Economics of Preventing Respiratory Syncytial Virus Lower Respiratory Tract Infections (RSV-LRTI) among US Infants with Nirsevimab

A SUMMARY REPORT COMPARING MODELS FROM:

Sanofi AND *University of Michigan and CDC*

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NCIRD/CDC

ACIP Meeting, February 23, 2023

Disclaimer*: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.*

Conflict of interest

- **Sanofi model**: Alexia Kieffer et al., [complete authors list and affiliations, upon request]
  - Sanofi manufactures nirsevimab
  - Evidera (San Francisco, London) was funded by Sanofi

- **UM-CDC model**: David W Hutton et al. from Univ Michigan, …, ***Ismael R Ortega-Sanchez*** *et al.* from CDC [complete authors list and affiliations, upon request]
  - All authors: No conflicts of interest

Overview

Policy questions:

- Should one dose of nirsevimab be recommended
  - a) at birth for all infants born during October to March ***and***
  - b) for all infants born during April through September and <8 months of age when entering first RSV season?

- Should nirsevimab be recommended for children <20 months of age entering their second RSV season who remain at increased risk of severe disease?

Economic analysis

Question: Is the use of nirsevimab against RSV LRTI in all infants <8 months entering their first RSV season or born during season (and in high-risk children <20 months entering the 2nd season) *cost-effective*?

Comparator

Standard of care (SoC)
Infants in first season
(and high-risk in 2nd season)

Intervention

Giving nirsevimab to infants in first season
(and high-risk in 2nd season)

Base-case scenario: What is the incremental *cost-effectiveness* of using nirsevimab in all infants <8 months entering their first RSV season or born during season (and in high-risk children <20 months entering second season) relative to "Standard of Care"?

Standard of Care (SoC) = Palivizumab only for infants eligible as per AAP recommendations, and no immunization for all other pre-term and term infants

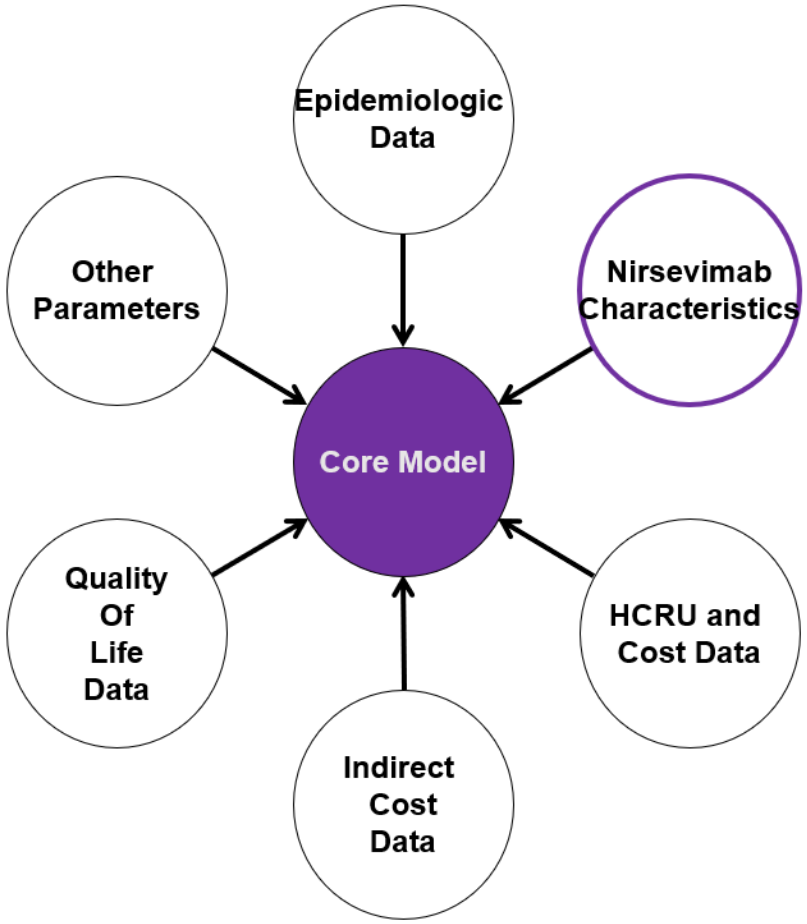
Focus on key features for model comparison

- Modeling approach
  - Targeted population(s)
  - Perspective (healthcare vs. societal)
  - Intervention strategies and comparators
- Inputs for RSV disease burden, nirsevimab efficacy, and costs
  - Incidence of RSV disease, rates of outcomes
  - Direct and indirect costs of RSV disease
  - Intervention: efficacy, duration of protection, safety and program costs
- Assumptions
  - Strong, influential assumptions

Modeling design and assumptions

	Sanofi	UM-CDC
Static analytical decision-making models	✓	✓
Sensitivity analyses (and probabilistic simulation)	✓(✓)	✓
Hypothetical population: All infants < 8 months (high risk children 8-19 months)	✓(✓)	✓(✓)
Time Frame: First year after a dose of nirsevimab (2nd season, 2nd dose for high-risk 8-19 months only)	✓ (✓)	✓ (✓)
Analytic Horizon: two years or seasons (for temporary disability) and Life Expectancy (for premature mortality)	✓ ✓	✓ ✓
Discount rate: 3%	✓	✓
Year of economic outcomes measured: 2022	✓	✓
Societal perspective (and healthcare perspective)	✓(✓)	✓(✓)

