27a

Respiratory syncytial virus

The disease

Respiratory syncytial virus (RSV) is an enveloped, negative-sense, single-stranded RNA virus that belongs to the *Orthopneumovirus* genus of the Pneumoviridae family in the order *Mononegavirales* (Rima *et al* 2017). Two surface glycoproteins on the virus have important functions in cell infection. The attachment glycoprotein G binds the virus to a host cell and trimeric fusion (F) glycoprotein joins the viral envelope with the host cell's plasma membrane, so the virus can enter the host cell. The F protein also stimulates the fusion of the plasma membranes of infected cells creating multi-nucleated syncytia, which can be observed in tissue culture. Two major subtypes (A and B, sometimes referred to as subgroups) of RSV have been identified based on structural variations in the G protein. The predominance of each subtype changes over successive seasons; studies find an inconsistent relationship between subtype and disease severity (see Ciarlitto *et al.,* 2019).

RSV is a common cause of respiratory tract infections. It usually causes a mild self-limiting respiratory infection in adults and children, but it can be severe in infants and older adults who are at increased risk of acute lower respiratory tract infection (LRTI; sometimes termed lower respiratory tract disease, LRTD), including bronchiolitis in infants. RSV bronchiolitis in the pre-immunisation era was an important cause of emergency department attendances (Williams *et al.*, 2023) and amongst the leading causes of infant hospital admissions, with an average annual admission rate of 35.1 per 1000 infant under one year old (Reeves *et al.,* 2017).

Humans are the only known reservoir of RSV. RSV is readily transmissible, with mean estimates of the basic reproduction number around 4.5 (Reis and Shaman., 2018). The incubation period is considered to range from two to eight days and infectious period from three to eight days. The virus is spread from respiratory secretions through close contact with infected persons via respiratory droplets or contact with contaminated surfaces or objects. At least half of children experience an RSV infection in the first year of life and almost all will by the age of two (Henderson *et al.,* 1979, Berbers *et al.*, 2021). Previous infection by RSV confers only partial immunity to RSV and so individuals may be infected repeatedly with the same or different strains of RSV (Oshansky *et al.,* 2009, Berbers *et al.*, 2021).

Those infected by RSV experience a range of acute respiratory infection (ARI) symptoms such as rhinitis, cough, shortness of breath, wheeze, lethargy and sometimes fever (Hall, 2001, Dietz *et al*., 2024). RSV LRTI can include pneumonia in all ages, and bronchiolitis in young children, in whom it may also cause decreased oral intake. RSV also causes croup and otitis media in children (Johnson, 2009; Phillips *et al.*, 2020).

RSV associated infant mortality is highest in low- and middle-income countries, but RSV has a significant disease burden and related healthcare utilisation in high-income countries (Greenough *et al.*, 2004; Li *et al.*, 2022). In the UK prior to the introduction of universal RSV

immunisation the virus was estimated to cause annually around 33,500 hospitalisations in children under 5 years (Reeves *et al*., 2017) and 20 to 30 child deaths (Cromer *et al.*, 2017). Most RSV admissions happen to full-term children without underlying risk factors. Birth months August to November are a risk factor for admission (Reeves *et al.,* 2019): these infants are younger, with correspondingly smaller airways, during peak RSV seasonal activity and have less well-developed immune systems than older infants. Prematurity is similarly an important risk factor for admission in infancy (Boyce *et al.*, 2000).

Predisposing clinical risk factors for severe RSV disease amongst infants include congenital heart disease, chronic lung disease, chromosomal abnormalities, neuromuscular disorders, large airway abnormalities, and immunodeficiency, particularly multimorbidity (Thorburn, 2009). Clinically high-risk infants have been found to account for around 5% of RSV admissions, but 21% of estimated bed days (Reeves *et al.*, 2019). In children considered high risk due to prematurity or chronic respiratory disease, hospitalisation with RSV has a risk of death of around three per cent (Müller-Pebody *et al.*, 2002). Social and demographic risk factors associated with severe RSV disease include being male, exposure to environmental tobacco smoke or indoor air pollution, having young siblings, and day care attendance (Simoes, 2003; Sommer *et al.*, 2011; DiFranza *et al.*, 2012; Havdal *et al*., 2022, Vartiainen *et al.*, 2023).

Paediatric RSV infection may be associated with acute complications including apnoea and hypoxemia, cardiovascular abnormalities (such as tricuspid regurgitation and arrythmias), and secondary bacterial infections (Leung *et al.,* 2005). It remains to be resolved whether there is a causal association between RSV bronchiolitis in early life and development of asthma later in childhood, versus predisposition towards both (see Fauroux *et al*., 2017, Driscoll *et al.*, 2020, Rosas-Salazar *et al*., 2023).

The exact burden of disease in elderly adults is comparatively poorly understood due to a relative lack of testing, although it is considered to have a substantial morbidity and mortality. RSV has been estimated to account for 175,000 annual GP episodes in those age 65 years and older in the UK (Fleming *et al* 2015), and an estimated 5000-7500 deaths in older adults in England and Wales every winter, the vast majority of which occur in adults age 75 years and older (Hardelid *et al* 2013). Enhanced surveillance is required to strengthen estimates.

RSV LRTI is now recognised to have a significant burden in immunocompromised and elderly adults. It may manifest as exacerbations of underlying chronic obstructive pulmonary disease or cardiovascular disease. In immunocompromised patients, RSV can cause severe infections with mortality rates as high as 80% (Falsey and Walsh, 2000). Immunosenescence of T-cell responses may be a factor in vulnerability to severe RSV infection in older adults (Cherukuri *et al.,* 2013).

History and epidemiology of the disease

RSV infections occur year-round but primarily within the period October to March, and with most infections occurring in a relatively short epidemic of about six weeks (Figure 1). Whilst the occurrence of the mid-winter peak is predictable, its size varies from year-to-year. Seasons can be dominated by subtype A or B or a mixture of both (Figure 2). Activity was disrupted by respiratory transmission control measures during the COVID-19 pandemic (Bardsley *et al.*, 2023).

