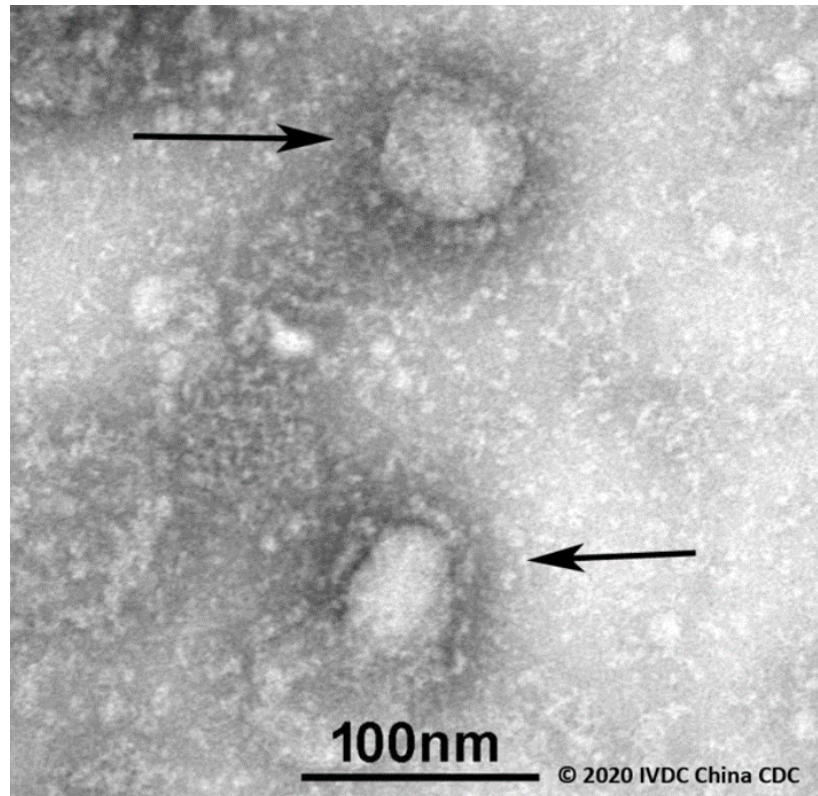


COVID-19 Vaccine

Jan. 27, 2021

Ira Berkower, JE 1969

The virus



The vaccine



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How to make and test a vaccine against COVID-19

Four vaccine questions:

- a. Does prior infection protect? Yes
- b. How many serotypes? One
- c. Are vaccine targets identified? Yes, the spike protein
- d. What type of vaccine platform to use?

Four basic types of vaccine

Killed virus

- Salk: fully inactivated
protein retains native folding

• Recombinant viral components

- Protein
- Viral DNA
- messenger RNA

Live, attenuated Covid virus strain

Sabin like

virus grows without spreading to CNS

Take one Covid gene and transfer into a more acceptable live attenuated viral vector

