Potential Public Health Impact of Bivalent Respiratory Syncytial Virus Stabilized Prefusion F Subunit Vaccine (RSVpreF) Among Older Adults in Canada

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INTRODUCTION

- Respiratory syncytial virus (RSV) is an important causative pathogen of lower respiratory tract disease (LRTD) among adults, and can lead to significant morbidity and mortality, especially among older adults and those with certain medical conditions[1-4]
- Pfizer's novel RSV vaccine (RSVpreF) was recently approved by Health Canada to prevent RSV-LRTD in adults aged ≥60 years

OBJECTIVE

To project the potential public health impact of vaccination with RSVpreF compared to no vaccination among adults aged 60-99 years in Canada over 3 years

METHODS

Model Overview

- Population-based, multi-cohort, Markov-type model to depict clinical/economic outcomes of RSV-LRTD and expected impact of vaccination with RSVpreF over three years
- Model population (N=9.6M) characterized by age (60-64, 65-74, 75-84, and 85-99y) and comorbidity profile (with vs. without chronic or immunocompromising medical conditions [CMC+ vs. CMC-])
- Clinical outcomes and economic costs projected monthly, from model entry through end of modelling horizon, including:
  - Clinical outcomes: medically attended RSV-LRTD by care setting (hospital [RSV-H], emergency department [RSV-ED] physician office/hospital outpatient [RSV-PO/HO]), and RSV-related deaths
  - Economic costs: direct medical care costs and indirect costs associated with morbidity- and mortality-related work loss

Estimation of Model Inputs

- Model inputs that vary by age and comorbidity profile are detailed in Table 1
- Population was characterized by age and comorbidity using Statistics Canada[5] and survey data[6]
- RSV-H incidence was from a recently published model-based study;[7] incidence of ambulatory RSV-LRTD was calculated by applying the ratio of incidence of RSV-ED vs. RSV-H and RSV-PO/HO vs. RSV-H from a US meta-analysis to Canadian RSV-H incidence rates:[8]
  - Incidence rates were allocated across comorbidity profiles[9] and calendar months[10]
- Case-fatality rates (CFR) due to RSV-H[2] were allocated across comorbidity profiles based on relative risks of pneumonia-related mortality[11]; CFR assumed to be 0 for ambulatory RSV-LRTD
- General population mortality rates[12] were allocated across comorbidity profiles based on assumption
- Setting-specific direct medical costs per episode of RSV-LRTD (RSV-H: $14,023; RSV-ED: $341; RSV-PO/HO: $125) were based on Canadian sources[3,13,14]
- Indirect (i.e., non-medical) costs were estimated using Canadian data[2,15-19]
- RSVpreF uptake based on pneumococcal vaccine uptake[20]; timing based on influenza vaccine[21]
- Vaccine effectiveness (VE) was based on RENOIR results from end of season 1 and end of season 2; assumptions on waning of effectiveness were applied to RENOIR data[22-27] (Figure 1)
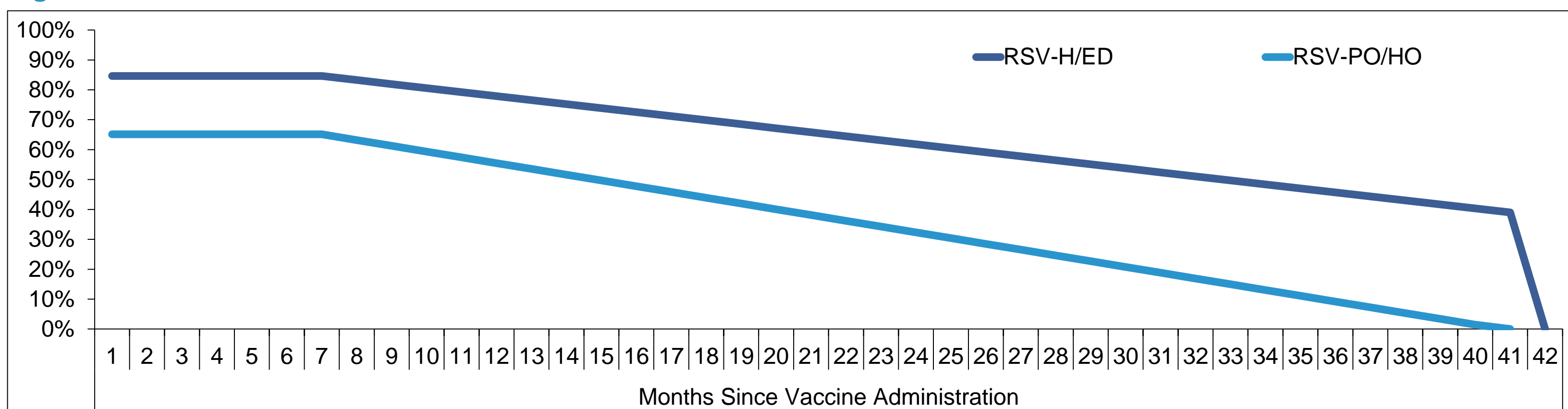
Analyses

