101034339 – PROMISE

Preparing for RSV Immunisation and Surveillance in Europe

WP1 – RSV epidemiology and impact of COVID-19

D1.8 Modelled impact of COVID-19 on RSV seasonality in Europe

Lead contributor	Susanne Heemskerk (8 - NIVEL)
	s.heemskerk@nivel.nl
Other contributors	Peter Spreeuwenberg (8 - NIVEL)
	Christos Baliatsas (8 - NIVEL)
	†John Paget (8 - NIVEL) † Deceased on 4 November 2023
Reviewers	Anne Teirlinck (7 - RIVM); Michiel van Boven (7 - RIVM); Philip Joosten (18 - GSK)

Document History

Version	Date	Description
V0.1	29/03/2024	First Draft
V0.2	11/04/2024	Draft after WP1 feedback
V0.3	02/05/2024	Draft after review comments
V1.0	15/05/2024	Final Version

Table of contents

Definitions

- **Participants** of the PROMISE Consortium are referred to herein according to the following codes:
    1. **UEDIN**. The University of Edinburgh (United Kingdom)
    2. **UMCU**. Universitair Medisch Centrum Utrecht (Netherlands)
    3. **UA**. Universiteit Antwerpen (Belgium)
    4. **Imperial**. Imperial College of Science, Technology and Medicine (United Kingdom)
    5. **UOXF**. The Chancellor, Masters and Scholars of the University of Oxford (United Kingdom)
    6. **THL**. Terveyden Ja Hyvinvoinnin Laitos (Finland)
    7. **RIVM**. Rijksinstituut voor Volksgezondheid en Milieu (Netherlands)
    8. **NIVEL**. Stichting Nedelands Instituut voor Onderzoek van de Gezondheidzorg (Netherlands)
    9. **TUCH**. Varsinais-Suomen Sairaanhoitopiirin Kuntayhtymä (Finland)
    10. **TEAMIT**. TEAM IT Research, S.L. (Spain)
    11. **ReSViNET**. Stichting Resvinet (Netherlands)
    12. **SSI**. Statens Serum Institut (Denmark)
    13. **SERGAS**. Servizo Galego de Saúde (Spain)
    14. **PENTA**. Fondazione PENTA - For the treatment and care of children with HIV and related diseases - ONLUS (Italy)
    15. **FISABIO**. Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (Spain)
    16. **MLU**. Martin-Luther-Universitaet Halle-Wittenberg (Germany)
    17. **SP**. Sanofi Pasteur, S.A. (France)
    18. **GSK**. GlaxoSmithKline Biologicals, S.A. (Belgium)
    19. **JANSSEN**. Janssen Pharmaceutica, N.V (Belgium)
    20. **Novavax**. Novavax, Inc. (United States)
    21. **Pfizer**. Pfizer Limited (United Kingdom)
    22. **AZ**. AstraZeneca AB (Sweden)

- **Grant Agreement**. (Including its annexes and any amendments) The agreement signed between the beneficiaries of the action and the IMI2 JU for the undertaking of the PROMISE project (Grant Agreement No. 101034339).
- **Project**. The sum of all activities carried out in the framework of the Grant Agreement.
- **Work plan**. Schedule of tasks, deliverables, efforts, dates and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.
- **Consortium**. The PROMISE Consortium, comprising the above-mentioned participants.
- **Consortium Agreement**. The agreement concluded amongst PROMISE participants for the implementation of the Grant Agreement. The agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

Abbreviations

Acronym / Abbreviation	Meaning
ARI	Acute respiratory infection
ECDC	European Centre for Disease Prevention and Control
EU/EEA	European Union and European Economic Area
ILI	Influenza-like illness
JRC	Joint Research Centre
NPIs	Non-pharmaceutical interventions
RSV	Respiratory syncytial virus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
TESSy	The European Surveillance System

Abstract

Background: During the COVID-19 pandemic, atypical respiratory syncytial virus (RSV) circulation patterns emerged, characterised by the absence or occurrence of RSV outside the typical winter season. This study investigates the impact of COVID-19 and associated non-pharmaceutical interventions (NPIs) on RSV seasonality.

Methods: The onset, offset, and peak of RSV epidemics from 2018-2022 across 12 European countries were determined using the 3% positivity threshold method (the 3% positivity threshold method defines an epidemic period when the percentage of sentinel and non-sentinel surveillance specimens testing RSV-positive exceed 3%). A multilevel longitudinal logit regression model for proportions was employed to assess the associations between five NPIs (closure of educational institutions, protective mask use, workplace measures, public gathering restrictions, and closure of public spaces) and RSV, utilising RSV surveillance data obtained from the ECDC Surveillance Atlas of Infectious Diseases, two NPI databases (ECDC-JRC and Oxford), and COVID-19 surveillance data obtained from “Our World in Data”.

Results: Before 2020, consistent RSV seasonality patterns were observed across countries, however, the seasonal increase of RSV-positive cases in winter remained absent during the 2020-2022 COVID-19 pandemic period. Analyses of the association between single NPIs and RSV yielded contradictory results: The associations differed between the models using either ECDC-JRC or Oxford NPI data not only in magnitude but also in the direction of the coefficients. Public gathering restrictions and the closure of public spaces exhibited significant negative associations with RSV incidence. However, this was only observed when using RSV surveillance data from the whole year and not when only examining weeks with increased RSV activity.

Conclusions: This study emphasises the importance of standardising data collection internationally during pandemics. This exercise also emphasises the need for standardised procedures for infectious disease modelling. The large differences between countries in how each country implemented various NPIs, and how each country coped with existing surveillance of RSV during a period of “exhaustion of public health means”, make it a challenge to understand the RSV infection dynamics during this period. Therefore, caution is advised when drawing conclusions about the relationship between NPIs and RSV.

1. Introduction

Respiratory syncytial virus (RSV) is a leading cause of respiratory infections in infants and young children. This viral respiratory infection has been extensively studied for its distinct seasonality, typically peaking during the winter months across Europe (1, 2). However, the emergence of the COVID-19 pandemic and implementation of various associated non-pharmaceutical preventive measures disrupted this typical pattern, resulting in atypical RSV circulation patterns occurring outside the usual winter season timeframe in various countries (2-8). Nevertheless, research on the relationship between the COVID-19 pandemic and the observed alterations in RSV seasonality is still scarce.

The global response to the COVID-19 pandemic involved various non-pharmaceutical interventions (NPIs) that were implemented to control the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (9). In Europe, these measures were documented mainly in two publicly available databases: 1) the European Centre for Disease Prevention and Control (ECDC) in collaboration with the Joint Research Centre (JRC) Response Measures Database and 2) the Oxford COVID-19 Government Response Tracker. NPIs ranged from national school closures and lockdowns to individual mask mandates (10, 11). A recent comparative analysis of the NPI data in these two databases revealed notable differences in the recorded timing of the measures, even with seemingly similar definitions (12); see Annex 1. This emphasised the need for further exploration of the timing and implementation of various NPIs. Furthermore, given the remarkable change observed in RSV seasonality, it was hypothesised that the pandemic-related NPIs had an impact on the seasonality of respiratory virus circulation, particularly on RSV.

Understanding changes in RSV seasonality is crucial for optimising public health responses, forecasting future epidemiological trends, and guiding timely interventions, such as vaccination or passive immunisation. This study aims to assess the impact of the COVID-19 pandemic and the associated NPIs on RSV seasonality, as evidenced through surveillance data. RSV epidemics will be assessed annually for various countries. Additionally, exploratory analysis will determine the impact of NPIs on RSV during the whole year and also focus on weeks with increased RSV activity (i.e., from onset to peak of an RSV epidemic). This timeframe is crucial as it is anticipated to show the most pronounced effects of NPIs on RSV transmission dynamics.

