UK Health Security Agency

The impact of RSV infection and rationale for RSV vaccination programmes

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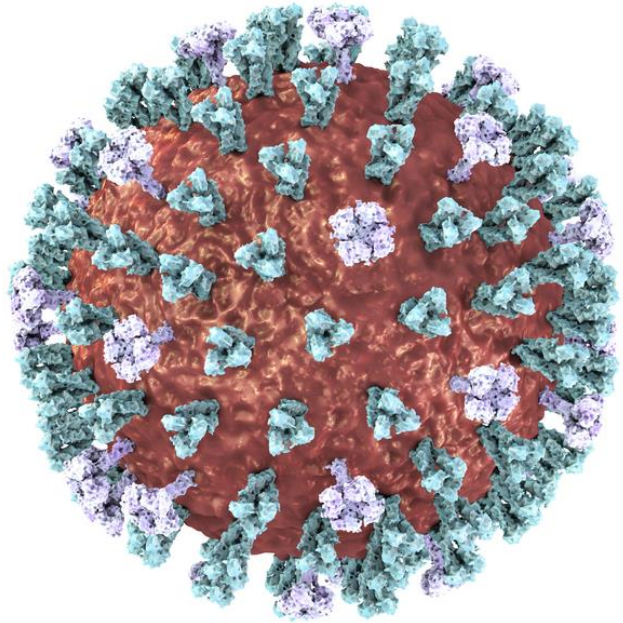
UKHSA

What is Respiratiry Syncytial Virus (RSV)

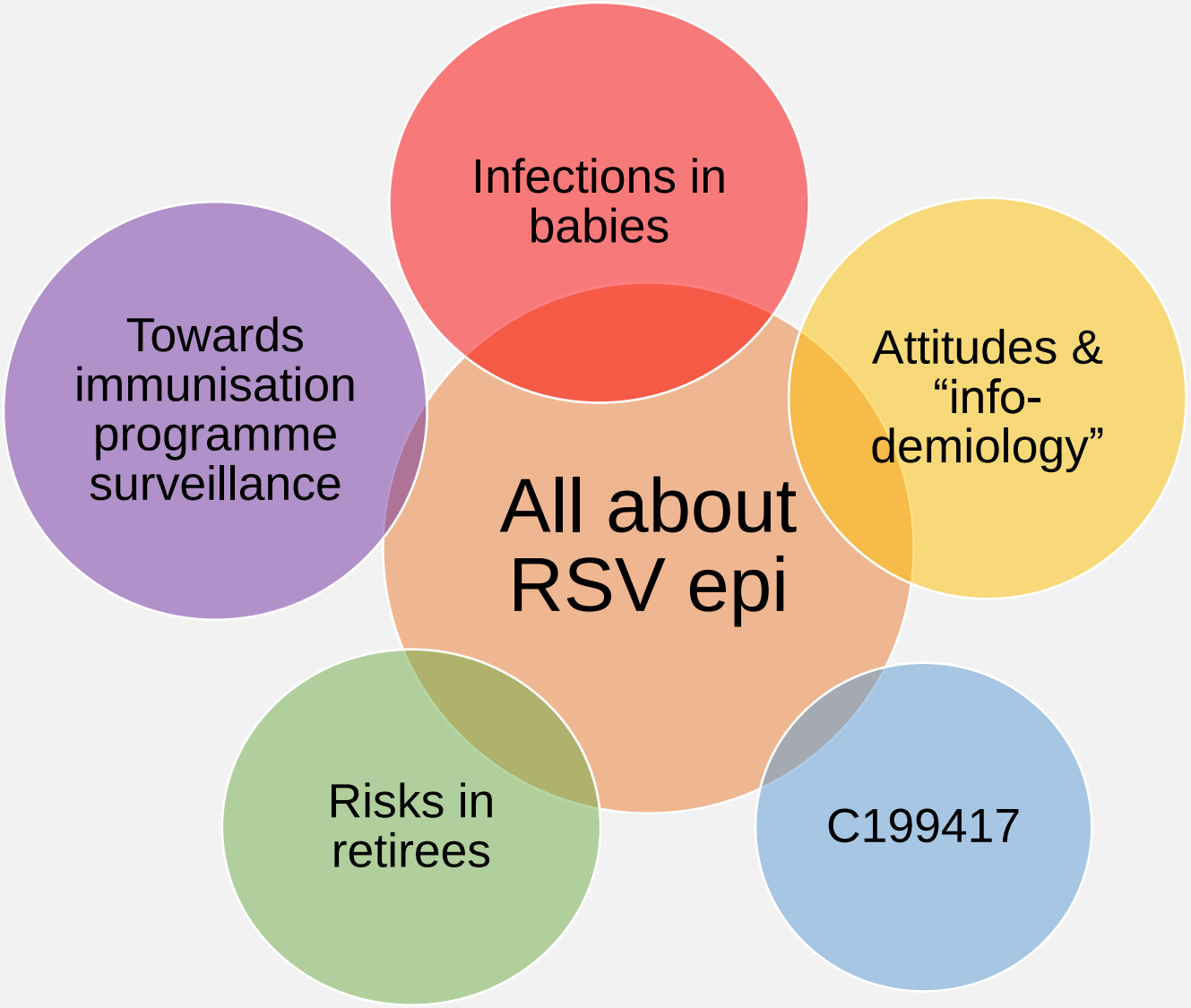
- An enveloped RNA virus that belongs to the *Paramyxoviridae* family (the same family as the human parainfluenza viruses and mumps and measles viruses)
- A common cause of respiratory tract infections
- Usually a mild self-limiting respiratory infection in young adults and children but can be severe in infants and older adults who are at increased risk of acute lower respiratory tract infection
- Best known for causing bronchiolitis in infants but is a major cause of hospitalisation in older adults
- previous infection may only confer partial immunity to RSV and so individuals may be infected repeatedly with the same or different strains of RSV
- the antibodies that develop following early childhood infection do not prevent further RSV infections throughout life
- predisposing factors include prematurity, cardiopulmonary disease, immunodeficiency, and may also include other factors such as tobacco exposure, day care attendance, overcrowding, lack of breastfeeding, and admission to hospital during the RSV season
- In older adults similar risk factors to flu
- No specific treatment for RSV



Transmission of RSV

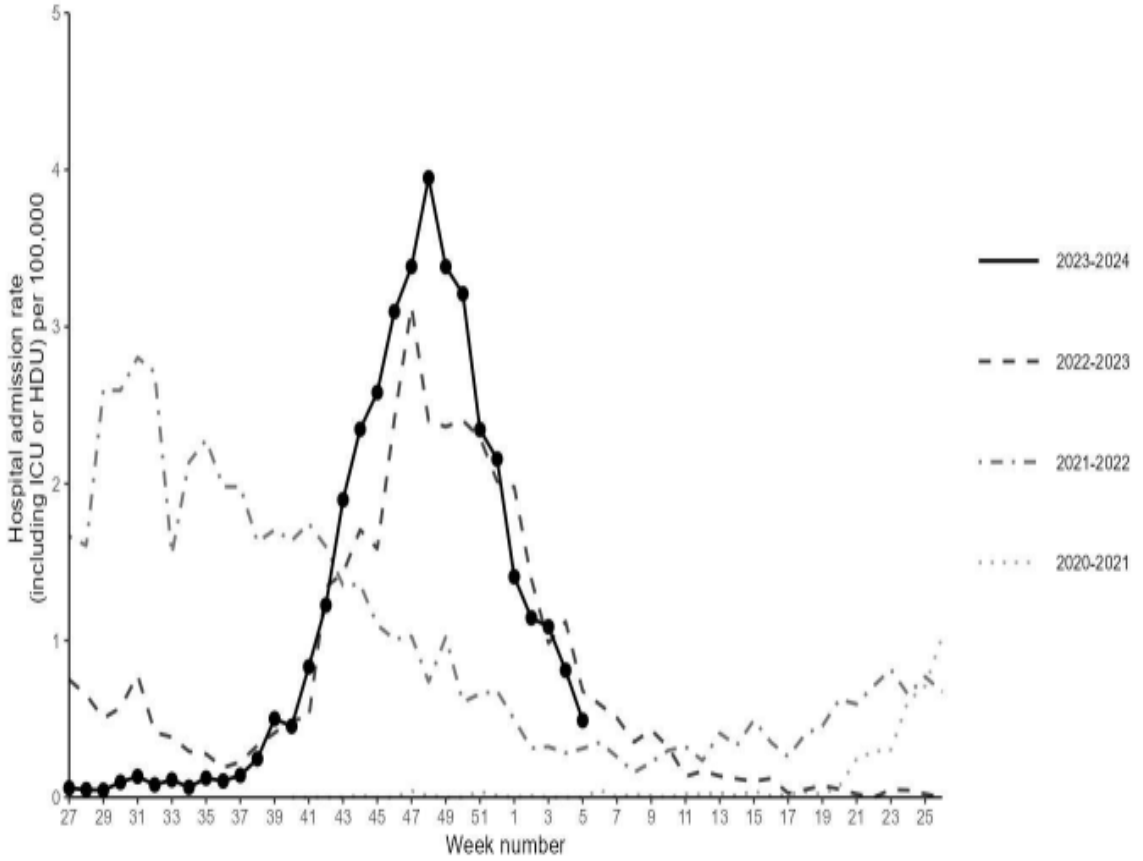
- RSV is highly communicable, but humans are the only known reservoir
- the incubation period (time between infection and appearance of symptoms) varies from 2 to 8 days (usually 3 to 5 days)
- the virus is spread from respiratory secretions following close contact with an infected person, via respiratory droplets or contact with contaminated surfaces or objects
- the virus can survive on surfaces or objects for about 4 to 7 hours

“The key objective of surveillance is to provide information to guide interventions.” Peter Nsubuga



