Economic Analysis of RSVpreF Maternal Vaccination

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SCHOOL OF PUBLIC HEALTH
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Research team

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Conflicts of interest statements

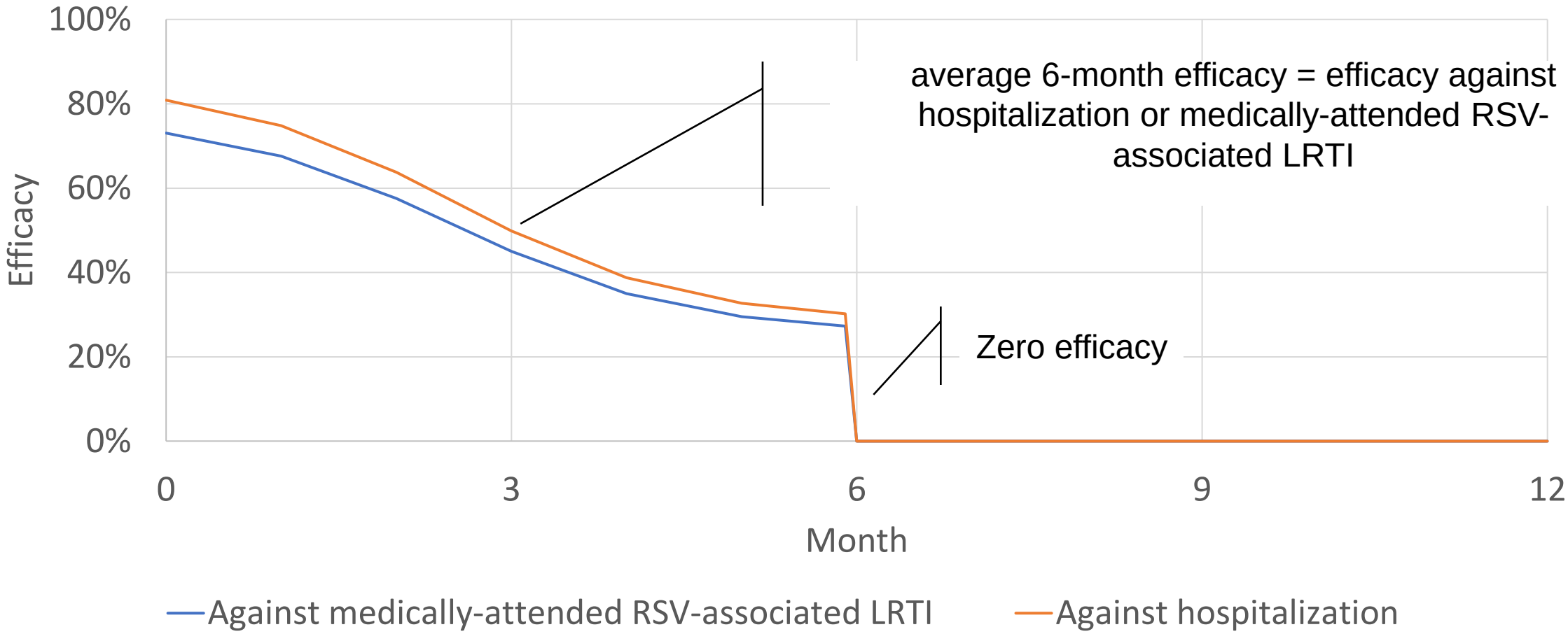
- Authors have no known conflict of interests.

Updates Since June 21 Presentation

- Additional vaccine efficacy scenario
- Additional timing scenarios
  - Months of year to administer
  - 32 $^{0}/_{7}$ - 36 $^{6}/_{7}$ weeks gestation
- Updated cost/dose

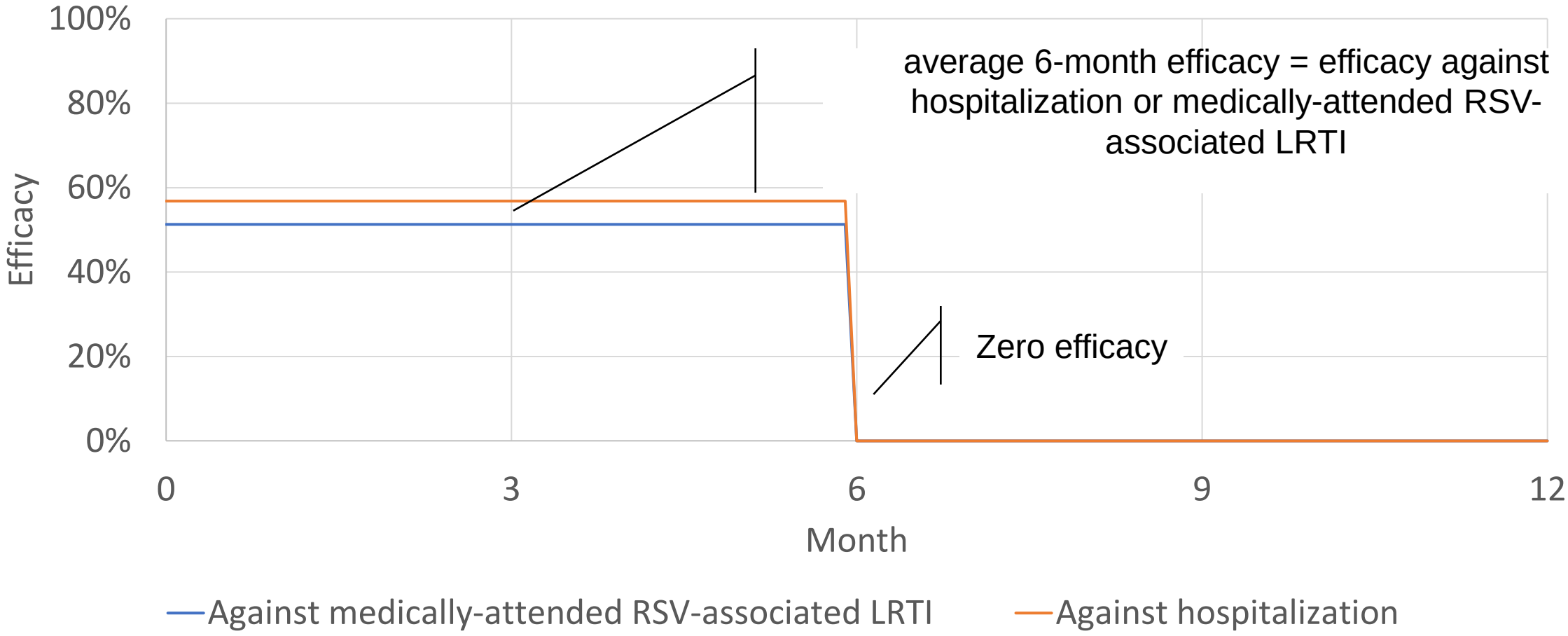
Economic Analysis of RSV Vaccination in Older Adults, June 21, 2023

Methods: RSVpreF efficacy



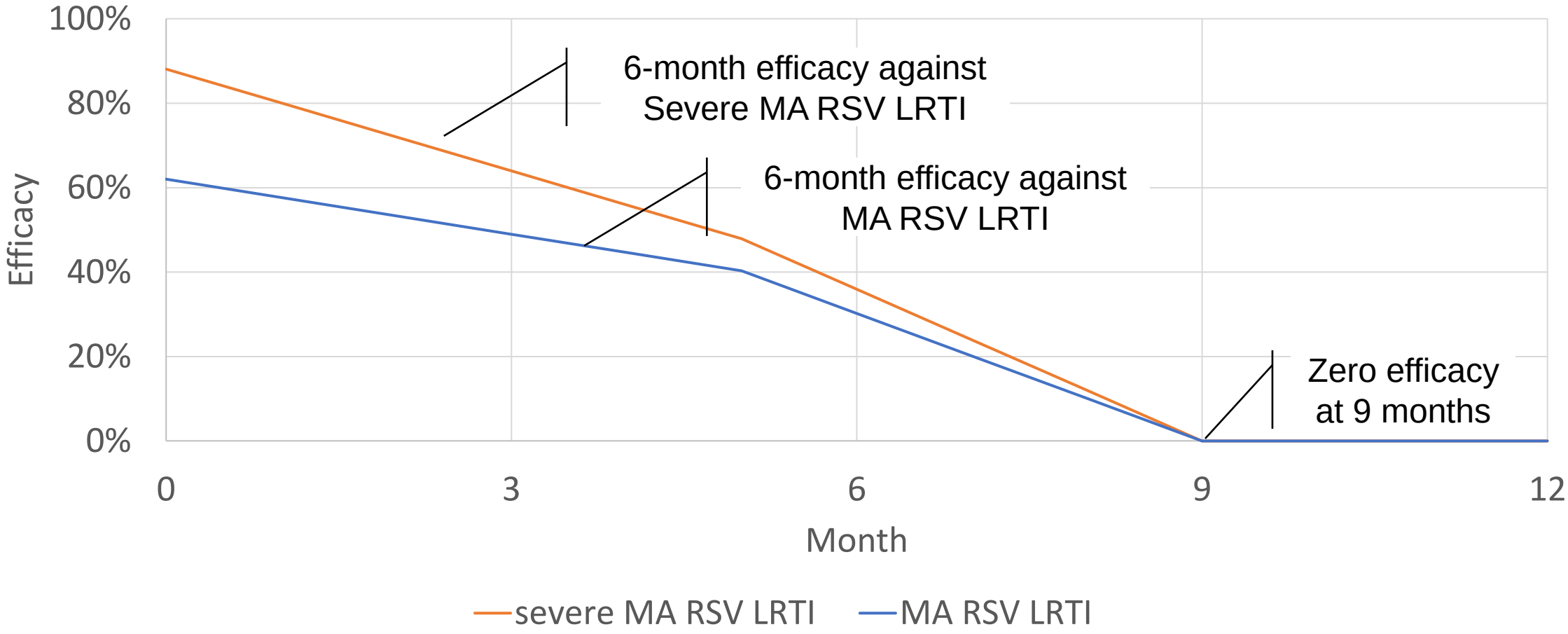
Source: Kampmann et al 2023
LRTI= Lower respiratory tract infection

Methods: RSVpreF efficacy alternate flat scenario



Source: Kampmann et al 2023
LRTI= Lower respiratory tract infection

Methods: RSVpreF efficacy
Optimistic scenario: Severe Efficacy with VE to 9 months



MA: Medically-attended, LRTI: Lower Respiratory Tract Infection

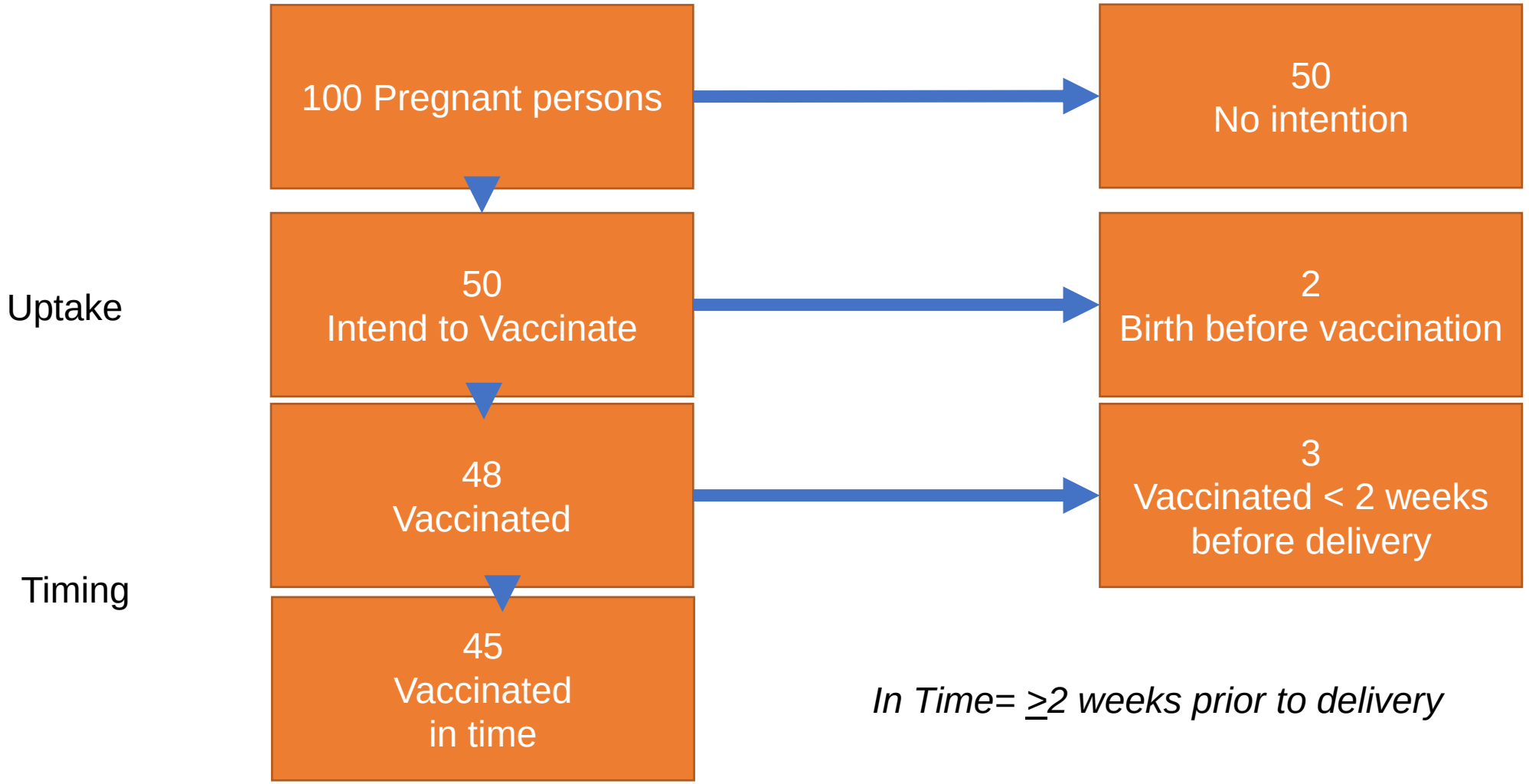
Methods: Provision of RSVpreF

- Base case:
  - Year round
- Scenarios
  - Individual Months
  - Ranges of Months
    - April-February
    - May-February
    - June-February
    - August-January
    - September-January
    - September-December

Methods: Provision of RSVpreF

- Mother vaccinated
  - During 32 $^{0}/_{7}$ - 36 $^{6}/_{7}$ weeks gestation, evenly distributed
- Birth
  - Must be >2 weeks after vaccination for protective efficacy to pass to infant, based on historical gestational age

Methods: Provision of RSVpreF

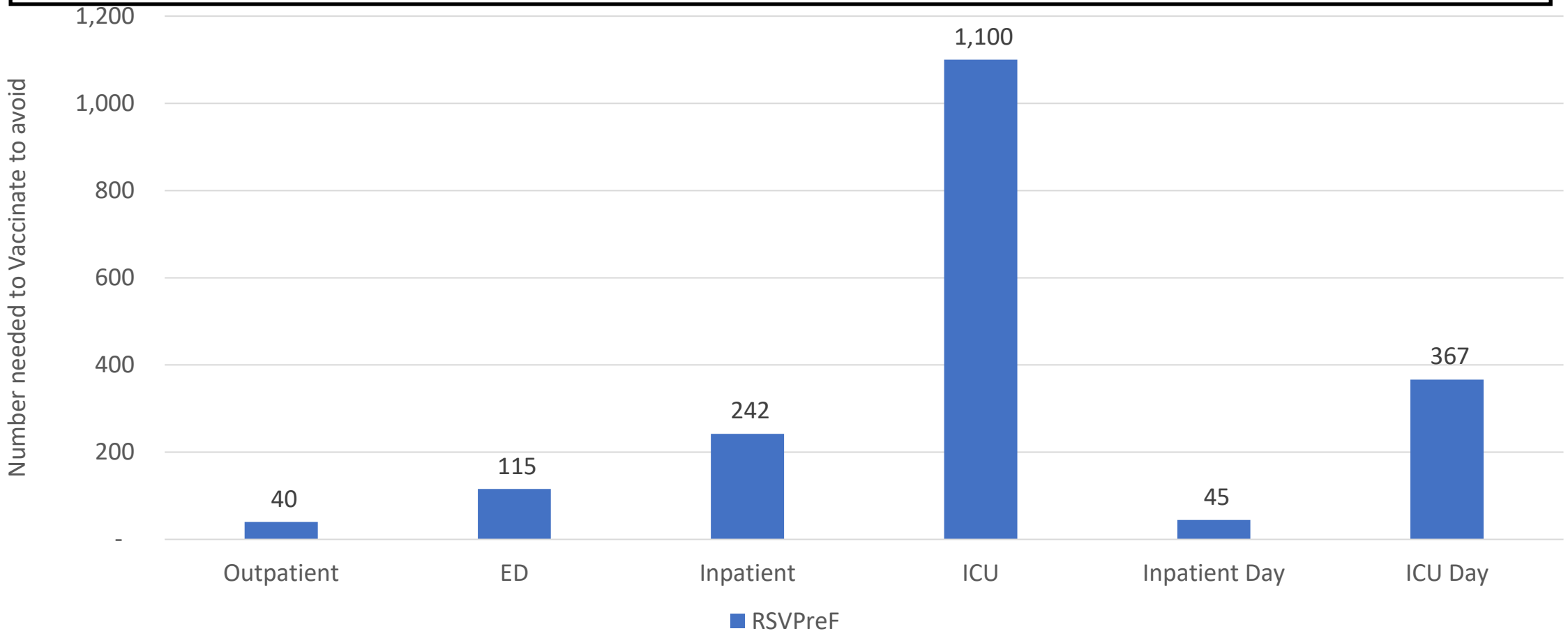


In Time= ≥2 weeks prior to delivery

Results: Base case

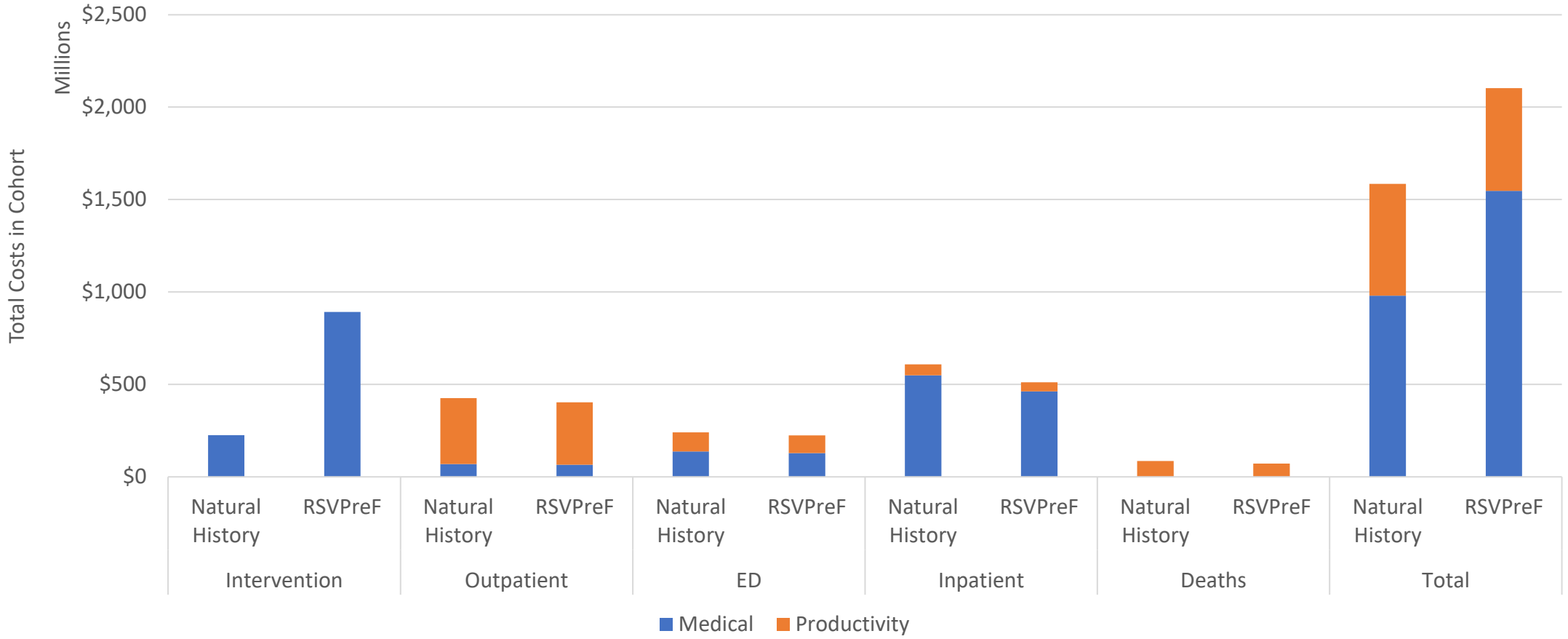
- Base case:
  - **Population of annual US births (3.66 million)**
  - 50% intended uptake in the RSVpreF group
  - First RSV season
  - **$295/dose**
  - RSVpreF only impacts lower respiratory tract infections