Inputs and main outcomes

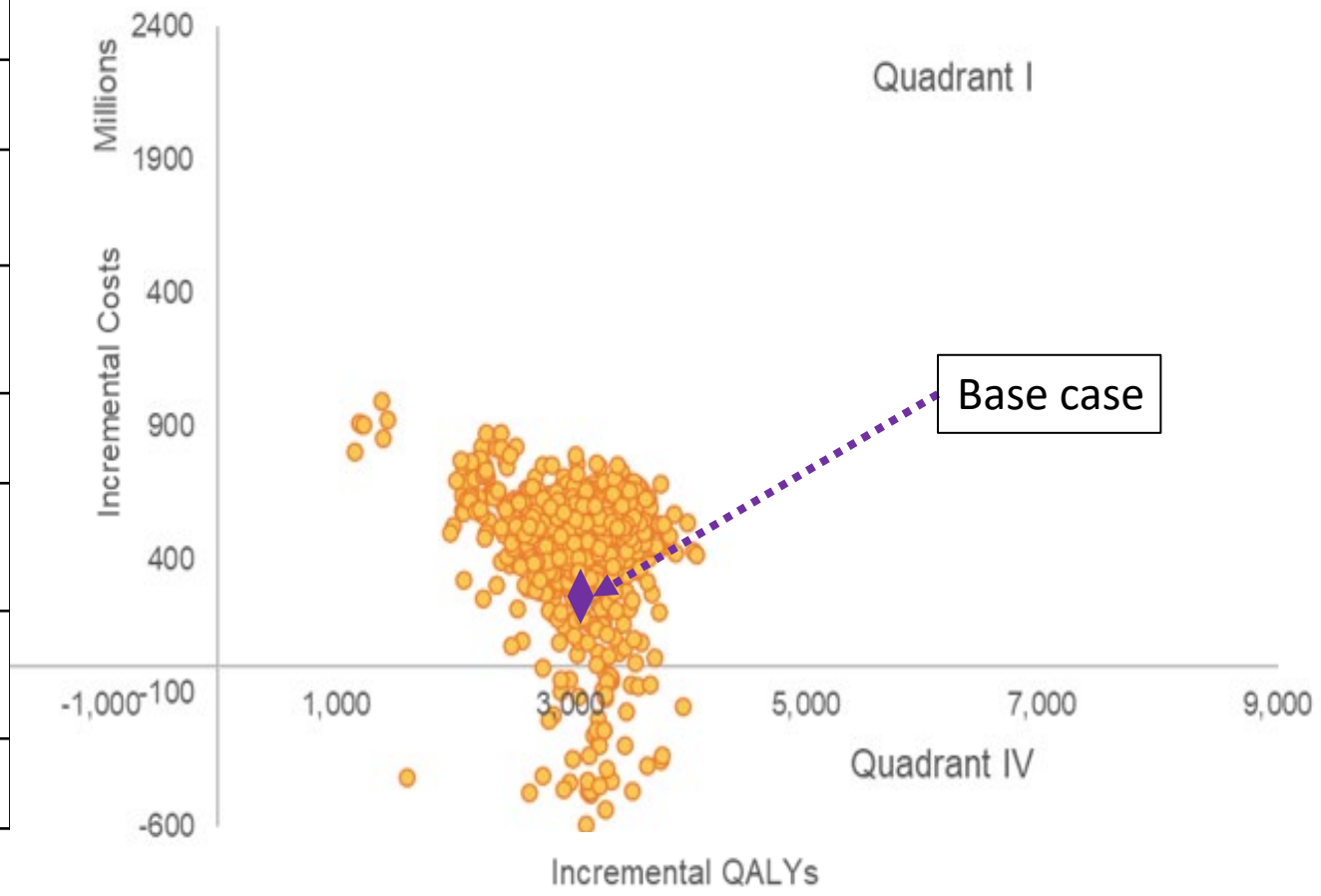


	Sanofi	UM-CDC
Prevention of:		
• MA RSV LRTI	✓	✓
• RSV LRTI hospitalizations	✓	✓
• RSV-associated deaths	✓	✓
QALYs saved	✓	✓
$/QALY saved	✓	✓
Number needed to immunize (NNI) to avert an:		
• MA RSV LRTI	✓	✓
• RSV LRTI hospitalization	✓	✓
• RSV-associated death	✓	✓

HCRU = health care resource use, MA = Medically attended, LRTI= Lower respiratory tract infection, QALY= quality-adjusted life year

Sanofi model: Base case estimates for all infants <7 months in Season 1, nirsevimab cost $500/dose & PSA

