RSV Genomic Surveillance – Operational Considerations

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Operationalizing RSV Genomic Sequencing within GISRS: From Specimen to Public Health Insight. August 13, 2025

World Health Organization

EPIDEMIC
&PANDEMIC
PREPAREDNESS
&PREVENTION

Disclosures

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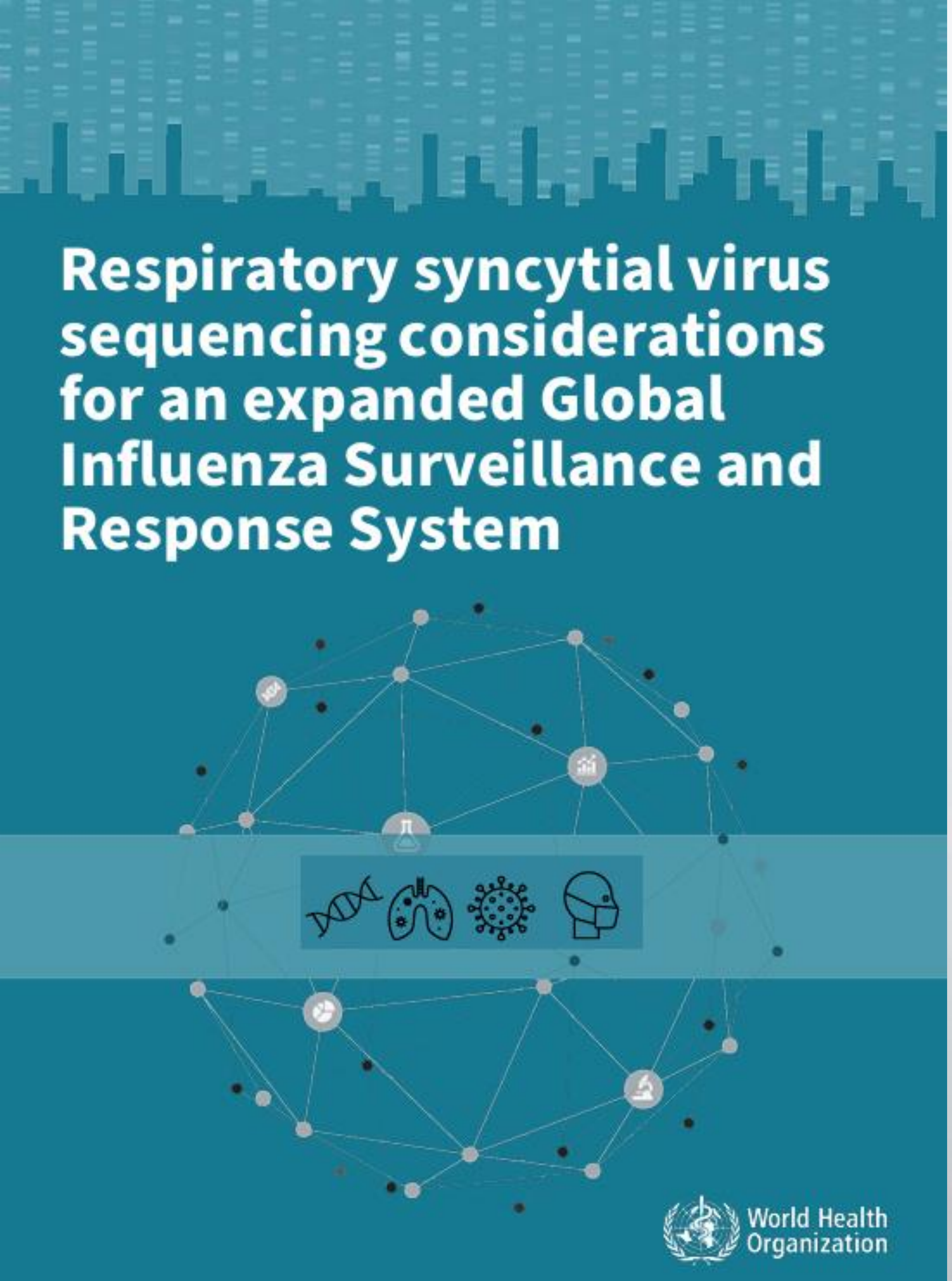
Outline of the talk

- Background for RSV surveillance
  - Burden of disease
  - New interventions
- RSV specimen collection
- Sample sizes
- Storage, transport, and handling to preserve RNA quality
- Integration with Influenza and SARS-CoV-2 specimen workflows



Respiratory syncytial virus sequencing considerations for an expanded Global Influenza Surveillance and Response System

World Health Organization

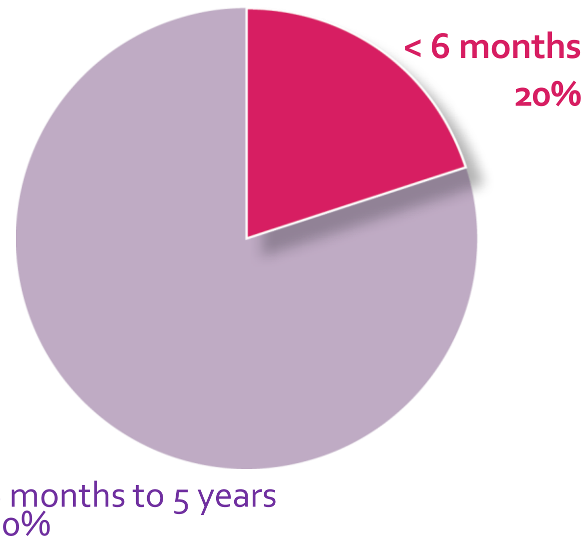
Talk based on recommendations published June 2025

Annual global pediatric RSV disease burden (< 5 years of age)[1]

