

Cover Page

Statement 1: This manuscript has not been submitted or accepted elsewhere. It has not been posted on any preprint server.

Statement 2: All authors fulfill the criteria given in the authorship paragraph; including that all authors have seen and approved the content and have contributed significantly to the work.

Statement 3: No writing assistance other than copy editing was provided in the preparation of the manuscript.

List of Unbiased Reviewers

1. Maria Zambon - Maria.Zambon@ukhsa.gov.uk – Director of Reference Microbiology at UKHSA
2. Jess Belser - jax6@cdc.gov – Scientist at US CDC specializing in influenza virus and other respiratory viruses
3. Ron Fouchier – r.fouchier@erasmusmc.nl – Deputy Head of the Erasmus MC Department of Viroscience
4. Connor Bamford – C.Bamford@qub.ac.uk – Virologist Queen’s University Belfast
5. Yi-Mo Deng – yi-mo.deng@influenzacentre.org – Head, Genetic Analysis Unit WHO collaborating center for reference and research on influenza Melbourne Australia
6. Magdi Samaan – saadsamaanm@who.int – WHO GISRS Team – Laboratory, Global Influenza Program
7. William Davis – fwb0@cdc.gov – Scientist at US CDC specializing in influenza virus and other respiratory viruses

**Respiratory Syncytial Virus European Laboratory Network 2022 Survey: Need
for Harmonization and Enhanced Molecular Surveillance**

Authors: Lance D. Presser¹, Willem M. R. van den Akker¹, Adam Meijer¹ *for PROMISE investigators*

1 – National Institute for Public Health and the Environment, PO Box 1, 3720, BA, Bilthoven, The Netherlands

2 – RSV-LabNet Group is composed of members listed in acknowledgements section

Correspondence: Adam Meijer, adam.meijer@rivm.nl

Total Figures: 1

Total Tables: 3

Abstract Word Count: 179

Total Word Count: 2304

Abstract

Respiratory syncytial virus (RSV) is a common pathogen causing mostly cold-like symptoms, but in very young infants and elderly individuals it can lead to severe disease and even death. There are currently promising developments both in vaccine development and in therapeutics which are expected to be approved soon. To get an impression within European countries of the laboratory diagnostics and surveillance activities, in anticipation of these developments, we queried the members of the European Respiratory Syncytial Virus Laboratory Network (RSV-LabNet, under the umbrella of the PROMISE project) via an online survey. The answers from the Consortium members showed scattered monitoring and the application of a broad array of techniques in the laboratories. A majority of the members expressed strong interest in harmonization and collaboration for setting up surveillance programs and the need for sharing laboratory protocols. The additional value of RSV whole-genome sequencing is broadly appreciated but implementation requires further development and closer collaboration. The RSV-LabNet can have an important responsibility in establishing contacts, exchange of expertise and providing a platform for communication to advance diagnostics, preparedness, and surveillance.

Keywords: RSV, Respiratory syncytial virus, Laboratory Network, diagnostics, PROMISE, IMI, vaccine development, antibody therapeutics, surveillance

Introduction

Respiratory syncytial virus (RSV) is a common respiratory virus that usually causes mild, cold-like symptoms. RSV is a known cause of substantial morbidity and mortality in young children and elderly adults globally. It is estimated that worldwide, RSV is responsible for between 25.4-44.6 million cases of acute lower respiratory tract infections in children 0-5 years of age and ~1.5 million cases of acute respiratory infection in older adults in industrialized countries [1,2]. The largest burden of RSV-attributable deaths, ~97% across all age groups, were in low- and middle-income countries (LMICs) [1].

Common symptoms of RSV infections in children usually include rhinorrhea (runny nose), cough, wheezing, and low-grade fever. More severe presentation of RSV infections such as bronchiolitis, pneumonia and atypical extrapulmonary disease can lead to hospitalization. Comorbidities such as chronic lung and/or heart disease increase the risk of severe RSV disease. Importantly, natural immunity to RSV is not long-lasting which means that individuals are at risk of reinfections throughout their lifetime [3].

