5to Panel Virtual
COVID-19: Estrategias de Tratamiento, Vacunas y Antivirales.

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UNIVERSITY OF PUERTO RICO

MEDICAL SCIENCES CAMPUS

Proposed Plan

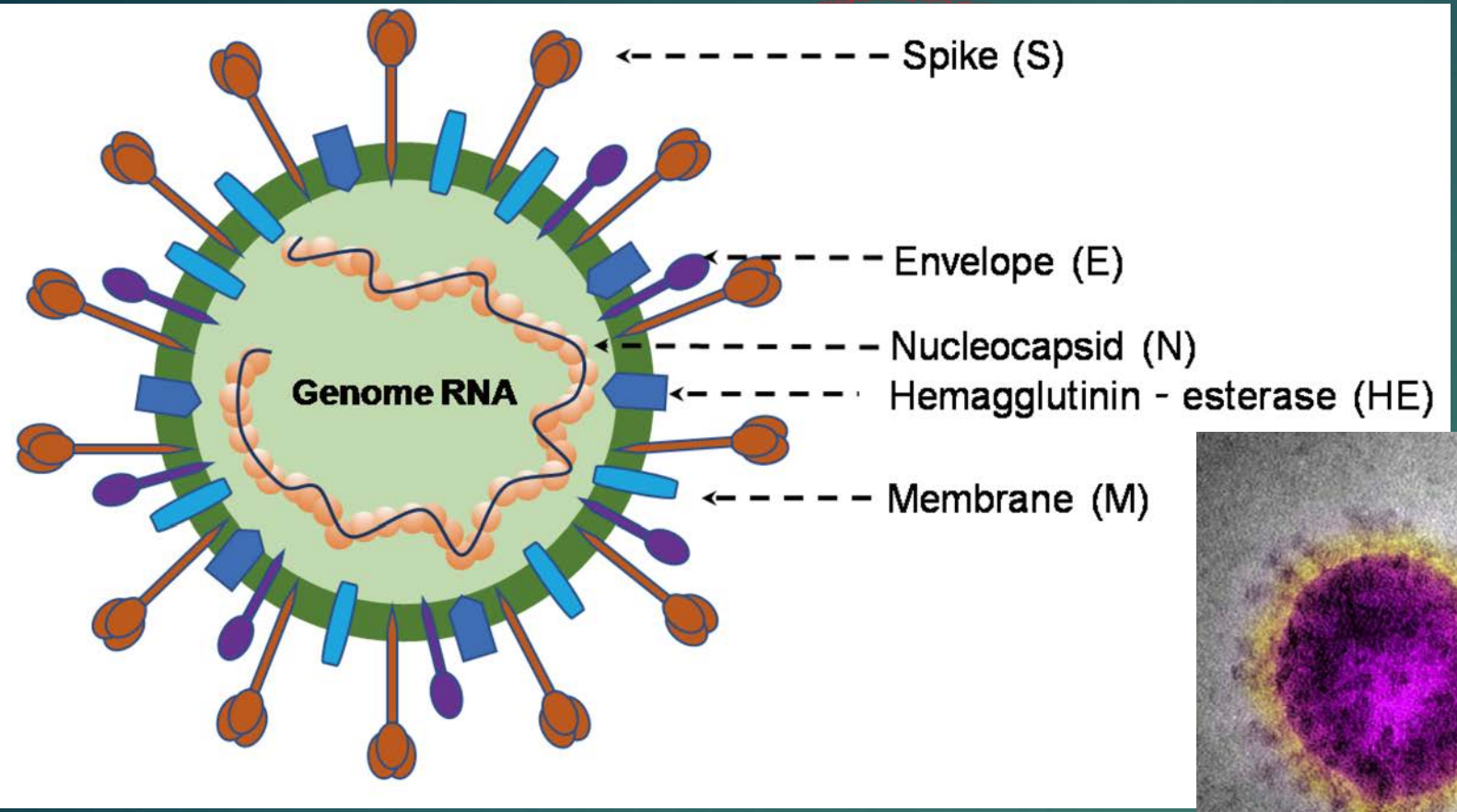
- Introduction to Coronavirus Family (1')
- SARS-CoV-2 infectiousness compared with other related infectious diseases and role of the herd immunity (4')
- Overview of Current Vacccines Candiates (1')
- Mechanism of protection by mRNA Vaccine (3')
- Mecanism of Protection by Adenovirus Vaccine (3')
- The interesting case of BCG (Tuberculosis) Vaccine (5')
- Challenges to Develop an effective Vaccine (3')

Human Coronavirus Family

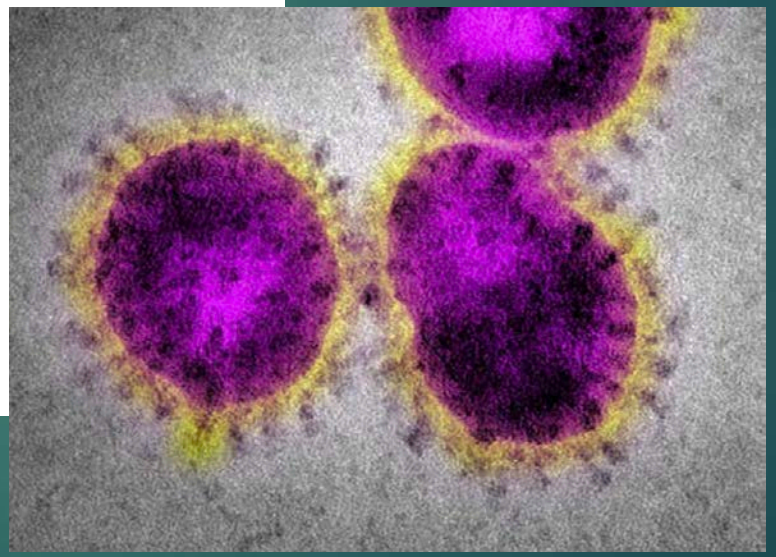
- **Human Coronavirus Types**
  - Human coronaviruses were first identified in the mid-1960s. The seven coronaviruses that can infect people are:
- **Common human coronaviruses**
    - 229E (alpha coronavirus)
    - NL63 (alpha coronavirus)
    - OC43 (beta coronavirus)
    - HKU1 (beta coronavirus)
- **Other human coronaviruses**
- SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS) (2002-2003)
- MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS) (2012-2013)
- SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19)

Content source: National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases

Human Coronavirus Family



https://www.mdpi.com/1999-4915/12/4/372/htm#cite

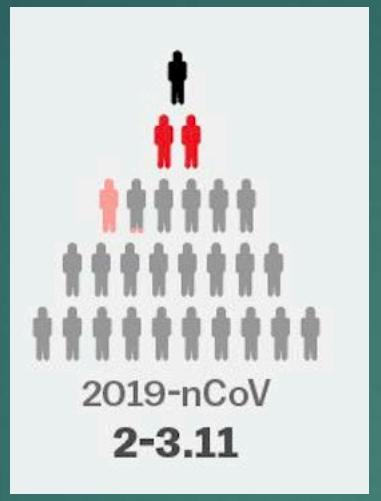


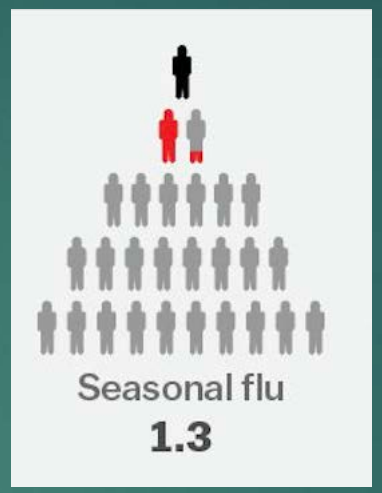
Electron micrograph of Coronavirus, the cause of Severe Acute Respiratory Syndrome (SARS)Scott Camazine/Alamy

How infectious can be SARS-Cov-2 and implications for human immunity

R_0

Average number of people who will catch a disease from one contagious person





https://www.businessinsider.com/coronavirus-contagious-r-naught-average-patient-spread-2020-3

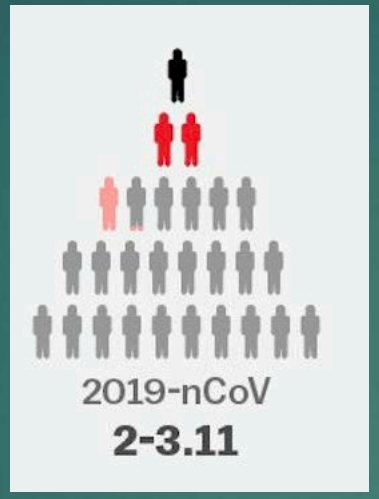
SOURCES: Travel Medicine, PLOS One, JAMA Pediatrics, MDPI, NCBI, New England Journal of Medicine, "The Spread and Control of Norovirus Outbreaks Among Hospitals in a Region"

How infectious can be SARS-Cov-2 and implications for human immunity

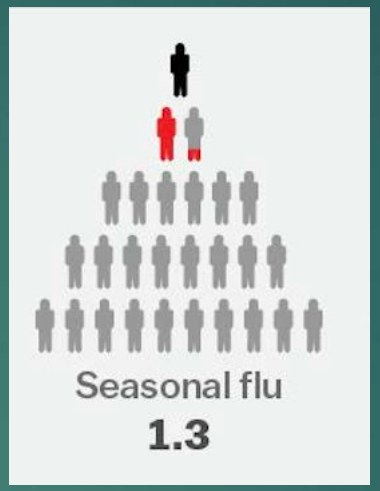
R_0

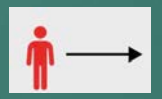
Average number of people who will catch a disease from one contagious person

x 10 cycles



+59,000





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https://www.businessinsider.com/coronavirus-contagious-r-naught-average-patient-spread-2020-3

SOURCES: Travel Medicine, PLOS One, JAMA Pediatrics, MDPI, NCBI, New England Journal of Medicine, "The Spread and Control of Norovirus Outbreaks Among Hospitals in a Region"

Herd Immunity and COVID-19

- Herd immunity happens when so many people in a community become immune to an infectious disease that it stops the disease from spreading.
- This can happen in two ways:
  - Many people contract the disease and in time build up an immune response to it (**natural immunity**).
  - Many people **are vaccinated** against the disease to achieve immunity.