Results: Number Needed to Vaccinate



Cohort: 3.66 million births, assuming 50% intended uptake in RSVpreF group

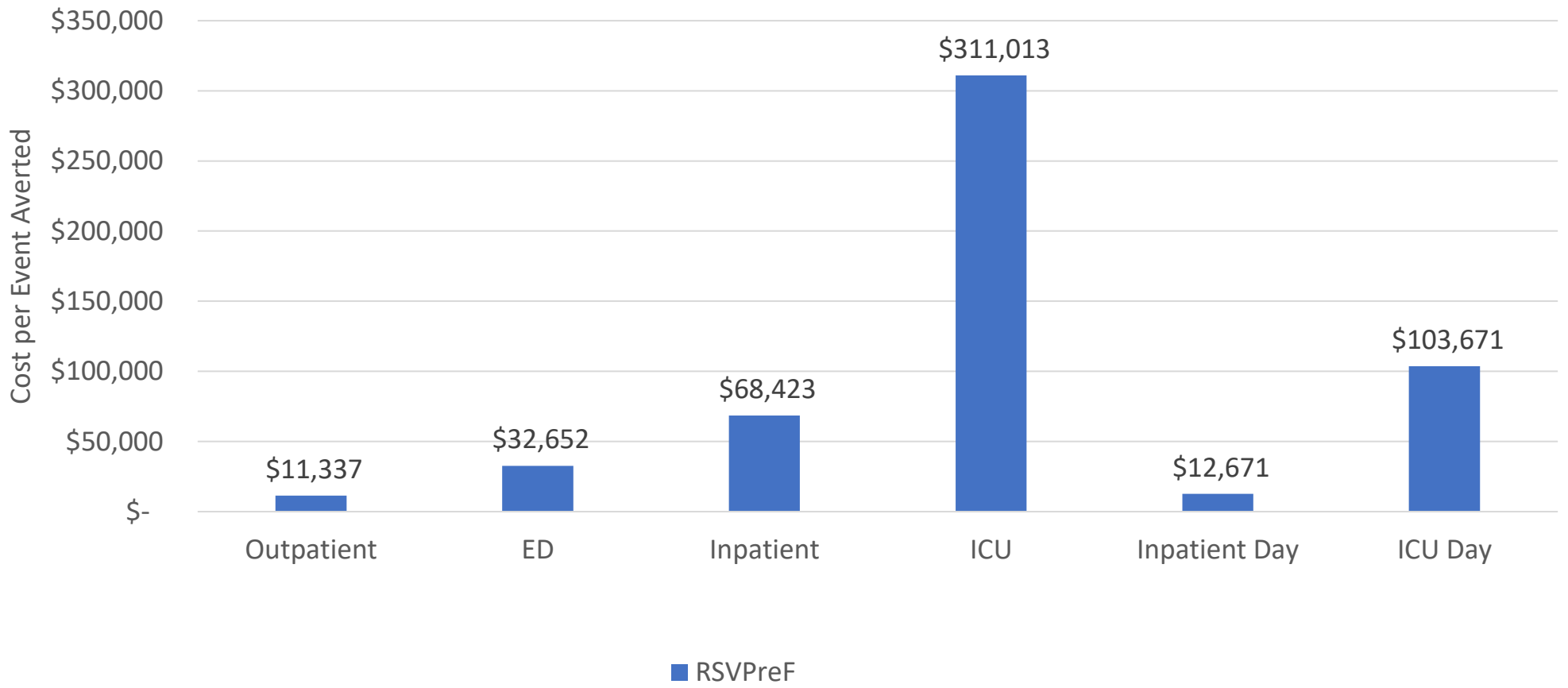
Results: Costs



Cohort: 3.66 million births, assuming 50% intended uptake in RSVpreF group

Base costs of RSVpreF: $295/dose, both natural history and RSVPreF involve palivizumab for high-risk children

Results: Cost per Event Averted



Base costs of RSVpreF: $295/dose

Results: Cost-Effectiveness

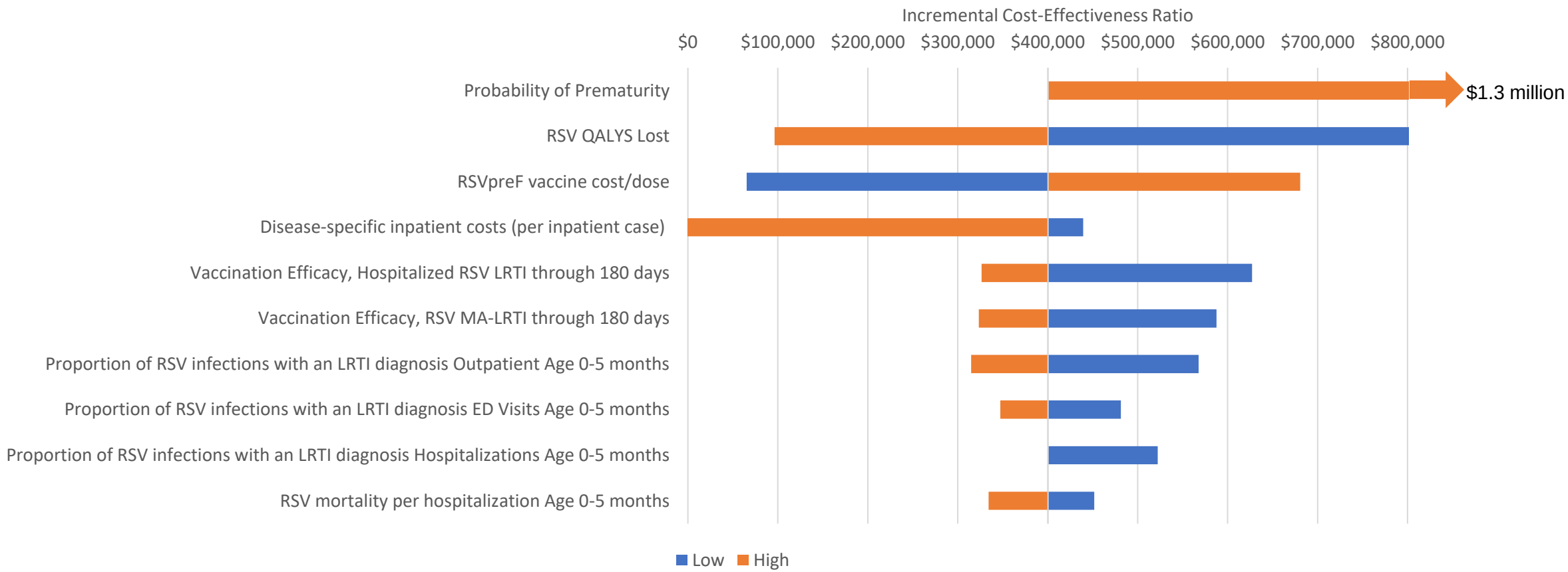
Overall	Costs ($)	QALYs lost	ICER ($/QALY) Vs. NH
Natural History	1,585,172,002	18,151	
RSVpreF	2,103,215,047	16,857	400,304

Cohort: 3.66 million births, assuming 50% intended uptake in RSVpreF group, ICER is not affected by uptake

Base costs of RSVpreF: $295/dose

QALY= quality-adjusted life-year; ICER= incremental cost-effectiveness ratio

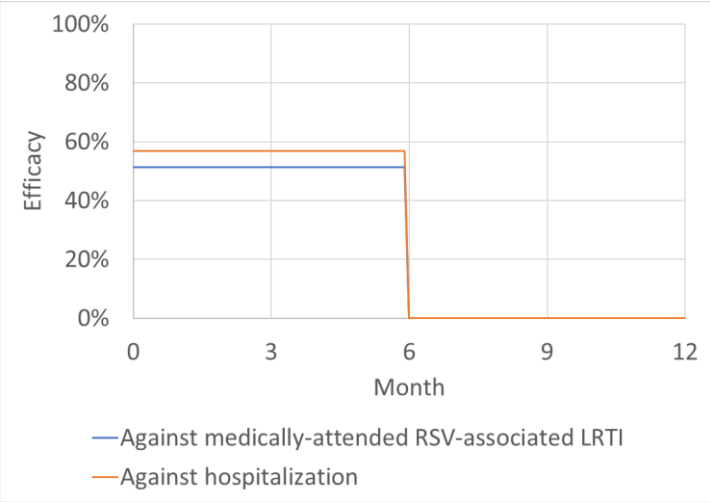
Sensitivity: Tornado RSVpreF



Base cost of RSVpreF: $295/dose
MA= Medically-attended
LRTI= Lower respiratory tract infection
QALY= Quality adjusted life year

Methods: RSVpreF efficacy "flat efficacy" scenario

Overall	Costs ($)	QALYs lost	ICER ($/QALY)
Natural History	1,585,172,002	18,151	
RSVpreF	2,094,993,469	16,757	365,669

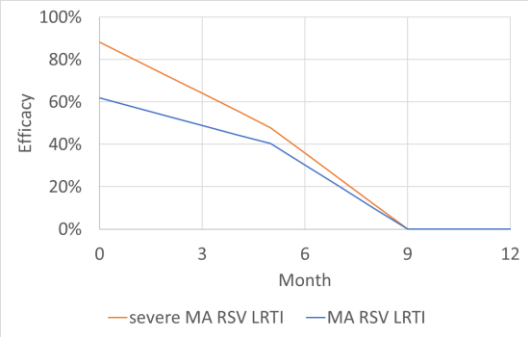


Slightly lower costs with RSVpreF, slightly fewer QALYs lost, slightly lower ICER

ICER: Incremental cost-effectiveness ratio
LRTI= Lower respiratory tract infection

Sensitivity Analysis: More Optimistic Efficacy

Overall	Costs ($)	QALYs lost	ICER ($/QALY) Vs. NH
Natural History	1,585,172,002	18,151	
RSVpreF	2,056,423,553	16,504	286,179



MA: Medically-attended, LRTI: Lower Respiratory Tract Infection

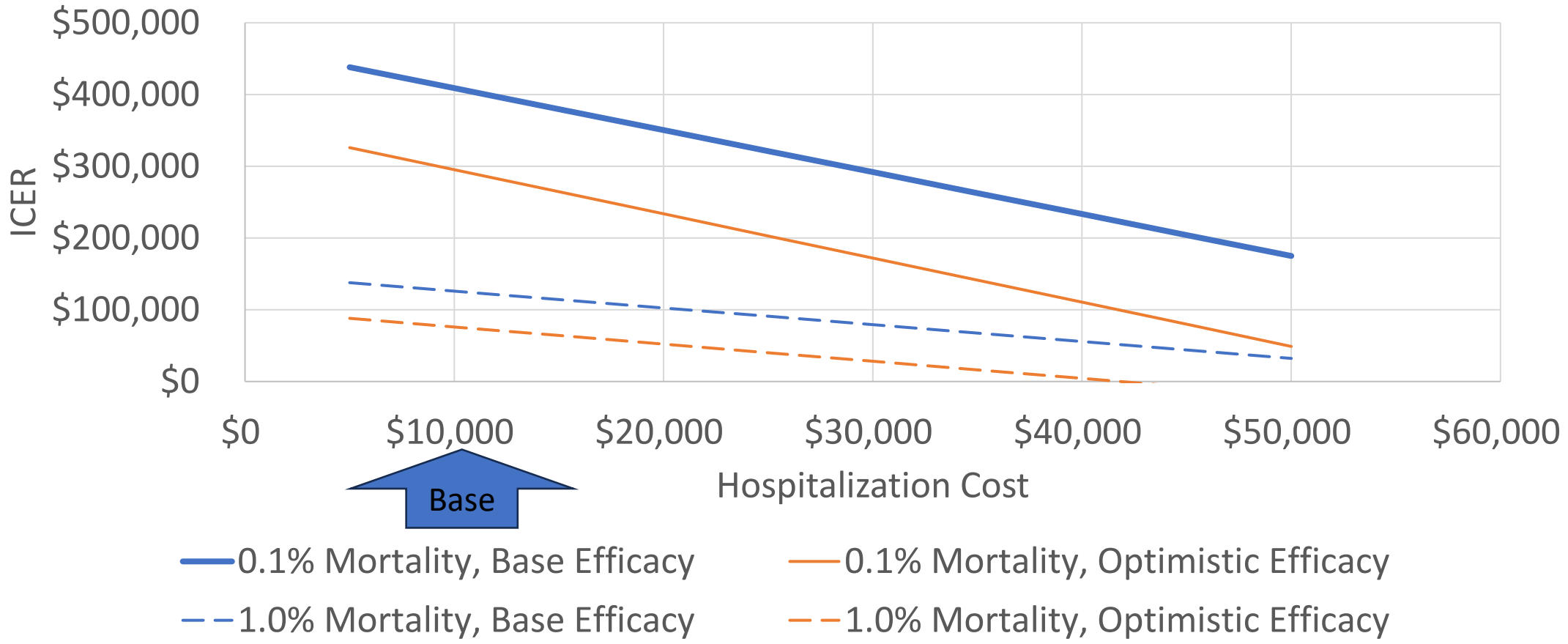
Higher and longer efficacy

Cohort: 3.66 million births, assuming 50% intended uptake in RSVpreF group, ICER is not affected by uptake

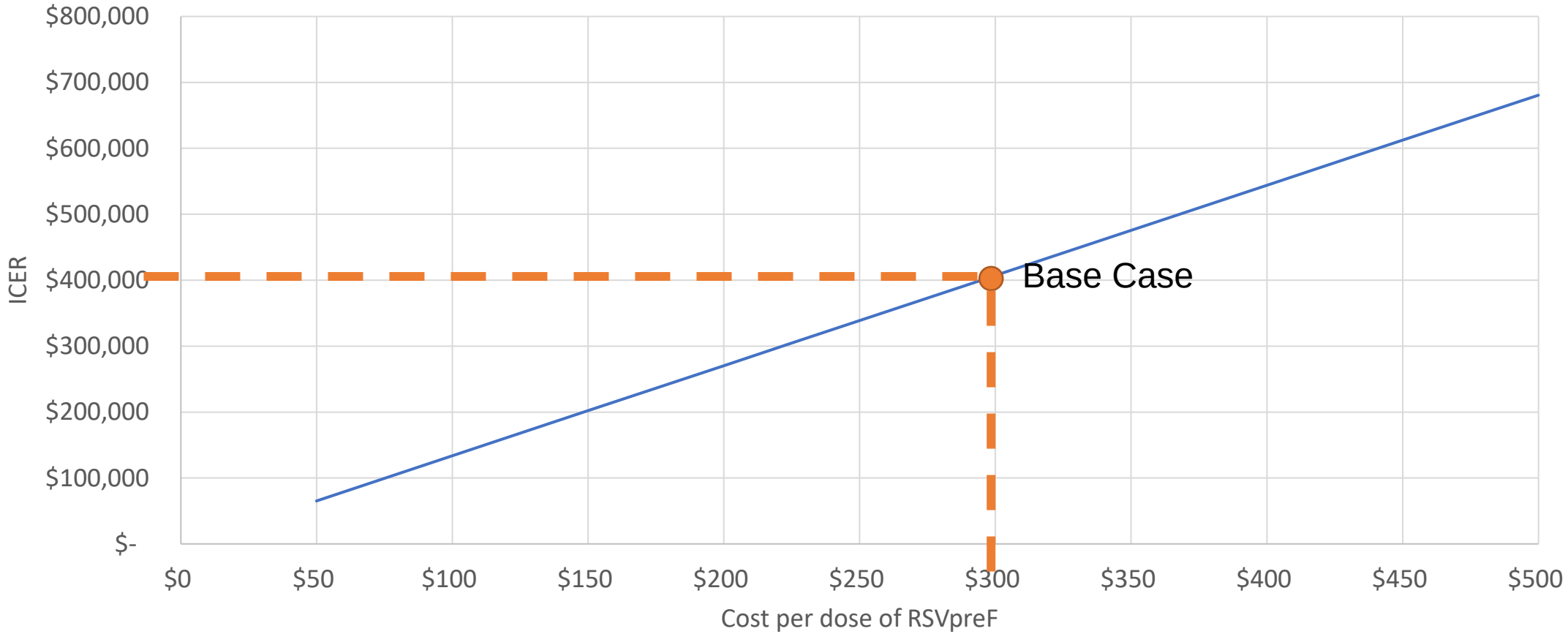
Base costs of RSVpreF: $295/dose

QALY= quality-adjusted life-year; ICER= incremental cost-effectiveness ratio

Sensitivity: Varying Efficacy, Hospitalization Cost, and Mortality



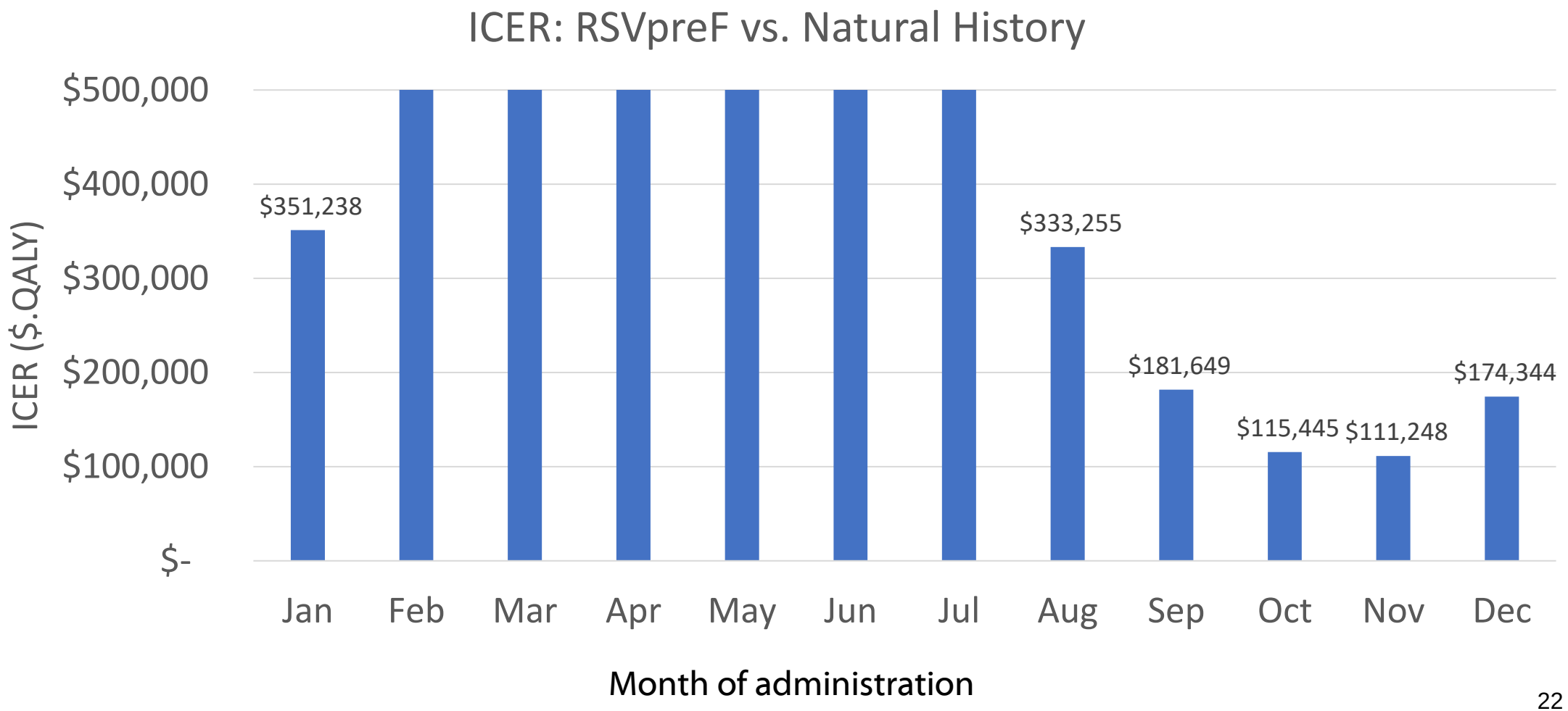
Sensitivity: Cost RSVpreF



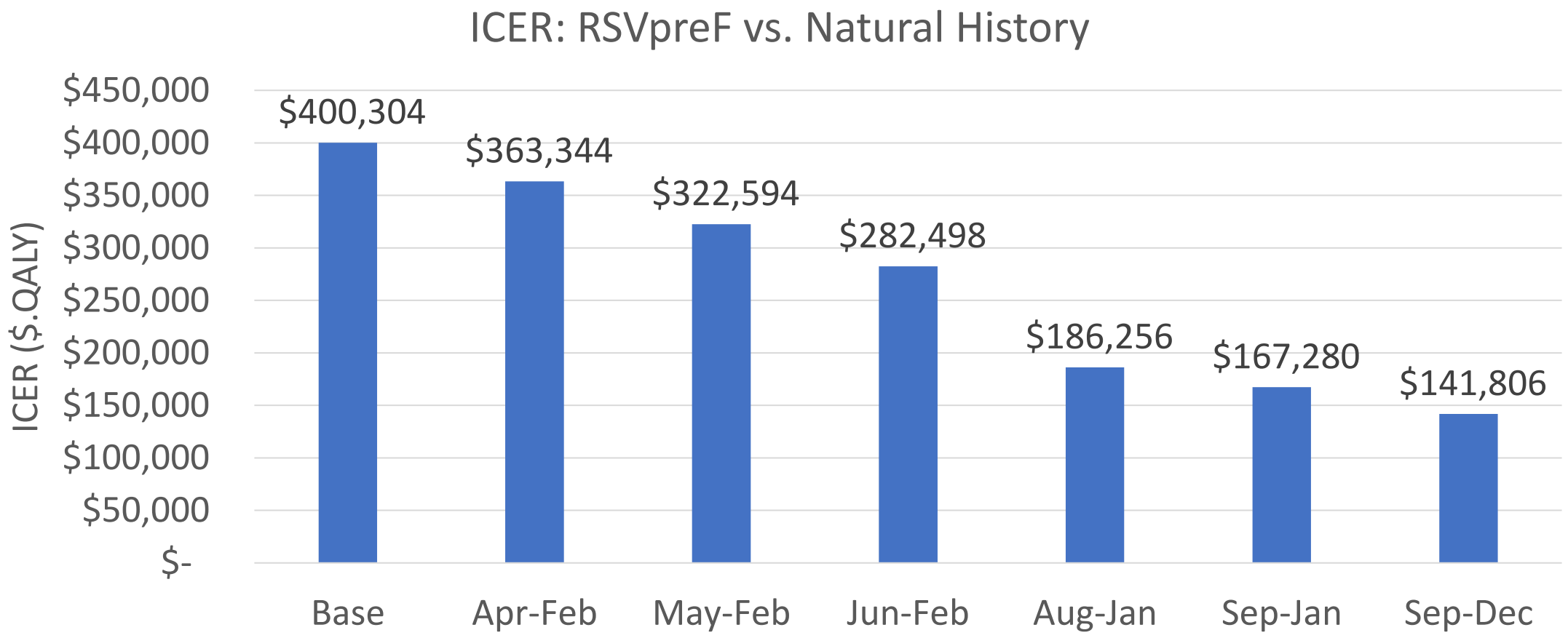
Results: RSVpreF timing scenarios

- Scenarios
  - Base: vaccine given year-round
  - By Month
  - During April-February
  - During May-February
  - During June-February
  - During August-January
  - During September-January
  - During September-December

