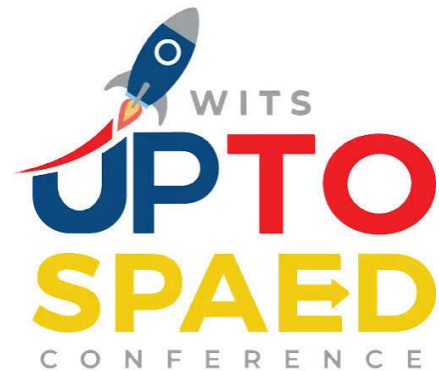




NIRSEVIMAB & THE PREVENTION OF RSV

Dr Despina Demopoulos

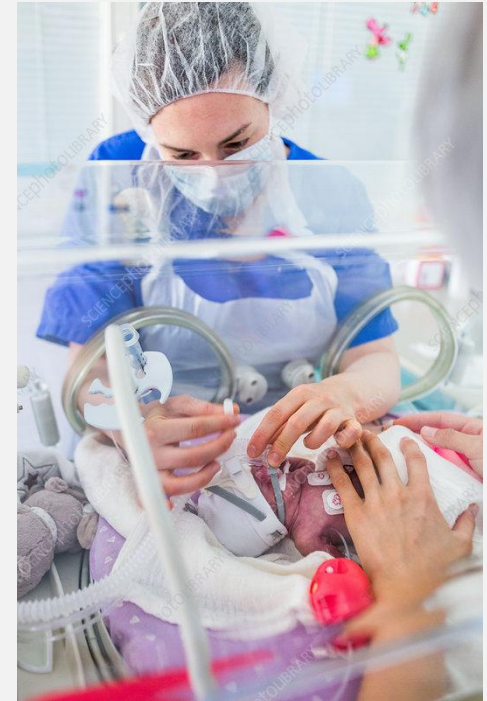
DISCLAIMER

- This presentation is intended for educational purposes only and does not replace independent professional judgment.
- Previous sponsorship: Pfizer, Sanofi, GSK

OVERVIEW

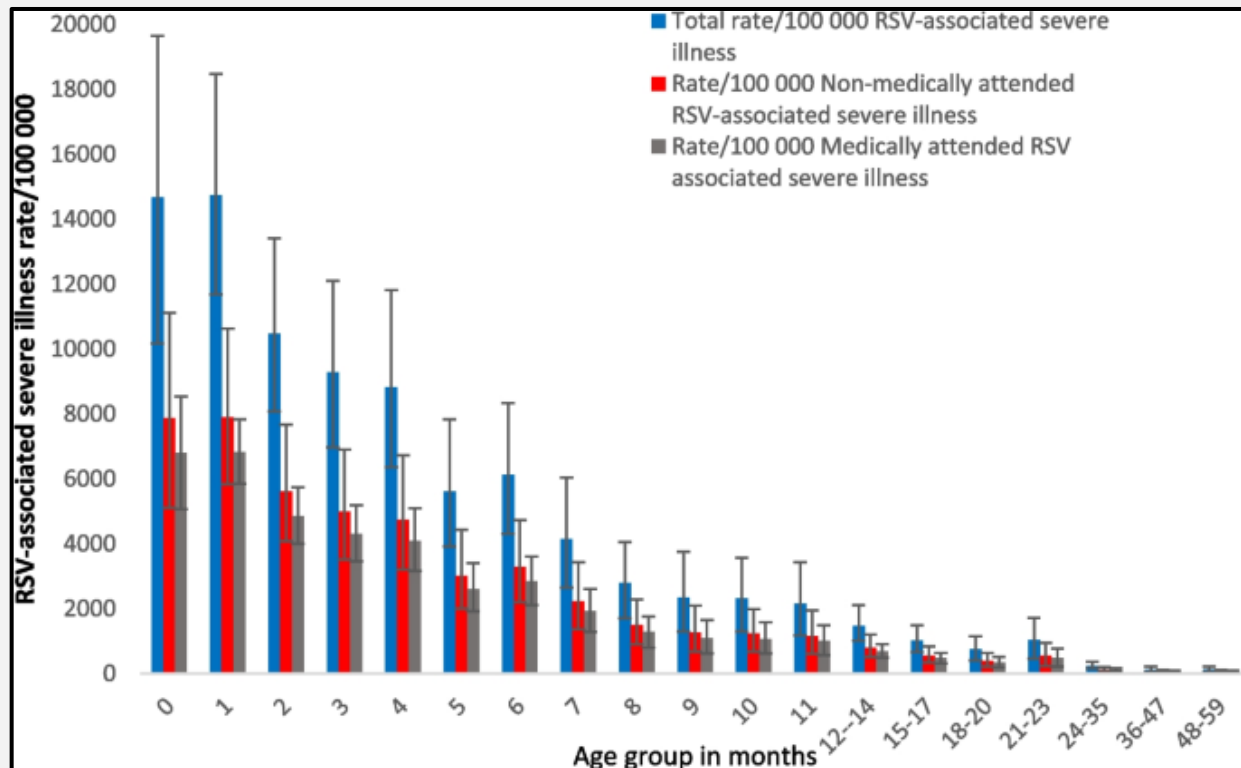
- A clinical perspective on RSV & Nirsevimab
- RSV burden – Global to Local
- Nirsevimab Clinical Efficacy
- Nirsevimab Global RWE Effectiveness & Public Health impact
- Recommendations & Implementation considerations

RSV SEASON



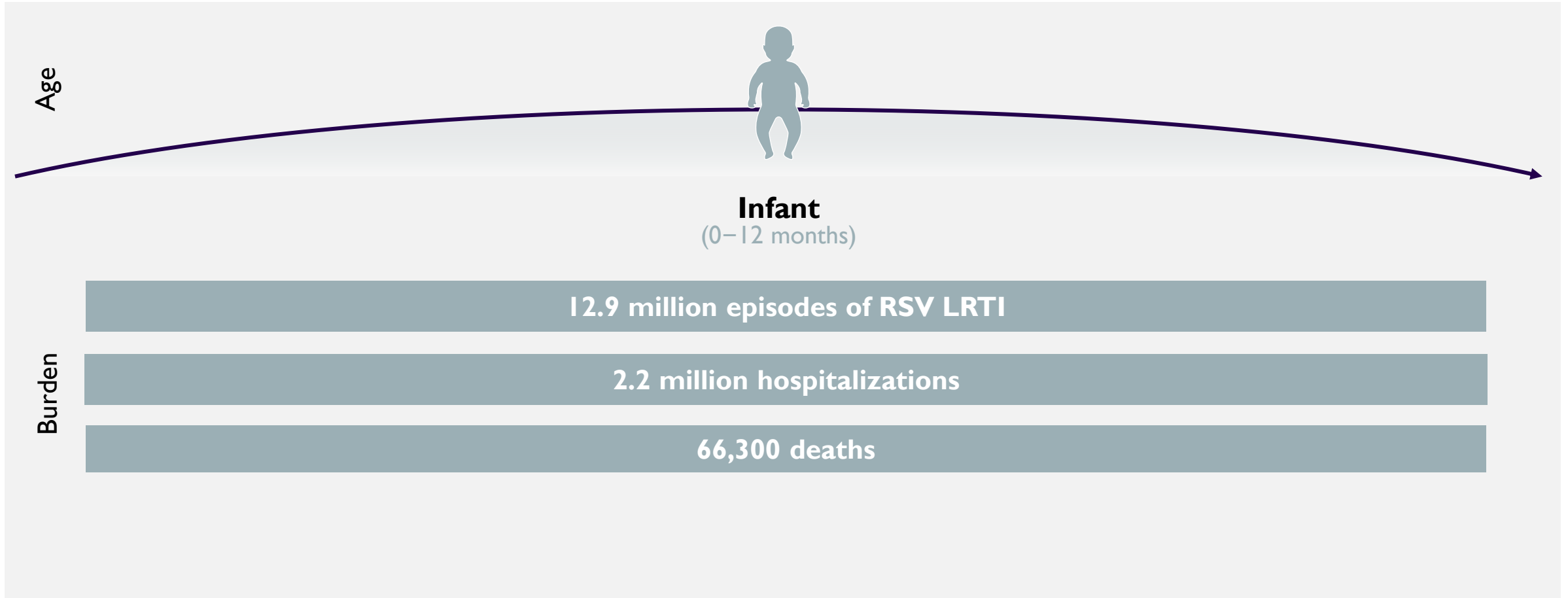
RSV CLINICAL PERSPECTIVES

- RSV causes significant infant hospitalisations in South Africa



Moyes, J., Tempia, S., Walaza, S. et al. The burden of RSV-associated illness in children aged < 5 years, South Africa, 2011 to 2016. *BMC Med* **21**, 139 (2023). <https://doi.org/10.1186/s12916-023-02853-3>

RSV CAUSES SUBSTANTIAL DISEASE BURDEN ON NEWBORNS AND INFANTS GLOBALLY EACH YEAR



COMPARISON OF RSV IMPACT ACROSS DIFFERENT HEALTHCARE SETTING – SOUTH AFRICA

Hospitalisations¹ (Drakenstein Birth Cohort, n=1136)

- **430 hospitalisation episodes** among 314 children (28%) in first 2 years
- **LRTI = 49% (169/346)** of post-discharge hospitalisations
- **RSV responsible for ~31% of LRTIs (~52 RSV hospitalisations)**
- In **first 6 months**, RSV-LRTI caused **22% of all hospitalisations (36/164)**

Outpatient / Ambulatory Visits²

- **Ambulatory RSV LRTI:** ~0.05 episodes per child-year
- Burden is **~3–4x higher than hospitalised RSV cases**
- Majority of RSV disease is managed in **clinics/outpatient settings**

1.Zar HJ et al., Drakenstein Child Health Study, abstract 2023
2.Zar HJ et al., Lancet Glob Health 2020





LEADING CAUSE OF LRTI AND HOSPITALIZATIONS IN ALL INFANTS

RSV accounted for **22%** of all-cause hospitalizations and **41%** of LRTI-hospitalisations in the first **6 months** of life¹

SA Birth Cohort, DCHS

In babies **< 1 month old**, about **14,674 out of every 100,000 (≈15%)** were hospitalised with severe RSV

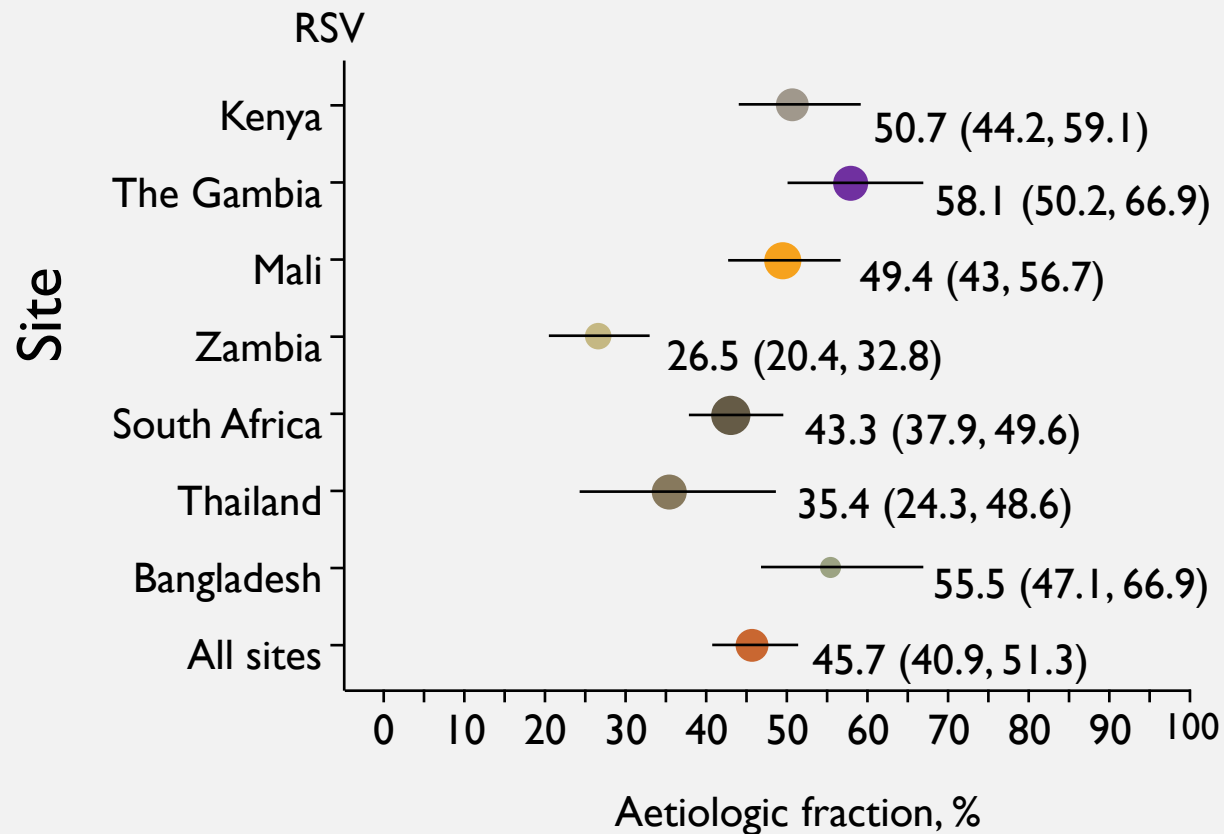
- **~96,783 cases** in infants **<1-year** annually

Infants **< 1 month old** - **extraordinarily high-risk window** — essentially, **1 in 7 newborns** in that age group lands in hospital with RSV

RSV is the **leading cause** of **LRTIs** in infants **<1 year**, responsible for:
20–40% of pneumonia cases
40–80% of bronchiolitis cases

1. Zar HJ, Barnett W, Stadler A, Gardner-Lubbe S, Myer L, Nicol MP. Aetiology of childhood pneumonia in a well-vaccinated South African birth cohort: a nested case-control study of the Drakenstein Child Health Study. *Lancet Respir Med*. 2016 Jun;4(6):463–72.

RSV IS THE LEADING ATTRIBUTABLE PATHOGEN-SPECIFIC CAUSE OF SEVERE OR VERY SEVERE PNEUMONIA IN INFANTS 1 TO 5 MONTHS OF AGE: PERCH STUDY



Prevention of RSV is a clear public health priority for high-income and low- to middle-income countries.

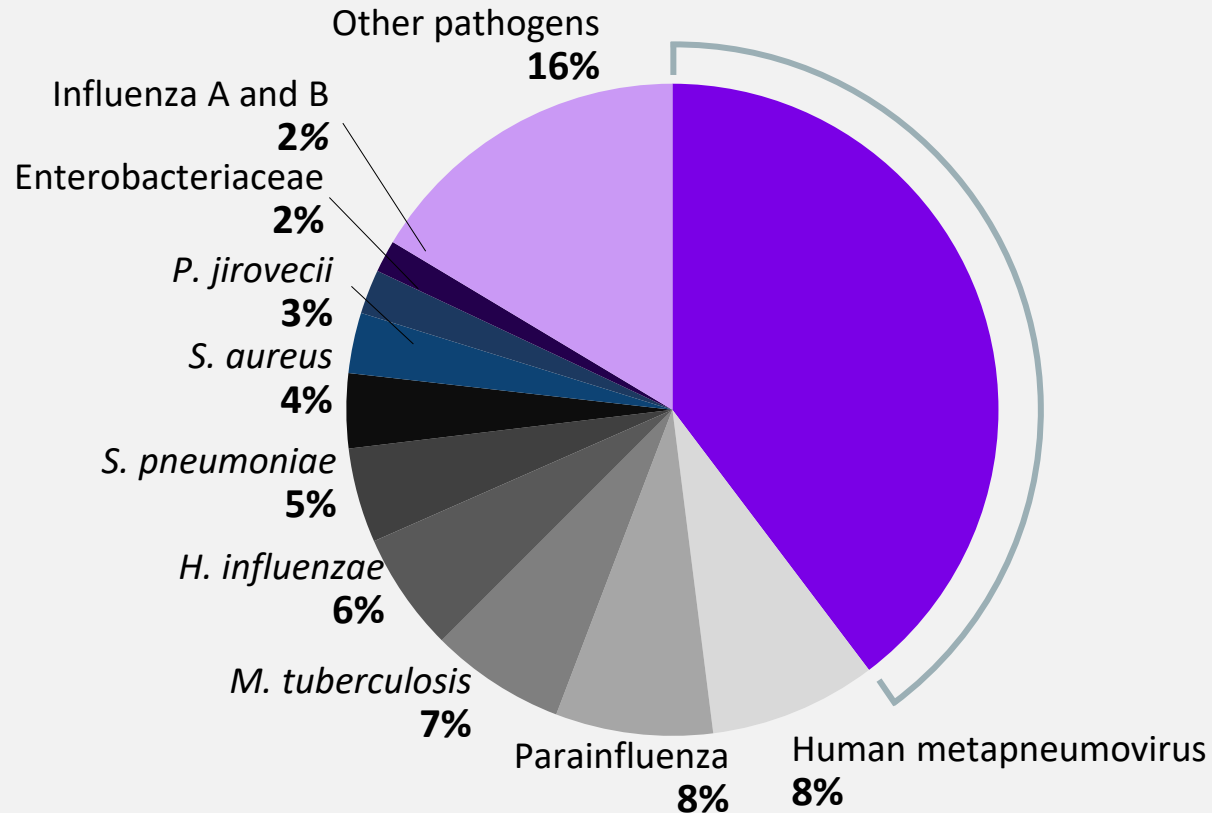
- Children 1 to 5 months of age make up 41% of all RSV cases, with CFR of 10.6%
- Overall, 47.3% of all deaths occurred in 1 to 5 months of age group

CFR, case fatality rate; PERCH, Pneumonia Etiology Research for Child Health; RSV, respiratory syncytial virus.

Figure courtesy of Dr Madhi. Publication: 1. Pneumonia Etiology Research for Child Health (PERCH) Study Group. [Lancet](#). 2019;394(10200):757-779. 2. Pneumonia Etiology Research for Child Health (PERCH) Study Group. Supplementary appendix. [Lancet](#). 2019;394(10200):757-779.

RSV IS THE LEADING CAUSE OF SEVERE PNEUMONIA REQUIRING HOSPITAL ADMISSION AMONG INFANTS <1 YEAR IN LOW-INCOME COUNTRIES

Aetiology of severe pneumonia in infants <1 year in seven countries^{1,a}



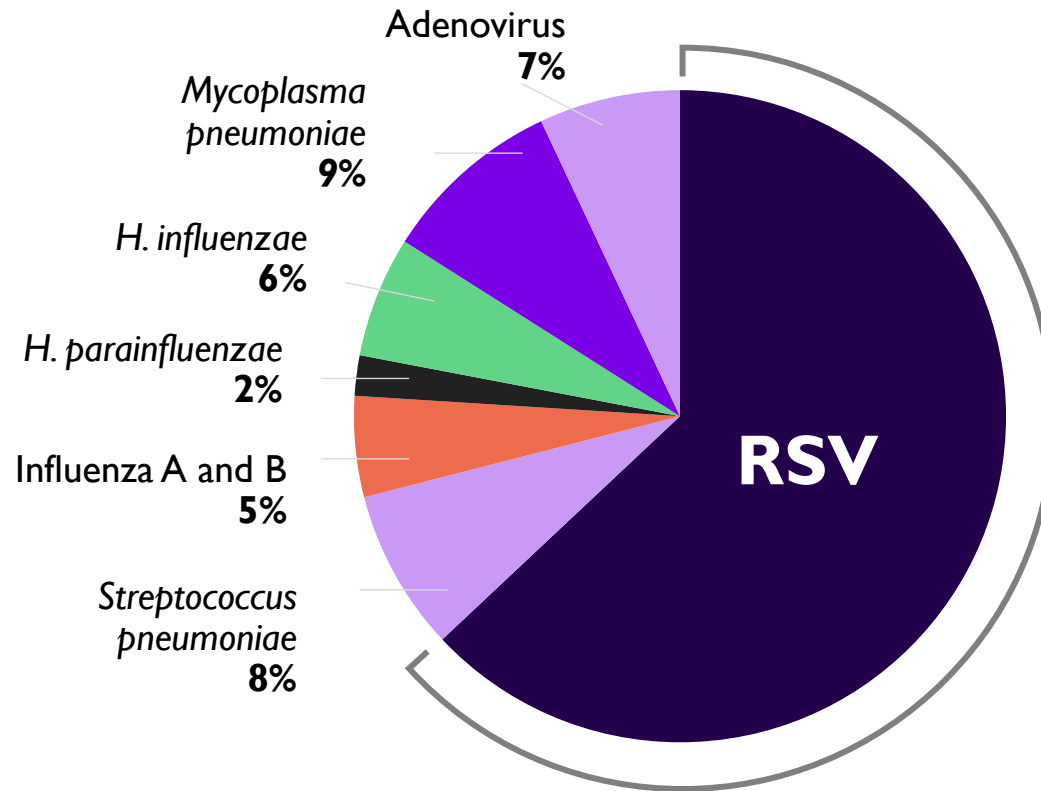
40%

of cases of severe pneumonia are caused by RSV

^aSeven low-income countries include Bangladesh, The Gambia, Kenya, Mali, South Africa, Thailand, and Zambia. Note that numbers are rounded, so may not add up to 100%.
RSV: respiratory syncytial virus.
1. Pneumonia Etiology Research for Child Health (PERCH) Study Group. *Lancet*. 2019;394(10200):757-779.

RSV ACCOUNTS FOR ALMOST 2/3 OF ACUTE RESPIRATORY INFECTIONS IN INFANTS AND YOUNG CHILDREN WORLDWIDE

Aetiology of acute respiratory infections in infants and young children

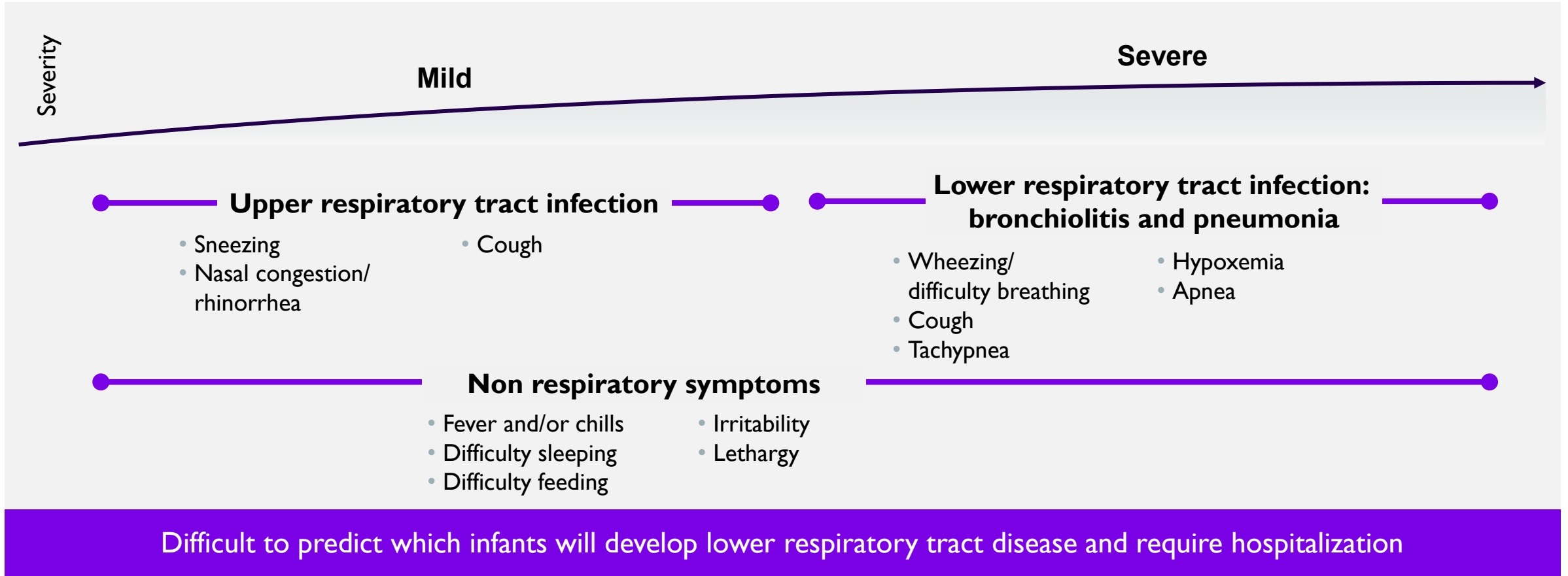


63%

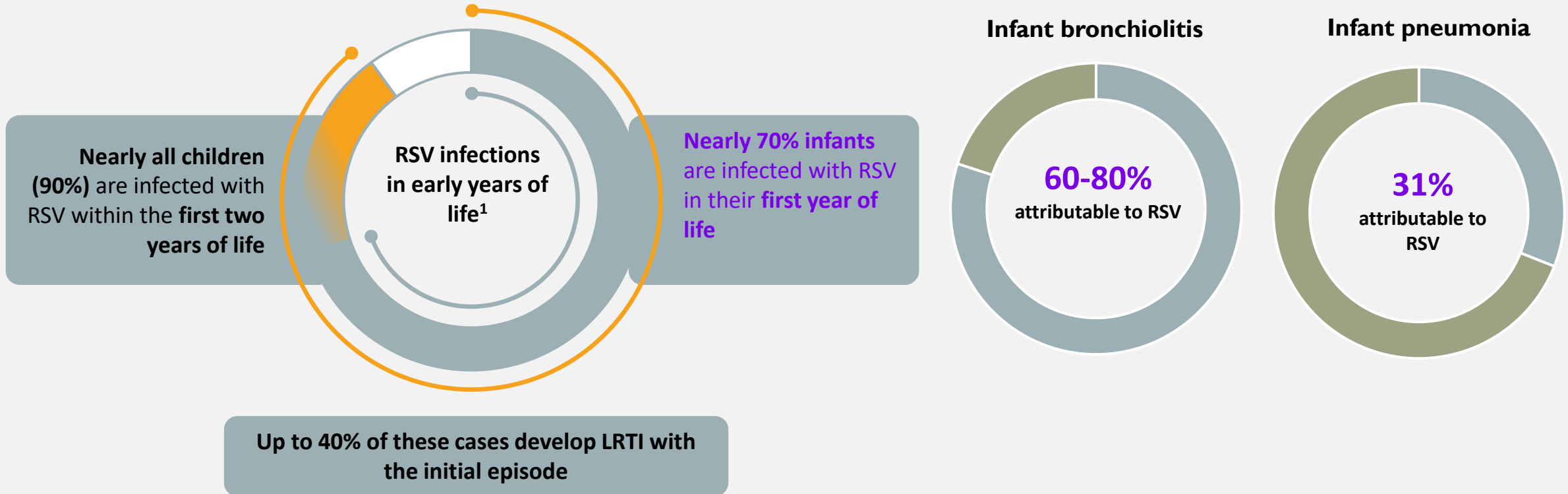
The World Health Organization estimates that **RSV** accounts for >60% of acute respiratory infections in young children and

