Vaccine Update for Older Adults: What Do I Need to Know

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2023 Toronto Geriatrics Update Course
Friday November 10th
11:00 – 11:50 AM EST

Sinai Health | Healthy Ageing and Geriatrics

UHN Toronto General Toronto Western Princess Margaret Toronto Rehab Michener Institute

Conflict of Interest Disclosure

- **Relationships with commercial interests:**
- **Speakers Bureau/Honoraria: Amgen, Allergan, BioSyent, Eisai, GSK, Merck, Moderna, NovoNordisk, Novartis, Pfizer, Sunoviun, Searchlight, Sequeris**
- **Consulting Fees: Merck, MDBriefcase, The Rounds, STA communications, Meducom, PeerVoice, MedCan**

- **Other:**
- **Board Member Immunize Canada,**
- **Women's Brain Health Initiative**
- **Past-President, Federation of Medical Women of Canada**
- **Chair, HPV Prevention Week 2017-2023**

Objectives

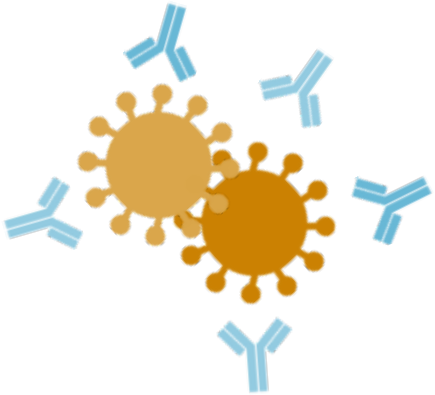
1. Review up to date epidemiology of COVID-19, RSV, Influenza & Pneumococcal disease, also Shingles. in older Canadian adults
2. Review the risk factors for the common respiratory pathogens, and understand the effect of age on immune response
3. Discuss the new NACI recommendations for COVID-19 and pneumococcal conjugate vaccines.
4. Identify populations at risk and treatment criteria for antiviral treatment in those with COVID-19 infection

Why are Older Adults at Greater Risk?

Immunosenescence is a heightened susceptibility to influenza-related complications in older adults due to the natural and progressive weakening of the immune system over time.[1,2]

The lower immune response can result in:

- Higher incidence and severity of infectious diseases[1,2]
- Lower strength and persistence of antibody responses to vaccines[1,2]

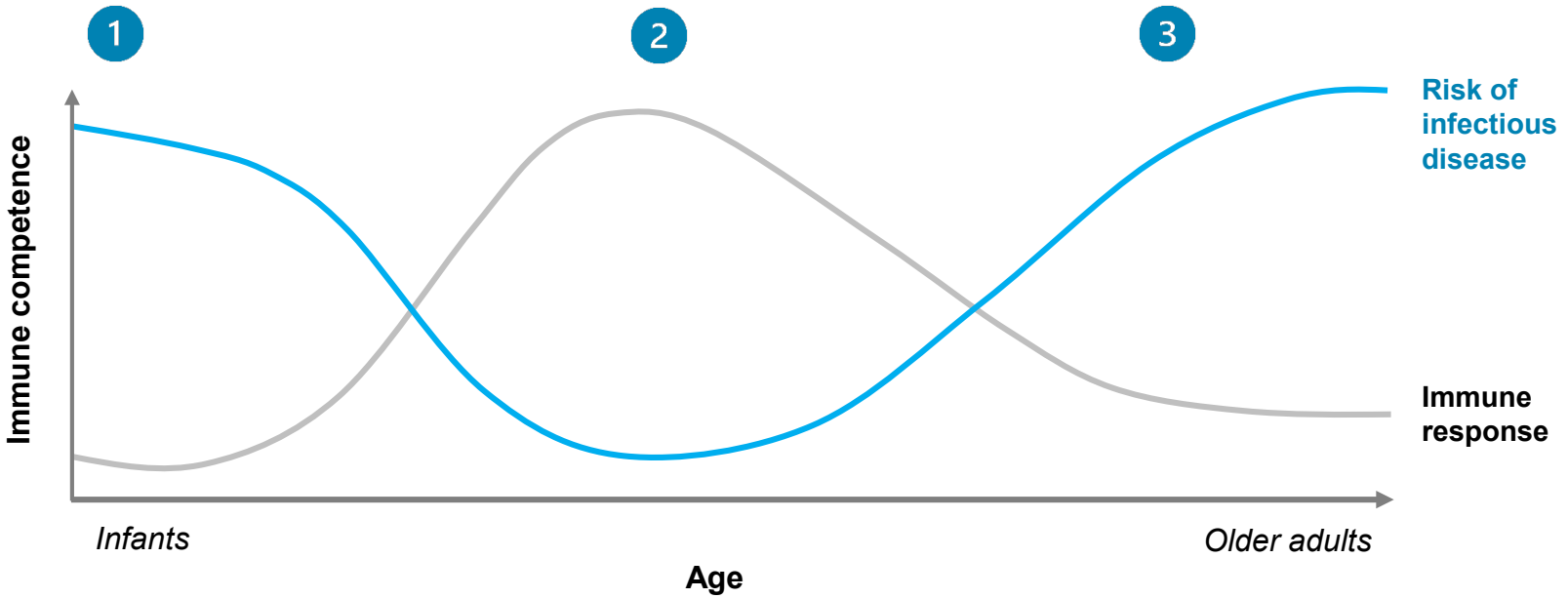


In older adults, influenza vaccine effectiveness is roughly half of that in healthy adults.[3]

References:
1. McElhaney JE, et al. (2016). Frontiers in Immunology, 7(41), 1-11.
2. Doherty M, et al. (2016). Vaccine, 3, 6681-6690.
3. National Advisory Committee on Immunization (NACI). Statement on Seasonal Influenza Vaccine for 2016–2017. Accessed on April 5, 2017.

The immune system changes over an individual's life

Age-related decline in immunity (immunosenescence) → changes in **composition** and **function** of immune cells[3]

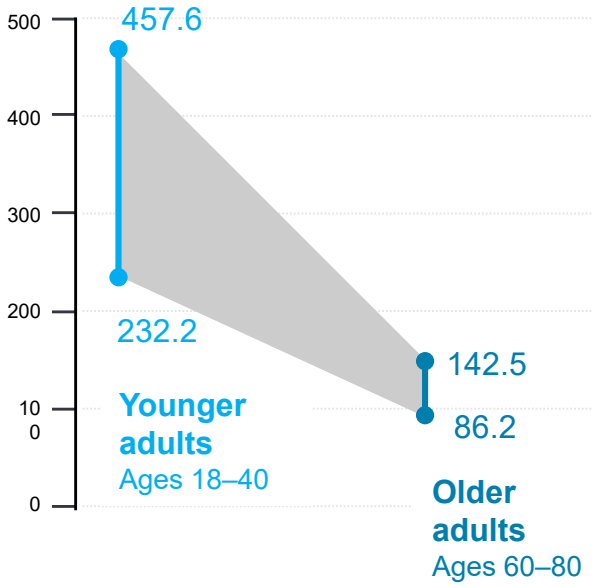


1. Simon AK, et al. Proc Biol Sci. 2015;282:20143085. 2. Del Giudice G, et al. NPJ Aging Mech Dis. 2017;4:1. 3. Crooke SN, et al. Exp Gerontol. 2019;124:110632.

Age-related decline in immunity presents a challenge in RSV vaccine development

Baseline RSV-specific cellular immune response[1]

RSVPreF3 CD4+ T cells (GMF range)



T-cell response declines with age, making it challenging for older adults to:[2,3]

- mount immunity to RSV infection
- achieve high levels of protection following vaccination

GMF, geometric mean frequency.

1. Leroux-Roels I, et al. J Infect Dis. 2023;227(6):761-772. 2. Stephens LM and Varga SM. Vaccines (Basel) 2021;9(6):624. 3. Cherukuri A et al. Clin Vaccine Immunol 2013;20:239–247.

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Reduced responsiveness to vaccination in older adults requires novel strategies

Vaccine formulations with **higher antigen content**, such as high-dose influenza vaccines[1]

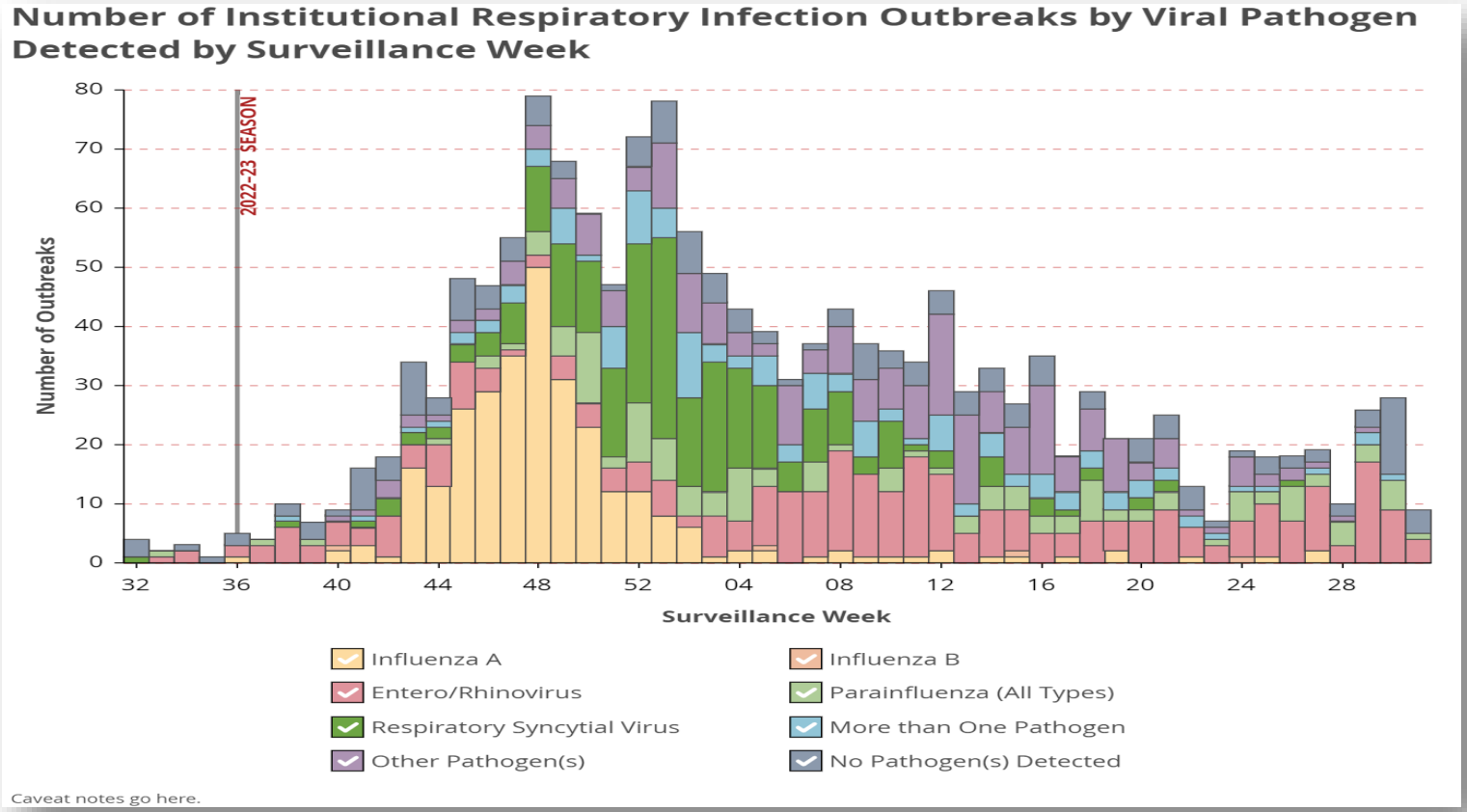
Vaccine formulations with **adjuvants**, such as MF59 or AS01[2,3]

Alternative **administration routes**, such as intradermal[4]

AS01, Adjuvant System 01; MF59, microfluidised emulsion 59.

1. Robertson CA et al. Expert Rev Vaccines. 2016;15:1495–1505. 2. Coleman BL et al. Influenza Other Respir Viruses. 2021;15:813–823. 3. Chlibek R et al. J Infect Dis 2013;208:1953–1961. 4. Arakane R et al. Vaccine 2015;33:6650–6658;

Respiratory Outbreaks in Institutional Settings Public Health Ontario (2022-23)



Ontario Agency for Health Protection and Promotion (Public Health Ontario).Technical notes: Ontario respiratory pathogen bulletin data caveats and glossary. Toronto, ON: King's Printer for Ontario; 2022.

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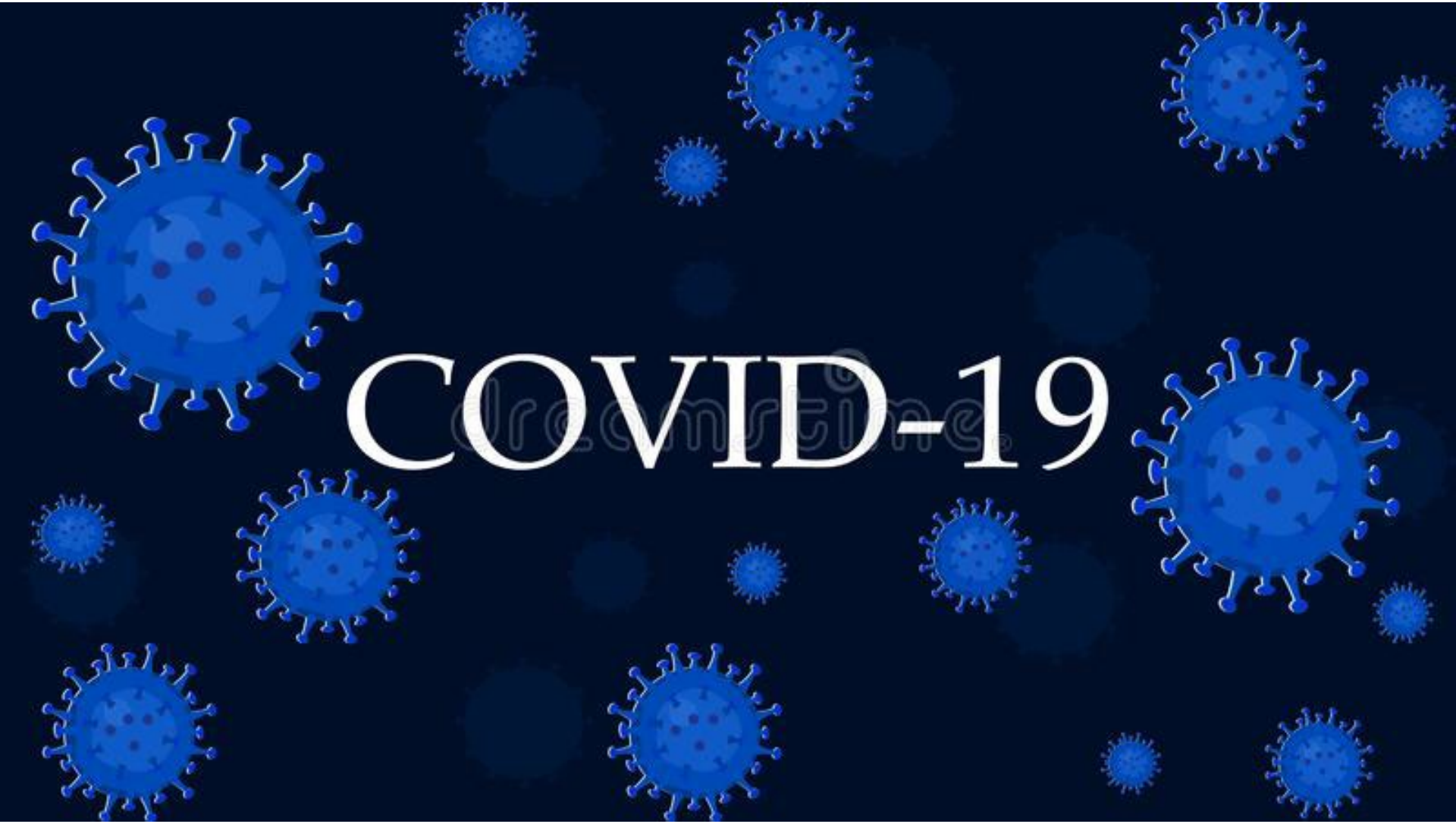
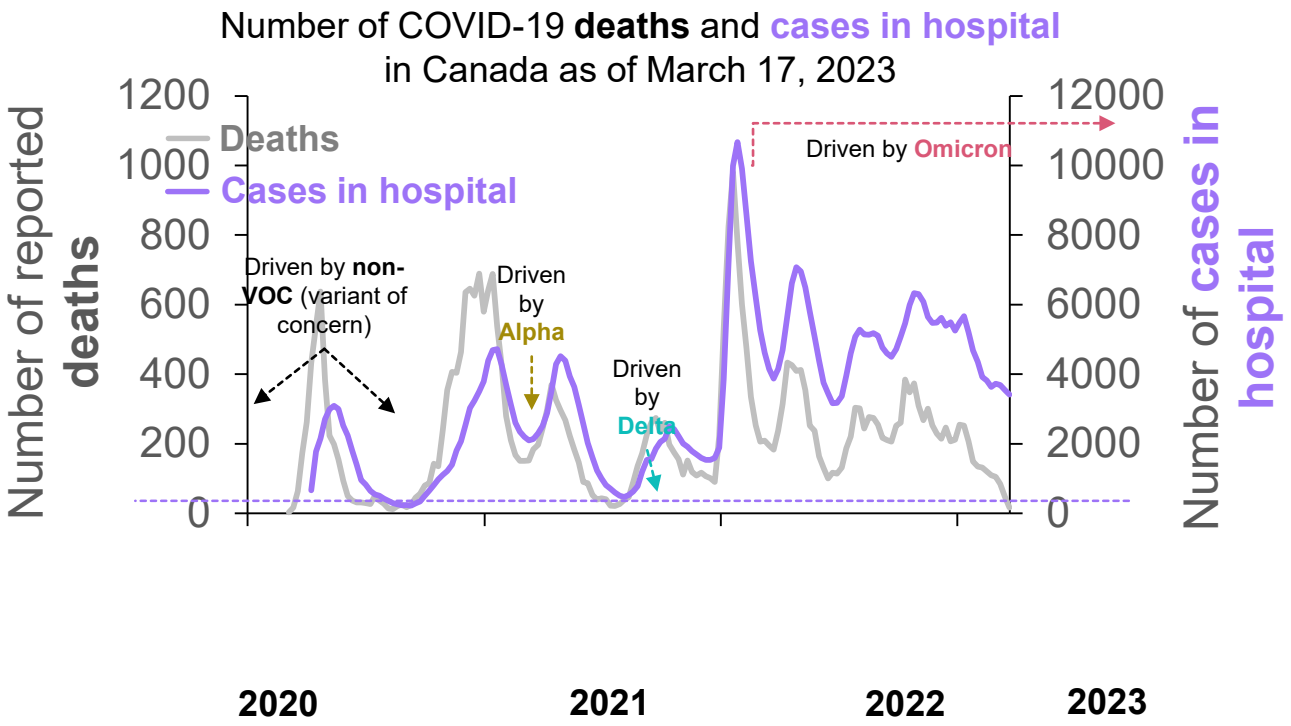

