



Future of COVID-19 Immunizations

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Land acknowledgement

BC Children's Hospital Research Institute operates on the traditional, ancestral, and unceded territory of the Coast Salish peoples — x^wməθk^wəy̓əm (Musqueam), Sḵw̓x̓wú7mesh (Squamish), and Səlílwətaʔ/Selilwitulh (Tsleil-Waututh) Nations.



BC Immunization Forum 2022 Presenter Disclosure

- Manish Sadarangani
- **Relationships with financial sponsors:**
 - Supported via salary awards from
 - BC Children's Hospital Foundation
 - Canadian Child Health Clinician Scientist Program
 - Michael Smith Health Research BC
 - Have been an investigator on projects funded by GlaxoSmithKline, Merck, Moderna, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo and VBI Vaccines



Disclosure of Financial Support

- **Potential for conflict(s) of interest:**

- The University of British Columbia has received research funding from GlaxoSmithKline, Merck, Moderna, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo and VBI Vaccines for studies conducted by Manish Sadarangani
- Different COVID-19 vaccines, including some developed and/or licensed by these companies will be discussed in this program



Mitigating Potential Bias

- Generic vaccine names will be used
 - Company names may be mentioned initially purely for clarity
- No specific recommendations will be made on use of a specific product
- Slide deck has been approved by program organizers






Outline

- Current COVID-19 vaccines
- Recently approved COVID-19 vaccines
- Current state of COVID-19 immunization programs
- Possible future scenarios



COVID-19 vaccines for Canada – Health Canada approvals

Platform	Vaccine	Health Canada	Age	Primary series	Booster
	BNT162b2 (Pfizer/BioNTech)	Approved	5y+	2 doses (21 days apart)	+6 months (18y+)
	mRNA-1273 (Moderna)	Approved	12y+	2 doses (1 month apart)	+6 months
	ChAdOx1-S (Oxford University/Astra Zeneca)	Approved	18y+	2 doses (4-12 wks apart)	No
	Ad26.COVS.2.S (Janssen)	Approved	18y+	Single dose	No
	NVX-CoV2373 (Novavax)	Approved	18y+	2 doses (21 days apart)	No
	CoVLP-AS03 (Medicago)	Approved	18- 64y	2 doses (21 days apart)	No
	Adjuvanted vaccine (Sanofi Pasteur/GlaxoSmithKline)	Under review			

<https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines.html>



COVID-19 vaccines for Canada – NACI recommendations

Age	Primary series (healthy individuals)	Booster
<5 years	No vaccine available	N/A
5-11 years	2 doses BNT162b2 (pediatric)	No
12-17y	2 doses BNT162b2 (preferred) or mRNA-1273	Specific populations only
18-29y	2 doses BNT162b2 (preferred) or mRNA-1273 or ChAdOx1-S or Ad26.COVS.2 or NVX-CoV2373	BNT162b2 or mRNA-1273 after 6 months
30y+	2 doses BNT162b2 or mRNA-1273 (preferred) or ChAdOx1-S or Ad26.COVS.2 or NVX-CoV2373	BNT162b2 or mRNA-1273 after 6 months

Optimal interval between doses for primary series (where applicable): 8 weeks
Vaccines may be used in heterologous (mix and match) combinations

