The 2022 – 2023 Influenza Season: Influenza in the Older Adult (65+) – "*It's Not Just a Cold*"

Welcome

September 8, 2023 – Calgary, Alberta

Presented by Anjli Acharya, B.Sc. (Pharm)

Sponsored by SANOFI PASTEUR

Disclosure

Presenter's Name: Anjli Acharya

I have the following relationships with commercial interests:

- Advisory Board/Speakers Bureau: GSK virtual advisory board herpes zoster - June 2022, Sanofi Quadrivalent Recombinant Influenza Vaccine (RIV4*) Speaker Bureau (Online/Virtual) June 2022
- Funding (Grants/Honoraria) : [n/a]
- Research/Clinical Trials: [n/a]
- Speaker/Consulting Fees: Sanofi Pasteur, GSK

Speaking Fees for current program:

- I have received a speaker's fee from Sanofi Pasteur for this learning activity

SPCA.FLHD.19.08.0052

Commercial Support Disclosure

This learning activity has received financial support from Sanofi Pasteur in the form of an unrestricted educational speaker honoraria.

SPCA.FLHD.19.08.0052

Learning Objectives

1. Recognize the importance of influenza vaccination in adults over the age of 65 for limiting the medical and functional impact of influenza in this population.

2. Describe the burden of influenza disease beyond the respiratory system and the concept of immunosenescence.

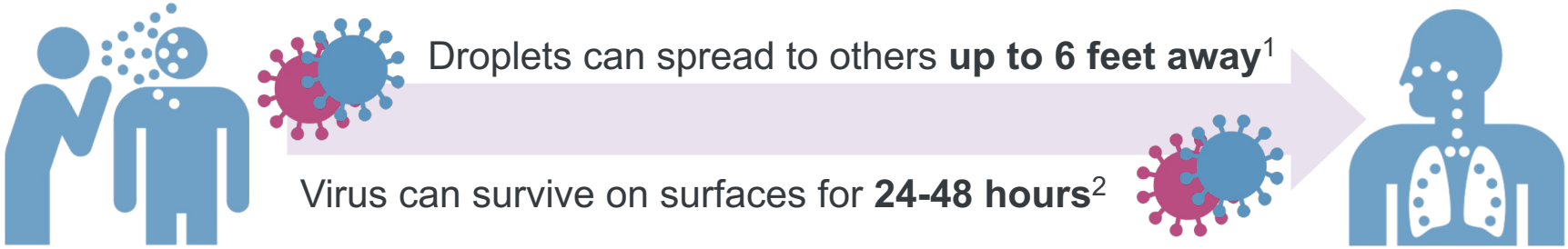
3. Review seasonal flu vaccines available for adults aged 65 and older based on the National Advisory Committee on Immunization (NACI) Statement for 2022-2023 including a brief pneumococcal vaccine update.

4. Address patients' and caregivers' concerns around vaccine selection and hesitancy to immunize.

Influenza and Older Adults

Influenza in Older Adults: A Highly Contagious Respiratory Infection

Transmission occurs mainly by droplets made when someone with the flu coughs or sneezes



Older adults can be at **increased risk of exposure** due to close living quarters and shared caregivers in long-term care[3]

Older adults are more susceptible to the flu due to **immunosenescence**:

A natural and progressive weakening of the immune system with age

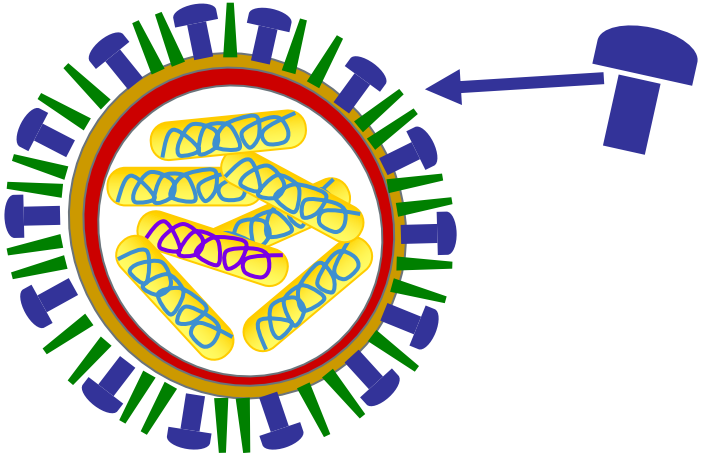
- **Higher incidence** and **severity** of infectious diseases, including influenza[4,5]
- **Lower strength** and **persistence** of antibody responses to vaccines[4,5]

References

1. Centers for Disease Control and Prevention. (2018). How Flu Spreads. Retrieved from https://www.cdc.gov/flu/about/disease/spread.htm
2. Kramer, A., et al. (2006). *BMC Infect Dis, 6*, 130.
3. Pop-Vicas, A., & Gravenstein, S. (2011). *Gerontology, 57*(5), 397-404.
4. Doherty, M., et al. (2016). *Vaccine, 34*(52), 6681-6690.
5. McElhaney, J. E., et al. (2016).. *Front Immunol, 7*, 41.

SPCA.FLHD.19.08.0052

Influenza Virus



Hemagglutinin (H) Protein

- Helps the influenza virus get into our cells

Influenza vaccines teach our immune systems to recognize the hemagglutinin (H) protein and neutralize the virus

However, influenza viruses survive as a population of viruses, with **varying hemagglutinin proteins**

1. Bouvier NM, Palese P. The Biology of Influenza Viruses. Vaccine. 2008;26(Suppl 4):D49-D53.
2. Center for Disease Control and Prevention. CDC Public Health Grand Rounds: Public Health Response to Severe Seasonal Influenza. January 16, 2018. Retrieved from: https://www.cdc.gov/grand-rounds/pp/2018/20180116-severe-influenza-H.pdf

Diversity of the Influenza Viruses

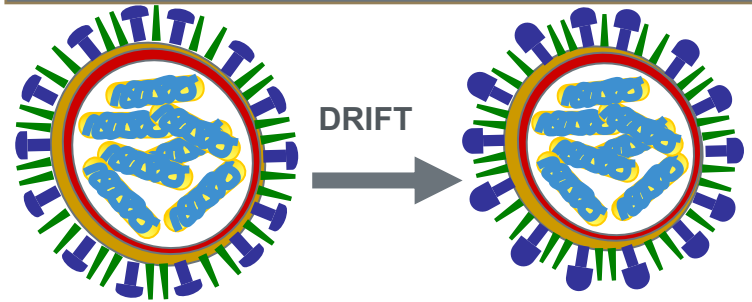
 Influenza A Virus	 Influenza B Virus
Can cause **epidemics and pandemics**[2]	Generally causes milder **epidemics**[2]
Can cause **serious** disease[2]	Causes **fewer cases** of disease than A, but can cause serious disease[2]
Circulates in both **animal** and **human** species[1,2]	Predominately circulates in **human** populations[1,2]
Cause of **seasonal, avian and swine influenza**[2]	Cause of **seasonal influenza**[2]
Up to 198 potential subtypes, all with numerous potential strains[4]	**2 circulating lineages, each with numerous potential strains**[4]

1. Bouvier NM, Palese P. (2008). The Biology of Influenza Viruses. Vaccine;26(Suppl 4):D49-D53.
2. Taubenberger JK, Morens DM. (2008). . Annu Rev Pathol;3:499-522
3. McCauley et al. (2012). Ninth Report of the International Committee on Taxonomy of Viruses. Virus Taxonomy. p749-761.
4. Centers for Disease Control and Prevention (19 Nov, 2019). Types of Influenza. https://www.cdc.gov/flu/about/viruses/types.htm

Influenza Viruses are constantly evolving

Antigenic **DRIFT**

Minor changes associated with annual outbreaks or limited epidemics[1,2]

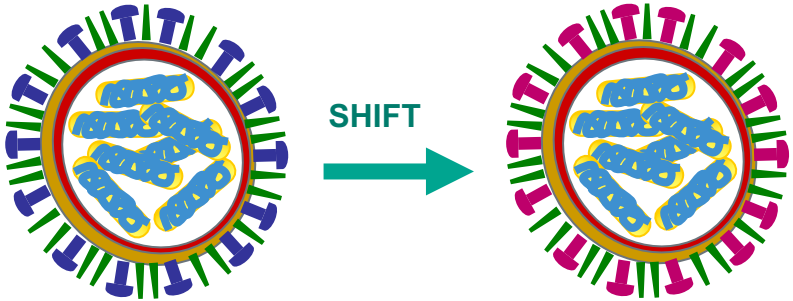


H1N1 Strain 03 → H1N1 Strain 05

Requires updating vaccine strains to match predicted strains that will be circulating[1,2]

Antigenic **SHIFT**

Major change resulting in new subtype with a new HA protein (and sometimes NA), and can lead to pandemics[1,2]



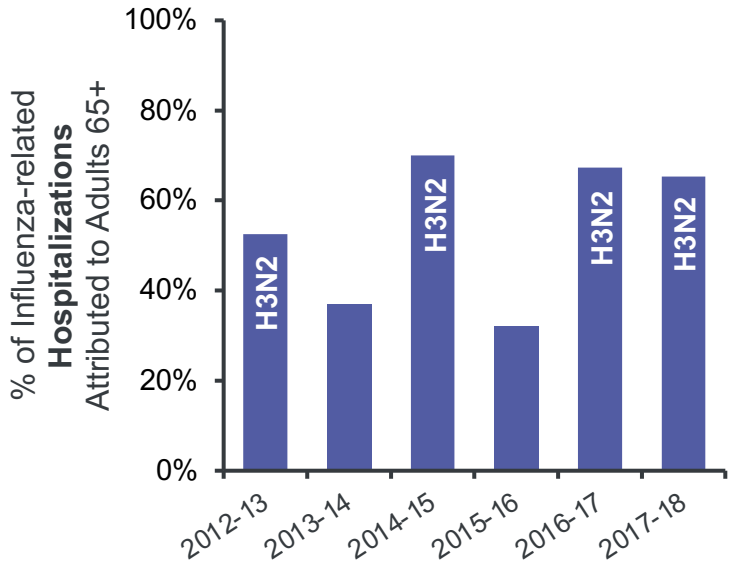
H1N1 → H3N1

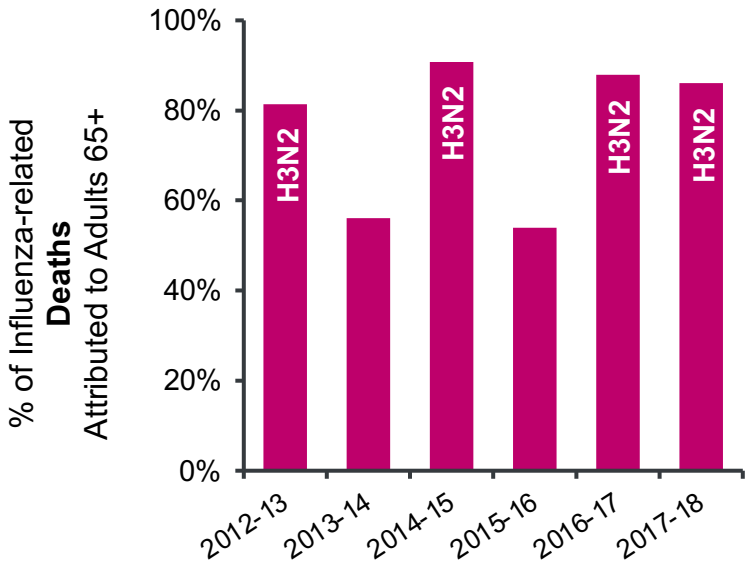
Antigenic drift and shift can result in novel influenza viruses

Individuals with immunity to the original strain/subtype **will not** have immunity to the new strain/subtype[1,2] .

