

# COVID-19 Science and Policy Symposium Webinar (New Zealand)

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## Answers to Outstanding Questions About COVID-19 Vaccines Will Dictate the Success or Failure of the Rollout

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# Disclosure statement

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- I have never received research funding from industry
- I have received funding from the following government agencies:
  1. Canadian Institutes of Health Research
  2. Natural Sciences and Engineering Research Council of Canada
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  4. Ontario COVID-19 Rapid Research Funding
  5. National Research Council of Canada – Pandemic Response Challenge Program

# Preamble

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- As a viral immunologist who develops immunization strategies to prevent infectious diseases and treat cancers, I teach the value of high-quality, well-validated vaccines and passionately promote their use
- Vaccines are, by far, the most efficient type of medicine; they cost-effectively save millions of people from sickness and/or death
- For the sake of global health, we need people to **maintain faith in vaccines**
- ‘Anti-vaxxers’ vs. vaccine hesitancy
  - Anti-vaxxer: tends to hold an extreme, negative view of all vaccines, regardless of the scientific data
  - Vaccine hesitancy: unsure of commitment to taking a vaccine because of outstanding questions
- As a public servant in the academic sector with expertise in developing vaccines, I view it as a responsibility to highlight outstanding questions and provide fact-based assessments of their potential implications

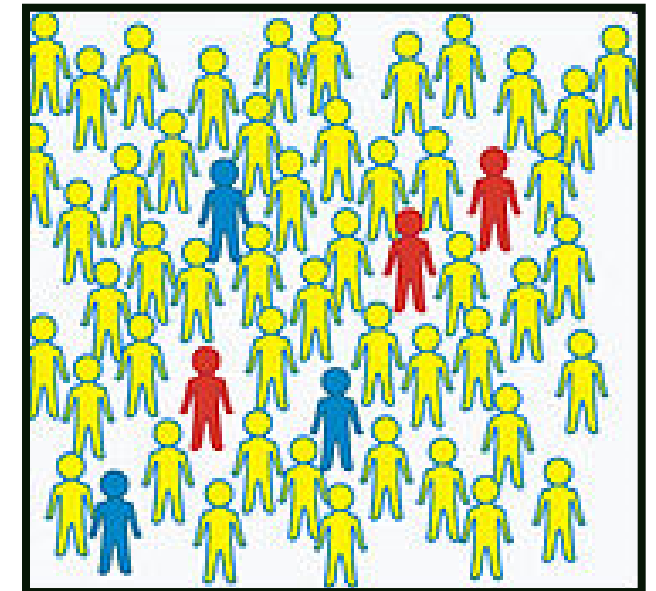
# COVID-19 Vaccines: How do They Work?



1. A COVID-19 vaccine **must** provide two things:
  - a) the virus or a piece(s) of the virus
  - b) a danger signal
2. A good vaccine simulates the natural infection, thereby inducing an appropriate immune response **without causing disease**
3. Then, when a person becomes infected the first time, their immune system thinks it is seeing the virus for the second time ('immunological memory')
4. Therefore, the response will be faster and more robust, and the virus will be cleared without the person experiencing disease
5. Vaccination can accelerate progress towards 'herd immunity'



[https://seuss.fandom.com/wiki/Thing\\_One\\_and\\_Thing\\_Two](https://seuss.fandom.com/wiki/Thing_One_and_Thing_Two)



# COVID-19 Vaccine Development: A 'Record'-Shattering Pace

- Prior to this pandemic, vaccines took ~10 years to traverse the clinical trial pipeline and receive regulatory approval
- The previous record was an 'astounding' 4 years
- COVID-19 vaccines reached the public rollout phase in <1 year (but by 'cutting corners')
- This means we are lacking information about COVID-19 vaccines that was always available for previous vaccines
- There is a lack of peer-reviewed data (much won't be released for ~2 years)
- Further, the nature of SARS-CoV-2 and perplexing decisions during the rollout are raising additional questions



COVID-19 vaccines have raised hopes that the pandemic is nearing an end. Hopefully, this is true. But here are some potential sticking points...



