

Respiratory Syncytial Virus (RSV) vaccination for older adults

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**Anna Funk,
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BCCDC**



**Ayisha Khalid,
Epidemiologist,
BCCDC**



**Lea Separovic,
Epidemiologist,
BCCDC**

Question for the group

- **Should provinces publicly fund a program of RSV vaccination for older adults?**
 - **Usual considerations:**
 - From which perspective and for what purpose
 - To reduce individual risks of RSV infection and/or severe outcomes?
 - To reduce population impact of RSV?
 - To reduce health care impact of RSV?
 - Burden of disease, vaccine characteristics, programmatic
 - **Special considerations:**
 - As yet, no NACI statement
 - Limited evidence
 - Relative prioritization:
 - Additional RSV technologies and target groups ahead
 - Subgroups of risk
 - NNV and cost

Open Forum Infectious Diseases

MAJOR ARTICLE



Leveraging Influenza Virus Surveillance From 2012 to 2015 to Characterize the Burden of Respiratory Syncytial Virus Disease in Canadian Adults ≥ 50 Years of Age Hospitalized With Acute Respiratory Illness

May ElSherif,¹ Melissa K. Andrew,^{1,⊕} Lingyun Ye,¹ Ardith Ambrose,¹ Guy Boivin,² William Bowie,³ Marie-Pierre David,⁴ Olivier Gruselle,⁴ Scott A. Halperin,¹ Todd F. Hatchette,¹ Jennie Johnstone,⁵ Kevin Katz,⁶ Joanne M. Langley,^{1,⊕} Mark Loeb,⁷ Donna MacKinnon-Cameron,¹ Anne McCarthy,⁸ Janet E. McElhaney,^{9,a} Allison McGeer,¹⁰ Andre Poirier,¹¹ Jean-Yves Pirçon,⁴ Jeff Powis,¹² David Richardson,¹³ Makeda Semret,^{14,⊕} Stephanie Smith,¹⁵ Daniel Smyth,¹⁶ Sylvie Trottier,² Louis Valiquette,¹⁷ Duncan Webster,¹⁸ Shelly A. McNeil,^{1b} and Jason J. LeBlanc,^{1,b} for the Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN) and the Toronto Invasive Bacterial Diseases Network (TIBDN)

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ElSherif incidence estimation¹, 2012-13 to 2014-15

Data and specimens on Canadian older adults (≥ 50 years of age) admitted to hospital with ARI², collected prospectively Nov-May of 2012-13 to 2014-15 seasons by the CIRN SOS network³

RSV
hospitalization
incidence
per 100K
population

=

Proportion of ARI
hospitalizations
with RSV in CIRN
SOS data⁴

×

ARI hospitalizations
from CIHI's Discharge
Abstract Database

Statistics Canada's
population census data

¹ ElSherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023:ofad315.

² ARI defined by CIRN SOS as: pneumonia, acute exacerbation of COPD or asthma, unexplained sepsis, or any RTI or influenza-like symptom (e.g. dyspnea, cough, sore throat, myalgia, arthralgia, fever, delirium/altered level of consciousness, CHF).

³ Systematic prospective surveillance for ARI in hospitalized adults. Comprises 40 academic and community hospitals in New Brunswick, Nova Scotia, QC, ON, Manitoba, AB, BC. Demographic and medical details collected by interview and/or chart review.

⁴ Nasopharyngeal swabs collected and NAAT tested for RSV.

EISherif estimates of % ARI hospitalization with RSV by age group

Variable		% ARI hospitalizations with RSV [95% CI] ¹		
		RSV-A	RSV-B	RSV total
Season	2012/2013	2.7 [2.1 to 3.4]	1.8 [1.3 to 2.3]	4.5 [3.7 to 5.4]
	2013/2014	2.0 [1.5 to 2.5]	2.2 [1.7 to 2.8]	4.2 [3.5 to 4.9]
	2014/2015	2.0 [1.4 to 2.7]	4.3 [3.4 to 5.3]	6.2 [5.2 to 7.4]
Gender	Female	2.8 [2.3 to 3.4]	3.0 [2.5 to 3.5]	5.8 [5.1 to 6.5]
	Male	1.5 [1.2 to 2.0]	2.1 [1.7 to 2.6]	3.6 [3.1 to 4.3]
Age, years	50 to 59	1.1 [0.6 to 2.0]	3.0 [2.1 to 4.2]	4.1 [3.0 to 5.5]
	60 to 64	3.6 [2.4 to 5.2]	2.1 [1.2 to 3.4]	5.7 [4.2 to 7.6]
	65 to 69	2.9 [1.9 to 4.3]	2.7 [1.7 to 4.0]	5.5 [4.1 to 7.3]
	70 to 79	2.0 [1.4 to 2.7]	2.6 [1.9 to 3.4]	4.6 [3.7 to 5.6]
	≥80	2.2 [1.7 to 2.8]	2.5 [1.9 to 3.1]	4.6 [3.9 to 5.4]
Overall		2.2 [1.9 to 2.6]	2.6 [2.2 to 2.9]	4.8 [4.3 to 5.3]

~5% of ARI hospitalizations among older adults associated with RSV – similar by age subgroup¹

Of those hospitalized:
 ~14% admitted to ICU
 ~6% died
 [not sub-stratified by age]

¹ EISherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023:ofad315.

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~5% of ARI hospitalizations among older adults associated with RSV – similar by age subgroup^{1,2}

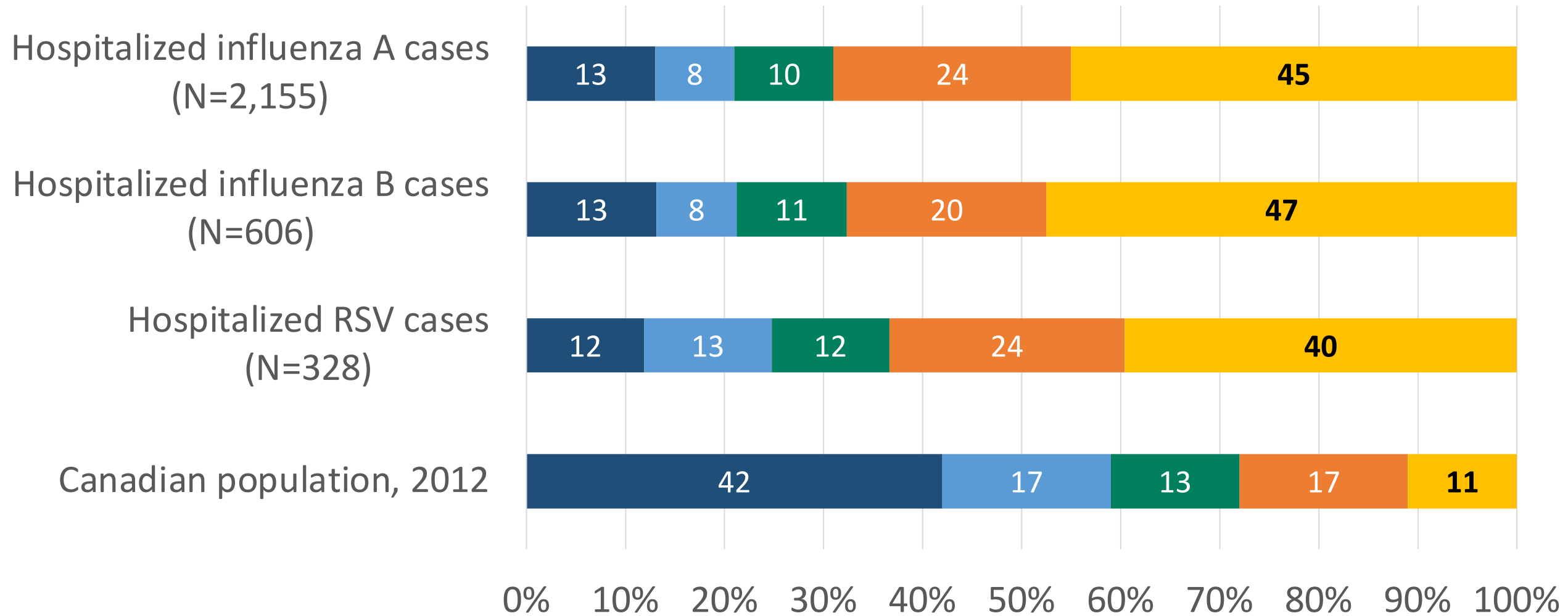
~35% of ARI hospitalizations among older adults associated with influenza A/B²

