

What does a Phase III trial mean?

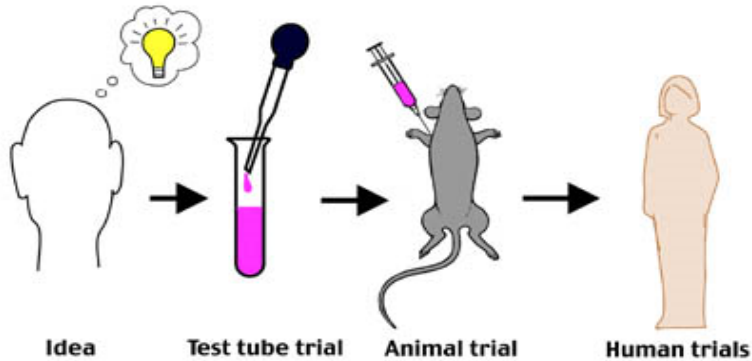
R. Scott McClelland, MD, MPH
University of Washington,
Seattle WA

7 October 2020

Topics

- What does a Phase III vaccine trial mean?
 - ◆ What does this look like in the context of the COVID-19 vaccine effort?

Development pathway for vaccines

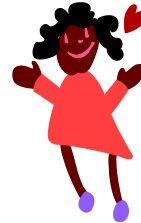


Randomized, double-blind,
placebo-controlled clinical trials

Phase 1- is it safe?



Phase 2- is it effective?

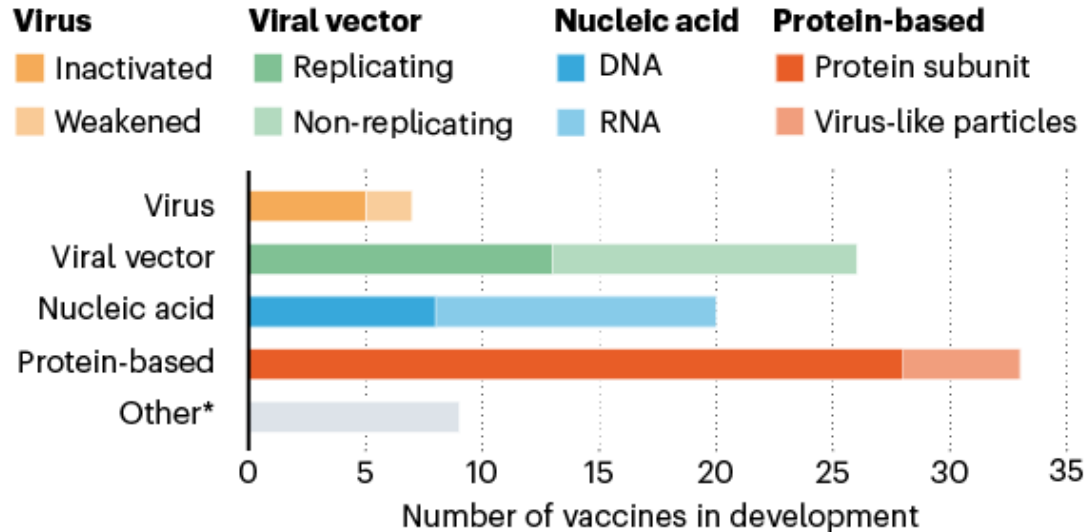


Phase 3- does it protect against disease?