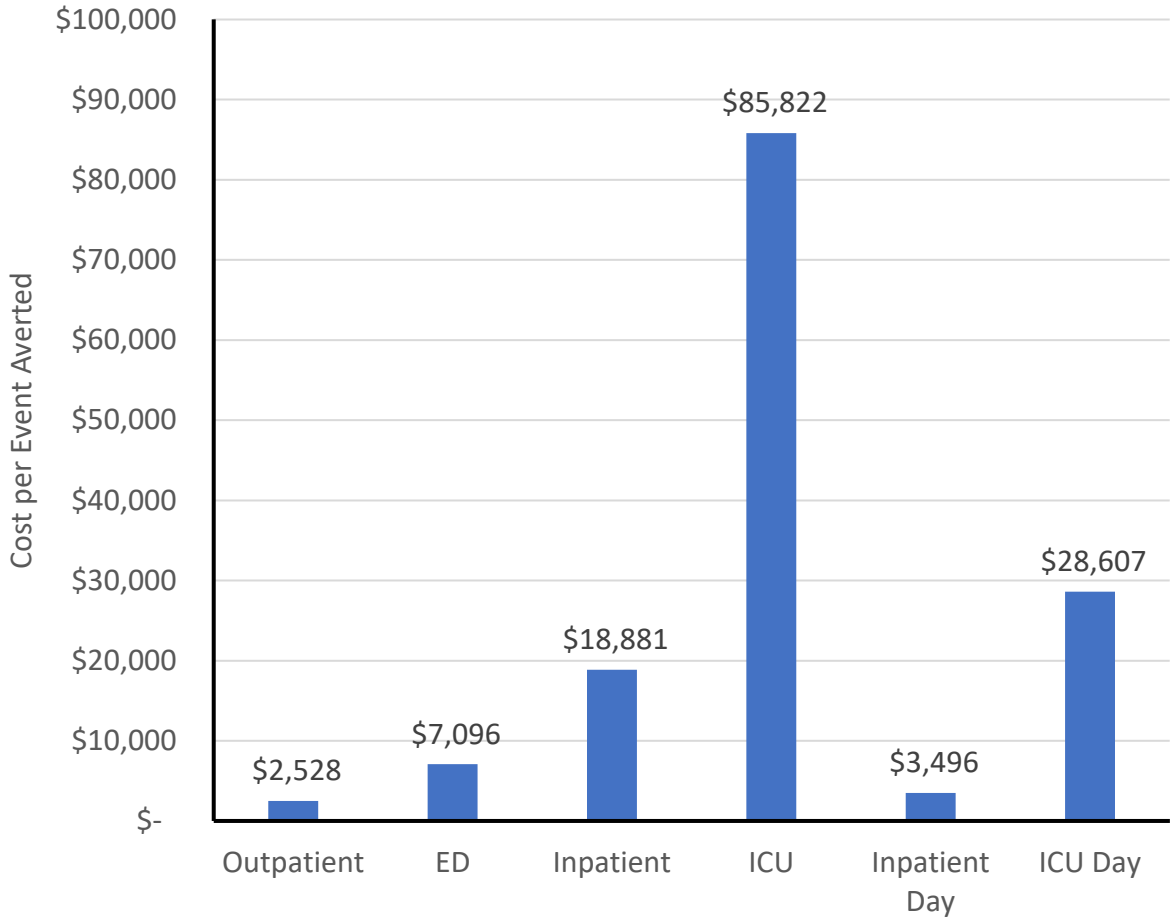
Summary outcomes	Base-Case
$/QALY gained	$70,430
$/RSV MA LRTI case averted	$798
$/RSV-associated LRTI hospitalization averted	$9,387
$/RSV-assoc. death averted	>$5.6Million
NNI to avert an RSV-MA LRTI case	5
NNI to avert an RSV-associated LRTI hospitalization	43
NNI to avert a death	55,957



Probabilistic sensitivity analysis (PSA)

UM-CDC: Base case estimates for all infants <8 months, Season 1, nirsevimab cost $300/dose

Summary outcomes	Base-Case
$/QALY gained	$102,805
$/RSV-MA LRTI case averted	$2,100
$/RSV-associated LRTI hospitalization averted	$18,881
$/RSV-assoc. death averted	n/r
NNI avert an RSV-MA LRTI case	14
NNI avert an RSV-assoc. LRTI hospitalization	130
NNI avert an RSV-assoc. death	n/r



