GenEpi-BioTrain - Virtual training 13 - RSV Insights

RSV Surveillance, Immunisation and Public Health Policy

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Intended Learning Objectives

Specific objectives of this session:

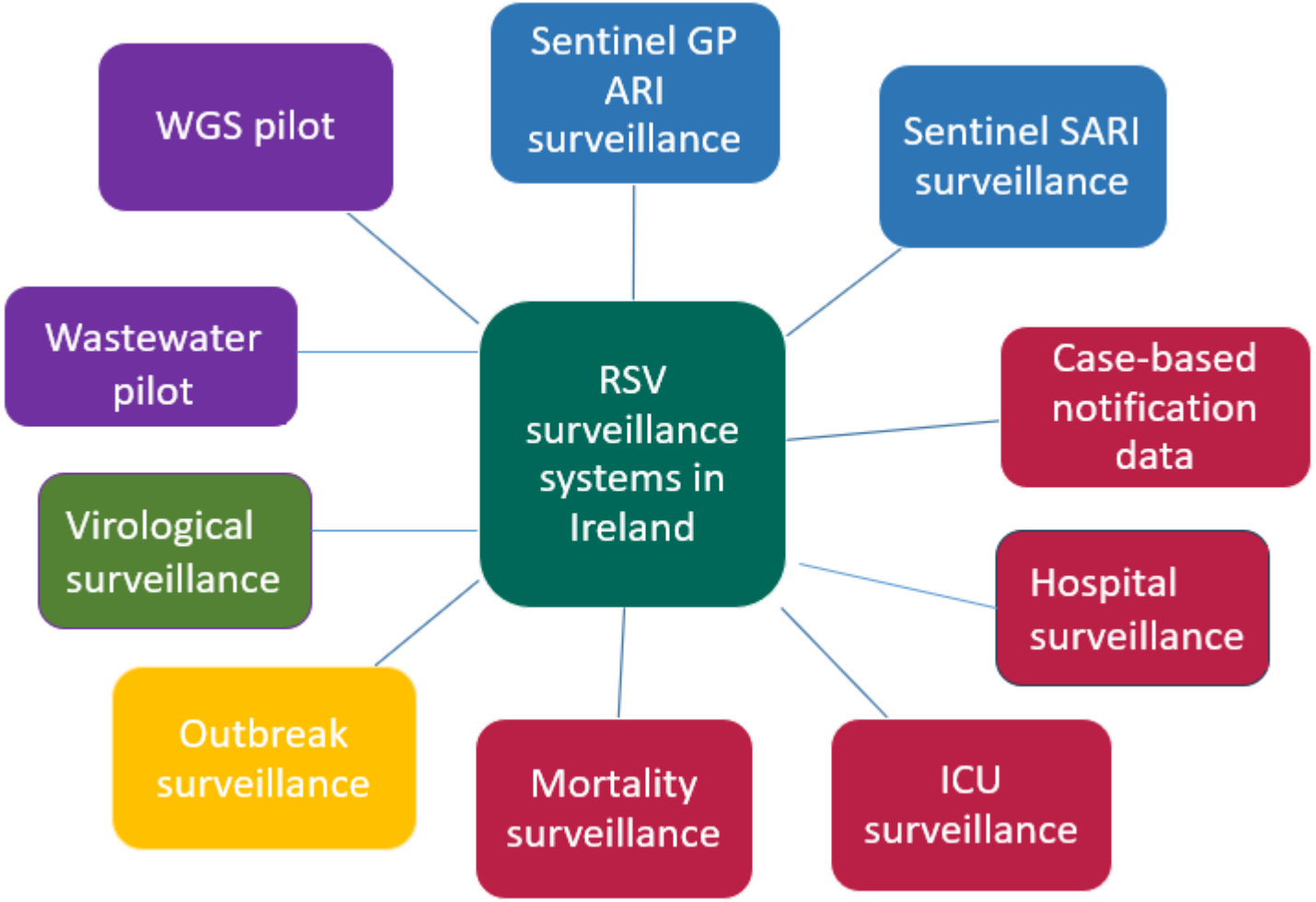
1. Learn about RSV surveillance systems in Ireland
2. Learn about RSV epidemiology in Ireland
3. Learn about RSV immunisation strategies
4. Awareness of the need for sampling frameworks/genomic strategies

Outline

This session consists of the following elements

1. Brief introduction to RSV surveillance in Ireland
2. RSV as a notifiable disease
3. RSV case definitions
4. RSV epidemiology
5. RSV immunisation
6. Back to surveillance - objectives, sampling frameworks and strategies

RSV surveillance in Ireland



- HPSC has developed a mosaic of integrated respiratory virus surveillance systems
- Priority surveillance objectives

Integrated Reports - Health Protection Surveillance Centre

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Question # 1

RSV as a notifiable disease

- Worldwide, RSV is associated with 34 million cases of acute respiratory tract infection (ARI) annually, over 3 million hospitalisations and more than 50,000 deaths in children below the age of 5 years.
- RSV became notifiable in Ireland in 2012 - one of the first countries in Europe
- RSV is also notifiable in the UK, Germany, Australia, Japan, New York State
- In the European Union RSV is not *currently* a mandatory notifiable disease

RSV as a notifiable disease in Ireland

Benefits

- Wealth of RSV surveillance data over a number of years
- Timing of RSV seasons (previously for Palivizumab and now for Nirsevimab/other immunisation programmes)
- Burden on the population and health system
- Baseline data – prior to the implementation of RSV immunisation programme(s)
- Solid base for further RSV research/epidemiological studies

Challenges

- In 2012 – additional workloads for regional Departments of Public Health

Innovation

- Innovative technical solutions to reduce notification workloads
- In 2020/2021 - Robotic Process Automation (RPA) developed for COVID-19 notifications
- In 2022 – RPA technology was further developed for RSV (and influenza)

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Question # 2

RSV Case Definitions

RSV case definition in Ireland

Clinical criteria

Any person presenting with a compatible clinical illness. Primary infection with RSV manifests clinically as pneumonia, bronchiolitis, tracheobronchiolitis or upper respiratory tract infection (often accompanied by fever and otitis media).

Laboratory criteria

At least one of the following four:

- Isolation of respiratory syncytial virus (RSV) in tissue cell culture from respiratory secretions
- Identification of RSV RNA in respiratory specimens by RT-PCR or other nucleic acid testing technique
- Identification of RSV-specific viral antigen in respiratory specimens
- 4-fold or greater rise in RSV antibody titre in paired acute and convalescent sera

Case classification

Confirmed case - Any person meeting the clinical and laboratory criteria

Case Definitions - Health Protection Surveillance Centre

ARI, ILI and SARI case definitions

Acute respiratory infection (ARI)

Sudden onset of symptoms

AND

at least one of the following four respiratory symptoms:

- Cough, sore throat, shortness of breath, coryza

AND

A clinician's judgement that the illness is due to an infection

EU case definitions

Influenza-like illness (ILI)

Sudden onset of symptoms

AND

at least one of the following four systemic symptoms:

- Fever or feverishness, malaise, headache, myalgia

AND

at least one of the following three respiratory symptoms:

- Cough, sore throat, shortness of breath

EU case definitions

Severe Acute Respiratory Infection (SARI)

A person hospitalised for at least 24 hours with ARI, with at least one of the following symptoms:

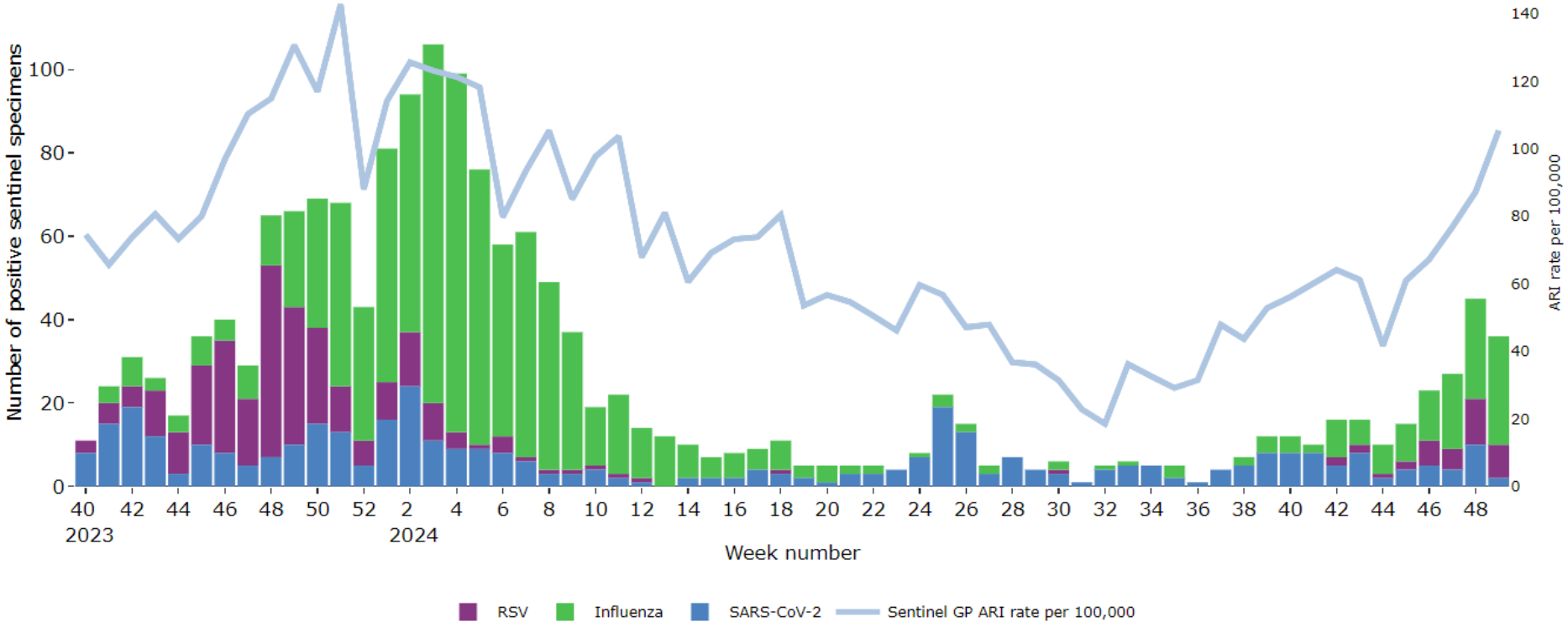
- cough, fever, shortness of breath

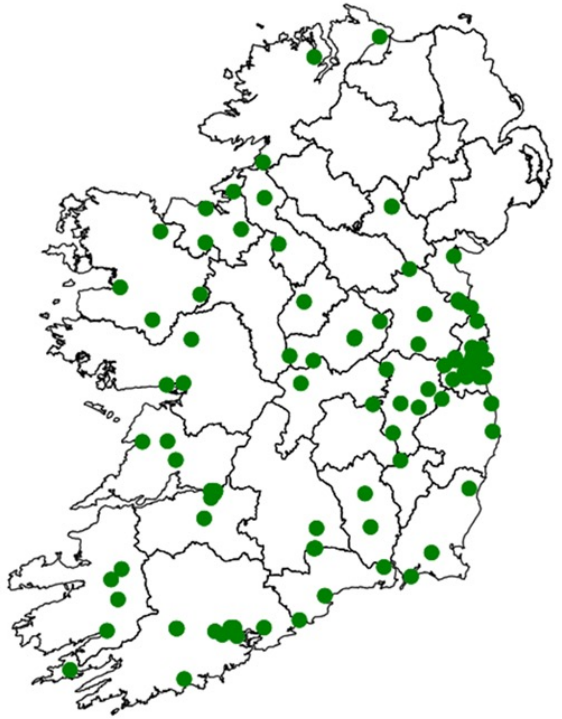
OR

- sudden onset of anosmia, ageusia or dysgeusia with onset of symptoms within 14 days prior to hospital admission.

RSV epidemiology in Ireland

Sentinel GP surveillance, Ireland

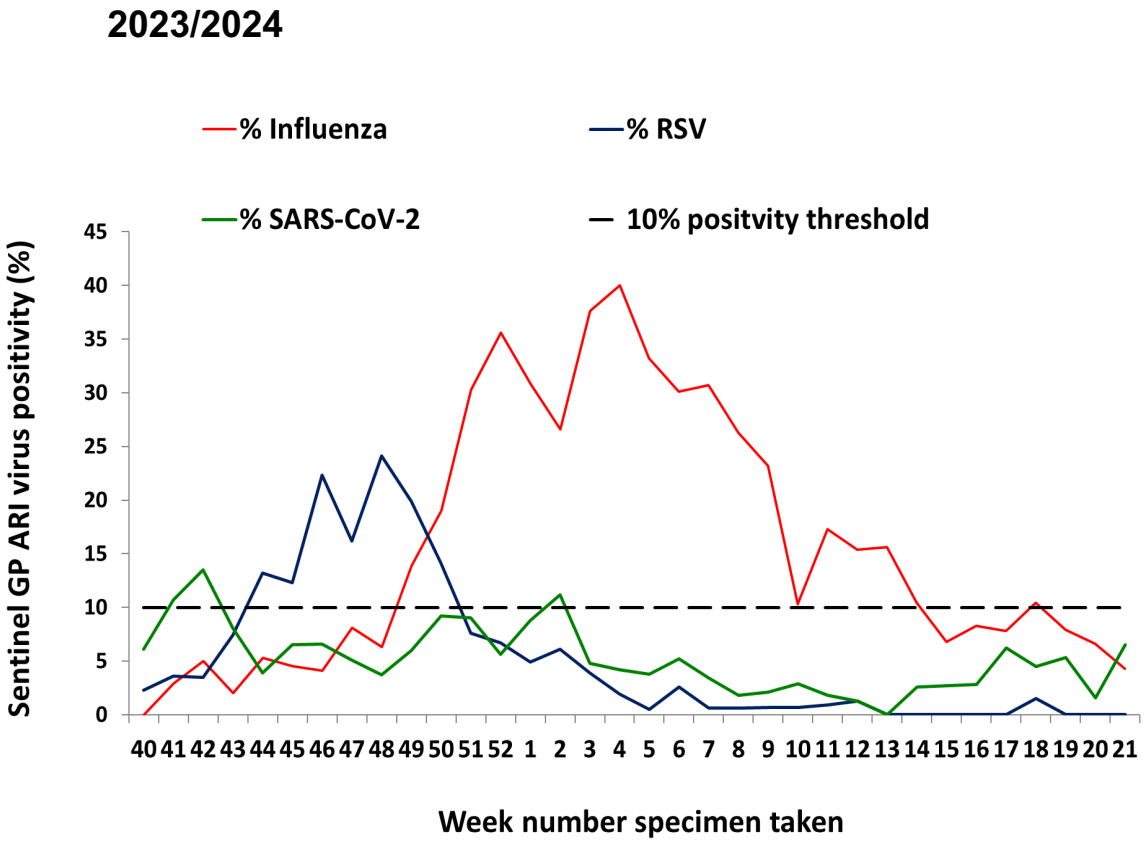


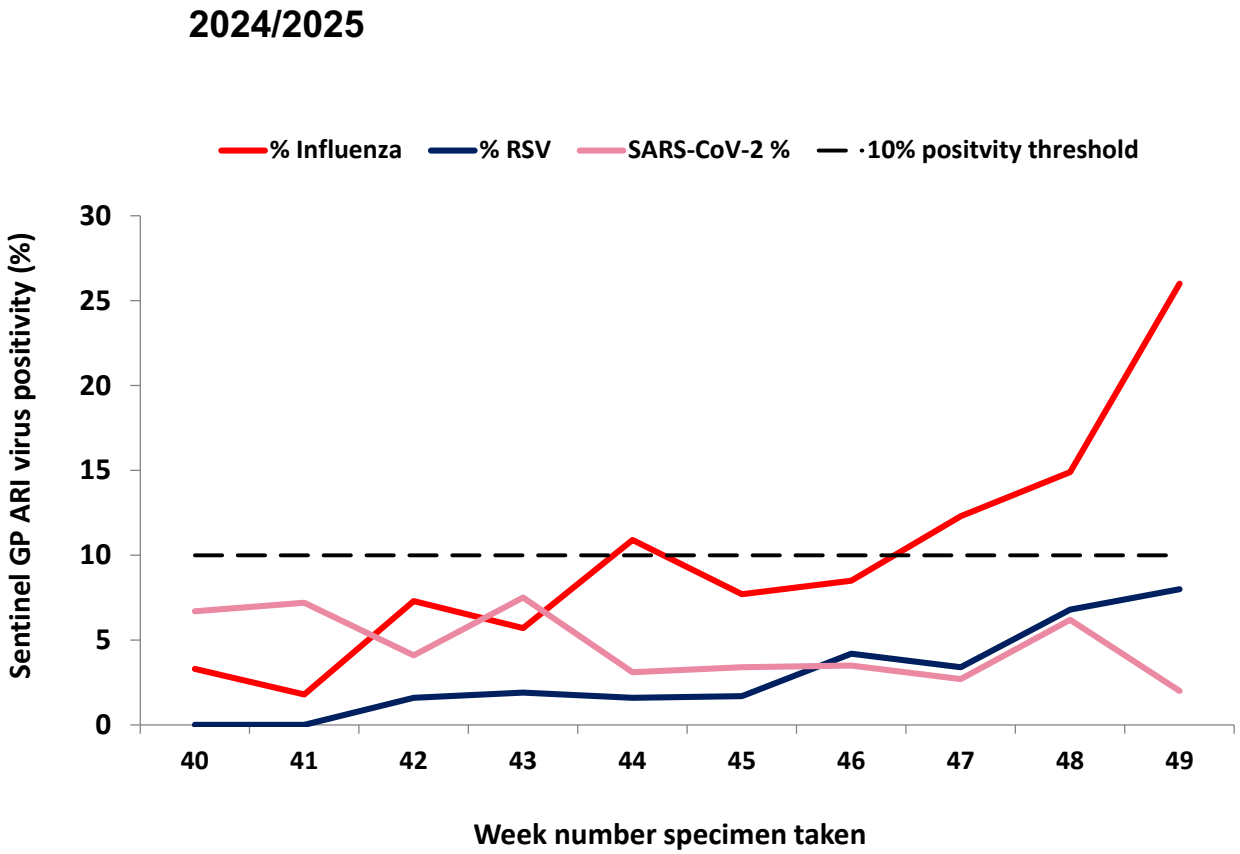


- Irish sentinel GP network established in 2000 – originally to monitor influenza-like illness (ILI)
- Network was strengthened and expanded – 10.6% population coverage
- ARI surveillance implemented during the 2023/2024 season
- First five ARI patients presenting per practice – systematically tested for RSV, influenza, SARS-CoV-2 and ORVs

