COVID-19 Vaccine Update

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CANADIAN IMMUNIZATION RESEARCH NETWORK

Disclosures

- **Research Funding**
  - Government
    - CIHR
    - Public Health Agency of Canada
    - Public Works Canada
  - Industry
    - GlaxoSmithKline
    - Sanofi Pasteur
    - Pfizer
    - Merck
    - Janssen
    - Entos
    - IMV
    - CanSino
    - VBI
  - The CIRN SOS Network is funded by CIHR, PHAC and by collaborative agreements or investigator-initiated research agreements with GSK (influenza) and Pfizer (CAP/IPD), respectively

- **Consultant/Advisory Board/Committee**
  - Government
    - NS Dept of Health Experts Group
    - C19 Vaccine Expert Panel
    - DHW COVID-19 Key Populations Task Group
  - Industry
    - GlaxoSmithKline
    - Sanofi Pasteur
    - Merck
    - Pfizer
    - Medicago

Learning Objectives

- To review current data on authorized and anticipated vaccinations for COVID-19
- To review NACI recommendations for COVID-19 vaccination
- To discuss use of mRNA vaccines in those who are pregnant or breastfeeding, immunocompromised or have underlying autoimmune conditions
- To review process for AEFI reporting following COVID vaccines.

Vaccine Platform Refresher

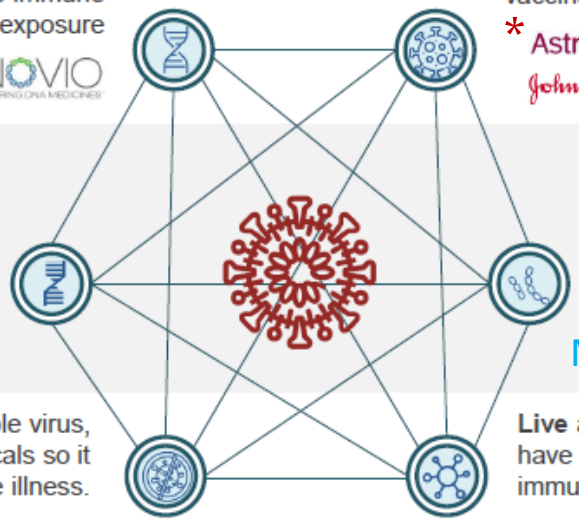
DNA-based vaccines work by inserting synthetic DNA of viral gene(s) into small DNA molecules (called plasmids). Cells take in the DNA plasmids and follow their instructions to build viral proteins, which are recognized by the immune system, and prepare it to respond to disease exposure

SANOFI INOVIO

Viral vector vaccines insert a gene for a viral protein into another, harmless virus (replicating or non-replicating), which delivers the viral protein to the vaccine recipient, triggering an immune response.

* AstraZeneca MERCK CanSinoBIO

Johnson&Johnson *



RNA vaccines introduce an mRNA sequence coded for a disease-specific antigen. Once this antigen is reproduced within the body, it is recognized and triggers an immune response

Pfizer* moderna* CUREVAC

Subunit vaccines introduce a fragment of the virus into the body. This fragment is enough to be recognized by the immune response and stimulate immunity.

NOVAVAX* Clover Biopharmaceuticals

Medicago* GSK/Sanofi*

Inactivated vaccines consist of the whole virus, which has been killed with heat or chemicals so it can't cause illness.

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sinovac

Live attenuated vaccines are made up of whole viruses that have weakened in a lab. They tend to elicit a stronger immune response than inactivated vaccines.

AVAC 25 Years and Counting

* Advanced Purchase Agreements with Canadian Government Phase 3

Canada's vaccine pipeline

Canada has secured vaccine access from 7 leading candidates	6 of 7 candidates require 2 doses, at different intervals	Health Canada has received submissions for authorization from 4 vaccine candidates
Pfizer BIONTECH	2 doses: → 21 days apart →	✓
moderna	2 doses : → 28 days apart →	✓
janssen	1 dose :	✓
NOVAVAX Creating Tomorrow's Vaccines Today	2 doses : → 21 days apart →	
SANOFI gsk	2 doses : → 21 days apart →	
medicago gsk	2 doses : → 21 days apart →	
AstraZeneca	2 doses : → 28 days apart →	✓

SARS-CoV-2 virion

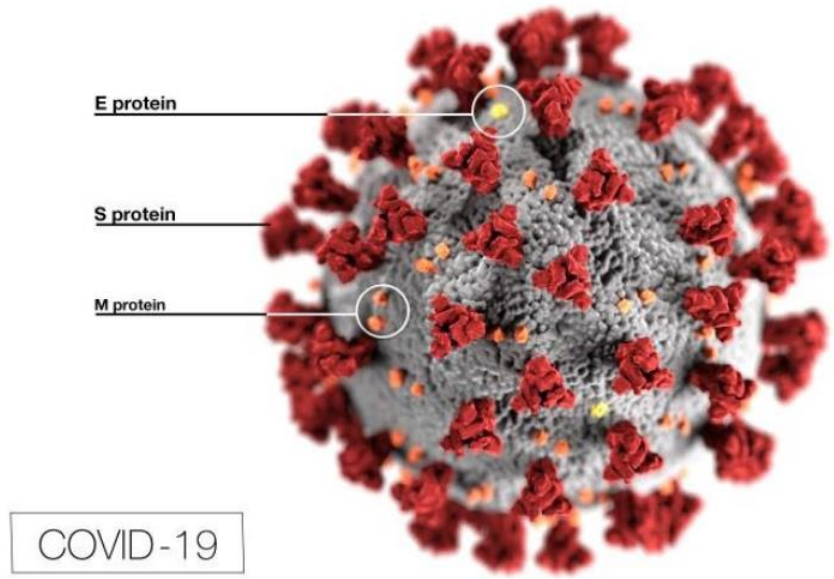
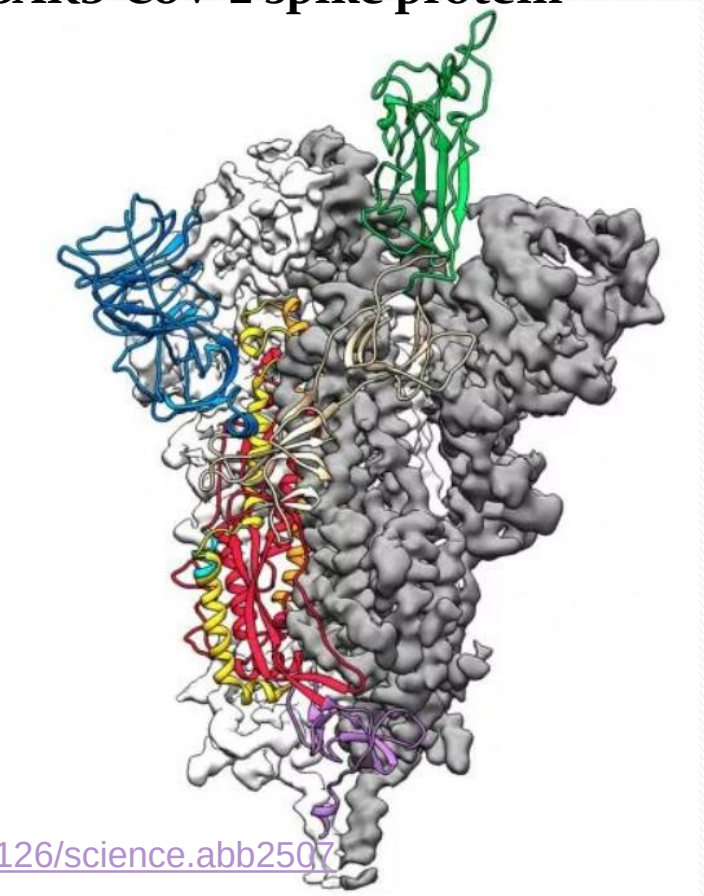