COVID-19

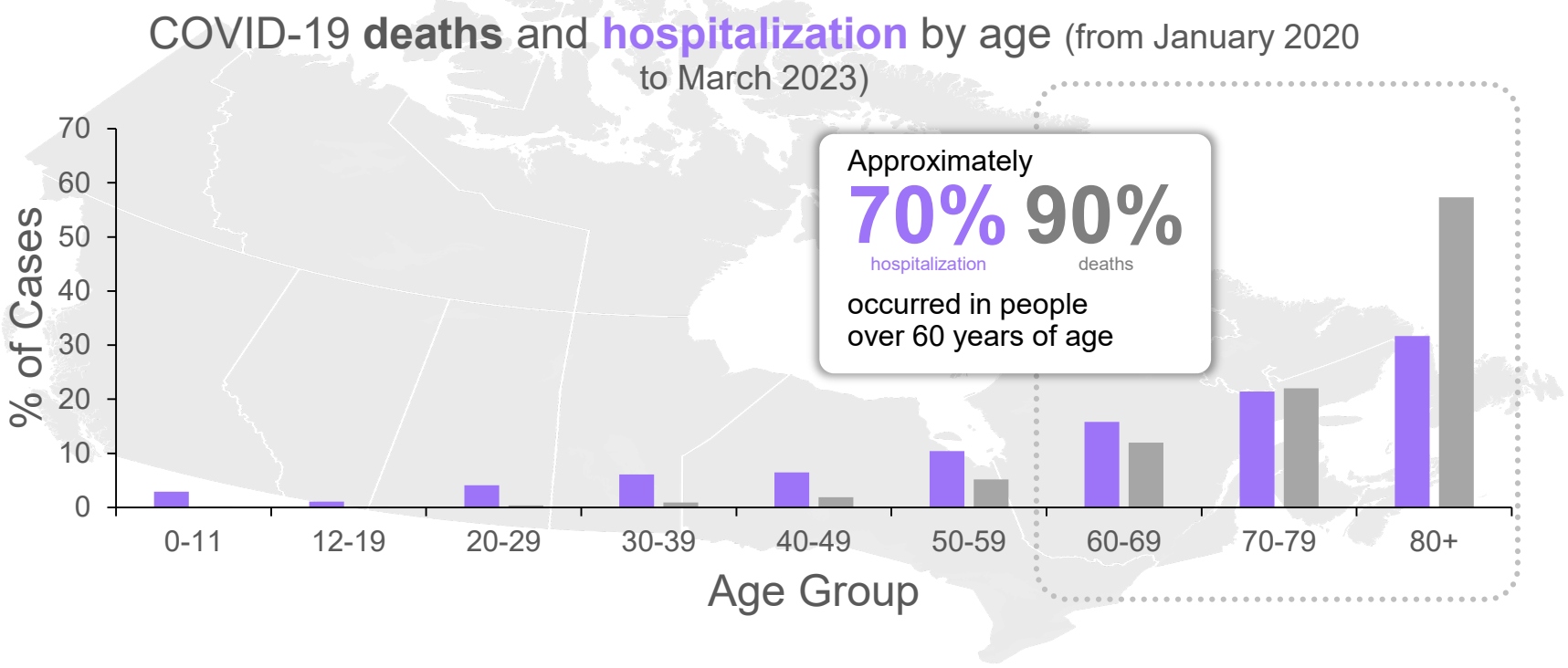
COVID-19 in Canada
Epidemiology Overview

As of September 8, 2023, 11:44 am ET



https://health-infobase.canada.ca/covid-19/

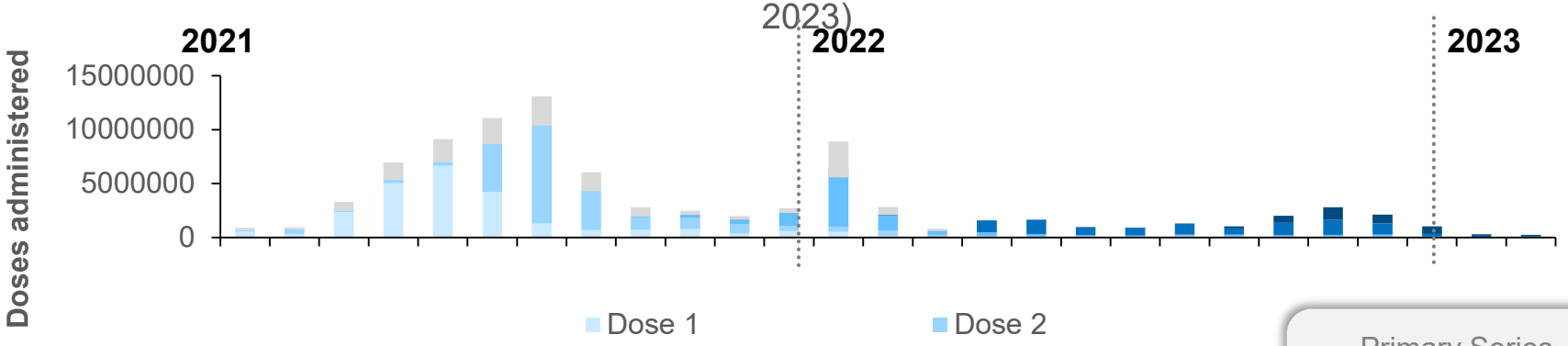
COVID-19 in Canada
Epidemiology Overview



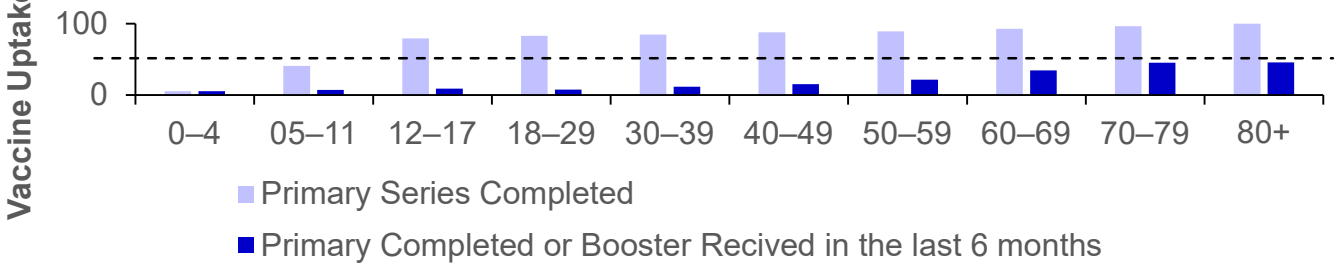
https://health-infobase.canada.ca/covid-19/

COVID-19 in Canada
Vaccination Status

Number of COVID-19 Vaccine Doses Administered in Canada (as of March 26, 2023)



COVID-19 Vaccine Uptake by Age Group (As of March 26, 2023)



Primary Series Completed

80.7%

(Excluding QC)

Primary Completed or Booster Dose Received

22.4%

(in last 6 months)

https://health-infobase.canada.ca/covid-19/

Risk Factors For Severe COVID-19

COVID-19

Biological

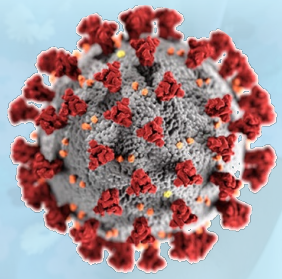
- Old age
- Obesity
- Pregnancy and recent pregnancy
- Disabilities (e.g. Down syndrome, learning, intellectual, or developmental disabilities; ADHD; cerebral palsy; congenital disabilities; spinal cord injuries)

Behavioral

- Smoking, current or former

Medical

- Cancer
- Cerebrovascular disease
- Chronic kidney disease
- Certain Chronic liver diseases
- Certain Chronic lung diseases
- Cystic fibrosis
- Diabetes mellitus, type 1 and type 2
- Heart conditions
- HIV infection
- Certain Mental health disorders
- Primary immunodeficiency diseases
- Solid organ or blood stem cell transplant
- Tuberculosis



https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/signs-symptoms-severity.html#a3;

NACI Guidance on COVID-19 Vaccine Booster Doses[1,2]

<table>
<tr><th>Population by age</th><th>Primary Series</th><th>Booster Before 2022 Fall</th><th>2022 Fall Booster</th><th>2023 Spring Additional Booster[2]</th></tr>
<tr><td>Adults ≥ 80 years</td><td rowspan="3">Should be offered</td><td rowspan="3">Should be offered</td><td rowspan="3">Should be offered</td><td rowspan="2">May be offered</td></tr>
<tr><td>Long Term Care, Congregate living for senior, complex medical need</td></tr>
<tr><td>Adults 65-79 years</td><td>May be offered
Particularly if not previously infected</td></tr>
<tr><td rowspan="2">Adults 18-64 years</td><td rowspan="2">Should be offered</td><td rowspan="2">Should be offered</td><td>Should be offered
(High-risk Population)</td><td>May be offered
(High-risk Population)</td></tr>
<tr><td>May be offered
(General Population)</td><td>-</td></tr>
<tr><td rowspan="2">Adolescents 12-17 years</td><td rowspan="2">Should be offered</td><td>Should be offered</td><td>Should be offered
(High-risk Population)</td><td>-</td></tr>
<tr><td>-</td><td>May be offered
(General Population)</td><td>-</td></tr>
<tr><td rowspan="2">Children 5-11 years</td><td rowspan="2">Should be offered</td><td>-</td><td>Should be offered
(High-risk Population)</td><td>-</td></tr>
<tr><td>-</td><td>May be offered
(General Population)</td><td>-</td></tr>
<tr><td>Children 6 months to < 5 years</td><td>May be offered</td><td colspan="3">No authorized product; not recommended</td></tr>
</table>

NACI Guidance on COVID-19 Vaccine Booster Doses
Additional Booster Dose in The Spring of 2023 For High-Risk Individuals

Starting in the spring of 2023, NACI recommends that **an additional booster dose** may be offered as per the recommended interval to the following individuals who are at increased risk of severe illness from COVID-19:

- Adults 80 years of age and older
- Adult residents of long-term care homes and other congregate living settings for seniors or those with complex medical care needs
- Adults 18 years of age and older who are moderately to severely immunocompromised (due to an underlying condition or treatment)
- Adults 65 to 79 years of age, particularly if they do not have a known prior history of SARS-CoV-2 infection

- **Bivalent Omicron-containing mRNA COVID-19 vaccines** are **the preferred booster** products for all individuals 5 years of age and older.
- When COVID-19 booster doses are offered, they should be provided using **the recommended interval of 6 or more months** since the previous COVID-19 vaccine dose or SARS-CoV-2 infection (whichever is later)

Individuals who have not received previously recommended doses, including a primary series or **fall 2022 booster dose**, are recommended to receive them now.

For more information, please refer to *Guidance on COVID-19 vaccine booster doses: Initial considerations for 2023*.

https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/national-advisory-committee-immunization-guidance-additional-covid-19-booster-dose-spring-2023-individuals-high-risk-severe-illness-due-covid-19/statement.pdf

NACI Guidance on COVID-19 Vaccine in the Fall of 2023

Individuals have not been immunized

- Individuals **5 years of age and older** **should be** immunized with a primary series of an mRNA vaccine.
- Children **6 months to under 5 years of age** **may be** immunized with a primary series of an mRNA vaccine.

Particularly important for

- **Adults 65 years of age or older**
- **Residents of long-term care homes and other congregate living settings**
- Individuals with underlying medical conditions that place them at higher risk of severe COVID-19

Individuals have previously been immunized

Should be immunized with **a dose of the new formulation of COVID-19 vaccine** in the authorized age group if it has been at least 6 months from the previous COVID-19 vaccine dose or known SARS-CoV-2 infection

- Individuals who are pregnant
- Individuals in or from First Nations, Métis and Inuit communities*
- Members of racialized and other equity-deserving communities
- People who provide essential community services

https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-guidance-use-covid-19-vaccines-fall-2023.html#_Recommendations

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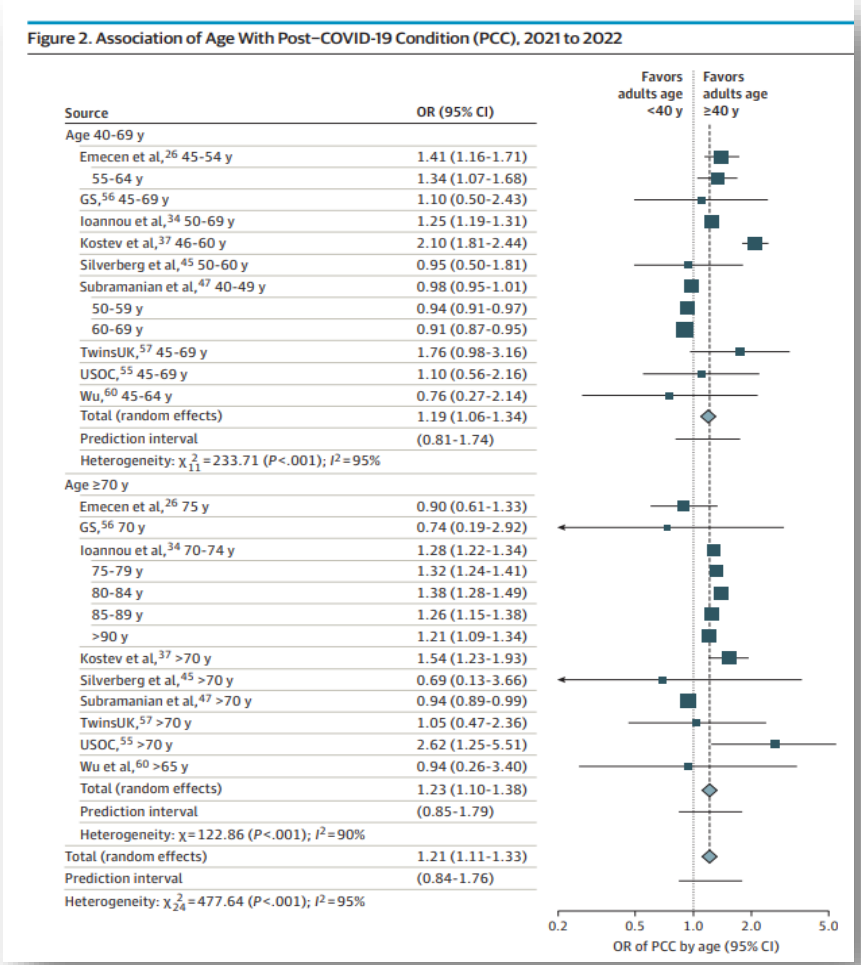
Older Age is Associated With Higher Risk of Long COVID

- In this meta-analysis, 9 studies including a total of 324,950 patients investigated age as a risk factor for PCC
  - Older individuals (40-69 and ≥70 years) had a significantly higher risk of ongoing persistent PCC symptoms compared with adults (18-39 years)

Figure 2. Association of Age With Post–COVID-19 Condition (PCC), 2021 to 2022



The dotted line in Figure 2 represents the point of no difference between the 2 groups, and the dashed line represents the average effect of all studies when pooled together.
PCC, post−COVID-19 condition; OR; odds ratio.
Tsampasian V. *JAMA Intern Med.* 2023.