<https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html>



NVX-CoV2373: Phase 3 trial

- 5 mcg recombinant nanoparticle spike protein
- 50 mcg Matrix-M adjuvant

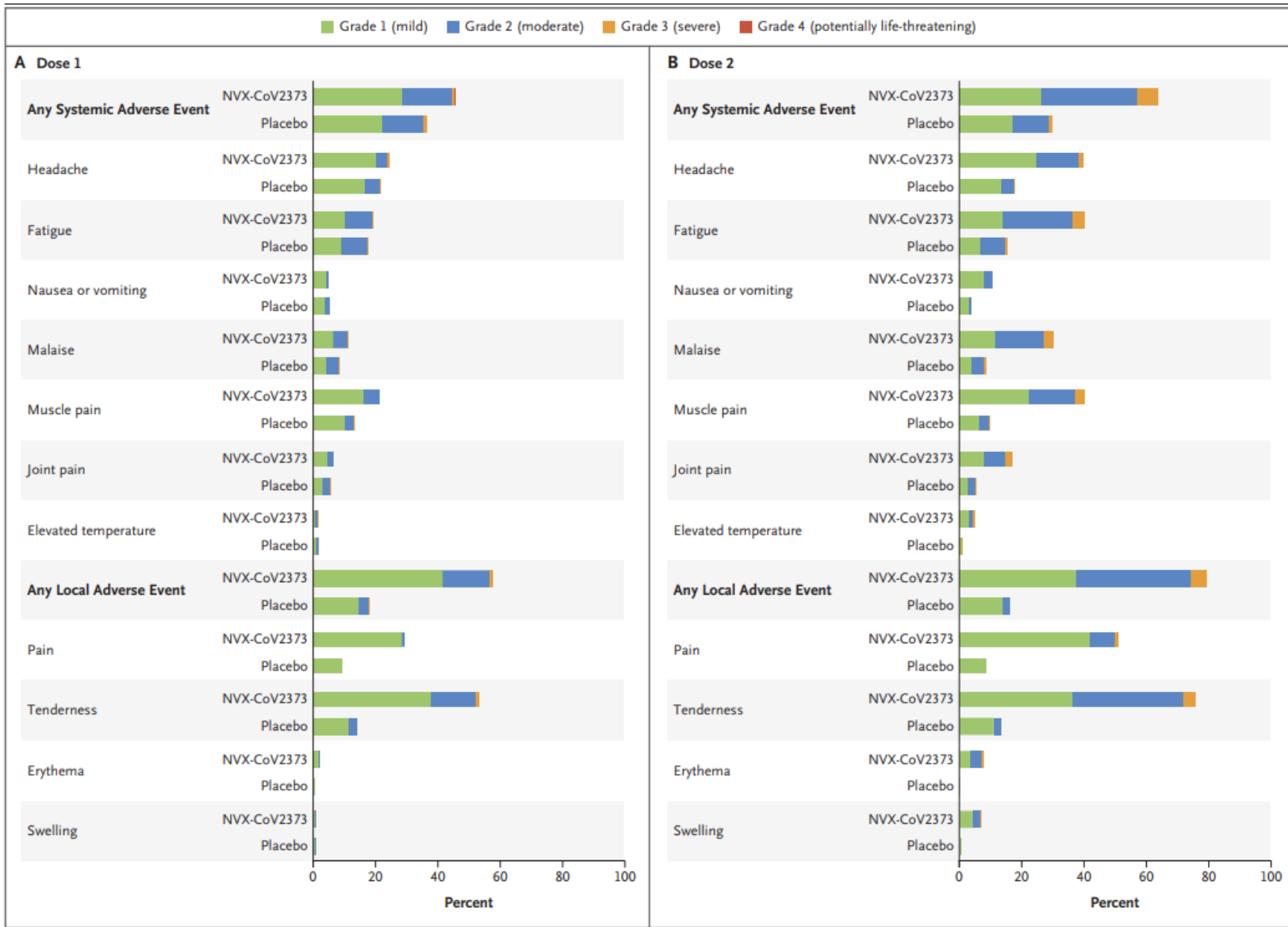
- 2 doses
- 21 days apart

- UK trial: 18-84yo
 - 15,139 participants: 7,020 vaccine, 7,019 placebo

- USA/Mexico trial:
 - 29,582 participants: 19,714 vaccine, 9,868 placebo



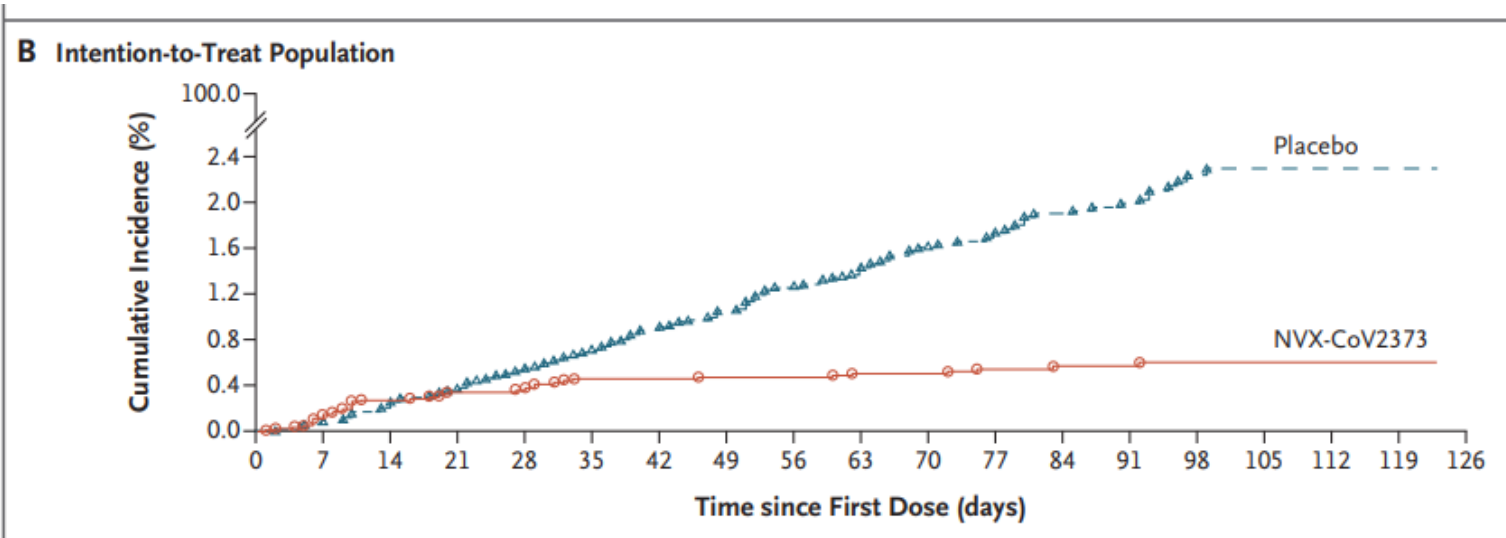
NVX-CoV2373: Safety



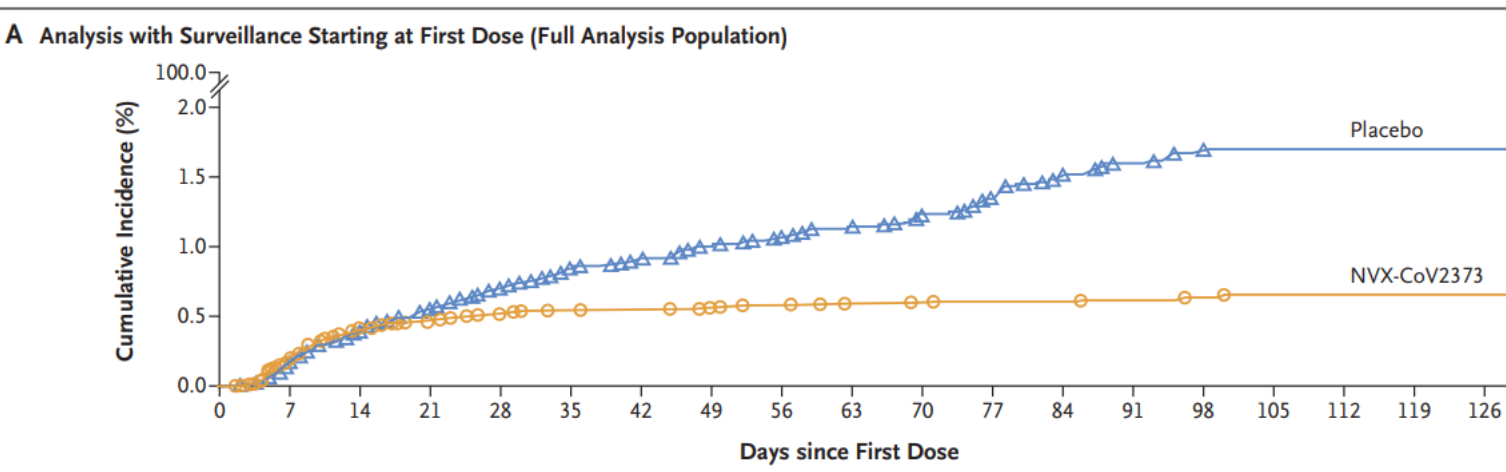
Heath et al. NEJM 2021



NVX-CoV2373: Efficacy



Efficacy: 89.7%



Efficacy: 90.4%

Heath et al. NEJM 2021
Dunkle et al. NEJM 2021



CoVLP-AS03

- 3.75 mcg spike protein virus-like particle expressed in tobacco plants
- AS03 adjuvant (used in H1N1 influenza vaccines)