LEADING CAUSE OF SEVERE RESPIRATORY INFECTION

33 million

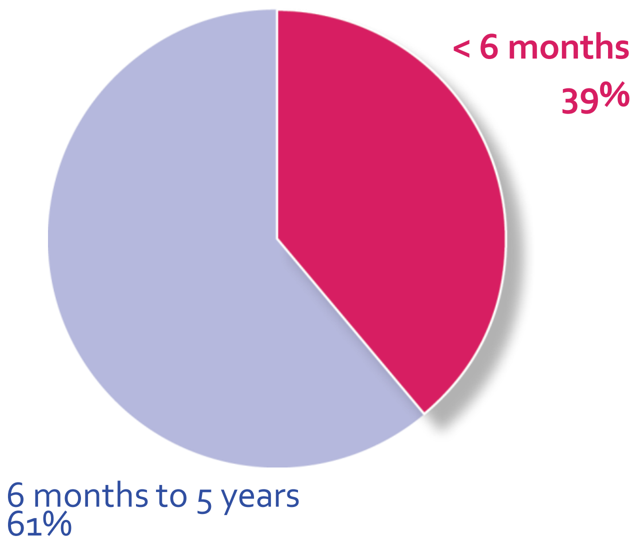
episodes



LEADING CAUSE OF PEDIATRIC HOSPITALIZATION

3.6 million

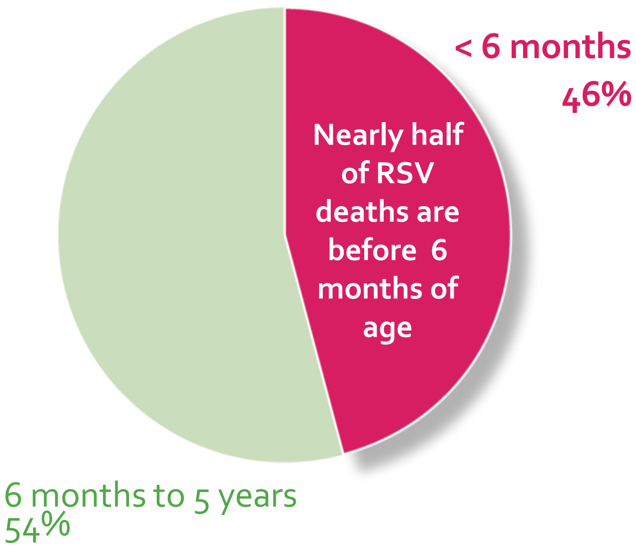
hospitalizations



IMPORTANT CAUSE OF PEDIATRIC MORTALITY

101,000

deaths



1 IN EVERY **28** DEATHS

before 6 months of age globally is due to RSV[2]

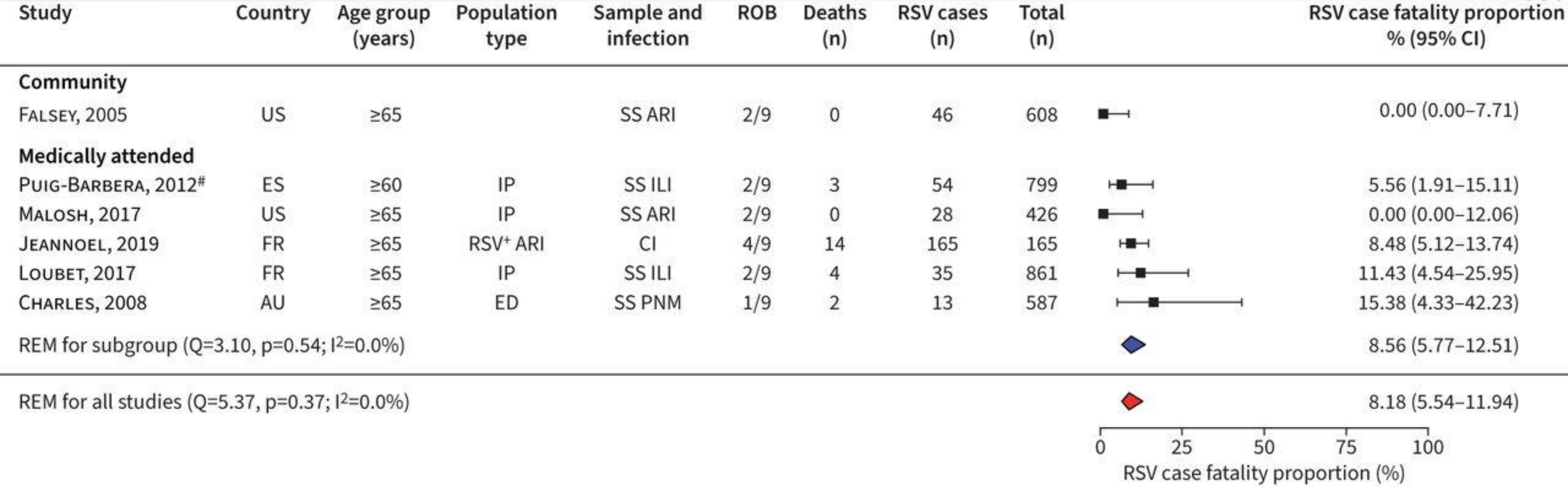
TOTAL GLOBAL CHILD MORTALITY DUE TO RSV

3.6%	**2.3%**
< 6 MONTHS	< 5 YEARS

Reference: [1] Li Y, et al. *Lancet* 2022. [2] PERCH Study Group. *Lancet*. 2019.

Original slide developed by the World Health Organization and PATH. August 2024.