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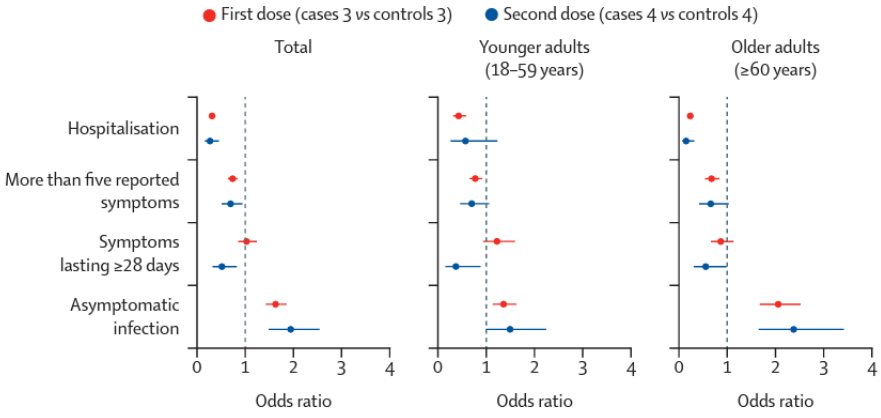
Vaccination in Older Individuals (≥60 years of age) Reduced the Risk of COVID-19 Symptoms Long-term

- In a prospective case-controlled study, vaccination was associated with **reduced odds** of
  - Hospitalisation or having more than five symptoms in the first week of illness following the first or second dose
  - Long-duration (≥28 days) symptoms following the second dose
- Infected individuals who were previously vaccinated reported most symptoms with less frequency compared with non-vaccinated, infected individuals
- Vaccinated participants were more likely to be completely asymptomatic, especially if they were ≥60 years of age

Currently COVID-19 vaccines licensed in Canada are not indicated for the prevention of long COVID.

Disease severity and duration in SARS-CoV-2-infected vaccinated vs unvaccinated participants



- Individuals who reported a SARS-CoV-2-positive RT-PCR test, had used the app for at least 14 consecutive days after testing positive and had received first vaccine dose (**Cases 3**) or not (unvaccinated; **Controls 3**);
- Individuals who reported a SARS-CoV-2-positive RT-PCR test, had used the app for at least 14 consecutive days after testing positive and had received a second vaccine dose (**Cases 4**) or not (unvaccinated; **Controls 4**);

Antonelli M et al. *Lancet Infect Dis* 2022; 22: 43–55.

Treatments for COVID-19 Authorized for use in Canada[1-13]

As of November 17, 2022, there were seven drugs authorized for the treatment of COVID-19 in Canada,[1] though there are currently others under review in Canada and around the world.[2,3]

Antiviral agents[4–6]

Drug	Company	Type
Nirmatrelvir-ritonavir tablets (Paxlovid™)[7]	Pfizer	Protease inhibitor
Remdesivir (Veklury®)[8]	Gilead	Adenosine nucleotide prodrug

Monoclonal antibodies

Drug	Company	Type
Sotrovimab[9]	GlaxoSmith Kline	Recombinant human IgG1 antibody
Casirivimab and imdevimab[10] †	Hoffman LaRoche	Recombinant human IgG1 antibodies
Bamlanivimab[11] †	Eli Lily	Recombinant human IgG1 antibody
Tixagevimab and cilgavimab (Evusheld™)[12]	AstraZeneca	Anti-SARS-CoV-2 spike protein monoclonal antibodies
Tocilizumab (Actemra™)[1]	Hoffmann LaRoche	Recombinant human IgG1 antibody

For current list of authorized medications, please click the following: Government of Canada: Drug and Vaccine Authorizations for COVID-19

† On January 24, 2022, the FDA announced revision of the authorizations for two monoclonal antibody treatments – bamlanivimab and etesevimab (administered together) and REGEN-COV (casirivimab and imdevimab) – to limit their use to only when the patient is likely to have been infected with or exposed to a variant that is susceptible to these treatments. Because data show these treatments are highly unlikely to be active against the omicron variant, which is circulating at a very high frequency throughout the United States, these treatments are not authorized for use in any U.S. states, territories, and jurisdictions at this time.[13]

Reference: 1. Government of Canada. Drug and vaccine authorizations for COVID-19: List of authorized drugs, vaccines and expanded indications. Accessed November 28, 2022, at: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/authorization/list-drugs.html#wb-auto-4. **2.** Government of Canada. Drug and health product submissions under review. Accessed November 28, 2022, at: https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/submissions-under-review/new-drug-submissions-under-review.html. **3.** U.S. Food and Drug Administration. Accessed November 28, 2022, at: https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap. **4.** Hu S, Jiang S, Qi X, *et al.* Races of small molecule clinical trials for the treatment of COVID-19: An up-to-date comprehensive review. *Drug Dev Res* 2021 Nov 11;10.1002/ddr.21895. **5.** Bernal AJ, Gomez da Silva MM, Musungaie DB, *et al.* Molnupiravir for oral treatment of Covid-19 in nonhospitalized patients. *N Engl J Med* 2021;Dec 16;NEJMoa2116044. **6.** Owen DR, Allerton CMN, Anderson AS, *et al.* An oral SARS-CoV-2 Mpro inhibitor clinical candidate for the treatment of COVID-19. *Science* 2021;374(6575):1586–1593. **7.** Paxlovid Product Monograph. Pfizer Canada ULC, June 13, 2022. **8.** Veklury Product Monograph. Gilead sciences Canada Inc., November 22, 2021. **9.** Sotrovimab Product Monograph. GlaxoSmithKline Inc., September 14, 2021. **10.** Casirivimab and imdevimab Product Monograph. Hoffman LaRoche Ltd., June 9, 2021. **11.** Bamlanivimab Product Monograph. Eli Lilly Canada Inc., April 14, 2021. **12.** Evusheld Product Monograph. AstraZeneca Canada Inc., November 9, 2022. **13.** U.S. Food and Drug Administration. Coronavirus (COVID-19) Update: FDA limits use of certain monoclonal antibodies to treat COVID-19 due to the omicron variant. Accessed November 28, 2022, at: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-limits-use-certain-monoclonal-antibodies-treat-covid-19-due-omicron.

Research

Population-based evaluation of the effectiveness of nirmatrelvir–ritonavir for reducing hospital admissions and mortality from COVID-19

Kevin L. Schwartz MD MSc, Jun Wang MSc, Mina Tadrous PharmD PhD, Bradley J. Langford PharmD, Nick Daneman MD MSc, Valerie Leung BScPhm MBA, Tara Gomes PhD, Lindsay Friedman MPH, Peter Daley MD, Kevin A. Brown PhD

Cite as: *CMAJ* 2023 February 13;195:E220-6. doi: 10.1503/cmaj.221608

April 10

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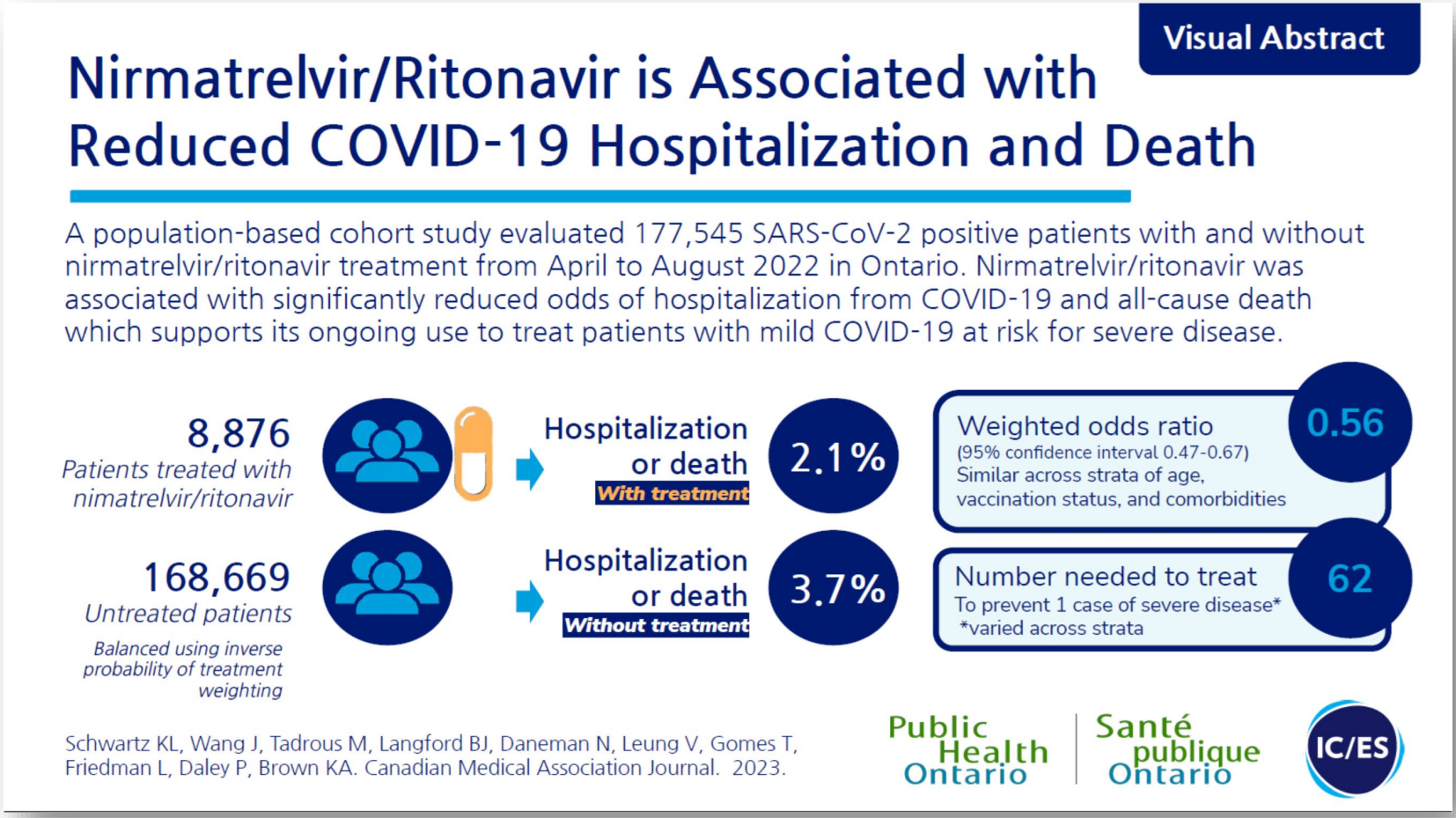
Population-based evaluation of the effectiveness of nirmatrelvir–ritonavir for reducing hospital admissions and mortality from COVID-19 (Ontario)



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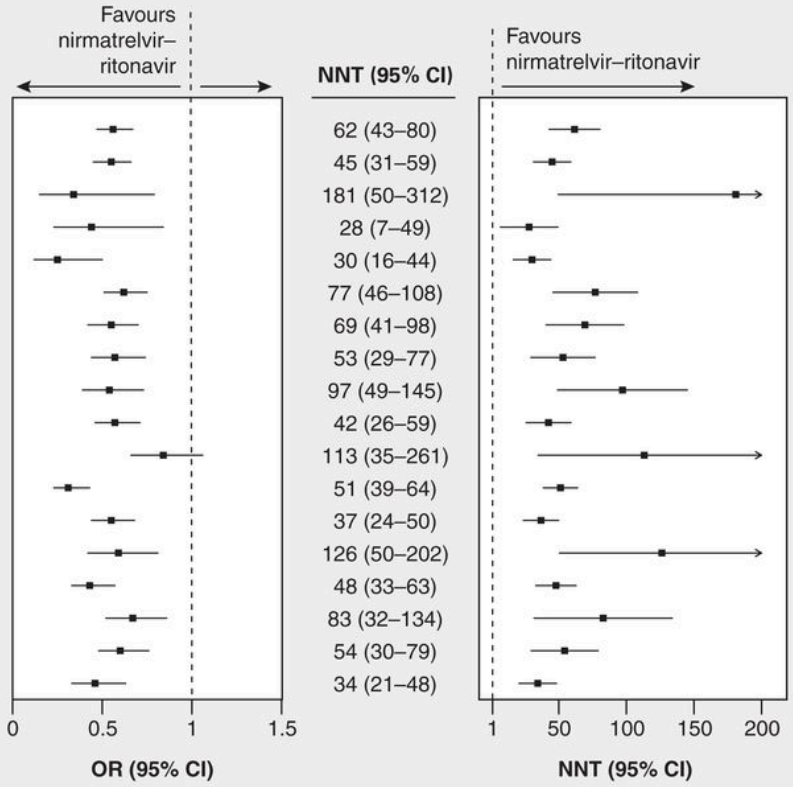
Population-based evaluation of the effectiveness of nirmatrelvir–ritonavir for reducing hospital admissions and mortality from COVID-19 (Ontario)

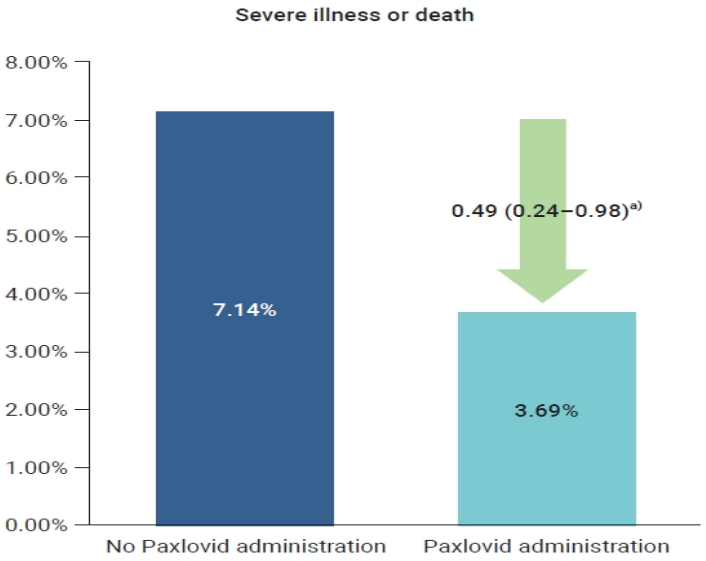
Subgroup	Nirmatrelvir–ritonavir weighted, %	Unexposed weighted, %	OR (95% CI)	NNT (95% CI)
Primary analysis	2.1	3.7	0.56 (0.47–0.67)	62 (43–80)
Age ≥ 70 yr	2.8	5.0	0.55 (0.45–0.66)	45 (31–59)
Age < 70 yr	0.3	0.8	0.34 (0.15–0.79)	181 (50–312)
No vaccine	3.0	6.6	0.44 (0.23–0.84)	28 (7–49)
Vaccine doses: 1–2	1.1	4.4	0.25 (0.12–0.50)	30 (16–44)
Vaccine doses: 3 or more	2.2	3.5	0.62 (0.51–0.75)	77 (46–108)
Last vaccine dose: 14–179 d	1.8	3.2	0.55 (0.42–0.70)	69 (41–98)
Last vaccine dose: 180 or more d	2.6	4.5	0.57 (0.44–0.74)	53 (29–77)
Comorbidities: 3 or more	1.2	2.3	0.54 (0.39–0.73)	97 (49–145)
Comorbidities: < 3	3.3	5.7	0.57 (0.46–0.71)	42 (26–59)
Long-term care resident	4.7	5.6	0.84 (0.66–1.06)	113 (35–261)
Not in long-term care	0.9	2.9	0.31 (0.23–0.43)	51 (39–64)
OST risk group: high	3.5	6.2	0.55 (0.44–0.68)	37 (24–50)
OST risk group: standard	1.1	1.9	0.59 (0.42–0.81)	126 (50–202)
April to June 2022	1.6	3.7	0.43 (0.33–0.57)	48 (33–63)
July to August 2022	2.6	3.8	0.67 (0.52–0.86)	83 (32–134)
DDI level 2	2.9	4.8	0.60 (0.48–0.76)	54 (30–79)
No DDI	2.6	5.5	0.46 (0.33–0.63)	34 (21–48)



Kevin L. Schwartz et al. CMAJ 2023;195:E220-E226

CMAJ·JAMC

Effectiveness of Paxlovid in LTC/Nursing Home Settings



- Long-term care facilities in South Korea (Feb-April 2022).
- The rate of severe illness or death in the group given Paxlovid was 51% lower than that of the non-Paxlovid group.
- Compared to unvaccinated patients, patients who had completed 3 doses of the vaccine had a 71% reduced rate of severe illness or death and a 65% reduced death rate.

Park H, et al. The effectiveness of Paxlovid treatment in long-term care facilities in South Korea during the outbreak of the Omicron variant of SARS-CoV-2. Osong Public Health Res Perspect. 2022;13(6):443-447.

