Protecting Your At-Risk Patients from Respiratory Infections

Thinking beyond influenza is as Easy as 1-2-3

Presenter Disclosure

- Presenter's Name: Jen Belcher
- I have the Relationships with commercial interests:
  - Advisory Board/Speakers Bureau – Pfizer, Sanofi-Pasteur

- Speaking Fees for current program:
  - I have received a speaker's fee from Pfizer Canada for this learning activity

Presenter Disclosure

- Presenter's Name: Michael Boivin
- I have the Relationships with commercial interests:
  - Advisory Board/Speakers Bureau – SDM, Abbvie, Novo-Nordisk, Emergent BioSolutions, Astra Zeneca
  - Funding (Grants/Honoraria) : Merck, Teva, Pfizer, Abbott Diabetes, Valneva, Novo Nordisk, Khiron, Tilray, Canopy, Moderna
  - Speaker/Consulting Fees: J & J, Sanofi-Pasteur, Abbvie, Ascensia, Pfizer, Astra Zeneca
- Speaking Fees for current program:
  - I have received a speaker's fee from Pfizer Canada for this learning activity

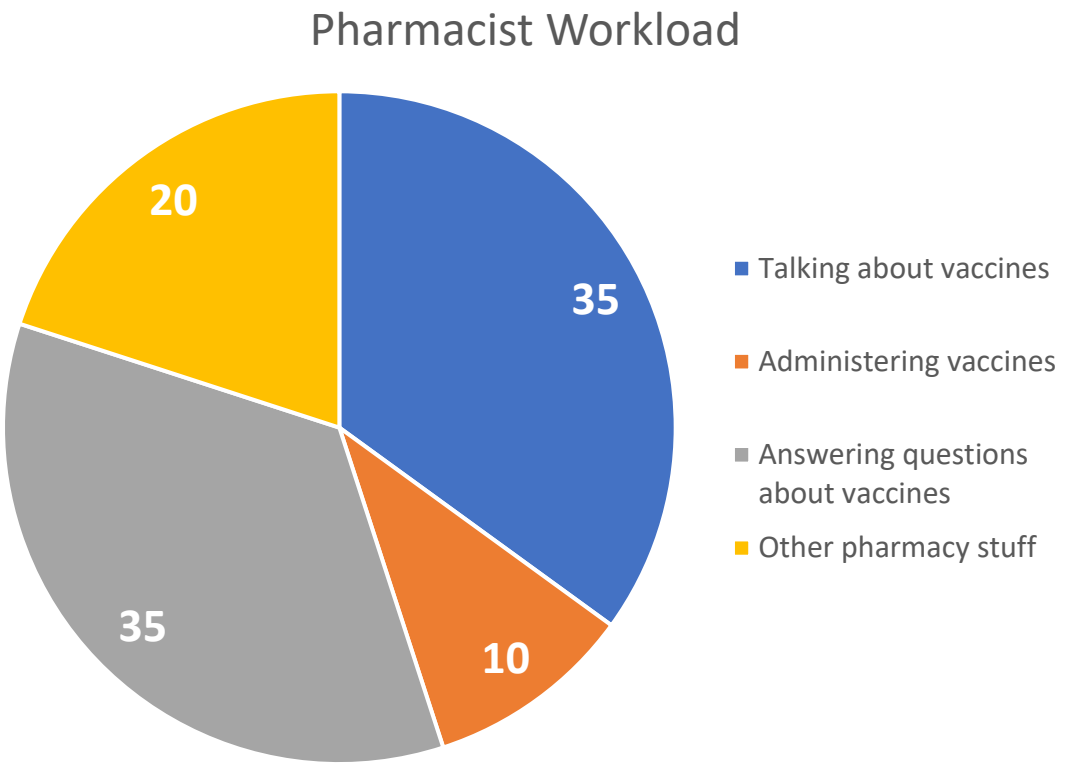
Commercial Support Disclosure

- This learning activity has received financial support from Pfizer Canada in the form of an unrestricted educational grant

Learning Objectives

1. Determine different strategies to reduce the risk and maximize protection for patients at risk of respiratory tract infections
2. Identify patients at risk for severe outcomes from pneumococcal and COVID-19 infections
3. Explain practical implementation of these recommendations in pharmacy practice
4. Summarize the role of antiviral therapy in patients once infected with COVID-19

Vaccines, Vaccines, Vaccines



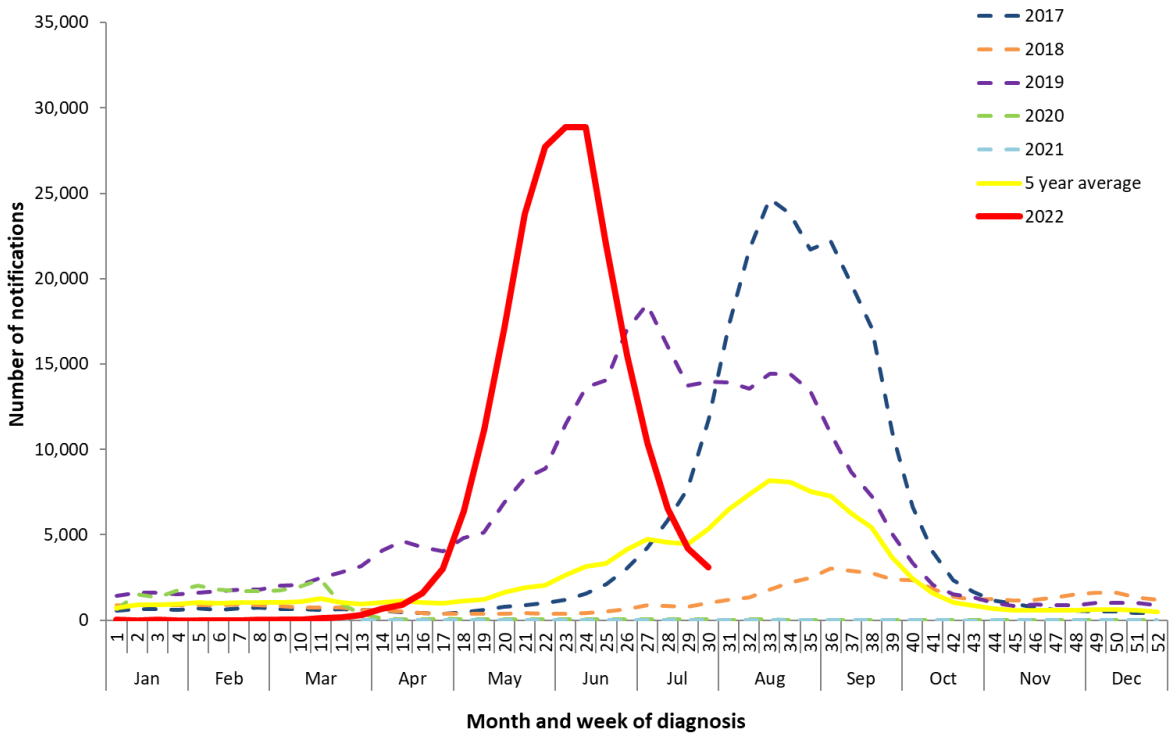
Why Vaccination is Crucial at this Point?

- Immunization coverage across the world
  - Dropped from 86% in 2019 to 81% in 2021
- An estimated **25 million children** under the age of 1 year did not receive basic vaccines, which is the highest number since 2009
- The number of girls not vaccinated against human papillomavirus (HPV) increased by 3.5 million, compared to 2019.
- In 2021, the number of completely unvaccinated children increased by 5 million since 2019.
- Some studies showed up to **80% reduction** in routine vaccination

WHO. https://www.who.int/news-room/fact-sheets/detail/immunization-coverage. SeyedAlinaghi S, Karimi A, Mojdeganlou H, et al. Impact of COVID-19 pandemic on routine vaccination coverage of children and adolescents: A systematic review. *Health Sci Rep*. 2022;5(2):e00516. doi:10.1002/hsr2.516

They are Predicting a **Twindemic** Party

Notifications of laboratory-confirmed influenza, Australia, 01 January 2017 to 31 July 2022, by month and week of diagnosis



The Department of Health and Aged Care. https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-ozflu-flucurr.htm

As Public Health Restrictions are Removed – Increase in Infectious Disease

Time to Party like it's 2018!

What We Are Going to Cover Today?

Prevent Person from getting ill

Adult immunization

Reduce the risk of severe outcomes with tools like Paxlovid

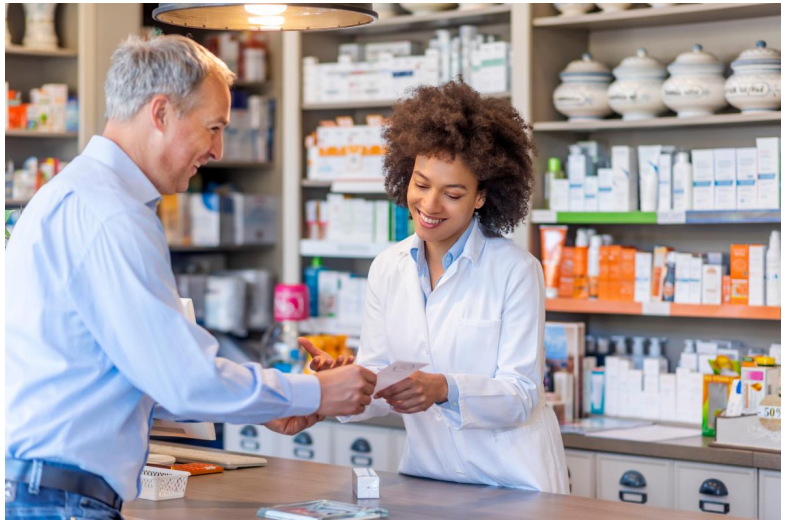
We know they are coming in for the influenza vaccine – **Proactively protect** them against other respiratory infections

Importance of Thinking Beyond Influenza – Maximizing patient protection opportunities

Patient Case – Evelyn

- Background:
  - 60 years old
  - Obesity, hypertension, dyslipidemia, type 2 diabetes, COPD
  - Patient had COPD exacerbation 3 months requiring ED visit
- Medications:
  - Aclidinium/formoterol 400/12 mcg BID
  - Metformin 1000 mg BID
  - Dapagliflozin 10 mg daily
  - Sitagliptin 100 mg daily
  - Atorvastatin 40 mg daily
  - Ramipril/HCTZ 10/12.5 mg daily
- Discussion:
  - She is in for the flu shot
  - She had 2 total doses of COVID-19 (last dose was July 2021) – Waiting for an omicron specific vaccine