RSV is a member of the Paramyxoviridae family and is a non-segmented, negative-sense, single stranded, enveloped RNA virus. The RSV genome contains 10 genes encoding 11 proteins, among which are the glycoprotein (G) and fusion protein (F) playing a role in attachment and entry of the virus in the human cell. These proteins are targets for immunization [4]. Laboratory detection of RSV infections is performed primarily by antigen detection, nucleic acid amplification tests (NAATs), and virus culture. RSV is divided into subtypes A and B based on antigenic differences of the glycoprotein G, and most commonly, the G gene region is used for molecular typing [5-10]. However, as the RSV genome is more variable than previously thought [10], genotyping by whole genome sequencing (WGS) is being developed by numerous groups.

Before the SARS-CoV-2 pandemic, both RSV subtypes would co-circulate during epidemic seasons, following an irregular, alternating prevalence pattern, subtype A having a higher cumulative

prevalence than subtype B [11]. However, the previously documented seasonal patterns of RSV have been disrupted by the SARS-CoV-2 pandemic and the nonpharmaceutical interventions directed against it [12-14].

Several new RSV vaccine and therapeutic candidates are currently undergoing development [4]. In Europe and the broader region, RSV is not a notifiable disease which is why RSV data are fragmented and harmonization of data and practices is necessary. Prior to the implementation of vaccines and therapeutics, baseline data on RSV surveillance and diagnostics is required.

In order to collect the required information, the “Preparing for RSV immunization and surveillance in Europe” (PROMISE) project <https://imi-promise.eu/> endeavors to share all data generated as part of routine RSV surveillance by national public health institutes (NPHIs) and make available regular reports based on surveillance data to the community. This is essential to improving awareness on respiratory infections in the community, building public confidence and awareness, and guiding the development of therapeutic and preventive solutions in the long term.

The PROMISE surveillance network has epidemiology and virology components. The epidemiology component will focus on data collection and producing a surveillance bulletin and the virology component on establishing a laboratory network for RSV. Ideally this will result in an integrated epidemiological and virological surveillance in which epidemiological observations can be explained by virus characteristics. In addition, it will provide the basis for vaccine effectiveness studies, like those routinely running for influenza effectiveness [15,16].

The objective of the present survey conducted among all European Union (EU) and European Economic Area (EEA) countries in July-September 2022, was to gather knowledge on the current practices of RSV laboratory diagnostics. This knowledge could identify best practices and provide benchmarking data thereby informing and strengthening RSV surveillance in the EU/EEA countries.

Methods

National coordinators, and national laboratory focal and operational contact points for respiratory viruses from EU/EEA countries were invited to participate in the survey. The online questionnaire (Appendix 1) on the National Institute for Public Health and the Environment for the Netherlands, or Rijksinstituut voor Volksgezondheid en Milieu (RIVM) FORMDesk platform (<https://en.formdesk.com>) contained questions primarily about laboratory diagnostics and testing practices. The survey also contained questions related to surveillance systems and future planning for WGS. Virologists from the public health organizations responded to the survey.

Online Questionnaire

The questionnaire was divided into three sections. The first section was the introduction section covering surveillance questions, and basic laboratory testing questions (e.g., what specimen types are used in your laboratory). The second section was the molecular diagnostics section, which included, among others, specific questions on extraction and PCR platforms, kit information, primer and probe information and sequencing protocols. The final section asked questions about future coordination of the RSV laboratory network.

Study period

The invitation to participate in the survey was sent out on multiple occasions between July and September 2022. Data from the online questionnaire was exported to and analyzed in Microsoft Excel. Data analysis was performed in two phases. Following the initial data cleaning process, respondents were contacted again to clarify answers when necessary. A map of participating countries was created with the Emma application (ECDC).

Ethical statement

Ethical approval was not needed for this survey.

Results

Participating (public health) Institutes across Europe

All EU countries except Cypress, Estonia, and Luxembourg responded to the questionnaire. Greece responded to the invite, but the National Influenza Reference Laboratory in Thessaloniki reported no RSV samples for testing the past few years, so they did not complete the survey. No European Free Trade Association (EFTA) countries (Iceland, Lichtenstein, Switzerland, and Norway) responded, though they were invited to participate. In some countries, two institutions provided responses (Netherlands, France, Spain). In total, 28 institutes in 26 countries provided answers to the questions. A map of countries that responded/participated in the survey is shown in Figure 1.

