The COVID CONVERSATIONS

Informed. Insights. Ideas.

Virulent Variants, Booster Vaccines and the Next Phase of the COVID-19 Pandemic

September 13, 2021 | 1:00 – 2:30 P.M. ET

Canadian Pharmacists Association

Association des pharmaciens du Canada

Disclosures

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- **Financial Disclosures (Include all Pharmaceutical Companies)**
  - **Grants/Research Support:** CIHR
  - **Speaking Engagements/Honoraria:** Merck, Pfizer, Sanofi Pasteur, AVIR Pharma, Immunize Canada, Federation of Medical Women in Canada
  - **Consulting Fees:** Merck, Pfizer, Sanofi Pasteur, GSK
- I had full editorial control over the content of this presentation and wish to advise that it may contain content that is not consistent with the approved Canadian Product Monographs

Disclosures

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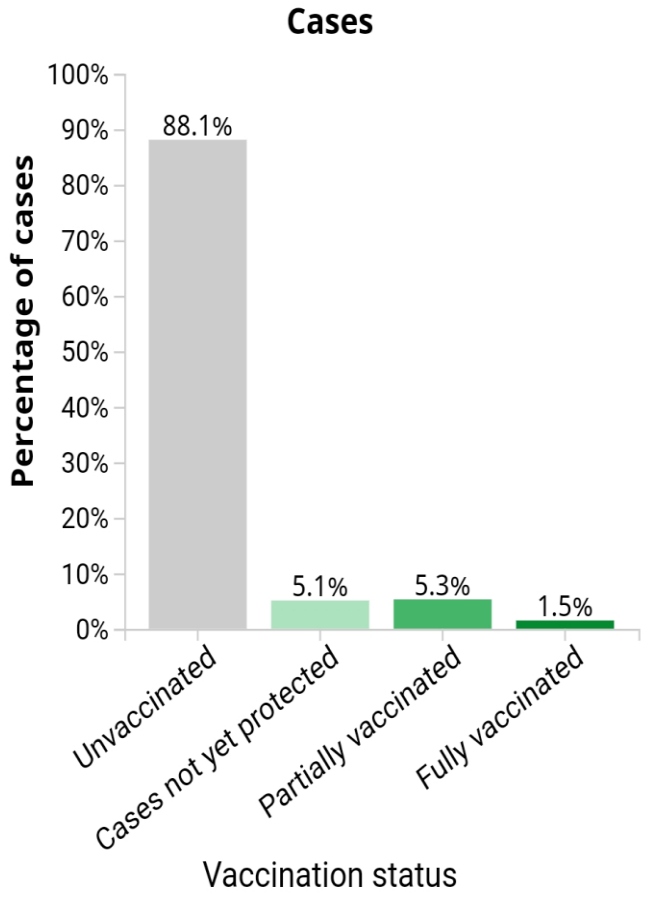
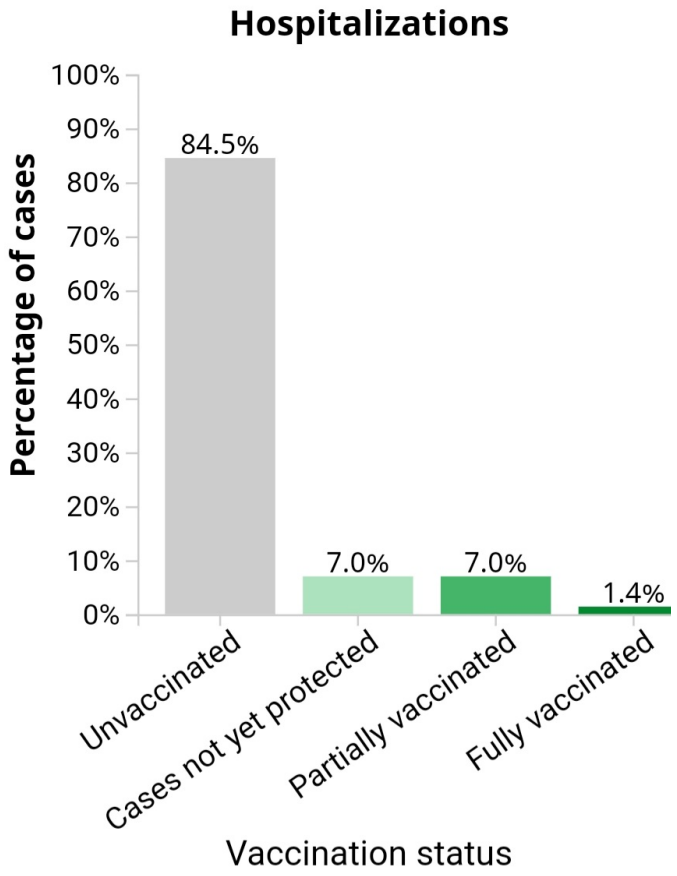
  - **Advisory Board/Speakers Bureau –** AA Pharma, Sanofi Pasteur
  - **Speaker/Consulting Fees:** Eli Lily, Novartis, Boeringher Ingelhiem, Mckesson Canada, Ensemble IQ, Sanofi Pastuer, Valneva
- Other: Current/past Employee of UBC Faculty of Pharmaceutical Sciences
- I had full editorial control over the content of this presentation and wish to advise that it may contain content that is not consistent with the approved Canadian Product Monographs