Bouvier NM, Palese P. The Biology of Influenza Viruses. Vaccine. 2008;26(Suppl 4):D49-D53.
Taubenberger JK, Morens DM. The Pathology of Influenza Virus Infections. Annual review of pathology. 2008;3:499-522

The Most Severe Outcomes for Adults 65+ Occur During A/H3N2 Seasons





Fraction of reported influenza-related hospitalizations or deaths attributed to adults 65+.
H3N2 labels indicate seasons where >88% of subtyped cases were A/H3N2 (unmarked seasons were <10%).
Adapted from FluWatch reports from the Public Health Agency of Canada[1-6].

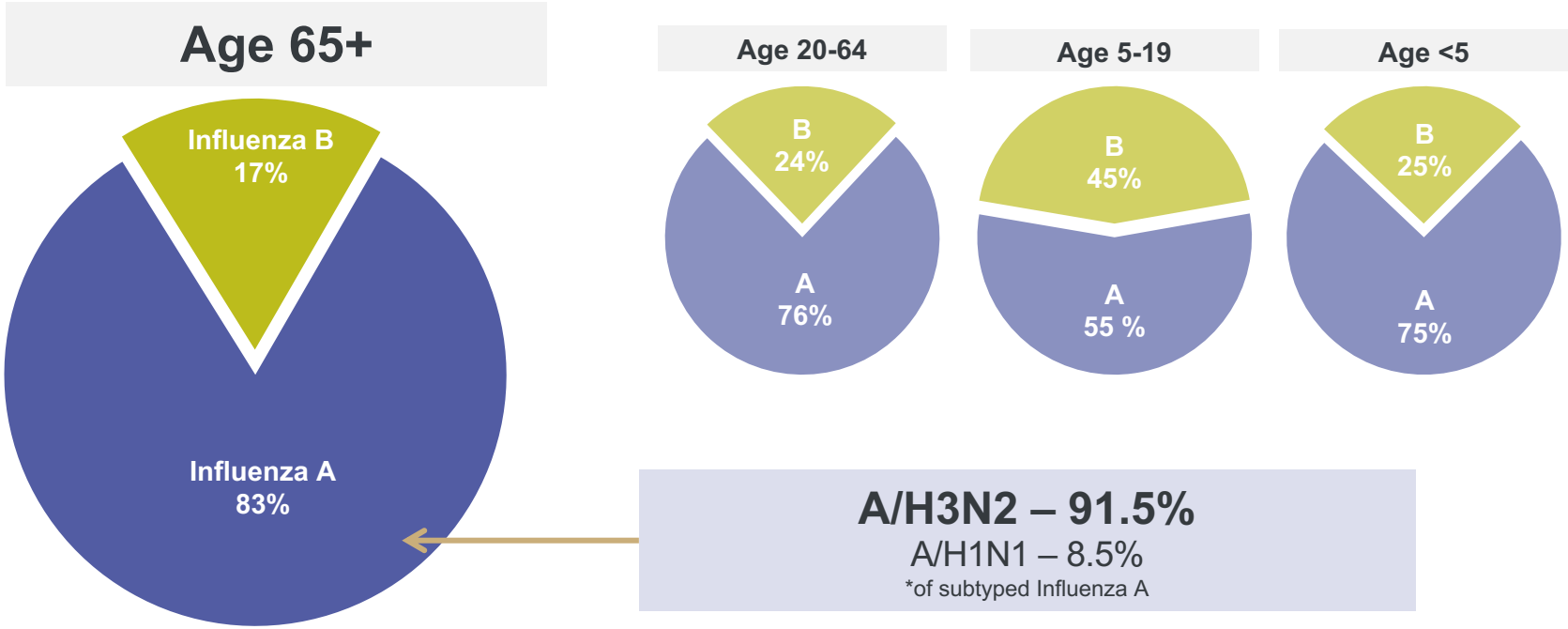
Adults 65+ account for a **majority** of influenza-related hospitalizations and deaths during **A/H3N2 seasons**

References:
1-7. Public Health Agency of Canada. (2012-2018). FluWatch reports. *See slide notes for full references.*

SPCA.FLHD.19.08.0052

Influenza in Adults 65+ is Predominantly Caused by the A/H3N2 Strain

Relative contribution of influenza strain in laboratory-confirmed influenza cases in Ontario (2010-2017)[1]



SPCA.FLHD.19.08.0052

References:

1. Public Health Ontario. (2018). Influenza Vaccines for Children and Adults 65 Years of Age and Over for the 2018-2019 Influenza Season https://www.publichealthontario.ca/-/media/documents/influenza-vaccines-2018-19.pdf?la=en (Accessed Feb 28, 2019)

Influenza: More than just a ‘cold’

Influenza is a severe respiratory illness that can have serious consequences[1]

Symptoms[1]	Cold	Influenza
Fever	Rare	**Usual**
Headache	Rare	**Usual**
Chest discomfort, coughing	Sometimes (mild)	**Usual**
Aches and pain	Sometimes (mild)	**Usual**
Extreme fatigue	Unusual	**Usual**
Weakness	Sometimes (mild)	**Usual**
Stuffy, runny nose	Common	Common
Sneezing	Sometimes	Common
Sore throat	Common	Common
Potential complications	Sinus congestion, earache	**Pneumonia, worsening chronic conditions, life-threatening**

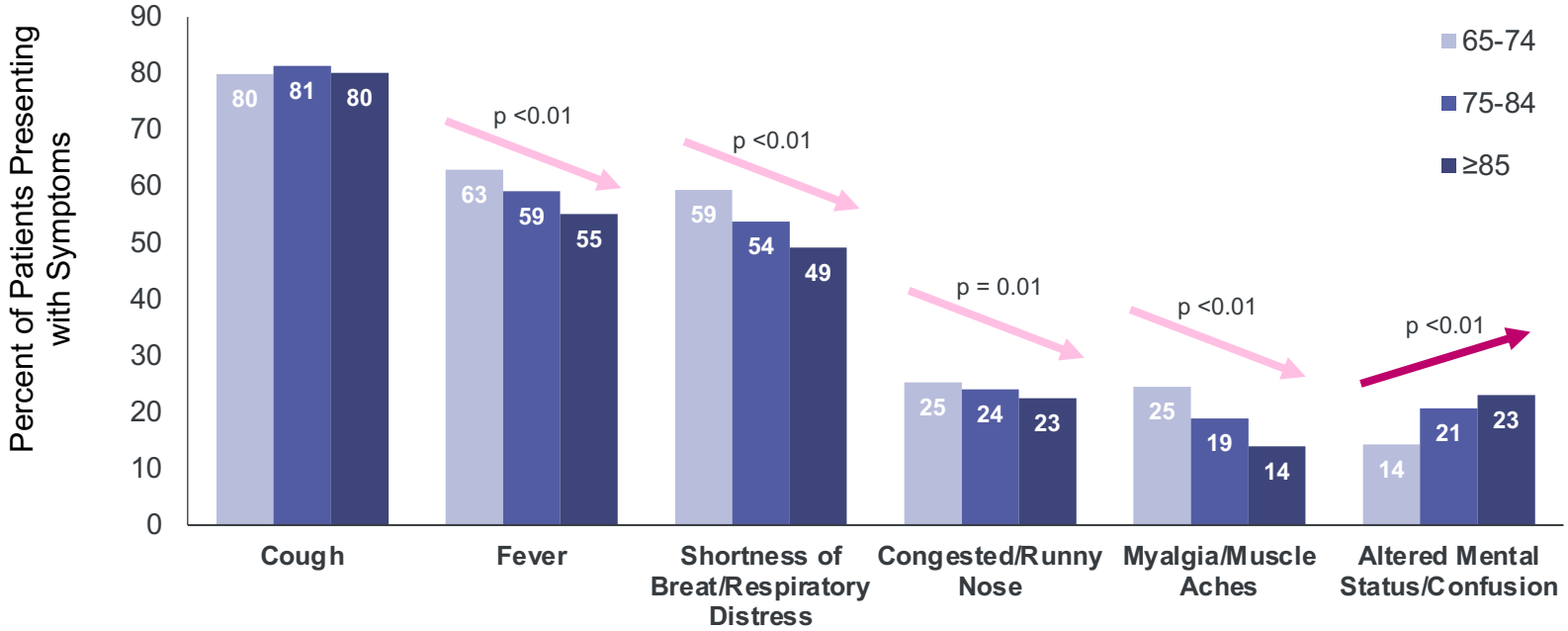
COVID-19

References

1. KFL&A Public Health. (2019). Flu Facts. Retrieved from https://www.kfhn.ca/news-events/news-patient-info/flu-facts/

Older Adults May Present with Different Symptoms of Influenza

Among adults age 65+ hospitalized with influenza, the clinical presentation varied by age



Acute signs or symptoms at admission of older adult patients hospitalized with laboratory confirmed influenza (N = 10,548) during the 2014/15 season in the US. Top 6 shown, adapted from Czaja *et al*.[1]

SPCA.FLHD.19.08.0052

Influenza: Impact on the Canadian Healthcare System

SPCA.FLHD.19.08.0052

The true burden of influenza may be **under appreciated** because incidents are often underreported.[1] The estimated burden of influenza in Canada includes:

175,000

Emergency room visits[2]

12,200

Hospital admissions[1]

3,500

Deaths[1]

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

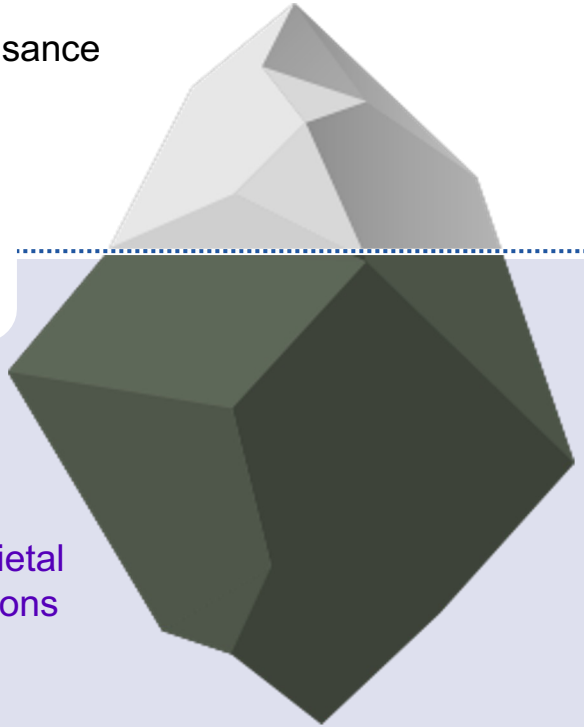
References:

National Advisory Committee on Immunization (NACI). (2019). Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2019-2020.
National Advisory Committee on Immunization (NACI). (2016). A Review of the Literature of High Dose Seasonal Influenza Vaccine for Adults 65 Years and Older.
BC Centre for Disease Control. (2013). BC Influenza Prevention Policy: a discussion of the evidence

The True Public Health Impact Of Influenza Is Underappreciated[1, 2]

Perception
Influenza is just a short-term nuisance & vaccination isn't worth it

Laboratory-confirmed or diagnosed influenza is only the tip of the iceberg



- **Fever**
- **Headache**
- **Muscle pain**
- **Cough**

- **Pneumonia**
- **Heart attack, stroke**
- **Exacerbation of underlying chronic illnesses (e.g. diabetes, asthma, COPD)**
- **Loss of independence**
- **Death**

But
True medical, economical & societal burden of influenza & complications is underappreciated[1]

SPCA.FLHD.19.08.0052

Centers for Disease Control and Prevention. Disease Burden of Flu. Accessed October 19, 2021. Retrieved from: https://www.cdc.gov/flu/about/burden/index.html
European Center for Disease Prevention and Control. Factsheet about Seasonal Influenza. Accessed October 19, 2021. Retrieved from: https://www.ecdc.europa.eu/en/seasonal-influenza/facts/factsheet

Hospitalization Due to Influenza can Result in Serious Outcomes

The Canadian Immunization Research Network (CIRN) found that the **average hospitalization** due to influenza in adults (16+):

Lasted for **10.8 days**
(95% CI: 10.3 – 11.3)

… and frequently led to serious outcomes

61.7% in-hospital complications

14.4% ICU admission

8.6% mechanically ventilated

5.7% 30-day hospital readmission

9.3% 30-day mortality

2011/12 – 2013/14 average of 2943 hospitalizations from AB, BC, ON, QC, NB, NS[1]

Reference:
1. Ng, C., et al. (2018). *Influenza Other Respir Viruses, 12*(2), 232-240.

Hospitalization and Mortality Occurs Disproportionately in Adults 65+

While Canadian adults age 65+ represented **only about 17%** of the Canadian population[1]

they accounted for up to

62% of **hospitalizations** due to influenza†

and

78% of **deaths** due to influenza†

† Based on Canadian provincial and territorial influenza surveillance data published in FluWatch reports from 2013 through 2018. Rates presented represent an average of these seasons.[2]

References:
1. Statistics Canada. (2017). 91-215-X Annual Demographic Estimates: Canada, Provinces and Territories, 2017.
2. Public Health Agency of Canada. (2013-2018). FluWatch reports. (see full references in notes)

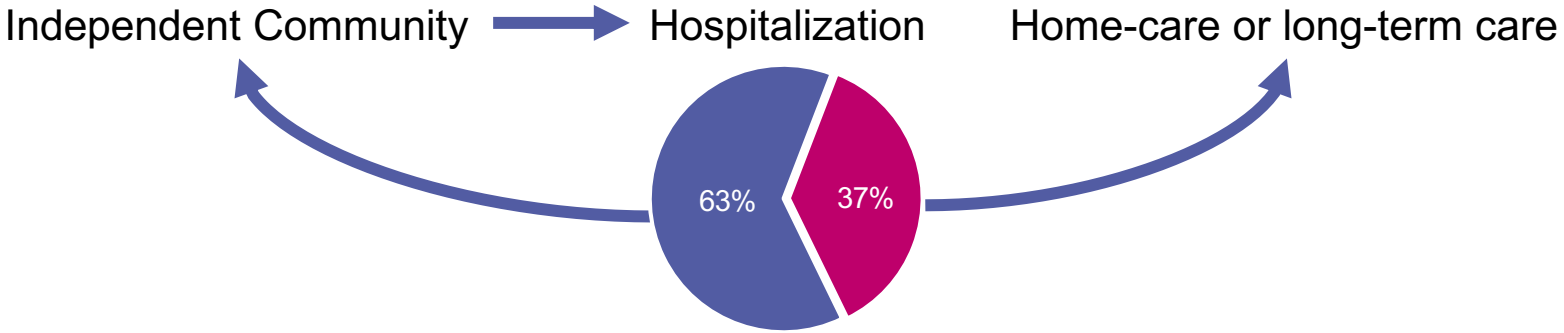
Hospitalization of Older Adults Can Lead to a Loss of Independence

Loss of independence

was the biggest fear of a majority of polled Canadians age 65+[1]

Hospitalization can lead to long-term dependence

Over one third of community-dwelling Ontarians age 65+ discharged from non-elective hospital stays were discharged to **home-care** or **long-term care**[2]



References:
1. Canadian Association of Retired Persons. (2016). Important Survey on Seniors' Health. http://www.carp.ca/2017/07/03/preventing-seasonal-flu-canada
2. Gruneir, A., et al. (2018). *CMAJ, 190*(38), E1124-E1133.

Hospitalization of Older Adults Can Lead to Functional Decline

Usual Aging	Hospitalization & Bed Rest	Disability	Dependency
↓ Strength, stability ↓ Bone density Fragile skin Urinary incontinence	Altered diet Immobilization Accelerated bone loss Pressure sore	Dehydration, malnutrition Deconditioning Syncope Fall, fracture	In-home care Long-term care

*Adapted from Creditor[1]

Heart and Stroke Foundation of Canada. "Make Health Last. What will your last 10 years look like?" Online video clip. Youtube. February 4, 2013

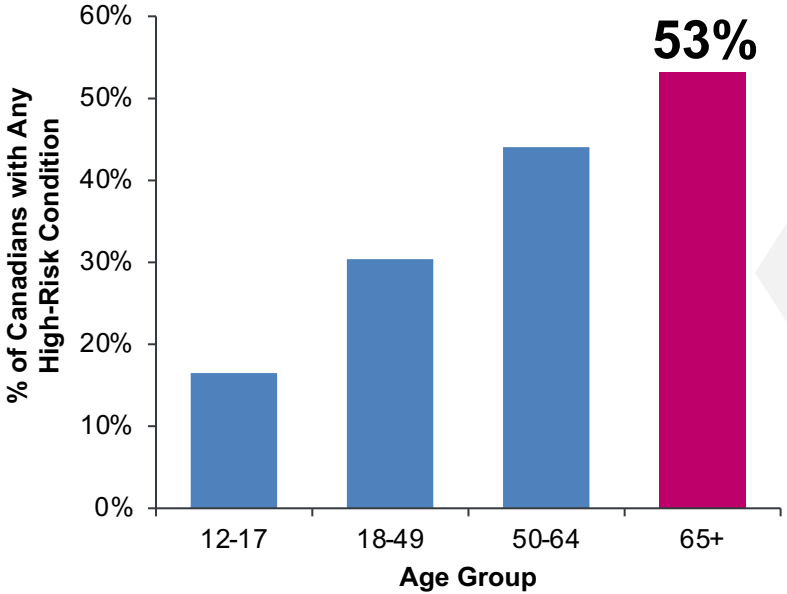
Influenza can produce **significant**, **long-lasting** functional decline in older adults[2]

References:
1. Creditor, M. C. (1993). *Ann Intern Med, 118*(3), 219-223.
2. Pop-Vicas, A., & Gravenstein, S. (2011). *Gerontology, 57*(5), 397-404.

Serious Outcomes of Influenza in Older Adults

Older Adults are at Risk of Influenza Exacerbating Chronic Conditions

The presence of **underlying comorbid conditions** further increases the risk of death from influenza[1]



High-Risk Chronic Conditions

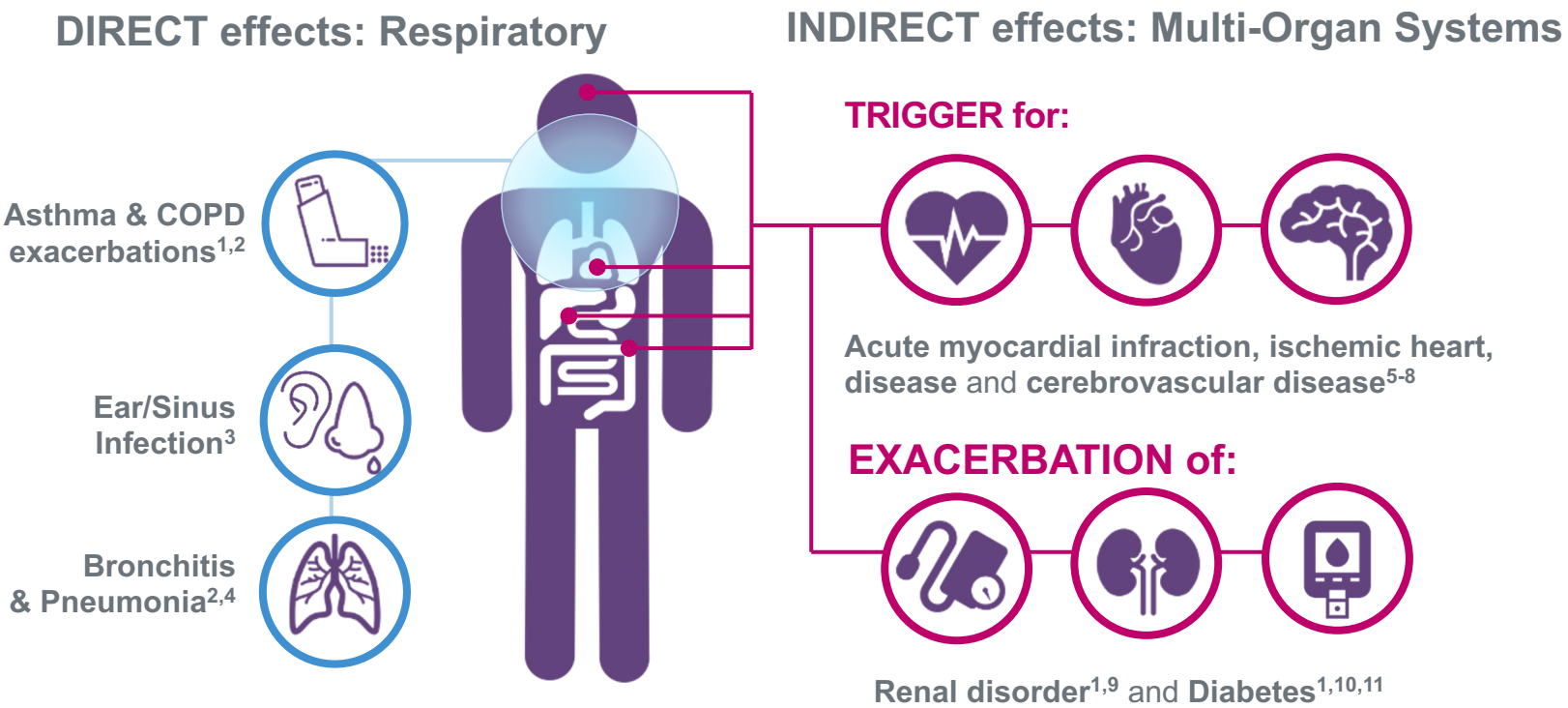
Over half of Canadians age 65+ reported having **AT LEAST** one of the following high-risk conditions[2]

- Asthma
- Cancer
- COPD
- Diabetes
- Obesity
- Heart disease
- Stroke

SPCA.FLHD.19.08.0052

References:
1. Pop-Vicas, A., & Gravenstein, S. (2011). *Gerontology, 57*(5), 397-404.
2. Statistics Canada. (2019). *Canadian Community Health Survey, 2015-2016: Annual component[public-use microdata file]*.