Results: RSVpreF timing scenarios



Results: RSVpreF timing scenarios



Limitations

- Model Structure
  - No risk groups
  - No dynamic transmission. No impact of the vaccine on transmission and indirect effects
- Uncertain inputs
  - RSVpreF cost
  - QALYs lost
  - Upper respiratory tract infections
  - Prematurity
- **Assumption: no infants will be receiving nirsevimab**

Summary

- RSVpreF may improve RSV outcomes, but will also increase costs
- RSVpreF has the potential to be cost-effective
- Results sensitive to:
  - Rate of prematurity
  - Cost per dose (~65,000 –68$/QALY)
  - Hospitalization Costs (Cost-saving – 440,000 $/QALY)
  - Efficacy (~280,000 – 680,000 $/QALY)
  - QALYs lost (~100,000 – 800,000 $/QALY)
  - Month of Administration (~110,000 – Millions $/QALY)

QALY: Quality-Adjusted Life-Year

Economics of combined use of Pfizer maternal RSVpreF vaccine and nirsevimab

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Methods: Study questions

- On August 3, 2023, the Advisory Committee on Immunization Practices (ACIP) recommended use of nirsevimab
- How should we think about combinations of RSVpreF and nirsevimab?
  - If we know RSVpreF has been administered in time, how cost-effective is it to provide nirsevimab?
  - If we know the infant will receive nirsevimab, how cost-effective is it to provide RSVpreF?

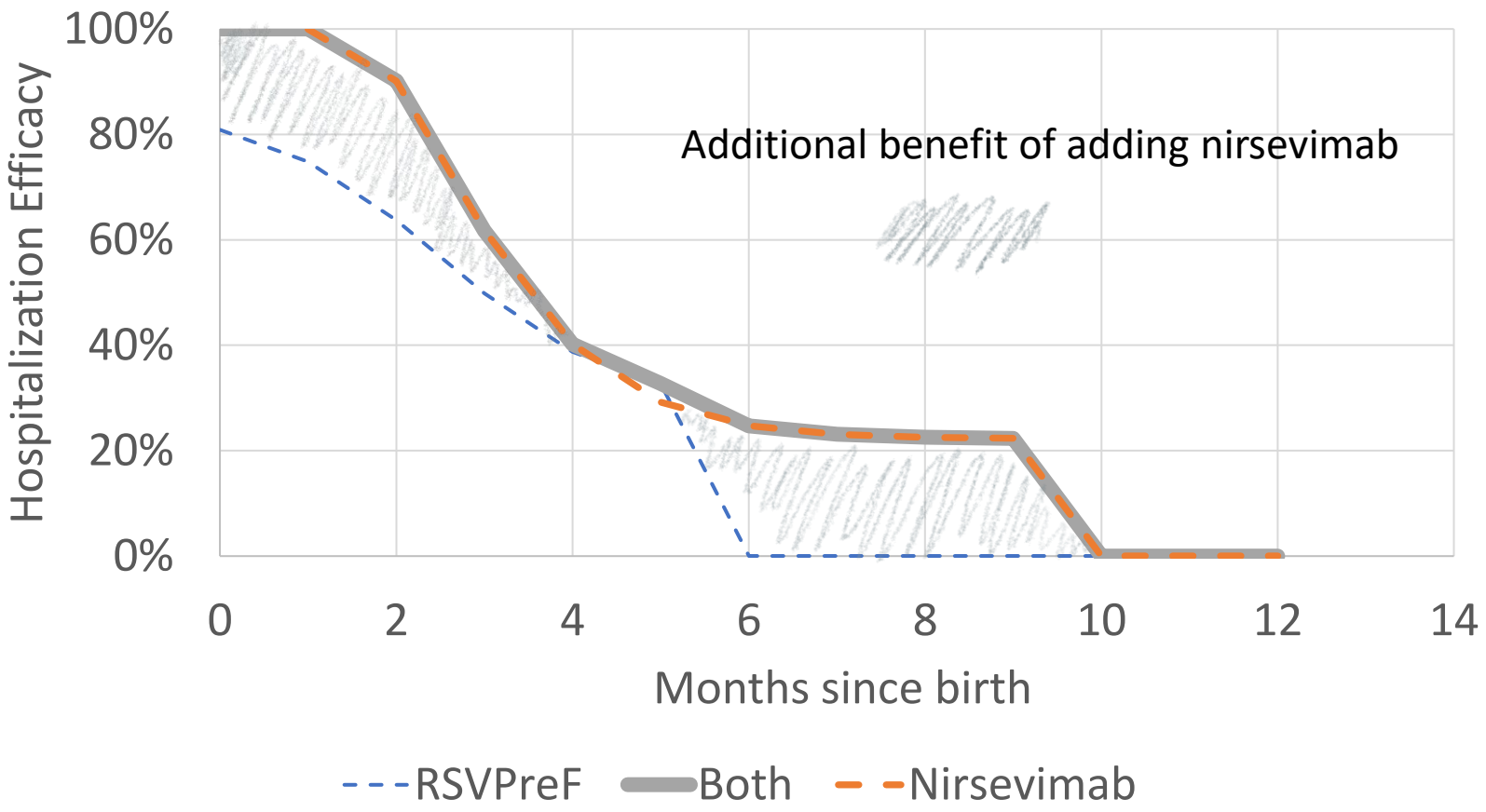
Updates since June

- RSVpreF will be administered in weeks 32-36
  - Because of this, we are assuming the infant is full-term, and therefore, there is no need for palivizumab for any newborns considered in this analysis
- Consideration of higher-risk populations (but assuming they are not premature)
- New timing of RSVpreF administration

Methods: Intervention effectiveness

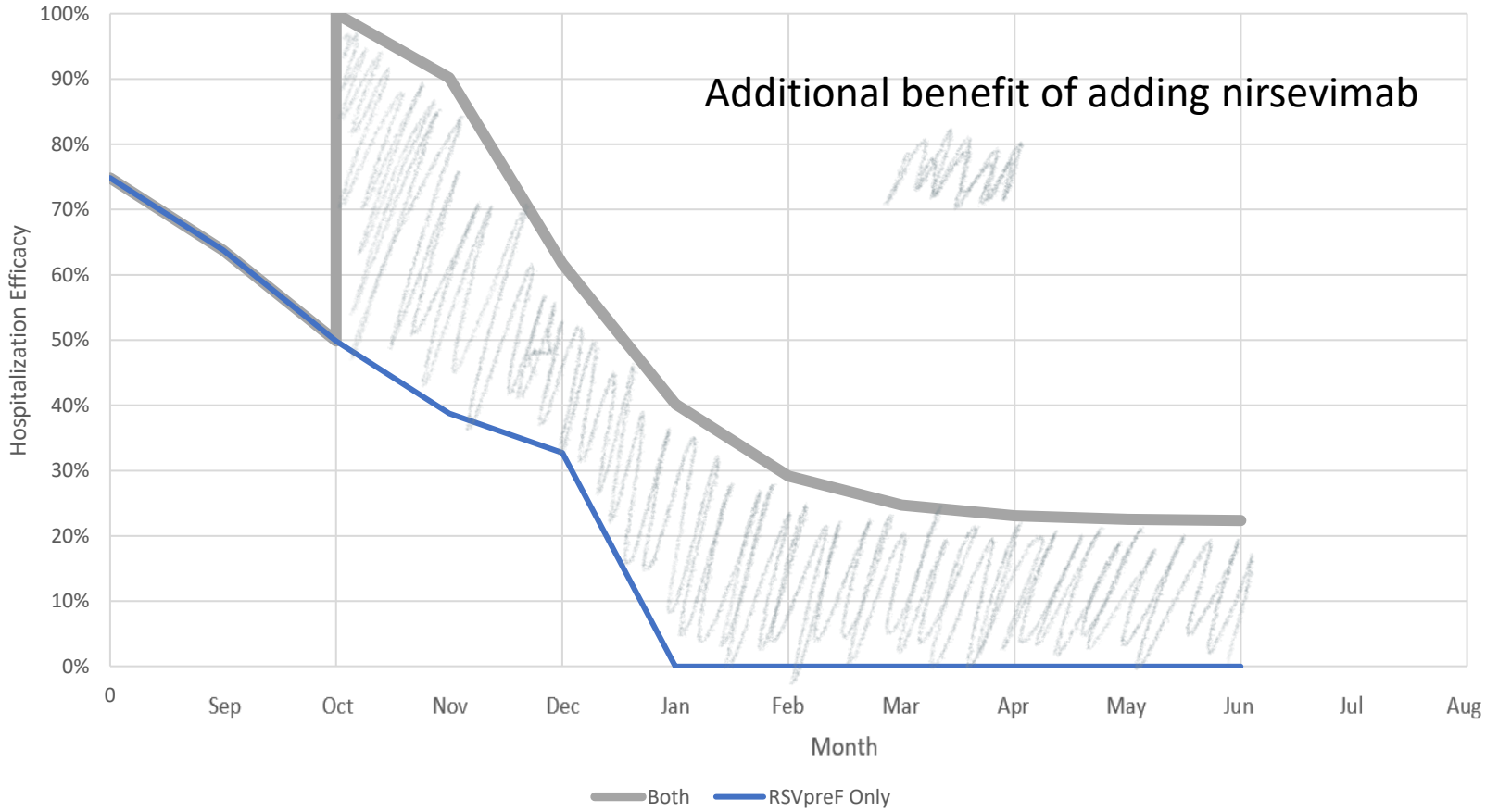
- NO evidence of efficacy on the combined use of these products
- Assumption:
  - Efficacy equal to the highest of nirsevimab or RSVpreF:
    - Efficacy would not be higher than from the most effective product

Methods: Intervention effectiveness



* Assuming administration of nirsevimab at birth

Methods: Intervention effectiveness Example: Off-peak (Aug) birth



Note: Peak infections are typically Dec-Feb

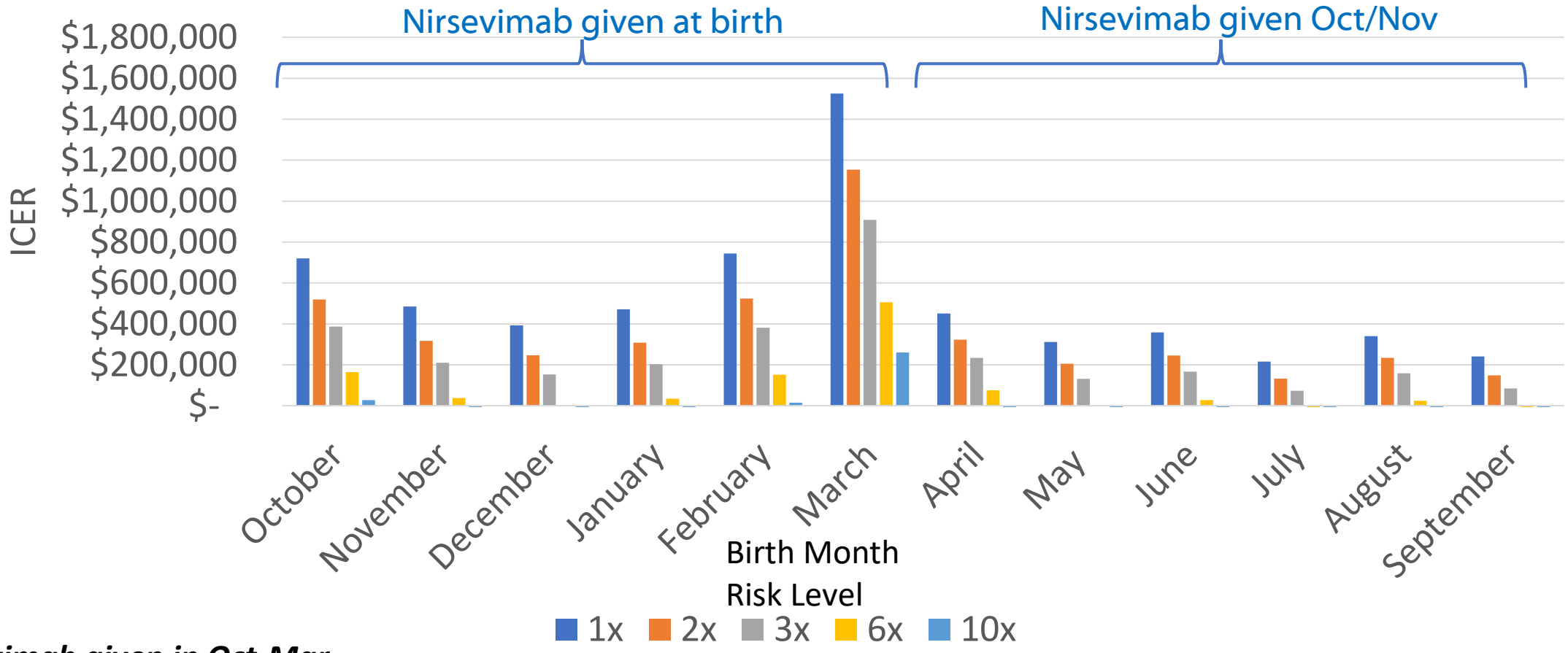
Incremental benefit of adding nirsevimab on top of RSVpreF

- For infants of persons vaccinated with RSVpreF during pregnancy at least 2 weeks prior to delivery

Results: Incremental benefit of adding nirsevimab on top of RSVpreF: Higher Risk

- Higher-Risk
  - Increased multiplier on
    - risk of hospitalization
  - No change in
    - Outpatient incidence
    - ED incidence
    - Cost/outcome
    - QALYs/outcome

Results: Incremental benefit of adding nirsevimab on top of RSVpreF: By Month and Risk

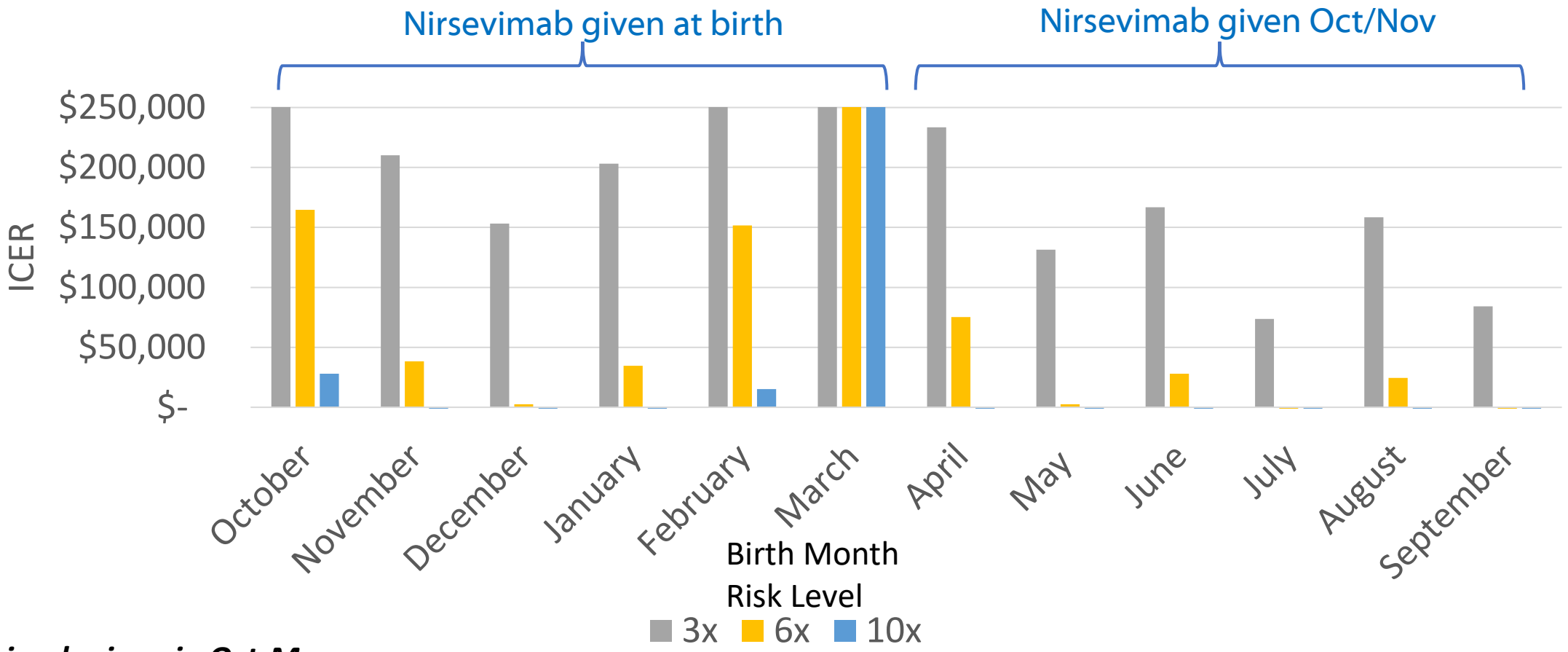


Nirsevimab given in Oct-Mar

ICER= Incremental cost effectiveness ratio ($/QALY)

If the 10x bars are "missing", providing nirsevimab is cost-saving.