Responses from Introduction Section

A sample of the responses to the introduction section are shown in Table 1. RSV is notifiable in approximately half the countries that responded. Germany is unique in that only one federal state (Saxony) lists RSV as notifiable. While RSV is not considered a notifiable disease in many of the countries, most countries perform some level of RSV surveillance and 22 of the 28 institutes that responded fulfill reference laboratory functions (as defined by ECDC) for RSV [17]. Notably, in four countries that responded, there is no designated reference laboratory for RSV.

The determination of RSV status is diagnosed at different levels by the diagnostic laboratories that answered the survey. Many of the laboratories (23/27) surveyed do perform subtyping, but less than half (10/27) generate sequencing data (Table 1).

Laboratories were also asked if specimens tested for RSV were also tested for other respiratory viruses. Of the 28 responding laboratories, 27 indicated that they do perform tests for other respiratory viruses with a wide range of viruses including, but not limited to, influenza virus, adenovirus, rhinovirus, parechovirus, SARS-CoV-2, human metapneumovirus, and bocavirus (Table 1).

168

169 **Responses to the Molecular Diagnostics Section**

170 Table S2 includes questions regarding the diagnostics of RSV. The laboratories were asked questions
171 regarding their diagnostic capacity for RSV testing. Of interest to the RSV-LabNet was the range of
172 workflows for RSV molecular diagnostics. There was a wide range of specimen types, RNA isolation
173 methods/kits, RT-PCR methods/kits, and gene targets (Table S2). Many of the laboratories (21/27)
174 participate in one or more annual External Quality Assessments (EQAs) from a variety of providers
175 (Table S2 footnote).

176 Another area of interest is the sequencing methods used for RSV. Ten of the laboratories that
177 responded to the survey do some sequencing for RSV (either or both G and F genes, or WGS), while
178 17 laboratories responded that they do not perform any sequencing. The laboratories that do
179 perform sequencing primarily perform the task for the purpose of genotyping the virus.

180 Nine laboratories are performing virus isolation using Hep-2, HeLa, MDCK, and other cell lines (Table
181 S2). Only one laboratory responded that they are working on an RSV reverse genetics system. As
182 many of the laboratories that responded are NPHIs, most RSV samples are shipped from other
183 locations which may have an effect on sample viability and downstream virus isolation [18].

184 **Responses to future planning for RSV-LabNet section**

185 As there are anticipated approvals of new RSV vaccines and therapeutics coming in the next few
186 years, and there has been a large shift in respiratory virus surveillance due to the SARS-CoV-2
187 pandemic, our survey asked questions regarding future planning for RSV surveillance. The questions
188 we asked were directed at sharing of protocols and data, as both of these will be crucial for the
189 progress of RSV diagnostics and surveillance systems across Europe. Many of the laboratories
190 expressed interest in sharing diagnostics protocols, for the purpose of development (in the case of
191 WGS) and to better harmonize RSV diagnostics. Most laboratories that completed the survey also

already share RSV data with either the European Centre for Disease Prevention and Control (ECDC) or the World Health Organization (WHO), with only four out of 27 laboratories not sharing any of their RSV data on one of the major international platforms (Table S3).

Discussion

The purpose of this questionnaire, developed as part of the 'Preparation for future RSV product assessment' work package for the PROMISE project (<https://imi-promise.eu/surveillance/rsvlabnet/>), was to obtain an overview of the current status of the European RSV surveillance and diagnostics laboratory practices and capabilities. A focus point was to see if there is some consensus or concerted preparation for the impending implementation of RSV vaccines and novel therapeutic options. This survey also serves as an update to a previous survey performed in 2017 as part of the REspiratory Syncytial virus Consortium in EUrope (RESCEU) project, [19]. This survey performed as part of the PROMISE project expands on the former RESCEU survey with more detail on laboratory systems and diagnostics for RSV, with the purpose of identifying what is needed for further building of a European RSV laboratory network.