2. Methods

2.1. RSV surveillance data

RSV surveillance data were obtained from the ECDC Surveillance Atlas of Infectious Diseases, which collects data through The European Surveillance System (TESSy) (13). TESSy includes sentinel surveillance in primary care and non-sentinel surveillance in primary care and/or hospital facilities. The dataset contains sentinel and non-sentinel RSV data from 26 EU/EEA countries including the number of RSV detections, total specimens tested, and the percentage of sentinel and non-sentinel surveillance specimens testing RSV-positive. RSV data from countries were included if the following criteria were met: 1) ≥3 years of sufficient RSV detections available since 2018, 2) ≥50 RSV detections per year (defined as week 27 through week 26), 3) percentage of RSV-positive tests or total number of specimens tested available (non-sentinel surveillance). Additionally, for the purpose of sensitivity analyses, seasons with substantial testing (>500 tests) were included, even if RSV detections were below the ≥50 threshold. Data from the following countries were considered to be eligible based on these criteria: Bulgaria, Denmark, Estonia, France, Germany, Iceland, Ireland, Latvia, the Netherlands, Slovenia, Spain, and Sweden. In these countries, non-sentinel data were chosen for consistency, except for Germany and the Netherlands, where sentinel data were included because almost no non-sentinel data was available.

2.2. Non-pharmaceutical intervention databases

Two NPI databases were used: 1) the ECDC-JRC Response Measures Database and 2) the Oxford COVID-19 Government Response Tracker. The ECDC-JRC NPI database is an archive of NPIs introduced by 30 countries in the EU/EEA from 01 January 2020 to 30 September 2022. Data entered into this database were collected by a dedicated team at ECDC, with measures implemented between January and March 2020 retrospectively gathered. This database contains measures organised at three levels to increase specificity and provide a detailed explanation on the aim of the measure (10). These data were downloaded from the ECDC website. The Oxford NPI database collects government response measures in more than 185 countries worldwide from 01 January 2020 to 31 December 2022. Data entered into this database were collected by a team of over 1500 volunteers and were published in real time to understand variations in government responses. This database contains 23 indicators recorded on an ordinal scale that represents the level of strictness of the measure (11). Oxford NPI data were downloaded directly from the “Our World in Data” platform.

We selected five measures that we assumed were relevant to RSV transmission: 1) closure of educational institutions, 2) protective mask use, 3) workplace measures, 4) public gathering restrictions, and 5) closure of public spaces. Measures with the most similar definitions in both databases were included in our analyses. Detailed definitions of the measures can be found in Supplementary Table 1. We synchronised the two databases and combined measures to ensure consistency in their definitions. More specifically, the strictest measures were selected from both databases. For the ECDC-JRC NPI database, this means that measures were considered for inclusion when the status was mandatory, the implementation was full, the geographical level was national and the target group was the general population; the only exception was school closures, where the target groups consisted of students and teachers. This means that voluntary, partial and regional/local measures were not considered. For the Oxford NPI database, the highest stringency levels were selected for all five NPI measures included. Lastly, all included NPI variables in both databases were transformed into weekly measures.

2.3. COVID-19 surveillance data

SARS-CoV-2 surveillance data were extracted from “Our World in Data” (14). We used the number of daily confirmed COVID-19 cases and tests per country provided by the John Hopkins repository. The total number of cases and tests per week was calculated to match the weekly RSV surveillance data.

2.4. Statistical analysis

We determined the onset and offset weeks of RSV epidemics in each country using the 3% positivity threshold method (15). The onset and offset weeks were defined as the first and last two consecutive weeks in which the percentage of sentinel or non-sentinel surveillance specimens testing RSV-positive exceeded 3%. This threshold was chosen to capture most RSV cases during the annual epidemics and because the percentage of RSV-positive tests outside the epidemic seasons was typically <3%. The peak week of the RSV epidemics was defined as the week with the highest percentage of RSV-positive cases.

A multilevel longitudinal logit regression model for proportions was employed to assess the association between NPIs and RSV seasonality, taking into account the hierarchical structure of the data. In this model, the percentage of RSV-positive tests (proportion) per week served as the dependent variable, with the total number of tests conducted in that week as the denominator. The multilevel structure incorporated “country” as level 1 units and “seasonal week (1-52 or 53)” as level 2. For each year, a separate intercept was allowed in the model, allowing for variability of RSV in a year (and, therefore, accounting for differences in RSV seasonality between countries). The average progression of seasonal weeks within a year (starting in week 27) was modelled as a polynomial fixed effect (to the 3rd order). Individual NPIs from either the ECDC-JRC database or the Oxford database were included as independent variables (fixed effects). The model was estimated with MLwiN using PQL first-order, RIGLS).

First, separate models were developed for individual NPIs for the ECDC-JRC and Oxford databases. Next, the individual NPIs were added together to a multivariate model. The analyses were adjusted for the potential confounding effect of COVID-19-positive tests by incorporating weekly COVID-19 surveillance data as fixed effects (a multivariate model with and without COVID-19 was developed). To further explore the association between NPIs and RSV during the early stages of the annual epidemics, the weeks from the start to the peak of the RSV epidemic were incorporated as fixed effects into the model (varying between countries and years). This association reflects whether an NPI had a clear effect on RSV epidemics during weeks in which RSV activity was increasing.

Two different scenarios were considered in the model analysis: 1) ≥50 RSV tests per week and 2) ≥50 RSV tests per week, excluding weeks with RSV rate=0 and without considering seasonal fluctuations (no polynomial modelling of the “seasonal week” variable).

The results of the investigated associations were presented as regression coefficients (β) with standard errors (SE). Two-tailed tests were used to assess statistical significance, with a p-value <0.05 considered statistically significant. Descriptive analyses were conducted using Stata SE version 16.0 (StataCorp, 2019, College Station, TX), and multilevel analyses were performed using MlwiN (Centre for Multilevel Modelling, University of Bristol, Bristol, UK).

The strength of the findings was evaluated based on statistical significance, the strength of the assessed associations, consistency in the observed associations regarding direction and strength (e.g., across different databases and scenarios), plausibility (considering existing literature), and relevance to public health or clinical practice.

3. Results

Individual NPIs showed different associations with RSV in the univariate model compared to the same NPIs in the multivariate model (the direction of the coefficients was sometimes even reversed). This was observed for both databases and several NPIs. This applied to the scenarios with and without the correction of COVID-19. Therefore, we have decided not to show this data and to focus on the multivariate model, where COVID-19 surveillance data is taken into account (see Table 1). Table 1 shows the variation of RSV between years and the variation between weeks within a year. It also shows the correlation between COVID-19 surveillance data and RSV. Furthermore, it shows the associations of individual NPIs with RSV throughout the entire year (defined as week 27 through week 26) and specifically during periods of increasing RSV circulation (from the onset to the peak of RSV epidemics).

3.1. Description of RSV seasonality

The seasonality of RSV across different countries revealed a consistent pattern – see Supplementary Figure 1 for an overview of the percentage of RSV-positive detections per country and see Supplementary Table 2 for the onset, offset, and peak of RSV epidemics per country for 2018-2022. More specifically, RSV epidemics typically occurred from late fall to early spring, with peaks observed from November to March, although slight variations in the timing of RSV epidemics and peaks from year to year were observed. Differences in RSV seasonality before and during the COVID-19 pandemic were mainly observed by the low rate and seasonal delay of RSV-positive cases during the 2020-2022 seasons. Specifically in 2020-2021, where almost no RSV was detected in Denmark, Estonia, Germany, Ireland, Latvia, the Netherlands, Slovenia, Spain, and Sweden. Additionally, in the Netherlands, two epidemic periods were observed during the 2021-2022 season (Supplementary Table 2).

3.2. Association between RSV and NPIs based on the ECDC-JRC data

The association between NPIs and RSV per database are provided in Table 1. Examining RSV surveillance data for the whole year (defined as week 27 through week 26) in relation to ECDC-JRC revealed significant negative associations between RSV presence and specific NPIs; namely, protective mask use ($\beta=-0.23$, SE=0.01, $p<0.01$), public gathering restrictions ($\beta=-0.57$, SE=0.03, $p<0.01$), and closure of public spaces ($\beta=-2.19$, SE=0.03, $p<0.01$). The negative estimates for these NPIs suggest a protective effect of the NPI studied, indicating a decrease in RSV transmission associated with the implementation of these interventions. However, when focusing on weeks with increased RSV activity (from the onset to peak of RSV epidemics), where stronger effects are expected than when using year-round data, only workplace measures ($\beta=-0.92$, SE=0.42, $p=0.03$) exhibited a significant negative association. Conversely, analyses yielded significant positive associations with RSV for protective mask use, public gathering restrictions, and closure of public spaces.

