The Science of Vaccines

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30 May, 2023
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.
Disclosures

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  • BC Children’s Hospital Foundation
  • Michael Smith Foundation for Health Research

• **Research/Project Funding**
  • Merck, Moderna, VBI Vaccines, GlaxoSmithKline, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo

• All funds have been paid to my institute
• I have not received any personal payments
My Brief

• Advances in vaccine technology to improve vaccine delivery and efficacy
  • Reflections from COVID-19 vaccines

• New vaccines on the horizon for chronic and emerging infections
  • Respiratory infections: COVID-19, influenza, RSV
  • Antimicrobial resistance
  • Controlled human infection models (CHIMs)

• Novel strategies for addressing the challenge of vaccine hesitancy
  • The importance of your role
Vaccine technologies
The global vaccination system has been stress-tested!
Some of the major ongoing challenges – game-changers?

• Vaccine platforms
  • Flexible, adaptable
  • Large scale manufacturing
  • Low cost

• Non-injectable administration

• Fewer doses – ideally single dose
  • Needs better understanding of how vaccines work

• Thermostable
  • In particular heat-stable
### Current vaccine approaches

<table>
<thead>
<tr>
<th>Whole-Pathogen Vaccines</th>
<th>Viral Vectors</th>
<th>Subunit Vaccines</th>
<th>Nucleic Acids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated influenza</td>
<td>rVSV-ZEBOV</td>
<td>Acellular</td>
<td>BNT162b2,</td>
</tr>
<tr>
<td>Inactivated influenza</td>
<td>(Ebola)</td>
<td>pertussis</td>
<td>mRNA1273</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>rVSV-ZEBOV</td>
<td>MenC,</td>
<td>ZyCoV-D</td>
</tr>
<tr>
<td>Polio</td>
<td>(Ebola)</td>
<td>MenACWY</td>
<td>(COVID-19)</td>
</tr>
<tr>
<td>Inactivated influenza</td>
<td>ChAdOx1-S</td>
<td>Tetanus</td>
<td>(COVID-19)</td>
</tr>
<tr>
<td>Ad26CoV2S (COVID-19)</td>
<td>Polio</td>
<td>HPV</td>
<td>(COVID-19)</td>
</tr>
<tr>
<td>Inactivated influenza</td>
<td>Ad26CoV2S</td>
<td>Polio</td>
<td></td>
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<tr>
<td>Ad26CoV2S (COVID-19)</td>
<td>Ad26CoV2S</td>
<td>Polio</td>
<td></td>
</tr>
<tr>
<td>Acellular pertussis</td>
<td>MenC,</td>
<td>Tetanus</td>
<td></td>
</tr>
<tr>
<td>MenACWY</td>
<td>Hepatitis B</td>
<td>Diphtheria</td>
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</tr>
<tr>
<td>PCV</td>
<td>Hepatitis B</td>
<td>Hepatitis B</td>
<td></td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Hepatitis</td>
<td>BNT162b2,</td>
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<tr>
<td>Hepatitis B</td>
<td>BNT162b2,</td>
<td>mRNA1273,</td>
<td></td>
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<td>mRNA1273,</td>
<td>mRNA1273,</td>
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<tr>
<td></td>
<td>mRNA1273,</td>
<td>ZyCoV-D,</td>
<td></td>
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<td></td>
<td>mRNA1273,</td>
<td>(COVID-19)</td>
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<tr>
<td></td>
<td>mRNA1273,</td>
<td>(COVID-19)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mRNA1273,</td>
<td>(COVID-19)</td>
<td></td>
</tr>
</tbody>
</table>

