COVID-19 Vaccine
Development, Efficacy & Safety

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Normal Times: **Sequential** Vaccines Development

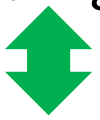
- Vaccine development and all phases of human testing – 10-15 years
- Regulatory review and approval (Health Canada), recommendations for use (National Advisory Committee on Immunization) – mos to yrs
- Provincial scheduling, safety standards, procurement, provision via Public Health or practitioners – mos to yrs
- Disease effectively and safely prevented

COVID-19: **Concurrent** Vaccine Development

- Vaccine development based on existing science and all phases of human testing with adaptive clinical trial designs – <1 year

- Advance purchase agreements (and production), rolling submissions for HC review & approval, preliminary NACI guidance on prioritizing populations to immunize efficiently, effectively and equitably – months

- Concurrent provincial scheduling, safety standards – weeks-months



- Disease effectively and safely prevented **→ Rapid, not rushed**

What's missing after rapid vaccine development and regulatory approval?

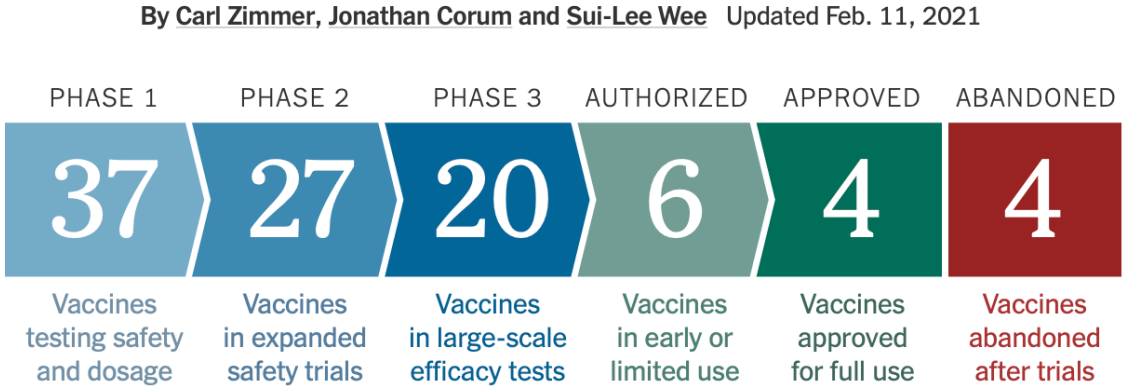
- **Safety** ✓ ✓
  - 2 month followup sufficient since adverse events very unlikely to emerge > 6 weeks after vaccine administration
  - Frequency of events may ↑ or ↓ over time e.g., anaphylaxis

- **Efficacy** ✓ ✗
  - Longer term duration of protection (>2-3 months) not known
  - **But** >90% short term efficacy could not be ignored during raging pandemic

- **Populations** ✓ ✗
  - Not all populations studied e.g., children, pregnant/breastfeeding women, immunocompromised persons

COVID-19 Vaccine Pipeline

- New York Times Vaccine Tracker (Jan 28)
  - 69 vaccines in human vaccine trials, ≥ 89 in preclinical evaluation



https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html,

COVID-19 Vaccines for Canada & Interim Authorization Status

Vaccine	Vaccine Type	Doses to Canada	Efficacy to prevent any COVID-19 Infection	Authorization
Pfizer	2 dose mRNA encoding spike	76 million	**95% efficacy** (≥7 days after 2nd dose) vs PCR+ infection	✓ **Dec 9, 2020**
Moderna	2 dose mRNA encoding spike	56 million	**94% efficacy** (≥14 days after 2nd dose)	✓ **Dec 23, 2020**
AstraZeneca Verity Pharma	2 dose viral vector with spike DNA	20 million	63% overall efficacy, highest in UK (72%), higher if 2nd dose after 12 weeks (78%)	Submitted Oct 1, 2020
Janssen/ Johnson & Johnson	1 dose viral vector with spike DNA	38 million	Press release: 66% overall efficacy vs moderate/severe disease: 72% efficacy in US; 57% efficacy in South Africa, >95% variants	Submitted Nov 30, 2020
Novavax	2 dose recombinant spike nanoparticle	76 million	Press release: 89% efficacy in UK, >50% variants; 49% efficacy in South Africa, >90% variants, 6% HIV+	Submitted Jan 29, 2021
Medicago	2 dose spike virus-like particle	76 million	Phase 2-3 RCTs have commenced	Not submitted
Sanofi & GSK	Protein subunit	72 million	Phase 1-2 trials – initial dose was not effective	Not submitted
7 VACCINES		**414 M doses!**		

