.*

Response to Reviewers' Comments

Reviewer #1

We appreciate the authors' revisions, especially the addition of bootstrapping values to lend statistical support to their findings, the addition of other diversity metrics, the inclusion of a specimen characteristics table, the improved contextualization of their finding, and their deposition of data in a BioProject. While a majority of initial concerns were addressed, there are a couple of outstanding issues that must be addressed prior to publication.

1) Lines 170-179: "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)." We appreciate the clarification of this point, which is bolstered by the addition of the bootstrapping values. While I would advocate for the removal of specimens with less than 90% coverage, I know that repeating these analyses can be computationally burdensome. As a compromise, and to ensure that readers can visualize this directly, please add a supplementary figure that shows a distribution of sequence coverage among the samples included in this study.

Response: *We have now added Supplementary Figure 1 to show the percentage coverage across genomes used in this study.*

2) Lines 340-346: "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 (Figure 2). Due to the increased testing regimes coupled with managed quarantine at the border for all arrivals besides those from Australia and the South Pacific, 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." It is fine that we disagree with the interpretation of these data. Given the limited sequencing information included in this study from 2018 and 2019 and the lack of a nearest common ancestor from Australia or another region of the South Pacific, I still believe that the origin of the emergent RSV-A strain in 2021 cannot be inferred. Without a clear discussion section, it is important that this point is thoroughly discussed and identifiable as speculation. Please expand on this in the text to include the points raised in your rebuttal.

Response: *We have added additional discussion on this point in the revised manuscript, including the discussion in the previous response as suggested.*

3) Lines 293-295: "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)." We appreciate the addition of this table, but its usability for cross-comparisons would be greatly enhanced by adding percentages to each category [i.e., #(%)] and by adding a total column at the far right. Also not that the cited statistic seems exclusive to this one comparison. Broader statistical comparisons are still lacking in Supplementary Figure 1 and Supplementary Table 3.

Response: *We have revised Supplementary Table 3 to include these additional columns as suggested.*

4) Although the text now provides more detail on the specific NPIs deployed in New Zealand in the introduction (Lines 75 – 81), no timeframe of these strategies was provided. Elaborating on whether these employed mitigation strategies were sustained throughout the pandemic or if there were breaks in between measures (such as the description of quarantine-free travel [Lines 90 – 103]) would provide more context for international readers.

Response: *We have now added dates to provide more context on the NPIs used in New Zealand.*

5) Line 253-256: "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 (Figure 1)." To further corroborate the study's conclusions and aforementioned inferences, the composition of hospital-based surveillance isolates should be stratified by the different listed categories (i.e., outpatient, inpatient, ICU, etc.). Since hospital systems may reinforce testing requisites/standards that do not directly correlate to the patient's clinical severity, additional stratification and caveat is needed.

Response: *We only have data for all hospital (including outpatients and admissions) as well as ICU separately. We have now included the percentage of ICU in the revised Supplementary Table 3, but it is also clear from Figure 1.*

6) Manuscript Structure: The authors do a better job at differentiating between results and speculation and I will defer to the editors if it is sufficient. Similarly, they have added some discussion of their limitations. However, I would again ask that the authors please call out each figure panel in the text to help the reader follow along with their argument and to direct their attention to specific analyses.

Response: *We have now added figure panel letters to the text.*

Reviewer #2

I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

Response: *We thank the Reviewer for their helpful review of our manuscript.*

Reviewer #3

The authors have addressed my comments, and I have no further comments.

Response: *We thank the Reviewer for their helpful review of our manuscript.*