Table 3. Results of Weighted Cox Proportional Hazard Regression After Propensity Score Weighting for Patients With COVID-19 Who Received Care From Community Geriatric Assessment Team

	Hospitalization		Death, ICU admission, or use of IMV	
COVID-19 oral antiviral use	Weighted HR (95% CI)	*P* value	Weighted HR (95% CI)	*P* value
Main analysis, time-dependent analysis[a]				
No oral antiviral use as reference				
No oral antiviral use	1 [Reference]	NA	1 [Reference]	NA
Use of molnupiravir	0.46 (0.37-0.57)	<.001	0.35 (0.23-0.51)	<.001
Use of nirmatrelvir/ritonavir	0.46 (0.32-0.65)	<.001	0.17 (0.06-0.44)	<.001
Use of molnupiravir as reference				
No oral antiviral use	2.18 (1.74-2.73)	<.001	2.90 (1.95-4.31)	<.001
Use of molnupiravir	1 [Reference]	NA	1 [Reference]	NA
Use of nirmatrelvir/ritonavir	1.00 (0.75-1.33)	.99	0.49 (0.20-1.20)	.12
Sensitivity analysis, 5-d landmark analysis[b]				
No oral antiviral use as reference				
No oral antiviral use	1 [Reference]	NA	1 [Reference]	NA
Use of molnupiravir	0.31 (0.21-0.46)	<.001	0.28 (0.13-0.62)	.002
Use of nirmatrelvir/ritonavir	0.27 (0.16-0.46)	<.001	0.14 (0.03-0.71)	.02
Use of molnupiravir as reference				
No oral antiviral use	3.24 (2.19-4.81)	<.001	3.56 (1.61-7.90)	.002
Use of molnupiravir	1 [Reference]	NA	1 [Reference]	NA
Use of nirmatrelvir/ritonavir	0.88 (0.58-1.34)	.55	0.52 (0.12-2.14)	.37

- Nursing homes in Hong Kong (Feb-April 2022).
- Compared with patients who did not use oral antivirals, nirmatrelvir/ritonavir users had a 69% lower risk of hospitalization

Ma BH, et al. Clinical Outcomes Following Treatment for COVID-19 With Nirmatrelvir/Ritonavir and Molnupiravir Among Patients Living in Nursing Homes. JAMA Netw Open. 2023;6(4):e2310887. doi:10.1001/jamanetworkopen.2023.10887

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Ministry of Health

COVID-19 Guidance for Public Health Units: Long-Term Care Homes, Retirement Homes, and Other Congregate Living Settings

Version 11 – June 26, 2023

- Health care providers should discuss potential treatment options (i.e., Paxlovid, Remdesivir) with residents and caregivers **in advance** of potential COVID-19 infection.

- This should include obtaining a **clinical assessment, up-to-date renal function tests and other relevant workup, medication reconciliation**, and goals of care. A physician or nurse practitioner must determine if treatment is right for a resident based on multiple factors such as clinical judgement, goals of care, the potential for drug-drug interactions or other medication contraindications, as well as other general considerations.

- Plans should also include steps for accessing treatment so it can be made available as quickly as possible.

Ministry of Health COVID-19 Guidance for Public Health Units: Long-Term Care Homes, Retirement Homes, and Other Congregate Living Settings Version 11 – June 26, 2023

- LTC homes are encouraged to pre-emptively:
  - Determine if a resident meets **eligibility, including reviewing medications for potential drug-drug interactions, and ordering a serum creatinine while the** residents are well.
  - Connect with their contracted pharmacy about including Paxlovid in their emergency box, especially if a home is in a remote area. (If a patient is not eligible for Paxlovid, there exist other therapeutic treatment options (i.e., Remdesivir). Residents and their caregivers are encouraged to proactively speak with their primary healthcare provider.
  - Health care providers and LTCHs should work with their Nurse-Led Outreach Teams or OH regional contact to access Remdesivir through local pathways.
- RHs and other CLSs are encouraged to provide information on COVID-19 therapeutics and encourage residents and clients to speak with their primary care provider to come up with a treatment plan in case they get sick, as appropriate.

Drugs that are contraindicated for concomitant use with Nirmatrelvir/Ritonavir

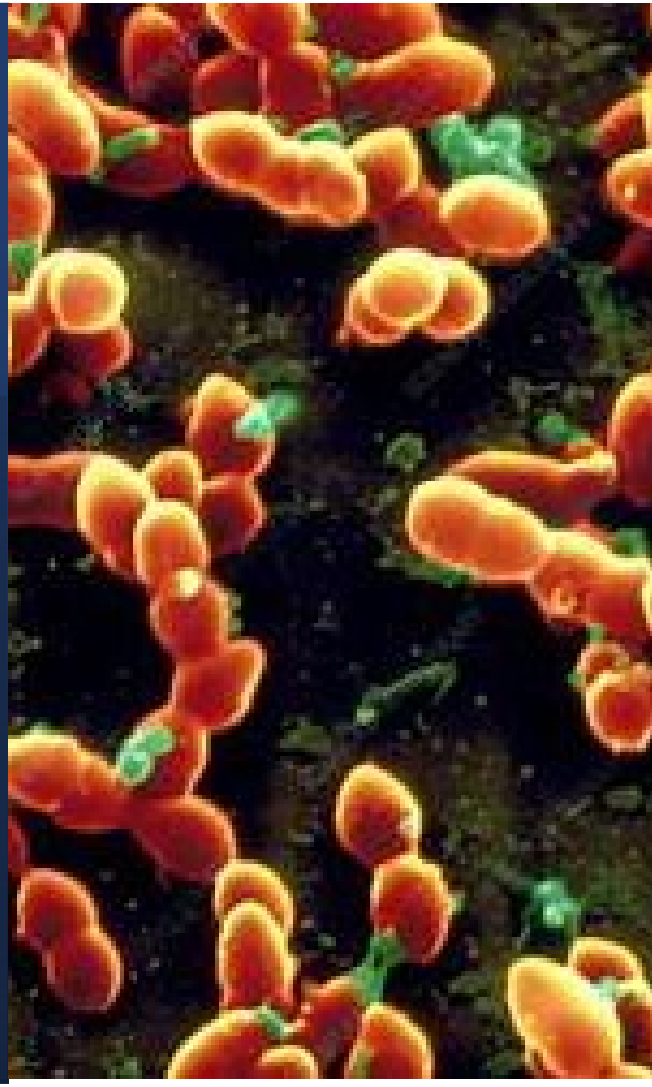
Drug class	Drugs within class that are contraindicated
Alpha1-adrenoreceptor antagonist	alfuzosin
Antianginal	ranolazine
Antiarrhythmics	amiodarone, bepridil[a], dronedarone, flecainide, propafenone, quinidine
Antibiotics	fusidic acid
Anticancer	Apalutamide, neratinib, venetoclax
Anticoagulants	rivaroxaban
Anticonvulsants	carbamazepine, phenobarbital, phenytoin
Antifungal	voriconazole
Antigout	colchicine (in renal or hepatic impairment)
Antihistamines	astemizole[a], terfenadine[a]
Antimycobacterial	rifampin
Antipsychotics	lurasidone, pimozide
Ergot derivatives	dihydroergotamine, ergonovine, ergotamine[a], methylergonovine[a]
GI motility agent	cisapride[a]
Herbal product	St. John's wort
Lipid-modifying agents • HMG-CoA reductase inhibitors • Microsomal triglyceride transfer protein inhibitor	 lovastatin, simvastatin lomitapide
Long-acting beta-adrenoceptor	salmeterol
PDE5 inhibitors	sildenafil[b], only when used for the treatment of PAH vardenafil, when used for the treatment of erectile dysfunction or PAH
Sedatives/Hypnotics	Oral midazolam[c], triazolam

a. Product no longer marketed in Canada; b. See Product Monograph for co-administration of sildenafil in patients with erectile dysfunction; c. See Product Monograph for parenterally administered midazolam. Oral formulation of midazolam is not marketed in Canada; d. See Product Monograph for coadministration of the maintenance dose of venetoclax.

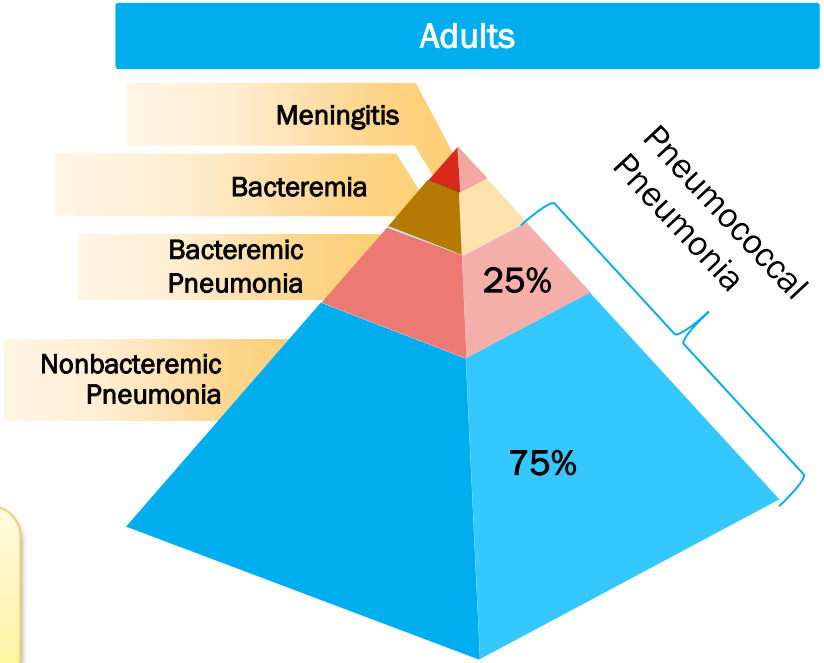
PAH = pulmonary arterial hypertension

Reference: 1. Paxlovid Product Monograph. Pfizer Canada ULC, December 8, 2022.

Invasive Pneumococcal Disease



S. pneumoniae is a major cause of human infection, mainly involving the respiratory tract



Among the > 100 recognized serotypes of *S. pneumoniae,* invasive disease caused by 24 serotypes can be prevented by vaccination*.

S. pneumoniae is commonly called pneumococcus; *24 would only be in patients receiving both doses of vaccine, including Pneu-P-23 and Pneu-C-13.
S, streptococcus

1. https://www.cdc.gov/pneumococcal/laboratorians.html;
2. Huang SS, et al. *Vaccine*. 2011;29:3398-3412. 3. Said MA, et al. *PLoS One*. 2013;8:e60273.

There are many risk factors for pneumococcal disease in adults

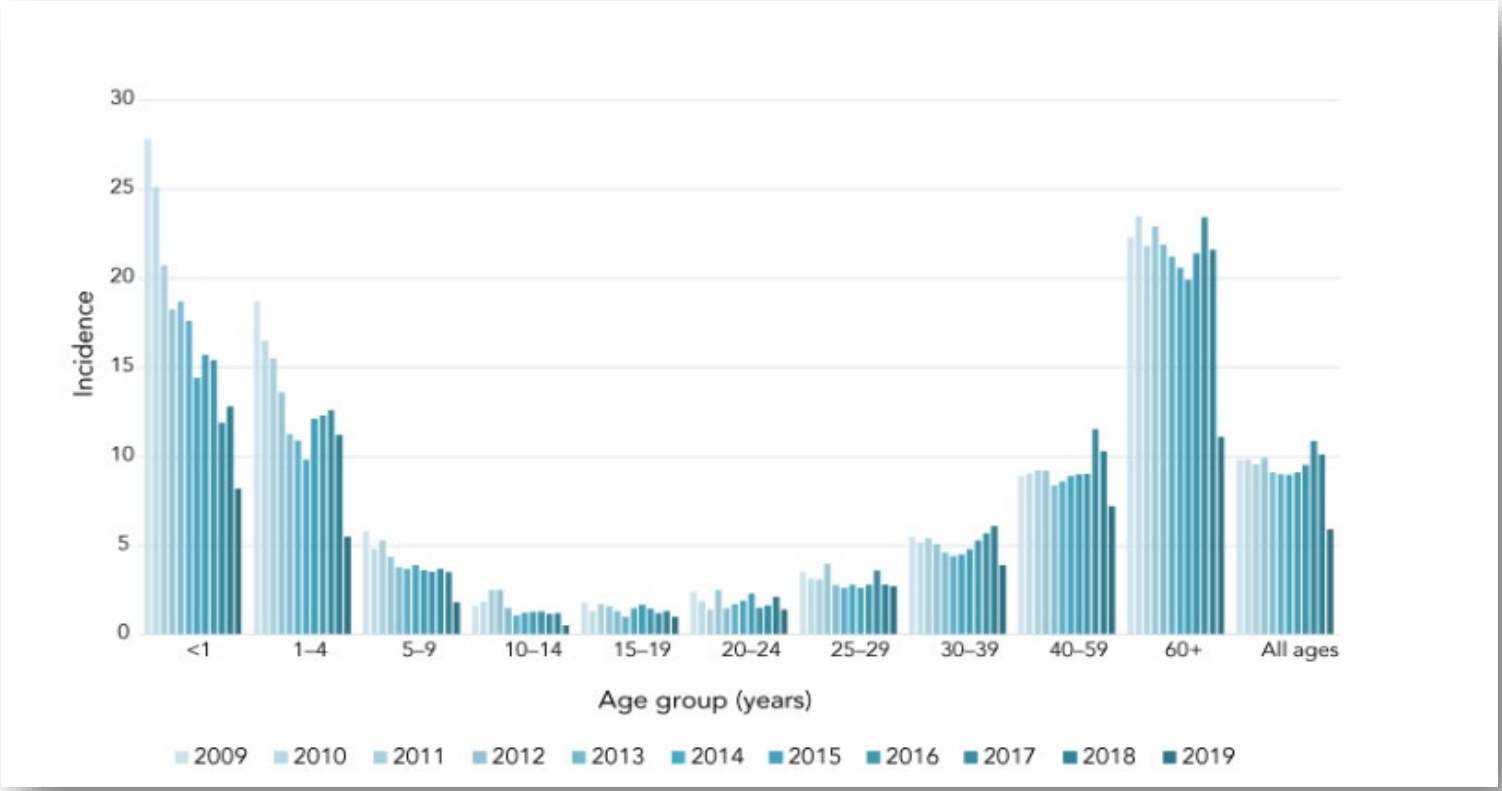
HOST FACTORS		External Factors	Behavioral Factors	Age
Immunocompetent	Immunocompromised			
• Chronic heart disease • Chronic lung disease • Diabetes • Functional or anatomic asplenia • Chronic liver disease • Cerebrospinal fluid leaks • Cochlear implants • Chronic renal failure, nephrotic syndrome*	• HIV infection • Cancer (solid, hematologic) • Solid organ transplantation • Autoimmune diseases • Immunosuppressive therapy • Primary immunodeficiencies • Prednisone (e.g. >20 mg/day)	• Socioeconomic • Environmental • Preceding viral respiratory infection (e.g., influenza) • Residence in an institution	• Smoking — • Alcohol abuse • Homelessness • Illicit drug use	• ≥ 65 years

* Unless immunosuppressed by long-term corticosteroids

1. Quach-Thanh C, et al. *Can Commun Dis Rep* 2013; 39(ACS-5):1-52.

Surveillance program

Annual incidence of invasive pneumococcal disease cases per 100,000 population In Canada by age group, 2010–2020



Invasive pneumococcal disease surveillance in Canada, 2020, CCDR 48(9) - Canada.ca

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NACI Strength of The Recommendations

In this NACI statement it also means

STRONG RECOMMENDATION

SHOULD BE OFFERED

A **strong recommendation** applies to ***most*** populations/individuals and **should be** followed unless a clear and compelling rational for an alternative approach is present.

In this NACI statement it also means

DISCRETIONARY RECOMMENDATION

MAY BE OFFERED

A **discretionary recommendation** **may be** offered for ***some*** populations/individuals in ***some*** circumstances. Alternative approaches **may be** reasonable.

Image source: Flaticon.com

Pneumococcal Conjugate Vaccination Guideline

Recommendations for Public Health Program Level Decision-Making

1

NACI recommends that the pneumococcal conjugate vaccine **PNEU-C-20** should be offered to pneumococcal vaccine naïve adults or adults whose vaccination status is unknown and who are

- *≥65 years of age*
- *50-64 years of age living with risk factors placing them at higher risk of pneumococcal disease*
- *18-49 years of age living with immunocompromising conditions*

Strong NACI recommendation

Should be offered

2

NACI recommends that **PNEU-C-15** *followed by* **PNEU-P-23** may be offered as an alternative to **PNEU-C-20** to pneumococcal vaccine naïve adults or adults whose vaccination status is unknown and who are

- *≥65 years of age*
- *50-64 years of age living with risk factors placing them at higher risk of pneumococcal disease*
- *18-49 years of age living with immunocompromising conditions*

Discretionary NACI recommendation

May be offered

Image source: Flaticon.com

Recommendations for Public Health Program Level Decision-Making

3

NACI recommends that the pneumococcal conjugate vaccine **PNEU-C-20**, should be offered to **adults ≥65 years of age** who have been immunized previously with

- ***PNEUP-23 alone***,
- ***PNEU-C-13 and PNEU-P-23 in series***, *if it has been at least 5 years from the last dose of a previous pneumococcal vaccine (PNEU-P-23 or PNEU-C-13).*

Strong NACI recommendation

Should be offered

4

NACI recommends that the pneumococcal conjugate vaccine **PNEU-C-20**, may be offered to **adults ≥65 years of age** who have been immunized previously with

- *PNEUC-13 alone, if it has been 1 year from the last dose of PNEU-C-13.*

Discretionary NACI recommendation

May be offered

Image source: Flaticon.com

Recommendations for Public Health Program Level Decision-Making

5

NACI recommends pneumococcal conjugate vaccine **PNEU-C-20** should be offered to **adults 18 years old or older** who

- received a hematopoietic stem cell transplant (HSCT) after consultation with transplant specialist.

A primary series of 3 doses of PNEU-C-20 starting 3-9 months after transplant should be administered at least 4 weeks apart, followed by **a booster dose of PNEU-C-20** 12 to 18 months post-transplant (6 to 12 months after the last dose of PNEU-C-20).