Vaccine Adverse Effects and Safety

- **Vaccine clinical trials – standard definitions**
  - *Solicited adverse events* (reactogenicity) – short term (1-2 weeks)
    - Local e.g., injection site pain, redness, swelling
    - Systemic e.g., fever, fatigue, headache, chills, muscle or joint pain, antipyretic use
  - *Unsolicited adverse events* – medium term (1-6 months)
    - Adverse events (AEs) – mild
    - Serious adverse events (SAEs) – disability, hospitalization, life-threatening, birth defects, death
  - *Grades* 1 (mild), 2 (moderate, interfere with daily activity), 3 (severe-medical attention), 4 (ED visit or hospitalization)
  - Determination of relatedness to vaccine or not

- **Vaccine program surveillance (passive or active) – standard approaches**
  - "AEFI" (Adverse Event Following Immunization)
  - Unfavourable new or more frequent events not related to known prior condition

Anaphylaxis After Pfizer COVID-19 Vaccine

- USA CDC (JAMA Feb 12, 2021)
  - 66 cases of anaphylaxis after 17.5 million doses Pfizer or Moderna vaccines
  - **Pfizer: 4.7 cases/million doses; Moderna: 2.5 cases/million doses**
    - 89% occurred ≤30 minutes of injection
    - 48% hospitalized (27% in ICU), no deaths
    - 82% after 1st dose, 79% history of allergies, 32% previous anaphylaxis

- NACI statement (Jan 12, 2021)
  - Polyethylene glycols (PEGs) may be main allergen of concern (in Pfizer & Moderna vaccines)
  - Contraindicated only if known allergy to vaccine components or previous dose
  - Prolonged observation >30 minutes if concerns

- Other vaccines – rate of anaphylaxis ~1-10/million doses

https://jamanetwork.com/journals/jama/fullarticle/2776557 https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html

COVID-19 Vaccine in Pregnancy and Breastfeeding

- NACI: May be offered to pregnant/breastfeeding individuals if a risk assessment deems that benefits outweigh potential risks for the individual and the fetus/infant, and if informed consent includes discussion about absence of evidence on the use of COVID-19 vaccine in this population
- Considerations:
  - Evidence evolving, no published data from clinical trials
  - Limited data from animal developmental & reproductive studies
  - Emerging data from vaccination in pregnant women
    - 10,000 in USA – no increase in miscarriage, preterm, stillborn vs usual population rates
  - Pregnant or breastfeeding women may have increased exposure or risk of severe disease
    - Evolving evidence of more severe disease if pregnant
  - "Usual" avoidance of COVID-19 – masks, distancing, handwashing

https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html,
https://www.sogc.org/common/Uploaded%20files/Latest%20News/SOGC_Statement_COVID-19_Vaccination_in_Pregnancy.pdf
https://drive.google.com/file/d/1_wHIYX-tGkGBPwuax7N8BxZPR4PTTCDm/view

Conclusions

- Development of COVID-19 vaccines has been rapid but not rushed
- Implementation of safe, highly effective vaccines after <1 year is astonishing
- More clinical trials, followed by longer term study and monitoring of vaccines will provide more complete understanding of impact of vaccines

COVID-19 Vaccines for Canada – References

Vaccine	Reference
Pfizer	https://www.nejm.org/doi/full/10.1056/NEJMoa2034577
Moderna	https://www.nejm.org/doi/full/10.1056/NEJMoa2035389
AstraZeneca Verity Pharma	https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1
Janssen / J&J	https://www.nejm.org/doi/full/10.1056/NEJMoa2034201 https://www.jnj.com/johnson-johnson-announces-single-shot-janssen-covid-19-vaccine-candidate-met-primary-endpoints-in-interim-analysis-of-its-phase-3-ensemble-trial
Novavax	https://www.nejm.org/doi/pdf/10.1056/NEJMoa2026920?articleTools=true https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3
Medicago	https://www.medrxiv.org/content/10.1101/2020.11.04.20226282v1
Sanofi & GSK	https://www.gsk.com/en-gb/media/press-releases/sanofi-and-gsk-announce-a-delay-in-their-adjuvanted-recombinant-protein-based-covid-19-vaccine-programme-to-improve-immune-response-in-the-elderly/