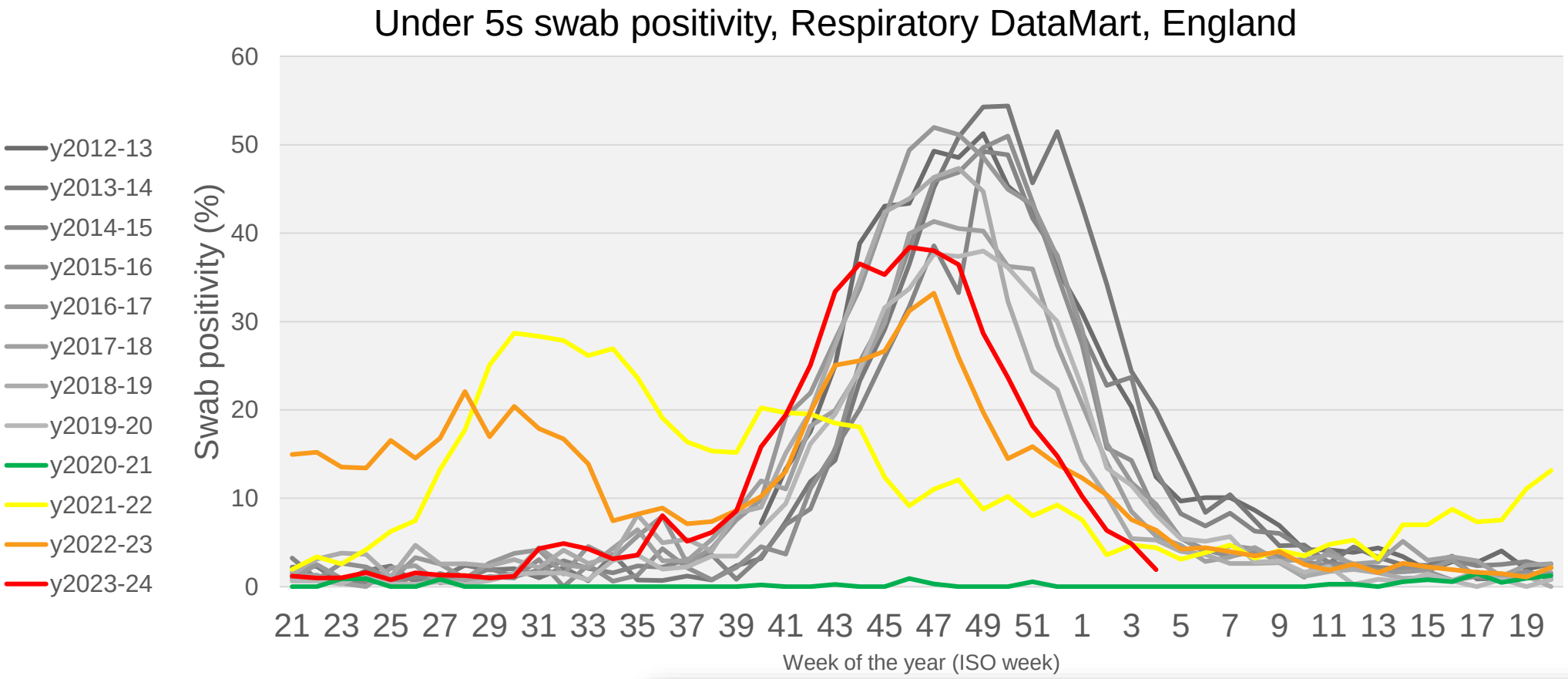
RSV epidemiology

- RSV infection is a winter virus, with RSV season in the UK starting from October, peaking in December and declining in March
- whilst the occurrence of the mid-winter peak is predictable, its size varies from year to year
- RSV infects up to 90% of children within the first 2 years of life and frequently reinfects older children and adults
- RSV accounts for approximately 33,500 hospitalisations annually in children aged under 5 years old
- it is a leading cause of infant mortality globally, resulting in 20 to 30 deaths per year in the UK
- UKHSA monitors levels of RSV activity in England throughout the RSV season - epidemiological data are available at [National flu and COVID-19 surveillance reports: 2023 to 2024 season - GOV.UK (www.gov.uk)]



Weekly overall hospital admission rates (including ICU or HDU) of RSV positive cases per 100,000 population reported through SARI Watch sentinel surveillance, England

Sentinel surveillance shows disruption and reestablishment of RSV seasonality



See also **Bardsley et al 2022, Lancet ID**, 23(1)56

and

Koltai et al 2022, Epidemics 100614

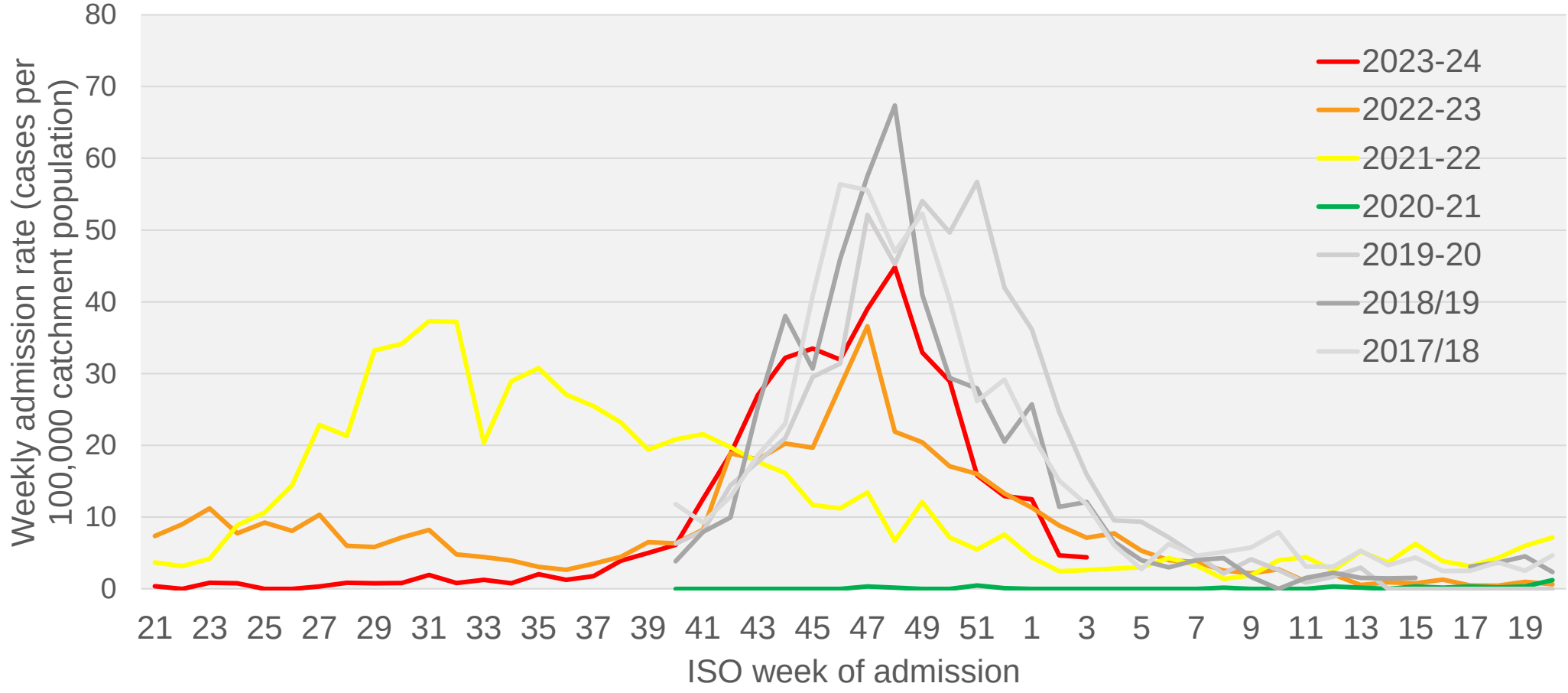
CEM/CMO/2021/014 29 June 2021

Palivizumab passive immunisation against respiratory syncytial virus (RSV) in at risk pre-term infants

Hospitalisation have followed a similar pattern

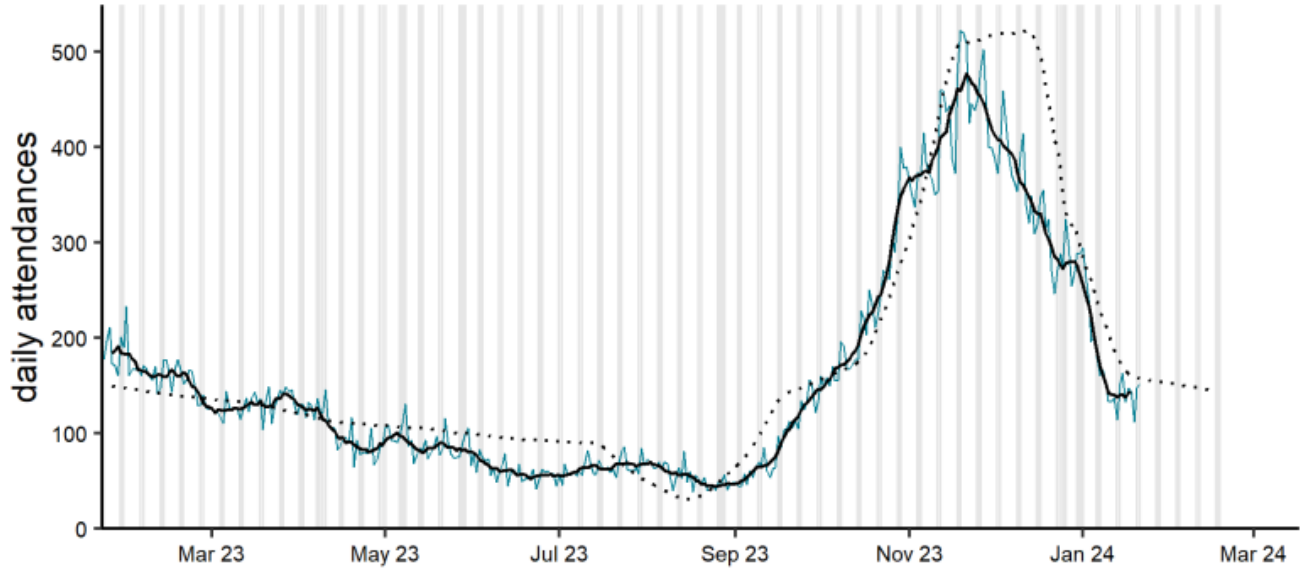
Do please sign up your Trust to RSV monitoring: sariwatch@ukhsa.gov.uk

SARI-WATCH RSV surveillance



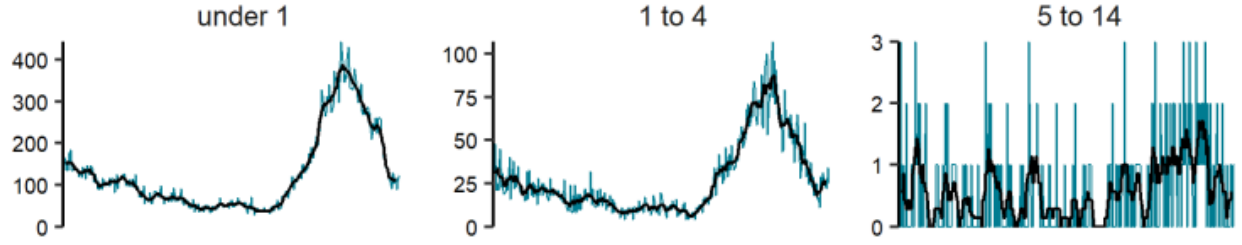
ED and critical care

Daily ED attendances for acute bronchiolitis nationally, England [note 12]