Protecting the patient is as Easy as 1-2-3

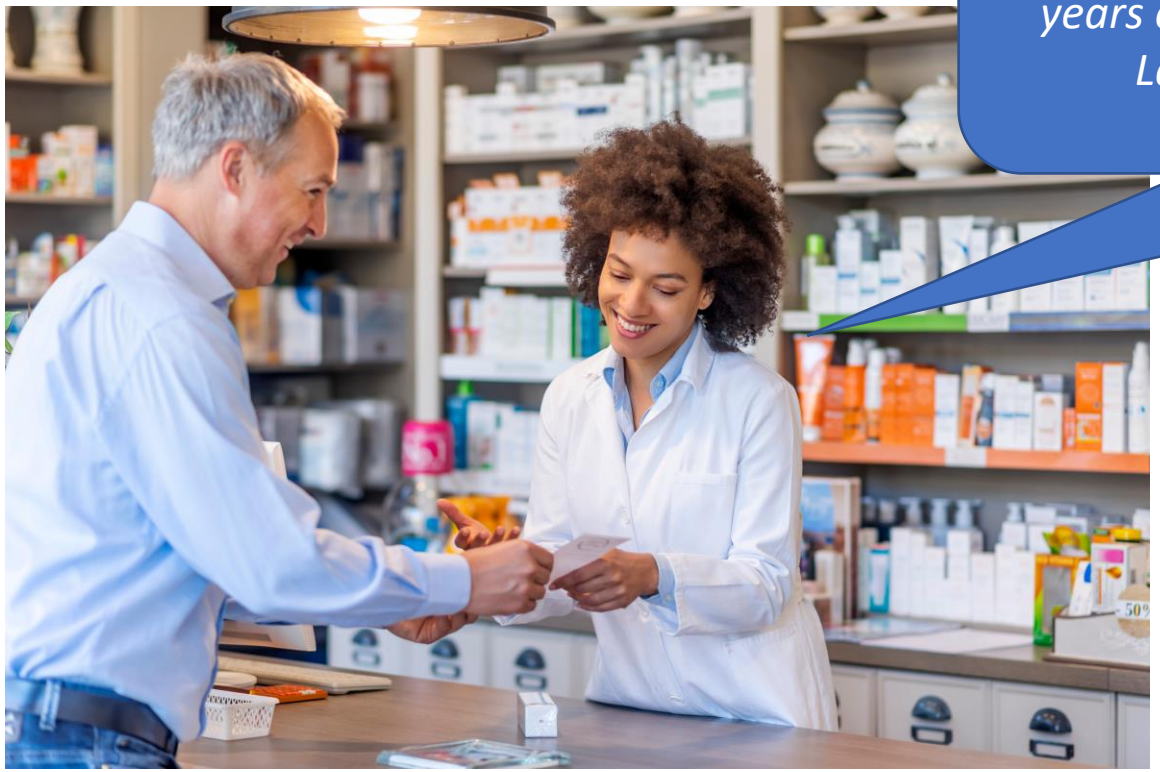


1. Ask

2. Educate

3. Immunize

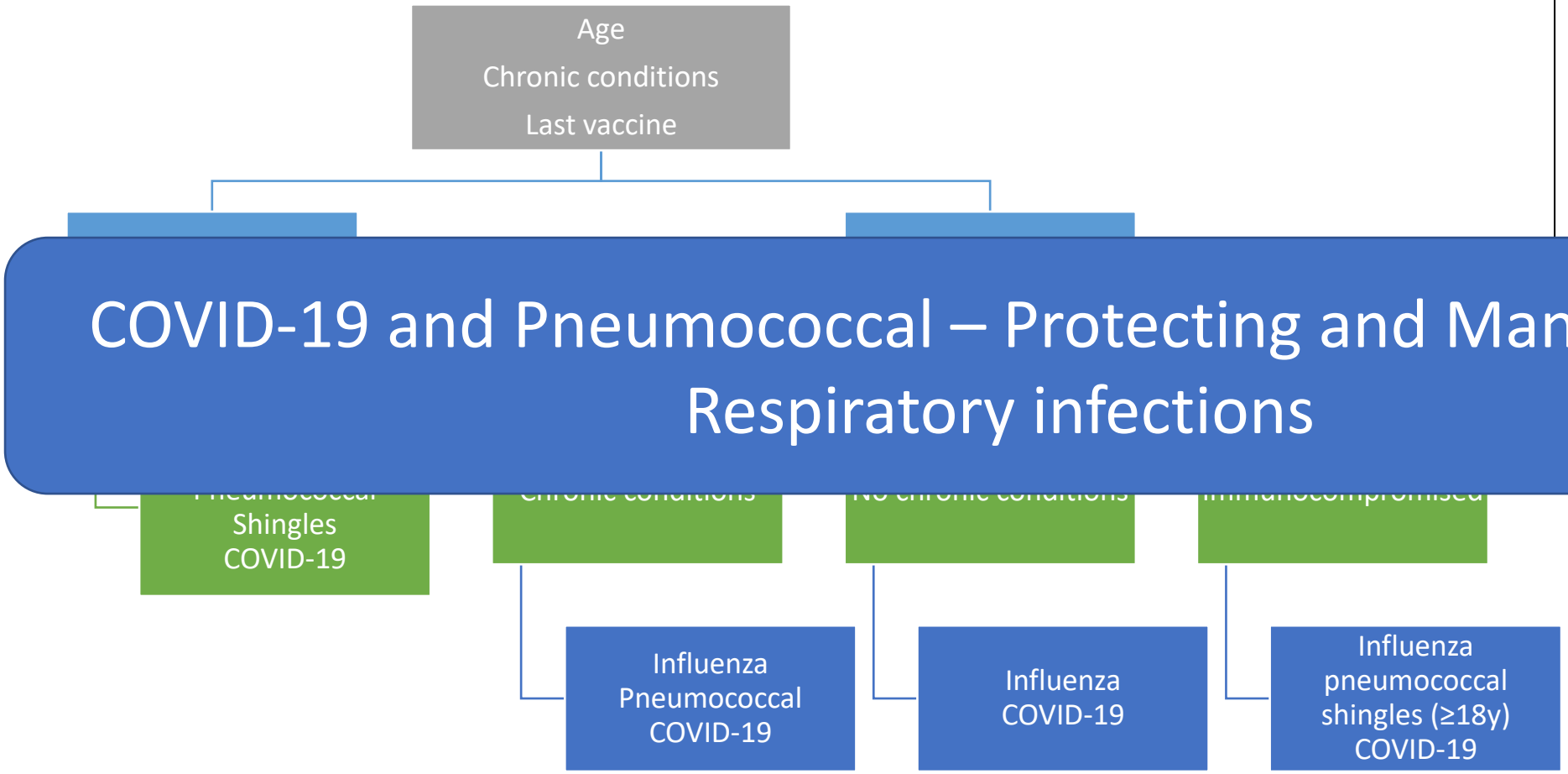
1. **Ask** Some Simple Questions to Determine Vaccines that are Required



"While you're here, we always like to check to see if you should receive any vaccines to protect your health. I see that your 54 years old. Can I please ask what medical conditions you have? Lastly, when is the last time you received a vaccine?"

- Simple questions:
  - Age of the patient
  - Medical conditions that they have
  - Last time they received a vaccine
- It is about gathering the information and recommending what they need

Key Pharmacy Vaccine Recommendations



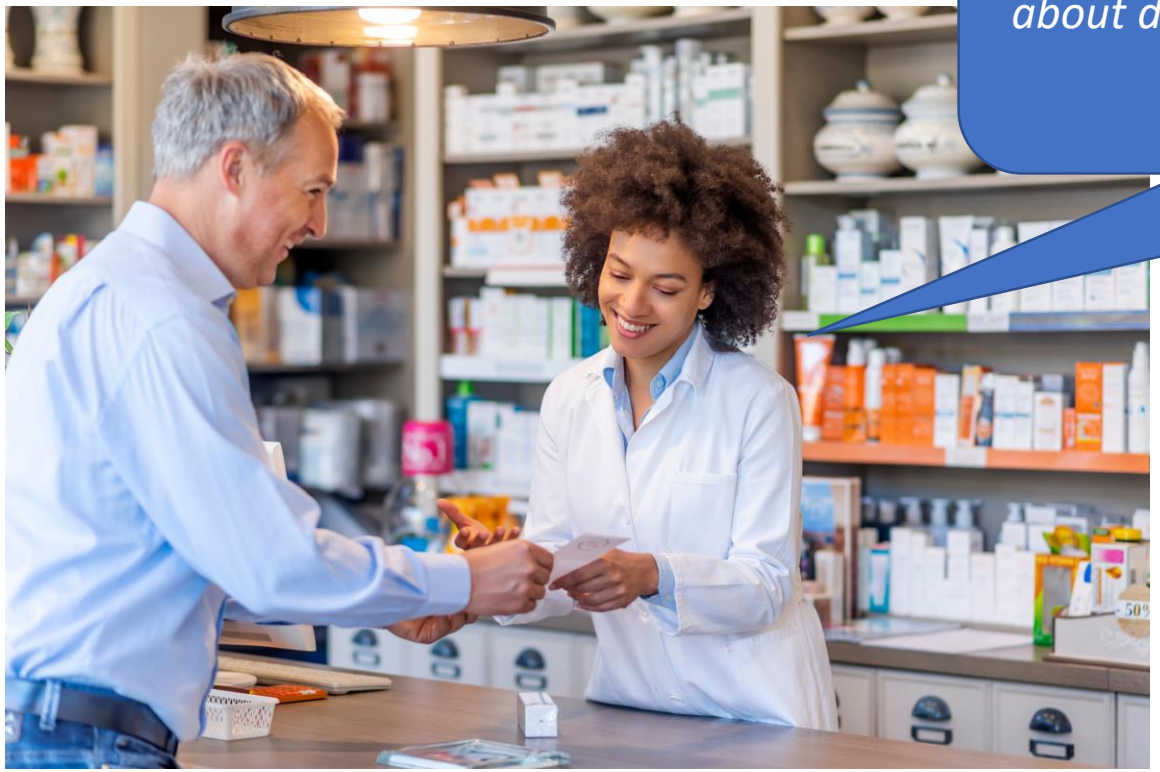
Tetanus-Diphtheria – every 10 years

Pertussis (whooping cough) – once in adulthood and every

COVID-19 and Pneumococcal – Protecting and Managing other Respiratory infections

1. **Ask** About Current Strategies to Protect or Manage Severe Infections

*"Has anyone told you that you are at higher risk of serious complications from chest infections. Has anyone talked to you about different things you can do **besides the vaccines** to prevent and treat the infection if you get sick?"*

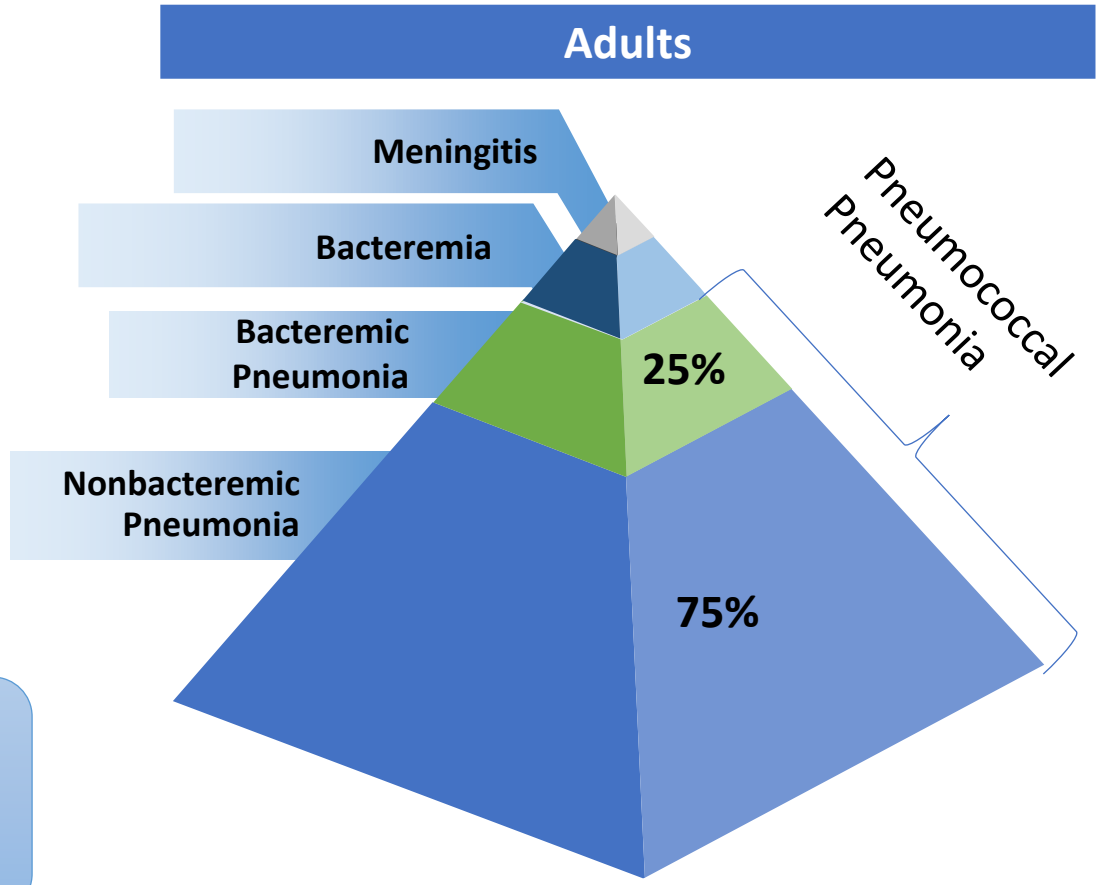


- What strategies are you currently using:
  - Masking
  - Gatherings
- COVID-19 treatment strategy notification
  - Informing patients that they are at risk of potential severe disease

Important Tip:

Proactively engage the patients at risk today, inform, prepare and encourage treatment.

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

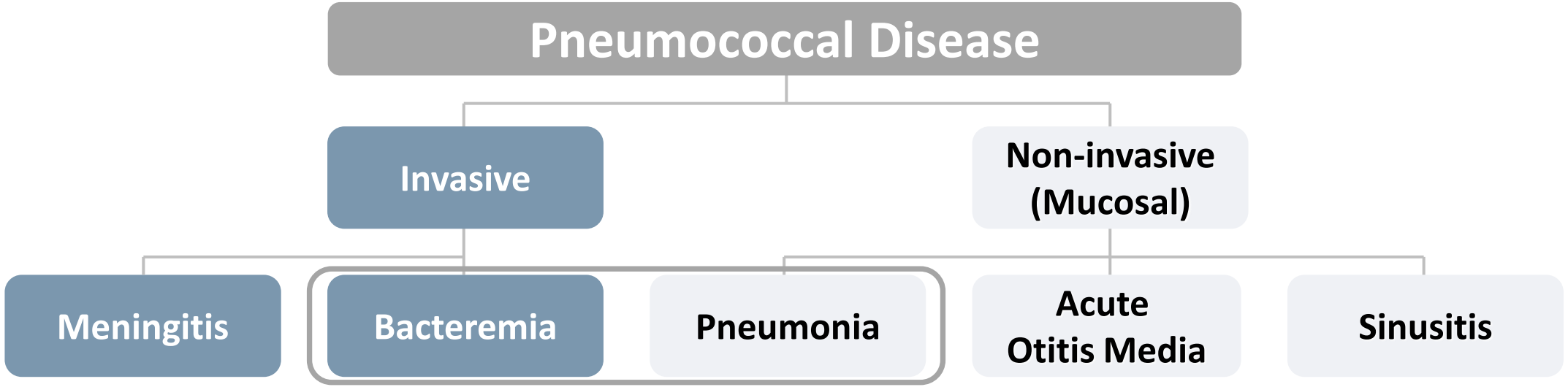


Among the > 100 recognized serotypes of *S. pneumoniae,* invasive disease caused by 24 serotypes can be prevented by vaccination*.

