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 — xʷməθkʷəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and Səl̓ílwətaʔ/Selilwitulh (Tsleil-Waututh) Nations.
BC Immunization Forum 2022 Presenter Disclosure

• Manish Sadarangani

• Relationships with financial sponsors:
  • Supported via salary awards from
    o BC Children’s Hospital Foundation
    o Canadian Child Health Clinician Scientist Program
    o 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
Disclaimer: I cannot predict the future
## COVID-19 vaccines for Canada – Health Canada approvals

<table>
<thead>
<tr>
<th>Platform</th>
<th>Vaccine</th>
<th>Health Canada</th>
<th>Age</th>
<th>Primary series</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BNT162b2 (Pfizer/BioNTech)</td>
<td>Approved</td>
<td>5y+</td>
<td>2 doses (21 days apart)</td>
<td>+6 months (18y+)</td>
</tr>
<tr>
<td></td>
<td>mRNA-1273 (Moderna)</td>
<td>Approved</td>
<td>12y+</td>
<td>2 doses (1 month apart)</td>
<td>+6 months</td>
</tr>
<tr>
<td></td>
<td>ChAdOx1-S (Oxford University/Astra Zeneca)</td>
<td>Approved</td>
<td>18y+</td>
<td>2 doses (4-12 wks apart)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Ad26.COV2.S (Janssen)</td>
<td>Approved</td>
<td>18y+</td>
<td>Single dose</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>NVX-CoV2373 (Novavax)</td>
<td>Approved</td>
<td>18y+</td>
<td>2 doses (21 days apart)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>CoVLP-AS03 (Medicago)</td>
<td>Approved</td>
<td>18-64y</td>
<td>2 doses (21 days apart)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Adjuvanted vaccine (Sanofi Pasteur/GlaxoSmithKline)</td>
<td>Under review</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

COVID-19 vaccines for Canada – NACI recommendations

<table>
<thead>
<tr>
<th>Age</th>
<th>Primary series (healthy individuals)</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 years</td>
<td>No vaccine available</td>
<td>N/A</td>
</tr>
<tr>
<td>5-11 years</td>
<td>2 doses BNT162b2 (pediatric)</td>
<td>No</td>
</tr>
<tr>
<td>12-17y</td>
<td>2 doses BNT162b2 (preferred) or mRNA-1273</td>
<td>Specific populations only</td>
</tr>
<tr>
<td>18-29y</td>
<td>2 doses BNT162b2 (preferred) or mRNA-1273 or ChAdOx1-S or Ad26.COV2.S or NVX-CoV2373</td>
<td>BNT162b2 or mRNA-1273 after 6 months</td>
</tr>
<tr>
<td>30y+</td>
<td>2 doses BNT162b2 or mRNA-1273 (preferred) or ChAdOx1-S or Ad26.COV2.S or NVX-CoV2373</td>
<td>BNT162b2 or mRNA-1273 after 6 months</td>
</tr>
</tbody>
</table>

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

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%**

Heath et al. NEJM 2021

**Efficacy: 90.4%**

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%

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 - Mix and match of the second COVID-19 vaccine dose for SAFety and IMMunogenicity (Co-PIs: Joanne Langley, Manish Sadarangani)

