# Economics of Preventing Respiratory Syncytial Virus Disease among US Infants by Maternal Vaccination Prior to Birth

**A SUMMARY REPORT COMPARING MODELS FROM:**

***Pfizer* AND *University of Michigan and CDC***

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NCIRD/CDC

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**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

- ***Pfizer* model**: Amy Law et al., [complete authors list and affiliations, upon request ]
  - *Pfizer* manufactures RSVpreF vaccine
  - Policy Analysis Inc. (Boston, MA, US) was funded by *Pfizer*

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

# Economic analysis

**Policy question:** Should *Pfizer* RSVpreF vaccine be recommended for pregnant mothers to be given during 32 through 36 weeks gestation to prevent RSV lower respiratory tract infection in infants?

**Question**: Is vaccinating pregnant mothers prior to birth to protect infants against RSV disease *cost-effective*?

**Comparator**

Unvaccinated Mothers + Standard of care (SoC) for Infants

**Intervention**

Vaccination of pregnant mothers prior to birth

**Base-case scenario:** What is the incremental *cost-effectiveness* of vaccinating pregnant mothers 32-36wGA and ≥2 weeks prior to birth with RSVPreF vaccine relative to "No vaccination"?

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

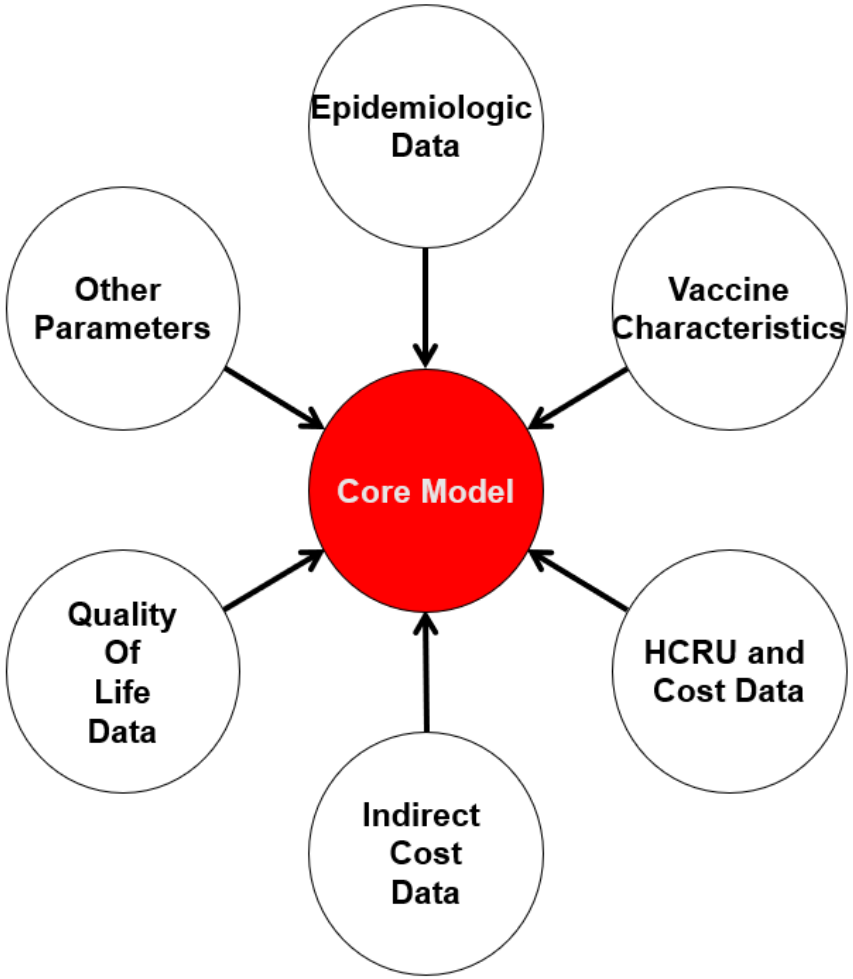
# Focus on key features for model comparison

- Modeling approach
  - Targeted population(s)
  - Perspective (healthcare vs. societal)
  - Intervention strategies and comparators
- Inputs for RSV disease burden, vaccine 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

| | *Pfizer* | UM-CDC |
|---|---|---|
| Static analytical decision-making models | ✓ | ✓ |
| Sensitivity analyses (and probabilistic simulation) | ✓(✓) | ✓ |
| Hypothetical population: All pregnant mothers, all year round | ✓ | ✓ |
| Time Frame:  First year after birth | ✓ | ✓ |
| Analytic Horizon: One year (for temporary disability) and Life Expectancy (for premature infant mortality) | ✓<br>✓ | ✓<br>✓ |
| Discount rate: 3% | ✓ | ✓ |
| Year of economic outcomes measured: 2022 | ✓ | ✓ |
| Societal perspective (and healthcare perspective) | ✓(✓) | ✓(✓) |

# Inputs and main outcomes




| | *Pfizer* | UM-CDC |
|---|---|---|
| Prevention of: | | |
| • RSV LRTI ED/OC visits | ✓ | ✓ |
| • RSV LRTI hospitalizations | ✓ | ✓ |
| • RSV-associated deaths | ✓ | ✓ |
| QALYs saved | ✓ | ✓ |
| **$/QALY saved** | ✓ | ✓ |
| Number needed to vaccinate (NNV) to avert an: | | |
| • RSV LRTI hospitalization | ✓ | ✓ |
| • RSV-associated death | ✓ | ✓ |