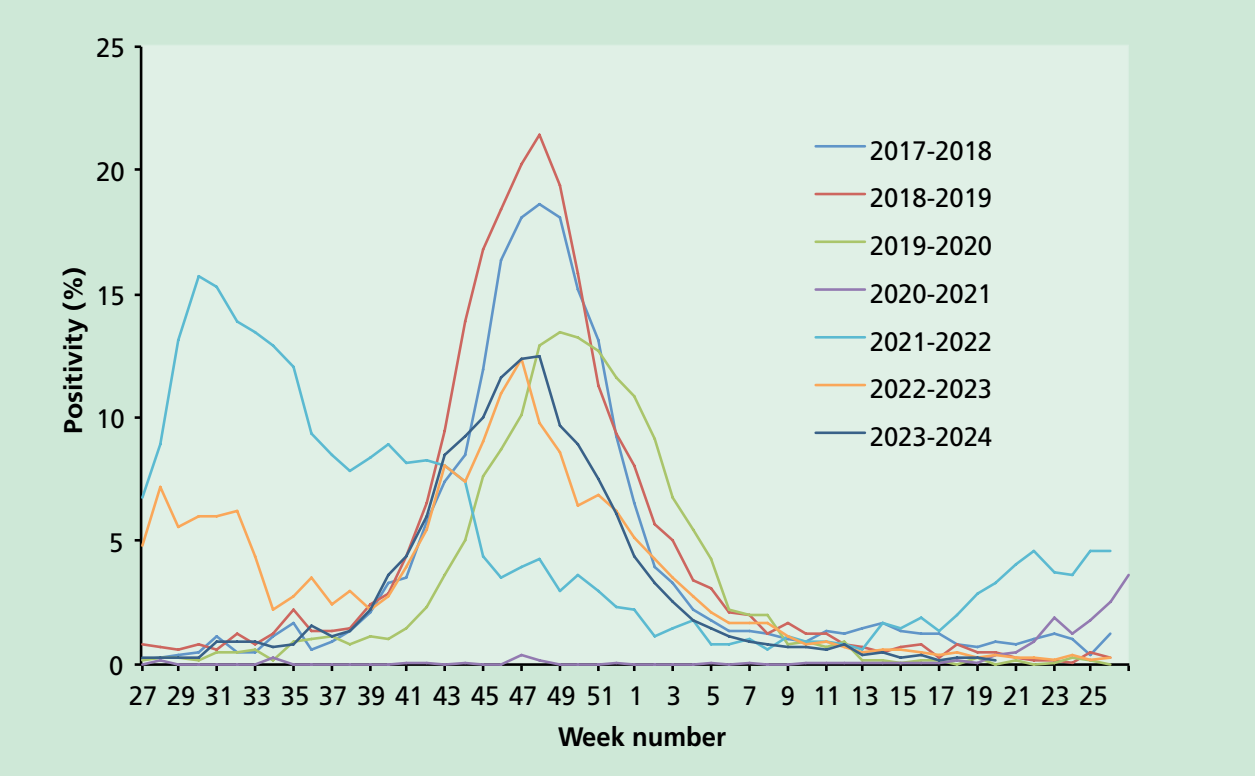

Figure 1. Weekly RSV swab positivity (%) by date of specimen, Respiratory DataMart 2017/18 to 2023/2024.

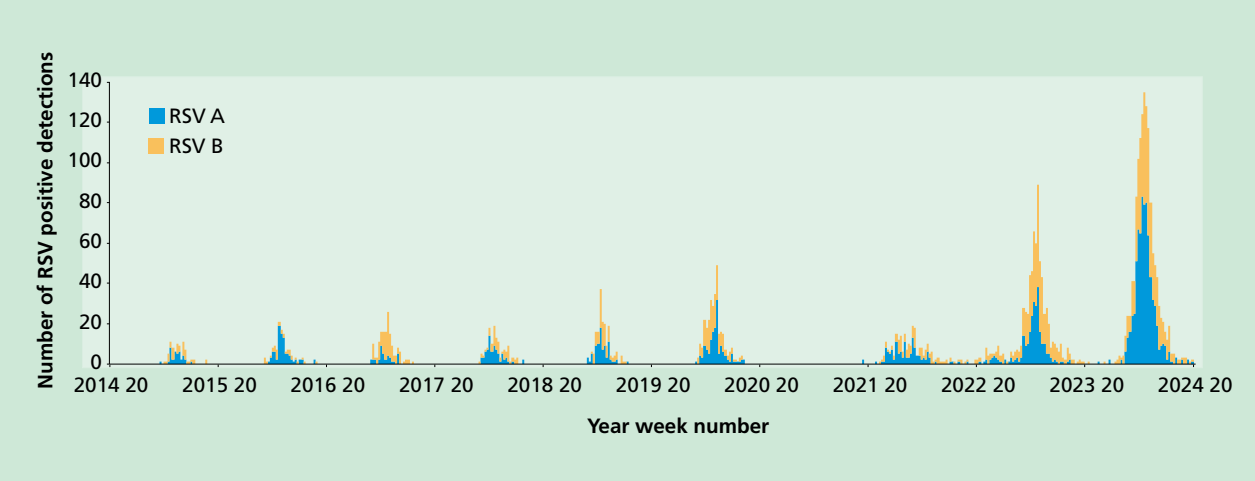

Figure 2. Primary care RSV detections by subtypes A and B in acute respiratory infection patients. Royal College of GPs Research and Surveillance Centre, Oxford and the UKHSA Respiratory Virus Unit. Note that testing has increased over time.

The UK Health Security Agency (UKHSA) monitors levels of RSV activity in England and publishes information throughout the RSV season. The epidemiological data are included in UKHSA's weekly national influenza reports (gov.uk/government/statistics/weekly-national-flu-reports).

RSV laboratory results are collected into national surveillance systems including sentinel Respiratory Datamart (figure 3) and the NHS-wide Second-Generation Surveillance System (SGSS). Data on RSV in primary care are collected as part of the Royal College of General

Practitioners UKHSA surveillance programme. Secondary care surveillance includes Emergency Department Syndromic Surveillance (of bronchiolitis), confirmed RSV admissions to wards and critical care (severe ARI) through the SARI Watch system (figure 4) and determining adult outcomes and incidence through the pilot Hospital ARI Surveillance System (HARISS). Monitoring for RSV strains that can evade immunity is important for RSV programmes globally (Simões *et al.,* 2021), as undertaken at UKHSA's Respiratory Virus Unit.

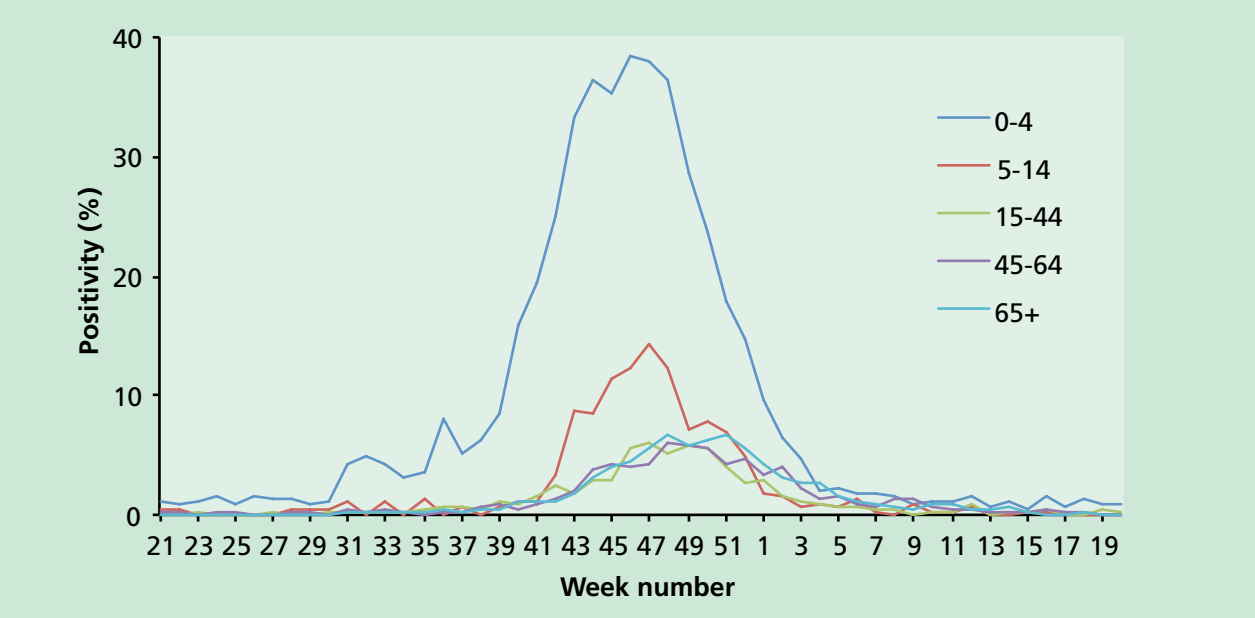

Figure 3. Weekly swab positivity (%) by age group and date of specimen, Respiratory DataMart 2023/2024