Sentinel GP RSV positivity

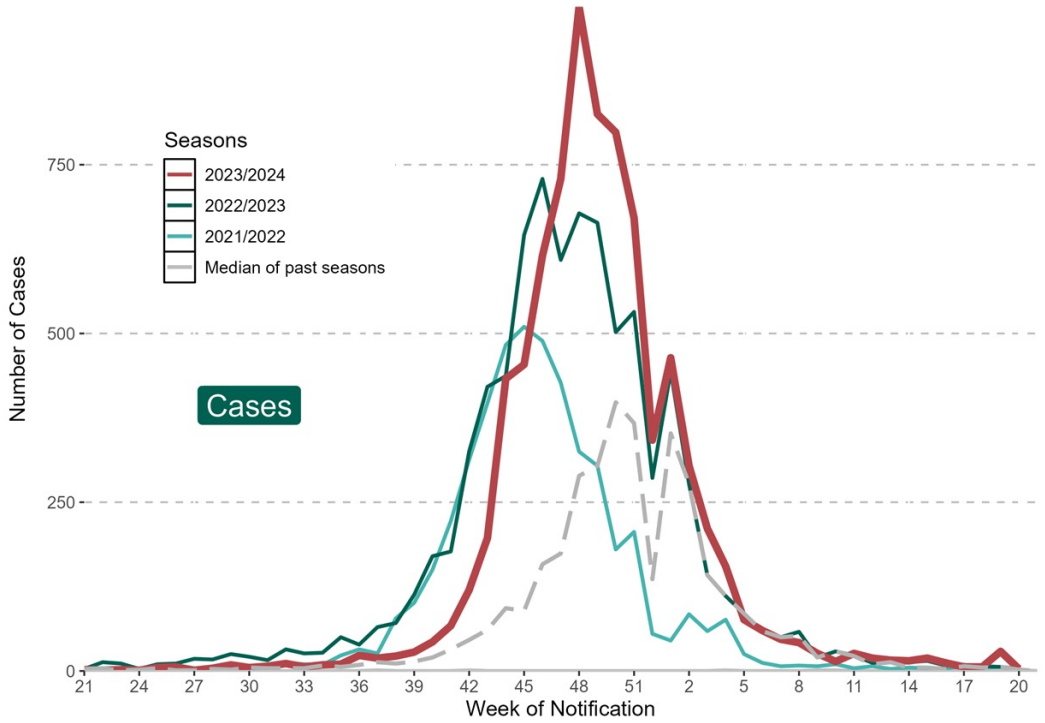
- 2023/2024 - RSV positivity peaked at **24.1%** in week 48 2023
- 2024/2025 - RSV positivity has not exceeded 10% positivity (to date)

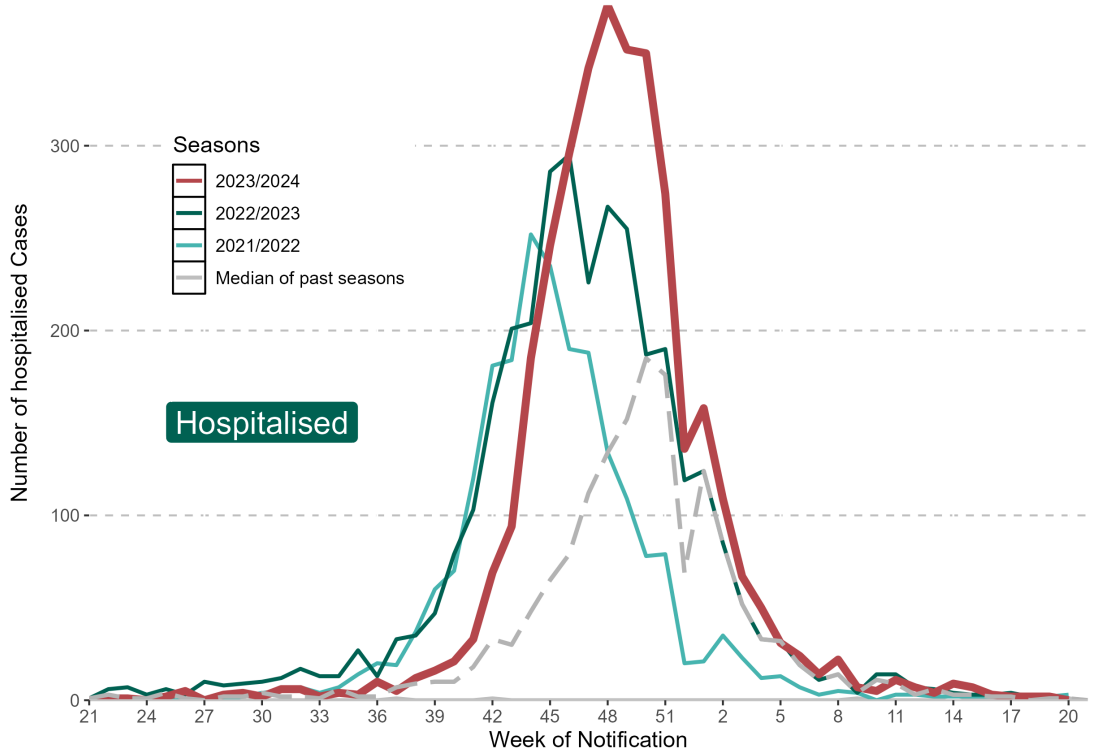




RSV case-based notification data, Ireland

- 2023/2024 severe RSV season – hospitalisations at highest level ever recorded at peak
- Improved case ascertainment and testing
- Timing of 2023/2024 season – slightly earlier than pre-pandemic seasons, shifting back to pre-pandemic seasonality