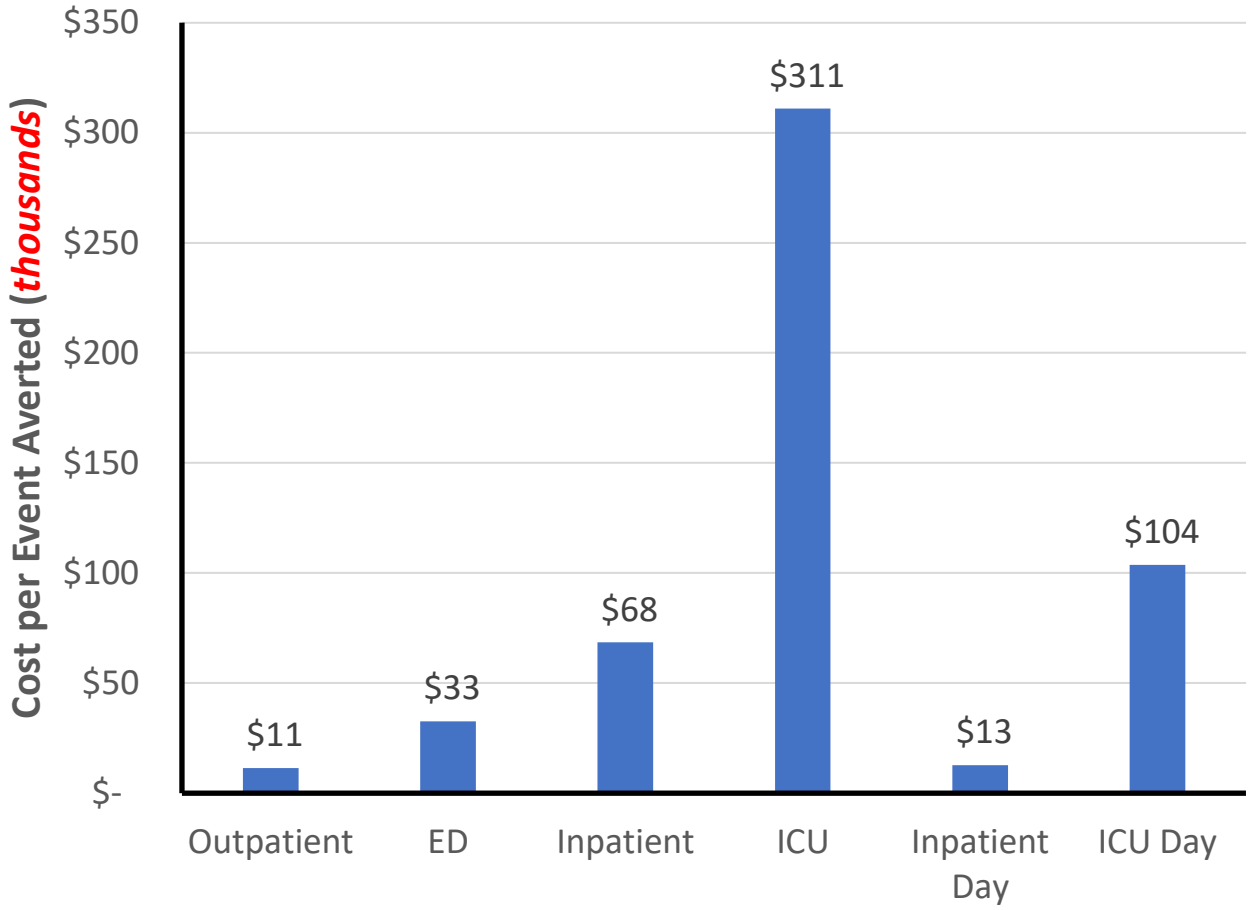


HCRU = health care resource use, ED= Emergency department, OC= outpatient clinic, LRTI= Lower respiratory tract infection, QALY= quality-adjusted life year

# UM-CDC: Base case estimates for maternal vaccination, Vaccination Window (VW) 32-36wGA, vaccine cost $295/dose

| Summary outcomes | Base-Case |
|---|---|
| $/QALY gained | $400,304 |
| $/RSV-associated ED/OC visit averted | $32,652 / $11,337 |
| $/RSV-associated LRTI hospitalization averted | $68,423 |
| $/RSV-assoc. death averted | >$71.5Million |
| NNV to avert an RSV-associated ED/ OC patient | 115 / 40 |
| NNV to avert an RSV-associated LRTI hospitalization | 242 |
| NNV to avert an RSV-associated death | 241,989 |

Assuming 50% uptake in vaccinated group
VW = vaccination window
wGA = weeks gestational age
LRTI= lower respiratory tract infection
OC = office clinic for outpatient care
ED = emergency department
NNV = Number needed to vaccinate