Strong NACI recommendation

Should be Offered

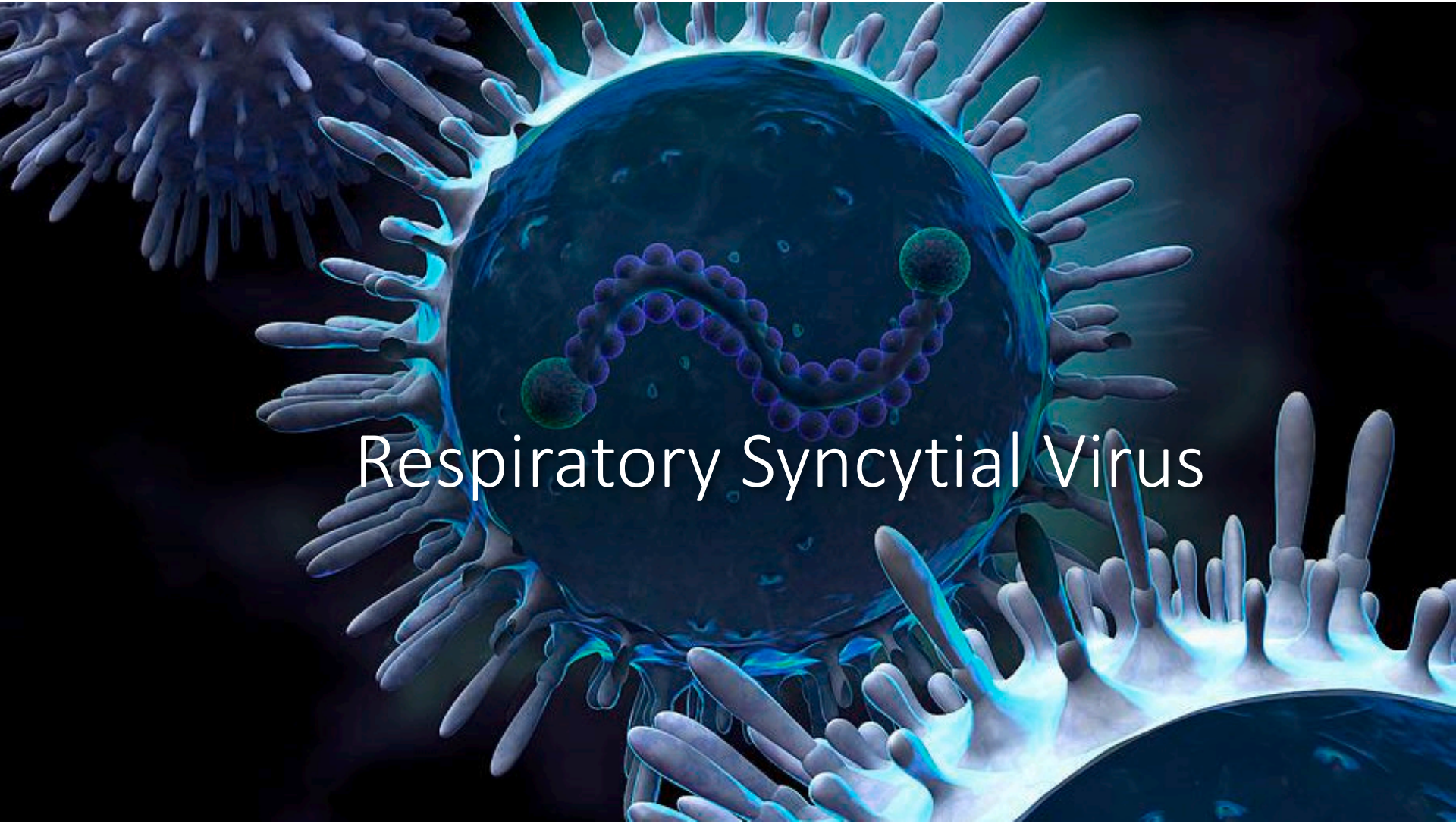
Image source: Flaticon.com

Recommendations for Public Health Program Level Decision-Making

Considerations for continued PNEU-C-13 and PNEU-P-23 use and other risk groups

NACI supports the continued use of **PNEU-C-13** and **PNEU-P-23** in adults *only* when **PNEU-C-15** and/or **PNEU-C-20** are unavailable or inaccessible.

At this time there are *no public health level recommendations* on the use of **PNEU-C-15** or **PNEU-C-20** for **adults 18-49 years of age with non-immunocompromising risk factors** that place them at high risk of IPD as additional analyses on the cost-effectiveness of conjugate PNEU-C-15 and PNEU-C-20 in this population are needed. **PNEU-C-15** or **PNEU-C-20** *may be considered* at clinical discretion for these adults.


Respiratory Syncytial Virus

Risk Factors for RSV

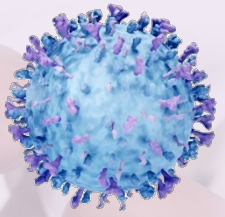
RSV

Biological

- Infants, especially premature infants or infants 6 months or younger
- Older adults, especially adults over the age of 65

Medical

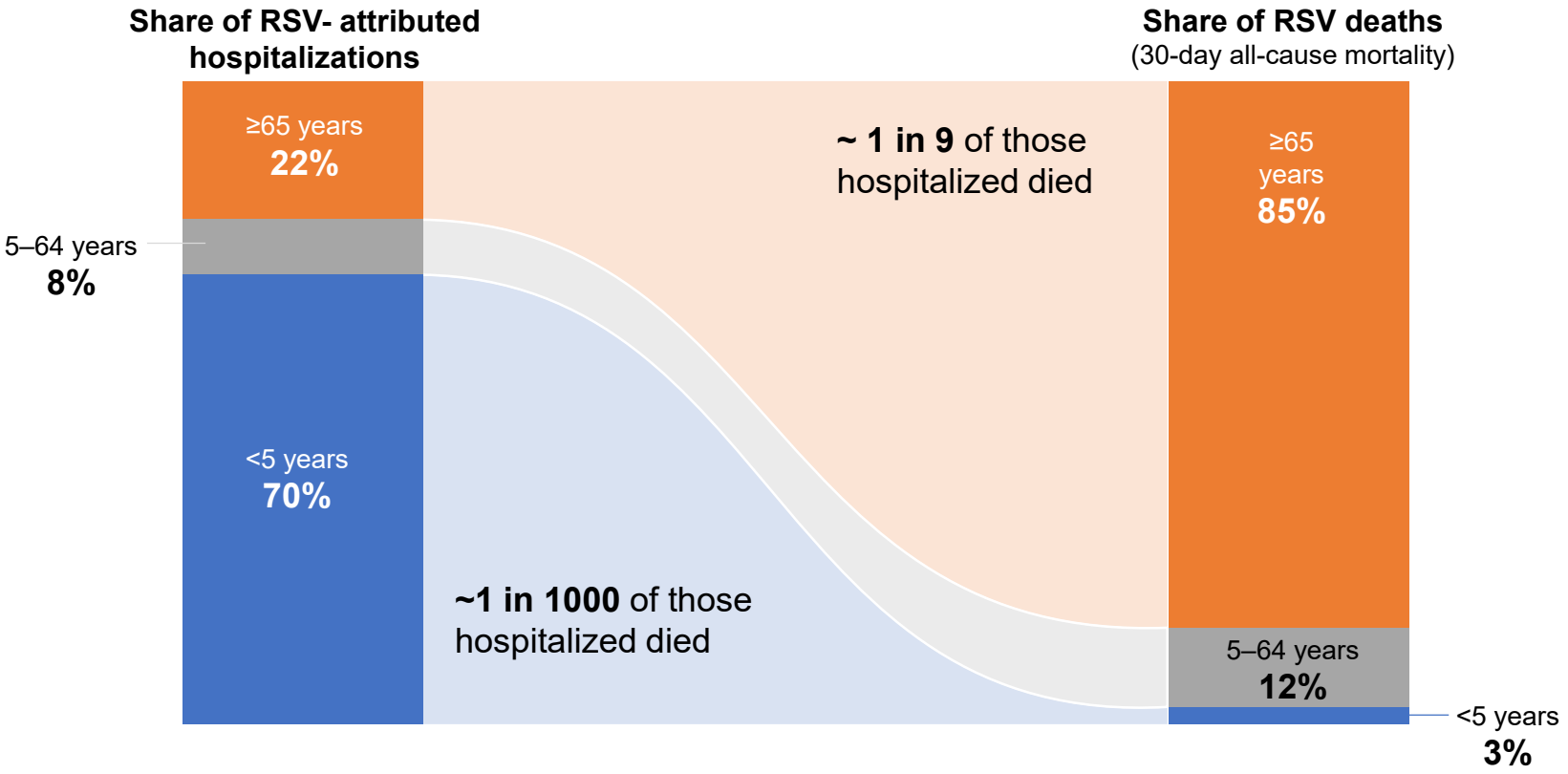
- Children with chronic lung disease
- Children with heart disease present from birth (congenital heart disease)
- Children or adults with weakened immune systems
- Children with neuromuscular disorders
- Adults with heart or lung disease



https://www.canada.ca/en/public-health/services/diseases/respiratory-syncytial-virus-rsv/prevention-risks.html#a3

Mortality:

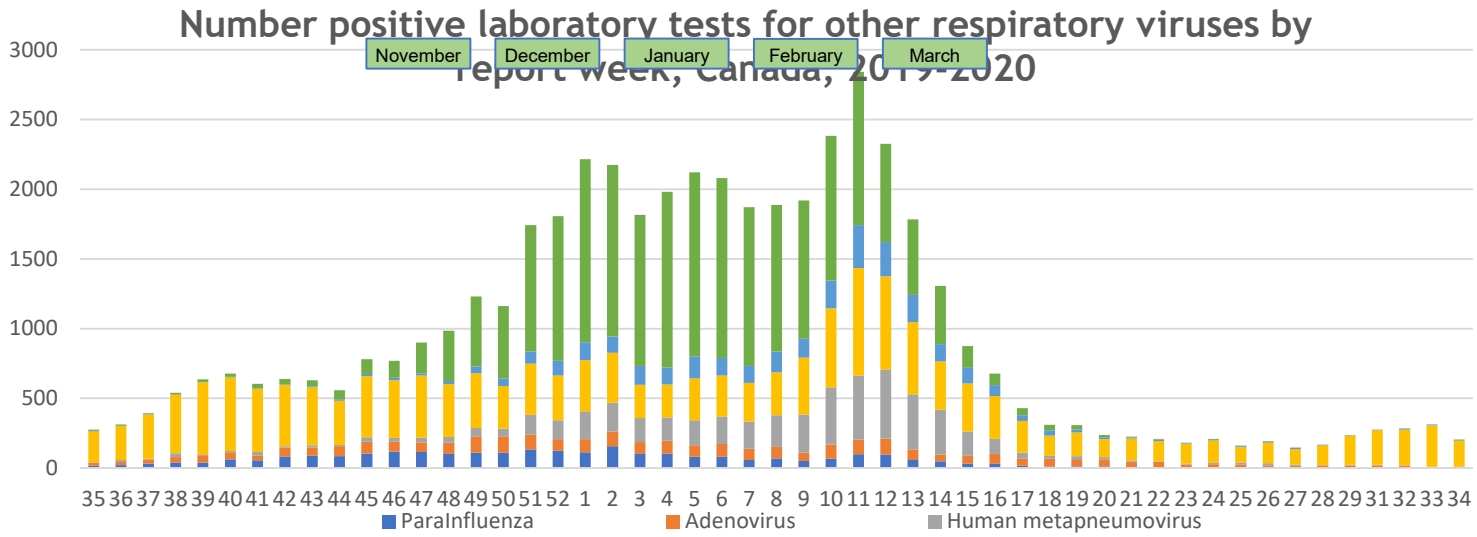
- Data from Ontario show that older adults make up a disproportionate number of RSV-attributed deaths



Ontario population-based laboratory and health administrative data, 2010/2011–2018/2019 respiratory virus seasons
From: Hamilton MA, et al. Influenza Other Respir Viruses. 2022;16(6):1072-1081.

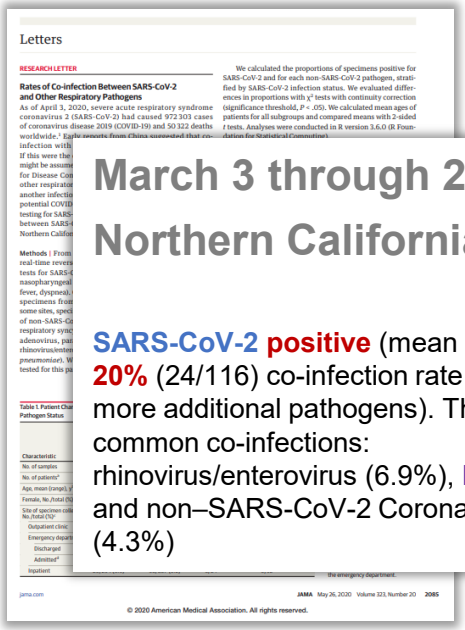
Respiratory Virus Detections/Isolations

By Season **2019-2020** (excluding SARS-CoV2)



Respiratory Virus Report, week 34 - ending August 22, 2020 - Canada.ca

Co-infections of SARS-CoV-2 with Respiratory Pathogens


Letters

RESEARCH LETTER

Rates of Co-infection Between SARS-CoV-2 and Other Respiratory Pathogens

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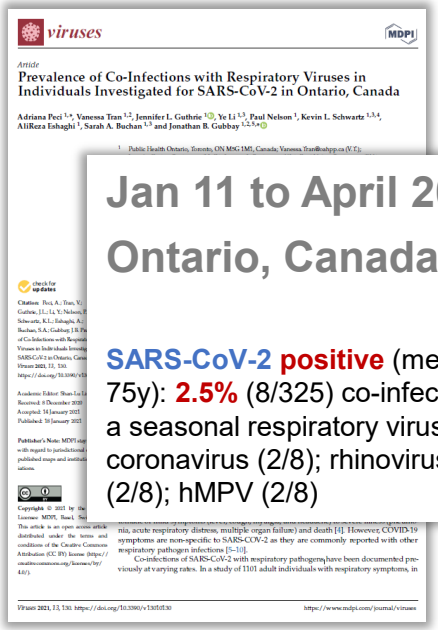
March 3 through 25, 2020

Northern California, US[1]

SARS-CoV-2 positive (mean age: 46.9y): **20%** (24/116) co-infection rate (with 1 or more additional pathogens). The most common co-infections: rhinovirus/enterovirus (6.9%), **RSV** (5.2%), and non–SARS-CoV-2 Coronaviridae (4.3%)


viruses

MDPI

Article

Prevalence of Co-Infections with Respiratory Viruses in Individuals Investigated for SARS-CoV-2 in Ontario, Canada

Jan 11 to April 20, 2020

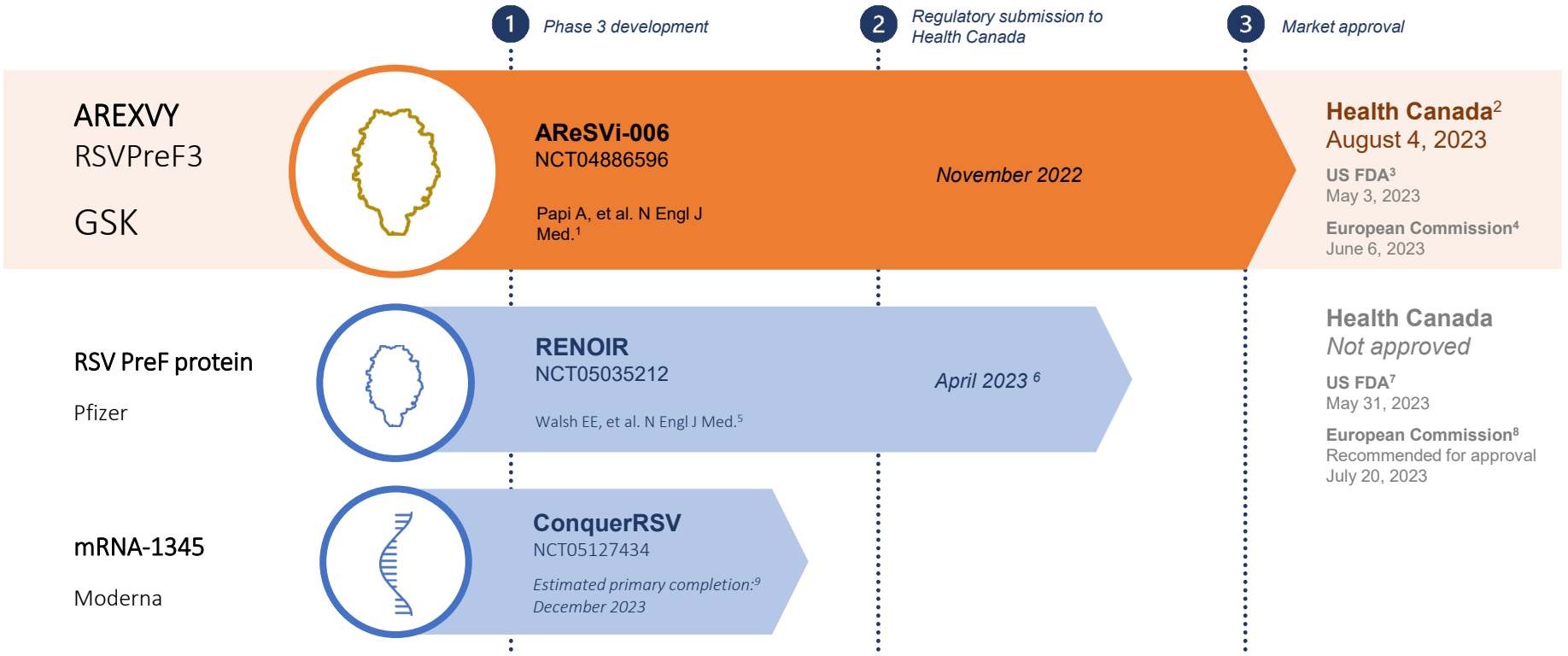
Ontario, Canada[2]

