



**College of  
Health Solutions**

**Arizona State  
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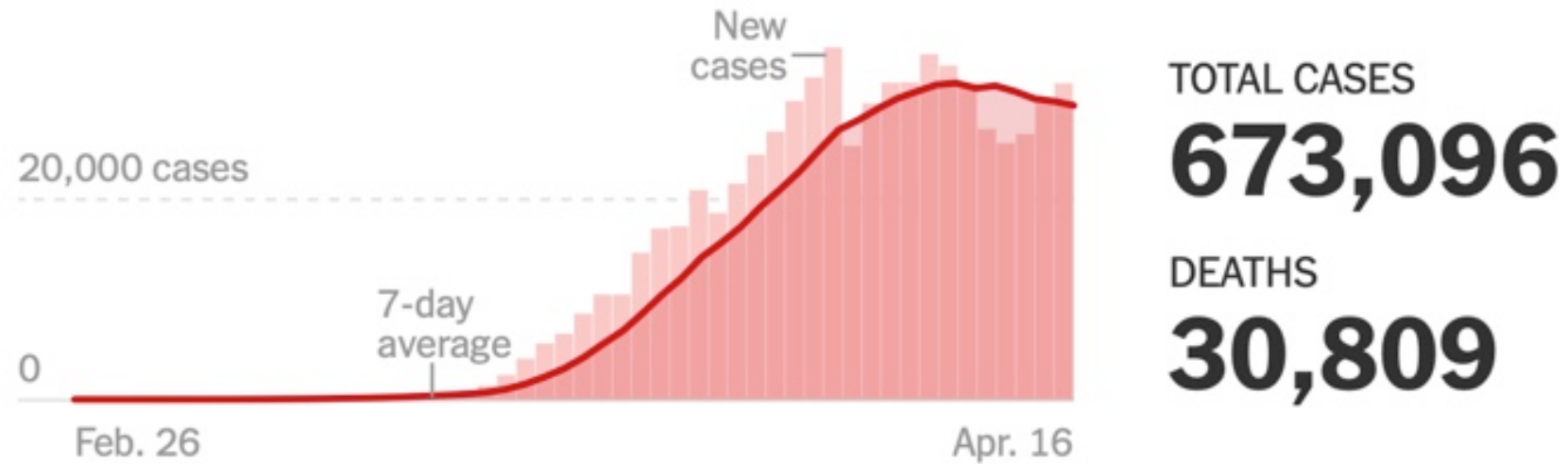
**Health  
Talks**

# **Diagnostics: Key to the Beginning, Middle and End of the COVID 19 Pandemic**

*Mara G. Aspinall  
Professor of Practice  
College of Health Solutions*



# The Devasting Impact of COVID-19



Source: Upshot by The New York Times Co; accessed 4/17/20; <https://www.nytimes.com/interactive/2020/03/21/upshot/coronavirus-deaths-by-country.html>