Cost per type of health outcome prevented

Assuming 100% uptake in nirsevimab group
n/r = not reported

Sanofi and UM-CDC models comparison: Selected outcome ratios for nirsevimab

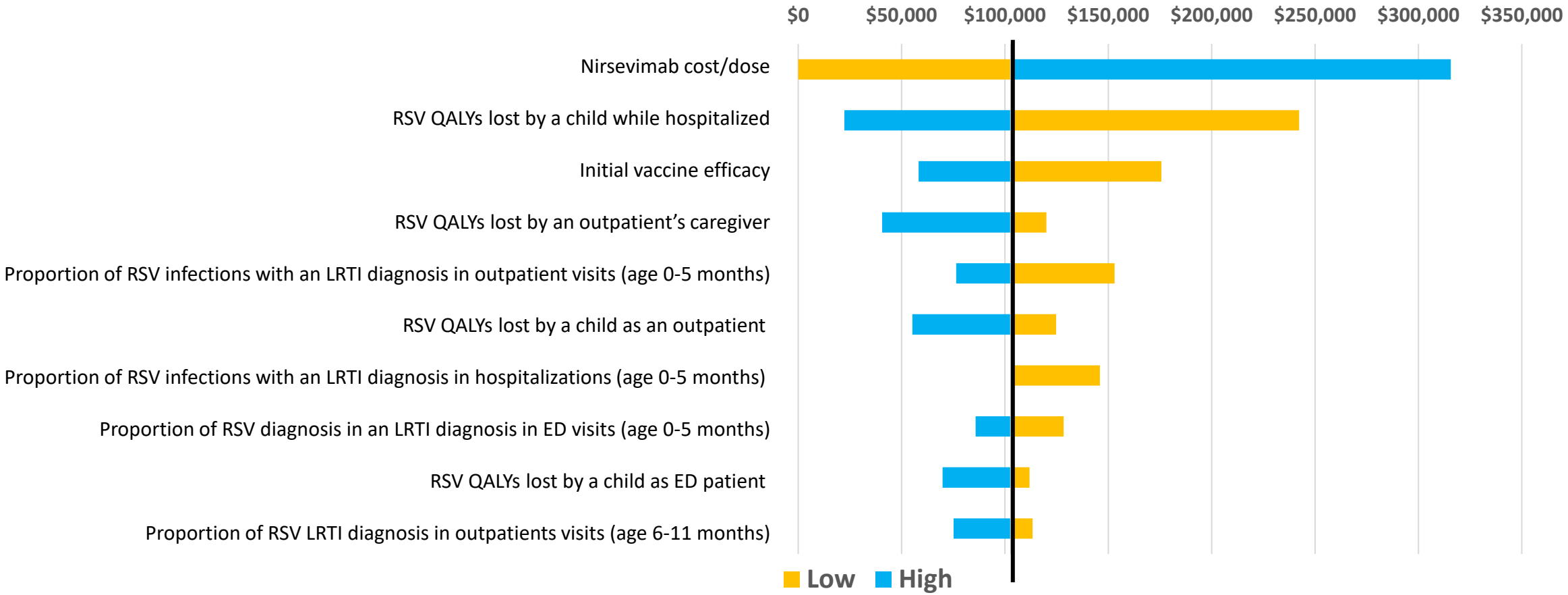
	UM-CDC model Price per dose $300	Sanofi model Price per dose $500
$ / QALY gained		
nirsevimab Season 1, infants	**$102,805**	**$70,430**
nirsevimab Season 2, high risk infants	$842,139[b]	$823,131[a]
nirsevimab Seasons 1 & 2 combined	n/r	$62,589
nirsevimab vs palivizumab, Season 2 PEP[c]	n/r	dominant
$ / hospitalization averted		
nirsevimab Season 1	$18,881	$9,387
nirsevimab Seasons 1 & 2 combined	n/r	$8,316

a. Pre-term infants only
b. High risk <19 months old infants (preterm + PEP) receiving a 2nd dose of nirsevimab in October
c. PEP= palivizumab eligible population

n/r = not reported

UM-CDC model: One-way Sensitivity Analyses (Season 1 only)

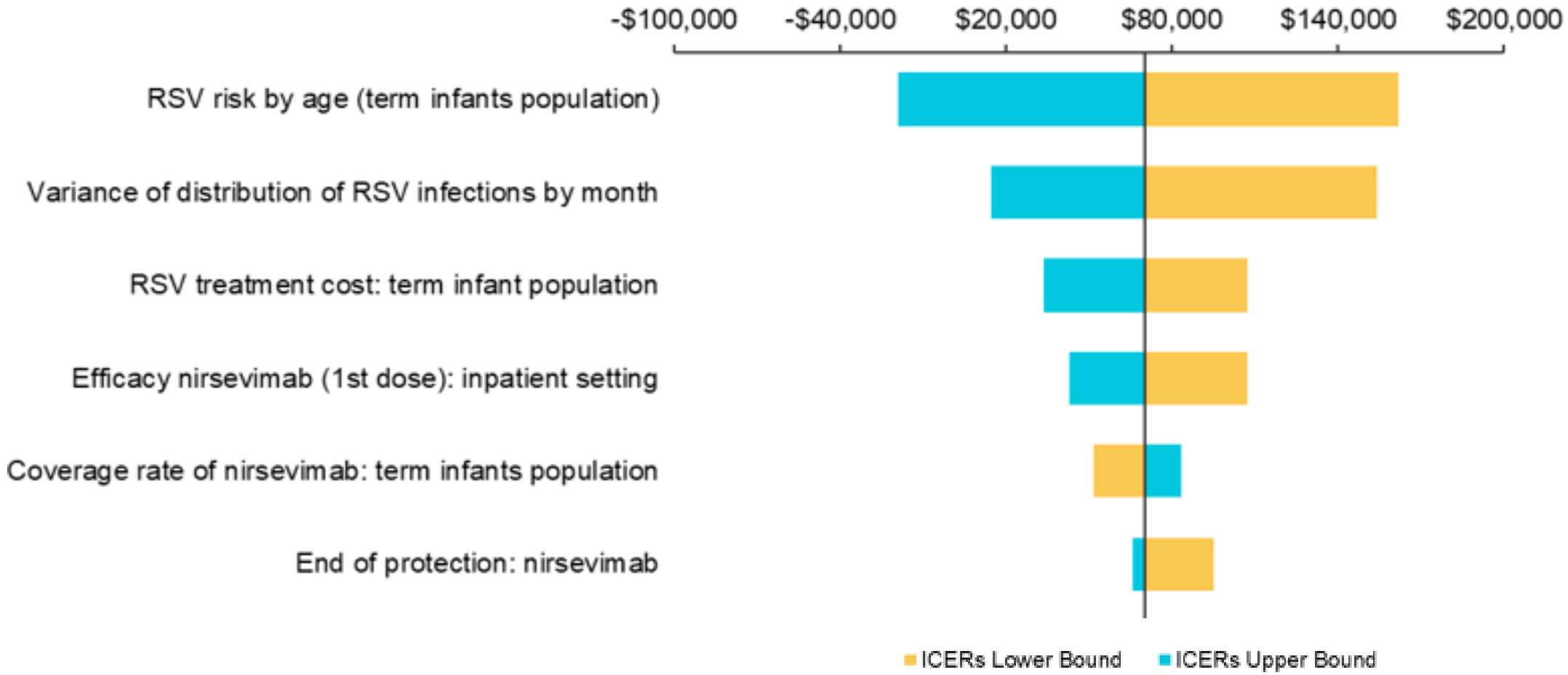
Base case: $102,805/QALY saved, nirsevimab cost $300/dose