3.3. Association between RSV and NPIs based on the Oxford data

When using RSV surveillance data for the whole year (defined as week 27 through week 26) and NPIs from the Oxford database, public gathering restrictions ($\beta=-0.88$, SE=0.02, $p<0.01$) and the closure of public spaces ($\beta=-0.56$, SE=0.02, $p<0.01$) exhibited significant negative associations with RSV, indicating a potential decrease in RSV transmission due to the implementation of these measures (Table 1). On the other hand, the use of protective masks was significantly and positively associated with RSV ($\beta=0.49$, SE=0.01, $p<0.01$), suggesting an increase in RSV transmission.

When the analyses focused solely on the weeks with increased RSV activity (from the onset to peak of RSV epidemics), significant positive associations were found for most of the measures, including school closures, protective mask use, workplace measures, and public gathering restrictions. The only exception was the closure of public spaces, which was negatively associated with RSV ($\beta=-0.33$, SE=0.04, $p<0.01$) during these weeks.

3.4. Comparison of ECD-JRC and Oxford model outcomes

When comparing the outcomes of the model using the ECD-JRC and Oxford databases notable discrepancies were observed in the associations between the individual NPIs and RSV (Table 1). These differences did not only concern the magnitude of associations but also the direction of the coefficients (whether positive or negative), ultimately leading to contradictory results.

3.4.1. Consistent findings between databases

In the analysis spanning the entire year (defined as week 27 through week 26), only two measures - public gathering restrictions and closure of public spaces - demonstrated significant negative associations with RSV in both databases. When analyses were restricted to weeks with increased RSV activity in the model (from the onset to peak of RSV epidemics), no negative associations were observed between RSV and NPIs corresponding between the databases. However, protective mask use and public gathering restrictions were positively associated with RSV in both datasets.

Notably, public gathering restrictions and closure of public spaces were the only corresponding measures between scenario 1 (≥50 RSV tests per week) and scenario 2 (≥50 RSV tests per week, excluding weeks where the RSV rate equals zero and not considering seasonal fluctuations) for both databases, demonstrating a significant negative association with RSV (Supplementary Table 3). However, this effect was only observed when using year-round surveillance data and was, therefore, not apparent when only examining weeks with increasing RSV activity.
No associations between COVID-19 surveillance data and RSV were observed in both databases (Table 1).

3.4.2. Contradictory findings between databases

Interestingly, protective mask use showed a significant negative impact on RSV in the ECD-JRC database, while demonstrating a positive association in the Oxford database when using year-round surveillance data. When only looking at weeks with increasing RSV activity, workplace measures showed a significant negative association with RSV using the ECD-JRC database but a positive association when using the Oxford database. Conversely, the closure of public spaces revealed the opposite effect in the two databases. When adopting a stricter model scenario (scenario 2), inconsistencies in the associations between individual NPIs and RSV were evident across the two databases (Supplementary Table 3). This scenario also showed conflicting results with scenario 1, revealing distinct associations for NPIs.

Table 1. Detailed findings on the association (regression coefficients) between NPIs and RSV, per database

	ECD-JRC NPIs			**Oxford NPIs**		
Parameter*	**Estimate**	**Sd. Error**	**P value**	**Estimate**	**Sd. Error**	**P value**
Year 2018	-1.44	0.60	0.02	-1.49	0.54	0.01
Year 2019	-1.32	0.60	0.03	-1.37	0.54	0.01
Year 2020	-2.41	0.60	<0.01	-2.31	0.54	<0.01
Year 2021	-1.06	0.60	0.08	-1.36	0.54	0.01
Year 2022	-2.73	0.60	<0.01	-2.96	0.54	<0.01
Week	-0.11	0.00	<0.01	-0.11	0.00	<0.01
Week^2	0.00	0.00	<0.01	0.00	0.00	<0.01
Week^3	0.00	0.00	<0.01	0.00	0.00	<0.01
RSV season	0.53	0.01	<0.01	0.46	0.01	<0.01
COVID-19	-0.03	0.00	<0.01	-0.01	0.00	<0.01
School closures	1.28	0.03	<0.01	0.01	0.04	0.74
Protective mask use	-0.23	0.01	<0.01	0.49	0.01	<0.01
Workplace measures	1.35	0.03	<0.01	-0.05	0.04	0.24
Public gathering restrictions	-0.57	0.03	<0.01	-0.88	0.02	<0.01
Closure of public spaces	-2.19	0.03	<0.01	-0.56	0.02	<0.01
I_school closures	0.05	0.44	0.91	0.25	0.12	0.03
I_protective mask use	0.19	0.05	<0.01	0.41	0.02	<0.01
I_workplace measures	-0.92	0.42	0.03	0.31	0.05	<0.01
I_public gathering restrictions	0.44	0.05	<0.01	0.45	0.03	<0.01
I_ closure of public spaces	1.10	0.42	0.01	-0.33	0.04	<0.01

* Year describes the variation between years for countries; week describes the variation between weeks within a year (polynomial); measure describes the interaction between individual NPIs and RSV during the whole year (defined as week 27 through week 26); I_measure describes the interaction between NPIs and RSV during weeks in which RSV activity is increasing (from the onset to peak of RSV epidemics). This model describes the outcome of scenario 1, i.e., ≥50 RSV tests per week.

4. Discussion

This study aimed to assess the association between NPIs and RSV seasonality using publicly accessible surveillance data and two different NPI databases. Before 2020, consistent RSV seasonality patterns were observed across all countries included in this analysis, with the absence of the usual seasonal increase in RSV-positive cases during the 2020-2022 seasons marking the COVID-19 pandemic period. Our study revealed conflicting findings regarding the impact of individual NPIs on RSV activity. Substantial disparities in associations emerged when using data from the ECDC-JRC and Oxford NPI databases, as indicated by variations in the direction and magnitude of the coefficients. Notably, public gathering restrictions and the closure of public spaces were the only measures that exhibited significant negative associations with RSV across both databases, suggesting a potential reduction in RSV due to the implementation of these measures. However, these associations were not observed when exclusively examining periods of increased RSV activity (from the onset to peak of RSV epidemics). These results underscore the challenges in drawing definitive conclusions regarding the relationship between NPIs and RSV.

Surprisingly, the majority of associations between individual NPIs and RSV deviated from the expected direction (negative or zero), suggesting an increase in RSV activity when NPIs were implemented (for both the univariate and multivariate models). These findings are in contrast to the existing literature. For instance, a recent study linked the reopening of schools and relaxation of stay-at-home measures to increased RSV activity (16). Notably, the study by Billard *et al*., 2022 also used the Oxford COVID-19 Government Response Tracker for the investigated NPIs. However, they studied whether or not NPIs resulted in a delayed onset of a seasonal RSV epidemic. The study by Billard *et al*., 2022 also took into account a 10-week time lag between NPIs and the start of an increase in RSV-positive cases. Another study reported similar results, suggesting that the reopening of schools correlated with a heightened risk of RSV resurgence (17). However, the latter study's results may not be directly comparable to our analyses due to a time-dependent analysis and a different method for assessing different NPIs and other exposures.

A critical aspect to consider when interpreting our findings is the quality of the data utilised. A previous comparative analysis highlighted disparities in the timing of interventions between the ECDC-JRC and Oxford NPI databases (12), see Annex I. It is, therefore, likely that the databases have collected different observations resulting in different associations between the individual NPIs and RSV epidemics in this study. The differences between the ECDC-JRC and Oxford NPI databases could be explained by discrepancies in the definitions of measures or variations in the registration of NPIs. Additionally, to achieve comparable definitions of measures across both databases, we standardised the granularity of the raw data during the construction of measures, potentially influencing the results. Our analysis does not provide sufficient evidence to determine which database performs better. Furthermore, the variability of NPIs within and between countries could also account for differences in model outcomes. Some countries, for example Spain, implemented not only national measures but also regional measures. Adherence to measures is also of importance both within individual countries and between countries, yet adherence to NPIs was not considered in our analysis.