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.

Invasive versus non-invasive pneumococcal disease



- Non-invasive forms of disease may become invasive (eg, pneumonia when accompanied by bacteremia)
- Serotype can be associated with disease severity and invasiveness

1. Aliberti S, Mantero M, Mirsaeidi M, et al. The role of vaccination in preventing pneumococcal disease in adults. *Clin Microbiol Infect* 2014;20(0 5):52058.
2. Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Pneumococcal Disease. Available at: https://www.cdc.gov/vaccines/pubs/pinkbook/pneumo.html Accessed November 10, 2017.
3. Jansen AG et al. *Clin Infect Dis.* 2009;49:e23-e29.

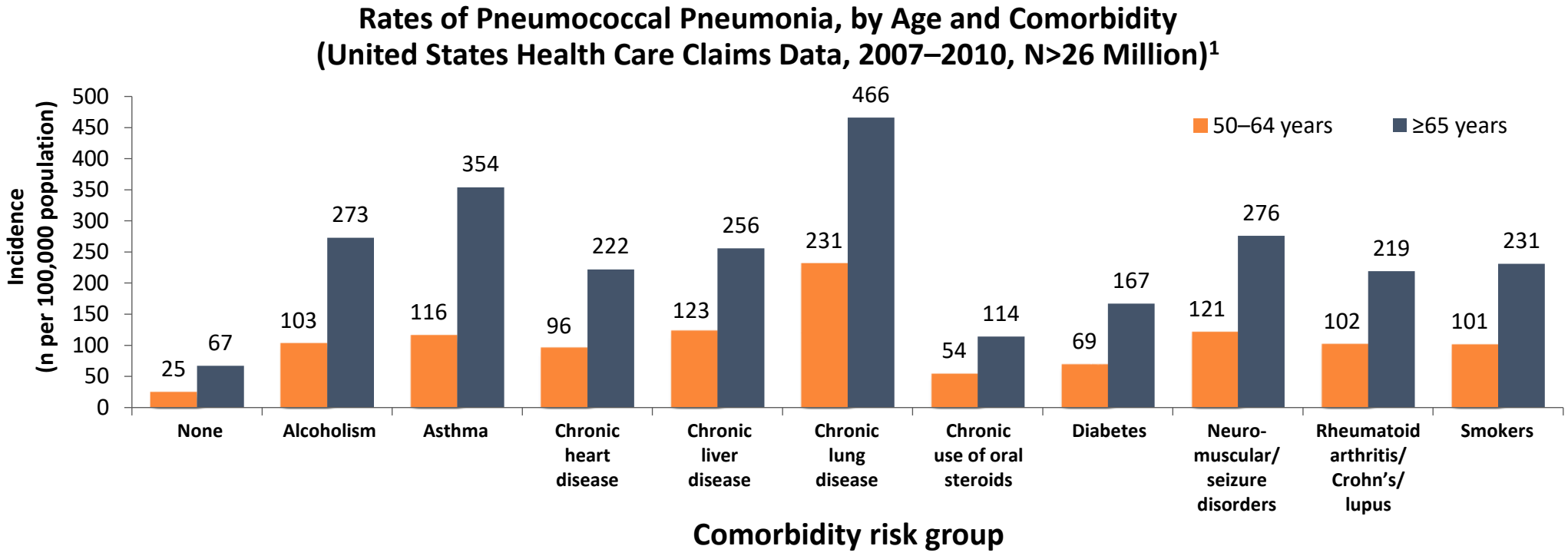
There are many risk factors for pneumococcal disease in adults

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.

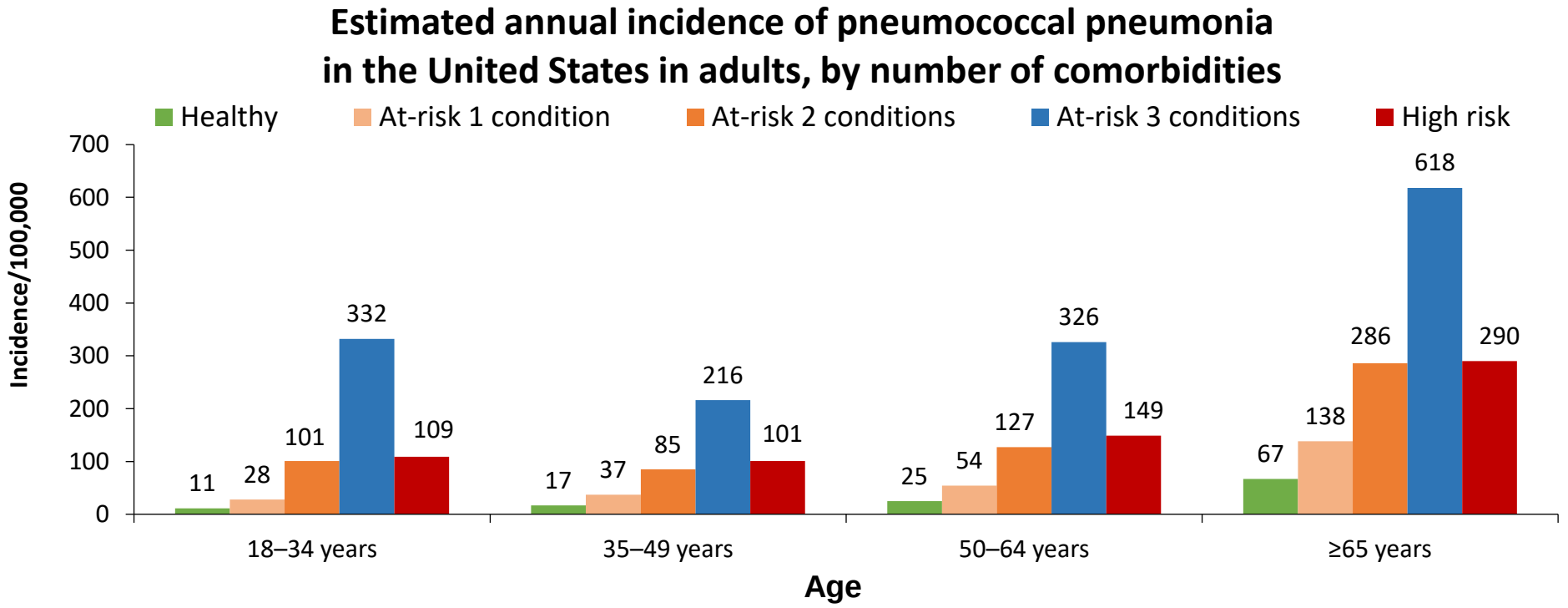
Age and comorbidities can increase pneumococcal pneumonia risk in adults



If the person has any disease related to kidney, lungs, heart, liver, or metabolic disease, they are at elevated risk

1. Shea KM, et al. *Open Forum Infect Dis* 2014;1(1):ofu024.

Multiple underlying medical conditions further increase pneumococcal pneumonia risk in adults

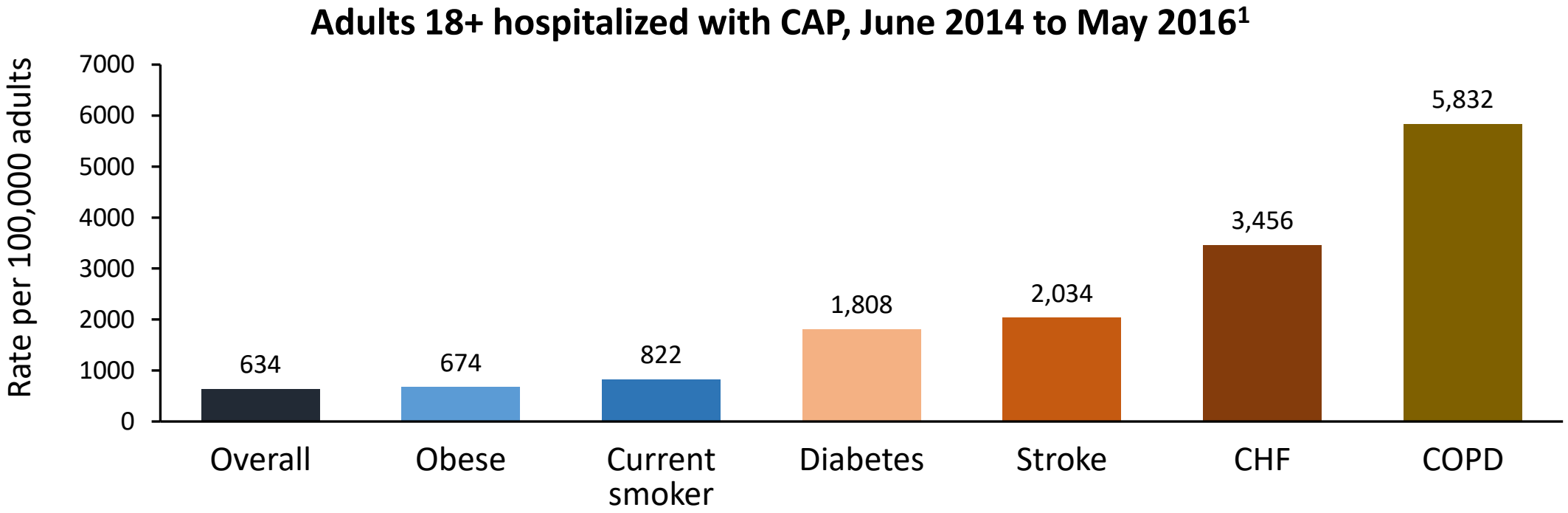


Persons with ≥2 at-risk conditions accounted for 9%–32% of all at-risk adults, depending on age

Note: At-risk—immunocompetent with ≥1 selected chronic condition, including alcoholism, asthma, chronic heart disease, chronic liver disease, chronic lung disease, diabetes, neuromuscular/seizure disorders, and smoking. Immunocompromised or immunosuppressed persons and those with a cochlear implant were classified as high-risk.

1. Shea KM, Edelsberg J, Weycker D, et al. *Open Forum Infect Dis* 2014;1(1).

Comorbid conditions can increase the risk of hospitalization due to community-acquired pneumonia



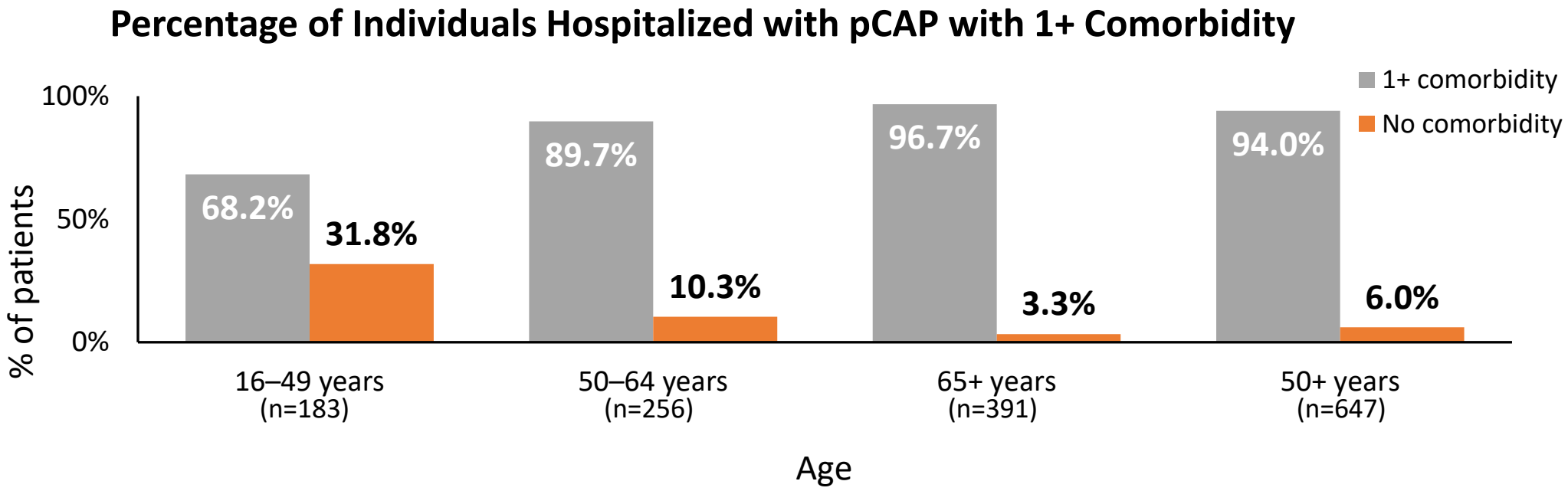
Pneumonia is one of the top 10 reasons the people went to the ED in Canada[2]

135,000 pneumonia-related ED visits in 2018[2]

CAP, Community-acquired pneumonia; CHF, Chronic heart failure; COPD, Chronic obstructive pulmonary disease; ED, emergency department

1. Ramirez JA, et al. Clin Infect Dis 2017; 65(11):1806-1; 2. National Institute of Ageing. As One Of Canada's Top Killers, Why Isn't Pneumonia Taken More Seriously? March 2019. https://static1.squarespace.com/static/5c2fa7b03917eed9b5a436d8/t/5d9de2f2353e453a7a90c74d/1570628341921/As%2BOne%2BOf%2BCanada%27s%2BTop%2BKillers%2C%2BWhy%2BIsn%27t%2BPneumonia%2BTaken%2BMore%2BSeriously.pdf

Patients with even one comorbidity are at increased risk of hospitalization across all age groups



Adults aged 50-64 years accounted for 33.1% of pCAP attributed to PCV13 serotypes, compared with 44.4% in adults aged ≥65 years

CAP, community-acquired pneumonia; pCAP, pneumococcal community-acquired pneumonia.