Vaccine development strategies

AN ARRAY OF VACCINES



* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

Phase 1 studies

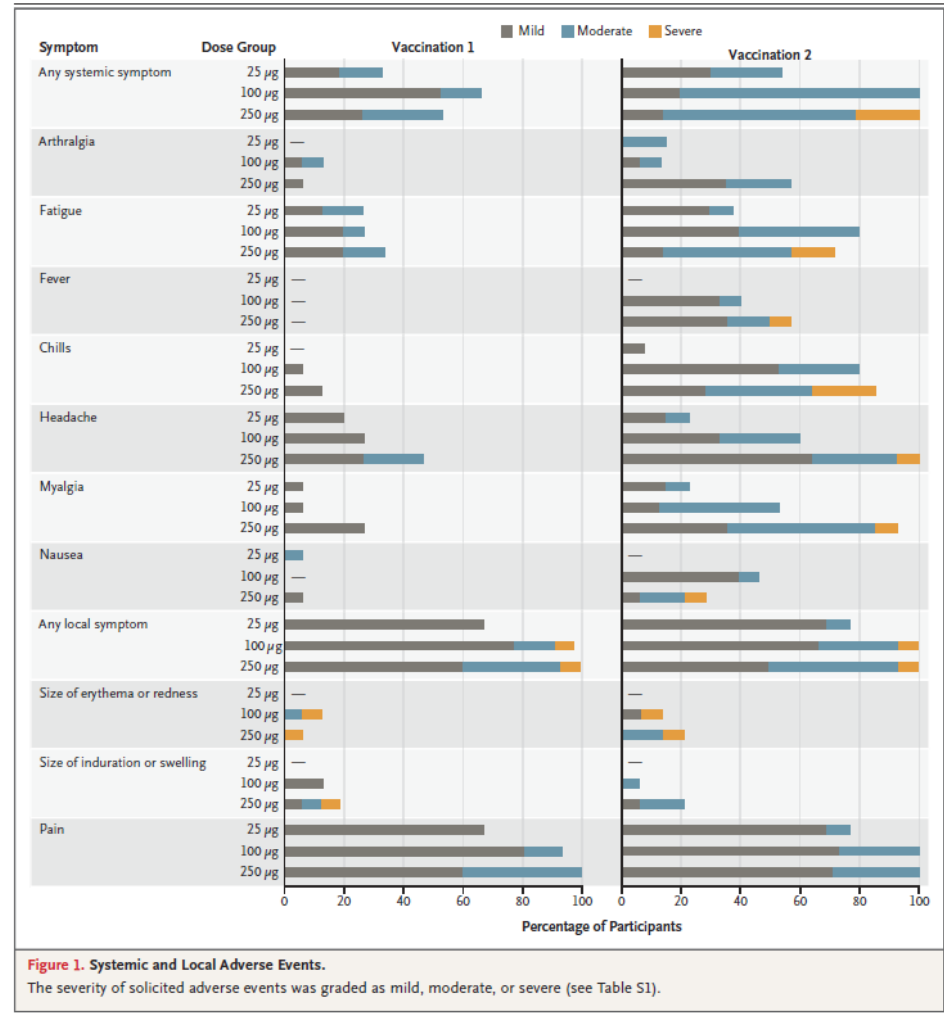
- First-in-man
- Is it safe?
- Does it result in an immune response?
- What is the best dose?
- Not always blinded or controlled
- 10's of people
- Very close monitoring
 - ◆ Observation in clinic for 60 min
 - ◆ Visit next day
 - ◆ Call at 48 hours
 - ◆ Visit at 7 days
 - ◆ Daily diary of fever and local site assessment

ORIGINAL ARTICLE

An mRNA Vaccine against SARS-CoV-2 — Preliminary Report

L.A. Jackson, E.J. Anderson, N.G. Roupael, P.C. Roberts, M. Makhene, R.N. Coler, M.P. McCullough, J.D. Chappell, M.R. Denison, L.J. Stevens, A.J. Pruijssers, A. McDermott, B. Flach, N.A. Doria-Rose, K.S. Corbett, K.M. Morabito, S. O'Dell, S.D. Schmidt, P.A. Swanson II, M. Padilla, J.R. Mascola, K.M. Neuzil, H. Bennett, W. Sun, E. Peters, M. Makowski, J. Albert, K. Cross, W. Buchanan, R. Pikaart-Tautges, J.E. Ledgerwood, B.S. Graham, and J.H. Beigel, for the mRNA-1273 Study Group*

- Phase 1, dose escalation
- 45 adults aged 18-55
- mRNA-1273, 2 doses
- All participants developed neutralizing Ab