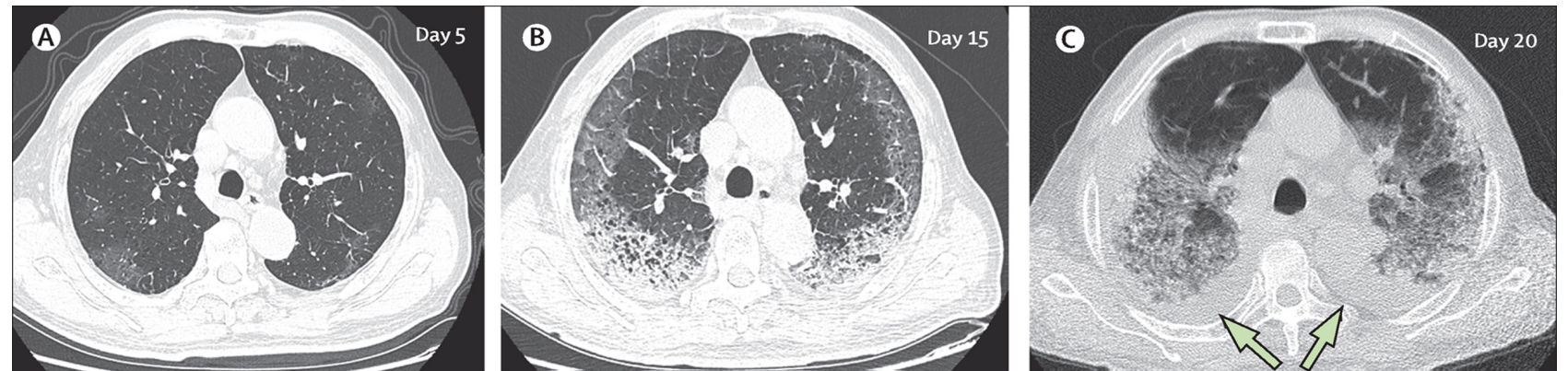
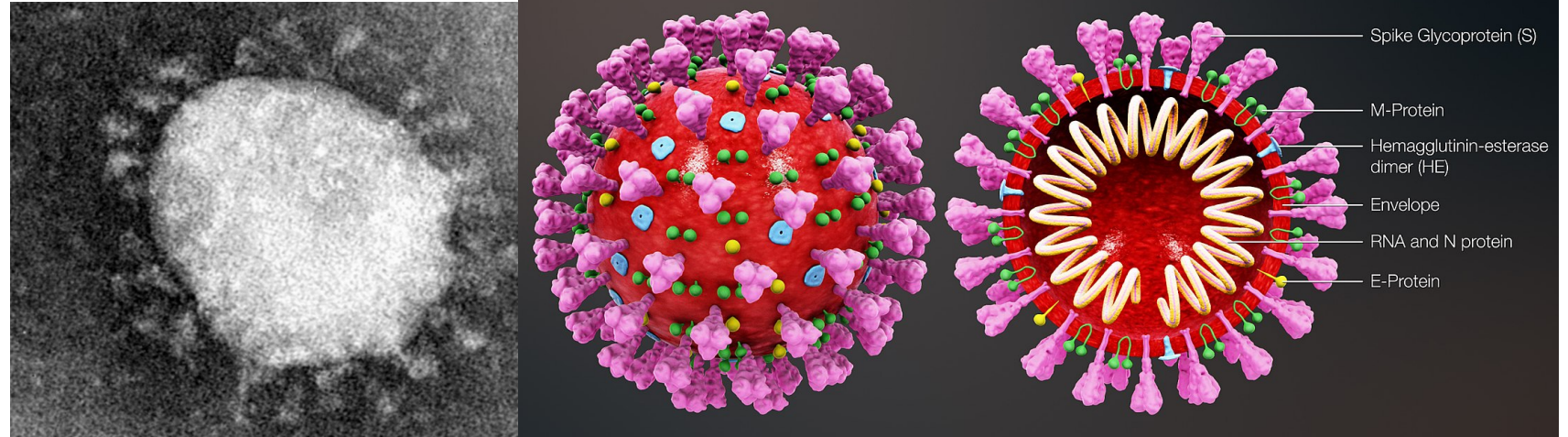


# The Virus vs. The Disease

**SARS-CoV2  
Virus**



**COVID-19  
Disease**



**Day 5**

**Day 15**

**Day 20**

**Source:** *The Lancet Infectious Diseases* 2020 20425-434DOI: (10.1016/S1473-3099(20)30086-4)



# Everyone wants diagnostics...

## Coronavirus Update: Medical Professionals Say They Still Don't Have Enough COVID-19 Tests To Meet Demand

April 9, 2020 at 11:37 pm Filed Under: Coronavirus, COVID-19, Jessica Layton, Local TV, New Jersey, Phil Murphy

The New York Times

Opinion

## The Real Tragedy of Not Having Enough Covid-19 Tests

## National shortages threaten COVID-19 testing while scientists try to get needed resources

Alessandro Marazzi Sassoon, Florida Today Published 11:39 a.m. ET March 19, 2020 | Updated 6:56 p.m. ET March 21, 2020