# What is the long-term safety of COVID-19 vaccines?

- COVID-19 vaccines are being distributed with uniquely short safety profiles (months-worth)
- Short-term safety profiles of the approved COVID-19 vaccines [looks good](#)
- However, induction of [anaphylactic reactions](#) in a very small percentage of vaccine [recipients](#) hasn't helped the optics for those with [vaccine hesitancy](#)
- Some questions have also arisen about vaccinating the frail elderly:
  - [23 frail elderly](#) individuals in Norway [died shortly after receiving the Pfizer vaccine](#)
  - UK [open letter](#): increase in non-COVID deaths in long term care homes compared to before the vaccinesIt is difficult to ascertain the reason for these deaths; they may have had nothing to do with the vaccines
- However, too many unpredicted severe long-term side-effects accruing over time could be cause for withdrawal of approval for a vaccine




# Is there an example of a long-term consequence of a vaccine?

Yes...


- In 2009 there was a swine flu pandemic
- One of the vaccines that was manufactured and distributed in Europe was called “Pandemrix-AS03”
- For ~2 years after the vaccine was used there were up to 14-fold and 7-fold increases in the diagnosis of narcolepsy in children/adolescents and adults, respectively
- Narcolepsy = a chronic sleep disorder with overwhelming fatigue, often accompanied by a sudden loss of muscle tone
- Likely due to autoimmunity against neurons in the brain

**PLOS ONE**

 OPEN ACCESS  PEER-REVIEWED

RESEARCH ARTICLE

## Increased Incidence and Clinical Picture of Childhood Narcolepsy following the 2009 H1N1 Pandemic Vaccination Campaign in Finland

Markku Partinen , Outi Saarenpää-Heikkilä, Ismo Ilveskoski, Christer Hublin, Miika Linna, Päivi Olsén, Pekka Nokelainen, Reija Alén, Tiina Wallden, Merimaaria Espo, Harri Rusanen, Jan Olme, Heli Sätälä, [ ... ], Turkka Kirjavainen [ view all ]

Published: March 28, 2012 • <https://doi.org/10.1371/journal.pone.0033723>

# What is the 'duration of immunity' of COVID-19 vaccines?

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- [Duration of immunity](#) = how long a person is protected after being vaccinated
- For previous vaccines, we could have reasonable confidence that immunity would last at least a few years prior to public rollouts
- COVID-19 vaccines only have a few months-worth of duration of immunity data
- If immunity declines before '[herd immunity](#)' is achieved, previously vaccinated individuals will become susceptible to infection again and the rollout could fail





# Are COVID-19 vaccines as effective as we have been told?

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- Public declarations of >90% effectiveness for the [Moderna](#) and [Pfizer](#) vaccines
- Unfortunately, Pfizer did not publicly disclose the fact that there were large numbers of suspected, but unconfirmed cases of COVID-19 that were excluded from their calculation of efficacy
- This was revealed in a [summary report](#) issued by the US-FDA
- Re-analysis with these new data was performed by the associate editor of the *British Medical Journal* (albeit in a non-peer reviewed opinion letter)
- Their new estimate = [19-29%](#) effectiveness
- This can't be confirmed or refuted until raw data are released to the scientific community

# FDA Briefing Document

## Pfizer-BioNTech COVID-19 Vaccine

Page 42:

Among 3410 total cases of suspected but unconfirmed COVID-19 in the overall study population, 1594 occurred in the vaccine group vs. 1816 in the placebo group. Suspected COVID-19 cases that occurred within 7 days after any vaccination were 409 in the vaccine group vs. 287 in the placebo group. It is possible that the imbalance in suspected COVID-19 cases occurring in the 7 days postvaccination represents vaccine reactogenicity with symptoms that overlap with those of COVID-19. Overall though, these data do not raise a concern that protocol-specified reporting of suspected, but unconfirmed COVID-19 cases could have masked clinically significant adverse events that would not have otherwise been detected.