- 2 doses, 21 days apart
- Canada, USA, UK, Mexico, Argentina, Brazil
- No related serious adverse events
- Generally mild to moderate reactogenicity for 1-3 days
- Fever in less than 10%
- Efficacy: 71%

<https://medicago.com/en/press-release/medicago-and-gsk-announce-positive-phase-3-efficacy-and-safety-results-for-adjuvanted-plant-based-covid-19-vaccine-candidate/>



MOSAIC-1 and MOSAIC-2 'mix and match' trials



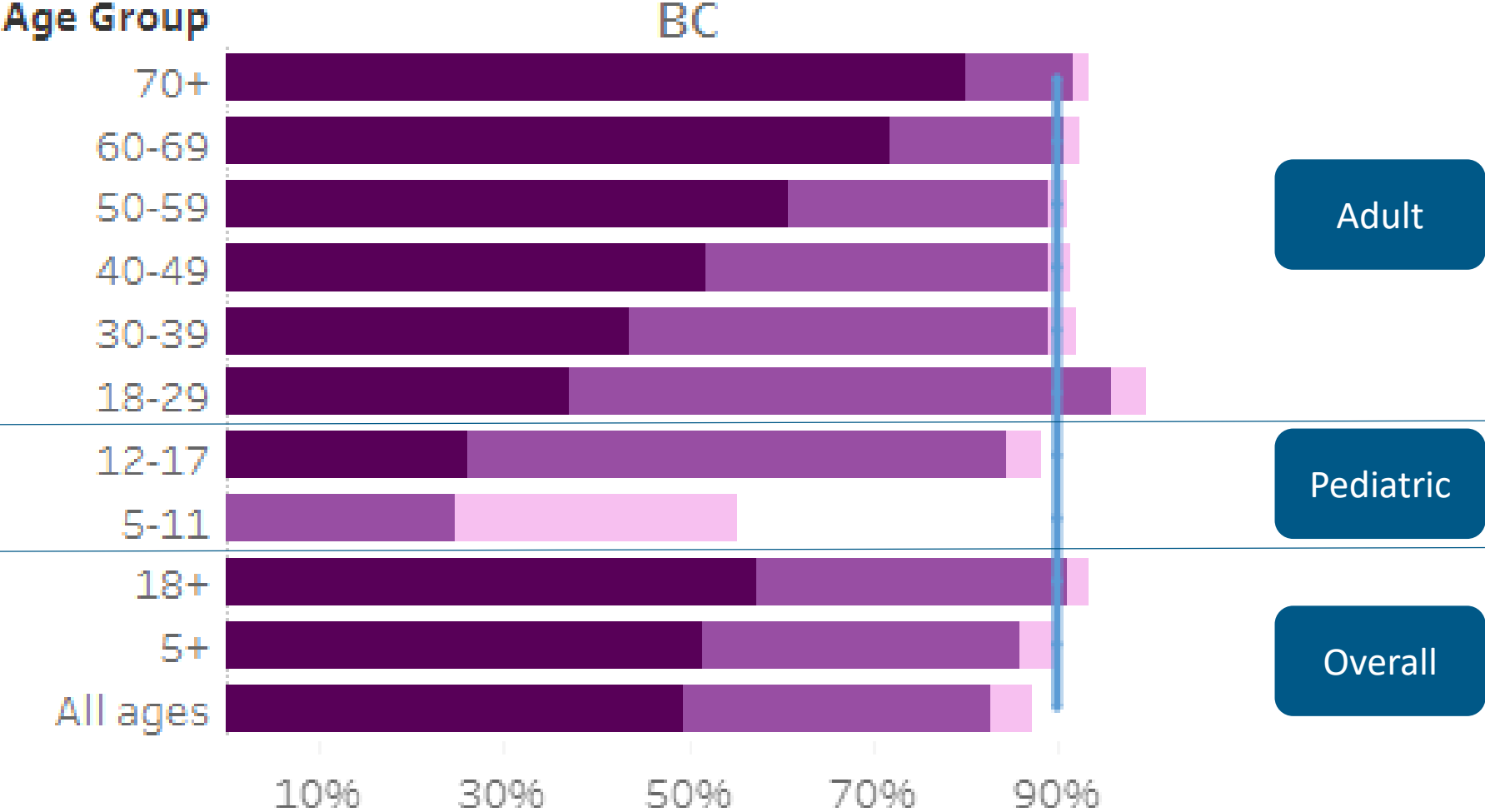
- Immunogenicity and adverse events following immunization with alternate schedules of authorized COVID-19 vaccines in Canada: MOSAIC study - **M**ix and **m**atch of the second COVID-19 vaccine dose for **S**Afety and **I**mmunogeni**C**ity (Co-PIs: Joanne Langley, Manish Sadarangani)