1. LeBlanc JJ et al. *Vaccine* 2022 Mar 18;S0264-410X(22)00246-8.

Mortality increases in the year post-discharge for people hospitalized with pneumonia

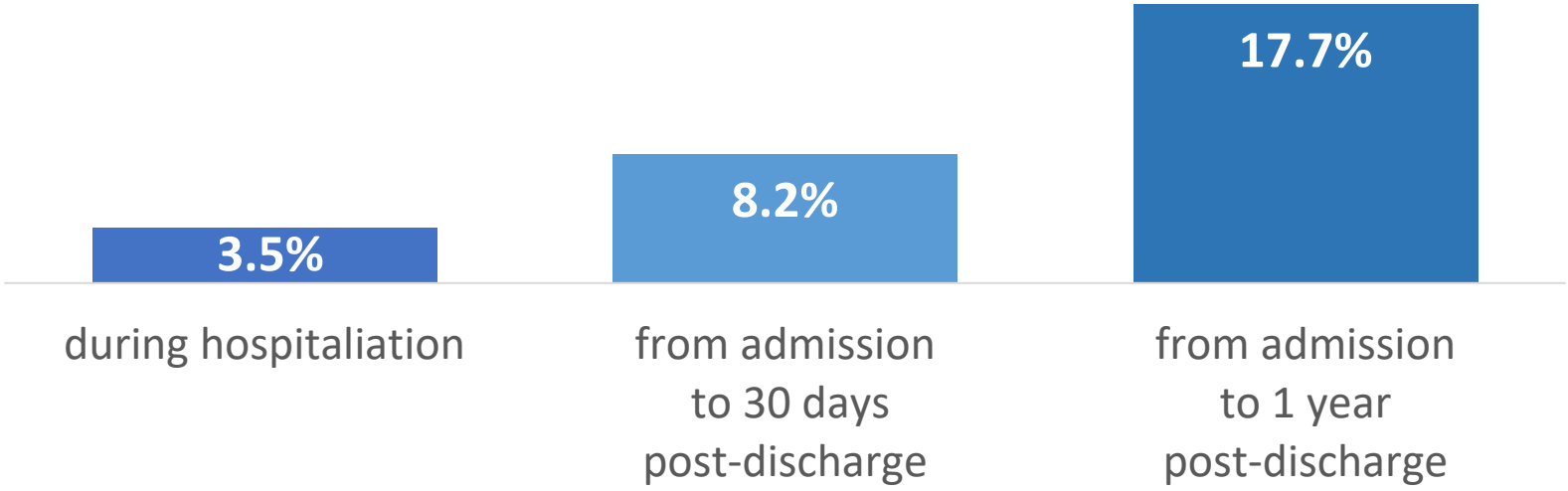
STUDY POPULATION

Pneumonia hospitalizations:
38,809

Mean age:
71 years

Risk:
33% at-risk
55% high-risk

Mortality over time in cohort of US adults hospitalized with pneumonia



Mortality within 1 –year post-discharge increases with age from 4.1% in those aged 18-49 to 26.0% in those ≥85 years

Note: At-risk includes chronic medical conditions; High-risk includes immunocompromised.

1. Averin A, et al. *Respir Med.* 2021;185:106476

Hospitalization due to pneumonia may be associated with cognitive impairment

% of patients who were hospitalized with CAP who had cognitive impairment that lasted for ≥1 year

- 25% had moderate-to-severe cognitive impairment
- 33% had mild cognitive impairment

Hospitalization for pneumonia is associated with:

- Functional decline
- ~2.5 x increase in risk of developing moderate-to-severe cognitive impairment

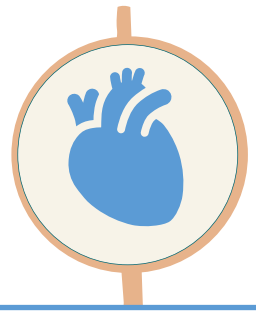
CAP, community acquired pneumonia

1. Girard TD, et al. *Society of General Internal Medicine*. 2018;33(6):929-35; 2. Davydow DS, et al. *Am J Med* 2013;126(7):615-624.

Hospitalization due to pneumonia may be associated with increased risk of cardiovascular issues

CV complications occur in a large portion of hospitalized patients with CAP:

- 17.7% overall cardiac complications
- 14.1% incident heart failure
- 5.3% acute coronary syndrome
- 4.7% incident arrhythmias



In individuals with **no history of heart failure**, CAP resulted in a:

- 12% increased risk of developing heart failure

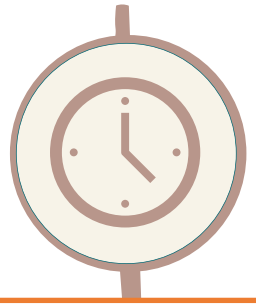
Patients admitted to hospital for pneumonia:

- 25% develop a major acute cardiac complication
- 60% increase in short-term mortality

CAP, community acquired pneumonia; CV, cardiovascular.

1. Corrales-Medina VF et al. *PLoS Med.* 2011;8(6):e1001048; 2. Eurich DT, et al. *British Medical Journal*. 2017;356(j413); 2. Corrales-Medina VF, et al. *Lancet.* 2013;381(9865):496-505.

Pneumococcal disease can affect quality of life



DAILY ACTIVITIES

Cough, weakness adversely affect capacity to carry out daily activities (e.g., housework, visiting places/others)[1]

CAREGIVER ASSISTANCE

Often need additional assistance from caregivers[1]

EMPLOYMENT

Employees with/without CAP averaged 4.7 vs 3.6 days of sick leave ($p < 0.0001$), >2x as likely to leave job ($p < 0.01$)[2]

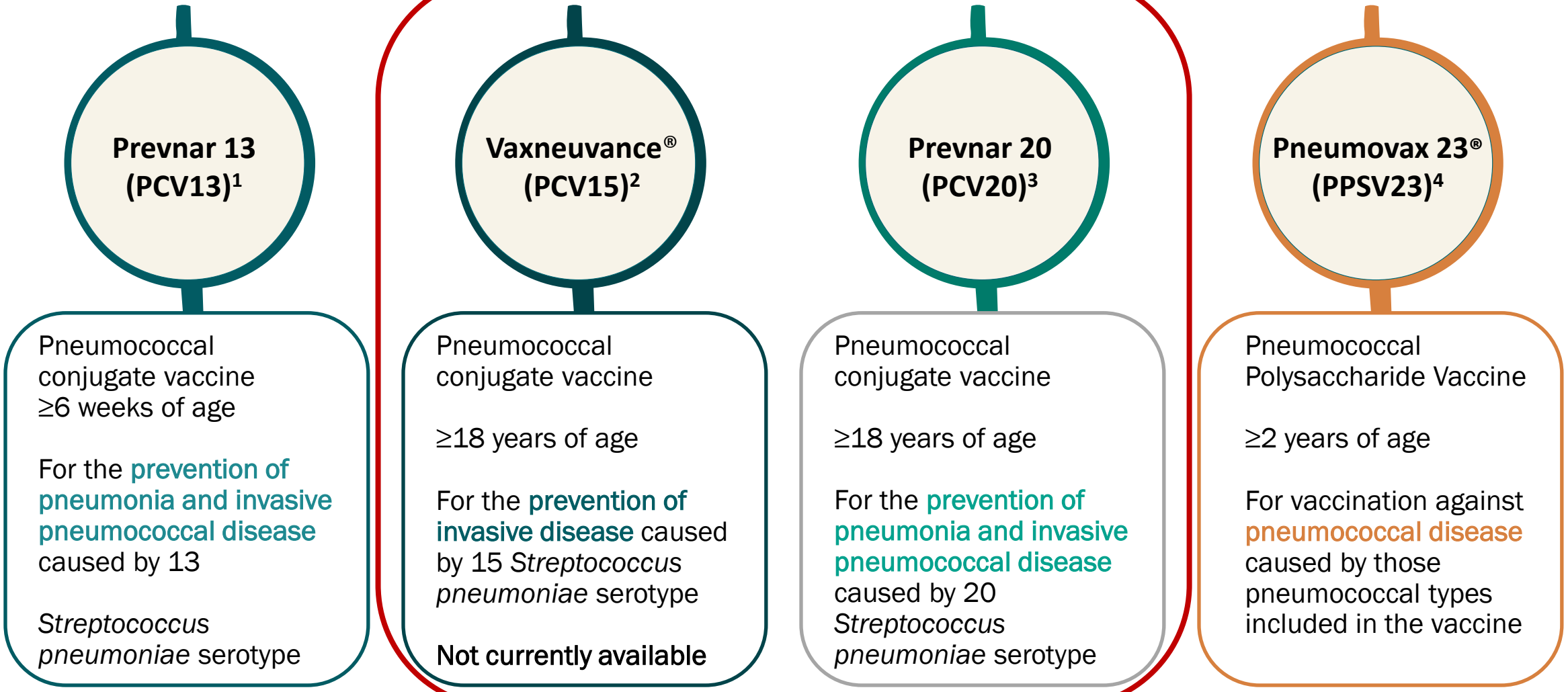
HEALTH-RELATED QUALITY OF LIFE

HRQoL persistently lower in CAP vs non-diseased persons[3]

ACS, Acute coronary syndromes; CAP, Community-acquired pneumonia; HRQoL, health-related quality of life.

1. Torres A, et al. *Thorax* 2015;70:984-989. 2. Kleinman NL, et al. *J Occup Environ Med* 2013;55:1149-1156.
3. Mangen MJ, et al. *BMC Infect Dis* 2017;17:208.

There are Many Pneumococcal Vaccines

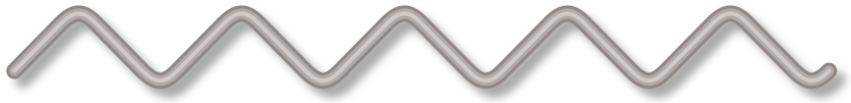


Note: PCV10 is also available but only for children; While PCV13 and PPSV23 are also available for children, the indications listed here are for adults ≥18 years of age. PCV15 is Health Canada approval but not yet available in Canada

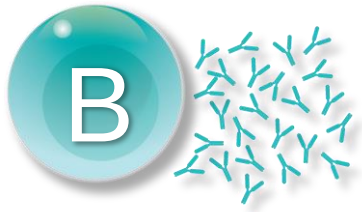
1. Prevnar 13® Product Monograph. Pfizer Canada. Revised Aug 8, 2019; 2. Vaxneuvance® Product Monograph. Merck Canada Inc. Nov 16, 2021; 3. Prevnar 20™ Product Monograph. Pfizer Canada. May 9, 2022; 4. Pneumovax 23® Merck Canada Inc. Revised April 15, 2016.

Conjugate vaccines produce a more robust response compared to polysaccharide vaccines

Polysaccharide vaccines[1,2]



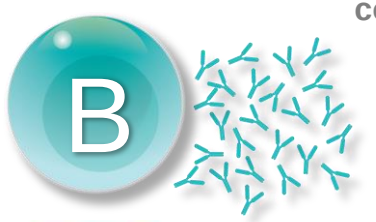
Polysaccharide antigens



- **B-cell activation** and antibody production
- **T-cell–independent** immune response that cannot be boosted

Conjugate vaccines[1-3]

Polysaccharide antigens
covalently linked to carrier protein



- **B-cell activation** and antibody production
- **T-cell–dependent** immune response
- **Memory B-cell activation** with booster response to revaccination

1. Siegrist CA. In: Vaccines. Plotkin SA, et al, eds. 5th ed. Philadelphia, PA: Saunders Elsevier; 2008:17-36. 2. Pollard AJ, et al. Nat Rev Immunol. 2009;9(3):213-220. 3. Clutterbuck EA, et al. Immunology. 2006;119(3):328-337.
4. de Roux A, et al. Clin Infect Dis. 2008;46(7):1015-1023.