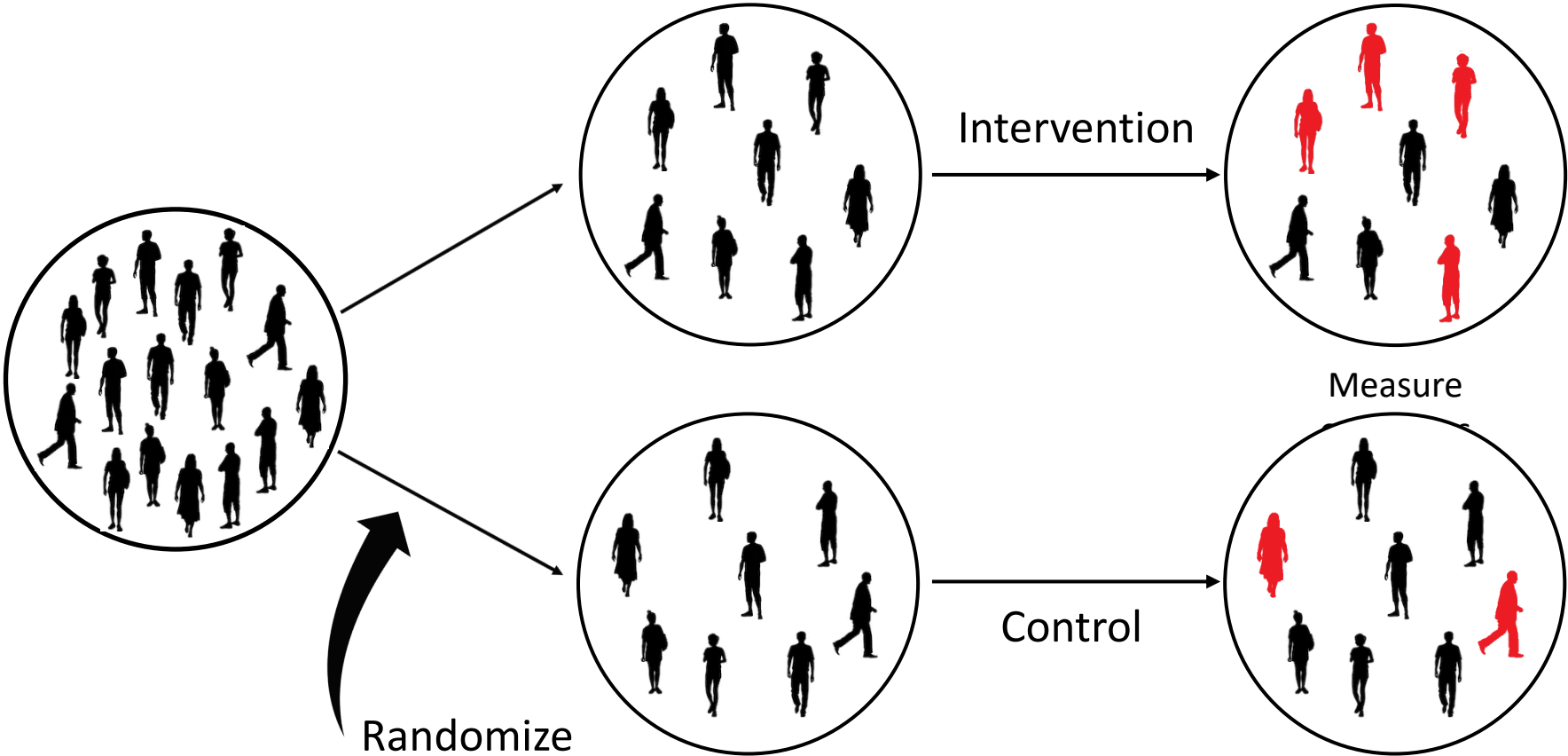
Phase 2 vaccine trial: does it work?

- Is it safe in different people – older, younger?
- Does it produce a good immune response?
- Can it protect against infection?
- 100's of people
- Frequent visits and blood draws

Phase 3

- Does it protect from infection?
- How does it compare with standard of care?
- If vaccinated people become infected, does it change the course of the disease?
- 1000's of people
- Endpoint – COVID-19 disease
- Some will become infected
- Comparison between the numbers infected in the vaccine vs placebo arms

