COVID-19 Vaccines

BC Immunization Forum

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2022 March 1

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Disclosure of Financial Support

- **This program has not received financial support**.
- **This program has not received in-kind support.**

- **<u>Potential for conflict(s) of interest</u>:**
  - Dr. Langley's employer, Dalhousie University, has received funding from Sanofi, GlaxoSmithKline, Moderna, Pfizer, Janssen, VIDO, VBI, whose product(s) are being discussed in this program. Dr. Langley holds the CIHR-GSK Chair in Pediatric Vaccinology at Dalhousie University.

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Objectives:

- To be aware of the COVID-19 vaccine landscape
- To review use of vaccines in Canada and the world

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Index case Dec 16, 2019

ProMED
INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

Published Date: 2019-12-30 23:59:00
Subject: PRO/AH/EDR> Undiagnosed pneumonia - China (HU): RFI
Archive Number: 20191230.6864153

UNDIAGNOSED PNEUMONIA - CHINA (HUBEI): REQUEST FOR INFORMATION
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A ProMED-mail post
http://www.promedmail.org
ProMED-mail is a program of the
International Society for Infectious Diseases
http://www.isid.org

Dec 30, 2019

[1]
Date: 30 Dec 2019
Source: Finance Sina [machine translation]
https://finance.sina.cn/2019-12-31/detail-iihnzahk1074832.d.html?from=wap

Wuhan unexplained pneumonia has been isolated test results will be announced [as soon as available]

On the evening of [30 Dec 2019], an "urgent notice on the treatment of pneumonia of unknown cause" was issued, which was widely distributed on the Internet by the red-headed document of the Medical Administration and Medical Administration of Wuhan Municipal Health Committee.

On the morning of [31 Dec 2019], China Business News reporter called the official hotline of Wuhan Municipal Health and Health Committee 12320 and learned that the content of the document is true.

12320 hotline staff said that what type of pneumonia of unknown cause appeared in Wuhan this time remains to be determined.

https://scholar.harvard.edu/files/kleelerner/files/20191230_promed_-_undiagnosed_pneumonia_-_china_hu-_rfi_archive_number-_20191230.6864153.pdf

- January 11, 2020: Viral genome sequence posted on GENBANK and Virologic.org
- March 11, 2020: Pandemic declared by World Health Organization
- March 16: first patient enrolled in a phase 1 vaccine trial (mRNA-1273)
- July 2020: phase 3 trials begin, multiple platforms (mRNA, Ad vectored, protein based)
- Dec 14, 2020: COVID-19 vaccine program begins in Canada

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WHO COVID vaccine target product profile

- Characteristics that are preferred or "critical or minimal"
- Target population – all ages (minimum adults including elderly)
- No contraindications (some e.g. immunocompromised possible)
- Safety/reactogenicity – favourable benefit/risk
- Efficacy ≥70% using endpoints of disease, severe disease; or ~50% point estimate of efficacy
- Single dose preferred
- Protection for a least 1 year (minimal 6 months)
- Capability to rapidly scale-up production at cost/dose that allows broad use including LMIC

who-target-product-profiles-for-covid-19-vaccines.pdf

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Vaccines WHO Vaccines with Emergency Use authorization (EUA) Qualification

- mRNA
  - Moderna
  - Pfizer
- Adenovirus vectored
  - Janssen
  - AstraZeneca (Vaxevria and COVIDSHIELD)
- Protein subunit
  - Novavax (Nuvaxoid and Covovax)
- Inactivated
  - Sinovac
  - Sinophar/BIBP
  - Bharat Biotech

11 vaccines in evaluation

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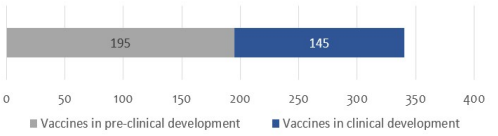
World Health Organization