>80% in infants
<1 year of age worldwide

THE SYMPTOMS OF RSV IN INFANTS RANGE FROM MILD TO SEVERE



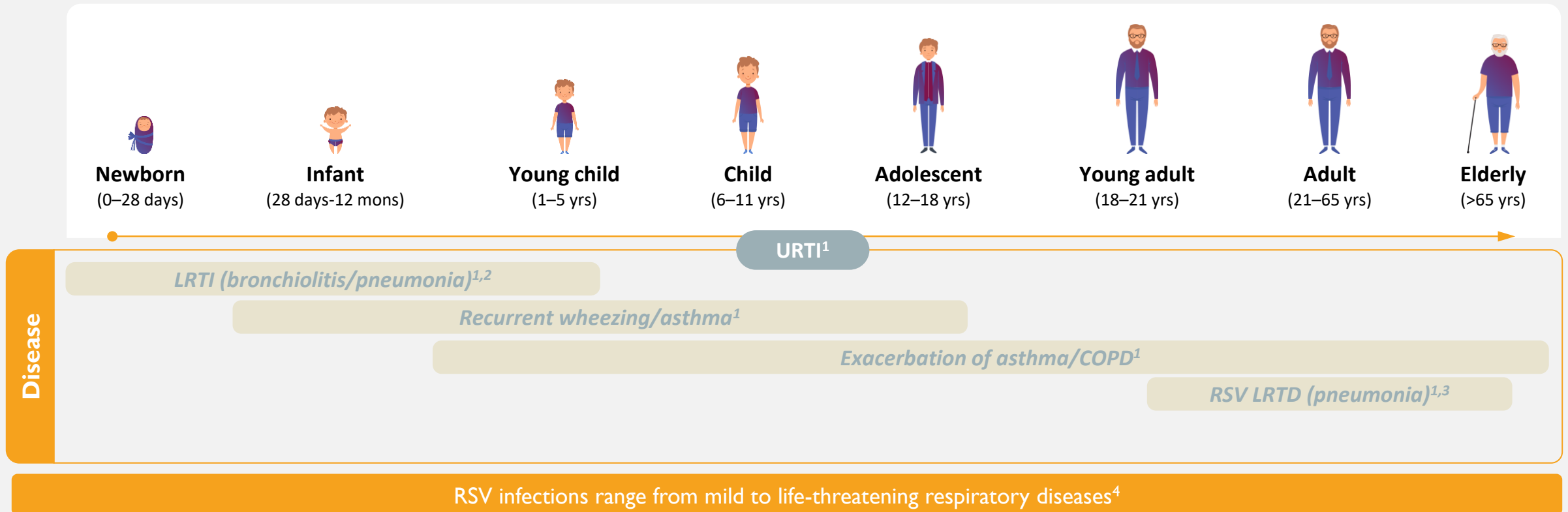
LOWER RESPIRATORY TRACT INFECTIONS IN EARLY YEARS OF LIFE



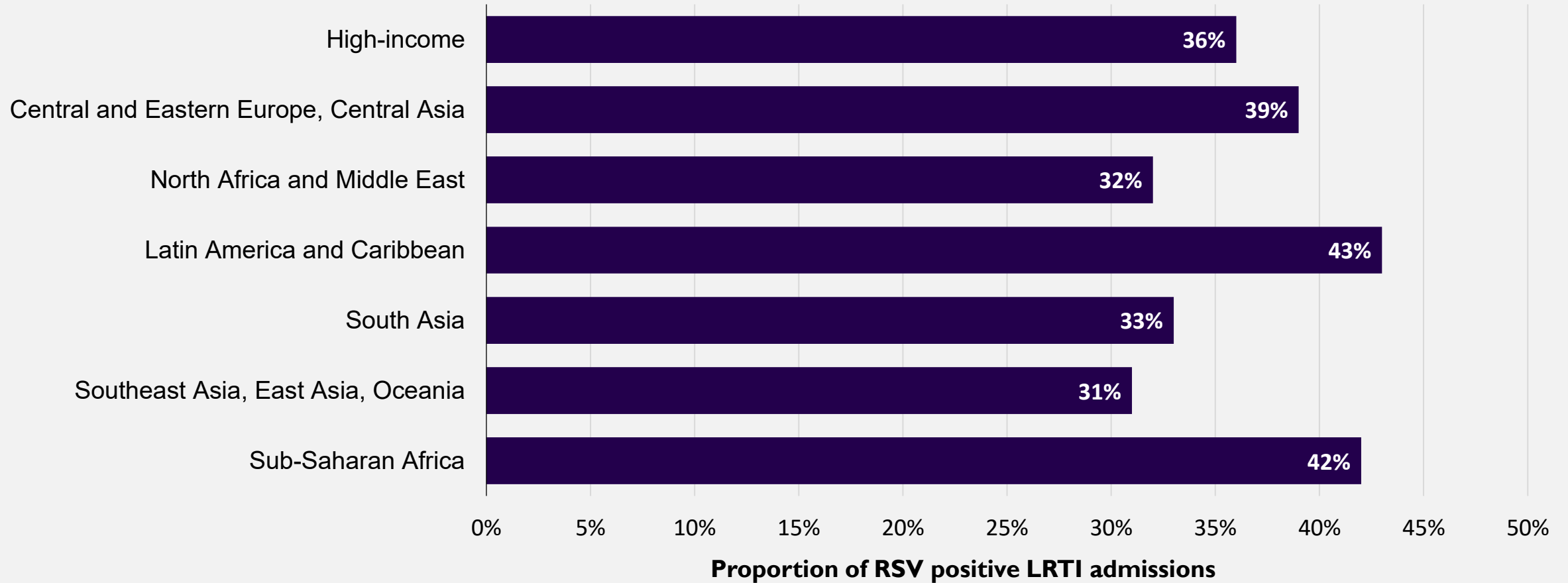
• LRTI: lower respiratory tract infection; RSV: respiratory syncytial virus.
• 1. Esposito S, et al. *Front Immunol.* 2022;13:880368. 2. Mazur NI, et al. *Lancet Infect Dis.* 2022;S1473-3099(22)00291-2.

SYMPTOMS VARY BY AGE-GROUPS

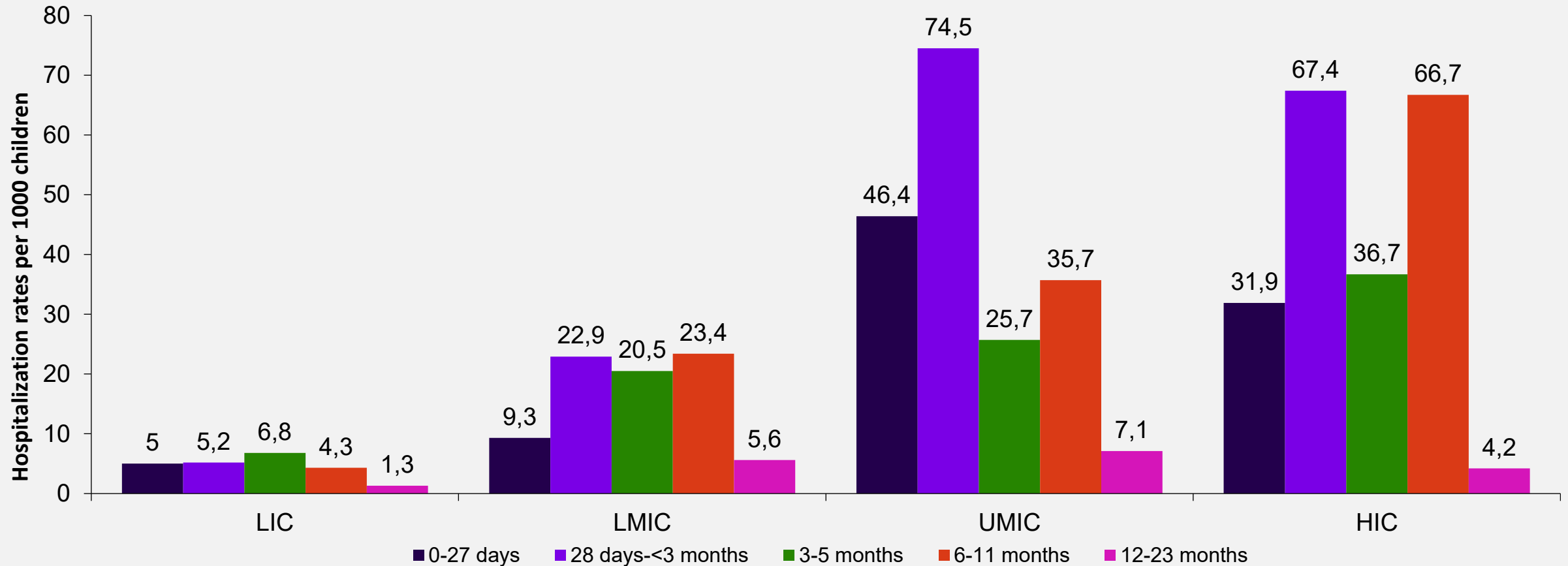
RSV causes disease that is recurrent throughout life, but more severe infections typically occur early and late in life



RSV IS A MAJOR CAUSE OF INFANT LRTI HOSPITALIZATION WORLDWIDE



INFANTS FROM ALL COUNTRIES ARE AT RISK OF HOSPITALIZATION FROM RSV-ASSOCIATED LRTIS



* HIC: high-income country; LIC: low-income country; LMIC: lower-middle-income country; LRTI, lower respiratory tract infection; RSV, respiratory syncytial virus; UMIC: upper-middle-income country.
* I. PATH. Advancing Maternal Immunization. Advancing RSV Maternal Immunization: A Gap Analysis Report. July 2018 <https://www.path.org/resources/advancing-rsv-maternal-immunization-gap-analysis-report/>

GLOBAL BURDEN OF RSV

A Global pneumonia



31% caused by RSV
33 million acute respiratory infections
3.1 million hospitalisations
118 200 deaths



Increased risk of obstructive airways
disease after RSV LRTI

B Respiratory syncytial virus deaths



More than 99% deaths occur in LMICs



24% access to intensive care



Location of RSV-related
paediatric deaths

20–50% in-hospital

50–80% out-of-hospital



Age at death

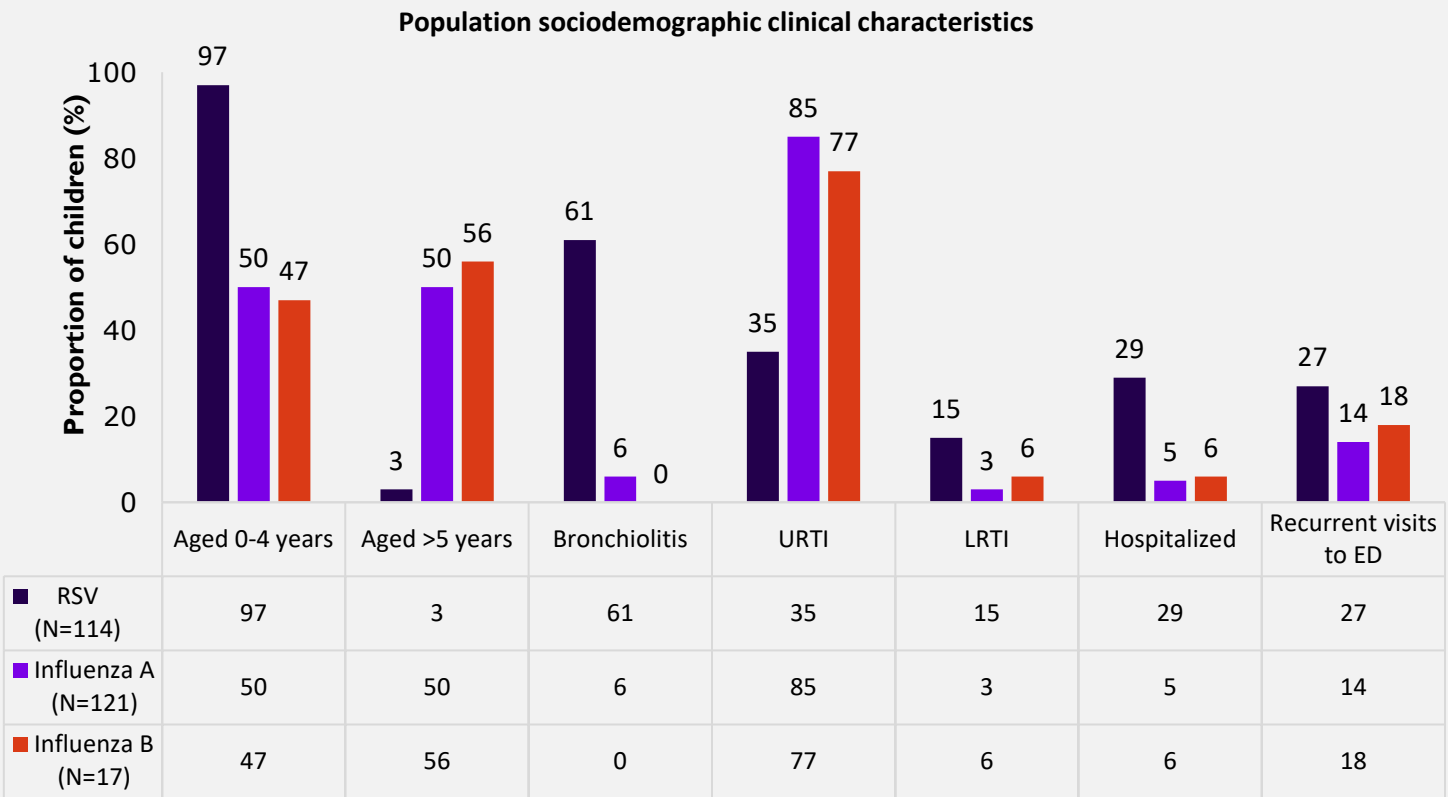
2–4 months

1–5 months

C Total costs

US\$3.13 billion direct medical costs (95% CI 2.27–5.13)
+8.7% direct non-medical costs
+36.7% indirect costs

CHILDREN WITH RSV HAD MORE SEVERE AND LONGER DURATION OF ILLNESS COMPARED WITH INFLUENZA



RSV vs. Influenza

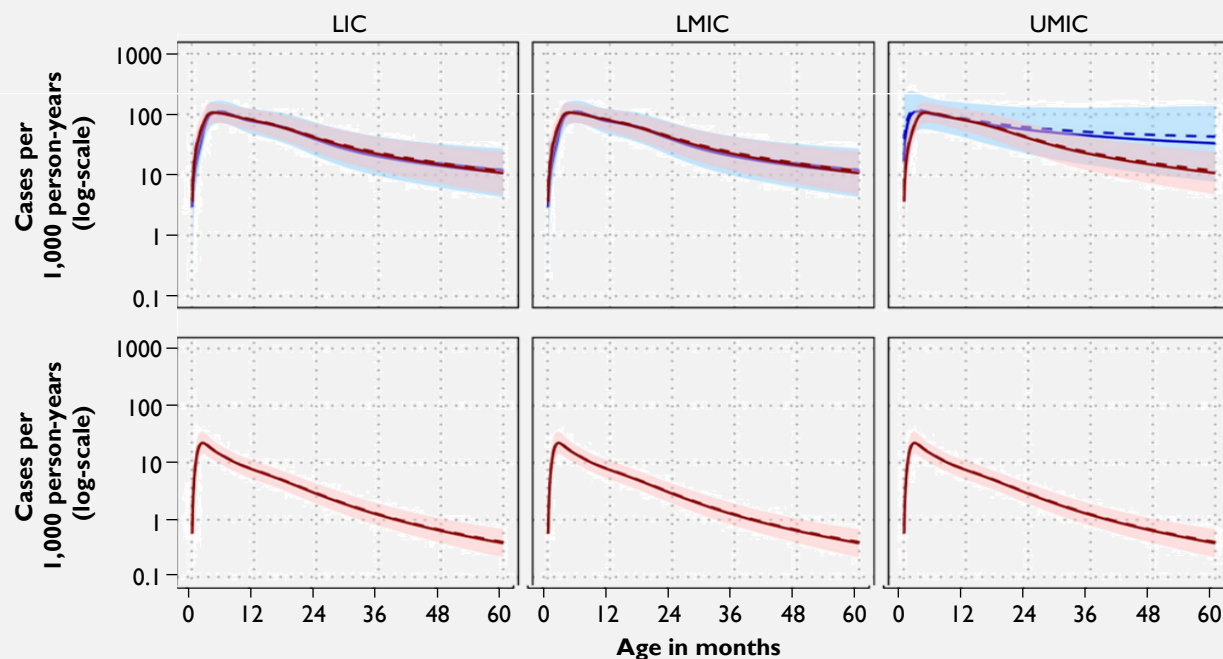
	Measure (95% CI)	P value
Hospitalization risk (Adjusted relative risk)	2.92 (1.14–7.47)	0.0249
Symptom duration (Adjusted hazard ratio)	2.16 (1.14–3.29)	0.0004

Children with RSV had:

- higher hospitalization risk compared with influenza
- longer illness duration compared with influenza

RSV DISEASE BURDEN ACROSS LICS, LMICS, AND UMICS

Splines of (A) community-based incidence, and
(B) hospital-based incidence of RSV*



In an average year, a total of **121 M cases** of RSV in infants <12 months



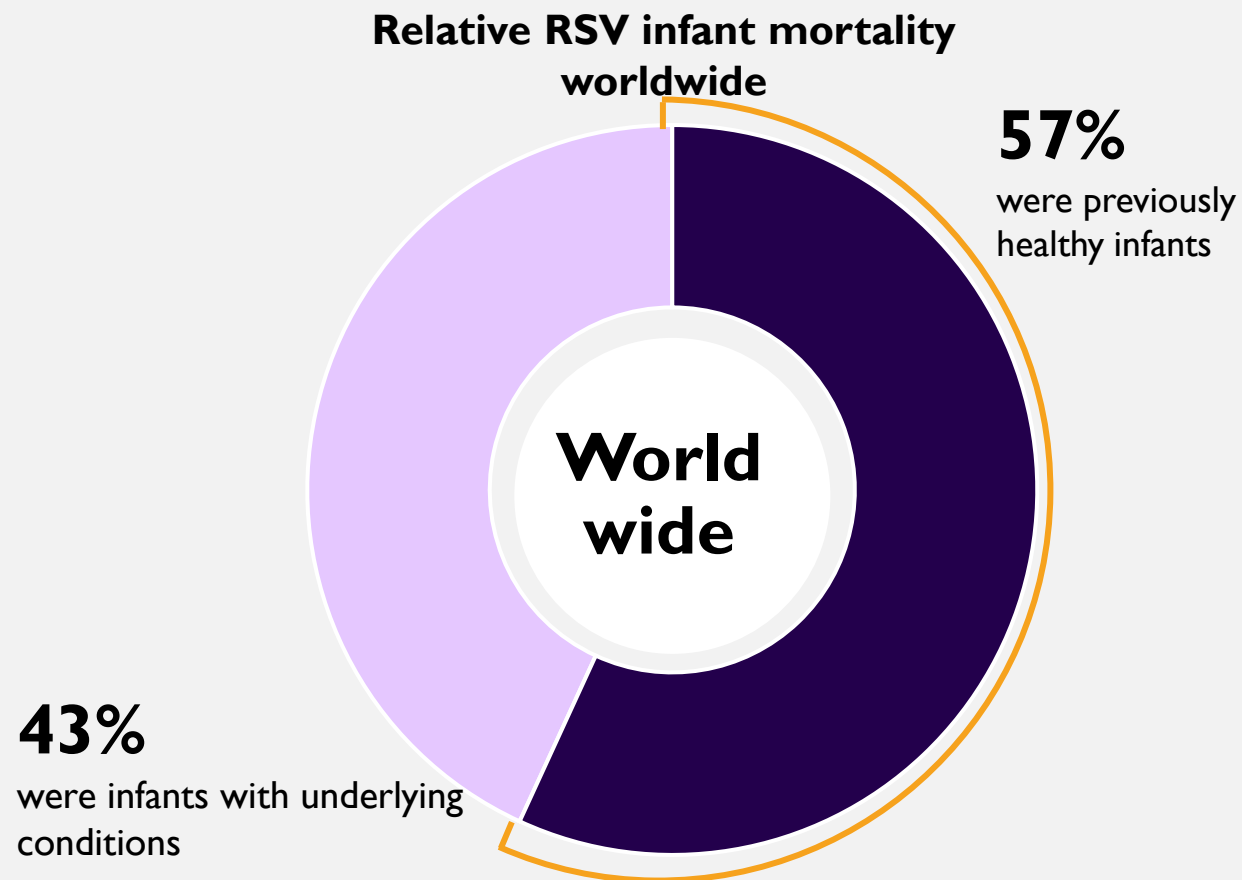
Probability of RSV hospitalization among infants <12 months is **11%** and CFR among hospitalized individuals is **0.53%**

The most common age for RSV infection

	Community-based incidence	Hospital-based incidence
Peak age	4.8 months	2.6 months
Mean age	18.9 months	15.8 months
Median age	14.7 months	11.6 months

**MOST HOSPITALIZATIONS FOR RSV
OCCUR IN HEALTHY FULL-TERM INFANTS**

RSV-LRTI IS A LEADING CAUSE OF MORBIDITY AND MORTALITY AROUND THE WORLD AFFECTING HEALTHY INFANTS



RSV-LRTI is the leading viral cause of infant mortality with 66,300 deaths in infants per year worldwide

Healthy infants comprise ~**57%** of RSV related deaths worldwide

- ^aCalculated from dataset that includes healthy pre-term infants (11%). ^b Healthy infant mortality varied from 44% in high-income countries to 53% in middle-income countries and 74% in low-income countries.
- RSV: respiratory syncytial virus; RSV-LRTI: respiratory syncytial virus-lower respiratory tract infection.
- 1. GBD 2016 Lower Respiratory Infections Collaborators. *Lancet Infect Dis.* 2018;18(11):1191-1210. 2. Shi T, et al. *Lancet.* 2017;390(10098):946-958. 3. Scheltema N, et al. *Lancet Glob Health.* 2017;5(10):e984-e991. 4. Li Y, et al. *Lancet.* 2022;399(10340):2047-2064.

**RSV IS ASSOCIATED WITH LONG-
TERM HEALTHCARE BURDEN**

BURDEN OF RSV EXTENDS BEYOND THE INITIAL MEDICAL CARE IN THE US



Short Term

RSV infection is associated with increased incidence of otitis media and pneumonia, and excessive antibiotic use



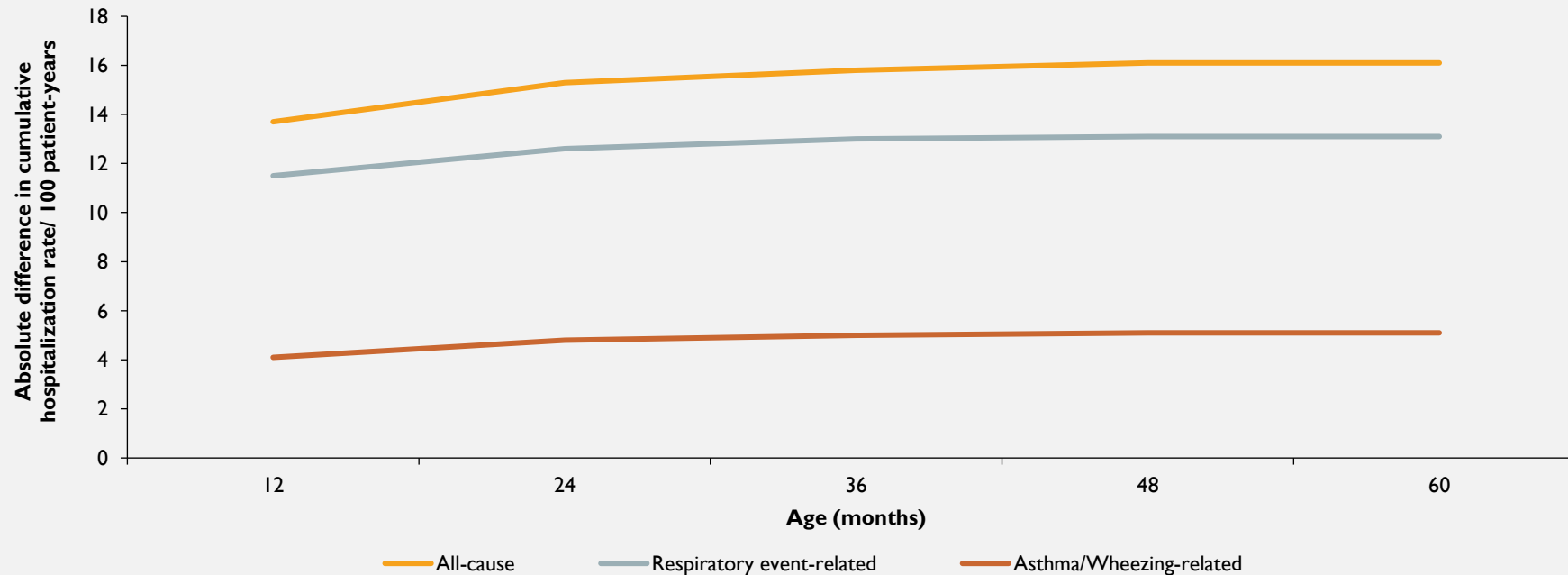
Long Term

RSV infection is associated with recurrent wheezing, reduced pulmonary function, and increased healthcare utilization

- ^aData representative for the second 6 months of life after considering an RSV infection in the first 6 months of life.
- RSV: respiratory syncytial virus.
- 1. Abreo A, et al. *Clin Infect Dis*. 2020;71(1):211-214. 2. Piedimonte G, et al. *Pediatr Rev*. 2014;35(12):519-530. 3. Driscoll AJ, et al. *Vaccine*. 2020;38(11):2435-2448. 4. Simoes EAF, et al. *J Infect Dis*. 2020;221(8):1256-1270.

CHILDREN HOSPITALIZED AS INFANTS FOR RSV INCUR GREATER HEALTHCARE RESOURCE UTILIZATION OVER THE FOLLOWING YEARS COMPARED WITH OTHER CHILDREN

Absolute difference in cumulative rate of hospitalization for infants hospitalized with RSV in the first year of life compared with healthy controls



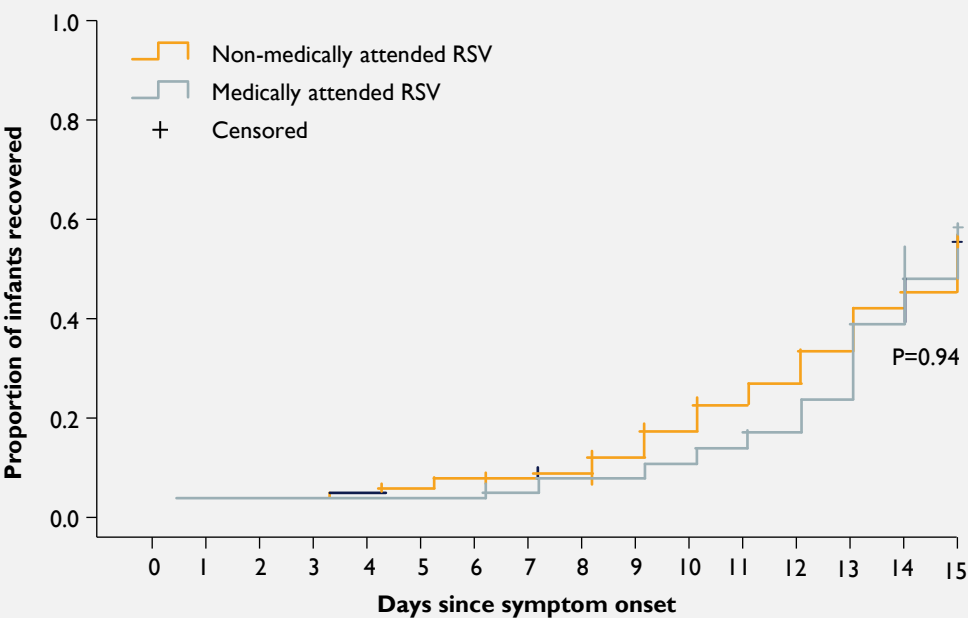
During follow up, there were 16 additional hospitalizations per year for every 100 full-term healthy infants previously hospitalized with RSV, compared with controls

- Rates were calculated as the no. of hospitalizations/100 patient-years since the index event and were for the full cohort. $P < 0.01$ for all data points.
- RSV: respiratory syncytial virus.
- I. Simões EAF, et al. *J Infect Dis.* 2020;221(8):1256-1270.