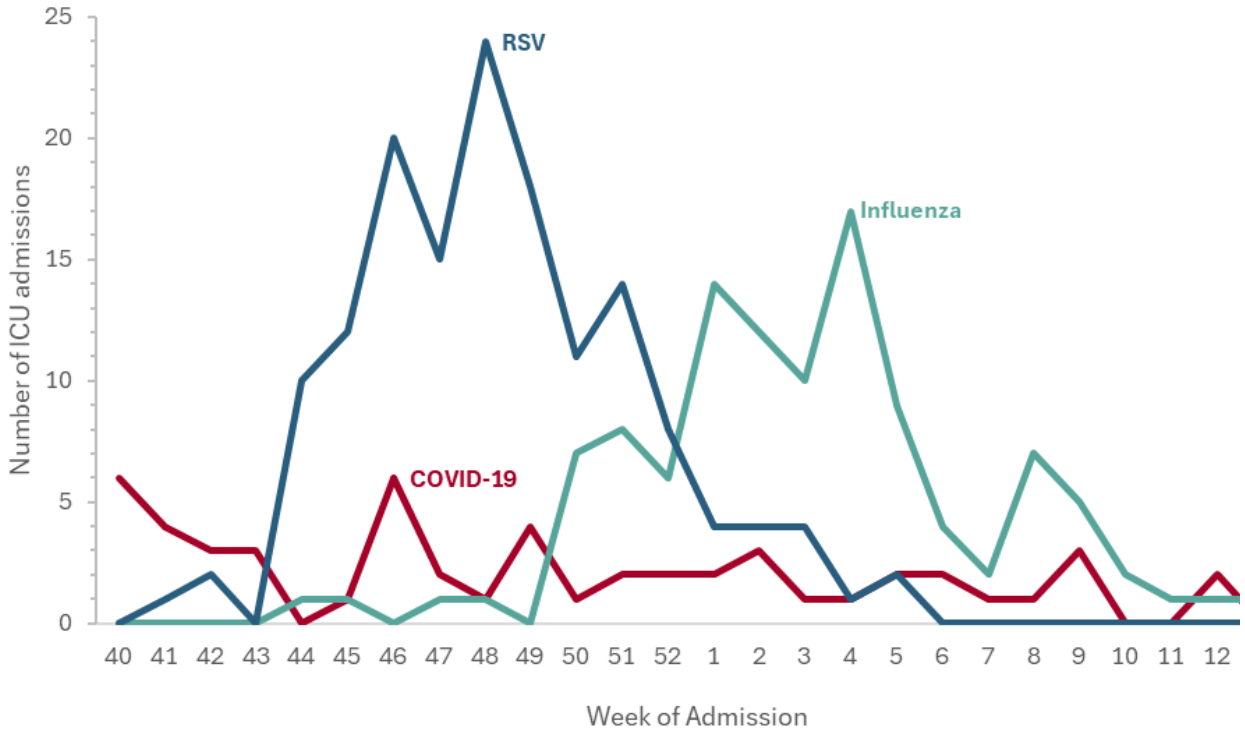


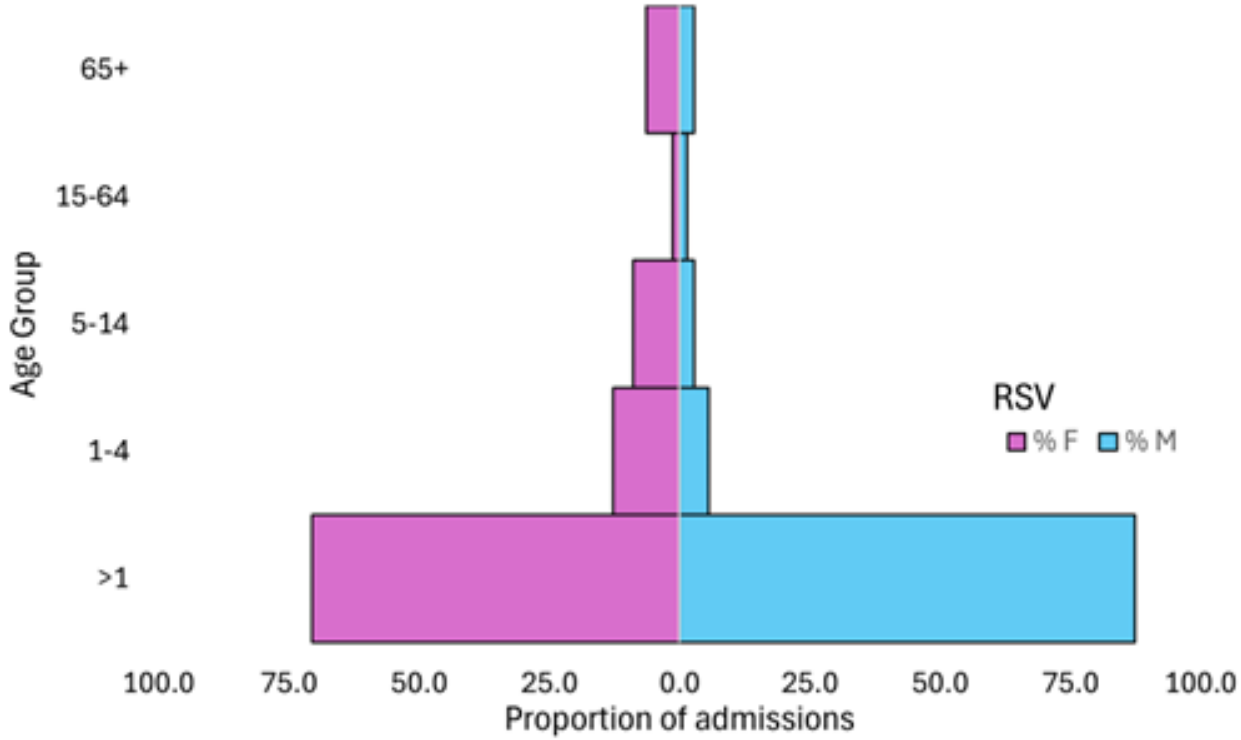


A review of the 2023/2024 influenza and respiratory syncytial virus (RSV) season in Ireland

RSV ICU surveillance, 2023/2024, Ireland

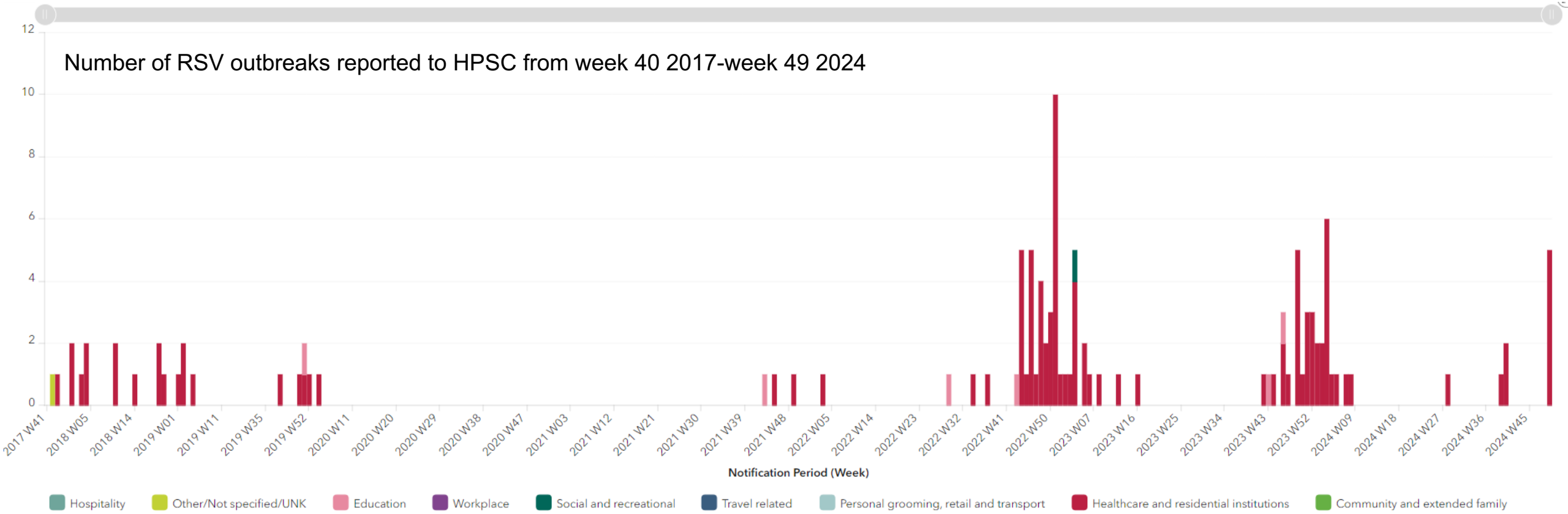
- RSV ICU surveillance began in the 2023/2024 season
  - 150 RSV cases admitted to ICU during the 2023/2024 season
  - 79% (118/150) of cases were aged <1 year of age





RSV outbreak surveillance, Ireland

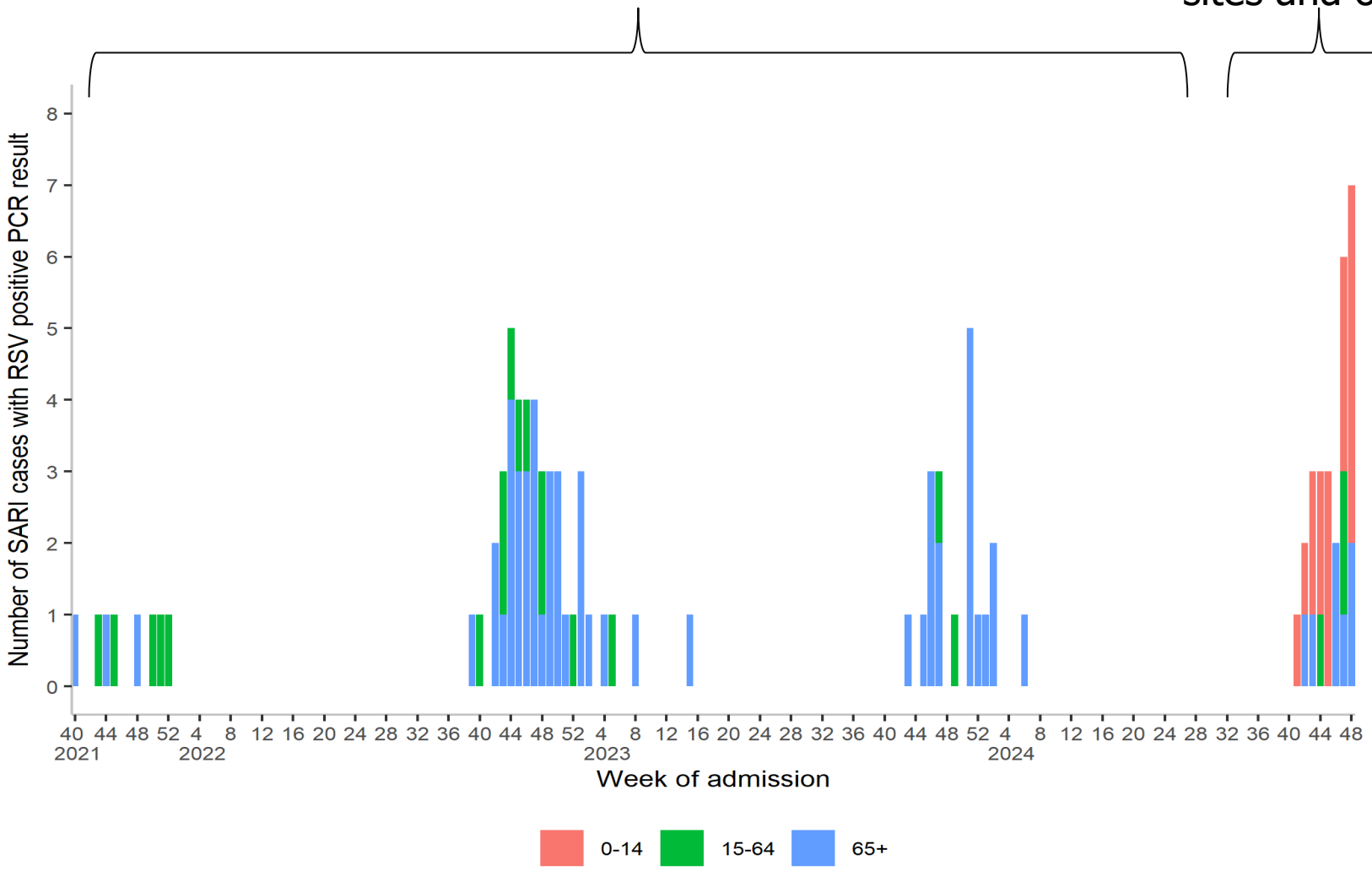
- Increased number of RSV outbreaks reported - 2022/2023 & 2023/2024 seasons
- Majority of outbreaks in health and care settings and residential institutions – underreporting of outbreaks in educational settings