Herd Immunity and COVID-19

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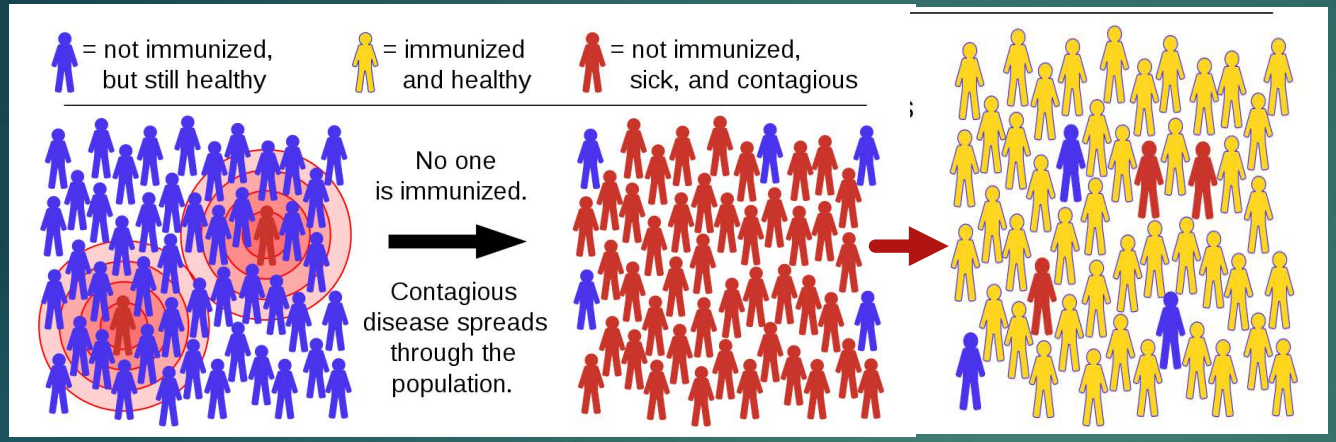
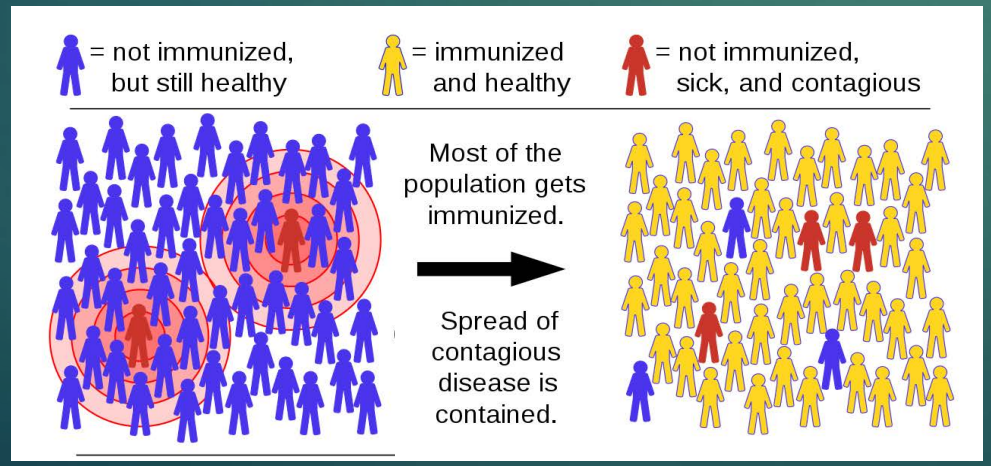


Problem

R_0 =2-2.5 need 60-66% of total persons infected

Ex: PR (~3 M) = 1,2 M
USA (~328M) = 196,8 M

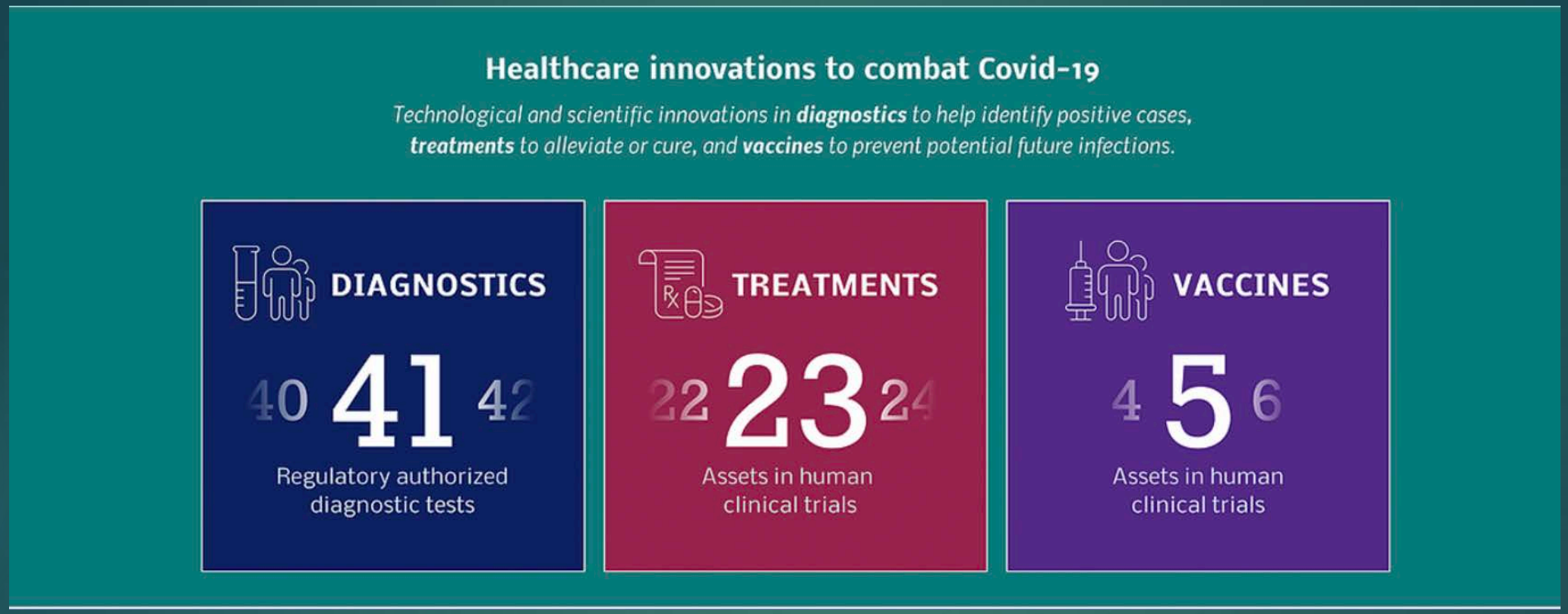
- Many people **are vaccinated** against the disease to achieve immunity.



Problem

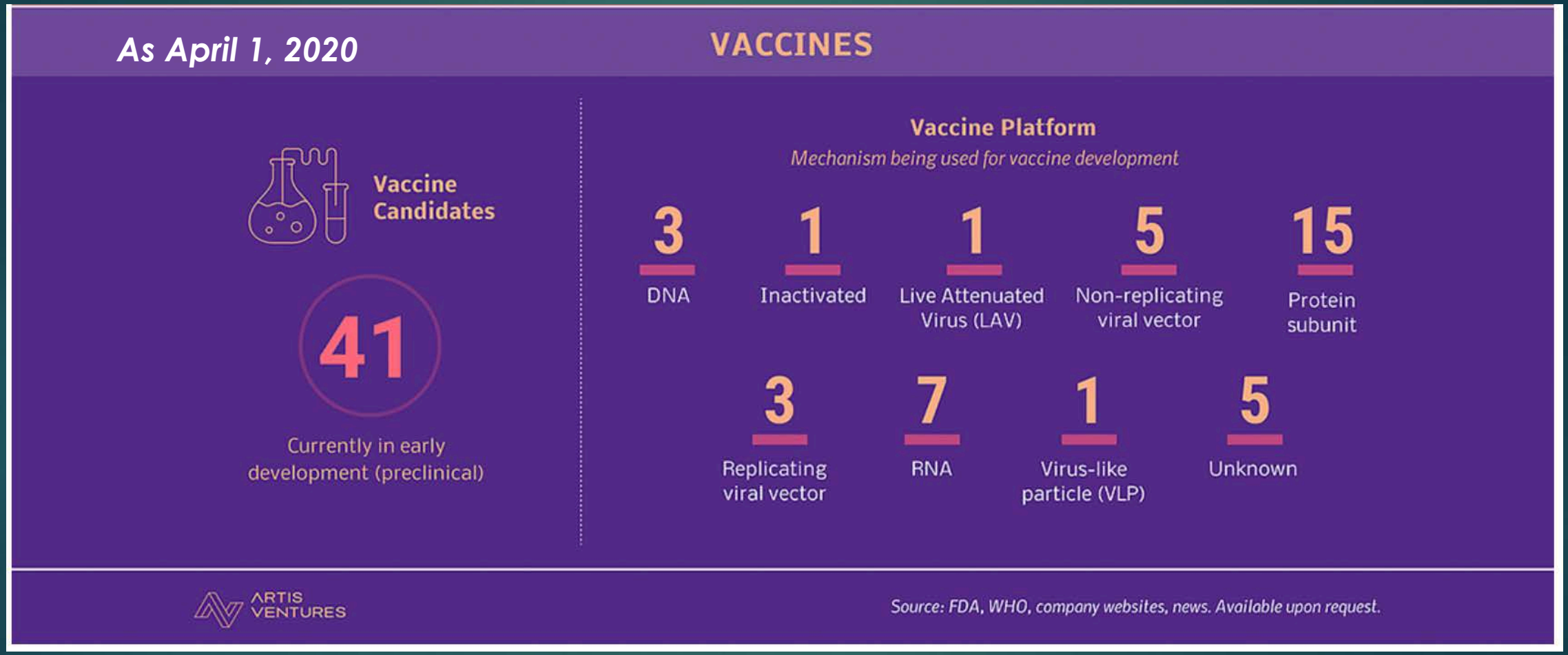
No Vaccine is available….YET

Tools to Combat Covid-19



Source: FDA, WHO, Companies web site.
Taken from www.visualcapitalism.com

VACCINE CANDIDATES



Source: FDA, WHO, Companies web site. Taken from www.visualcapitalism.com

https://www.who.int/blueprint/priority-diseases/key-action/Novel-Coronavirus_Landscape_nCoV-4april2020.pdf?ua=1

VACCINE CANDIDATES

VACCINES

Vasudev Bailey, PhD @vasudevbailey Zoe Guttendorf @zoeguttendorf

Vaccine	Company	Platform	Stage	Description	Location
1. mRNA-1273	Moderna NIAID (NIH)	RNA	Phase I-First Patient Dosed	First to dose a human in the US. Vaccine consists of a synthetic strand of mRNA designed to elicit an immune response to produce antibodies against SARS-CoV-2	

Source: FDA, WHO, Companies web site.
Taken from www.visualcapitalism.com

moderna

Biomedical Advanced Research and Development Authority

Moderna Announces Award from U.S. Government Agency BARDA for up to $483 Million to Accelerate Development of mRNA Vaccine (mRNA-1273) Against Novel Coronavirus

April 16, 2020

Award will fund development of mRNA-1273 to FDA licensure

Award will fund manufacturing process scale-up to enable large-scale production in 2020 for pandemic response

NIH-led Phase 1 study of mRNA-1273 has completed enrollment of 3 dose cohorts (25 µg, 100 µg and 250 µg); expanding to an additional 6 cohorts of older adults and elderly adults