INVESTIGATES

## Coroners worry Covid-19 test shortages could lead to uncounted deaths

By Blake Ellis, Melanie Hicken and Ashley Fantz, CNN Investigates

Updated 10:33 AM ET, Tue April 7, 2020

## Many Who Need Testing For COVID-19 Fail To Get Access

HEALTH

## Labs are testing 100,000 people each day for the coronavirus. That's still not enough.

Ken Alltucker USA TODAY

Published 6:00 a.m. ET Apr. 2, 2020

T Apr. 2, 2020

nature

NEWS EXPLAINER · 23 MARCH 2020

## Coronavirus tests: researchers chase new diagnostics to fight the pandemic

## WHY WIDESPREAD CORONAVIRUS TESTING ISN'T COMING ANYTIME SOON

By Robert P. Baird

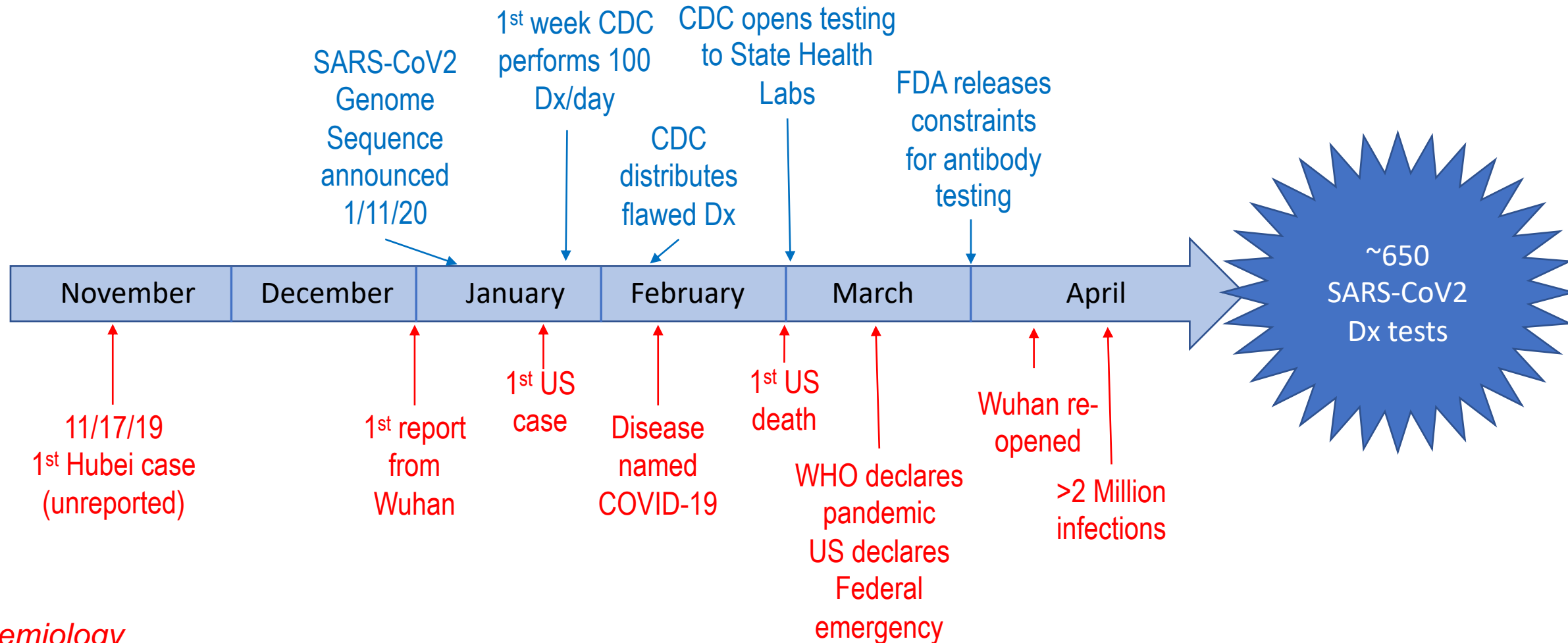
March 24, 2020





# Three Months since Virus Sequenced

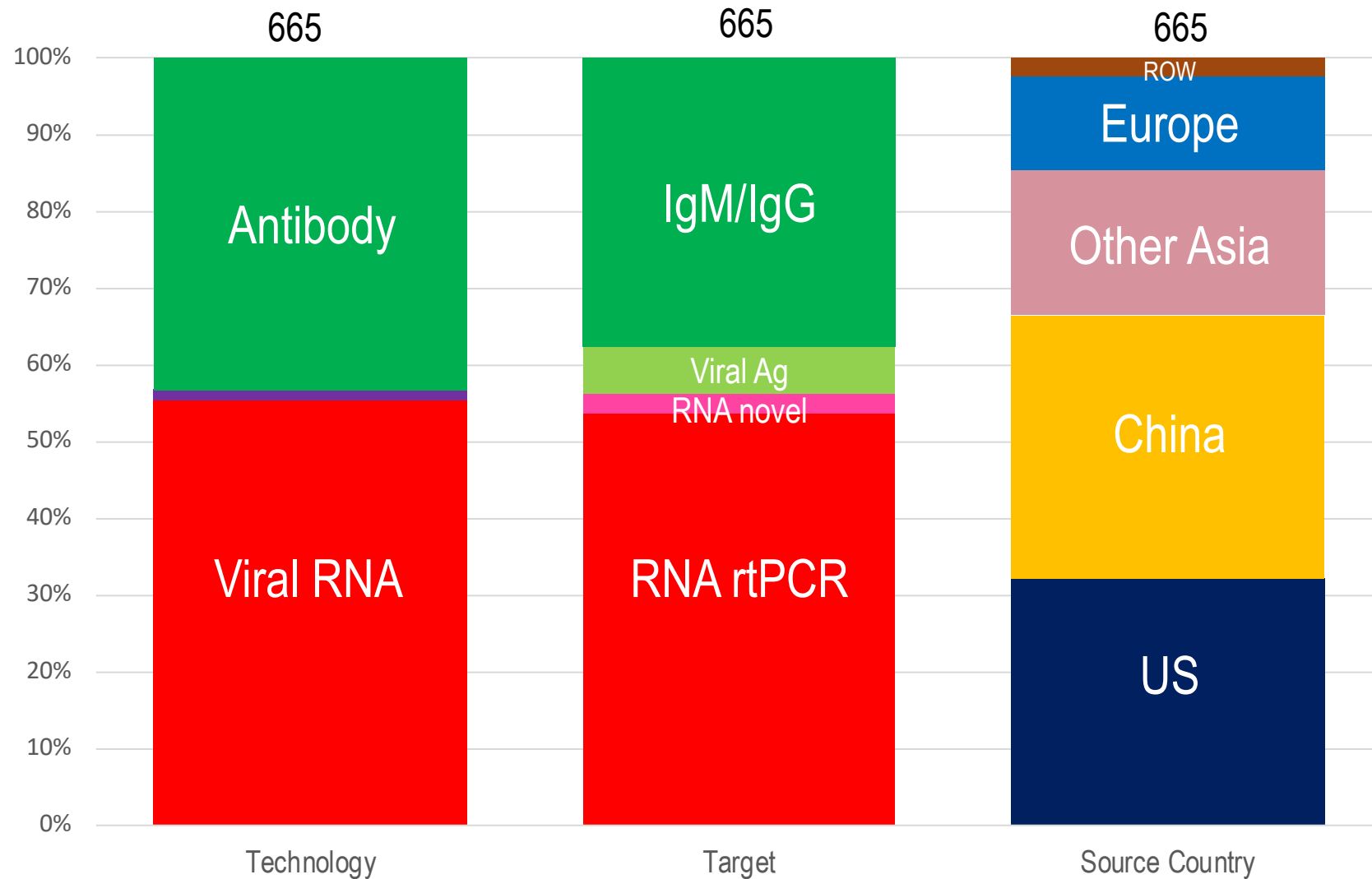
## Dx Testing



## Epidemiology



# Unprecedented # of Tests





# FDA: New Policies / Fast Action / Quality Control?



## Policy/Recommendation Highlights

	Applicable technologies	Validation?	Notification to FDA	EUA to FDA after testing initiated?	Location of Testing
Policy A	molecular, antigen, antibody	Yes	From high complexity lab	Yes	High complexity labs only
Policy B	molecular, antigen, antibody	Yes	From State; encouraged from labs	Not required	High complexity labs in certain states only
Policy C	molecular, antigen, antibody	Yes	From manufacturer	Yes	Clinical labs or point of care; not for home use
Policy D	antibody	Yes	From developer (manufacturer or high complexity lab)	Not required	Clinical labs or point of care; not for home use