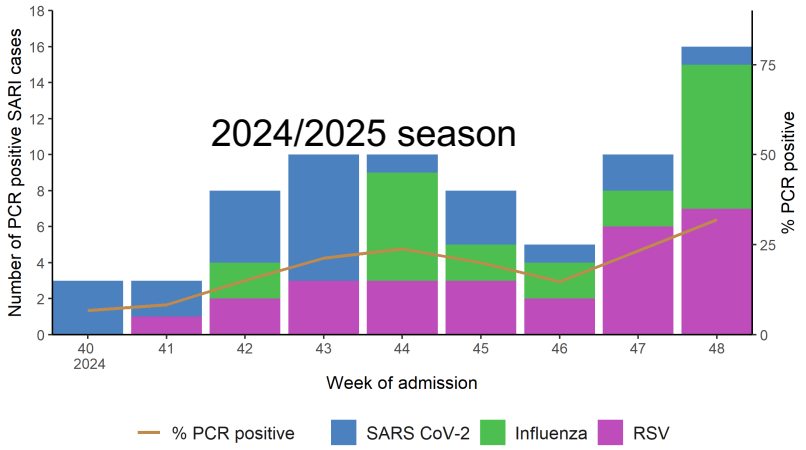


SARI RSV positive cases reported in Ireland, 2021/22 – 2024/25

One SARI hospital - adult only

Three SARI hospitals – two adult sites and one paediatric site

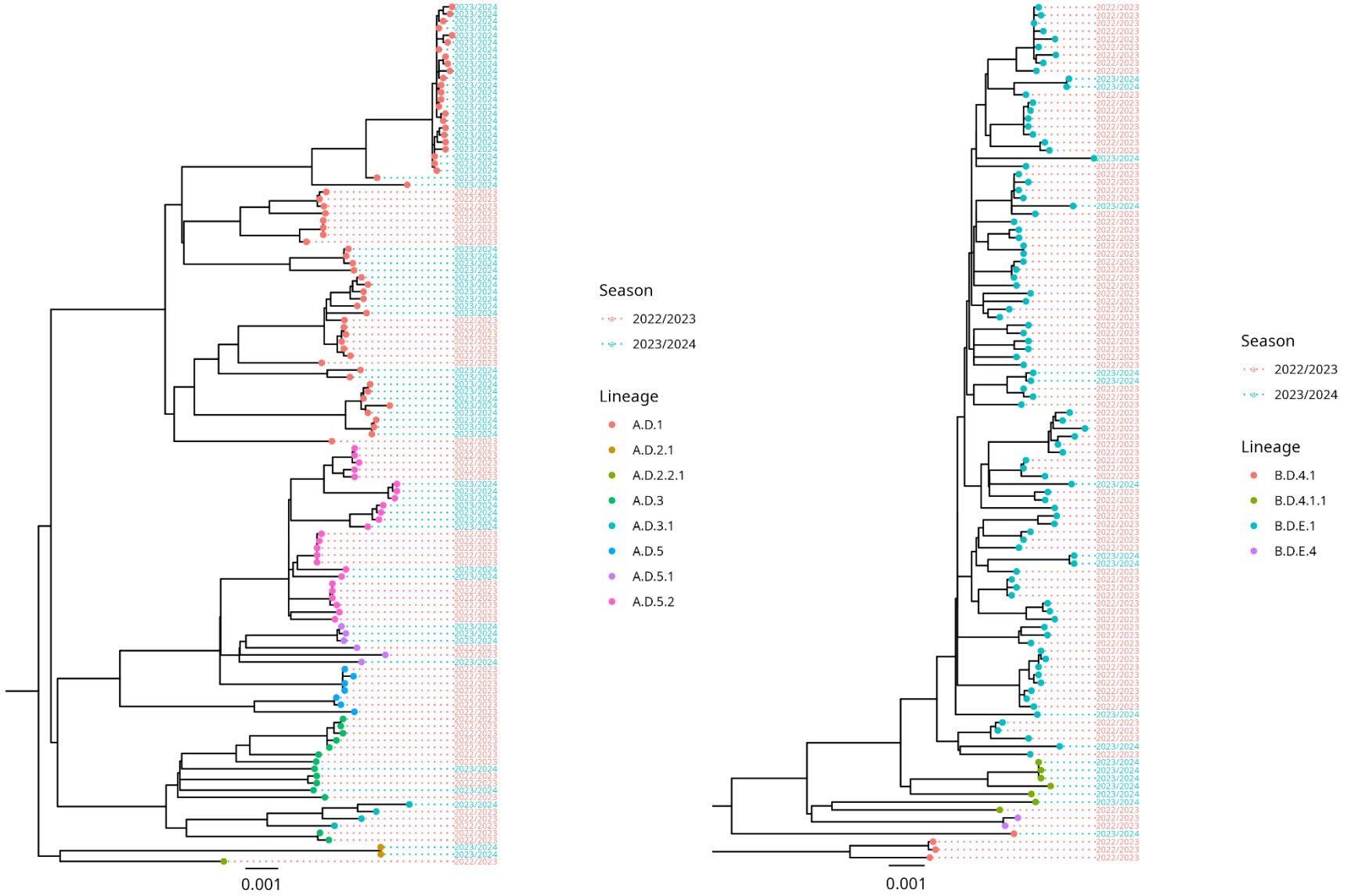




[Severe Acute Respiratory Infection surveillance programme expanded to new acute hospital sentinel sites]

[Severe Acute Respiratory Infections (SARI) - Health Protection Surveillance Centre]

RSV WGS pilot, 2022/2023 & 2023/2024, Ireland



- National Virus Reference Laboratory (NVRL), UCD Ireland conducted a pilot RSV WGS study
- Ongoing - link to epi data
- Future seasons
  - Sampling framework
  - Funding dependent

https://www.medrxiv.org/content/10.1101/2024.07.23.24310850v1

RSV Immunisation

National Immunisation Advisory Committee (NIAC) RSV recommendations, October 2023

1. **Passive immunisation of all infants against RSV during their first RSV season**
   "Two forms of passive immunisation for infants against RSV have recently been authorised in the EU; a long-acting monoclonal antibody (nirsevimab) which can be administered to the infant directly, and a maternal vaccine RSV preF (Abrysvo, Pfizer) which can provide infant protection through transplacental antibody transfer. Both products have acceptable safety and efficacy profiles. Further analysis of cost effectiveness and programmatic considerations is required to determine the most appropriate RSV passive immunisation strategy for Irish infants."

2. **RSV vaccination for those aged 65 years and older** with either RSV PreF3 (Arexvy, GSK) or RSV preF (Abrysvo, Pfizer). *"Further analysis of cost and product availability is needed to determine which product is more suitable for use in Ireland."*

Recommendations may be updated if more information becomes available

Royal College of Physicians of Ireland Website > Healthcare Leadership > NIAC > Advice Provided to the Department of Health (rcpi.ie)

National Immunisation Advisory Committee (NIAC) RSV recommendations for 2024/2025 season, April 2024

Passive immunisation with nirsevimab of:

- **all infants who are born during the RSV season.** These infants should receive nirsevimab ideally prior to discharge home from a maternity hospital
- **all high-risk infants aged ≤12 months** at the start of their first RSV season
- **all infants who are aged ≤6 months** at the start of the RSV season
- **all ex-preterm infants under 24 months of age with Chronic Lung Disease** in their second RSV season
- In the event of short supply or **programmatic limitations** youngest infants (**those born during the RSV season**) and **high-risk infants in their first RSV season** should be prioritised

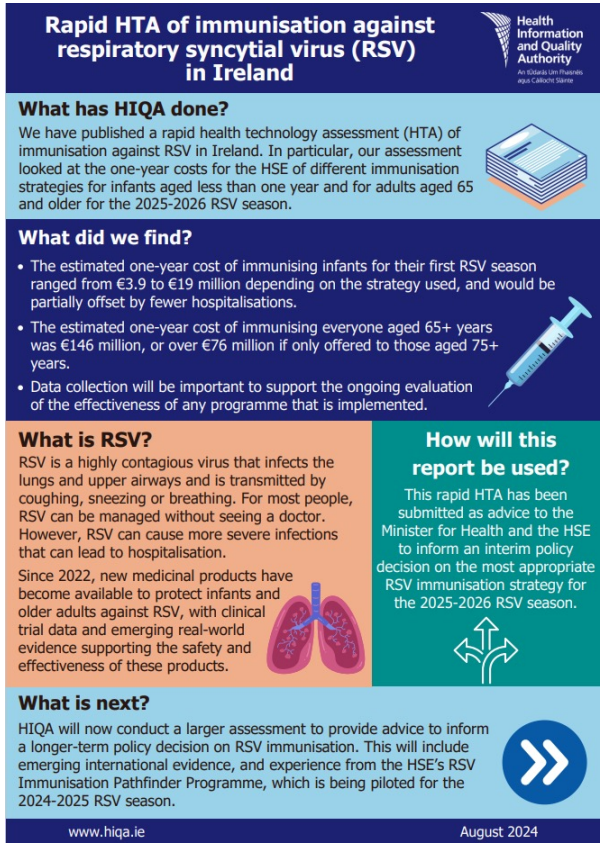
Royal College of Physicians of Ireland Website > Healthcare Leadership > NIAC > Advice Provided to the Department of Health (rcpi.ie)

RSV Immunisation in Ireland

- NIAC considers the evidence and provides advice to the Chief Medical Officer and the Department of Health (DOH)
- The Department and the Minister for Health make policy decisions on vaccines/immunisations which are implemented by the Health Service Executive (HSE)
- DOH requested RSV Health Technology Assessments (HTA) – HIQA – rapid and full HTA Home | HIQA
- HSE business case was submitted and approved by DOH for funding
- HSE agreed to establish RSV Nirsevimab Pathfinder Programme for 2024/2025 season
    - ‘Pathfinder’ initiative designed to explore and establish innovative approaches to improving health outcomes within a community or population

Health Technology Assessments

- Health Information and Quality Authority (HIQA) in Ireland Home | HIQA
- Health Technology Assessments (HTA) – HIQA – rapid and full HTA
- Rapid HTA - to inform an interim policy decision on the most appropriate RSV immunisation strategy for infants and or adults for the 2025-2026 season



Rapid HTA of immunisation against respiratory syncytial virus (RSV) in Ireland

Health Information and Quality Authority

What has HIQA done?

We have published a rapid health technology assessment (HTA) of immunisation against RSV in Ireland. In particular, our assessment looked at the one-year costs for the HSE of different immunisation strategies for infants aged less than one year and for adults aged 65 and older for the 2025-2026 RSV season.