SARS-CoV-2 positive (median age: 75y): **2.5%** (8/325) co-infection rate with a seasonal respiratory viruses: seasonal coronavirus (2/8); rhinovirus (2/8); **RSV** (2/8); hMPV (2/8)

1. Kim D. et al. JAMA. 2020 May 26; 323(20): 2085–2086.; 2. Peci A. et al. Viruses 2021, 13, 130.

Immunization strategies for RSV in older adults

RSV Vaccines: Here and Coming Soon

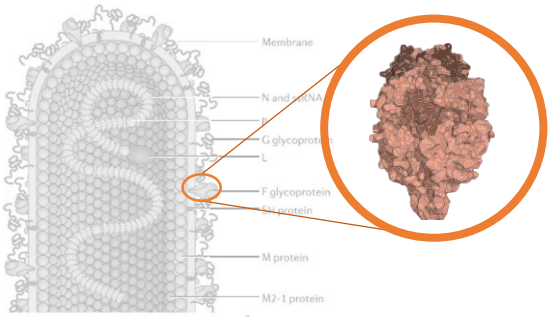


1. Papi A, et al. N Engl J Med. 2023;388(7):595-608. 2. GSK press release. Aug 4, 2023. https://ca.gsk.com/en-ca/media/press-releases/gsk-s-arexvy-the-first-respiratory-syncytial-virus-rsv-vaccine-for-older-adults-approved-in-canada/ 3. US Food and Drug Administration. https://www.fda.gov/vaccines-blood-biologics/arexvy 4. European Medicines Agency. https://www.ema.europa.eu/en/medicines/human/EPAR/arexvy 5. Walsh EE, et al. N Engl J Med. 2023;388(16):1465-1477. 6. Pfizer press release. Apr 14, 2023. https://www.pfizer.ca/en/media-centre/pfizer-canada-initiates-submission-to-health-canada-for-its-bivalent-respiratory-syncytial-virus-rsv-vaccine 7. US Food and Drug Administration. https://www.fda.gov/vaccines-blood-biologics/abrysvo 8. European Medicines Agency. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/abrysvo 9. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05127434

AREXVY combines a recombinant RSV-PreF3 antigen and an adjuvant with established activity in older adults

ANTIGEN

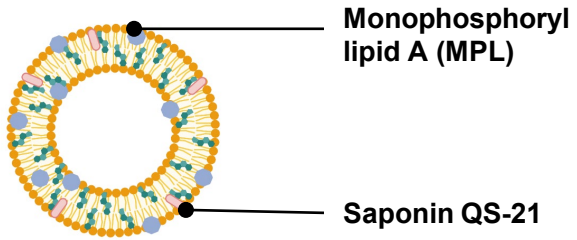
RSV-F stabilized in the prefusion state (120 µg)



The RSV-F antigen target is highly conserved between RSV-A and RSV-B subtypes[1]

ADJUVANT

AS01E adjuvant system: liposomes containing two immunostimulants that boost RSV-specific T-cell response[1,2]



Same adjuvant ingredients as the recombinant shingles vaccine Shingrix, with half the amount of MPL and QS-21[2,3]

Image of RSV adapted from: Battles MB, McLellan JS. Nat Rev Microbiol. 2019;17(4):233-245; Image of RSV-F reproduced from: Graham BS, et al. Curr Opin Immunol. 2015;35:30–38, with permission from Elsevier.
AS01E, Adjuvant System 01E (25 µg Quillaja saponaria Molina, fraction 21, 25 µg 3-O-desacyl-4'- monophosphoryl lipid A, combined in a liposomal formulation)

1. Graham BS et al. Curr Opin Immunol 2015;35:30–38. 2. AREXVY (RSV vaccine recombinant, AS01E adjuvanted). Product Monograph. Mississauga, ON: GlaxoSmithKline Inc; Aug 2023. 3. SHINGRIX (herpes zoster vaccine). Product Monograph. Mississauga, ON: GlaxoSmithKline Inc; Nov 2022.

ACIP recommends RSV vaccines for adults aged ≥60 under shared clinical decision-making based on risk assessment

Older adults who are at **highest risk for severe RSV disease** might **be most likely to benefit from vaccination**.

"Adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making."

ACIP recommendation
June 21, 2023

Chronic underlying medical conditions associated with increased risk
- Lung disease (such as chronic obstructive pulmonary disease and asthma)
- Cardiovascular diseases (such as congestive heart failure and coronary artery disease)
- Moderate or severe immune compromise*
- Diabetes mellitus
- Neurologic or neuromuscular conditions
- Kidney disorders
- Liver disorders
- Hematologic disorders
- Other underlying conditions that a health care provider determines might increase the risk for severe respiratory disease

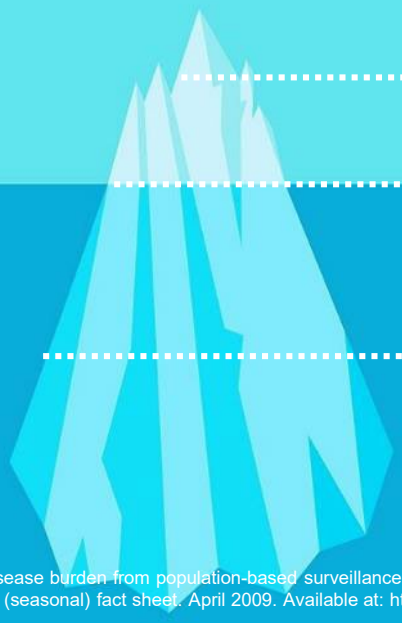
Other factors associated with increased risk
- Frailty
- Advanced age
- **Residence in a nursing home or other long-term care facility**
- Other underlying factors that a health care provider determines might increase the risk for severe respiratory disease

ACIP, Advisory Committee on Immunization Practices (US CDC)
Melgar M, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793–801.

Under-appreciated Burden of Influenza

TIP OF THE ICEBERG[1]

Annual influenza epidemics cause an estimated 250,000 – 500,000 deaths globally, infecting up to 15-20% of the population each season[2]



Laboratory-confirmed Deaths

Ascertained Cases

Laboratory-confirmed Cases

Unobserved Cases

Medically-attended cases
(not laboratory-confirmed)

Non Medically-attended cases
(not laboratory-confirmed)

Reference:
1. Reed C et al. Estimating influenza disease burden from population-based surveillance data in the United States. PloS one. 2015 Mar 4;10(3):e0118369.
2. World Health Organization. Influenza (seasonal) fact sheet. April 2009. Available at: http://www.who.int/mediacentre/factsheets/fs211/en/. Accessed November 12, 2013.

Influenza Remains a Serious Public Health Concern

In Canada, influenza is estimated to annually cause[1-3]:

3,500,000
Symptomatic Infections

2,300,000
Work absences

900,000
Physician office visits

175,000
Emergency Room visits

12,200
Hospital admissions

3,500
Deaths

Influenza-related deaths are highest among vaccine-preventable diseases.[3]

References:
1. National Advisory Committee on Immunization (NACI). A Review of the Literature of High Dose Seasonal Influenza Vaccine for Adults 65 Years and Older. Accessed on April 5, 2017.
2. National Advisory Committee on Immunization (NACI). Statement on Seasonal Influenza Vaccine for 2016–2017. Accessed on April 5, 2017.
3. https://www.publichealthontario.ca/en/LearningAndDevelopment/EventPresentations/Introducing_Flu_Other_Respiratory_Viruses_Research_Cohort_Kwong_2017.pdf
3. Symposium on Influenza Immunization in the Healthcare Workplace. University of Calgary Faculty of Medicine. A Report of Conference Proceedings. June 11, 2014.

Influenza Prevalence

- At least 5–15% of the population infected by influenza annually
- Influenza and pneumonia—top 10 leading causes of death in Canada
- Influenza is annually associated with
  - 12,200 hospitalizations
  - 3500 deaths

Public Health Agency of Canada. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023. Published June 8, 2022. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023.html. Monto AS, Ansaldi F, Aspinall R, et al. Influenza control in the 21st century: Optimizing protection of older adults. *Vaccine*. 2009;27(37):5043-5053. doi:10.1016/j.vaccine.2009.06.032

Influenza in Adults 65+: A Vulnerable Population

Older Canadians suffer disproportionately from influenza-related morbidity and mortality[1]:

Adults 65+ only represent 15% of the Canadian population[2], but in the 2016-17 influenza season, they accounted for[1]:

67% of hospitalizations due to influenza

AND

88% of deaths due to influenza

References:

1. Public Health Agency of Canada (PHAC). FluWatch. August 20 to August 26, 2017. Accessed on September 5, 2017.
2. Statistics Canada. (2015). Population projections for Canada (2013 to 2063), Provinces and Territories (2013 to 2038). Accessed on April 5, 2017.

Influenza and High Risk Groups

High risk groups for developing influenza-related complications[1]:

- **Adults 65+**
- Pulmonary disease
- Cardiovascular disorders
- Diabetes
- Liver disorders
- Kidney disorders
- Cancer
- Morbidly obese
- HIV/AIDS
- Children 6 to 59 mo.
- Pregnant Women

74% **OF CANADIANS 65+ reported having at least 1 chronic condition[1-2]***

**Arthritis, asthma, cancer, chronic pain, depression, diabetes, emphysema/ COPD, heart disease, high blood pressure, mood disorders, stroke*

KEY RISK FACTORS FOR INFLUENZA

Age 65+

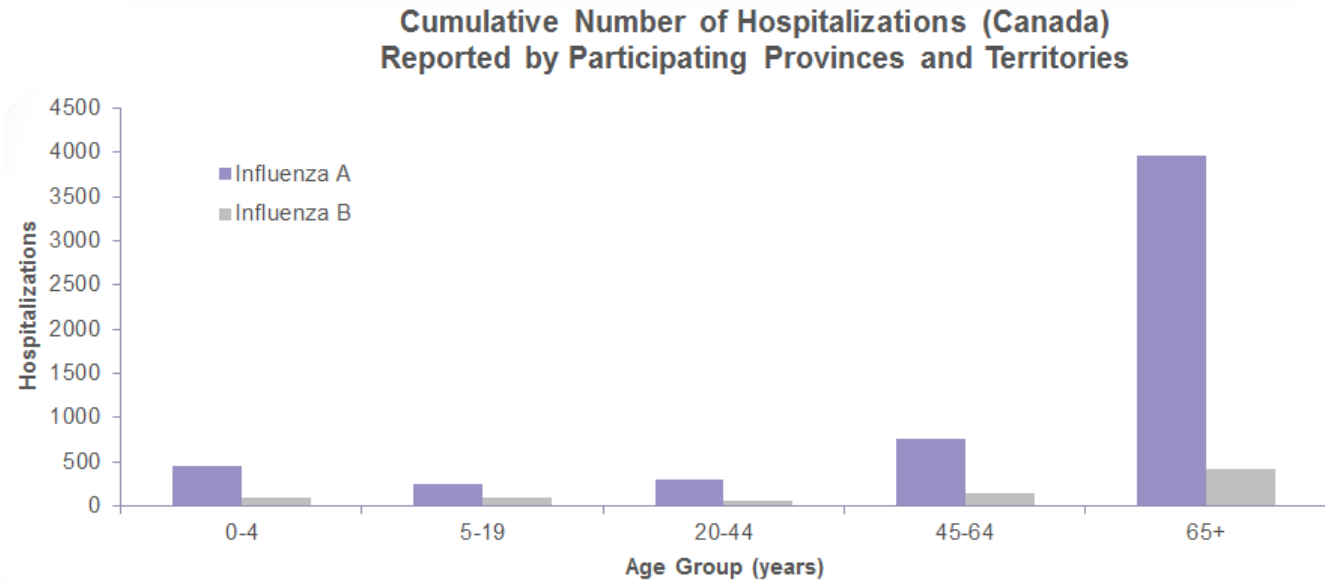
Chronic Medical Condition

Weakened Immune System

References:
1.An Advisory Committee Statement (ACS)/National Advisory Committee on Immunization (NACI): Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2017–2018.
2.CIHI: Seniors and the Health Care System: What Is the Impact of Multiple Chronic Conditions? 2011. Accessed at: https://secure.cihi.ca/free_products/air-chronic_disease_aib_en.pdf.

49

In 2016–2017, hospitalizations caused by influenza A and B were highest among adults over 65…[1]



- 88% of all hospitalizations were due to influenza A
  - 99% of these influenza A cases reported were the H3N2 subtype
  - Adults 65+ accounted for 67% of the hospitalizations

Influenza A (H3N2) was by far the leading cause of hospitalization among seniors.

References:

1. Public Health Agency of Canada (PHAC). (2017). FluWatch report: June 18 to July 22, 2015. Accessed on Aug 10, 2017.

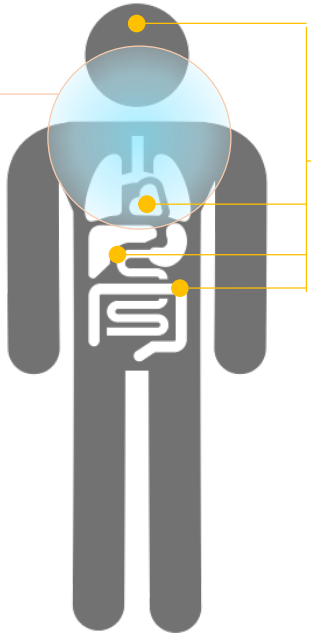
Potential Complications of Influenza

DIRECT effects: Respiratory

Asthma & COPD exacerbations[1,5]

Ear/Sinus Infection[2]

Bronchitis & Pneumonia[1,6]



INDIRECT effects: Multi-Organ Systems

TRIGGER for:

Acute myocardial infraction[3,4,7,8], Ischemic heart[3,4,8] disease and Cerebrovascular disease[3,4,9]

EXACERBATION of:

Renal disorder[1,10] and Diabetes[1,11]

References:

1. National Advisory Committee on Immunization (NACI): Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2016–2017. Accessed on April 5, 2017.
2. Norhayati MN, et al. (2015). Cochrane Database of Systematic Reviews.; (3): 1-54.
3. Udell JA, et al. (2013). JAMA; 310(16):1711-20.
4. Udell JA, et al. (2015). Expert Rev Cardiovasc Ther.;13(6):593-6.
5. Canadian Lung Association. Accessed on April 5, 2017.
6. CDC: The Pink Book: Course Textbook – 13th Edition (2015). Accessed on April 5, 2017.
7. Siriwardena AN, et al. (2010). CMAJ182(15):1617-1623.
8. CDC Morbidity and Mortailty Weekly Report. Accessed on April 5, 2017.
9. Grau AJ, et al. (2005). Stroke; 36(7):1501-1506.
10. Chen CI, et al. (2016). Medicine (Baltimore); 95(5):1–9.
11. Husein N, et al. (2013). Canadian Journal of Diabetes.; 37 Supplement 93.