Pneumococcal vaccine serotype overview

Vaccine	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	8	10A	11A	12F	15B	22F	33F	2	9N	17F	20
PCV13	●	●	●	●	●	●	●	●	●	●	●	●	●											
PCV15	●	●	●	●	●	●	●	●	●	●	●	●	●						●	●				
PCV20	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●				
PPSV23	●	●	●	●		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

Predominant serotypes causing IPD in Canada in 2019: **3** (12%), **22F** (10%), **4** (7%), **9N** (7%) and **8** (6%)[1]

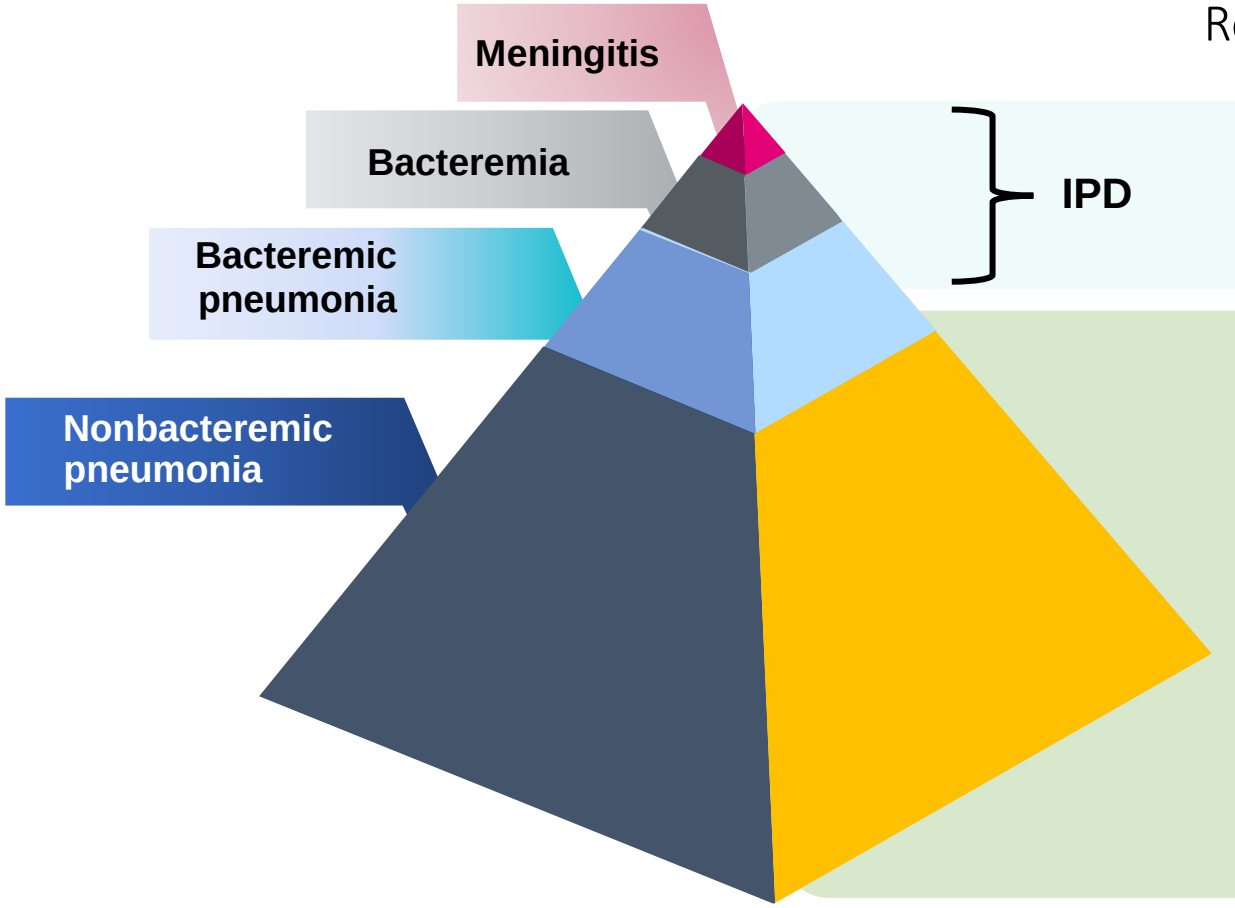
Serotypes in Canada in 2019 with highest rates of antimicrobial resistance: **33F** (89%), **7C** (73%), **19 A** (62%)[1]

Predominant vaccine-preventable serotypes in adults hospitalized with pCAP or IPD in 2017: **22F, 11A, 9N, 33F**[2]

IPD, invasive pneumococcal disease; pCAP, pneumococcal community-acquired pneumonia; PCV13, 13-valent pneumococcal conjugate vaccine; PCV-15, 15-valent pneumococcal conjugate vaccine; PCV20, 20-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine.

1. https://www.canada.ca/en/public-health/services/publications/drugs-health-products/national-laboratory-surveillance-invasive-streptococcal-disease-canada-annual-summary-2019.html. 2. LeBlanc JJ, et al. *Vaccine* 2022;40(18):2635-2646.

CAPiTA Study: Efficacy of PCV13 in preventing vaccine-type pneumococcal CAP and IPD



Reduction in Pneumococcal Disease with PCV13

IPD

75%
p < 0.001

Secondary end point:
Prevention of first episode of VT IPD

45%
p = 0.007

Secondary end point:
Prevention of first episode of VT nonbacteremic/ non-invasive pneumococcal CAP

46%
p < 0.001

Primary end point:
Prevention of first episode of VT pneumococcal CAP

Conducted in non-institutionalized adults ≥65 years of age (n=84,496)

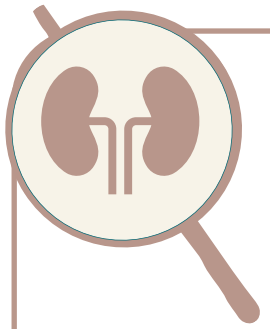
CAP, community-acquired pneumonia; CAPiTA, Community-Acquired Pneumonia Immunization Trial in Adults; IPD, Invasive pneumococcal disease; VT, Vaccine type

1. Bonten MJM, et al. *N Engl J Med* 2015;372:1114–1125; 2. Patterson S, et al. *Trials in Vaccinology* 2016;5:92-96.

Patients with comorbidities and older age are at an increased risk for pneumococcal pneumonia

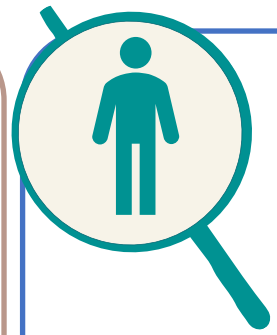
Immunosuppressive drugs/conditions

4.1 - 13.3 x greater risk



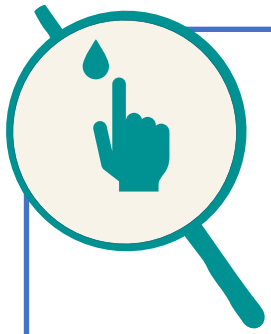
Chronic renal failure

4.2 – 6.5 x greater risk



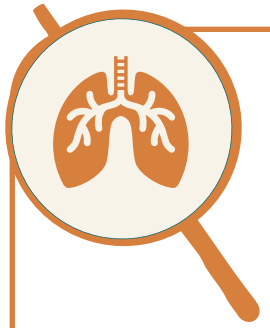
Age (≥65)

2.7 x greater risk (compared to those aged 50-64)



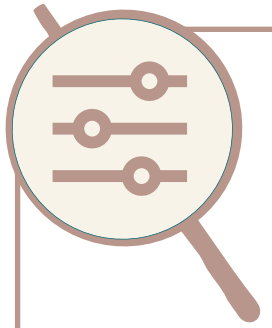
Diabetes

2.8 – 3.0 x greater risk



Asthma

4.9 – 5.9 x greater risk



≥3 Comorbidities

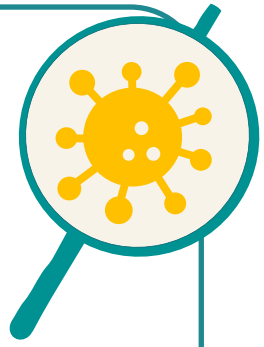
9.2 – 12.8 x greater risk

Rate ratios presented for those aged 50-64 years and ≥60 years relative to healthy counterparts. Rate ratios are presented for pneumococcal pneumonia, but similar rates were found for all-cause pneumonia and for invasive pneumococcal disease.

1. Shea KM, et al. *Open Forum Infect Dis*. 2014;1(1):ofu02

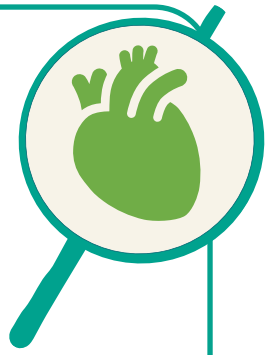
Medications that should flag vaccine discussion

Immunocompromised



- Biologics
- Methotrexate
- Long-term prednisone
- Chemotherapy
- Anti-rejection drugs
- Start early with patients not yet on immunosuppressive therapy, e.g., :
  - Rheumatoid arthritis
  - Inflammatory bowel disease
  - Psoriasis

Cardiovascular

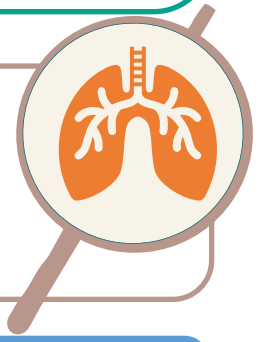


- Beta-blockers
- DOACs
- Warfarin
- ASA
- Medications for HF (e.g. nitrates, neprilysin inhibitor/ARB, MRA)

Metabolic

- Any medication to treat diabetes

Respiratory

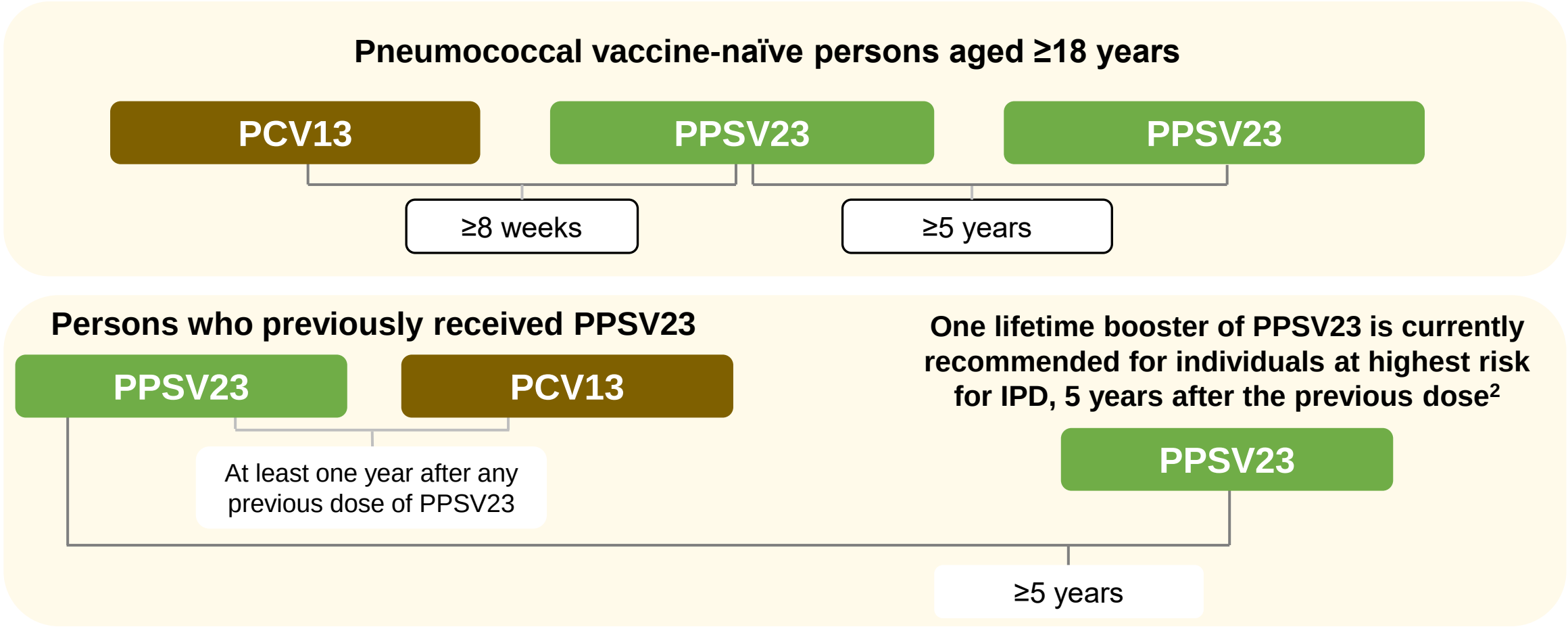


- Anyone using moderate dose inhalers consistently

"Did you know you are at higher risk of pneumonia, have you gotten your pneumonia shot?"