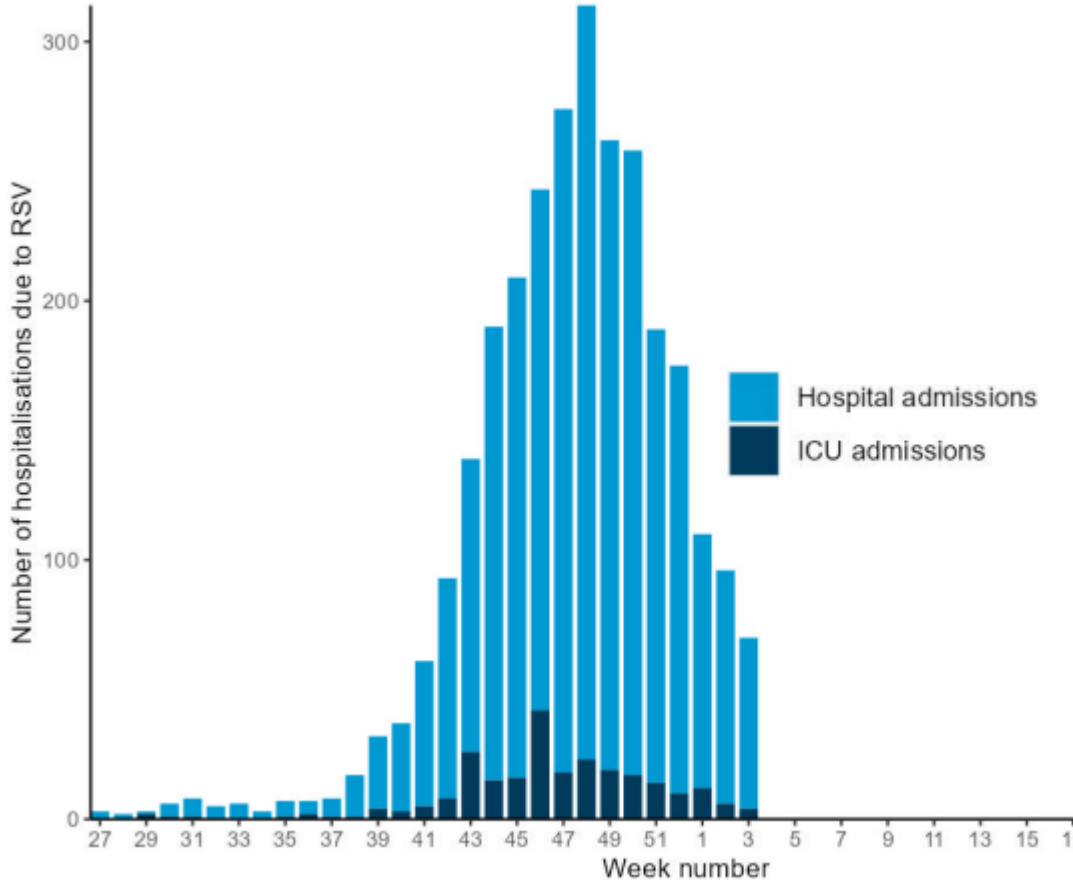


See [note 10] as above.

Daily ED attendances for acute bronchiolitis by age group, England [note 12]

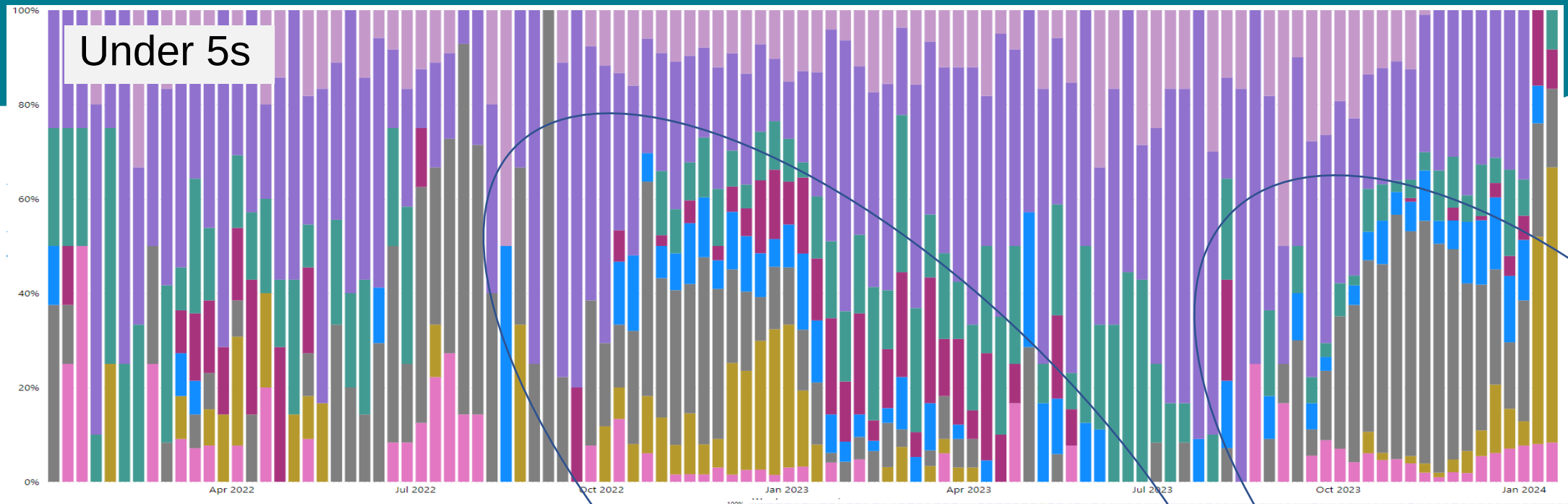


Weekly count hospital admissions of RSV positive cases reported through SARI Watch sentinel surveillance by level of care, England



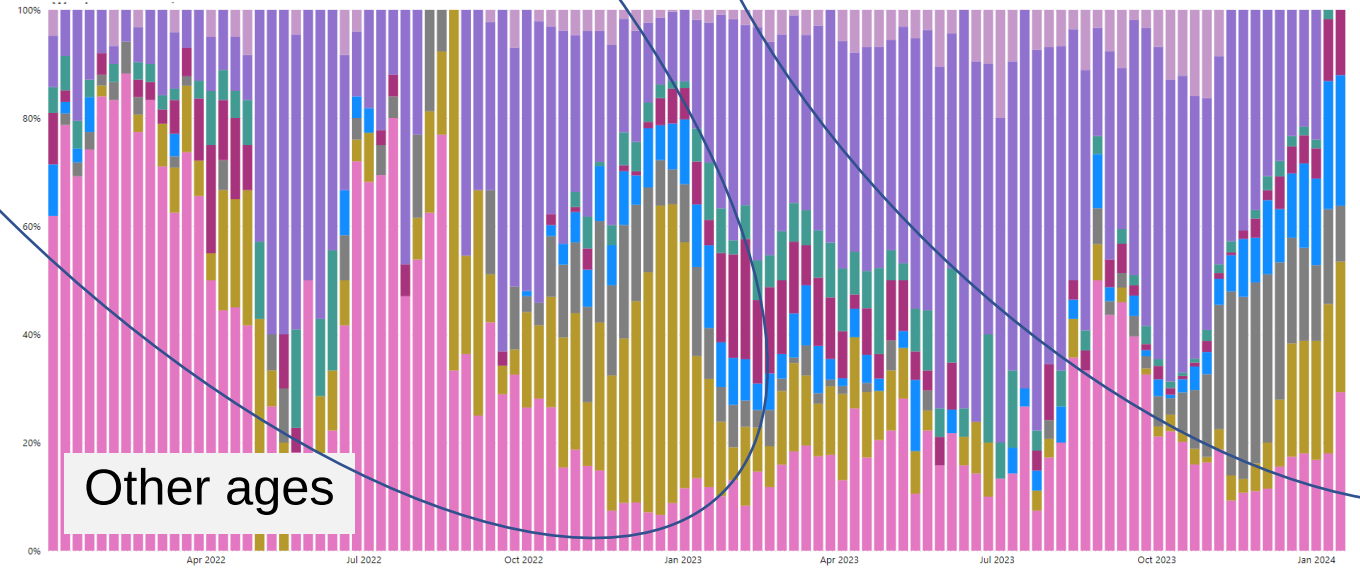
gov.uk/government/collections/weekly-national-flu-reports