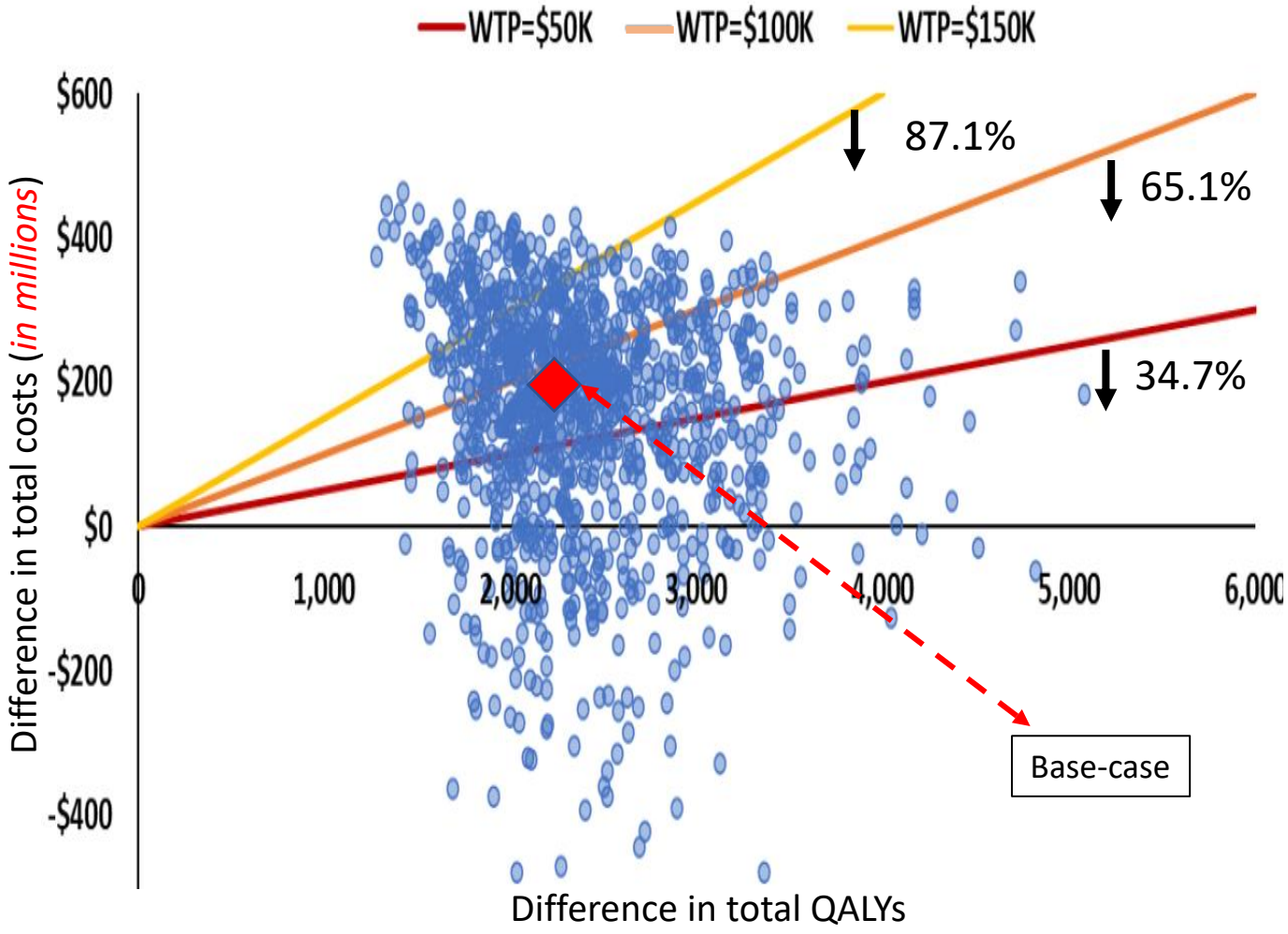



**Cost per type of health outcome prevented (*in thousands*)**

# *Pfizer* model: Base case estimates for maternal vaccination, VW 32-36wGA, vaccine cost $295/dose & PSA

| Summary outcomes | Base-Case |
|---|---|
| $/QALY gained | $84,690 |
| $/RSV-associated ED/OC visit averted | $6,145/ $2,101 |
| $/RSV-associated LRTI hospitalization averted | $14,932 |
| $/RSV-associated death averted | >$7.7Million |
| NNV to avert an RSV-associated ED/OC patient | 66 / 22 |
| NNV to avert an RSV-associated LRTI hospitalization | 159 |
| NNV to avert an RSV-associated death | 82,243 |

Assuming 54.9% uptake in vaccinated group and 93.2% born ≥2 weeks after adm.
VW = vaccination window
wGA = weeks gestational age
LRTI= lower respiratory tract infection
OC = office clinic
ED = emergency department
NNV = Number needed to vaccinate
WTP = Willingness to pay




**Probabilistic sensitivity analysis (PSA)**

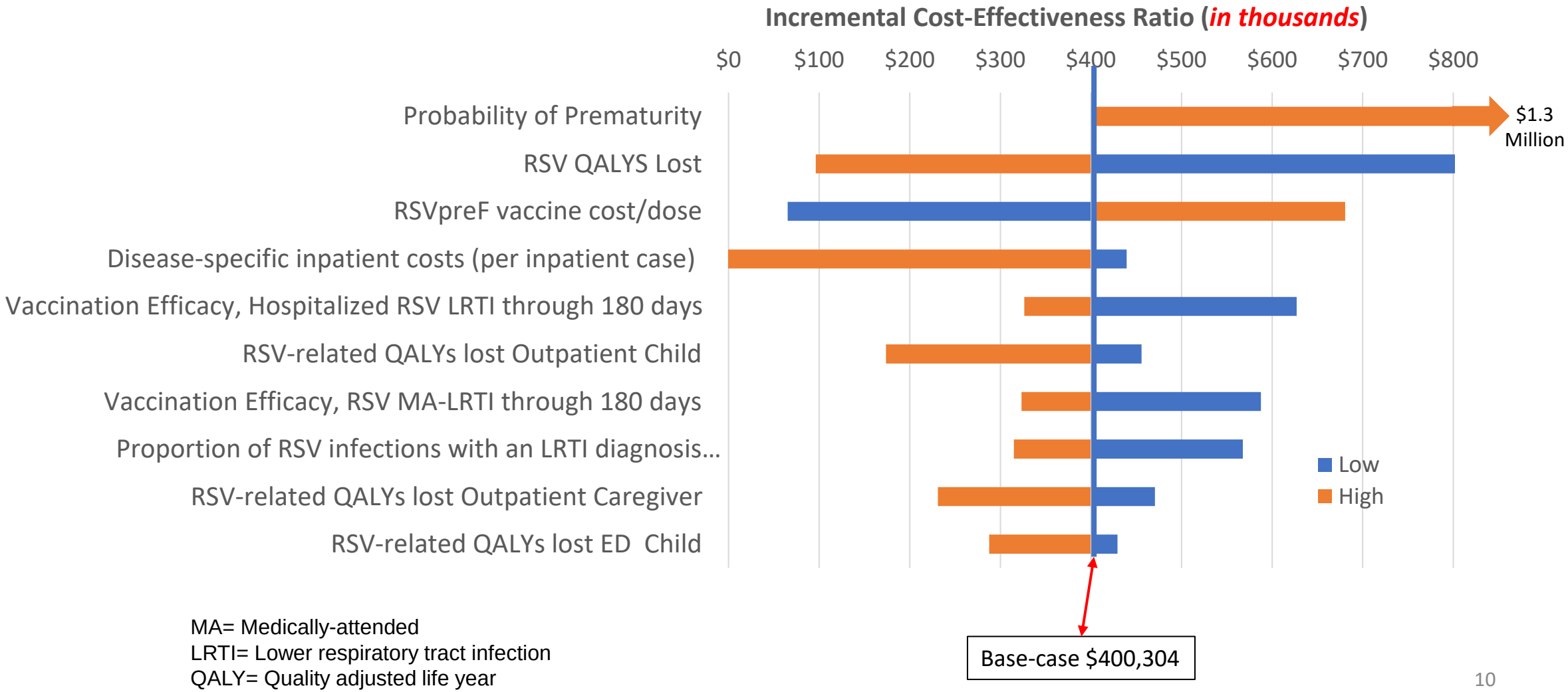
# *Pfizer* and UM-CDC models comparison: base-case selected outcome ratios for maternal vaccination

| | **UM-CDC model**<br>**Price per dose $295**<br>**VW=32-36wGA**<br>**Year-round administration** | ***Pfizer* model**<br>**Price per dose $295**<br>**VW=32-36wGA**<br>**Year-round administration** |
|---|---|---|
| **$ / QALY gained** | **$400,304** | **$84,690** |
| $ / RSV LRTI hospitalization averted | $68,423 | $14,932 |
| $ / Death averted among RSV LRTI hospitalized infants | >$71.5Million | >$7.7Million |
| **NNV to prevent a** | | |
| RSV LRTI associated hospitalization | 242 | 159 |
| Death among RSV LRTI hospitalized infants | 241,989 | 82,243 |