¹ EISherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023;ofad315.

² Relative RSV versus influenza percentages similar in separate analysis by Gilca et al for those ≥ 65 years (8% and 36%, respectively). See: Gilca R et al. Open Forum Infect Dis 2014 Sep 22; 1(2):ofu086. doi: 10.1093/ofid/ofu086.

ElSherif proportion flu/RSV hospitalizations by age group, 2012-14

■ 50-59 ■ 60-64 ■ 65-69 ■ 70-79 ■ 80+ years



ElSherif estimates of RSV hospitalization incidence by age group

Table 1. Estimated Respiratory Syncytial Virus Hospitalization Rates Among Canadian Adults Aged ≥ 50 Years

Virus	Age Group, y	Seasonal Incidence Rates per 100 000 Population (95% CI) ^a			
		2012–2013	2013–2014	2014–2015	2012–2015
RSV (total)	50–59	9.3 (3.3–15.3)	11.8 (6.6–16.9)	8.2 (4.2–12.1)	13.9 (9.9–17.9)
	60–69	46.6 (30.9–62.4)	36.7 (25.6–47.8)	51.1 (29.8–72.5)	43.7 (34.2–51.2)
	70–79	105.4 (70.8–140.0)	66.4 (50.0–87.9)	103.7 (63.8–143.6)	88.6 (71.0–106.1)
	≥ 80	254.0 (179.9–328.1)	173.9 (124.9–222.9)	487.4 (369.3–605.5)	282.5 (238.2–326.8)
	50–64	32.0 (20.3–43.8)	27.3 (18.7–35.9)	28.1 (17.0–37.5)	33.6 (26.9–40.3)
	≥ 50	63.9 (52.6–75.1)	47.2 (39.5–54.8)	54.5 (62.3–88.4)	64.8 (58.4–71.1)
	≥ 65	80.7 (64.5–96.9)	57.0 (46.3–67.7)	68.6 (83.2–123.6)	80.8 (71.7–89.9)
	≥ 60	101.6 (91.0–112.2)	105.5 (86.2–124.8)	73.1 (60.4–85.8)	145.5 (118.7–172.4)

Abbreviations: CI, confidence interval; RSV, respiratory syncytial virus.

^aFor incidence calculations for age groups, the proportion of RSV attributed to community-acquired pneumonia by the Canadian Immunization Research Network's Serious Outcomes Surveillance Network from November to May of each year was applied to census data during this period, and the seasonal proportions of individuals hospitalized with an acute respiratory infection from Canadian Institute for Health Information Discharge Abstract Database data (excluding the provinces of British Columbia and Québec).

¹ ElSherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023;ofad315.

² Statistics Canada. Research Highlights on Health and Aging. Released October 2016. ARCHIVED. Accessible online at: <https://www150.statcan.gc.ca/n1/pub/11-631-x/11-631-x2016001-eng.htm>

³ From British Columbia Chronic Disease Registry (BCCDR) at the BC Centre for Disease Control

EISherif estimates of RSV hospitalization incidence by age group

98% of hospitalized RSV cases in EISherif series had at least 1 comorbidity; 27% immunocompromising

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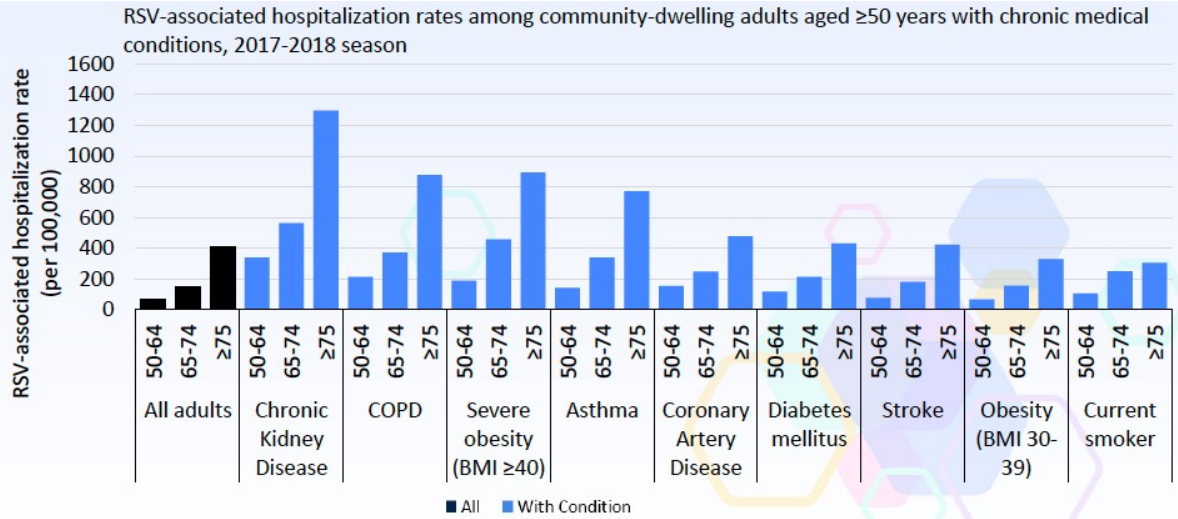
70% of adults 60-69 years; 80% of adults 70-79 years; 90% of adults 80+ years have at least 1 comorbidity in Canadian² and BC³ population

¹ EISherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023;ofad315.

