

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*

Ismael R. Ortega-Sanchez, PhD

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

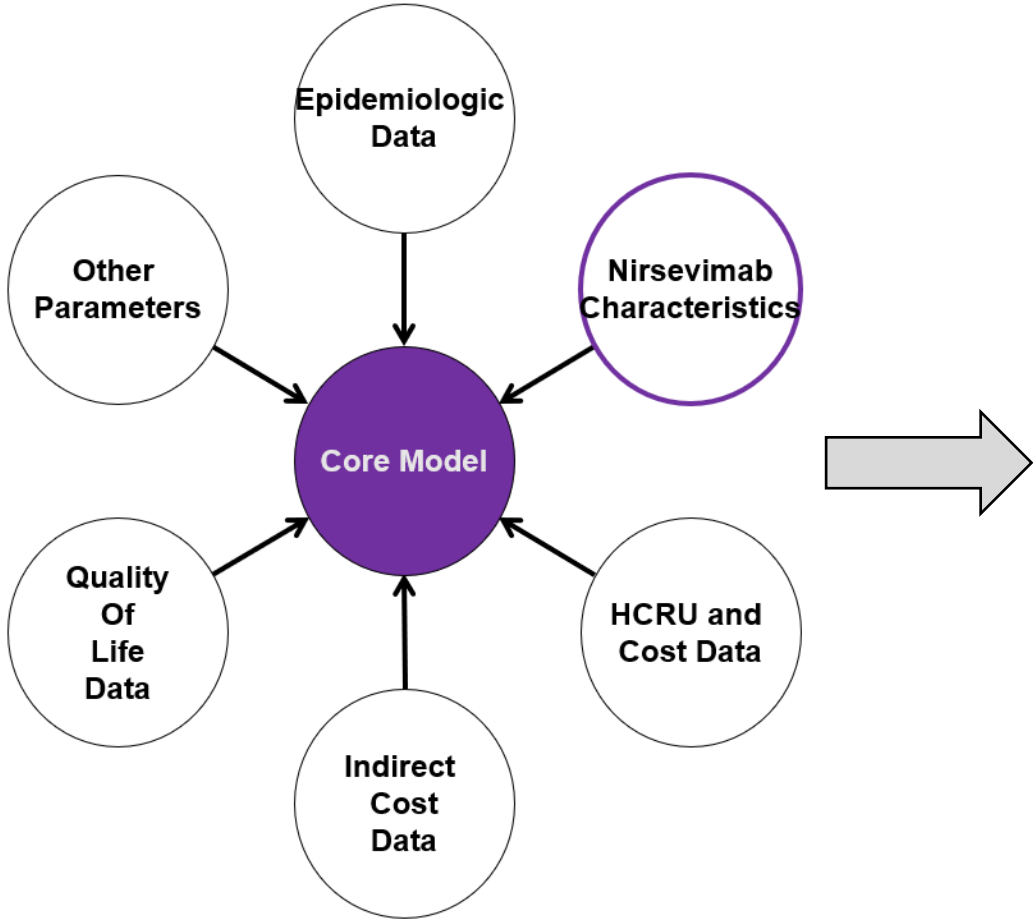
Focus on key features for model comparison

- 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 (2 nd 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



Prevention of:

- MA RSV LRTI
- RSV LRTI hospitalizations
- RSV-associated deaths

Sanofi	UM-CDC
✓	✓
✓	✓
✓	✓

QALYs saved
\$/QALY saved

✓	✓
✓	✓

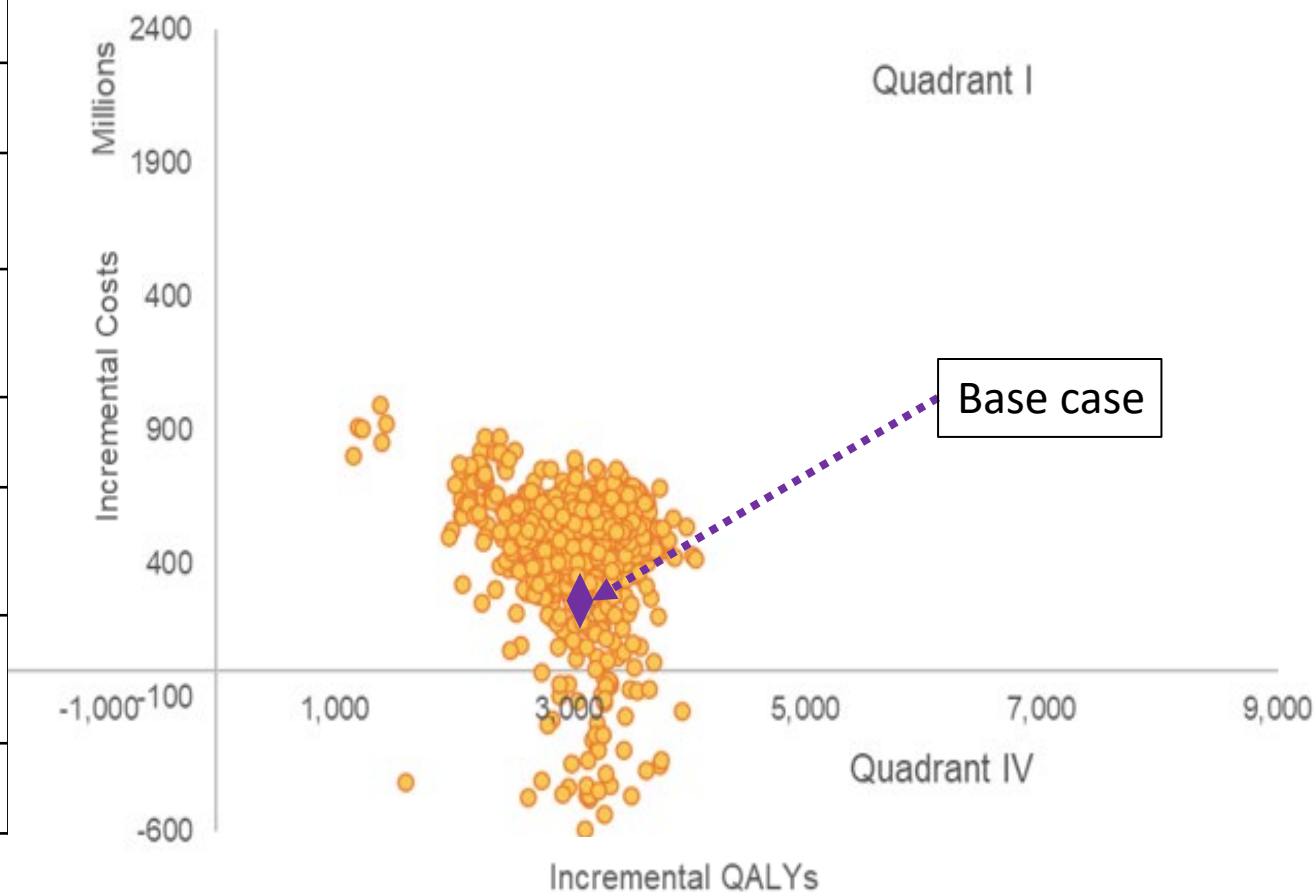
Number needed to
immunize (NNI) to avert an:

- MA RSV LRTI
- RSV LRTI hospitalization
- RSV-associated death

✓	✓
✓	✓
✓	✓

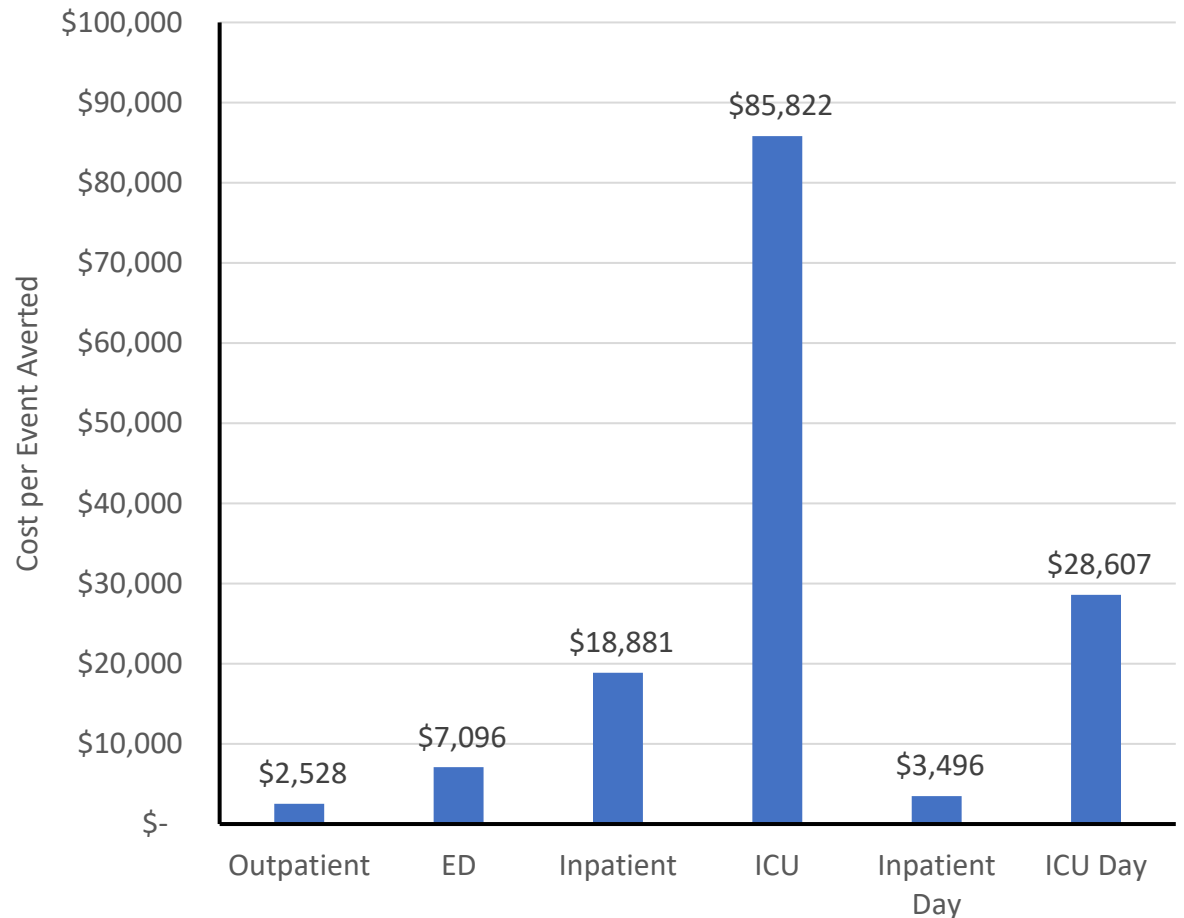
Sanofi model: Base case estimates for all infants <7 months in Season 1, nirsevimab cost \$500/dose & PSA

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



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

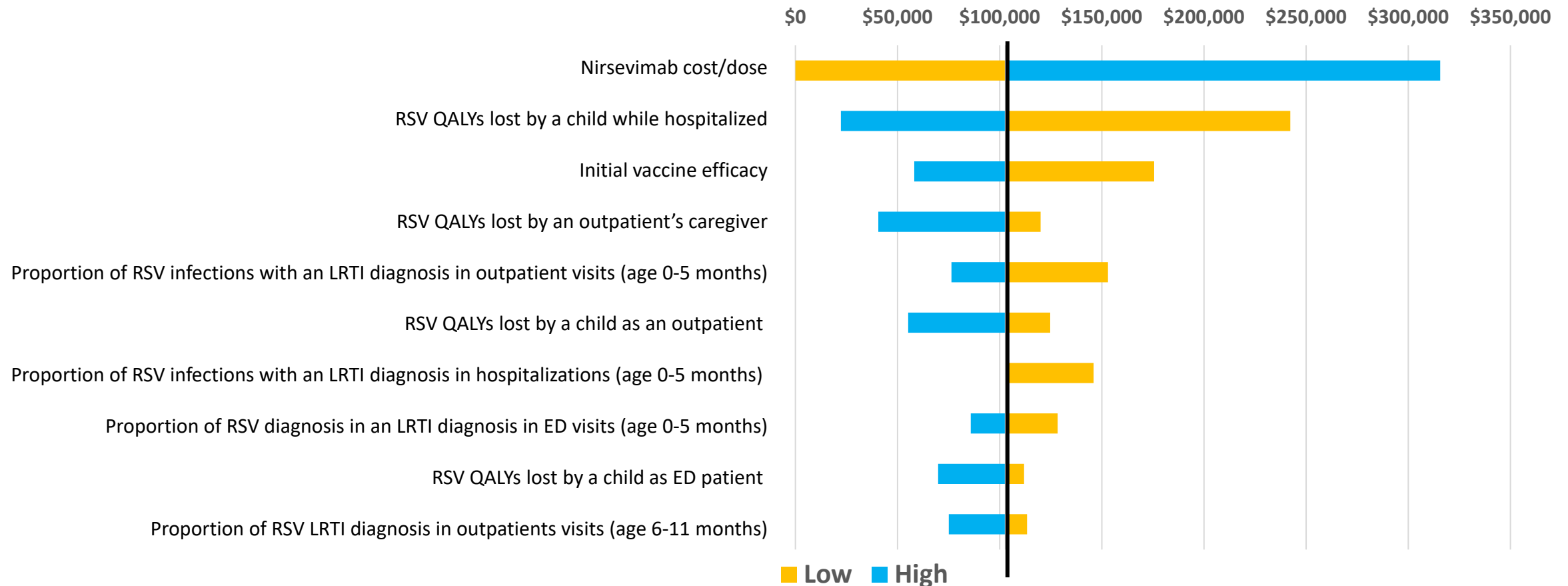
b. High risk <19 months old infants (preterm + PEP) receiving a 2nd dose of nirsevimab in October