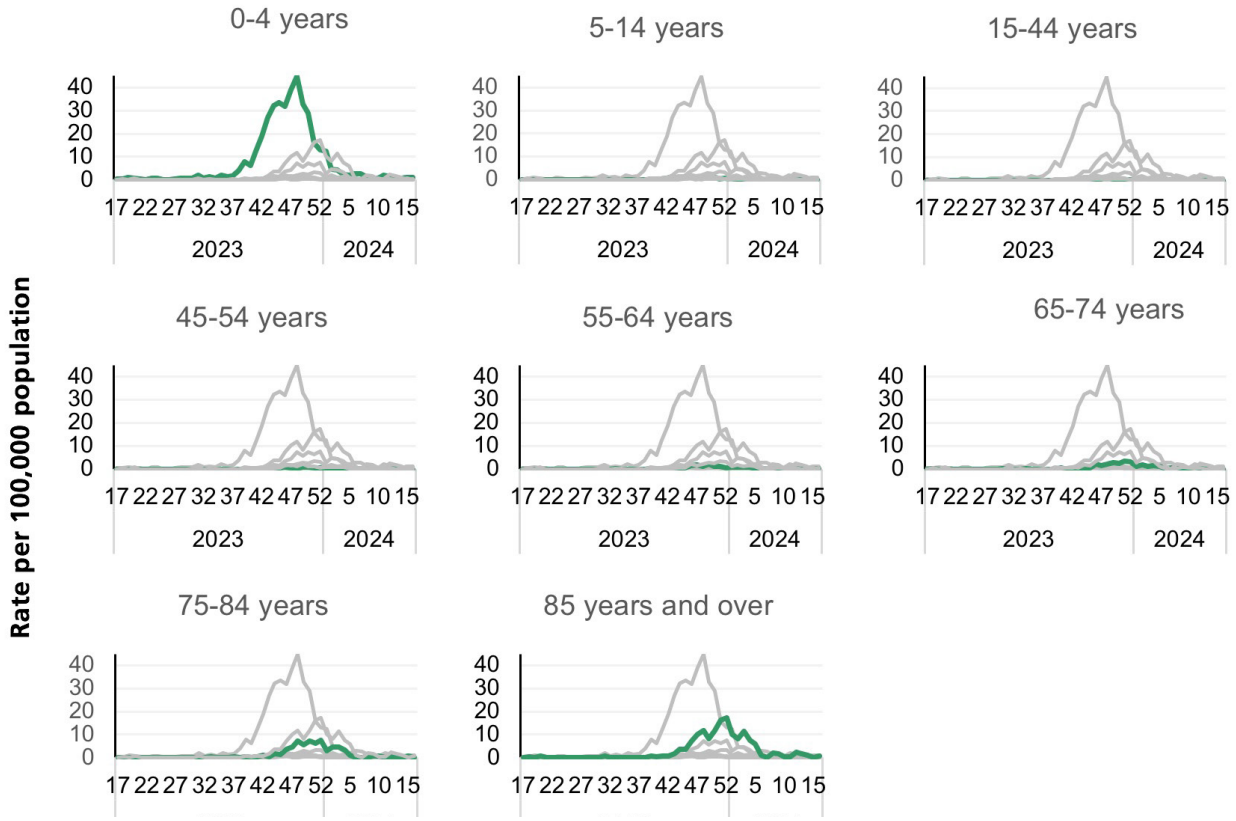

Figure 4. Weekly confirmed RSV hospital admission rates per 100,000 population, by age group, reported through SARI Watch sentinel surveillance, England, week 16 2023 to week 15 2024

RSV immunisation

RSV monoclonal antibody immunisation using palivizumab was first approved for use in infants in European countries in 1999, providing passive protection (EMEA 2010). Its high cost and moderate effectiveness meant that cost-effectiveness was only demonstrated for very high-risk infants (JCVI 2010). The UK selective immunisation programme has been delivered in secondary care by paediatric services.

Paediatric RSV vaccine development was effectively halted after trials in the late 1960s where severe, enhanced disease was observed when some vaccinated infants were later exposed to natural infection (Chin *et al.*, 1969; Fulginiti *et al.*, 1969; Kapikian *et al.*, 1969;Kim *et al.*, 1969). This observation was limited to younger infants who had not been exposed to infection prior to vaccination and may have resulted from low avidity neutralising antibody responses, T-helper type 2 oriented immune responses, and immune complex deposition in airways. Subsequently, the mechanism was considered to be caused by the inactivation step of vaccine production which used formalin to kill the virus. This led to the experimental vaccine displaying post-fusion F glycoprotein instead of the pre-fusion form found in natural infection and thus associated with the abberant immune responses (Killikelly, Kanekiyo and Graham, 2016).

Discovery of the crystal structures of the prefusion and postfusion forms of the RSV F protein has enabled rational design of vaccines and monoclonal antibodies including F-protein vaccines stabilised in the pre-fusion formation (McLellan *et al* 2013; Che *et al.*, 2023).

From late 2022 a number of products have been licensed internationally for protection against RSV LRTI in infants and in adults. RSV immunisation programmes are projected to have substantial health benefits (Hodgson *et al.*, 2024).

Adult protection against RSV LRTI is through vaccination for active immunity (see chapter 1). Evaluation of the first season of the US older adult vaccination programme showed effectiveness of 80% (95%CI: 71 to 85%) against RSV-associated hospitalisation in the immunocompetent and 73% (95%CI: 48 to 85%) in those with immunocompromise (Payne *et al.*, 2024).

At time of writing there are no approved RSV vaccines for infants; such an approach is unlikely to provide protection during the most vulnerable first months of life due to the immaturity of the immune system. Vaccine development for older infants requires clinical trials to determine efficacy and safety, including assurances around the possibility of vaccine-associated enhanced respiratory disease. Infant RSV protection is therefore through passive immunity, either by vaccination of the pregnant mother for transplacental passive immunisation of the baby *in-utero* or by direct administration to the infant of a monoclonal antibody. There is some evidence that passive monoclonal antibody administration with nirsevimab provides better protection against disease than against infection (Wilkins *et al.*, 2023). Immunised infants can therefore acquire natural infection and start to develop active immunity against RSV. This appears to confer protection into the second season, with no excess of deferred disease seen in immunised group in the MELODY trial (Dagan *et al.*, 2024). The same mechanism is likely to apply to passive immunity derived from maternal vaccination.

For maternal vaccination, while the major mechanism of infant protection is transplacental antibody transfer, there may also be protective effects from antibody transfer in breast

milk, and from indirect protection by reducing the risk of infection and/or degree of infectiousness in the mother and therefore chance of infecting the infant. Lactational antibody transfer and indirect protective effects ("cocooning") would also be expected to apply where vaccine is given too late in pregnancy for good transplacental transfer and with immediate postnatal maternal vaccination.