What did we find?

- The estimated one-year cost of immunising infants for their first RSV season ranged from €3.9 to €19 million depending on the strategy used, and would be partially offset by fewer hospitalisations.
- The estimated one-year cost of immunising everyone aged 65+ years was €146 million, or over €76 million if only offered to those aged 75+ years.
- Data collection will be important to support the ongoing evaluation of the effectiveness of any programme that is implemented.

What is RSV?

RSV is a highly contagious virus that infects the lungs and upper airways and is transmitted by coughing, sneezing or breathing. For most people, RSV can be managed without seeing a doctor. However, RSV can cause more severe infections that can lead to hospitalisation.

Since 2022, new medicinal products have become available to protect infants and older adults against RSV, with clinical trial data and emerging real-world evidence supporting the safety and effectiveness of these products.

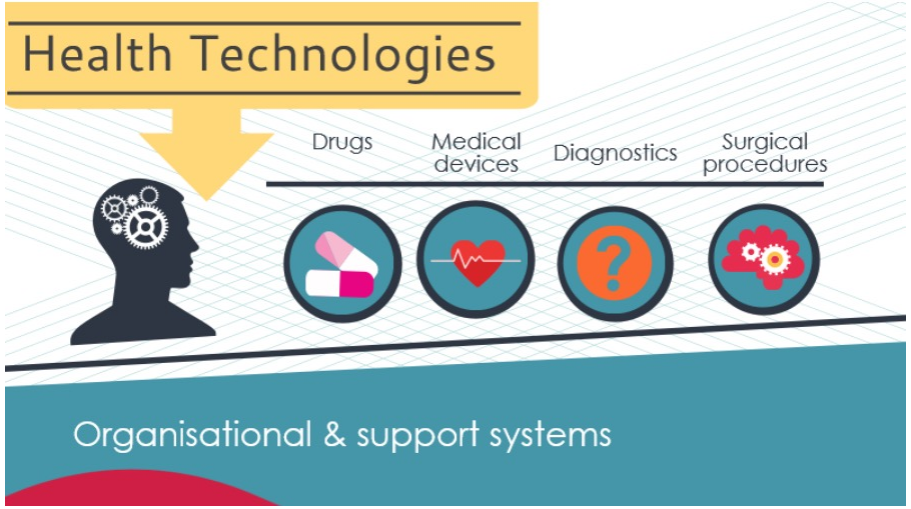
How will this report be used?

This rapid HTA has been submitted as advice to the Minister for Health and the HSE to inform an interim policy decision on the most appropriate RSV immunisation strategy for the 2025-2026 RSV season.

What is next?

HIQA will now conduct a larger assessment to provide advice to inform a longer-term policy decision on RSV immunisation. This will include emerging international evidence, and experience from the HSE's RSV Immunisation Pathfinder Programme, which is being piloted for the 2024-2025 RSV season.

www.hiqa.ie August 2024



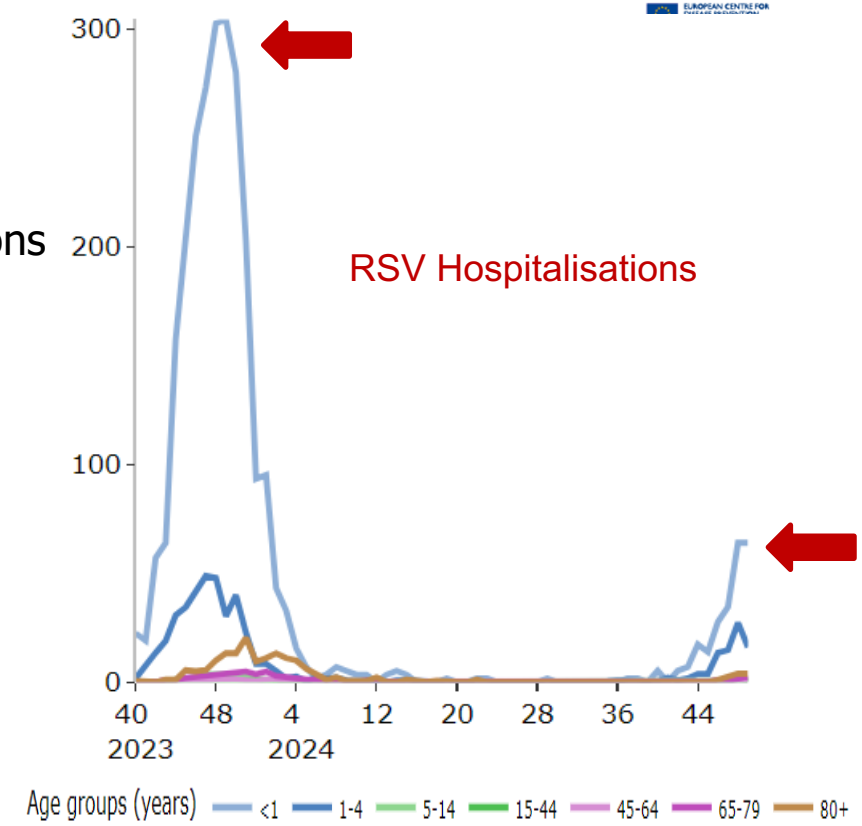
RSV Nirsevimab Pathfinder programme in Ireland

- RSV Nirsevimab Pathfinder Programme implemented for 2024/2025 season
- Commenced on Sunday 1st September 2024
- **All infants born between 1st September 2024 - 28 February 2025** to receive Nirsevimab in maternity hospital units on day 2 of life
- **At risk infants who previously received Palivizumab** also to receive Nirsevimab
- Challenges – funding, resources, data management, short timeline

RSV immunisation for newborns - HSE.ie

RSV surveillance in Ireland, 2024/2025 (up to week 49 2024)

- Number of notified **cases** and **hospitalisations** to date, **lower** than recent seasons
- **Later season** than recent years, similar to pre-pandemic pattern
- Overall rates highest in those aged <1 year – at significantly lower level
- 460 hospitalisations weeks 40-49 2024, compared to 1972 weeks 40-49 2023
- 14 ICU cases and no deaths notified for the season to date (weeks 40-49 2024)



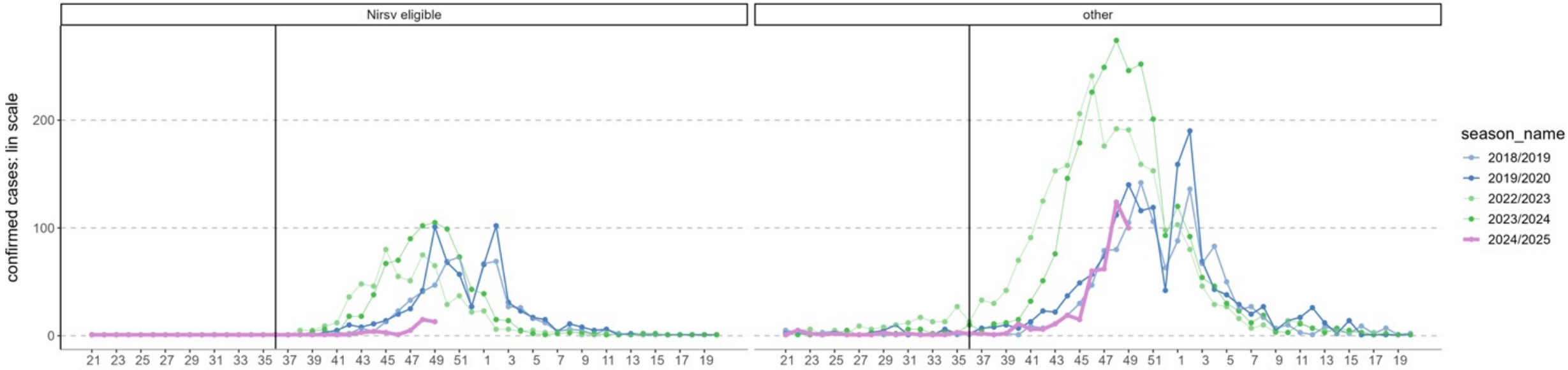
Since the implementation of Nirsevimab programme, 01/09/2024

- Over **12,000** infants immunised; cumulative uptake **83%** (by 08/12/2024)

- 41 notified RSV cases, including **24 hospitalisations** & **5 ICU admissions** in infants born since 01/09/2024
- 656 notified RSV cases, including **413 hospitalisations** & **64 ICU admissions** in infants born during the same time-period in 2023

RSV epidemiology during first twelve weeks of RSV Nirsevimab Pathfinder Programme in Ireland

RSV hospitalised cases in Ireland by season
Epi curves 1) for infants born Sept-Feb 2) all others



Notes

- Figure on left refers to all laboratory confirmed RSV hospitalised cases notified in infants born between September-February and aged <6 months
- Other – refers to all other laboratory confirmed RSV hospitalised cases notified (excluding infants born Sep-Feb)

RSV hospitalised cases – for infants born Sept-Feb*
Fitted Curves and growth rates