Results: Incremental benefit of adding nirsevimab on top of RSVpreF: By Month and Risk

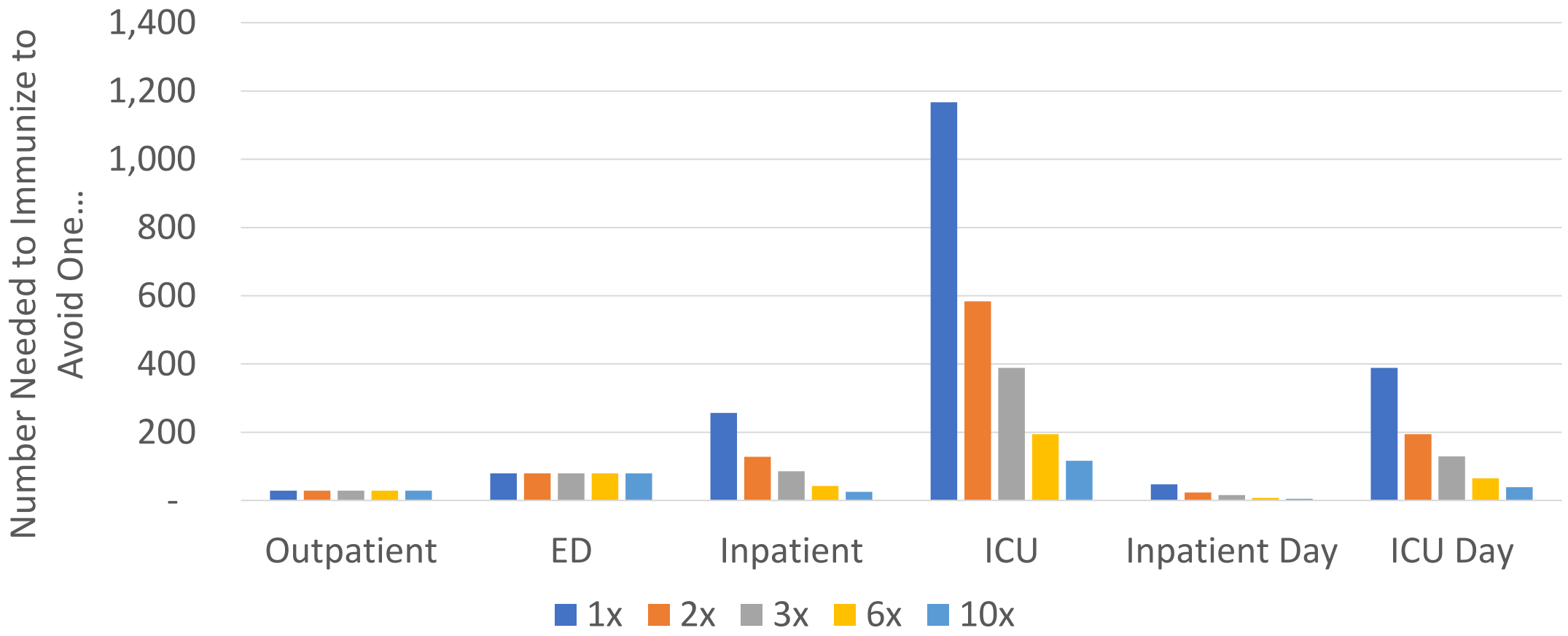


Nirsevimab given in Oct-Mar

ICER= Incremental cost effectiveness ratio ($/QALY)

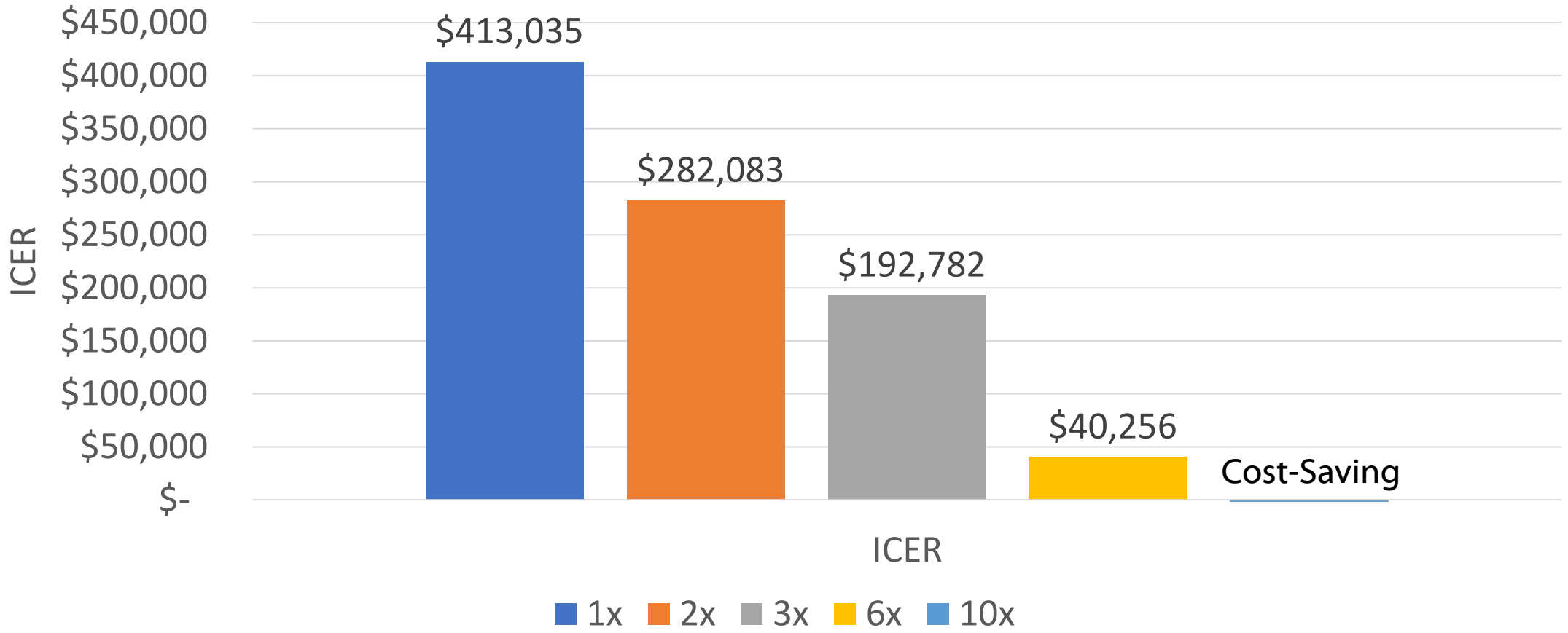
If the 10x bars are "missing", providing nirsevimab is cost-saving.

Results: Adding nirsevimab to *all* infants born year-round to vaccinated mothers



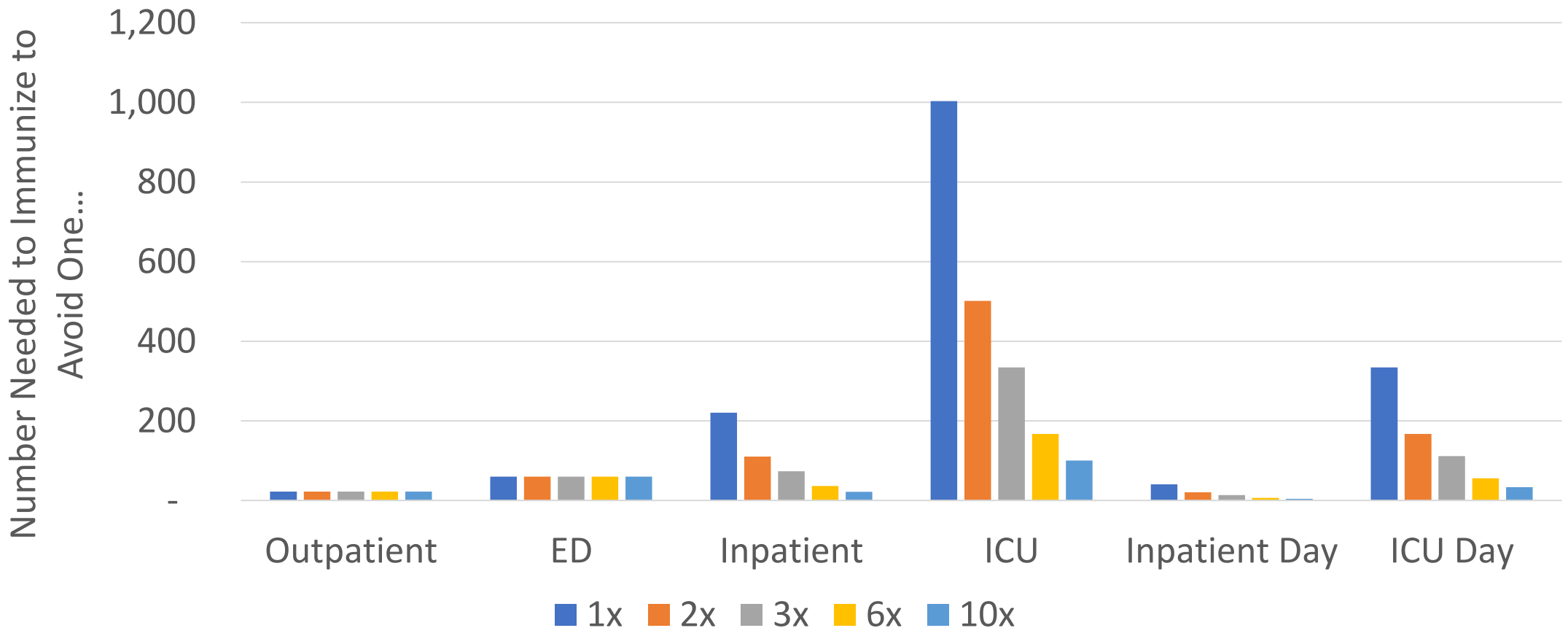
Nirsevimab given at birth for babies born October-March, and in October/November for babies born in April through September to mothers who received RSVpreF at least 2 weeks prior to delivery

Results: Adding nirsevimab to *all* infants born year-round to vaccinated mothers



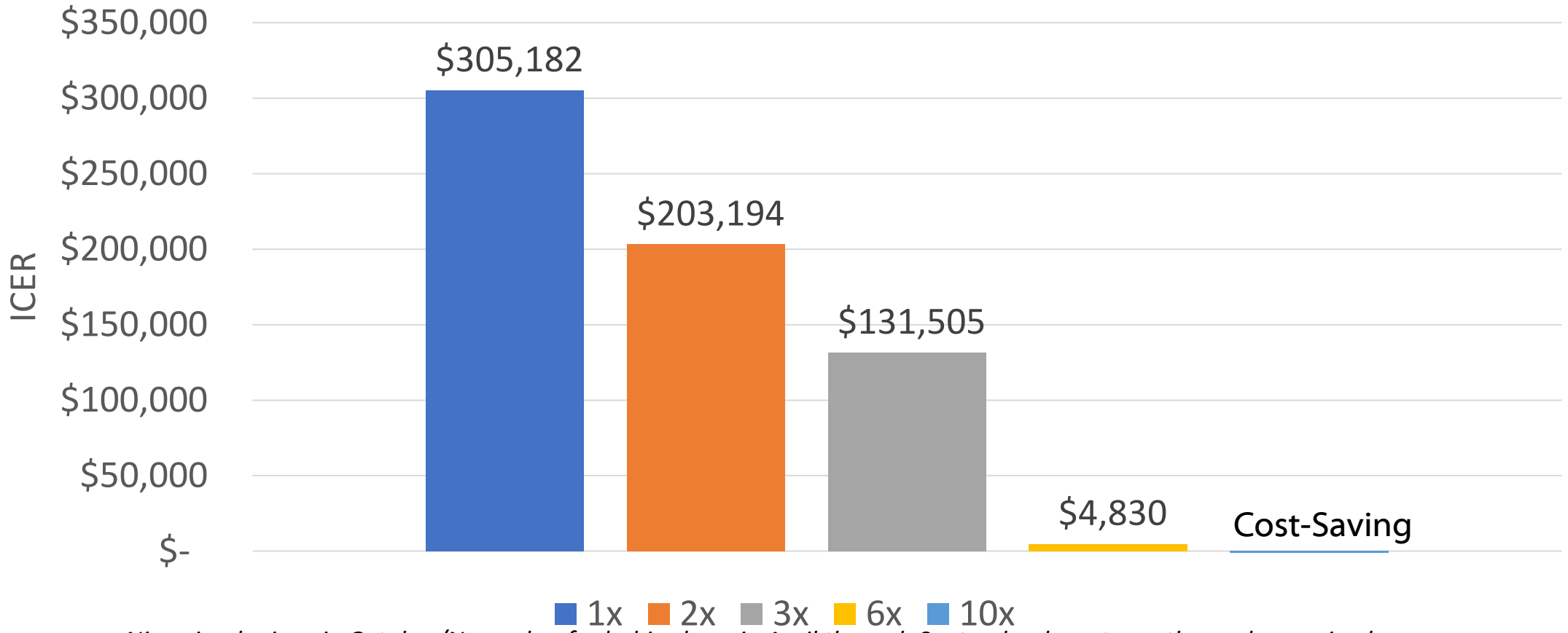
Notes: Nirsevimab given at birth for babies born October-March, and in October/November for babies born in April through September to mothers who received RSVpreF at least 2 weeks prior to delivery
ICER= Incremental cost effectiveness ratio; QALY= Quality-adjusted life-year

Results: Adding nirsevimab at the start of the season only for infants born Apr-Sept



Nirsevimab given in October/November for babies born in April through September born to mothers who received RSVpreF at least 2 weeks prior to delivery

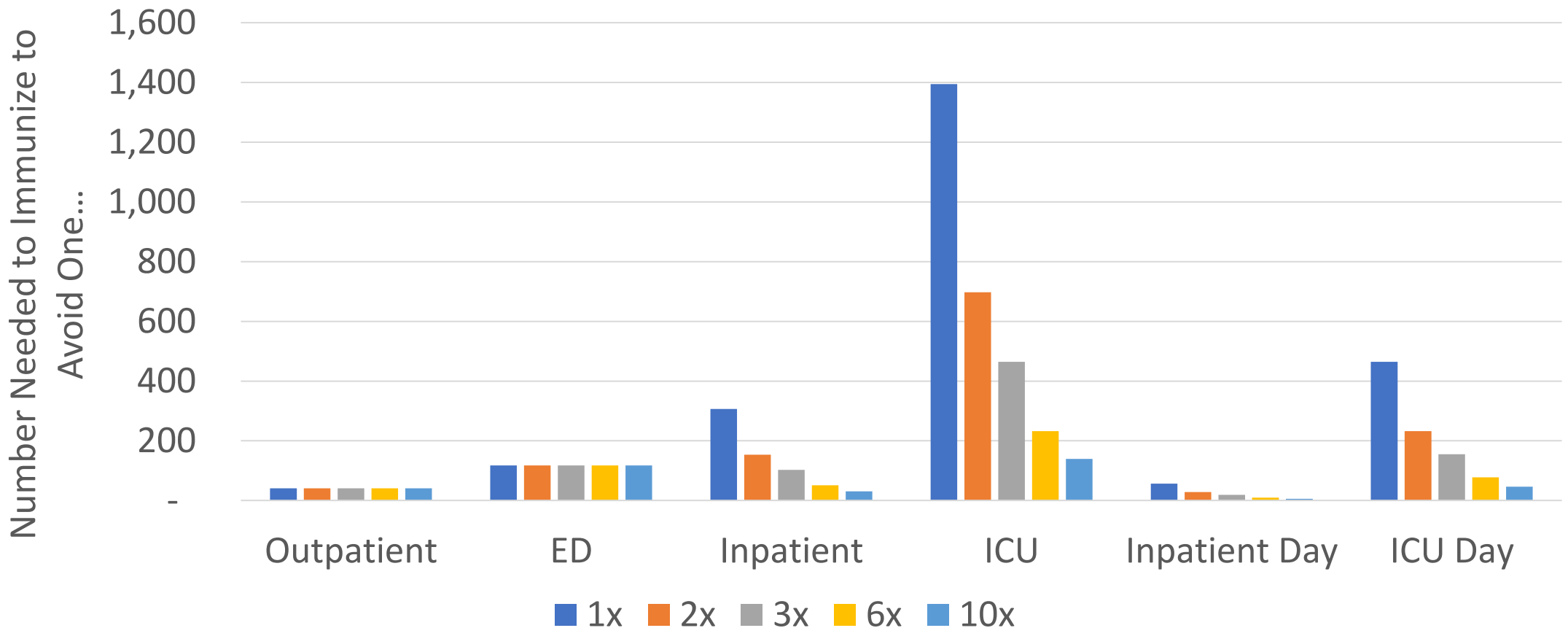
Results: Adding nirsevimab at the start of the season only for infants born Apr-Sept



Nirsevimab given in October/November for babies born in April through September born to mothers who received RSVpreF at least 2 weeks prior to delivery

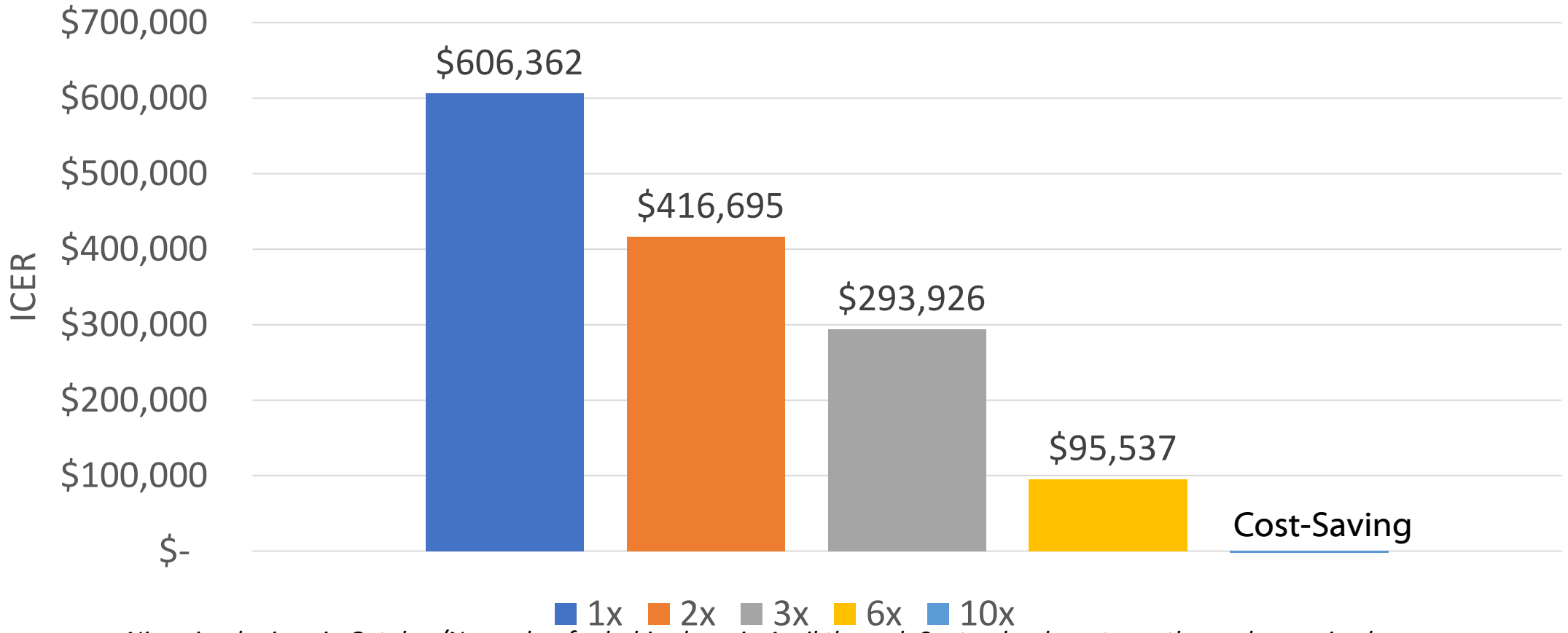
ICER= Incremental cost effectiveness ratio; QALY= Quality-adjusted life-year

Results: Adding nirsevimab during the season for infants born Oct-Mar



Nirsevimab given in October/November for babies born in April through September born to mothers who received RSVpreF at least 2 weeks prior to delivery

Results: Adding nirsevimab during the season for infants born Oct-Mar



Nirsevimab given in October/November for babies born in April through September born to mothers who received RSVpreF at least 2 weeks prior to delivery