Image: CDC/Alissa Eckert

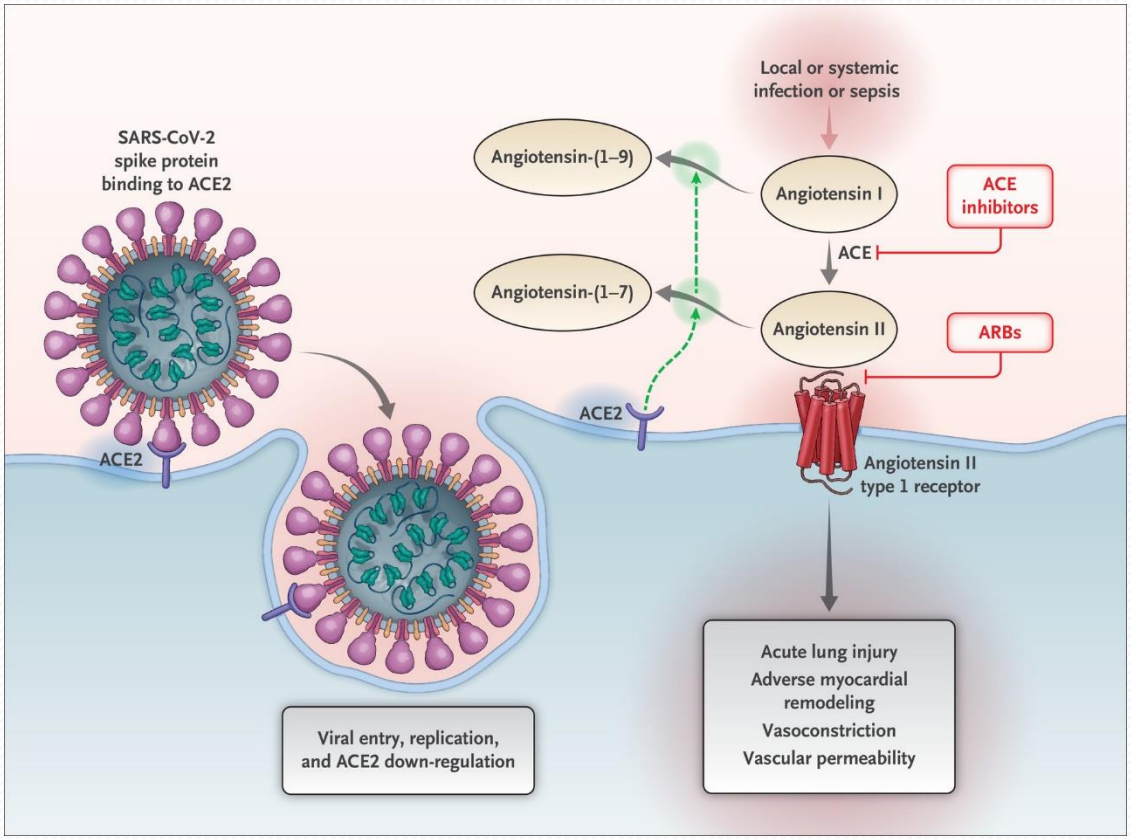
SARS-CoV-2 spike protein



DOI: 10.1126/science.abb2507

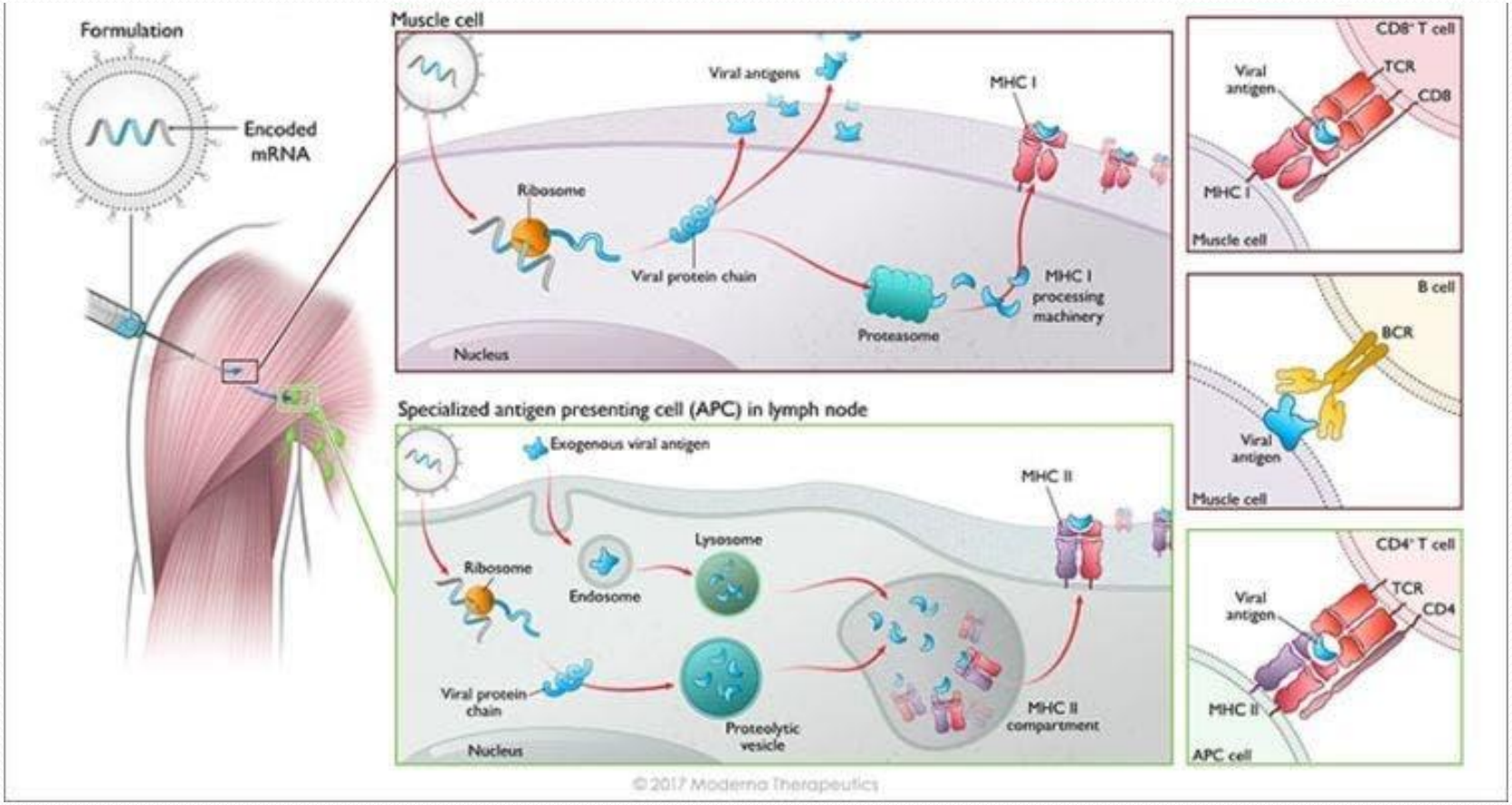
This is the 3D atomic scale map or molecular structure of the SARS-2-CoV protein "spike" which the virus uses to invade human cells.
(Image: © Jason McLellan/Univ. of Texas at Austin)

SARS-CoV-2 cell entry



N Engl J Med 2020; 382:1653-1659
DOI: 10.1056/NEJMsr2005760

mRNA Vaccines: Mechanism of Action



Two Nucleic Acid-based Vaccine Platforms: DNA vs mRNA

	DNA	mRNA
Stability	DNA **more stable** than RNA and remains intact longer inside and outside the cell	RNA **far less stable**, need technologies to try to increase stability ("jiggle factor")
Mechanism of Action	DNA needs to get inside cell then inside nucleus; DNA must be transcribed to mRNA then translated to protein to elicit Ab and CMI response.	RNA only needs to enter cell for translation alone. Only needs to cross one membrane so can be delivered via lipid coating – "lipid nanoparticle"
Risk of genomic integration	Some risk	No Risk

mRNA-based Vaccine Platform

Advantages	- Quick manufacturing and interchangeable Ag - Anticipated inductions of cellular and humoral responses
Disadvantages	- No authorized RNA vaccines; unknown stability, durability and long term safety - Supply chain is materials may be unstable

Manufacturer	Platform	Stage of Development
Moderna (NIH) (US)	Non-replicating mRNA lipid nanoparticle	Phase 3 in US
BioNTech/Pfizer (Germany and US)	Non-replicating modified mRNA lipid nanoparticle	Phase 2/3 in US and Germany Phase 1/2 in Japan
Chulalongkorn University	mRNA encoding SARS-CoV-2 spike	Phase 1/2 in Thailand

Moderna and BioNTech/Pfizer have signed Advanced Purchase Agreements with the Canadian Government