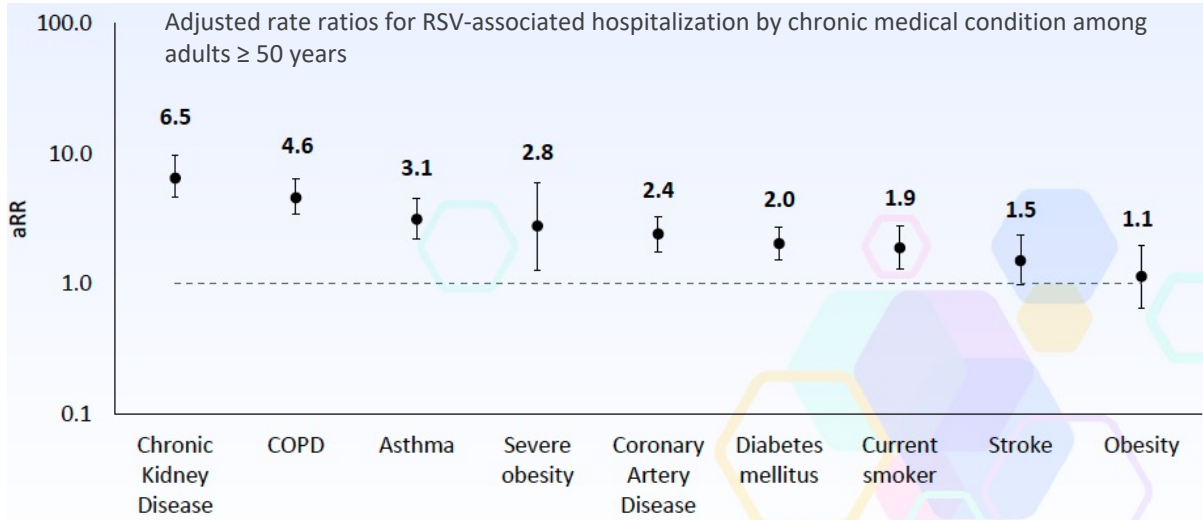
² Statistics Canada. Research Highlights on Health and Aging. Released October 2016. ARCHIVED. Accessible online at: <https://www150.statcan.gc.ca/n1/pub/11-631-x/11-631-x2016001-eng.htm>

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Select comorbidities increase risk, preliminary data, United States



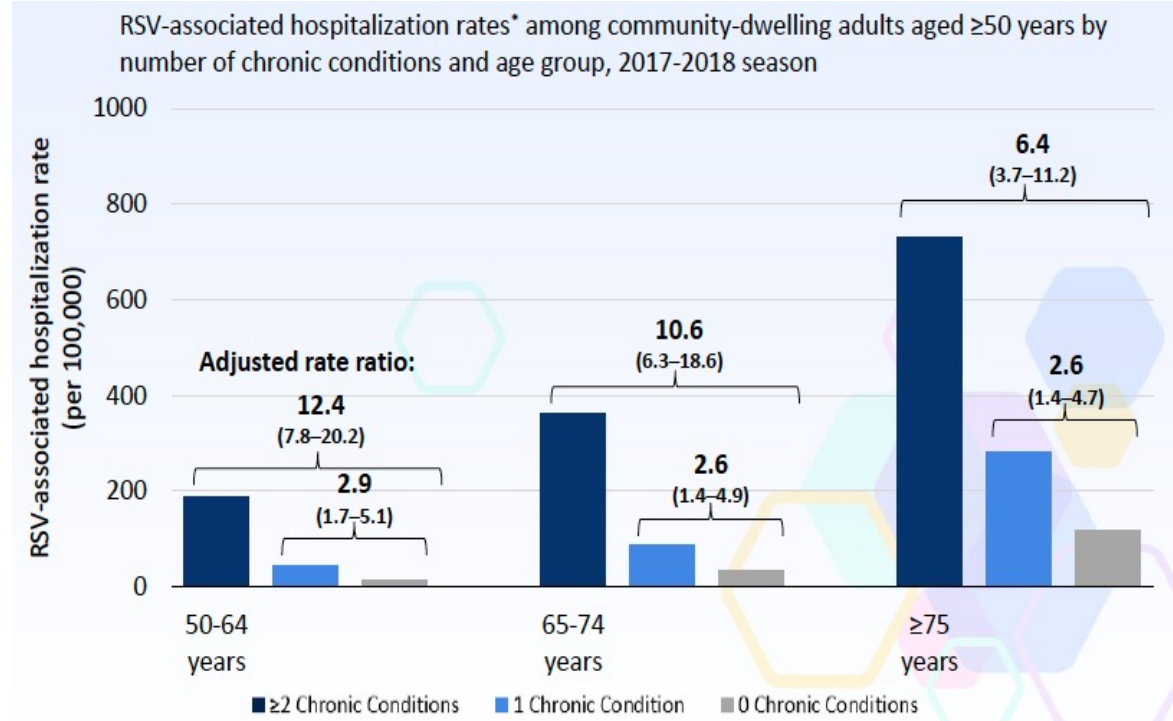
Data are preliminary and unpublished. Rates of laboratory-confirmed RSV-associated hospitalization account for under-detection of RSV infection among hospitalized adults and sensitivity of diagnostic tests; rates exclude residents of nursing homes and long-term care facilities and are not adjusted for sex or race/ethnicity group.



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From: Woodruff RSV Vaccines Adults February 29, 2024:

<https://www.cdc.gov/vaccines/acip/meetings/slides-2024-02-28-29.html>



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Extrapolating ElSherif estimates to BC population

- ElSherif et al RSV hospitalization incidence estimates¹ applied to BC population²
 - Not accounting for RSV attribution or for comorbidity (thereby tending to over-estimate)
 - Correction (multiplier) factors ranging 1.5 to 3.25^{3,4,5} to address sensitivity of NAAT assay, specimen type

Age Group (years)	Average 2012-2014 hospitalization incidence per 100K	Population size (2023)	Approximate number of hospitalizations annually with/without correction factor (CF)		
			Without CF	CF = 1.5x	CF = 3x
60-69	43.7	704 K	300	450	900
70-79	88.6	491 K	400	600	1300
≥ 65	80.8	1.09 M	900	1300	2600
≥ 80	282.5	260 K	700	1100	2200

1. ElSherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023;ofad315.
2. Population data obtained online from Statistics Canada, for the years 2012-2015: <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000501>. Exact population estimates applied in derivations.
3. McLaughlin JM, Khan F, Begier E, Swerdlow DL, Jodar L, Falsey AR. Rates of Medically Attended RSV Among US Adults: A Systematic Review and Meta-analysis. Open Forum Infect Dis 2022;9:ofac300.
4. Li Y, Kulkarni D, Begier E, Wahli-Singh P, Wahli-Singh B, Gessner B, Nair H. Adjusting for case under-ascertainment in estimating RSV hospitalization burden of older adults in high-income countries: a systematic review and modelling study. Infect Dis Ther 2023;12:1137-49.
5. Ramirez J, Carrico R, Wilde A, et al. Diagnosis of respiratory syncytial virus in adults substantially increases when adding sputum, saliva, and serology testing to nasopharyngeal swab RT-PCR. Infect Dis Ther 2023;12:1593-1603
6. From Melgar, RSV Vaccines – Adult. Etr (incl GRADE) for 2 vaccines (GSK & Pfizer) (slide 8). February 23, 2023. Available: <https://www.cdc.gov/vaccines/acip/meetings/slides-2023-02-22-24.html>

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In BC, during the six month period spanning August-February 2023, among those 60-69 years, 70-79 years and ≥ 80 years there were ~ 700, ~1400 and ~2400 hospitalizations with COVID-19, exceeding all but the most extreme CF-adjusted estimates for RSV.

1. ElSherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023;ofad315.
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RSV vaccines for older adults

- **AREXVY, GSK¹: RSVPreF3 OA (recombinant subunit vaccine, AS01_E adjuvanted)**
 - Recombinant RSV surface F glycoprotein (based on RSV-A subtype) stabilized in prefusion trimeric form with AS01_E adjuvant (latter as per zoster vaccine but at a lower dose)
 - *Authorized for adults ≥ 60 years in US in May 2023 and in Canada in August 2023^{2,3,4}*
- **ABRYSVO, Pfizer Inc⁵: Bivalent RSVPreF (no adjuvant)**
 - Recombinant RSV surface F glycoprotein (based on both RSV-A and RSV-B subtypes) stabilized in prefusion form
 - *Authorized for adults ≥ 60 years in US in May 2023 and in Canada January 2024^{3,6,7}*
 - *Authorized for pregnant women in US in August 2023 and in Canada January 2024^{6,8}*
- **In the pipeline: Moderna mRNA-1345 vaccine for use in adults aged ≥60 years**
 - *Authorization pending*

1. Papi A, Ison MG, Langley JM, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. N Engl J Med 2023;388:595-608.

2. Government of Canada. Health Canada. Drug product database. Product monograph including patient medication information. AREXVY. Available: https://pdf.hres.ca/dpd_pm/00071904.PDF

3. Government of Canada. Respiratory syncytial virus (RSV): Canadian Immunization Guide. Available: <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/respiratory-syncytial-virus.html>

4. FDA approves first RSV vaccine. Arexvy approved for individuals 60 years of age and older. Available: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-respiratory-syncytial-virus-rsv-vaccine>

5. Walsh EE, Perez Marc G, Zareba AM, et al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. N Engl J Med 2023;388:1465-77

6. Government of Canada. Health Canada. Drug product database. Product monograph including patient medication information. ABRYSVO. Available: https://pdf.hres.ca/dpd_pm/00073900.PDF

7. US FDA approves Abrysvo, Pfizer's vaccine for the prevention of respiratory syncytial virus (RSV) in older adults. Available: <https://www.pfizer.com/news/press-release/press-release-detail/us-fda-approves-abrysvo-tm-pfizers-vaccine-prevention>

8. FDA approves first vaccine for pregnant individuals to prevent RSV in infants. Available: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-vaccine-pregnant-individuals-prevent-rsv-infants>

Vaccine efficacies, clinical trial and CDC calculated, ≥ 60 years

Adapted from: Melgar RSV Vaccines Adults (slide 10) February 29, 2024: <https://www.cdc.gov/vaccines/acip/meetings/slides-2024-02-28-29.html> with references from Ortega-Sanchez Economics of vaccinating US adults ≥60 years-old against Respiratory Syncytial Virus (slide 18) June 21, 2023: <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/05-RSV-Adults-Ortega-Sanchez-508.pdf>

Outcome (RSV-associated)	AREXVY, GSK ¹ VE (95% CI)		ABRYSCO, Pfizer ² VE (95% CI)	
	Season 1 (0-7 months post-injection)	Season 2 (13-18 months post-injection) ³	Season 1 (0-7 months post-injection)	Season 2 (8-14 months post-injection) ³
Outpatient visits⁴ <i>Trial efficacy against medically-attended ARI due to RSV</i>	79.0% (54.3, 91.5)	27.8% (0, 60.4)	65.2% (36.0, 82.0)	55.0% (0, 82.0)
Hospitalizations <i>Trial efficacy against medically-attended LRTD/LRTI due to RSV</i>	87.5% (58.9, 97.6) ⁵	52.9% (0, 81.2) ⁵	84.6% (32.0, 98.3) ⁶	75.0% (0, 97.4) ⁶

Clinical trials under-enrolled adults ≥ 75 years in whom VE estimates may be lower

¹ GSK Phase 3 Trial; interim analysis 2023; CDC-calculated vaccine efficacy in participants ages ≥60 years

² Pfizer Phase 3 Trial; interim analysis 2023; CDC-calculated vaccine efficacy in participants ages ≥60 years

³ Efficacy estimates are not directly comparable. Clinical trials used different outcome definitions and the follow up time differed substantially across trials. Efficacy estimates are associated with much uncertainty.

⁴ CDC-calculated VE against medically-attended RSV acute respiratory illness (ARI)

⁵ CDC-calculated VE against medically-attended RSV lower respiratory tract disease (LRTD)

⁶ CDC-calculated VE against medically-attended RSV lower respiratory tract illness (LRTI) with at least 3 lower respiratory symptoms

Vaccine safety

- A small number of inflammatory neurological events (notably Guillain Barré Syndrome, GBS) were found during clinical trials among older adults
 - AREXVY (GSK): 1 GBS \leq 42 days (9 days) post-vaccination among 18,304 vaccinees \geq 60 years*[‡]
 - ABRYSSVO (Pfizer): 2 GBS \leq 42 days (10, 14 days) post-vaccination among 20,255 vaccinees \geq 60 years *[‡]
- In November 2024, post-marketing surveillance in the United States identified a higher than expected number of GBS cases in the Vaccine Adverse Event Reporting System (VAERS), triggering further in-depth investigation
- At US ACIP meeting on February 29, 2024, the first preliminary 2023-24 safety surveillance data were presented from several surveillance systems

*Melgar et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices - United States, 2023. Am J Transplant. 2023;23(10):1631-1640.

[‡]Shimabukuro slide 4, RSV Vaccines Adults February 29, 2024:
<https://www.cdc.gov/vaccines/acip/meetings/slides-2024-02-28-29.html>

Preliminary US risk-benefit assessment

Adapted from: Britton RSV Vaccination in Older Adults: Working Group Interpretations, slide 10, February 29, 2024:

<https://www.cdc.gov/vaccines/acip/meetings/slides-2024-02-28-29.html>

	Disease-associated hospitalizations preventable per million vaccinated ¹ (95% CI)		Potential vaccine-associated GBS cases per million vaccinated ≥ 65 years ^{2,3} (95% CI)	
	Over two seasons, ≥ 60 years:			
RSV	AREXVY (GSK)	2,400 (1,800 - 3,700)	AREXVY (GSK)	10 (2 - 18)
	ABRYSVO (Pfizer)	2,700 (2,100 - 4,200)	ABRYSVO (Pfizer)	25 (7 - 43)
	(if 6% died: 140 – 160 preventable deaths)		Expected background rate	5 (4.8 - 5.4) ^{4,5}
Influenza	Over one season, ≥ 65 years:		Variable & inconsistent by season. At most ~1-2 excess cases per million vaccinated ^{6,7}	
	2,000 (300 - 5,500)			

Abbreviations: CMS = Centers for Medicare & Medicaid Services, FDA = U.S. Food and Drug Administration, GBS = Guillain-Barre syndrome

¹ Ranges of preventable outcomes were calculated using adjusted 95% confidence interval of RSV-associated incidence of the outcome observed in RSV-NET. Uncertainty in vaccine efficacy was not incorporated into ranges of preventable outcomes.