- **Future vaccine “platforms”**
  - RNA
  - Viral vector
  - Others in development

https://asm.org/resource-pages/vaccine-resources
RNA vaccines

Conventional mRNA

- Cap
- 5’UTR
- GOI
- 3’UTR
- AAAAA

Self-amplifying mRNA

- Cap
- 5’UTR
- Alphavirus nsPs
- GOI
- 3’UTR
- AAAAA

Formulation for delivery

Cell entry

Endosome

Proteasome

Ribosome

Protein production

Surface presentation for antibody induction

Surface presentation for CTL induction

TLR3, TLR7, TLR9

RIG-I, MDA5

RNA sensing

Self-amplification

Replicase

Ribosome

Proteasome

Peptide-MHC presentation for CTL induction

Peptide-MHC presentation for antibody induction

Sandbrink and Shattock. Frontiers in Immunology 2020
COVID-19 mRNA vaccines: THE GOOD

• High vaccine efficacy

BNT162b2

Polack et al. NEJM 2020; Baden et al. NEJM 2020

mRNA-1273
COVID-19 mRNA vaccines: THE GOOD

- High vaccine efficacy
- Rapid development

Polack et al. NEJM 2020; Baden et al. NEJM 2020

Ball. Nature 2020
COVID-19 mRNA vaccines: THE GOOD

- High vaccine efficacy
- Rapid development
- Adapt to variants

Polack et al. NEJM 2020; Baden et al. NEJM 2020

Ball. Nature 2020

Noh et al. Nature 2021
COVID-19 mRNA vaccines: THE BAD

• Adverse events
  • Very frequent local and systemic reactions
  • Rare, severe events
    o Myocarditis, pericarditis
      • Young adults, adolescents
      • Males > Females
    o Bell’s palsy (facial paralysis)

• Cold chain
  • BNT162b2: -90°C to -50°C
  • mRNA-1273: -50°C to -15°C

• Need for boosters
COVID-19 mRNA vaccines: THE BAD

• Adverse events
  • Very frequent local and systemic reactions
  • Rare, severe events
    o Myocarditis, pericarditis
      • Young adults, adolescents
      • Males > Females
    o Bell’s palsy (facial paralysis)

• Cold chain
  • BNT162b2: -90°C to -50°C
  • mRNA-1273: -50°C to -15°C

• Need for boosters
COVID-19 mRNA vaccines: THE UGLY

- Poor global coverage
- High cost

Potential Total Cost Scenarios for One Dose of a COVID-19 Vaccine/Booster per Adult

<table>
<thead>
<tr>
<th>Type of Purchase</th>
<th>Price/Dose ($)</th>
<th>Source</th>
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</thead>
<tbody>
<tr>
<td>Federal (Bivalent)</td>
<td>$29</td>
<td></td>
</tr>
<tr>
<td>Commercial (Low)</td>
<td>$96</td>
<td></td>
</tr>
</tbody>
</table>
COVID-19 self-amplifying RNA vaccine

Safety and immunogenicity of a self-amplifying RNA vaccine against COVID-19: COVAC1, a phase I, dose-ranging trial

COVAC1 phase 2a expanded safety and immunogenicity study of a self-amplifying RNA vaccine against SARS-CoV-2

<table>
<thead>
<tr>
<th>Vaccine dose</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 mcg</td>
<td>5</td>
<td>3</td>
<td>8</td>
<td>8</td>
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<tr>
<td>0.3 mcg</td>
<td>0</td>
<td>13</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>1.0 mcg</td>
<td>7</td>
<td>19</td>
<td>43</td>
<td>48</td>
</tr>
<tr>
<td>2.5 mcg</td>
<td>0</td>
<td>17</td>
<td>39</td>
<td>43</td>
</tr>
<tr>
<td>5.0 mcg</td>
<td>4</td>
<td>26</td>
<td>39</td>
<td>35</td>
</tr>
<tr>
<td>10.0 mcg</td>
<td>0</td>
<td>35</td>
<td>61</td>
<td>57</td>
</tr>
</tbody>
</table>

Note: conventional mRNA vaccine dose 30-100 mcg (adult)

Vaccine dose | Week 2 | Week 4 |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 mcg + 10 mcg</td>
<td>80</td>
<td>80</td>
</tr>
</tbody>
</table>

Pollock et al. eClinicalMedicine 2023; Szubert et al. eClinicalMedicine 2023
mRNA vaccines for other pathogens?