- Base case analyses evaluated RSVpreF vs. no intervention among all adults aged 60-99 years
- Sensitivity and scenario analyses evaluated impact of changes in key model parameters and assumptions (i.e., RSV-H rates, CFR,[28] vaccine uptake, vaccine duration of protection [DoP], medical care costs)
- Subgroup analyses evaluated public health impact among alternative populations (i.e., aged ≥65y, CMC+)
- In all analyses, costs and benefits were discounted 1.5% annually; costs were reported in 2022 CAD

Table 1. Model parameter values

	Age/Comorbidity Profile							
	60-64 years		65-74 years		75-84 years		85-99 years	
	CMC-	CMC+	CMC-	CMC+	CMC-	CMC+	CMC-	CMC+
Population (in thousands)	1,720	852	2,410	1,649	1,091	1,010	380	472
RSV rates (annual, per 100K)								
Hospitalized	14	240	18	331	32	492	63	613
ED	74	187	77	211	81	239	91	259
PO/HO	1,266	2,192	1,163	2,288	1,085	2,330	978	2,371
RSV-H CFR (per 100)	2.3	7.9	4.2	8.2	8.6	10.6	13.5	15.8
Gen. population mortality (annual, per 100)	0.7	1.2	1.2	2.2	3.4	5.9	9.5	16.6
Vaccine uptake	48.3%	48.3%	48.3%	48.3%	65.4%	65.4%	65.4%	65.4%

Figure 1. Vaccine effectiveness*

*While VE is assumed to last through 4 RSV seasons, effectiveness beyond the 3rd year is not relevant for this analysis

RESULTS

Base Case Analyses

- Over 3 years, use of RSVpreF prevented 19,476 cases of RSV-H, 14,242 cases of RSV-ED, 107,170 cases of RSV-PO/HO, and 2,084 RSV-related deaths (Table 2)
- Total costs were reduced by $0.5 billion (medical care: -$0.4B; non-medical: -$0.1B)
- While hospitalizations comprised only 14% of the reduction in total RSV-LRTD cases, they accounted for 95% of the reduction in total medical care costs (Figure 2, Figure 3)

Table 2. Base case results

	Current Scenario	Hypothetical Scenario	Difference
Clinical outcomes			
No. of cases			
Hospital	49,199	29,723	-19,476
Emergency department	36,926	22,685	-14,242
Physician office/hospital outpatient	433,414	326,244	-107,170
No. of deaths	5,092	3,008	-2,084
Economic costs (millions)			
Medical care	$936	$578	-$358
Non-medical	$338	$228	-$110
Medical + non-medical	$1,274	$806	-$468