SUBSTANTIAL BURDEN TO INFANTS, FAMILIES, AND SOCIETY EVEN WHEN MEDICAL ATTENDANCE IS NOT REQUIRED

In **50.5%** (49/97) of episodes, parents still reported respiratory symptoms on **≥day 15**

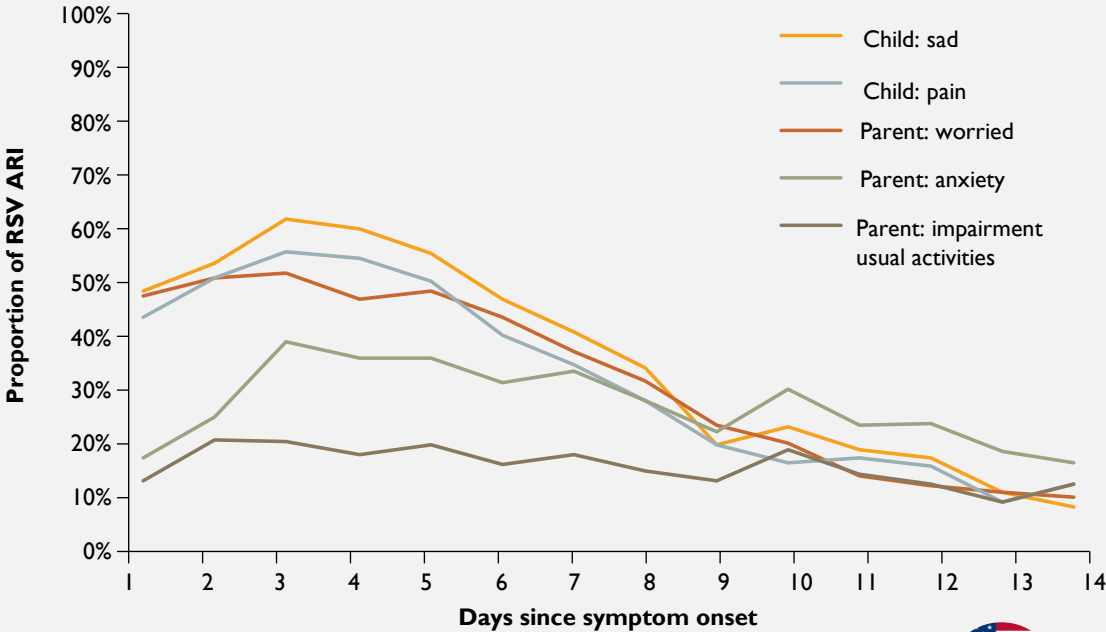
Time to recovery of respiratory symptoms in nonmedically attended (dark) and medically attended (light) RSV acute respiratory infections. Time to recovery was compared between groups with a log-rank test.



Number at risk	Day 0	Day 5	Day 10	Day 15
Non-MA RSV	97	94	79	49
MA RSV	102	102	90	50

Problems in each of the 5 HRQoL dimensions were most common during **days 2 to 5**

Proportion of nonmedically attended RSV episodes in which parents reported any problem in 5 health-related quality-of-life dimensions. ARI, acute respiratory infection; RSV, respiratory syncytial virus.



• HRQoL: health-related quality of life; MA: medically attended; RSV: respiratory syncytial virus.
• 1. Hak SF, et al. *J Infect Dis.* 2024;229(Supplement_1):S40-S50.

RISK OF RSV INFECTION AND WHEEZING WITH NIRSEVIMAB



A population-based cohort study

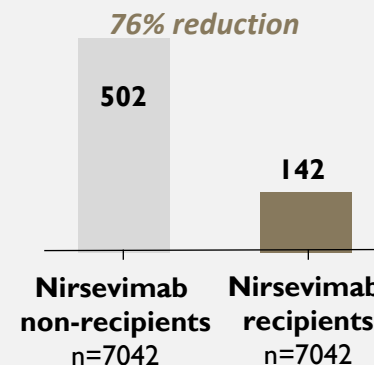
Objectives

To compare the rate of RSV infections and wheezing events in infants who received nirsevimab prophylaxis with those who did not in the 2023–24 RSV season

Methods

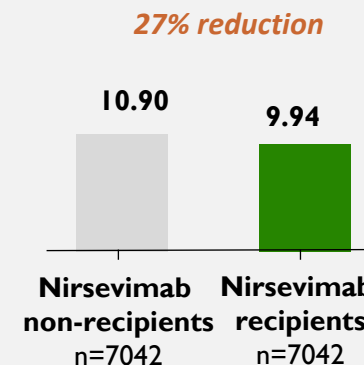
Population-based cohort study using TriNetX Research Network in infants (<12 months) who had an encounter for routine immunizations from 1 October 2023 to 31 March 2024

Total number of RSV infections‡



HR: 0.24, 95% CI: 0.17–0.33

Cases per 1000 person-months



HR: 0.73, 95% CI: 0.58–0.93

Infants who received nirsevimab had a **significantly lower risk** of **RSV infection**, and a **lower risk** of **wheezing**, compared with infants who did not receive nirsevimab

In this real-world, post-approval analysis, nirsevimab administration is associated with a reduced risk of RSV infection and wheezing in infants

RSV-LRTI ASSOCIATED WITH RECURRENT WHEEZE OF EARLY CHILDHOOD AND ASTHMA

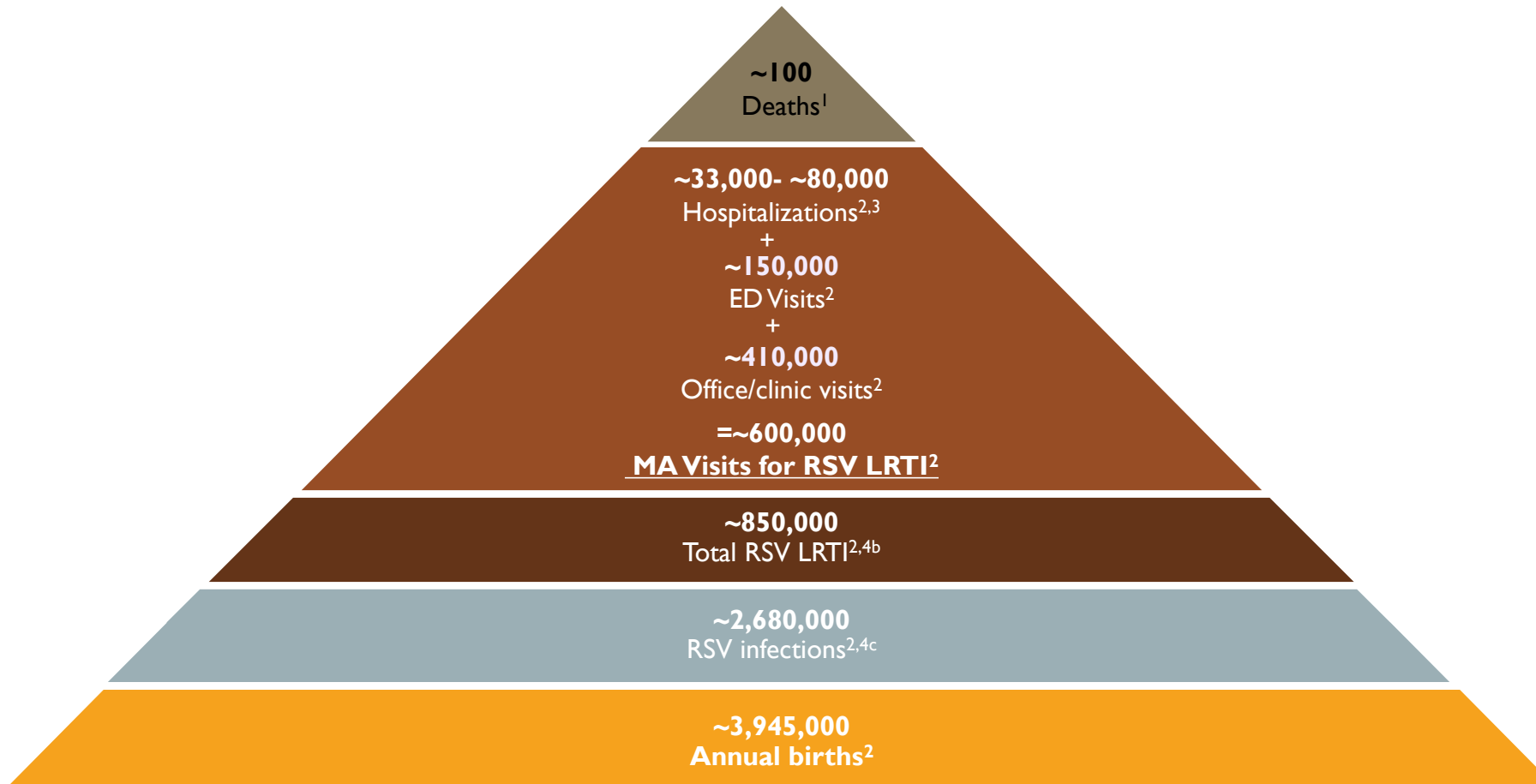
RSV-LRTI in infancy is associated with later development of RWEC or asthma, although evidence for a causal association is mixed and inconclusive



Severe RSV infection, with lower respiratory tract involvement, is more strongly associated with the development of RWEC/asthma than non-severe RSV infection

- RWEC: recurrent wheeze of early childhood; RSV-LRTI: respiratory syncytial virus lower respiratory tract infection; RSV: respiratory syncytial virus.
- I. Driscoll AJ, et al. *Vaccine*. 2020;38(11):2435-2448.

ANNUAL RSV BURDEN IN US INFANTS <12 MONTHS OF AGE



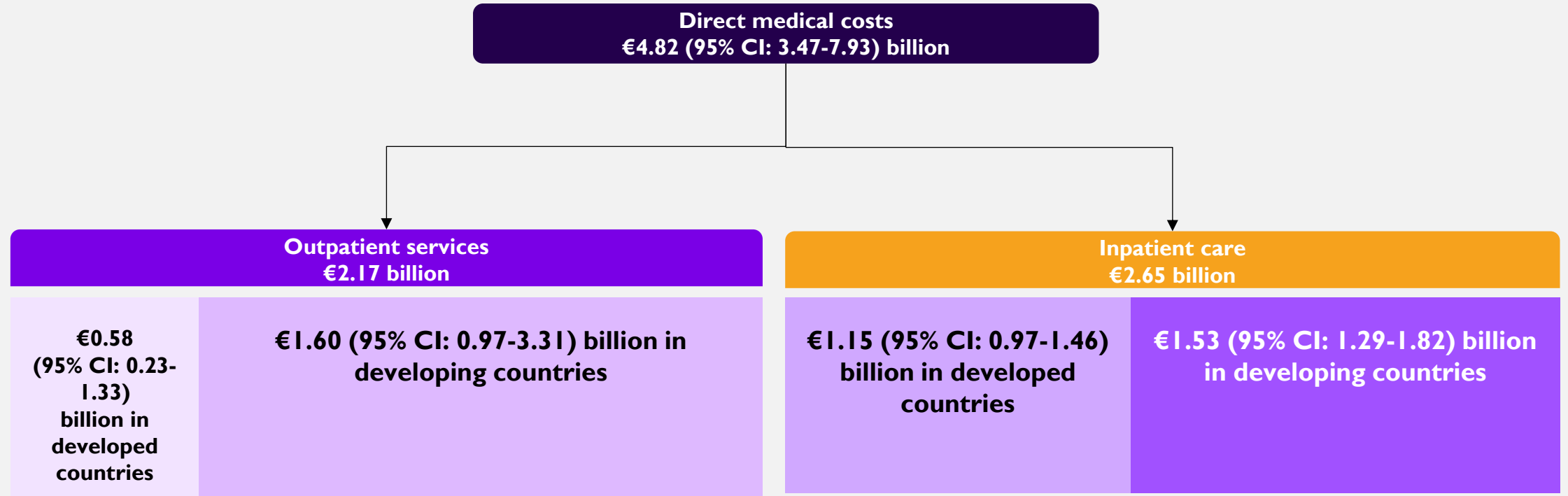
1 in 7
Infants develop LRTI
requiring medical
attention annually

a. Estimated typical RSV season based on references.¹⁻⁴ **b.** Calculated using the birth cohort from Rainisch and the RSV LTRI rate of 21.6% from Glezen WP, et al. **c.** Calculated using the birth cohort from Rainisch and the RSV infection rate of 68% from Glezen WP et al.

ED, emergency department; **LRTI**, lower respiratory tract infection; **RSV**, respiratory syncytial virus.

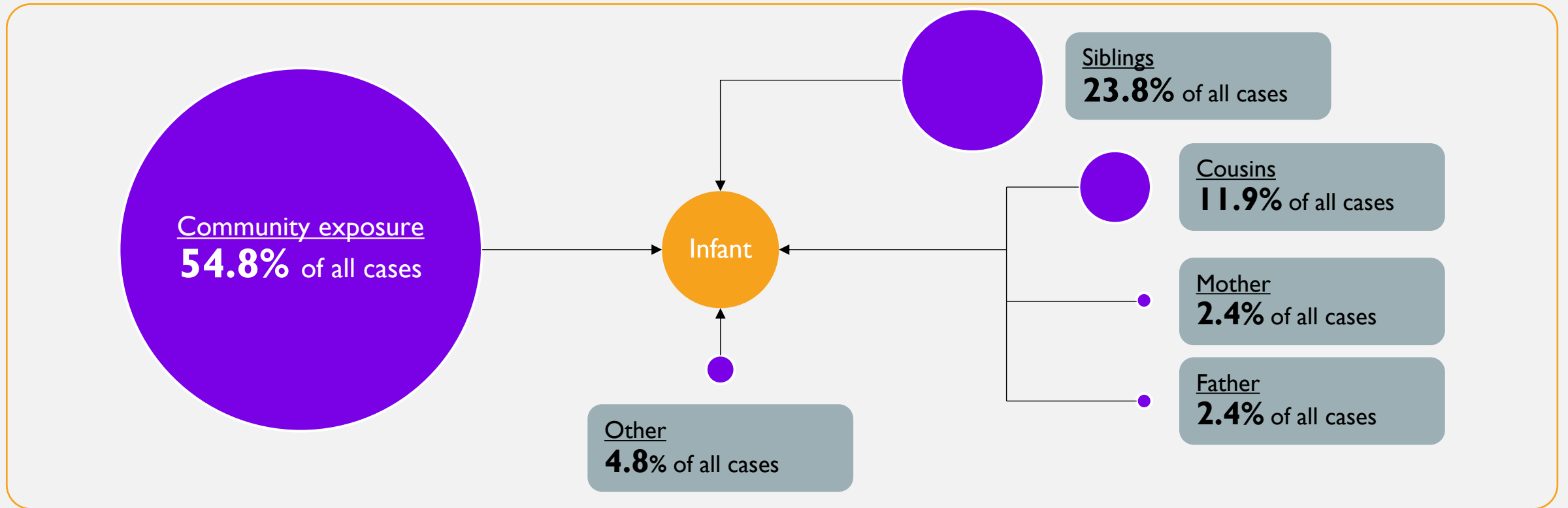
References: 1. Hansen CL, et al. *JAMA Netw Open.* 2022;5(2):e220527. 2. Rainisch G, et al. *Vaccine.* 2020;38(2):251-257. 3. McLaughlin JM, et al. *J Infect Dis.* 2020;jiaa752. 4. Glezen WP, et al. *Am J Dis Child.* 1986;140(6):543-546.

RSV-ALRI RESULTS IN €4.82 BILLION DIRECT MEDICAL COSTS GLOBALLY^{1,A}



- ^aCosts are given in 2017 EUR.
- CI: confidence interval; RSV-ALRI: respiratory syncytial virus-acute lower respiratory tract infections.
- 1. Zhang S, et al. *J Infect Dis.* 2020;222(suppl 7):S680-S687.

MOST INFANTS ARE EXPOSED TO RSV INFECTION IN THE COMMUNITY AND THROUGH OTHER CHILDREN



Network showing the sources of infection to the infant, as identified by social relationships in Kenya. The size of the circles is proportional to the number of cases.

TREATMENT OF RSV

When to take a baby with RSV to the hospital

"Caving in" of their chest when breathing.



 <p>Blue or gray lips, mouth or fingernails.</p>	 <p>Short, shallow or fast breathing.</p>	 <p>Flaring of nostrils when breathing.</p>
 <p>Noisy breathing.</p>	 <p>Signs of dehydration.</p>	 <p>Pauses in breathing.</p>

 Cleveland Clinic

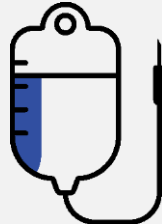


CURRENT TREATMENT IS LIMITED TO SUPPORTIVE CARE



RESPIRATORY SUPPORT AND MONITORING

IMPORTANT:
Provide respiratory
support including
oxygen, possibly
ventilation



HYDRATION

Assess skin turgor
(tightness,
elasticity) and urine
output

Consider IV fluids if
marked respiratory
distress



FEVER

Manage with
acetaminophen
which also helps to
decrease
respiratory effort
and maintain
hydration



STEROIDS

DO NOT GIVE
steroids or
adrenaline/
epinephrine



ANTIBIOTICS

Inappropriate
antibiotic use poses
antimicrobial
resistance threat

ICU ADMISSION

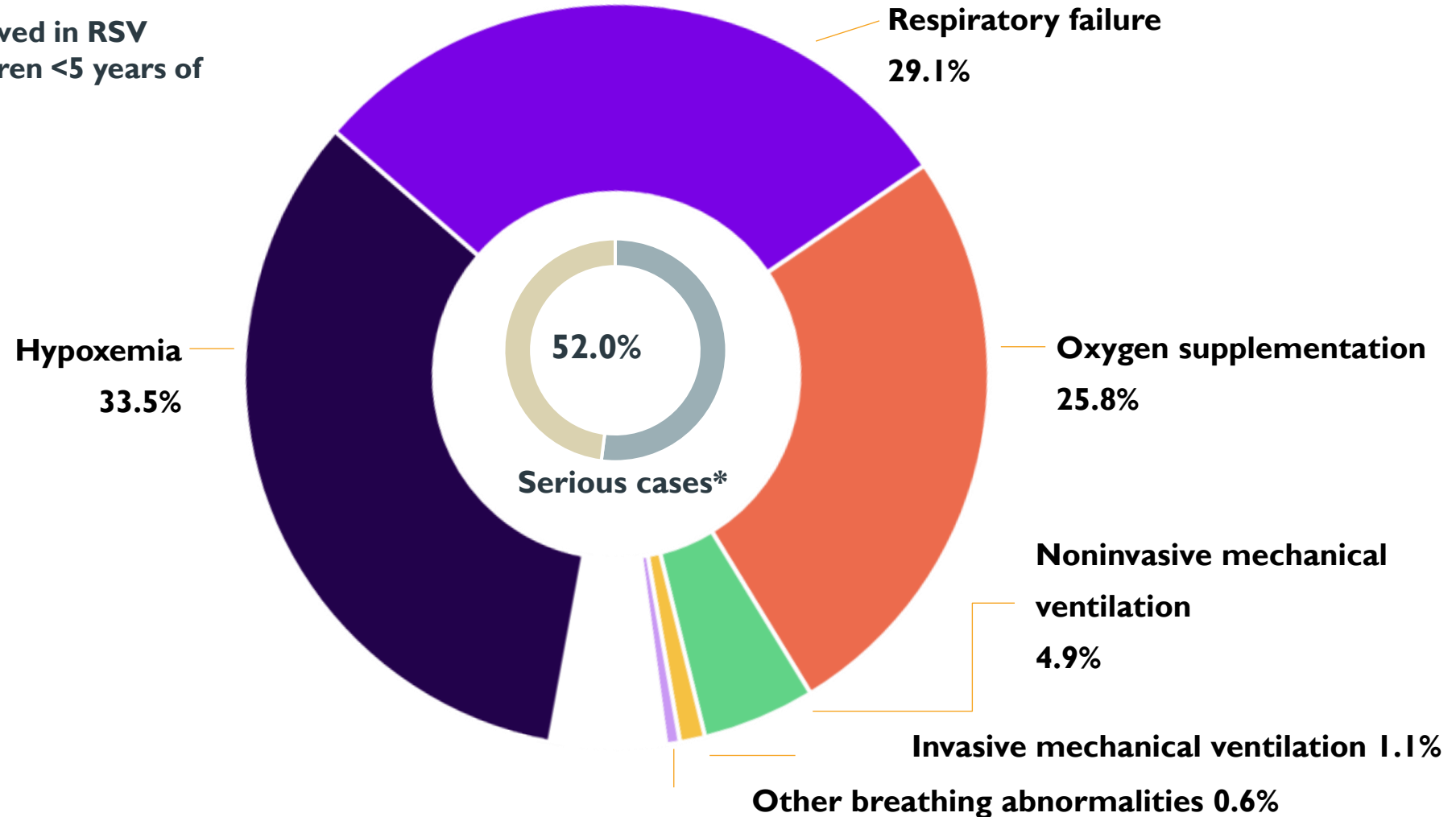
- **Supportive therapy**
- **Oxygenation, respiratory support, hydration, and monitoring.**
- Rescue therapies:
 - HFOV for severe ARDS
 - ECMO in refractory respiratory failure



ONLY SUPPORTIVE CARE IS AVAILABLE FOR INFANTS WITH SEVERE RSV

N

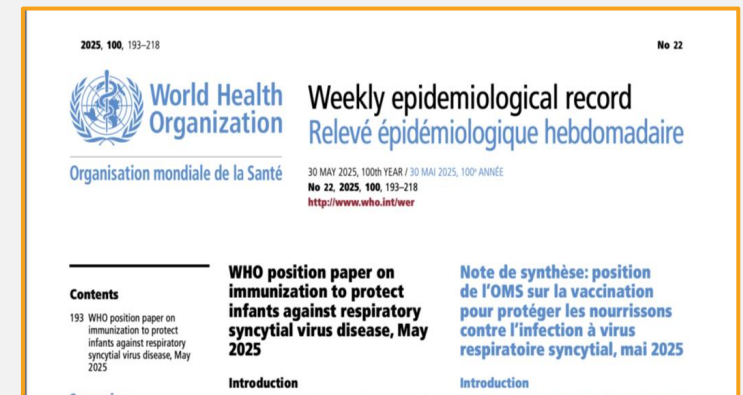
Severity markers observed in RSV hospitalizations in children <5 years of age, in Spain



*Cases with Severity Markers

WHO STRATEGIC ADVISORY GROUP OF EXPERTS (SAGE) ON IMMUNIZATION SEPT 2024

- All countries should introduce passive immunization for the prevention of severe RSV disease in young infants
- Decisions to include the maternal RSV vaccine and/or the long-acting monoclonal antibody would need to consider the cost, financing, supply, anticipated coverage and feasibility
- Single dose of maternal RSV vaccine should be administered in the third trimester of pregnancy and post-marketing surveillance would be necessary



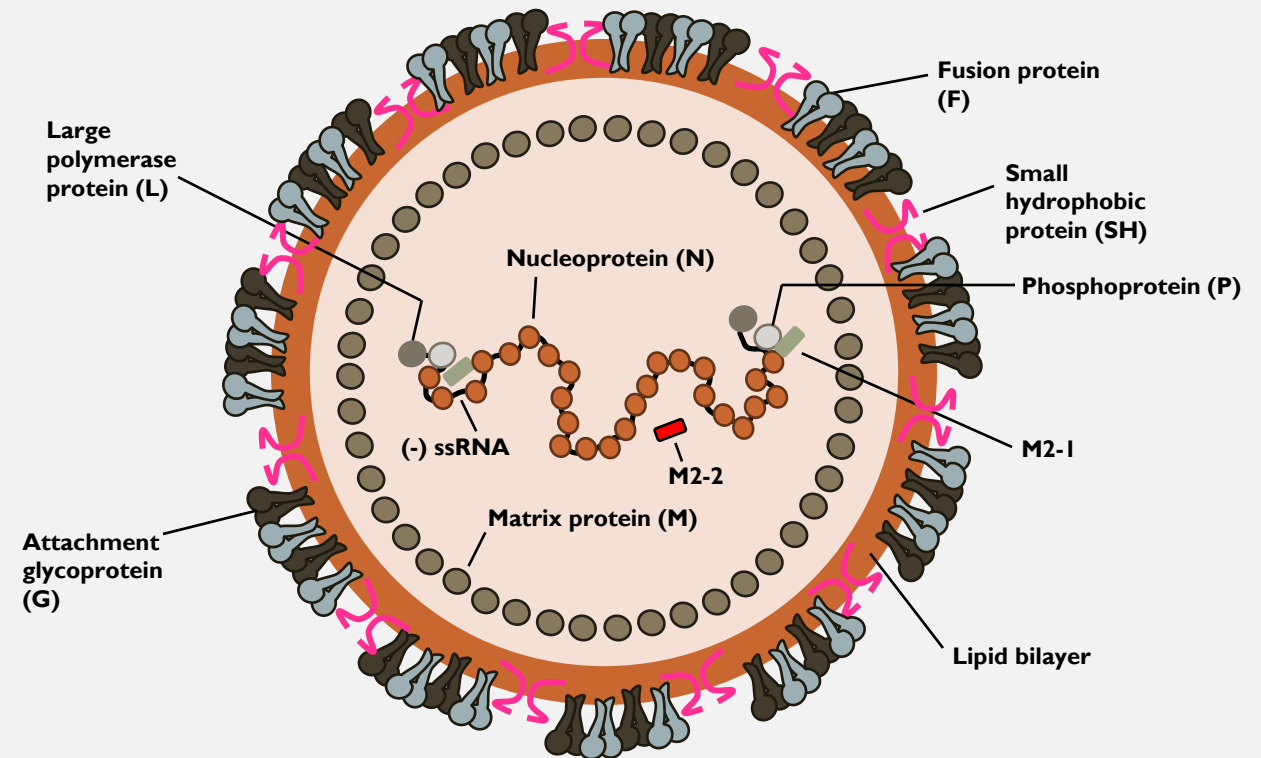
KEY FEATURES OF RSV

Characteristics

- Categorized into 2 co-circulating subgroups, A and B, based on differences in the G protein
- Contains several membrane proteins; the F protein is responsible for fusion to host cells

Infection

- Spread from person to person via respiratory droplets
- Fomite spread- contact with contaminated surfaces
- Lack of long-term immunity after infection leads to frequent reinfection

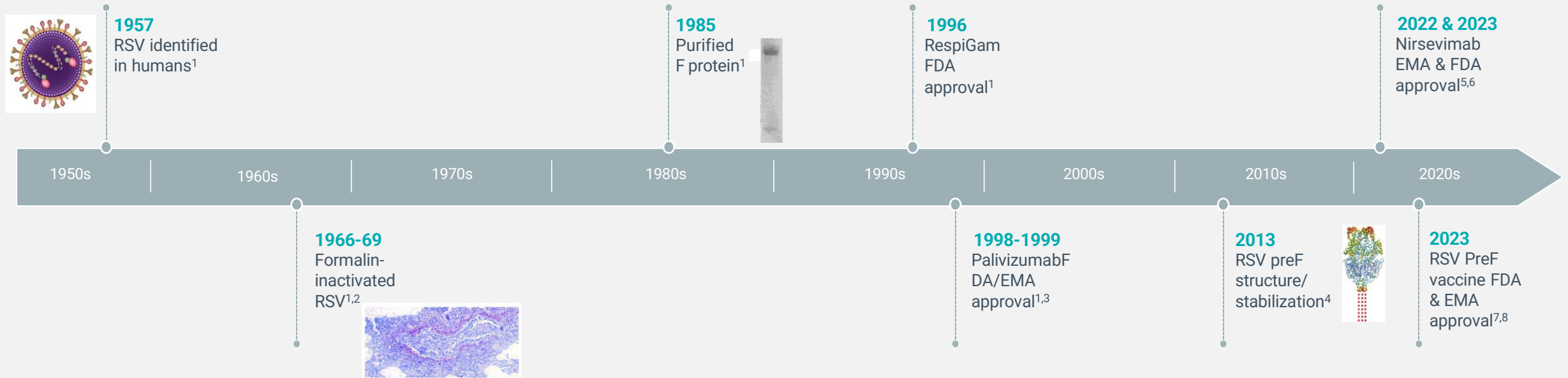


SELECT MILESTONES IN RESEARCH AND DEVELOPMENT: NEW RSV PREVENTATIVE OPTIONS ARE AVAILABLE TO PROTECT INFANTS FROM RSV

No Preventative Options Available

Limited Preventative Options Available

New Preventative Options Available



RSV VACCINES AND MONOCLONAL ANTIBODIES TARGETING F PROTEIN

AstraZeneca/Sanofi Infants	(mAb)		July 2023
GSK Older adults	(protein)	 + AS01e	May 2023
Pfizer Maternal, older adults	(protein)	 + 	August 2023 May 2023
Janssen Older adults	(Ad26 + pre-F protein)	 + 	Phase 3 published Feb 2023
Moderna Older adults	(mRNA)		Phase 3 initiated Feb 2022
Merck Infants	(mAb)		Phase 3 initiated Nov 2021