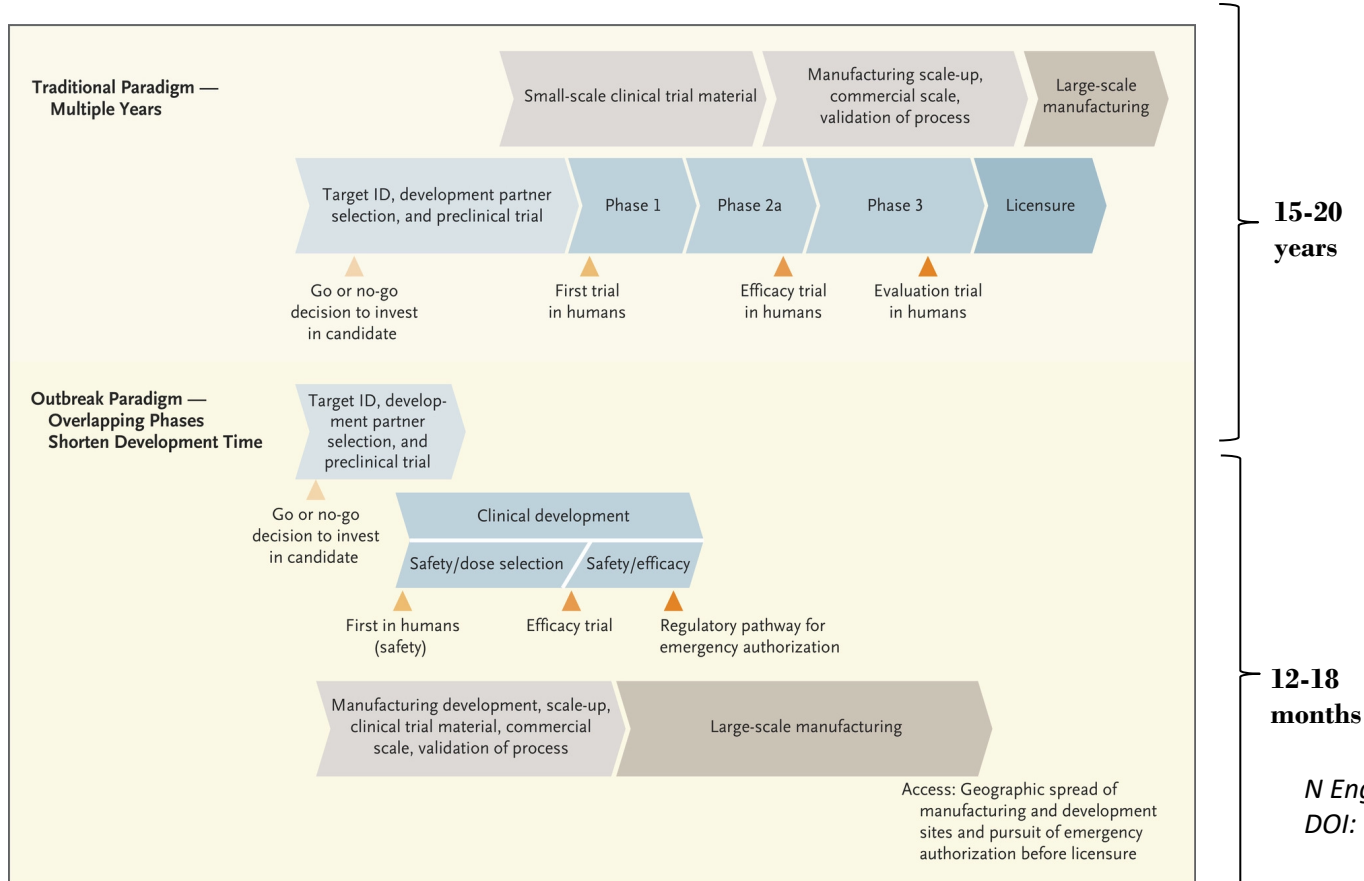
Randomized, double-blind, controlled trials