Figure 2. Clinical outcomes associated with RSV-LRTD, overall and by care setting
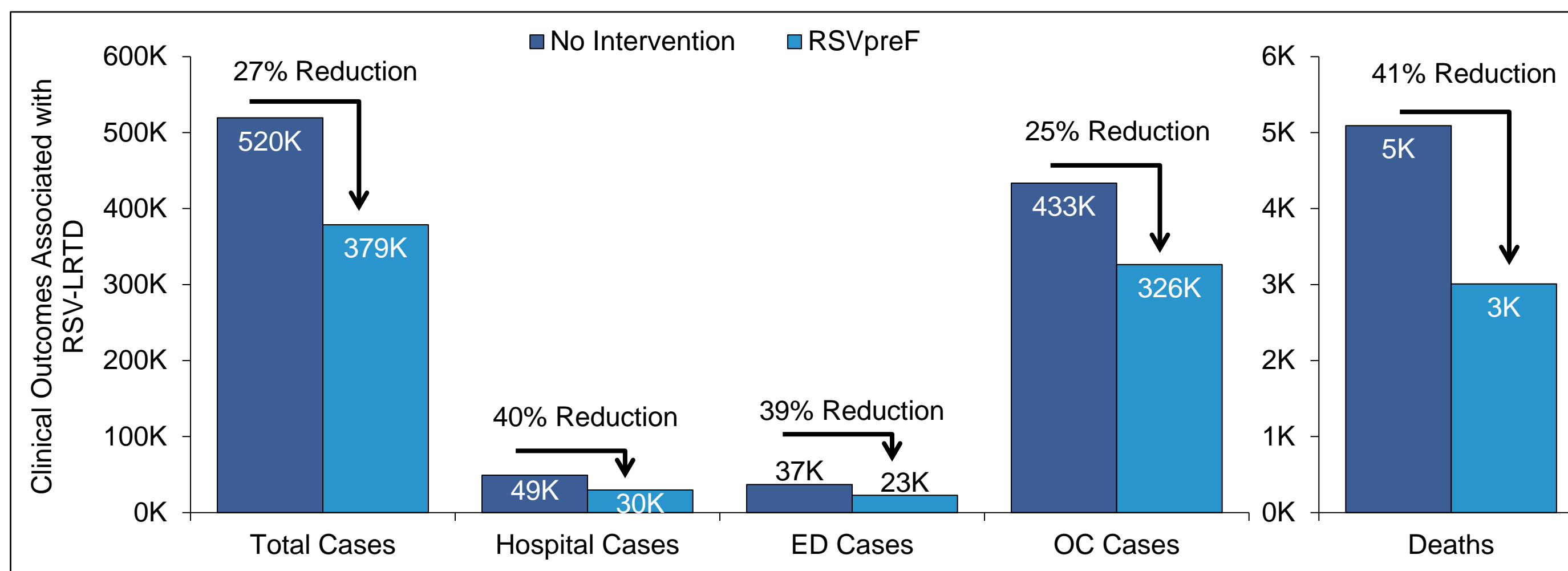
*Note vertical axes differentiating quantity of RSV-LRTD-related deaths