MATERNAL IMMUNISATION

- Pfizer's Abrysvo® (RSVpreF)
- WHO prequalified (Mar 2025) SAHPRA approved (Dec 2024)
- NAGI recommends public rollout
- Available privately



MONOCLONAL ANTIBODY: NIRSEVIMAB

- Long-acting antibody for direct infant protection
- Single dose per RSV season
- SAHPRA approved (Oct 25) Beyfortus®
- WHO recommends for infants whose mothers weren't vaccinated



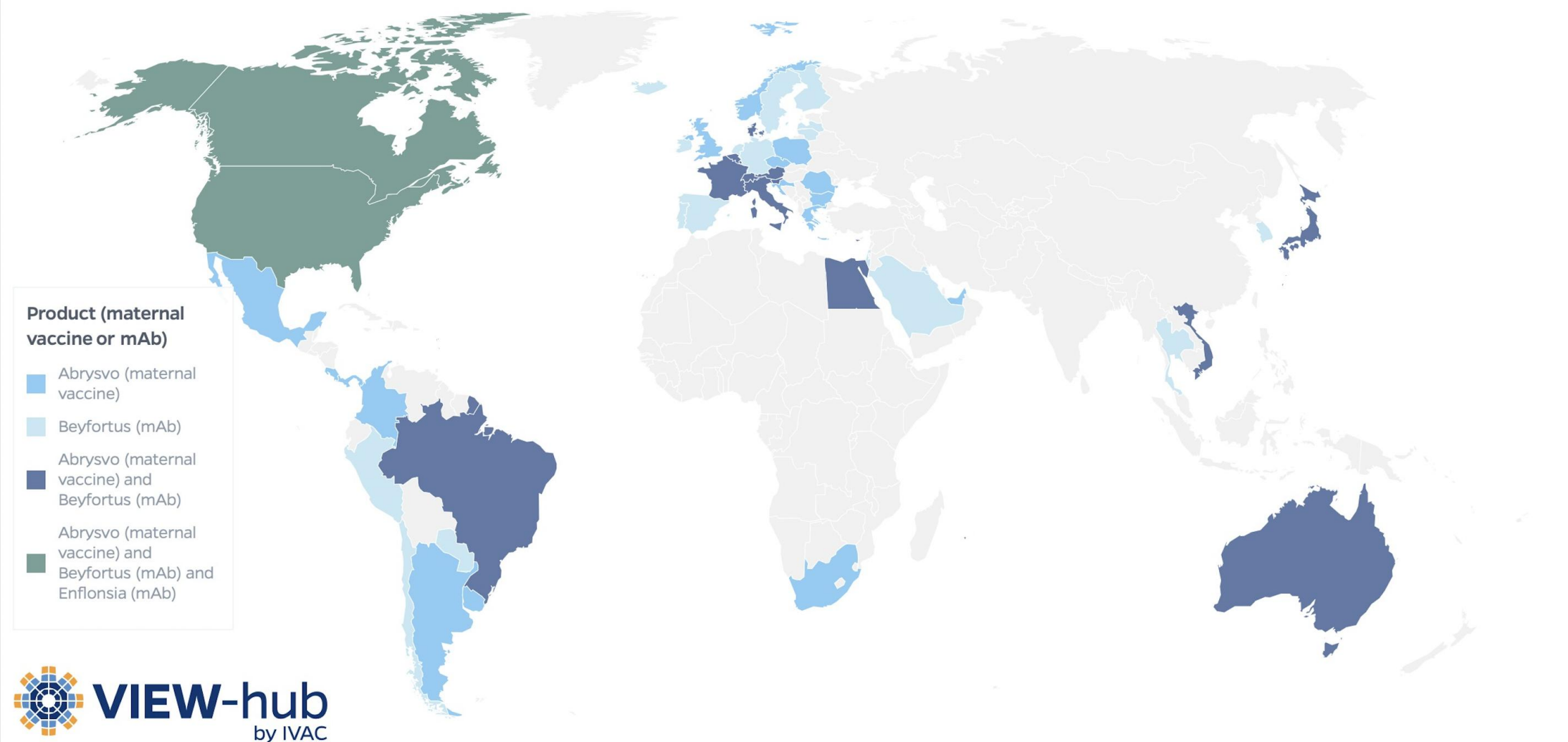
NIRSEVIMAB IN SOUTH AFRICA

For full prescribing information refer to the professional information approved by the medicines regulatory authority.

S4 BEYFORTUS 50 mgTM; BEYFORTUS 100 mgTM (solution for injection). QUALITATIVE AND QUANTITATIVE COMPOSITION: One mL solution for injection contains 100 mg nirsevimab. Each BEYFORTUS 50 mg pre-filled syringe contains 50 mg of nirsevimab in 0,5 mL (100 mg/mL). Each BEYFORTUS 100 mg pre-filled syringe contains 100 mg of nirsevimab in 1 mL (100 mg/mL).
REGISTRATION NUMBER: BEYFORTUS 50 mg: A59/30.1/0957; BEYFORTUS 100 mg: A59/30.1/0958.
HOLDER OF CERTIFICATE OF REGISTRATION: sanofi-aventis south africa (pty) ltd., Reg. no.: 1996/010381/07, Floor 5, Building I, Hertford Office Park, 90 Bekker Road, Midrand, 2196.
Tel: (011) 256 3700

For Medical Information enquiries, kindly contact: Zavaccine.queries@sanofi.com

RSV ► mAb or Maternal Vaccine Introduction ► Product (maternal vaccine or mAb)





PASSIVE IMMUNISATION

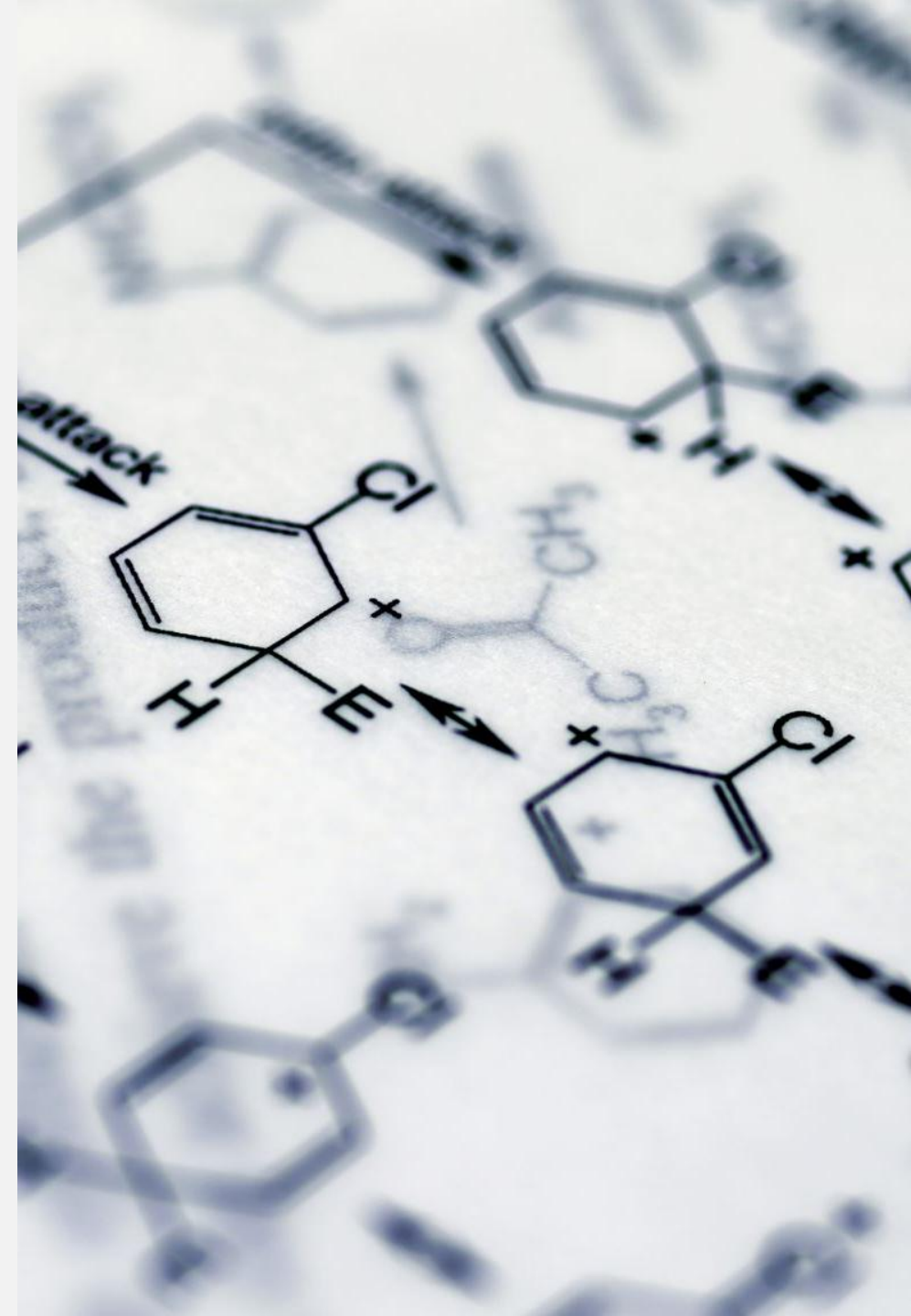
DEFINITION

- Administration of pre-formed antibodies directed against a particular pathogen to combat or prevent disease
- Rather than waiting the required 7–10 days for one's own adaptive immune response to either a pathogen or vaccine immunogen → immediate protection by the injected antibodies



EXAMPLES

- **Human immunoglobulin preparations** (e.g., IVIG)
- **Specific hyperimmune sera** (e.g., hepatitis B immunoglobulin, varicella-zoster immunoglobulin)
- **Monoclonal antibodies** (e.g., nirsevimab for RSV)



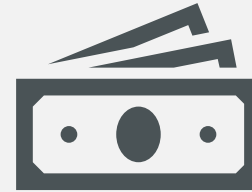
PASSIVE IMMUNISATION



Immediate Protection



Short term Immunity-
weeks to months



Can be expensive

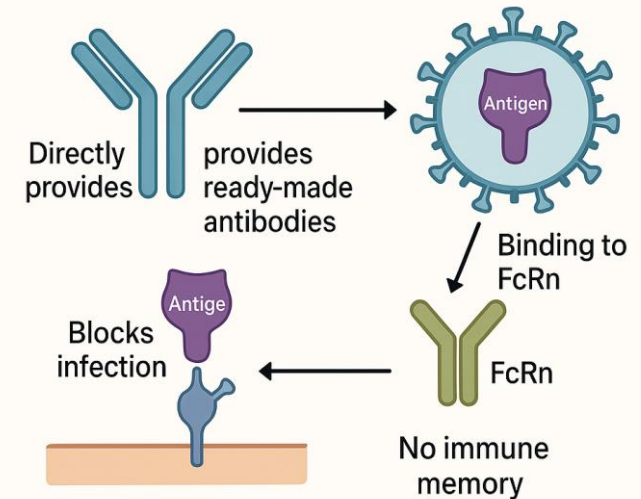


LONG ACTING MONOCLONAL ANTIBODIES

MONOCLONAL AB

- Nirsevimab → binds RSV pre-fusion F protein → blocks viral fusion → prevents RSV entry → virus cannot replicate
- YTE Fc modification → prolonged recycling via FcRn → long half-life → single seasonal dose

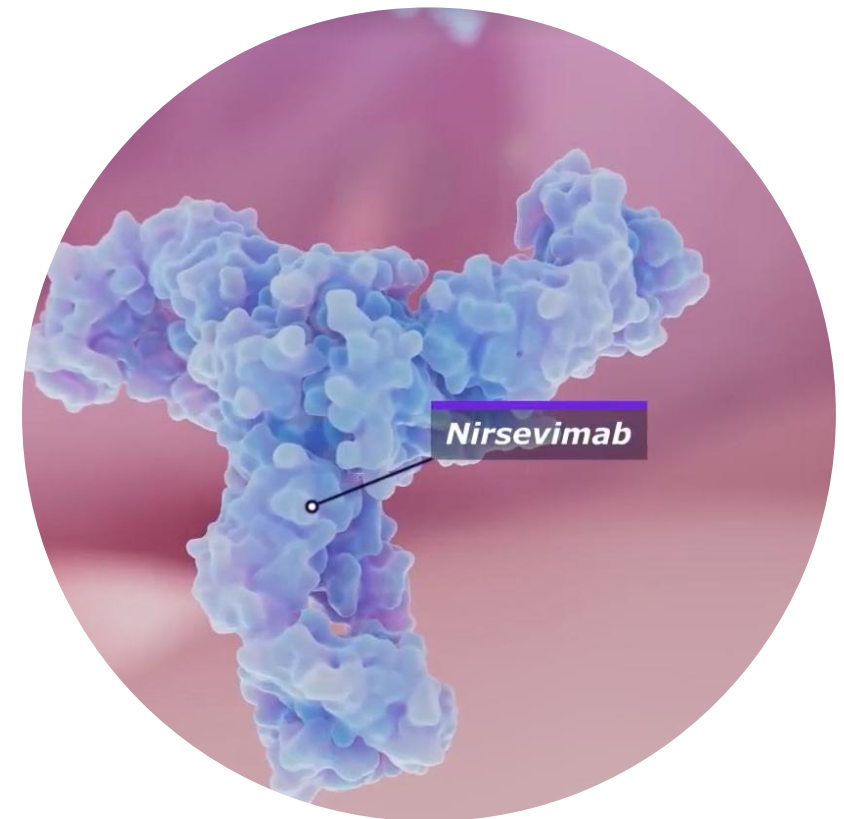
Long-Acting Monoclonal Antibody Provides Passive Immunisation



OVERVIEW OF NIRSEVIMAB

Technology

- Fully human, high-potency IgG1 kappa mAb derived from human B cells
- Extended half life using YTE technology
- Recombinant antibody produced in CHO cells by recombinant DNA technology



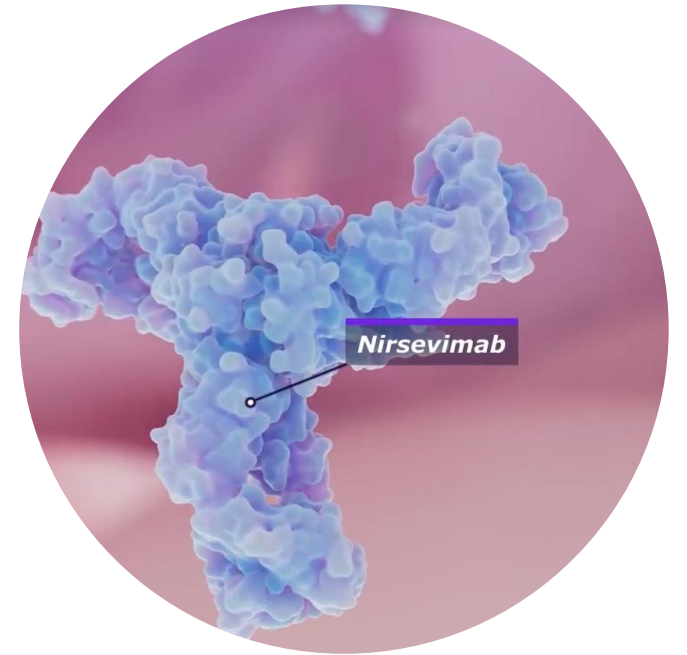
OVERVIEW OF NIRSEVIMAB

Highlights of properties

- Offers rapid and direct protection against medically attended RSV LRTD
- Extended half-life offers season-long protection with a single dose
- Pre-filled syringe presentation allows simple weight-banded dosing (50mg if <5kg and 100mg if ≥5kg)

Efficacy and safety across the 3 complimentary pivotal studies

- A single dose of nirsevimab demonstrated efficacy to protect infants against RSV LRTD in full term and preterm infants
- Favorable safety profile demonstrated in 3 studies across the full birth cohort

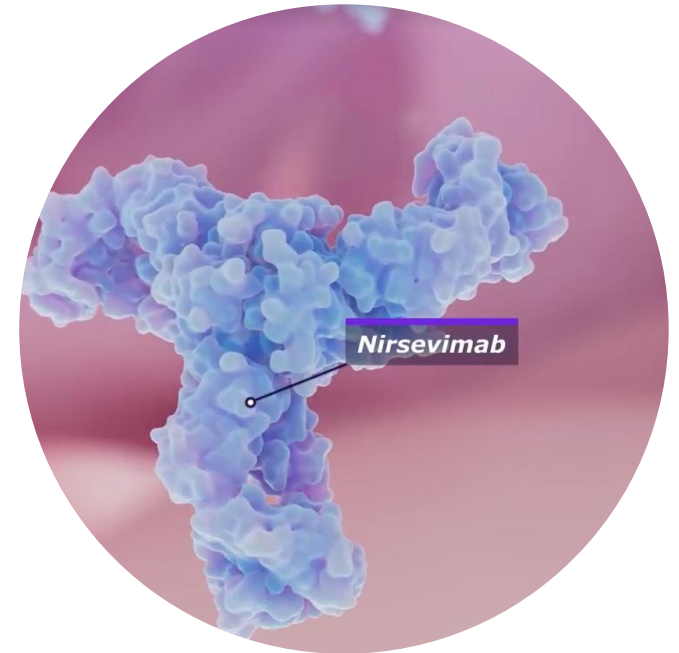


OVERVIEW OF NIRSEVIMAB

Journey to approval

- In October and November 2022, nirsevimab received approval in Europe and the UK, respectively
- In July 2023, the FDA approved nirsevimab to protect infants against RSV (for the 2023/2024 season)
- Nirsevimab is currently **approved in 62 countries** and **recommended by the governmental authorities of 29 countries**

1. EMA, Beyfortus Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/beyfortus-epar-product-information_en.pdf. [accessed July 2025].
2. FDA. Beyfortus Prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761328s000lbl.pdf. [accessed July 2025].



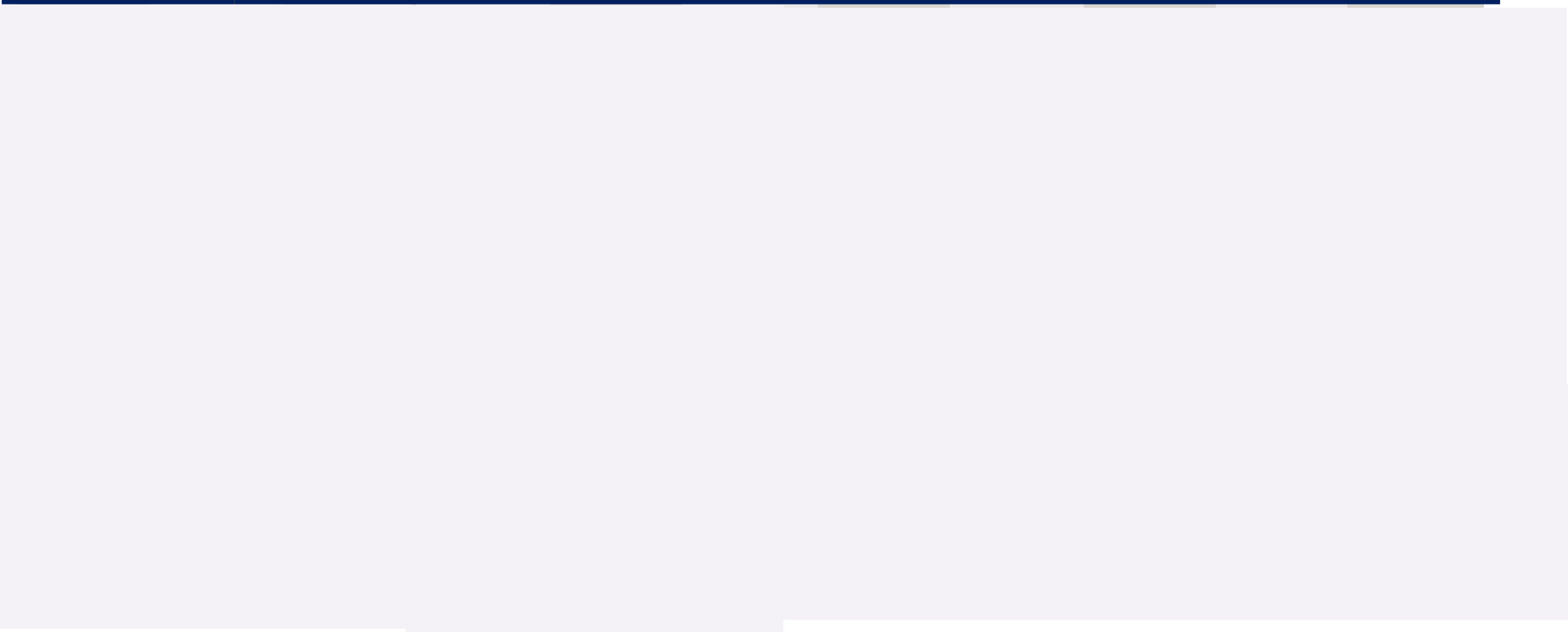
NIRSEVIMAB

- Brand name: Beyfortus™ - AstraZeneca/Sanofi
- IMI, **single dose** (long-acting)
- Can be administered simultaneously with other childhood vaccines
- Dosed by weight/age
 - 50 mg if <5 kg
 - 100 mg if ≥5 kg
 - 200 mg (2x100 mg) for high-risk children entering 2nd RSV season
- Stored in refrigerator at 2-8°C
 - May be kept at room temperature (20-25°C) for up to 8 hours



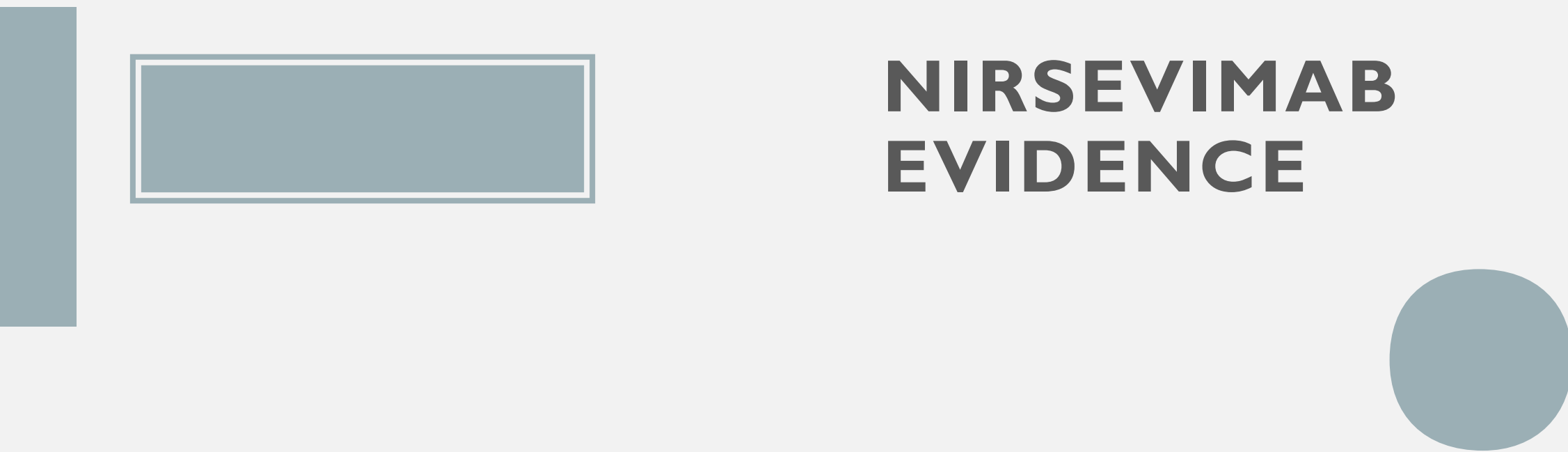
CLINICAL DEVELOPMENT OF NIRSEVIMAB

2014 2015 2016 2017 2018 2019 2020 2021 2022 2023 2024



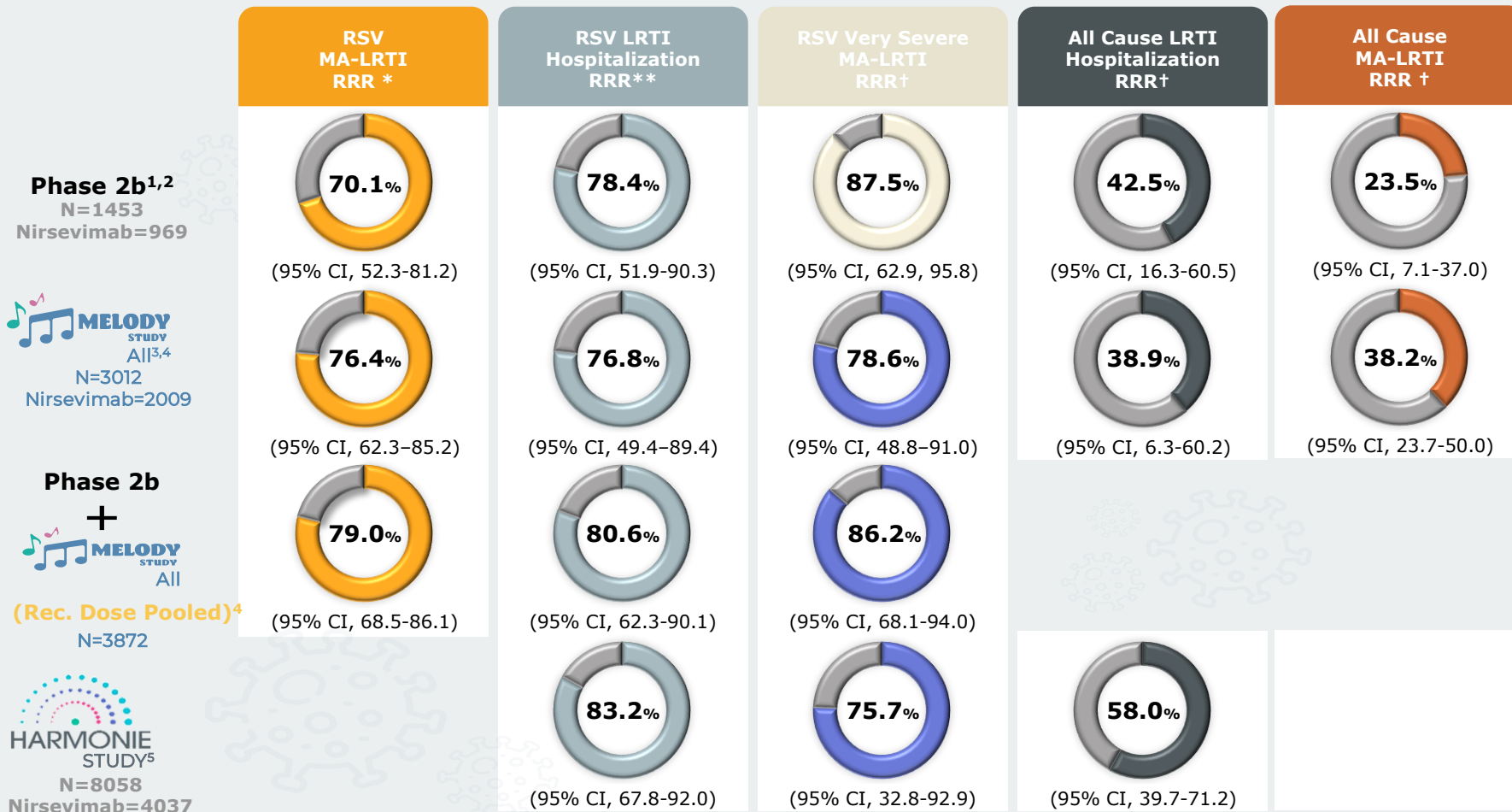
NIRSEVIMAB CLINICAL DEVELOPMENT PROGRAM

	Phase 2b Study (POC/Pivotal trial)	Phase 3 – MELODY Study (Pivotal trial)	Phase 2/3 – MEDLEY First and Second Season Study (Pivotal trial)
Study Population	<ul style="list-style-type: none"> 1453 healthy infants 29 to <35 wGA Not eligible to receive palivizumab (AAP or other local guidelines) 	<ul style="list-style-type: none"> 3012 healthy infants ≥35 wGA <ul style="list-style-type: none"> Primary cohort: 1490 infants Full cohort: 3012 infants Not eligible to receive palivizumab 	<ul style="list-style-type: none"> 615 preterm infants born ≤35 wGA <ul style="list-style-type: none"> 200 preterm infants born <29 wGA 310 infants with CLD of prematurity or CHD CLD/CHD infants were given a second dose in the second season: (N/N); palivizumab infants were re-randomized 1:1 to either 200 mg nirsevimab followed by four once-monthly doses of placebo (P/N) or five once-monthly intramuscular doses of palivizumab (15 mg/kg weight per dose) (P/P).
Interventions	<ul style="list-style-type: none"> 2:1 Randomization Single Dose of Nirsevimab 50 mg : Placebo 	<ul style="list-style-type: none"> 2:1 Randomization Single dose of Nirsevimab : Placebo Dosing: 50 mg if <5 kg or 100 mg if ≥5 kg 	<ul style="list-style-type: none"> 2:1 Randomization Single dose of Nirsevimab: Palivizumab <ul style="list-style-type: none"> Nirsevimab Dosing single dose: 50 mg if <5 kg or 100 mg if ≥5 kg (first season), 200mg if second season. Followed by 4 once-monthly placebo doses Palivizumab Dosing: 5 monthly doses of 15 mg/kg
Primary Endpoint	Incidence of RSV confirmed MA-LRTI through 150 days after administration of the dose		Safety & tolerability of nirsevimab
Secondary Efficacy Endpoints	Incidence of RSV-LRTI hospitalization through 150 days after administration of the dose		<ul style="list-style-type: none"> Descriptive efficacy of nirsevimab in reducing RSV confirmed MA-LRTI and RSV-LRTI hospitalization Pharmacokinetics for extrapolation of efficacy observed in healthy infants