Group	1 st dose	2 nd dose	Interval
1	mRNA-1273	mRNA-1273	Short
2	mRNA-1273	mRNA-1273	Long
3	mRNA-1273	BNT162b2	Short
4	mRNA-1273	BNT162b2	Long
5	BNT162b2	BNT162b2	Short
6	BNT162b2	BNT162b2	Long
7	BNT162b2	mRNA-1273	Short
8	BNT162b2	mRNA-1273	Long
9	ChAdOx1-S	mRNA-1273	Short
10	ChAdOx1-S	mRNA-1273	Long
11	ChAdOx1-S	Pfizer/BioNTech	Short
12	ChAdOx1-S	Pfizer/BioNTech	Long

Group	1 st dose	2 nd dose	3 rd dose
1b	BNT162b2	BNT162b2	BNT162b2
2b	BNT162b2	BNT162b2	mRNA-1273
3b	mRNA-1273	mRNA-1273	BNT162b2
4b	mRNA-1273	mRNA-1273	mRNA-1273
5b	mRNA-1273, BNT162b2 (any order)		mRNA-1273
6b	mRNA-1273, BNT162b2 (any order)		BNT162b2
7b	ChAdOx1-S	Any mRNA	BNT162b2
8b	ChAdOx1-S	Any mRNA	mRNA-1273