<table>
<thead>
<tr>
<th>Group</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>mRNA-1273</td>
<td>mRNA-1273</td>
<td>Short</td>
</tr>
<tr>
<td>2</td>
<td>mRNA-1273</td>
<td>mRNA-1273</td>
<td>Long</td>
</tr>
<tr>
<td>3</td>
<td>mRNA-1273</td>
<td>BNT162b2</td>
<td>Short</td>
</tr>
<tr>
<td>4</td>
<td>mRNA-1273</td>
<td>BNT162b2</td>
<td>Long</td>
</tr>
<tr>
<td>5</td>
<td>BNT162b2</td>
<td>BNT162b2</td>
<td>Short</td>
</tr>
<tr>
<td>6</td>
<td>BNT162b2</td>
<td>BNT162b2</td>
<td>Long</td>
</tr>
<tr>
<td>7</td>
<td>BNT162b2</td>
<td>mRNA-1273</td>
<td>Short</td>
</tr>
<tr>
<td>8</td>
<td>BNT162b2</td>
<td>mRNA-1273</td>
<td>Long</td>
</tr>
<tr>
<td>9</td>
<td>ChAdOx1-S</td>
<td>mRNA-1273</td>
<td>Short</td>
</tr>
<tr>
<td>10</td>
<td>ChAdOx1-S</td>
<td>mRNA-1273</td>
<td>Long</td>
</tr>
<tr>
<td>11</td>
<td>ChAdOx1-S</td>
<td>Pfizer/BioNTech</td>
<td>Short</td>
</tr>
<tr>
<td>12</td>
<td>ChAdOx1-S</td>
<td>Pfizer/BioNTech</td>
<td>Long</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>3rd dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b</td>
<td>BNT162b2</td>
<td>BNT162b2</td>
<td>BNT162b2</td>
</tr>
<tr>
<td>2b</td>
<td>BNT162b2</td>
<td>BNT162b2</td>
<td>mRNA-1273</td>
</tr>
<tr>
<td>3b</td>
<td>mRNA-1273</td>
<td>mRNA-1273</td>
<td>BNT162b2</td>
</tr>
<tr>
<td>4b</td>
<td>mRNA-1273</td>
<td>mRNA-1273</td>
<td>mRNA-1273</td>
</tr>
<tr>
<td>5b</td>
<td>mRNA-1273, BNT162b2 (any order)</td>
<td>mRNA-1273</td>
<td></td>
</tr>
<tr>
<td>6b</td>
<td>mRNA-1273, BNT162b2 (any order)</td>
<td>BNT162b2</td>
<td></td>
</tr>
<tr>
<td>7b</td>
<td>ChAdOx1-S</td>
<td>Any mRNA</td>
<td>BNT162b2</td>
</tr>
<tr>
<td>8b</td>
<td>ChAdOx1-S</td>
<td>Any mRNA</td>
<td>mRNA-1273</td>
</tr>
</tbody>
</table>
Current status of vaccination in BC

http://www.bccdc.ca/health-professionals/data-reports/covid-19-surveillance-dashboard
Current status of vaccination in BC

The future is about boosters (in Canada)

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): 56%
  • Range: 0.07% to 94.93%
  • 43 countries at less than 20%

Globally, initial vaccine rollout is ongoing

http://https://ourworldindata.org/covid-vaccinations
Respiratory viruses are all seasonal, but not the same

Influenza

2019-2020

RSV

2020-2021

2021-2022

Future boosters depends on virus evolution...

- **UK Scenario 1: Reasonable best-case**

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

Future boosters depends on virus evolution...

• **UK Scenario 1: Reasonable best-case**
  - Further variants with minimal escape from vaccine/infection-induced immunity
  - **Existing vaccines annually for vulnerable only**

• **UK Scenario 2: Central optimistic**
  - 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**

Future boosters depend on virus evolution...

- **UK Scenario 3: Central pessimistic**
  - Unpredictable emergence of variants for many years, at least once per year
  - Vaccines effective against severe outcomes
  - **Widespread annual vaccination with updated vaccines**

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For a detailed understanding of the key scenarios and their implications, please refer to the linked document:

Future boosters depends on virus evolution...

• UK Scenario 3: Central pessimistic

<table>
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<th>Transmissibility</th>
<th>Immune escape</th>
<th>Intrinsic severity</th>
<th>Realised severity</th>
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• 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

<table>
<thead>
<tr>
<th>Transmissibility</th>
<th>Immune escape</th>
<th>Intrinsic severity</th>
<th>Realised severity</th>
</tr>
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</table>

• 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

- Egg-based vaccine strain virus
- Mass-production of viruses
- Purification
- Formulation and filling
- Shipping
- Vaccination

- Cell-based vaccine

Chen et al. J Biomed Sci 2020
Combined COVID-19/Influenza vaccine?
Broadly-protective beta coronavirus vaccine?

**Example BPCoV2 ideal Target Product 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.

**Schematic ‘bookends’ for the new CFP:**

- Broadly Protective SARS-COV-2 (prevent disease caused by all VOC & emergent variants);
- Multivalent variant formulations or smart immunogen design;
- Broadly Protective Beta-COV (prevent disease caused by top Beta-CoV threats);
- 2022-2023;
- 2022-2023;
- 2024+.

**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 Betacoronaviruses 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.
Thank you

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