We observe a wide variety of applied laboratory techniques being used as well as a range of different surveillance and reporting mechanisms. Within this scattered diagnostics landscape, many different assays are in use. The vast majority are NAATs which utilize a number of different RSV gene targets and are the most sensitive pathogen detection method. The diversity of workflows for RSV diagnostics across Europe suggests a need for EQAs to evaluate the quality and accuracy of these workflows, and for those laboratories that do not currently participate, it would be highly recommended moving forward, especially if the laboratory has ISO accreditation.

Broad RSV NAAT sensitivity and specificity was most recently demonstrated via a WHO EQA panel for RSV in 2019-2020 [20]. In the WHO EQA, 98.8% of the participating laboratories had correct identification within the expected RSV Ct range, while two labs reported results with RSV Ct values two standard deviations above the mean value of other laboratories [20]. Also, of the 28

217 participating laboratories in the WHO EQA, 2/28 incorrectly reported the presence of RSV in the
218 negative specimen [20].

219 There are several initiatives for sequencing (including WGS) but systems have not been settled yet
220 and protocols are still in development at the moment of this manuscripts writing. Broadly, there is a
221 need for harmonization (diagnostics and quality assessments) and guidance and it is our hope that
222 the RSV-LabNet, as part of the PROMISE project will act as a hub for harmonization and
223 improvement of RSV diagnostics.

224 One of the key areas that needs to be addressed globally will be WGS and genotyping of RSV. As we
225 have seen with other respiratory viruses (SARS-CoV-2, influenza virus) it is of importance to have
226 active molecular epidemiology-based surveillance programs to accurately assess spread, burden,
227 and to monitor vaccine and therapeutic effectiveness. There are notable developments with regard
228 to sequencing of RSV samples which might give insight into the degree of variation among circulating
229 strains and be informative about changes in the characteristics of the virus. Also, given the
230 increasing likelihood of multiple approved vaccines and therapeutics for RSV in the near future, it
231 will be important for diagnostics and surveillance laboratories to perform WGS to monitor important
232 mutations which may affect vaccine efficacy or show reduced efficacy of the therapeutics.

233

234 Currently, RSV sequencing in diagnostic laboratories is mostly restricted to the variable regions or
235 regions covering antigenic epitopes within the G and F genes, respectively, although it is moving
236 toward WGS. WGS of RSV is shown in several recent studies and it results in partially different clade
237 assignment of strains [6-9, 21]. We recommend the continued development of WGS for RSV, which
238 is important for molecular epidemiology studies of RSV, and also will provide more detail than the
239 current methodology (F and G gene sequencing) on how RSV responds to vaccine and therapeutic
240 monoclonal antibody introduction. From information within the network, several laboratories are
241 investigating whether such WGS analysis can be implemented at their institutes. However,

implementation of WGS of RSV is technically demanding, expensive, and many laboratories expressed their need for guidance through this survey. Another aspect of RSV sequencing will be the continued development of a standard genotyping system. At this time, there are multiple suggestions for such a system, but each has its own positives and negatives, and regardless of the standard chosen, continued development will be necessary [6-9, 21]. To address this situation, our work package group within PROMISE has established an RSV genotyping working group and are working toward a unified method.

Overall, based on the results of this survey we found an active, though fragmented, diagnostic picture for RSV in Europe. Two separate events, the recent focus on respiratory disease following the SARS-CoV-2 pandemic and the development of multiple vaccine and therapeutic candidates for RSV, are driving the need for RSV diagnostic improvement and harmonization. As part of the PROMISE project, RSV-LabNet will facilitate this harmonization by sharing protocols, working toward a standard (updated) genotyping method, developing and sharing WGS protocols, and communicating openly with European and global partners.

Acknowledgements

We thank all the RSV-LabNet survey participants (listed below). We also want to acknowledge our colleagues in the PROMISE consortium (listed below). The institutions of the following co-authors are partners in Preparing for RSV Immunization and Surveillance in Europe (PROMISE); LP, WA, AM (RIVM). 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 EFPIA.