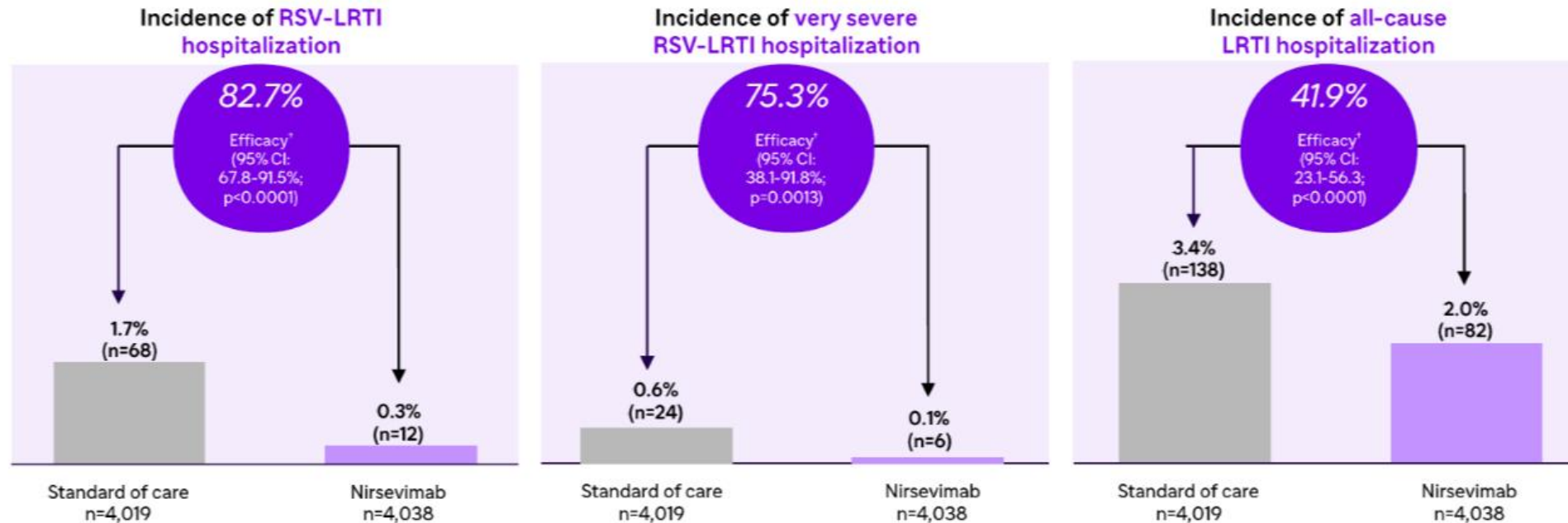
NIRSEVIMAB EVIDENCE

NIRSEVIMAB DEMONSTRATED CONSISTENT EFFICACY AGAINST MA RSV-LRTI ASSOCIATED HOSPITALIZATIONS AND ALL CAUSE HOSPITALIZATIONS IN CLINICAL TRIALS AS WELL AS IN CLOSE-TO-REAL-LIFE CONDITIONS STUDY (HARMONIE)



HARMONIE

REDUCTIONS IN RSV-LRTI RELATED HOSPITALIZATIONS WITH NIRSEVIMAB IS SUSTAINED THROUGH 180-DAY POST-DOSING



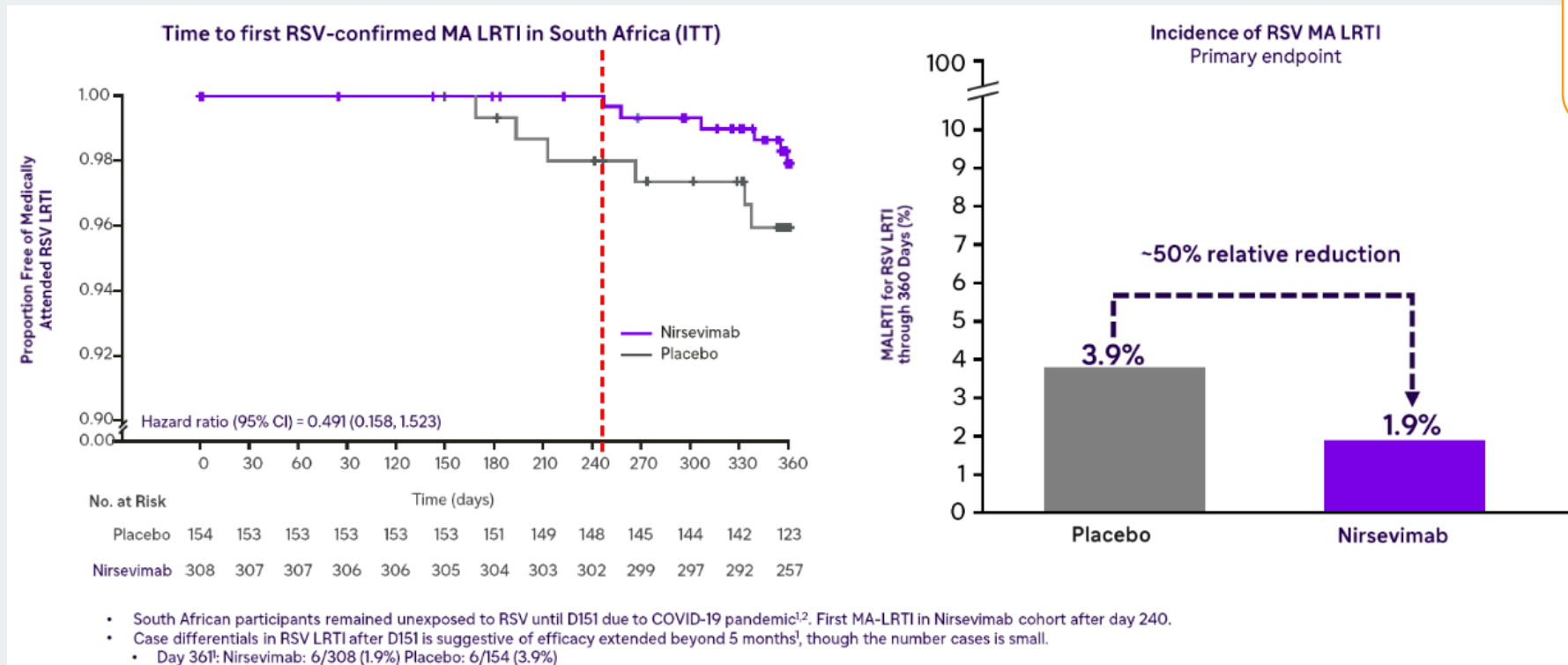
Nirsevimab demonstrated a significant beneficial efficacy at 180 days post-dose; therefore, offering consistent and sustained protection against RSV LRTI hospitalization in infants for at least 6 months

*This study reports the outcomes through 180 days of follow up, extending it past the end of the RSV season for most participants; †All outcome results were calculated by the exact method using binomial distribution accounting for the follow-up time; Efficacy was calculated as 1 minus the incidence rate ratio accounting for the follow-up time post-dosing/randomization; Previously, outcomes as of the end of the RSV season (February 28 2023) have been reported.
CI, confidence interval; LRTI, lower respiratory tract infection; RSV, respiratory syncytial virus.
Reference: Munro APS, et al. *The Lancet*. 2025, 9(6):404-412

MELODY SOUTH AFRICAN COHORT: 360 DAYS FOLLOW-UP

- Cases in the context of delayed RSV in circulation

Harmonie Extension
Study confirms
maintained efficacy over 6
months



*These are EXPLORATORY results. ITT population—participants from South Africa. Kaplan–Meier curve from a time-to-event analysis shows an estimate of the proportion of participants who were free from a medically attended RSV-associated LRTI. The hazard ratio and corresponding 95% CIs were obtained from a proportional-hazard model. Tick marks indicate censored data. CI: Confidence Interval; COVID-19: Corona virus disease- 2019; ITT: Intent-to-treat; LRTI: Lower respiratory tract infection; MA: Medically attended; RSV: Respiratory syncytial virus.

References: 1. Hammit LL, et al. *N Engl J Med*. 2022;386:837–846. 2. Tempia S, et al. *Euro Surveill*. 2021;26(29):2001600.

FAVOURABLE SAFETY PROFILE ACROSS INFANT STUDIED POPULATIONS & REAL-WORLD SETTINGS

Favorable safety profile across all infants, regardless of gestational age at birth or underlying health conditions

Safety	Phase 2b ¹ 29-<35 wGA		MELODY ^{2,3} ≥35 wGA		MEDLEY ^{4*}			
					Preterm		CHD/CLD	
Variables	Placebo (N=479)	Nirsevimab (N=968)	Placebo (N=996)	Nirsevimab (N=1998)	Palivizumab (N=206)	Nirsevimab (N=406)	Palivizumab (N=98)	Nirsevimab (N=208)
Serious adverse events	16.9%	11.2%	7.4%	6.3%	6.3%	8.6%	25.5%	21.6%
Adverse events of Grade 3 or higher	12.5%	8.0%	3.8%	3.1%	3.9%	4.4%	17.3%	15.4%
Adverse events of special interest	0.6%	0.5%	0.0%	0.2%	0.0%	0.2%	0.0%	1.0%
Deaths	3	2	0	4	0	2	1	3

- None of the serious adverse events or deaths were considered as related to nirsevimab
- In the HARMONIE study (n=4016 infants who received nirsevimab in the safety analysis set), no safety concerns were raised during the trial⁵

Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

Laura L. Hammitt, M.D., Ron Dagan, M.D., Yuan Yuan, Ph.D., Manuel Baca Cots, M.D., Miroslava Bosheva, M.D., Shabir A. Madhi, Ph.D., William J. Muller, Ph.D., Heather J. Zar, Ph.D., Dennis Brooks, M.D., Amy Grenham, M.Sc., Ulrika Wählby Hamrén, Ph.D., Vaishali S. Mankad, M.D., Pin Ren, Ph.D., Therese Takas, B.Sc., Michael E. Abram, Ph.D., Amanda Leach, M.R.C.P.C.H., M. Pamela Griffin, M.D., and Tonya Villafana, Ph.D., for the MELODY Study Group*

ABSTRACT

BACKGROUND

Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infection and hospitalization in infants. Nirsevimab is a monoclonal antibody to the RSV fusion protein that has an extended half-life. The efficacy and safety of nirsevimab in healthy late-preterm and term infants are uncertain.

METHODS

We randomly assigned, in a 2:1 ratio, infants who had been born at a gestational age of at least 35 weeks to receive a single intramuscular injection of nirsevimab or placebo before the start of an RSV season. The primary efficacy end point was medically attended RSV-associated lower respiratory tract infection through 150 days after the injection. The secondary efficacy end point was hospitalization for RSV-associated lower respiratory tract infection through 150 days after the injection.

RESULTS

A total of 1490 infants underwent randomization: 994 were assigned to the nirsevimab group and 496 to the placebo group. Medically attended RSV-associated lower respiratory tract infection occurred in 12 infants (1.2%) in the nirsevimab group and in 25 infants (5.0%) in the placebo group; these findings correspond to an efficacy of 74.5% (95% confidence interval [CI], 49.6 to 87.1; $P < 0.001$) for nirsevimab. Hospitalization for RSV-associated lower respiratory tract infection occurred in 6 infants (0.6%) in the nirsevimab group and in 8 infants (1.6%) in the placebo group (efficacy, 62.1%; 95% CI, −8.6 to 86.8; $P = 0.07$). Among infants with data available to day 361, antidrug antibodies after baseline were detected in 58 of 951 (6.1%) in the nirsevimab group and in 5 of 473 (1.1%) in the placebo group. Serious adverse events were reported in 67 of 987 infants (6.8%) who received nirsevimab and in 36 of 491 infants (7.3%) who received placebo.

CONCLUSIONS

A single injection of nirsevimab administered before the RSV season protected healthy late-preterm and term infants from medically attended RSV-associated lower respiratory tract infection. (Funded by MedImmune/AstraZeneca and Sanofi; MELODY ClinicalTrials.gov number, NCT03979313.)

From the Department of International Health, Johns Hopkins University, Baltimore (L.L.H.), and AstraZeneca, Gaithersburg (Y.Y., D.B., A.G., P.R., T.T., M.E.A., A.L., M.P.G., T.V.) — both in Maryland; the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel (R.D.); Quirónsalud Málaga Hospital, Málaga, Spain (M.B.C.); University Multi-profile Hospital for Active Treatment, St. George Medical University, Plovdiv, Bulgaria (M.B.); the South African Medical Research Council Vaccines and Infectious Diseases Analytics Research Unit and African Leadership in Vaccinology Expertise, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg (S.A.M.); and the Department of Paediatrics and Child Health, Red Cross Children's Hospital, and the Medical Research Council Unit on Child and Adolescent Health, University of Cape Town, Cape Town (H.J.Z.) — all in South Africa; Ann and Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago (W.J.M.); AstraZeneca, Gothenburg, Sweden (U.W.H.); and AstraZeneca, Durham, NC (V.S.M.). Dr. Villafana can be contacted at tonya.villafana@astrazeneca.com or at AstraZeneca, One MedImmune Way, Gaithersburg, MD 20878.

*A list of the MELODY Study Group members is provided in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2022;386:837–46.

DOI: 10.1056/NEJMoa2110275

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Efficacy

- **78.4% (95% CI: 51.9–90.3)**
- **29 to <35 weeks**

- **76.8% (95% CI: 49.4–89.4)**
- **near term or term infants**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 30, 2020

VOL. 383 NO. 5

Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants

M. Pamela Griffin, M.D., Yuan Yuan, Ph.D., Therese Takas, B.S., Joseph B. Domachowski, M.D., Shabir A. Madhi, M.B., B.Ch., Ph.D., Paolo Manzoni, M.D., Ph.D., Eric A.F. Simões, M.D., Mark T. Esser, Ph.D., Anis A. Khan, Ph.D., Filip Dubovsky, M.D., Tonya Villafana, Ph.D., and John P. DeVincenzo, M.D., for the Nirsevimab Study Group*

ABSTRACT

BACKGROUND

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection in infants, and a need exists for prevention of RSV in healthy infants. Nirsevimab is a monoclonal antibody with an extended half-life that is being developed to protect infants for an entire RSV season with a single intramuscular dose.

METHODS

In this trial conducted in both northern and southern hemispheres, we evaluated nirsevimab for the prevention of RSV-associated lower respiratory tract infection in healthy infants who had been born preterm (29 weeks 0 days to 34 weeks 6 days of gestation). We randomly assigned the infants in a 2:1 ratio to receive nirsevimab, at a dose of 50 mg in a single intramuscular injection, or placebo at the start of an RSV season. The primary end point was medically attended RSV-associated lower respiratory tract infection through 150 days after administration of the dose. The secondary efficacy end point was hospitalization for RSV-associated lower respiratory tract infection through 150 days after administration of the dose.

RESULTS

From November 2016 through November 2017, a total of 1453 infants were randomly assigned to receive nirsevimab (969 infants) or placebo (484 infants) at the start of the RSV season. The incidence of medically attended RSV-associated lower respiratory tract infection was 70.1% lower (95% confidence interval [CI], 52.3 to 81.2) with nirsevimab prophylaxis than with placebo (2.6% [25 infants] vs. 9.5% [46 infants]; $P < 0.001$) and the incidence of hospitalization for RSV-associated lower respiratory tract infection was 78.4% lower (95% CI, 51.9 to 90.3) with nirsevimab than with placebo (0.8% [8 infants] vs. 4.1% [20 infants]; $P < 0.001$). These differences were consistent throughout the 150-day period after the dose was administered and across geographic locations and RSV subtypes. Adverse events were similar in the two trial groups, with no notable hypersensitivity reactions.

CONCLUSIONS

A single injection of nirsevimab resulted in fewer medically attended RSV-associated lower respiratory tract infections and hospitalizations than placebo throughout the RSV season in healthy preterm infants. (Funded by AstraZeneca and Sanofi Pasteur; ClinicalTrials.gov number, NCT02878330.)

From AstraZeneca, Gaithersburg, MD (M.P.G., Y.Y., T.T., M.T.E., A.A.K., F.D., T.V.); SUNY Upstate Medical University, Syracuse, NY (J.B.D.); Medical Research Council: Respiratory and Meningeal Pathogens Research Unit, and Department of Science and Technology/National Research Foundation South African Research Chair, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg (S.A.M.); the Division of Pediatrics and Neonatology, Department of Maternal, Neonatal, and Infant Medicine, Nuovo Ospedale Degli Infermi, Biella, and Neonatology and NICU, Sant'Anna Hospital, AOU Città della Salute e della Scienza, Turin — both in Italy (P.M.); the University of Colorado School of Medicine, Aurora (E.A.F.S.); and the Children's Foundation Research Institute at Le Bonheur Children's Hospital, Memphis, TN (J.P.D.V.). Address reprint requests to Dr. Villafana at R&D Biopharmaceuticals, AstraZeneca, 1 MedImmune Way, Gaithersburg, MD 20878, or at tonya.villafana@astrazeneca.com.

*A list of investigators in the Nirsevimab Study Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was updated on July 30, 2020, at NEJM.org.

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DOI: 10.1056/NEJMoa1913556
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ORIGINAL ARTICLE

Nirsevimab for Prevention of Hospitalizations Due to RSV in Infants

S.B. Drysdale, K. Cathie, F. Flamein, M. Knuf, A.M. Collins, H.C. Hill, F. Kaiser, R. Cohen, D. Pinquier, C.T. Felter, N.C. Vassilouthis, J. Jin, M. Bangert, K. Mari, R. Nteene, S. Wague, M. Roberts, P. Tissi res, S. Royal, and S.N. Faust, for the HARMONIE Study Group*

ABSTRACT

BACKGROUND

The safety of the monoclonal antibody nirsevimab and the effect of nirsevimab on hospitalizations for respiratory syncytial virus (RSV)–associated lower respiratory tract infection when administered in healthy infants are unclear.

METHODS

In a pragmatic trial, we randomly assigned, in a 1:1 ratio, infants who were 12 months of age or younger, had been born at a gestational age of at least 29 weeks, and were entering their first RSV season in France, Germany, or the United Kingdom to receive either a single intramuscular injection of nirsevimab or standard care (no intervention) before or during the RSV season. The primary end point was hospitalization for RSV-associated lower respiratory tract infection, defined as hospital admission and an RSV-positive test result. A key secondary end point was very severe RSV-associated lower respiratory tract infection, defined as hospitalization for RSV-associated lower respiratory tract infection with an oxygen saturation of less than 90% and the need for supplemental oxygen.

RESULTS

A total of 8058 infants were randomly assigned to receive nirsevimab (4037 infants) or standard care (4021 infants). Eleven infants (0.3%) in the nirsevimab group and 60 (1.5%) in the standard-care group were hospitalized for RSV-associated lower respiratory tract infection, which corresponded to a nirsevimab efficacy of 83.2% (95% confidence interval [CI], 67.8 to 92.0; $P<0.001$). Very severe RSV-associated lower respiratory tract infection occurred in 5 infants (0.1%) in the nirsevimab group and in 19 (0.5%) in the standard-care group, which represented a nirsevimab efficacy of 75.7% (95% CI, 32.8 to 92.9; $P=0.004$). The efficacy of

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Prof. Faust can be contacted at s.faust@soton.ac.uk or at the NIHR Southampton Clinical Research Facility and Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, or the Faculty of Medicine and Institute for Life Sciences, University of Southampton, Tremona Road, Southampton, SO16 6YD, United Kingdom.

A list of the investigators in the HARMONIE Study Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Drysdale, Cathie, Flamein, Knuf, and Collins and Dr. Tissi res, Dr. Royal, and Prof. Faust contributed equally to this article.

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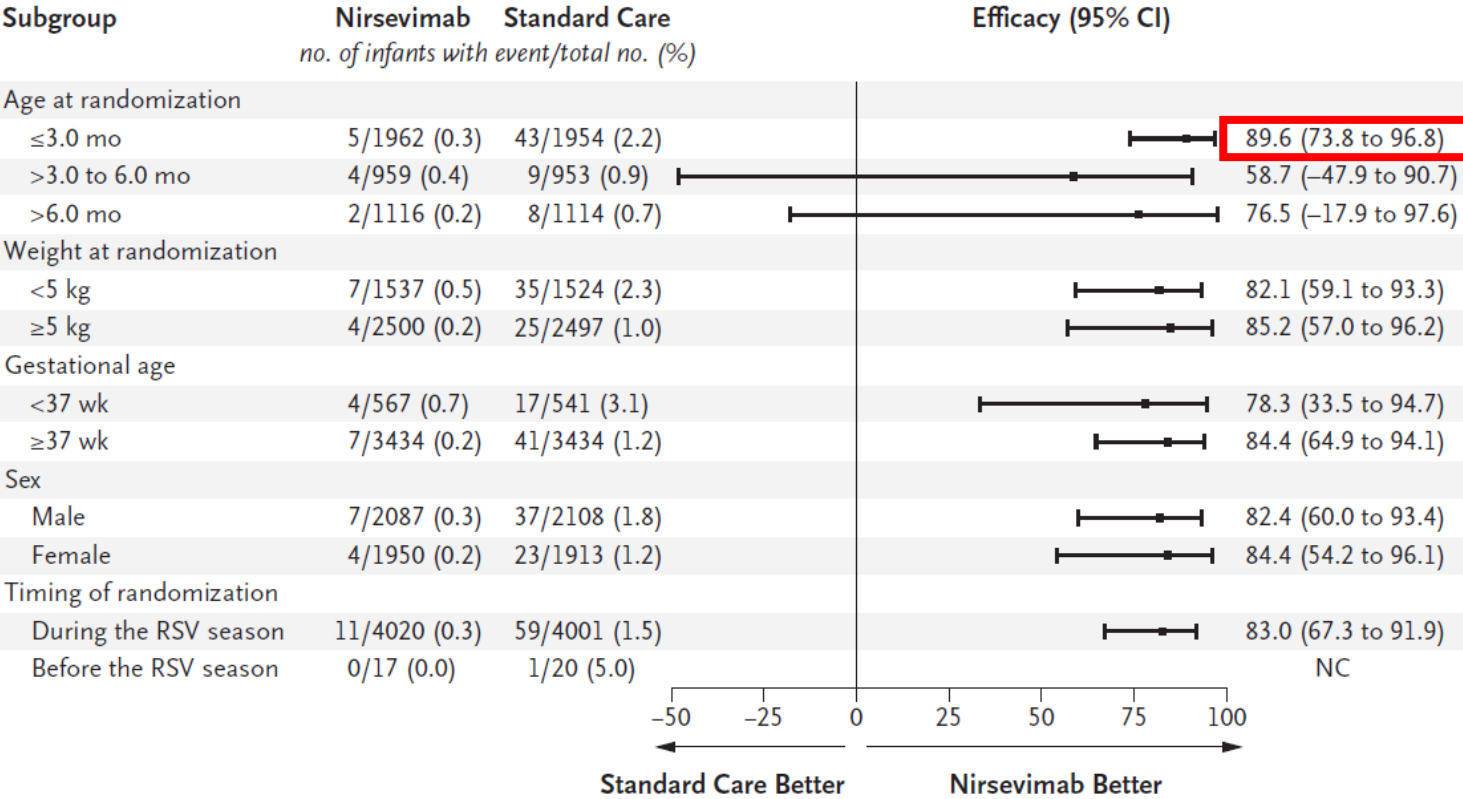


Figure 2. Hospitalization for RSV-Associated Lower Respiratory Tract Infection According to Subgroup.

ALL-CAUSE LRTI

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

Laura L. Hammitt, M.D., Ron Dagan, M.D., Yuan Yuan, Ph.D., Manuel Baca Cots, M.D., Miroslava Bosheva, M.D., Shabir A. Madhi, Ph.D., William J. Muller, Ph.D., Heather J. Zar, Ph.D., Dennis Brooks, M.D., Amy Grenham, M.Sc., Ulrika Wählby Hamrén, Ph.D., Vaishali S. Mankad, M.D., Pin Ren, Ph.D., Therese Takas, B.Sc., Michael E. Abram, Ph.D., Amanda Leach, M.R.C.P.C.H., M. Pamela Griffin, M.D., and Tonya Villafana, Ph.D., for the MELODY Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE



Nirsevimab for Prevention of RSV in Term and Late-Preterm Infants

TO THE EDITOR: Nirsevimab, a monoclonal anti- The case definition of medically attended

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VOL. 383 NO. 5

Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants

M. Pamela Griffin, M.D., Yuan Yuan, Ph.D., Therese Takas, B.S., Joseph B. Domachowski, M.D., Shabir A. Madhi, M.B., B.Ch., Ph.D., Paolo Manzoni, M.D., Ph.D., Eric A.F. Simões, M.D., Mark T. Esser, Ph.D., Anis A. Khan, Ph.D., Filip Dubovsky, M.D., Tonya Villafana, Ph.D., and John P. DeVincenzo, M.D., for the Nirsevimab Study Group*

19. Table S5. Incidence of All-cause LRTI and Hospitalization for All-cause LRTI Through 150

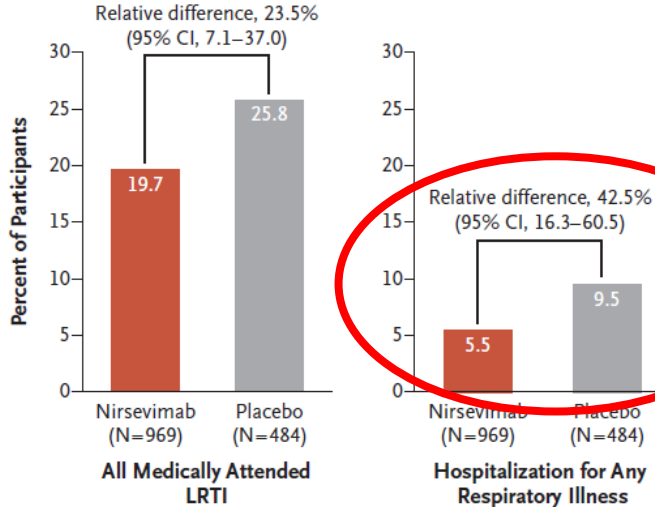
Days Post-dose (ITT Population*) and Efficacy of Nirsevimab Compared to Placebo.