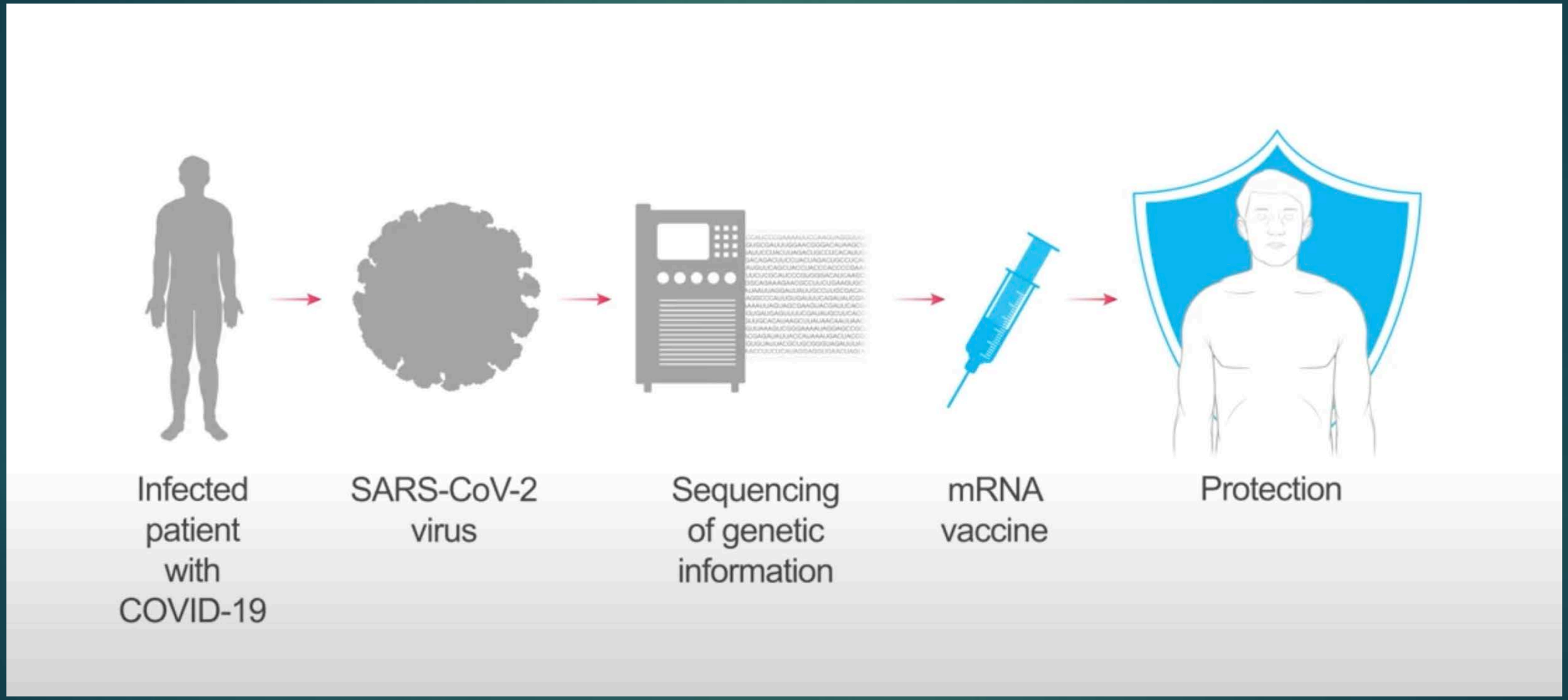
Phase 2 study expected to begin in Q2 2020, following safety data from ongoing Phase 1 study

Moderna to hire up to 150 new team members to support efforts

Conference call to be held on Friday, April 17 at 8:00 a.m. ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 16, 2020-- Moderna, Inc., (Nasdaq: MRNA) a clinical stage biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, today announced an agreement for a commitment of up to $483 million from the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS), to accelerate development of the Company's mRNA vaccine candidate (mRNA-1273) against the novel coronavirus (SARS-CoV-2).

How mRNA 1273 Vaccine works



https://youtu.be/qJlP91xjvsQ

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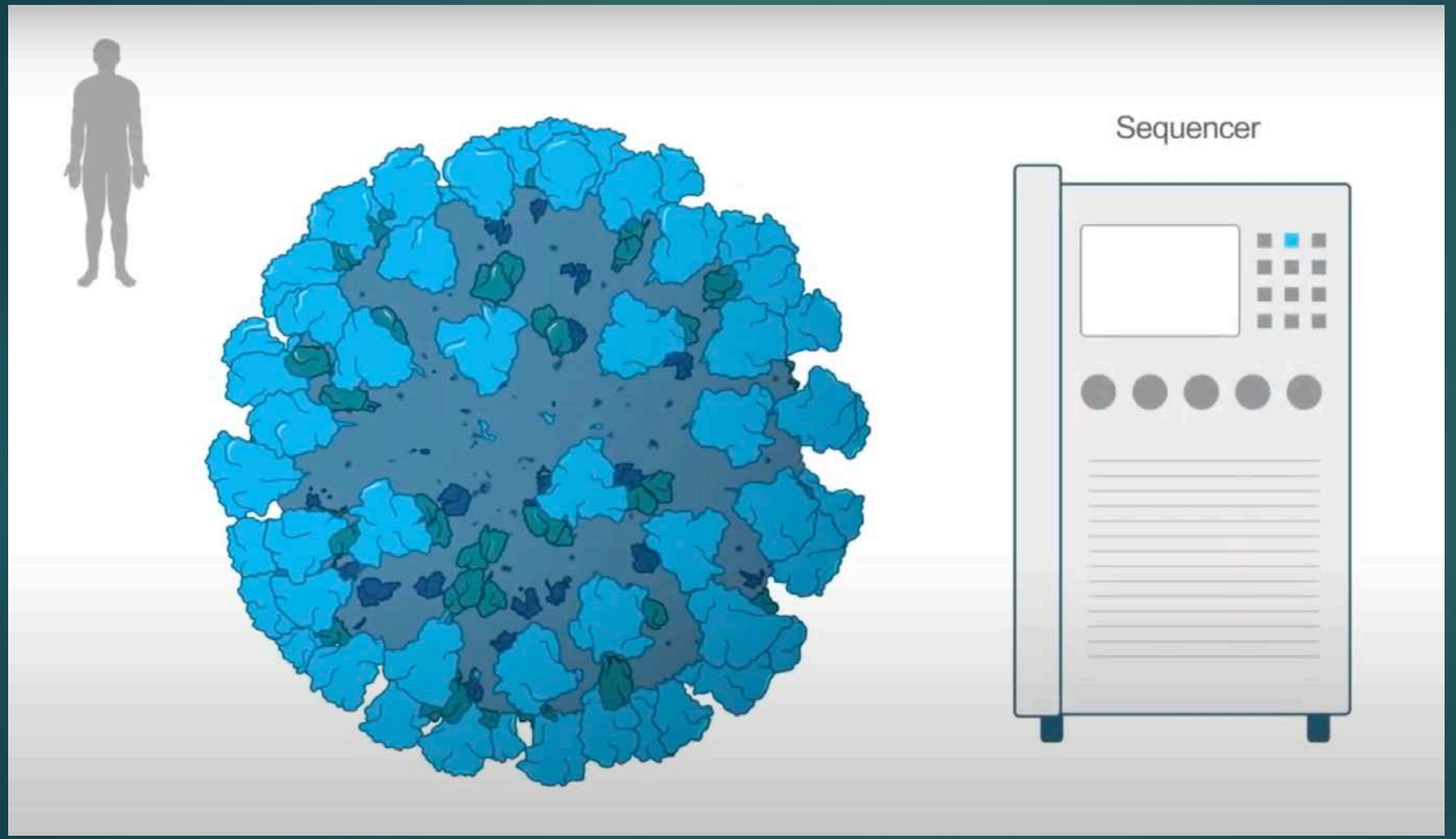

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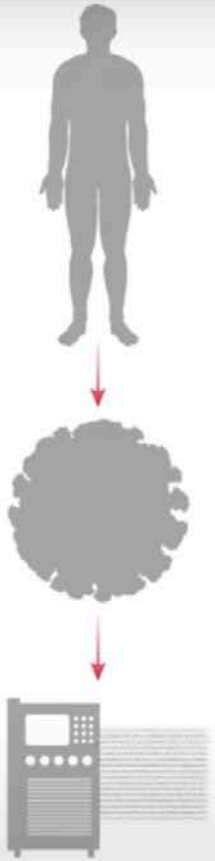
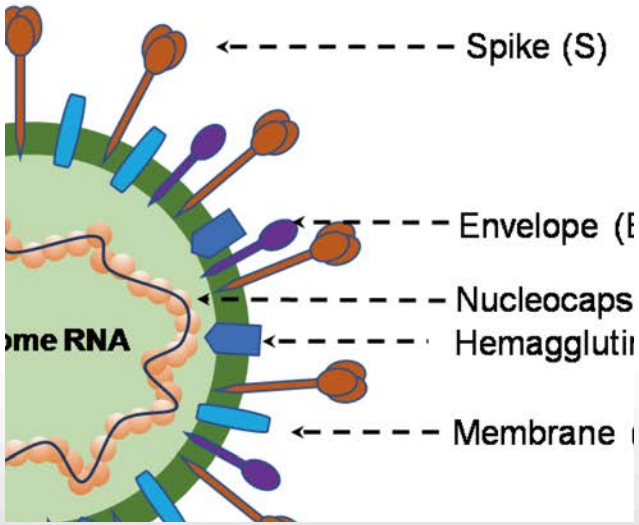