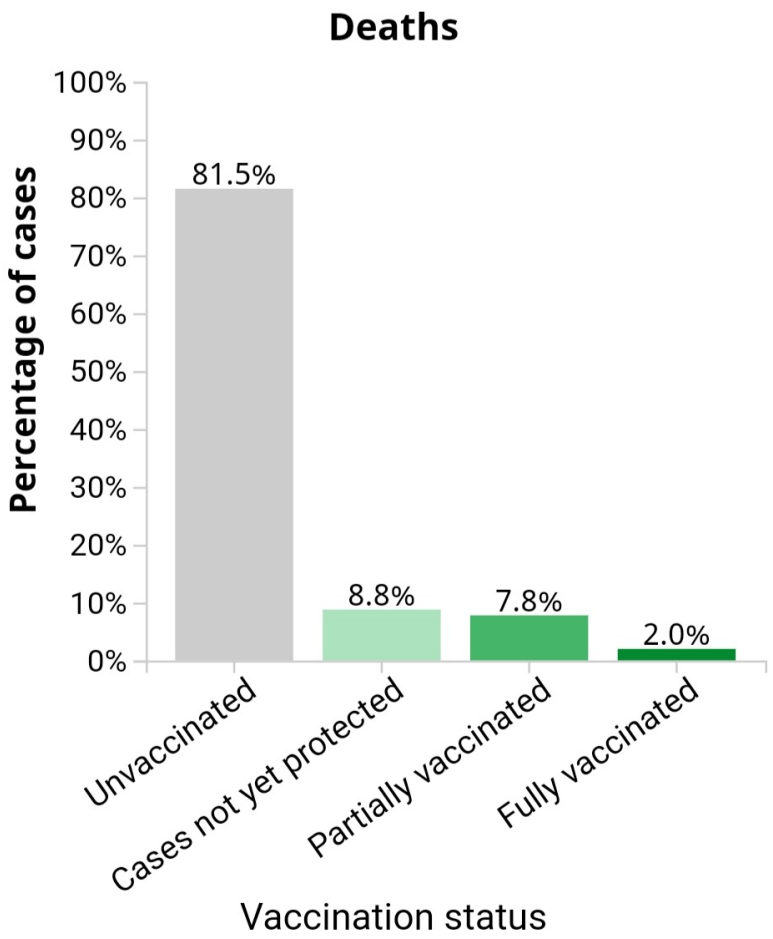
Learning Objectives

- What have we learned so far about SARS-COV2 infection in humans?
- What impacts have the emergence of "new variants" had on the pandemic and vaccine "effectiveness“
- What is the current evidence and subsequent role of "booster" COVID-19 vaccine doses?
- What is the current situation going into the fall regarding disease risk and vaccination options for children less than 12 years of age

PHAC Epidemiology Update as of Sept 7, 2021







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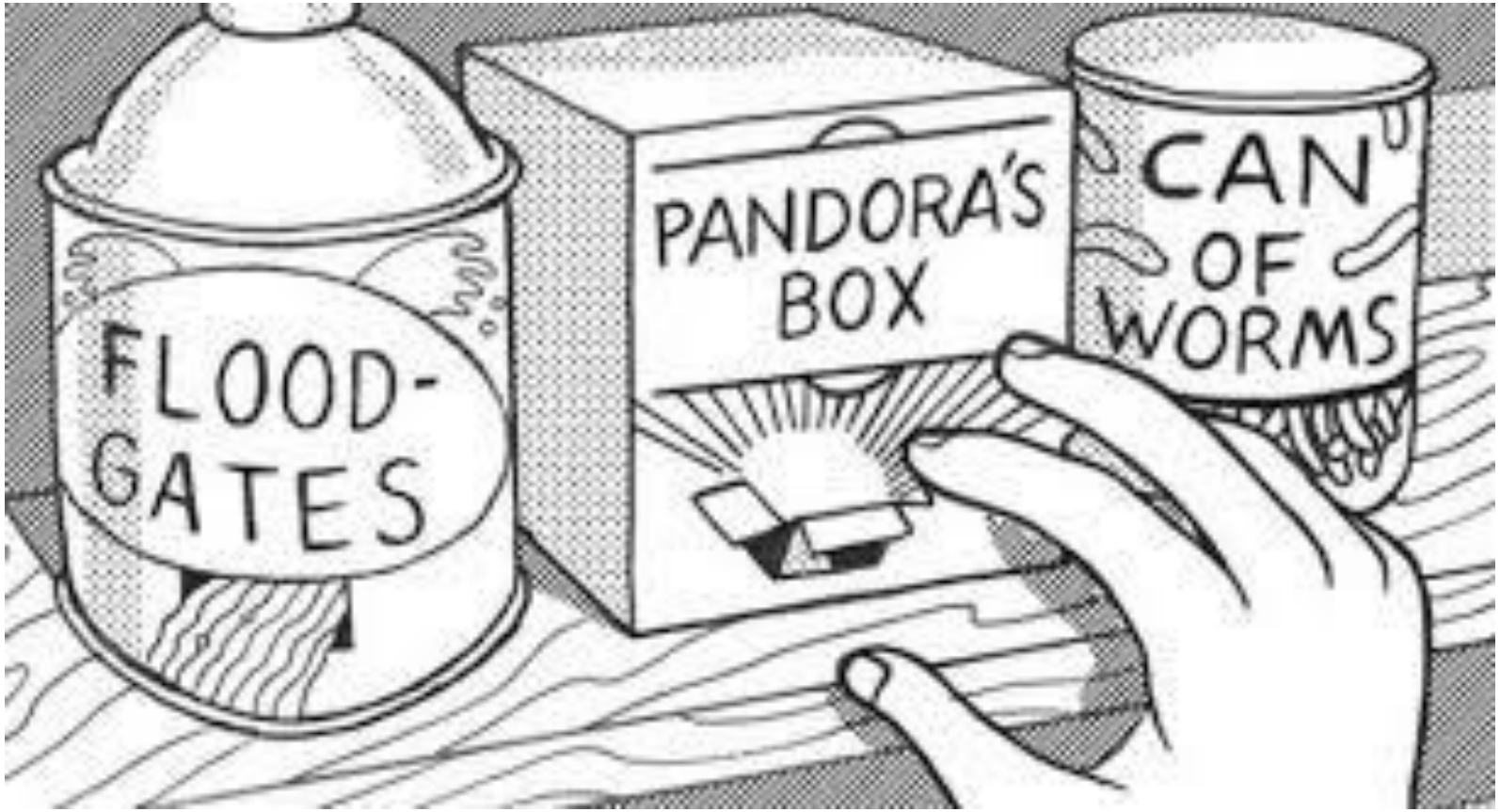
Question #1: What have we learned so far about SARS-COV2 infection in humans?



- **Multisystem Inflammatory Syndrome in Children (MIS-C)**
  - Post-viral hyperinflammatory condition affecting multiple organ systems
  - Usually seen 2-6 wks after the peak of COVID-19 outbreak in community

- **<u>CDC Case Definition</u>:**
- <21 yo presenting with ***fever, laboratory evidence of inflammation***, and evidence of ***clinically severe illness requiring hospitalization***, with ***multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological);*** AND

- No alternative plausible diagnoses; AND

- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.

- **Multisystem Inflammatory Syndrome in Adults (MIS-A)**
- ≥21yo hospitalized for ≥24h, or with an illness resulting in death, without a more likely alternative diagnosis with at least 3 of the following:
- Primary clinical criteria
  - Severe **cardiac** illness *Includes myocarditis, pericarditis, coronary artery dilatation/aneurysm, or new-onset right or left ventricular dysfunction (LVEF<50%), 2nd/3rd degree A-V block, or ventricular tachycardia. (Note: cardiac arrest alone does not meet this criterion)*
  - **Rash AND non-purulent conjunctivitis**
- Secondary clinical criteria
  - New-onset **neurologic** signs and symptoms *Includes encephalopathy in a patient without prior cognitive impairment, seizures, meningeal signs, or peripheral neuropathy (including Guillain-Barré syndrome)*
  - **Shock or hypotension** not attributable to medical therapy (e.g., sedation, renal replacement therapy)
  - **Abdominal pain, vomiting, or diarrhea**
  - **Thrombocytopenia** (platelet count <150,000/ microliter)
- Laboratory evidence of inflammation AND SARS-CoV-2 infection.