Influenza Causes Direct and Indirect Complications

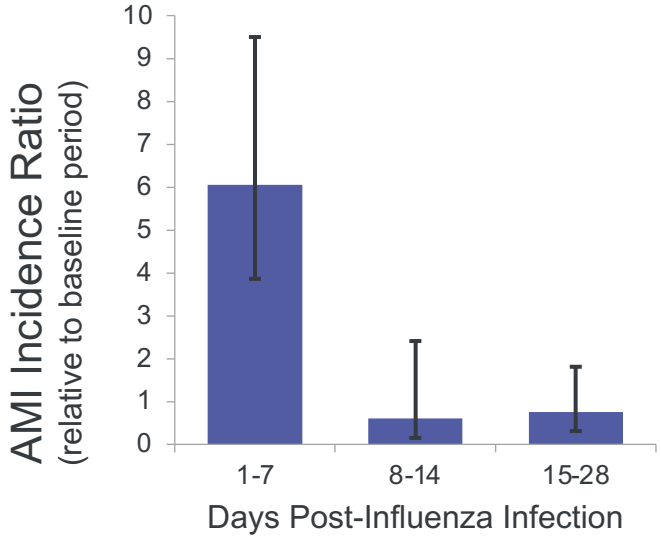


References:

1. National Advisory Committee on Immunization (NACI). (2019). Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2019-2020.
2. Kopsaftis, Z., et al. (2018). *Cochrane Database Syst Rev, 6*, CD002733.
3. Norhayati, M. N., et al. (2017). *Cochrane Database Syst Rev, 10*, CD010089.
4. Walter, N. D., et al. (2010). *Clin Infect Dis, 50*(2), 175-183.
5. Udell, J. A., et al. (2013). *JAMA, 310*(16), 1711-1720.
6. Udell, J. A., et al. (2015). *Expert Rev Cardiovasc Ther, 13*(6), 593-596.
7. Kwong, J. C., et al. (2018). *N Engl J Med, 378*(4), 345-353.
8. Boehme, A. K., et al. (2018). *Ann Clin Transl Neurol, 5*(4), 456-463.
9. Chen, C. I., et al. (2016). *Medicine (Baltimore), 95*(5), e2588.
10. Lau, D., et al. (2014). *Diabetologia, 57*(4), 690-698.
11. Campbell, A., et al. (2010). *CMAJ, 182*(4), 349-355.

Influenza is Associated with Increased Risk of Acute Myocardial Infarction

The incidence of acute myocardial infarction (AMI) is **6x** higher during the 7 days post-influenza



Incidence ratio (±95% CI) for acute myocardial infarction (AMI) following influenza infection, relative to control interval. Adapted from [1]

The incidence ratio (IR) for AMI was *higher in adults 65+*

Age 65+	IR: **7.31** (4.53 – 11.79)
Age <65	IR: 2.38 (0.59 – 9.66)

And even in adults with *no previous history of AMI*

No previous AMI	IR: **6.93** (4.24–11.33)
Previous AMI	IR: 3.53 (1.12 – 11.14)

References:
1. Kwong, J. C., et al. (2018). *N Engl J Med, 378*(4), 345-353.

The NEW ENGLAND JOURNAL of MEDICINE

Heart and Lung Disease Increase the Risk of Influenza-Attributed Death

For Canadians aged 65+ admitted to hospital with a respiratory complication, the risk for **influenza-attributed death** was:

5x greater among those with chronic heart diseases[1]

12x greater among those with chronic lung diseases[1]

20x greater among those with **both** chronic heart and lung conditions[1]

References:
1. Schanzer, D. L., et al. (2008). *Vaccine, 26*(36), 4697-4703.

Influenza is More Frequent and Severe in Patients with Diabetes

Adults with diabetes are more susceptible to serious influenza-attributable illness:

- Canadian adults with diabetes had a **6% higher risk of hospitalization due to influenza** (95%CI 2%-10%) compared to adults without diabetes (Manitoba 2000-08)[1]

Among patients in Canada hospitalized with influenza during the 2009 H1N1 pandemic, patients with diabetes were at a **higher risk of severe outcomes**[2]

2.2-fold (95%CI 1.7 – 3.0) relative risk of **ICU Admission**

2.7-fold (95%CI 1.5 – 4.7) relative risk of **Death**

References:
1. Lau, D., et al. (2014). *Diabetologia, 57*(4), 690-698.
2. Campbell, A., et al. (2010). *CMAJ, 182*(4), 349-355.

Pneumococcal Disease and Influenza

Some pneumococcal diseases are vaccine preventable.

Pneumococcal disease is caused by different types of *Streptococcus pneumoniae ('strep') bacteria.*

- These bacteria can cause ear infections, sinus infections or bronchitis.
- They can cause serious and life-threatening infections of the lungs (pneumonia), of the blood (bacteremia) and the lining that covers the brain (meningitis).
- Permanent complications include brain damage and deafness.
- For every 100 people who get pneumococcal disease, up to 7 could die.
- People with certain medical conditions have a high risk of having pneumococcal disease.

Bacterial pneumonia is a secondary cause of infection and complication in influenza infections

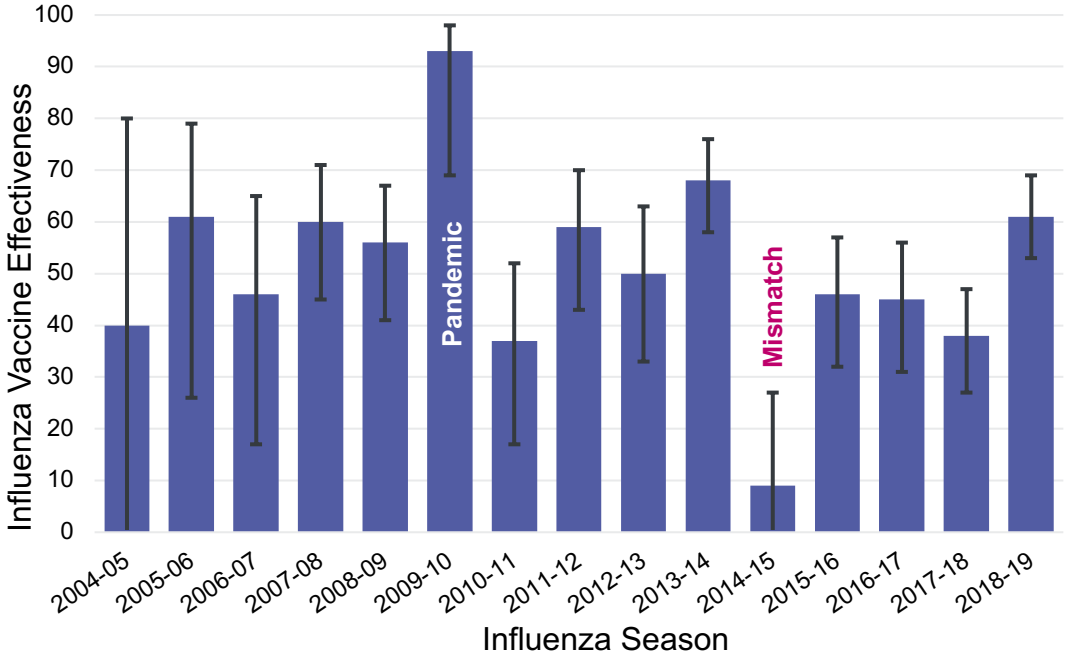
SPCA.FLHD.19.08.0052

Influenza Vaccination for Older Adults

Vaccination is Effective in Preventing Influenza

Canadian surveillance data consistently demonstrates the **protective benefit** of vaccination against influenza[1]

However, in older adults, vaccine efficacy is about **half** of that in healthy adults[2]



Annual estimates of influenza vaccine effectiveness (all ages, all subtypes) from case-control test negative design studies of Canada's Sentinel Physician Surveillance Network.[1]

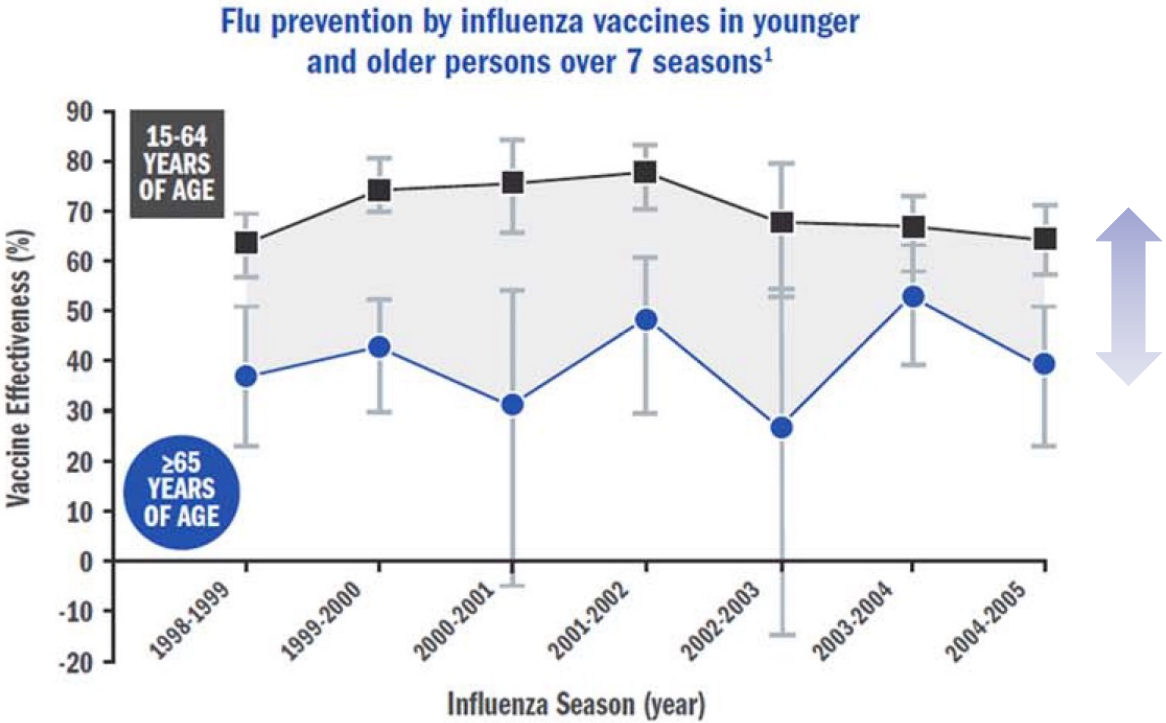
SPCA.FLHD.19.08.0052

Reference

. B.C. Centre for Disease Control. (2019) Influenza vaccine effectiveness findings from the Canadian SPSN over the past 15 years. http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Publications/Epid/Influenza%20and%20Respiratory/SPSN_VE_By_Year_Table.pdf

. National Advisory Committee on Immunization (NACI). (2019). Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2019-2020.