JCVI advice

JCVI has recommended that high risk infants (see later) receive nirsevimab, or palivizumab if nirsevimab is unavailable (February 2023).

For a universal programme for infant protection, JCVI has advised either maternal immunisation with Pfizer pre-F vaccine (Abrysvo®) or infant immunisation with nirsevimab (Beyfortus®) would be suitable for a national programme. JCVI has also advised (October 2024) that a long-acting monoclonal immunisation should be considered for very and extremely preterm infants (born before 32 weeks), who are unlikely to benefit from maternal vaccination, to be offered in or immediately preceding their first RSV season.

For older adults, the committee initially advised (June 2023) that GSK's adjuvanted pre-F vaccine (Arexvy®), Pfizer's Abrysvo® or Moderna's mRNA-1345 mRESVIA vaccine (subject to licensure) would all be suitable for a national programme. The committee has since noted (October 2024) that more recent data give greater certainty on the durability and efficacy of Arexvy and Abrysvo than Moderna's mRNA vaccine, which remains unlicensed in the UK at time of writing.

JCVI has noted there were few participants age 80 years+ in the pivotal clinical trials, and that further data are required on clinical protection in this group.

See JCVI's 2023 statement for further details and below for details of the product in use in the national programmes.

RSV vaccines

There are two licensed RSV vaccines in the UK: Pfizer's Abrysvo® and GSK's Arexvy®. Whereas the GSK product is only approved for use in older adults, the Pfizer product is approved for use in both older adults and pregnant women. The Pfizer vaccine has been procured for use in the national programmes for protection of older adults and for vaccination of pregnant women for infant protection.

Pfizer RSV pre-F vaccine (Abrysvo®)

Abrysvo® is a recombinant RSV vaccine. It is bivalent, containing recombinant RSV prefusion F protein (pre-F) antigens developed from each of subtypes A and B. Abrysvo® is licensed for prevention of RSV LRTI in individuals from 60 years of age and to protect infants from RSV LRTI through vaccination of pregnant women. The maternal indication is licensed by the Medical and Healthcare products Regulatory Agency (MHRA) as between 28 and 36 weeks gestation (see Recommendations, below, for off-label use).

Maternal (antenatal) vaccination has been demonstrated to be efficacious against RSV LRTI in infants from birth through to 6 months of age (Kampmann *et al.,* 2023). The pivotal phase 3, multi-country, randomised, double-blind, placebo-controlled trial assessed the prevention of RSV LRTI and severe RSV LRTI (co-primary efficacy endpoints) in infants born to pregnant individuals vaccinated between weeks 24 and 36 of gestation. Vaccine was administered to 3,695 pregnant women with uncomplicated, singleton pregnancies; 3,697

received placebo. In the final analysis, vaccine efficacy (VE) against severe RSV LRTI was 82.4% (95%CI: 57.5 to 93.9%) at 90 days and 70.0% (95%CI: 50.6 to 82.5%) at 180 days. VE against RSV LRTI was 57.6% (95%CI: 31.1 to 74.6%) at 90 days and 49.2% (95%CI: 31.4 to 62.8%) at 180 days (Munjal *et al.,* 2024; Simões *et al*., 2025). VE estimates by RSV subtype have overlapping confidence intervals. A posthoc analysis of vaccination by gestational week suggests the possibility of higher VE when the vaccine is given from week 28, compatible with efficacy against severe RSV LRTI of around 80% over 180 days. There are data showing antibody transfer to the infant even where the mother delivered within two weeks of immunisation (Kampmann, 2024; Simões *et al*., 2025). Preliminary evaluation of the first season of the maternal programme in Argentina found infants under 6 months age had 68% (95%CI 56.2 to 76.6%) protection against RSV hospitalisation and 73.9% (95%CI: 53.2 to 85.4%) against severe hospitalised RSV LRTI (Pérez Marc and Rearte, 2024).

For older adults, the pivotal phase 3, multi-country, randomised, double-blind, placebo-controlled trial recruited from the age of 60 years to assess Abrysvo's efficacy against RSV LRTI with 2+ or 3+ symptoms (Walsh *et al.*, 2023). Participants were randomised to receive vaccine (n=18,488) or placebo (n=18,479), stratified by ages 60-69 years (63%), 70-79 years (32%) and ≥80 years (5%). Stable chronic underlying conditions were present in 52% of participants; immunocompromised individuals were excluded. At the end of the first RSV season VE against RSV LRTI with ≥2 symptoms was 65.1% (95%CI: 35.9 to 82.0%) and with ≥3 symptoms 88.9%, (95%CI: 53.6 to 98.7%) (Pfizer 2024). VE estimates by RSV subtype have overlapping confidence intervals (Walsh *et al.*, 2023). In the second season, VE was 77.8% against LRTI with 3+ symptoms (95%CI: 51.4 to 91.1%) and 55.7% (95%CI: 34.7 to 70.4%) against 2+ symptoms (Pfizer 2024).

GSK adjuvanted RSV pre-F vaccine (Arexvy®)

Arexvy® is a recombinant adjuvanted RSV vaccine licensed in adults 60 years of age and older. It contains a pre-fusion F protein with an adjuvant ($AS01_E$, a proprietary combination of saponin and monophosphoryl lipid A) which was found to improve immunogenicity, including CD4+ T cell responses, over unadjuvanted formulations (Leroux-Roels *et al.*, 2023). This adjuvant is a lower dose of the adjuvant used in the inactivated shingles vaccine Shingrix® and has also been used widely in the GSK malaria vaccine Mosquirix®.

Efficacy against RSV LRTI in adults 60 years and older was evaluated in a phase 3, multi-country, randomised, observer-blind, placebo-controlled trial. Participants were randomised to single dose Arexvy (n=12,466) or placebo (n=12,494). Fixty-six percent of participants were age 60-69 years. At baseline, 39.3% of participants had at least one comorbidity of interest; immunosuppression was an exclusion criterion.

In the primary analysis, after median 6.7 months follow-up, VE against RSV LRTI was 82.6% (96.95%CI: 57.9% to 94.1%). Against the secondary endpoint of severe RSV LRTI, VE was 94.1% (95% CI: 62.4 to 99.9%). Protection against LRTI caused by RSV subtypes A and B appears equivalent (Papi *et al.,* 2023). Efficacy against LRTI was 58.5% (95%CI: 33.9 to 75.0%) in the second season and 48.0% (95%CI 8.7 to 72.0%) in the third season. Cumulative efficacy against severe LRTI was 72.3% (95%CI: 51.3 to 85.2%) over three seasons (Gerber 2024).

RSV monoclonal antibodies for passive immunisation

There are two RSV monoclonal antibody immunisations for young children licensed in the UK. These should be used in line with JCVI advice on immunisation of high-risk children (see Recommendations section below).

