Health Economic Impact of Maternal Bivalent Stabilized Prefusion F Subunit Vaccine for Prevention of Respiratory Syncytial Virus Infections Among Infants in Germany

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INTRODUCTION

- Respiratory syncytial virus (RSV) causes substantial respiratory illnesses among young children worldwide, with infants under 6 months being most prone to develop severe infection[1,2]
- In Germany, incidence of RSV-attributable hospitalization is highest among infants—especially those aged <6 months[3]—and the associated economic burden on the German healthcare system is considerable[4]
- Bivalent stabilized prefusion F subunit vaccine (RSVpreF) was recently granted market authorization in Germany for prevention of lower respiratory tract disease due to RSV (RSV-LRTD) in infants from birth through 6 months of age via active immunization of pregnant women between weeks 24 and 36 of gestation[5]

OBJECTIVES

- **To evaluate the potential health benefits and additional costs associated with the implementation of a maternal RSVpreF vaccination program in Germany**

METHODS

Model Overview

- Population-based cohort model to evaluate clinical outcomes/economic costs of RSV-LRTD during first year of life, and expected impact of RSVpreF vs. no intervention:
  - Clinical outcomes: RSV-LRTD by setting (hospital [RSV-H], ambulatory [RSV-Amb]), attributable deaths
  - Economic costs: direct costs related to medical care and vaccination, indirect (i.e., non-medical) costs related to caregiver work loss and future lost earnings associated with premature RSV-LRTD-related death
- Model population was characterized by month of age, calendar month of birth, and term status defined by gestational age in weeks (wGA) at birth (full-term, ≥37 wGA; late preterm, 32-36 wGA; early preterm, 28-31 wGA; extreme preterm, ≤27 wGA)

Estimation of Model Inputs

- Model inputs that vary by age and term status are detailed in Table 1 and Figure 1
- Infants in model population (N = 778,262 live births)[6] were distributed by term status (full term: 91.6%; late preterm: 6.9%; early preterm: 0.9%; extreme preterm: 0.6%)[7,8]
- RSV-H incidence rates by month of age were specific to Germany,[4] whereas RSV-Amb rates were derived from UK data[9,10]:
  - RSV rates were further allocated by term status and calendar month[4]
- Case fatality was assumed to occur among hospitalized cases only and was invariant by term status (aged <6 mo: 0.05 per 100; aged 6-<12 mo: 0.1 per 100), based on rates in high income countries from a published global meta-analysis[2]
- Rates of general population mortality among infants aged <1 month and aged 1-<12 months in Germany[11] were allocated across term status using US data[12]
- Monthly VE for full term infants was consistent with values employed by Hodgson et al., which were derived based on efficacy observed in Phase III clinical trial, "MATISSE," assuming that vaccine provided some protection throughout the first year of life (i.e., beyond age 6 months as indicated on the European Medicines Agency label)[13,14]
- Direct medical costs per RSV-H episode (full term: 4,651 €; late and early preterm: 6,487 €; preterm: 7,178 €) were based German administrative data[4]; cost per RSV-Amb episode (100 €) was from Ehlken et al.[15]
- Vaccine price: 214 €; administration fee: 10.39 €[16]
- Indirect costs were estimated based on German labor force, morbidity, and mortality data[17-19] as well as average RSV episode duration[20]

Analyses

Base Case

- Base case analyses evaluated the public health and economic impact of RSVpreF vs. no intervention among infants in Germany aged <1 year under two alternative vaccination schedules:
  - Year-round administration assumed uptake across all calendar months
  - Seasonal administration assumed uptake from June through February (i.e., protection during Oct-Mar RSV season)
- RSVpreF uptake was assumed to be 40% among eligible pregnant women[21] and was assumed to occur between 24-36 weeks gestation, with 10% of vaccine administered between 24-32 weeks and 90% between 33-36 weeks
- Costs, reported in 2023 EUR,[22] were discounted at an annual rate of 3%

Scenario

- A scenario analysis considering higher uptake of 60% with year-round administration was also conducted

Sensitivity

- Deterministic sensitivity analyses (DSA) were conducted to evaluate impact of ±20% variation on RSV incidence, cost of RSV, and initial VE in both hospital and ambulatory settings

Table 1. Base case model parameter values for RSV incidence and general infant mortality (per 1,000)