- **Influenza**

  Moderna announces mixed results for influenza mRNA vaccine candidate

  By Rachel Arthur
  20-Feb-2023 - Last updated on 20-Feb-2023

  Phase 3 interim data showed the mRNA vaccine candidate generated a strong immune response against Influenza A; but failed to demonstrate it was at least as effective as an existing vaccine against Influenza B.

  The Phase 3 study looked at the safety and immunogenicity of a single dose of mRNA-1010 during the Southern Hemisphere influenza season: enrolling 6,102 adults across Argentina, Australia, Colombia, Panama and the Philippines.

- **RSV**

  mRNA vaccine effective against RSV respiratory disease

  Nature Medicine explores the latest translational and clinical research news, with Moderna's clinical trial of a vaccine against respiratory syncytial virus in older adults.

  Moderna has announced topline results for its mRNA-based vaccine against respiratory syncytial virus (RSV) infection in adults 60 years of age and older. mRNA-1345 targets the RSV fusion (F) glycoprotein and, according to the press release, is 83.7% effective at preventing lower-respiratory-tract disease. It is the latest in a string of positive results from

https://www.biopharma-reporter.com/Article/2023/02/20/moderna-announces-mixed-results-for-influenza-mrna-vaccine-candidate;
https://www.nature.com/articles/d41591-023-00017-7
Viral vector vaccines

**VIRAL-VECTOR VACCINES**

**Replicating viral vector (such as weakened measles)**
The newly approved Ebola vaccine is an example of a viral-vector vaccine that replicates within cells. Such vaccines tend to be safe and provoke a strong immune response. Existing immunity to the vector could blunt the vaccine’s effectiveness, however.

**Non-replicating viral vector (such as adenovirus)**
No licensed vaccines use this method, but they have a long history in gene therapy. Booster shots can be needed to induce long-lasting immunity. US-based drug giant Johnson & Johnson is working on this approach.

Callaway. Nature 2020
COVID-19 Viral vector vaccines: THE GOOD

• High efficacy
• Rapid development
• Adapt to variants

Voysey et al. Lancet 2020
COVID-19 Viral vector vaccines: THE BAD

• Adverse events
  • Very frequent local and systemic reactions
  • Rare, severe events
    o Thrombosis with thrombocytopenia (TTS)
    o Vaccine-induced immune thrombotic thrombocytopenia (VITT)
    o Capillary leak syndrome
    o Guillain-Barré syndrome

• Cold chain

• Need for boosters
COVID-19 Viral vector vaccines: THE UGLY

• Anti-viral immunity

• High cost
Avoiding anti-viral immunity

Use of different vectors/platforms for priming and booster doses?
  - ‘Heterologous prime-boost’

Adjuvants

Mucosal administration

McCann et al. Curr Opin Immunol 2022
Non-injectable administration

- Mucosal immunity

- Current
  - Oral rotavirus vaccine
  - Oral polio vaccine (plan to phase out as part of global eradication plan)
  - Live attenuated influenza vaccine

- Future
  - Epicutaneous (e.g., microneedles, microinjectors, patches)
  - Other mucosally administered
    - Intranasal, inhaled, oral
Epicutaneous vaccine administration

The safety, immunogenicity, and acceptability of inactivated influenza vaccine delivered by microneedle patch (TIV-MNP 2015): a randomised, partly blinded, placebo-controlled, phase 1 trial


Safety and immunogenicity of the epicutaneous reactivation of pertussis toxin immunity in healthy adults: a phase 1, randomized, double-blind, placebo-controlled trial

Clinical Microbiology and Infection 27 (2021) 878–885

Understanding how vaccines work → Rational vaccine design

Pulendran et al. Immunity 2010
Pulendran et al. PNAS 2014
The dawn of ‘precision vaccinology’?