Nirsevimab (Beyfortus®)

Nirsevimab, known as MEDI8897 during early development (Domachowske *et al*., 2018), is a recombinant monoclonal antibody produced in a mammalian cell line. It provides passive immunity and was approved by the MHRA on 9 November 2022 for prevention of RSV LRTI in infants. Nirsevimab is directed against the Ø (slashed zero) antigenic site of the F prefusion protein of RSV. This inhibits the membrane fusion required for viral entry to human airway cells. Nirsevimab has an extended half-life, and the duration of protection is at least five months based on clinical and pharmacokinetic data (Wilkins *et al.*, 2023). Clinical trials have shown nirsevimab be safe and effective at reducing medically attended LRTI in pre-term and term infants (Griffin *et al*., 2020; Hammitt *et al.*, 2022; Domachowske *et al.*, 2022). In the pivotal phase 3 multi-country, randomised, double-blind, placebo-controlled, randomised trial, amongst infants receiving pre-seasonal nirsevimab, 1.2% developed RSV LRTI compared to 5% of the placebo group, which corresponds to an efficacy of 74.5% (95% confidence interval (CI): 49.6 to 87.1%) (Hammitt *et al.*, 2022). A phase 3b trial demonstrated efficacy of 83.2% (95%CI: 67.8 to 92.0%; P<0.001) in preventing hospitalisation for RSV-associated LRTD (Drysdale *et al.*, 2023). In preterm infants born at 29 to 34 weeks gestation, a phase IIb study found 70.1% (95%CI: 52.3 to 81.2%) lower incidence of medically attended RSV LRTI (2.6% vs. 9.5%) with nirsevimab than placebo (Griffin *et al.,* 2020). Nirsevimab has been shown to be comparable with palivizumab in a safety study of higher-risk infants (Domachowske *et al.*, 2022).

Post-licensure use of nirsevimab prophylaxis for infants with low- and high- risk of RSV LRTD has been evaluated in the USA and parts of Europe. Preliminary surveillance by the US Centers for Disease Control and Prevention (CDC) found effectiveness of 90% (95%CI: 75 to 96%) against RSV-associated hospitalisation (Moline *et al*., 2024). In Galicia, Spain, effectiveness was found to be 82.0% (95%CI: 65.6 to 90.2%) against RSV-associated LRTD hospitalisation (Ares-Gomez *et al.,* 2024). Effectiveness against critical care admission in France has been estimated as 75.9% (95%CI: 48.5 to 88.7%) (Parieau *et al.,* 2024).

Palivizumab (Synagis®)

Palivizumab is a humanised monoclonal antibody (IgG11K) produced using recombinant DNA techniques in a mammalian cell line. It provides passive immunity against RSV disease. Palivizumab is directed against an epitope in the A antigenic site of the F protein responsible for fusing the virus and the host cell and therefore works by inhibiting the virus from entering the host cell (Johnson *et al.,* 1997, Harkensee *et al.,* 2006). Palivizumab has been shown to be safe and effective in reducing RSV hospitalisation rates and serious complications among high-risk children (Impact-RSV Study Group, 1998; Feltes *et al.,* 2003) with an effectiveness around 55% (Garegnani *et al*., 2021). Palivizumab has a half-life in the body in the range of 18 to 21 days. Monthly administration during the RSV season is required to maintain its concentration at a protective level (Johnson *et al*., 1997).

Synagis® solution for injection is the only licensed form of palivizumab available in the UK. The licensed indication is the prevention of serious RSV LRTD requiring hospitalisation in children under two years of age that are at high risk for RSV disease, due to prematurity

(including chronic lung disease of prematurity) or haemodynamically significant congenital heart disease, as detailed in the summary of product characteristics (SmPC).

Storage

RSV immunisations should be stored in their original packaging in a refrigerator at 2°C to 8°C.

Heat speeds up the decline in potency of most vaccines and monoclonal antibodies, thus reducing their shelf life. Storage below 2°C may cause loss of potency and freezing can also cause hairline cracks in the container, leading to contamination of the contents. However, excursion from the recommended conditions does not necessarily require that the product should be disposed of or require that the patient needs an additional dose if the product has been administered. See the chapter 3 section on fridge failure or disruption of the cold chain, SmPCs, and the UKHSA programme information for healthcare professionals. Information should be sought from manufacturers' medical information departments: contact details are in the SmPCs.

RSV immunisations should ordinarily be used immediately after being taken from the fridge (and reconstituted if applicable) to reduce the risk of administration errors, minimise waste, and from a microbiological perspective. There is some data on known room temperature stability in the pre-administration period. After reconstitution Abrysvo® (Pfizer Pre-F vaccine) and Arexvy® (GSK adjuvanted Pre-F vaccine) are stable for 4 hours at room temperature. Beyfortus (nirsevimab) is stable at room temperature for 8 hours. Synagis (palivizumab) has some data supporting stability at room temperature for at least 8 hours.

Presentation

Abrysvo® (Pfizer RSV pre-F vaccine) is presented as a single dose pack for reconstitution. Each pack comprises a vial of dry powder with a synthetic chlorobutyl rubber stopper and a flip-off cap, a glass prefilled syringe of water for injection with a plunger stopper of synthetic chlorobutyl rubber and a synthetic isoprene/bromobutyl blend rubber tip cap on top of luer adaptor, a sterile vial adaptor, and a 25g 1 inch needle for administration.

Arexvy® (GSK adjuvanted pre-F vaccine) comes as a vial of powdered antigen with a vial of aduvant suspension for reconstitution. The powdered antigen vial (type I glass) has a butyl rubber stopper and a mustard green flip-off cap. The adjuvant suspension vial (type I glass) has a butyl rubber stopper and a brown flip-off cap.

Beyfortus® (nirsevimab) is a colourless to yellow solution, supplied as either a 50mg in 0.5ml or 100mg in 1ml pre-filled syringe.

Synagis® (palivizumab) is a clear or slightly opalescent liquid, supplied in either 50mg in 0.5 ml or 100mg in 1ml vials, with chlorobutyl rubber stoppers and flip-off caps.

Dosage and schedule

Dosages and schedules should be used in accordance with the Recommendations section later in this chapter.

Vaccines dosage and schedules

For both Abrysvo and Arexvy, the full duration of protection in older adults is unknown but is at least two years. There are no current data to support revaccination of older adults after a first dose.

Abrysvo® Pfizer RSV pre-F vaccine

Abrysvo® is approved by regulators for pregnant individuals and older adults. A single dose of 0.5 mL should be administered using the full volume of the reconstituted, drawn up syringe.

For pregnant individuals, Abrysvo should be administered from week 28 gestation and can be given up until delivery. Vaccine should be offered in each pregnancy. Ideally it should be given in week 28 or soon after, so there is sufficient time for the mother to make high levels of antibody and for these to transfer across the placenta, including if the baby is born prematurely. Women may still be vaccinated later in pregnancy, including off-label after week 36 of pregnancy but this may not offer as high a level of passive protection to the baby. There is some evidence that good transplacental antibody transfer can take place within two weeks of vaccination (Kampmann 2024), so even doses later in pregnancy may offer some protection to the infant. Babies born to women who have had Abrsyvo® can be safely breastfed. Vaccines given to the mother close to delivery, including soon after delivery, may offer indirect protection by preventing maternal infection/infectiousness and through antibody transfer in breastmilk.

GSK adjuvanted RSV pre-F vaccine (Arexvy®)

Arexvy® is approved by the medicine regulators for use in older adults only. The regimen is a single dose of 0.5ml, once reconstituted.

Monoclonal antibody dosage and schedules

For the selective immunisation of high-risk children, monoclonal antibodies are given seasonally, usually in or from around calendar week 40 in early October. See Recommendations section for eligibility and choice of monoclonal antibody product. In the rare event of disrupted RSV seasonality (as occurred during the COVID-19 pandemic) alternative schedules may be needed. Advice from national authorities should be followed.