Influenza→ Inflammation→ Potential AMI[1-5]

1

High-risk Plaque Formation

2

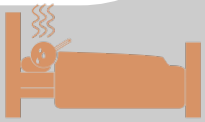
Infections like influenza may result in **exacerbation** of underlying inflammatory processes of athlerosclerosis

"**The influenza virus has extensive effects on inflammatory and coagulation pathways**, which might lead to destabilization of vulnerable atherosclerotic plaques and thus coronary artery occlusion – the major cause of **acute myocardial infarction (AMI)**"[3]

4

Inflammation → Plaque Rupture → Coagulation Cascade → **Acute Coronary Syndrome**

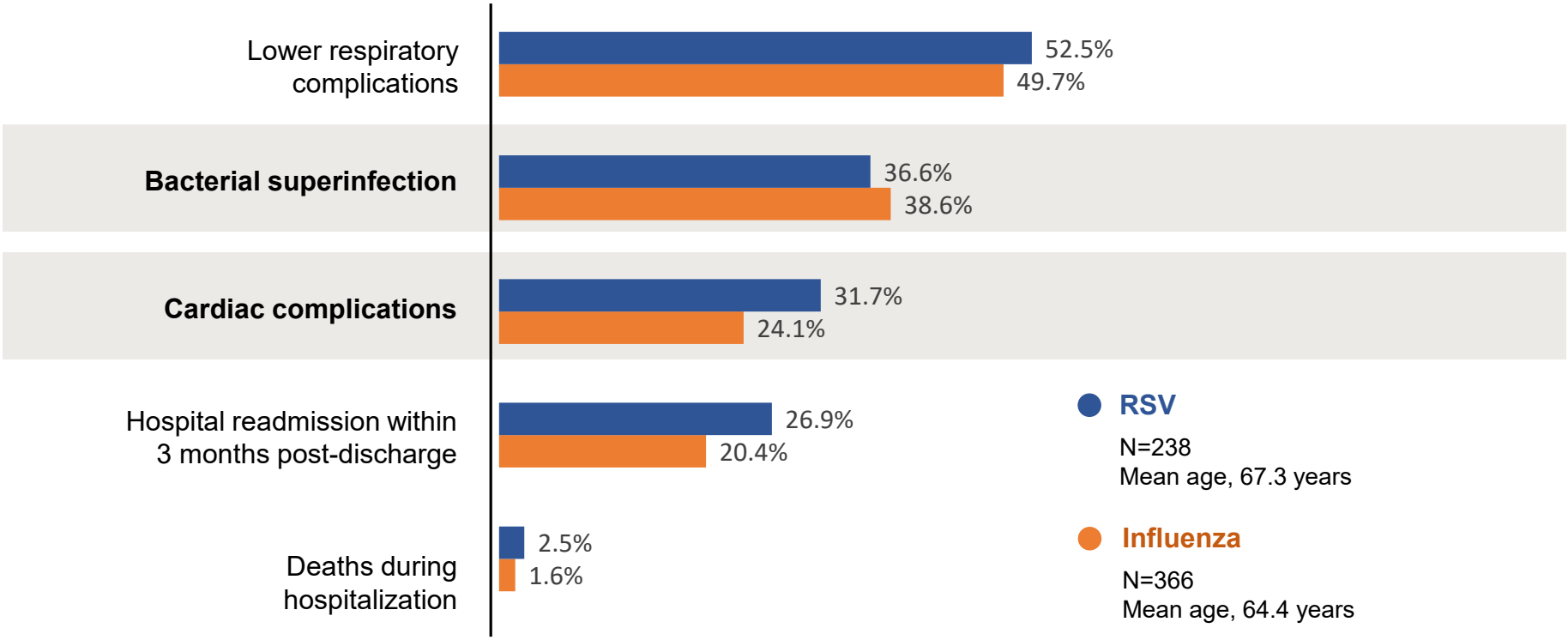
3



Severe inflammation during acute infection

References:
1. Madjid M. Eur Heart J. 2007;28 (10):1205-1210.
2. Ross R. Nature. 1993;362(6423): 801-809.
3. Warren-Gash C, et al. Lancet Infect Dis. 2009;9(10):601-610.
4. Harskamp RE, van Ginkel MW. Ann Med. 2008;40(2):121-128.
5. Phrommintikul A, et al. Eur Heart J. 2011;32(14):1730-1735.

Rates of complications and mortality in adults hospitalized with ARTI are similar between RSV and influenza



ARTI, acute respiratory tract infection

HARTI global study results from: 1. Falsey AR, et al. Open Forum Infect Dis. 2021;8(11):ofab491.

Higher influenza-attributed mortality is associated with chronic conditions

For persons aged 65 years and over, the risk for influenza-attributed death was[1]:

5x greater among those with chronic heart diseases

12x greater among those with chronic lung diseases

20x
greater among those with **both** chronic heart and lung conditions

References:
1. Schanzer DL, et al. (2008). Vaccine, 26, 4697–4703.
2. National Advisory Committee on Immunization (NACI). Statement on Seasonal Influenza Vaccine for 2016–2017. Accessed on April 5, 2017.

Influenza-Related Risk Factors for Complications

- All children 6–59 months of age
- Adults and children with the following chronic health conditions:
  - Cardiac or pulmonary disorders
  - Diabetes and other metabolic diseases
  - Cancer, immune compromising conditions
  - Renal disease
  - Anemia or hemoglobinopathy
  - Neurologic or neurodevelopment conditions
  - Morbid obesity (defined as BMI of 40 kg/m^2 and over), and
- Children 6 months to 18 years of age undergoing treatment for long periods with acetylsalicylic acid (ASA)
- All pregnant individuals
- People of any age who are residents of nursing homes and other chronic care facilities
- Adults aged ≥65 years, and
- Indigenous peoples

Residents of nursing homes and other chronic care facilities are at much higher risk of influenza infections, where their comorbidities increase the risks of complications

Public Health Agency of Canada. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023. Published June 8, 2022. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023.html. Accessed June 16, 2022

BMI, Body Mass index

A Common Influenza Trajectory in Older Adults

Vaccines Indicated in Older Adults

Product Category	Vaccine Type	Indication
Standard dose, unadjuvanted, quadrivalent, IM administered, egg-based	IIV4-SD	≥ 6 months
Recombinant, unadjuvanted, quadrivalent, IM administered	RIV4	≥ 18 years
Adjuvanted, trivalent, IM administered, egg-based	IIV3-adj	≥ 65 years
High-dose, unadjuvanted, quadrivalent, IM administered, egg-based	IIV4-HD	≥ 65 years
Standard dose, unadjuvanted, quadrivalent IM administered, cell culture-based	IIV4-CC	≥ 6 months

Enhanced influenza vaccines include RIV4, IIV3-adj and IIV4-HD

Public Health Agency of Canada. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023. Published June 8, 2022. Accessed June 16, 2022. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023.html

High-Dose Influenza Vaccine (IIV4-HD)

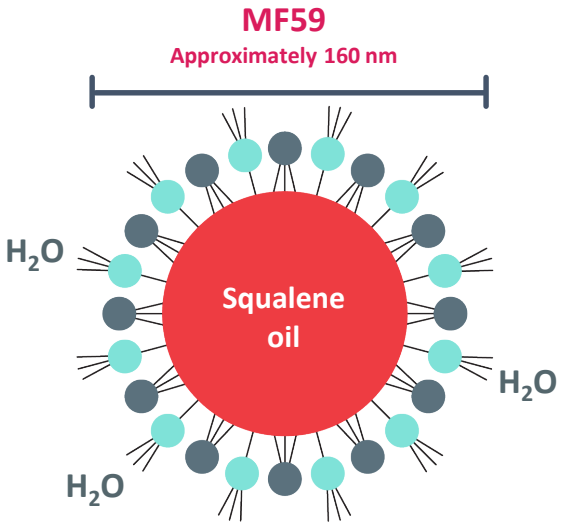
- Contains 4 X dose of hemagglutinin (HA)—60 µg of each strain
- Two RCTs of HD versus SD vaccine
  - Individual: ↓ Influenza cases in older adults
  - Cluster randomized: ↓ Hospitalizations for respiratory-related illness in nursing-home residents
- NACI Recommendation: IIV-HD preferred to IIV-SD formulations
- Safety - Higher rates of some systemic and local reactions than IIV3-SD
  - Especially malaise, myalgia and moderate to severe fever
  - Most resolve within 3 days
  - No increase in risk of serious adverse effects

Public Health Agency of Canada. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023. Published June 8, 2022. Accessed June 16, 2022. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023.html.
DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults. *N Eng J Med.* 2014;371(7):635-645. doi:10.1056/NEJMoa1315727. Gravenstein S, Davidson HE, Taljaard M, et al. Comparative effectiveness of high-dose versus standard-dose influenza vaccination on numbers of US nursing home residents admitted to hospital: a cluster-randomised trial. *The Lancet Resp Med.* 2017;5(9):738-746. doi:10.1016/S2213-2600(17)30235-7.

HA: hemagglutinin; IIV3-SD: trivalent inactivated influenza vaccine standard dose; IIV4-HD: inactivated influenza vaccine high dose; IIV4-SD: inactivated influenza vaccine standard dose; µg: microgram; NACI: National Advisory Committee on Immunization; RCT: randomized controlled trials.

Adjuvanted-Trivalent Influenza Vaccine (IIV3-adj)

- Contains 15 µg of HA (influenza A H3N2, H1N1 and influenza B strain Victoria) with MF59 adjuvant
- Compared to IIV3-SD
  - ↓ Influenza cases (observational)
  - ↓ Hospitalization risk for influenza or pneumonia (observational)
  - ↓ Cases of acute coronary and cerebrovascular event hospitalization (observational)
- Safety
  - Higher risk of mild-to-moderate local reactions compared to IIV3-SD
  - Acceptable safety profile in adults aged ≥65 years



Public Health Agency of Canada. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023. Published June 8, 2022. Accessed June 16, 2022. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023.html. Frey SE, Reyes MRA-DL, Reynales H, et al. Comparison of the safety and immunogenicity of an MF59®-adjuvanted with a non-adjuvanted seasonal influenza vaccine in elderly subjects. *Vaccine*. 2014;32(39):5027-5034. doi:10.1016/j.vaccine.2014.07.013. Van Buynder PG, Konrad S, Van Buynder JL, et al. The comparative effectiveness of adjuvanted and unadjuvanted trivalent inactivated influenza vaccine (TIV) in the elderly. *Vaccine*. 2013;31(51):6122-6128. doi:10.1016/j.vaccine.2013.07.059. Mannino S, Villa M, Apolone G, et al. Effectiveness of Adjuvanted Influenza Vaccination in Elderly Subjects in Northern Italy. *Am J Epidemiol*. 2012;176(6):527-533. doi:10.1093/aje/kws313. Domnich A, Arata L, Amicizia D, Puig-Barberà J, Gasparini R, Panatto D. Effectiveness of MF59-adjuvanted seasonal influenza vaccine in the elderly: A systematic review and meta-analysis. *Vaccine*. 2017;35(4):513-520. doi:10.1016/j.vaccine.2016.12.011. Lindert K, Leav B, Heijnen E, Barrett J, Nicolay U. Cumulative clinical experience with MF59-adjuvanted trivalent seasonal influenza vaccine in young children and adults 65 years of age and older. *International Journal of Infectious Diseases*. Published online March 20, 2019. doi:10.1016/j.ijid.2019.03.020

HA: hemagglutinin; H_2O: water; IIV3-adj: adjuvanted inactivated influenza vaccine; IIV3-SD: trivalent inactivated influenza vaccine standard dose; nm: nanometre.

Educating Older Adults About Influenza

- Influenza rates were low during the COVID-19 pandemic, but influenza activity increased at the start of 2022
- Older adults are at significant risk of complications from influenza including:
  - ↑ frailty and ↓ quality of life
  - ↑ risk of hospitalization and death
  - ↑ CV risk
  - Worsening of comorbidities
- Influenza can lead to a downward spiral of the health of the infected older adult

Key Learning Points

- The 2023/24 influenza season is expected to be very busy as the COVID-19 public health measures have been reduced
- Influenza and RSV are associated with significant morbidity and mortality risk in older adults
- Enhanced vaccines for Influenza offer effectiveness advantages over IIV-SD
- Influenza significantly increases the risk of bacterial pneumonia[1,2]
- **Up to 40% of pneumonia cases in hospitalized patients can be traced to viral infections[3]**

Herpes zoster (HZ) is caused by reactivation of varicella zoster virus (VZV) in adults[1]

1 Primary VZV infection: chickenpox

(varicella)

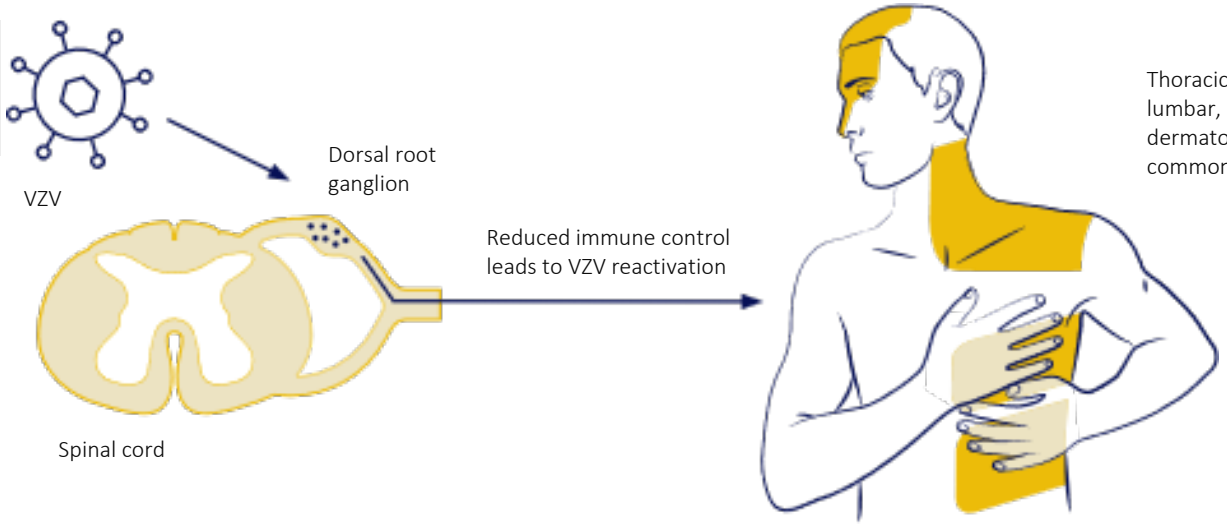
2 Latency

After control of the primary infection, the virus remains dormant within sensory neurons[1]

3 Reactivation: shingles

Reactivated virus travels along sensory nerve pathways to the skin, producing a painful rash[2]

≥90% of Canadian adults have been infected with VZV[3]



The lifetime risk of HZ is **~1 in 3**[5]

~1 in 17 patients with HZ experience recurrent episodes[6,7]

Figure adapted from: Gershon AA, et al. Nat Rev Dis Primers. 2015;1:15016.

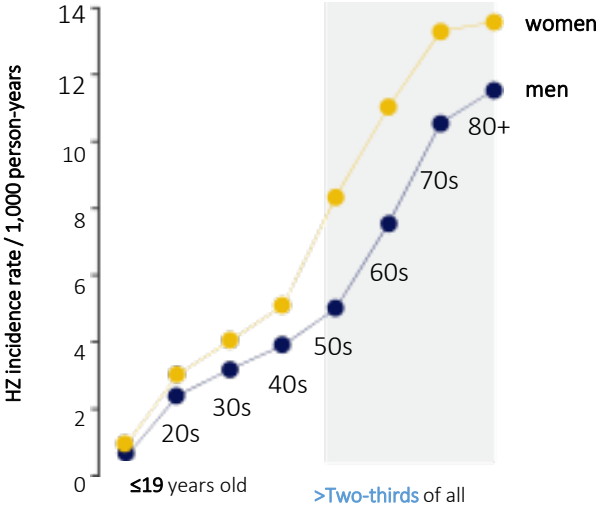
ACS, acute coronary syndrome; CI, confidence interval; CV, cardiovascular; *adjusted for age, sex, diabetes, hypertension, body mass index, current smoking, cholesterol and use of antibiotics in the last 3 months

1. Gershon AA, et al. Nat Rev Dis Primers. 2015;1:15016. 2. Weinberg JM. J Am Acad Dermatol. 2007;57(6 Suppl):S130-S135. 3. Ratnam S. Can J Infect Dis. 2000;11(5):249-253. 4. Carbone V, et al. Minerva Stomatol. 2004;53:49–59. 5. Brisson M, et al. Epidemiol Infect. 2001;127(2):305-314. 6. Kawai K, et al. BMJ Open. 2014;4(6):e004833. 7. Shiraki K, et al. Open Forum Infect Dis. 2017;4(1):ofx007.

Anyone infected with VZV is at risk of developing HZ. However, certain individuals are at increased risk[1].