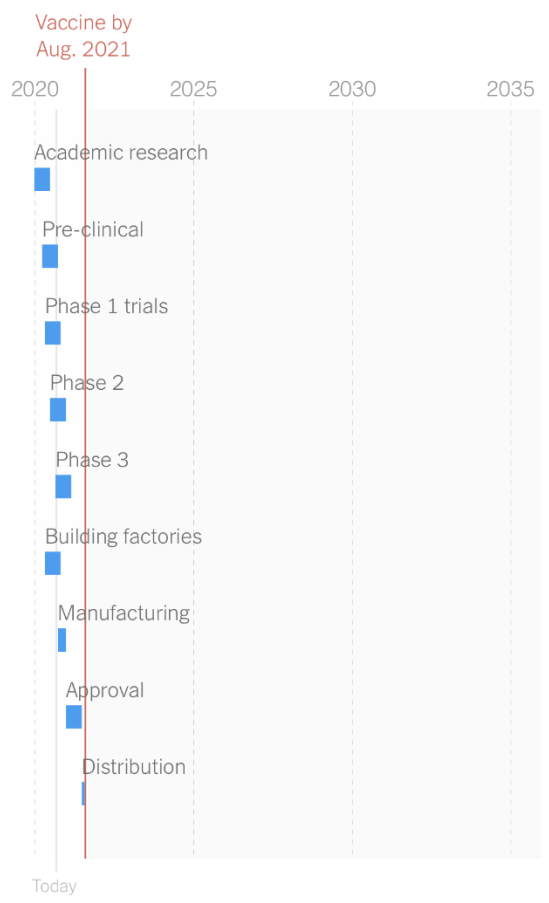
Vaccine Safety Monitoring

- Vaccines are biologic agents and can lead to physiologic effects or adverse events.
- Novel adjuvant
- Careful monitoring during clinical trials
- Long term follow-up
- Post-licensure monitoring
 - ◆ CDC network at HMO's
 - ◆ Passive reporting via VAERS (<https://vaers.hhs.gov/>)
- Postmarketing safety of 57 FDA-approved vaccines: cohort study

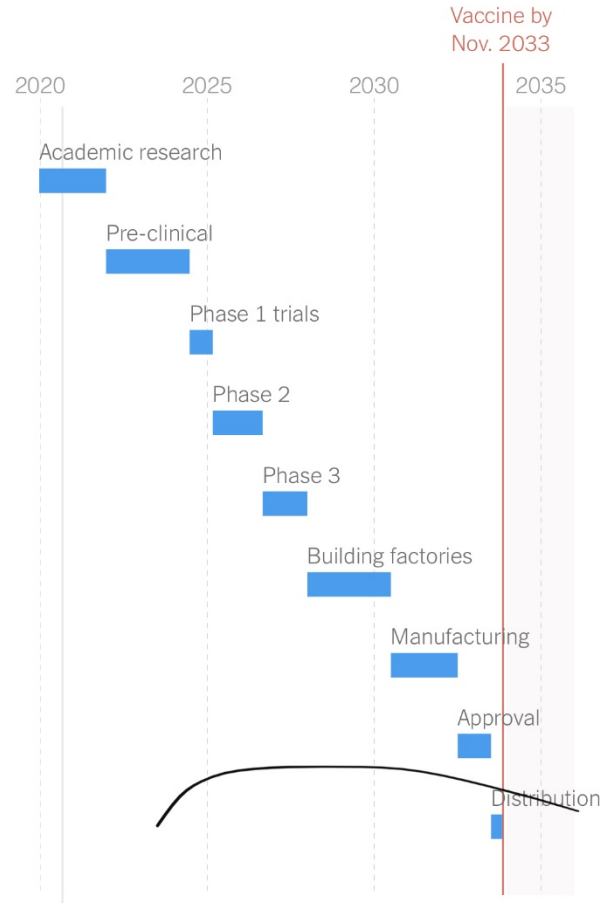
Vaccine Development: A Lengthy, Risky and Expensive Process



N Engl J Med 2020; 382:1969-1973
DOI: 10.1056/NEJMp2005630



Goal Typical



Goal Typical

NYT, April 30, 2020

[Volunteer](#)

[Clinical Studies](#)

[What to Expect](#)

[Science](#)

[FAQ](#)

[About Us](#)

Join our COVID-19 Volunteer
Screening Registry

[Volunteer Now](#)



Thank you!

www.preventcovid.org

- UWVR
 - HMC, NJB, 908 Jefferson Street
- STVU
 - Cabrini Tower, 901 Boren Avenue