RSV circulates across age groups



SARS-CoV-2 Influenza RSV hMPV

OtherCoronavirus Adeno Rhino Entero

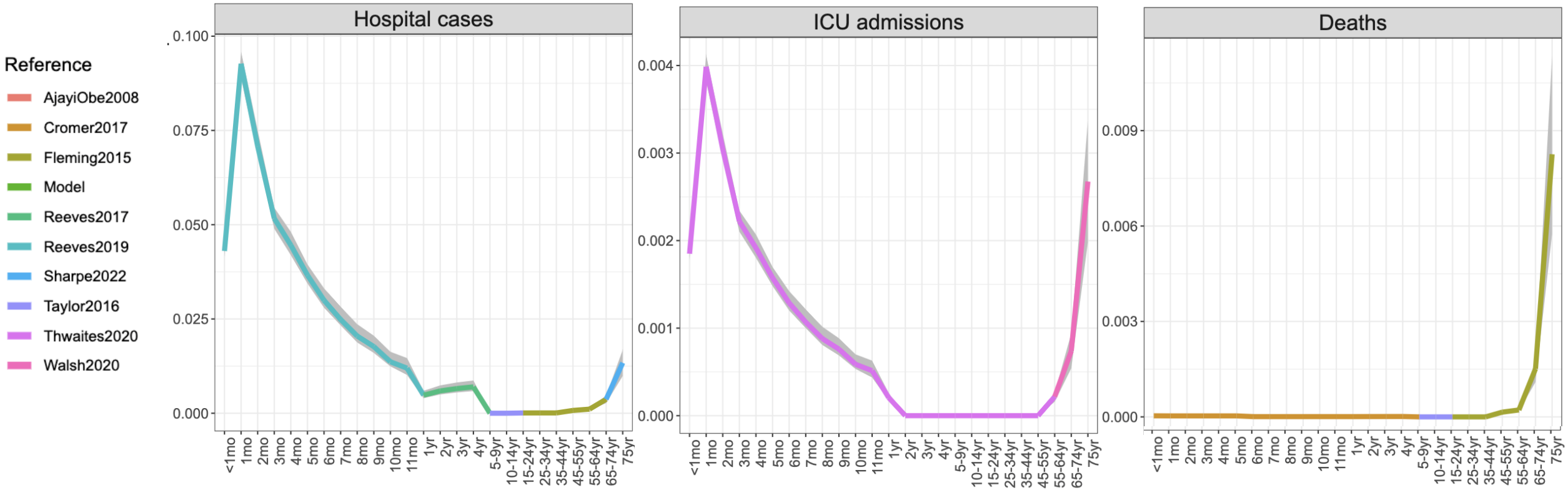


RCGP & UKHSA Resp Virus Unit

gov.uk/government/collections/weekly-national-flu-reports

RSV across the life-course

Risk of event per infection, by age group, synthesis by David Hodgson, LSHTM



See Hodgson *et al* 2024, Lancet Reg H Eur

Impact of RSV infection in children

- winter respiratory illness, infects 90% of children under 2 years – usually mild, cold-like symptoms
- can cause severe disease (bronchiolitis) in infants, especially very young infants born prematurely who have predisposing conditions such as lung or heart disease or children who are immunodeficient
- bronchiolitis is a common cause of hospitalisation in children aged under one year;1-3% of RSV infected children require hospitalisation; 33,500 hospitalisations annually in children aged under 5 years old
- NG/IV fluids, oxygen, mechanical ventilation, antibiotics (secondary infections)
- in ‘high-risk’ children the mortality rate is about 3%; there are 20 to 30 deaths per year in the UK
- Green Book Chapter 27a Respiratory syncytial virus

Socio-demographic risk factors for RSV

Severe LRT disease

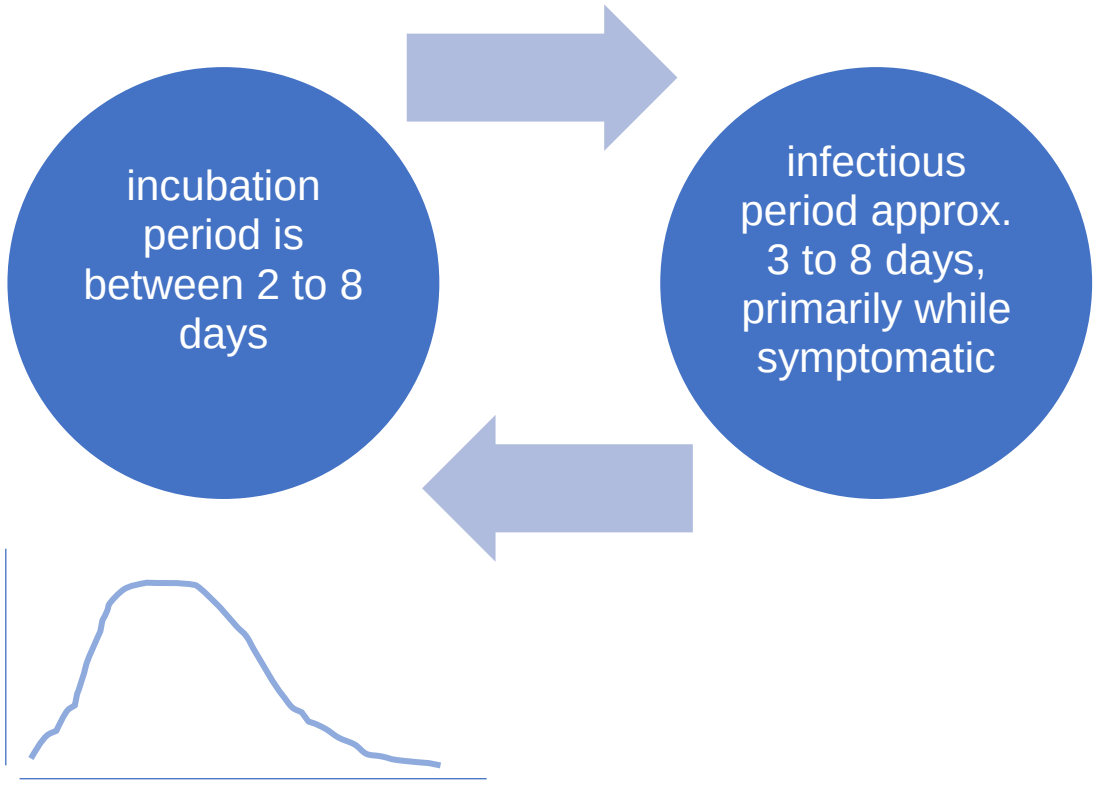
- <6mo at start of RSV season
- Multiple birth
- Male
- Young siblings
- Larger households (5+/6+)
- Indoor (tobacco) smoke exposure
- ?Lower socioeconomic status
- ?Lower parental education
- Malnutrition/SGA
- ?FHx atopy/asthma
- Low cord serum RSV IgG
- (Living at altitude)

Infection

- Birth immediately prior to or in RSV season
- Day care
- Siblings in school or day care
- Not breastfed - ?as co-factor

See Sommer, Rech & Simões, 2011 Open Micro J
DiFranza et al 2012 BMC Paeds

When do secondary cases arise in households?



Tang, Y. W., & Crowe, J. E. 2011 in Versalovic et al.
Walsh et al 2013 J inf Dis

Burden by age and birth month, Reeves et al

RSV-associated admissions peaked in infants aged 6 weeks, and those born September to November

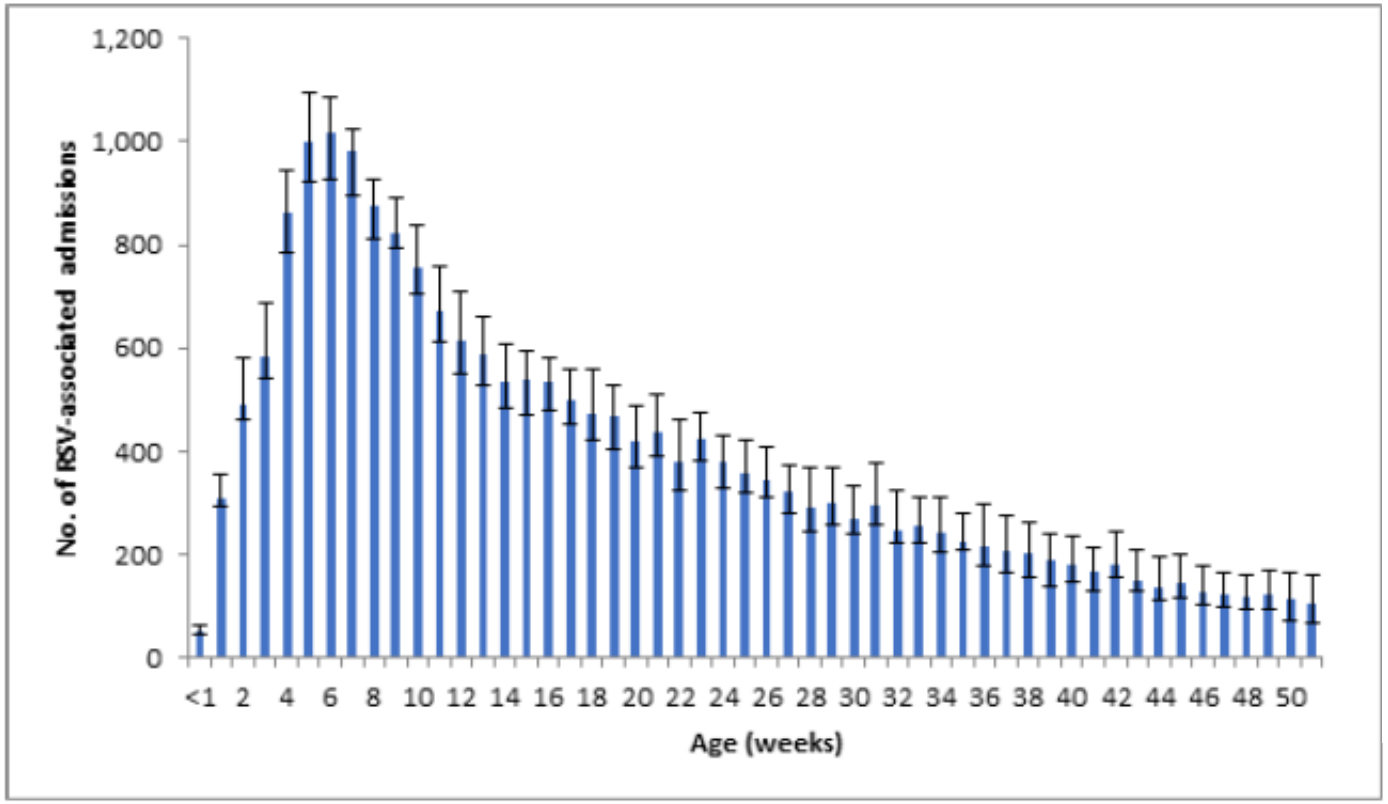


Figure 3. Annual estimated number of RSV-associated admissions, by age in weeks.