Assuming 100% uptake in nirsevimab group

Sanofi model: One-way Sensitivity Analyses (Season 1 only)

Base case: $70,430/QALY saved, nirsevimab cost $500/dose



Sanofi and UM-CDC models comparison: Selected influential inputs

- RSV-hospitalization rate
  - Sanofi: Age and term-specific hospitalization rates reported in McLaurin (2016)[a]
  - UM-CDC: From RSV-associated hospitalization rates[b] among children aged ≤2 years
- Unitary medical cost of RSV hospitalization
  - Sanofi: Cost varies by term at birth and by whether Intensive Care Unit or Mechanical Ventilator were needed as reported in McLaurin (2016)[b]
  - UM-CDC: Unit cost was a weighted average by term at birth and age as reported in Bowser (2022)[c]
- RSV season & intervention period
  - Sanofi: MA RSV season based on Rainisch (2020)[d] but intervention ends in February
  - UM-CDC: RSV-season and intervention period based on CDC surveillance data (2016-2019)[c]
- Initial efficacy & waning
  - Sanofi: Constant first 5 months as in trials, linear decay from month 6 to month 10
  - UM-CDC: Sigmoid decay up to 10 months; average residual protection in first 5 months equals constant efficacy from trials

a McLaurin et al. *J Perinatol*. 2016;36(11):990-996
b CDC unpublished data from the New Vaccine Surveillance Network (NVSN) (December 2016 to September 2020)
c Bowser et al., *J Infect Dis*. 2022 Aug 15; 226(Suppl 2): S225–S235
d Rainisch et al. *Vaccine*. 2020;38(2):251-257

Sanofi and UM-CDC models comparison: Differences in key inputs

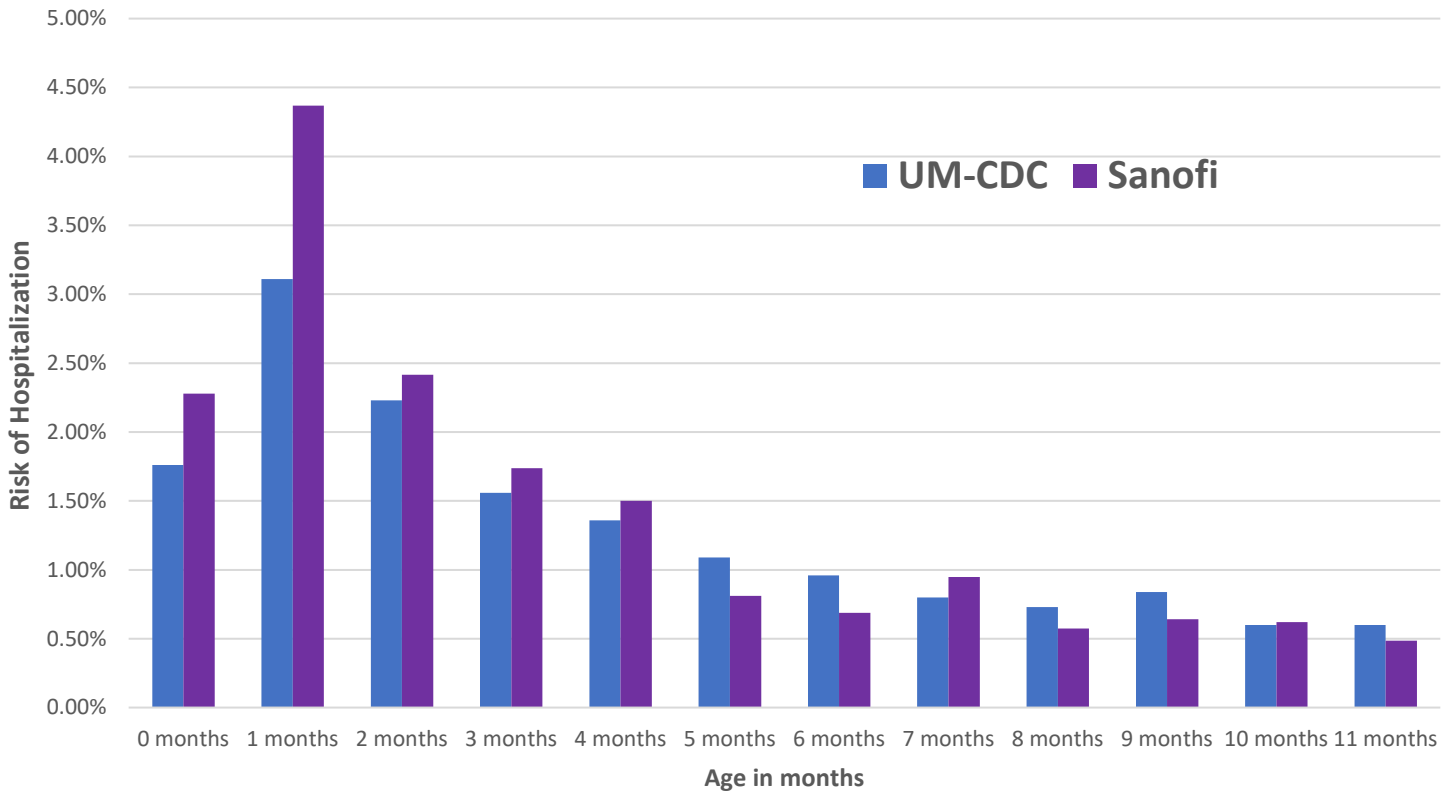
	UM-CDC	Sanofi
Risk of RSV hospitalization (Infants <12 months of age)	1.30% (0.60% - 3.11%)[a]	1.42% (0.49% - 4.37%)[b]
Medical costs per RSV hospitalization	$11,487 ($11,042 - $11,993)[c]	$18,790 – $28,812 (age- and term dependent)[d]
Medical costs per RSV outpatient visit	$82 ($46 - $118)[c]	$153 (no variation reported)