Similarly, RSV surveillance data exhibited variability not only between countries but also between different years within the same country, influenced by differences in testing and surveillance systems across Europe (18, 19). The 3% positivity threshold method used in this study effectively captured peaks during RSV epidemics; see Supplementary Figure 1. However, in instances where RSV circulates continuously over an extended period, such as observed in Bulgaria during 2020-2022 and in the Netherlands during 2021-2022, this method may not be as suitable for identifying epidemics. RSV surveillance data from TESSy, originally established to monitor influenza, were used for this study. Other studies used different RSV surveillance outputs (16). Using surveillance data from Tessy may not be perfectly suited for measuring RSV. The European Influenza Surveillance Network (EISN) reports RSV data to TESSy through both acute respiratory infection (ARI) and influenza-like illness (ILI) sentinel and non-sentinel surveillance systems (1). The ILI case definition is not optimal for capturing RSV because this can lead to under-detection of RSV in countries employing this case definition (20). Additionally, non-sentinel data were used for most countries, except for Germany and the Netherlands. The majority of RSV-positive cases reported to TESSy come from non-sentinel surveillance, collecting data based on diagnostic needs. Non-sentinel surveillance is likely to have been impacted by the COVID-19 pandemic, resulting in underreporting of RSV-positive cases. COVID-19 was incorporated into our analysis. At the beginning of the COVID-19 pandemic, SARS-CoV-2 surveillance was also mainly non-sentinel, leading to an underestimation of COVID-19-positive cases during the spring and summer of 2020 (21). However, since COVID-19 was only used as a control variable, this is not expected to have influenced our results.

The main strength of this study is the use of two NPI databases involving many European countries. This enables a comprehensive assessment of the association between NPIs and RSV. However, several limitations should be acknowledged. First is the reliance on publicly available databases, which may not always provide an optimal quality of the data. The clear differences between the NPI databases and the variability between and within countries of the RSV surveillance data underscores the necessity for caution when interpreting the results. Furthermore, the study did not account for potential confounding factors, such as social adherence to measures and weather conditions (e.g., temperature) (22). Incorporating these variables can enhance the accuracy of future models and provide a more nuanced understanding of the relationship between NPIs and the occurrence of seasonal RSV epidemics. Additionally, exploring country-specific associations between NPIs and RSV may offer more accurate insights into the various associations.

The above-mentioned shortcomings lead to the following recommendations for future studies and RSV surveillance: First, European RSV surveillance should be standardised, ideally to match international influenza surveillance. This also includes the standardisation of a uniform case definition for RSV (23). Moreover, improving European consistency and uniformity when registering NPIs, including standardised definitions across databases, will improve data quality and facilitate more robust analyses. Overall, the conflicting findings and methodological limitations highlighted in this study underscore the complexity of the impact of the COVID-19 pandemic and associated NPIs on RSV seasonality.

5. Conclusion

In conclusion, the present study highlights the complexity of assessing the association between NPIs during the recent COVID-19 pandemic and RSV seasonality. While some NPIs exhibited negative associations with RSV epidemic occurrence, suggesting a potential protective effect, conflicting findings were also observed, questioning the quality of the databases used for this analysis and challenging existing literature. Methodological limitations were characterised by important differences between the ECDC-JRC and Oxford NPI databases, probably implementation differences between countries of NPIs and by high variability in RSV surveillance data between countries. This emphasises the necessity for caution when interpreting these results. This study also underscores the importance of rigorous surveillance, also during pandemics, leading to improved data quality on the incidence and prevalence of infection. This will improve our ability to model infectious diseases like RSV and be able to improve our understanding of RSV dynamics during pandemics.

6. Recommendations for future work

Due to the ending of the project and data quality limitations, the possibilities for further analysis for the purpose of this deliverable are limited. Therefore, the following recommendations were made for a scientific publication:

- Investigation of the differences between the two NPI databases used in this analysis; for instance, to identify specific differences and overlap between the databases. This should be determined per country.
- Evaluate the possibility of incorporating more precise sources of RSV surveillance outcome data; different sources from different countries should be included to improve the analysis outcomes.
- When using RSV surveillance data from the ECDC, it is necessary to explore the testing policies implemented by each country and determine if there were any alterations to these policies during the pandemic.
- Improvement of analysis strategy:
  - Develop country-specific models of the association between NPIs and RSV seasonality.
  - Explore grouping and combining NPI measures. Additionally, use the Oxford stringency index to explore the overall effect of NPIs on RSV seasonality.
  - Incorporate RSV incubation period by adding a 1- or 2-week lag effect.