Vaccine characteristics

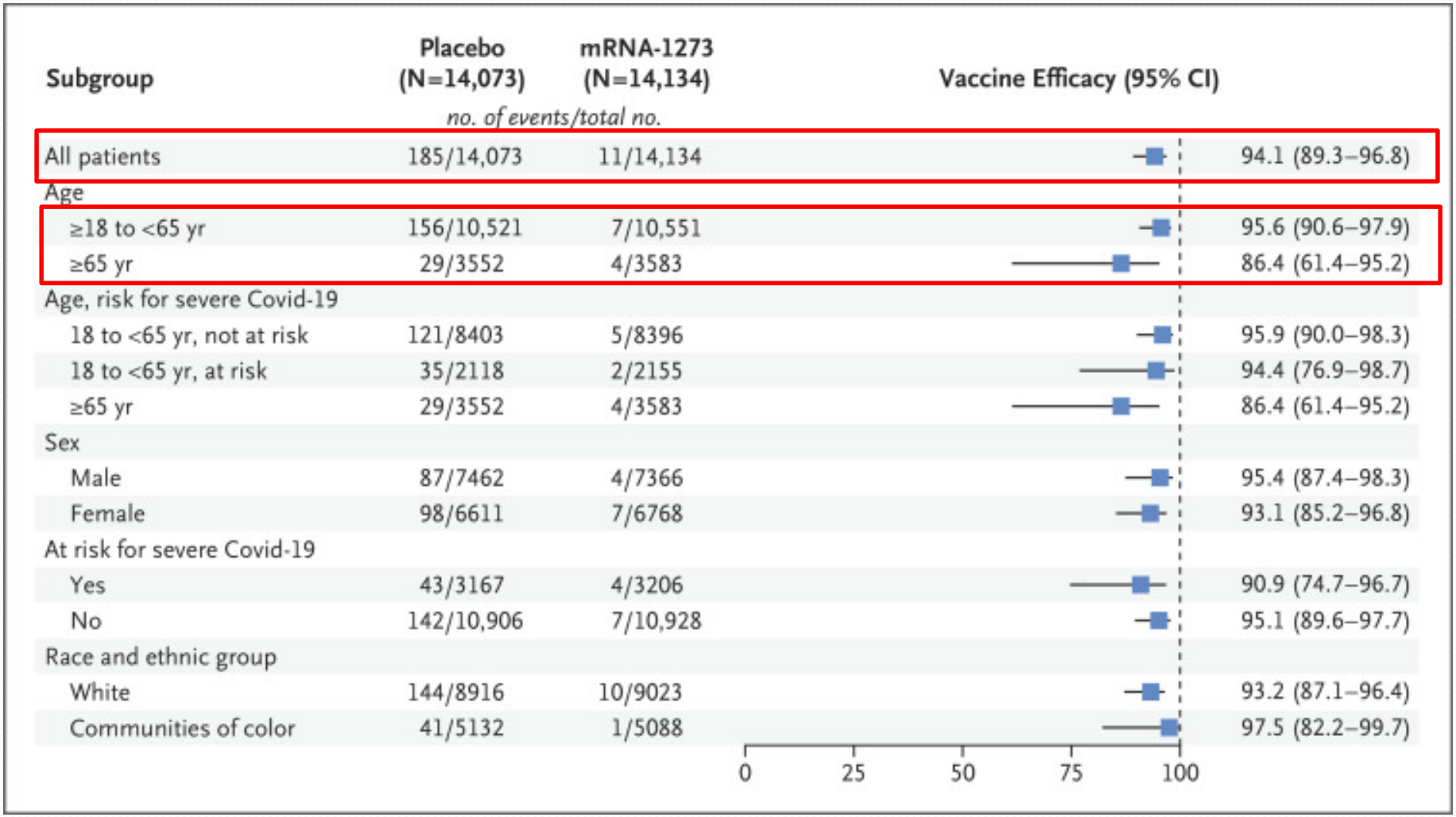
	Moderna (mRNA-1273)	Pfizer/BioNTech (BNT162b2)
Vaccine components	mRNA formulated into a lipid nanoparticle (LNP)	mRNA formulated into a lipid nanoparticle (LNP)
Authorized population	18y +	16y +
Vial size	10 dose multi-vial	5 (6) dose multi-vial
Reconstitution	None needed	Normal saline
Administration and dosing	2 x 0.5ml IM; 28d apart	2 x 0.3ml IM; 21d apart (alt 28d schedule OK per NACI)
Freezer storage	-20°C	-75°C
Transport	Frozen only (-20°C)	Ultrafrozen only (-75°C)
Fridge storage	30d	5d
Room temperature (unpunctured)	12h	2h
Once punctured	6h	6h

mRNA Vaccines: Summary Results

	Moderna (mRNA-1273)[1]	Pfizer/BioNTech (BNT162b2)[2]
	Phase 3 - Age: 18+ - Size: 30,420 in US - dosing: 2xIM, 28d	Phase 3 - Age: **12-15y, 18-55y, 65-85y** - Size: 43,000 in US - Dosing: 2xIM, 21d
Efficacy Data	*Final Analysis* 185 Placebo/ 11 vaccine Data from 2 months post dose 2 **Primary endpoint**: 94.1% vaccine efficacy (89.3- 96.8%) **Efficacy in 65+: 86.4% (61.4-95.2)** **Secondary endpoint**: 30 severe cases and 1 death- all in Placebo group	Final analysis at 170 cases (162 Placebo/ 8 vaccine) Data from 1 week after dose 2 **Primary endpoint**: 95% vaccine efficacy (90.3-97.6%) **Efficacy in 65y+: 94% (66.7-99.9)** **Secondary endpoint:** 10 severe cases- 9 in Placebo group.
Safety Data	Median follow up only approx. 2mos; quite reactogenic; no serious safety concerns	Median follow up only approx. 2mos; quite reactogenic; no serious safety concerns

[1]NEJM 2020:Dec 30 [2]NEJM 2020:Dec 10

Moderna: VE by subgroup



NEJM 2020; Dec 30

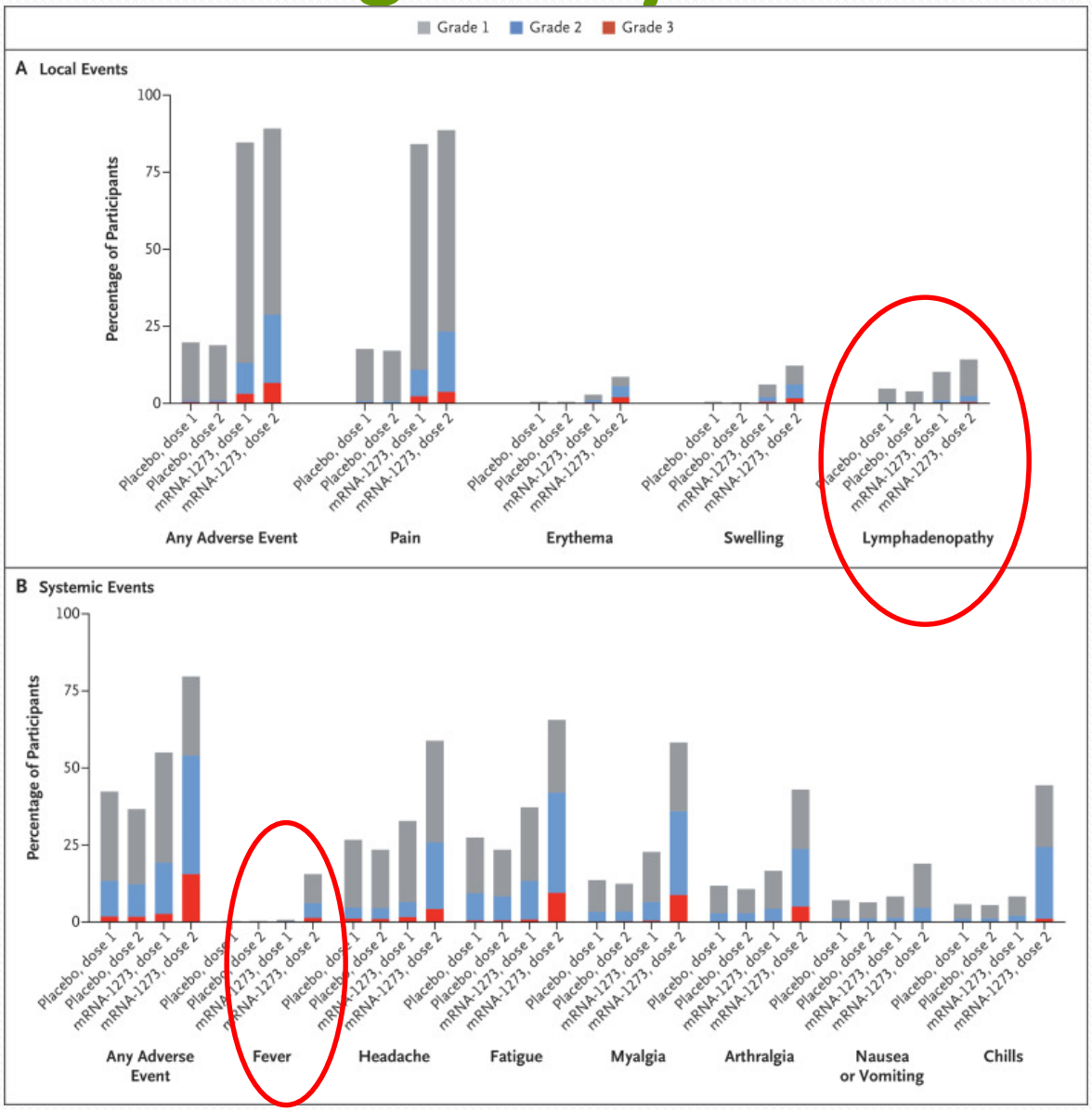
Pfizer/BioNTech: VE by subgroup

Table 3. Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection before 7 Days after Dose 2.