Summary Information on Vaccine Products in Clinical Development

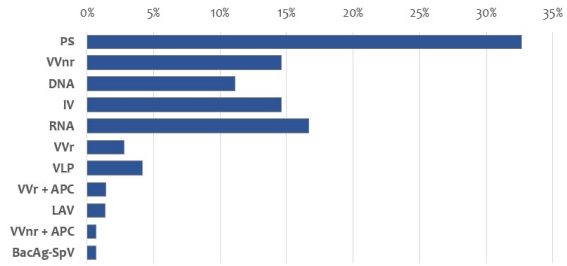
1. - Number of vaccines in clinical development	145
2. - Number of vaccines in pre-clinical development	195



3. - Candidates in clinical phase

Filter: All — Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	47	33%
VVnr	Viral Vector (non-replicating)	21	15%
DNA	DNA	16	11%
IV	Inactivated Virus	21	15%
RNA	RNA	24	17%
VVr	Viral Vector (replicating)	4	3%
VLP	Virus Like Particle	6	4%
VVr + APC	VVr + Antigen Presenting Cell	2	1%
LAV	Live Attenuated Virus	2	1%
VVnr + APC	VVnr + Antigen Presenting Cell	1	1%
BacAg-SpV	Bacterial antigen-spore expression vector	1	1%
		145	



https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines

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Abandoned vaccines

- mRNA
  - Imperial College Morningside sRNA Jan 27, 2021 "not the time to start an efficacy trial" and "not a satisfying immune response" *https://doi.org/10.1016/j.eclinm.2021.101262 (phase 1)*
  - Sanofi Translate Bio mRNA MRT5500 phase ½ trial data Sept 2021: nAB in 91 to 100% at day 14; "sufficient mRNA vaccine expected" *https://www.sanofi.com/en/media-room/press-releases/2021/2021-09-28-18-44-47-2304800*
  - CUREVAC mRNA; 48% efficacy in phase 3 trial; "pandemic window closing"; focussing on 2nd generation vaccine
- DNA
  - Oncosec CORVax12 protein plasmid DNA vaccine (codes for spike and IL-12) phase 1 in Jan 2021, abandoned Nov 2021 *NCT04627675*
- Virus vectored
  - Merck/Themis Bioscience/Institut Pasteur (measles virus vector) phase 1 trial results weaker than natural infection
  - Merck/IAVI viral vector (vesiculostomatitis virus) phase 1 trial results weaker than natural infection *NCT04569786*
  - Altimmune AdCOVID nasal spray Ad5 phase 1; substantially lower antibody levels that authorized vaccines *NCT04679909*
- Protein subunit
  - University of Queensland CSL MF59 adjuvanted, stabilized in pre-fusion conformation with a novel molecular clamp (sclamp) 99% had nAB; false positive HIV tests *https://dx.doi.org/10.2139/ssrn.3769210*
  - RIBSP QazCoVac-P subunit vaccine Khazkhstan *NCT04930003*
  - SK bioscience South Korea NBP2001 phase 1 completed
- Inactivated
  - Iran Ministry of Defence inactivated coronavirus vaccine, Fakhravac

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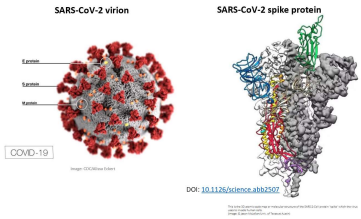
COVID-19 vaccines procured by Government of Canada

- Lipid Nanoparticle-messenger RNA (mRNA)
  - Moderna 56 M doses
  - Pfizer-BioNTech 80 M doses
- Viral vector (adenovirus)
  - Janssen (Johnson and Johnson) 38 M doses
  - AstraZeneca-Oxford 20 M doses
- Subunit protein, adjuvanted
  - Novavax 76 M doses *(approved Feb 2022)*
  - Sanofi Pasteur – GSK 72 M doses *(approval pending, rolling submission)*
- Virus-like particle
  - Medicago 76M doses *(approved Feb 2022)*



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COVAX

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- Vaccines pillar of the *Access to COVID-19 Tools (ACT)* Accelerator, launched April 2020 by WHO, European Commission, France; now led by CEPI, GAVI, UNICEF, WHO
  - Goal is to accelerate development, production, and access
  - Global risk-sharing mechanism for pooled procurement equitable access to vaccines
- Doses for at least 50% of global population
- Diverse and actively managed portfolio of vaccines
- Options for countries:
  - Committed purchase
    - Lower upfront payment
    - Purchase allocated vaccines
  - Optional purchase
    - Larger upfront payment
    - Purchase vaccine of choice