ICER= Incremental cost effectiveness ratio; QALY= Quality-adjusted life-year

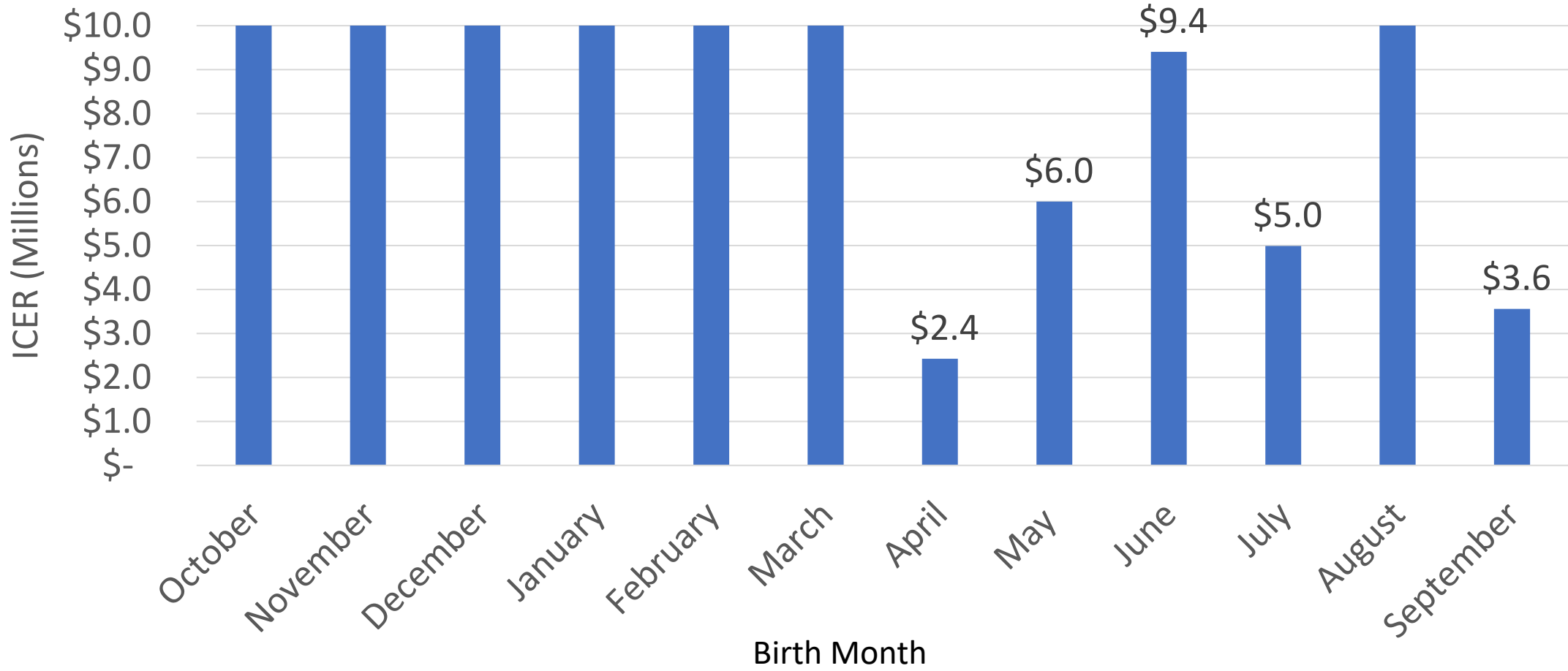
Summary: Incremental benefit of adding nirsevimab on top of RSVpreF

- Additional benefit beyond RSVpreF protection
- ICERs are high, but could be lower for higher-risk populations, particularly if born off-peak

Incremental benefit of adding RSVpreF on top of nirsevimab

- If you know the infant will be receiving nirsevimab

Results: Incremental benefit of adding RSVpreF on top of nirsevimab



ICER= Incremental cost effectiveness ratio

Summary: Incremental benefit of adding RSVpreF on top of nirsevimab

- Very marginal additional benefit beyond nirsevimab protection
- ICERs are extremely high

Overall summary: Combinations

- Limitation:
  - No efficacy data for combination of products
- Nirsevimab may add additional protection on top of RSVpreF, particularly for higher-risk infants.
- Adding RSVpreF on top of nirsevimab adds marginal effectiveness at very high cost in the general population

Thank You

- Please send comments to:
- dwhutton@umich.edu

Appendix to Economics of Pfizer maternal RSVpreF vaccine

Research team

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CDC

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- Andrew Leidner, PhD

Conflicts of interest statements

- Authors have no known conflict of interests.

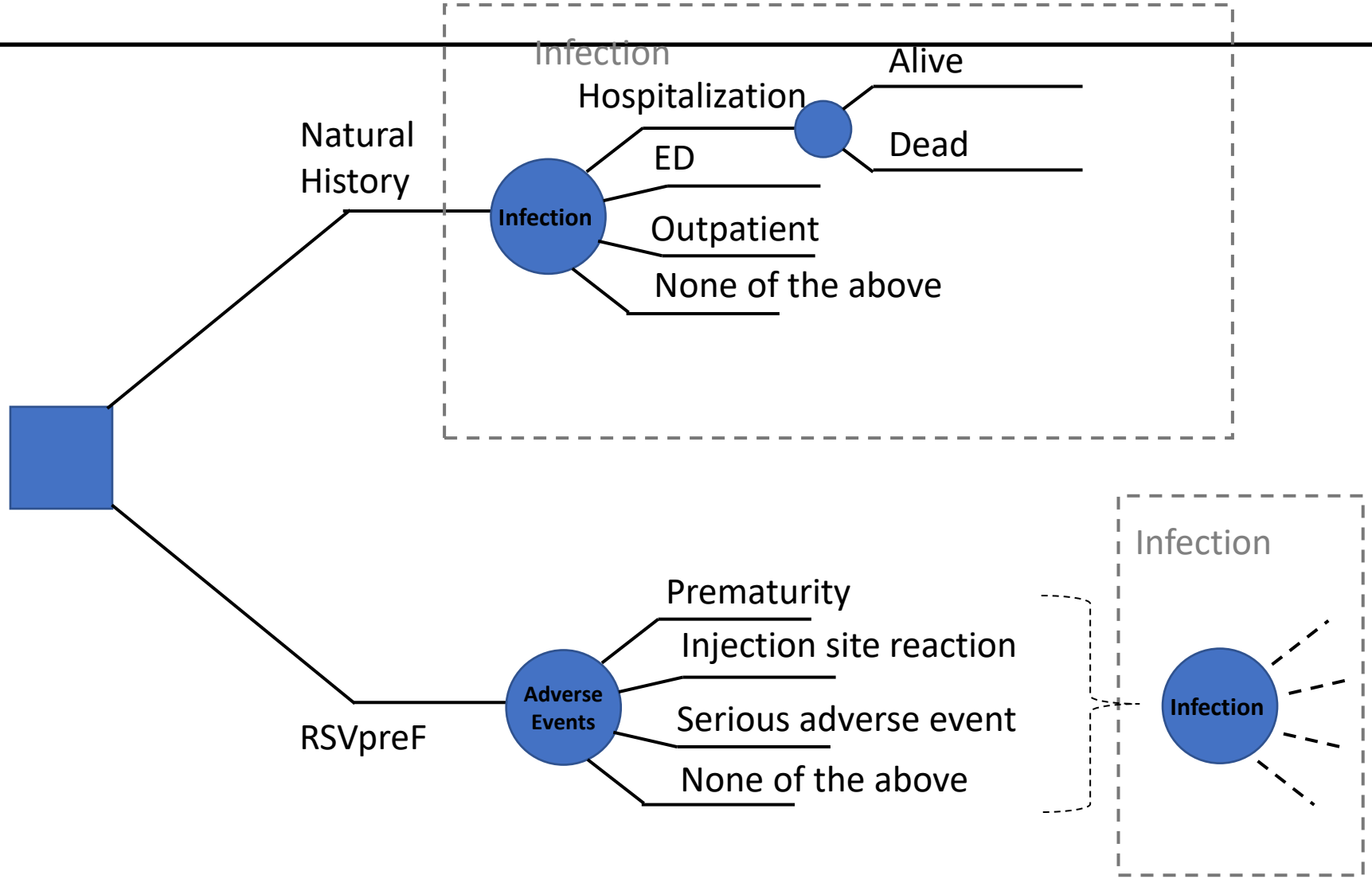
Methods: Study question

- Determine the cost-effectiveness of RSVpreF by:
  - Evaluating the population impact in terms of
    - annual resource utilization
    - total cases
    - total costs
    - deaths
    - quality-adjusted life-years (QALYs)
  - Comparing the incremental cost-effectiveness ratio (ICER) of RSVpreF to natural history/no vaccine.
  - Running scenario analyses outcomes that explore key areas of uncertainty.
- Perspective: Societal

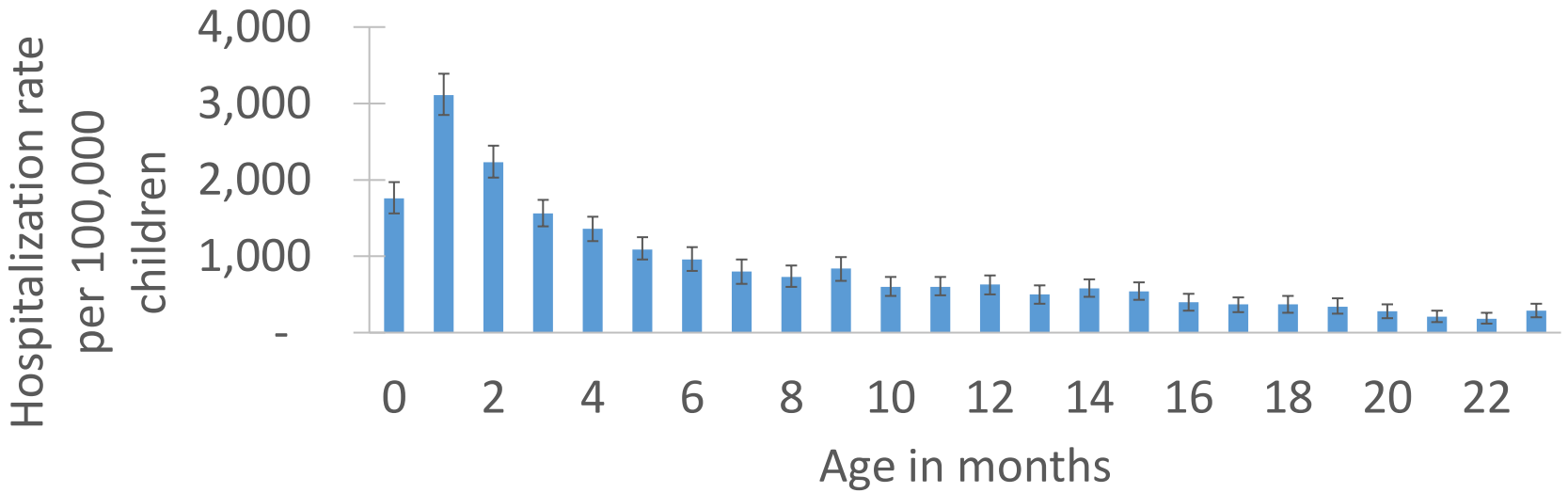
Methods: Intervention(s)

- Target population: US pregnant persons
- Interventions:
    1. No vaccination (Natural history)
    2. RSVpreF against RSV illness
- Timeframe: 1 year (1 RSV season)
- Analytic horizon: infant's lifetime
- Discount rate: 3%

Methods: Decision tree model



Methods: Epidemiology Hospitalization



	Base Case	Range	Source
Respiratory syncytial virus (RSV) incidence, per 100,000	See Above	See Above	CDC NVSN, December 2016 to September 2020
Proportion with LRTI			
Age 0-5 months	1.0	0.5-1.0	Rainisch, 2020
Age 6-11 months	1.0	0.5-1.0	Rainisch, 2020

CDC New Vaccine Surveillance Network (NVSN) hospitalization rates for children under 2 years of age from December 2016 to September 2020

Methods: Epidemiology
ED and Outpatient

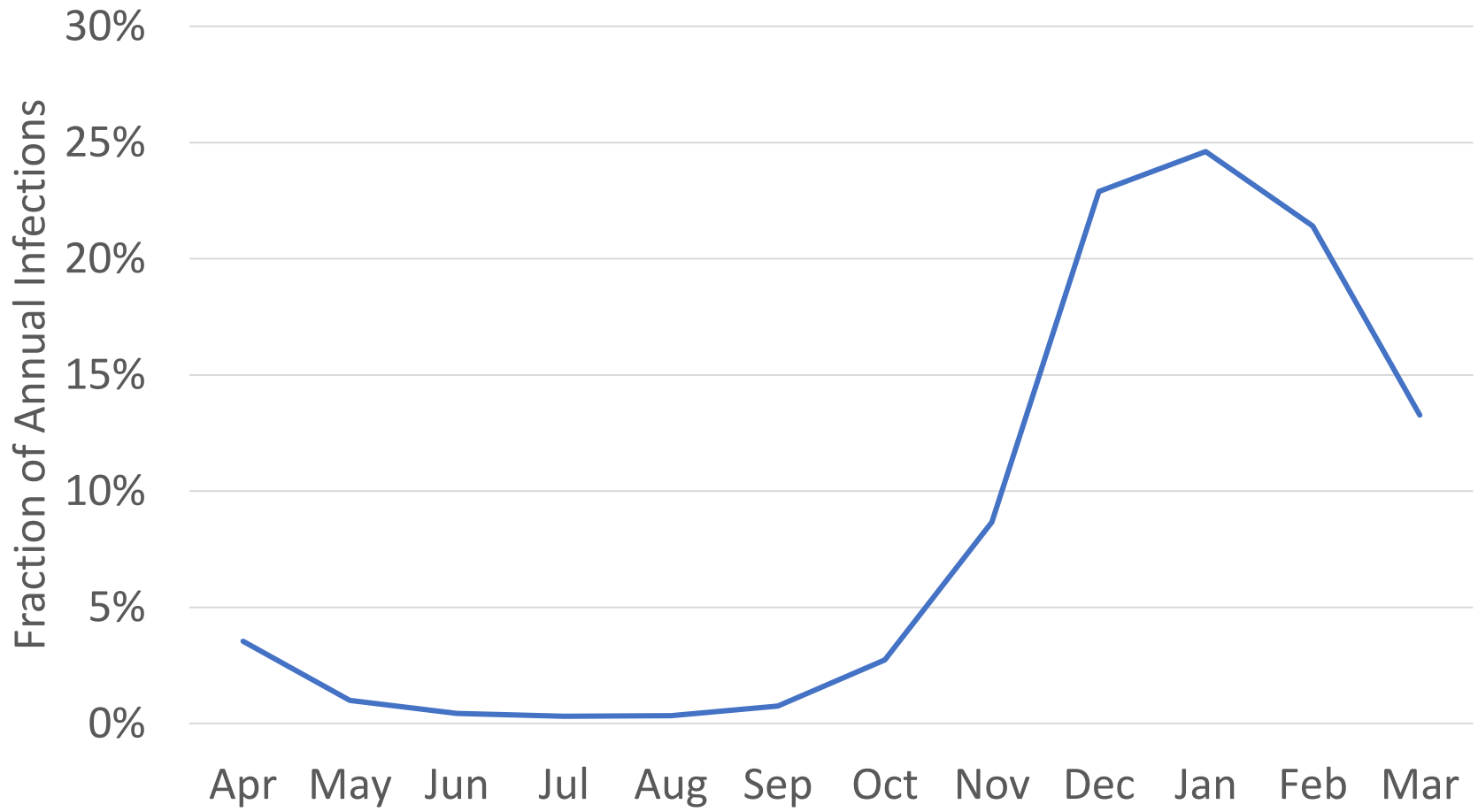
Respiratory syncytial virus (RSV) incidence, per 100,000	Base Case	Range	Source
Emergency Department			
Age 0-5 months	7,500	5,500 – 7,500	Lively 2019 (base case and range), Hall 2009 (range)
Age 6-11 months	5,800	5,700 – 5,800	Lively 2019 (base case and range), Hall 2009 (range)
Age 12-23 months	3,200	3,200 – 5,300	Hall 2009 (base case and range), Lively 2019 (range)
Proportion with LRTI			
Age 0-5 months	0.65	0.25-1.0	Rainisch, 2020
Age 6-11 months	0.5	0.25-1.0	Rainisch, 2020
Outpatient			
Age 0-5 months	21,600	13,200 – 21,600	Lively 2019 (base case and range), Hall 2009 (range)
Age 6-11 months	24,600	17,700 – 24,600	Lively 2019 (base case and range), Hall 2009 (range)
Age 12-23 months	18,440	6,600 – 29,620	Jackson 2021 (base case and range), Hall 2009 (range)
Proportion with LRTI			
Age 0-5 months	0.65	0.25-1.0	Rainisch, 2020
Age 6-11 months	0.3	0.1-1.0	Rainisch, 2020

LRTI= Lower respiratory tract infection

Methods: Epidemiology
Mortality

	Base Case	Range	Source
RSV mortality per hospitalization			
Age 0-5 months	0.10%	0.04-0.20%	Hansen 2022, Doucette 2016
Age 6-11 months	0.10%	0.04-0.20%	Hansen 2022, Doucette 2016
Age 12-23 months	0.3%	0.28%-0.34%	Gupta 2016

Seasonality



Source: National Respiratory and Enteric Virus Surveillance System (NREVSS) (2015-2019)

Methods: Efficacy

Variable	Base case value	Range for sensitivity analysis	Source
RSVpreF			
Initial efficacy (months 0-5) against medically-attended RSV-associated LRTI	51.3%	29.4% - 66.8%	Kampmann et al, 2023
Initial efficacy (months 0-5) against hospitalized RSV-associated LRTI	56.8%	10.1% - 80.7%	Kampmann et al, 2023
Efficacy months 6-12	0		

Assumed 0% efficacy against upper respiratory tract infections
LRTI= Lower respiratory tract infection

Methods: Medical Costs

Variable	Value	Range	Source
Disease-specific hospitalization costs (per hospitalization)			
Age 0-11 months	$11,487	4,804 - 86,646	Bowser 2022
Age 12- 23 months	$11,469	4,804 - 86,646	
Disease-specific ED costs (per ED visit)	$563	544 - 581	Bowser 2022
Disease-specific outpatient costs (per outpatient visit)	$82	46 - 118	Bowser 2022

- Bowser, 2022 is a systematic review using studies from 2014-2021
- Funded by Sanofi
- All numbers updated to 2022 dollars using GDP Deflator

Methods: Productivity costs

Variable	Value	Range	Source
Productivity burden of RSV disease (caregiver losses)			
Days of lost productivity			
Outpatient*	2.5	0-5	Fragaszy, 2018; Petrie, 2016; Van Wormer, 2017
ED*	2.5	0-5	Fragaszy, 2018; Petrie, 2016; Van Wormer, 2017
Hospitalization^	7.4	0-14	
Lifetime productivity for those <1 year old (lost from death)	1,795,936	1,346,951-2,244,919	Grosse, 2019

*Productivity for outpatient and ED based on adult influenza
^Hospitalization productivity loss = length of hospitalization + 2 days

Methods: Intervention cost

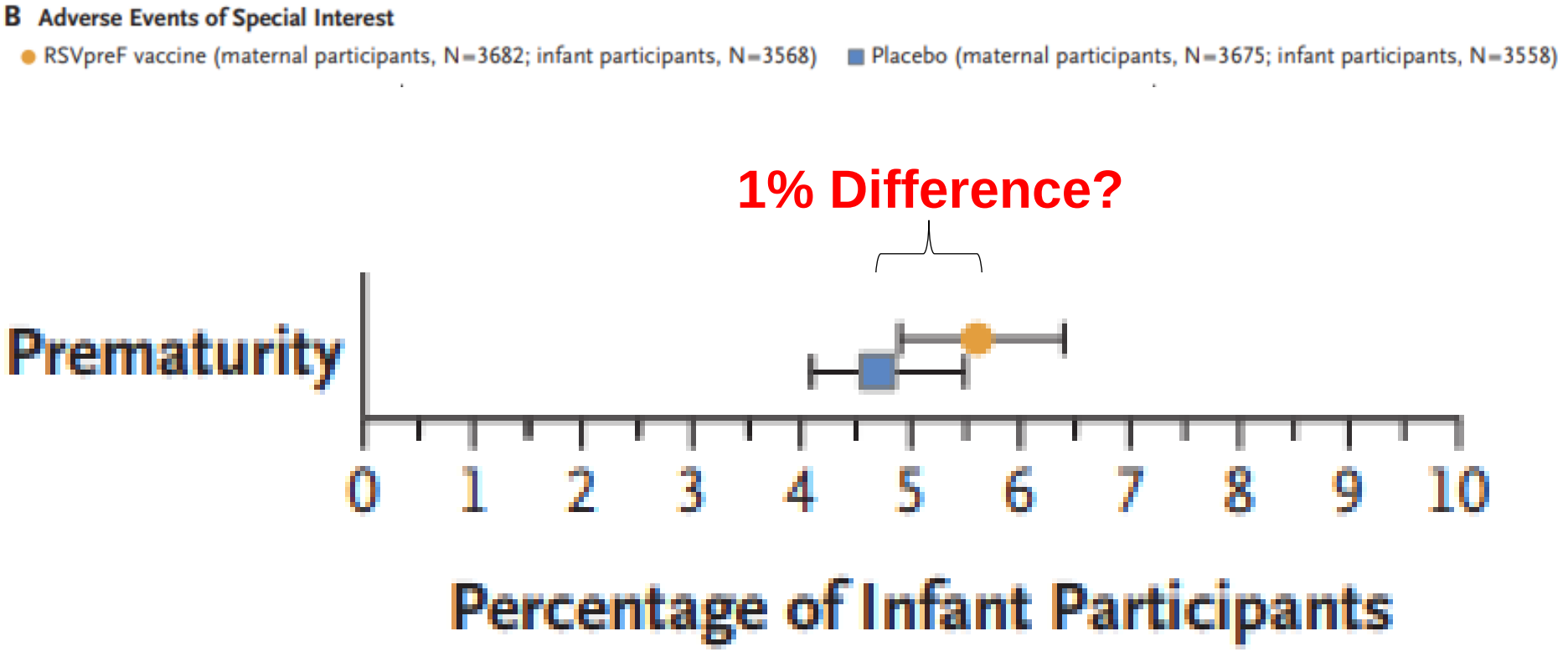
Variable	Value	Range	Source
Immunization-related costs			
RSVpreF, per dose	$295	50 – 500	Assumption: Manufacturer costs for adult vaccine
RSVpreF administration	$16.96	15 - 22	Medicare: HCPCS 90460

Both assume no additional visits, but do include costs of administration

Methods: Adverse event costs

Variable	Value	Range	Source
RSVpreF Maternal Adverse Events			
Rate of injection site reaction	0.41	0.38 – 0.44	Pfizer Phase 3 Trial
Probability of healthcare visit, given injection site reaction	0.02	0.015 – 0.025	Curran, 2020
Cost of outpatient visit	$367.76	23.15 – 1,758	(Deluca, 2023)
Recipient time, physician office for injection site reaction (hours)	2	1 - 3	Assumption
Hypothetical serious adverse event	0.000001	0 - 0.0002	Base: Prosser, 2006 High: 95% CI Phase 3 data for RSV adult vaccines

Methods: Prematurity?