a Data from CDC-funded New Vaccine Surveillance Network (NVSN) (December 2016 to September 2020) (range values are the lowest and highest within the first 11 months of age)
b Weighted average term-specific populations shares (range values are the lowest and highest within the first 11 months of age)
c Adapted from Bowser et al., *J Infect Dis*. 2022 Aug 15; 226(Suppl 2): S225–S235 (A systematic review study funded by Sanofi)
d Costs in the base-case varied by age, term at birth and by whether Intensive Care Unit or Mechanical Ventilator were needed while hospitalized using percentages as wights; data reported in McLaurin (2016)

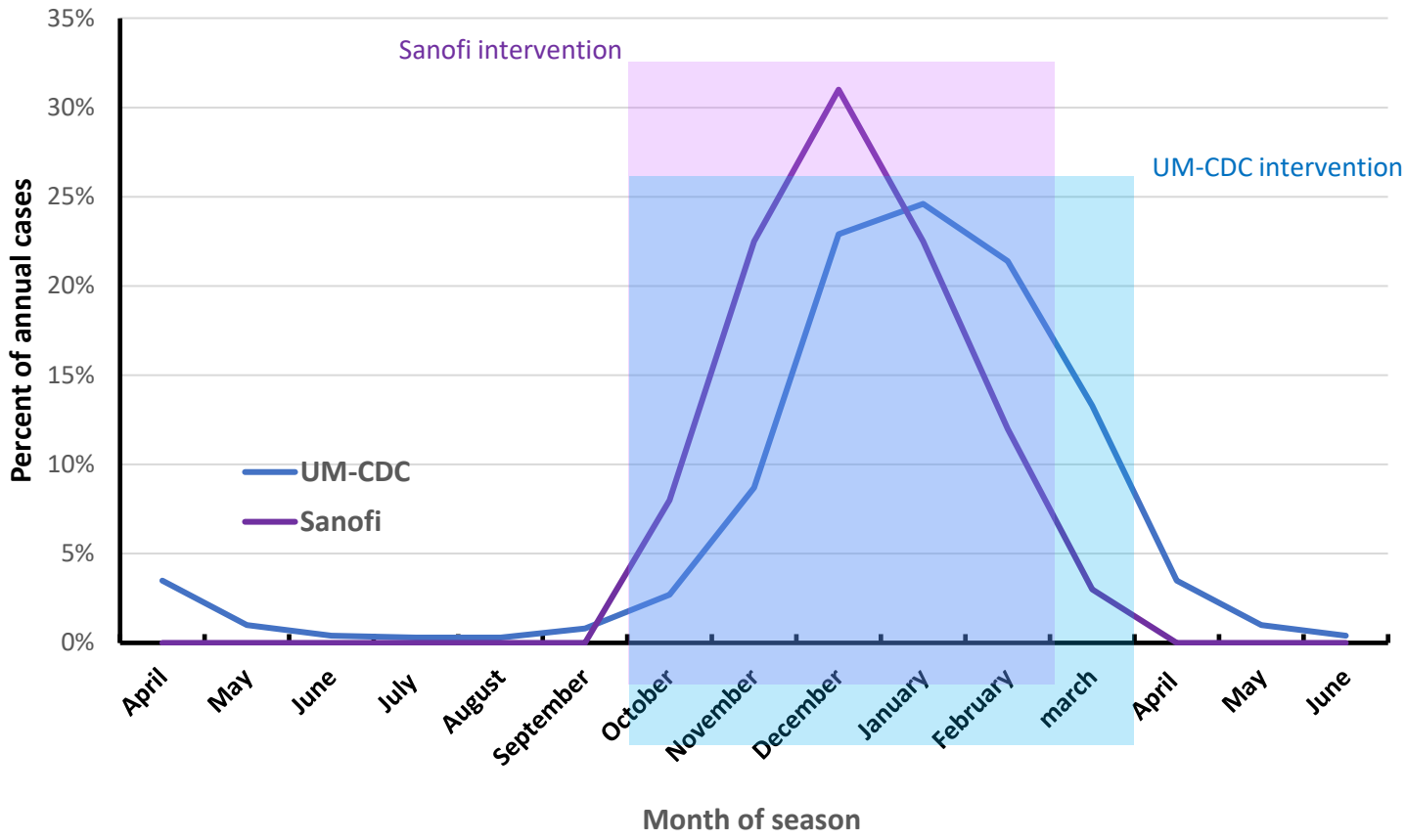
Sanofi and UM-CDC models comparison: Base-case risk of RSV-related hospitalization by age