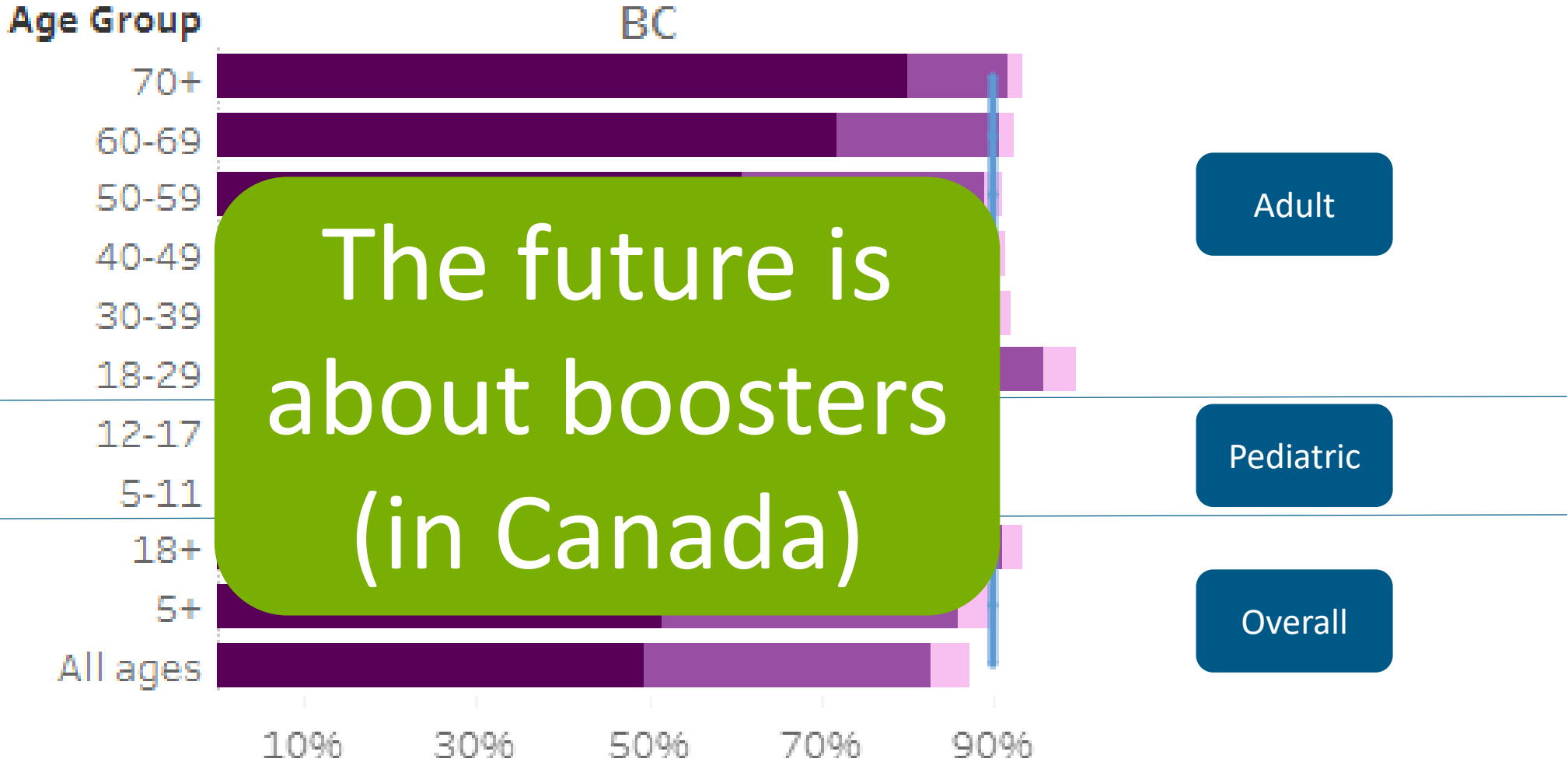


Current status of vaccination in BC



<http://www.bccdc.ca/health-professionals/data-reports/covid-19-surveillance-dashboard>

Current status of vaccination in BC



<http://www.bccdc.ca/health-professionals/data-reports/covid-19-surveillance-dashboard>

Global COVID-19 vaccine coverage

- 10.8 billion doses administered
- At least one dose: 63%
- Completely vaccinated (primary series) 1.560%
 - Range: 0.07% to 94.93%
 - 43 countries @less than 20%

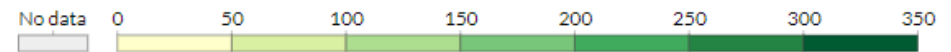
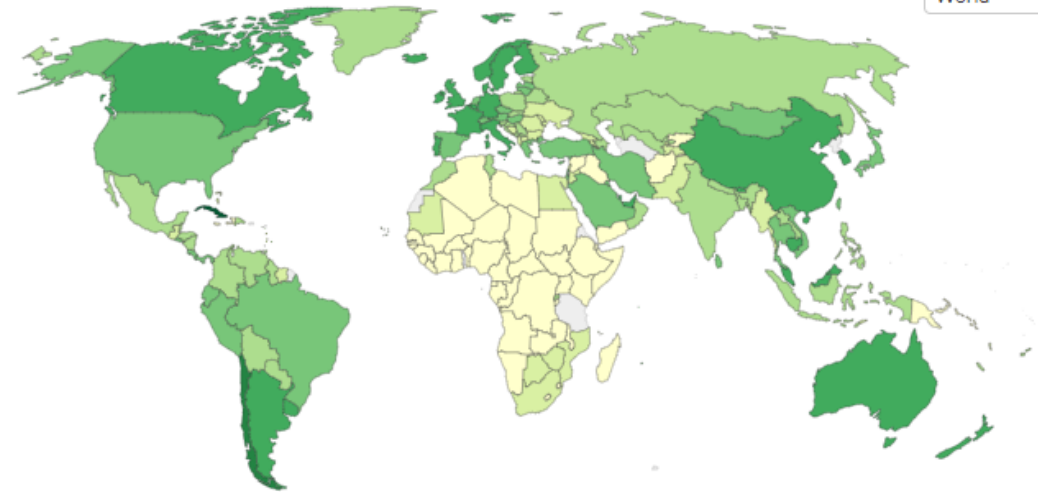
Globally, initial vaccine rollout is ongoing

COVID-19 vaccine doses administered per 100 people, Feb 28, 2022

All doses, including boosters, are counted individually. As the same person may receive more than one dose, the number of doses per 100 people can be higher than 100.

Our World in Data

World

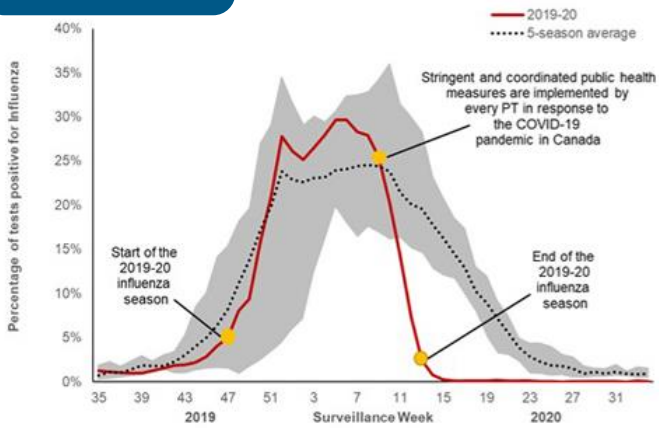


Source: Official data collated by Our World in Data - Last updated 1 March 2022, 11:20 (London time)
OurWorldInData.org/coronavirus • CC BY

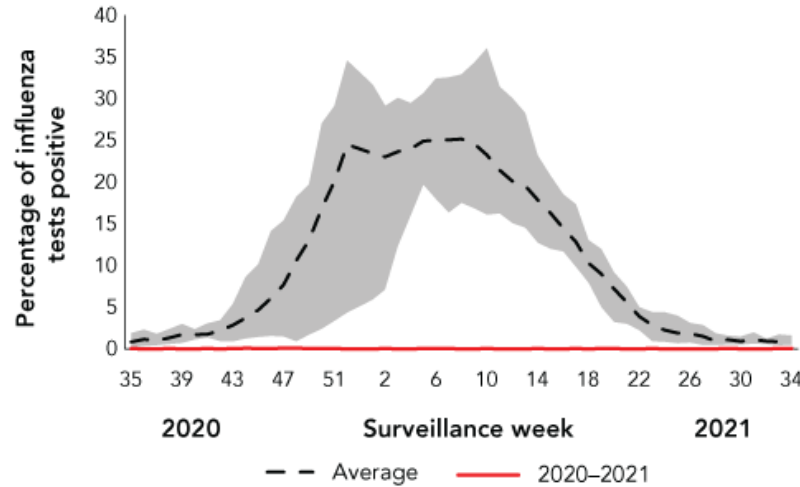
Respiratory viruses are all seasonal, but not the same