Kampmann B, Madhi SA, Munjal I, Simões EA, Pahud BA, Llapur C, Baker J, Pérez Marc G, Radley D, Shittu E, Glanternik J. Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. New England Journal of Medicine. 2023 Apr 5.

Methods: Prematurity scenario

Variable	Value	Range	Source
RSVpreF infant adverse events			
Higher Rate of Prematurity	**0%**	**0-2%**	Pfizer Phase 3 Trial
Outcomes, per prematurity			
Lifetime cost of late prematurity			
Medical	$ 23,241	$11,621 – $46,482	Waitzman, Jalali, Grosse, 2021
Productivity	$ 11,447	$5,724 – $22,894	Waitzman, Jalali, Grosse, 2021
QALYs lost from late prematurity	0.03	0 – 1.2	Werner, Hauspurg, Rouse, 2015 Petrini et al, 2008, Hirvonen et al, 2014, Crump et al, 2021, Darcy-Mahoney et al, 2016, Carroll et al, 2009, Payakachat et al, 2014

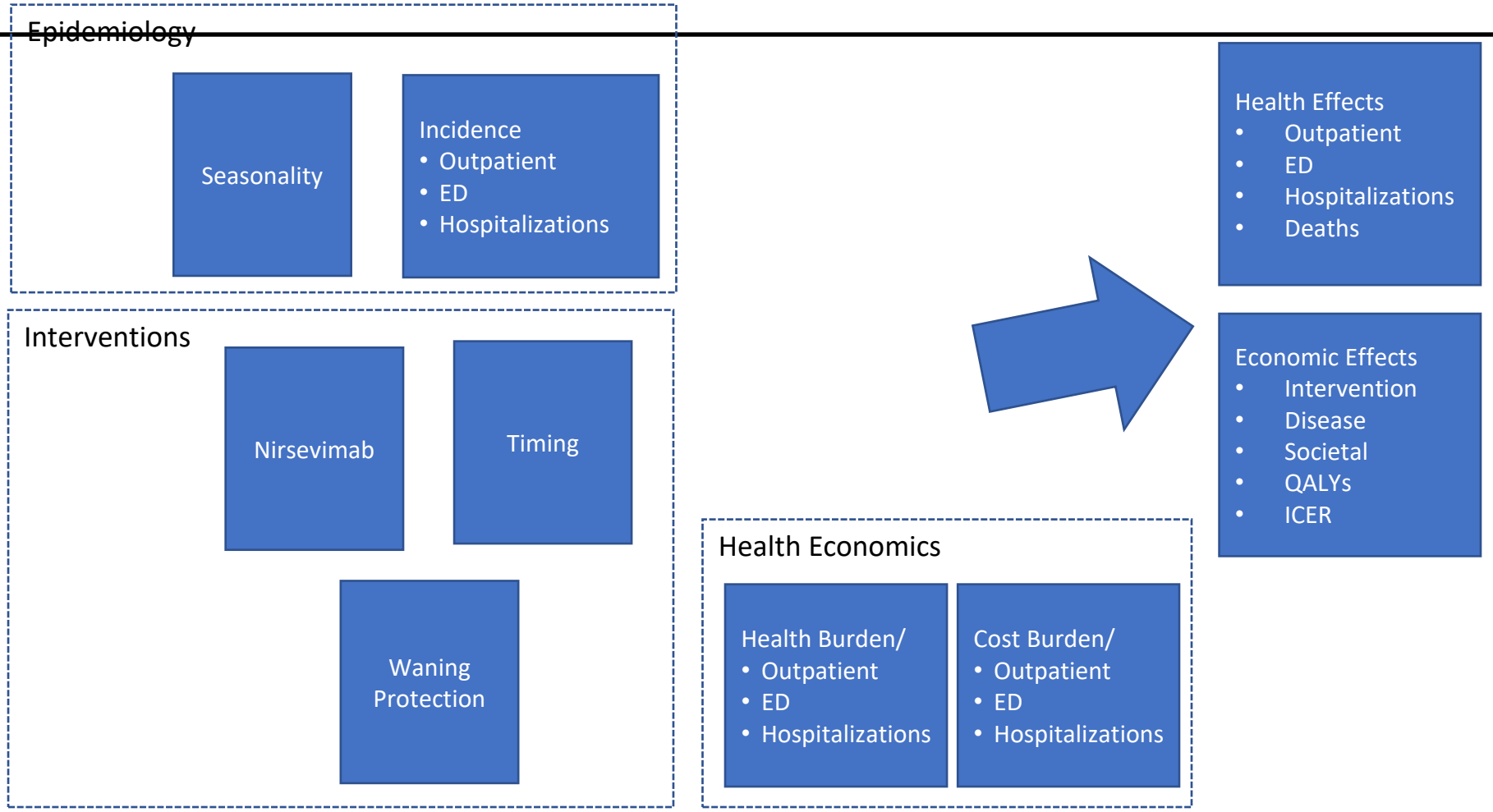
* All costs updated to 2022 using GDP Deflator

Methods: RSV health-related quality of life

Measured in
Days Lost

LRTI quality-adjusted life DAYS lost	Base	Lower (Regnier)	Upper (JIVE)
Outpatient: Child	3.1	1.8	16.6
Outpatient: Caregiver	1.5	0	9.1
ED: Child	4.9	2.9	16.6
ED: Caregiver	2.5	0	9.1
Hospitalized: Child	6.2	3.7	26.5
Hospitalized: Caregiver	2.4	0	13.6

Methods: Epidemiological model



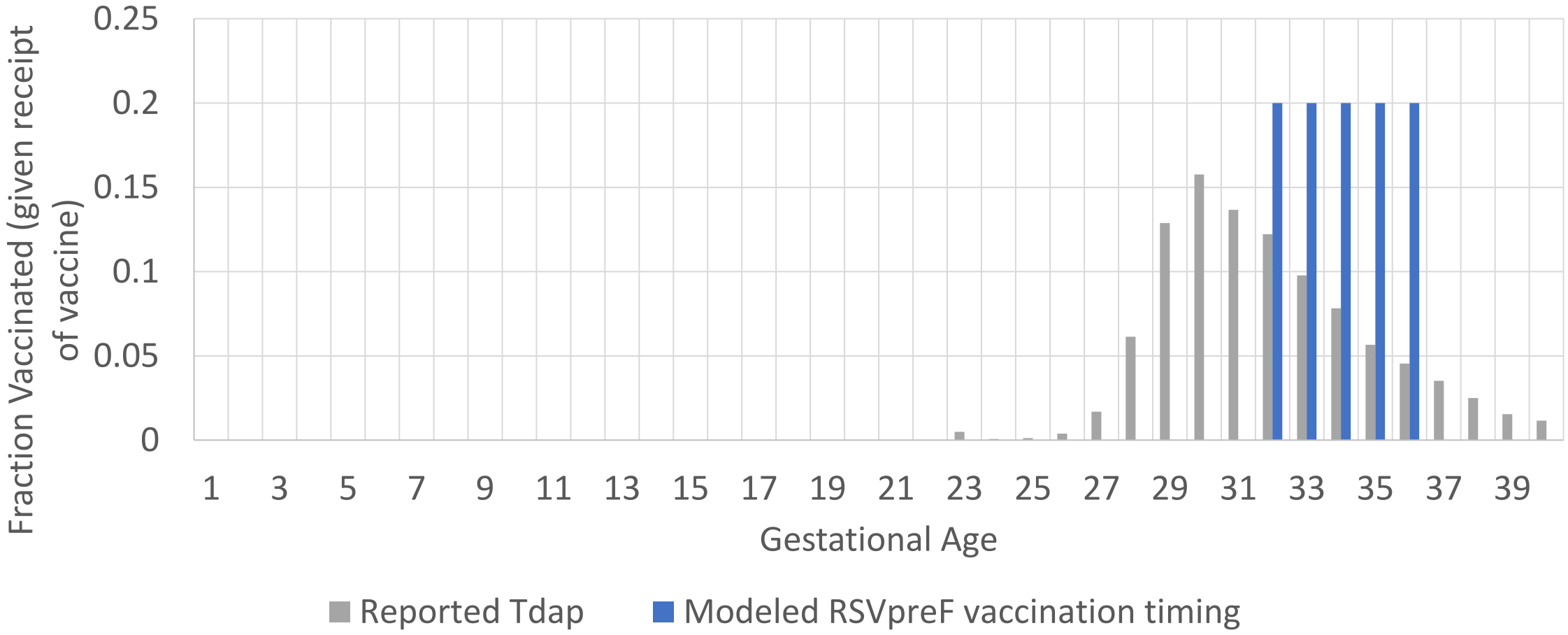
Methods: Inputs

- Incidence
  - Raw reported incidence may be underreported because of imperfect PCR sensitivity, so we consider an additional scenario in sensitivity analysis:
    - based on CDC Unpublished re-analysis of raw data from Zhang et al study which found decreased RSV PCR sensitivity in light of paired serology testing (adjustment factor: 87.6%).

Health-Related Quality-of-Life

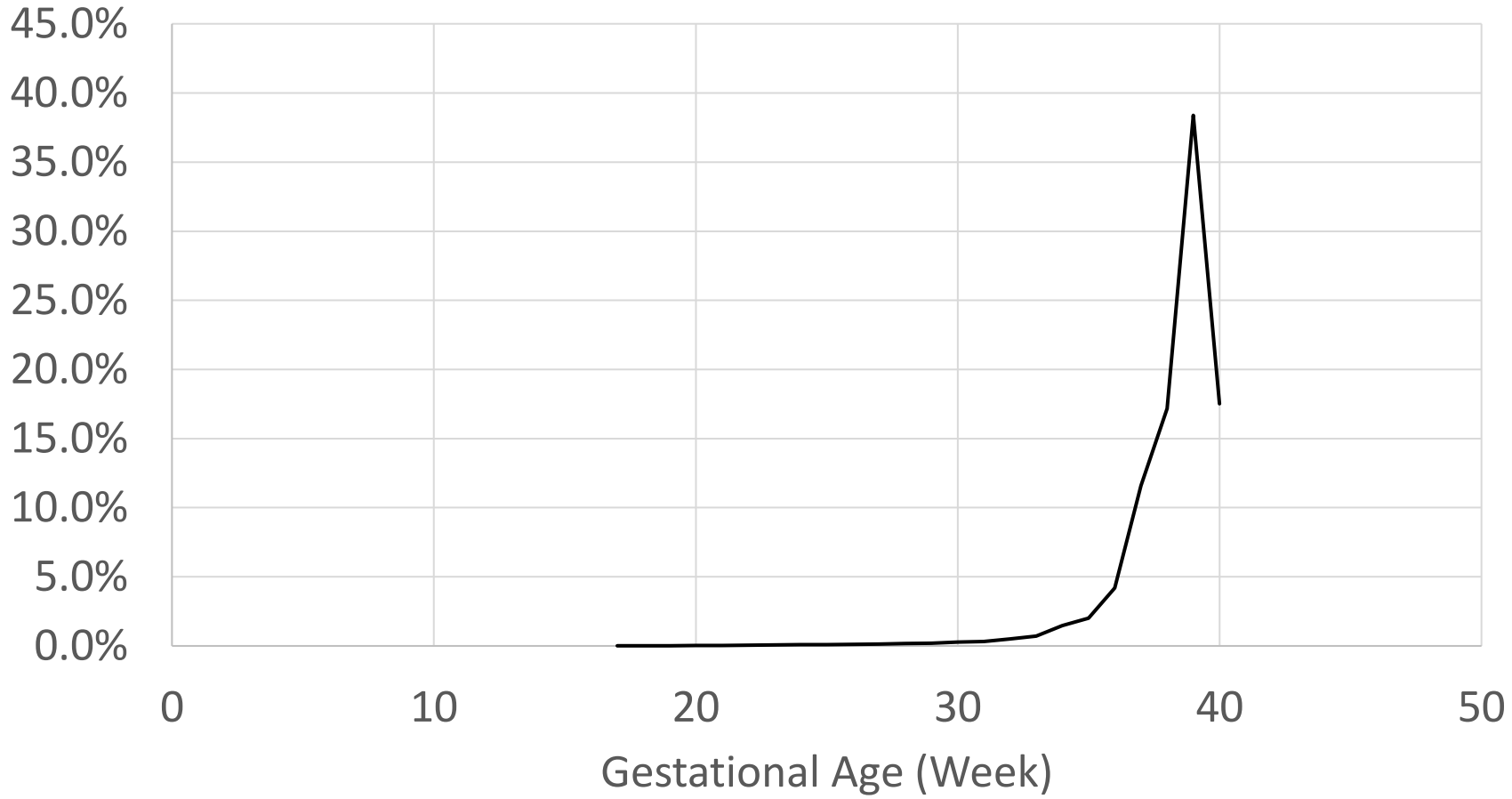
- Sources
  - Glaser (2022)
    - Estimate based on comparison of utility losses between premature children who had RSV vs. premature children without RSV and their caregivers
    - Used as base case for hospitalization for children and their caregivers
  - Regnier (2013)
    - Estimate QALY losses for hospitalization, ED visits, and outpatient visits for children with pertussis
    - Use relative QALYs between hospitalization, ED, and outpatient to estimate base losses for ED and outpatient in base case
  - JIVE RSV Utilities Survey (2021)
    - Estimates QALY losses for hospitalization and outpatient visits for child and caregiver
    - Estimates may be impacted by COVID-related concerns about respiratory viruses
    - Inform upper bound of range

Methods: Provision of RSVpreF



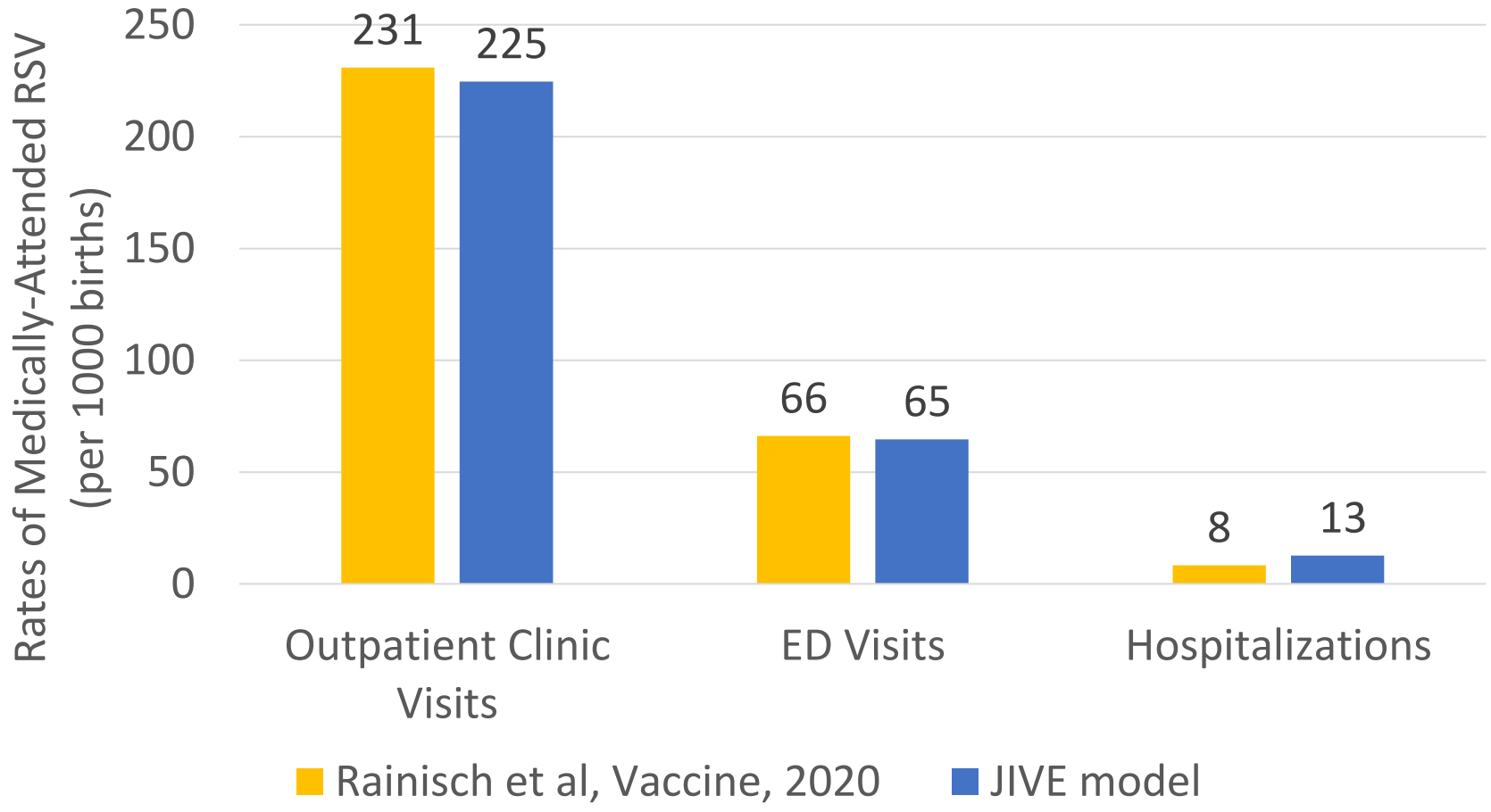
Timing of those who received vaccination during pregnancy
RSVpreF is assumed to start earlier at week 24 (vs. week 27)

Methods: Birth Timing



Source: NCHS from 2019 and 2021

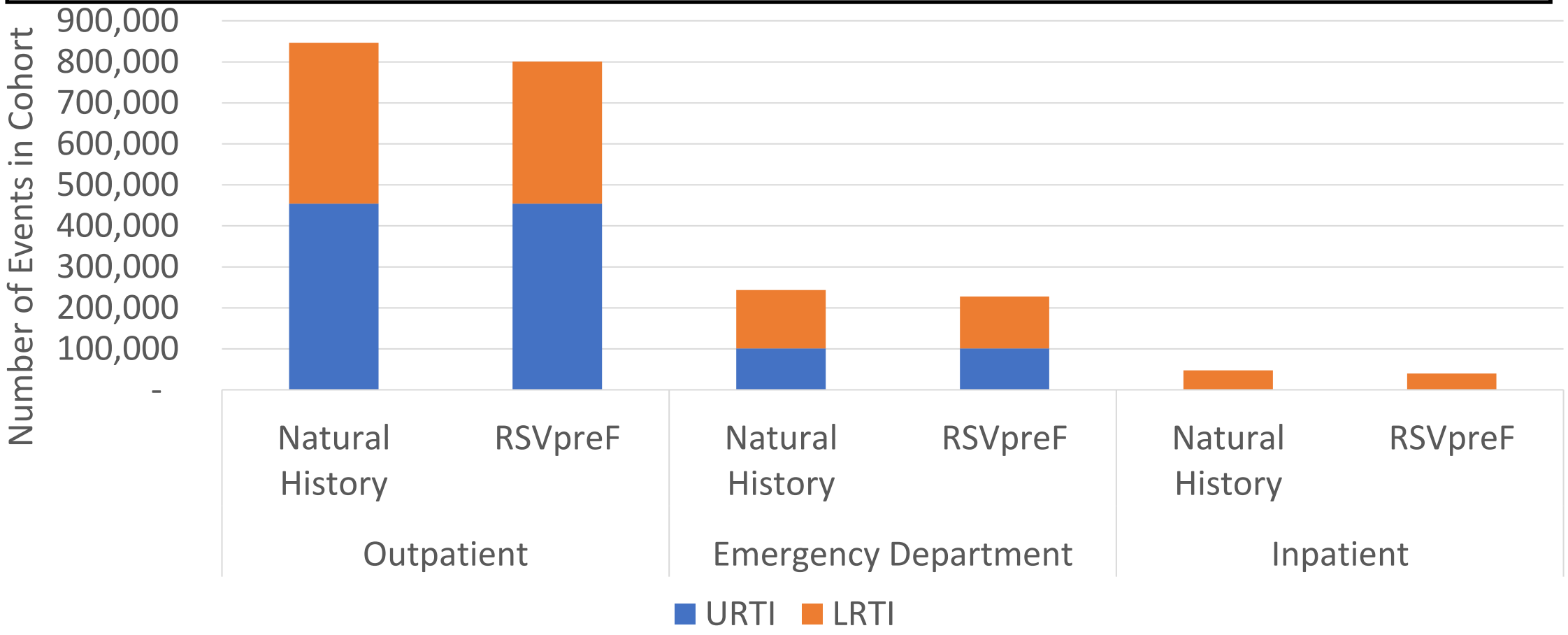
Validation


Rates of Medically-Attended RSV (per 1000 births)
250
200
150
100
50
0
231
225
66
65
8
13
Outpatient Clinic Visits
ED Visits
Hospitalizations
Rainisch et al, Vaccine, 2020
JIVE model