Fig 1: Confirmed hospitalised cases

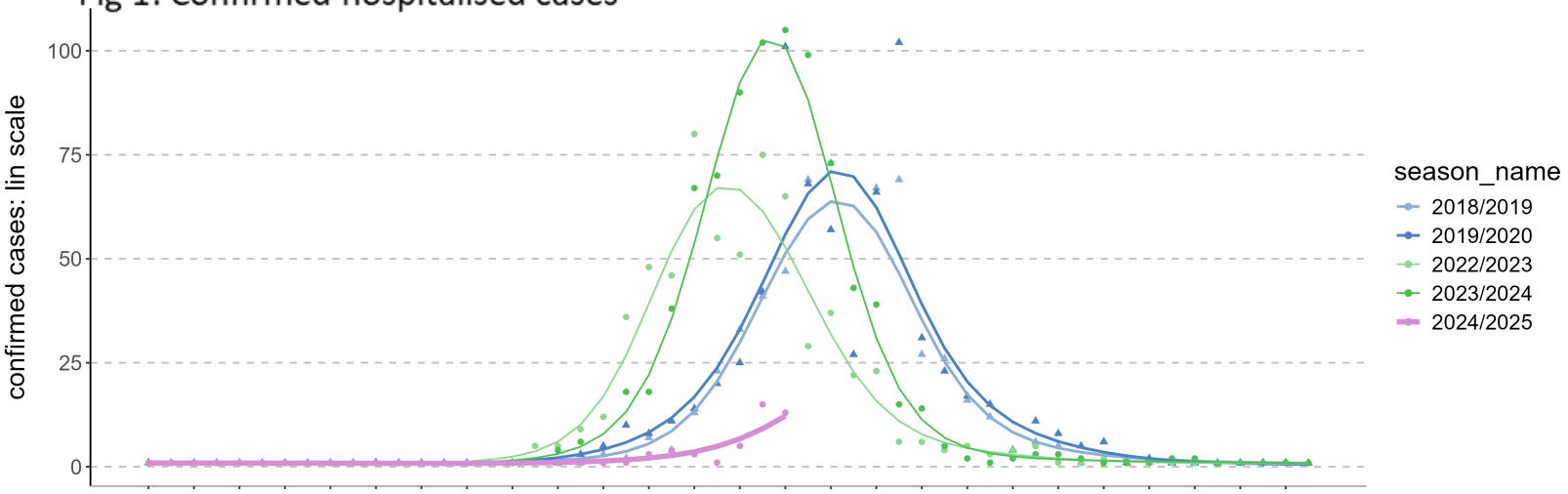
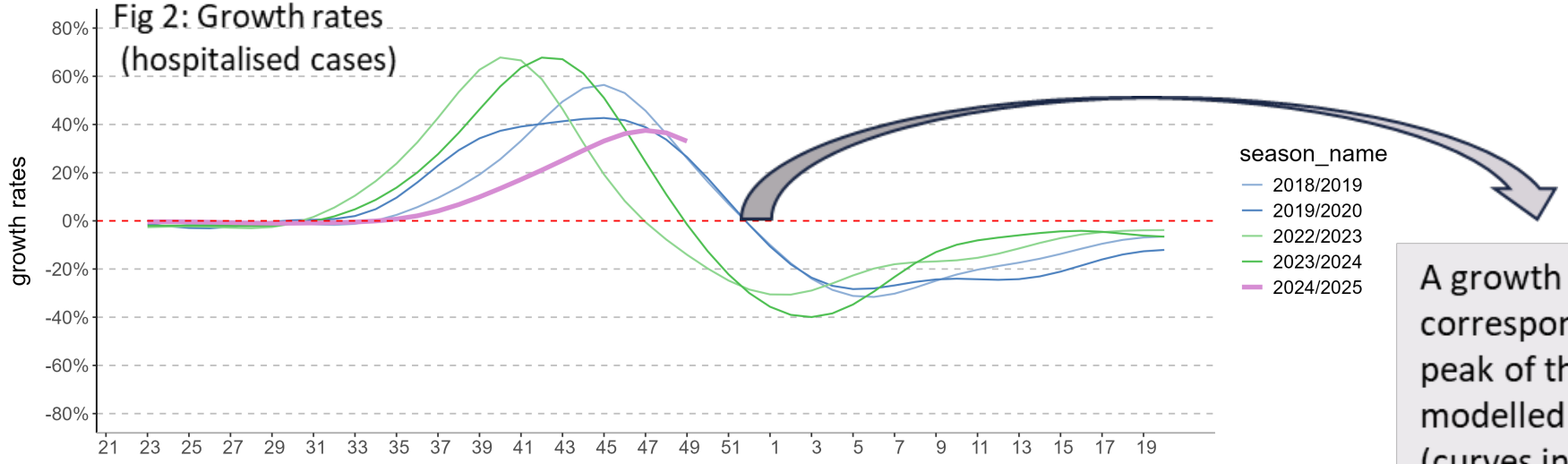


Fig 2: Growth rates (hospitalised cases)



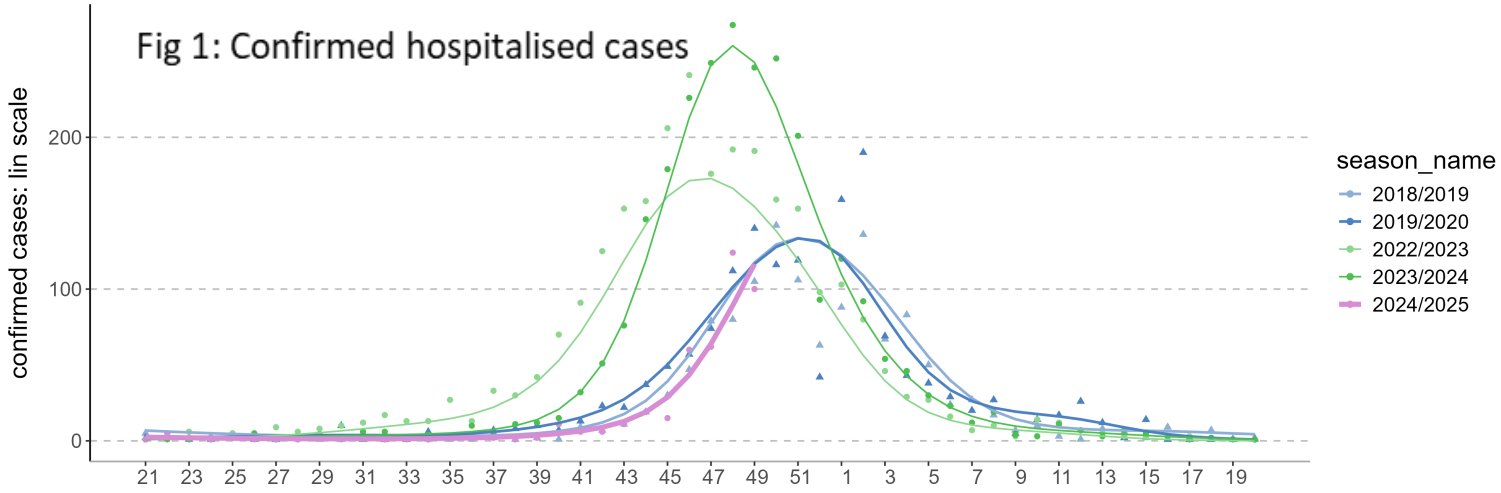
A growth rate of 0% corresponds to peak of the modelled data (curves in Fig 1) .

Technical Note: The curves are fitted to the observed hospitalised counts using Generalised Additive Models (GAMs)

The **most recent growth rate, week 49** based on modelled curve is approximately **33%,** down from fastest rate of 38% in week 47.

*Infants born Sept – Feb and less than six months at confirmed case date.

RSV hospitalised cases – All other cases*
Fitted Curves and growth rates



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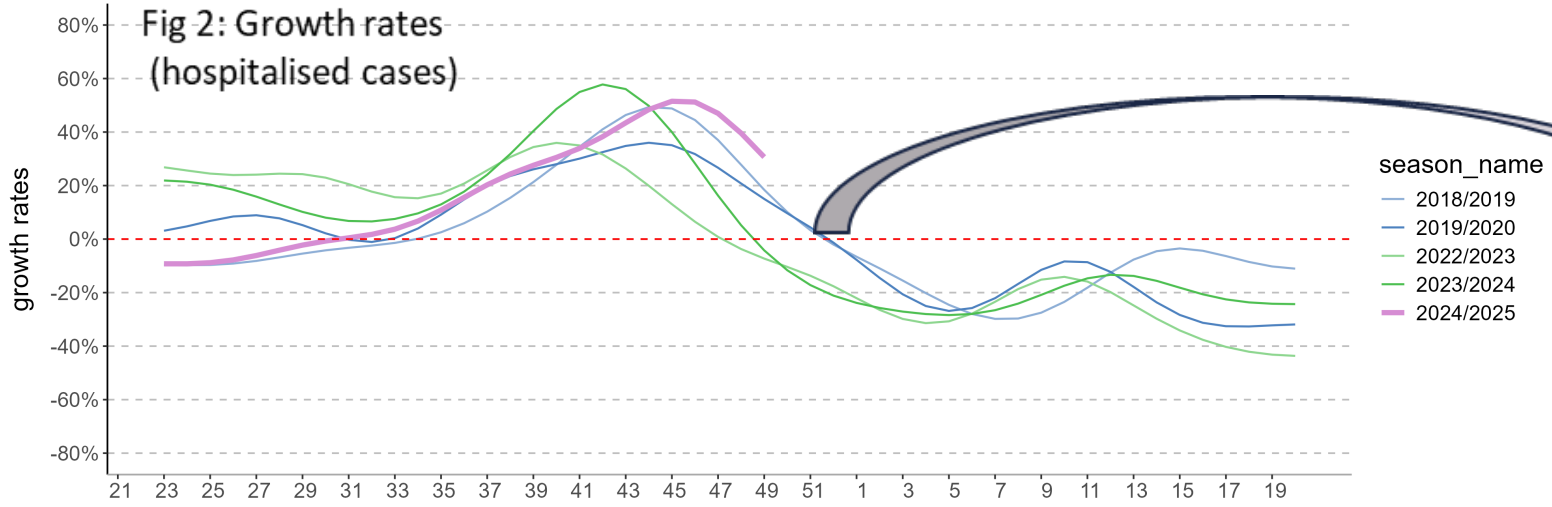


A growth rate of 0% corresponds to peak of the modelled data (curves in Fig 1) .