Influenza

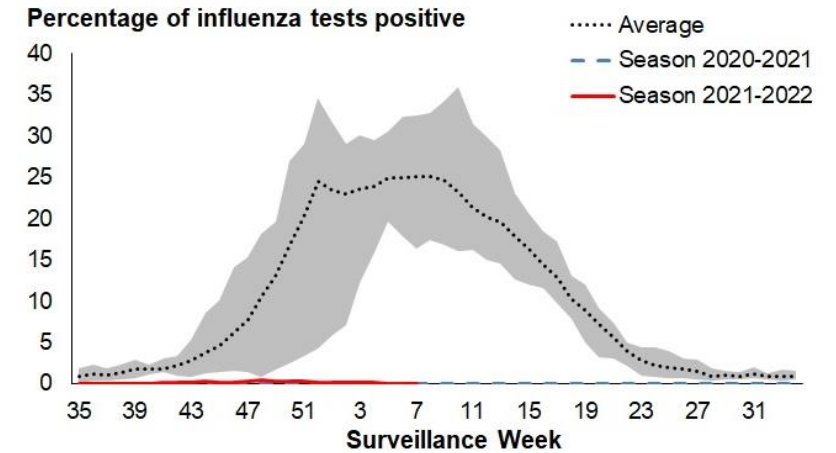
2019-2020



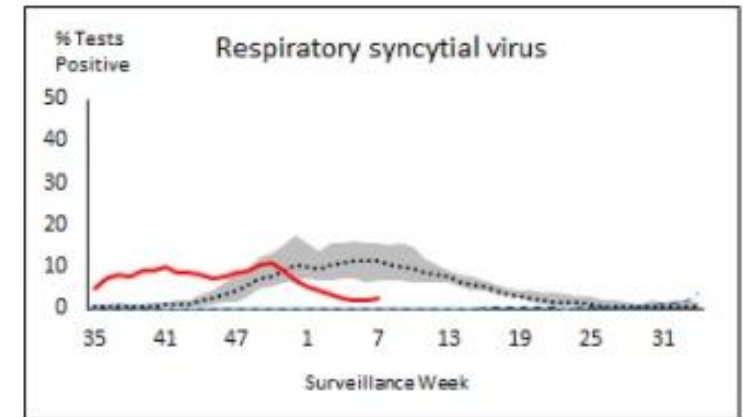
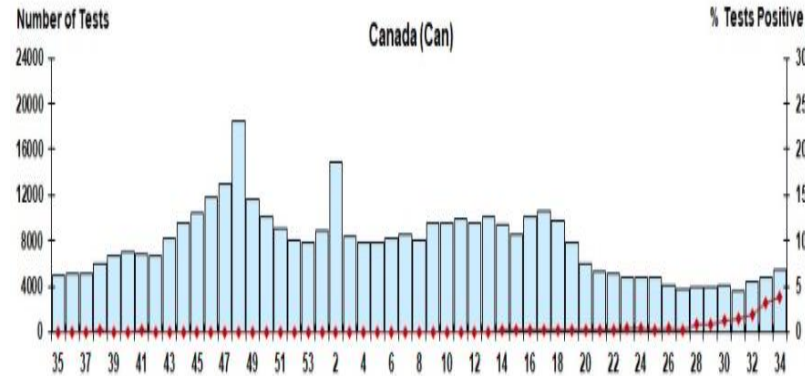
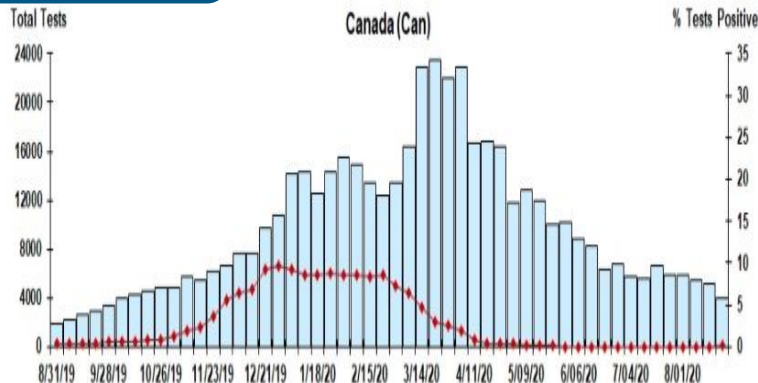
2020-2021



2021-2022



RSV






<https://www.canada.ca/en/public-health/services/diseases/flu-influenza/influenza-surveillance.html#a2>



Future boosters depends on virus evolution...

Key:
(Relative to Omicron characteristics)

 Less / better  Equal to  More / worse




- UK Scenario 1: Reasonable best-case

Transmissibility	Immune escape	Intrinsic severity	Realised severity
			

- Further variants with minimal escape from vaccine/infection-induced immunity
- Existing vaccines annually for vulnerable only**

Future boosters depends on virus evolution...