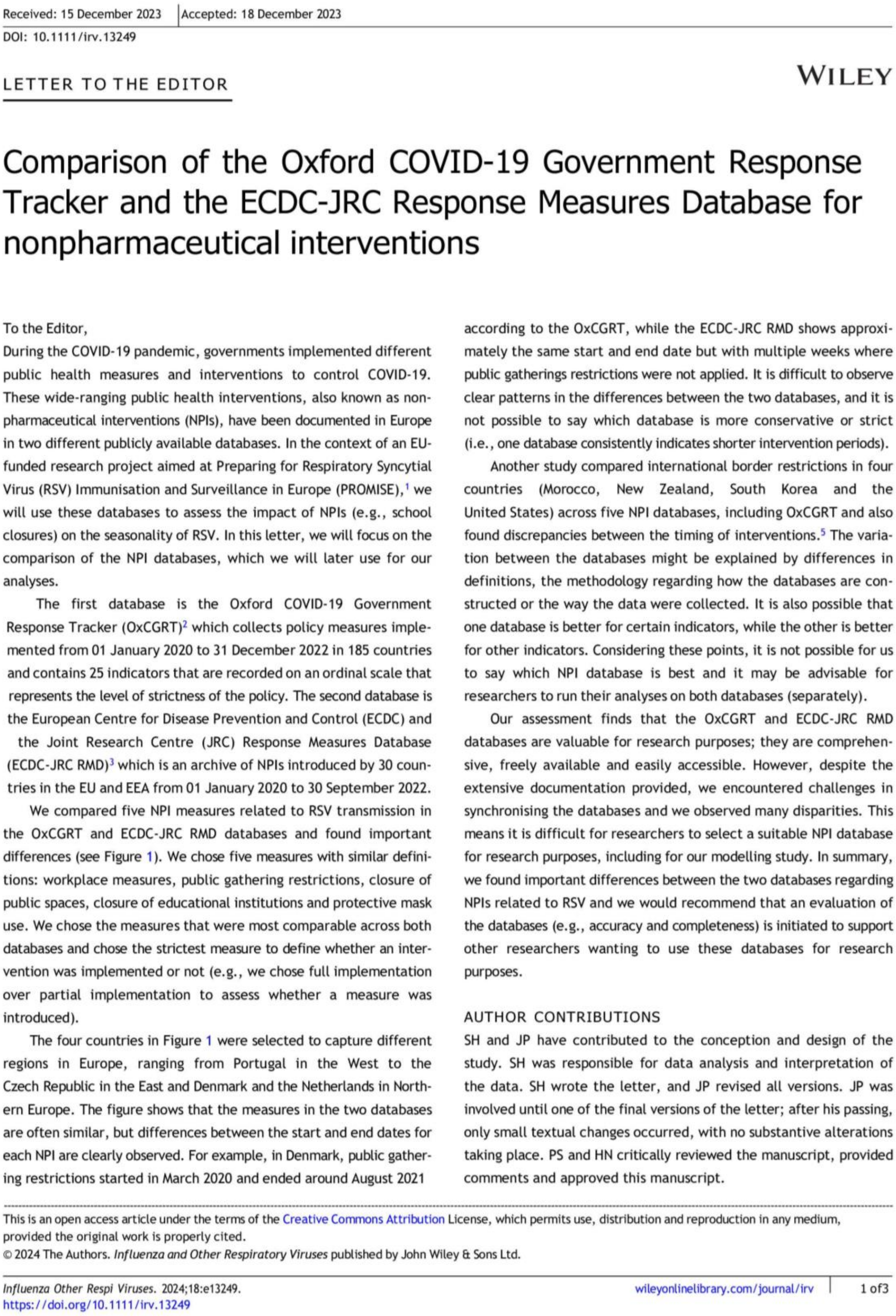
7. References

1) Broberg EK, Waris M, Johansen K, Snacken R, Penttinen P. Seasonality and geographical spread of respiratory syncytial virus epidemics in 15 European countries, 2010 to 2016. Euro Surveill. 2018;23(5).
2) Li Y, Wang X, Blau DM, Caballero MT, Feikin DR, Gill CJ, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. Lancet. 2022;399(10340):2047-64.
3) van Summeren J, Meijer A, Aspelund G, Casalegno JS, Erna G, Hoang U, et al. Low levels of respiratory syncytial virus activity in Europe during the 2020/21 season: what can we expect in the coming summer and autumn/winter? Euro Surveill. 2021;26(29).
4) Delestrain C, Danis K, Hau I, Behillil S, Billard MN, Krajten L, et al. Impact of COVID-19 social distancing on viral infection in France: A delayed outbreak of RSV. Pediatr Pulmonol. 2021;56(12):3669-73.
5) Eden JS, Sikazwe C, Xie R, Deng YM, Sullivan SG, Michie A, et al. Off-season RSV epidemics in Australia after easing of COVID-19 restrictions. Nat Commun. 2022;13(1):2884.
6) Huang QS, Wood T, Jelley L, Jennings T, Jefferies S, Daniells K, et al. Impact of the COVID-19 nonpharmaceutical interventions on influenza and other respiratory viral infections in New Zealand. Nat Commun. 2021;12(1):1001.
7) Jiang ML, Xu YP, Wu H, Zhu RN, Sun Y, Chen DM, et al. Changes in endemic patterns of respiratory syncytial virus infection in pediatric patients under the pressure of nonpharmaceutical interventions for COVID-19 in Beijing, China. J Med Virol. 2023;95(1):e28411.
8) Olsen SJ, Winn AK, Budd AP, Prill MM, Steel J, Midgley CM, et al. Changes in Influenza and Other Respiratory Virus Activity During the COVID-19 Pandemic - United States, 2020-2021. MMWR Morb Mortal Wkly Rep. 2021;70(29):1013-9.
9) European Centre for Disease Prevention and Control. Guidelines for non-pharmaceutical interventions to reduce the impact of COVID-19 in the EU/EEA and the UK. Stockholm, 2020.
10) Lionello L, Stranges D, Karki T, Wiltshire E, Proietti C, Annunziato A, et al. Non-pharmaceutical interventions in response to the COVID-19 pandemic in 30 European countries: the ECDC-JRC Response Measures Database. Euro Surveill. 2022;27(41).
11) Hale T, Angrist N, Goldszmidt R, Kira B, Petherick A, Phillips T, et al. A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). Nat Hum Behav. 2021;5(4):529-38.
12) Heemskerk S, Spreeuwenberg P, Nair H, Paget J. Comparison of the Oxford COVID-19 Government Response Tracker and the ECDC-JRC Response Measures Database for nonpharmaceutical interventions. Influenza Other Respir Viruses. 2024;18(1):e13249.
13) European Centre for Disease Prevention and Control. Surveillance Atlas of Infectious Diseases [Internet]. [Available from: https://www.ecdc.europa.eu/en/surveillance-atlas-infectious-diseases.
14) Mathieu E, Ritchie H, Rodés-Guirao L, Appel C, Giattino C, Hasell J, et al. Coronavirus Pandemic (COVID-19) [Online Resource]. 2020 [Available from: https://ourworldindata.org/coronavirus.

15) Grilc E, Prosenc Trilar K, Lajovic J, Sočan M. Determining the seasonality of respiratory syncytial virus in Slovenia. Influenza Other Respir Viruses. 2021;15(1):56-63.
16) Billard MN, van de Ven PM, Baraldi B, Kragten-Tabatabaie L, Bont LJ, Wildenbeest JG. International changes in respiratory syncytial virus (RSV) epidemiology during the COVID-19 pandemic: Association with school closures. Influenza Other Respir Viruses. 2022;16(5):926-36.
17) Li Y, Wang X, Cong B, Deng S, Feikin DR, Nair H. Understanding the Potential Drivers for Respiratory Syncytial Virus Rebound During the Coronavirus Disease 2019 Pandemic. J Infect Dis. 2022;225(6):957-64.
18) Presser LD, van den Akker WMR, Meijer A. Respiratory Syncytial Virus European Laboratory Network 2022 Survey: Need for Harmonization and Enhanced Molecular Surveillance. J Infect Dis. 2024;229(Supplement_1):S34-s9.
19) Mollers M, Barnadas C, Broberg EK, Penttinen P, Teirlinck AC, Fischer TK. Current practices for respiratory syncytial virus surveillance across the EU/EEA Member States, 2017. Euro Surveill. 2019;24(40).
20) Korsten K, Adriaenssens N, Coenen S, Butler CC, Verheij TJM, Bont LJ, et al. World Health Organization Influenza-Like Illness Underestimates the Burden of Respiratory Syncytial Virus Infection in Community-Dwelling Older Adults. The Journal of Infectious Diseases. 2021;226(Supplement_1):S71-S8.
21) Allan M, Lièvre M, Laurenson-Schafer H, de Barros S, Jinnai Y, Andrews S, et al. The World Health Organization COVID-19 surveillance database. Int J Equity Health. 2022;21(Suppl 3):167.
22) Li Y, Wang X, Broberg EK, Campbell H, Nair H. Seasonality of respiratory syncytial virus and its association with meteorological factors in 13 European countries, week 40 2010 to week 39 2019. Euro Surveill. 2022;27(16).
23) Teirlinck AC, Broberg EK, Stuwitz Berg A, Campbell H, Reeves RM, Carnahan A, et al. Recommendations for respiratory syncytial virus surveillance at the national level. Eur Respir J. 2021;58(3).

ANNEXES

ANNEX I. Letter to the editor



Received: 15 December 2023 | Accepted: 18 December 2023
DOI: 10.1111/irv.13249

LETTER TO THE EDITOR

WILEY

Comparison of the Oxford COVID-19 Government Response Tracker and the ECDC-JRC Response Measures Database for nonpharmaceutical interventions

To the Editor,

During the COVID-19 pandemic, governments implemented different public health measures and interventions to control COVID-19. These wide-ranging public health interventions, also known as nonpharmaceutical interventions (NPIs), have been documented in Europe in two different publicly available databases. In the context of an EU-funded research project aimed at Preparing for Respiratory Syncytial Virus (RSV) Immunisation and Surveillance in Europe (PROMISE),[1] we will use these databases to assess the impact of NPIs (e.g., school closures) on the seasonality of RSV. In this letter, we will focus on the comparison of the NPI databases, which we will later use for our analyses.

The first database is the Oxford COVID-19 Government Response Tracker (OxCGRT)[2] which collects policy measures implemented from 01 January 2020 to 31 December 2022 in 185 countries and contains 25 indicators that are recorded on an ordinal scale that represents the level of strictness of the policy. The second database is the European Centre for Disease Prevention and Control (ECDC) and the Joint Research Centre (JRC) Response Measures Database (ECDC-JRC RMD)[3] which is an archive of NPIs introduced by 30 countries in the EU and EEA from 01 January 2020 to 30 September 2022.

We compared five NPI measures related to RSV transmission in the OxCGRT and ECDC-JRC RMD databases and found important differences (see Figure 1). We chose five measures with similar definitions: workplace measures, public gathering restrictions, closure of public spaces, closure of educational institutions and protective mask use. We chose the measures that were most comparable across both databases and chose the strictest measure to define whether an intervention was implemented or not (e.g., we chose full implementation over partial implementation to assess whether a measure was introduced).

The four countries in Figure 1 were selected to capture different regions in Europe, ranging from Portugal in the West to the Czech Republic in the East and Denmark and the Netherlands in Northern Europe. The figure shows that the measures in the two databases are often similar, but differences between the start and end dates for each NPI are clearly observed. For example, in Denmark, public gathering restrictions started in March 2020 and ended around August 2021 according to the OxCGRT, while the ECDC-JRC RMD shows approximately the same start and end date but with multiple weeks where public gatherings restrictions were not applied. It is difficult to observe clear patterns in the differences between the two databases, and it is not possible to say which database is more conservative or strict (i.e., one database consistently indicates shorter intervention periods).