Burden of RSV- older adults



Study	Country	Age group (years)	Population type	Sample and infection	ROB	Deaths (n)	RSV cases (n)	Total (n)	RSV case fatality proportion % (95% CI)
Community									
Falsey, 2005	US	≥65		SS ARI	2/9	0	46	608	0.00 (0.00–7.71)
Medically attended									
Puig-Barbera, 2012#	ES	≥60	IP	SS ILI	2/9	3	54	799	5.56 (1.91–15.11)
Malosh, 2017	US	≥65	IP	SS ARI	2/9	0	28	426	0.00 (0.00–12.06)
Jeannoel, 2019	FR	≥65	RSV$^+$ ARI	CI	4/9	14	165	165	8.48 (5.12–13.74)
Loubet, 2017	FR	≥65	IP	SS ILI	2/9	4	35	861	11.43 (4.54–25.95)
Charles, 2008	AU	≥65	ED	SS PNM	1/9	2	13	587	15.38 (4.33–42.23)
REM for subgroup (Q=3.10, p=0.54; I^2=0.0%)									8.56 (5.77–12.51)
REM for all studies (Q=5.37, p=0.37; I^2=0.0%)									8.18 (5.54–11.94)

Nguyen-Van-Tam et al (2022) European Respiratory Review

RSV interventions

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ARTICLES · Online first, July 18, 2025 · *Open Access*

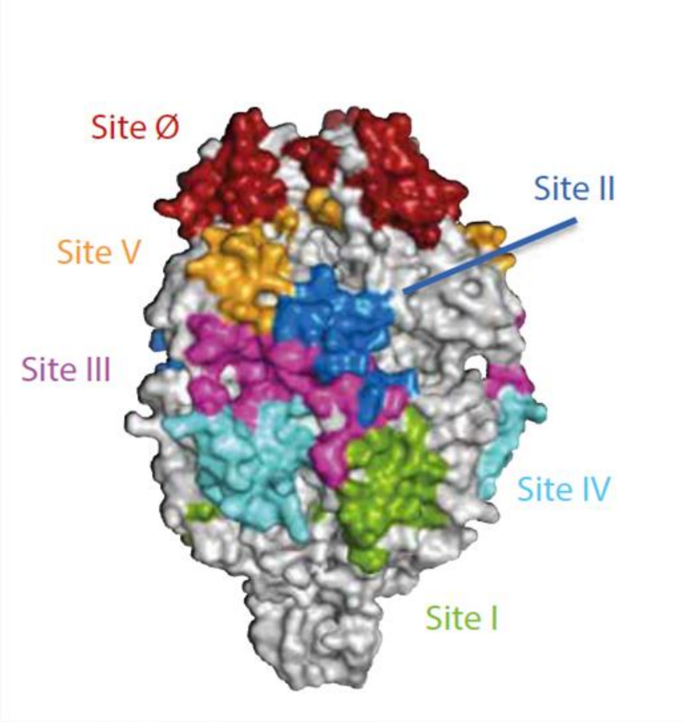
Bivalent prefusion F vaccination in pregnancy and respiratory syncytial virus hospitalisation in infants in the UK: results of a multicentre, test-negative, case-control study

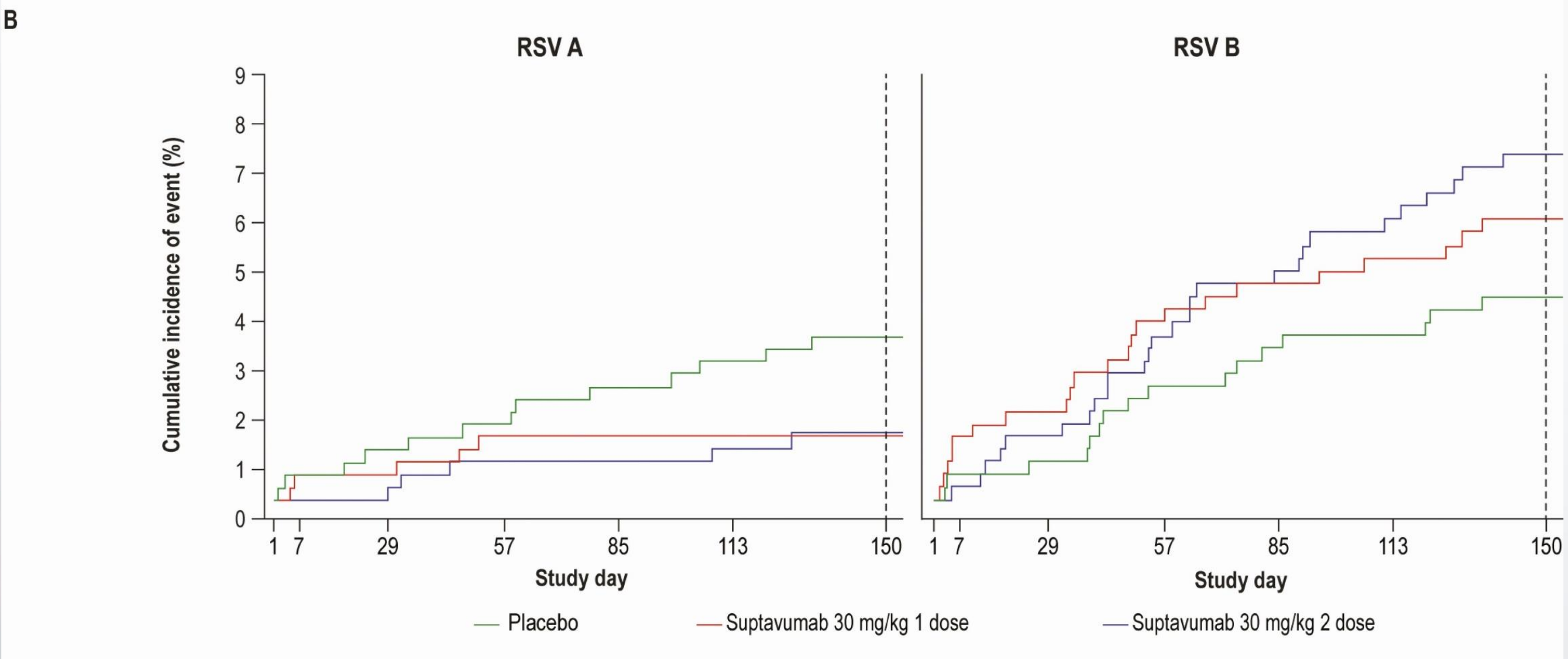
Thomas C Williams, PhD [a,b,*] · Robin Marlow, PhD [c,d,*] · Prof Steve Cunningham, PhD [b,e] · Simon B Drysdale, PhD [f,g] · Helen E Groves, MB BCh BAO PhD [h] · Samantha Hunt, BSc [i] · et al. Show more