c. PEP= palivizumab eligible population

n/r = not reported

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

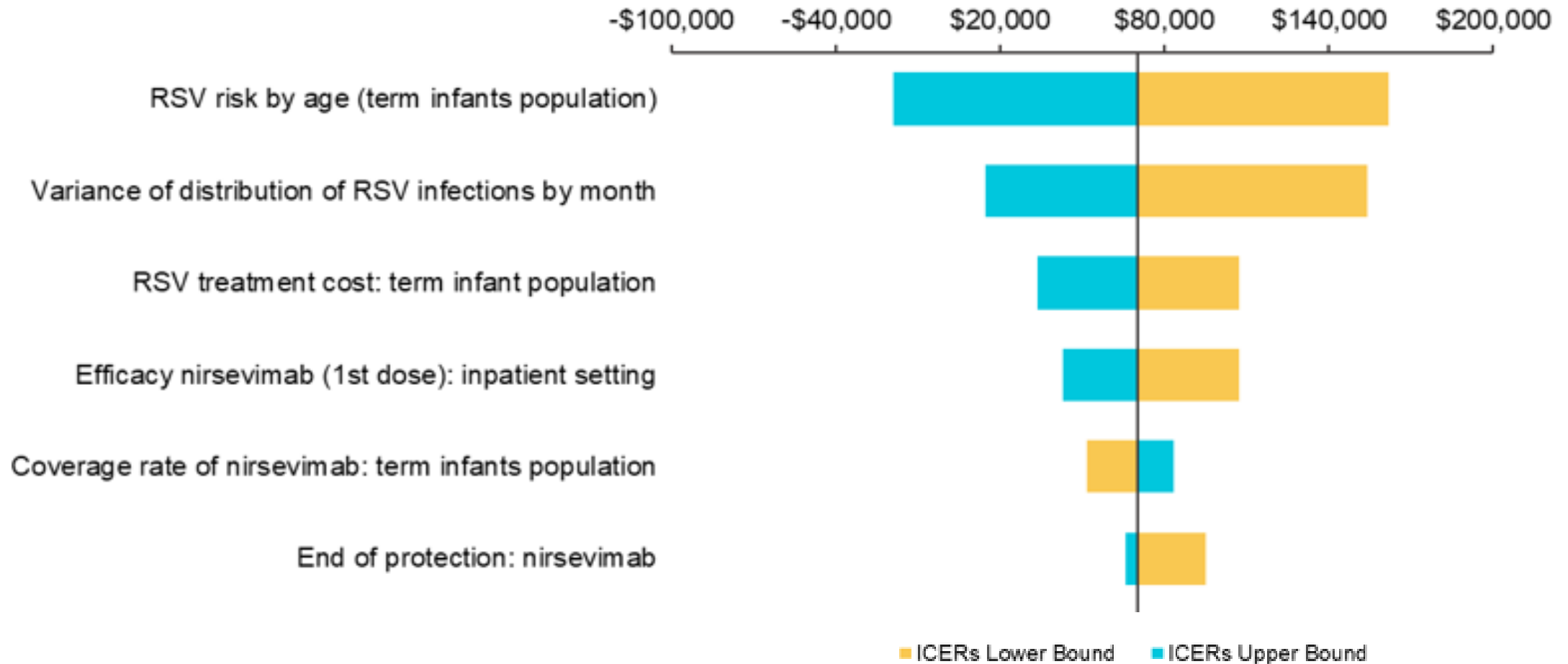
Base case: \$102,805/QALY saved, nirsevimab cost \$300/dose