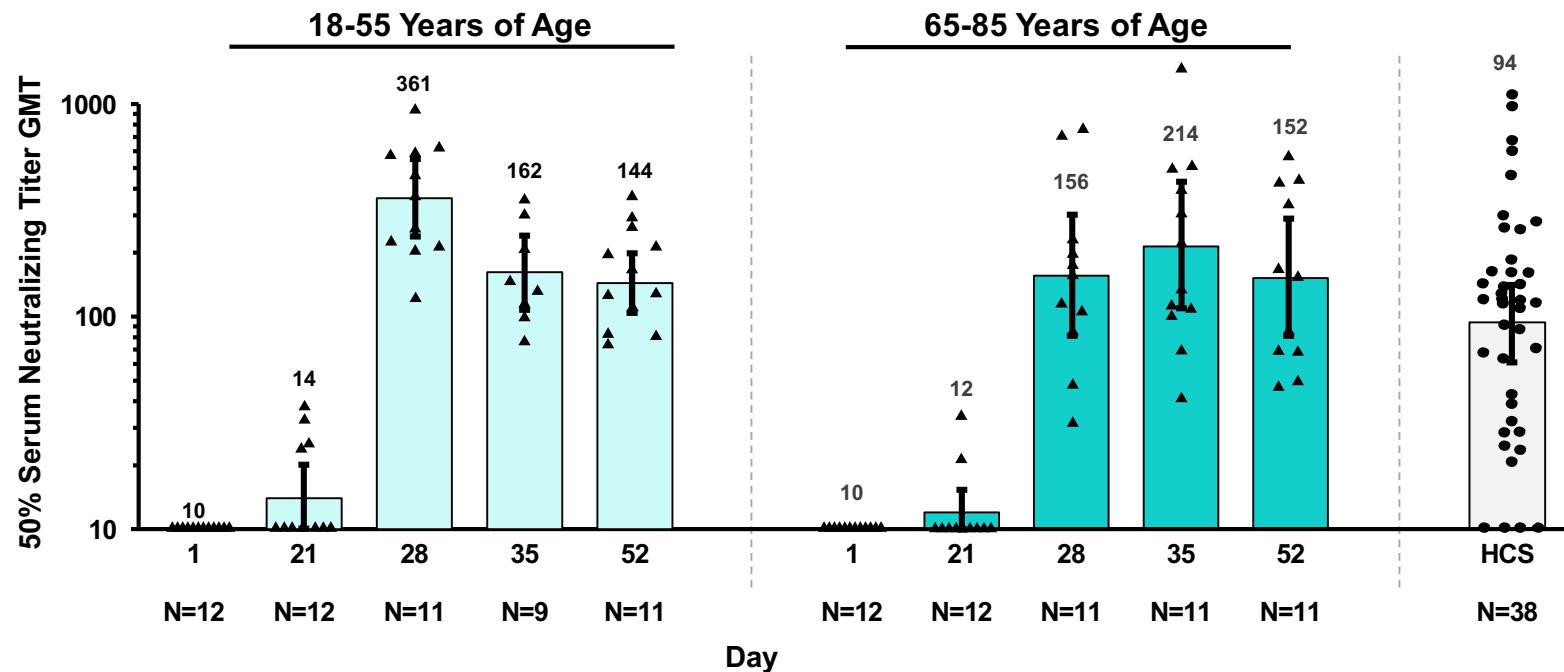
Adeno virus

Rubella vaccine strain

DNA → mRNA → Protein

Typical vaccine testing: phase 1 safety testing n =20 24
 phase 2 immunogenicity n=200 195
 phase 3 efficacy n=2000 17,500

Phase 1-2: Antibody Titers Comparable or Higher than Natural Infection

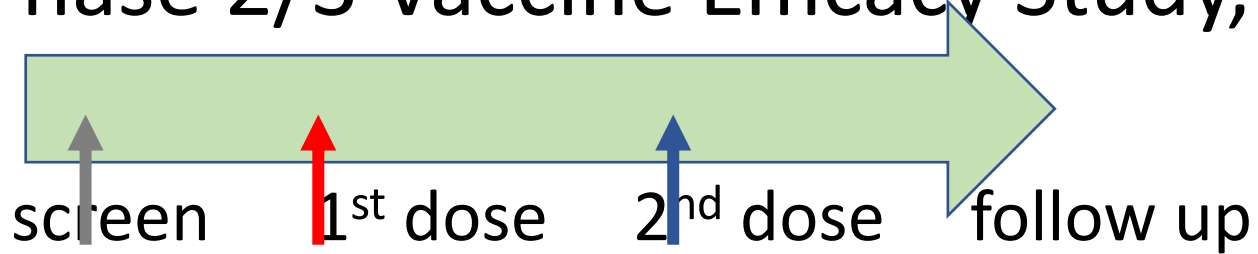


Walsh EE, et al. *N Engl J Med.* 383: 2439, 2020.