Rationale for the recommendations

- Rapid progress in development of new RSV interventions
  - Monoclonal antibodies, vaccines and antivirals
- RSV immunization now recommended for infants, pregnant persons and older adults globally
- Goal of the sequencing programme:
  1. Understand current global genetic diversity of RSV
  2. Understand the spread of lineages globally
  3. Support the use of molecular diagnostics
  4. Inform the development and introduction of interventions
- Genomic sequencing - part of integrated surveillance strategies to understand challenges to the effectiveness of newly introduced interventions

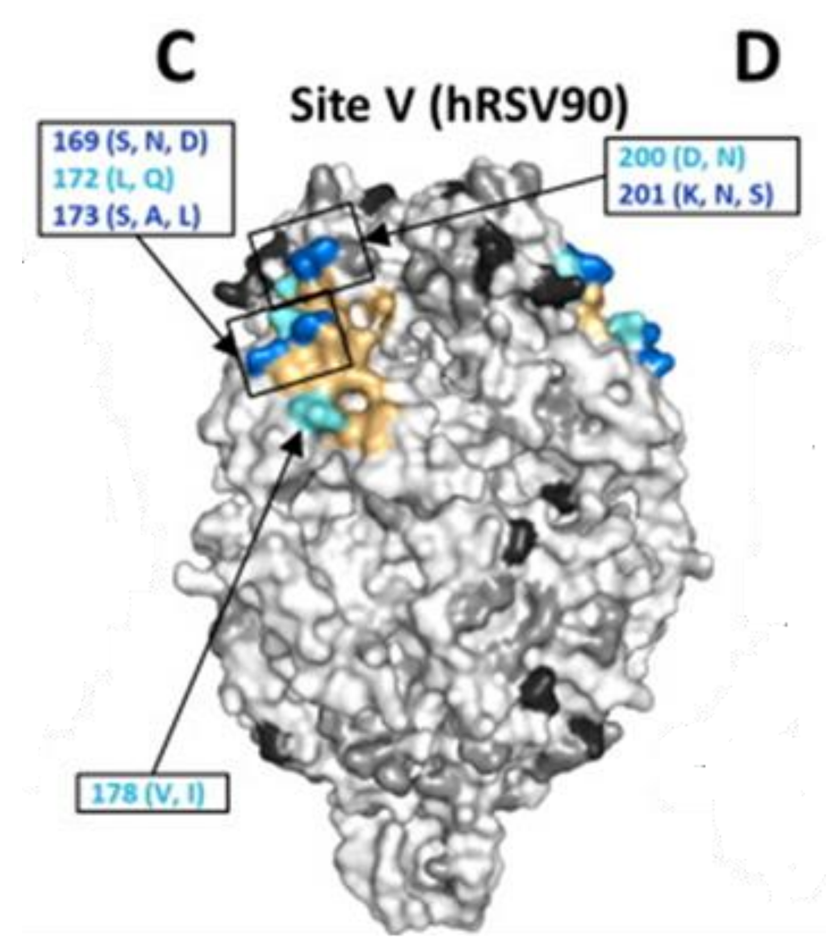
Why do we need global RSV genomic surveillance? Suptavumab case study