# Are COVID-19 vaccines as effective as we have been told?

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- The effectiveness reported for Sinovac Biotech's currently unapproved vaccine dropped from 78% early in a clinical trial in Brazil to 50.38% in the late stages of the trial when a previously excluded group was incorporated into the analysis
- Cut-off for approval of COVID-19 vaccines was set at 50% effectiveness
- If efficacy is less than 'advertised', COVID-19 vaccines will under-perform relative to expectations

# What are the risks of using COVID-19 vaccines in ways for which they were not approved?

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- Due to logistical challenges of rolling out two-shot vaccines and with the goal of maximizing how many and how quickly people can be vaccinated, some considerations are being given to using vaccines...  
...in [single-dose](#) regimens, combining vaccines from [different](#) manufacturers, or altering [intervals](#) between doses
- Reported effectiveness of COVID-19 vaccines only holds true beginning one to two weeks after the second immunization and using the recommended interval and dose
- Performance and safety of vaccines cannot be guaranteed if administered differently than the way in which they obtained regulatory approval
- Example: A single/delayed-dose regimen of the Pfizer vaccine was used in [Israel](#); it was reported to perform worse than Pfizer's publicized 52% effectiveness and a large # of vaccinated people got COVID-19
- Deviations in protocols should not be tolerated unless backed up by data



# What are the risks of using COVID-19 vaccines in ways for which they were not approved?

## Case Series Drug Analysis Print

### Name: COVID-19 mRNA Pfizer- BioNTech vaccine analysis print analysis print

Report Run Date: 31-Jan-2021  
Earliest Reaction Date: 19-Jan-2001

Data Lock Date: 28-Jan-2021 19:00:04  
MedDRA Version: MedDRA 23.1

Reaction Name	Total	Fatal
<b>Pregnancy conditions</b>		
<i>Abortions spontaneous</i>		
Abortion spontaneous	4	0
<i>Maternal complications of pregnancy NEC</i>		
Morning sickness	1	0
<i>Normal pregnancy, labour and delivery</i>		
Pregnancy	3	0
<b>Pregnancy conditions SOC TOTAL</b>	<b>8</b>	<b>0</b>

### Of concern:

- Growing #s of headlines proposing vaccination of pregnant individuals and children
- Should not be done without demonstration of safety and efficacy in a phase 3 clinical trial



# What is the risk of emergence of SARS-CoV-2 variants that can evade vaccine-induced immunity?

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- [Several novel variants](#) of SARS-CoV-2 have been identified
- Coronaviruses copy their genetic material in a way that inherently induces random [mutations](#)
- The risk of emergence of mutants that can evade vaccine-induced immunity cannot be accurately quantified
- But, the way COVID-19 vaccines are being rolled out might increase the potential for this to occur for two reasons:
- First, the current vaccines confer narrowly focused immunity that targets a single viral [spike protein](#)
- SARS-CoV-2 only needs to mutate one protein to evade vaccine-induced immunity
- Secondly, the vaccination program is being rolled out in piece-meal fashion
- Slow expansion of narrowly focused immunity among people that are surrounded by others that are not immune provides the time and contact with a ‘reservoir population’ that a virus would need to generate random variants that can ‘probe their potential’ to re-infect vaccinated individuals
- If a variant emerges that has altered its spike protein enough to bypass vaccine-induced immunity, this could be a recipe for failure of the rollout
- If this happens, vaccines may need to be re-engineered to express a novel version of the spike protein, preferably with other proteins added to broaden immunity
- Importantly, acquisition of natural immunity, which targets multiple components of the virus, may reduce the risk of re-infection with variants that can bypass spike protein-specific immunity



# Can 'herd immunity' still be achieved if COVID-19 vaccines don't do the job?

- Probably!
- Most people that have been infected with SARS-CoV-2 have naturally acquired immunity that can [protect](#) them from re-infection
- There is even evidence that pre-existing immunity against other coronavirus, including those that merely cause colds, can [cross-protect](#) some people against SARS-CoV-2
- This is what our immune systems are designed to do
- However, more than a year into the pandemic a huge unanswered question is:

## **How close/far are we from natural herd immunity?**

- In most places, we have done a poor job of tracking this
- Acquisition of natural immunity by an ever-growing number of people means fewer people require vaccination to reach herd immunity
- Bonus: natural immunity = broader immunity; these people should be less susceptible to re-infection if an immuno-evasive SARS-CoV-2 variant emerges