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)

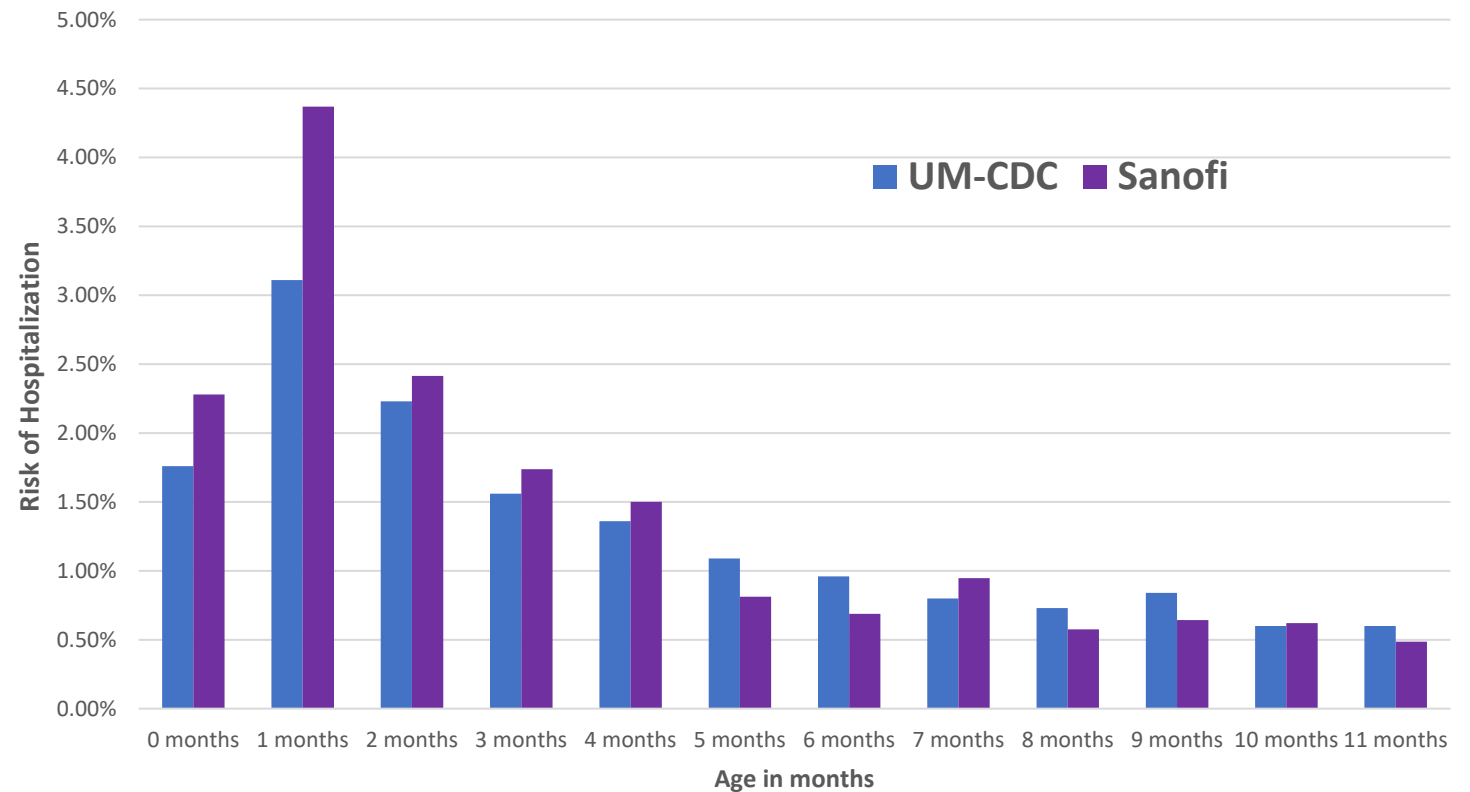
c Adapted from Bowser et al., *J Infect Dis.* 2022 Aug 15; 226(Suppl 2): S225–S235 (A systematic review study funded by Sanofi)