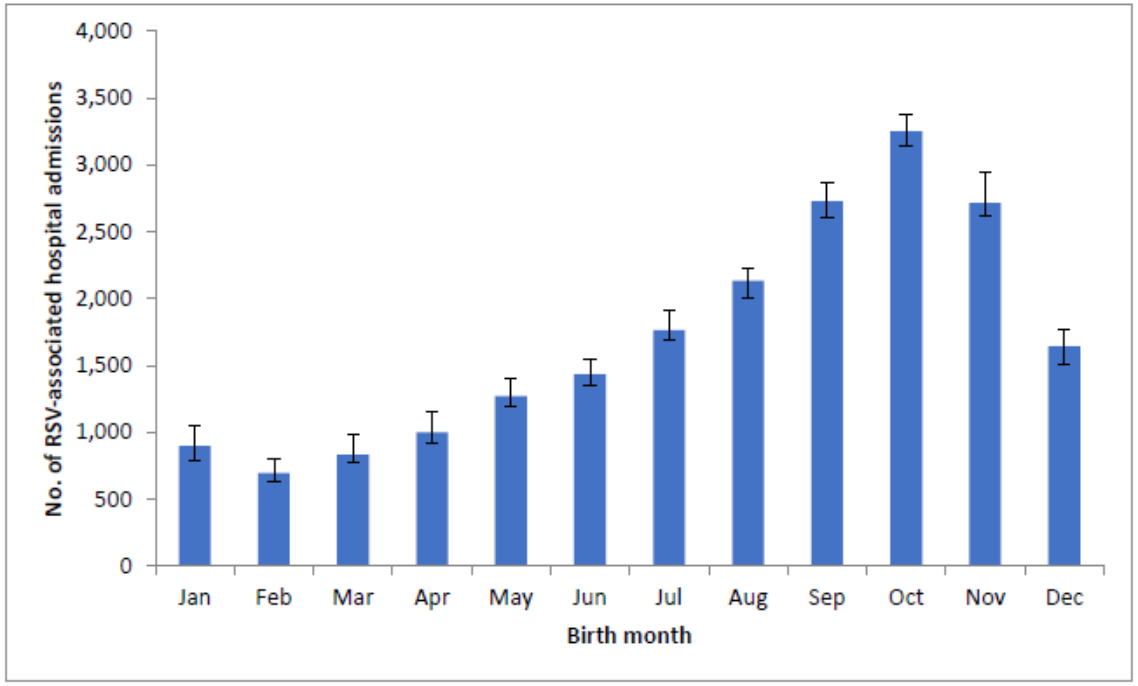


Figure 4. Annual estimated number of RSV-associated admissions, by birth month.

5% of RSV-associated admissions were in high-risk infants, requiring 21% of the estimated bed days.

High-risk groups: CLD inc BPD, CHD, prematurity, immunodeficiency, neurological

Mortality

Cromer et al 2017 (Lancet PH) estimates 25 deaths/year in under 5s

NCMD Dec 2023 report Apr 2019 Mar 2022:

“RSV was recorded in 40 deaths over the 3 year period [2 epidemic seasons] and was identified where infection provided a complete and sufficient explanation of death in 18 cases”

RSV older adult disease

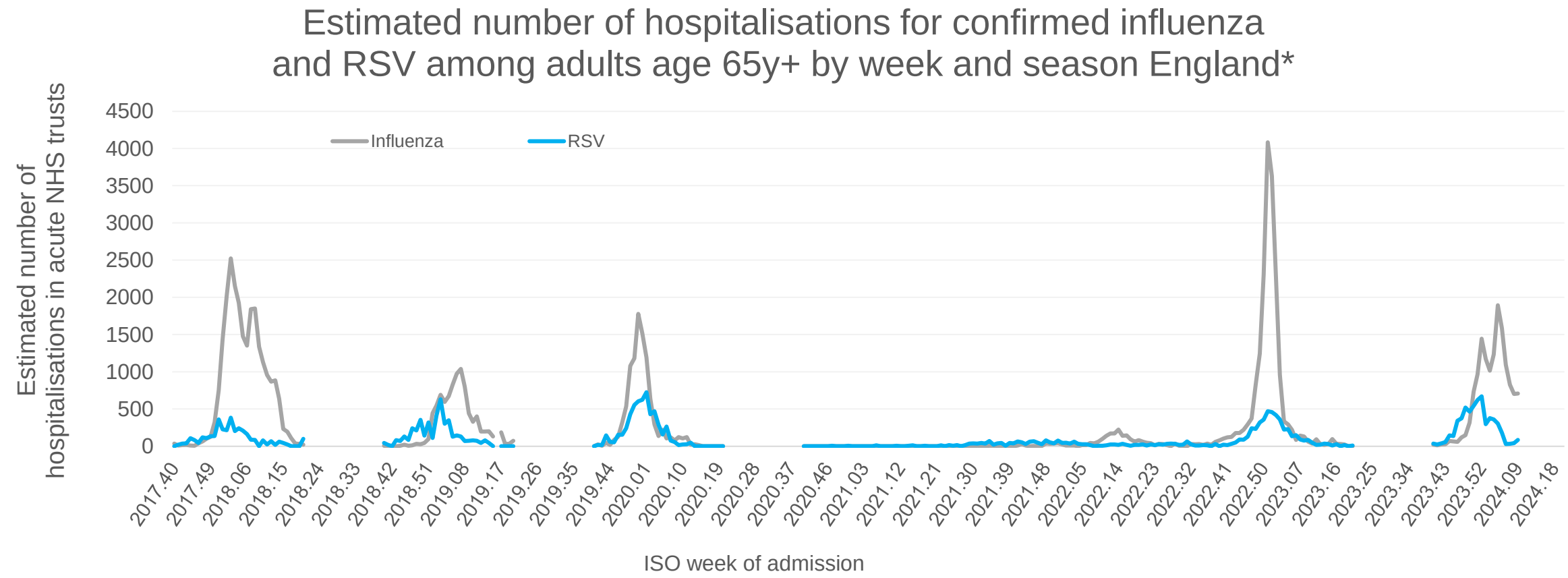
- Clinical syndrome can include:
  - Productive cough
  - Difficult/fast breathing
  - Wheeze
  - Fever
- Commonly diagnosed as pneumonia

See e.g. Chuaychoo 2019

- RSV can be an important pathogen in those with chronic airway disease, cancer, immunosuppression and chronic heart disease

See *Falsey 2000*

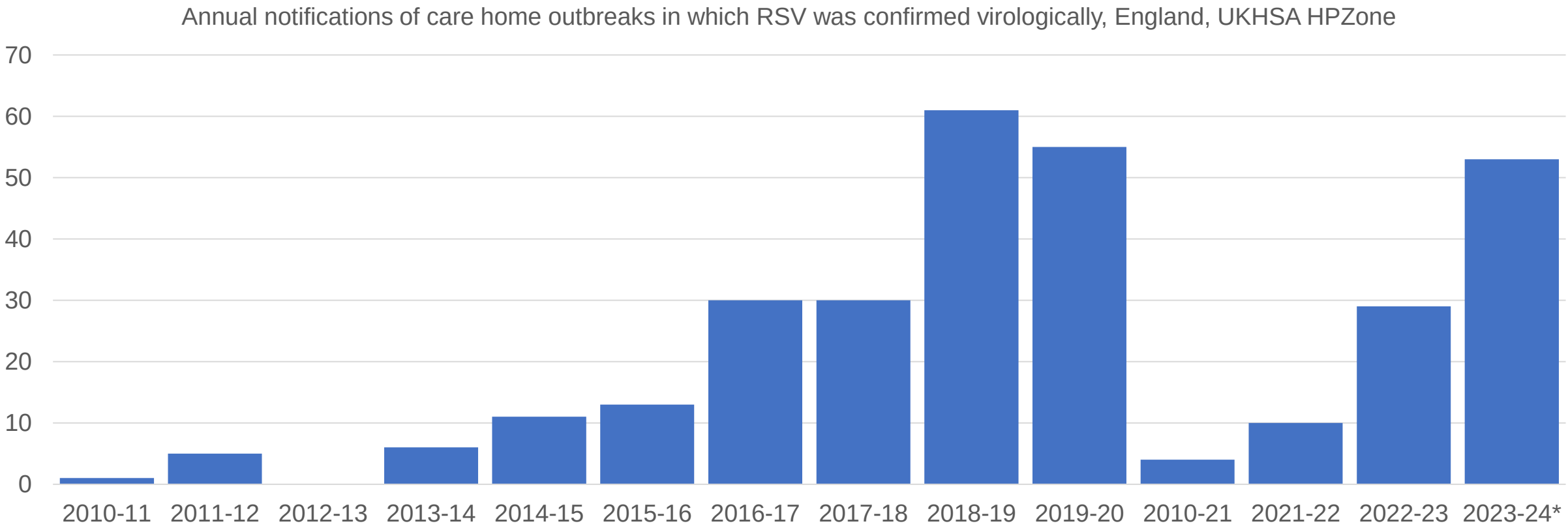
RSV admissions, England sentinel hospital surveillance



*estimates based on sentinel surveillance (SARI-Watch, UKHSA) and ONS population data including 2021 census

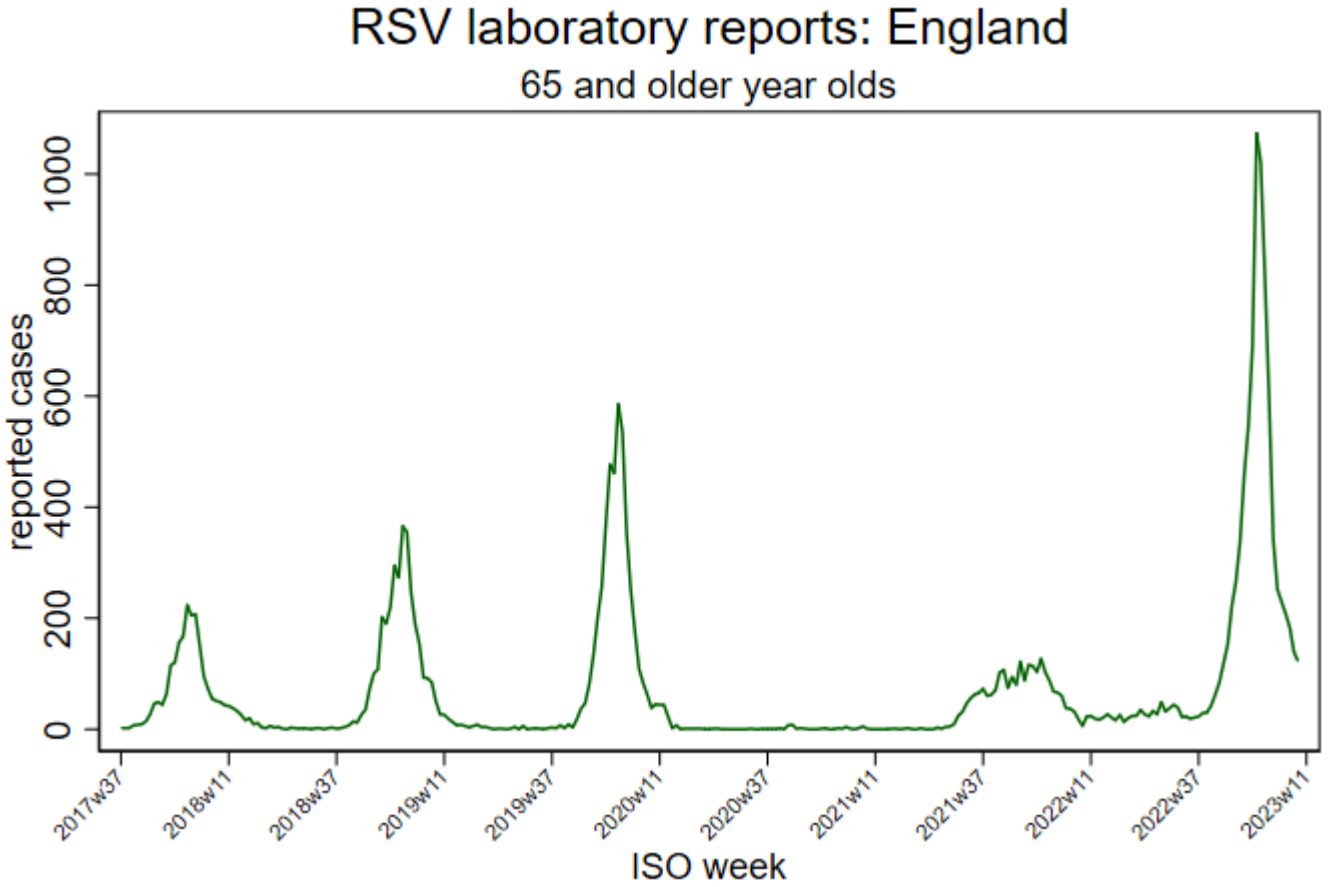
Equivalence of testing practices cannot be assumed; also need to consider detectability of RSV

Increased visibility of RSV as a cause of care home outbreaks



*To week 9, 2024

Virological diagnosis as a clinical norm?