Assuming 50% (UM-CDC) and 54.9% (Pfizer) uptake in vaccinated group and 100% (UM-CDC) to 93.2% (Pfizer) born ≥2 weeks after administration.
VW = Vaccination window
LRTI= lower respiratory tract infection
NNV = Number needed to vaccinate
Note: Both models vaccination window = 32-36wGA only (wGA = weeks gestational age)

# UM-CDC model: One-way Sensitivity Analyses

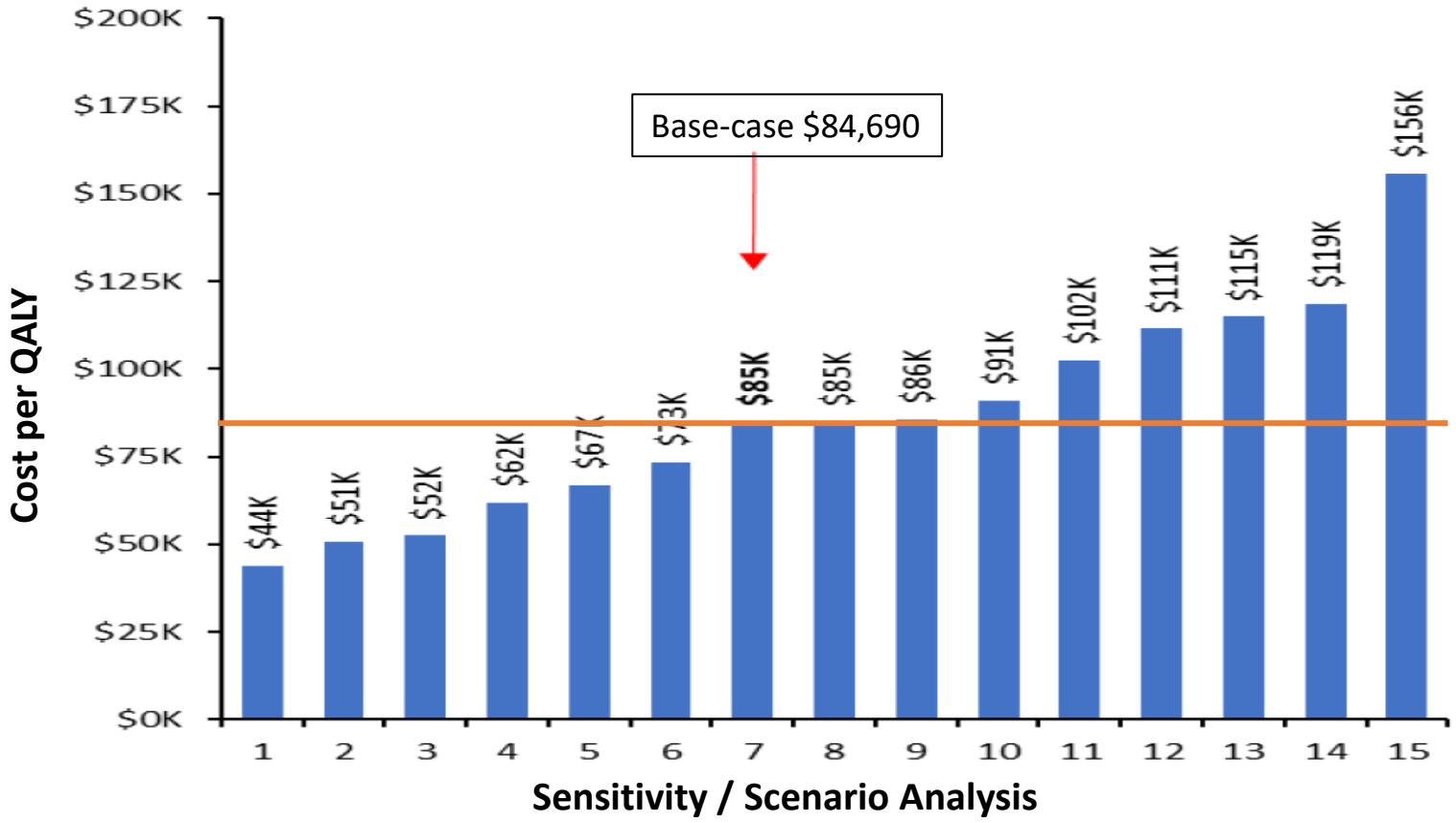
## Base case: $400,304/QALY saved, vaccine price $295/dose




MA= Medically-attended
LRTI= Lower respiratory tract infection
QALY= Quality adjusted life year

# *Pfizer* model: One-way Sensitivity Analyses

## Base case: $84,690/QALY saved, Vaccine cost $295/dose




| | |
|---|---|
| 15) | VE lower bound |
| 14) | RSV-H medical care cost lower bound |
| 13) | US healthcare system perspective |
| 12) | DoP = 6 months |
| 11) | RSV-H CFR lower bound (overall = 0.1%) |
| 10) | Vaccine uptake 32-36 wGA (uniform) |
| 9) | Disutilities form Glasser (RSV-H) and Reigner (RSV-ED, RSV-OC) |
| 8) | Uptake = 100% |
| **7)** | **Base case** |
| 6) | VE for late PT = for FT |
| 5) | Palivizumab scenario |
| 4) | DoP = 12 months |
| 3) | RSV-H CFR upper bound (overall=0.53%) |
| 2) | RSV-H medical care cost upper bound |
| 1) | VE upper bound |