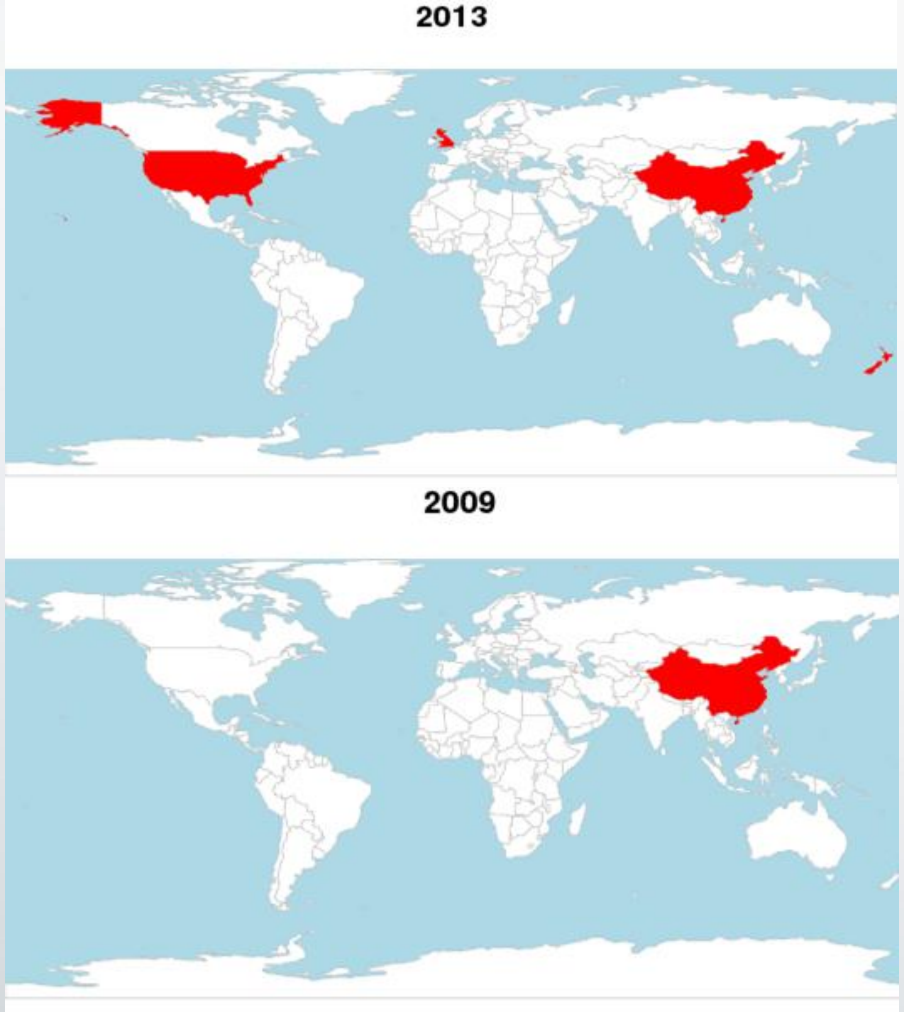




Mas et al (2018) *Vaccine*; Simoes et al (2021) *CID*

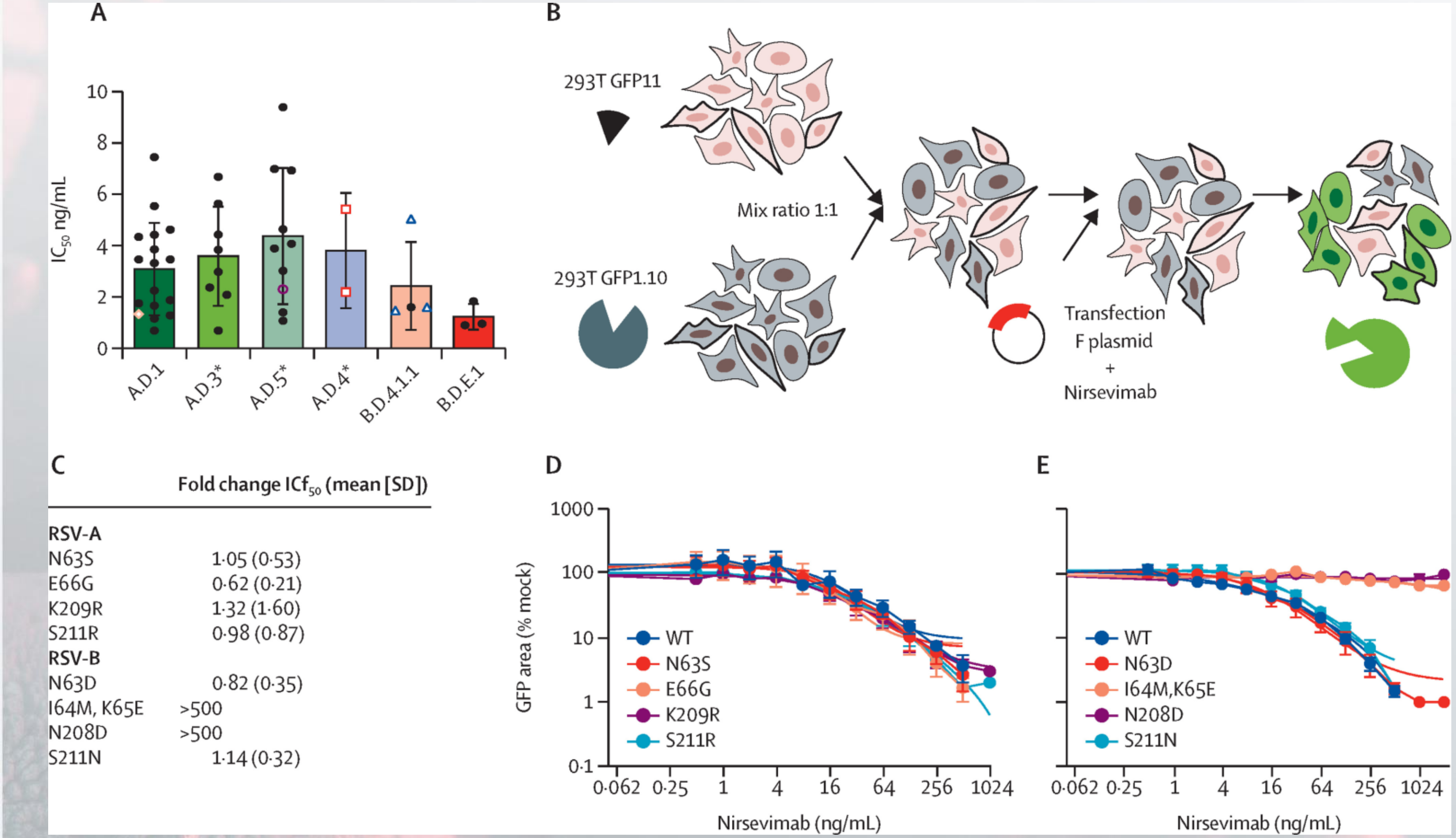
Why did suptavumab fail?