Model Parameter	<1	1-<2	2-<3	3-<4	4-<5	5-<6	6-<7	7-<8	8-<9	9-<10	10-<11	11-<12
Rates of RSV episodes												
Hospital												
Full term	29.7	55.9	43.8	36.9	35.6	31.1	28.1	24.3	18.3	16.8	16.9	16.9
Late/early preterm	38.7	72.7	57.0	47.9	46.3	40.4	36.5	31.5	23.9	21.9	22.0	22.0
Extreme preterm	41.6	78.3	61.4	51.6	49.9	43.5	39.3	34.0	25.7	23.5	23.7	23.7
Ambulatory												
Full term	42.7	94.1	117.3	116.5	132.8	144.9	61.2	47.9	64.2	52.5	55.9	59.7
Late/early preterm	55.5	122.4	152.5	151.5	172.6	188.4	79.6	62.3	83.5	68.3	72.7	77.6
Extreme preterm	59.8	131.8	164.3	163.2	185.9	202.9	85.7	67.1	89.9	73.6	78.2	83.6
General infant mortality												
Full term	0.7	1.9	1.2	0.9	0.7	0.6	0.5	0.4	0.3	0.2	0.2	0.2
Late preterm	8.1	9.0	5.8	4.3	3.5	2.7	1.8	1.3	1.1	0.8	0.7	0.7
Early preterm	38.8	22.7	14.6	10.7	8.8	6.9	4.5	3.3	2.7	2.1	1.7	1.8
Extreme preterm	155.5	33.5	21.6	15.8	13.1	10.1	6.6	4.8	4.0	3.0	2.5	2.6

Figure 1. Vaccine effectiveness, by age (based on Hodgson et al. 2024)
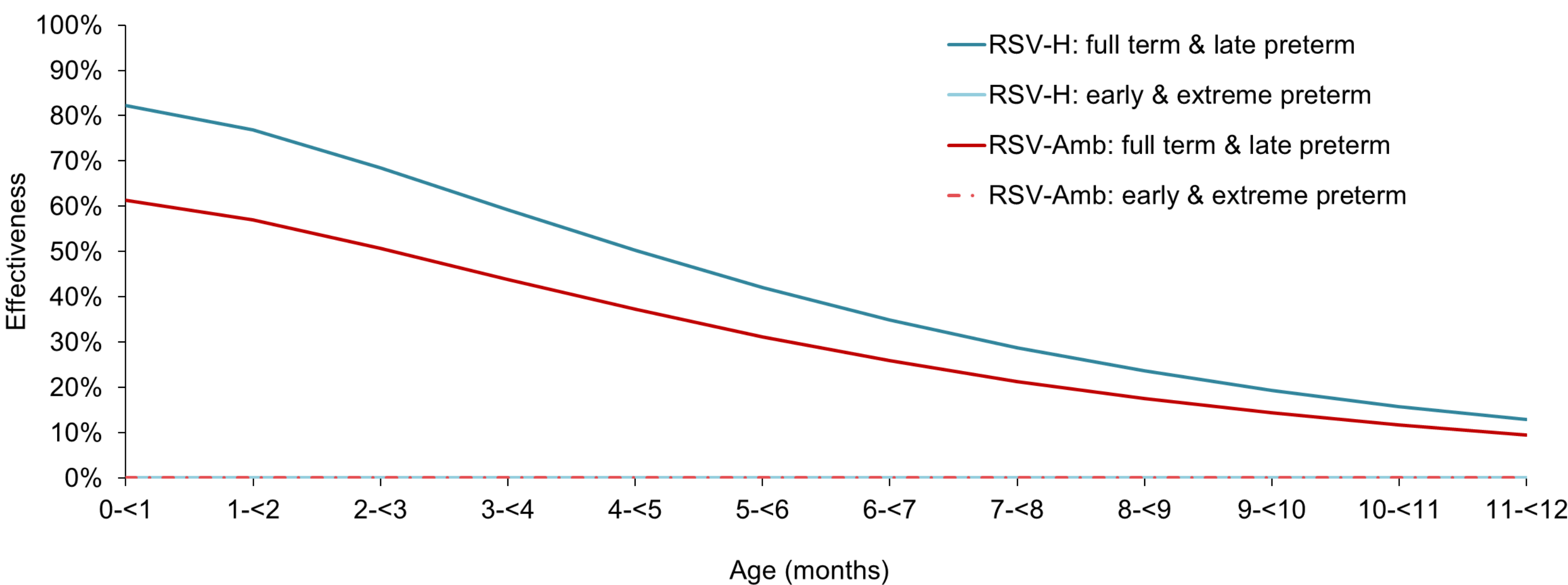
RESULTS

Base Case Analyses

- Year-round administration of RSVpreF prevented 19% of RSV-H cases, 13% of RSV-Amb cases, and 17% of RSV-related deaths compared to no intervention (Figure 2a, Table 2); corresponding total costs increased by 34% (i.e., due to net costs associated with 305,579 vaccinations) (Figure 2b)
- Seasonal administration of RSVpreF prevented 13% of RSV-H cases, 9% of RSV-Amb cases, and 10% of RSV-related deaths compared to no intervention; corresponding total costs increased by 12% (i.e., due to net costs associated with 146,064 vaccinations)