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- UK Scenario 1: Reasonable best-case

Transmissibility	Immune escape	Intrinsic severity	Realised severity
			

- Further variants with minimal escape from vaccine/infection-induced immunity
- Existing vaccines annually for vulnerable only**

- UK Scenario 2: Central optimistic

Transmissibility	Immune escape	Intrinsic severity	Realised severity
			




- Annual seasonal infection with good and bad years
- Significant waning of immunity and/or new major variants
- Annual vaccination for vulnerable every year and all in some years**

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1054323/S1513_Viral_Evolution_Scenarios.pdf



Future boosters depends on virus evolution...

Key:
(Relative to Omicron characteristics)

 Less / better  Equal to  More / worse

- UK Scenario 3: Central pessimistic




Transmissibility	Immune escape	Intrinsic severity	Realised severity
			

- Unpredictable emergence of variants for many years, at least once per year
- Vaccines effective against severe outcomes
- **Widespread annual vaccination with updated vaccines**



Future boosters depends on virus evolution...

Key:
(Relative to Omicron characteristics)

 Less / better  Equal to  More / worse

- UK Scenario 3: Central pessimistic

Transmissibility	Immune escape	Intrinsic severity	Realised severity
			

- Unpredictable emergence of variants for many years, at least once per year
- Vaccines effective against severe outcomes
- Widespread annual vaccination with updated vaccines**

- UK Scenario 4: Reasonable worst-case

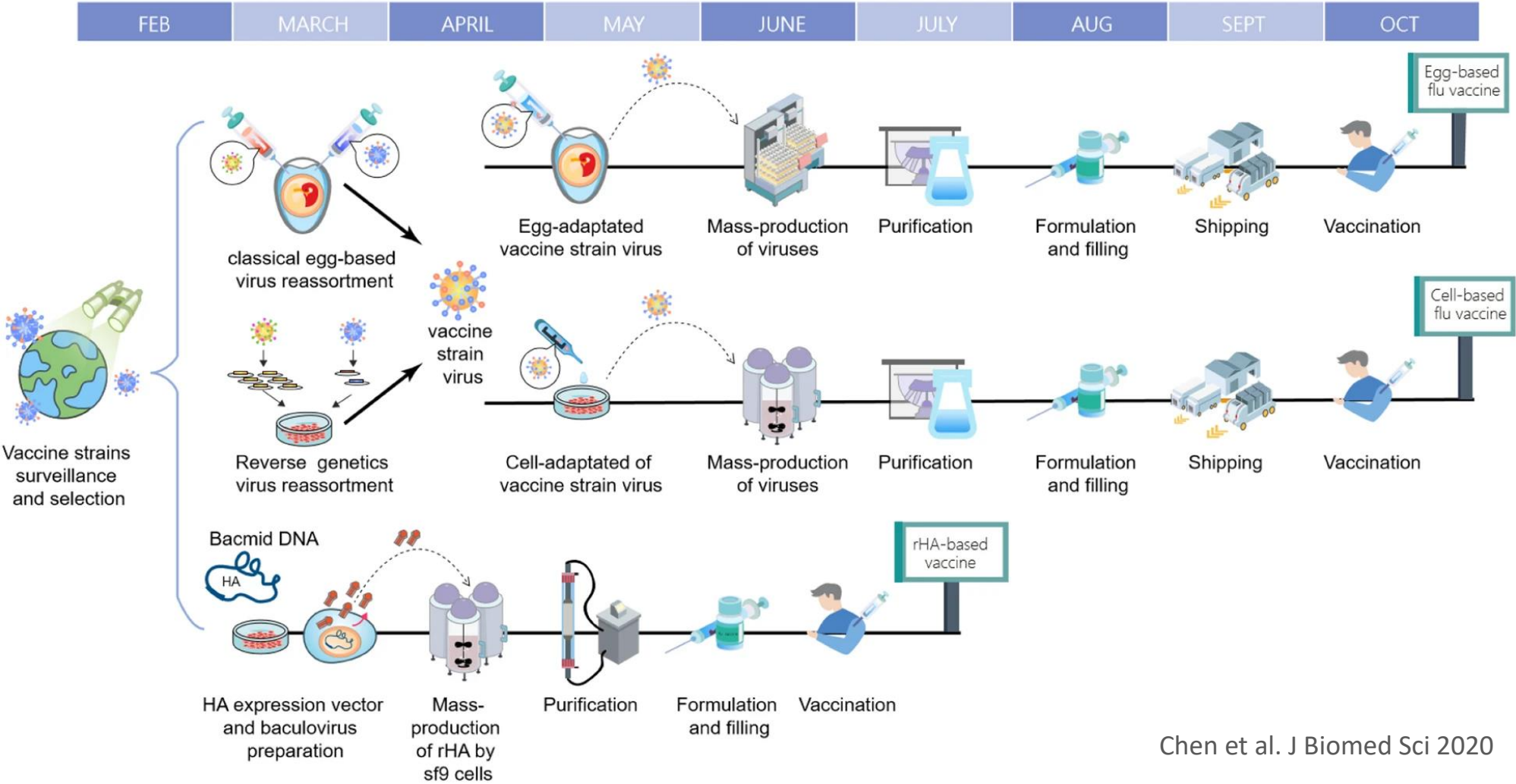
Transmissibility	Immune escape	Intrinsic severity	Realised severity
			