PROMISE Investigators: Jeroen Aerssens, Gabriela Ispas (Janssen, Beerse, Belgium); Bahar Ahani (AstraZeneca, Gaithersburg, Maryland, USA); Jessica Atwell, Elizabeth Begier, Tin Tin Htar (Pfizer, Paris, France); Mathieu Bangert, Rolf Kramer, Charlotte Vernhes (Sanofi Pasteur, Lyon, France); Philippe Beutels (University of Antwerp, Antwerpen, Belgium); Louis Bont (University Medical Centre Utrecht, Utrecht, the Netherlands); Harry Campbell, Harish Nair, You Li, Richard Osei-Yeboah, Xin

Wang (University of Edinburgh, Edinburgh, UK); Rachel Cohen, Gael Dos Santos, Theo Last (GlaxoSmithKline, Wavre, Belgium); Veena Kumar (Novavax, Gaithersburg, Maryland, USA); Nuria Machin (Teamit Research, Barcelona, Spain); Hanna Nohynek (Finnish National Institute for Health and Welfare, Helsinki, Finland); Peter Openshaw (Imperial College London, London, UK); John Paget (Netherlands Institute for Health Services Research, Utrecht, the Netherlands); Andrew Pollard (University of Oxford, Oxford, UK); Anne Teirlinck (National Institute for Public Health and the Environment, Bilthoven, the Netherlands)

RSV-LabNet Group

Adam Meijer – Netherlands – Rijksinstituut voor Volksgezondheid en Milieu (RIVM)
 Algirdas Griskevicius – Lithuania – National Public Health Surveillance Laboratory
 AnnaSara Carnahan – Sweden – Public Health Agency
 Catherine Moore – Wales – Public Health Wales
 Charlene Bennett – Ireland – National Virus Reference Laboratory
 Cyril Barbezange – Belgium – Sciensano
 Edita Staronová – Slovak Republic – Public Health Authority
 Gatis Pakarna – Latvia – Riga East University Hospital
 Graziella Zahra – Malta – Mater Dei Hospital
 Helena Jirincova – Czech Republic – National Institute of Public Health
 Inmaculada Casas – Spain – Instituto de Salud Carlos III
 Iván Sanz – Spain – National Influenza Centre - Valladolid
 Janine Reiche – Germany – Robert Koch Institute (RKI)
 Katarina Prosenc Trilar – Slovenija – National Laboratory for Health Environment and Food
 Lidia Brydak – Poland – National Institute of Public Health
 Maja Ilic – Croatia – Institute of Public Health
 Maria Exindari – Greece – National Influenza Reference Laboratory
 Martine Valette – France – National Influenza Centre - Lyon
 Mihaela Lazar – Romania – Cantacuzino National Military Medical Institute for Research and Development
 Mónika Rózsa – Hungary – National Public Health Center
 Monika Redlberger-Fritz – Austria – Center of Virology Medical University Vienna
 Neli Korsun – Bulgaria – National Centre of Infectious and Parasitic Diseases
 Niina Ikonen – Finland – Finnish Institute for Health and Welfare
 Ramona Trebbien – Denmark – Statens Serum Institut (SSI)
 Raquel Guiomar – Portugal – National Institute of Health Doctor Ricardo Jorge
 Richard Molenkamp – Netherlands – Erasmus Universitair Medisch Centrum
 Rory Gunson – Scotland – West of Scotland Specialist Virology Centre
 Simona Puzelli – Italy – Istituto Superiore di Sanità
 Sylvie van der Werf – France – Institut Pasteur

Missing European Free Trade Association (EFTA) countries - Iceland, Liechtenstein, Norway, and Switzerland. Missing European Union (EU) countries – Cypress, Estonia, Luxembourg, and Greece (no samples)

Table 1. Introduction questions regarding RSV surveillance and testing (for RSV-LabNet)