	Placebo (N=1003)	Nirsevimab (N=2,009)	Efficacy	
			RRR	95% CI
All-cause LRTI, n (%)	139 (13.9)	171 (8.5)	38.2	23.7, 50.0
All-cause LRTI hospitalization, n (%)	37 (3.7)	45 (2.2)	38.9	6.3, 60.2

* All infants who underwent randomization.

CI, confidence interval; ITT, intent-to-treat population; LRTI, lower respiratory tract infection; RRR, relative risk reduction.

A Medically Attended LRTI or Respiratory-Related Hospitalization for Any Cause



HOSPITAL ADMISSION FOR RSV



vaccines



Systematic Review

Impact of Nirsevimab Immunization on Pediatric Hospitalization Rates: A Systematic Review and Meta-Analysis (2024)

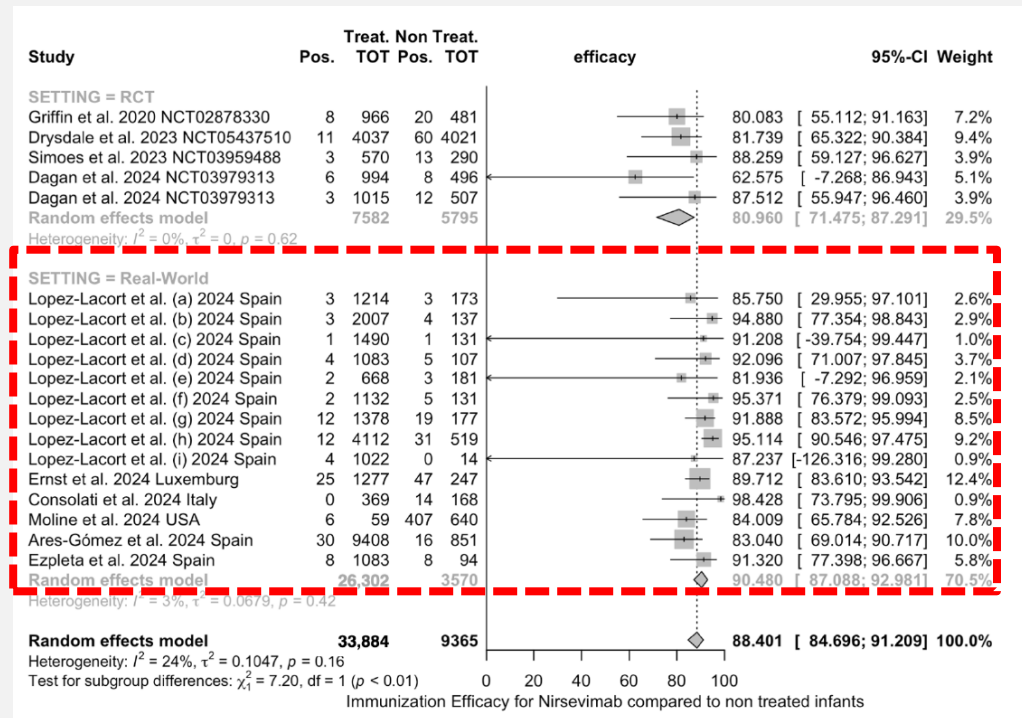
Matteo Riccò ^{1,*}, Antonio Cascio ², Silvia Corrado ³, Marco Bottazzoli ⁴, Federico Marchesi ⁵, Renata Gili ⁶, Pasquale Gianluca Giuri ⁷, Davide Gori ⁸ and Paolo Manzoni ⁹

- ¹ AUSL-IRCCS di Reggio Emilia, Servizio di Prevenzione e Sicurezza Negli Ambienti di Lavoro (SPSAL), Local Health Unit of Reggio Emilia, 42122 Reggio Emilia, Italy
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 - ³ ASST Rhodense, Dipartimento Della Donna e Area Materno-Infantile, UOC Pediatria, 20024 Milano, Italy
 - ⁴ Department of Otorhinolaryngology, APSS Trento, 38122 Trento, Italy
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 - ⁷ Department of Medicine and Diagnostics, AUSL di Parma, 43100 Parma, Italy
 - ⁸ Department of Biomedical and Neuromotor Sciences, University of Bologna, 40126 Bologna, Italy; davide.gori4@unibo.it
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Abstract: A systematic review with a meta-analysis was performed to gather available evidence on the effectiveness of monoclonal antibody nirsevimab in the prevention of lower respiratory tract diseases (LRTDs) due to respiratory syncytial virus (RSV) in children and newborns (CRD42024540669). Studies reporting on real-world experience and randomized controlled trials (RCTs) were searched for in three databases (PubMed, Embase, and Scopus) until 1 May 2024. Our analysis included five RCTs, seven real-world reports, and one official report from the health authorities. Due to the cross-reporting of RCTs and the inclusion of multiple series in a single study, the meta-analysis was performed on 45,238 infants from 19 series. The meta-analysis documented a pooled immunization efficacy of 88.40% (95% confidence interval (95% CI) from 84.70 to 91.21) on the occurrence of hospital admission due to RSV, with moderate heterogeneity (I^2 24.3%, 95% CI 0.0 to 56.6). Immunization efficacy decreased with the overall length of the observation time (Spearman's $r = -0.546$, $p = 0.016$), and the risk of breakthrough infections was substantially greater in studies with observation times >150 days compared to studies lasting <150 days (risk ratio 3.170, 95% CI 1.860 to 5.323). Heterogeneity: $I^2 = 3\%$, $\tau^2 = 0.0679$, $p = 0.42$



Citation: Riccò, M.; Cascio, A.; Corrado, S.; Bottazzoli, M.; Marchesi, F.; Gili, R.; Giuri, P.G.; Gori, D.; Manzoni, P. Impact of Nirsevimab Immunization on Pediatric Hospitalization Rates: A Systematic Review and Meta-Analysis (2024).



This meta-analysis was performed on 45,238 infants from 19 series (US and three European countries)

EFFECTIVENESS OF NIRSEVIMAB ON PICU ADMISSIONS

European Journal of Pediatrics
<https://doi.org/10.1007/s00431-024-05634-z>

RESEARCH

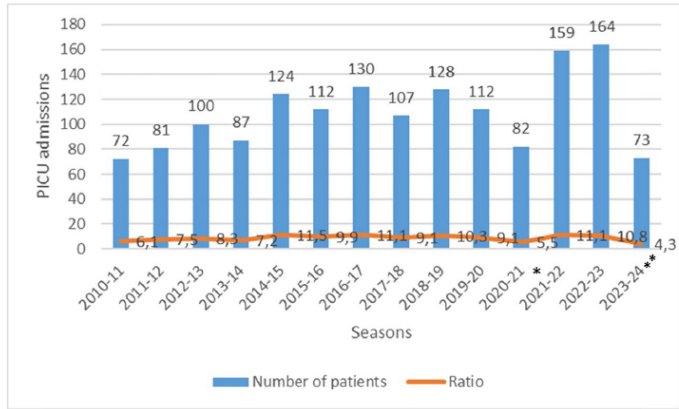


Impact of universal immunization program with monoclonal antibody nirsevimab on reducing the burden of serious bronchiolitis that need pediatric intensive care

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Fig. 2 Number of PICU admissions and ratio of RSV-bronchiolitis per 100 PICU admissions for each season, from the 2010–2011 season through the 2023–2024 season. *SARS-CoV-2 pandemic season; **Post-nirsevimab season (until February 4, when data collection closed)



vaccines



Article

Effectiveness of Nirsevimab Immunoprophylaxis Administered at Birth to Prevent Infant Hospitalisation for Respiratory Syncytial Virus Infection: A Population-Based Cohort Study

Guillermo Ezpeleta¹, Ana Navascués^{2,3}, Natividad Viguria^{3,4} , Mercedes Herranz-Aguirre^{3,4}, Sergio Enrique Juan Belloc⁵, Juan Gimeno Ballester⁶, Juan Carlos Muruzábal⁷ , Manuel García-Cenoz^{1,3,8} , Camino Trobajo-Sanmartín^{1,3,8} , Aitziber Echeverría^{1,3,8}, Iván Martínez-Baz^{1,3,8} , Noelia Vera-Punzano^{1,3} , Itziar Casado^{1,3,8}, Héctor López-Mendoza¹, Carmen Ezpeleta^{2,3} and Jesús Castilla^{1,3,8,*}

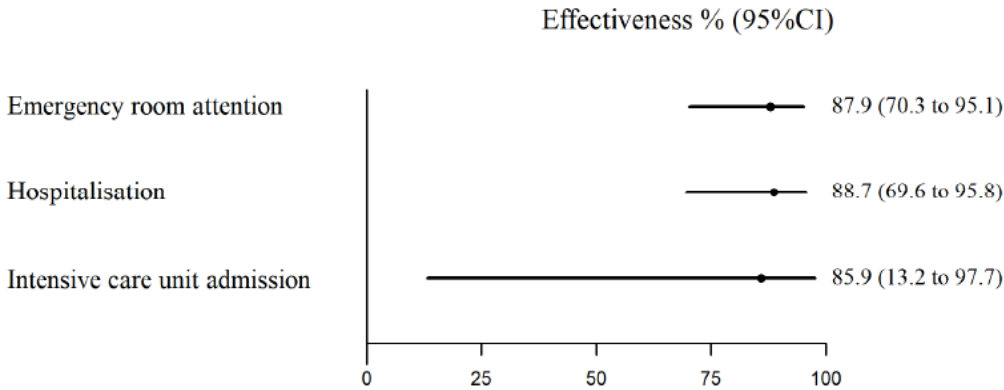


Figure 3. Effectiveness of nirsevimab in preventing laboratory-confirmed respiratory syncytial virus cases.

EFFECTIVENESS - ALL-CAUSE LRTI & HOSPITALIZATION

	Nirsevimab non-recipients			Nirsevimab recipients			Incidence rate ratio (95% CI)	Effectiveness, % (95% CI)*
	Events	Number analysed	Person-years	Events	Number analysed	Person-years		
RSV-related LRTI hospitalisation								
Intention-to-treat analysis†	16	851	207.03	30	9408	1877.71	0.18 (0.10-0.34)	82.0 (65.6-90.2)
Sensitivity analysis‡	19	855	207.55	25	9404	1877.64	0.13 (0.07-0.23)	87.5 (76.6-93.2)
Severe RSV-related LRTI with oxygen support								
Intention-to-treat analysis†	10	851	207.03	15	9408	1877.71	0.13 (0.06-0.31)	86.9 (69.1-94.2)
Sensitivity analysis‡	11	855	207.55	13	9404	1877.64	0.10 (0.04-0.23)	90.0 (76.6-95.7)
Severe RSV-related LRTI with intensive care unit admission	0	851	207.03	10	9408	1877.71	NA	NA
Severe RSV-related LRTI with non-invasive mechanical ventilation	0	851	207.03	7	9408	1877.71	NA	NA
Severe RSV-related LRTI with invasive mechanical ventilation	0	851	207.03	0	9408	1877.71	NA	NA
All-cause LRTI hospitalisation	43	826	206.80	150	9237	1861.84	0.31 (0.22-0.44)	69.2 (55.9-78.0)
All-cause hospitalisations	77	817	205.81	289	9072	1840.74	0.34 (0.26-0.44)	66.2 (56.0-73.7)

LRTI=lower respiratory tract infection. NA=not applicable. RSV=respiratory syncytial virus. *Nirsevimab effectiveness was estimated from incidence rate ratios calculated using Poisson regression models, which were adjusted for enrolment group (catch-up and seasonal), sex, and health district area. Only patients with non-zero follow-up time were included. †For the main analysis (intention-to-treat analysis), any event that took place after immunisation with nirsevimab was considered a case; all analyses were done in this population unless otherwise indicated. ‡For the sensitivity analysis, after the reviewers' and expert advisory committee's assessment of the event's relation to RSV infection and considering the definition of breakthrough cases, patients immunised but not meeting these criteria were allocated to the non-nirsevimab group. §All-cause hospitalisations include non-LRTI hospitalisations.

Table 2: Nirsevimab effectiveness against NIRSE-GAL study endpoints estimated in infants for the first 3 months of the 2023-24 vaccination campaign using Poisson regression models

Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study

Sonia Ares-Gómez*, Narmeen Mallah*, Maria-Isolina Santiago-Pérez*, Jacobo Pardo-Seco*, Olalla Pérez-Martínez, María-Teresa Otero-Barris, Nuria Suárez-Gaiche, Rolf Kramer, Jing Jin, Leticia Platero-Alonso, Rosa-Maria Álvarez-Gil, Olga-Maria Ces-Ozores, Victoria Nartallo-Penas, Susana Mirás-Carballid, Marta Piñeiro-Sotelo, Alberto Malvar-Pintos, Juan-Manuel González-Pérez, Carmen Rodríguez-Tenreiro-Sánchez, Irene Rivero-Calle, Antonio Salas, Carmen Durán-Panoranda, Federico Martínón-Torres,* on behalf of the NIRSE-GAL study group

Summary
Background Galicia (Spain) was one of the first regions worldwide to incorporate nirsevimab for universal respiratory syncytial virus (RSV) prophylaxis in infants into its immunisation programme. The NIRSE-GAL longitudinal population-based study aimed to assess nirsevimab effectiveness in preventing hospitalisations (ie, admittance to hospital).

Method: The 2023-24 immunisation campaign with nirsevimab in Galicia began on Sept 25, 2023, and concluded on March 31, 2024. The campaign targeted three groups: infants born during the campaign (seasonal group), infants younger than 6 months at the start of the campaign (catch-up group), and infants aged 6-24 months with high-risk factors at the start of the campaign (high-risk group). Infants in the seasonal group were offered immunisation on the first day of life before discharge from hospital. Infants in the catch-up and high-risk groups received electronic appointments to attend a public hospital or health-care centre for nirsevimab administration. For this interim analysis, we used data collected from Sept 25 to Dec 31, 2023, from children born up to Dec 15, 2023. Data were retrieved from public health registries. Nirsevimab effectiveness in preventing RSV-associated lower respiratory tract infection (LRTI) hospitalisations; severe RSV-related LRTI requiring intensive care unit admission, mechanical ventilation, or oxygen support; all-cause LRTI hospitalisations; and all-cause hospitalisations was estimated using adjusted Poisson regression models. Data from five past RSV seasons (2016-17, 2017-18, 2018-19, 2019-20, and 2022-23), excluding the COVID-19 pandemic period, were used to estimate the number of RSV-related LRTI hospitalisations averted along with its IQR. The number needed to immunise to avoid one case in the 2023-24 season was then estimated from the averted cases. Nirsevimab safety was routinely monitored. The NIRSE-GAL study protocol was registered on ClinicalTrials.gov (NCT06180993), and follow-up of participants is ongoing.

Conclusion: The 2023-24 immunisation campaign with nirsevimab in Galicia began on Sept 25, 2023, and concluded on March 31, 2024. The campaign targeted three groups: infants born during the campaign (seasonal group), infants younger than 6 months at the start of the campaign (catch-up group), and infants aged 6-24 months with high-risk factors at the start of the campaign (high-risk group). Infants in the seasonal group were offered immunisation on the first day of life before discharge from hospital. Infants in the catch-up and high-risk groups received electronic appointments to attend a public hospital or health-care centre for nirsevimab administration. For this interim analysis, we used data collected from Sept 25 to Dec 31, 2023, from children born up to Dec 15, 2023. Data were retrieved from public health registries. Nirsevimab effectiveness in preventing RSV-associated lower respiratory tract infection (LRTI) hospitalisations; severe RSV-related LRTI requiring intensive care unit admission, mechanical ventilation, or oxygen support; all-cause LRTI hospitalisations; and all-cause hospitalisations was estimated using adjusted Poisson regression models. Data from five past RSV seasons (2016-17, 2017-18, 2018-19, 2019-20, and 2022-23), excluding the COVID-19 pandemic period, were used to estimate the number of RSV-related LRTI hospitalisations averted along with its IQR. The number needed to immunise to avoid one case in the 2023-24 season was then estimated from the averted cases. Nirsevimab safety was routinely monitored. The NIRSE-GAL study protocol was registered on ClinicalTrials.gov (NCT06180993), and follow-up of participants is ongoing.

Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study

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2023/ 2024 immunization campaign in Spain wherein 9408 infants received Nirsevimab

	Immunised infants (n=145 087)		Non-immunised infants (n=9086)		Effectiveness of nirsevimab (95% CI)
	Events	Person-years	Events	Person-years	
RSV-related LRTI hospitalisation	957	72 128·31	327	5787·48	76·41% (72·57–79·72)
RSV-related ICU hospitalisation	189	72 479·82	81	5789·00	84·94% (79·47–88·95)
All-cause LRTI hospitalisation*	1689	71721·89	438	5776·54	66·50% (61·97–70·50)
All-cause hospitalisation†	6714	66 897·67	1776	5830·63	47·90% (44·35–51·21)

Effectiveness of nirsevimab was estimated using the stratified Cox proportional hazards model with time-variant covariates (including age, sex, gestational age in weeks, region, and rurality). Computation of effectiveness against RSV-related LRTI (requiring ICU or not) excluded 240 additional participants, all-cause LRTI excluded 390, and all-cause hospitalisation excluded 4194 from the seasonal cohort who had the corresponding outcome between Oct 1, 2023, and April 1, 2024. Patients with non-zero follow-up time were included. ICU=intensive care unit. LRTI=lower respiratory tract infection. RSV=respiratory syncytial virus. *Including hospitalisations with primary ICD-10 diagnosis codes J-209 to J-229 and those associated with RSV. †Including hospitalisations unrelated to RSV.

Table 2: Primary and secondary endpoints

Effectiveness and impact of nirsevimab in Chile during the first season of a national immunisation strategy against RSV (NIRSE-CL): a retrospective observational study



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Summary

Background Nirsevimab for the prevention of respiratory syncytial virus (RSV) was introduced in some countries in the northern hemisphere in 2023. Chile was the first to implement a universal strategy in the southern hemisphere. We aimed to evaluate the effectiveness and impact of nirsevimab during the 2024 RSV season in Chile.

Methods Roll-out of the strategy began on April 1, 2024, and ended on Sept 30, 2024, targeting infants born between April 1, 2024, and Sept 30, 2024 (seasonal newborn cohort), and infants born between Oct 1, 2023, and March 31, 2024 (catch-up cohort). Using historical surveillance and hospital discharge data from ten hospitals that perform universal RSV testing for all patients admitted due to lower respiratory tract infection (LRTI), we identified a set of ICD-10 codes most closely related to RSV admissions during the 2019, 2022, and 2023 RSV seasons. These codes were applied to a national database of three consolidated nationwide government registries to identify RSV-related LRTI hospitalisations (primary endpoint) among infants who received or did not receive nirsevimab. Secondary endpoints were RSV-related intensive care unit (ICU) admission, all-cause LRTI hospitalisation, and all-cause hospitalisation occurring at least 7 days after birth. Nirsevimab effectiveness was estimated using a stratified Cox proportional

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[https://doi.org/10.1016/S1473-3099\(25\)00314-7](https://doi.org/10.1016/S1473-3099(25)00314-7)

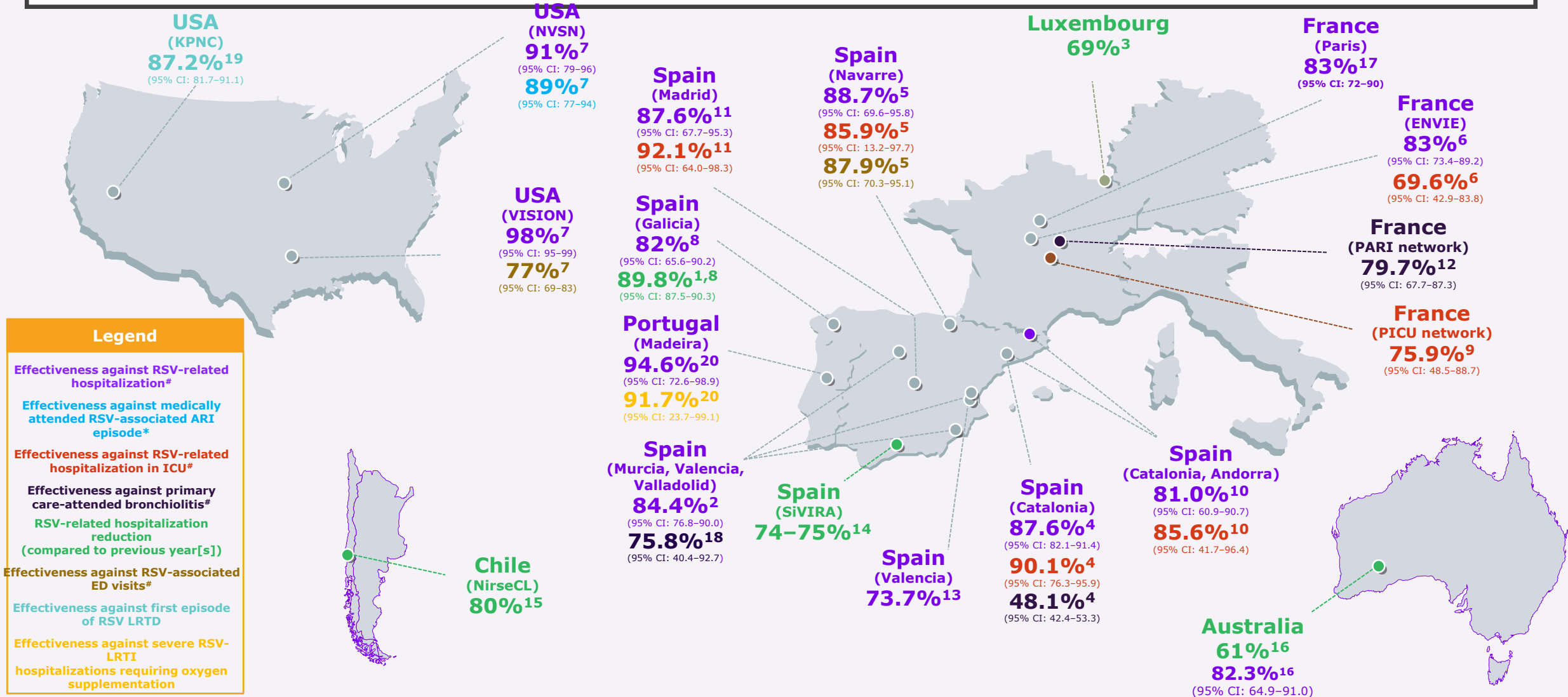
*Contributed equally

For the Spanish translation of the abstract see Online for appendix 1

Departamento de Pediatría y Cirugía Infantil, Facultad de Medicina (J P Torres MD PhD),

NNI of 1 in 35

SUMMARY OF REAL-WORLD IMPACT ON RSV-RELATED OUTCOMES



NIRSE-CL STUDY



A retrospective observational study during the first season of a national immunization strategy against RSV in Chile

Objectives

- To evaluate the effectiveness and impact of nirsevimab during the 2024 RSV season in Chile

Outcomes

Primary:

- RSV-related LRTI hospitalization

Secondary:

- Severe RSV-related LRTI hospitalization requiring ICU admission (RSV-related ICU admission)
- All-cause LRTI hospitalization
- All-cause hospitalization occurring at least 7 days after birth

Methods

- Roll-out of the national campaign from April 1, 2024 to Sept 30, 2024, communication campaign led by the MOH
- Targeted groups:
 - **Seasonal newborn cohort** (infants born April 1 2024 - Sept 30 2024), immunized at birth before hospital discharge
 - **Catch-up cohort** (infants born Oct 1 2023 - March 31 2024), immunized in vaccination centers
 - **High risk cohort:** infants with high-risk conditions who previously would have been eligible for palivizumab (*not included in analysis*)

Statistical Analysis

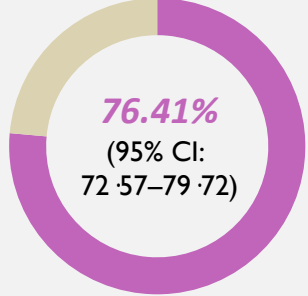
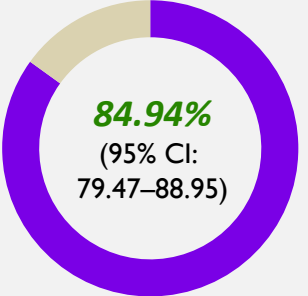
- All eligible infants with **complete data on RSV-associated LRTI hospitalization** episodes were considered in the primary endpoint analysis
- Eligible infants in the were followed up from birth (seasonal cohort) or from the beginning of the campaign (catch-up cohort) until the first occurrence of the outcome, death, or end of the immunization strategy, whichever occurred first
- Nirsevimab effectiveness was determined by estimating the HR between immunized and nonimmunized infants

NIRSE-CL STUDY



Effectiveness of nirsevimab against RSV-related LRTI and ICU hospitalizations

Coverage rates ²	Newborns [†]	Infants (catch-up) [‡]
	97.3%	90.4%

	Immunized infants (n=145,087)		Non-immunized infants (n=9,086)		Effectiveness of nirsevimab (95% CI)		
	Events	PY	Events	PY			
RSV-related LRTI hospitalization	957	72,128.31	327	5,787.48	76.41% (72.57–79.72)		<i>effective against RSV-related LRTI hospitalization</i>
RSV-related ICU hospitalization	189	72,479.82	81	5,789.00	84.94% (79.47–88.95)		<i>Effective against RSV-related ICU hospitalization</i>
All-cause LRTI hospitalization*	1689	71,721.89	438	5,776.54	66.50% (61.97–70.50)		
All-cause hospitalization [†]	6714	66,897.67	1776	5,830.63	47.90% (44.35–51.21)		

The estimated **effectiveness of nirsevimab** against RSV-related LRTI hospital admissions are **76.41%** and **84.94%** for severe RSV-related ICU admissions

NIRSE-GAL STUDY: RATIONALE

NIRSE-GAL study

- Prospective, population-based, longitudinal study in Galicia, Spain
- Galicia: One among the first globally to introduce nirsevimab as universal RSV prophylaxis in infants within National Immunization Program
- 3-year follow-up period (2023-2026)
- Aims: Assess nirsevimab effectiveness in preventing hospitalizations
- Impact assessed by comparing post-implementation data with historical cohorts (2016–2023)

First-season findings (2023-2024)

- Reductions observed:
 - 89.2% in RSV-related LRTI hospitalizations
 - 95.2% among seasonally born infants
- NNI to prevent one RSV-related LRTI hospitalization:
 - 30 overall
 - 16 for seasonally born infants

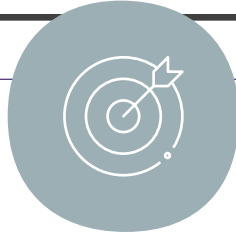
- Although the first-season effectiveness of nirsevimab is well established, evidence characterizing its impact on hospitalization and primary-care outcomes during the second RSV season remains limited.