Tsang et al. Trends in Immunol 2020
Safety and immunogenicity of a thermostable ID93 + GLA-SE tuberculosis vaccine candidate in healthy adults

Gerhardt et al. bioRxiv 2021
New vaccines
Seasonal influenza vaccine pathway

Current influenza vaccine productions

<table>
<thead>
<tr>
<th>FEB</th>
<th>MARCH</th>
<th>APRIL</th>
<th>MAY</th>
<th>JUNE</th>
<th>JULY</th>
<th>AUG</th>
<th>SEPT</th>
<th>OCT</th>
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</tr>
</tbody>
</table>

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

Cell-based flu vaccine

Vaccine strains surveillance and selection

classical egg-based virus reassortment

Reverse genetics virus reassortment

Bacmid DNA

HA expression vector and baculovirus preparation

Mass-production of rHA by sf9 cells

Purification
Formulation and filling
Vaccination

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

Example BP-CoV2 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;

Multivalent variant formulations or smart immunogen design

Schematic ‘bookends’ for the new CFP

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;
# Universal influenza vaccine

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain specific</td>
<td>Current circulating strains</td>
</tr>
<tr>
<td>Subtype specific</td>
<td>All strains within a single HA subtype (e.g., H1)</td>
</tr>
<tr>
<td>Multisubtype</td>
<td>Multiple HA subtypes within single group (e.g., H1/H5/H9)</td>
</tr>
<tr>
<td>Pan-group</td>
<td>Covering all group 1 or 2 influenza A viruses</td>
</tr>
<tr>
<td>Universal</td>
<td>All influenza A viruses (with or without influenza B viruses)</td>
</tr>
</tbody>
</table>

A universal influenza vaccine should:

- Be at least 75% effective against symptomatic influenza virus infection;
- Protect against group I and group II influenza A viruses (influenza B virus would be a secondary target);
- Have durable protection that lasts at least 1 year and preferably through multiple seasons;
- Be suitable for all age groups.

Courtesy: Gary Nabel

Erbelding et al. JID 2018
A universal influenza vaccine should:

- Be at least 75% effective against symptomatic influenza virus infection;
- Protect against group I and group II influenza A viruses (influenza B virus would be a secondary target);
- Have durable protection that lasts at least 1 year and preferably through multiple seasons;
- Be suitable for all age groups.

Erbelding et al. JID 2018; Vogel and Manicassamy. Front Microbiol 2020
Clinical trial of mRNA universal influenza vaccine candidate begins
# Respiratory syncytial virus (RSV)

## RSV Vaccine and mAb Snapshot

### TARGET INDICATION:
- P = Pediatric
- M = Maternal
- E = Elderly

<table>
<thead>
<tr>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>MARKET APPROVED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LIVE-ATTENUATED/CHIMERIC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blue Lake</td>
<td>Codagenix</td>
<td>Melissa Vaccines</td>
<td>Sanofi</td>
</tr>
<tr>
<td>RSV/RSV</td>
<td>LID/NIAID/NIH</td>
<td>RSV</td>
<td>LID/NIAID/NIH</td>
</tr>
<tr>
<td>Pontificia Universidad Católica de Chile</td>
<td>SIPL, St Jude Hospital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCC/RSV</td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>PROTEIN-BASED</strong></th>
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</thead>
<tbody>
<tr>
<td>• PARTICLE</td>
</tr>
<tr>
<td>• SUBUNIT</td>
</tr>
<tr>
<td>Icosavaxx</td>
</tr>
<tr>
<td>RSV/MMPV/VLP</td>
</tr>
<tr>
<td>Virometix</td>
</tr>
<tr>
<td>VLP</td>
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</table>

<table>
<thead>
<tr>
<th><strong>NUCLEIC ACID</strong></th>
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</thead>
<tbody>
<tr>
<td>Moderna</td>
</tr>
<tr>
<td>RNA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>RECOMBINANT VECTORS</strong></th>
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</thead>
<tbody>
<tr>
<td>Janssen Pharmaceutical</td>
</tr>
<tr>
<td>Adenovirus</td>
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<table>
<thead>
<tr>
<th><strong>IMMUNOPROPHYLAXIS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gates MIRI</td>
</tr>
<tr>
<td>Anti-F mAb</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Merck</td>
</tr>
<tr>
<td>Anti-F mAb</td>
</tr>
</tbody>
</table>