CEPI Gavi The Vaccine Alliance unicef World Health Organization

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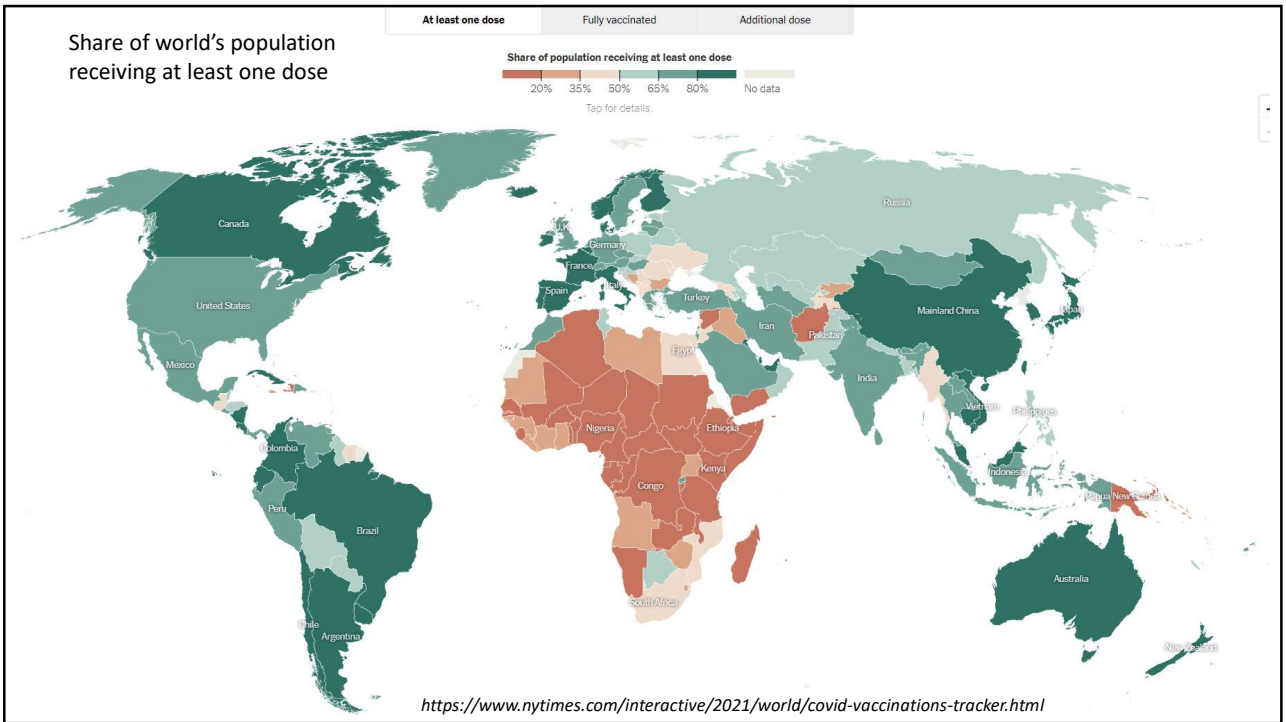
Share of world's population receiving at least one dose