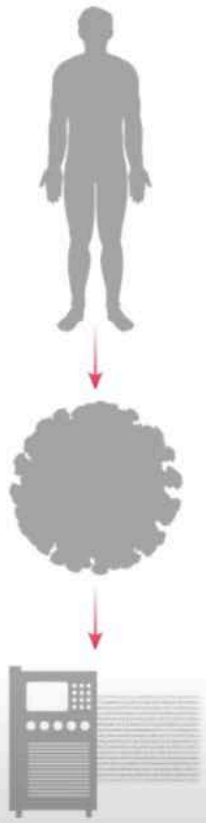


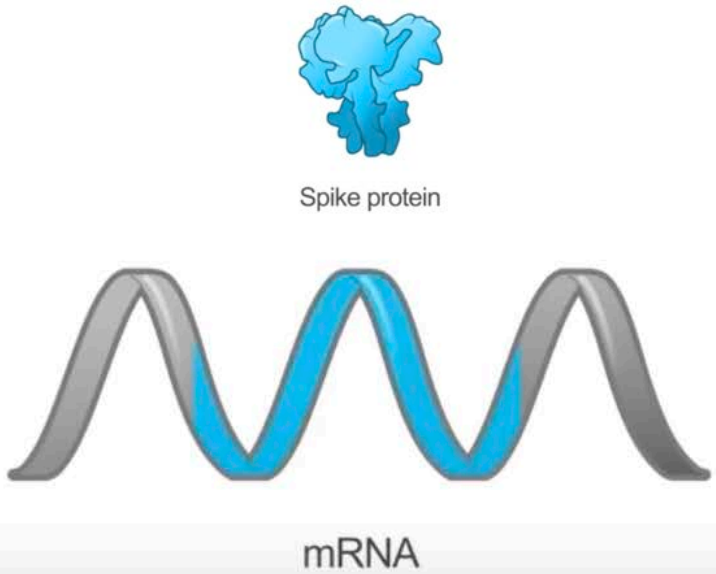
Genetic information

UCCUACUCAGACUGCCUCACAUUGAGGCCCAUUGUGAUUUCAGAUAUCGAC
GUAGGGUUGCACCGUACGCAUGUAAAAUUAGUAGCGAAGUACGAUUCACGA

Spike protein

How mRNA 1273 Vaccine works





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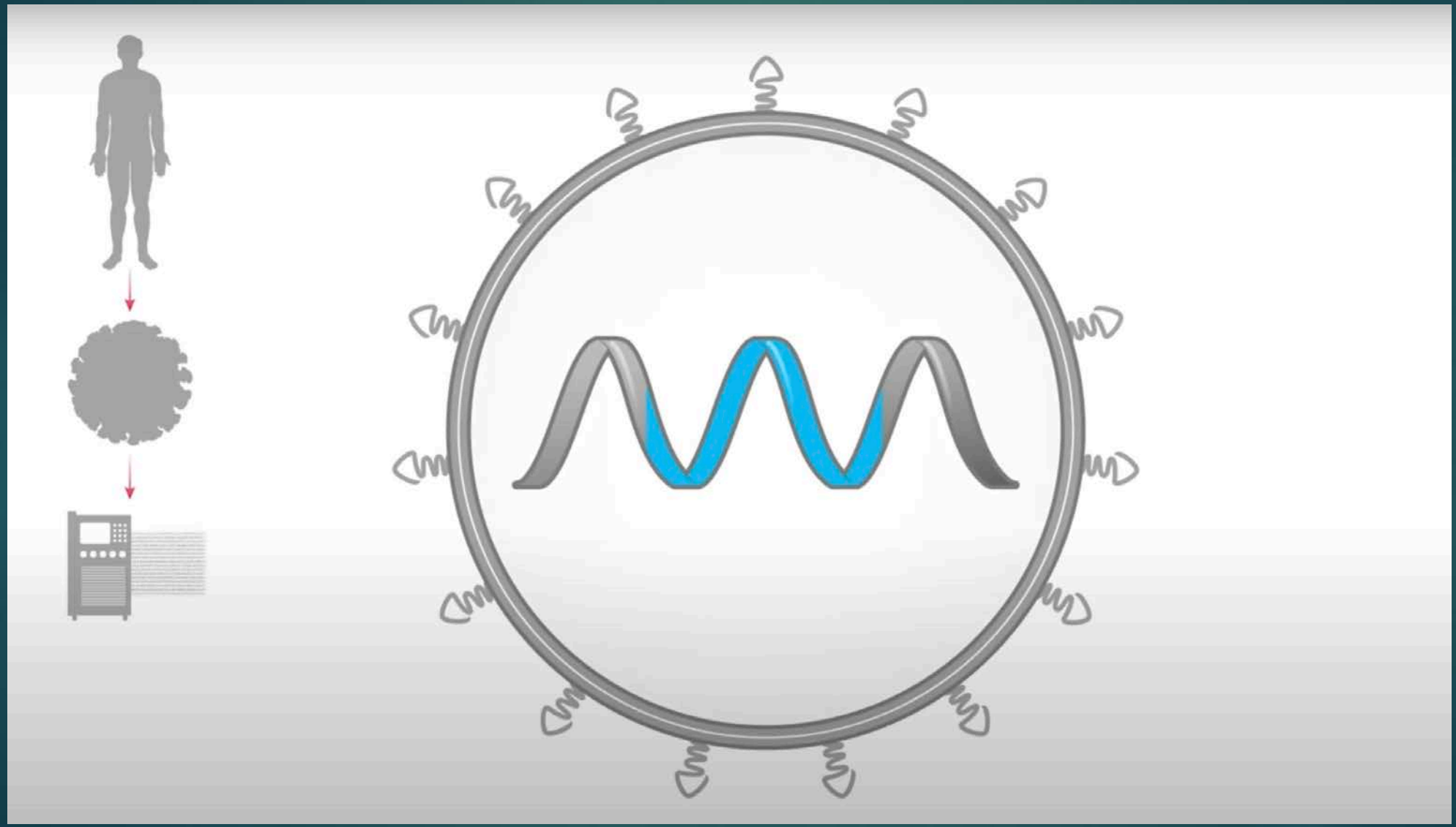

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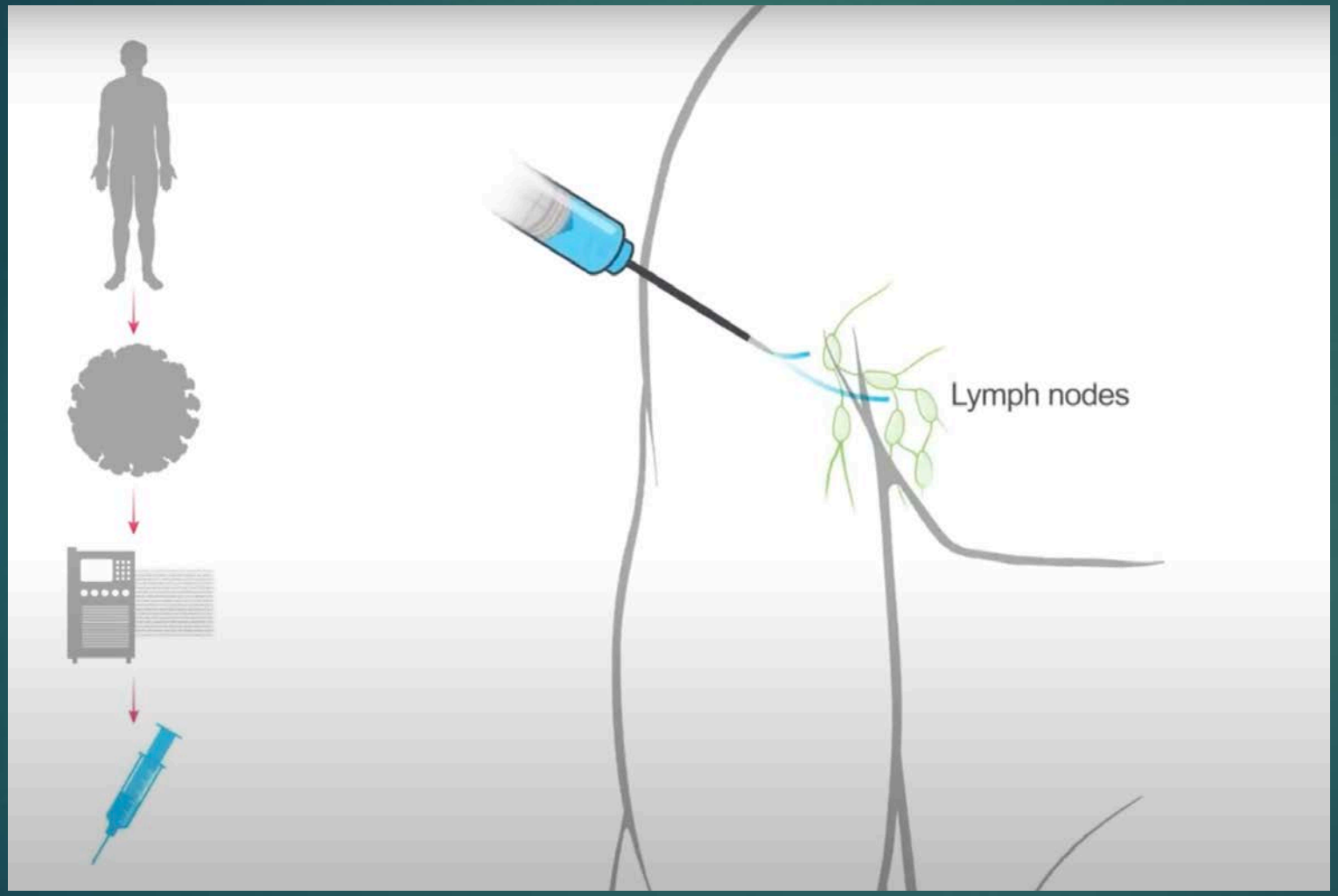

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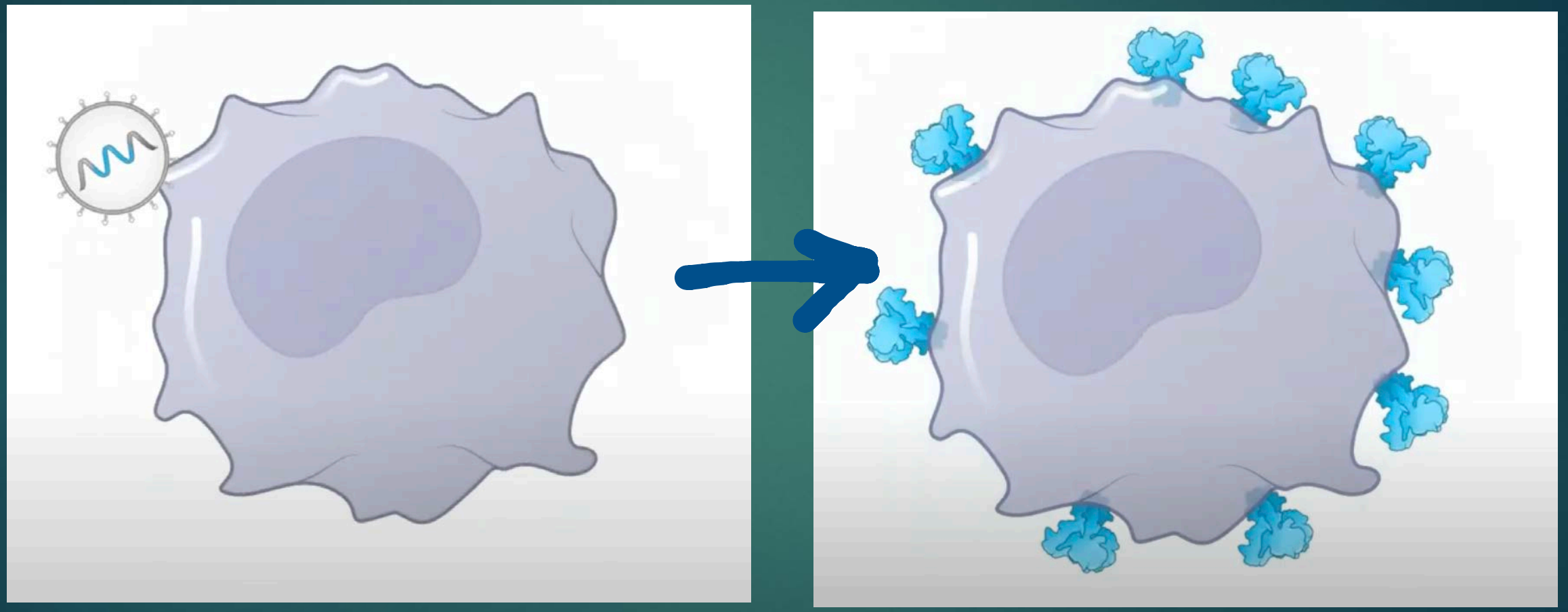

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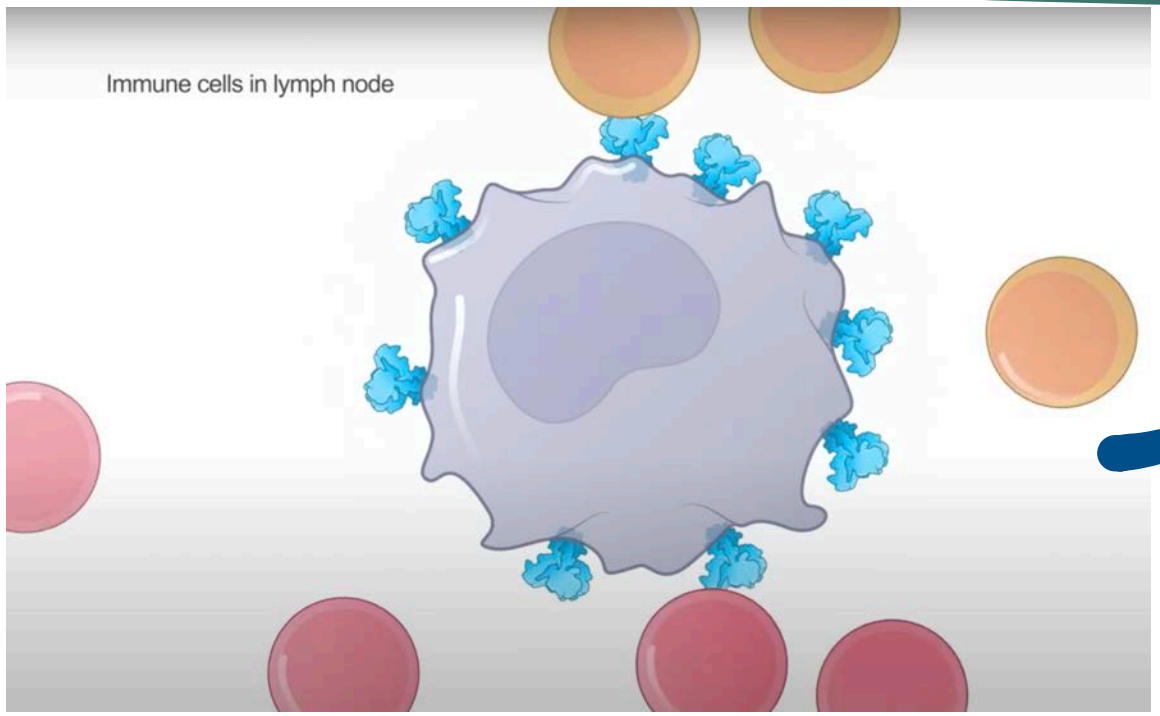