Questions	Responses
Is RSV notifiable in your country or region? (n=28)	Yes - 10, No - 15, Other - 3
Does your country currently perform RSV surveillance? (n=28)	Yes - 24, No - 4
What systems are used for RSV surveillance? (multiple answers possible)	Primary care surveillance - 17 Hospital based surveillance - 16 Laboratory surveillance - 20
Does your institute fulfill national RSV reference laboratory function? (n=28)	Yes - 22, No - 6 (other laboratory in country = 2, no reference laboratory in country = 4)
At what level is RSV determined in your institution? (n=27)	RSV +/-, No subtyping, No sequencing - 4 RSV +/-, Subtyping (A/B), No sequencing info - 13 RSV pos/neg, subtyping (A/B), sequencing info - 10
At your institute are RSV specimens also tested for other viruses? (n=28)	Yes - 27 No - 1

316

317 **Appendix 1**

318 RSV-LabNet Survey.pdf

319 **Supplementary**

Table S2. Molecular diagnostics questions regarding RSV testing

320

Questions	Responses
-----------	-----------

What type of specimen(s) do you use for RSV diagnostics? (multiple answers possible)	Nasopharynx swab - 26, Nasal swab - 16, Nasal aspirate - 11, Oropharynx swab - 22, Naso- and oropharynx swab - 21, Mid turbinate swab - 3, BAL -14, Sputum - 11
Do you perform RNA isolation? (method used) (n=27)	Automated - 23, Manual - 5
Do you use an RNA isolation kit? (n=28)	Kit - 27, In-house method - 1
Do you use an integrated extraction and amplification system? (n=27)	Yes - 7 (Cepheid - 4, Roche -1, Hologic - 3, Biofire - 2) No - 21
For RT-PCR or NAAT, do you use a kit or in-house method? (n=28)	Kit - 14, In-house method - 14
What gene(s) does your assay target? (multiple answers possible)	M - 6, N - 11, F - 5, L - 2, G - 3, M2-1 - 1, M2-2 - 1
Does your lab use rapid antigen tests? (n=28)	Yes - 1, No - 27
Does your lab use RSV serology? (n=25)	No - 19, Yes, for diagnostics - 5 Yes, to determine immune status - 1
Does your lab perform sequencing for RSV samples? (multiple answers possible)	WGS - 7, F gene - 4, G gene - 8, No - 13
What platform do you use to sequence RSV samples?	Illumina - 11, ABI/Sanger - 7, Nanopore - 4
In your lab are there annual evaluations of RSV assay performance by EQA? (n=27)	Yes - 21 ^a , No - 6

Is your lab currently performing virus isolation for RSV? (n=27)	Yes - 9, No - 18
--	------------------

a. EQA providers: WHO, QCMD, UK NEQAS, INSTAND

Table S3. Future planning for RSV-LabNet

Questions	Responses
Is your lab willing to share diagnostic protocols for RSV with the PROMISE Consortium? (n=27)	Yes - 20 No - 1 Other - 6
Does your laboratory currently report RSV data to TESSy or the WHO RSV surveillance project? (n=27)	TESSy - 16 WHO - 1 Both - 6 ^a Neither - 4
Is your laboratory willing to contribute to a new data collection platform, if one was created for PROMISE (to be handed over to ECDC after program is finished)? (n=26)	Yes - 18 No - 0 Other - 8 ^b

a. Officially, the WHO RSV dashboard https://ais.paho.org/phil/viz/ed_who_rsv.asp has stopped updating in 2021.

b. These laboratories were often positive to this question, but wanted to make certain it would not disrupt or interfere with other data collection platforms.

References

- Li Y, Wang X, Blau DM, 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):2047-2064.