Older individuals

Age-related decline in immunity is the dominant driver of shingles. Older age is also associated with an increased risk of HZ complications.[1,2]



>Two-thirds of all shingles cases occur in those ≥50 years old[1]

Immunocompromised adults

Immunodeficient conditions and/or treatment with immunosuppressive agents or chemotherapy can increase the risk of HZ.[3-11] For example, the incidence of HZ is higher in adults with:

- Bone marrow/stem cell transplant
- Organ transplant
- Hematologic malignancies
- Solid tumours
- Human immunodeficiency virus (HIV)
- Systemic lupus erythematosus (SLE)
- Rheumatoid arthritis (RA)
- Inflammatory bowel disease (IBD)
- Psoriasis

Additional risk factors[11]

Family history of HZ

Certain chronic conditions

E.g., asthma, chronic obstructive pulmonary disease (COPD), diabetes, depression, cardiovascular conditions, chronic renal disease

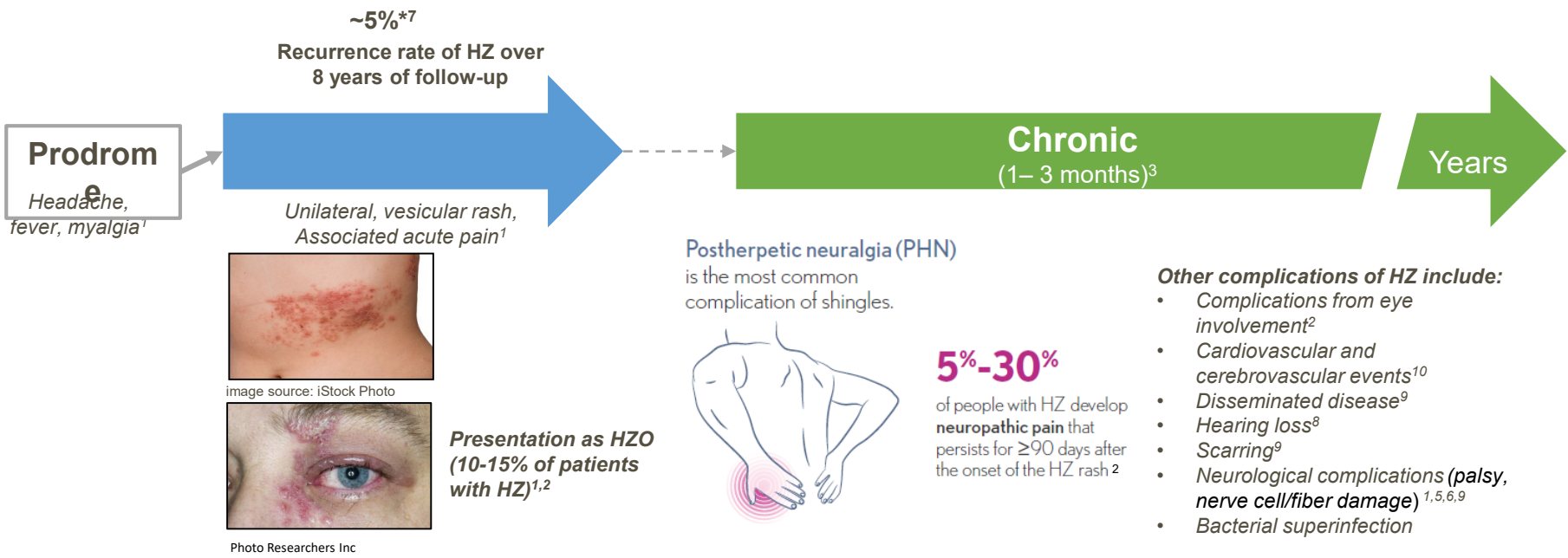
Physical trauma, psychological stress

Younger immunocompromised patients (aged 18 to 49 years) have an equivalent or higher risk of HZ than older immunocompetent patients (>50 years old)

Data sourced from Johnson BH, et al. 2015

1. Government of Canada. August 2018. Accessed August 2022. www.canada.ca/en/public-health/services/publications/healthy-living/ canadian-immunization-guide-part-4-active-vaccines/page-8-herpes-zoster-(shingles)-vaccine.html. 2. John A, Canaday DH. Infect Dis Clin North Am. 2017;31:811–826. 3. Chen SY, et al. Infection. 2014;42(2):325-334. 4. Khan N, et al. Clin Gastroenterol Hepatol. 2018;16(12):1919-27.e3. 5. Veetil BM, et al. Arthritis Care Res (Hoboken). 2013 Jun;65(6):854-61. 6. Chakravarty EF. Rheum Dis Clin North Am. 2017;43(1):111-121. 7. Blank LJ, et al. J Acquir Immune Defic Syndr. 2012;61(2):203-207. 8. Habel LA, et al. Cancer Epidemiol Biomarkers Prev. 2013;22(1):82-90. 9. Mao J, et al. Medicine (Baltimore). 2017;96(48):e8746. 10. Tseng HF, et al. Clin Infect Dis. 2014;59(7):913-919. 11. Marra F, et al. Open Forum Infect Dis. 2020;7:1–8.

The natural course of HZ consists of an acute phase which can be followed by chronic complications



HZO, herpes zoster ophthalmicus; PHN, postherpetic neuralgia

1. Harpaz R, et al. *MMWR Recomm Rep* 2008;57:1–30; 2. Kawai K, *et al. BMJ Open* 2014;4:e004883; 3. Opstelten W, *et al. Fam Pract* 2002;19:471–5; 4. Dworkin RH, *et al. J Pain* 2008;9:S37–4; 5. Dworkin RH, *et al. Clin Infect Dis* 2007;44:S1–26; 6. Nagel MA and Gilden D. *Curr Neurol Neurosci* rep 2015:15:16; 7. Yawn BP, *et al. Mayo Clin Proc* 2011;86:88–93; 8. Centers for Disease Control and Prevention. MMWR. 2008 June;57(RR-5):1-30. 9. Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook, Australian Government Department of Health and Aged Care, Canberra, 2022, immunisationhandbook.health.gov.au (Accessed April 2023). 10. Erskine, N; PLoS One; 2017;12:1-18.

More than just a rash, HZ can be debilitating to daily life

Overall impact of HZ complications

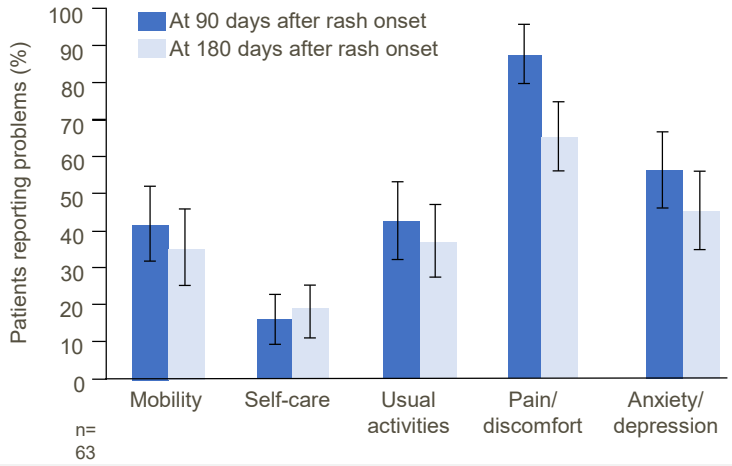
High pill burden
Polypharmacy is common to relieve pain and prevent or alleviate HZ complications[1]

Lower quality of life
97% of patients report with difficulties performing activities of daily living[2]

Increased absenteeism
>50% of working patients take time off work due to HZ[3,4]

Immunocompromised individuals are disproportionately affected.
They are more likely to experience HZ recurrence, atypical and/or more severe disease, and complications[5,6]

PHN has a persistent impact on health-related quality of life[7,8]



Changes in QoL closely correlated with the severity of pain and persisted as long as clinically significant pain continued

Data collected from 261 outpatients aged ≥50 years with HZ recruited from the clinical practices of 83 physicians within 14 days after rash onset between October 2005 and July 2006
HZ, herpes zoster; PHN, post-herpetic neuralgia; QoL, quality of life. Reproduced from Drolet M *et al. CMAJ* 2010;182:1731–1736 with permission from Joule Inc.

1. Gater A, et al. BMC Public Health. 2015;15:193. 2. Van Oorschot D, et al. Infect Dis Ther. 2022 Feb;11(1):501-516 (supplementary data). 3. Gater A, et al. BMC Infect Dis. 2014;14:402. 4. Weinke T, et al. J Public Health. 2010;18:367–374. 5. Dworkin RH, et al. Clin Infect Dis. 2007;44:S1–26. 6. Gershon AA, et al. Nat Rev Dis Primers. 2015;1:15016. 7. Drolet M et al. CMAJ 2010;182:1731–1736. 8. Drolet M, et al. Vaccine. 2012;30(12):2047-2050.

SHINGRIX

Non-live adjuvanted recombinant zoster vaccine (RZV)[1]
SHINGRIX®

For the prevention of herpes zoster (HZ) in:

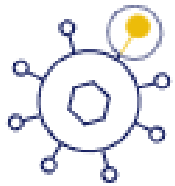
- Adults 50 years of age or older;
- Adults 18 years of age or older who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy

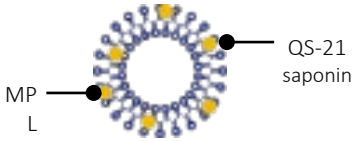
SHINGRIX components[2]

Antigen + **Adjuvant**

Glycoprotein E (gE)
elicits anti-VZV immunity

AS01B system shapes and enhances the immune response





Two immunostimulants delivered in liposomes

Figure adapted from: Heineman TC, et al. Curr Opin Immunol. 2019;59:42-48.

NACI recommends that SHINGRIX be offered to individuals ≥50 years of age who have previously been vaccinated with live zoster virus vaccine (strong recommendation)[3]

1. SHINGRIX [product monograph]. Mississauga, ON: GlaxoSmithKline Inc. Revised November 24, 2021. Accessed August 2022. https://ca.gsk.com/en-ca/products/shingrix/ 2. Heineman TC, et al. *Curr Opin Immunol.* 2019;59:42-48. 3. © All rights reserved. An Advisory Committee Statement (ACS), National Advisory Committee on Immunization (NACI) – Updated Recommendations on the Use of Herpes Zoster Vaccine. Public Health Agency of Canada, modified: 2018. Adapted and reproduced with permission from the Minister of Health, 2018.

SHINGRIX provides strong, durable protection against both herpes zoster and its complications

Two doses of SHINGRIX appear to offer clinical benefit through Year 10 after vaccination.[1-3]

ZOE-50/ZOE-70 pivotal phase 3 trials

High level of protection[1,2]

Age (years)	50–59	60–69	70–79	≥80
% Efficacy Against HZ*	**96.6%**	**97.4%**	**91.3%**	**91.4%**
(95% CI)	(89.6–99.4)	(90.1–99.7)	(86.0–94.9)	(80.2–97.0)

* Pooled data for subjects receiving full HZ series

Reduced risk of PHN and non-PHN complications by[4]:

91.2% (Age ≥50 years)

88.8% (Age ≥70 years)

ZOE-50/ZOE-70 long-term follow-up

Sustained efficacy and immune responses[3]

During follow-up period	Since vaccination
81.6%	**89.0%**
(75.2-86.6)	(85.6-91.3)

Across the long-term follow-up,

Anti-gE antibodies

gE-specific CD4[2+] T-cells

Remained >5x above pre-vaccination levels

Predictive modelling suggests cellular and humoral immune responses will remain above the observed baseline for at least **20 years after initial vaccination**[5,6]

1. Lal H, et al. N Engl J Med. 2015;372:2087-2096. 2. Cunningham AL, et al. N Engl J Med. 2016;75:1019 1032. 3. Strezova A, et al. Open Forum Infect Dis. 2022;9(10):ofac485. 4. Kovac M, et al. Vaccine. 2018;36(12):1537-1541. 5. Hastie A, et al. J Infect Dis. 2021;224(12):2025-2034. 6. Schwarz TF, et al. Hum Vaccin Immunother. 2018;14(6):1370-1377.

National Advisory Committee of Immunization (NACI) Recommendations for HZ vaccine use

National Advisory Committee on Immunization (NACI)[1]

≥50 years of age (strong recommendation)

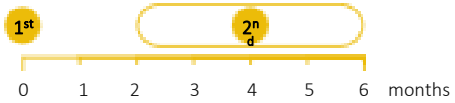
SHINGRIX (not LZV) may be considered for immunocompromised adults ≥50 years of age based on a case-by case assessment of the benefits vs risks

(discretionary recommendation; based on expert opinion)

Persons **can be vaccinated** with SHINGRIX regardless of[2,3]:

- **Varicella vaccination**
  People who have had the chickenpox vaccine may still be susceptible to shingles[4]
- **History of chickenpox**
  People who do not recall a history of varicella infection may receive SHINGRIX with no need for serology
- **History of HZ**
  Wait at least 1 year after the HZ episode
- **Vaccination with SHINGRIX**
  Wait at least 1 year after receiving SHINGRIX

SHINGRIX dosing schedule[5]



Patients who are or will be immunocompromised may receive the second dose 1 to 2 months after the initial dose. NACI also allows for 12 months between doses with no need to restart the series.

Both NACI and CIQ recommend administering SHINGRIX before initiating immunosuppressive treatment that might lead to immunodeficiency[1,6]

* E.g., rheumatoid arthritis, systemic lupus erythematosus, chronic inflammatory bowel disease, chronic obstructive pulmonary disease or bronchial asthma, chronic kidney disease, and insulin-dependent diabetes.

SHINGRIX® is a 2-dose series.
Prioritize series completion to ensure patients are fully protected.[5,7] For a subset of patients, an opportune time to immunize against HZ is at the time of referral for a tuberculosis (TB) test prior to starting immunosuppressive therapy.

1. © All rights reserved. An Advisory Committee Statement (ACS), National Advisory Committee on Immunization (NACI) – Updated Recommendations on the Use of Herpes Zoster Vaccine. Public Health Agency of Canada, modified: 2018. Adapted and reproduced with permission from the Minister of Health, 2018. 2. Government of Canada. August 2018. Accessed August 2022. www.canada.ca/en/public-health/services/publications/healthy-living/ canadian-immunization-guide-part-4-active-vaccines/page-8-herpes-zoster-(shingles)-vaccine.html 3. Ministère de la Santé et des Services sociaux du Quebec. February 2022. Accessed August 2022. https://www.msss.gouv.qc.ca/professionnels/ vaccination/piq-vaccins/zona-su-vaccin-sous-unitaire-contre-le-zona/. 4. Gershon AA, et al. Nat Rev Dis Primers. 2015;1:15016. 5. SHINGRIX [product monograph]. Mississauga, ON: GlaxoSmithKline Inc. Revised November 24, 2021. Accessed August 2022. https://ca.gsk.com/en-ca/products/shingrix/ 6. © Gouvernement du Québec, 2019. Comité sur l'immunisation du Québec. 7e éd. Section Zona-SU. The original French version of this information was published in 2019 by the Department of Health and Social Services. The Dept. declines any responsibility for any damage, loss or injury that may result from this translation into English. In case of contradiction between the English and French versions of this information, the latter it will prevail. The Government of Quebec is and remains the only copyright owner of the work in French. 7. McGirr A, et al. Vaccine. 2021;39(25):3397-3403.

Co-administration of vaccines

NACI's general recommendation on coadministration:

- In general, inactivated vaccines may be administered concomitantly with, or at any time before or after, other inactivated vaccines or live vaccines.
- Exceptions include different formulations of vaccine that protect against the same disease, which should be administered at different visits (for example, pneumococcal conjugate and pneumococcal polysaccharide vaccines).
- Different injection sites and separate needles and syringes should be used for concomitant parenteral injections.

https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-10-timing-vaccine-administration.html

Co-administration of vaccines

SHINGRIX

Studies in immunocompetent subjects ≥50 years of age evaluated the immunogenicity and safety of two doses of SHINGRIX when the first dose was concomitantly administered with another unadjuvanted vaccine:

1st dose of SHINGRIX vaccine[1]

Pneumovax 23[2]

PCV13[3]

Boostrix[4]

Fluarix Quadrivalent[5]

Moderna's original C-19 mRNA as a booster[6]

Co-administration of SHINGRIX with the above listed vaccines does not interfere with the immune response to any of the antigens in either vaccine.

1. SHINGRIX (herpes zoster vaccine). Product Monograph. Mississauga, ON: GlaxoSmithKline Inc; Nov 2022. 2. Maréchal C et al. Vaccine 2018;36:4278-4286; 3. Min J.-Y. et al. J Infect 2022;84:490-498; 4. Strezova A et al. Vaccine 2019;37:5877-5885; 5. Schwarz TF et al. J Infect Dis 2017;216:1352-1361; 6. Naficy A et al. doi: https://doi.org/10.1101/2023.03.10.23286967

Co-administration of vaccines

AREXVY

ACIP advises that co-administration of RSV vaccines with other adult vaccines is acceptable*

In clinical studies, co-administration of an RSV vaccine with a seasonal influenza vaccine (quadrivalent, high dose, and adjuvanted influenza vaccines) met non-inferiority criteria for immunogenicity**

Seasonal influenza vaccines

COVID-19 vaccines

Pneumococcal vaccines

Td/Tdap

Recombinant zoster vaccine (Shingrix)

Evidence of increased reactogenicity with coadministration of RSV and influenza vaccines is mixed.

*Given the lack of data on coadministration of RSV with other recommended vaccines, **ACIP recommends that decisions to co-administer should consider:**

- Patient immunization status for recommended vaccines
- Feasibility of the patient attending multiple appointments
- Risk for acquiring vaccine-preventable disease
- Vaccine reactogenicity profiles
- Patient preferences

**Except the FluA/Darwin H3N2 strain when AREXVY was co-administered with adjuvanted quadrivalent inactivated influenza vaccine. RSV and influenza antibody titers were somewhat lower with
coadministration; however, the clinical significance of this is unknown.
ACIP, Advisory Committee on Immunization Practices.
Melgar M, et al. MMWR Morb Mortal Wkly Rep 2023;72:793–801.
https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-10-timing-vaccine-administration.html

Practice points: Optimizing adult immunizations

1 DISCUSS
Make it routine

Build a habit of talking about vaccination.

Prioritize prevention.
Ensure immunization discussions aren't lost amid other concerns.

Take responsibility for the discussion.
Don't assume another HCP will take the lead.

2 RECOMMEND
Make it clear

Make the recommendation.
HCP recommendations are a major factor in achieving high rates of vaccine uptake.[51]

Communicate with authenticity and confidence.
Consider sharing if you or a family member have received the vaccine. The actions of a trusted professional are often more compelling than data.

Keep patients accountable.
Follow up with patients who want to "think about it." Document patient decisions to opt out of vaccination and consider asking for a signature to acknowledge this refusal.

Take a presumptive approach.
Telling rather than asking about vaccinations is seen as a stronger recommendation.[52]

3 ADMINISTER
Make it easy

Consider co-administration where appropriate.

Summary/Goals

1. Let's normalize the conversation re vaccine and disease prevention

2. Each patient, each visit should be updated, and reviewed before the onset of the fall respiratory diseases

3. Understanding the value of adult vaccine, let's educate and advocate

4. Adult vaccine is an ongoing process of prevention and good health, stabilizing those with comorbid conditions, preventing increasing frailty

Thank You!

Questions?

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