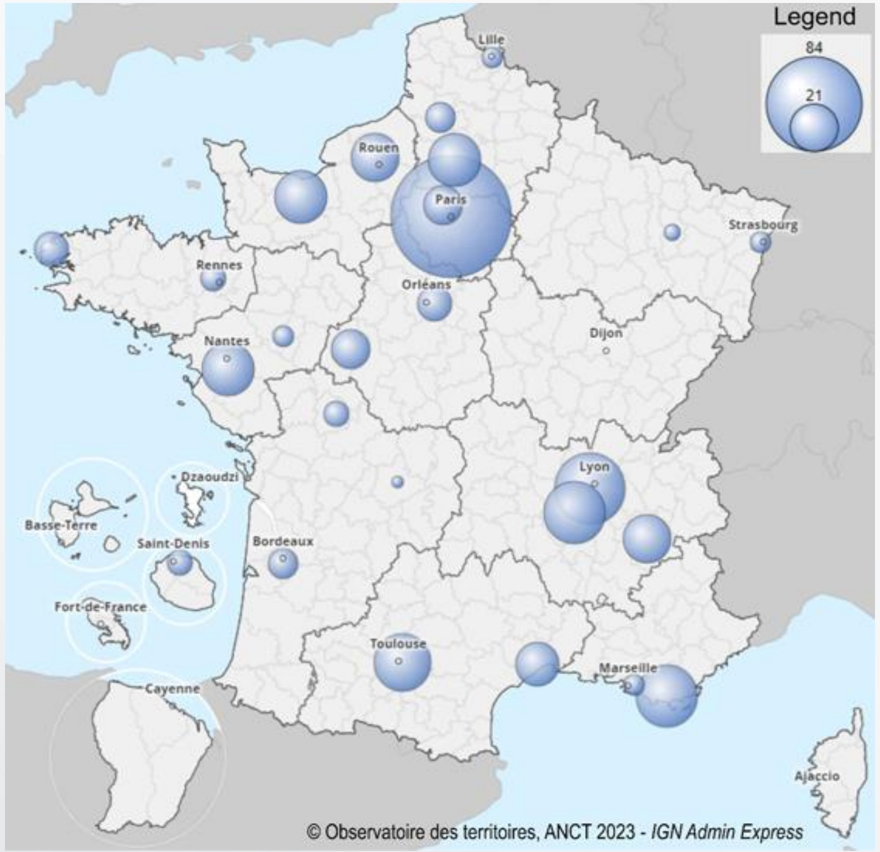


Mas et al (2018) *Vaccine*

Nirsevimab surveillance in France



	Fold change ICf$_{50}$ (mean [SD])
RSV-A	
N63S	1·05 (0·53)
E66G	0·62 (0·21)
K209R	1·32 (1·60)
S211R	0·98 (0·87)
RSV-B	
N63D	0·82 (0·35)
I64M, K65E	>500
N208D	>500
S211N	1·14 (0·32)



© Observatoire des territoires, ANCT 2023 - *IGN Admin Express*

Fourati et al (2025) *Lancet ID*

Objectives of the sequencing recommendations

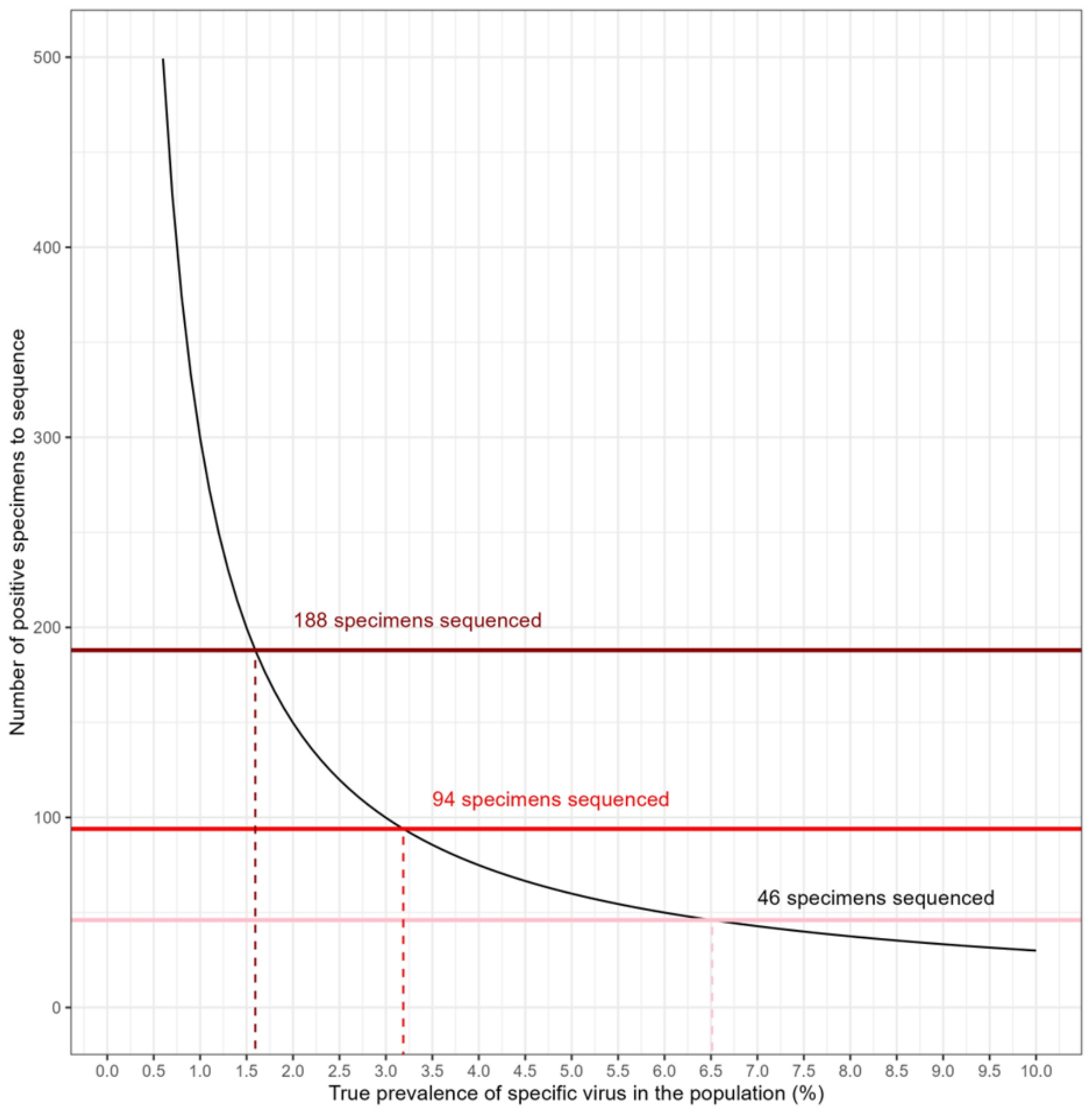
1. Outline standards for RSV specimen collection and diagnostic testing for **high quality sequencing**
2. **Improve access to tools** for RSV sequence data generation, analysis and interpretation
3. Ensure **timely sharing** of RSV sequence data
4. **Strengthen capacity** within participating laboratories and ensure the **sustainability** of integrated respiratory virus surveillance
5. Adopt and repurpose existing sequencing technologies to **maximise the use of existing laboratory infrastructure,** which can then be applied to other pathogens or emergencies