IMPACT OF UNIVERSAL NIRSEVIMAB PROPHYLAXIS IN INFANTS ON HOSPITAL AND PRIMARY CARE OUTCOMES ACROSS TWO RESPIRATORY SYNCYTIAL VIRUS SEASONS IN GALICIA, SPAIN (NIRSE-GAL): A POPULATION-BASED PROSPECTIVE OBSERVATIONAL STUDY

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ACROSS TWO SEASONS



The objective of this publication was to assess the **medium-term impact** of universal infant RSV prophylaxis with **nirsevimab** across **inpatient and outpatient settings** during **two consecutive RSV seasons**

Impact of universal nirsevimab prophylaxis in infants on hospital and primary care outcomes across two respiratory syncytial virus seasons in Galicia, Spain (NIRSE-GAL): a population-based prospective observational study



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Summary

Background Real-world evidence on nirsevimab impact beyond the first season when given under universal immunisation programmes is emerging. We aimed to assess the medium-term impact of universal infant respiratory syncytial virus (RSV) prophylaxis with nirsevimab across inpatient and outpatient settings during two consecutive RSV seasons.

Methods NIRSE-GAL is an ongoing, population-based, prospective, longitudinal study in Galicia, Spain. For this study, we included all infants eligible for nirsevimab in the 2023–24 RSV campaign in Galicia, followed up from their first RSV season (2023–24) until the end of their second RSV season (2024–25). The primary endpoint was RSV-related lower respiratory tract infection (LRTI) hospitalisation. Secondary endpoints were LRTI hospitalisation, acute bronchitis or bronchiolitis and pneumonia admissions, all-cause hospitalisations, and primary health-care outcomes (acute bronchitis or bronchiolitis, wheezing or asthma, LRTI, respiratory infections, acute otitis media, and all otitis diagnoses). The first recurrences of these endpoints were also assessed as secondary endpoints. Impact was estimated by Poisson regression models using weekly incidence rates of historical non-pandemic seasons (2017–18 to 2022–23) as comparators, adjusted for RSV seasonality, and evaluated across three follow-up periods: the first RSV season, the second RSV season, and up to 18 months. This study is registered with ClinicalTrials.gov, NCT06180993.

Findings Of 12 492 eligible infants, 11 796 received nirsevimab (94·4% coverage). Compared with historical cohorts, RSV-related LRTI hospitalisations decreased by 85·9% (95% CI 80·2–90·0) in the first season and 55·3% (22·5–74·3) in the second, with an estimated 123 infants needing to be immunised to prevent a second-season admission. First LRTI hospitalisations decreased by 59·8% (46·5–69·8) in the first season and 48·1% (33·1–59·7) over 18 months. Acute bronchitis or bronchiolitis admissions decreased by 59·0% (37·9–72·9) in the first season and 58·7% (40·6–71·3) over 18 months. All-cause hospitalisation declined by 20·3% (3·1–34·4) in the first season, with no significant reduction thereafter. First recurrent admissions in the second season decreased by 78·2% (25·6–93·6) for RSV-related LRTI, 62·4% (30·9–79·6) for LRTI, and 76·9% (5·3–94·4) for acute bronchitis or bronchiolitis. First outpatient visits declined during the first season for bronchitis or bronchiolitis (30·8% [17·5–41·9]), LRTI (33·4% [21·6–43·4]), and wheezing or asthma (27·7% [14·9–38·5]). First recurrent outpatient visits also declined, by 52·5% (39·7–62·6) for acute bronchitis or bronchiolitis, 28·2% (17·8–37·3) for wheezing or asthma, and 47·3% (35·3–57·2) for LRTI.

Interpretation Universal infant nirsevimab prophylaxis markedly reduced RSV-related hospitalisations and outpatient morbidity, with sustained reductions in RSV-related LRTI hospitalisations into the second season and no signal of adverse shift in RSV morbidity. These findings provide robust population-level evidence that could be valuable for infant immunisation policies and cost-effectiveness models.

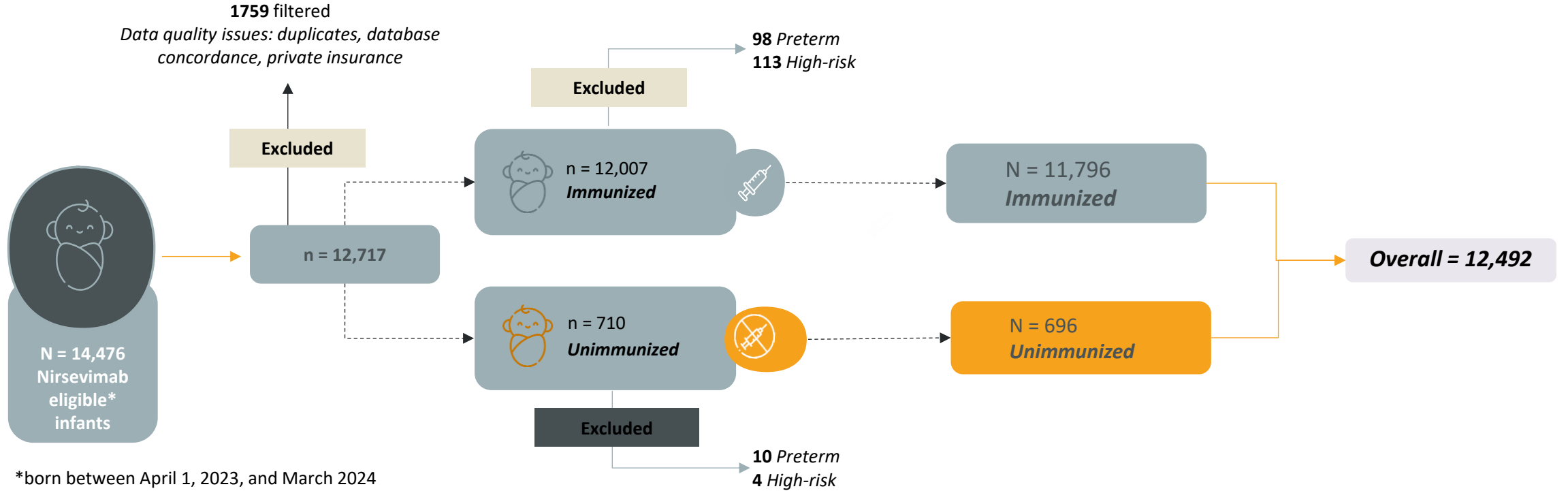
Lancet Infect Dis 2026

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For the Spanish translation of the abstract see Online for appendices

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STUDY DESIGN



Nirsevimab-eligible infants were classified into two cohorts:

- *Seasonal cohort* (infants born during the nirsevimab campaign)
- *Catch-up cohort* (infants <6 months at campaign start, including high-risk infants)

Statistical analysis

- RSV seasonality adjusted using polynomial time-trend models
- Impact assessed using Poisson regression models comparing weekly incidence in nirsevimab-eligible cohort (2023-24) with non-immunized historical cohorts (2016-2023)

CONCLUSION

Universal infant prophylaxis → reduction in first and recurrent admissions and outpatient visits for acute bronchitis/bronchiolitis and LRTI during infants' first RSV season



Reduced RSV-related LRTI hospitalizations
sustained across 2 seasons 85.9% (first season) and 55.3% (second season)



Reduced all-cause hospitalizations
by ~20% during the first season



Lowered primary care visits for acute bronchitis/bronchiolitis, wheezing/asthma, and LRTI by ~30% during the first season



No signal of disease enhancement or severity shift during the second season

EFFECTIVENESS OF NIRSEVIMAB AGAINST RSV AND RSV-RELATED EVENTS IN INFANTS (BEAR STUDY)



Amber Hsiao, John Hansen, Bruce Fireman,
Julius Timbol, Ousseney Zerbo, Karine Mari,
Christopher Rizzo, William La Via, Ruvim Izikson, Nicola P. Klein

Hsiao A, et al. *Pediatrics*. 2025;156(2):e2024069510.
Available at: <https://doi.org/10.1542/peds.2024-069510>.

BEAR STUDY

- **Study objective**

- To evaluate the real-world effectiveness of *nirsevimab* against **PCR-confirmed RSV-LRTD and RSV-associated healthcare utilization** in healthy term infants at Kaiser Permanente Northern California during 2023–2024 RSV season


n = 49,680
KPNC infants
born between
April 1, 2023,
and April 30,
2024

Among immunized infants



45.3%

Immunized in November



30.8%

Immunized in December

Hospitalization

89%

OR: 0.11
(0.01–0.85)
 $P = 0.035$

ED visits

70%

OR: 0.30
(0.13–0.67)
 $P = 0.003$

**Reduction in odds among infants with
RSV-LRTD episode (95% CI)**

SUMMARY



Reduction in **RSV-LRTD** by **87.2%** ($P < 0.0001$)



Reduction in **RSV-LRTD hospitalization** by **98.0%** ($P < 0.0001$)



Reduction in any PCR-confirmed **RSV infection (with or without LRTD)** by **71.0%** ($P < 0.0001$)



Among infants with RSV-LRTD, **fewer medical encounters and lower odds of hospitalization**

RWE SUMMARY OF RSV-RELATED OUTCOMES



>400,000*

Infants who received nirsevimab have been included in RWE studies, with **many more RWE studies planned and ongoing**



>50*

publications on uptake, effectiveness, and public health impact of nirsevimab

A large body of RWE is available for nirsevimab, demonstrating efficacy against RSV-related hospitalization, ICU admission, and LRTI incidence

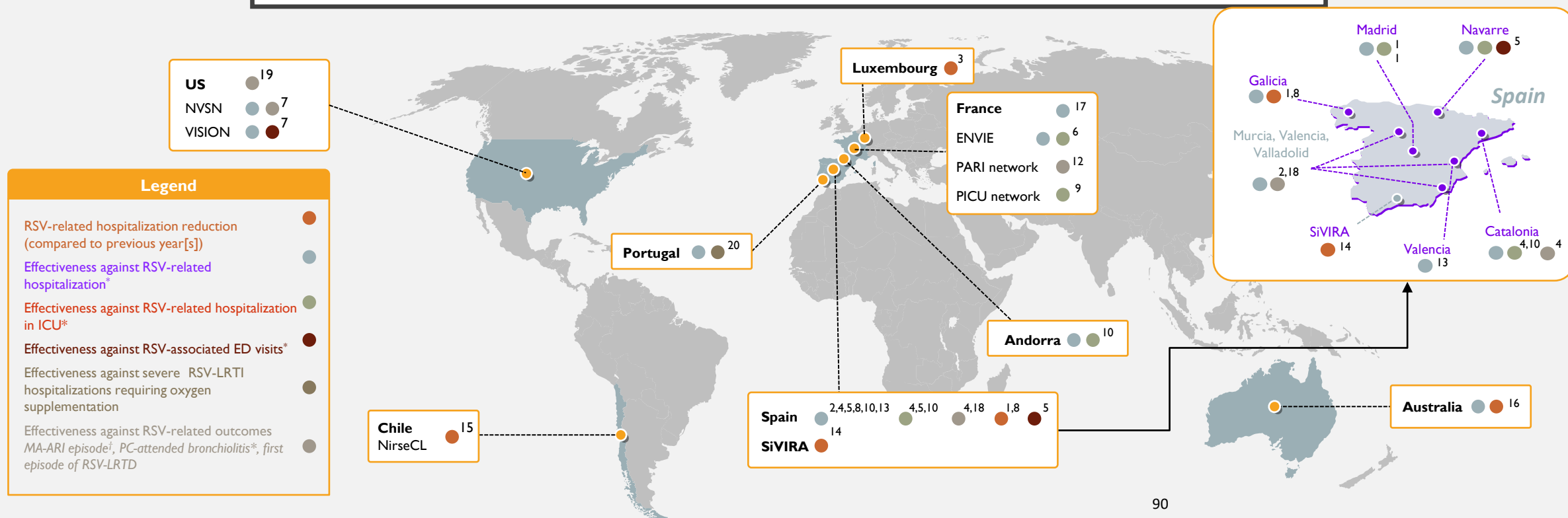
RWE confirms the effectiveness of nirsevimab to prevent RSV LRTD in infants and demonstrates the public health impact that RSV prevention for the broad infant population can have

* As of July 2025

ICU, intensive care unit; LRTD, lower respiratory tract disease; LRTI, lower respiratory tract infection; RSV, respiratory syncytial virus; RWE, real-world evidence.

References: 1. Data on file, Sanofi. 2.Sumsuzzman D, et al. *Lancet*. 2025. DOI: 10.1016/S2352-4642(25)00093-8.

SUMMARY OF REAL-WORLD IMPACT ON RSV-RELATED OUTCOMES



EFFECTIVENESS AGAINST RSV-RELATED HOSPITALIZATIONS



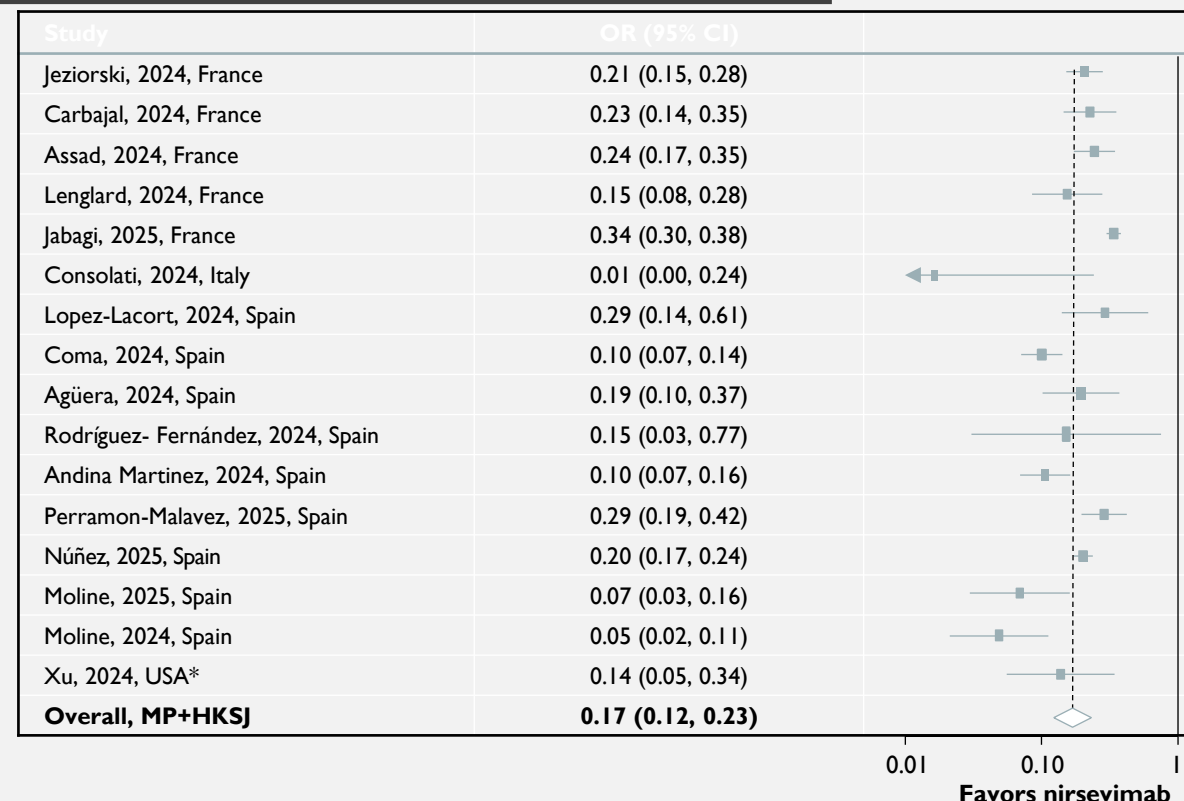
Nirsevimab is **83% effective**

(OR: 0.17, 95% CI: 0.12–0.23, $p < 0.0001$)

against **reducing** the risk of

RSV-related hospitalizations

- **Nirsevimab** group = **1,585 events**, among 85,242 infants
- **Control** group = **3,978 events**, among 51,893 infants



Nirsevimab demonstrated consistent reduction in the risk of RSV-related hospitalization in infants who received nirsevimab, compared with those that did not receive nirsevimab

Overall, 16 studies reported data on RSV-related hospitalizations in infants aged 0–12 months

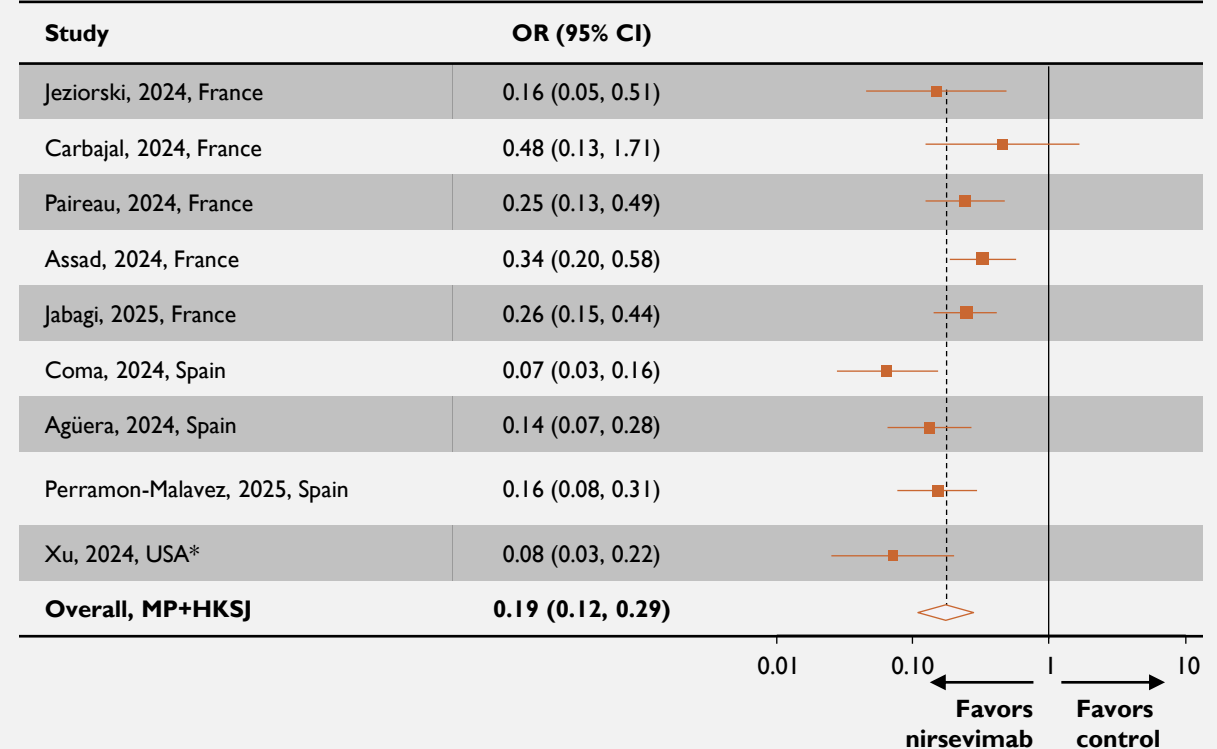
EFFECTIVENESS AGAINST RSV-RELATED ICU ADMISSIONS



Nirsevimab is **81% effective**
(OR: 0.19, 95% CI: 0.12–0.29, $p < 0.0001$)
against **reducing** the risk of
RSV-related ICU hospitalizations

- **Nirsevimab** group = **176 events**, among 79,545 infants
- **Control** group = **618 events**, among 48,023 infants

Effectiveness of nirsevimab in reducing RSV-related ICU admissions



Nirsevimab demonstrated consistent reduction in the risk of ICU admission in infants who received nirsevimab, compared with those that did not receive nirsevimab

Overall, 9 studies reported data on RSV-related ICU admissions in infants aged 0-12 months

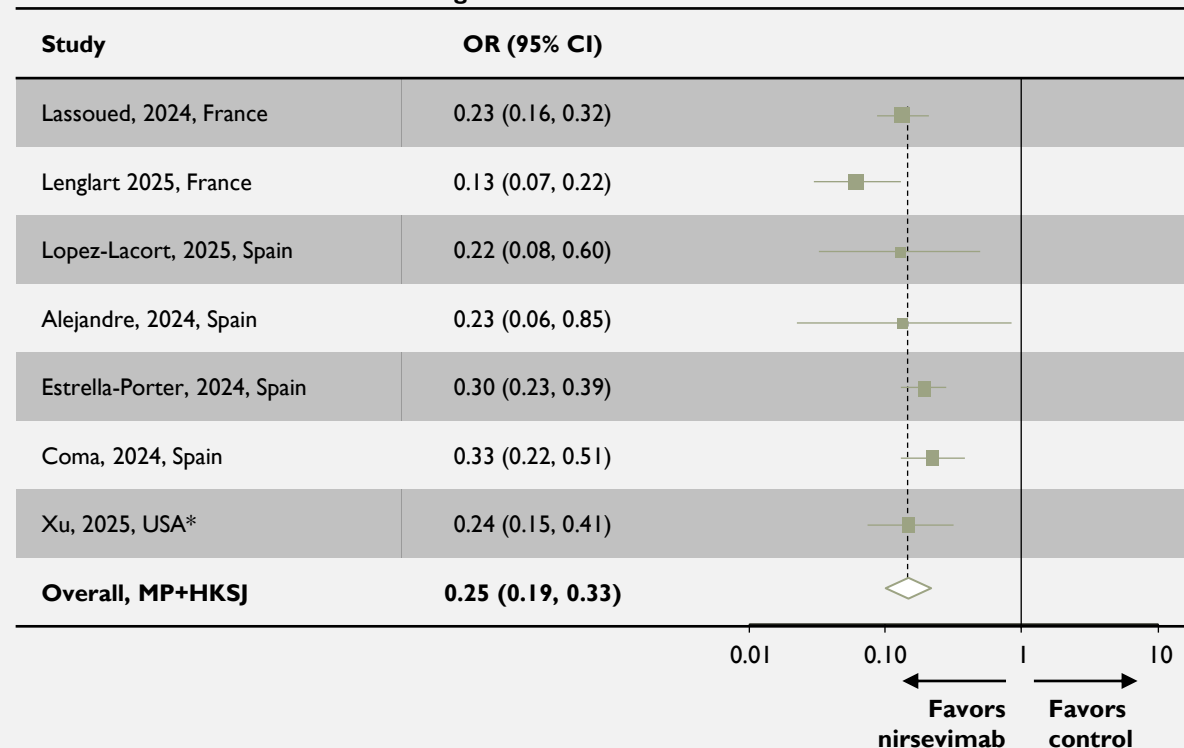
EFFECTIVENESS AGAINST RSV-RELATED LRTI INCIDENCE



Nirsevimab is **75% effective**
(OR: 0.25, 95% CI: 0.19–0.33, $p < 0.0001$)
against **reducing** the risk of
RSV-related LRTI incidence

- **Nirsevimab** group = **392 events**, among 48,303 infants
- **Control** group = **1,049 events**, among 9,569 infants

Effectiveness of nirsevimab in reducing RSV-related LRTI incidence



Nirsevimab demonstrated consistent reduction in the risk of RSV-related LRTI incidence in infants who received nirsevimab, compared with those that did not receive nirsevimab

Overall, 7 studies reported data on RSV-related LRTI incidence in infants aged 0-12 months

SUMMARY

01

Nirsevimab was *received by 3961 infants* during its clinical development program and *demonstrated efficacy and a favorable safety profile*

02

Since nirsevimab has been approved, *>50* studies on uptake, effectiveness, and public health impact* have been published *including >400,000* nirsevimab recipients*

04

In a recent population-based study, *the risk of wheezing was reduced in infants that had received nirsevimab* compared to those that did not

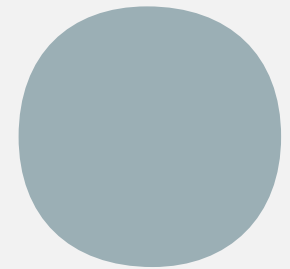
03

Real-world evidence confirms the *effectiveness of nirsevimab against RSV-related hospitalizations, ICU admissions, and LRTI incidence*



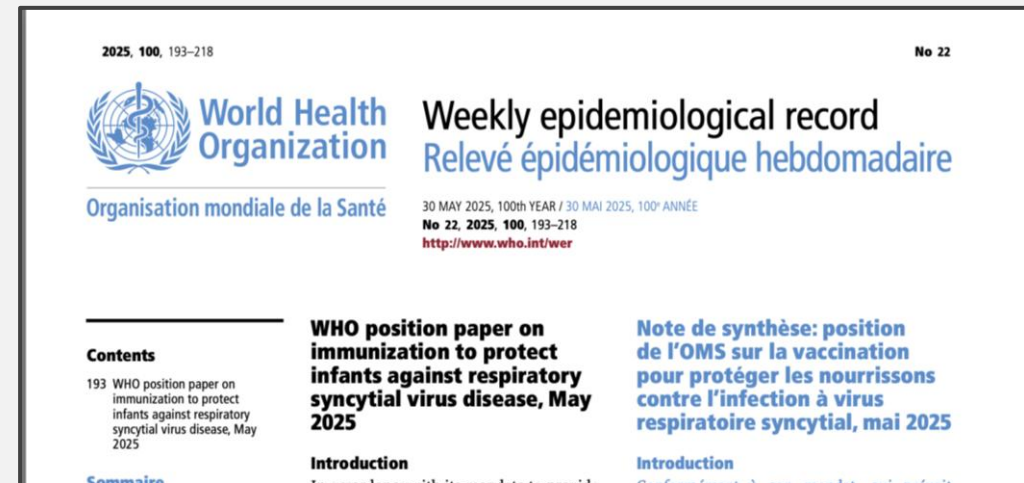


RECOMMENDATIONS



WHO STRATEGIC ADVISORY GROUP OF EXPERTS (SAGE) ON IMMUNIZATION SEPT 2024

- All countries should introduce passive immunization for the prevention of severe RSV disease in young infants
- Decisions to include the maternal RSV vaccine and/or the long-acting monoclonal antibody would need to consider the cost, financing, supply, anticipated coverage and feasibility
- Single dose of maternal RSV vaccine should be administered in the third trimester of pregnancy and post-marketing surveillance would be necessary



Expanding the reach of RESPIRATORY SYNCYTIAL VIRUS disease prevention

New immunization tools to protect in early life

Respiratory syncytial virus (RSV) is a major, under-recognized public health problem causing more severe respiratory infections and hospitalizations in infants and young children each year than any other pathogen. Now, new tools for early RSV prevention are licensed and globally recommended—meaning the chance to address this pervasive virus has never been better.

What is RSV and its disease burden?

Virtually everyone gets RSV, usually by age 2. RSV disease is often mild, like a cold, but can be severe (or deadly) for young children. Though an child can get severely ill or hospitalized due to RSV, infants are the most vulnerable due to easily blocked small airways. Serious complications include bronchiolitis and pneumonia and can harm lung health long term. RSV can occur seasonally in many areas and year-round in others.

A communications toolkit is available to help you learn more about RSV prevention and spread the word.
bit.ly/RSVInfoToolkit





Maternal vaccine



Monoclonal antibody

RATIONALE

Vaccination in pregnancy can directly enhance the pregnant vaccinee's immunity and increase natural antibody transfer to baby across the placenta for protection in early life.

Directly immunizing infants soon after birth or before/during first RSV season provides antibodies for critical protection in early life.

HOW IT WORKS

Pre-F protein in the vaccine induces antibodies that neutralize the virus.

mAbs are manufactured antibodies to the RSV pre-F protein that neutralize the virus.

TIMING

Defined vaccination window needed to optimize protection for infant. (WHO recommends 3rd trimester of pregnancy as defined in local context. Windows can vary by regulatory authority and country.)

At birth with other birth dose vaccinations (e.g., hepatitis B; BCG, OPV) or before/during the infant's first RSV season.