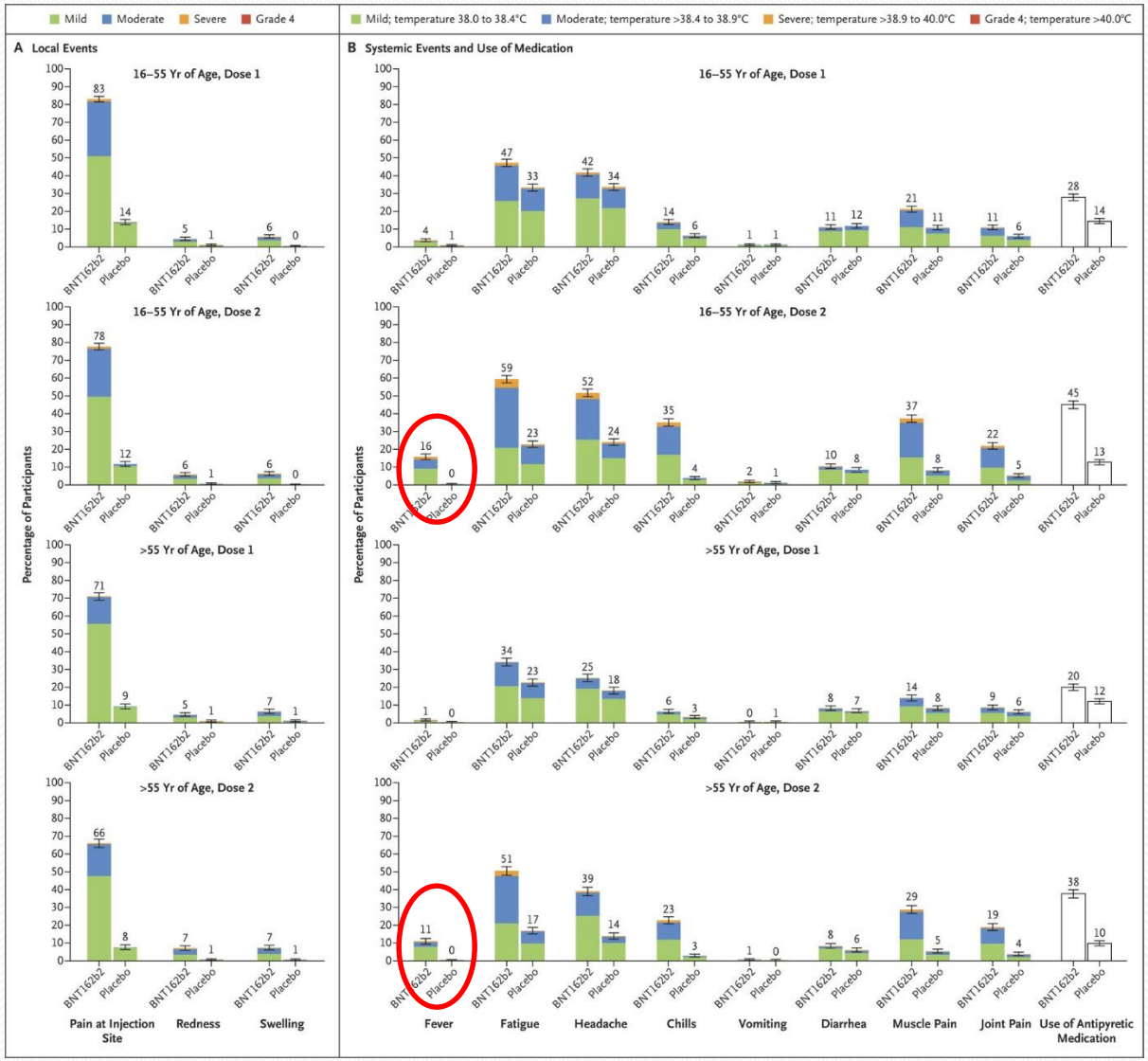
Efficacy End-Point Subgroup	BNT162b2 (N=18,198)		Placebo (N=18,325)		Vaccine Efficacy, % (95% CI)†
	No. of Cases	Surveillance Time (No. at Risk)*	No. of Cases	Surveillance Time (No. at Risk)*	
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.0–97.9)
Age group					
16 to 55 yr	5	1.234 (9,897)	114	1.239 (9,955)	95.6 (89.4–98.6)
>55 yr	3	0.980 (7,500)	48	0.983 (7,543)	93.7 (80.6–98.8)
≥65 yr	1	0.508 (3,848)	19	0.511 (3,880)	94.7 (66.7–99.9)
≥75 yr	0	0.102 (774)	5	0.106 (785)	100.0 (–13.1–100.0)
Sex					
Male	3	1.124 (8,875)	81	1.108 (8,762)	96.4 (88.9–99.3)
Female	5	1.090 (8,536)	81	1.114 (8,749)	93.7 (84.7–98.0)
Race or ethnic group‡					
White	7	1.889 (14,504)	146	1.903 (14,670)	95.2 (89.8–98.1)
Black or African American	0	0.165 (1,502)	7	0.164 (1,486)	100.0 (31.2–100.0)
All others	1	0.160 (1,405)	9	0.155 (1,355)	89.3 (22.6–99.8)
Hispanic or Latinx	3	0.605 (4,764)	53	0.600 (4,746)	94.4 (82.7–98.9)
Non-Hispanic, non-Latinx	5	1.596 (12,548)	109	1.608 (12,661)	95.4 (88.9–98.5)
Country					
Argentina	1	0.351 (2,545)	35	0.346 (2,521)	97.2 (83.3–99.9)
Brazil	1	0.119 (1,129)	8	0.117 (1,121)	87.7 (8.1–99.7)
United States	6	1.732 (13,359)	119	1.747 (13,506)	94.9 (88.6–98.2)

* Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.
† The confidence interval (CI) for vaccine efficacy is derived according to the Clopper–Pearson method, adjusted for surveillance time.
‡ Race or ethnic group was reported by the participants. "All others" included the following categories: American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported.

Moderna: Reactogenicity



Pfizer/BioNTech: reactogenicity



Implications for Occupational Health

- Local and systemic AEs common, particularly after Dose 2
- ~15% will experience fever post-dose 2; fatigue, headache and chills common (worse post dose 2)
- No role for prophylactic acetaminophen/ibuprophen but can be used to treat symptoms
- HCW meeting COVID case definition (fever OR 2 or more of sore throat, runny nose, headache or SOB) should NOT REPORT TO WORK and should arrange a COVID test
- Attempt to avoid many people from same clinical area being vaccinated on same day to avoid service implications of AEs

Allergic reactions and anaphylaxis post dose 1 Pfizer/BioNTech vaccine (CDC, MMWR Jan 15)

- Vaccine contraindicated in persons with allergy to polyethylene glycol (PEG) or prior dose of vaccine
- Caution in patients with hx of anaphylaxis to another vaccine or injectable product- proceed but observe x 60 min
- No special precautions in patients with anaphylaxis to foods, oral medications, insect stings

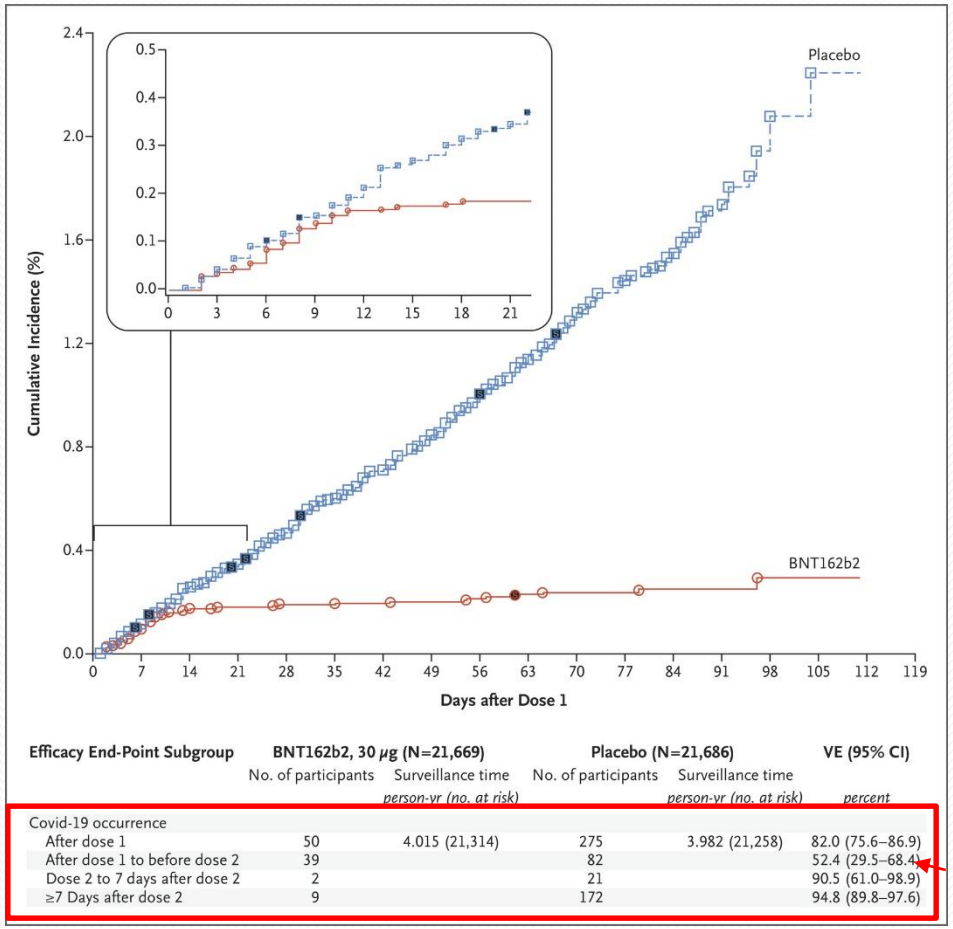
Allergy cont.

- 21 cases anaphylaxis reported in US in Dec following Dose 1 Pfizer- rate **11.1/mil** doses administered (vs 1.35/mil for influenza vaccine)
- Median onset 13 minutes (range 2-150 min); 71% occurred within 15min
- 4 patients hospitalized (3 in ICU)
- 81% had hx of allergies (1/3 hx of anaphylaxis)
- Early tx with IM epi critical
- Given timing, should we extend observation period in people with Hz of anaphylaxis or multiple allergies?