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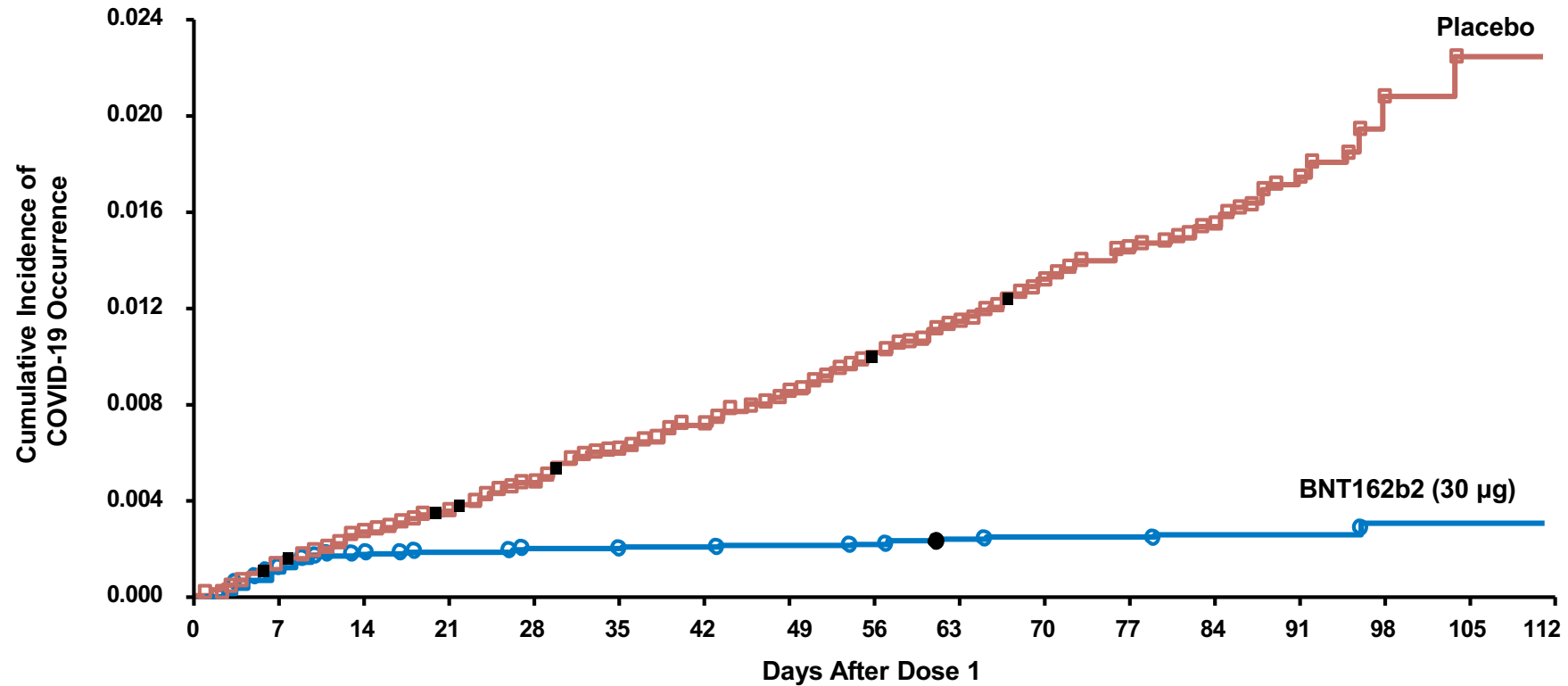
Phase 2/3 Vaccine Efficacy Study,

- Timeline



- Screen healthy adults, PCR negative, age 16-55, 56-64, and 65+. Randomly assigned to control or vaccine group 1:1
- Subjects are given two doses, 21 days apart.
- Follow up beginning after the 1st dose and lasting 6 months. Return for symptoms. Confirm diagnosis by PCR.
- They were exposed to Covid under real-world conditions: dose and route.

Cumulative Incidence of COVID-19 After Dose 1



Note: 95% of cases are in the control group

Vaccine group early vs. late

Solid fill marker indicates subjects with severe COVID-19 disease

Vaccine induced protection of different clinical groups

		Vaccine Group	Controls				
Entire study	n=	17411	17511				$VE = 1 - V/C$
	infections	8	162				95%
severe disease							
	infections	1	9				88%
65+	n =	4622	4665				
	infections	1	24				96%

Future studies

- Duration of protection? Currently up to 120 days.
- Does vaccine prevent asymptomatic infections?
- Transmission from asymptomatic infections?

Additional Issues:

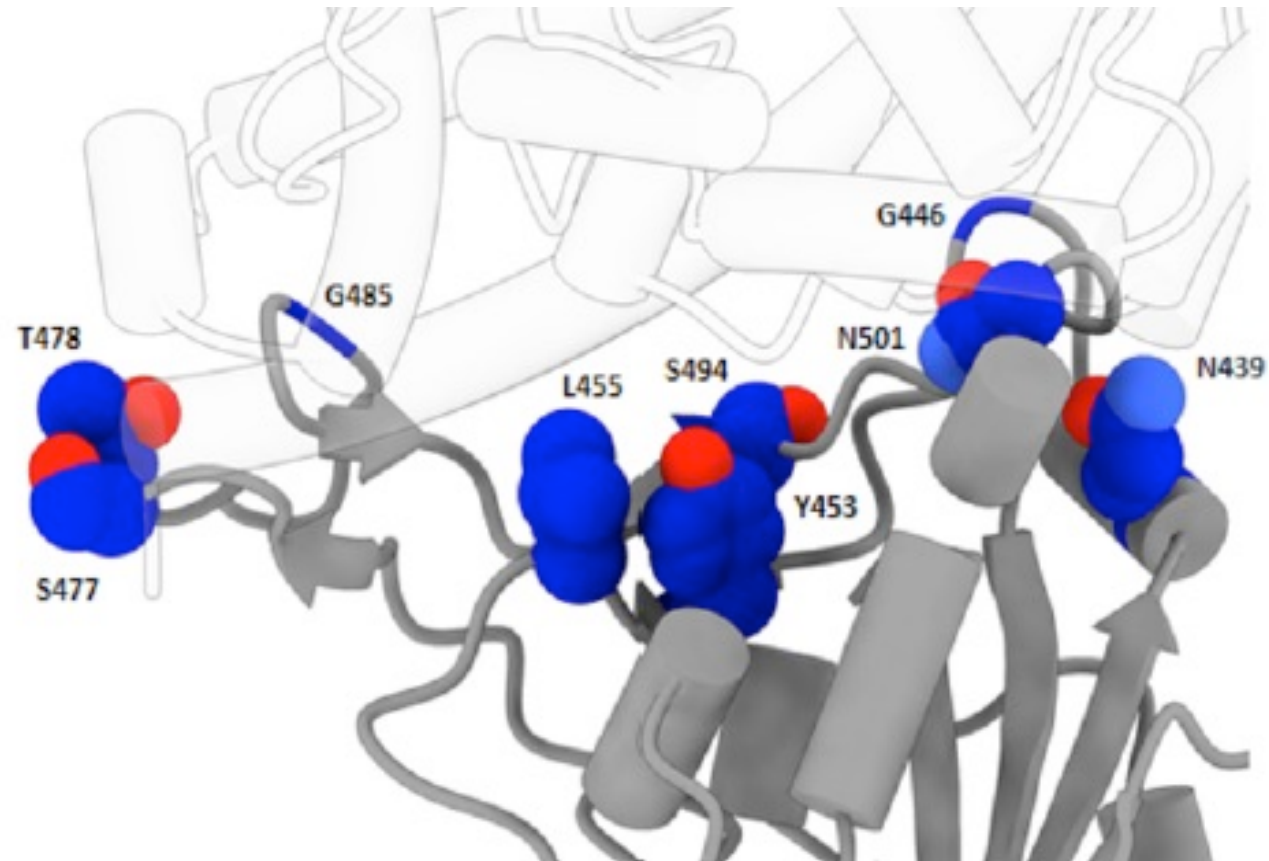
- Virus variants can arise over time and quickly spread worldwide
Test these for: greater infectivity, disease severity, and antibody escape.
- Herd immunity: propagation ratio R_0
Depends on vaccine efficacy X coverage.
Will need about 60 % coverage to achieve this.
- New vaccines to Increase supply, prevent mucosal spread, and improve acceptance among children and parents.