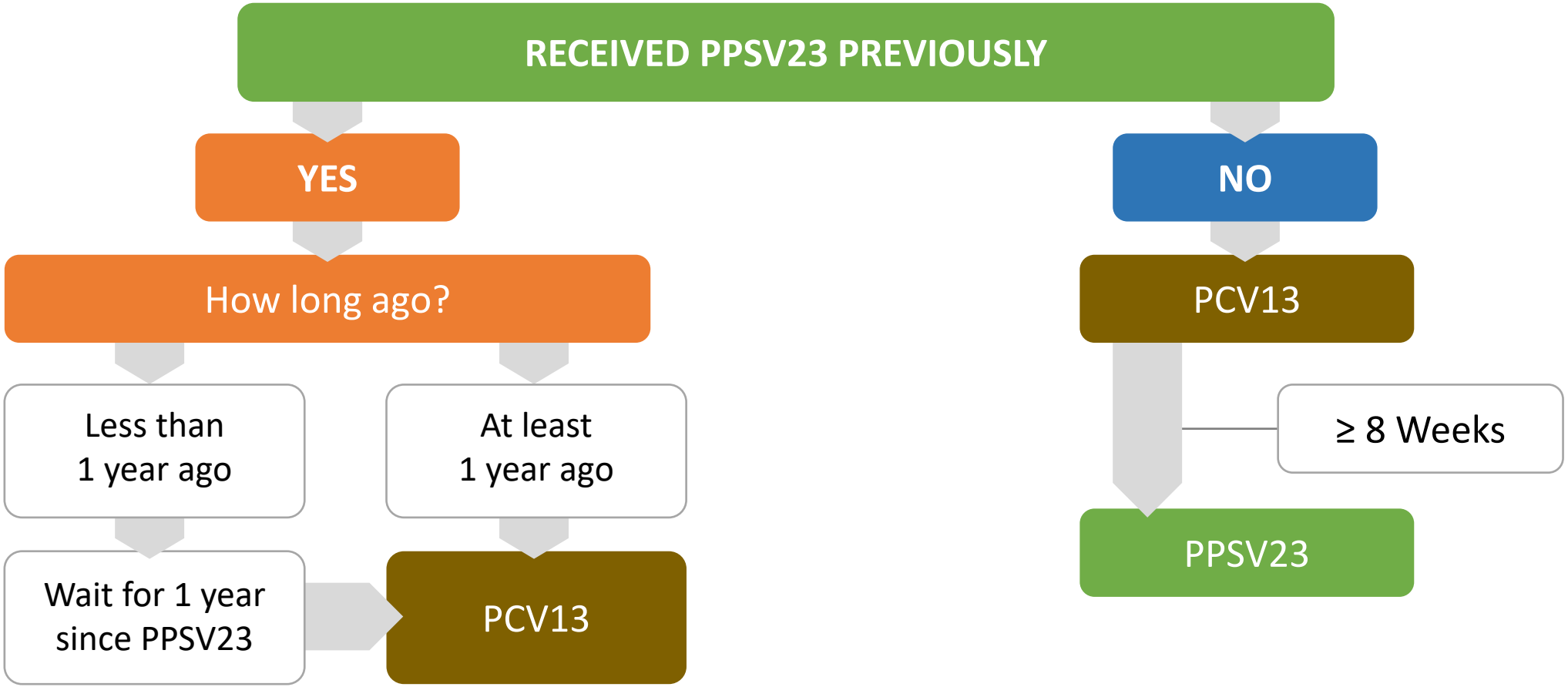
ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; DOACs, direct oral anticoagulants; HF, heart failure; MRA, mineralocorticoid receptor antagonists.

NACI 2016 recommendations for pneumococcal vaccines in immunosuppressed adults



1. Government of Canada. Canadian Immunization Guide: Part 4 – Active Vaccines. Pneumococcal Vaccine. Available at: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-16-pneumococcal-vaccine.html#a19
2. Public Health Agency of Canada. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Re-Immunization with Polysaccharide 23-Valent Pneumococcal Vaccine (Pneu-P-23). April 2015. Available at: https://www.canada.ca/en/public-health/services/publications/healthy-living/re-immunization-with-polysaccharide-23-valent-pneumococcal-vaccine-pneu-p-23.html

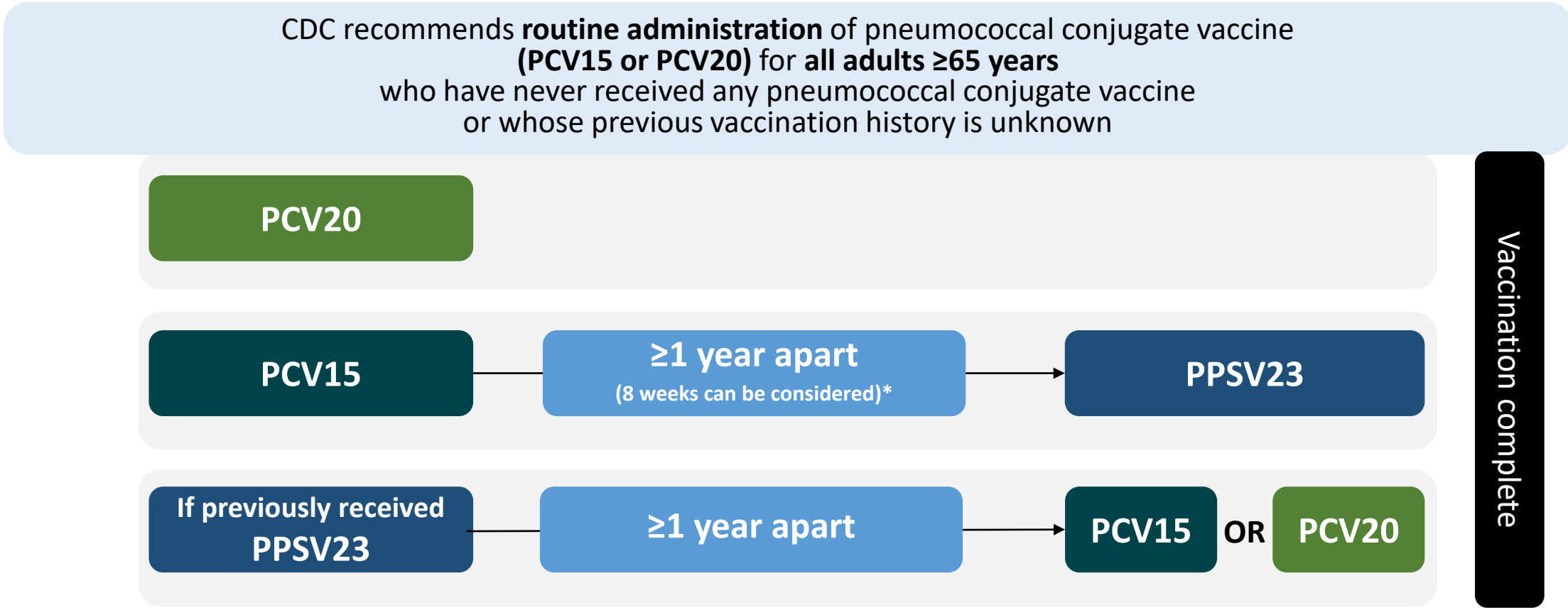
NACI 2016 recommendations for pneumococcal vaccines in immunocompetent adults ≥ 65 years



Note: PCV15 and PCV20 are Health Canada approved, but have not yet been incorporated into the NACI recommendations.

1. Public Health Agency of Canada. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Update on the use of 13-valent pneumococcal conjugate vaccine (PNEU-C-13) in addition to 23-valent pneumococcal polysaccharide vaccine (PNEU-P-23) in immunocompetent adults 65 years of age and older – Interim Recommendations. October 2016.

While NACI has not yet updated its guidelines, the CDC 2022 guidelines include PCV15 and PCV20



Note: PCV15 is Health Canada approved, but not yet available in Canada

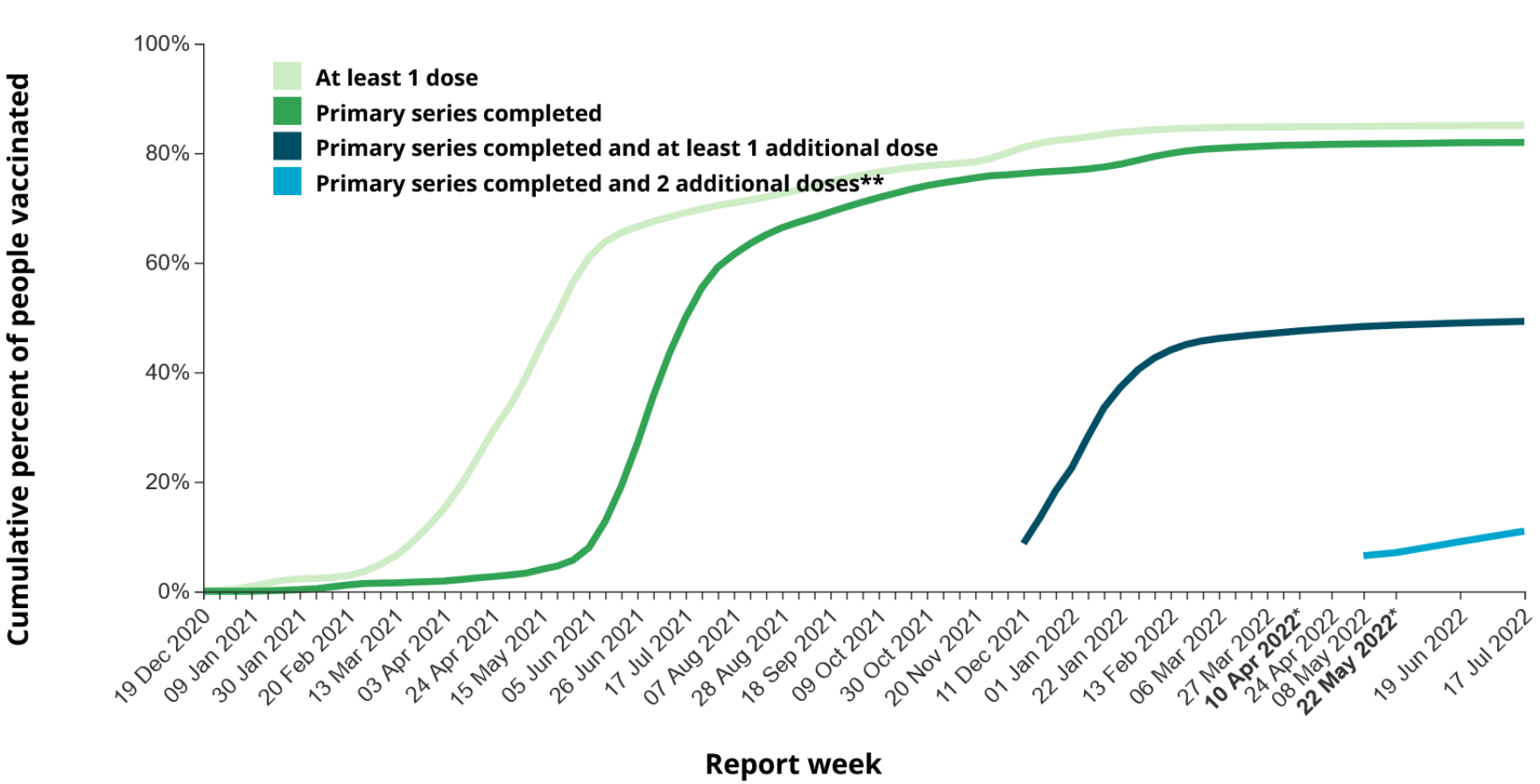
*The minimum interval is 8 weeks and can be considered in adults with an immunocompromising condition†, cochlear implant, or cerebrospinal fluid leak

†Immunocompromising conditions include chronic renal failure, congenital or acquired asplenia, generalized malignancy, HIV infection, Hodgkin disease, iatrogenic immunosuppression, leukemia, lymphoma, multiple myeloma, nephrotic syndrome, sickle cell disease or other hemoglobinopathies, and solid organ transplant.

CDC, Centers for Disease Control; PCV, pneumococcal conjugate vaccine; PPSV. Pneumococcal polysaccharide vaccine.

https://www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf [Accessed April 28, 2022]

2. Educate – COVID-19 Prevention Update

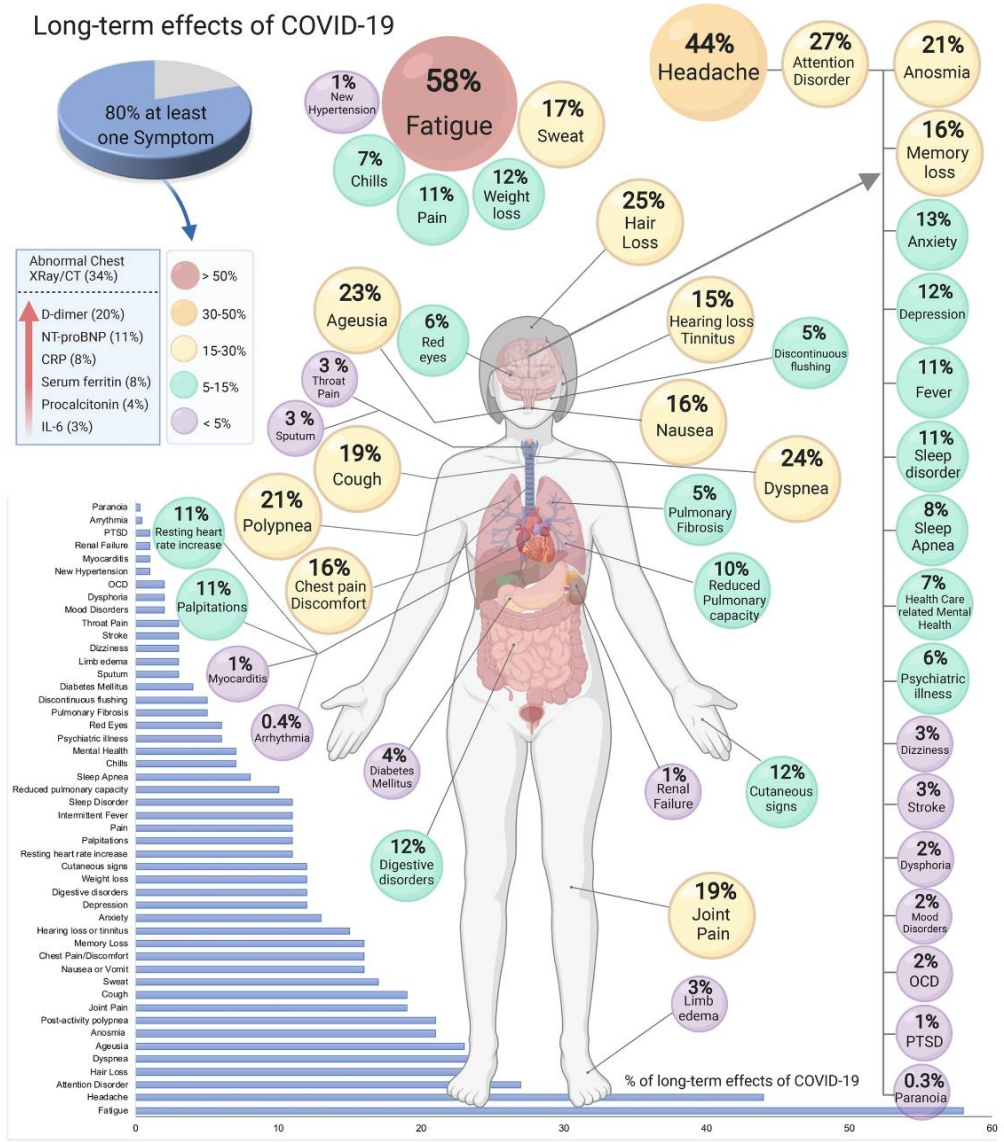


Why bother getting a booster now. I think I will just wait for my Omicron Booster.