Rationale for delayed dosing (or single dose)

- mRNA vaccines authorized on a 2 dose 0, 21d (Pfizer) or 0, 28d (Moderna) schedule
- In some jurisdictions with significant community transmission and deaths, consideration of immunizing as many people as possible with 1st dose to achieve early, broad population protection being recommended
- Given anticipated vaccine supply, this will mean delaying (or omitting) Dose 2
- **Pros:**
  - Short term efficacy of first dose appears high
  - Maximizes number of people protected quickly
  - In general, increased interval between doses in a series not detrimental and potentially improves immunogenicity
- **Cons:**
  - Establishing large cohorts of partially immune people in the face of a highly prevalent infection could lead to development or selection for viral variants
  - Peak humoral and CMI responses occur after dose 2
  - Infections between dose 1 and delayed dose 2 could erode confidence in vaccine leading to lower overall 2-dose completion

Pfizer/BioNTech: Single dose efficacy

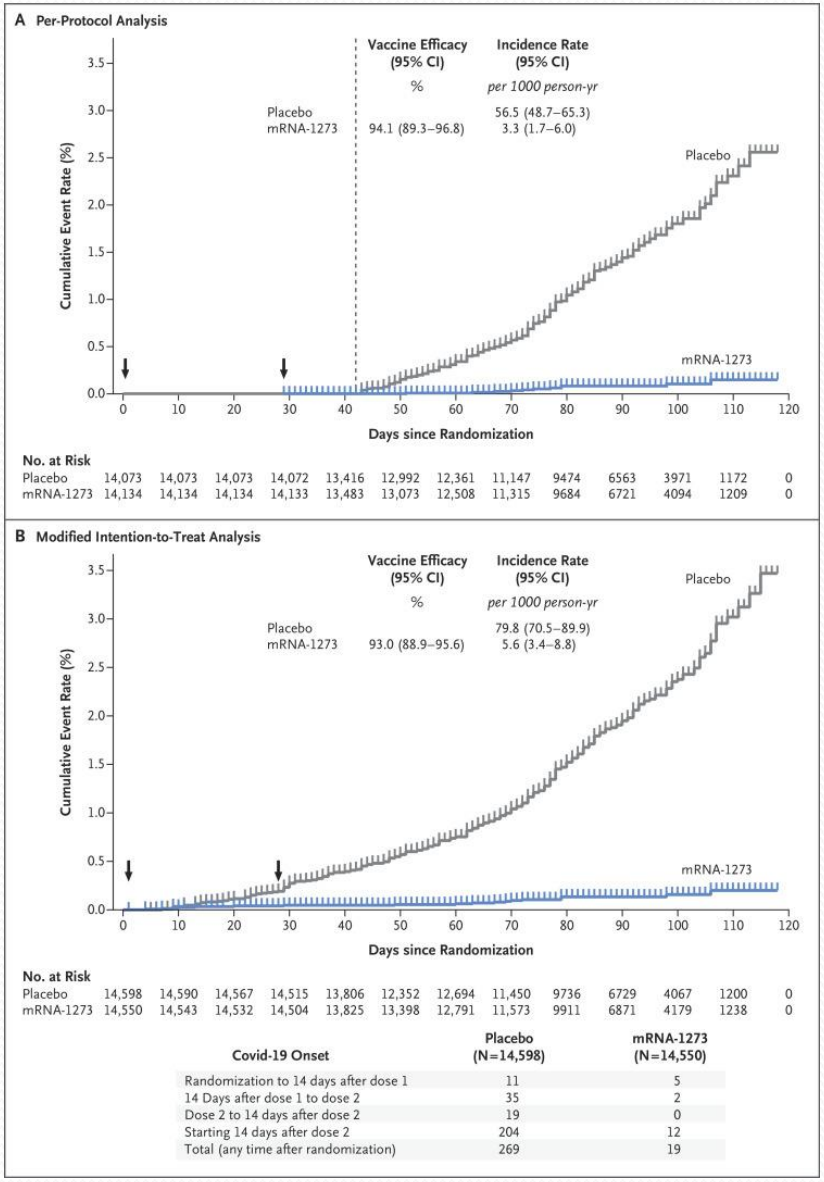


Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669) No. of participants	BNT162b2, 30 μg (N=21,669) Surveillance time *person-yr (no. at risk)*	Placebo (N=21,686) No. of participants	Placebo (N=21,686) Surveillance time *person-yr (no. at risk)*	VE (95% CI) *percent*
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

VE 14d after dose 1 to before dose 2 = **92.3% (69-98%)**

NB- Median duration of follow-up = 28d

Moderna: Single dose efficacy



Covid-19 Onset	Placebo (N=14,598)	mRNA-1273 (N=14,550)
Randomization to 14 days after dose 1	11	5
14 Days after dose 1 to dose 2	35	2
Dose 2 to 14 days after dose 2	19	0
Starting 14 days after dose 2	204	12
Total (any time after randomization)	269	19

Single dose efficacy:
After Dose 1 to before Dose 2: **80.2%** (55.2- 92.5%)
14d after dose 1 to before dose 2: **92.1%** (68.8- 99.1%)

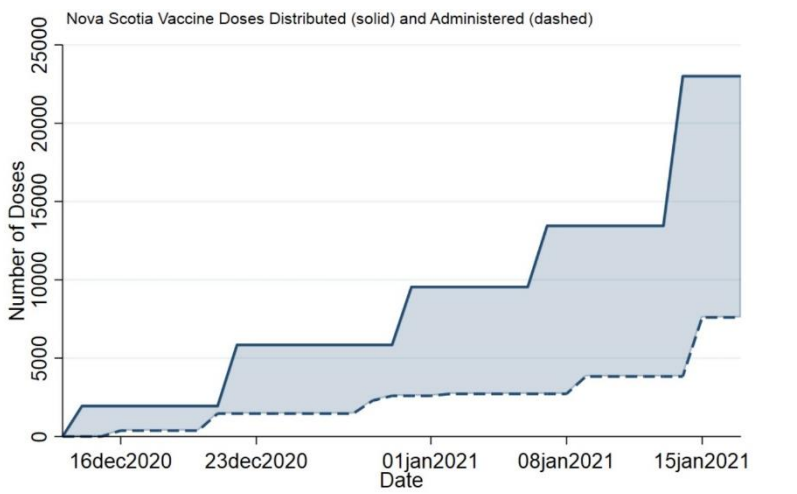
NB: Median duration of follow-up= 28d

What are jurisdictions doing?

- **WHO:** Use recommended intervals except in exceptional circumstances (vaccine supply + epi); max interval= 42d
- **UK:** 0, 3-12 week schedule
- **US:** 0, 21-25 (Pfizer) or 0, 28-32d (Moderna) but no upper limit on timing of second dose
- **US FDA:** schedule changed not routed in evidence and may jeopardize public health
- **Canada:** NACI (Jan 12)- VE data for both mRNA vaccines based on 2 dose schedule 3-6 weeks (42d)apart; 2 dose duration of protection ≥14weeks; give dose 2 by day 42

What are we doing in NS?

- Given current epi and anticipated vaccine supply, plan to stick to 2 dose schedule at 0, 21 or 0, 28 (consider harmonized 0, 28d schedule for both)
- To ensure adequate supply to give second dose on time, 2nd dose will be held in reserve until supply more certain (Note Pfizer delay this week – decreased supply by 40-50% for 4 weeks)



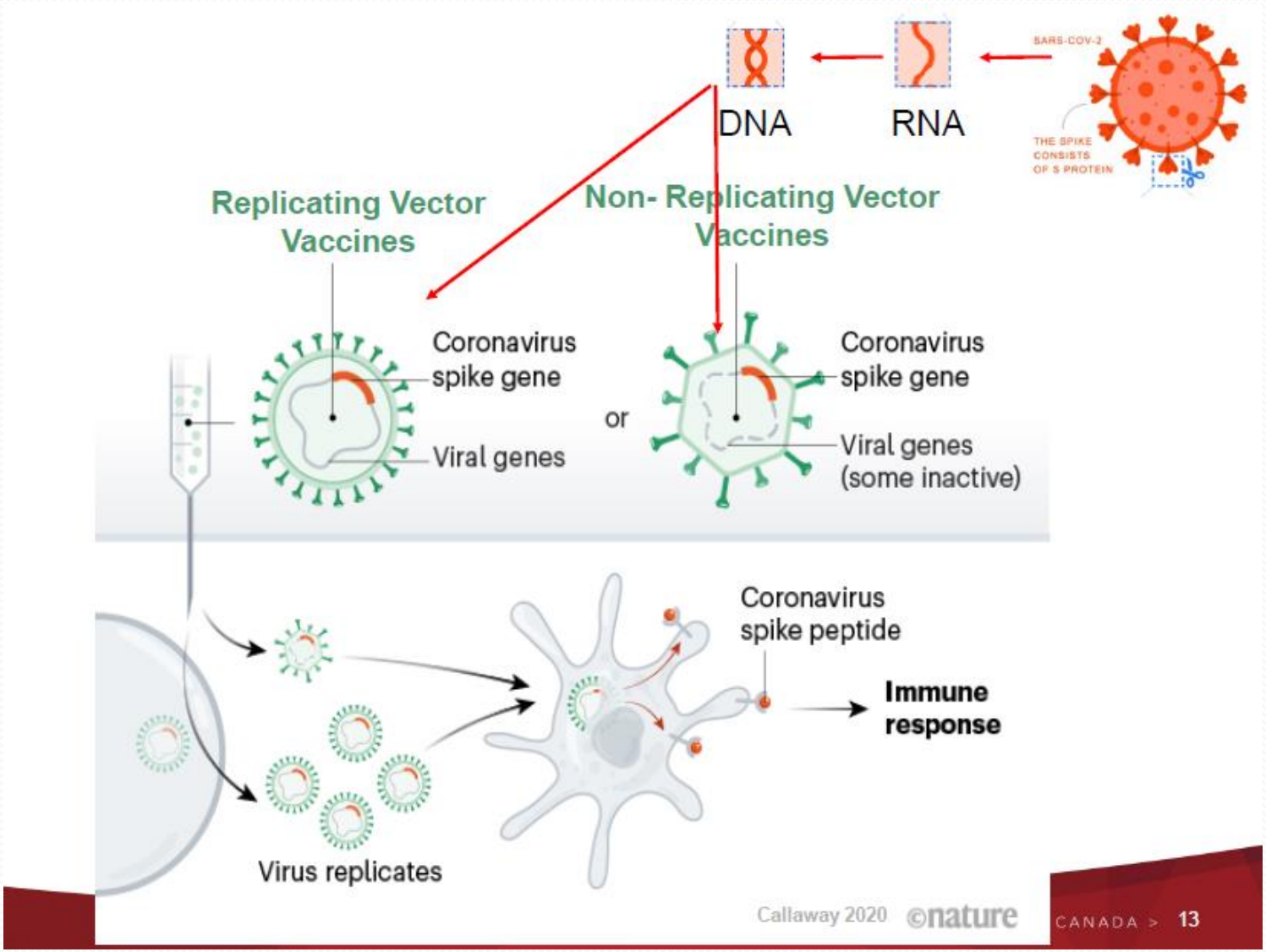
Source: Berry I, Soucy J-PR, Tuite A, Fisman D. Open access epidemiologic data and an interactive dashboard to monitor the COVID-19 outbreak in Canada. CMAJ. 2020 Apr 14;192(15):E420. doi: https://doi.org/10.1503/cmaj.75262.