2. Shi T, Denouel A, Tietjen AK, et al. Global disease burden estimates of respiratory syncytial virus – associated acute respiratory infection in older adults in 2015: A systematic review and meta-analysis. *J Infect Dis* 2020; 222(Suppl 7):S577-S583.
3. StatPearls. Respiratory Syncytial Virus Infection. <https://www.ncbi.nlm.nih.gov/books/NBK459215/>. Accessed 07 January 2023.
4. PATH. RSV Vaccine and mAb Snapshot. <https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/>. Accessed 07 January 2023.
5. Borchers AT, Chang C, Gershwin ME, Gershwin LJ. Respiratory Syncytial Virus – A Comprehensive Review. *Clin Rev Allergy & Immuno* 2013; 45:331-379.
6. Goya S, Galiano M, Nauwelaers I, et al. Toward unified molecular surveillance of RSV: A proposal for genotype definition. *Influenza Other Respir Viruses* 2020; 14(3):274-285.
7. Ramaekers K, Rector A, Cuypers L, et al. Towards a unified classification for human respiratory syncytial virus genotypes. *Virus Evolution* 2020; Vol. 6, Issue 2 July.
8. Munoz-Escalante JC, Comas-Garcia A, Bernal-Silva S, et al. Respiratory syncytial virus A genotype classification based on systematic intergenotypic and intragenotypic sequence analysis. *Scientific Reports* 2019; 9:20097
9. Salimi V, Viegas M, Trento A, Agoti CN, et al. Proposal for human respiratory syncytial virus nomenclature below the species level. *Emerg Infect Dis* 2021; Jun;27(6):1-9.
10. Yu JM, Fu YH, Peng XL, Zheng YP, He JS. Genetic diversity and molecular evolution of human respiratory syncytial virus A and B. *Scientific Reports* 2021; 11:12941.
11. Li Y, Wang X, Broberg EK, et al. 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).
12. Staadegaard L, Meijer A, Rodrigues AP, et al. Temporal variations in respiratory syncytial virus epidemics, by virus subtype, 4 countries. *Emerg Infect Dis* 2021; 27(5)
13. Staadegaard L, Caini S, Wangchuk S, et al. Defining the seasonality of respiratory syncytial virus around the world: National and subnational surveillance data from 12 countries. *Influenza Other Respir Viruses* 2021; 15(6):732-741.
14. Moss crop LG, Williams TC, Tregoning JS. Respiratory syncytial virus after the SARS-CoV-2 pandemic-what next? *Nat Rev Immuno* 2022; 22:589-590.
15. Rose A, Kissling E, Emborg H-D, et al. Interim 2019/20 influenza vaccine effectiveness: six European studies, September 2019 to January 2020. *Euro Surveill.* 2020;25(10).
16. Rose AMC, Kisslin E, Gerasim A, et al. Vaccine effectiveness against influenza A(H3N2) and B among laboratory-confirmed, hospitalized older adults, Europe, 2017-2018: A season of B lineage mismatched to the trivalent vaccine. *Influenza Other Respir Viruses.* 2020 Feb 5.
17. ECDC. Core functions of microbiology reference laboratories for communicable diseases technical report. https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/1006_TER_Core_functions_of_reference_labs.pdf. Accessed 28 July 2023.
18. Teirlinck AC, Broberg EK, Berg AS, et al. Recommendations for respiratory syncytial virus surveillance at the national level. *Euro Respi Journal.* 2021 58:200376
19. Mollers M, Barnadas C, Broberg EK, et al. Current practices for respiratory syncytial virus surveillance across the EU/EEA Member States, 2017. *Euro Surveill.* 2019 Oct;24(40) 1900157.
20. Williams T, Jackson S, Barr I, et al. Results from the second WHO external quality assessment for the molecular detection of respiratory syncytial virus, 2019-2020. *Influenza Other Respir Viruses* 2023; January;17(1):e13073
21. Chen J, Qui X, Avadhanula V, et al. Novel and extendable genotyping system for human respiratory syncytial virus based on whole-genome sequence analysis. *Influenza Other Respir Viruses* 2022; May;16(3):492-500.

Footnote Page

Conflict of Interest Statement: The authors note no potential conflicts of interest.

Funding Statement: The institutions of the following co-authors are partners in Preparing for RSV Immunization and Surveillance in Europe (PROMISE); LP, WA, AM (RIVM). 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 EFPIA.

Mention of any meeting(s) where the information has previously been presented: Preliminary data from this survey was presented at the virtual PROMISE RSV-LabNet Introduction Meeting 13 December 2022. There was no abstract submitted, as it was not specifically a scientific meeting, but more an organizational kick-off meeting.

Corresponding author contact information: Adam Meijer – adam.meijer@rivm.nl
Dutch National Institute for Public Health and the Environment (RIVM)
PO Box 1 3720 BA Bilthoven
Antonie van Leeuwenhoeklaan 9 3721 MA Bilthoven
T +31 08 868 935 95
M +31 06 311 464 42