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

Long COVID Update

- 1 in 8 people (12.74%) develop long COVID
- Not directly linked to severity of original infection
- Many people with long COVID during alpha variant still have persistent symptoms
- **Vaccine reduces risk by 41% of long COVID**
- Each breakthrough infection increases the risk of long COVID



Long-term effects of coronavirus disease 2019 (COVID-19). The meta-analysis of the studies included an estimate for one symptom or more reported that 80% of the patients with COVID-19 have long-term symptoms. *CRP* C-reactive protein, *CT* computed tomography, *IL-6* Interleukin-6, *NT-proBNP* (NT)-pro hormone BNP, *OCD* Obsessive Compulsive Disorder, *PTSD* Post-traumatic stress disorder. This figure was created using Biorender.com.

Ballering AV, Zon SKR van, Hartman TC olde, Rosmalen JGM. Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study. *The Lancet*. 2022;400(10350):452-461. doi:10.1016/S0140-6736(22)01214-4

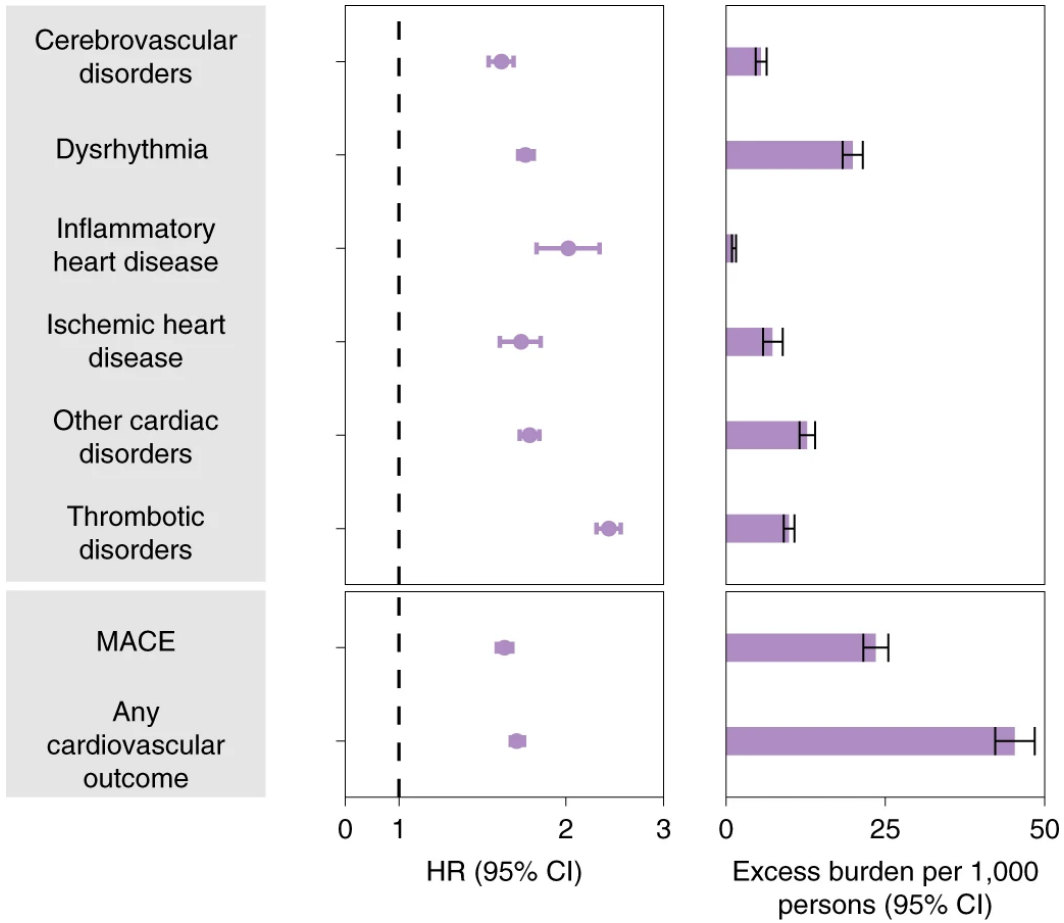
Office for National Statistics. Self-reported long COVID after two doses of a coronavirus (COVID-19) vaccine in the UK. Published online January 26, 2022:5.

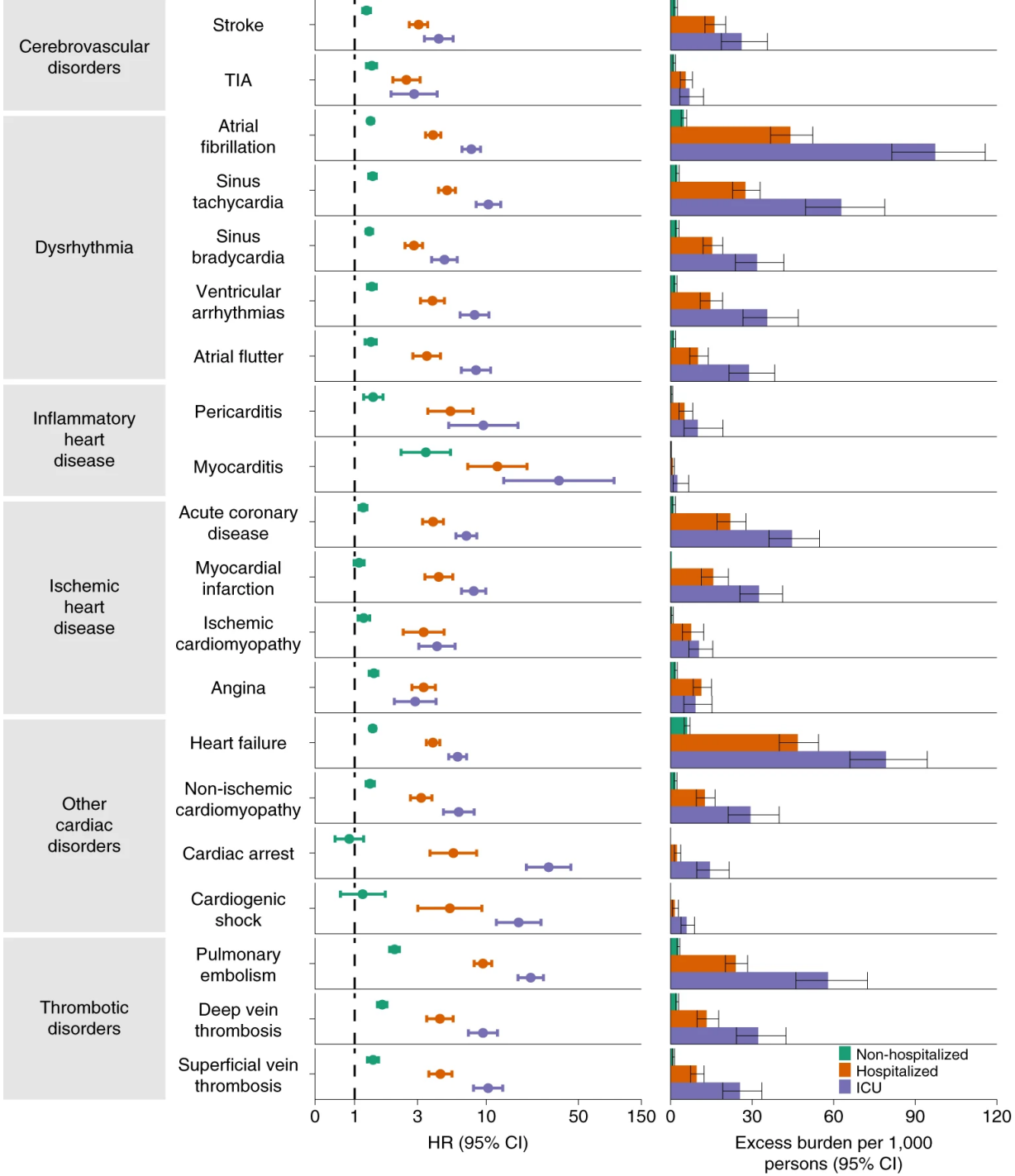
Al-Aly Z, Bowe B, Xie Y. *Outcomes of SARS-CoV-2 Reinfection*. In Review; 2022. doi:10.21203/rs.3.rs-1749502/v1

Lopez-Leon S, Wegman-Ostrosky T, Perelman C, et al. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *Sci Rep*. 2021;11:16144. doi:10.1038/s41598-021-95565-8

COVID-19 Schools Infection Survey, England: long COVID and mental health, March 2022\

CV Outcomes Post-COVID Update

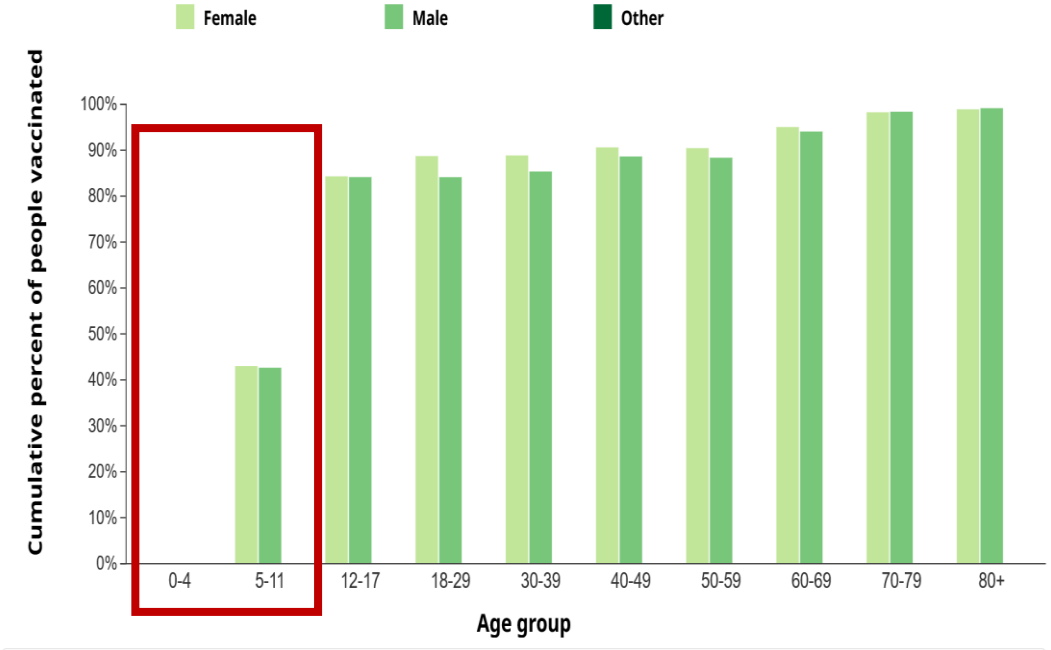




Xie Y, Xu E, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. *Nat Med*. Published online February 7, 2022:1-8. doi:10.1038/s41591-022-01689-3

Pediatric COVID Vaccine Update

- Most children are asymptomatic when infected (15%-65%)
- Pediatric hospitalization with Omicron was 5 X higher than with delta
- MIS-C – fortunately rare
- The prevalence of long COVID symptoms - 4 to 66% in children and adolescents
  - Nearly 1 in 50 (1.8%) primary school pupils and nearly 1 in 20 (4.8%) secondary school pupils had experienced long COVID