**UPDATED: May 4, 2023**

https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/
RSV – recent successes

• Vaccine efficacy 83% in adults aged 60y+

• Immunoprophylaxis – nirsevimab – efficacy ~60-80%
NEWS ANALYSIS

Maternal RSV vaccine: Further analysis is urged on preterm births

A “safety signal” in a similar respiratory syncytial virus (RSV) vaccine has led to trials being stopped and prompted calls for a cautious approach to using the vaccine in pregnant women, reports Hristio Boytchev

Hristio Boytchev

Experts have called for further analysis of trial data and post-approval monitoring of Pfizer’s maternal RSV vaccine candidate after GSK’s trials of a similar product were halted over a rise in preterm births and neonatal deaths.
Vaccines against antimicrobial resistance

Fig. 1. Strategic objectives of the Global Action Plan on Antimicrobial Resistance

- Investing in new medicines, diagnostic tools, vaccines and other interventions
- Improving awareness and understanding of antimicrobial resistance through effective communication, education and training
- Optimizing the use of antimicrobial medicines in human and animal health
- Strengthening the knowledge and evidence base through surveillance and research
- Reducing the incidence of infection through effective sanitation, hygiene and infection prevention measures, including vaccines
Vaccines against antimicrobial resistance

1. Expanding use of licensed vaccines to maximize impact on AMR

**Fig. 3. Impact of pneumococcal vaccine on rates of drug-resistant invasive pneumococcal disease (IPD) in the United States of America**

- Introduction of PCV13
- 63% Mecloides
- 81% Cephalosporins
- 81% Tetracyclines
- 83% Penicillins

% change in antibiotic resistant cases between 2009 and 2013
Vaccines against antimicrobial resistance

1. Expanding use of licensed vaccines to maximize impact on AMR

2. Developing new vaccines that contribute to prevention and control of AMR

3. Expanding and sharing knowledge of vaccine impact on AMR

<table>
<thead>
<tr>
<th>Pipeline Feasibility Group</th>
<th>Description</th>
<th>Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high</td>
<td>AMR priority pathogens for which licensed vaccines already exist</td>
<td>Salmonella enterica ser. Typhi, Streptococcus pneumoniae, Haemophilus influenzae type b, Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>High</td>
<td>AMR priority pathogens for which a vaccine candidate is in late-stage development (Phase 3) and vaccines would be suitable to target AMR infections caused by these priority pathogens in the coming years</td>
<td>Extraintestinal pathogenic Escherichia coli (ExPEC), Salmonella enterica ser. Paratyphi A, Neisseria gonorrhoeae, Clostridioides difficile</td>
</tr>
<tr>
<td>Moderate</td>
<td>AMR priority pathogens for which a vaccine candidate has either been identified in early clinical trials or been identified as a feasible vaccine target during expert review. Vaccines may be feasible solutions to target AMR infections, with moderate feasibility of vaccine development</td>
<td>Enterotoxigenic Escherichia coli (ETEC), Klebsiella pneumoniae, Non-typhoidal Salmonella, Campylobacter spp., Shigella spp.</td>
</tr>
</tbody>
</table>

Frost et al. Hum Vacc Immun 2022
Controlled human infection models (CHIMs)