Virological diagnosis as a clinical norm?

UKHSA with University of Nottingham and sentinel hospitals is setting up “**HARISS**” the **Hospital Acute Respiratory Infection Surveillance System**

- Standardised testing for patients admitted with compatible syndromes
- Gathers clinical data on older adults diagnosed with RSV or other viral respiratory infection
- Follows up outcomes
- A future platform for vaccine effectiveness monitoring

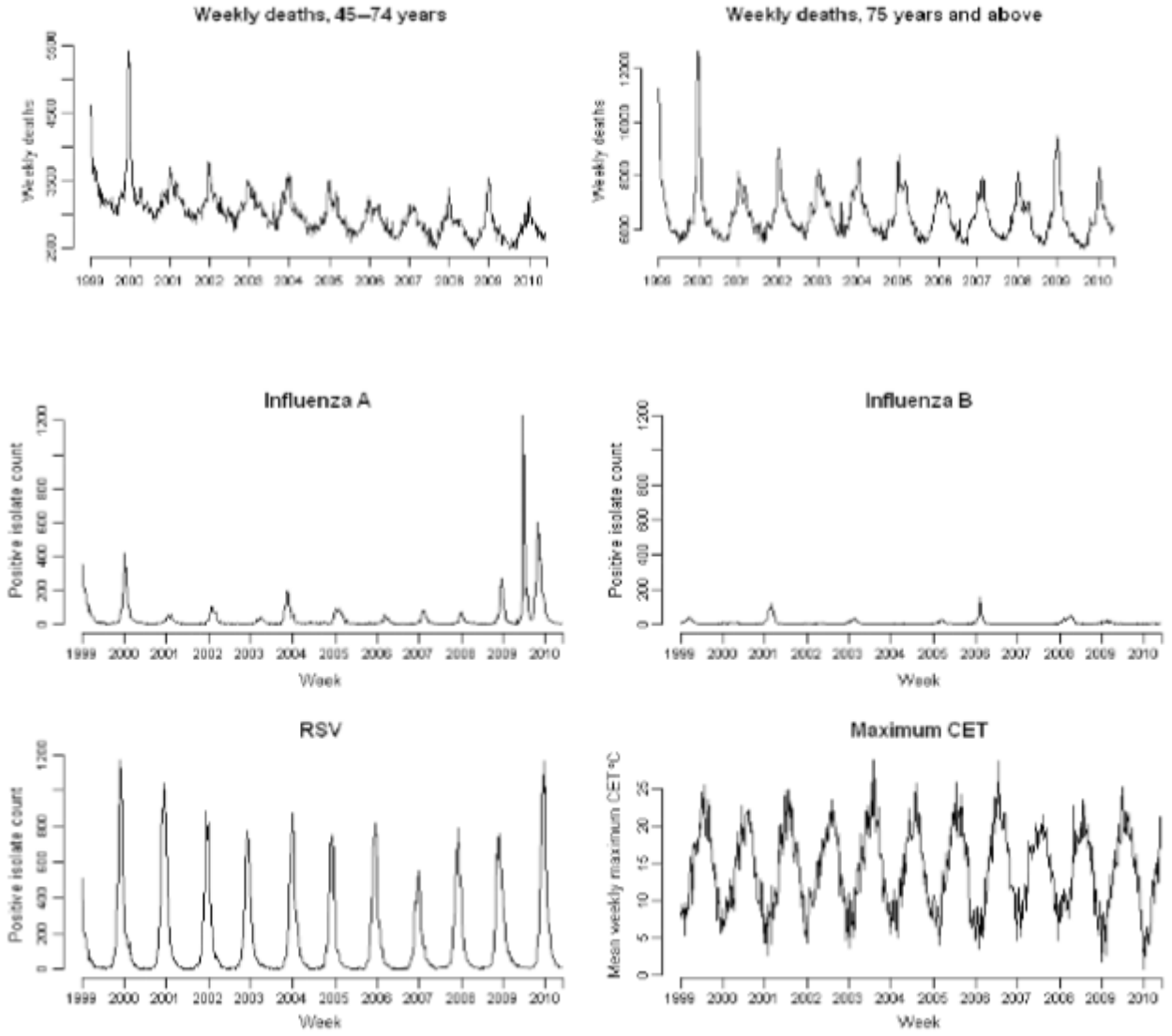
Dr Rebecca Symes, Prof Jamie Lopez Bernal & Prof Wei-Shin Lim

How do we know the burden when we don't test every patient?
HPA mortality estimate, 1999-2010

Statistical regression approach, comparing week-to-week trends in deaths with those for different pathogens, and temperature in England

- 7000-25000 influenza attributable deaths annual, mostly 75yo+
- 5000-7500 RSV attributable deaths annually, mostly 75yo+

Hardelid, Pebody and Andrews, 2013



IRV

Who might benefit most? UKHSA epidemiological analysis by *Dr Freja Kirsebom*

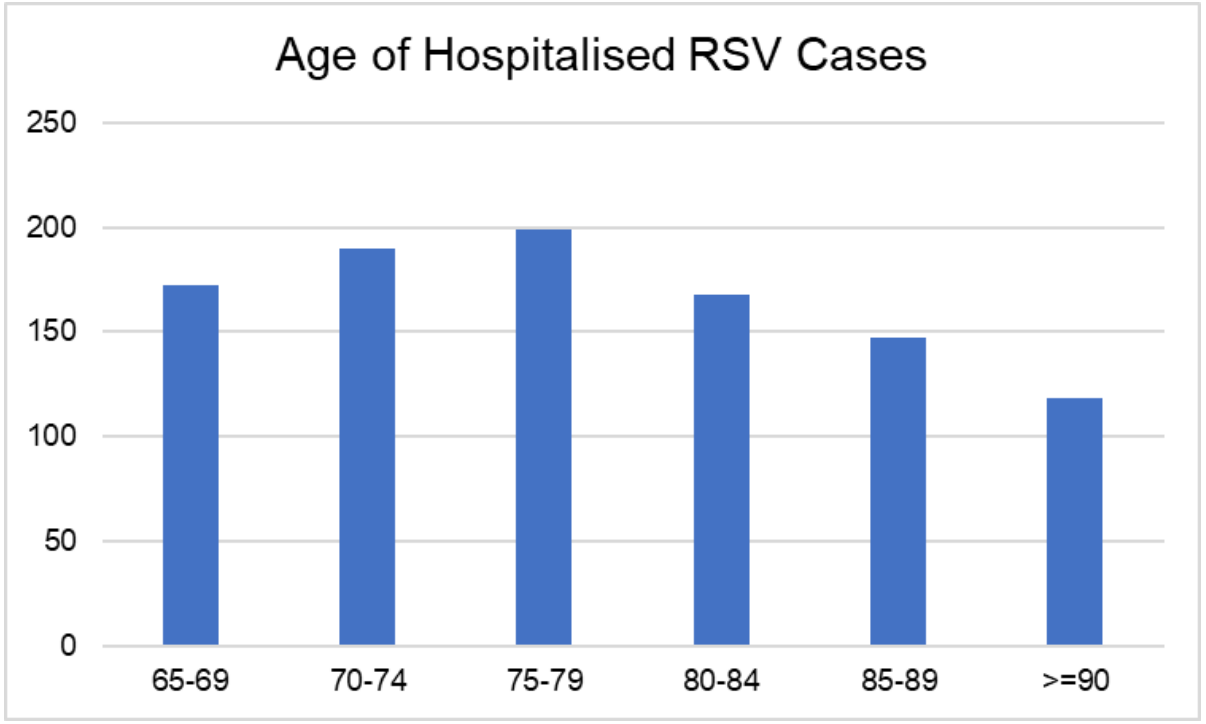
unpublished

- RSV-associated admission **by age group** within the 65yo+ populations
- Examine **primary diagnoses** in RSV associated admissions
- Identify **clinical risk groups** that may be associated with raised rates of admission (caused by) RSV
- Examine **mortality** in the RSV-diagnosed, with 28 days and 365 days

Who is admitted for RSV?

unpublished

- 40% of all older adult RSV tests were linked/linkable to an admission
- More RSV admissions in the 75yo+ than 65-74yo.