Literature Review of MIS-A

- 9 cases reported worldwide
- All hospitalized; 1 death

- Clinical features:
  - Occurrence in post-acute phase
  - Fever
  - Digestive symptoms
  - Cardiac involvement
  - Elevated inflammatory markers

Long COVID

- Post-acute COVID-19 is a syndrome with persistent or delayed symptoms lasting or appearing more than 3 weeks since illness-onset

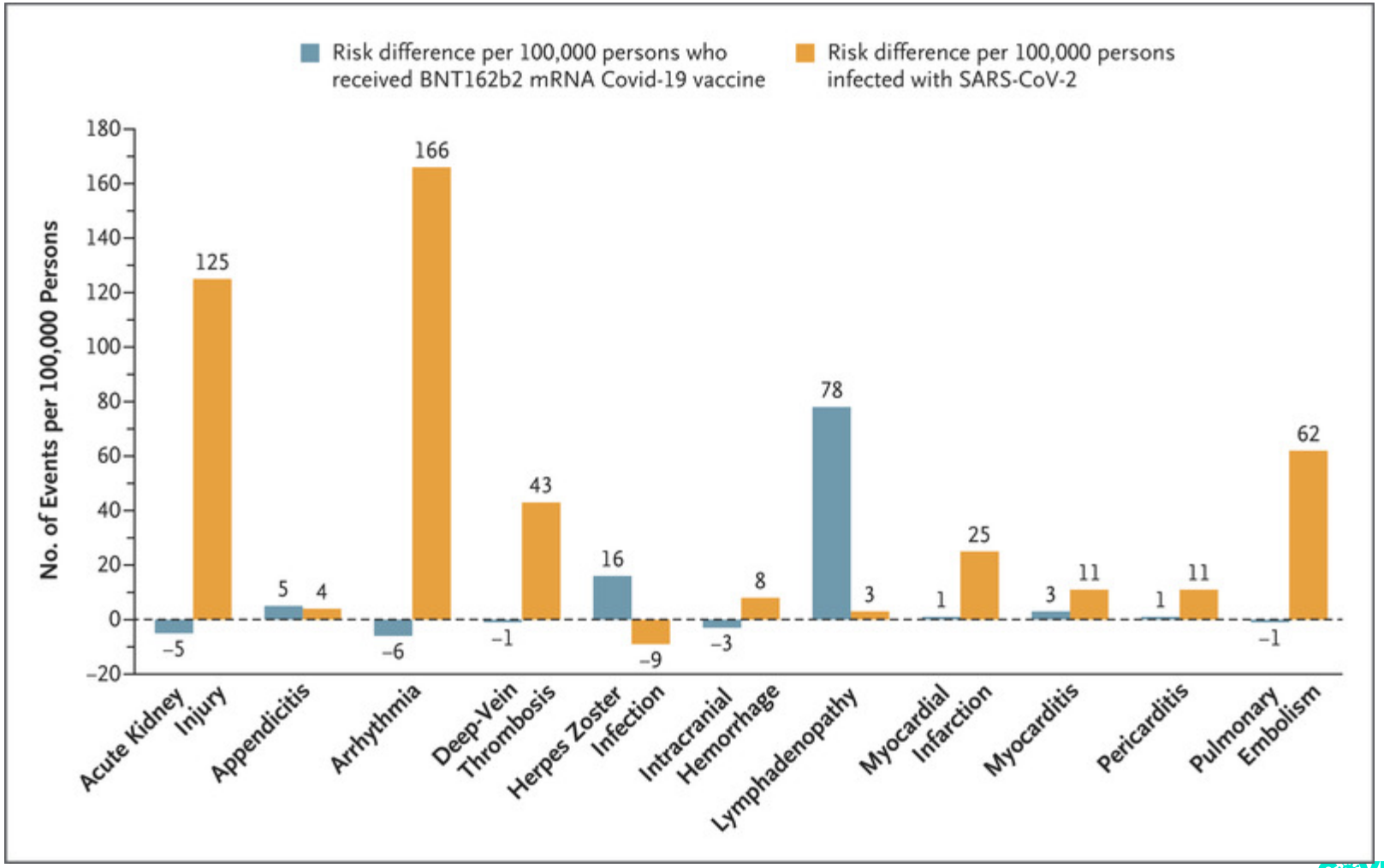
- Difficulty breathing or shortness of breath
- *Tiredness or fatigue
- Symptoms that get worse after physical or mental activities
- Difficulty thinking or concentrating (sometimes referred to as “brain fog”)
- *Cough
- Chest or stomach pain
- *Headache
- Fast-beating or pounding heart

- Can occur in anyone who has had COVID-19, even mild illness or initially asymptomatic

- Joint or muscle pain
- Pins-and-needles feeling
- Diarrhea
- *Sleep problems
- Fever
- Llightheadedness
- Rash
- Mood changes
- Change in smell or taste
- Changes in period cycles