### TABLE 38 Summary recommendations for the continued development and utilization of human challenge models for 17 infectious diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Challenge agent(s)</th>
<th>Recommendation from the literature review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td><em>Plasmodium falciparum</em></td>
<td>Proceed. Few concerns identified, if any.</td>
</tr>
<tr>
<td>Cholera</td>
<td><em>Vibrio cholerae</em></td>
<td></td>
</tr>
<tr>
<td>Pneumococcus</td>
<td><em>Streptococcus pneumoniae</em></td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Live oral rotavirus vaccine</td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>Oral poliovirus vaccine</td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>Influenza strains pertinent to the development of universal influenza vaccines</td>
<td></td>
</tr>
<tr>
<td>Typhoid/Paratyphoid</td>
<td><em>Salmonella Typhi</em> and <em>Salmonella Paratyphi</em> serovars</td>
<td></td>
</tr>
<tr>
<td>ETEC</td>
<td>ETEC strains expressing selected toxins and colonization factors</td>
<td>Proceed with caution. Minor concerns identified.</td>
</tr>
<tr>
<td>Shigellosis</td>
<td><em>Shigella flexneri</em> serotypes and <em>Shigella sonnei</em></td>
<td></td>
</tr>
<tr>
<td>Norovirus</td>
<td>Norovirus genogroups and genotypes</td>
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</tr>
<tr>
<td>RSV</td>
<td>RSV strains of genogroups A and B</td>
<td></td>
</tr>
<tr>
<td>Dengue</td>
<td>Attenuated dengue virus serotypes 1 through 4</td>
<td></td>
</tr>
<tr>
<td>Malaria</td>
<td><em>Plasmodium vivax</em></td>
<td>Address major concerns before proceeding.</td>
</tr>
<tr>
<td>Campylobacteriosis</td>
<td><em>Campylobacter jejuni</em> serotypes</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Bacillus Calmette-Guérin</td>
<td></td>
</tr>
<tr>
<td>Pertussis</td>
<td><em>Bordetella pertussis</em></td>
<td></td>
</tr>
<tr>
<td>Cryptosporidiosis</td>
<td><em>Cryptosporidium parvum</em> and <em>Cryptosporidium hominis</em></td>
<td></td>
</tr>
<tr>
<td>COVID-19</td>
<td>SARS-CoV-2</td>
<td></td>
</tr>
</tbody>
</table>

*COVID-19, Coronavirus disease 2019; ETEC, enterotoxigenic *Escherichia coli*; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.*
Vaccine hesitancy
What is vaccine hesitancy?

Vaccine hesitancy continuum

Accept all

Accept but unsure

Accept some, delay, refuse some

Refuse but unsure

Refuse all

Should we be worried about vaccine hesitancy?

- Global state of vaccine confidence

**Figure 2 Confidence in the safety of vaccines**

Wiegand et al. SSRN 2023
We are failing to vaccinate the world

Vaccines save lives, but far too many children in the world are not being vaccinated. The COVID-19 pandemic only added to their numbers. The children who are missing out live in the poorest, most remote and most marginalized communities. To reach them, it is vital to prioritize investment in primary health care and in the health workers – mostly women – who deliver services. It is essential, too, to build confidence in vaccines and to make the most of a host of new ideas and technologies that can boost the power of vaccines and ensure they reach every child.

Over the past decade or so, despite growing efforts to expand immunization, there has been little progress in reducing the number of zero-dose children. Reaching every child remains a challenge.

**Figure 1. Zero-dose children globally, 2000–2021**

- **2000:** 22.3 million
- **2010:** 15.4 million
- **2021:** 18.2 million


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**For Every Child, Vaccination**

**1 in 5** children are zero-dose (unvaccinated) and under-vaccinated, leaving them vulnerable to a range of vaccine-preventable diseases.

**1 in 5** children have no protection at all against measles, a childhood killer.

**7 in 8** eligible girls are not vaccinated against human papillomavirus (HPV), which can cause cervical cancer.
Pillars of vaccine confidence

- Trust
- Safety
- Effectiveness
- Importance
- Religious compatibility
What can you do?

- You are the most trusted source of information...