Admission causes and underlying risk conditions

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Top five admissions groupings:

- Pneumonia/pneumonitis
- Exacerbation of chronic disease
- Acute lower respiratory tract infection
- [RSV]
- Cancer

At least 85% of RSV-admitted older patients are within an influenza clinical risk group:

- 60% heart/vascular disease
- 41% chronic respiratory disease
- Kidney, neurological, immunocompromise, endocrine disorders/diabetes also common

During the hospital stay

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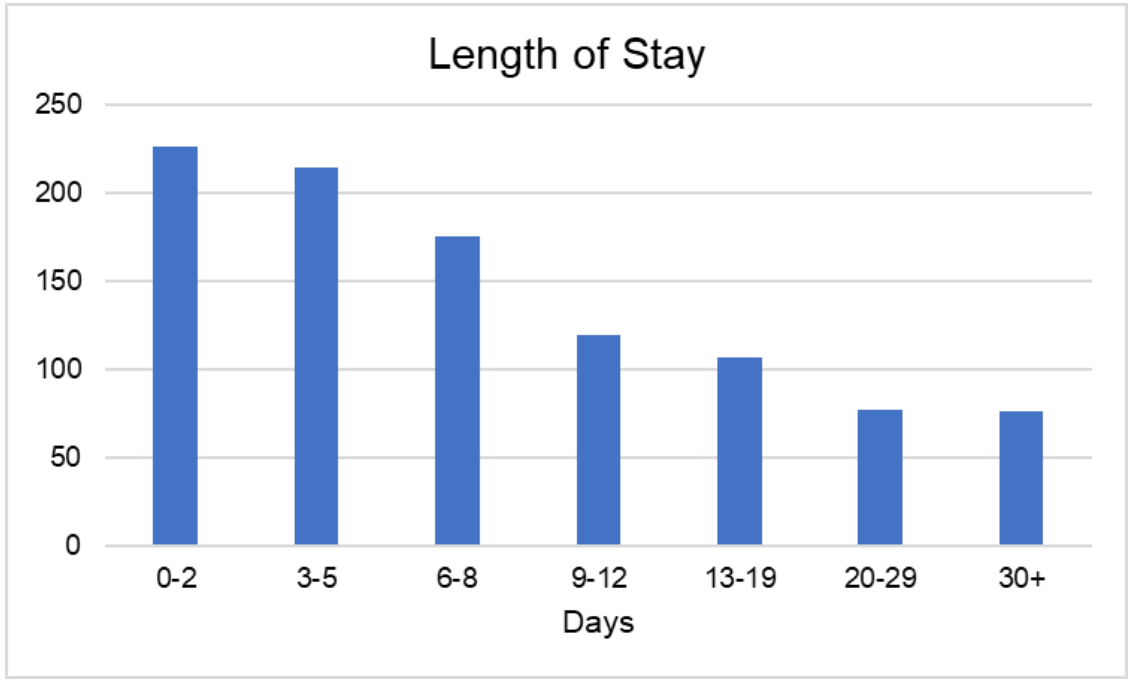
- 11.6% of tests from hospitalised cases (115/994) required oxygen, mechanical ventilation and/or ICU

- Length of stay is heavy-tailed
  - many discharged within 5 days but longer stays are common



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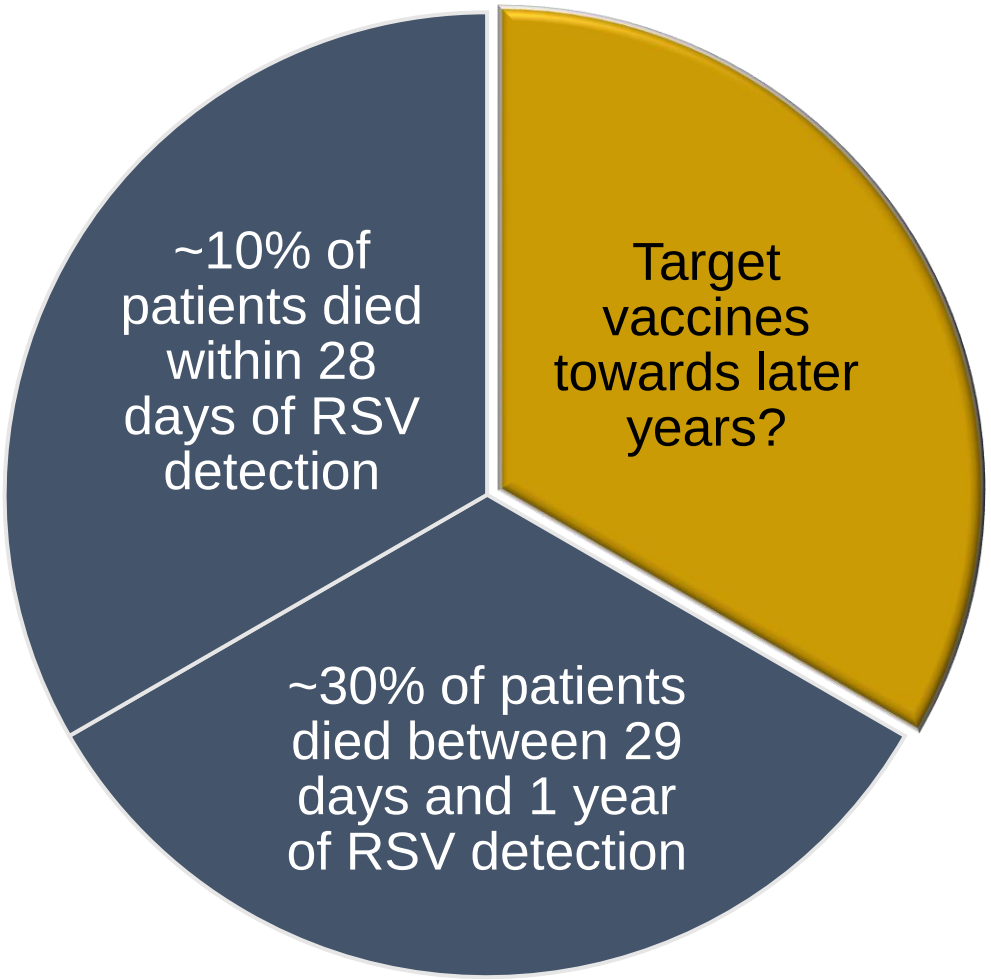
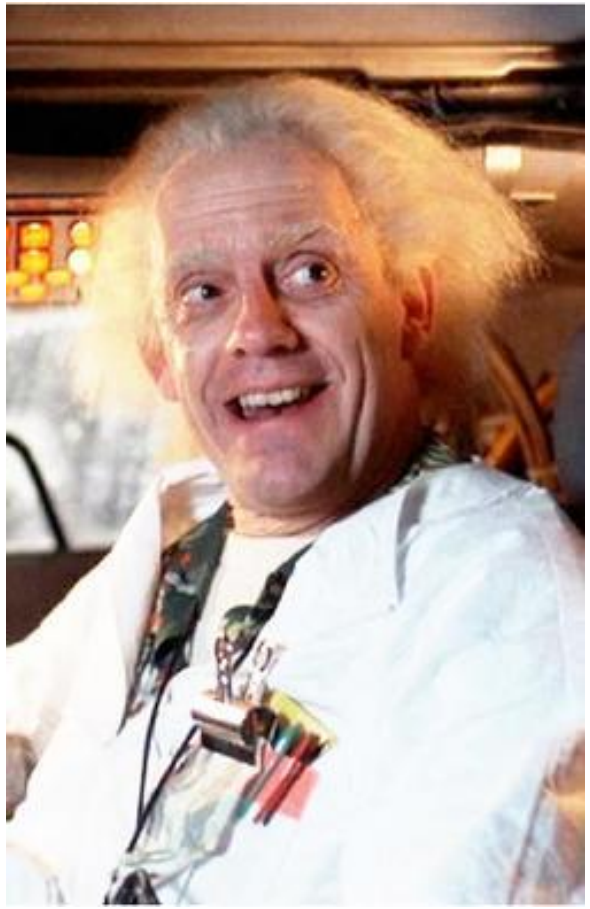
Deaths following an RSV detection



Which RSV patient worries you the most?



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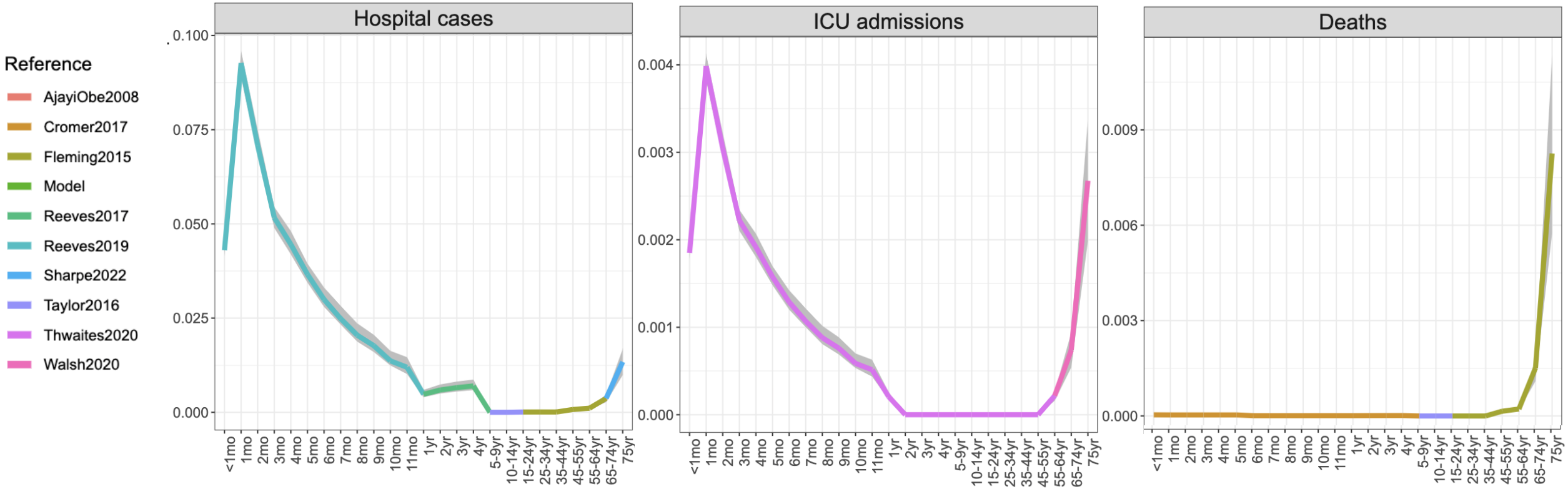

See Hodgson *et al* 2024, Lancet Reg H Eur

Universal vaccination programme to protect neonates and infants?

- JCVI September 2023:
- either **a seasonal, seasonal with catch-up or year-round passive immunisation (monoclonal antibody) programme for newborns** or a **seasonal or year-round maternal active immunisation programme (vaccine)** could be cost effective over a range of potential prices that combine the cost of the product and its administration.
- JCVI advises a **preference for a year-round offer** for a passive immunisation or maternal immunisation programme **to ensure high uptake and for reasons of operational effectiveness** because this would be less complex and resource intensive to deliver, compared with running seasonal campaigns

JCVI advice, June 2023

"The committee notes an RSV vaccine programme for adults aged 75 years and above could be cost effective at a potential price that combines the cost of the product and its administration, noting that this would be influenced by multi-year protection from a single dose.