² Among Medicare beneficiaries ≥ 65 years, May-December 2023. Must have been enrolled in Medicare Parts A, B and D. Must not have had a diagnostic code for GBS in the 365 days preceding vaccination. GBS cases observed after RSV vaccination during a 42-day risk interval, adjusted for delays in claims data and adjustment for positive-predictive value of diagnostic codes in identifying chart-confirmed GBS. These are rates of GBS identified by inpatient claims data and are decreased by 29% to account for the positive predictive value of diagnostic codes in identifying chart-confirmed GBS cases. A GBS background rate is not subtracted from these rates.

³ Due to delays in claims data, not all participants have accrued 42 days of effective follow up time. GBS observation rates per 1million doses over a **21-day risk interval** were also calculated (**GSK Arexvy: 5 cases [1–9], Pfizer Abrysvo: 13 cases [3–22]**).

⁴ Historical background rate may not be applicable to persons electing to receive RSV vaccination using shared clinical decision-making. On average, recipients of each of the two vaccines may be at different baseline risk of GBS. More robust analysis, such as a self-controlled case series, is needed to confirm and quantify a risk of Guillain-Barre syndrome after RSV vaccination.

⁵ The lower and upper bounds of the 95% confidence interval for the expected cases both round to 5. With additional precision: 5.06 expected GBS cases (95% CI 4.76 –5.38) per 1 million doses administered to adults ages 65 years and older.

⁶ Vellozzi C, Iqbal S, and Broder K. Guillain-Barré Syndrome, Influenza, and Influenza Vaccination: The Epidemiologic Evidence, *Clinical Infectious Diseases*, Volume 58, Issue 8, 15 April 2014, Pages 1149–1155, <https://doi.org/10.1093/cid/ciu005>.

⁷ Committee to Review Adverse Effects of Vaccines; Institute of Medicine; Stratton K, Ford A, Rusch E, et al., editors. *Adverse Effects of Vaccines: Evidence and Causality*. Washington (DC): National Academies Press (US); 2011 Aug 25. 6, Influenza Vaccine. Available from: [https://www.ncbi.nlm.nih.gov/books/NBK190013/Influenza_Vaccine_-_Adverse_Effects_of_Vaccines_-_NCBI_Bookshelf_\(nih.gov\)](https://www.ncbi.nlm.nih.gov/books/NBK190013/Influenza_Vaccine_-_Adverse_Effects_of_Vaccines_-_NCBI_Bookshelf_(nih.gov)).

Vaccine safety

- A small number of inflammatory neurological events (notably Guillain Barré Syndrome, GBS) were found during clinical trials among older adults
 - AREXVY (GSK): 1 GBS \leq 42 days (9 days) post-vaccination among 18,304 vaccinees \geq 60 years*[‡]
 - ABRYSVO (Pfizer): 2 GBS \leq 42 days (10, 14 days) post-vaccination among 20,255 vaccinees \geq 60 years *[‡]
- In November 2024, post-marketing surveillance in the United States identified a higher than expected number of GBS cases in the Vaccine Adverse Event Reporting System (VAERS), triggering further in-depth investigation
- At US ACIP meeting on February 29, 2024, the first preliminary 2023-24 safety surveillance data were presented from several surveillance systems
- **Conclusions:**
 - **Overall favorable benefit-risk ratio for both vaccines, but GBS safety signal requiring ongoing monitoring and more definitive evaluation**
 - **Benefits would more clearly outweigh potential risks among those of advanced age or with comorbidity**

Number needed to vaccinate (NNV)

- **NNV = number of people we need to vaccinate to prevent one outcome**
 - E.g., to prevent one hospitalization, one death
- **Varies with incidence and vaccine efficacy (VE)**
 - As incidence or VE increase, NNV decreases
- **Can multiply vaccination costs by NNV to ballpark the cost to prevent one outcome**
 - Can compare cost to prevent one outcome to the cost to treat one outcome
 - E.g., ratio of cost to prevent one hospitalization versus cost to pay for one hospitalization

$$\begin{aligned} \text{NNV} &= \frac{1}{\text{Absolute Risk Reduction}} = \frac{1}{\text{Incidence}_{\text{unvaccinated}} - \text{Incidence}_{\text{vaccinated}}} \\ &= \frac{1}{\frac{n_{\text{unvaccinated}}}{N_{\text{unvaccinated}}} - \frac{n_{\text{vaccinated}}}{N_{\text{vaccinated}}}} \end{aligned}$$

NNV to prevent hospitalization and ratio of costs to prevent vs to treat

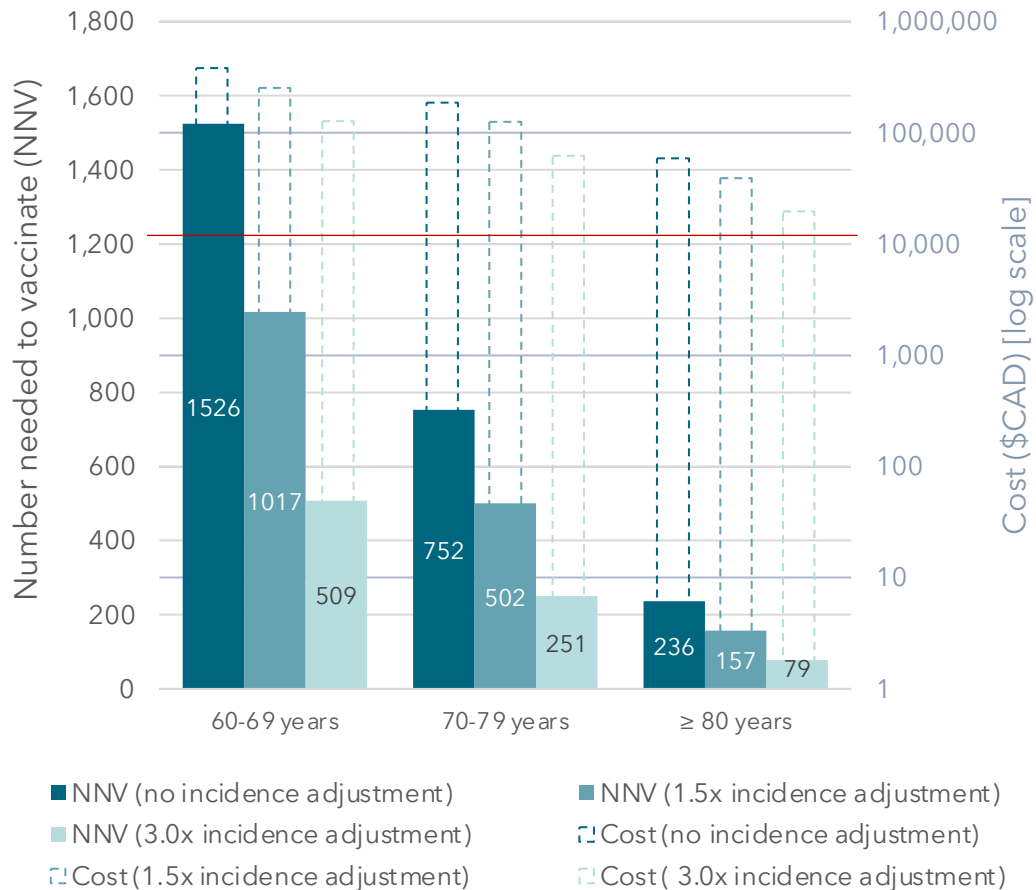
- NNV assumptions:
 - Incidence per El Sherif et al¹
 - Not accounting for RSV attribution or comorbidity
 - VE: 85% season 1, 65% season 2 (not varied by age)
- Cost assumptions:
 - Vaccine price per dose: \$250
 - RSV hospitalization: \$20,000 for 60-69y; \$15,000 for $\geq 70y$ ¹