Figure 3. Medical costs of RSV-LRTD, overall and by care setting
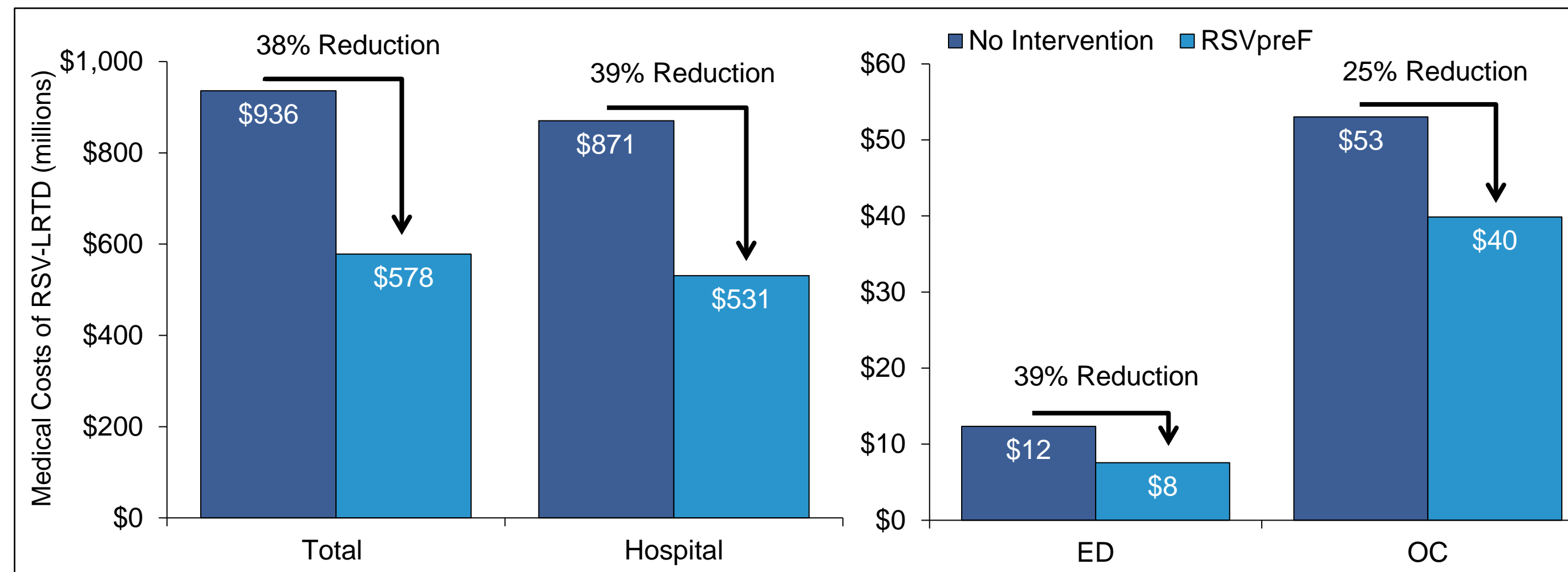
*Note, vertical axes differentiating costs associated with differing RSV-LRTD severity

Deterministic Sensitivity and Scenario Analyses

- Increasing vaccine uptake to 80% had the greatest impact on results, preventing >65K additional cases, nearly 800 deaths and >$225M in costs, compared to base case (Table 3)
- Changes to RSV-H incidence (±20% of base case) resulted in differences of ~4,000 cases and $86 million in total costs, compared to base case
- All other scenario analyses had relatively minimal effects on public health impact

Table 3. Scenario analysis results

	Total Cases Prevented	Deaths Prevented	Total Costs (millions) Prevented
Base case	140,888	2,084	$468
Vaccine uptake = 80% (all ages/comorbidities)	206,634	2,863	$694
Conservative duration of protection	139,729	2,057	$462
CFR from Nguyen-Van-Tam	140,911	1,668	$475
RSV-H incidence lower bound (80%)	137,036	1,668	$383
RSV-H incidence upper bound (120%)	144,740	2,501	$554
Medical costs lower bound (90%)	140,888	2,084	$432
Medical costs upper bound (110%)	140,888	2,084	$504

Subgroup Analyses

- Targeting all adults aged ≥60 years with RSVpreF vaccination would prevent 50,221 more cases than targeting only CMC+ adults and 28,112 more cases than targeting only adults aged ≥65 years (Figure 4)
- Targeting all adults aged ≥60 years would prevent 164 and 195 additional RSV-LRTD-related deaths, compared to targeting only CMC+ adults or adults aged ≥65 years, respectively
- Targeting all adults aged ≥60 years would save $56 million and $105 million more in total costs than targeting only CMC+ adults or adults aged ≥65 years, respectively