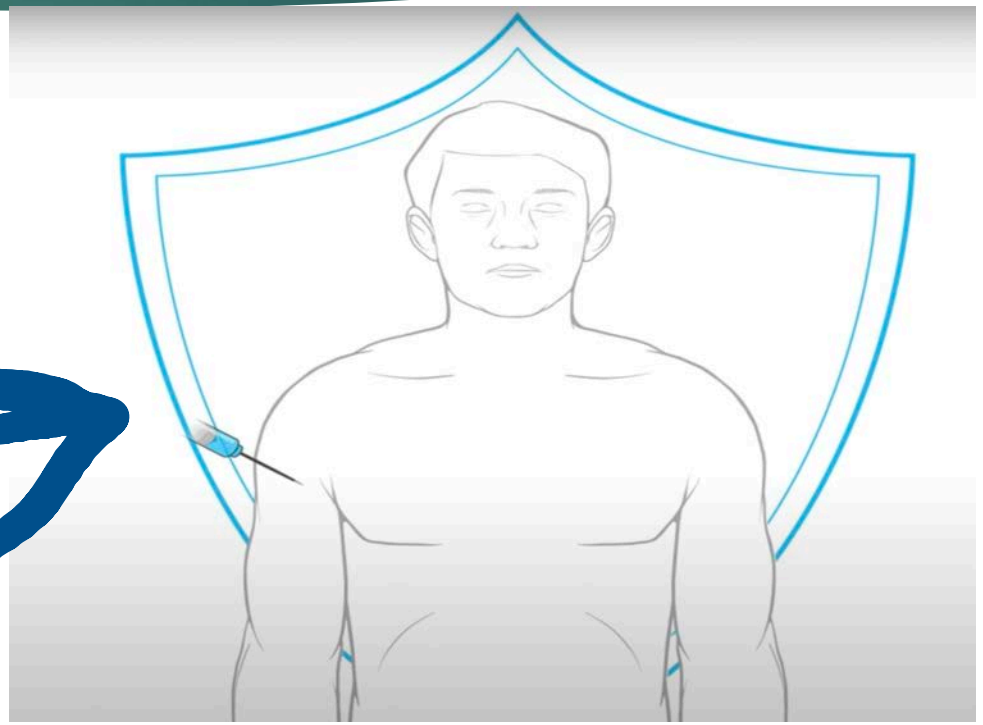

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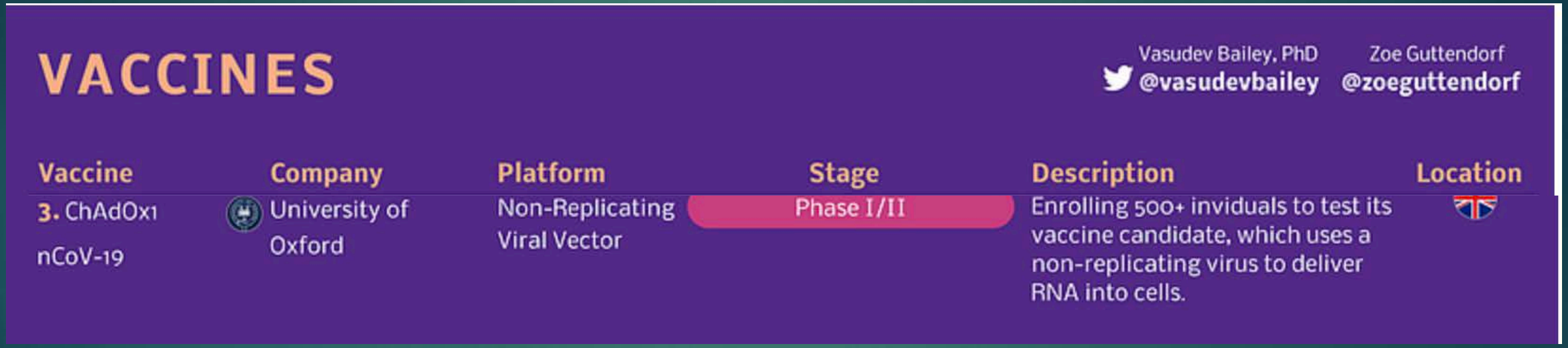
Vaccine	Company	Platform	Stage	Description	Location
2. Ad5-nCoV	CanSino Bio	Non-Replicating Viral Vector	Phase I	Benefits from previous success in the Ebola virus (time to market ~3 years). The vaccine being developed is based on viral vectors (adenoviruses) to deliver antigens to express the SARS-CoV-2 spike protein	

Source: FDA, WHO, Companies web site.
Taken from www.visualcapitalism.com

VACCINE CANDIDATES



VACCINES

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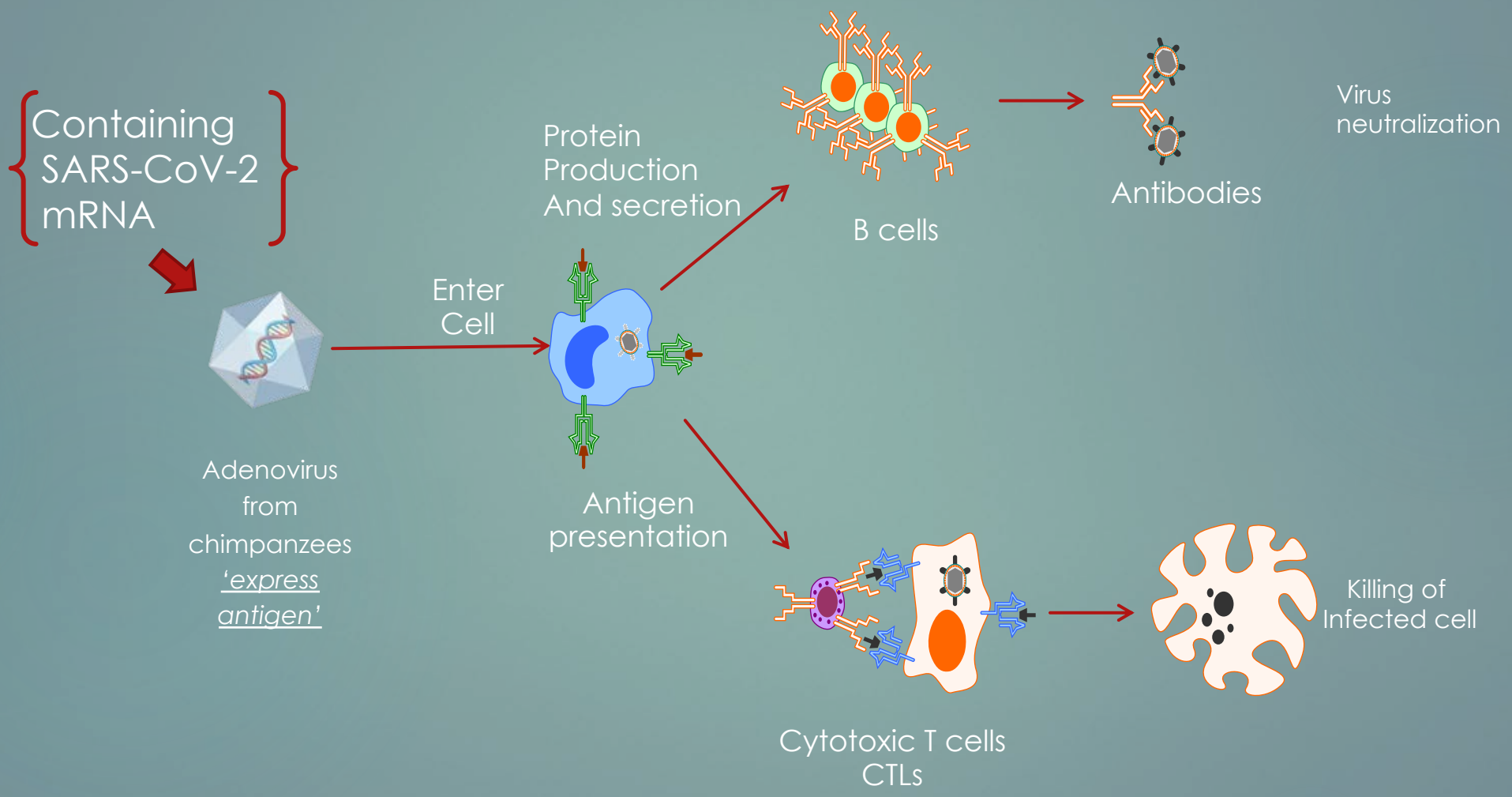
Vaccine	Company	Platform	Stage	Description	Location
3. ChAdOx1 nCoV-19	University of Oxford	Non-Replicating Viral Vector	Phase I/II	Enrolling 500+ inviduals to test its vaccine candidate, which uses a non-replicating virus to deliver RNA into cells.	

Source: FDA, WHO, Companies web site.
Taken from www.visualcapitalism.com

Recombinant adenoviruses induce balanced immune responses: Antibodies and T cells



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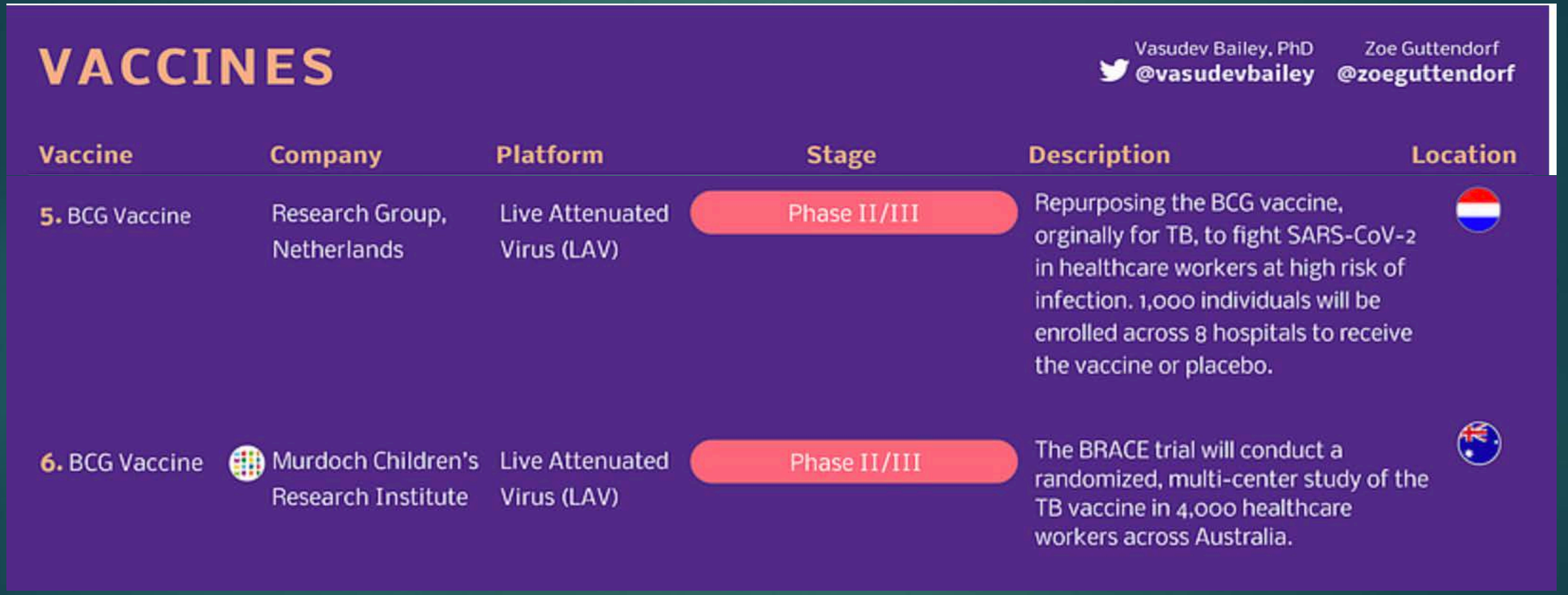

VACCINES

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Vaccine	Company	Platform	Stage	Description	Location
5. BCG Vaccine	Research Group, Netherlands	Live Attenuated Virus (LAV)	Phase II/III	Repurposing the BCG vaccine, orginally for TB, to fight SARS-CoV-2 in healthcare workers at high risk of infection. 1,000 individuals will be enrolled across 8 hospitals to receive the vaccine or placebo.	
6. BCG Vaccine	Murdoch Children's Research Institute	Live Attenuated Virus (LAV)	Phase II/III	The BRACE trial will conduct a randomized, multi-center study of the TB vaccine in 4,000 healthcare workers across Australia.	