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NNV and cost to prevent 1 RSV hospitalization

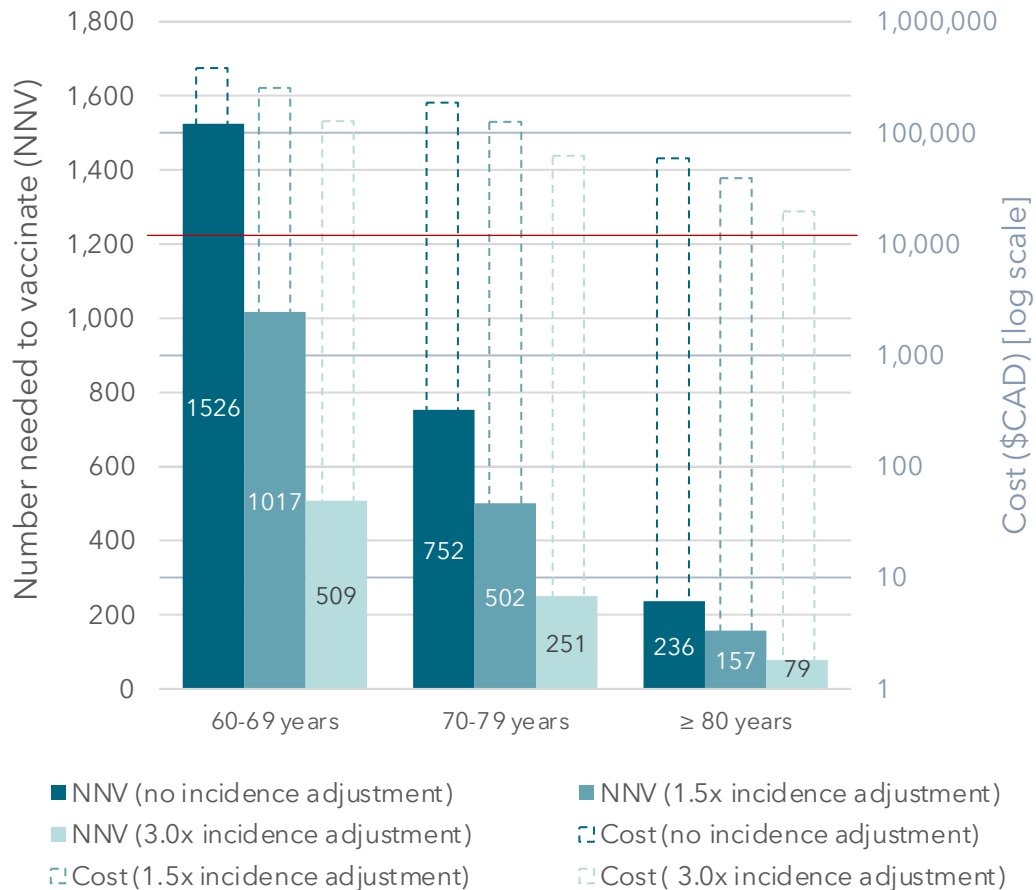


¹ ElSherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023;ofad315.

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NNV and cost to prevent 1 RSV hospitalization



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Derived NNV estimates to prevent one RSV hospitalization

- 500-1500 among adults 60-69 years
 - 250 to 750 among adults 70-79 years
 - 100 to 200 among adults ≥ 80 years
- ↑ 2x if VE halved

US derived NNV estimates to prevent one RSV hospitalization

- 400 to 1100 among adults ≥ 65 years

Canadian estimates to prevent one influenza hospitalization²

- Higher incidence, lower VE → comparable NNV

Influenza NNV (2012-2019) ²	Overall			With comorbidity			Without comorbidity		
	30%	50%	60%	30%	50%	60%	30%	50%	60%
VE:	30%	50%	60%	30%	50%	60%	30%	50%	60%
≥ 65 years	772	463	386	458	275	229	2497	1498	1248
≥ 75 years	365	219	182	298	179	149	1206	724	1206
≥ 85 years	301	180	150	223	134	111	807	484	403

² Carazo S, Guay C-A, Skowronski DM et al. Clin Infect Dis 2023 Oct 11:ciad627. Doi: 10.1093/cid/ciad627.

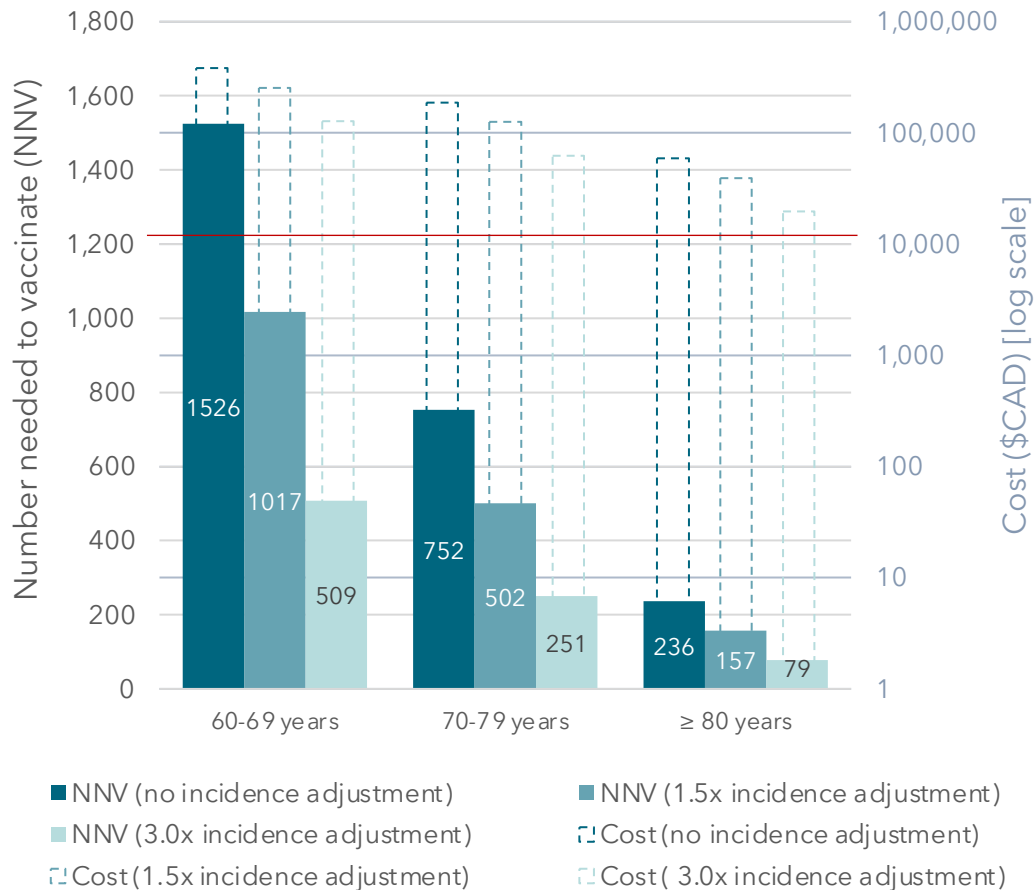
¹ ElSherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023:ofad315.