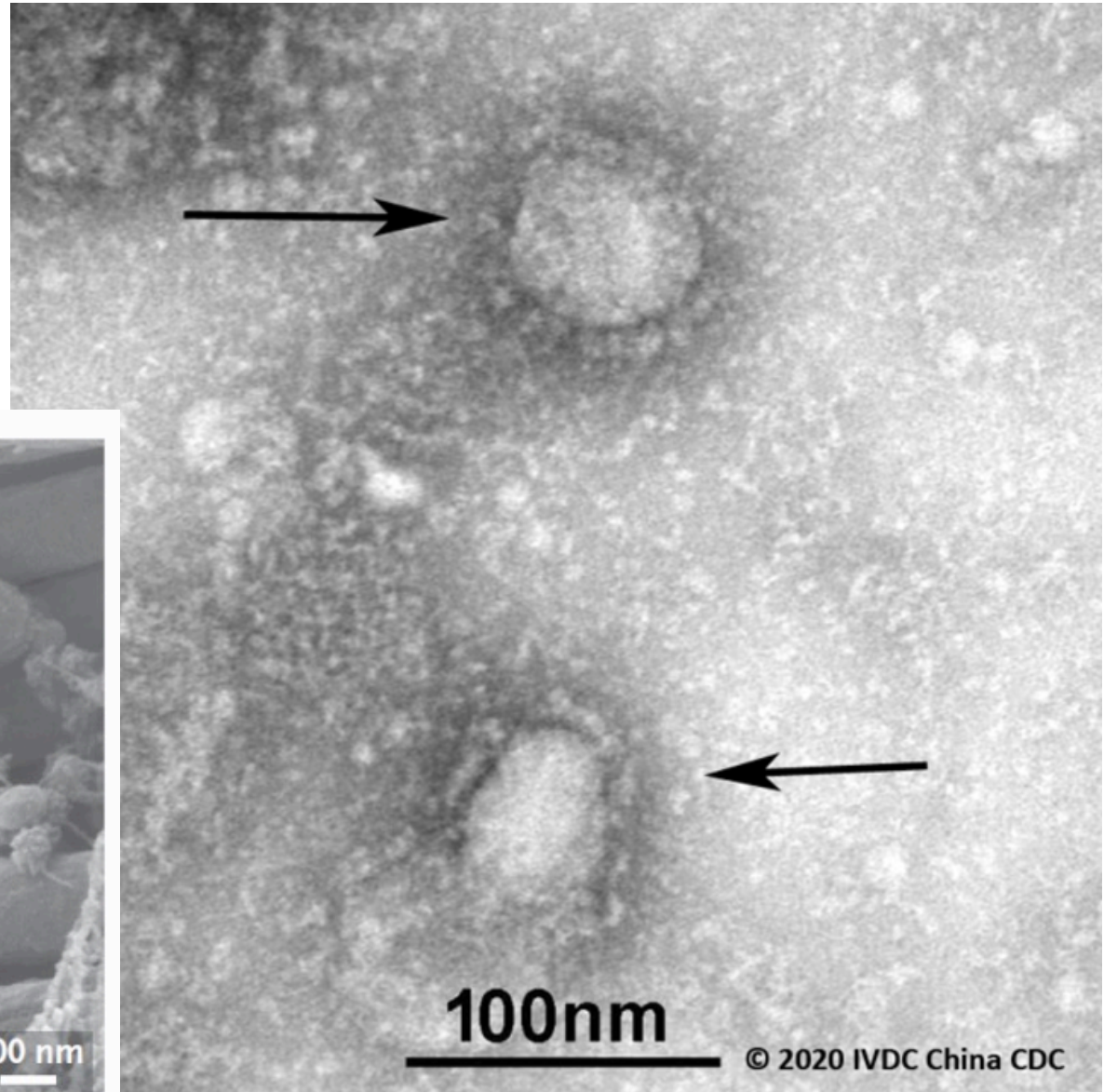
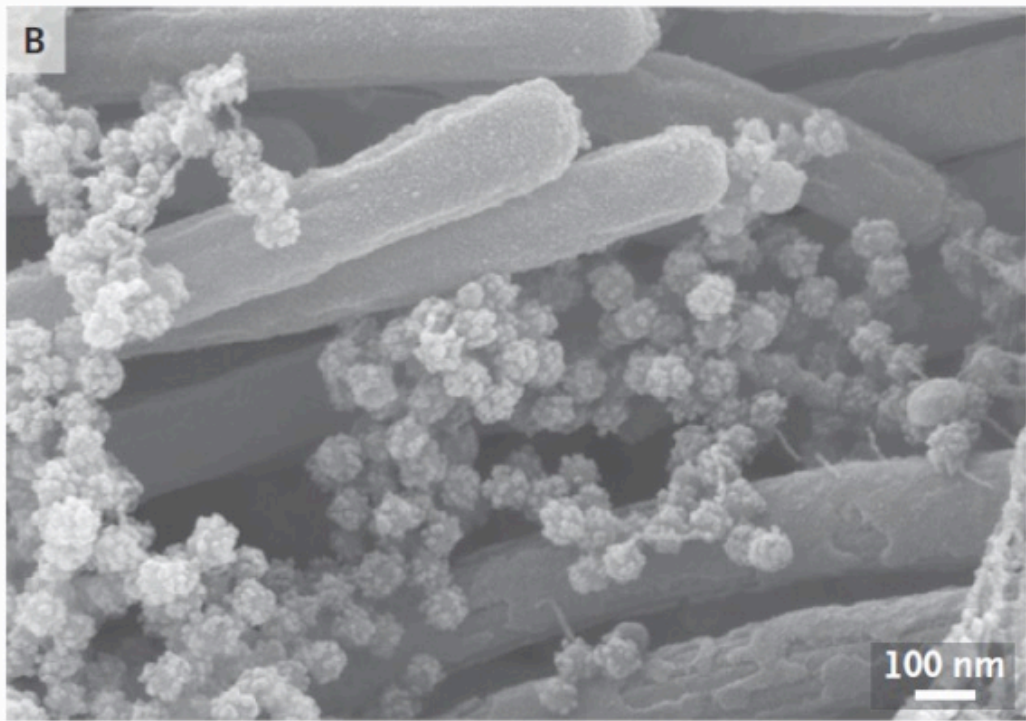
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Video: spread of COVID variants worldwide

<https://www.gisaid.org/phylogenetics/global/nextstrain/>

COVID variants near the receptor binding domain





From: Camille Ehre, Baric Lab, NEJM 2020