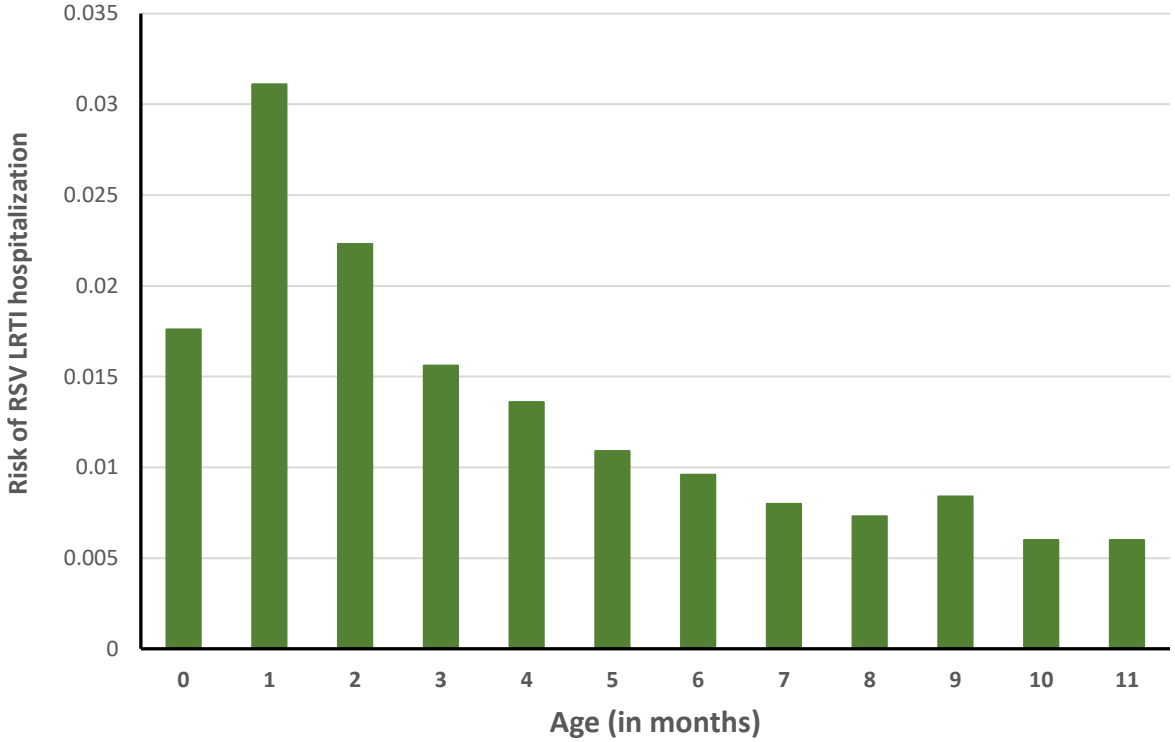
CFR= Case fatality ratio
DoP = Duration of protection
VE= Vaccine efficacy
PT = Preterm
FT = Full term

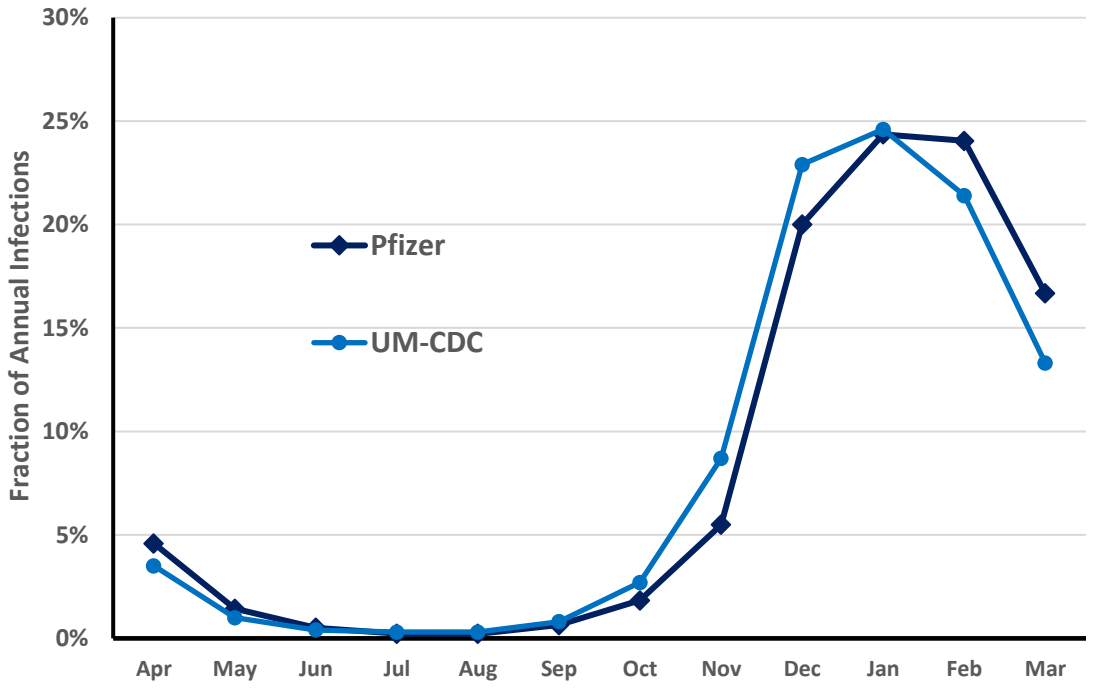
RSV-H = RSV-associated hospitalization
RSV-ED = RSV-associated emergency department care
RSV-OC = RSV-associated outpatient care

# *Pfizer* and UM-CDC models comparison: Selected influential inputs

- RSV-hospitalization risk and RSV seasonality
- Vaccine efficacy
- Duration of protection and waning
- RSV Case fatality rate
- Medical cost of RSV hospitalization, ED and Outpatient care
- Vaccine associated adverse events
- Quality of life lost by patients and caregivers