JCVI currently does not have a preference among the products it has reviewed as efficacy is broadly comparable and there are no head-to-head **studies to allow direct comparison, and so subject to licensure, they can be considered equally suitable for an older adult RSV immunisation programme at this time.**"

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Opportunity

RSV immunisations (2024)

Secretary of State for Health and Social Care acting as part of the Crown through UK Health Security Agency

F02: Contract notice

Notice reference: 2024/S 000-002471

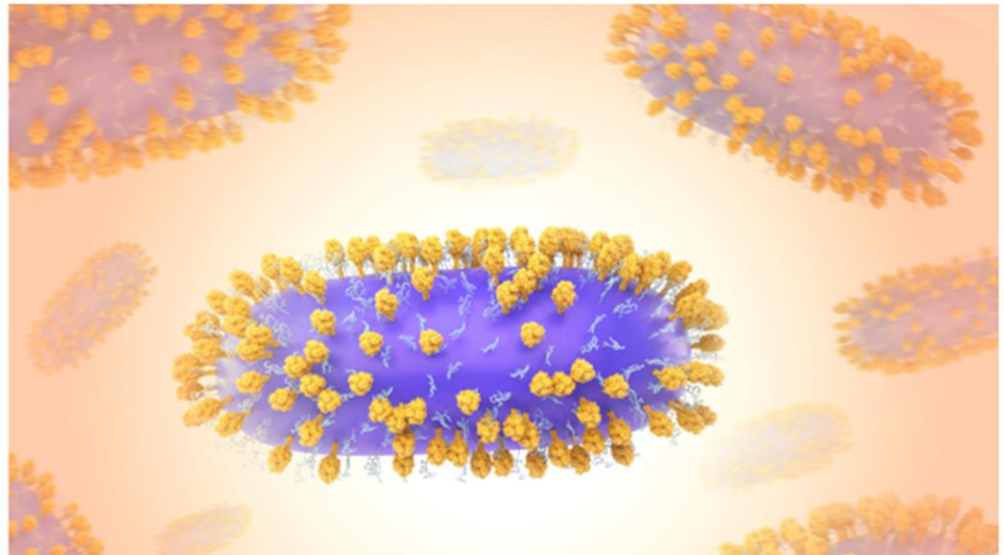
Published 24 January 2024, 4:13pm

UK Health Security Agency

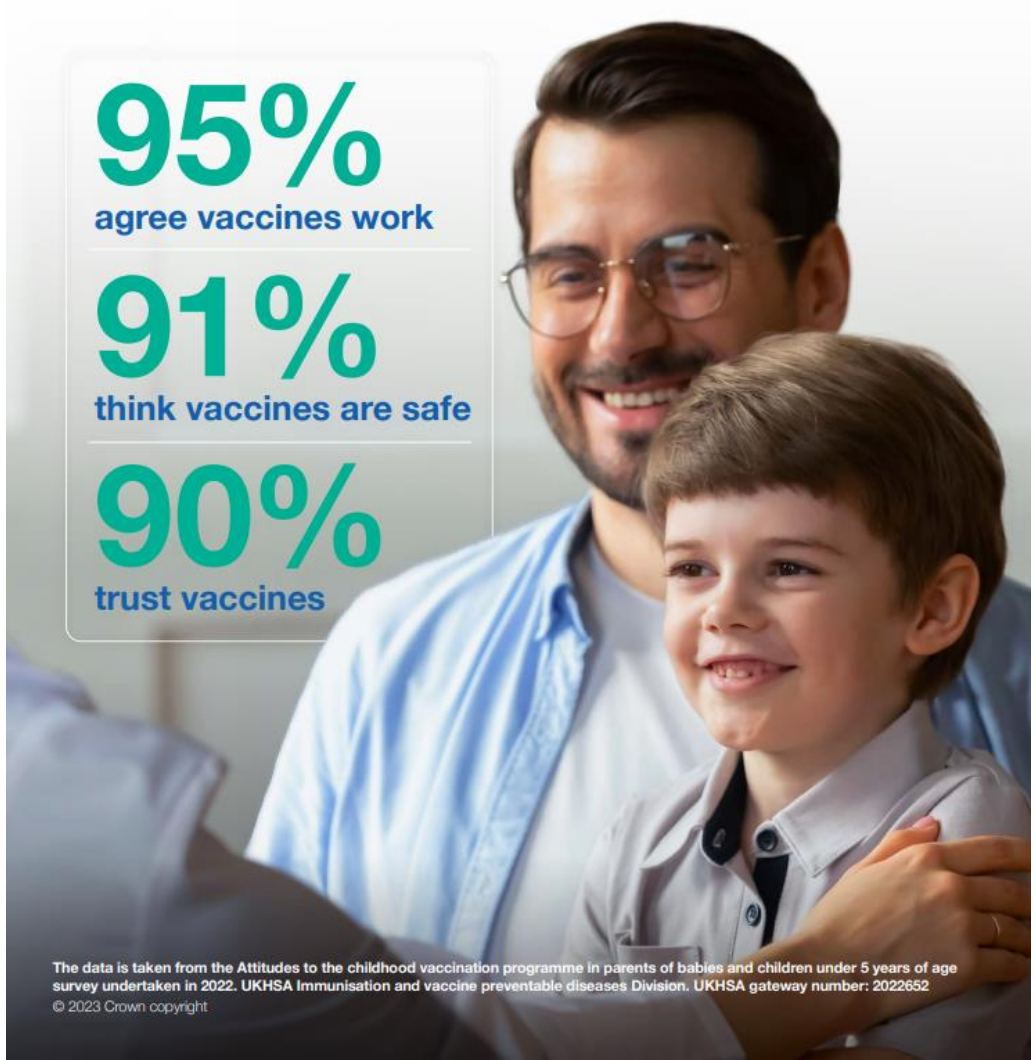
Respiratory syncytial virus (RSV) immunisation surveillance strategy

Infant protection and older adult programmes

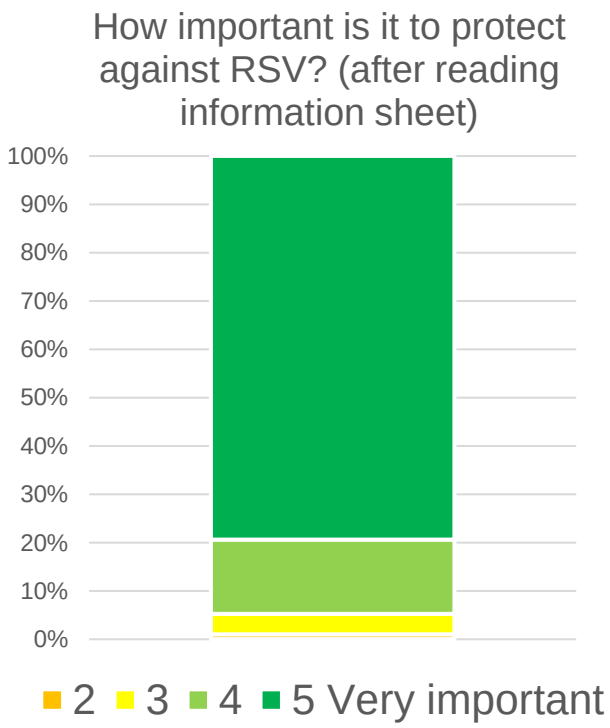
Draft

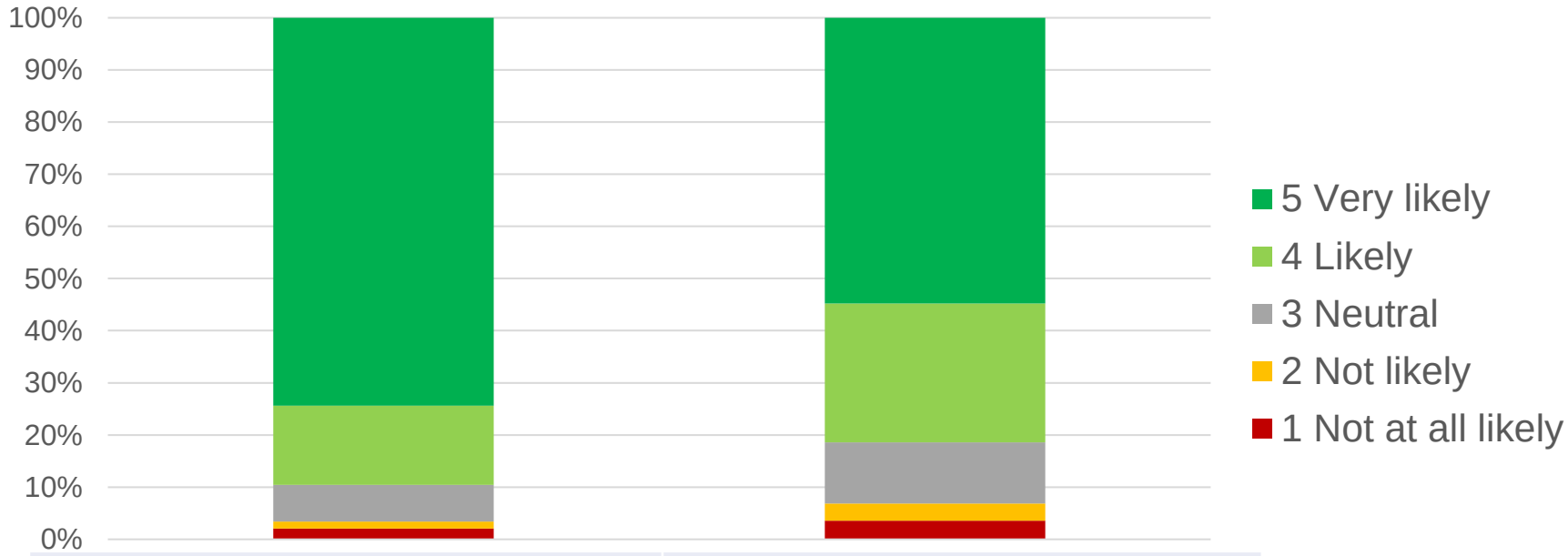


Parent attitudes tracker survey



Would pregnant women / new parents be likely to accept RSV immunisations? (n=1061)





89.5% indicated likely to accept **maternal vaccine**

81.4% indicated likely to accept **infant immunisation**

Factor associated with reduced acceptance on univariable analysis (multivariable currently inconclusive): having a religion, black ethnicity, Asian (infant immunisation only), ?maternal disability, single parent, previously unvaccinated in pregnancy, most deprived (maternal only), currently pregnant (infant only)

What next?