Source: FDA, WHO, Companies web site.
Taken from www.visualcapitalism.com

Could a 100-year-old vaccine protect against COVID-19?

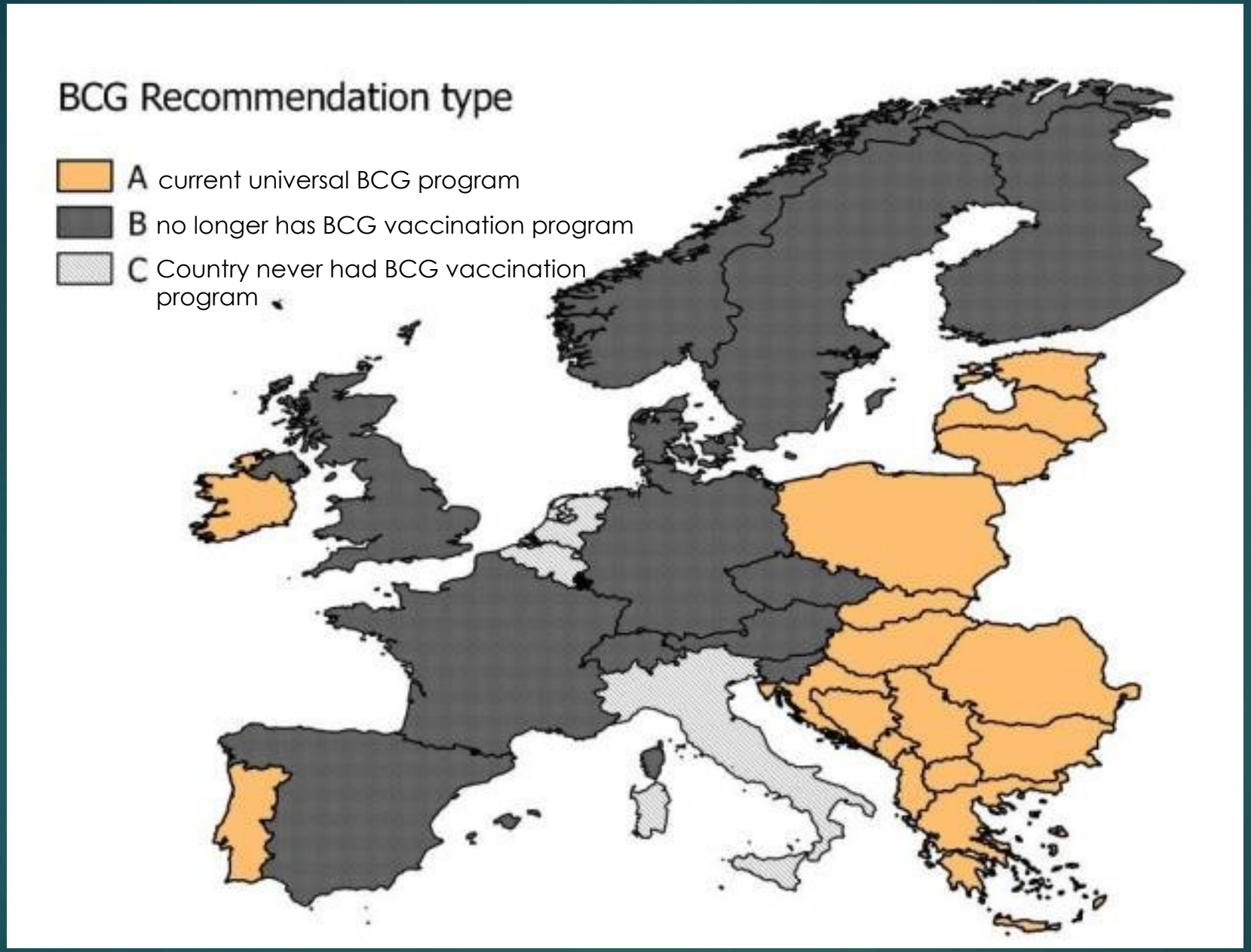
- Jean Antoine Villemin first recognized bovine tuberculosis in 1854
- In 1882, Robert Koch identified the *Mycobacterium tuberculosis* as *the cause of human TB.*
- The BCG strain was isolated after subculturing 239 times during 13 years. Developed by Albert Calmette and Camille Guerin (Bacillus Calmette–Guérin, BCG).
- The BCG vaccine was first used in humans in 1921.

https://www.livescience.com/coronavirus-protection-using-tuberculosis-vaccine.html

Could a 100-year-old vaccine protect against COVID-19?

- BCG vaccination exist in 131 countries;
- 21 countries have no current program of national BCG vaccination;
- Status for 26 countries is unknown.

from: https://www.researchgate.net/publication/340224580_BCG_vaccination_may_be_protective_against_Covid-19 [accessed Apr 19 2020].



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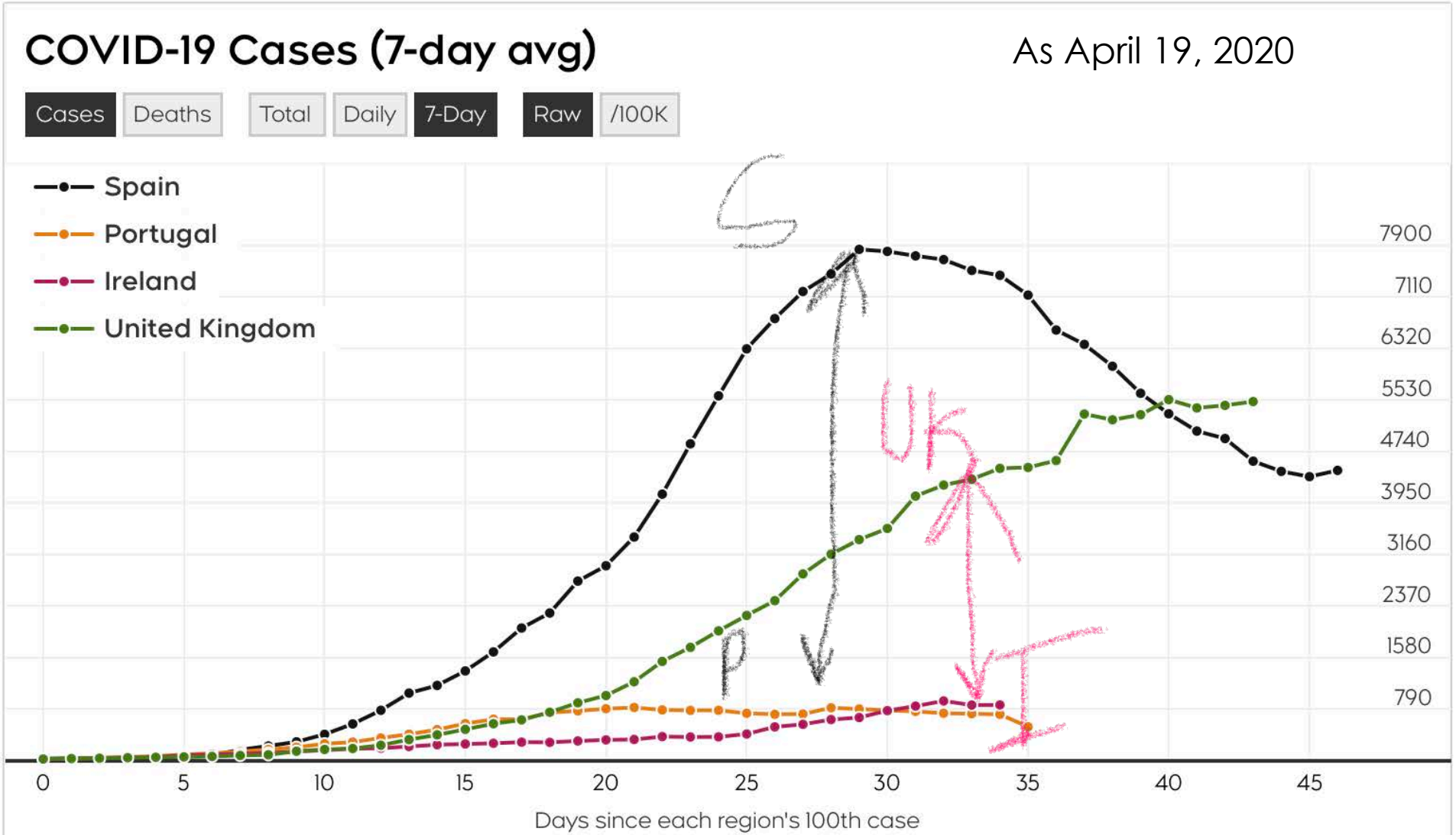


https://www.ctvnews.ca/health/coronavirus/

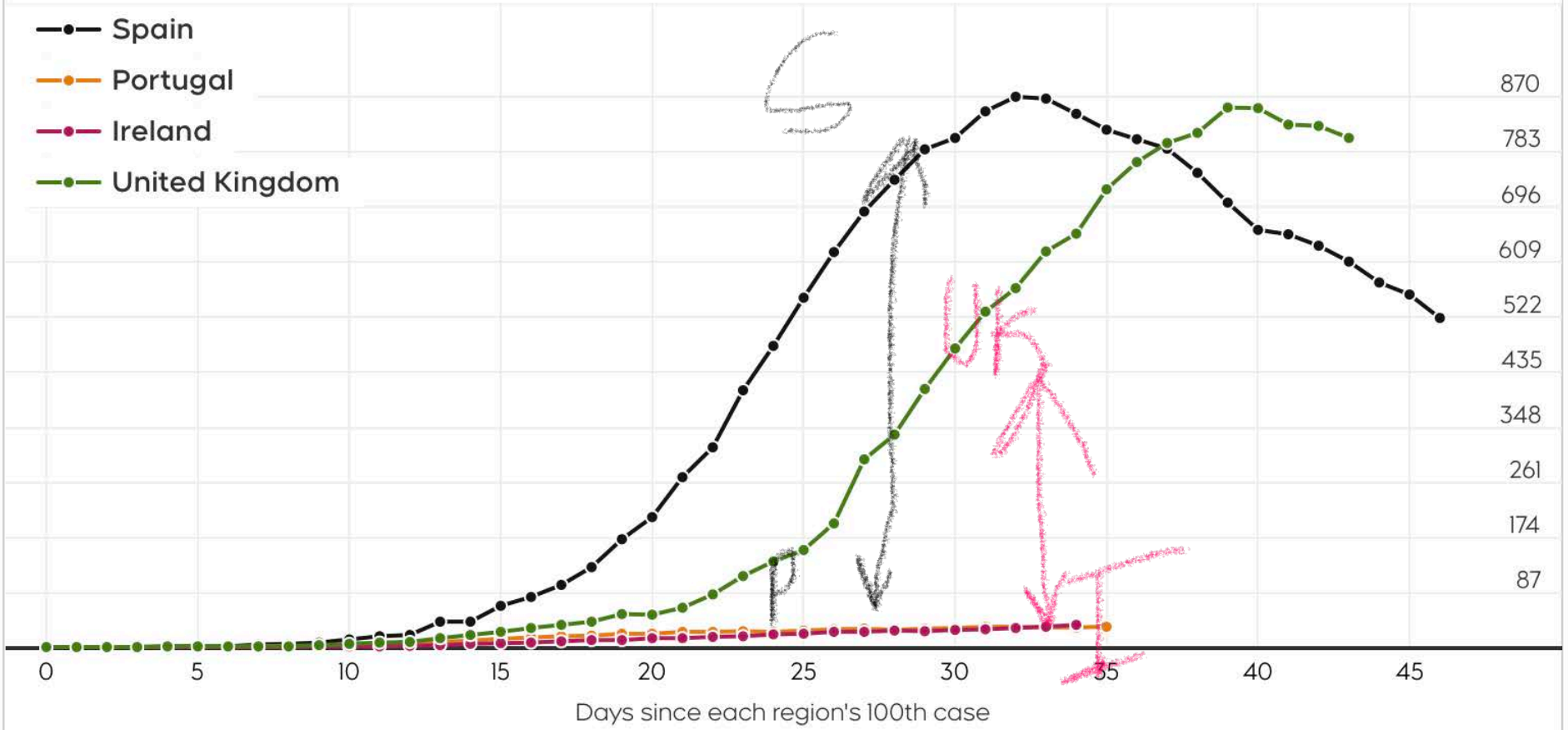
Choose regions

Spain | Portugal | Ireland | United Kingdom

COVID-19 Deaths (7-day avg)