# *Pfizer* and UM-CDC: comparison of base-case risk of RSV-related hospitalization by age and RSV Seasonality




**Risk of RSV Hospitalization**: ***Pfizer*** and **UM-CDC**: Based on laboratory-confirmed RSV-associated hospitalization by age in months from New Vaccine Surveillance Network (NVSN) data for children under 2 years of age (December 2016 to September 2020). Risk estimates are based only on RSV cases that manifest as LRTI.
**RSV Seasonality:** ***Pfizer***: based on Midgley et al. *J Infect Dis* 2017. (data based in NRVSS) https://pubmed.ncbi.nlm.nih.gov/28859428/#full-view-affiliation-1
**UM-CDC*:*** based on National Respiratory and Enteric Virus Surveillance System (NREVSS) (2015-2019)

# *Pfizer* and UM-CDC: Differences in initial vaccine efficacy

| | UM-CDC | *Pfizer* | |
|---|---|---|---|
| | | **Full Term** | **Late Preterm** |
| Initial vaccine efficacy against RSV LRTI hospitalization (%) | Month 0 = 81.0<br>Average Month 0-6 = 56.8 [a] | 88.1<br>Severe MA RSV-LTRI [b] | 73.4<br>Severe MA RSV-LRTI [b, c] |
| Initial vaccine efficacy against Medically attended RSV associated LRTI for ED and Outpatient care (%) | Month 0 = 73.0<br>Average Month 0-6 = 51.3 [a] | 47.6 [b] | 39.7 [c] |
| **For Scenario Analysis only**: Initial efficacy against RSV URTI treated in Outpatient care (%) | 37.9 [d] | 47.6 [b] | 39.7 [c] |

NOTE: None of Pfizer Phase 3 (i.e., MATISSE) endpoint definitions overlapped ideally with the case definition used for the US burden data.

a. CDC: Average between efficacy for full term and preterm reported from Phase 3 were used. VE for RSV-LRTI hospitalization is an average over months 0-6 reported in Phase 3 trial, and RSV-positive MA-LRTI for VE against RSV-LRTI in the ED and outpatient. Kampmann et al *New England Journal of Medicine*. 2023 Apr

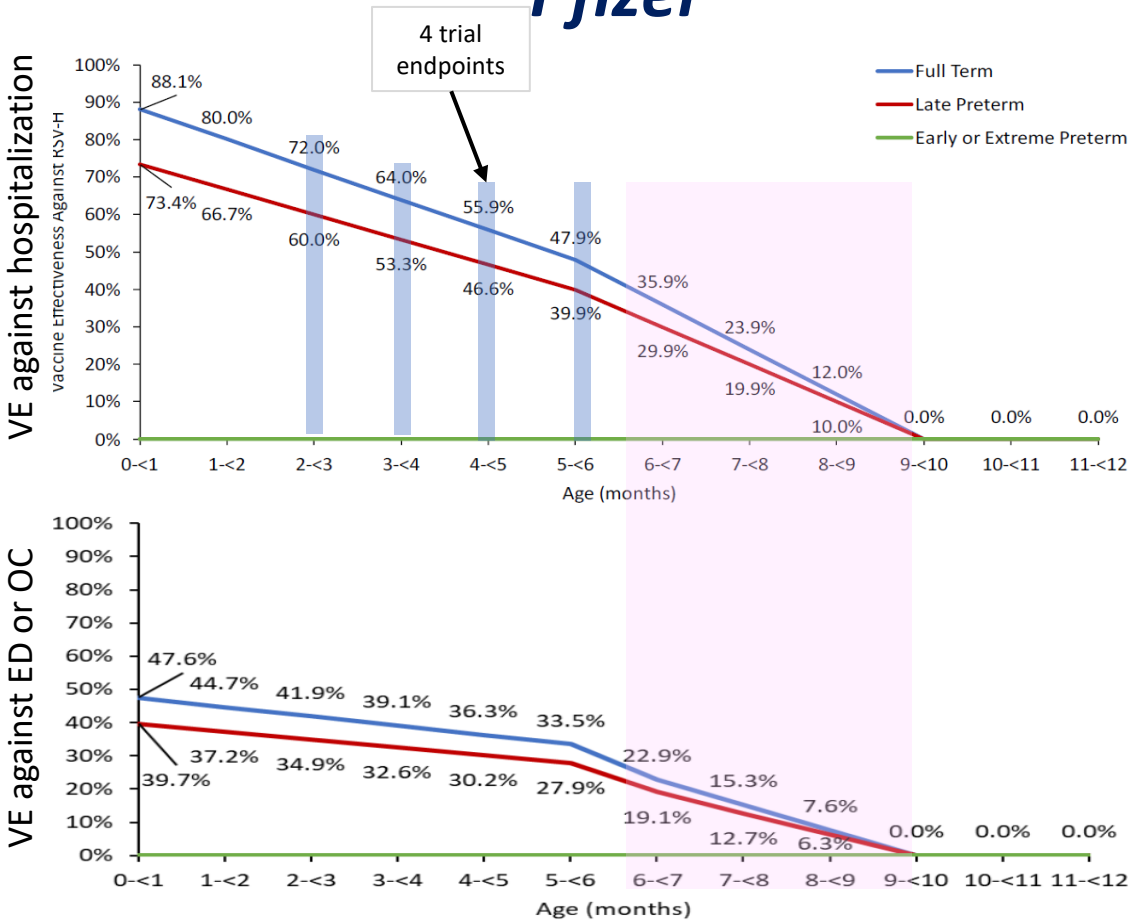
b. Pfizer: Efficacy against severe RSV-positive MA-LRTI was used as a proxy for VE against RSV-LRTI requiring hospitalization, and efficacy against RSV-positive MA-LRTI was used as a proxy for VE against RSV-LRTI treated in the ED. Pfizer: Kampmann et al *New England Journal of Medicine*. 2023 Apr

c. VE for late preterm infants was assumed to be 83.3% of corresponding values for full term infants. VE for URTI was assumed equal to VE for MA LRTI in ED care