Influenza Vaccines are Among the most Effective Means to Prevent Influenza But are Generally Less Effective in Adults 65+



Average vaccine effectiveness by age from the French Sentinel Network, 1998-2005.
Adapted from Legrand, J., et al. (2006).[1]

SPCA.FLHD.19.08.0052

References:
1. Legrand, J., et al. (2006). *Vaccine, 24*(44-46), 6605-6611.

Vaccination is Associated with Reduced Severity of Influenza Infections

Pneumonia and Influenza together are top 10 cause of death in Canada

Among adults age 65+ hospitalized with lab-confirmed influenza (US, 2013-14), patients who were vaccinated against influenza had:

Lower odds of severe outcomes[1]

61% (95%CI 34% - 83%) lower odds of **in-hospital death**

37% (95%CI 19% - 52%) lower odds of **ICU admission**

.. and **shorter lengths of stay** (LoS)[1]

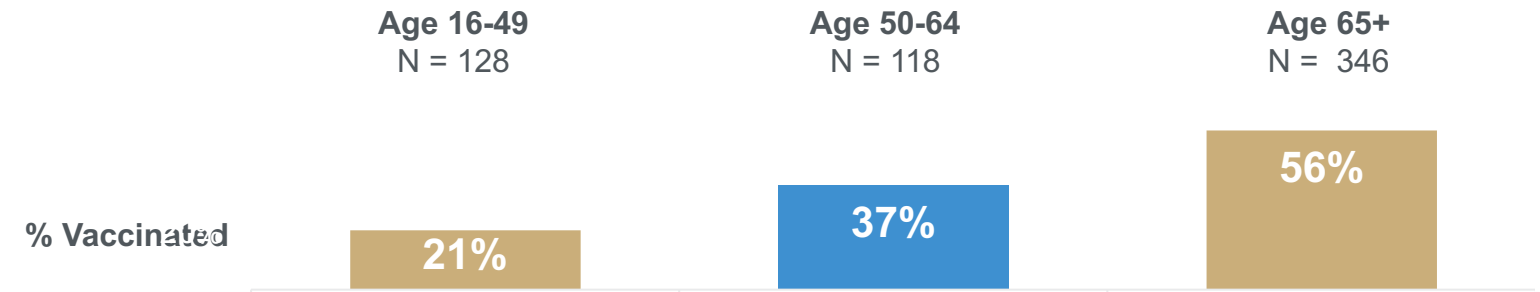
34% (95%CI 6% - 73%) higher odds of a **shorter ICU LoS**

24% (95%CI 13% - 37%) higher odds of a **shorter hospital LoS**

SPCA.FLHD.19.08.0052

Reference:
1. Arriola, C., et al. (2017). *Clin Infect Dis, 65*(8), 1289-1297.

Adults aged 50 to 64 who were hospitalized with influenza were **less likely to be vaccinated and more likely to be admitted to the ICU**, as compared to those 65+



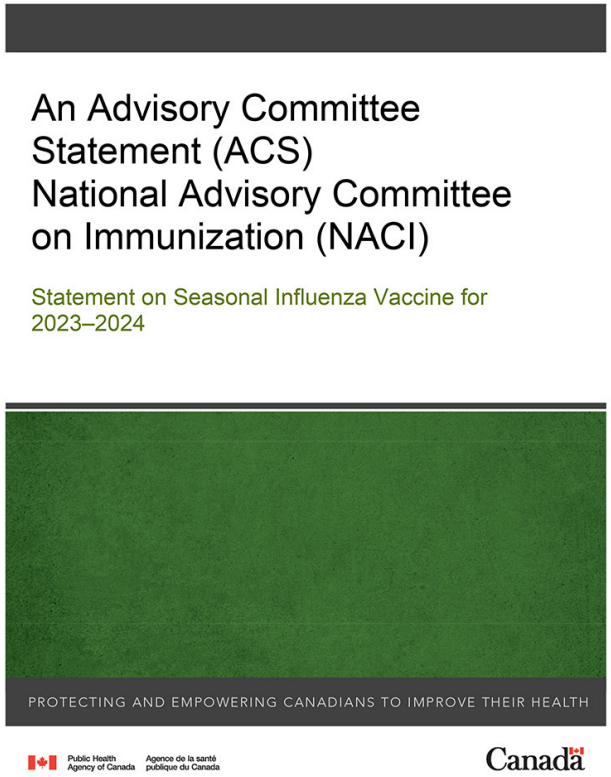
	Age 16-49 N = 128	Age 50-64 N = 118	Age 65+ N = 346
ICU Admissions	16 (12.5%)	**20 (16.9%)**	39 (11.3%)
Deaths	1 (0.8%)	3 (2.5%)	42 (12.1%)

Influenza-related hospitalizations in Canada by age via Serious Outcomes Surveillance Network (2011/2012)[1]

1. Thompson WW, et al. Epidemiology of Seasonal Influenza: Use of Surveillance Data and Statistical Models to Estimate the Burden of Disease*J Infect Dis.* 2006;194(suppl 2):S82-S91.
2. McNeil. Monitoring of Immunization and Outcomes: Experience of the Canadian Serious Outcomes Surveillance Network. 2018 Adult Immunization Forum. June 8, 2018. Retrieved from: https://immunisationcoalition.org.au/wp-content/uploads/2018/06/1-Shelly-McNeil.pdf

Influenza Vaccine Recommendations in Canada

NACI Influenza Statement



National Advisory Committee on Immunization (NACI)

- NACI is a national advisory committee of experts in medicine and public health that provides ongoing and timely medical, scientific, and public health advice
- NACI makes recommendations for the use of vaccines currently or newly approved for use in humans in Canada, and identifies groups at risk for vaccine-preventable diseases for whom vaccination should be targeted
- NACI knowledge syntheses, analyses, and recommendations on vaccine use in Canada are included in published literature reviews, statements, and updates

Reference:
1. National Advisory Committee on Immunization (NACI). (2023). *Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2023- 2024*

NACI Canadian Immunization Guide:
Chapter on Influenza and Statement on Seasonal Influenza Vaccine

Influenza vaccines are recommended for all individuals 6 mo and older, with particular focus on people at high risk of influenza-related complications or hospitalizations, including:

Individuals with chronic illnesses

- Cardiac or pulmonary disorders
- Diabetes and other metabolic diseases
- Cancer or immune compromising conditions
- Renal disease
- Rheumatologic disease
- Neurologic or neurodevelopment conditions
- Morbid obesity (BMI ≥40)

SPCA.FLHD.19.08.0052

al Advisory Committee on Immunization (NACI). (2023). *Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2023- 2024*

Recommendation Bodies: Influenza Statements

World Health Organization

"The most effective way to prevent influenza and/or severe outcomes from influenza is vaccination."[1]

Public Health Agency of Canada

"Vaccination is the most effective way to prevent influenza and its complications."[2]

Reference:
1. WHO. (2018, June 14). Influenza. Retrieved from http://www.who.int/influenza/vaccines/en/
2. National Advisory Committee on Immunization. (2019). *Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2019–2020.*

WHO Recommended Vaccine Composition

The World Health Organization recommended the following influenza strains for the 2023-2024 Northern Hemisphere influenza season[1]

SPCA.FLHD.19.08.0052

Reference:
1. https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2023-2024-northern-hemisphere-influenza-season#:~:text=For%20quadrivalent%20egg%2D%20or%20cell,Yamagata%20lineage)%2Dlike%20virus.

Influenza Vaccines in Canada

9 influenza vaccines are authorized for use in Canada by NACI in the 2023/2024 season[1]

- **Live attenuated influenza vaccine (LAIV)**
  - Intranasal spray of live attenuated influenza virus mainly for pediatric use

- **Recombinant influenza Vaccine (RIV4)**
  - Baculovirus vector for protein expression
- **Inactivated influenza vaccine (IIV4-cc)**
  - Standard dose propagated in a mammalian cell line
- **Inactivated influenza vaccines (IIV4-SD)**
  - Split virus and subunit vaccines available
- **High-dose inactivated influenza vaccine (IIV4-HD)**
  - TIV containing 4x the dose of regular influenza vaccines for adults aged 65+
- **Adjuvanted, inactivated influenza vaccine (IIV3-Adj)**
  - Pediatric and adult 65+ formulation
  - TIV containing MF59 adjuvant - an oil-in-water emulsion aged 65+

Available for use for adults **age 65+**

Reference:
1. National Advisory Committee on Immunization (NACI). (2023). *Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2023- 2024*

Comparison of Inactivated Influenza Vaccine Manufacturing Technologies

Egg-Based

- Adapt wild-type virus to grow in eggs
- Inactivated split-virus/subunit or live-attenuated vaccine
- Initial manufacturing step requires that CVVs adapt to grow well in avian cell substrate

Subject to egg-adapted mutations

IIV3-SD, IIV4-SD, IIV4-HD

Egg-Based Adjuvanted

- Manufactured using egg-based process
- Inactivated subunit vaccine formulated with MF59 adjuvant
- Initial manufacturing step requires that CVVs adapt to grow well in avian cell substrate

Subject to egg-adapted mutations

IIV3-Adj

Cell Culture Based

- Adapt wild-type virus to grow in mammalian cell culture (MDCK cells)
- Inactivated subunit vaccine
- Initial manufacturing step requires that CVVs adapt to grow well in mammalian cell line.