- Repeated and unpredictable emergence of variants with significant immune escape
- Driven by high global incidence, incomplete global vaccination, animal reservoirs**
- Voluntary protective behaviours are largely absent and/or a source of societal conflict**
- Widespread annual vaccination with updated vaccines – feasibility?**



Seasonal influenza vaccine pathway

Current influenza vaccine productions

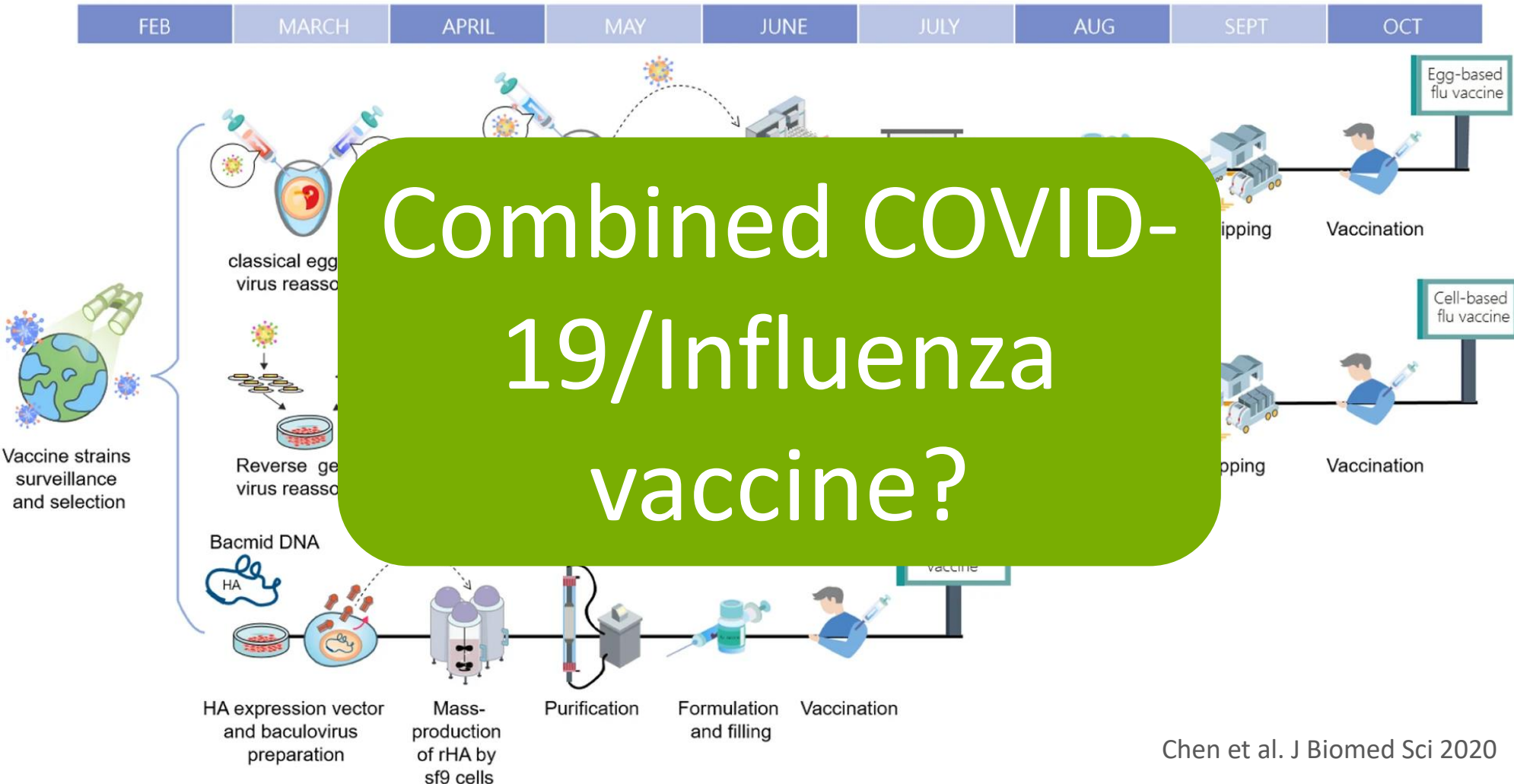


Chen et al. J Biomed Sci 2020



Seasonal influenza vaccine pathway

Current influenza vaccine productions



Chen et al. J Biomed Sci 2020



Broadly-protective beta coronavirus vaccine?

Schematic 'bookends' for the new CFP

Example BPCoV2 ideal Target Product Profile:

Profile:

- 80% or more efficacy against moderate-to-severe disease caused by variants;
- Prevention of viral infection and transmission
- Thermostable at 4-8° C
- Use in all ages and pregnant women
- Use in the immunocompromised
- Potential as booster vaccine

Broadly Protective SARS-COV-2

(prevent disease caused by all VOC & emergent variants)

B1.351
P1
B1.1.7
Other VOC

2022-2023

Broadly Protective Beta-COV

(prevent disease caused by top Beta-CoV threats)

SARS-COV-1
MERS
SARS-COV-2 (+VOC)
USAID
PREDICT
identified 113
novel Beta-CoV

2024+

Multivalent variant formulations or smart immunogen design

Example of a BPBC ideal Target Product Profile:

- Active immunization of at-risk individuals, based on specific risk factors, to prevent disease and mortality (proxy - robust [80%] neutralization against a panel of Betacoronaviuses predictive of protection against disease).
- Prevention of virus infection and transmission
- Thermostable at 4-8° C
- Use in all age groups and pregnant women
- Use in the immunocompromised
- Suitable for use in outbreak situation



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Thank you