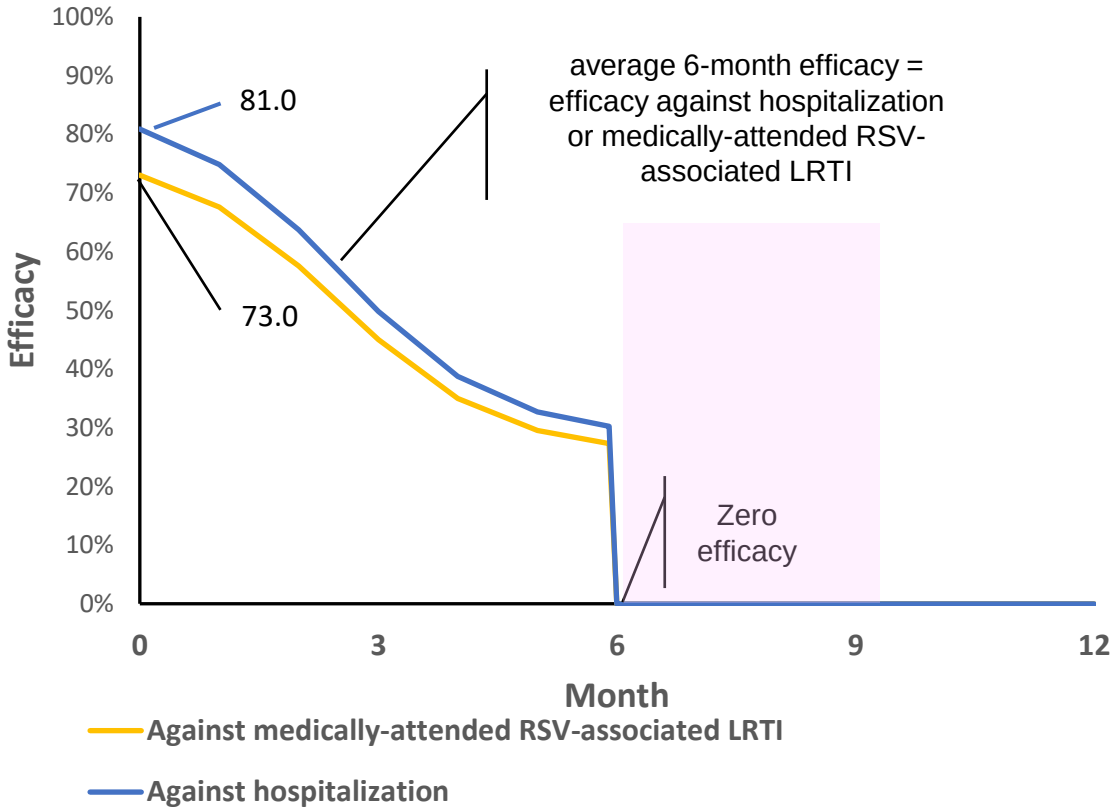
d. Based on overall respiratory tract efficacy from phase 3 trial (Kampmann et al *New England Journal of Medicine*. 2023 Apr )

# *Pfizer* and UM-CDC: Assumption on duration of protection (DoP)

## *Pfizer*




## UM-CDC




The pink-shaded areas denote a higher level of uncertainty of the waning assumption beyond available phase 3 data

**UM-CDC**: Average between efficacy for full term and preterm were used for DoP for RSV-LRTI hospitalization over months 0-6 and RSV-positive MA-LRTI for DoP against RSV-LRTI in the ED and outpatient also over months 0-6. Both reported in Phase 3 trial, Kampmann et al *New England Journal of Medicine*. 2023 Apr

# *Pfizer* and UM-CDC models comparison: Differences in key inputs

| | UM-CDC | *Pfizer* |
|---|---|---|
| Case fatality rate (CFR) among RSV-hospitalized infants <12 months of age | **0.10%** (0.04% - 0.20%)[a] | 0.10% (full term) 0.80% (all preterm) [b] |
| Medical costs per RSV hospitalization | **$11,487** ($4,804 - $86,646)[c] | Average: **$20,483** [d] $13,171 – $33,876 (full term) $19, 415 – $51,343 (late preterm) |
| Medical costs per RSV ED visit | **$563** ($544 -$581)[c] | Average: **$1,840** [d] $1,620 – $2,520 (full term) $1,787 – $2,779 (late preterm) |
| Medical costs per RSV outpatient visit | **$82** ($46 - $118)[c] | Average: **$348** [d] $292 – $730 (full term) $328 – $823 (late preterm) |

a. RSV mortality per hospitalization: 0.10% (range 0.04-0.20%) in 0-5months, 0.10% (range 0.04-0.20%) in 6-11months.
b. Case fatality due to RSV-Hospital in full term infants per 100 cases = 0.1 (based on Li et al CEA-RSV in children 2022). In pre-term infants CFR per 100= 0.8 (assumes 16.3% of all RSV-Hosp are among preterm)
c. Adapted from Bowser et al., *J Infect Dis*. 2022 Aug 15; 226(Suppl 2): S225–S235 (A systematic review using studies from 2014-2021. Cost updated to 2022 using the GPD deflator)
d. Source: Pfizer data on file. Costs in the base-case varied by age and term at birth. Weighted average cost among full and late preterm infants in commercially insured and Medicaid populations

# *Pfizer* and UM-CDC: Vaccine-associated adverse events

| | UM-CDC | *Pfizer* | Source |
|---|---|---|---|
| Rate of injection site reaction | **0.41** (0.38 – 0.44) | **0.41** (0.38 – 0.44} | *Pfizer* Phase III Trial |
| Probability of healthcare visit, given injection site reaction | **0.02** (0.015 – 0.025) | **0.02** (0.015 – 0.025) | Curran, 2020 |
| Cost of outpatient visit | **$367.76** (23.15 – 1,758) | **$367.76** (23.15 – 1,758) | (Deluca, 2023) also in *Pfizer* CEA technical report (August 2023) |
| Recipient time, physician office for injection site reaction (hours) | **2** (1 – 3) | n/r | Assumption |
| Hypothetical serious adverse event | **0.000001** ( 0 - 0.0002) | n/r | Base: Prosser, 2006<br>High: 95% CI Phase 3 data for RSV adult vaccines |
| Potential risk increase of prematurity | **0.0%** ( 0 – 2%) | n/r | *Pfizer* Phase III Trial<br>Kampmann et al *New England Journal of Medicine*. 2023 Apr |

Note: Values in bold are used for the base-case scenario. Range values in parenthesis for sensitivity analyses
n/r = not reported