Methods: Maternal Adverse Event Health Effects

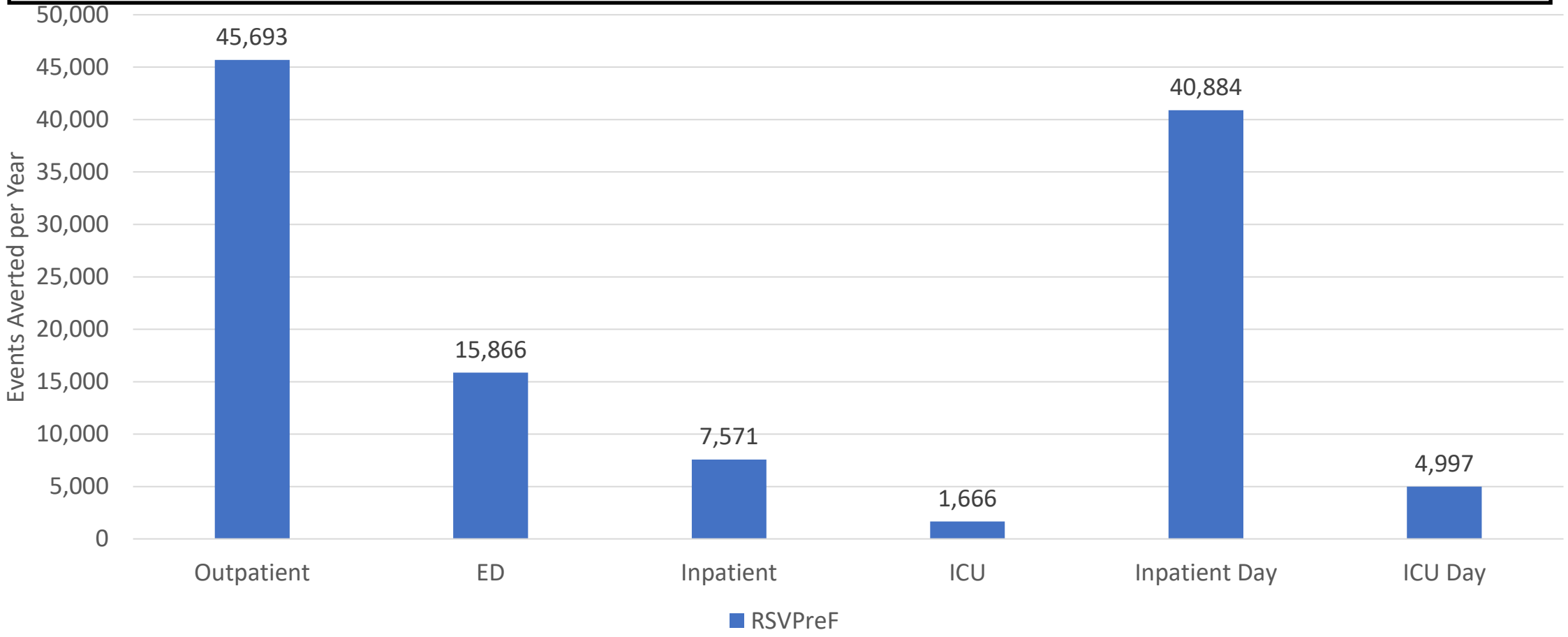
Variable	Value	Range	Source
Adult Quality-Adjusted Life-Years lost due to adverse events			
Injection Site Reaction	0		Assumed
Serious Adverse Event	0.141	0.092-0.199	Prosser, 2006

Results: Health outcomes



Cohort: 3.66 million births, assuming 50% intended uptake in RSVpreF group
URTI= upper respiratory tract infection; LRTI= lower respiratory tract infection

Results: Events Averted



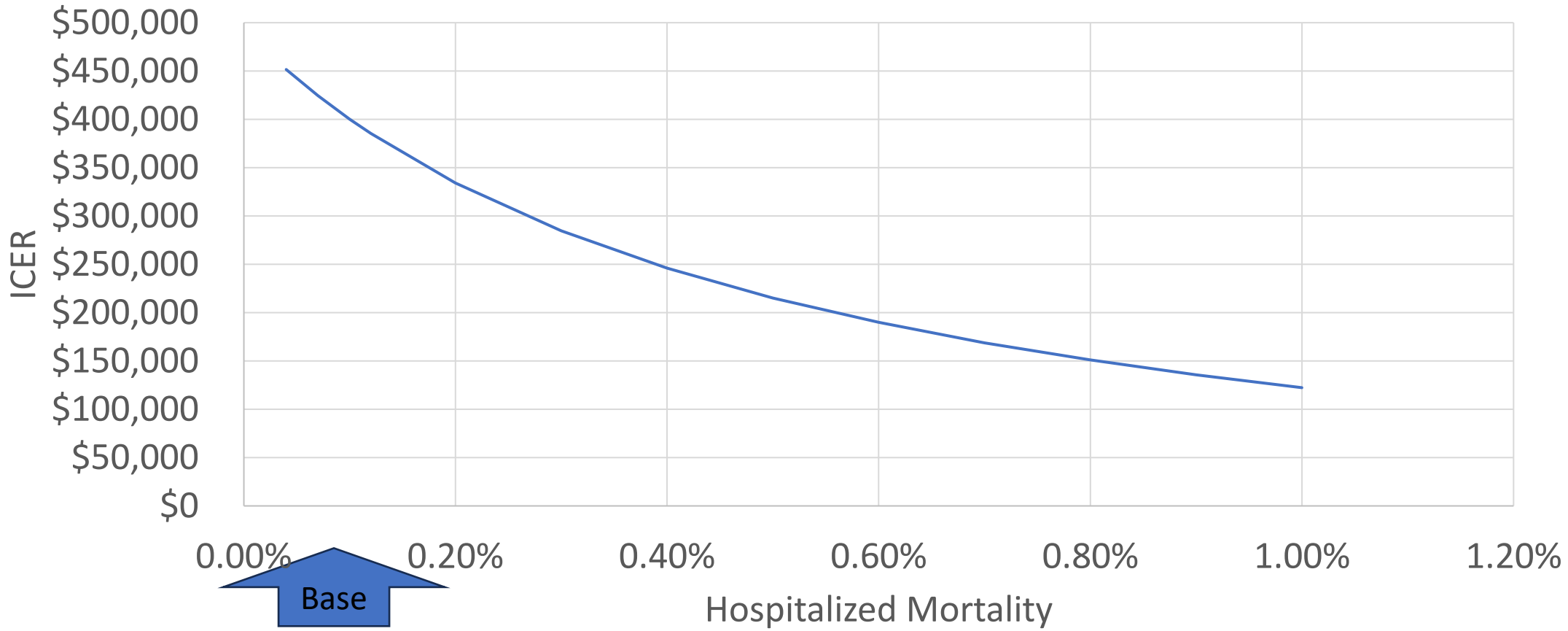
Cohort: 3.66 million births, assuming 50% intended uptake in RSVpreF group

Results: QALYs Lost

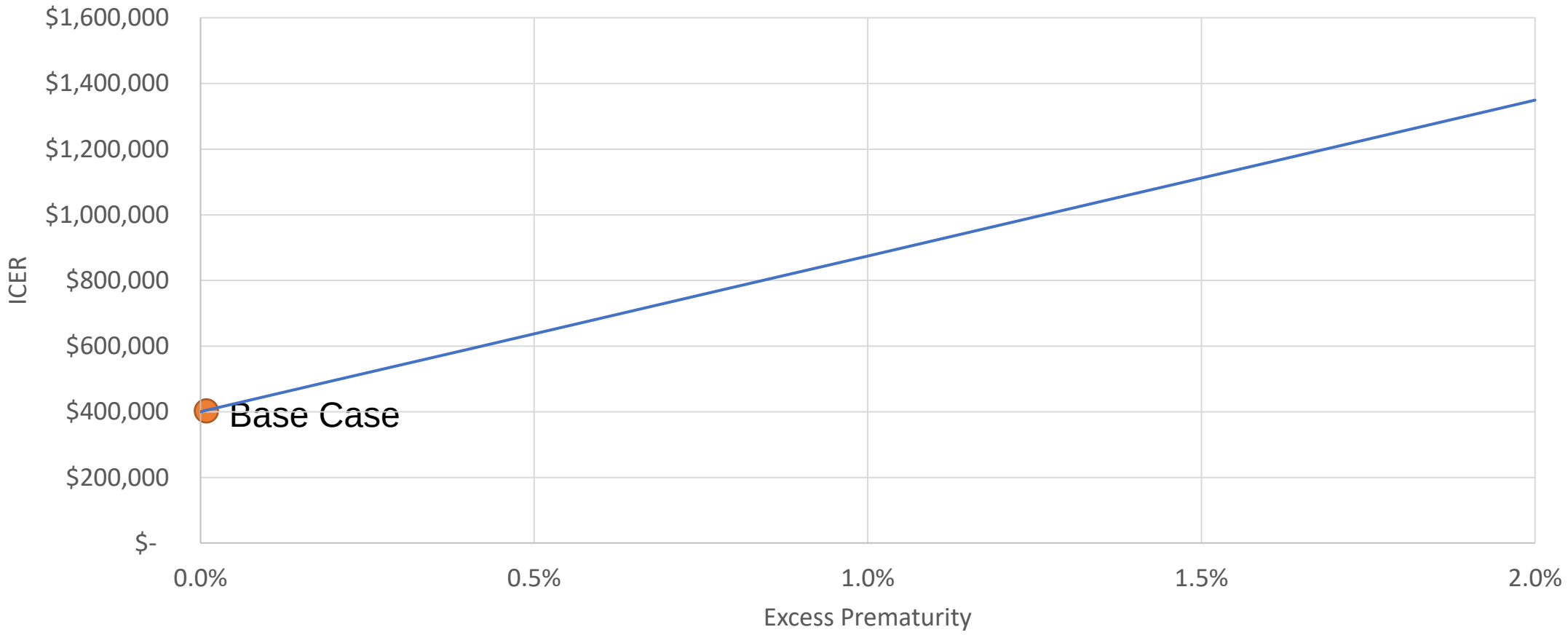
	Adverse Events	Outpatient		ED		Inpatient		Deaths	Total		Grand
		Child	Caregiver	Child	Caregiver	Child	Caregiver	Child	Child	Caregiver	Total
Natural History		7,153	3,580	3,290	1,645	807	320	1,356	12,606	5,545	18,151
RSVpreF	0.2495	6,766	3,387	3,075	1,538	679	269	1,141	11,663	5,194	16,857

Cohort: 3.66 million births, assuming 50% intended uptake in RSVpreF group
QALY= quality-adjusted life-year

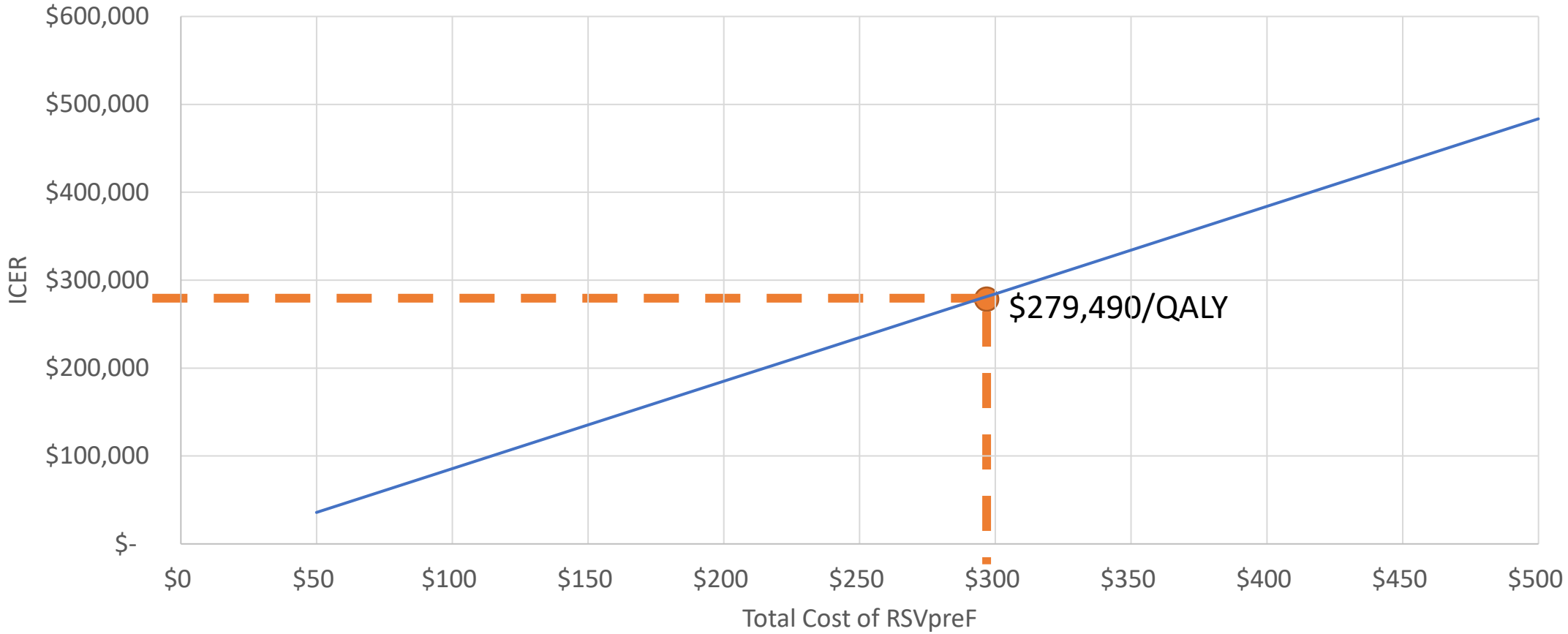
Sensitivity: Hospitalization Mortality



Scenario: Prematurity



Scenario: Upper Respiratory Tract Infection Effect



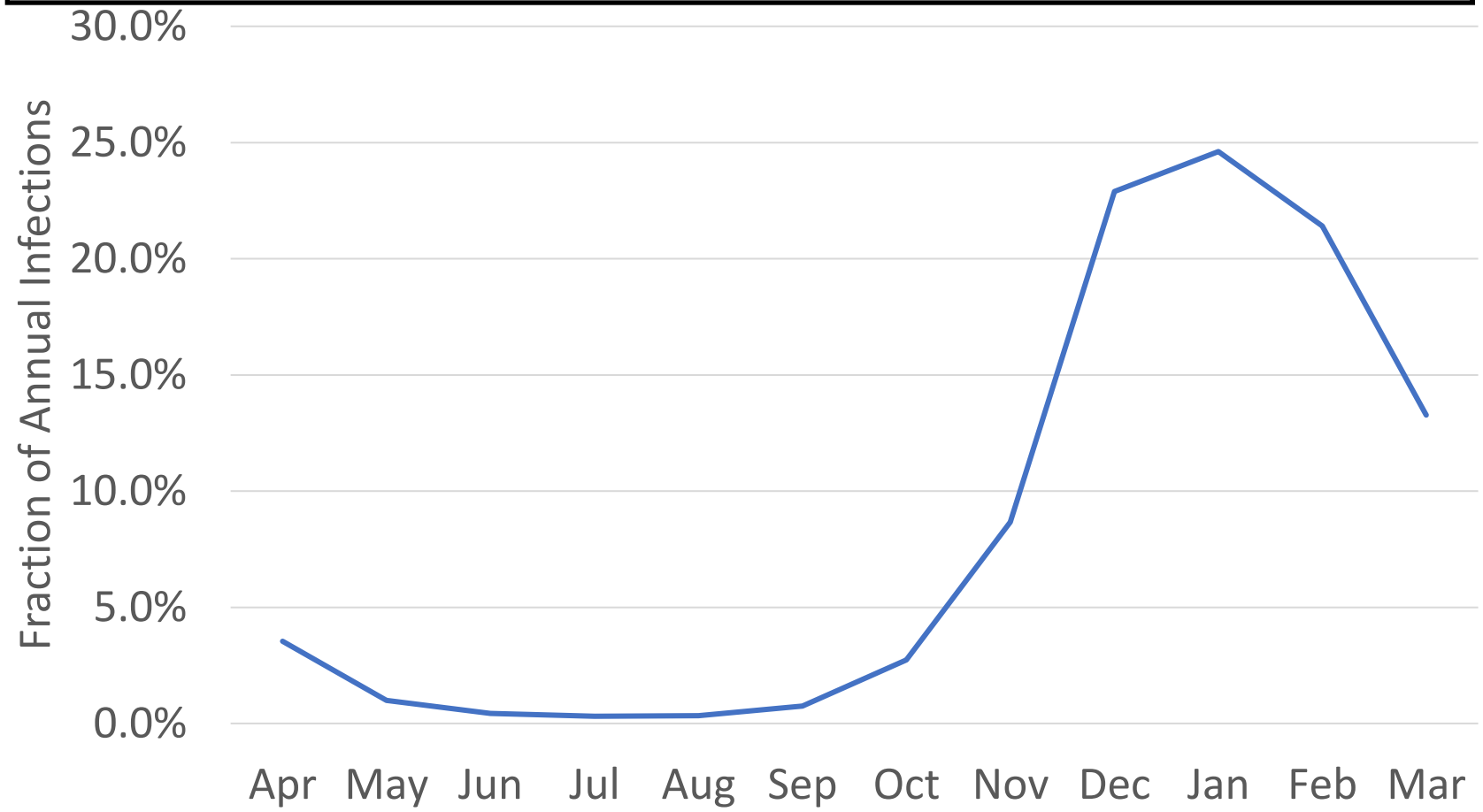
RSVpreF is assumed to have 37.9% efficacy for upper respiratory tract infections based on overall respiratory tract efficacy from phase 3 trial (Kampmann, 2023)
ICER= incremental cost effectiveness ratio; QALY= Quality adjusted life year

Appendix to Economics of combined use of Pfizer maternal RSVpreF vaccine and nirsevimab