*most commonly reported in children

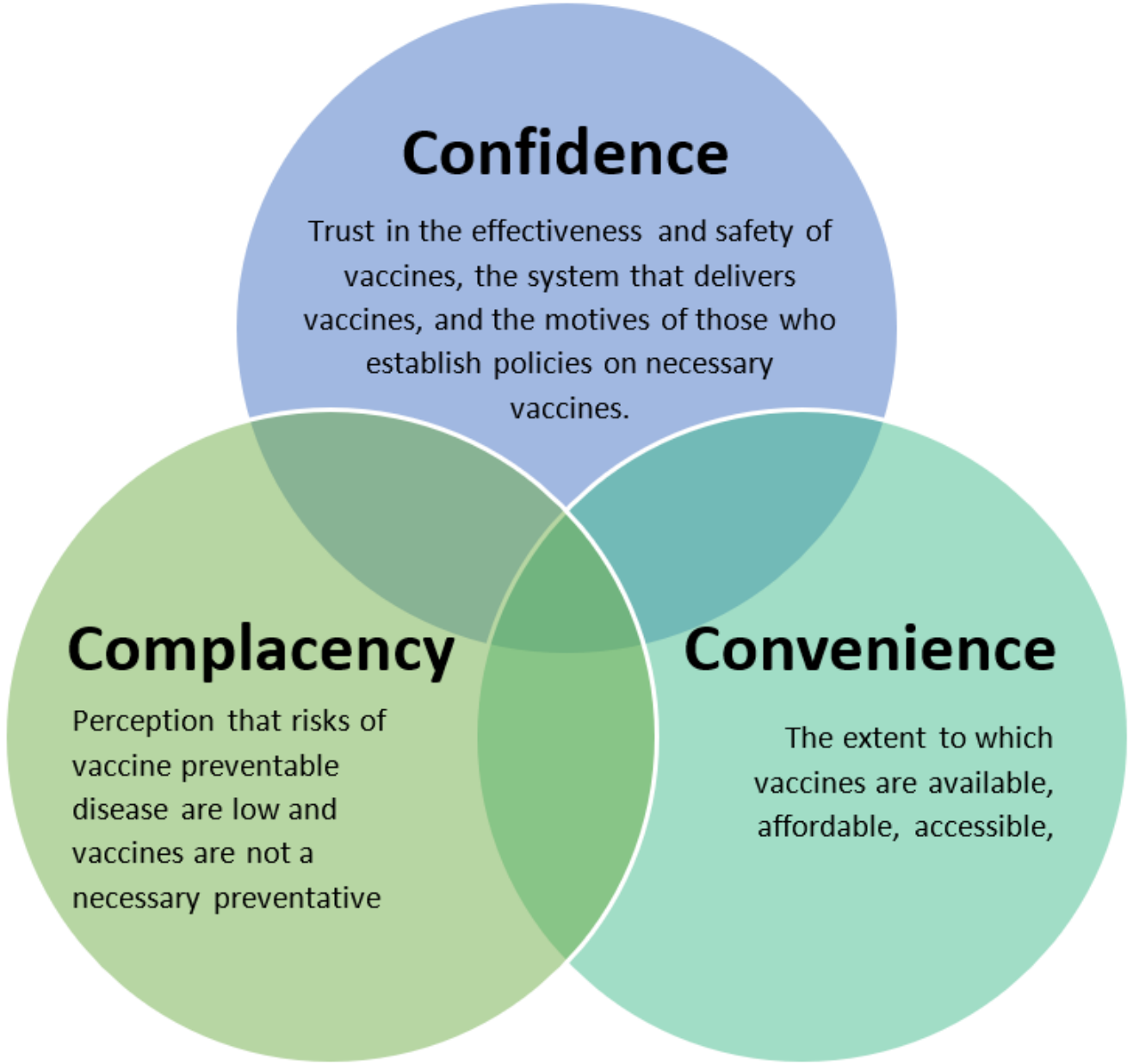
Myocarditis after mRNA Vaccines



Absolute Excess Risk of Various Adverse Events after Vaccination or SARS-CoV-2 Infection

August 25, 2021 DOI: 10.1056/NEJMoa2110475

Vaccine Hesitancy



VANCOUVER | News

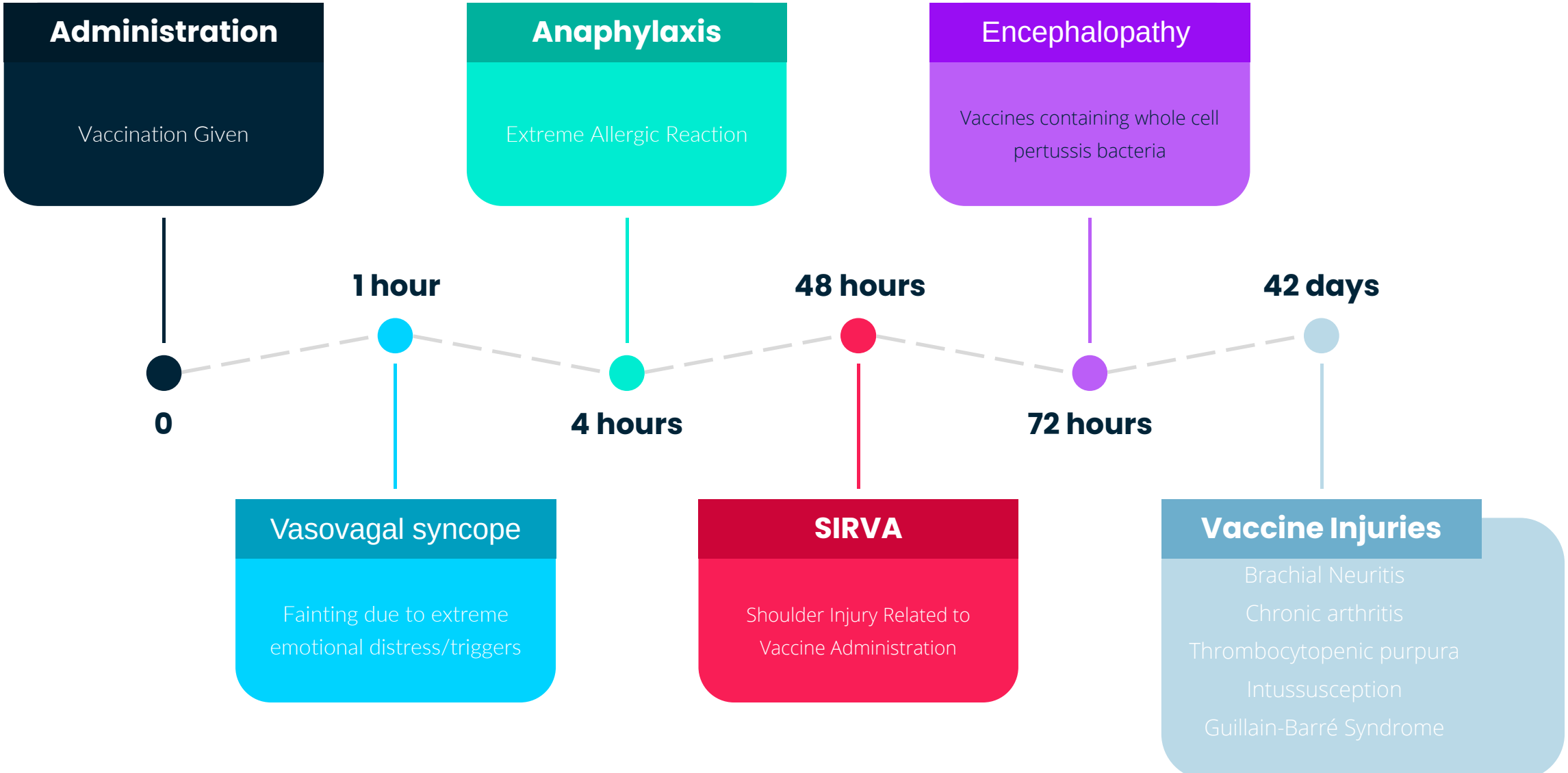
'Long COVID' clinics expanding as thousands of British Columbians struggle with symptoms

2 Month Follow Up – Is it enough?

- *From a safety perspective, a 2-month median follow-up following completion of the full vaccination regimen will allow identification of potential adverse events that were not apparent in the immediate postvaccination period. Adverse events considered plausibly linked to vaccination generally start within 6 weeks of vaccine receipt.*

Vaccine Adverse Event

TImeline



HRSA
Health Resources & Services Administration

According to the CDC, from 2006 to 2018 over 3.7 billion doses of covered vaccines were distributed in the U.S. For petitions filed in this time period, 7,565 petitions were adjudicated by the Court, and of those 5,297 were compensated. This means for every 1 million doses of vaccine that were distributed, approximately 1 individual was compensated.