Subject to cell-adapted mutations

IIV4-CC

Recombinant

- Uses genetic sequence for influenza HA protein
- Program SF+ cells/other expression system to produce HA protein

Exact match to recommended strains

RIV4

(1) CDC. (2019). Key Facts About Seasonal Flu Vaccine. (2) Chen H, et al. *Mol Biol Evol. 2016. 33(12):3133-3143* (3) Robertson JS, et al. *J Gen Virol. 1993. 74 (Pt 10):2047-51* (4) CDC. 2018). How Influenza (Flu) Vaccines Are Made. (5) Wu NC, et al. *PLoS pathogens, 2017. 13(10), e1006682* (6) Zost SJ, et al. *PNAS. 2017 114 (47) 12578-12583*

NACI Statement (2023-2024)

Influenza Vaccine Recommendations for Adults 65+

Recipient	Vaccine types available	Recommendations on choice of influenza vaccine	
		Individual-level Decision-making	**Public health level Decision-making**
65 years and older	• IIV3-Adj • IIV4-cc • IIV4-HD • IIV4-SD • RIV4	•**IIV-HD should be used over IIV-SD, given the burden of influenza A(H3N2) disease and the good evidence of IIV3-HD providing better protection** compared to IIV3-SD in adults 65 years of age and older. •Other than a recommendation for using IIV-HD over IIV-SD formulations, NACI has not made comparative individual-level recommendations on the use of the other available vaccines in this age group.In the absence of a specific product, any of the available age-appropriate influenza vaccines should be used.	• **Any of the available influenza vaccines should be used** • There is insufficient evidence (cost-effectiveness assessments have not been performed) to make comparative public health program-level recommendations on the use of the available vaccines

SPCA.FLHD.19.08.0052

Reference:
1. National Advisory Committee on Immunization (NACI). (2023). *Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2023- 2024*

NACI Statement (2023-2024)

Vaccine Characteristics NACI-Efficacy and Effectiveness

"The comparison of vaccine characteristics across vaccine types, in the table below, may be considered in making a decision on the preferred vaccine option(s) for use by an individual or a public health program."

Considerations	Influenza vaccine type				
	IIV3-Adj	IIV4-HD	IIV4-SD	IIV4-cc	RIV4
Efficacy and effectiveness	Overall, insufficient comparative evidence with IIV3-SD to draw conclusion.	Expected better protection compared with IIV3-SD, particularly against influenza A(H3N2).			
		Better protection against the influenza B strain not contained in IIV3-HD.	Better protection against the influenza B strain not contained in IIV3-SD.	Expected better protection against the influenza B strain not contained in IIV3-SD.	Expected better protection against the influenza B strain not contained in IIV3-SD.
					Potentially better Protection compared with IIV4-SD.

SPCA.FLHD.19.08.0052

Vaccine Characteristics NACI - Immunogenicity

"The comparison of vaccine characteristics across vaccine types, in the table below, may be considered in making a decision on the preferred vaccine option(s) for use by an individual or a public health program."

Considerations	Influenza vaccine type				
	IIV3-Adj	IIV4-HD	IIV4-SD	IIV4-cc	RIV4
Immunogenicity	Non-inferior Immune response compared to IIV3-SD. Superiority to IIV3-SD has not been consistently demonstrated.	Expected **superior** immune response to influenza A strains compared to IIV3-SD. Superior Immune response to the additional B Strain compared to IIV3-HD.	Non-inferior immune response to the strains contained in IIV3-SD with superior immune response to the additional B strain.	Non-inferior immune response to the strains contained in IIV3-cc. Superior immune response against the influenza B strain not contained in IIV3-SD. Non-inferior response expected compared to IIV3-SD.	Expected non-inferior immune response compared to IIV4-HD,IIV4-cc, IIV3-HD, IIV3-Adj.

Vaccine Characteristics NACI - Safety

"The comparison of vaccine characteristics across vaccine types, in the table below, may be considered in making a decision on the preferred vaccine option(s) for use by an individual or a public health program."

Considerations	Influenza vaccine type				
	IIV3-Adj	IIV4-HD	IIV4-SD	IIV4-cc	RIV4
Safety	**Higher** rate of injection site reactions than IIV3-SD. Higher or comparable systemic reactions compared to IIV3-SD; systemic reactions were mild to moderate and transient. SAEs were comparable to IIV3-SD and were uncommon.	**Higher** rate of some systemic reactions than IIV4-SD and the same is expected compared to IIV3-SD; most systemic reactions were mild and transient. SAEs were rare and similar in frequency to IIV4-SD and the same is expected compared to IIV3-SDb	Pre-licensure clinical trials and post-marketing surveillance showed a similar safety profile to IIV3-SD.	Pre-licensure clinical trials showed a similar safety profile to IIV3-cc. Similar safety profile to IIV3-SD is expected.	Pre-licensure clinical trials showed a similar safety profile to IIV4-SD, IIV3-HD and IIV-Adj. Similar safety profile to IIV3-SD is expected.

High-Dose Influenza Vaccine Post-Licensure Efficacy Trial (FIM12): Superiority Demonstrated vs Standard-Dose Influenza Vaccine

High-dose influenza vaccine was developed by in response to requests for a **high-dose trivalent inactivated influenza vaccine** that would **improve antibody responses** and **better protect adults age 65+** against influenza

To **induce higher antibody levels** in adults age 65+, the High-Dose vaccine is formulated to contain:

4x the hemagglutinin antigen content compared to standard-dose vaccines[1]

High-Dose influenza vaccine is formulated to contain 60 µg hemagglutinin (HA) of each influenza strain per 0.5 mL dose, 4 times the HA content of standard-dose influenza vaccines (15 µg HA/strain)[1]

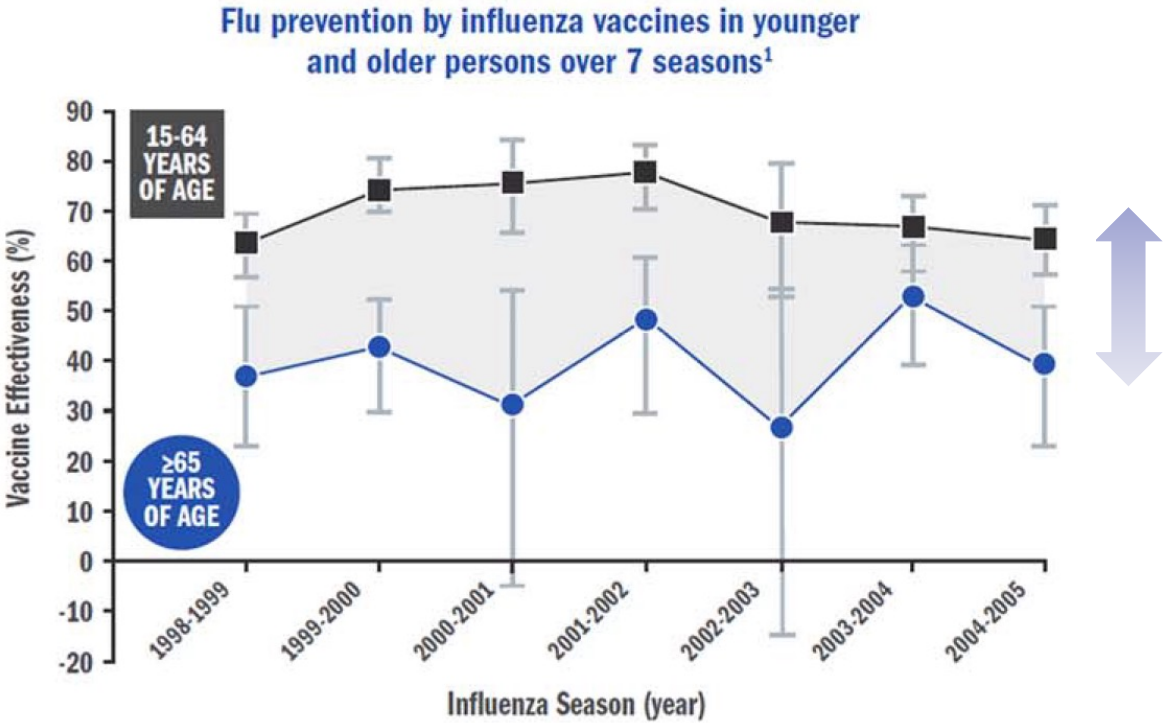
High-Dose demonstrated **superior efficacy** in preventing lab-confirmed influenza in adults age 65+:

24.2% (95%CI 9.7-36.5%) More efficacious than standard-dose influenza vaccines[1]

High dose influenza (IIV3-HD) demonstrated a relative vaccine efficacy of 24.2% (95%CI: 9.7-36.5%) compared to standard-dose IIV3-HD in preventing laboratory-confirmed influenza illness in adults age 65+ during the 2011-12 and 2012-13 seasons (1.4% of HD recipients and 1.9% of SD recipients had laboratory-confirmed influenza caused by any viral type or subtype).[2]

References:
1. Sanofi Pasteur Limited. (2019). *FLUZONE High-Dose Vaccine [Canadian Product Monograph].*
2. DiazGranados, C. A., et al. (2014). *N Engl J Med, 371*(7), 635-645

Influenza Vaccines are Among the most Effective Means to Prevent Influenza But are Generally Less Effective in Adults 65+



Average vaccine effectiveness by age from the French Sentinel Network, 1998-2005.
Adapted from Legrand, J., et al. (2006).[1]

References:
1. Legrand, J., et al. (2006). *Vaccine, 24*(44-46), 6605-6611.

NACI 2018

- There is good evidence that Fluzone® High-Dose provides superior protection[1]

(e.g., decrease in ILI, influenza-related death and all-cause hospitalization compared with standard-dose TIV in the elderly (Grade A Evidence)"[1]

ECDC 2020

- "Overall, high-dose influenza vaccines may provide better protection against laboratory- confirmed influenza and proxy outcome measures"[2]

STIKO 2021

- "Evidence of relative efficacy/effectiveness and safety is better for HD than for the three other enhanced vaccines"
- "HD shows small but significant superiority against lab-confirmed influenza and not lab-confirmed endpoints. For the other vaccines, this statement can not be made with such certainty currently"[3]

US CDC 2022

- "It was acknowledged that the most data, for the most outcomes, are available to support the high dose vaccine"[4]

NCIRS 2022

- "For HD-IIV vs. SD-IIV in 65+, the overall certainty of evidence in GRADE was rated as "Moderate"
- For MF59 vs. SD-IIV in 65+, the overall certainty of evidence in GRADE was rated as "Low"[5]

NACI

Recommendation season 2022-23[6]

- IIV-HD should be used over IIV-SD (Individual recommendation)
- Any available influenza vaccine (Public level)

STIKO

Recommendation season 2022-23[7]

- Preferential recommendation for all persons ≥ 60 years of age with inactivated, high-dose quadrivalent influenza vaccine

ACIP

Recommendation season 2022-23[4]

- "ACIP recommends that adults aged ≥65 years preferentially receive any one of the HD or adjuvanted influenza vaccines HD-IIV4, RIV4, or aIIV4"

ATAGI

Recommendation season 2023[5]

- "HD-IIV is recommended in preference to SD-IIV in adults aged ≥65 years"
- Same for Adjuvanted
- "Neither adjuvanted nor HD IIV is recommended in preference to the other in 65+"

MAT-CA-2300111 V1.0 February 2023

1. NACI: - (publications.gc.ca) ; 2. ECDC : https://www.ecdc.europa.eu/sites/default/files/documents/seasonal-influenza-vaccines-systematic-review-efficacy.pdf 3.STIKO https://edoc.rki.de/handle/176904/7510 ; 4.CDC Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022–23 Influenza Season | MMWR (cdc.gov) ; 5.NCIRS https://www.ncirs.org.au/our-work/australian-immunisation-handbook/influenza-grade-assessments ; 6. Canadian Immunization Guide Chater on Influenza and Statement on Seasonal Influenza Vaccine for 2022-2023 Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023 - Canada.ca ; 7. STIKO Epidemiologisches Bulletin 27 January 2022 Epidemiologisches Bulletin 4/2022 (rki.de)