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)

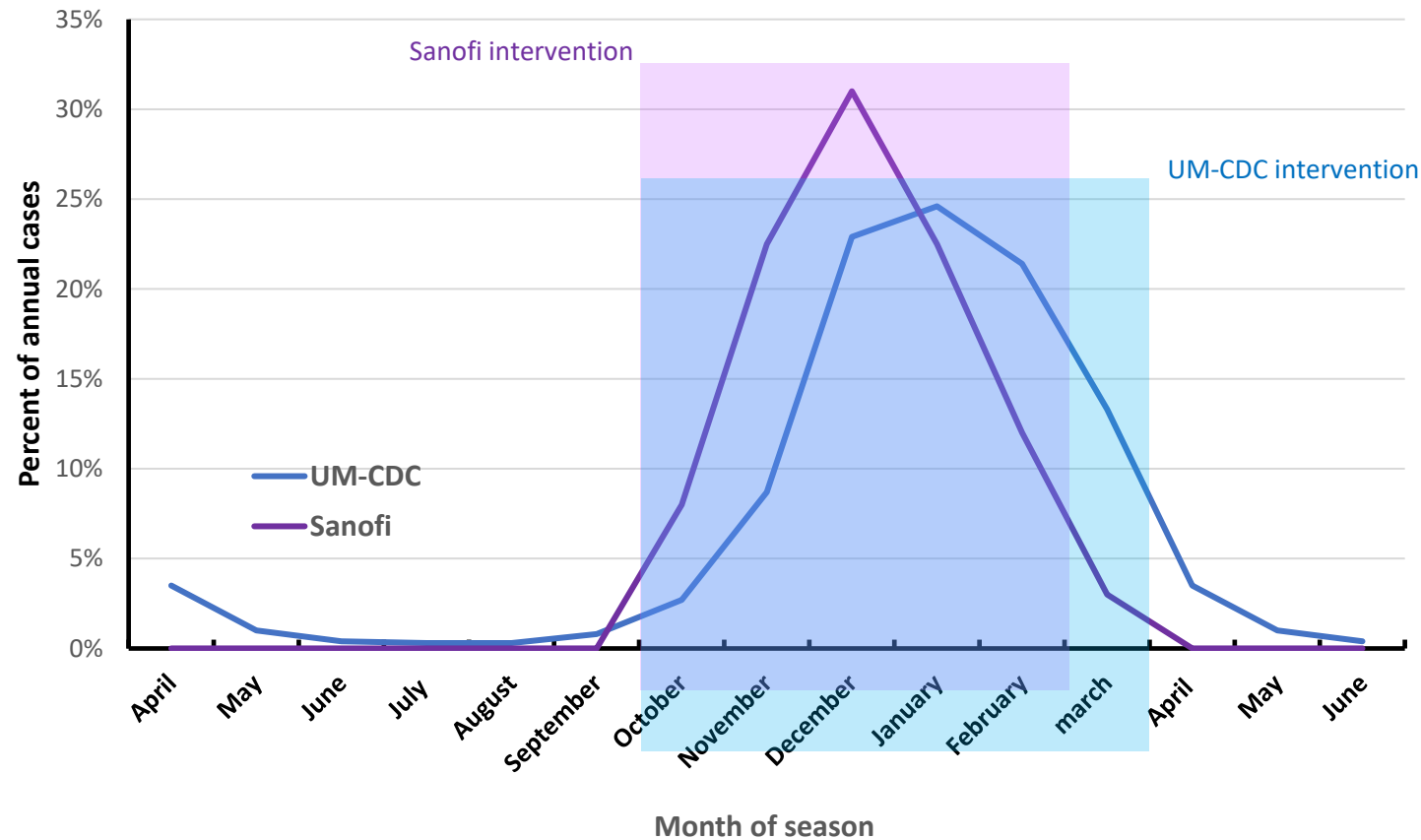
Sanofi and UM-CDC models comparison: Base-case risk of RSV-related hospitalization by age

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 1 st to Feb 29 th)	At birth, if born October 1 st to March 31 st
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) 61