Nirsevimab (Beyfortus®)

The nirsevimab dose for children weighing less than 5kg is 50mg, and for children weighing 5kg or more it is 100mg. The full volume of the appropriate strength prefilled syringe should be used. A single dose is expected to protect for at least 5 months, a full RSV season. Therefore the dose should ordinarily be administered around calendar week 40 (the start of October). If an infant or child is newly identified as high-risk (see box 1) during the season, a single dose of nirsevimab should be given, up to the end of calendar week 8 (late February).

For those born in season or scheduled to leave hospital during the RSV season, the nirsevimab dose should be given while an inpatient. As the duration of protection is season-long, the dose does not need to wait until near discharge, and there may be merit in giving it earlier to allow time for absorption and distribution before the infant goes home.

Palivizumab (Synagis®)

The recommended dose of palivizumab is 15mg/kg of body weight, given once a month. Where possible, the first dose should be administered at the start of the RSV season (calendar week 40). Subsequent doses should be administered monthly throughout the RSV season up to a maximum of five doses.

If the course of treatment begins later in the RSV season (for example, infants are born or leaving hospital within the RSV season, or clinical risk is identified in season) up to five doses should be given one month apart until the end of calendar week 8 (late February). As the risk of acquiring RSV infection while in the neonatal unit is extremely low, and palivizumab requires monthly re-administration, infants in neonatal units who are in the appropriate risk groups should receive an RSV monoclonal antibody immunisation 24 to 48 hours before being discharged from hospital. Those infants that have begun a course of palivizumab treatment but are subsequently hospitalised should continue to receive palivizumab whilst they remain in hospital. Where a palivizumab course has been interrupted the doses should be restarted and administered monthly for the remainder of the RSV season but need not be given after the end of calendar week 8.

Administration

The vaccines Abrysvo® (Pfizer RSV pre-F) and Arexvy® (GSK adjuvanted RSV pre-F) are given by intramuscular injection, preferably in the deltoid muscle. The SmPCs/package inserts should be consulted for reconstitution steps. For Abrysvo®, Pfizer UK also provides a video of reconstitution steps pfizerpro.co.uk/medicine/abrysvo/dosing/preparation.

The monoclonal antibody immunisations nirsevimab (Beyfortus®) and palivizumab (Synagis®) are given by intramuscular injection, preferably in the anterolateral aspect of the thigh.

Individuals with bleeding disorders may be immunised intramuscularly if, in the opinion of a doctor familiar with the individual's bleeding risk, immunisations or similar small volume intramuscular injections can be administered with reasonable safety by this route. If the individual receives medication/treatment to reduce bleeding, for example treatment for haemophilia, intramuscular immunisation can be scheduled shortly after such medication/ treatment is administered. Individuals on stable anticoagulation therapy, including individuals on warfarin who are up-to-date with their scheduled INR testing and whose latest INR is below the upper level of the therapeutic range, can receive intramuscular vaccination. A fine needle (23 or 25 gauge) should be used for the immunisation, followed by firm pressure applied to the site without rubbing for at least 2 minutes (Kroger *et al.*, 2023). The individual/parent/carer should be informed about the risk of haematoma from the injection.

Disposal

Equipment used for immunisation, including used vials, syringes, or partially discharged product should be disposed of at the end of a session by placing in a proper, puncture-resistant 'sharps' box according to local authority regulations and guidance in the technical memorandum 07-01 (NHS England 2022).

Recommendations for the use of RSV immunisations

The objective of the RSV immunisation programme is to lower the incidence and severity of RSV LRTI in:

- older people
- infants through maternal vaccination as part of the routine immunisation programme
- infants and young children at high risk of severe RSV disease

Immunisation programme letters

England
https://www.gov.uk/government/collections/respiratory-syncytial-virus-rsv-vaccination-programme

Northern Ireland
https://bso.hscni.net/directorates/operations/family-practitioner-services/pharmacy/contractor-information/contractor-communications/communications-general-information-circulars/

Scotland
https://www.gov.scot/publications/rsv-vaccination-cmo-letter-to-health-boards/

Wales
https://www.gov.wales/introduction-rsv-vaccination-programme-2024-whc2024032-html

National programme for adults aged 75 to 79 years

JCVI has advised that a one-off catch-up campaign should be introduced, and a routine programme routine programme for those turning 75 years old.

A single dose of Abrysvo (Pfizer RSV pre-F vaccine) should be offered to all adults turning 75 years old and as a catch-up programme for all adults aged 75-79 years old, noting that the timing of the offer will be important in ensuring protection ahead of and during any subsequent RSV season. Please see national programme letters for further details.

National programme for infant protection through maternal vaccination

Abrysvo® (Pfizer RSV Pre-F vaccine) should be offered to all pregnant women from week 28 gestation**,** in every pregnancy. Vaccination should ideally be offered in week 28 or soon after to maximise the likelihood that a baby will be optimally protected from birth. For further information see the earlier section on dosage and schedule.

Selective immunisations for high risk infants and young children

To reduce the risk of severe disease, eligible high-risk infants and young children are recommended to receive RSV monoclonal antibody immunisation seasonally, in or from around week 40 (the start of October). This should be offered regardless of whether the mother was vaccinated during the pregnancy.

- Nirsevimab (Beyfortus®) is the recommended first-line immunisation, if available.
- Palivizumab (Synagis®) is recommended if nirsevimab is not available.

Patients started on palivizumab should usually continue on this through the season, even if nirsevimab subsequently becomes available during the RSV season.

All children in the following high-risk groups (Box 1) are recommended to receive an RSV monoclonal antibody immunisation, based on an analysis of the cost-effective use of palivizumab prophylaxis (JCVI 2010, JCVI 2023). There is no RSV monoclonal programme currently for very/extremely premature infants, other than those included in the high-risk groups.

Box 1

High Risk due to chronic lung disease of prematurity (CLD), also known as bronchopulmonary dysplasia (BPD)

Pre-term infants who have moderate or severe CLD. Moderate or severe CLD is defined as 'preterm infants with compatible x-ray changes who continue to receive supplemental oxygen or respiratory support at 36 weeks post-menstrual age'.[1] Children who fall into the light and dark red shaded area of Table 1 should be offered prophylaxis

Infants with respiratory diseases who are not necessarily pre-term but who remain in oxygen at the start of the RSV season are also considered to be at higher risk

These infants may include those with conditions including:

- pulmonary hypoplasia due to congenital diaphragmatic hernia
- other congenital lung abnormalities (sometimes also involving congenital heart disease or lung malformation)
- interstitial lung disease

and including those receiving long term ventilation (LTV) at the onset of the season.[2]

High Risk due to Congenital Heart Disease (CHD)

Preterm infants with haemodynamically significant, acyanotic CHD at the chronological ages at the start of the RSV season and gestational ages at birth covered within the light red shaded area in Table 1.

Cyanotic or acyanotic CHD plus significant co-morbidities particularly if multiple organ systems are involved.

High Risk due to Severe Combined Immunodeficiency Syndrome (SCID)

Children less than 24 months of age with SCID – the most severe form of inherited deficiency of immunity, who are unable to mount either T-cell responses or produce antibody against infectious agents – until immune reconstituted.