Join BC ECHO for Post-COVID-19 Recovery

Register now >

Price: FREE

Format: Online

Duration: Monthly 1-hour sessions

Certification: Each session offers 1 Mainpro+ credit or 1 MOC (Section 1) Group Learning credit

Burden on “Other vaccine Preventable Diseases”

Influenza
Pneumonia
HPV
Shingles
Meningitis

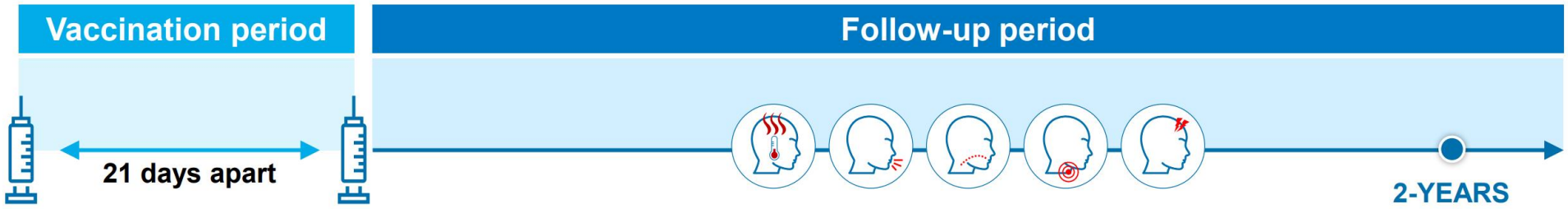
Question #2: What impacts have the emergence of "new variants" had on the pandemic and vaccine "effectiveness"

- Viruses continually mutate
- Variants of concern (VOC) have potential for increased transmissibility, more severe disease, reduced effectiveness of treatments or vaccines, diagnostic detection failures
- Real-world studies demonstrate reduced vaccine effectiveness against confirmed and symptomatic infection (72% - 88%) from Delta variant
- However, vaccine effectiveness against hospitalizations was 93-100%
- VOCs are being monitored with no current recommendations for targeted vaccines

HEALTH AND SCIENCE

Fully vaccinated people are still getting infected with Covid. Experts explain why