Credit: @WilsonKM2

Do mRNA vaccines prevent asymptomatic infection?

- No data for Pfizer/BioNTech
- Moderna- pre dose 2 – asymptomatic infn in 15/14,000 (0.1%) in vaccine arm vs 39/14,000 (0.3%) in placebo arm suggesting reduction in asymptomatic infection of about 2/3
- Very small sample, single timepoint
- Give lack of data, no change in PH/IPAC recommendations for vaccinated vs unvaccinated
- Education critical as this is sometimes motivating factor for seeking vaccination

Viral Vector Vaccines



Viral Vector Vaccines

Advantages	- Established activation of humoral and cellular responses without an adjuvant - Potential boosted immunity to vector virus - Technology authorized in 3 vaccines – 2x Ebola and a dengue/yellow fever vaccine
Disadvantages	- Potential for reduced immune responses due to vector seropositivity (increased impact with age) - Potential blunting of response to Dose 2 and to future vaccines using the same platform

COVID-19 Viral Vector-Based Vaccines:

Organizations	Platform	Stage of Development
Janssen/Johnson&Johnson	Non-replicating Adenovirus 26 viral vector	Phase 3 in US
AstraZeneca / University of Oxford (UK)	Non-replicating Chimpanzee adenovirus viral vector	Phase 3 clinical trials in UK, South Africa, Brazil, US and Russia
CanSino Biological Inc. (China)	Non-replicating Adenovirus 5 viral vector	Phase 3 in Pakistan and Russia
Gamaleya Research Institute (Russia)	Combination of Non-replicating Ad5 and Ad26 platforms	Phase 3 in Russia*
Johnson&Johnson/Beth Israel (US)	Non-replicating adenovirus 26 viral vector	Phase 1/2 in US
Reithera (Italy)	Non-replicating simian adenovirus vector	Phase 1 in Italy
Merck/Themis/Institut Pasteur (US/Aus/France)	Replicating measles virus vaccine platform	Phase 1 in France
University of Hong Kong/Xiamen University (China)	Replicating flu virus vaccine platform	Phase 1 in China

Janssen/Johnson&Johnson and AstraZeneca/University of Oxford have made a commitment in principle to supply vaccines to the Canadian government.

*Approved by Russian Government

Viral Vector Vaccines: Summary of Results

	AstraZeneca/Oxford	Janssen/J&J
	Phase 3 - Age: 18+ - Size: 17,177 UK and Brazil - dosing: 2xIM, 29d	Phase 1/2 - Age: 20y+ - Size: 805 - **1xIM**
Efficacy Data	**Symptomatic illness** >14d post dose 2: 63.1% (51.8-71.7) 54.9% (32.7-69.7) if interval <6wk **82.4%** (62.7- 91.7) if interval >12wks **Asymptomatic illness** >14d post dose 2: **2.0%** (-50.7- 36.2) Symptomatic illness >21d post dose 1: **76%** (59-86) (x 3 mos)	Humoral: Ag-binding and neutralizing Ab Cellular: -Th1 biased CD4 response Effect of Immune Responses to Vector: Not assessed
Safety Data	N/A: trial paused for investigation a neurological in a participant	Reactogenicity within normal range

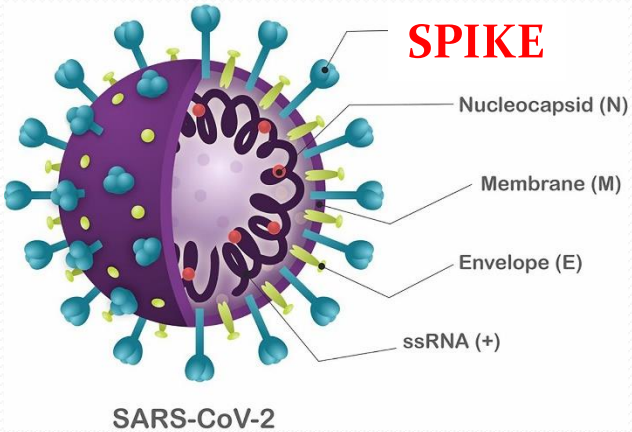
1Lancet 2020: Dec 8; 2NEJM 2021: Jan 14

Subunit Protein-based vaccines: Mechanism of Action

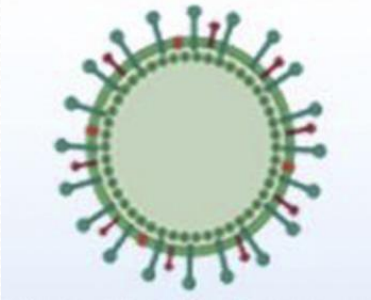
Adjuvant

Matrix M is a nanoparticle composed of saponins, cholesterol and lipids

Vaccine nanoparticle



SARS-CoV-2



Virus-like particle (VLP)

Subunit Protein Vaccine Platform

Advantages	-platform has been used in previously authorized vaccines -fast design and relatively rapid production
Disadvantages	-antigens are less immunogenic and may need an antigen

Manufacturer	Platform	Stage of Development
Medicago	VLPs containing spike	Phase 2/3 in Canada
Novavax	Spike protein with Matrix M adjuvant	Phase 3 in UK
Sanofi/GSK collaboration	Spike protein with GSK adjuvant	Phase 1/2 in US
Kentucky Bioprocessing	Protein subunit/KBP-COVID-19	Phase 1/2 in US
Anhui Zhifel Biologics	Recombinant protein subunit	Phase 2 in China
Federal Budgetary Research Institution	Protein subunit/SARS-CoV-2 antigens	Phase 1/2 in Russia
Finlay Vaccine Institute	Protein subunit/FINLAY-FR-1	Phase 1/2 in Cuba

Medicago, Novavax and Sanofi/GSK have signed Advanced Purchase Agreements with the Canadian Government

Protein Subunit Vaccines: Summary of *Early-stage* Results

	Novavax	Medicago
	Phase 2b/3 - Age: 18-84y (27%>65y) - Size: 15000 - dosing: 2xIM, 21d	Phase 1 - Age: 18-55y - Size: 180 - Dosing: 2xIM, 21d
Immunogenicity Data	Symptomatic inf'n 7d post dose 2: **89.3%** (75.2-95.4)(50% were UK variant) - 95.6% original strain - 85.6% UK variant - Phase 2b SA (90% of cases **SA variant**) - VE **60%** (19.9-80.1)	<u>Humoral</u>: Ag binding and neutralizing Ab - Very strong responses in ASO3 adjuvant group, 10x that of convalescent sera <u>Cellular</u>: - Th 1 biases CD4 response
Safety Data	Reactogenicity within normal range	Reactogenicity within normal limits

Key Messages

- Novel technology, not previously used in vaccines authorized for use in humans, represents the front runners of COVID-19 vaccines in development
- All vaccines to be used in Canada, regardless of platform, must be authorized by Health Canada

Based on very limited data:

- mRNA vaccines from Pfizer and Moderna induce protection very soon after their second dose and provide short term protection after one dose
- All vaccine platforms covered today induce humoral and cellular responses in the majority of vaccine recipients
  - Protein-based vaccine (Novavax, Medicago) induce very high humoral response

NACI Recommendations

- https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html
- Updated Jan 12, 2021

Data limitations

- No safety or efficacy data in:
  - Women who are pregnant or breastfeeding
  - People who are immunosuppressed
  - People with underlying autoimmune conditions
- NACI recommends that these people be offered vaccination “if risk assessment deems that the benefit outweighs potential risks and if informed consent included discussion about the absence of evidence on the use of COVID-19 in these populations”

Recommendations: Summary

1) NACI recommends that a complete series should be offered to individuals in the authorized age group without contraindications

- ≥16y Pfizer
- ≥18y Moderna

- Efforts should be made to adhere to recommended schedules; if delay necessary, give dose 2 within 42d