### Most of the time, we can trust...

<table>
<thead>
<tr>
<th>Source</th>
<th>Strong intention to vaccinate their child</th>
<th>Somewhat disagree</th>
<th>Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>The pharmaceutical industry to do what is in the best interest of the public</td>
<td><img src="chart1" alt="Percentage" /></td>
<td><img src="chart2" alt="Percentage" /></td>
<td><img src="chart3" alt="Percentage" /></td>
</tr>
<tr>
<td>The media to report fairly and accurately</td>
<td><img src="chart4" alt="Percentage" /></td>
<td><img src="chart5" alt="Percentage" /></td>
<td><img src="chart6" alt="Percentage" /></td>
</tr>
<tr>
<td>The academic researchers to do what is in the best interest of the public</td>
<td><img src="chart7" alt="Percentage" /></td>
<td><img src="chart8" alt="Percentage" /></td>
<td><img src="chart9" alt="Percentage" /></td>
</tr>
<tr>
<td>The public health authorities to do what is in the best interest of the public</td>
<td><img src="chart10" alt="Percentage" /></td>
<td><img src="chart11" alt="Percentage" /></td>
<td><img src="chart12" alt="Percentage" /></td>
</tr>
<tr>
<td>The government to do what is in the best interest of the public</td>
<td><img src="chart13" alt="Percentage" /></td>
<td><img src="chart14" alt="Percentage" /></td>
<td><img src="chart15" alt="Percentage" /></td>
</tr>
<tr>
<td>Doctors to do what is in the best interest of the public</td>
<td><img src="chart16" alt="Percentage" /></td>
<td><img src="chart17" alt="Percentage" /></td>
<td><img src="chart18" alt="Percentage" /></td>
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</tbody>
</table>

Dubé et al. Vaccine 2018
You have the power to address vaccine hesitancy


**IMMUNIZE**

**STEP 1**
Assume person will immunize. Use a presumptive statement.
- Person consents with no further questions? Person is hesitant?

**STEP 2**
Give your strong recommendation.
- Person consents with no further questions? Person is still hesitant?

**STEP 3**
Explore the reason for hesitancy.
- Listen to what the person says.
- Use motivational interviewing techniques to determine the cause of hesitancy.

**STEP 4**
Ask permission to address concerns.
- If person agrees, use the Ask-Provide-Verify approach to deliver information to address concerns.

**STEP 5**
Ask again if you can immunize.
- Person consents with no further questions? Person is hesitant?

**THE SKILLS OF MI (OARS + Ask-Provide-Verify)**

<table>
<thead>
<tr>
<th>Open-Ended Questions</th>
<th>Affirmations</th>
<th>Reflections</th>
<th>Summaries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Questions that don't result in &quot;yes&quot; or &quot;no&quot; answers.</td>
<td>Validate strengths, efforts, and accomplishments.</td>
<td>Encourage deeper consideration or meaning.</td>
<td>Ensure clear communication.</td>
</tr>
</tbody>
</table>

- Example: "What do you think about vaccines?"
- Example: "You are great at seeking out information."
- Example: "You're worried about vaccines overwhelming your child's immune system."
- Example: "You feel it's important to protect your child, but you're worried about the number of vaccines."

**Ask**
Ask what the person already knows.

- Example: "Can you tell me what you already know about the immune system and vaccines?"

**Provide**
Provide information.

- Example: "Your baby's immune system is amazing and can safely handle multiple vaccines given at the same time..."

**Verify**
Verify understanding of the information.

- Example: "Does this information make sense?"

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- "I hope I was able to address your concerns regarding the safety of vaccines. I really want to ensure your daughter is protected against these diseases. Can I provide the immunizations now?"
Summary

• COVID-19 has enabled rapid optimization of vaccine platforms
  • RNA and viral vector potentially promising for future vaccines
  • Multiple issues that remain to be resolved
  • Other platforms also in development

• Potential game-changers would be
  • Non-injectable administration
  • Need for a single vaccine dose
  • Long-term thermostable vaccines

• Vaccines will be a vital part of our strategy against antimicrobial resistance
• New and improved vaccines against respiratory viruses are coming soon...
• Do not under-estimate your role in addressing vaccine hesitancy
Thank you

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