Sanofi and UM-CDC: Initial nirsevimab efficacy and uptake

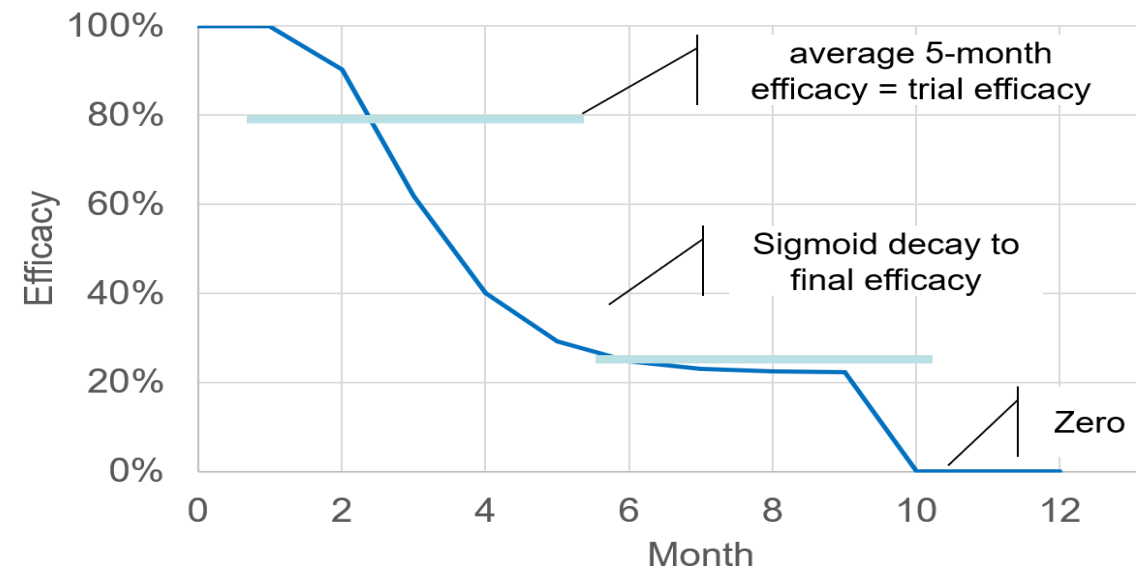
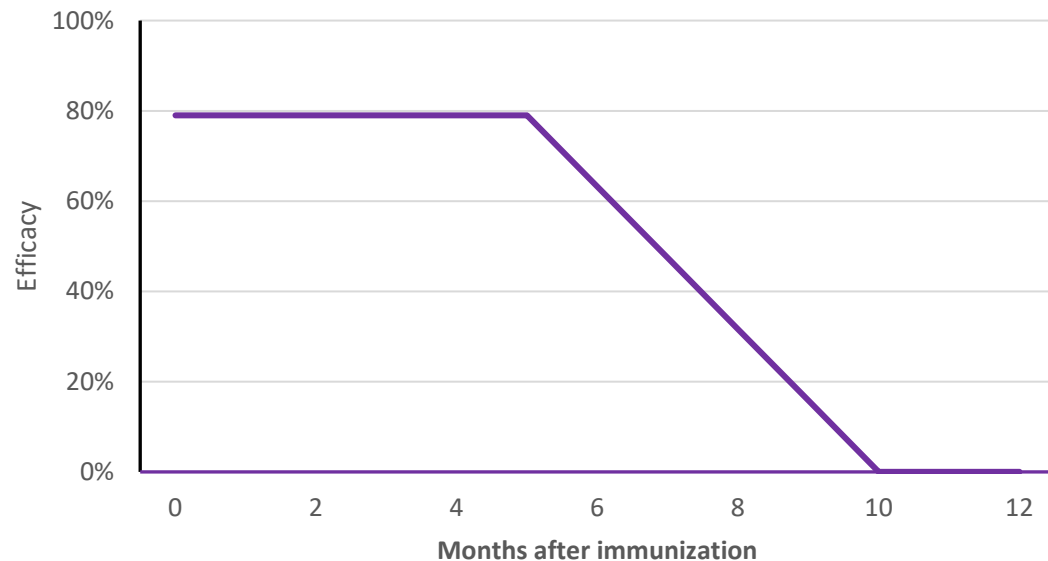
	UM-CDC	Sanofi
Initial efficacy against MA RSV LRTI: Inpatient and outpatient (%) ^a	80.0 (68.5 – 86.1) ^a	79.0 (68.5 – 86.1) ^{a, b}

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

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

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