https://www.nytimes.com/interactive/2021/world/covid-vaccinations-tracker.html

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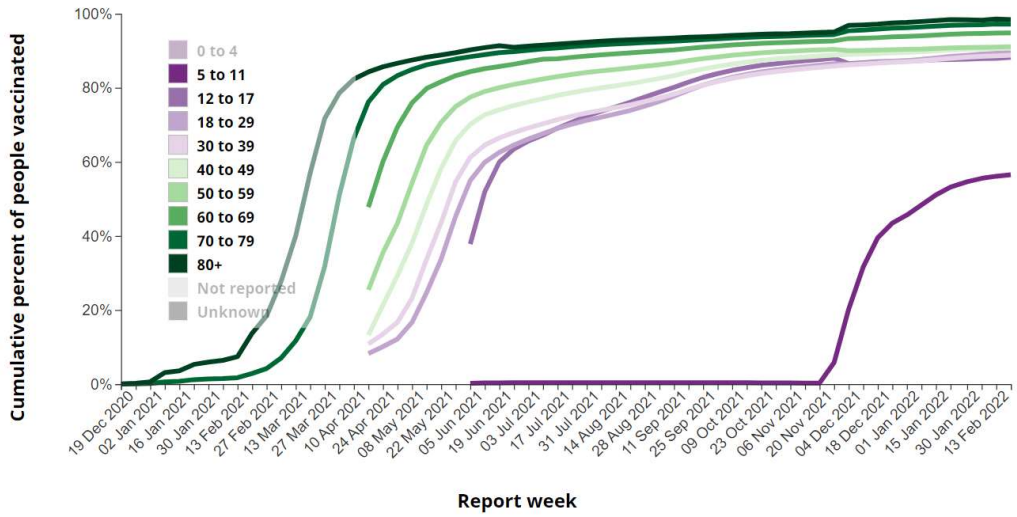
Cumulative percentage of Canadians who have received a COVID-19 vaccine by age group and report week, Feb 20, 2022



https://health-infobase.canada.ca/covid-19/vaccination-coverage/#a5

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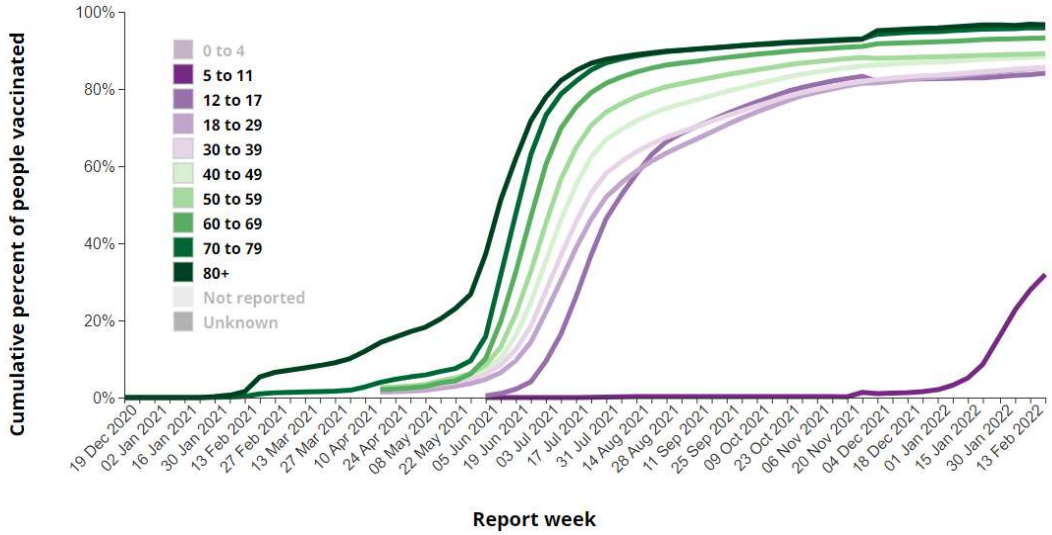
Cumulative percentage of people who are fully vaccinated (two doses) with a COVID-19 vaccine in Canada by age group and report week Feb 2022



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Homologous priming (1,2):
-~33% Pfizer
-~10% Moderna