UM-CDC model: Laboratory-confirmed RSV-associated hospitalization rates from New Vaccine Surveillance Network (NVSN) data for children under 2 years of age (December 2016 to September 2020)

Sanofi model: Age and term-specific weighted average of hospitalization rates in infants using reported rates in McLaurin (2016)



Sanofi and UM-CDC models comparison: RSV-season and intervention*



Sanofi Intervention	UM-CDC Intervention
WiS (Within RSV season). All Infants born in-season (i.e., October 1st to Feb 29th)	At birth, if born October 1st to March 31st
WiS: All infants 0-3 months of age at the start of RSV season (i.e., in October)	In October, if born in April June August
OoS (Out of RSV season): All infants born OoS at the start of the RSV season (i.e., in October)	In November, if born in May July September

* RSV-season and Intervention period in UM-CDC model are based on NREVVS seasonality (2016-2019).
Intervention period in Sanofi model ends in February (a month short from end of MA RSV season, Rainisch et al., *Vaccine*. 2020;38(2):251-257. Technical appendix)

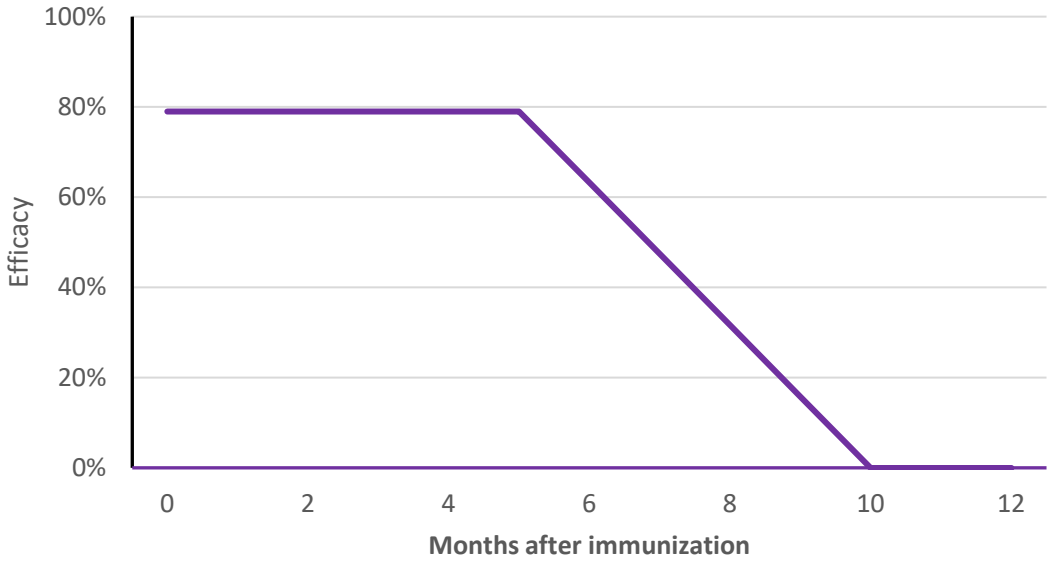
Sanofi and UM-CDC: Initial nirsevimab efficacy and uptake

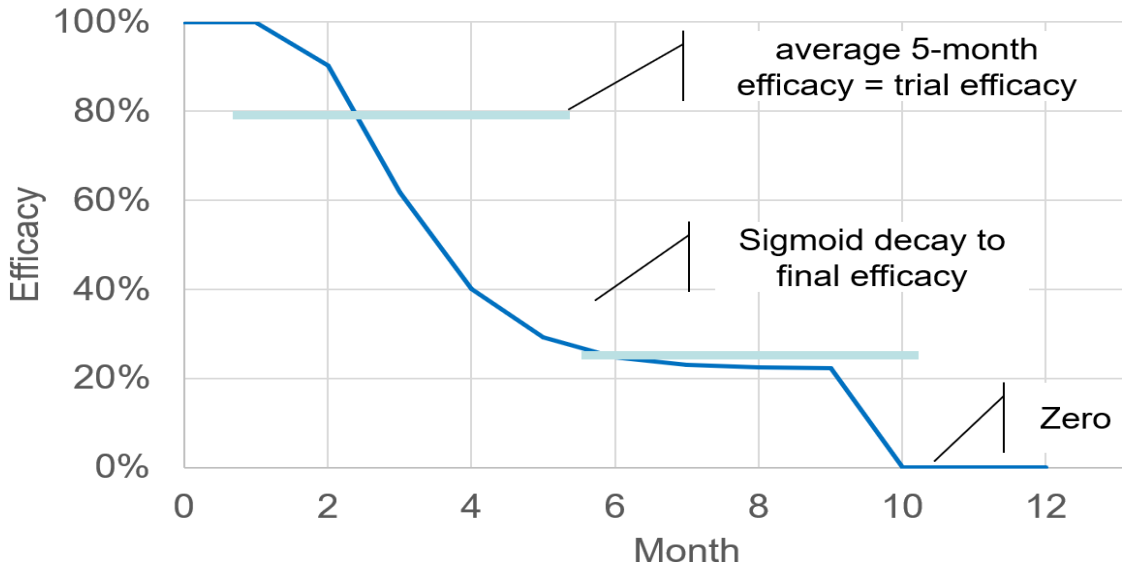
	UM-CDC	Sanofi
Initial efficacy against MA RSV LRTI: Inpatient and outpatient (%)[a]	80.0 (68.5 – 86.1)[a]	79.0 (68.5 – 86.1)[a, b]