PRODUCT CHARACTERISTICS

- Given in one dose
- At least 5-6 months protection after birth

- Given in one dose
- At least 5-6 months protection after administration (longer lasting than palivizumab)

	Likely advantages	Possible challenges
Maternal vaccine	<ul style="list-style-type: none"> Existing tetanus and other maternal immunization programs may be leveraged Offering RSV vaccine during ANC may also benefit ANC coverage, uptake, and perceived quality of care Vaccine safety monitoring systems could also track pregnancy and other maternal/child health outcomes 	<ul style="list-style-type: none"> ANC/EPI coordination and readiness needs may be uncharted in some countries Reaching pregnant patients in specific vaccine-eligible gestational age windows Missing protection of infants born before the vaccine-eligible window begins Expanding pregnancy registry surveillance/linking mother-infant records
Long acting mAbs	<ul style="list-style-type: none"> Delivered similarly to BCG, hepatitis B, OPV birth doses Intramuscular injection, like many vaccines Robust immunization infrastructure/systems in place Skilled workforce familiar with nuances of immunization 	<ul style="list-style-type: none"> Identifying and reaching infants born outside formal healthcare settings mAbs may be new policy and regulatory territory for some countries Cost and supply barriers to access
Common across products	<ul style="list-style-type: none"> Both products will protect babies during the most critical first six months of life Provide passive protection against RSV Only one dose needed, which simplifies delivery Potential to be cost-effective in low- and middle-income economies (context dependent) 	<ul style="list-style-type: none"> Awareness gaps or reluctance/hesitancy may affect demand/acceptability/uptake Additional services may strain health system components Seasonal dosing could be logistically challenging Competing immunization and MCH program priorities



HEALTHCARE DELIVERY

The dawn of preventing respiratory syncytial virus lower respiratory tract infections in children

Z Dangor,¹ MMed (Paed), PhD ; S A Madhi,¹ MMed (Paed), PhD ; H J Zar,² FC Paed (SA), PhD ;
D Demopoulos,³ MMed (Paed)  on behalf of the South African Paediatrics Association*

¹ South African Medical Research Council Vaccines and Infectious Diseases Analytics Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

² Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, and South African Medical Research Council Unit on Child and Adolescent Health, Faculty of Health Sciences, University of Cape Town, South Africa

³ Department of Critical Care, Wits Donald Gordon Medical Centre and Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

* South African Paediatrics Association Executive: Chairperson: Despina Demopoulos, Secretary: Lindo Radebe, Treasurer: Andrew Redfern, Ex Officio: Ziyaad Dangor, Executive Members: Mignon McCulloch, Mark Atkins, Martie Wege, Shaegan Irusen, Samina Yakoob, Zinhle Vilakazi

Corresponding author: Z Dangor (ziyaad.dangor@wits.ac.za)

RSV SA



Palivizumab

Effectiveness

- 51% (RR 0.49, 95%CI: 0.37-0.64) against RSV hospitalization
- ~80% in high-risk groups

Nirsevimab

Efficacy

- 78.4% (95% CI: 51.9–90.3) in 29 to <35 weeks
- 76.8% (95% CI: 49.4–89.4) in near term or term infants

OPPORTUNITIES

Recommended by AAP for infants <12-months of age that have/are

- <29 weeks gestation,
- CHD - haemodynamically significant lesions,
- CLD of prematurity

- IMI, single dose (long-acting)
- Can be administered simultaneously with other childhood vaccines
- Affordable to medical aids (\$200-\$500)
- Useful in circumstances where mother did not receive vaccine or in cases of preterm infants

LIMITATIONS IN SA CONTEXT

- Cost (\$3000-\$12000)
- Logistical monthly dosing during RSV season

- Unlikely to be affordable by state unless limited to high-risk groups
- Delivery platform needs to be determined



Maternal Bivalent RSV prefusion F protein-based vaccine

Efficacy

VE for severe medically attended RSV-LRTI:

- 81.8% (95% CI: 40.6–96.3) at 90 days after birth
- 69.4% (95% CI: 44.3–84.1) at 180 days after birth

OPPORTUNITIES

- Single dose to pregnant women
- Cost \$20
- Cost effective
- Driven through antenatal platform with Tdap

LIMITATIONS IN SA CONTEXT

- Reduced transplacental transfer in HIV-infected women
- Safety surveillance
- Willingness of pregnant people to accept multiple vaccines in pregnancy

JOINT STATEMENT

Joint statement for the prevention of RSV in young infants in South Africa

Despina Demopoulos¹, Nicolette du Plessis², Amy Wise³, Refiloe Masekela*^{4,5} and Ziyaad Dangor*⁶

Supported by the South Africa Paediatric Association, South African Thoracic Society, Southern African Society for Paediatric Infectious Diseases, and South African Society of Obstetrics and Gynaecology.

¹ Wits Donald Gordon Medical Centre, University of the Witwatersrand, Faculty of Health Sciences, Johannesburg, South Africa.

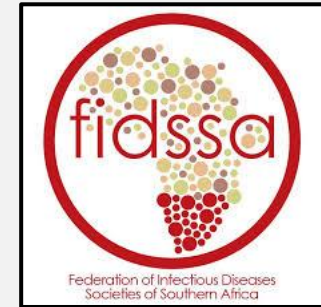
² Department of Paediatrics, University of Pretoria and Kalafong Provincial Tertiary Hospital, Gauteng, South Africa.

³ Department of Obstetrics and Gynaecology, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.

⁴ Department of Paediatrics and Child Health, Nelson R Mandela School of Medicine, College of Health Sciences, University of KwaZulu Natal, Durban, South Africa

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⁶ South Africa Medical Research Council Vaccines and Infectious Diseases Analytics Research Unit, University of the Witwatersrand, Faculty of Health Science, Johannesburg, South Africa



Accepted for publication June 2026 AJTCCM

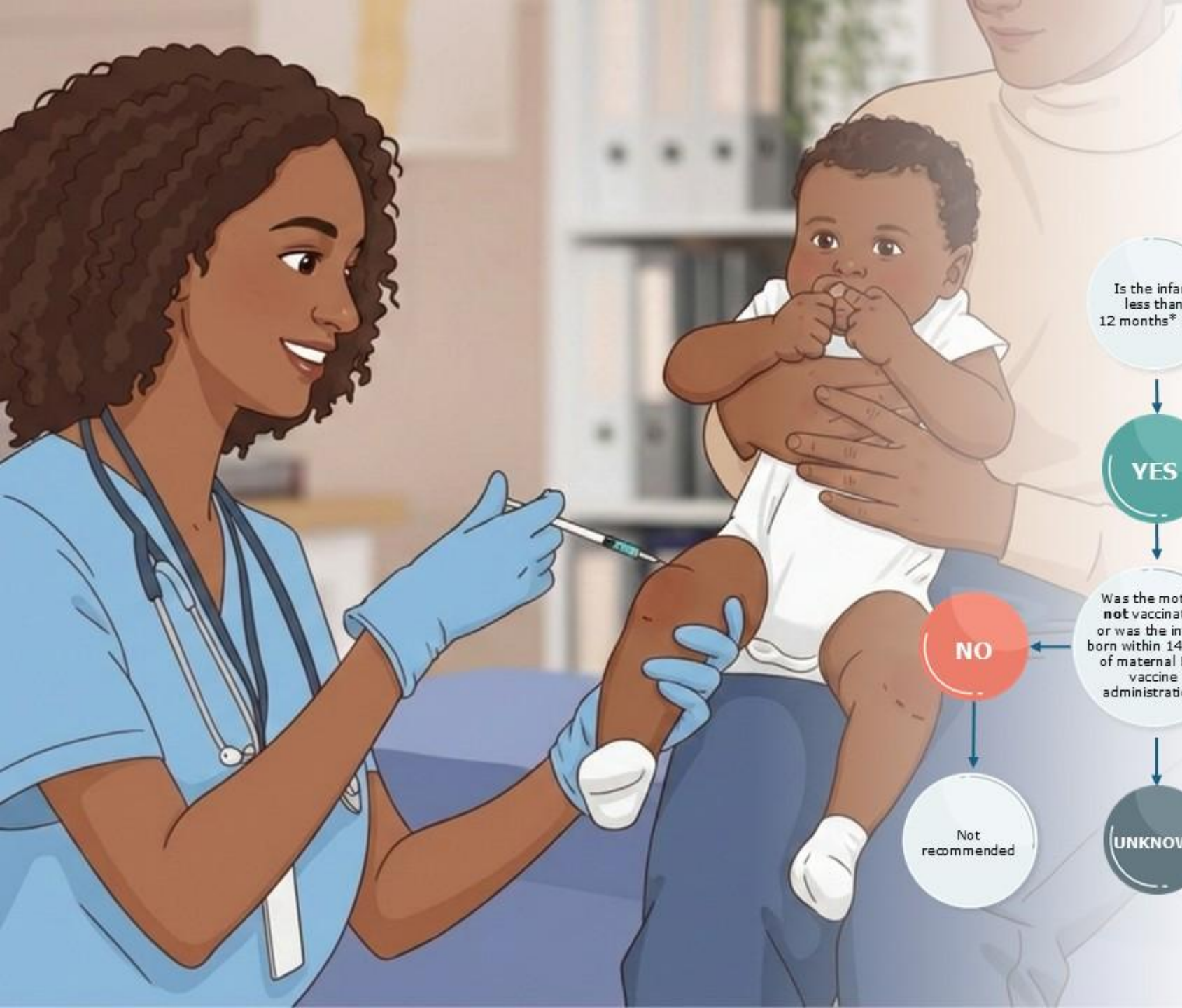


All pregnant women are to be offered the maternal RSV vaccine

all year-round

28-36 weeks' gestation

Single dose of 0.5ml IMI



Is it shortly before or during RSV season (Feb-May)?

YES

NO

Is the infant less than 12 months* old?

YES

Was the mother **not** vaccinated or was the infant born within 14 days of maternal RSV vaccine administration?

NO

Not recommended

UNKNOWN

Is the child 12-24 months** and meets the high-risk criteria?

NO

YES

What is the child's weight today?

< 5 kg

Nirsevimab 50 mg IMI stat

≥ 5 kg

Nirsevimab 100mg IMI stat

Not recommended

RECOMMENDATIONS

- RSV Maternal vaccine to all women in 3rd trimester
- Nirsevimab to infant:
 - Unvaccinated women or preterm newborns (<37 weeks), or
 - Baby is born within a month of the mother receiving her RSV vaccine
- High Risk Infant
 - congenital heart disease
 - chronic lung disease
 - HIV
 - inborn errors of immunity
 - neurological or neuromuscular disease





COMPARATIVE IMPLEMENTATION FEATURES

Country/Region	Start Season	Target Population	Delivery Strategy	Coverage	Impact/Effectiveness
Spain (Galicia, national) 	2023–24	All infants in 1st RSV season; catch-up; some HR infants up to 24m	Newborn before discharge + primary care catch-up	86–97% in-season; catch-up 45–97%	~70–90% effectiveness vs RSV hospitalisation
France 	2023–24	Infants <12m (priority newborns)	Maternity wards; outpatient for older infants (supply-limited)	Lower for non-newborns due to supply	~76–81% vs severe RSV/ICU
United States 	2023–24	Infants in 1st season; some HR infants 2nd season	Hospitals (where available) + paediatric outpatient	Pooled uptake ~51% (state variation)	~90% effectiveness vs hospitalisation (early RWE)
Chile (national) 	Winter 2024	All newborns; catch-up infants	Hospitals + national health system; integrated data	98% newborns; 83% catch-up by mid-season	~86% vs PICU; ~75% vs overall hospitalisation
Australia (WA) 	2024	All infants; HR in 2nd season	State-wide program via hospitals/clinics	Pilot/early program (regional)	Real-world reduction in RSV hospitalisations

KEY SUCCESS FACTORS FOR NIRSEVIMAB IMPLEMENTATION

SPAIN



- Strong commitment and recognition of the unmet need from **scientific & medical societies, policy makers and public health experts**
- Consider nirsevimab immunization as any other vaccine-like/immunization tool to capitalize on existing vaccination processes
- Robust information and **education campaign** to HCPs and lay public leading to a very high acceptance from the start of the program
- **Hospital-based roll-out** for babies born in season, enabling rapid immunization of the target population before the start of RSV circulation (flexible hours)

United States



- Inclusion in NIP schedule
 - Recognition of significant public health burden in infants
 - Review of data started prior to product approval
- Inclusion in **Vaccines for Children program** – government purchase program for un/under-insured
- **Flexibility** in VFC rules
 - Allowed to 'borrow' doses between private and public stock
 - Birthing hospitals don't have to stock every other vaccine
- **Rapid coverage by private insurance** (ahead of mandate)
- Coordinated educational campaign for parents and providers between CDC, AAP, and other professional societies

Luxembourg



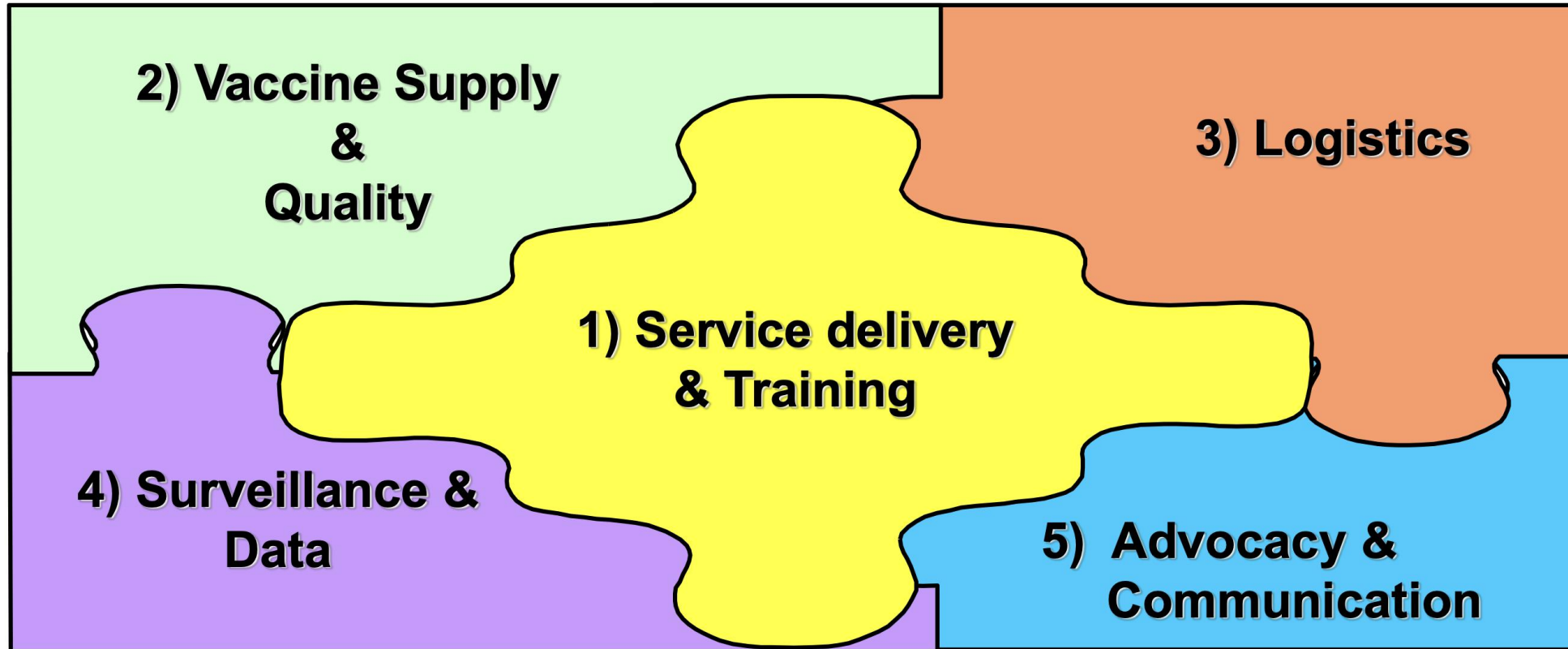
- After a surge in RSV cases and related hospitalizations in 2022, **RSV became a laboratory-notifiable infection** in Luxembourg in early 2023.
- In 2023, we observed a reduced number of hospital and PICU admissions among infants with RSV infection, while screening and admission criteria did not change. This positive development contributed to the maintenance of routine hospital planning, allowing most scheduled medical interventions to proceed as planned, in contrast to the previous year.

France



- Drug pathway was used to allow timely recommendation for implementation of nirsevimab ahead of 2023-24 RSV season
- Nirsevimab was accepted by parents in levels much higher than expected
- Interim effectiveness analysis using sentinel hospitals demonstrated public health impact on nirsevimab usage in infants
- **Government centralized purchase** (Free of charge for parents and no advanced payment for providers)
- Strong communication plan in place from DGS

5 COMPONENTS OF AN IMMUNISATION PROGRAMME



health

Department:
Health
REPUBLIC OF SOUTH AFRICA



Discovery Health's Centre for Clinical Excellence has updated the funding policy for **Beyfortus® (nirsevimab)**.

Please find a summary of our funding decision below:

Indications:

- **Beyfortus® (nirsevimab)** is indicated for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in neonates and infants during their first RSV season.

Decision:

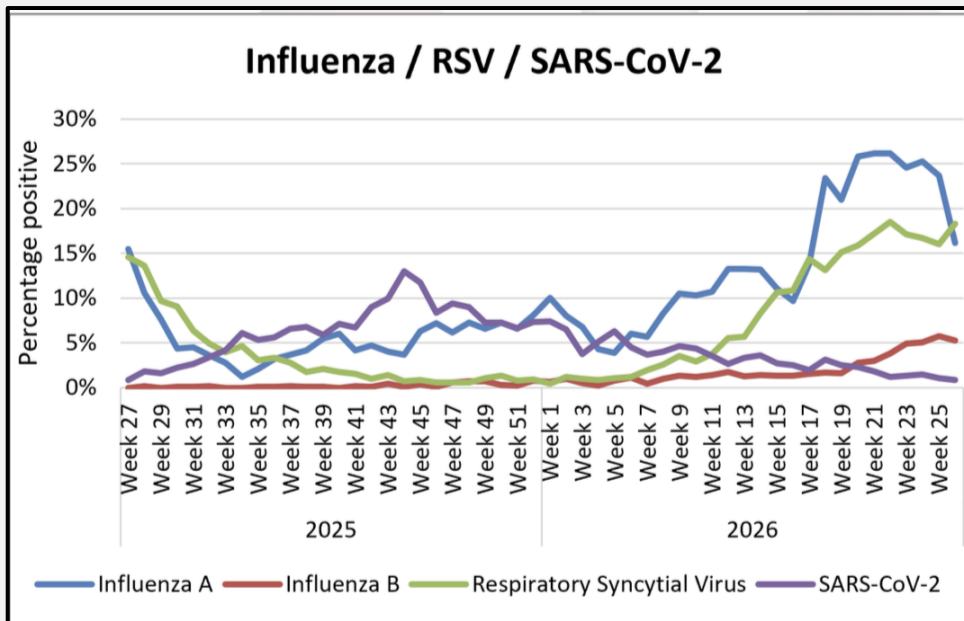
- **Beyfortus®** will be funded from the hospital benefit subject to preauthorisation and the rules of the member's chosen plan for the following eligible group:
 - Infants born during the RSV season
 - Premature and high-risk babies

Please note that:

- In all other cases, **Beyfortus®** will be funded from the Medical Savings Account and/or Above Threshold benefit accumulating to Prescribed Medicine Benefit sub-limit subject to the rules of the member's chosen plan and available funds.
- Clinical entry criteria may apply

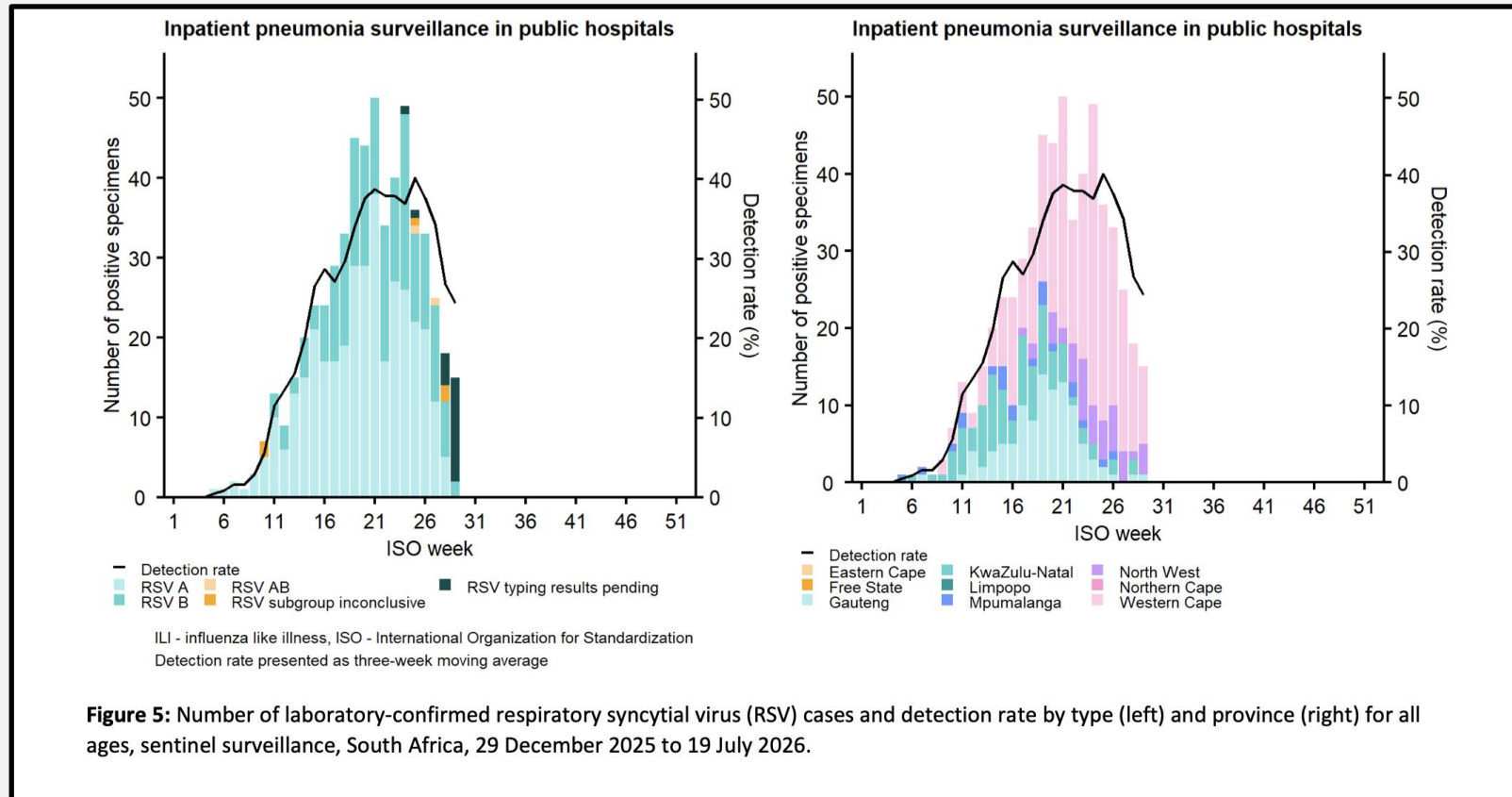


JUNE 2026



- RSV positivity remained high
- Combined RSV detection rates ranged from 16-18%
- Highest positivity rates were in those aged ≤ 5 years.





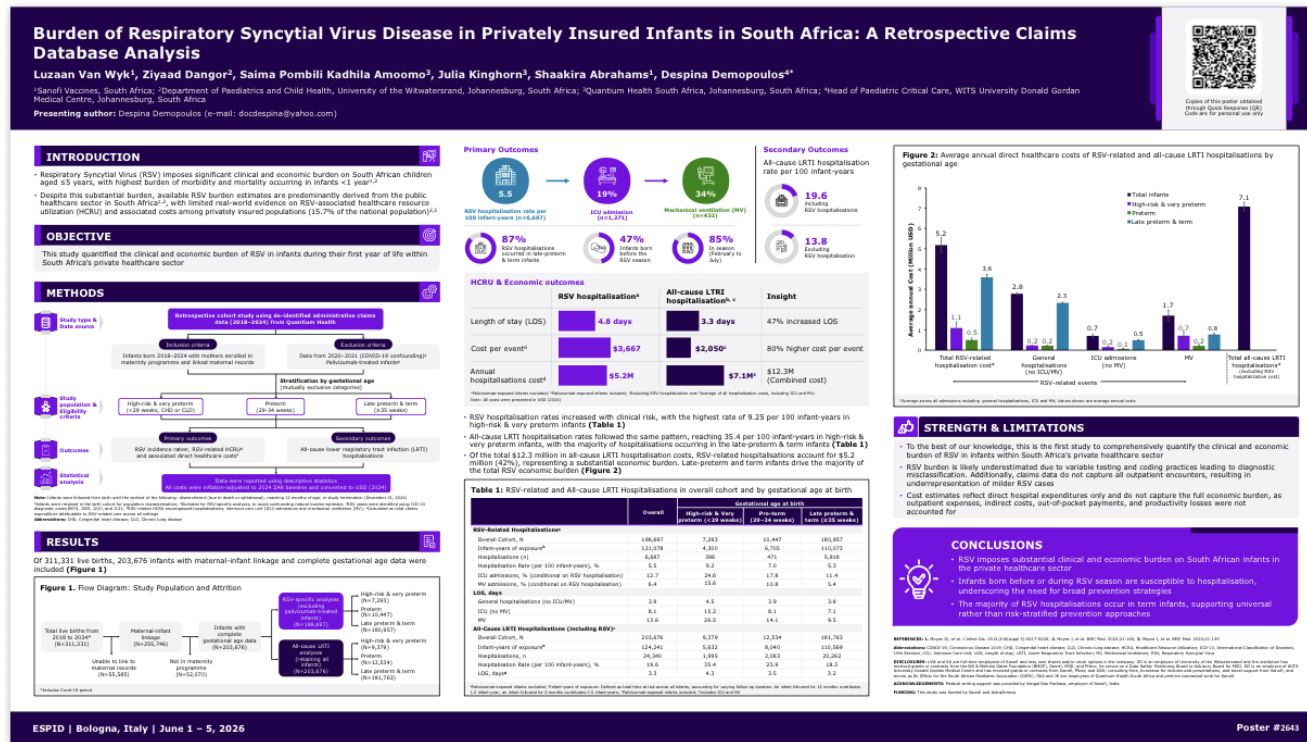
Week 29 (13 July 2026 to 19 July 2026):
9.6% cases of influenza
19.1% cases of respiratory syncytial virus (RSV)

ESPID 2026

- Substantial clinical and economic burden on South African infants in the private healthcare sector

- Infants born before or during RSV season are susceptible to hospitalisation

- Majority in term infants



DATA & SURVEILLANCE GAPS



ROBUST DATA ON RSV
INCIDENCE, SEASONALITY
AND IMPACT



NATIONAL-LEVEL DATA ON
RSV HOSPITALISATIONS AND
ECONOMIC BURDEN



ONGOING SAFETY
SURVEILLANCE ESSENTIAL

NEXT STEPS

1

Finalize national
RSV
immunization
policy

2

Conduct cost-
effectiveness &
affordability
analyses

3

Strengthen
antenatal &
newborn delivery
systems

4

Plan safety &
effectiveness
monitoring

5

Engage NDoH,
funders, and
providers

SUMMARY

- South Africa is ready for RSV prophylaxis rollout
- Nirsevimab can substantially reduce RSV burden in infants
- Collaboration, affordability & planning key to success

**LET'S
GET
MOVING**



thank
you
for
listening



A hand-drawn doodle on a white background. The text 'thank you for listening' is written in a casual, handwritten style. 'thank' is on the top line, 'you' is on the second line, 'for' is on the third line, and 'listening' is on the fourth line. To the left of 'thank' is a heart with three radiating lines. To the right of 'thank' is a star and two small plus signs. To the left of 'you' is a smiley face. To the right of 'listening' is a flower with a stem and leaf. A horizontal line with a heart in the center is positioned below the word 'listening'.