Contraindications/Precautions

- History of anaphylaxis to previous dose of vaccine or to any component of the vaccine or its containor
- Practically speaking, this means allergy to **polyethylene glycol (PEG)**
- **Precaution:** Anaphylaxis to another vaccine or injectable medication/product: may be vaccinated with 30-60min observation period
- Note: other allergies, including anaphylaxis to foods, latex, environmental allergens, insect stings are **NOT** a contraindication to vaccination; routine observation

2) **NACI recommends that all individuals should continue to practice recommended public health measures for prevention and control of SARS-CoV-2**

- Insufficient evidence on duration of protection and effectiveness in preventing asymptomatic transmission
- Preliminary data suggests mRNA vaccines (Moderna data) reduce risk but evidence insufficient to warrant change in practice
- No evidence to support COVID-19 vaccine for post-exposure prophylaxis

3) **NACI recommends that COVID-19 vaccine may be offered to individuals with prior COVID-19 infection**

- No role for COVID testing prior to vaccination (screen for symptoms to avoid transmission in clinic)
- No evidence of increased adverse events or decreased efficacy/immunogenicity in people with prior infection
- Reinfections, though rare, have been reported

Immunosuppressed persons

4) **NACI recommends the COVID-19 vaccine may be offered to persons who are immunosuppressed by disease or treatment if a risk assessment deems that benefits outweigh potential risks and if informed consent includes discussion about absence of evidence on use of COVID-19 vaccine in this population**

- Limited evidence that immunosuppression is an independent risk factor for severe COVID-19
- Most immunosuppressed persons were excluded from the clinical trials
- In general, non-live vaccines may be safely administered to IC people; no anticipated safety concerns
- immune response may be diminished; continue all other preventive measures

Persons with Autoimmune Conditions

5) **NACI recommends that COVID-19 vaccine may be offered to persons with an autoimmune disease if a risk assessment deems that benefits outweigh potential risks and if informed consent includes discussion about absence of evidence on use of COVID-19 vaccine in this population**

- Limited evidence that having an autoimmune condition is an independent risk factor for severe COVID-19; evidence evolving
- Limited data on COVID-19 vaccine in people with AI conditions; not excluded if not IS but small sample size
- Degree of autoimmunity varies by condition, severity and progression and use of immunosuppressive meds- risk/benefit must be individualized
- Previous use of mRNA technologies were used for treatment of cancer so required immune response directed at cancer cells; raised theoretical concern that mRNA vaccines against infections would elicit similar responses, eliciting inflammation and possibly exacerbating existing autoimmune diseases; lipid vacuole technology used to reduce this risk

Autoimmune cont

- Exacerbation of AI not seen with other vaccines
- Active infection also poses theoretical risk
- Benefit of vaccination must be balanced against this theoretical risk
- Patients with stable AI disease do not require specialist consultation (including those on immunosuppressants/immunomodulators)
- Patients with active/poorly controlled AI disease should discuss with their specialist

Pregnancy and Breastfeeding

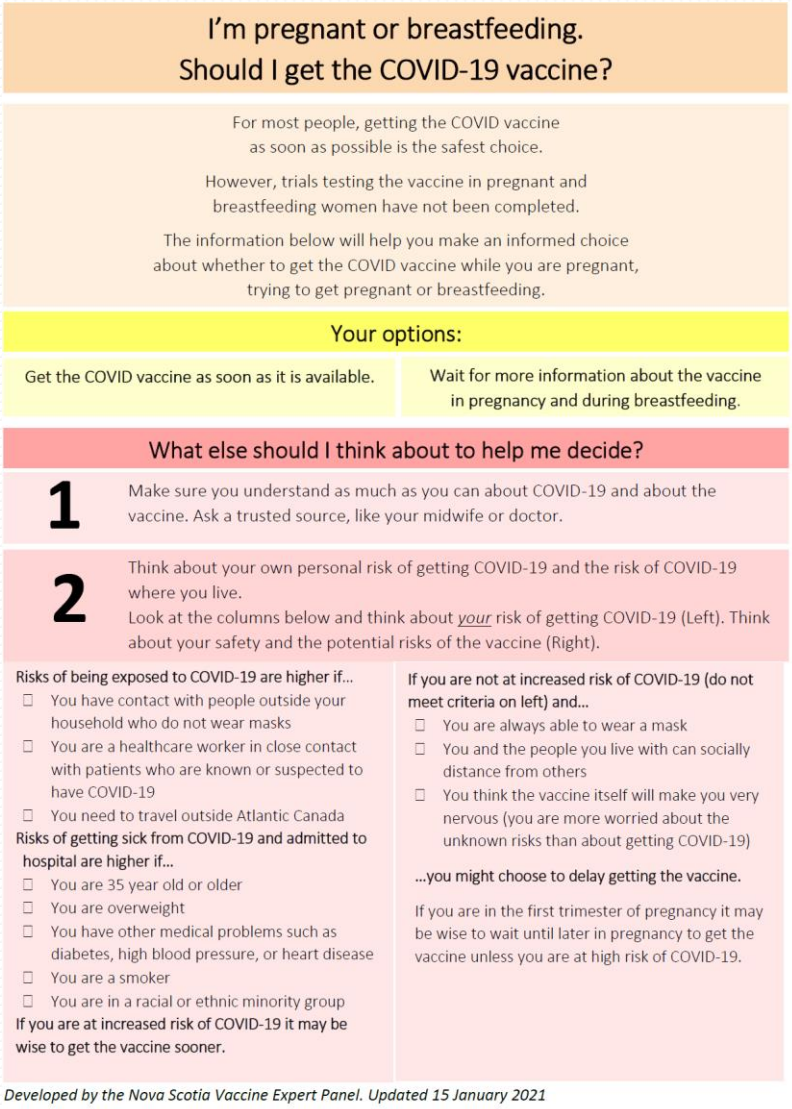
6/7) NACI recommends that COVID-19 vaccine may be offered to pregnant or breastfeeding individuals if a risk assessment deems that benefits outweigh potential risks for the individual and and the fetus and if informed consent includes discussion about absence of evidence on use of COVID-19 vaccine in this population

- Evidence of pregnancy as an independent risk factor for severe COVID-19 evolving: pregnant women >35y, obese, medical comorbidities, smoking, racial or ethnic minority appear to be at increased risk of hospitalization
- Pregnant and breastfeeding individuals excluded from trials
- No theoretical concerns about these vaccines in breastfeeding woman
- Vaccine not live so not contraindicated; animal studies reassuring thus far
- Decision to receive vaccine during pregnancy requires shared decision making; SOGC recommends that pregnant women should be offered vaccine

Pregnancy cont.

- Given lack of data and risk of fever post-dose 2, may wish to consider delaying vaccination until second TM
- Those in first TM should discuss risks and benefits with their maternity care provider
- Individuals who become pregnant during vaccine series should NOT be counselled to terminate
- Consider delaying second dose until after pregnancy or beyond first TM
- No data to guide recommendation about timing between vaccination and pregnancy; NACI conservatively recommends 28d post dose 2

Available Resources



I'm pregnant or breastfeeding. Should I get the COVID-19 vaccine?

For most people, getting the COVID vaccine as soon as possible is the safest choice.

However, trials testing the vaccine in pregnant and breastfeeding women have not been completed.

The information below will help you make an informed choice about whether to get the COVID vaccine while you are pregnant, trying to get pregnant or breastfeeding.

Your options:

Get the COVID vaccine as soon as it is available.	Wait for more information about the vaccine in pregnancy and during breastfeeding.

What else should I think about to help me decide?

1 Make sure you understand as much as you can about COVID-19 and about the vaccine. Ask a trusted source, like your midwife or doctor.

2 Think about your own personal risk of getting COVID-19 and the risk of COVID-19 where you live.
Look at the columns below and think about *your* risk of getting COVID-19 (Left). Think about your safety and the potential risks of the vaccine (Right).

Risks of being exposed to COVID-19 are higher if...

- ☐ You have contact with people outside your household who do not wear masks
- ☐ You are a healthcare worker in close contact with patients who are known or suspected to have COVID-19
- ☐ You need to travel outside Atlantic Canada

Risks of getting sick from COVID-19 and admitted to hospital are higher if...

- ☐ You are 35 year old or older
- ☐ You are overweight
- ☐ You have other medical problems such as diabetes, high blood pressure, or heart disease
- ☐ You are a smoker
- ☐ You are in a racial or ethnic minority group

If you are at increased risk of COVID-19 it may be wise to get the vaccine sooner.

If you are not at increased risk of COVID-19 (do not meet criteria on left) and...

- ☐ You are always able to wear a mask
- ☐ You and the people you live with can socially distance from others
- ☐ You think the vaccine itself will make you very nervous (you are more worried about the unknown risks than about getting COVID-19)

...you might choose to delay getting the vaccine.

If you are in the first trimester of pregnancy it may be wise to wait until later in pregnancy to get the vaccine unless you are at high risk of COVID-19.