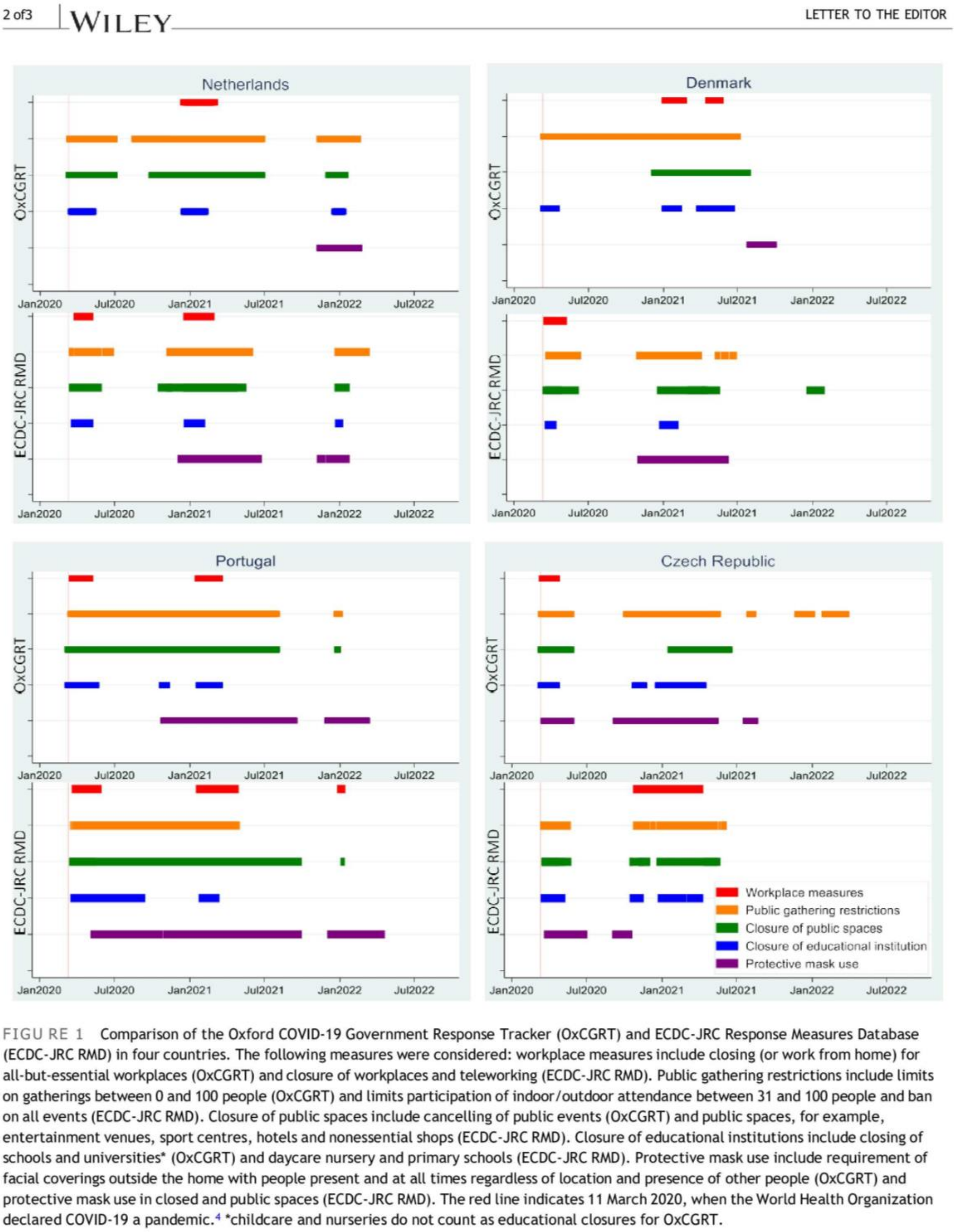
Another study compared international border restrictions in four countries (Morocco, New Zealand, South Korea and the United States) across five NPI databases, including OxCGRT and also found discrepancies between the timing of interventions.[5] The variation between the databases might be explained by differences in definitions, the methodology regarding how the databases are constructed or the way the data were collected. It is also possible that one database is better for certain indicators, while the other is better for other indicators. Considering these points, it is not possible for us to say which NPI database is best and it may be advisable for researchers to run their analyses on both databases (separately).

Our assessment finds that the OxCGRT and ECDC-JRC RMD databases are valuable for research purposes; they are comprehensive, freely available and easily accessible. However, despite the extensive documentation provided, we encountered challenges in synchronising the databases and we observed many disparities. This means it is difficult for researchers to select a suitable NPI database for research purposes, including for our modelling study. In summary, we found important differences between the two databases regarding NPIs related to RSV and we would recommend that an evaluation of the databases (e.g., accuracy and completeness) is initiated to support other researchers wanting to use these databases for research purposes.

AUTHOR CONTRIBUTIONS

SH and JP have contributed to the conception and design of the study. SH was responsible for data analysis and interpretation of the data. SH wrote the letter, and JP revised all versions. JP was involved until one of the final versions of the letter; after his passing, only small textual changes occurred, with no substantive alterations taking place. PS and HN critically reviewed the manuscript, provided comments and approved this manuscript.

Influenza Other Respi Viruses. 2024;18:e13249.
https://doi.org/10.1111/irv.13249
wileyonlinelibrary.com/journal/irv | 1 of3



FIGU RE 1 Comparison of the Oxford COVID-19 Government Response Tracker (OxCGRT) and ECDC-JRC Response Measures Database (ECDC-JRC RMD) in four countries. The following measures were considered: workplace measures include closing (or work from home) for all-but-essential workplaces (OxCGRT) and closure of workplaces and teleworking (ECDC-JRC RMD). Public gathering restrictions include limits on gatherings between 0 and 100 people (OxCGRT) and limits participation of indoor/outdoor attendance between 31 and 100 people and ban on all events (ECDC-JRC RMD). Closure of public spaces include cancelling of public events (OxCGRT) and public spaces, for example, entertainment venues, sport centres, hotels and nonessential shops (ECDC-JRC RMD). Closure of educational institutions include closing of schools and universities* (OxCGRT) and daycare nursery and primary schools (ECDC-JRC RMD). Protective mask use include requirement of facial coverings outside the home with people present and at all times regardless of location and presence of other people (OxCGRT) and protective mask use in closed and public spaces (ECDC-JRC RMD). The red line indicates 11 March 2020, when the World Health Organization declared COVID-19 a pandemic.[4] *childcare and nurseries do not count as educational closures for OxCGRT.

KEYWORDS

COVID-19, disease outbreaks, epidemiology, non-pharmaceutical interventions, public health

CONFLICT OF INTEREST STATEMENT

JP declares that Nivel has received unrestricted grants from the World Health Organization, Sanofi and the Foundation for Influenza Epidemiology outside the submitted work. HN reports grants from the World Health Organization, the National Institute for Health Research, Pfizer and Icosavax and personal fees from the Bill & Melinda Gates Foundation, Pfizer, GSK, Merck, AbbVie, Janssen, Icosavax, Sanofi, Novavax, outside the submitted work.

FUNDING INFORMATION

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement no. 101034339. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Associations.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/irv.13249.

DATA AVAILABILITY STATEMENT

All data are presented in the letter.

Susanne Heemskerk[1]
Peter Spreeuwenberg[1]
Harish Nair[2,3]
John Paget[1†] on behalf of PROMISE investigators

[1]*Netherlands Institute for Health Services Research (Nivel), Utrecht, the Netherlands*
[2]*Centre for Global Health, Usher Institute, University of Edinburgh, Edinburgh*
[3]*School of Public Health, University of the Witwatersrand, Johannesburg, South Africa*

Correspondence
Susanne Heemskerk, Netherlands Institute for Health Services Research (Nivel), Utrecht, the Netherlands.
Email: s.heemskerk@nivel.nl

†Deceased on 4 November 2023.