Scenario Analysis

- With higher year-round uptake, RSVpreF prevented 29% of RSV-H cases and 20% of RSV-Amb cases; total costs increased by 52% though medical care and indirect costs were lower by 28% and 25%, respectively

Sensitivity Analyses

- Changes to RSV-H incidence, costs, and initial VE had the biggest impact on total difference in costs between RSVpreF and no intervention
- While total number of RSV-Amb cases was affected by adjustments to RSV-Amb incidence and initial VE, total costs were similar to base case (i.e., within 100-200K €, strategy dependent)

Figure 2a. Total cases of RSV with use of RSVpreF vs. no intervention, base case and scenario analyses
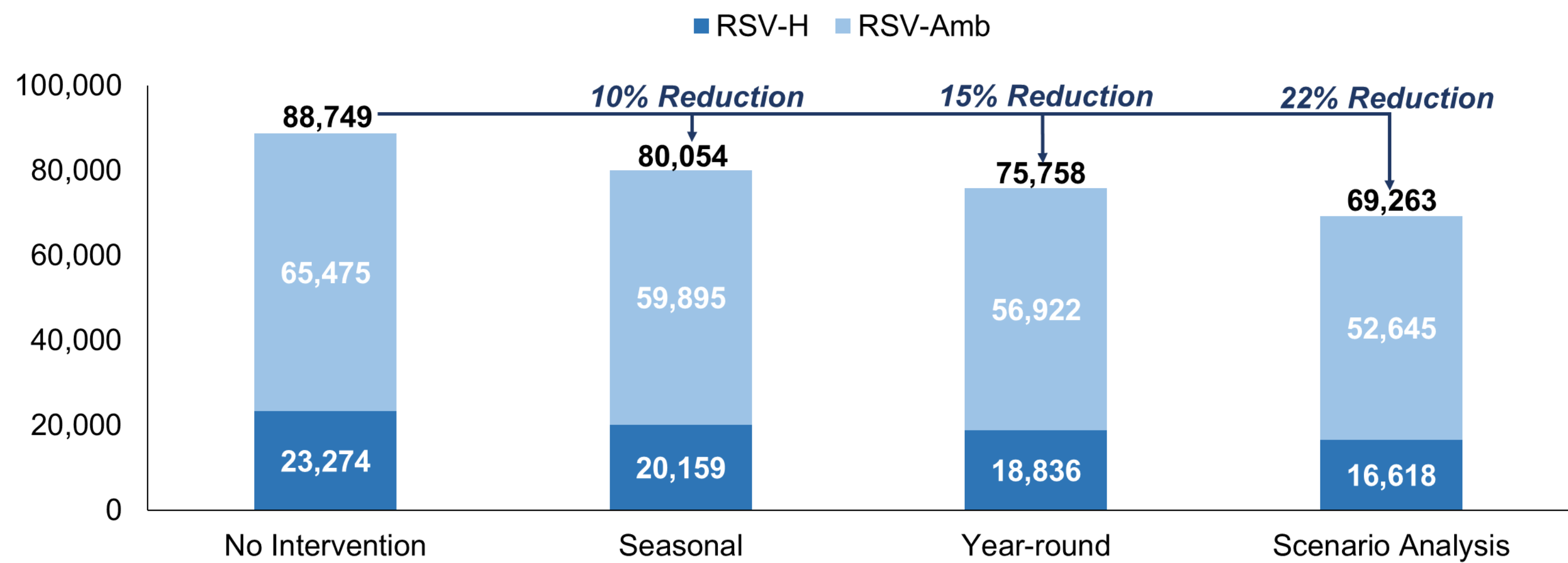