Developed by the Nova Scotia Vaccine Expert Panel. Updated 15 January 2021

Resources from Specialty care providers (samples)

- Canadian Association of Gastroenterology
- Society of Obstetricians and Gynaecologists of Canada
- Canadian Dermatology Association
- Canadian Rheumatology Association
- Canadian Association of Transplantation
- Canadian Association of Allergy and Immunology
- Canadian Association of Endocrinology and Metabolism

NS Approach to consent

- For patients with underlying conditions requiring discussion of risks/benefits in light of absence of data, discussion with a care provider- Primary care provider, specialist, vaccine expert, allergist, pharmacist
- Recommended provider to discuss consent dependent on underlying condition
- No written documentation required to be given to patient by provider; record in health record
- Supplemental consent/disclaimer document acknowledging consent discussion to be signed at time of vaccination

Management Pathways

	Pathway 1	Pathway 2	Pathway 3	Pathway 4
Category	1	2 & 3	4	5
Education	Information on website	Information on website	Information on website	Information on website
Education provider	Self +/- 811	Primary care provider or specialist	Specialist* or vaccine consultant	Allergist
Consent	Usual	Usual + disclaimer	Usual + disclaimer	Usual + disclaimer
Consent sign off	Usual	Primary care provider or specialist	Specialist* or Vaccine consultant	Allergist

* Includes maternity care provider for first TM of pregnancy

Category 1	Category 2	Category 3	Category 4	Category 5
• Breastfeeding individuals • Splenic disorders • HIV • Chronic kidney disease • Chronic liver disease • Diabetes mellitus • Non-hematologic malignancy in absence of neutropenia and check point inhibitors • Stable anticoagulation • Radiation therapy alone	• On immune suppressing doses of prednisone (> 20 mg/day > 2 weeks) • On monoclonal antibodies, plasma therapy , or plasmapheresis (delay 3 months)	• Pregnant individuals beyond the 1st trimester • Primary immune deficiency requiring IVIG or SCIG • Chronic granulomatous disease • Hyper IgE syndrome • Complement deficiency • Solid organ transplant after 1 month & no acute rejection • HSCT after 3-6 months & no GVHD • Stable autoimmune condition • Stable immunomodulator therapy • Bleeding disorder • History of Guillain Barre syndrome • History of Bell's palsy	• Active autoimmune condition • Anaphylaxis to injectable medication • Solid organ transplant with acute rejection • Pregnant individuals in the first trimester (consider delaying until at least the second trimester) • Cytotoxic chemotherapy with neutropenia • Leukemia • Within 3 months of stem cell transplant • On check point inhibitor • On CAR T-cell therapy • Interferonopathy	• Anaphylaxis or severe reaction to prior dose of COVID-19 vaccine • Anaphylaxis to any component of the COVID-19 vaccine

Other

- Vaccination series should be completed with same product (same lot number not necessary)
- Do not give simultaneously with other vaccines- wait 14 days
- Perform TST before COVID-19 vaccine OR defer until 4 weeks post dose 2 (per CDC)

Post-authorization monitoring

Safety surveillance, effectiveness, vaccine coverage, and herd immunity

Safety surveillance

- Clinical trials performed in 10's of thousands of individuals (most phase III trials were around 30,000 participants to detect 150-175 infection outcomes)
  - A trial of 30,000 has 95% likelihood to detect an adverse event with a frequency of 1/10,000
  - To detect a rare even (1/100,000-1,000,000) need to monitor 300,000-3,000,000 immunizations
- Passive safety surveillance is useful but insufficient to detect rare adverse events with certainty
- Active surveillance systems are being discussed for COVID-19 program roll out
  - Collaboration between PHAC, provinces
  - Canadian Immunization Research Network (CIRN)
    - Canadian Safety Network (CANVAS)
    - Serious Outcomes Surveillance Network (SOS)

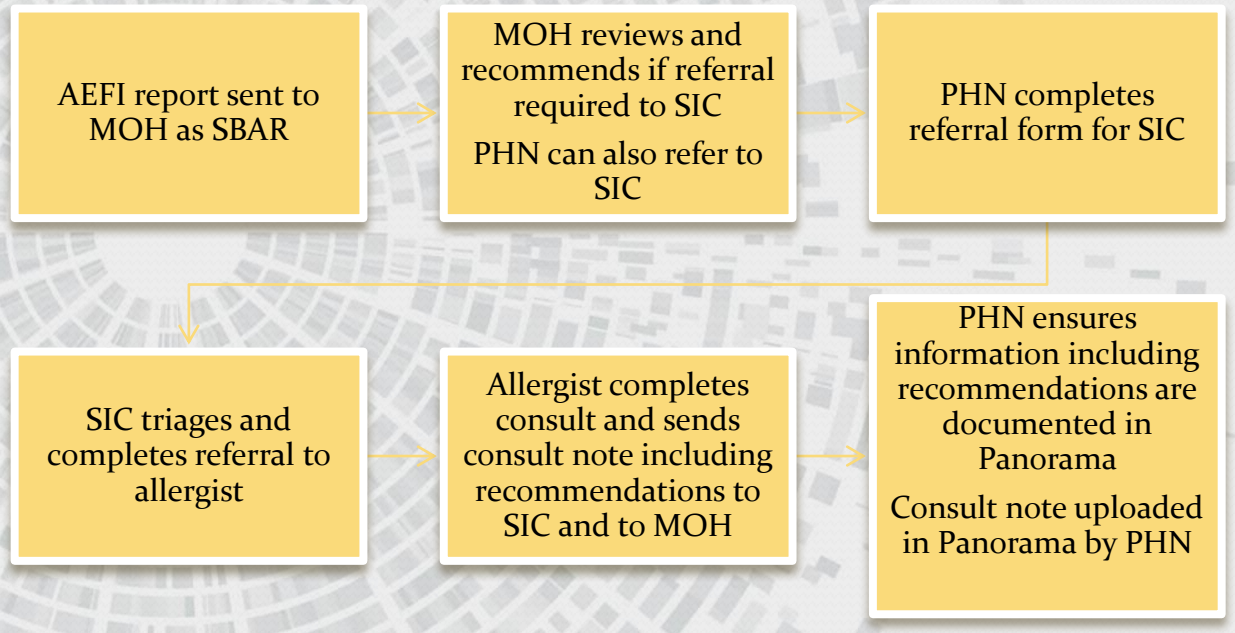
Vaccine effectiveness

- Efficacy (clinical trials) vs. effectiveness (vaccine performance under conditions of normal usage)
- Post use measures of effectiveness
  - Hospital-based surveillance systems
  - Administrative databases

Canadian Immunization Research Network

- Serious Outcomes Surveillance Network (SOS)
- Provincial Collaborative Network (PCN)

COVID19 AEFI Reporting Process

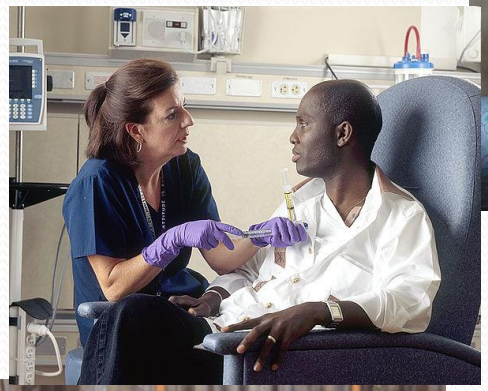


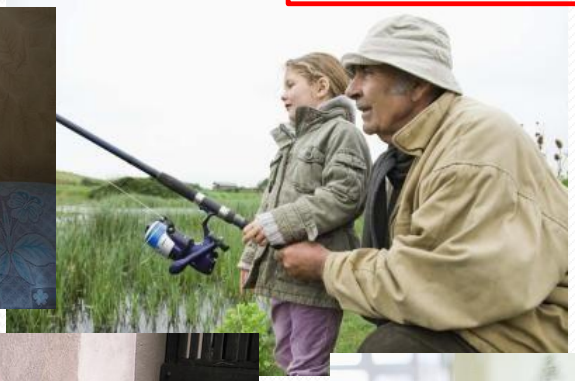
Summary and Conclusion

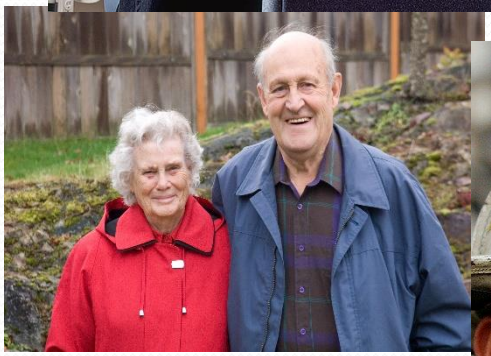
- Development of a COVID-19 vaccine has been an extraordinary endeavor accomplished in record time achieved through global coordination
  - However, we are only part way through the process
  - Successful implementation will require a similar level of focus and cooperation
- While a positive outcome is increasingly likely, it is not assured
  - So far, focus has been on the immunological and biological sciences
    - Need not to lose that focus
  - Focus on implementation science and social science will now take priority

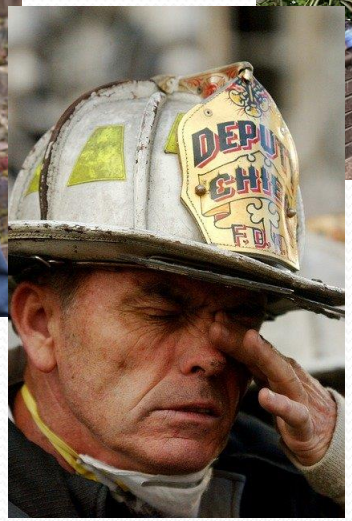
We're all in this together!

Insert your parent/grandparent here









Thanks!

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