Phase 2/3 Efficacy Analysis



Prior infection status

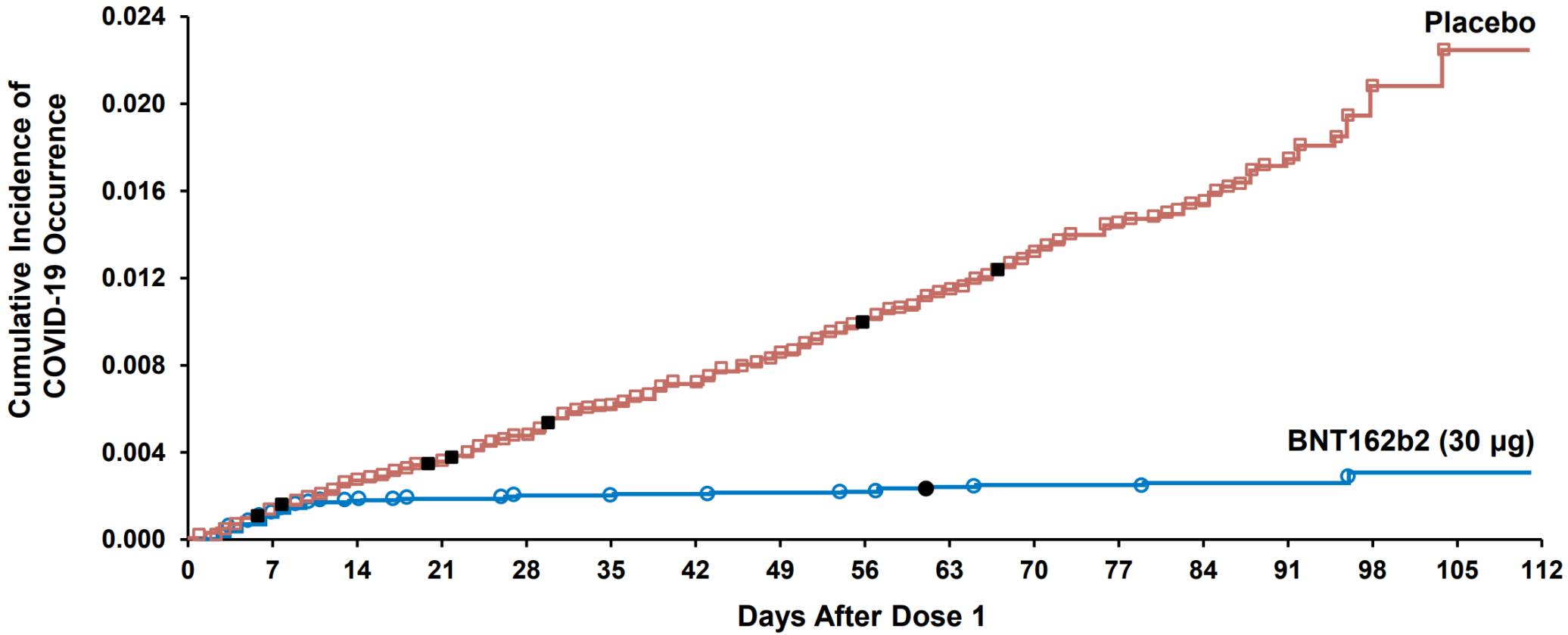
Before each dose

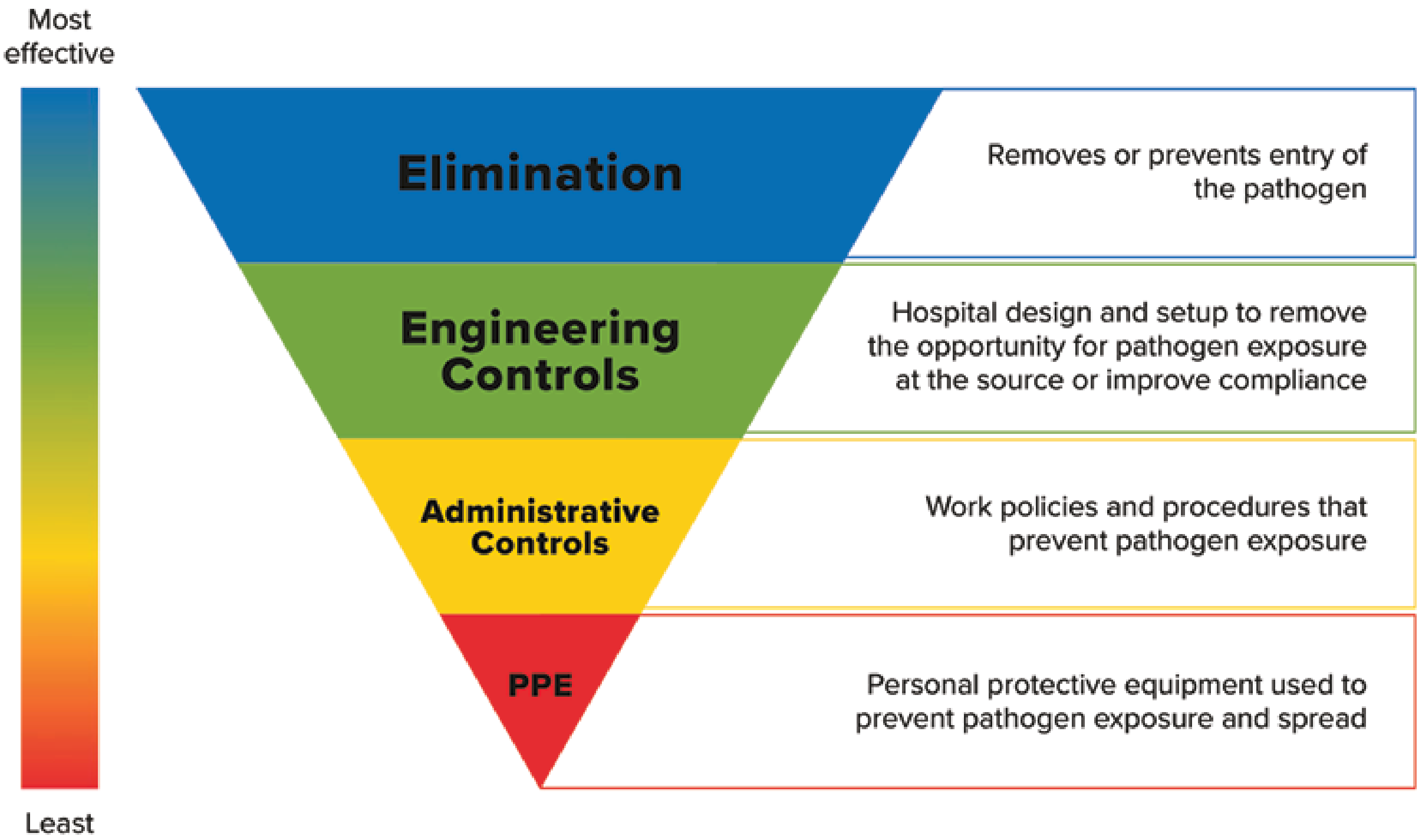
- Swab for SARS-CoV-2 PCR
- Blood for N-antigen antibodies

Active surveillance begins after 1st dose

Potential COVID-19 symptoms **TRIGGER** telehealth or in-person visit and nasal swab

Cumulative Incidence of COVID-19 After Dose 1




Most effective
Least
Elimination
Removes or prevents entry of the pathogen
Engineering Controls
Hospital design and setup to remove the opportunity for pathogen exposure at the source or improve compliance
Administrative Controls
Work policies and procedures that prevent pathogen exposure
PPE
Personal protective equipment used to prevent pathogen exposure and spread

Question #3: What is the current evidence and subsequent role of "booster" COVID-19 vaccine doses?

- Rationale for additional dose:
  - Vaccine-induced immunity wanes over time in those who developed adequate immunity after primary vaccine series →booster dose restores protection
  - Return to pre-pandemic behaviors increases exposure to high viral loads

- Immunocompromised individuals:
  - Are at increased risk of prolonged infection and severe COVID-19 disease (4-5X higher than general population)
  - Have reduced immune responses to 2-dose primary mRNA vaccine series
  - Have reduced vaccine effectiveness compared to general population
  - Have enhanced antibody responses with similar reactogenicity profile after 3rd dose

- Real world study in Israel (pre-print) suggests 70-84% reduction in risk of infection 14-20d after 3rd dose in 60+

https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/statement-september-10-2021-additional-dose-covid-19-vaccine-immunocompromised-following-1-2-dose-series.html

Additional Dose cont'd

- Aug.23/21: FDA approved emergency use authorization of 3rd dose of Pfizer (≥12yo) and Moderna (≥18yo) vaccines at least 28 days following the two-dose regimen of the same vaccine to who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise

- Sept.10/21: NACI recommends 3-dose mRNA primary vaccine series for moderate-severely immunocompromised. Those who received 1 or 2 dose complete primary vaccine series should receive additional dose of mRNA vaccine (no data on additional dose of viral vector vaccine in this population)
  - **minimal interval between the 1- or 2- dose primary series and the additional dose should be 28d**

- Informed consent should include discussion about the limited evidence for the use of an additional dose of any of the authorized COVID-19 vaccines, and unknown risk of myocarditis/pericarditis after 3rd dose of mRNA vaccine

Highly Vaccinated Israel Is Seeing A Dramatic Surge In New COVID Cases. Here's Why

August 20, 2021 · 11:01 AM ET
Heard on All Things Considered

DANIEL ESTRIN

3-Minute Listen + PLAYLIST

Demographic Characteristics
Phase 2/3 (N=43,448)

		BNT162b2 (30 µg) N=21,720 n (%)	Placebo N=21,728 N (%)	Total N=43,448 n (%)
Sex	Male	11,183 (51.5)	10,942 (50.4)	22,125 (50.9)
	Female	10,537 (48.5)	10,786 (49.6)	21,323 (49.1)
Race	White	17,839 (82.1)	17,857 (82.2)	35,696 (82.2)
	Black or African American	2,091 (9.6)	2,107 (9.7)	4,198 (9.7)
	All others	1,790 (8.2)	1,764 (8.1)	3,554 (8.2)
Ethnicity	Hispanic/Latino	5,672 (26.1)	5,668 (26.1)	11,340 (26.1)
	Non-Hispanic/non-Latino	15,928 (73.3)	15,940 (73.4)	31,868 (73.3)
	Not reported	120 (0.6)	120 (0.6)	240 (0.6)
Age	16-55 Years	12,780 (58.8)	12,822 (59.0)	25,602 (58.9)
	>55 Years	8,940 (41.2)	8,906 (41.0)	17,846 (41.1)
	16-64 Years	17,176 (79.1)	17,190 (79.1)	34,366 (79.1)
	65-74 Years	3,620 (16.7)	3,646 (16.8)	7,266 (16.7)
	≥75 Years	924 (4.3)	892 (4.1)	1,816 (4.2)

>9000 (20.9%)