Figure 2b. Total direct and indirect costs of RSV with use of RSVpreF vs. no intervention, base case and scenario analyses
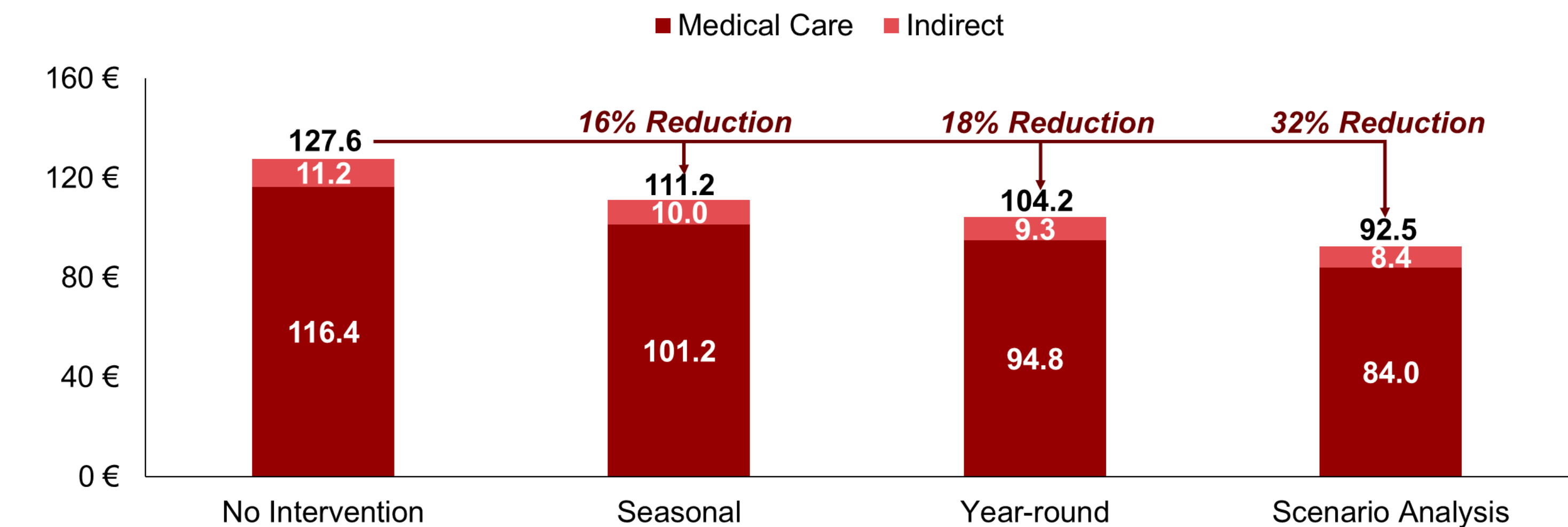

Table 2. Differences in clinical outcomes and economic costs with year-round and seasonal use of maternal vaccine vs. no intervention, deterministic sensitivity analyses (±20%)

Analysis	Year-round (vs. No Intervention)			Seasonal (vs. No Intervention)		
	Cases RSV-H	Cases RSV-Amb	Total Costs*	Cases RSV-H	Cases RSV-Amb	Total Costs*
Base case	-4,539	-8,746	44.9 €	-3,192	-5,725	16.1 €
RSV-H incidence, 80%	-3,631	-8,746	49.5 €	-2,553	-5,725	19.4 €
RSV-H incidence, 120%	-5,447	-8,746	40.3 €	-3,830	-5,725	12.9 €
RSV-Amb incidence, 80%	-4,539	-6,997	45.1 €	-3,192	-4,580	16.3 €
RSV-Amb incidence, 120%	-4,539	-10,496	44.7 €	-3,192	-6,870	16.0 €
Cost of RSV-H, 80%	-4,539	-8,746	49.2 €	-3,192	-5,725	19.2 €
Cost of RSV-H, 120%	-4,539	-8,746	40.7 €	-3,192	-5,725	13.1 €
Cost of RSV-Amb, 80%	-4,539	-8,746	45.1 €	-3,192	-5,725	16.2 €
Cost of RSV-Amb, 120%	-4,539	-8,746	44.8 €	-3,192	-5,725	16.0 €
RSV-H VE, 80%	-3,631	-8,746	49.5 €	-2,553	-5,725	19.4 €
RSV-H VE, 120%	-5,447	-8,746	40.3 €	-3,830	-5,725	12.9 €
RSV-Amb VE, 80%	-4,539	-6,997	45.1 €	-3,192	-5,725	16.1 €
RSV-Amb VE, 120%	-4,539	-10,496	44.7 €	-3,192	-6,870	16.0 €

*Total costs are the sum of medical care, vaccination, and indirect costs

LIMITATIONS

- Conservatively assumed 0% VE for early and extreme preterm infants
- Data from other high-income countries was applied in instances where German-specific data was not available (e.g., ambulatory RSV rates, case-fatality, work-loss days)
- Several benefits of maternal vaccination not accounted for, including: reduction in societal costs of RSV, reduction in long-term consequences of RSV, protection for vaccinated women, and indirect effects (herd immunity)

CONCLUSIONS

- **RSVpreF could substantially reduce the burden of RSV among infants, preventing 1.5x as many cases with year-round versus seasonal maternal vaccination, with even greater benefits with higher year-round vaccine uptake**
- **Our findings highlight the large potential impact of a maternal RSVpreF program on infants**

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