As April 19, 2020

Cases | Deaths | Total | Daily | 7-Day | Raw | /100K



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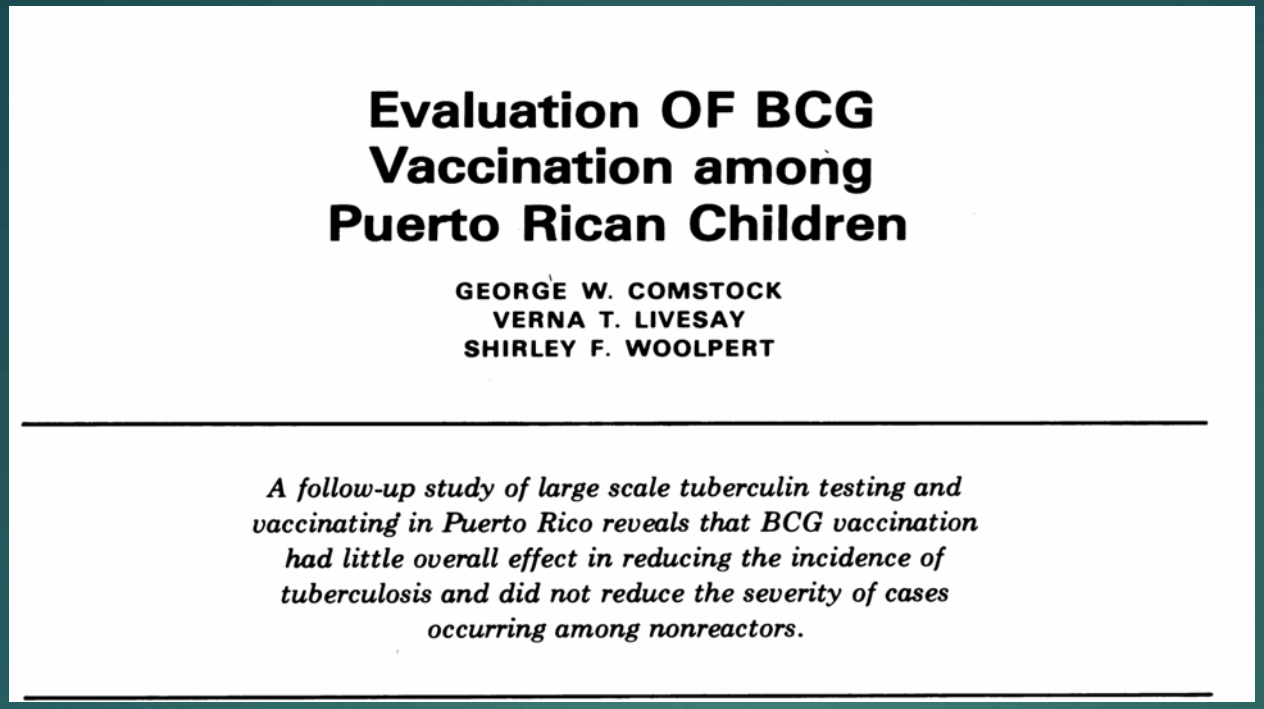
Choose regions

Spain | Portugal | Ireland | United Kingdom

Could a 100-year-old vaccine protect against COVID-19?

- As of March 2020, even though the tuberculosis vaccine does not directly protect against COVID-19 it has been thought to boost the immune systems and has been suggested for study.[94][95]
- Spanish, French, German and Dutch research entities are preparing trials using genetically-modified BCG vaccines.[96]
- BCG vaccine is in phase 3 trials in health care workers in Australia and Netherlands.[97]
- The WHO does not recommend its use for prevention as of 13 April 2020.[98]



Evaluation OF BCG Vaccination among Puerto Rican Children

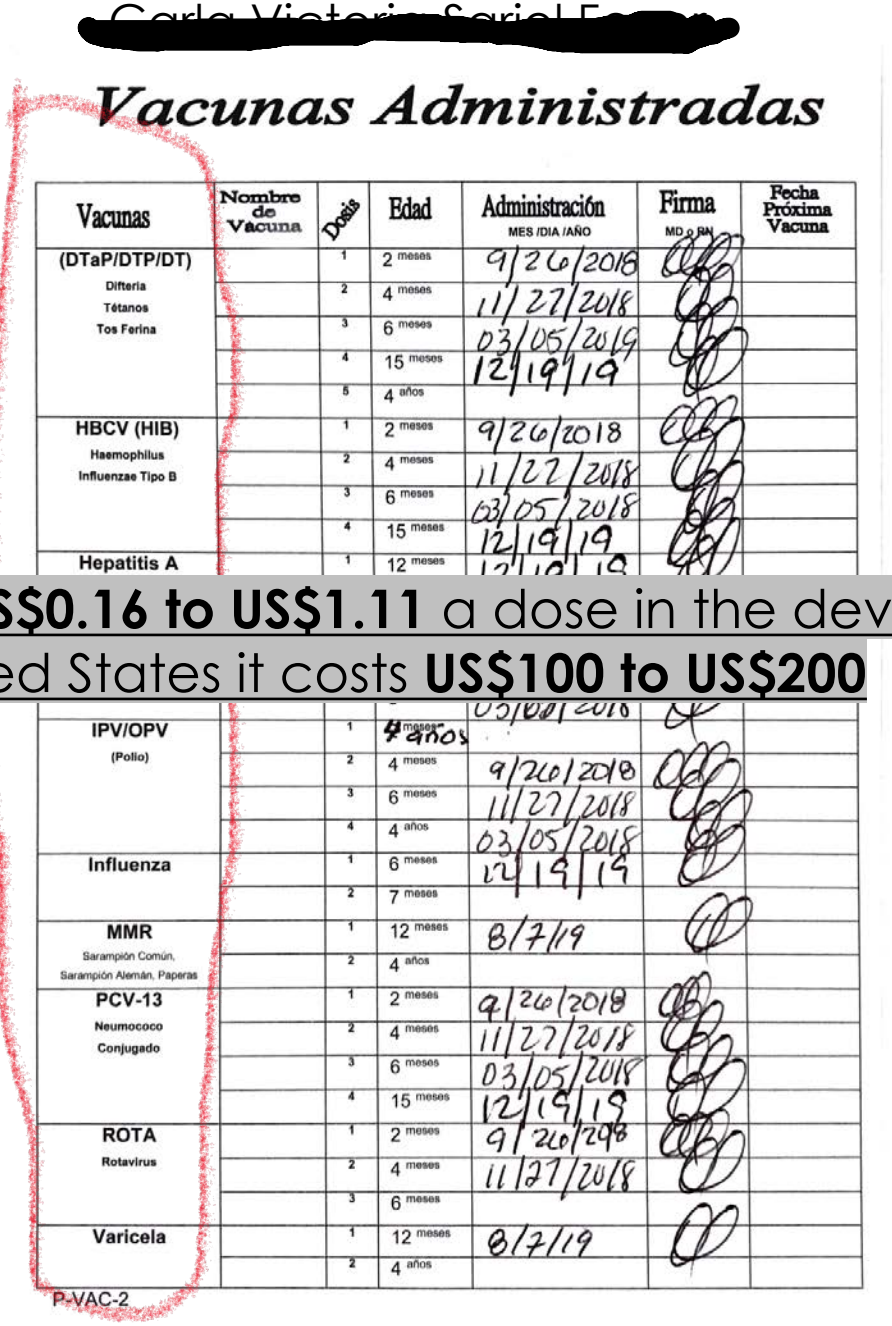
GEORGE W. COMSTOCK
VERNA T. LIVESAY
SHIRLEY F. WOOLPERT

A follow-up study of large scale tuberculin testing and vaccinating in Puerto Rico reveals that BCG vaccination had little overall effect in reducing the incidence of tuberculosis and did not reduce the severity of cases occurring among nonreactors.

- Tuberculin testing and vaccinating were started in September, 1949, and stopped in May, 1951.
- A total of 191,827 children (1-18 y/o) were included in the study population.

AJPH MARCH, 1974, Vol.64, No.3

Current Vaccine Schedulle in PR



Vacunas Administradas

Vacunas	Nombre de Vacuna	Dosis	Edad	Administración MES /DIA /AÑO	Firma MD o RN	Fecha Próxima Vacuna
(DTaP/DTP/DT) Difteria Tétanos Tos Ferina		1	2 meses	9/26/2018		
		2	4 meses	11/27/2018		
		3	6 meses	03/05/2019		
		4	15 meses	12/19/19		
		5	4 años			
HBCV (HIB) Haemophilus Influenzae Tipo B		1	2 meses	9/26/2018		
		2	4 meses	11/27/2018		
		3	6 meses	03/05/2018		
		4	15 meses	12/19/19		
Hepatitis A		1	12 meses			
IPV/OPV (Polio)		1	4 meses 4 años			
		2	4 meses	9/26/2018		
		3	6 meses	11/27/2018		
		4	4 años	03/05/2018		
Influenza		1	6 meses	12/19/19		
		2	7 meses			
MMR Sarampión Común, Sarampión Alemán, Paperas		1	12 meses	8/7/19		
		2	4 años			
PCV-13 Neumococo Conjugado		1	2 meses	9/26/2018		
		2	4 meses	11/27/2018		
		3	6 meses	03/05/2018		
		4	15 meses	12/19/19		
ROTA Rotavirus		1	2 meses	9/26/2018		
		2	4 meses	11/27/2018		
		3	6 meses			
Varicela		1	12 meses	8/7/19		
		2	4 años			