SPCA.FLHD.19.08.0052

High-Dose Influenza Vaccine: **Clinical Overview**

High-Dose Influenza Vaccine Post-Licensure Efficacy Trial (FIM12): Relative Efficacy Against Laboratory-confirmed Influenza Illness[1-3]

Compared to IIV3-SD, the benefit of IIV3-HD was demonstrated over two seasons, across age groups, influenza types, comorbidities, and frailty-associated conditions in 32,000 community-dwelling seniors

PRIMARY ENDPOINT

24.2%

more efficacious*
(95% CI: 9.7; 36.5)
HD (n = 228 breakthrough cases)
SD (n = 301 breakthrough cases)

Demonstrated SUPERIOR EFFICACY over IIV3-SD against laboratory-confirmed influenza illness caused by any virus type or subtype in adults age 65+[1]

Similar to Vaccine Strains[1]

35.4%
(95% CI: 12.5; 52.5)

Year 1 (vaccine matched)[3]

45.3%
(95% CI: 6.9; 68.6)

Year 2 (vaccine mismatched)[3]

20.7%
(95% CI: 4.4; 34.3)

65-74 Years of Age[2]

19.7%
(95% CI: 0.4; 35.4)

75+ Years of Age[2]

32.4%
(95% CI: 8.1; 50.6)

≥1 High-Risk Comorbidity[2]

22.1%
(95% CI: 3.9; 37.0)

1 Frailty-Associated Condition[2]

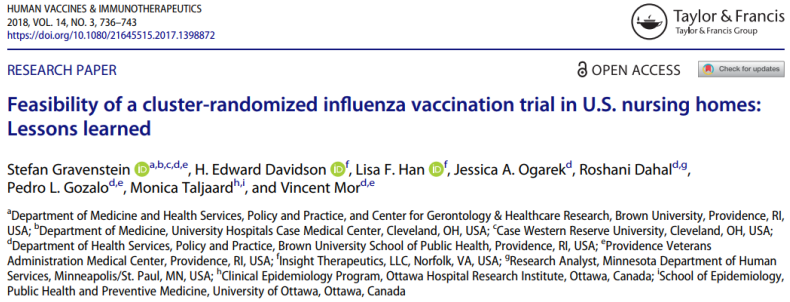
27.5%
(95% CI: 0.4; 47.4)

SPCA.FLHD.19.08.0052

References:
1. DiazGranados, C. A., et al. (2014). *N Engl J Med, 371*(7), 635-645
2. DiazGranados CA, et al. (2015). *Vaccine*, 33, 4565–4571.
3. DiazGranados, C. A., et al. (2014). *N Engl J Med, 371*(7), 635-645, supplementary appendix

Real-World Effectiveness in Nursing Home Residents

Cluster-randomized study designs developed by Gravenstein *et al* to evaluate efficacy of **IIV3-HD** vs **IIV3-SD** against multiple clinical outcomes



HUMAN VACCINES & IMMUNOTHERAPEUTICS
2018, VOL. 14, NO. 3, 736–743
https://doi.org/10.1080/21645515.2017.1398872

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

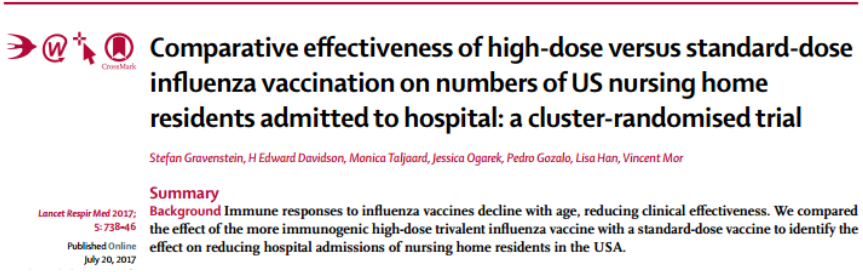
OPEN ACCESS

Check for updates

Feasibility of a cluster-randomized influenza vaccination trial in U.S. nursing homes: Lessons learned

Stefan Gravenstein[a,b,c,d,e], H. Edward Davidson[f], Lisa F. Han[f], Jessica A. Ogarek[d], Roshani Dahal[d,g], Pedro L. Gozalo[d,e], Monica Taljaard[h,i], and Vincent Mor[d,e]

[a]Department of Medicine and Health Services, Policy and Practice, and Center for Gerontology & Healthcare Research, Brown University, Providence, RI, USA; [b]Department of Medicine, University Hospitals Case Medical Center, Cleveland, OH, USA; [c]Case Western Reserve University, Cleveland, OH, USA; [d]Department of Health Services, Policy and Practice, Brown University School of Public Health, Providence, RI, USA; [e]Providence Veterans Administration Medical Center, Providence, RI, USA; [f]Insight Therapeutics, LLC, Norfolk, VA, USA; [g]Research Analyst, Minnesota Department of Human Services, Minneapolis/St. Paul, MN, USA; [h]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Canada; [i]School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, Ottawa, Canada



Comparative effectiveness of high-dose versus standard-dose influenza vaccination on numbers of US nursing home residents admitted to hospital: a cluster-randomised trial

Stefan Gravenstein, H Edward Davidson, Monica Taljaard, Jessica Ogarek, Pedro Gozalo, Lisa Han, Vincent Mor

Lancet Respir Med 2017; 5:738–46
Published Online July 20, 2017

Summary

Background Immune responses to influenza vaccines decline with age, reducing clinical effectiveness. We compared the effect of the more immunogenic high-dose trivalent influenza vaccine with a standard-dose vaccine to identify the effect on reducing hospital admissions of nursing home residents in the USA.

- Cluster randomization at **facility level** to receive either high-dose or standard-dose
  - Studies conducted over **two influenza seasons**
  - Pilot: 2012-13 season (39 nursing homes, 2,957 subjects)
  - Large scale study 2013-14 season (823 nursing homes, 53,008 subjects)

References:
1. Gravenstein, S., et al. (2018). *Hum Vaccin Immunother, 14*(3), 736-743.
2. Gravenstein, S. (2017). *The Lancet Respiratory Medicine, 5*(9), 738-746.

SPCA.FLHD.19.08.0052

Izurieta *et al* (2015): Relative Effectiveness of IIV3-HD vs IIV3-SD
Community Dwelling Medicare Recipients Age 65+ (2012-13)

IIV3-HD demonstrated **better protection** against influenza-related health outcomes, including **hospitalized influenza** and **ED visits**

Outcome	Outcomes per 10,000 person weeks		rVE (95% CI)
	IIV3-HD (n = 929,730)	IIV3-SD (n =1,615,545)	
Probable Influenza* (rapid influenza test and oseltamivir treatment)	1.01	1.30	**21.9%** (15.0-28.7)
Hospitalized influenza/ ED Visit	0.86	1.10	**21.6%** (16.1-26.7)

SPCA.FLHD.19.08.0052

***Primary outcome**
Abbreviations: ED, emergency department; rVE, Relative Vaccine Effectiveness; CI, confidence interval.

References:
1. Izurieta HS, et al. (2015). Lancet Infect Dis, 15, 293-300.

THE LANCET Infectious Diseases

Real-World Evidence – Conclusions

The relative effectiveness of IIV3-HD versus IIV3-SD has been demonstrated:

in community-dwelling seniors, and long-term care residents

for the prevention of all-cause, cardiorespiratory, and influenza/pneumonia hospitalizations

over 7 distinct influenza seasons (2010/11 through 2017/18)

Pneumococcal Vaccine Recommendations in Canada

Pneumococcal Guidelines

Pneumococcal Vaccine Timing for Adults

Make sure your patients are up to date with pneumococcal vaccination.

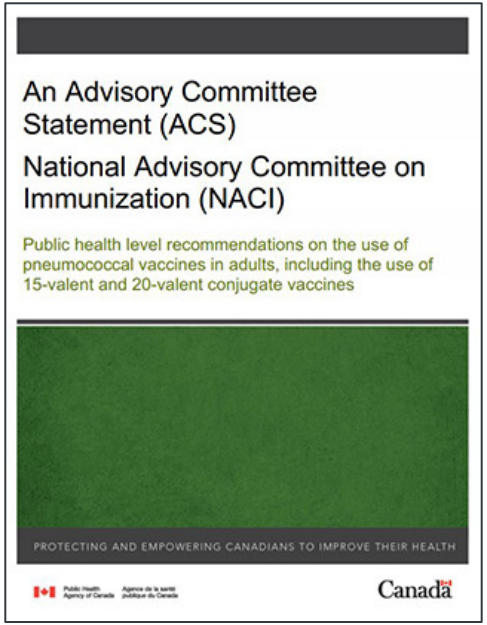
Adults ≥65 years old
Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	PCV20	PCV15 → ≥1 year† → PPSV23
PPSV23 only at any age	≥1 year → PCV20	≥1 year → PCV15
PCV13 only at any age	≥1 year → PCV20	≥1 year† → PPSV23
PCV13 at any age & **PPSV23** at <65 yrs	≥5 years → PCV20	≥5 years§ → PPSV23

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines
† Consider minimum interval (8 weeks) for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak (CSF) leak
§ For adults with an immunocompromising condition, cochlear implant, or CSF leak, the minimum interval for PPSV23 is ≥8 weeks since last PCV13 dose and ≥5 years since last PPSV23 dose; for others, the minimum interval for PPSV23 is ≥1 year since last PCV13 dose and ≥5 years since last PPSV23 dose

Shared clinical decision-making for those who already completed the series with PCV13 and PPSV23

Prior vaccines	Shared clinical decision-making option
Complete series: PCV13 at any age & **PPSV23** at ≥65 yrs	≥5 years → PCV20 — Together, with the patient, vaccine providers **may choose** to administer PCV20 to adults ≥65 years old who have already received PCV13 (but not PCV15 or PCV20) at any age and PPSV23 at or after the age of 65 years old.