Heterologous priming (1,2)
-~13% 2 mRNA's
-~4% AZ followed by mRNA

Vaccine series type	Vaccine included in the vaccine series	At least 1 dose	Partially vaccinated	Fully vaccinated	Fully vaccinated with an additional dose
Homologous series (series containing only 1 vaccine product)	Pfizer-BioNTech Comirnaty	12,880,415 (33.68%)	492,006 (1.29%)	12,388,409 (32.39%)	5,655,910 (14.79%)
	Pfizer-BioNTech Comirnaty pediatric 5-11 years	1,211,886 (3.17%)	575,482 (1.50%)	636,404 (1.66%)	31 (<0.01%)
	Moderna Spikevax	3,922,573 (10.26%)	193,544 (0.51%)	3,729,029 (9.75%)	1,847,936 (4.83%)
	AstraZeneca Vaxzevria/COVISHIELD	108,705 (0.28%)	13,656 (0.04%)	95,049 (0.25%)	664 (<0.01%)
	Janssen	30,839 (0.08%)	74 (<0.01%)	30,765 (0.08%)	203 (<0.01%)
	Non-Health Canada-approved vaccines	15,158 (0.04%)	5,330 (0.01%)	9,828 (0.03%)	0 (0%)
Heterologous series (mixed series)	The pediatric and adult Pfizer-BioNTech Comirnaty vaccines	10,599 (0.03%)	n/a	10,599 (0.03%)	230 (<0.01%)
	Either Pfizer-BioNTech Comirnaty vaccine with the Moderna Spikevax vaccine	5,007,660 (13.09%)	n/a	5,007,660 (13.09%)	4,160,174 (10.88%)
	AstraZeneca Vaxzevria/COVISHIELD with an mRNA vaccine (either Pfizer-BioNTech Comirnaty vaccine or Moderna Spikevax)	1,674,849 (4.38%)	n/a	1,674,849 (4.38%)	1,471,775 (3.85%)
	Novavax Nuvaxovid with an mRNA vaccine (either Pfizer-BioNTech Comirnaty vaccine or Moderna Spikevax)	4 (<0.01%)	n/a	4 (<0.01%)	0 (0%)
	Janssen with other Health Canada-approved vaccine(s)	8,451 (0.02%)	n/a	8,451 (0.02%)	7,737 (0.02%)
	Non-Health Canada-approved vaccine(s) and other Health Canada-approved vaccine(s)	40,582 (0.11%)	n/a	40,582 (0.11%)	8,895 (0.02%)
Other	Not reported	7,374,683 (19.28%)	295,969 (0.77%)	7,078,714 (18.51%)	4,076,003 (10.66%)
	Unknown	36,855 (0.10%)	1,107 (<0.01%)	35,748 (0.09%)	10,143 (0.03%)

https://health-infobase.canada.ca/covid-19/vaccination-coverage/#a5

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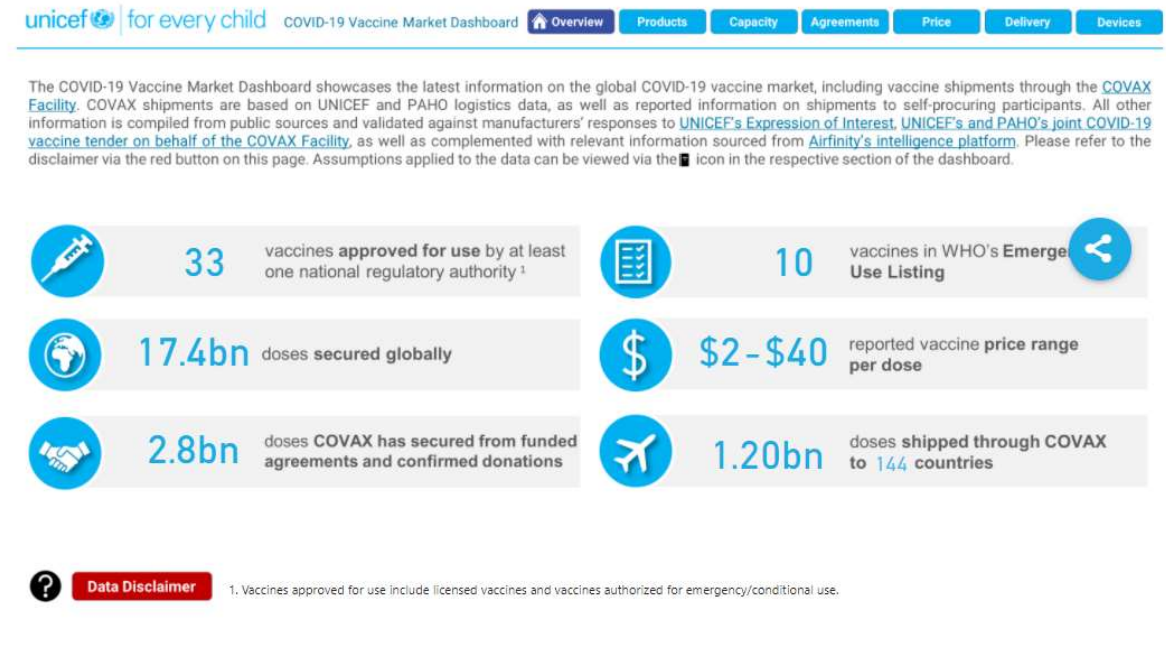