Sample types, timing, and patient groups

- Surveillance and sequencing strategies differ between countries
    - Use country's existing surveillance system criteria
- Aim for representativeness with sampling:
    - **Age groups** that are likely to be targeted by interventions
        - 0 - 11 months [maternal vaccines / infant monoclonal antibodies]
        - 12 - 23 months [pediatric vaccines / monoclonal antibodies in high risk]
        - ≥60 years, if a country is introducing vaccination in this older age group
        - Other age groups, dependent on resources and future interventions
    - Different **geographic locations** across the country
    - Different **time points** (early, middle, late season and out of season)
    - **Ranges of disease severity** (milder community cases, hospitalised)
- **Clinically significant cases,** such as fatal cases and breakthrough infections

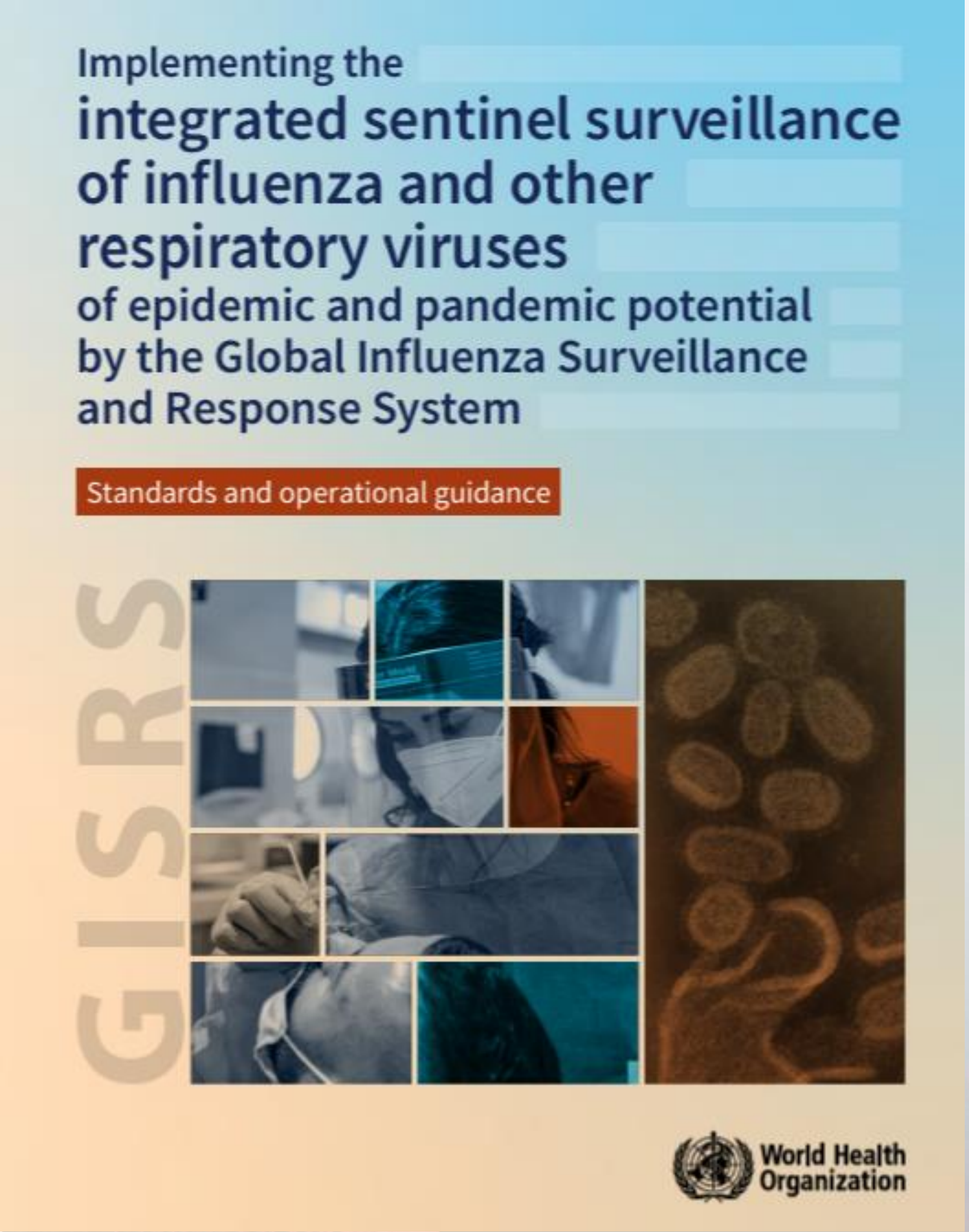
Sample size

- Identify main lineages circulating within a country at high prevalence, and minor lineages circulating globally at low prevalence
- Recommend 46 sequences per country per year
  - Identify lineages circulating at a prevalence of 10% (95% CI 4.2-22.0%)
  - Permit identification of a lineage circulating to a prevalence of **6.6% nationally**, and **0.27% globally**
- Choose proportion of RSV-A to RSV-B samples based on the circulating distribution