References:
1. Public health level recommendations on the use of pneumococcal vaccines in adults, including the use of 15-valent and 20-valent conjugate vaccines, Feb 2023
2. https://www.cdc.gov/vaccines/vpd/pneumo/hcp/pneumo-vaccine-timing.html CDC (2023)

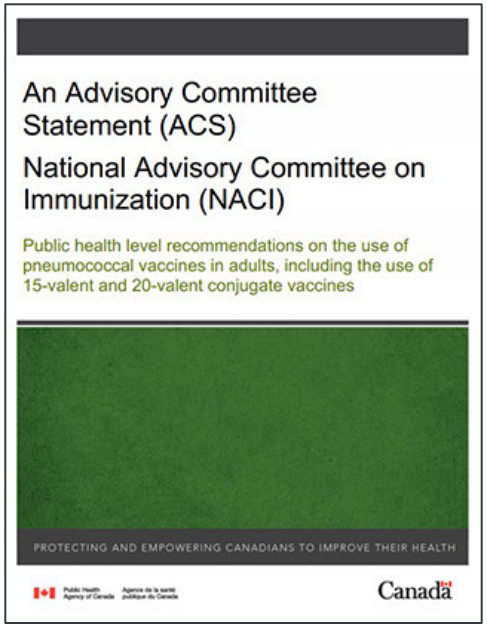
SPCA.FLHD.19.08.0052

Pneumococcal Guidelines - Alberta

AHS Provincial biologic vaccine pages and guidelines have **not** been updated

Most recent update:

- Patients with pneumococcal conjugate vaccine (PCV20) are not recommended to receive PneuC13
- A dose of PCV20 can be considered sufficient for individuals recommended PneuC13 or Pneu-C13 in combination with Pneumo-P23.
- Patients who have received PCV20 are not recommended to receive Pneumo-P at this time.
- Having received a dose of PCV 20 can be considered sufficient for individuals recommended Pneumo-P or Pneumo-P in combination with PCV13.

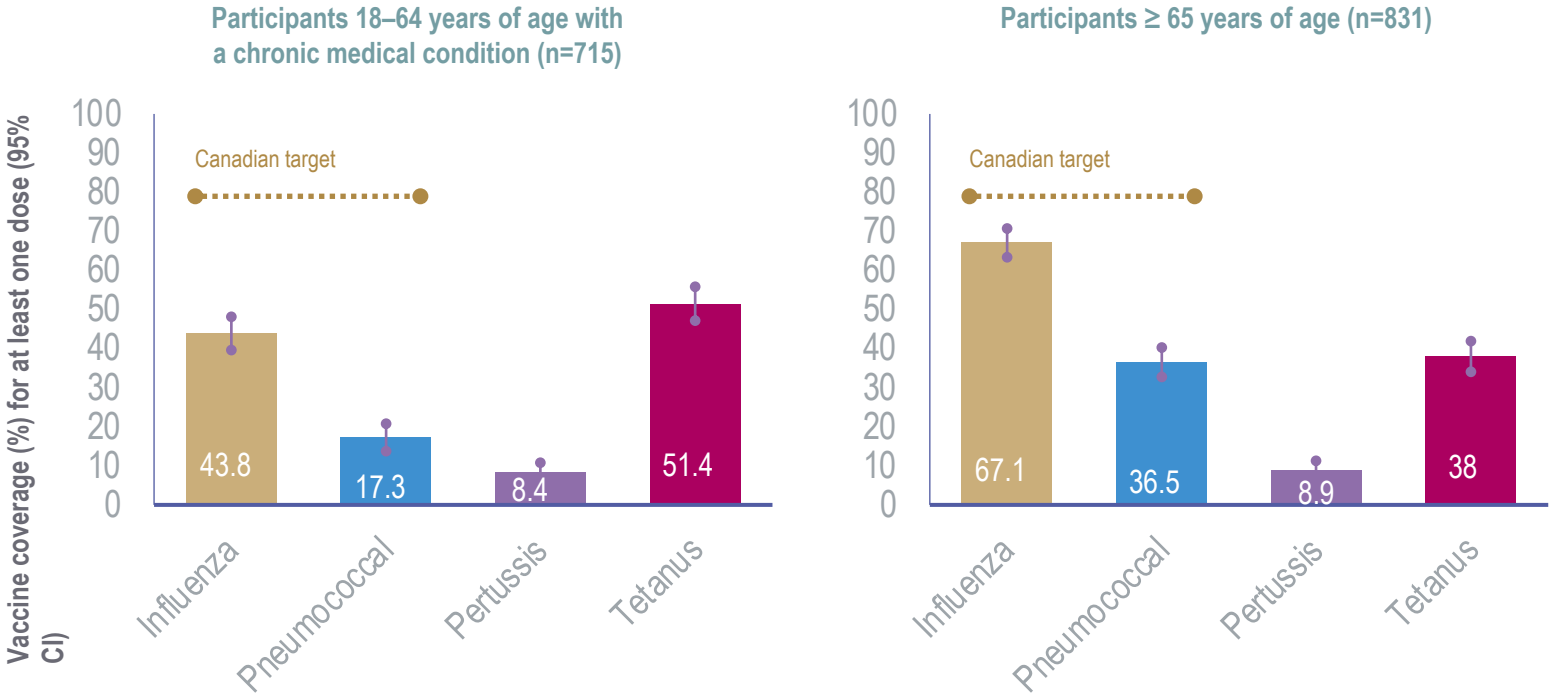


References:

1. Public health level recommendations on the use of pneumococcal vaccines in adults, including the use of 15-valent and 20-valent conjugate vaccines, Feb 2023
2. https://www.albertahealthservices.ca/assets/info/hp/cdc/if-hp-cdc-pnumo-polysac-vac-bio-pg-07-290.pdf (2023)

Improving Immunization Rates

Adult Immunization Targets



Government of Canada. Vaccine uptake in Canadian adults: results from the 2014 adult National Immunization Coverage Survey. 2016. Available at: https://www.canada.ca/en/public-health/services/publications/healthy-living/vaccine-uptake-canadian-adults-results-2014-adult-national-immunization-coverage-survey.html

NACI on Continuity of Immunization

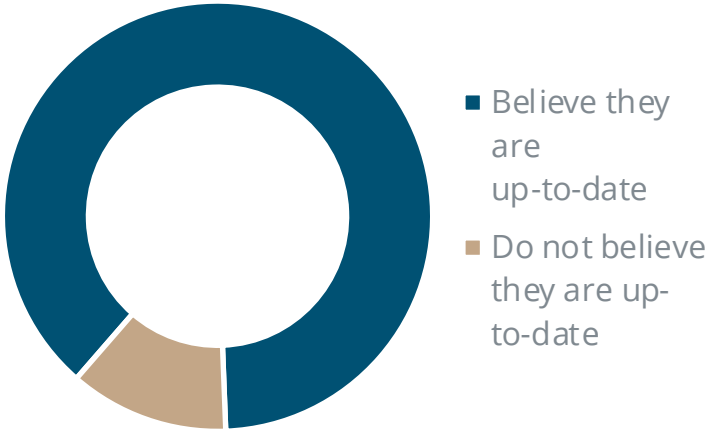
• Older adults are particularly susceptible to severe outcomes of COVID-19 and are at high risk for vaccine preventable diseases such as invasive **pneumococcal disease**, **influenza**, and **herpes zoster**.

•It would be preferable to offer immunization when it can be combined with another medical visit, and offering multiple vaccines if required, to minimize the risk of acquiring COVID-19 and to reduce the number of health care encounters.

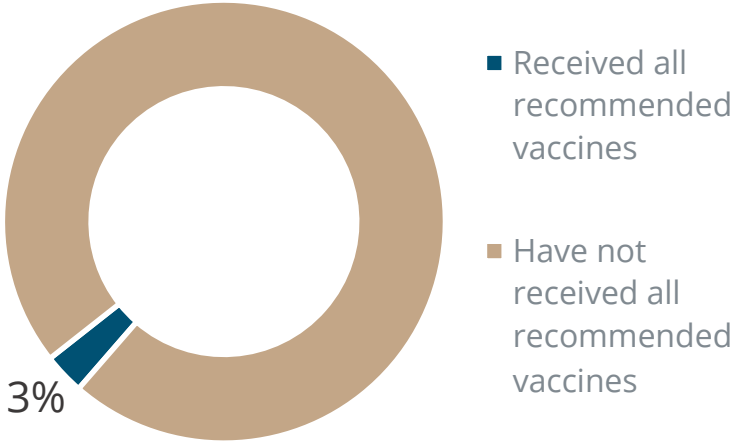
Canadian adults are not aware they lack recommended vaccines

According to the 2016 adult National Immunization Coverage Survey, many Canadians incorrectly believe they are up-to-date on their recommended vaccines

Percentage of Canadians who believe they are up-to-date on all vaccines recommended for their age and risk group



Percentage of Canadians who have received all vaccines recommended for their age and risk group



1. Public Health Agency of Canada. Available from: http://www.publications.gc.ca/site/eng/9.859558/publication.html.

SPCA.FLHD.19.08.0052

Perceived Barriers to Immunization

#1 Barrier to Vaccine Uptake Among Canadian Physicians[1]

Perceived Barriers of Cost

- **Cost** was seen as the number one barrier by **92% to 95%** of physicians
- Perceived barriers may **limit recommendations for vaccination**, particularly among older women or men

#1 Barrier to getting Vaccinated Among Canadian Adults[2]

Receiving an HCP Recommendation

- The number one reported barrier to vaccination for the general public was **not having a recommendation from an HCP**
- **Cost** was seen as a barrier by **only 18% (male)** and **19% (female) of participants**

- **It is important to counsel patients on all available vaccines, without making any presumptions as to what they can or cannot afford**

1. Steben et al. J Obstet Gynaecol Can. 2019;41:599-607; 2. Steben et al. J ObstetGynaecol Can. 2019;41:1125-33.

SPCA.FLHD.19.08.0052

Improving Influenza Immunization Programs

Increase immunization rates

Increasing disease awareness and vaccine acceptability to increase immunization rates

Increase vaccine protection

Ensuring the use of the most effective vaccines in order to reduce morbidity and mortality

Start the conversation ~~EARLY~~ Now – The summer months are the ideal time to plan for vaccination.

SPCA.FLHD.19.08.0052

Conclusions

Influenza Vaccine: Summary

Older adults experience a **high and broad burden from influenza** and are **least protected** by standard influenza vaccines[1]

High-dose influenza vaccine is the only vaccine for adults 65+ with **superior efficacy** over standard-dose vaccine (IIV3-SD) demonstrated in a randomized controlled trial[2]

High-dose influenza vaccine is **uniquely recommended** by NACI for adults age 65+[3]

Based on data collected among multiple settings, the high-dose vaccine is expected to **reduce hospitalizations**[4] and **avoid healthcare costs**[5] for adults age 65+

References:
1. Andrew, M. K., et al. (2018). *Drugs & Aging, 36*(1), 29-37.
2. DiazGranados, C. A., et al. (2014). *N Engl J Med, 371*(7), 635-645.
3. National Advisory Committee on Immunization (NACI). (2019). Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2019-2020.
4. Lee, J. K. H., et al. (2018). *Expert Rev Vaccines, 17*(5), 435-443
5. Becker, D. L.,et al. (2016). *Hum Vaccin Immunother, 12*(12), 3036-3042.

Vaccine: Summary

Public health authorities provincially have differing vaccine coverage and guidelines then their national counterparts

Conjugated Pneumococcal 20 is individually recommended for individuals over the age of 65

High risk patients may have coverage for pneumococcal 20 at a provincial level

Pneumococcal vaccines and flu vaccines (HD or Standard) may be given at the same time.

https://www.albertahealthservices.ca/assets/info/hp/cdc/if-hp-cdc-pnumo-polysac-vac-bio-pg-07-290.pdf

Thank You