Israel finds COVID-19 vaccine booster significantly lowers infection risk

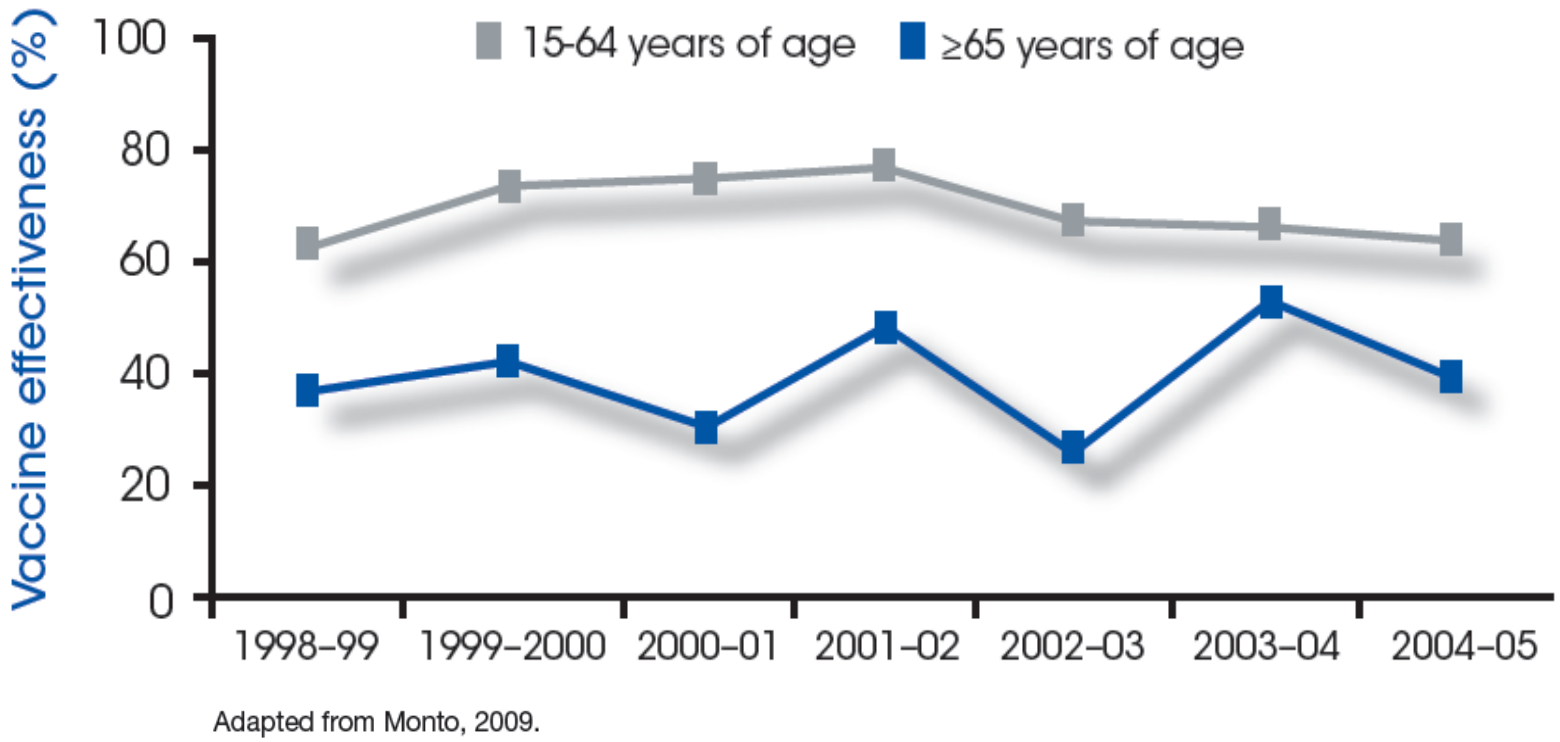
Reuters Staff
Contact

Published Sunday, August 22, 2021 5:39PM EDT

'Breakthrough' COVID-19 in older Israeli patients

An Israeli doctor and a COVID-19 expert weigh in on 'breakthrough' COVID affecting older patients and the need for a booster vaccine shot.

Standard-Dose Influenza Vaccine
Effectiveness by Age[1]



Adapted from Monto, 2009.

During the influenza seasons shown, the range of vaccine effectiveness was 62% to 76% in persons 15-64 years of age and 26% to 52% in those ≥65 years of age

Reference: 1. Monto AS, Ansaldi F, Aspinall R, et al. Influenza control in the 21st century: optimizing protection of older adults. *Vaccine.* 2009;27:5043-5053.

Influenza Vaccines in Canada

- **Inactivated influenza vaccines (TIV)**

  Influvac®, Fluviral®, Agriflu®, Trivalent vaccines available

- **Inactivated influenza vaccines (QIV)**

  Flulaval® Tetra, Fluzone®Quadrivalent, Afluria Quadrivalent

- **Live attenuated influenza vaccine (LAIV)**
  - **FluMist® Quadrivalent**
  - Intranasal spray of live attenuated influenza virus mainly for pediatric use
- **Cell-Based influenza vaccine (CBIV)**
  - **Flucellvax® Quadrivalent**
  - QIV made in cell-base instead of traditional eggs
- **High-dose inactivated influenza vaccine (HD-TIV)**
  - **FLUZONE® High-Dose**
  - TIV containing 4x the dose of regular influenza vaccines for adults aged 65+
- **Adjuvanted, inactivated influenza vaccine (ATIV)**
  - **FLUAD®/FLUAD Pediatric™**
  - TIV containing MF59 - an oil-in-water immunologic adjuvant

References:
An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI): Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2021-2022. Public Health Agency of Canada

Question # 4 - What is the current situation going into the fall regarding disease risk and vaccination options for children less than 12 years of age ?