Storage, transport, and handling to preserve RNA quality

- Same type of specimens collected for SARS-CoV-2 and influenza testing
- Recommended: nasal aspirates, nasal swabs, throat (OP) swabs, nasopharyngeal swabs, nasopharyngeal aspirates, combined NP/OP
- Viral/Universal transport medium (VTM/UTM)
- Stored and transported at 2-8°C, and RNA extracted within 72 hours
- Alternatively, freeze in -70°C freezer
- Freeze-thaw cycles should be minimized
- rRT-PCR testing – CDC IRR / commercial kits



Implementing the
integrated sentinel surveillance of influenza and other respiratory viruses
of epidemic and pandemic potential by the Global Influenza Surveillance and Response System

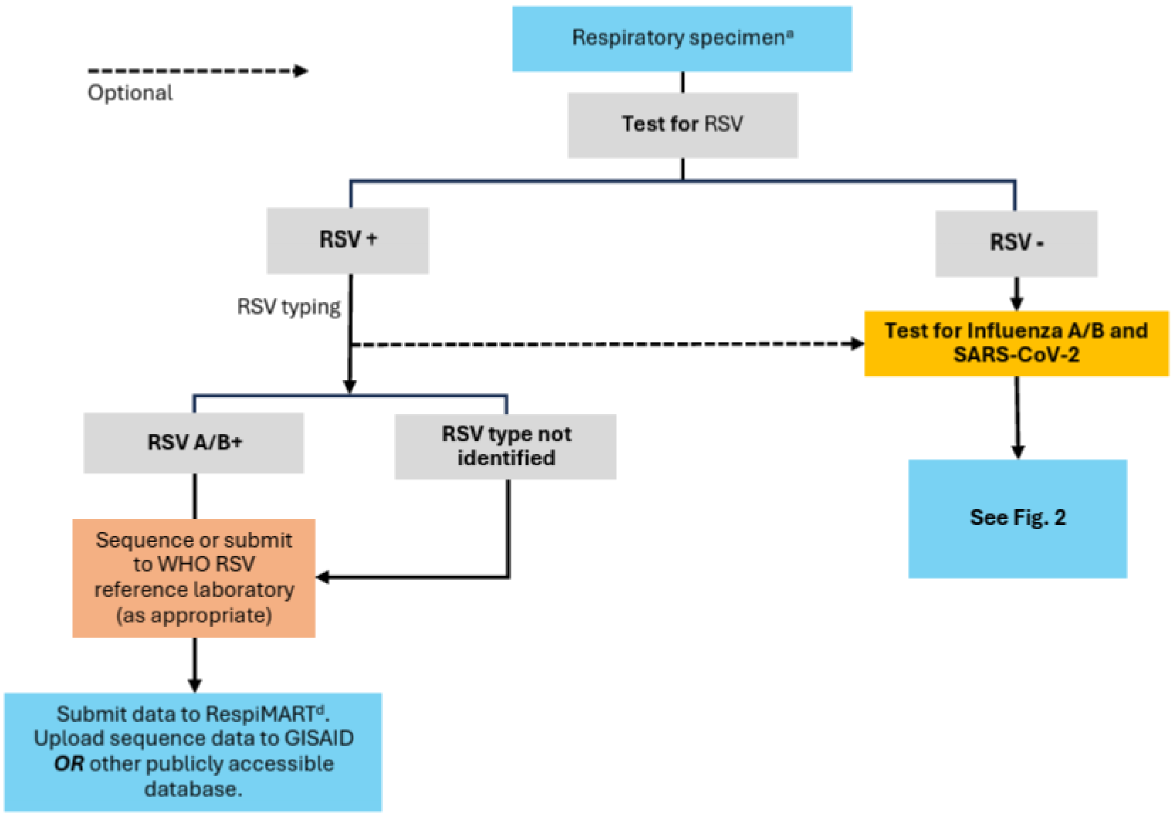
Standards and operational guidance

GISRS

World Health Organization

Integration with Influenza and SARS-CoV-2 specimen workflows

Fig. 3. Testing algorithm for RSV



Optional

Respiratory specimen[a]

Test for RSV

RSV +

RSV -

RSV typing

Test for Influenza A/B and SARS-CoV-2

RSV A/B+

RSV type not identified

See Fig. 2

Sequence or submit to WHO RSV reference laboratory (as appropriate)

Submit data to RespiMART[d]. Upload sequence data to GISAID *OR* other publicly accessible database.

Conclusion

1. Now is an exciting time for RSV surveillance as effective interventions are rolled out
2. The key to understanding RSV disease burden and the impact of interventions is accurate diagnostic testing
3. RSV sequence data generation embedded within GISRS will allow the detection of new variants that may impact on immunisation/vaccination effectiveness, and generate scientific insights into RSV transmission dynamics as infection rates fall
4. The expertise developed for RSV sequencing can also be applied to other pathogens (e.g. human metapneumovirus) or emergencies

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Questions?