P-VAC-2

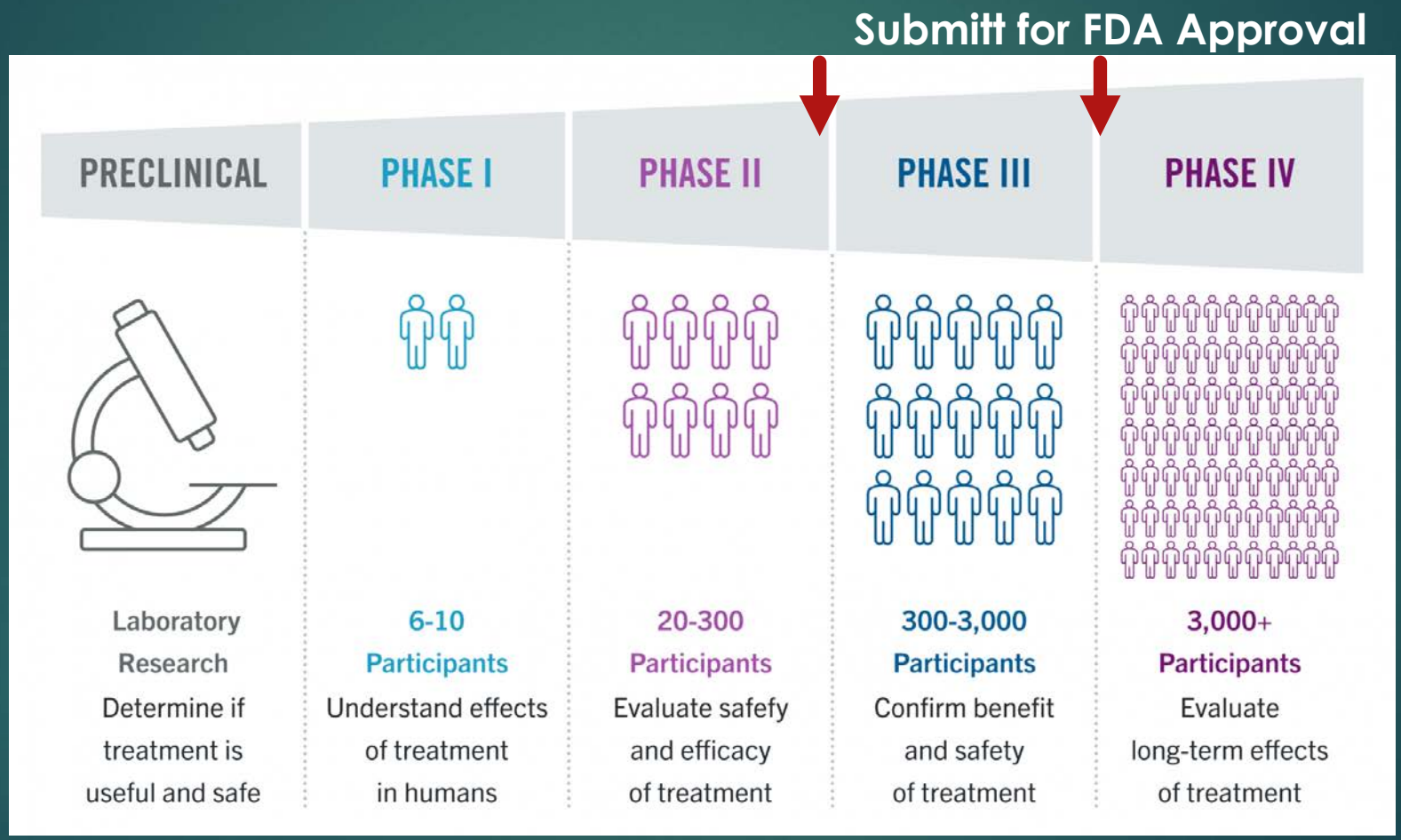
VER AL DORSO

The cost **US$0.16 to US$1.11** a dose in the developing world.[6][7]
In the United States it costs **US$100 to US$200**

Challenge to develop an effective and secure Vaccine at any time soon.

- No animal model that can recall the diseases like in humans.
  - From mice to humans
  - From Labs to humans
  - Several Preclinical studies in NHP

Challenge to develop an effective and secure Vaccine at any time soon.



Months to Years

Several months

Up to two years

One(1) to four (4) years

One (1) to several years

Challenge to develop an effective and secure Vaccine at any time soon.

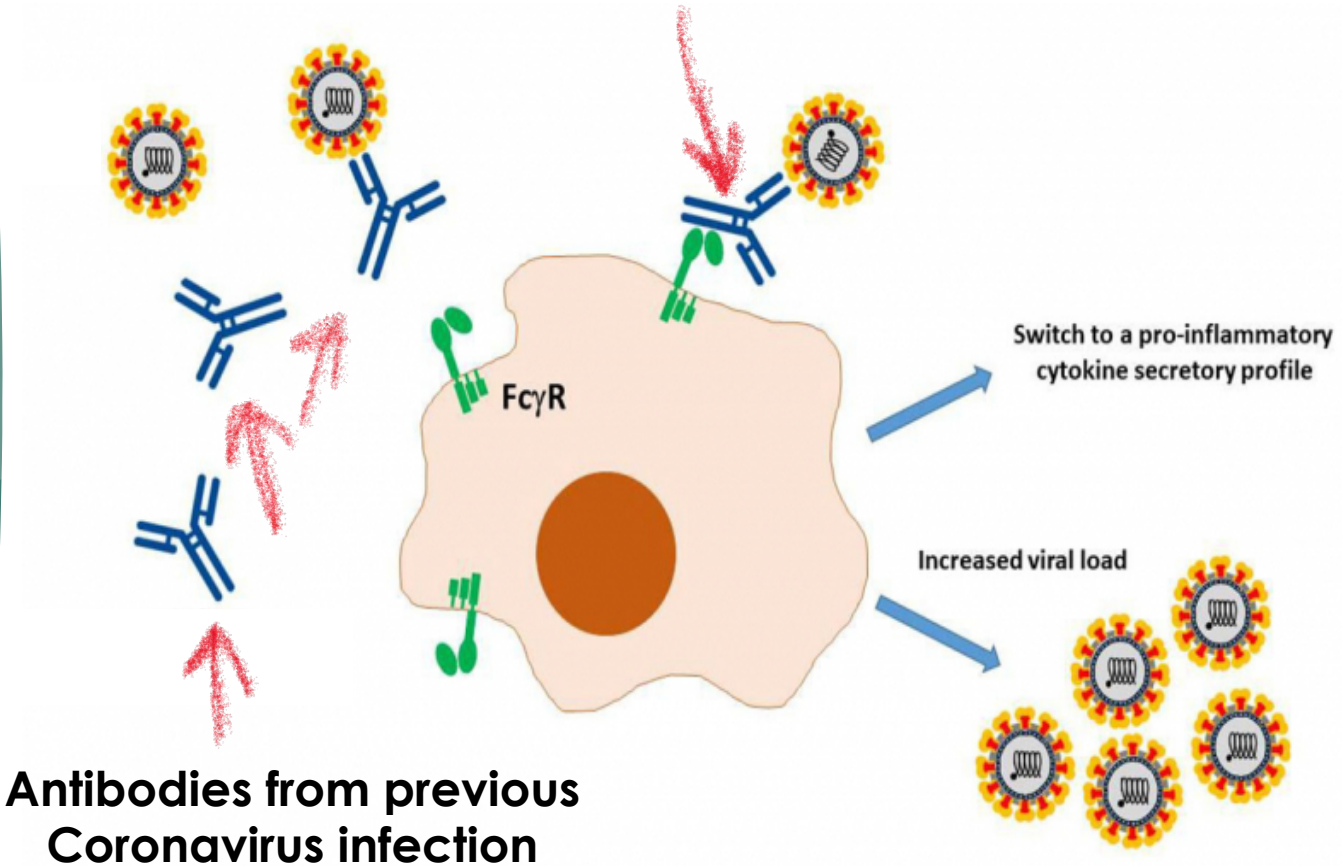
- Manufacture Capabilities

100 Tech Drive, Norwood, Massachusetts

Challenge to develop an effective and secure Vaccine at any time soon.

- SARS-CoV. enhancement was identified by Yang et al. [6] in 2005.
- It was hypothesized as being the reason for such a high mortality rate in China [7].
- At the time, the priming strains were thought to be human coronaviruses known to cause mild infection such as 229E [7].
- Yip et al. [8,9] revealed that **anti-Spike** protein antibodies were indeed responsible for the infection of immune cells.

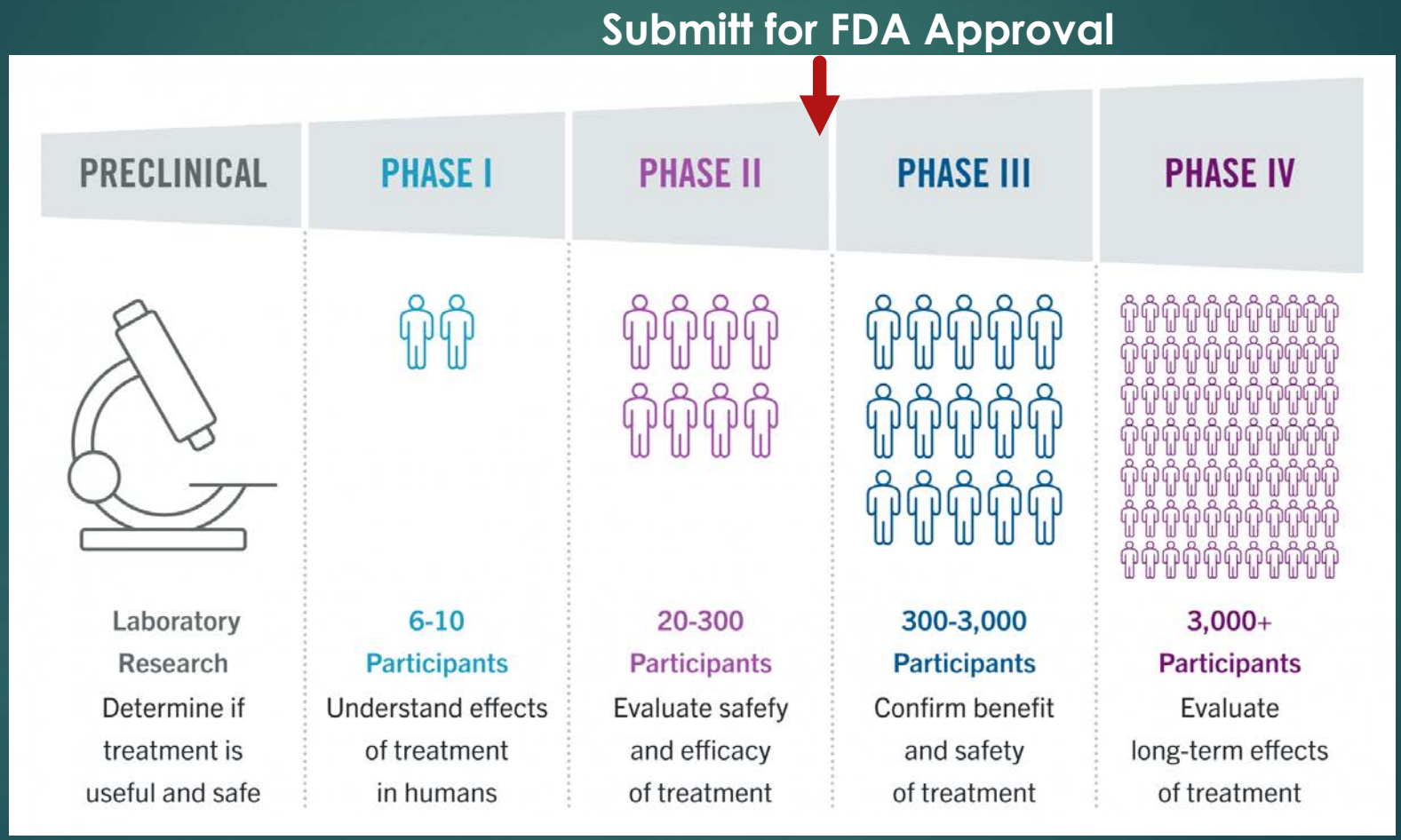
Antibody-Dependent Enhacement (ADE)



Antibodies from previous Coronavirus infection
OR
Vaccine induced??

DOIhttps://doi.org/10.4414/smw.2020.20249 Publication Date: 16.04.2020, Swiss Med Wkly. 2020;150:w20249

Challenge to develop an effective and secure Vaccine at any time soon.



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One (1) to several years

Thank you

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