a MELODY trial and Phase 2b recommended dose
b Assumed non-inferiority with palivizumab, Hammitt et al., *N Engl J Med.* 2022;386(9):837-846

Sanofi and UM-CDC: Assumption on duration of nirsevimab

Sanofi	Initial efficacy against MA LRTI = A constant protection over 5 months, Then, a linear decay of efficacy from month 6 to month 10 No residual protection after 10 months	**UM-CDC**	Initial efficacy against LRTI = Average 5 months efficacy equals to trial estimates Sigmoid decay up to 10 months and then 0% afterwards; Calibrated such that the first 5 months efficacy equals trial estimates





UM-CDC model: comparison of base case & selected scenarios

Scenario	UM-CDC
Nirsevimab cost per $500/dose (1st season)[c]	$244,677
Intervention period October to February	$107,963
Base case [a] (Nirsevimab cost $300/dose, 1st season)	**$102,805**
Prevention of All MA RSV visits (LRTI and URTI)[b]	$45,092
Nirsevimab cost per $200/dose (1st season)[c]	$31,869

a Base-case nirsevimab cost $300 per dose, immunization is for only the 1st season
b LRTI=Lower respiratory tract infection, URTI= Upper respiratory tract infection
c Cost per QALY saved estimated by varying nirsevimab cost per dose from $200 (low) to $500 (high), immunization is for only the 1st season

Limitations

- **Factors not considered that may result in overestimating the ICER (underestimating the cost-effectiveness) of nirsevimab immunization**
  - In base-case: both models assumed
    - No protection against URTI
    - No protection against asymptomatic/unattended LRTI
  - Neither model included RSV-related costs incurred after discharge from an RSV-associated hospitalization or emergency department visit:
    - Productivity losses incurred by caregivers after discharge
  - Both models assumed no indirect effects of nirsevimab immunization (i.e., no protection against RSV transmission)

Conclusion

- **Differences in key inputs among Sanofi and UM-CDC models explain differences in results:**
  - Nirsevimab cost per dose
  - Seasonality and intervention period
  - Duration of nirservimab efficacy
  - Hospitalization rates
  - Medical costs
- **Base-case in both models:**
  - Nirsevimab would significantly reduce RSV disease burden in infants
    - Data from clinical trials support impact estimates on disease reduction
  - Economic value of using nirsevimab in infants could be *cost-effective* or *costly*
    - Reasonable nirsevimab price and duration of protection combined with careful design of seasonal interventions would determine the ***cost-effectiveness*** value of routine prophylaxis among infants ≤7 months of age entering their first RSV season, and those born during the RSV season

Acknowledgements

From NCIRD/CDC

- Jamison Pike
- Jefferson Jones
- Meredith McMorrow
- Mila M. Prill
- Katherine E. Fleming-Dutra
- Michael Melgar

Also:

- Maternal/Pediatric RSV working group members

End of Summary

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Leftovers:

Note:

Economic evaluation:

Incremental cost-effectiveness ratio (*ICER*) **:**

$$ICER = \frac{C_{imm} - TC_{saved}}{HO_{SoC} - HO_{imm}}$$

Where:

- C_{imm} **=** Cost of intervention (nirsevimab program costs)
- TC_{saved} **=** Total savings (difference in RSV disease costs under Standard of care vs. nirsevimab immunization)
- HO_{imm} **=** Health outcome of immunization (ex., QALYs)
- HO_{SoC} **=** Health outcome of Standard of Care (ex., QALYs)

Both Cost and QALYs are discounted using:

- ***t =*** time in months/years after immunization *(t=0, 1, 2,…, T)*
- ***r =*** discount rate (3%)
- ***T =*** Analytical horizon (age-specific, in years)

Number needed to immunize (NNI) ratio**:**

$$NNI = \frac{\#\ Immunized}{\#\ HO_{saved}}$$

Where:

- ***# Immunized =*** number of individuals immunized against RSV during the time frame of the intervention
- $\#HO_{saved}$ **=** Number of health outcomes saved or prevented with immunization, ex.,
  - RSV cases saved,
  - RSV-outpatient visits prevented,
  - RSV-hospitalizations prevented,
  - lives saved