Where clinical judgement of other individual patient circumstances strongly suggests that prophylaxis would prevent serious RSV infection in infants who are at particular risk of complications from RSV, use of nirsevimab (first-line, if available) or palivizumab could be considered during the RSV season.

1 Post-menstrual age is calculated by adding the time elapsed between the first day of the last menstrual period to the day of delivery plus the time elapsed from birth.

2 The definition of LTV is 'any child who when medically stable, continues to require a mechanical aid for breathing, after an acknowledged failure to wean three months after the institution of ventilation' (Jardine and Wallis, 1998)

Table 1 – Recommended use of monoclonal antibodies in risk patients by gestational age[1]

	Gestational age at birth (weeks+days)						
Chronological age (months)	≤24+0	24+1 to 26+0	26+1 to 28+0	28+1 to 30+0	30+1 to 32+0	32+1 to 34+0	≥34+1
<1.5							
1.5 to <3							
3 to <6							
6 to <9							
9							

1 Light red shaded area denotes eligibility for premature infants with haemodynamically significant acynanotic congenital heart disease; light or dark red areas denote eligibility for preterm infants with chronic lung disease. See text for further details including eligibility for other conditions.

Co-administration with other immunisations and immunoglobulin products

If given at the same appointment as other immunisations, RSV immunisations should be given at separate sites, preferably in a different limb. If given in the same limb, they should be given at least 2.5cm apart (AAP 2024). The site at which each injection is given and the batch numbers of the immunisations should be recorded in the individual's records.

Older adults (age 75 to 79 years)

RSV vaccines can be safely co-administered with Shingrix shingles vaccine and pneumococcal vaccines. Some data indicates that, in older adults, administering Abrysvo® at the same time as seasonal influenza vaccine may reduce the immune response to the RSV vaccine (Athan *et al.*, 2023). There is also data that suggests that the response to the influenza A(H3N2) component of seasonal influenza vaccine (the influenza virus subtype which most severely affects older adults) may be diminished when RSV and seasonal influenza vaccines are co-administered to older adults, and that coadministration of COVID-19 vaccines may reduce the immune response to the RSV vaccine. The clinical significance of any reduced response is unknown, but influenza immune response is known to correlate with protection against infection, and there is emerging data that RSV immune response also correlates with clinical protection (Ma *et al.*, 2024). It is therefore recommended that RSV vaccine is not routinely scheduled to be given to an older adult at the same appointment or on the same day as an influenza or COVID-19. No specific interval is required between administering the vaccines. If it is thought that the individual is unlikely to return for a second appointment or immediate protection is necessary, Abrysvo® can be administered at the same time as influenza and/or COVID-19 vaccination. Reactogenicity for co-administered vaccines is expected to be consistent with the profiles of the individual products.

Maternal vaccination

Pregnant women can safely have Abrysvo co-administered with influenza vaccine, COVID-19 vaccine and/or anti-D immunoglobulin; there are no concerns around blunted responses or interactions. There is some data suggesting that coadministration of the RSV vaccine with pertussis-containing vaccines may reduce the response made to the pertussis

components (Peterson *et al.*, 2022). The clinical significance of this is unclear and any impact on protection is likely to be small; the key pertussis toxoid component is least affected. Giving the vaccines separately at the typical scheduled times (around 20 weeks for pertussis and from 28 weeks for RSV) will avoid any potential attenuation of antibody response to the pertussis containing vaccine. If a woman has not received a pertussis containing vaccine by the time she presents for Abrysvo® RSV vaccine, both vaccines can and **should** be given at the same appointment to provide timely protection against both infections to the infant. Reactogenicity for co-administered vaccines is expected to be consistent with the profiles of the individual products.

Infant monoclonal antibody immunisation

RSV monoclonal antibodies can be given at the same time or around the same as any vaccines scheduled to be administered as part of the routine childhood immunisation programme (nirsevimab SmPC; Esposito *et al.*, 2021). Monoclonal antibody passive immunisations are not expected to interfere with the active immune response to concurrent vaccines. Coadministration of nirsevimab or palivizumab in clinical trials alongside routine scheduled vaccine had safety and reactogenicity similar to that of scheduled vaccines alone.

Contraindications

There are very few individuals who cannot receive an indicated RSV vaccine or immunisation. Where there is doubt, appropriate advice should be sought from a specialist or the local immunisation team.

RSV vaccines should not be given to anyone who has had a confirmed anaphylactic reaction to a previous dose of an RSV vaccine, or any of the excipients in the RSV vaccine.

RSV monoclonal antibody immunisations should not be given to anyone who has had a confirmed anaphylactic reaction to any previous dose of nirsevimab, palivizumab or another humanised monoclonal antibody, or any excipient of the monoclonal antibody immunisation.

RSV vaccines - distinct from monoclonal antibody immunisations - should not be given to infants or young children outside of approved trials: safety for use in this group has not been assessed in clinical studies, and there is a theoretical possibility of predisposing naive infants to vaccine-associated enhanced disease (VAED).

The Abrysvo® and Arexvy® vaccines and nirsevimab (Beyfortus®) monoclonal antibody immunisation contain small amounts of polysorbate 80. Rarely, people may be allergic to polysorbate 80. However, polysorbate 80 is widely used in medicines and foods, and is present in many medicines including other monoclonal antibody preparations. Some injected influenza vaccines (including the main vaccine used in the 65-year-old-plus programme) contain polysorbate 80. Individuals who have tolerated injections that contain polysorbate 80 (including the adjuvanted influenza vaccine, and the GlaxoSmithKline vaccine Fluarix®) are likely to tolerate RSV vaccines (or monoclonal antibody immunisations) containing polysorbate 80.

Precautions

Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If an individual is acutely unwell, immunisation may be postponed until they

have fully recovered. This is to avoid confusing the diagnosis of any acute illness by wrongly attributing any sign or symptoms to the adverse effects of the vaccine.

See administration section for advice on immunisation of people with bleeding disorders, which includes thrombocytopenia.

A number of cases of Guillain-Barre syndrome (GBS) have been reported following vaccination with Pfizer Pre-F and GSK adjuvanted pre-F vaccines (see adverse events below). Individuals who have a history of GBS can be vaccinated as recommended for their age. There is evidence to suggest that having had a prior diagnosis of GBS does not predispose an individual to further episodes of GBS when immunised with other vaccines (Baxter *et al*, 2012). Although there is no current indication for revaccination, those who are diagnosed with GBS within six weeks of a dose of RSV vaccine, should be advised to seek medical advice before accepting a future offer of revaccination, on a precautionary basis.

Adverse reactions

Reports of adverse reactions can be found in the SmPCs. Anyone can report a suspected adverse reaction to the MHRA using the Yellow Card scheme (yellowcard.mhra.gov.uk). All suspected reactions should be reported for black triangle (▼) products. This black triangle is a standard symbol added to the product information of a vaccine during the earlier stages of its introduction, to encourage reporting of all suspected adverse reactions. Abrsyvo (Pfizer pre-F vaccine), Arexvy (GSK adjuvanted pre-F vaccine) and Beyfortus (nirsevimab) are all black triangle products.

Older adult vaccination

A clinical trial of older adults receiving Abrysvo (Pfizer Pre-F vaccine) found that the most common adverse events following immunisation was pain at the vaccination site (11% of recipients). Redness and swelling at the injection site were the next most commonly reported reactions.