NNV to prevent hospitalization and ratio of costs to prevent vs to treat

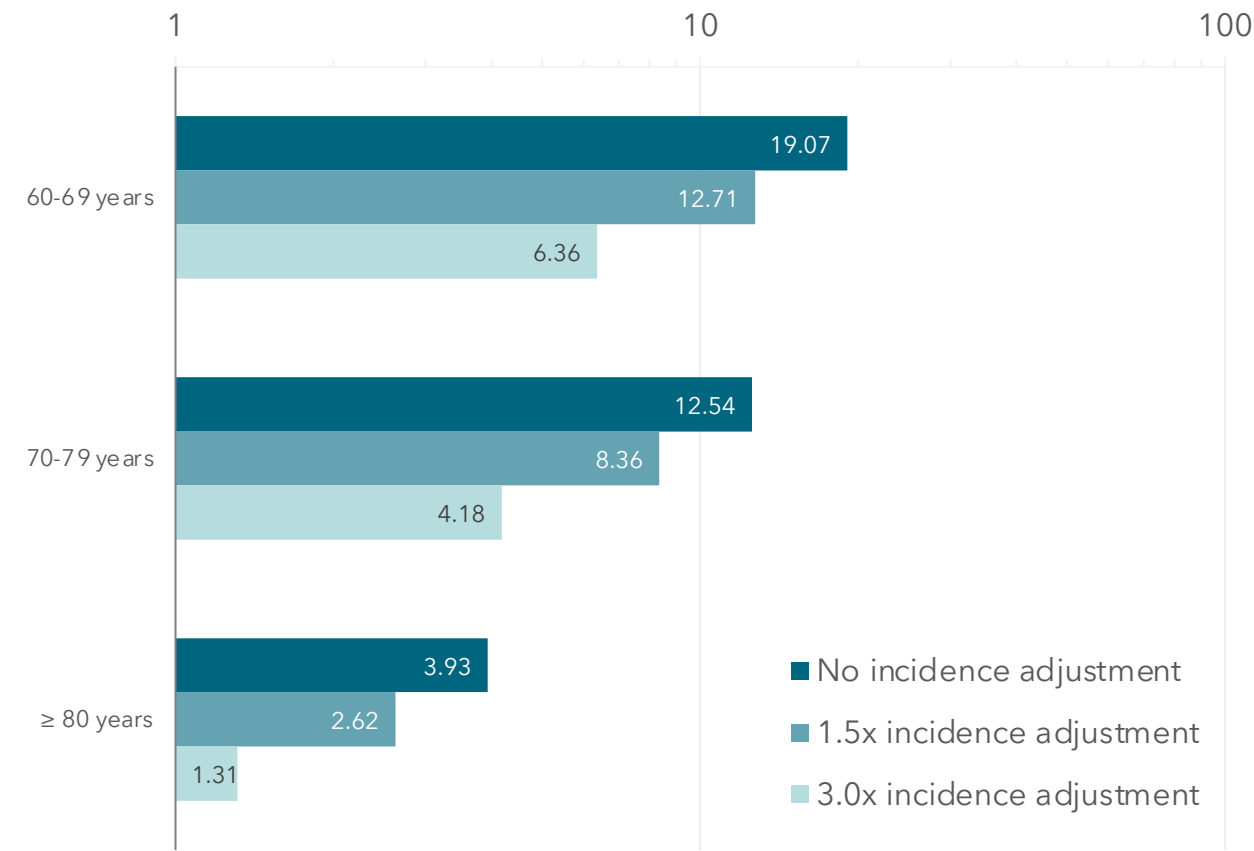
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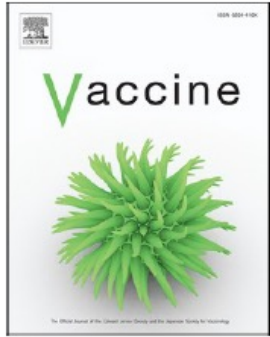
NNV and cost to prevent 1 RSV hospitalization



Ratio of cost to prevent vs to hospitalize



¹ ElSherif M et al. Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease (RSV) in Canadian adults ≥ 50 years hospitalized with acute respiratory illness. Open Forum Infect Dis 2023;ofad315.



Impact and cost-effectiveness analyses of vaccination for prevention of respiratory syncytial virus disease among older adults in Ontario: A Canadian Immunization Research Network (CIRN) study

Affan Shoukat ^a, Carolyn E. Bawden ^{a,b}, Gergely Röst ^c, Jason J. LeBlanc ^{d,e,f}, Alison P. Galvani ^g, Joanne M. Langley ^d, Seyed M. Moghadas ^{a,*}

Vaccine 2024 Feb 16:S0264-410X(24)00200-7. doi: 10.1016/j.vaccine.2024.02.041. Online ahead of print.

- **Simulation of older adults ≥ 60 years in Ontario**

- Scenario 1 (S1): LTCH residents
- Scenario 2 (S2): LTCH residents + community-dwelling adults
- Direct healthcare (inpatient and outpatient) and societal costs (loss of productivity)
- Time horizon: two RSV seasons post-vaccination
- Incidences from ElSherif et al without adjustment for assay sensitivity

Canadian cost-effectiveness: maximum price per dose

Shoukat A et al. Vaccine 2024 Feb 16:S0264-410X(24)00200-7.
doi: 10.1016/j.vaccine.2024.02.041. Online ahead of print.

	Maximum price per dose [\$ CAD] corresponding with willingness to pay (WTP) threshold					
Age and WTP per QALY:	≥ 60 years WTP¹ \$50K per QALY	≥ 60 years WTP ¹ \$70K per QALY	≥ 65 years WTP ¹ \$50K per QALY	≥ 65 years WTP ¹ \$70K per QALY	≥ 75 years WTP ¹ \$50K per QALY	≥ 75 years WTP ¹ \$70K per QALY
Scenario 1: LTCH only						
Healthcare	\$137-177	\$172-221				
Societal²	\$137-177	\$172-221				
Scenario 2: LTCH + community-dwelling						
Healthcare	\$68-87	\$88-111	\$82-104	\$105-132	\$140-174	\$174-216
Societal	\$114-143	\$134-168	\$126-157	\$148-185	\$184-227	\$218-269

¹ Willingness to pay (WTP) ranges displayed here combine varying assumption of sigmoidal versus linear pattern of waning vaccine efficacy (VE) over the two-year time horizon, respectively (always higher WTP with linear assumption), and the span of Arexvy (always slightly higher WTP with sigmoidal assumption) versus Abrysvo (always slightly higher WTP with linear assumption). Accordingly, the first WTP specified reflects Abrysvo value with sigmoidal assumption and the second WTP specified reflects Abrysvo value with linear assumption. Arexvy estimates are similar and fall within the same range. See publication for specific values by underlying assumption of VE waning and product.