ORCID

Susanne Heemskerk https://orcid.org/0009-0007-7267-0897
Harish Nair https://orcid.org/0000-0002-9432-9100
John Paget https://orcid.org/0000-0002-1503-2481

REFERENCES

1. PROMISE. Preparing for RSV immunisation and surveillance in Europe. Accessed October 3, 2023. https://imi-promise.eu/
2. Hale T, Angrist N, Goldszmidt R, et al. A global panel database of pandemic policies (Oxford COVID-19 government response tracker). *Nat Hum Behav*. 2021;5(4):529-538. doi:10.1038/s41562-021-01079-8
3. Lionello L, Stranges D, Karki T, et al. ECDC-JRC response measures database working group. Non-pharmaceutical interventions in response to the COVID-19 pandemic in 30 European countries: the ECDC-JRC response measures database. *Euro Surveill*. 2022;27(41):2101190. doi:10.2807/1560-7917.ES.2022.27.41.2101190
4. World Health Organization. Listings of WHO's response to COVID-19. Accessed October 3, 2023. https://www.who.int/news/item/29-06-2020-covidtimeline
5. Shen Y, Powell G, Ganser I, et al. Monitoring non-pharmaceutical public health interventions during the COVID-19 pandemic. *Sci Data*. 2021;8(1):225. doi:10.1038/s41597-021-01001-x

ANNEX II. Supplementary materials

Supplementary Table 1. Detailed definition of measures for ECDC-JRC Response Measures Database and Oxford COVID-19 Government Response Tracker

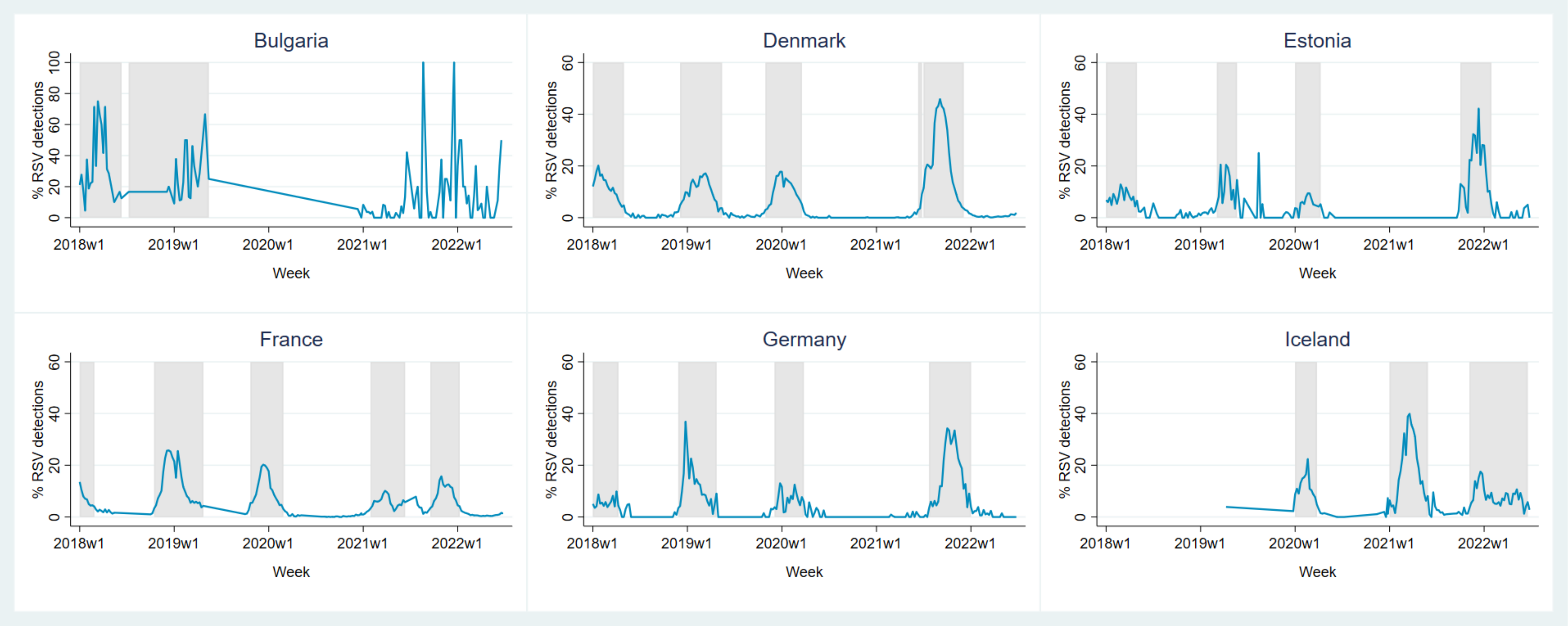
Measure	**ECDC-JRC Response Measures Database**	**Oxford COVID-19 Government Response Tracker**
Closure of educational institutions	Closure of educational institutions - Daycare nursery - Primary school	C1. Records closings of schools and universities* - Require closing all levels (stringency level 3)
Protective mask use	Protective mask use community - All public spaces - Closed public spaces (e.g., transportation facilities, supermarkets or working environments)	H6. Records policies on the use of facial coverings outside the home - Required in all shared/public spaces outside the home with other people present or all situations when social distancing not possible (level 3) - Required outside the home at all times regardless of location or presence of other people (level 4)
Workplace measures	Workplace measures - Closure of workplaces - Teleworking (specific recommendation of teleworking from home)	C2. Records closings of workplaces - Require closing (or work from home) for all-but-essential workplaces (e.g., grocery stores, doctors) (level 3)
Public gathering restrictions	Public gathering restrictions: Any measure or legislation which limits participation or attendance to a public event - Indoor over 50 (between 31 and 50 participants) and 100 (between 51 and 100 participants) - Outdoor over 50 (between 31 and 50 participants) and 100 (between 51 and 100 participants) - Ban on all events	C4. Records the cut-off size for limits on gatherings - Restrictions on gatherings between 11-100 people (level 3) - Restrictions on gatherings of 10 people or less (level 4)

Closure of public spaces	Closure of public spaces - Entertainment venues (e.g., arena, concert halls, theatre) - Gym, sports centres - Hotels and other accommodation - Non-essential shops - Place of worship - Restaurants or cafes - Other public spaces	C3. Records cancelling public events - Require cancelling (level 2)**

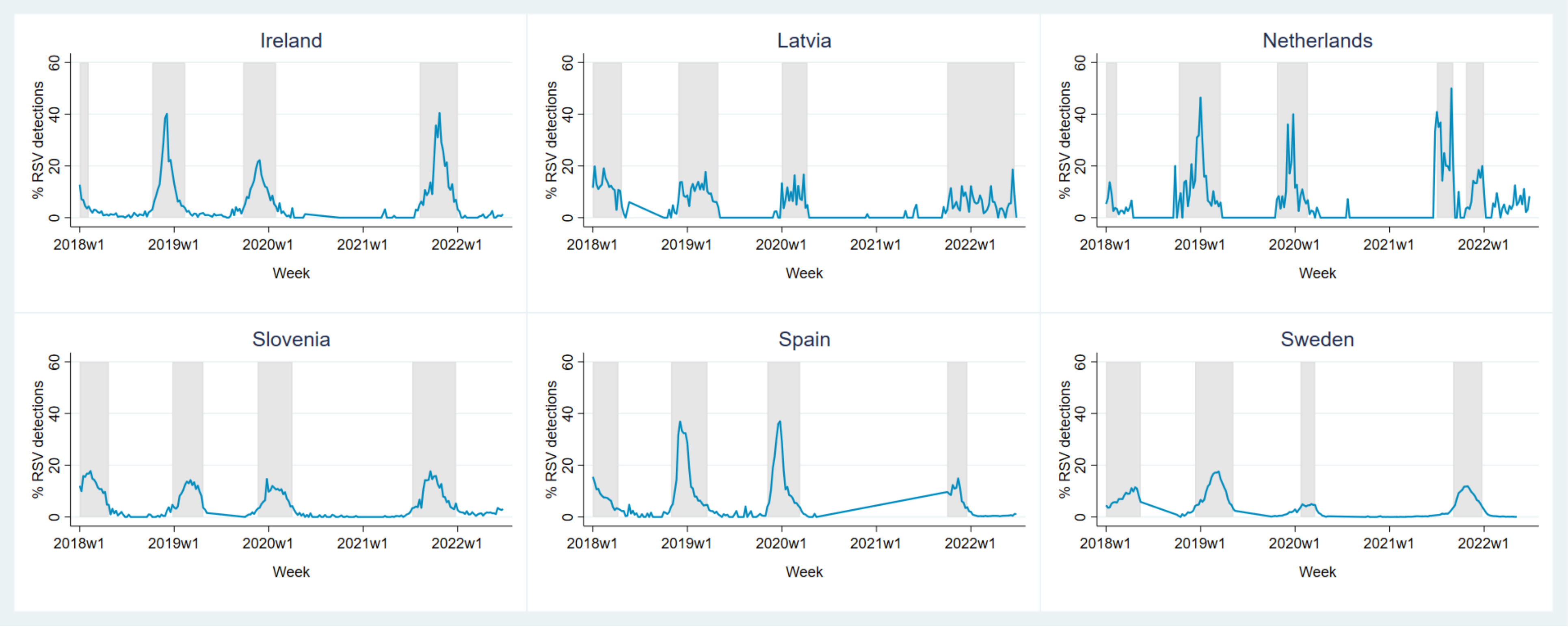
*C1 reports closures of both schools and universities. It does not report closures of childcare, nurseries, language courses, and driving schools, which are instead recorded as workplaces under C2.