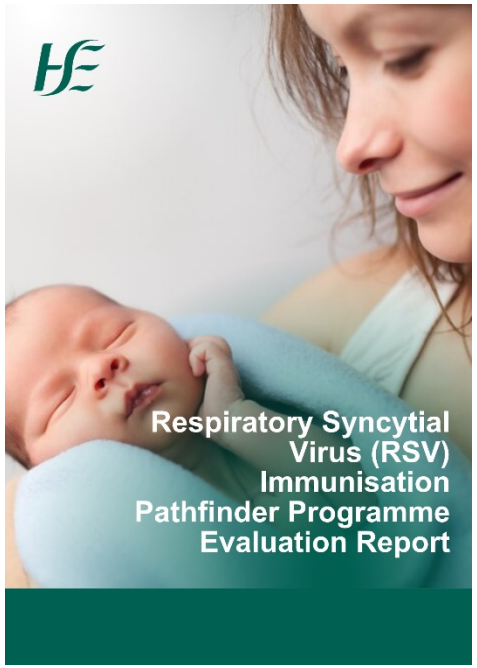
The most recent **growth rates (weeks 48-49)** based on modelled curve are approximately **35-40% and are starting to slow down.**

*See previous slide

RSV Immunisation Programme Evaluation

A comprehensive evaluation to assess the effectiveness and efficiency of the RSV Immunisation Pathfinder Programme has been requested by the Department of Health within 3 months of completion of the programme (i.e. May 2025)

This will be crucial to informing future RSV immunisation policy in Ireland



Evaluation Overview

1. Description of the RSV Programme

A description of the steps that were taken to establish and run the RSV Immunisation Programme

2. Reach & Uptake

Measurement of the proportion of eligible infants who received nirsevimab

Analysis of demographic factors influencing nirsevimab uptake

3. Impact

Assessment of the change to RSV-related hospitalisations and ICU admissions among infants eligible for nirsevimab compared to similar cohorts in previous RSV seasons

Evaluation Overview

4. Staff Survey

A survey of staff delivering the programme will be conducted in January and February 2025 to describe staff experiences

5. Parent Survey

A parent survey will be conducted to explore parental perspectives in relation to nirsevimab, including those who refused nirsevimab for their baby

6. Costs

A description of the costs associated with the deliver of the RSV Immunisation Programme (for the Department of Health only)

Back to RSV surveillance

RSV sampling framework/sequencing, Ireland

It is recommended that all hospital microbiology laboratories in Ireland refer the following RSV isolates to the National Virus Reference Laboratory (NVRL) for further testing:

- All **RSV hospitalised cases**, including those admitted to PICU in **infants born since the 1st September 2024**
- A systematic selection of **sentinel GP** Acute Respiratory Infection (ARI) specimens (**up to five ARI patients presenting to each practice each week**) are also tested by the NVRL
- **RSV positive** specimens from the designated SARI sentinel hospital sites in Ireland are referred to the NVRL, as per agreements with these sites.
- No genomic surveillance strategy in Ireland currently

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Question # 3

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Question # 4

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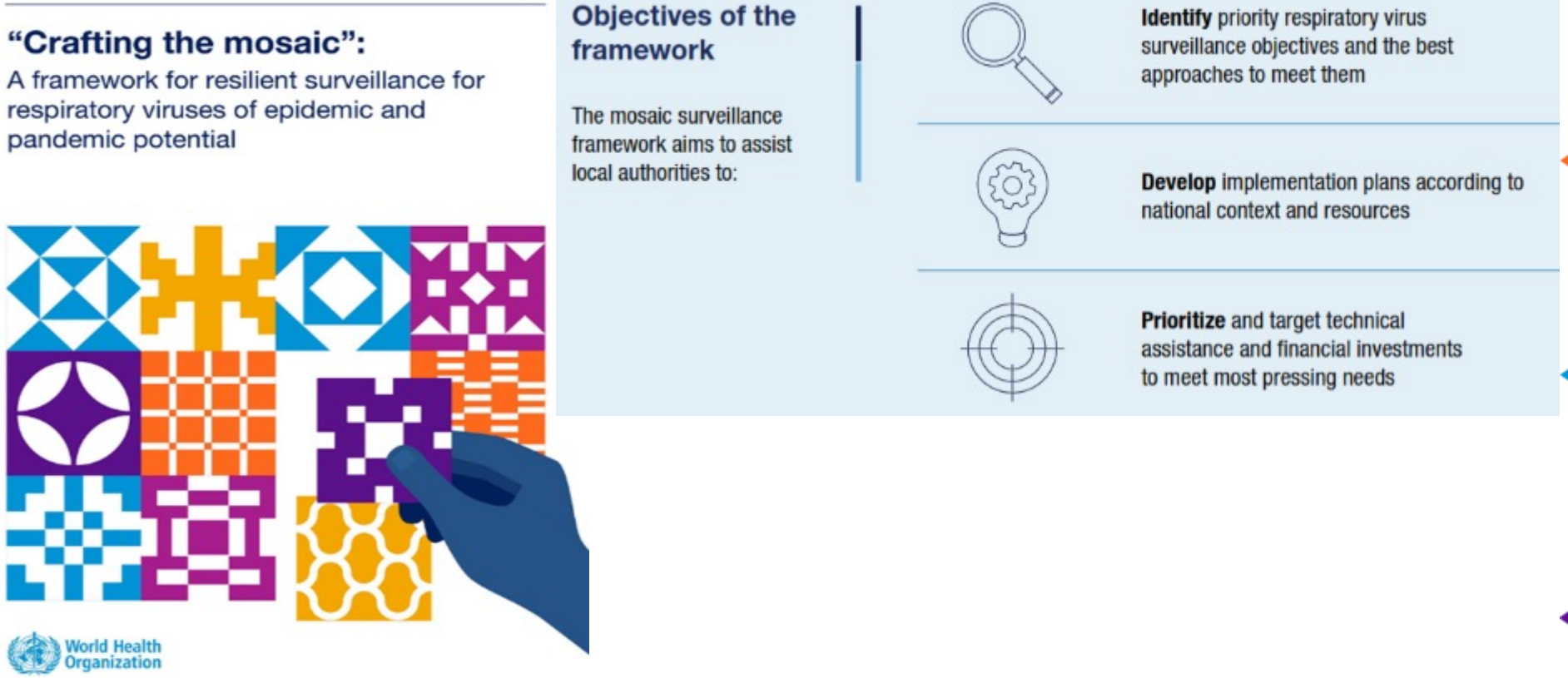
Question # 5

WHO Mosaic Respiratory Surveillance Framework



Objectives of the framework

The mosaic surveillance framework aims to assist local authorities to:

- **Identify** priority respiratory virus surveillance objectives and the best approaches to meet them
- **Develop** implementation plans according to national context and resources
- **Prioritize** and target technical assistance and financial investments to meet most pressing needs

WHO Mosaic Respiratory Surveillance Framework

WHO Mosaic Respiratory Surveillance Framework workshop at HPSC

In summary - RSV surveillance

- Identify priority RSV surveillance objectives (WHO Mosaic framework; other priority frameworks)
- Continue to strengthen RSV surveillance systems
- Need for robust RSV surveillance systems
  - To monitor the impact and effectiveness of interventions/immunisation programmes
  - To assess start/finish of RSV seasons – timing of RSV immunisation and impact on health service and population
- Establish expert groups for monitoring impact and effectiveness of RSV Nirsevimab/vaccines
- Develop sampling frameworks and genomic strategies for RSV and other respiratory viruses
- RSV research and collaborative work nationally and internationally

Acknowledgements

- HPSC Influenza/RSV team – Amy Griffin, Pamella Lima, Karen O'Reilly, Eva Kelly, Adele McKenna, Nancy Somi, Maureen O'Leary, Joan O'Donnell
- Eve Robinson, Ajay Oza, Gillian Cullen, Margaret Fitzgerald and all in the HPSC Respiratory Virus Unit; HPSC statistician – Katie O'Brien
- NHPO - Éamonn O'Moore, Lois O'Connor
- All data providers
- National Immunisation Advisory Committee (NIAC) secretariat
- RSV Nirsevimab pathfinder programme – Augustine Pereira, Michael Hanrahan, Ciaran Browne, all members of steering committee/working groups, all maternity sites, CHI – Crumlin and Temple Street, TCP homecare programme
- NVRL – Daniel Hare and Alan Rice

Acknowledgements

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References

- Integrated Reports - Health Protection Surveillance Centre
- Respiratory Virus Notification Data Hub
- Severe Acute Respiratory Infections (SARI) - Health Protection Surveillance Centre
- RSV epidemiology during first twelve weeks of RSV Nirsevimab Pathfinder Programme in Ireland
- Severe Acute Respiratory Infection surveillance programme expanded to new acute hospital sentinel sites
- HPSC launches new Integrated Respiratory Virus bulletin for Winter season
- A review of the 2023/2024 influenza and respiratory syncytial virus (RSV) season in Ireland
- New HSE immunisation programme to protect newborn babies against RSV
- WHO Mosaic Respiratory Surveillance Framework workshop at HPSC
- A review of the 2022/2023 RSV and influenza season in Ireland
- Epidemiology of Respiratory Syncytial Virus in Ireland for the 2022/2023 season to date
- Unusual seasonal patterns of Respiratory Syncytial Virus in Ireland during the COVID-19 pandemic
- Eurosurveillance | Establishing severe acute respiratory infection (SARI) surveillance in a sentinel hospital, Ireland, 2021 to 2022