Clinical trials of Arexvy (GSK adjuvanted Pre-F vaccine) found that the most common adverse events following immunisation were pain at the injection site (61% of vaccinees), fatigue (34%), myalgia (29%), headache (28%), and arthralgia (18%). Common adverse events (less than 10% of vaccinees) were redness and/or swelling at the injection site, fever or chills. For both vaccines, most reactions were mild and resolved within 1-2 days.

Guillain-Barre syndrome

A small number of cases of Guillain-Barré syndrome (GBS) were detected in phase 3 clinical trials and in post-marketing surveillance of older adults (Schwarz *et al*., 2023, Walsh *et al*., 2023). A study over the first season of vaccination in the USA, suggested that RSV vaccines were associated with an increased risk of GBS in the six weeks following administration. The risk was estimated at just under 10 cases of GBS for every million doses of the vaccine administered to older people. This compares to a background rate of GBS which is 11 per million per year in those aged 75-79 years. Overall the benefit of vaccination in preventing hospitalisation and death from RSV LRTI in the eligible group remains highly favourable relative to the risk of any serious adverse event.

Maternal vaccination

The most commonly reported adverse reactions reported by pregnant women receiving Abrysvo® (Pfizer pre-F vaccine) as part of a clinical trial were vaccination site pain (41%), headache (31%) and myalgia (27%). Most reactions were mild and resolved within a few days.

The trial had a slightly higher number of babies born prematurely in the vaccine arm than the placebo arm but this was not statistically significant and there was no temporal relationship between vaccination and premature birth (Kampmann *et al.*, 2023). There was no signal for any imbalance in premature births in high income countries of Europe and North America – the imbalance was observed in upper middle-income countries, predominantly South Africa, where the rate of preterm birth in the control arm was well below the national expected rate (Madhi *et al.*, 2025). In the month following immunisation, the period when vaccine-related adverse events are considered to be most plausible, the rate of preterm birth in the vaccine group was 2.1% and in the control group 1.9%, which was statistically equivalent (Kampmann *et al.*, 2023). In the two study arms the median gestational age at birth was equal at 39 weeks, and median birth weight equal at 3.3kg (Kampmann, Radley and Munjal, 2023). There was no mortality signal associated with prematurity, and the overall number of deaths by 24 months of age was 8 in the vaccination arm and 14 in the placebo arm (Madhi *et al.*, 2025). Independent safety studies from the first season in the US found no raised risk of preterm birth in vaccine recipients (Moro, 2024; Son *et al.*, 2024.) There are no safety concerns around congenital anomalies, which were less common in the vaccine arm (174, 5%) than the placebo group (203, 6%). JCVI has advised that it is reassured that the safety data for Abrysvo does not raise significant concerns about use in a programme, and the vaccine is approved by the MHRA on the basis of safety, quality and effectiveness (Wilkinson 2023).

Monoclonal antibody immunisations

In clinical trials of nirsevimab (Beyfortus®), the most frequent adverse reaction was rash (0.7%) occurring within 14 days of immunisation. The majority of cases were mild. Additionally, pyrexia and injection site reactions were reported in 0.5% and 0.3% of recipients within 7 days post dose, respectively. Most pyrexia cases were mild and all injection site reactions were non-serious.

Common (<10%) adverse reactions occurring with palivizumab (Synagis®) are fever, rash, and injection site reaction. The most serious adverse reactions occurring with palivizumab are anaphylaxis and other acute hypersensitivity reactions.

Management of cases, contacts and outbreaks

There is currently limited evidence to support the use of RSV vaccination or immunisations for post-exposure prophylaxis or to interrupt transmission during outbreaks.

Any case of RSV infection in an at-risk infant or child (or known exposure) should prompt a review of the patient's medical history to establish whether they are in a recognised risk group and whether they have been offered prophylaxis. Patients who have risk factors who have not previously been immunised should begin monoclonal antibody prophylaxis.

Hospital outbreaks of RSV should be reported to the Trust's infection prevention and control (IPC) team for advice on control.

Outbreaks of RSV in adult social care facilities should be notified to local health protection teams (HPTs) (or community IPC teams according to local arrangements) and managed in line with national guidance for HPTs.

Supplies

National routine immunisation programme

Immunisations for the national RSV programme are centrally purchased and provided free of charge. Products for private prescriptions, occupational health use or travel are NOT provided free of charge and should be ordered from the manufacturers.

Up to date information on vaccine products availability can be found in Vaccine Update (gov.uk/government/collections/vaccine-update).

In England vaccines can be ordered through ImmForm. Further information about ImmForm is available at https://www gov.uk/government/publications/how-to-register-immform-helpsheet-8 or by emailing helpdesk@immform.org.uk or calling 020 7183 8580. The vaccine is distributed by Movianto UK Ltd (Tel: 01234 248631).

In Scotland, supplies should be obtained from local childhood vaccine holding centres.

In Wales vaccines can be ordered through ImmForm. Any queries about vaccine supply in Wales should be directed to vpw.enquiries@wales.nhs.uk

In Northern Ireland, supplies should be obtained from local childhood vaccine holding centres. Details of these are available from the Regional Pharmaceutical Procurement Service (Tel: 028 9442 2089).

Immunisations for the high-risk infant programme

Monoclonal antibody immunisations for high-risk children should be ordered by hospital pharmacies in line with JCVI recommendations and NHS supply arrangements.

Beyfortus® (nirsevimab) is marketed by Sanofi UK and Ireland (customer services: 0800 854 430).

Synagis (palivizumab) is made by AstraZeneca (www.supplychain-astrazeneca.co.uk). Hospital pharmacies can order it from Phoenix Healthcare Distribution Ltd.

RSV vaccines for use outside of the routine programme

Abrysvo® Pre-F vaccine is manufactured by Pfizer (01304 616161) and for use outside of the programme is available from Alliance Healthcare (Cencora).

Arexvy® adjuvanted RSV Pre-F vaccine is manufactured by GSK (www.vaccines.co.uk) and is supplied by AAH Pharmaceuticals Ltd.

Summaries of product characteristics

Vaccines

Pfizer Pre-F vaccine (Abrysvo®)

Abrysvo powder and solvent for solution for injection Respiratory syncytial virus vaccine (bivalent, recombinant). Pfizer Limited, 2023. Date of revision of text 12/2024. https://www.medicines.org.uk/emc/product/15309/smpc

GSK adjuvanted Pre-F vaccine (Arexvy®)

Arexvy powder and suspension for suspension for injection Respiratory Syncytial Virus (RSV) vaccine (recombinant, adjuvanted) GlaxoSmithKline UK (GSK), 2023. Date of revision of the text 06/01/2025. https://www.medicines.org.uk/emc/product/14951

Monoclonal antibody immunisations

Nirsevimab: Beyfortus solution for injection in pre-filled syringe. Marketing Authorisation holder: AstraZeneca UK Limited, 2022. Date of revision of the text 08/11/2024. Jointly developed with Sanofi. https://products.mhra.gov.uk/search/?search=beyfortus&doc=Spc

Palivizumab: Synagis solution for injection. AstraZeneca UK Limited, 2021. Date of revision of the text 23/03/2023. https://www.medicines.org.uk/emc/product/6963

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