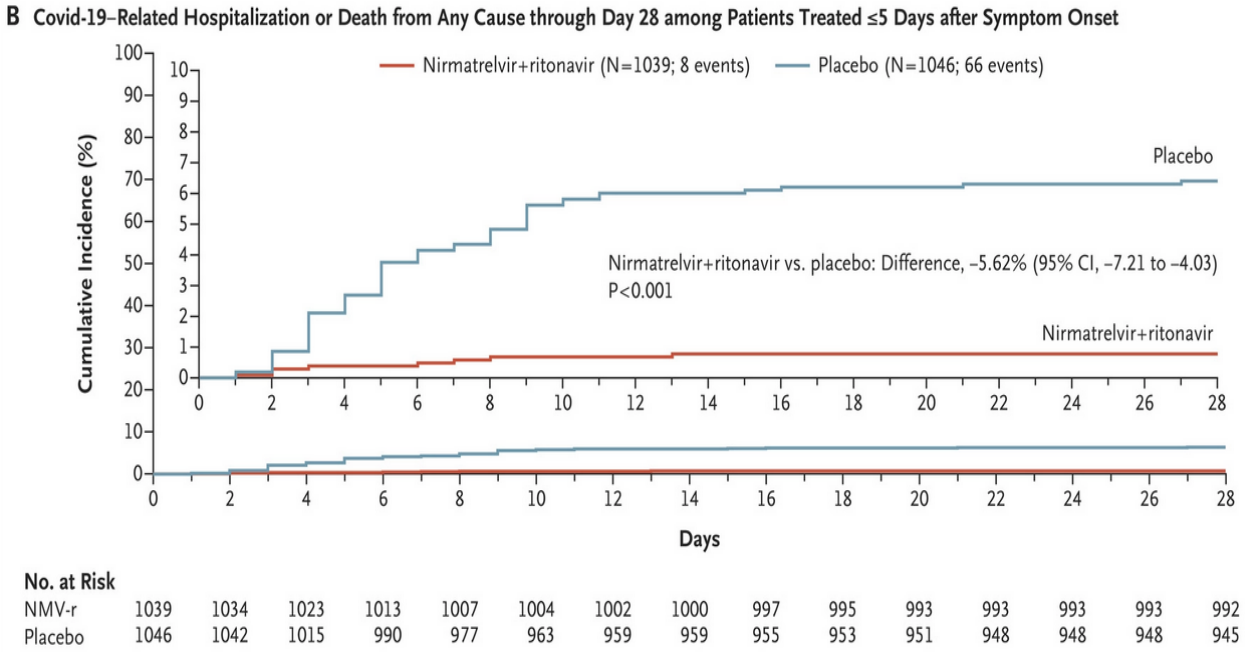


2. Educate – COVID-19 Treatment Update

- 300 mg of nirmatrelvir plus 100 mg of ritonavir

Treated ≤3 Days after Onset of Symptoms through Day 28 (modified intention-to-treat population)

	Nirmatrelvir Group N = 697	Placebo Group N = 682
Total number of patients with event	5	44
Covid-19–related hospitalization	5	44
Death from any cause	0	9
Estimated percentage with event (95% CI)	0.72 (0.30–1.73)	6.53 (4.90–8.68)
Difference ±SE from placebo — percentage points	−5.81±1.01	
Relative risk reduction	88.9%	



Hammond J, Leister-Tebbe H, Gardner A, et al. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19. *New England Journal of Medicine*. 2022;0(0):null. doi:10.1056/NEJMoa2118542

2. Educate – Who is a Candidate?

BC	Treatments (bccdc.ca) COVID-19 treatments - Province of British Columbia (gov.bc.ca)
AB	Outpatient Treatment for COVID-19 | Alberta Health Services
SK	https://www.saskatchewan.ca/government/news-and-media/2022/january/25/stick-it-to-covid-paxlovid-available-to-eligible-residents-january-26 paxlovid-patient-handout.pdf (usask.ca) COVID-19 Treatments | Testing Information | Government of Saskatchewan
MB	https://gov.mb.ca/covid19/treatment/index.html
ON	COVID-19 antiviral treatment | COVID-19 (coronavirus) in Ontario
QC	Oral treatment against COVID-19 (Paxlovid^{TM}) | Gouvernement du Québec (quebec.ca)
NB	COVID-19 treatments (gnb.ca) Coronavirus (COVID-19) Drug Therapies (gnb.ca)
NS	Questions about Paxlovid? COVID-19 medication tips from your local infectious diseases pharmacist | Nova Scotia Health Authority (nshealth.ca)
PEI	Caring for yourself or others with COVID-19 | Government of Prince Edward Island
NF	Treatments - COVID-19 (gov.nl.ca)
NWT	Addition of Paxlovid as Treatment Option for COVID-19 | Health and Social Services Authority (nthssa.ca)
YK	For COVID-19 Questions call 811

2. Educate - Proactively Identifying Patients at High Risk and Start Discussion

- Patients at high risk of severe COVID-19
  - Age 60 or over
  - Overweight or living with obesity (body mass index [BMI] over 25)
  - Chronic kidney disease
  - Diabetes
  - Immunocompromised (weakened immune system from medication or a disease)
  - Active cancer
  - Cardiovascular conditions like hypertension (high blood pressure) and heart disease
  - Lung disease, such as chronic obstructive pulmonary disease (COPD), asthma (moderate to severe), cystic fibrosis, and pulmonary hypertension
  - Current smoker
  - Sickle cell disease
  - Neurodevelopmental disorders like cerebral palsy and Down syndrome

PAXLOVID PM - https://covid-vaccine.canada.ca/info/pdf/paxlovid-pm-en.pdf

2. Educate – Tools

- Drug interactions are a concern for some patients
- Dosing in people with CKD requires adjustment
- Drug interaction tools
  - https://www.covid19-druginteractions.org/ (University of Liverpool)
  - https://www.antimicrobialstewardship.com/paxlovid-ddi-oncology (UHN interactions in oncology)
- Manufacturer has some tools as well to help

Updated: June 6, 2022

SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

UNIVERSITY OF WATERLOO | SCHOOL OF PHARMACY

Nirmatrelvir/ Ritonavir (Paxlovid™)

What Prescribers and Pharmacists Need to Know

Why is nirmatrelvir/ritonavir used to treat COVID-19?

COVID-19 has an initial phase of viral replication and a significant inflammatory response in moderate illness. This inflammation can lead to poor outcomes, including hospitalization, invasive ventilation, and death. However, treatments that target SARS-CoV-2 replication, if administered before the inflammatory phase of COVID-19, can improve outcomes.

Nirmatrelvir works by binding to the SARS-CoV-2 3CL protease, which ultimately causes viral replication to stop. Ritonavir is a potent CYP3A4 inhibitor. It is not active against SARS-CoV-2 but is administered as a "boosting agent" to slow the metabolism of nirmatrelvir, thus increasing concentrations of nirmatrelvir.

Nirmatrelvir/ritonavir is a highly effective outpatient therapy based on available data, but there is uncertainty about effect magnitude in target populations and high certainty for harm with ritonavir **if drug interactions are not mitigated.**

What is the benefit of nirmatrelvir/ritonavir for COVID-19?

The EPIC-HR study[1] has shown a benefit from treatment of adult outpatients with laboratory-proven SARS-CoV-2 infection who were not on supplemental oxygen and were within 5 days of symptom onset. The study suggests that nirmatrelvir/ritonavir may reduce the risk of hospitalization in these patients by 88%.

Research on nirmatrelvir/ritonavir was done in unvaccinated patients and prior to circulation of the Omicron variant. However, a study suggests that nirmatrelvir/ritonavir retains activity against the Omicron variant in vitro.[2] The Ontario Science Advisory Table recommends the use of nirmatrelvir/ritonavir in COVID-19 patients who are not on supplemental oxygen but are at high risk of progression to moderate or severe COVID-19.[3]

Who should receive nirmatrelvir/ritonavir?

Nirmatrelvir/ritonavir should be offered to patients at **higher risk** of severe COVID-19 *(proven by PCR* or a provider-administered rapid test),* who are not yet on supplemental oxygen, and who are within 5 days of symptom onset.

*PCR = polymerase chain reaction

AGE (years)	NUMBER OF VACCINE DOSES			RISK FACTORS
	0 doses	1 or 2 doses	3 doses	
<20[1]	**Higher risk** if ≥3 risk factors[2]	Standard risk[1]	Standard risk[1]	• Obesity (BMI ≥30 kg/m²) • Diabetes • Heart disease, hypertension, congestive heart failure • Chronic respiratory disease, including cystic fibrosis • Cerebral palsy • Intellectual disability • Sickle cell disease • Moderate or severe kidney disease (eGFR <60 mL/min) • Moderate or severe liver disease (e.g., Child Pugh Class B or C cirrhosis)
20 to 39	**Higher risk** if ≥3 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
40 to 69	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
≥70	**Higher risk**	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	
Immunocompromised[2] individuals of any age	**Higher risk**: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.[1,2]			
Pregnancy	**Higher risk**[3]	Standard risk	Standard risk	

1. Evidence for the safety and efficacy of sotrovimab and nirmatrelvir/ritonavir (Paxlovid) in children <18 years of age is limited. While early evidence on risk factors for moderate and severe COVID-19 in children is emerging, the ability to reliably predict disease progression in children remains very limited, and the frequency of progression is rare. While not routinely recommended in children <18 years of age, the use of these agents may be considered in exceptional circumstances (e.g., severe immunocompromise and/or multiple risk factors, clinical progression) on a case-by-case basis. Multidisciplinary consultation with Infectious Diseases (or Pediatric Infectious Diseases) and the team primarily responsible for the child's care is recommended to review the individual consideration of these medications.
2. Examples of immunocompromised or immunosuppressed individuals include receipt of treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment), receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency, Good's syndrome, hyper IgE syndrome), advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.
3. Therapeutics should always be recommended for pregnant individuals who have received zero vaccine doses.

From: "Clinical Practice Guideline Summary: Recommended Drugs and Biologics in Adult Patients with COVID-19. (Version 11.0)" https://covid19-sciencetable.ca/sciencebrief/#infectious-diseases-clinical-care.

Indigenous persons (First Nations, Inuit, or Métis), Black persons, and members of other racialized communities may be at high risk of disease progression due to disparate rates of comorbidity, increased vaccination barriers, and social determinants of health, and should be considered priority populations for access to COVID-19 therapeutics. Nirmatrelvir/ritonavir may be considered in pregnant or lactating patients on an individual basis if the benefits of treatment outweigh the potential risks.

2. Educate – Operationalizing COVID-19 Treatment

- Proactively identify those at risk
- Discuss their risk
- Ensure they are protected with the vaccine
- Engage the team
- Medication review today
- Prescription on file
- Drug interaction management plan on file

3. Immunize Today

- Get them protected today
- Coadministration
  - For individuals 5 years of age and older, COVID-19 vaccines may be given concurrently with (i.e., same day), or at any time before or after, non-COVID-19 vaccines (including live and non-live vaccines)
  - If more than one type of vaccine is administered at a single visit, they should be administered at different injection sites using separate injection equipment.

Public Health Agency of Canada. Initial guidance on a second booster dose of COVID-19 vaccines in Canada: NACI statement, April 5, 2022. Published April 20, 2022. Accessed June 6, 2022. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-second-booster-dose-covid-19-vaccines.html

Revisit our Patient – Evelyn

- Ask
  - 60 years of age, multiple comorbidities, had Pneu-P-23 when diagnosed with COPD
- Recommendations for vaccines
  - Pneumococcal
  - COVID-19 booster
  - Influenza
- Educate she is at high risk:
  - Medication review for Paxlovid
    - Script
    - Plan
- Immunize today

- Background:
  - 60 years old
  - Obesity, hypertension, dyslipidemia, type 2 diabetes, COPD
  - Patient had COPD exacerbation 3 months requiring ED visit
- Medications:
  - Aclidinium/formoterol 400/12 mcg BID
  - Metformin 1000 mg BID
  - Dapagliflozin 10 mg daily
  - Sitagliptin 100 mg daily
  - Atorvastatin 40 mg daily
  - Ramipril/HCT 10/12.5 mg daily
- Discussion:
  - She is in for the flu shot
  - She had 2 total doses of COVID-19 (last dose was July 2021) – Waiting for an omicron specific vaccine

Other Considerations

Vaccine hesitancy

- Vaccine hesitancy does not equal anti-vaccine
- Education alone will not address vaccine hesitancy
- Using the presumptive ask can help to reduce resistance to vaccines
- Explore the patient's reason for hesitancy, ask permission to address their concern
- If they refuse, don't dismiss, warn them of the signs of the condition and say that you will bring it up again
- Even though there doesn't seem to be hesitancy today due to the high demand for the vaccine, it is out there
  - Can start discussions with patients early to hear their thoughts and address concerns before you are standing there with a needle in hand and they are resisting

Discussing Unfunded Vaccines

- Many times patients are not offered vaccines as the cost is not covered under public vaccine program
  - Please do not assume they will reject an unfunded vaccine – Just offer
  - New vaccines could take years before they are included in the public program
- It is important to offer the vaccines that the patient is a candidate for
  - Explain benefits of getting it vs risk of not getting it
  - Discuss cost
  - Many private plans will cover the cost of these vaccines
- Offer and allow them to decide
  - It is amazing how perspective changes based on their personal history (e.g. know someone with pneumonia or shingles)

Key Learning Points

1. Proactively engage patients to ensure their vaccines are up to date
2. Many patients are at high risk of COVID-19, pneumococcal disease and influenza
3. Identify patients today and develop a plan to manage infection, should they develop COVID-19 symptoms
4. We can take an active role to continue to improve outcomes in the patients we see every day in practice