** When private gatherings of only 10 people or less are permitted (i.e., C4=4), this restriction would prevent public events from taking place, so we also report C3=2 (public events are required to be cancelled), unless there is a specific policy in place permitting public gatherings to go ahead.

Supplementary Figure 1. Percentage of RSV-positive detections of included countries; grey areas indicate RSV epidemics



Supplementary Figure 1 (continued). Percentage of RSV-positive detections of included countries; grey areas indicate RSV epidemics



Supplementary Table 2. Onset, peak and offset of the RSV epidemics and number of RSV detections per season of included countries

Country, season	**Start, week**	**Peak, week**	**End, week**	**RSV+ cases***	**Total specimens tested**	**Data source**
Bulgaria						Non-sentinel
2017-2018	34 - 2017	11 - 2018	24 - 2018	90	446	
2018-2019	28 - 2018	18 - 2019	20 - 2019	107	554	
2019-2020	-	-	-	-	-	
2020-2021	-	-	-	78	749	
2021-2022	-	-	-	54	334	
Denmark						Non-sentinel
2017-2018	46 - 2017	4 - 2018	18 - 2018	4504	42860	
2018-2019	49 - 2018	11 - 2019	20 - 2019	4184	42642	
2019-2020	44 - 2019	52 - 2019	12 - 2020	4471	56606	
2020-2021				127	25676	
2021-2022	24 - 2021	36 - 2021	49 - 2021	10961	121418	
Estonia						Non-sentinel
2017-2018	50 - 2017	9 - 2018	18 - 2018	571	8266	
2018-2019	10 - 2019	15 - 2019	21 - 2019	299	8027	
2019-2020	1 - 2020	8 - 2020	15 - 2020	260	5427	
2020-2021	-	-	-	0*	3031	
2021-2022	40 - 2021	50 - 2021	5 -2022	227	1976	
France						Non-sentinel
2017-2018	42 - 2017	47 - 2017	9 - 2018	11524	121938	
2018-2019	42 - 2018	50 - 2018	17 - 2019	14346	95902	
2019-2020	43 - 2019	50 - 2019	9 - 2020	11082	163805	
2020-2021	5 - 2021	13 - 2021	24 - 2021	5984	140983	
2021-2022	38 - 2021	44 - 2021	2 - 2022	13630	344604	
Germany						Sentinel
2017-2018	51 - 2017	52 - 2017	15 - 2018	254	6239	
2018-2019	48 - 2018	52 - 2018	17 - 2019	367	4205	
2019-2020	49 - 2019	8 - 2020	13 - 2020	201	4364	
2020-2021	-	-	-	10*	5849	
2021-2022	30 - 2021	40 - 2021	1 - 2022	805	7570	
Iceland						Non-sentinel
2019-2020	1 - 2020	8 - 2020	13 - 2020	270	3526	
2020-2021	1 - 2021	12 - 2021	22 - 2021	529	5285	
2021-2022	45 - 2021	51 - 2021	25 - 2022	552	8902	
Ireland						Non-sentinel
2017-2018	40 - 2017	49 - 2017	6 - 2018	1543	19168	
2018-2019	41 - 2018	49 - 2018	7 - 2019	1521	19981	
2019-2020	39 - 2019	48 - 2019	5 - 2020	1445	17913	

2020-2021	-	-	-	5*	4120	
2021-2022	32 - 2021	43 - 2021	1 -2022	825	8857	
Latvia						Non-sentinel
2017-2018	40 - 2017	2 - 2018	17 - 2018	519	5052	
2018-2019	48 - 2018	11 - 2019	18 - 2019	263	2924	
2019-2020	1 - 2020	13 - 2020	15 - 2020	110	1825	
2020-2021	-	-	-	4*	1706	
2021-2022	40 - 2021	48 - 2021	25 - 2022	114	2353	
Netherlands						Sentinel
2017-2018	46 - 2017	51 - 2017	7 - 2018	75	1272	
2018-2019	41 - 2018	1 - 2019	12 - 2019	105	955	
2019-2020	43 - 2019	52 - 2019	8 - 2020	93	1689	
2020-2021	-	-	-	5*	630	
2021-2022	27 - 2021	35 - 2021	36 - 2021	108	1520	
2021-2022	43 - 2021	52 - 2021	1 - 2022	108	1520	
Slovenia						Non-sentinel
2017-2018	50 - 2017	7 - 2018	17 - 2018	1537	17360	
2018-2019	52 - 2018	10 - 2019	17 - 2019	1228	17384	
2019-2020	47 - 2019	52 - 2019	14 - 2020	1369	18377	
2020-2021	-	-	-	31*	18686	
2021-2022	28 - 2021	38 - 2021	52 - 2021	1811	37013	
Spain						Non-sentinel
2017-2018	42 - 2017	49 - 2017	15 - 2018	3967	35381	
2018-2019	44 - 2018	49 - 2018	12 - 2019	4346	39503	
2019-2020	45 - 2019	52 - 2019	11 - 2020	4585	39095	
2020-2021	-	-	-	-	-	
2021-2022	40 - 2021	46 - 2021	51 - 2021	4949	286417	
Sweden						Non-sentinel
2017-2018	51 - 2017	17 - 2018	20 - 2018	4528	73795	
2018-2019	50 - 2018	11 - 2019	19 - 2019	7312	75623	
2019-2020	4 - 2020	10 - 2020	12 - 2020	1987	72364	
2020-2021	-	-	-	308	209830	
2021-2022	36 - 2021	44 - 2021	52 - 2021	16042	455049	

*Empty cells have <50 RSV detections per season, RSV detections with * also have <50 RSV detections per season but is included in the table because a lot of testing was performed (>500 tests).

The following countries did not have sufficient data: Belgium, Croatia, Cyprus, Czechia, Finland, Greece, Hungary, Italy, Lithuania, Luxembourg, Malta, Poland, Portugal, Romania, and Slovakia.

Supplementary Table 3. Detailed findings on the association (regression coefficients) between NPIs and RSV, per database*

	ECD-JRC NPIs			**Oxford NPIs**		
Parameter**	**Estimate**	**Sd. Error**	**P value**	**Estimate**	**Sd. Error**	**P value**
Year 2018	-2.08	0.53	<0.01	-2.08	0.49	<0.01
Year 2019	-1.93	0.53	<0.01	-1.94	0.49	<0.01
Year 2020	-2.94	0.53	<0.01	-2.82	0.49	<0.01
Year 2021	-1.90	0.53	<0.01	-1.93	0.49	<0.01
Year 2022	-3.97	0.53	<0.01	-3.96	0.49	<0.01
RSV season	0.53	0.01	<0.01	0.52	0.01	<0.01
COVID-19	-0.01	0.00	<0.01	0.00	0.00	<0.01
School closures	1.54	0.04	<0.01	0.36	0.05	<0.01
Protective mask use	-0.06	0.01	<0.01	0.50	0.01	<0.01
Workplace measures	0.66	0.03	<0.01	0.09	0.04	0.03
Public gathering restrictions	-0.50	0.03	<0.01	-1.03	0.01	<0.01
Closure of public spaces	-2.08	0.04	<0.01	-0.45	0.02	<0.01
I_school closures	-0.79	0.45	0.08	-0.55	0.12	<0.01
I_protective mask use	0.07	0.05	0.14	0.18	0.02	<0.01
I_workplace measures	-0.35	0.42	0.41	-0.05	0.05	0.28
I_public gathering restrictions	-0.12	0.05	0.02	0.50	0.03	<0.01
I_ closure of public spaces	1.46	0.42	<0.01	-0.35	0.04	<0.01

* Scenario 2: ≥50 RSV tests per week, model without seasonality (week variable) and weeks with RSV rate=0 deleted.

** Year describes the variation between years for countries; week describes the variation between weeks within a year (polynomial); measure describes the interaction between individual NPIs and RSV during the whole year (defined as week 27 through week 26); I_measure describes the interaction between NPIs and RSV during weeks in which RSV activity is increasing (from the onset to peak of RSV epidemics).