Figure 4. Subgroup analysis results: percent reduction in study outcomes vs. no intervention
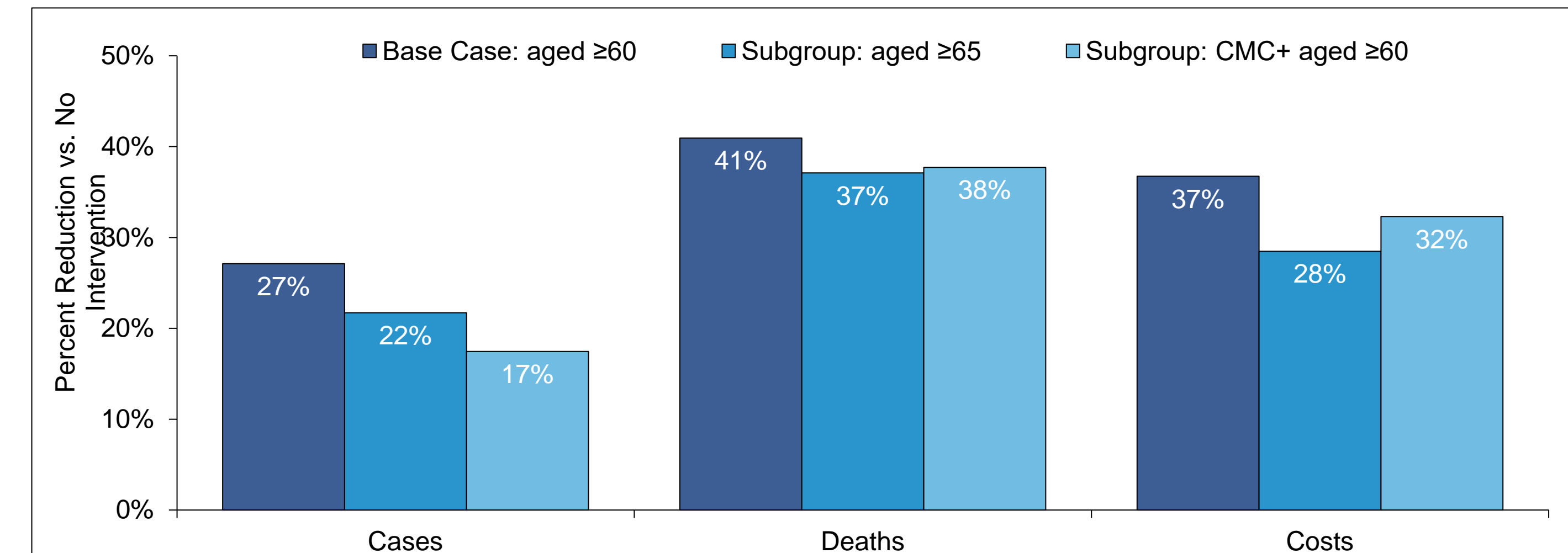
LIMITATIONS

- Given high VE throughout season 2, assumed linear waning up to 4 RSV seasons after average follow-up (16.4 months) in RENOIR
- VE vs. RSV-H was based on efficacy against medically-attended RSV-LRT illness with ≥3 symptoms as there were insufficient hospitalized RSV cases in RENOIR; VE vs. RSV-H is, therefore, likely conservative as vaccines are generally more protective against more severe disease (e.g., RSV-H)[29]
- RSV-H incidence was based on a modelling study which employed healthcare claims data from Ontario which may not be representative of Canada as a whole
- Canada-specific data were not available for incidence of RSV-ED or RSV-PO/HO, thus values were derived using ratios of hospitalized vs. ambulatory RSV from a US meta-analysis
- Some inputs (e.g., medical costs of RSV-H; work-days lost for RSV-H) are likely conservative

CONCLUSION

Findings suggest that an immunization program with RSVpreF among adults aged ≥60 years in Canada would considerably reduce the clinical and economic burden of RSV-LRTD

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