- Pfizer and Moderna mRNA vaccines authorized ≥12yo

- Pediatric COVID vaccine trials currently being conducted

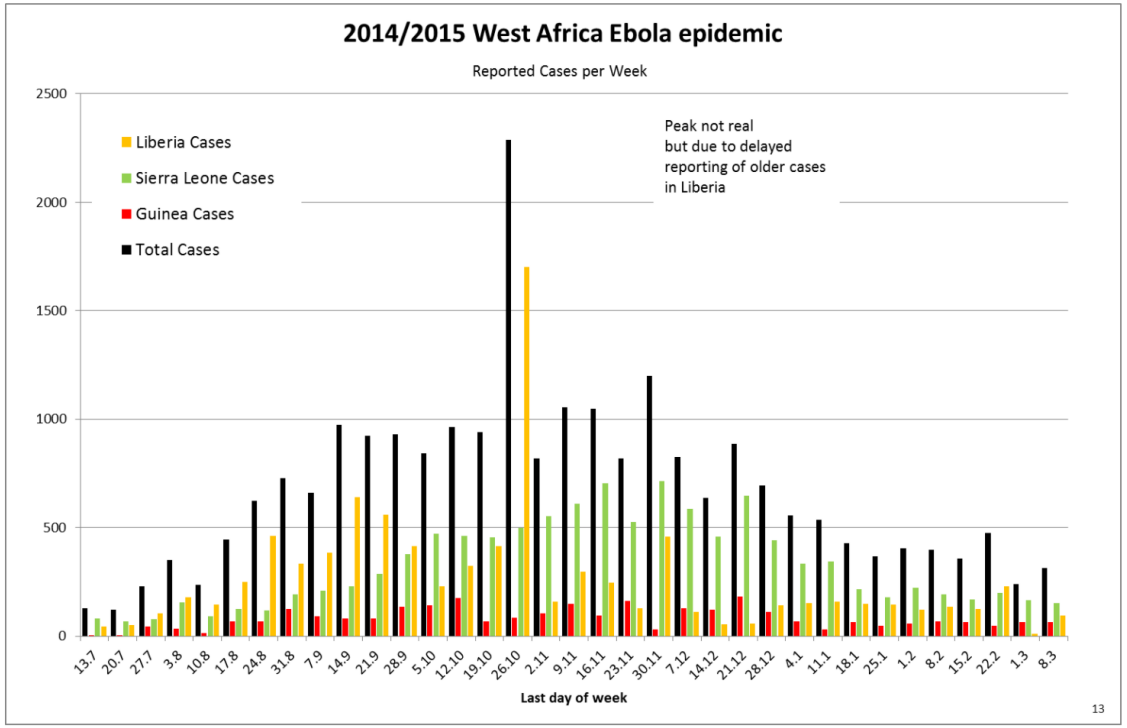
- MMWR report:
  - Hospitalization rates amongst unvaccinated 12-17yo was ~10X higher than vaccinated
  - Hospitalization rates amongst children ~4X higher in states with lowest overall vaccination coverage
  - No increase in disease severity despite increased cases in children
  - Community level vaccination is best way to protect children until direct immunization possible

- **Do not forget routine immunizations or vaccine-preventable diseases will come roaring back!!!!**

What history has shown

Over the years, outbreaks of a new disease have led to a reduction in routine vaccination rates — followed by a resurgence of previously dormant diseases.

One example happened in West Africa (Liberia, Guinea, and Sierra Leone), with the Ebola outbreak of 2014-2015. This led to a reduction in measles vaccination in the population. As a result, measles disease transmission drastically increased well above pre-Ebola levels.



NACI - Interim guidance on continuity of immunization programs during the COVID-19 pandemic

Adult immunizations: “Older adults are particularly susceptible to severe outcomes of COVID-19 and are at high risk for VPDs 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.”’**

https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-naci-interim-guidance-continuity-immunization-programs-during-covid-19-pandemic.html

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Coadministration?

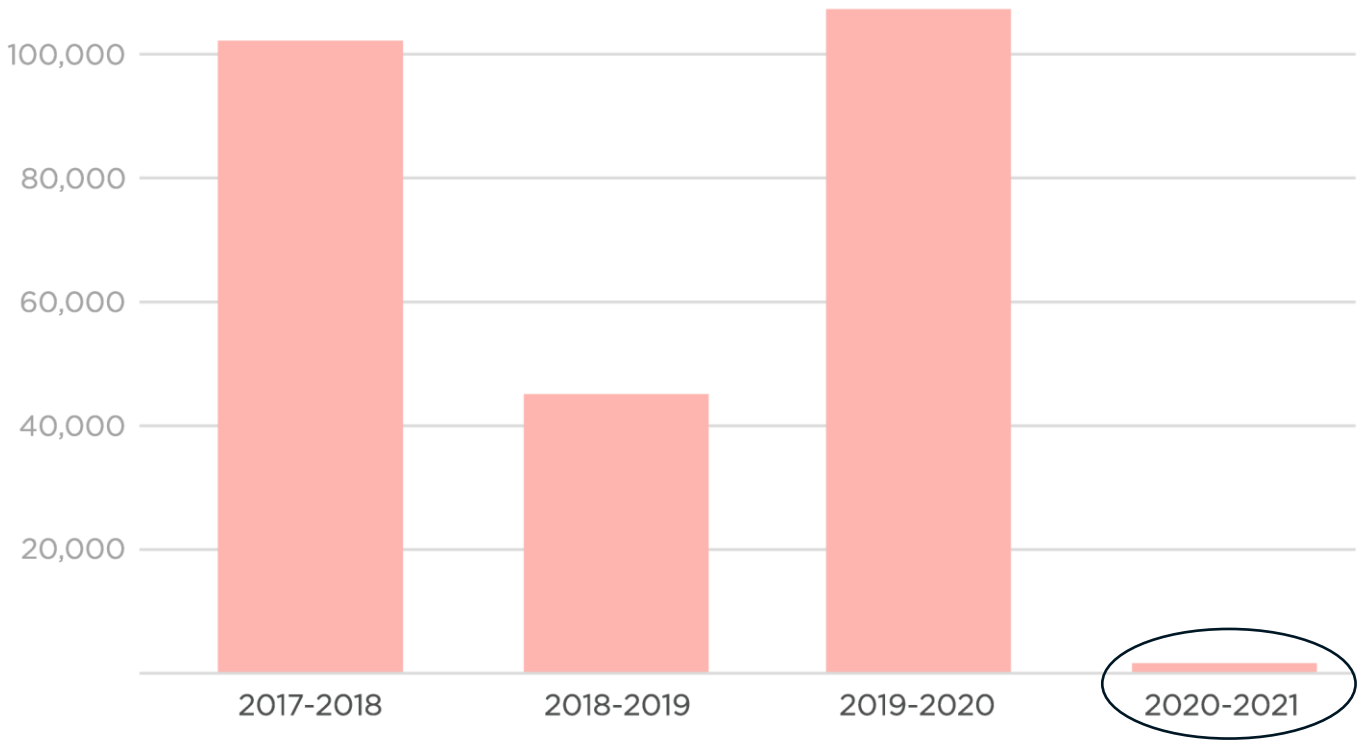
The BCCDC recommends that all COVID-19 vaccines (Pfizer, Moderna, AstraZeneca, Janssen) may be administered concomitantly or at any time before or after the administration of another inactivated or live vaccine.

While formal studies of coadministration have not been conducted yet, general guidelines on immunization are to use every visit as an opportunity to offer recommended vaccines.

— Healthcare Provider Q&A (bccdc.ca)

Few Americans have had confirmed flu cases this season

Positive lab tests through the fourth week of January



Source: Centers for Disease Control and Prevention

Vox

Workflow

- Websites
- Waitlists (Registration)
- Calling or lining up in crowded pharmacies
- Staffing
- Appointments vs Walk-ins
- Booking platforms
- Inventory
- 2nd dose recall (N/A for MOST Influenza vaccines)
- Access to Immunization Records

Thank you

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