# *Pfizer* and UM-CDC: Quality of life lost (*in days*) by RSV LRTI outcome for patients & caregivers

| | UM-CDC* | *Pfizer*** |
|---|---|---|
| Outpatient: Child | **3.1** (1.8 - 16.6) | **2.22** |
| Outpatient: Caregiver | **1.5** (0 - 9.1) | **1.5** |
| ED: Child | **4.9** (2.9 – 16.6) | **2.22** |
| ED: Caregiver | **2.5** (0 - 9.1) | **2.5** |
| Hospitalized: Child | **6.2** (3.7 – 26.5) | **5.7** |
| Hospitalized: Caregiver | **2.4** (0 – 13.6) | **2.4** |
| **Scenario Analysis**: Vaccine-related increased risk of prematurity *** | 11 (0 – 438) | n/r |

* Base case values are from EGlasser et al 2022, lower values are based in Regnier et al 2013, higher values are based in JIVE (unpublished data)

** Patient values are base in Roy 2013, Caregiver values are based on Hutton. Economic Analysis of Nirsevimab in Pediatric Populations. ACIP; February 23, 2023.

Note: Values in bold are used for the base-case scenario. Range values in parenthesis for sensitivity analyses

*** Sources: Werner, et al 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

n/r = not reported

# *Pfizer* and UM-CDC models comparison: $/QALY for selected scenarios in UM-CDC model

| | | UM-CDC |
|---|---|---|
| | UM-CDC model Base-case | **$400,304** |
| A | Cost of RSV-LRTI hospitalization: **$20,000 or $50,000** (i.e., 85% to 450% increase, base-case cost= $11,487) | **$350,500** - $174,987 |
| B | UM-CDC model with same **VE duration of protection as *Pfizer***: 6 months slowly, linearly declining efficacy and declining faster after month 6 reaching 0% at month 9 | $286,769 |
| C | CFR among RSV LRTI hospitalization: **1%** (base-case = 0.1%) | $122,539 |
| **D** | **Combining A and B vs. Combining A, B and C** | **$233,736 -** $52,108 |
| E | Increase in the risk of prematurity in **one- or two-percent points** (base-case risk of prematurity after vaccination = 0% increase ) | $874,609 - **$1.3 Million** |
| F | Vaccine administration timing: **September-January vs. February-July** (base-case, year-round) | <$200,000 - **$Millions** |
| G | Vaccine cost = **$50/dose or $500/dose** (base-case vaccine cost = $295/dose) | $65,304 - **$680,609** |
| H | VE for URTI = 37.9% (Base-case = 0% VE against URTI) | $279,490 |

# *Pfizer* and UM-CDC models comparison: $/QALY for selected scenarios in *Pfizer* model (I)

| | ***Pfizer*** |
|---|---|
| ***Pfizer*** model base-case | **$84,690** |
| VE for late preterm infants assumed same as for full term infants [a] | $73,404 |
| Vaccine Efficacy**: 80% or 120%** of base case values | $155,834 - $43,813 |
| Trial-based VE over 6 months, **then 0% VE** or **linear waning to 0% VE at 12 months** | $111,473 - $61,925 |
| Overall CFR among RSV hospitalized: **0.1% or 0.53%** [b] | $102,431 - $52,000 |
| Costs of RSV-Hospitalization **80% or 120%** of base-case) | $118,625 - $50,755 |
| Vaccination window: 32-36 wGA only (**uniform: 20% in each week**) [c] | $91,036 |
| Maternal vaccine and palivizumab in <1y infants **vs.** palivizumab only for prevention of RSV | $66,796 |

a. Base-case assumes for late pre-term a VE =83% of the VE for full term (VE = Vaccine efficacy)
b. CFR among RSV hospitalized: 0.1% (RR of RSV-H death = 1 for full term and preterm infants). For CFR 0.53% (using CFR values from full term = 0.3% and preterm = 1.7%)
c. wGA = weeks gestational age

# *Pfizer* and UM-CDC models comparison: $/QALY for selected scenarios in *Pfizer* model (II)

| | | ***Pfizer*** |
|---|---|---|
| A | ***Pfizer*** model with selected UM-CDC Inputs | $343,000 |
| B | *Pfizer* model with selected UM-CDC Inputs **except for *Pfizer* initial VE assumptions** | $265,000 |
| C | *Pfizer* model with selected UM-CDC Inputs **except for** *Pfizer* initial VE assumptions and ***Pfizer* DoP** | $173,000 |
| D | *Pfizer* model with selected UM-CDC Inputs **except for** *Pfizer* initial VE assumptions, *Pfizer* DoP and ***Pfizer* Medical costs** | **$83,000** |
| E | *Pfizer* model with selected UM-CDC Inputs **except for** *Pfizer* initial VE assumptions, *Pfizer* DoP, *Pfizer* Medical costs and **Palivizumab use** | $67,000 |

DoP = Duration of protection
VE = vaccine efficacy

# Limitations

- **Factors not considered that may result in overestimating the ICER (underestimating the cost-effectiveness) of maternal vaccination**
  - In base-case: both models assumed
    - No protection against URTI
    - No benefits of vaccination for vaccinated pregnant women
    - No out-of-pocket cost accrued by caregivers during infants RSV illness
  - 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 vaccination (i.e., no protection against RSV transmission)

# Conclusion

- **Differences in key inputs among *Pfizer* and UM-CDC models explain differences in results:**
  - Initial vaccine efficacy and assumptions about protection waning
  - Medical costs
  - Quality of life associated with RSV LRTI outcomes for patient and caregivers
  - Vaccine related adverse events
- In addition, the **UM-CDC** also identified two important factors that could drive the results
  - Hypothetically severe vaccine-associated adverse events
  - Timing of vaccination to RSV season
- **Base-case in both models:**
  - Maternal vaccination would significantly reduce RSV disease burden and costs in infants
    - Data from clinical trials used in both models support the reduction in RSV disease and associated costs
  - Economic value of vaccinating pregnant people to protect infants could increase costs
    - Reasonable vaccine price and duration of protection combined with careful design of seasonal interventions would determine the ***cost-effectiveness*** value of routine vaccination of pregnant people during the 32-36wGA

# Acknowledgements

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- Andrew Leidner
- Meredith McMorrow

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