https://www.unicef.org/supply/covid-19-vaccine-market-dashboard

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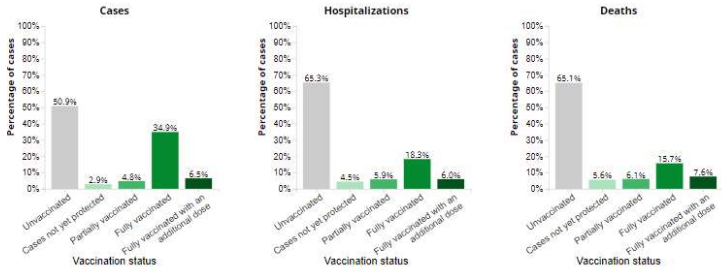

https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html

COVID-19 cases by vaccination status

- Authorized vaccines were highly effective in randomized controlled trials leading to their approval
- Vaccine effectiveness against severe outcomes was good to excellent during Delta, Omicron
- Vaccine effectiveness against "infection" is low to absent during Omicron period

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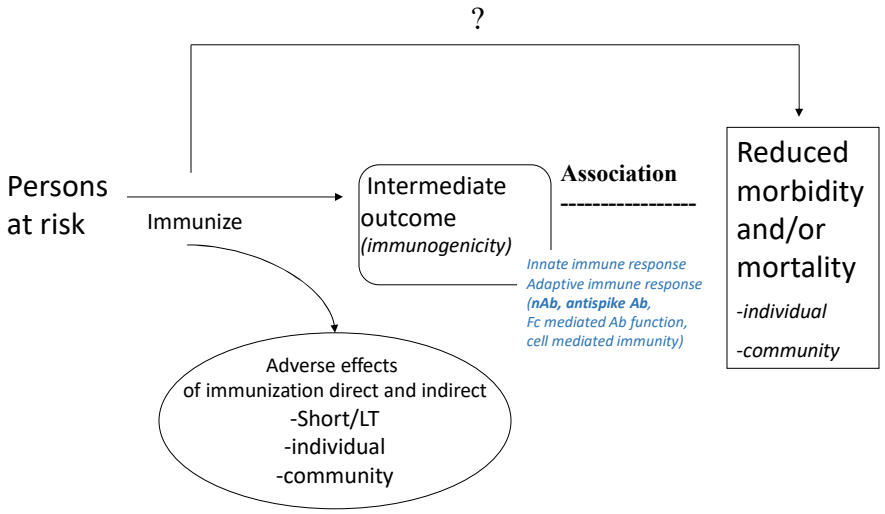
An analytic framework for immunization

(after United States Task Force on Preventive Health Care)



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How correlates are determined

- Levels of passively administered or maternal antibody that protect
- Analysis of immune responses in protected and unprotected subjects in efficacy trials
- Observations made on vaccine failures, e.g. immunocompromised patients
- Human challenge studies
- Extrapolation from animal challenge studies, including immunodeficiency

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Potential protective adaptive immune mechanisms induced by vaccination

- Serum antibody
  - Neutralizing
  - Non-neutralizing (ADCC, etc)
  - Functionality (opsonophagocytosis)
  - Avidity
- Mucosal antibody
  - IgA locally produced
  - IgG produced from serum
- CD4 + T cells
  - B cell helper
  - T cell helper
  - Th17
  - Cytokines
  - Lysis
  - Tregs
- CD8+ cells
  - Lysis
  - Avidity

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Summary: COVID-19 vaccines

- Highly effective vaccines were developed rapidly during the COVID-19 vaccine pandemic
- Canada did not develop a vaccine to mitigate the high incidence periods of the pandemic, but now has the potential to domestically produce at least one vaccine, potentially three vaccines
- Remaining questions:
  - What outcomes do we want to prevent?
  - Which useful correlates of protection will be accepted?
  - What will be the vaccine schedule in the future?

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