² Market/non-market productivity for LTCH residents was considered negligible. Therefore there is no change in PPD for healthcare-only vs societal costs.

Summary

- **Should provinces publicly fund a program of RSV vaccination for older adults?**

Summary

- **Should provinces publicly fund a program of RSV vaccination for older adults?**
- **There is a vaccine preventable burden of severe RSV-related ARI in older adults**
 - *From an individual perspective*
 - **Older individuals may wish to avail themselves of protective vaccine**
 - Benefits more clearly outweigh potential risks among those of advanced age or with comorbidity
 - *From a population/public health perspective requiring prioritized allocation of resources*
 - **RSV burden in older adults appears to be less than influenza or currently COVID-19**
 - **NNV to prevent hospitalization appears to be comparable to influenza in older adults**
 - Taking into account variation in incidence and VE
 - **Cost-effectiveness contingent upon price per dose, which is 5-10x higher for RSV than for influenza**
 - At currently anticipated costing, cost-effectiveness is not clearly established
 - Cost-effectiveness may be improved:
 - Among those of advanced age or with comorbidity
 - If protection persists longer than two years
 - With competitive (lower) pricing following authorization of additional products
- **In the context of great uncertainty and a changing landscape**
 - A graduated approach is most prudent pending better understanding of cost effectiveness (and safety signals)

Authorized vaccine use, United States and Canada

- **US, CDC recommendation for 2023-24**
 - Adults ≥ 60 years may receive a single dose of RSV vaccine using shared clinical decision-making
 - Co-administration with other vaccines considered acceptable
 - Estimated vaccine coverage: 14-22% depending upon data source
 - Considering shift away from shared decision-making approach for next season
- **In Canada, NACI recommendation still awaited**
- **Only Ontario introduced a program for adults ≥ 60 years in 2023-24**
 - Initially for ≥ 60 -year-olds:
 - Living in long-term care homes, elder care lodges, retirement homes licensed to provide dementia care
 - In December 2023, expanded to ≥ 60 -year-olds who are:
 - Hospital assisted living care patients
 - Receiving dialysis
 - Transplant recipients
 - Experiencing homelessness
 - Indigenous, including those in urban dwellings
 - No co-administration; 14-day waiting period between RSV vaccine and other vaccines
 - No pharmacist administration

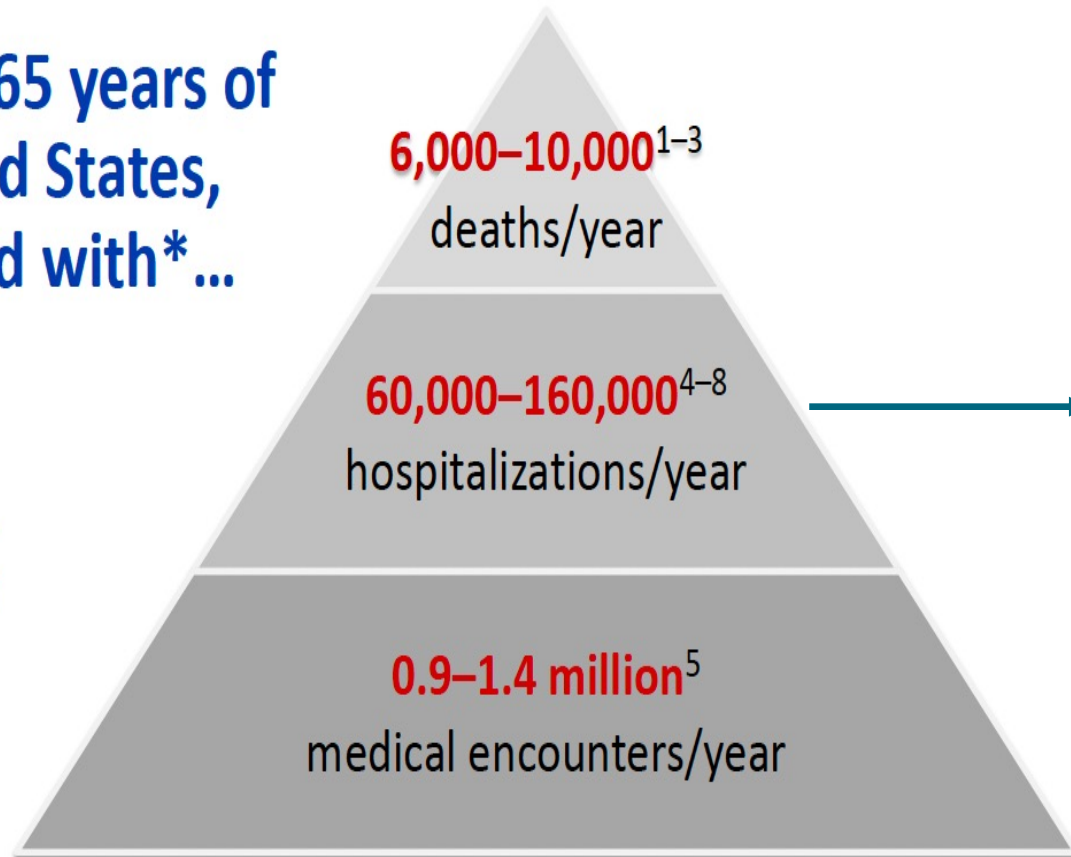
Canadian estimates of RSV burden in older adults are limited

From Melgar, RSV Vaccines – Adult. Etr (incl GRADE) for 2 vaccines (GSK & Pfizer) (slide 8). February 23, 2023.

Available: <https://www.cdc.gov/vaccines/acip/meetings/slides-2023-02-22-24.html>

Among adults ≥ 65 years of age in the United States, RSV is associated with* ...

*There is substantial uncertainty in burden of disease, reflected in wide ranges here.



Canada $\sim 11.5\%$ of US population:
 $\sim 7000 - 18,000$ RSV hospitalizations per year among adults ≥ 65 years

BC $\sim 1.5\%$ of US population:
 $\sim 1000 - 2400$ RSV hospitalizations per year among adults ≥ 65 years

1. Thompson et al, JAMA (2003): <https://doi.org/10.1001/jama.289.2.179>
2. Matias et al, Influenza Other Respi Viruses (2014): <https://doi.org/10.1111/irv.12258>
3. Hansen et al, JAMA Network Open (2022): <https://doi.org/10.1001/jamanetworkopen.2022.0527>
4. Widmer et al, JAMA Network Open (2012): <https://doi.org/10.1093/infdis/jis309>

5. McLaughlin et al, Open Forum Infect Dis (2022): <https://doi.org/10.1093/ofid/ofac300>
6. Zheng et al, Pneumonia (2022): <https://doi.org/10.1186/s41479-022-00098-x>
7. Branche et al, Clinical Infect Dis (2022): <https://doi.org/10.1093/cid/ciab595>
8. CDC RSV-NET data 2016–2020 (unpublished)