Methods: Study questions

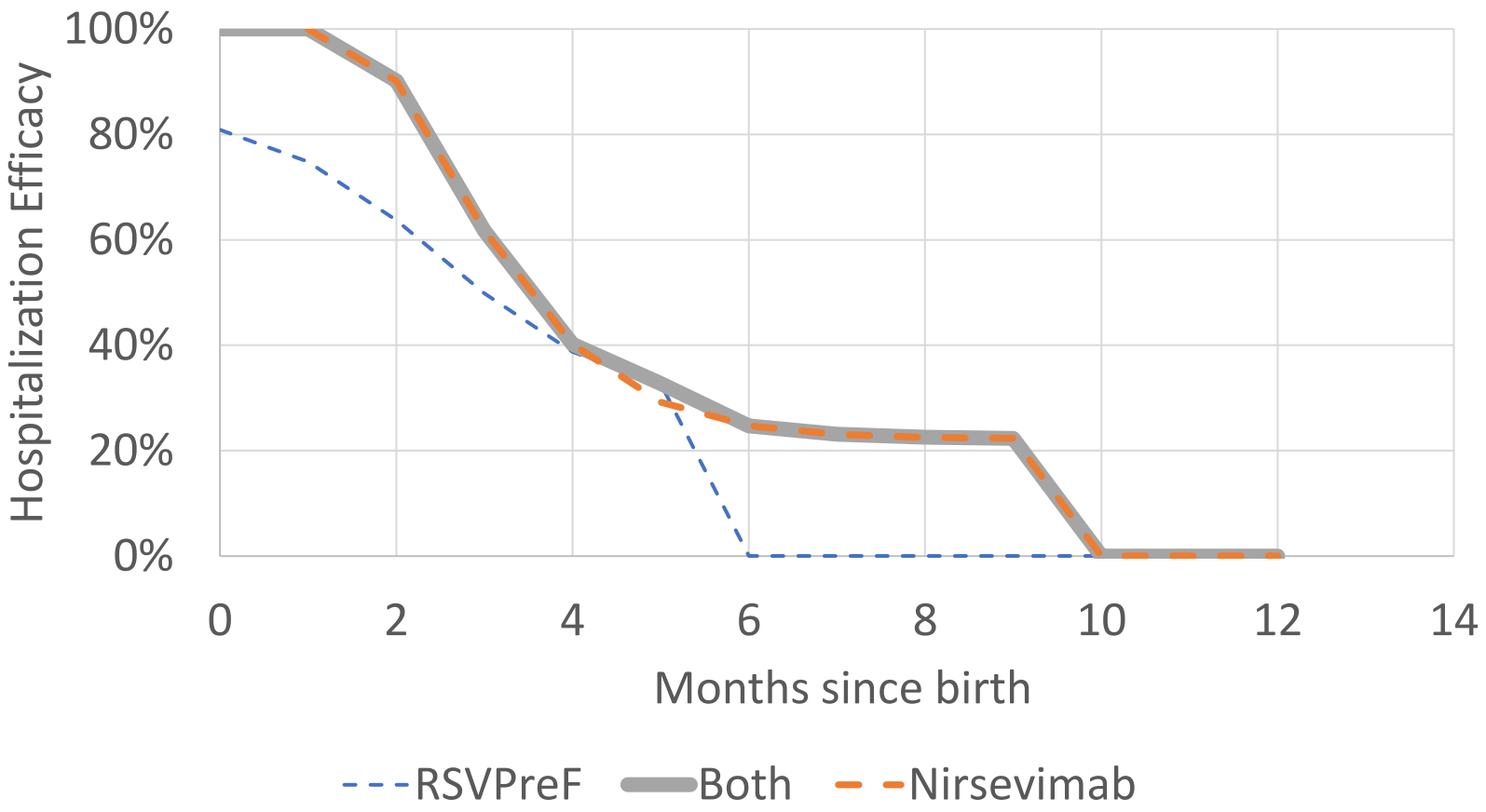
- Determine the cost-effectiveness of:
  - Nirsevimab in children born to mothers who received RSVpreF at least 2 weeks prior to delivery
  - RSVpreF for pregnant persons who will give nirsevimab to their newborns
- Single individual
- Evaluate by month of year
- Perspective: Societal
- Timeframe: 1 year (1 RSV season)
- Analytic horizon: infant's lifetime
- Discount rate: 3%

Reminder: Seasonality



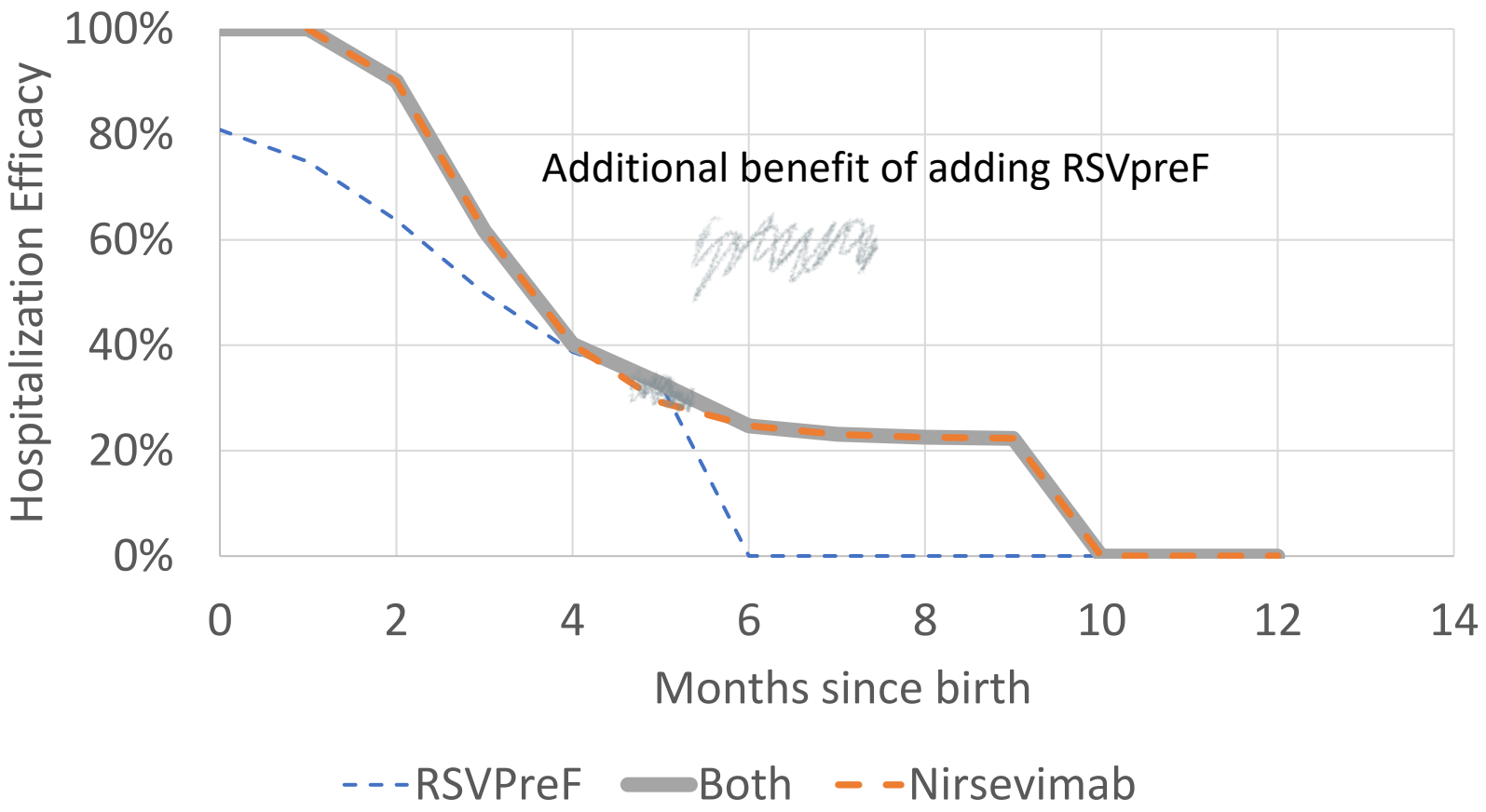
Source: National Respiratory and Enteric Virus Surveillance System (NREVSS) (2015-2019)

Methods: Intervention effectiveness



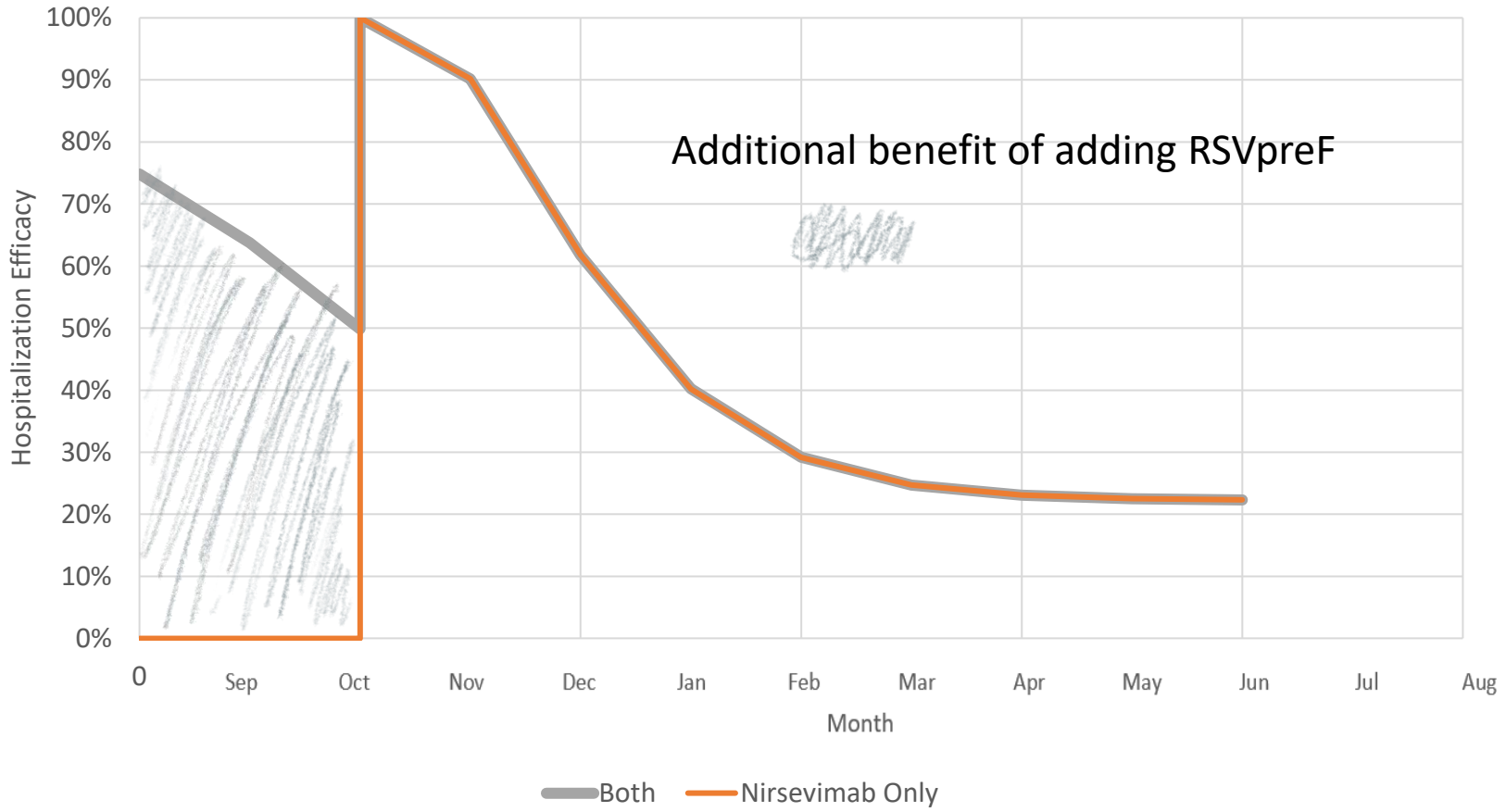
* Assuming administration of nirsevimab at birth

Methods: Intervention effectiveness

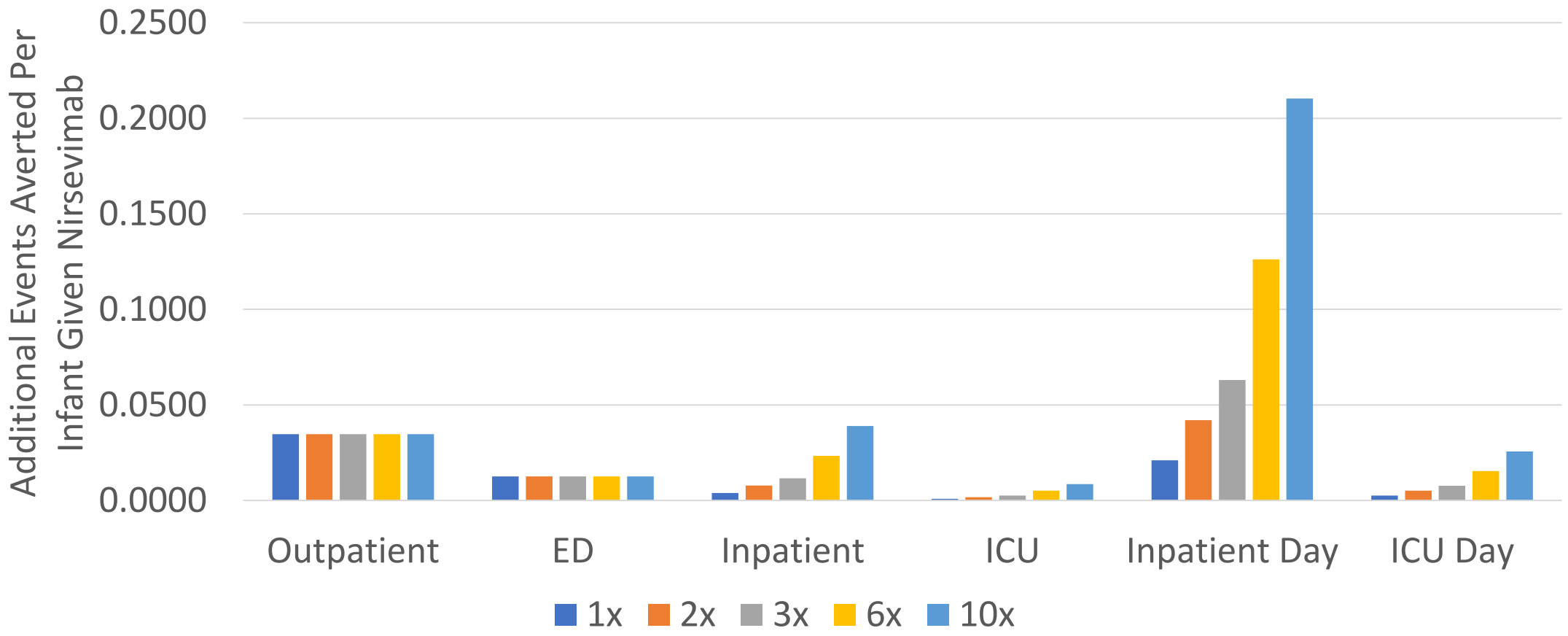


* Assuming administration of nirsevimab at birth

Methods: Intervention effectiveness example: Off-peak (Aug) birth

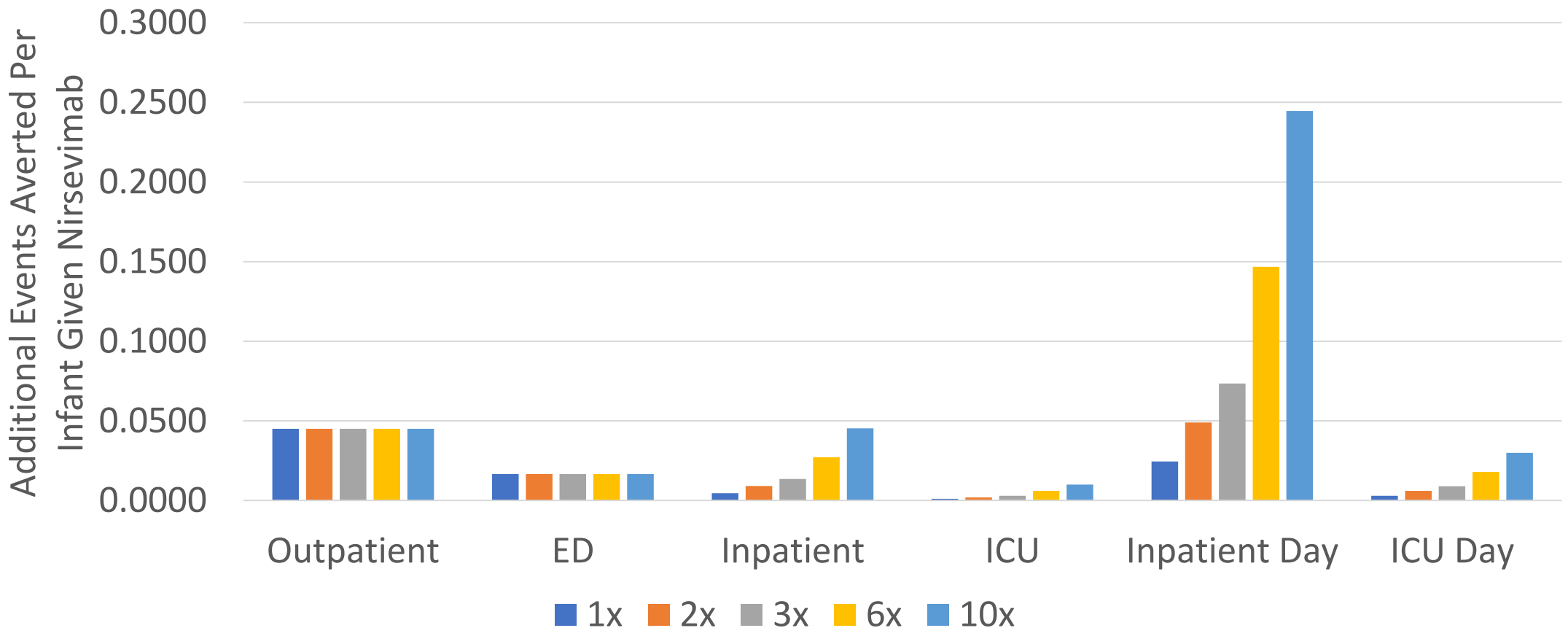


Results: Adding nirsevimab to *all* infants born to vaccinated mothers



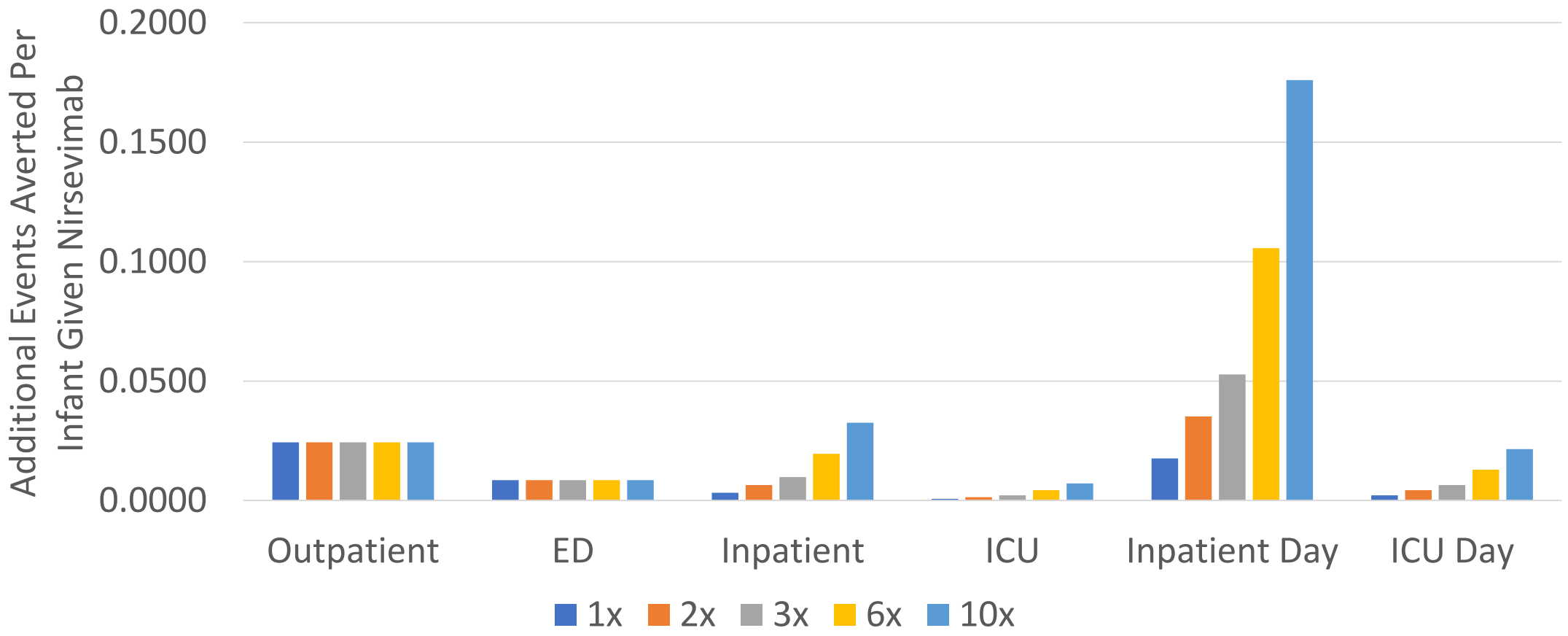
Nirsevimab given at birth for infants born October-March, and in October/November for infants born in April through September

Results: Adding nirsevimab at the start of the season only for infants born Apr-Sept



Nirsevimab given in October/November for babies born in April through September born to mothers who received RSVpreF

Results: Adding nirsevimab during the season for infants born Oct-Mar



Nirsevimab given in October/November for babies born in April through September born to mothers who received RSVpreF