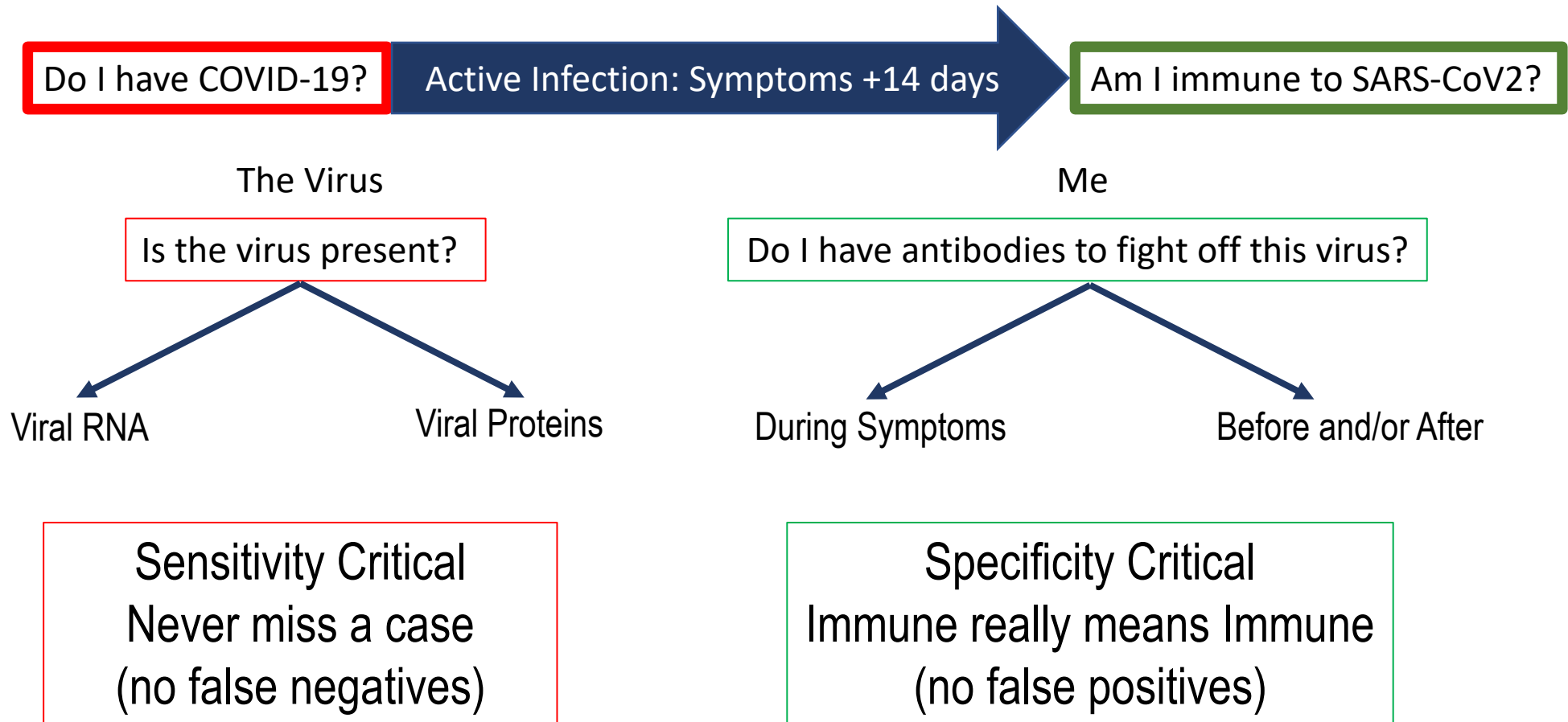
# If there are so many tests – why can't I get one?

- What is the difference between a test for the virus and a test for antibodies for the virus?
- Does it matter if I use a nasal or oral swab; or a spit or sputum; or blood sample?
- How do we use testing to reopen society?



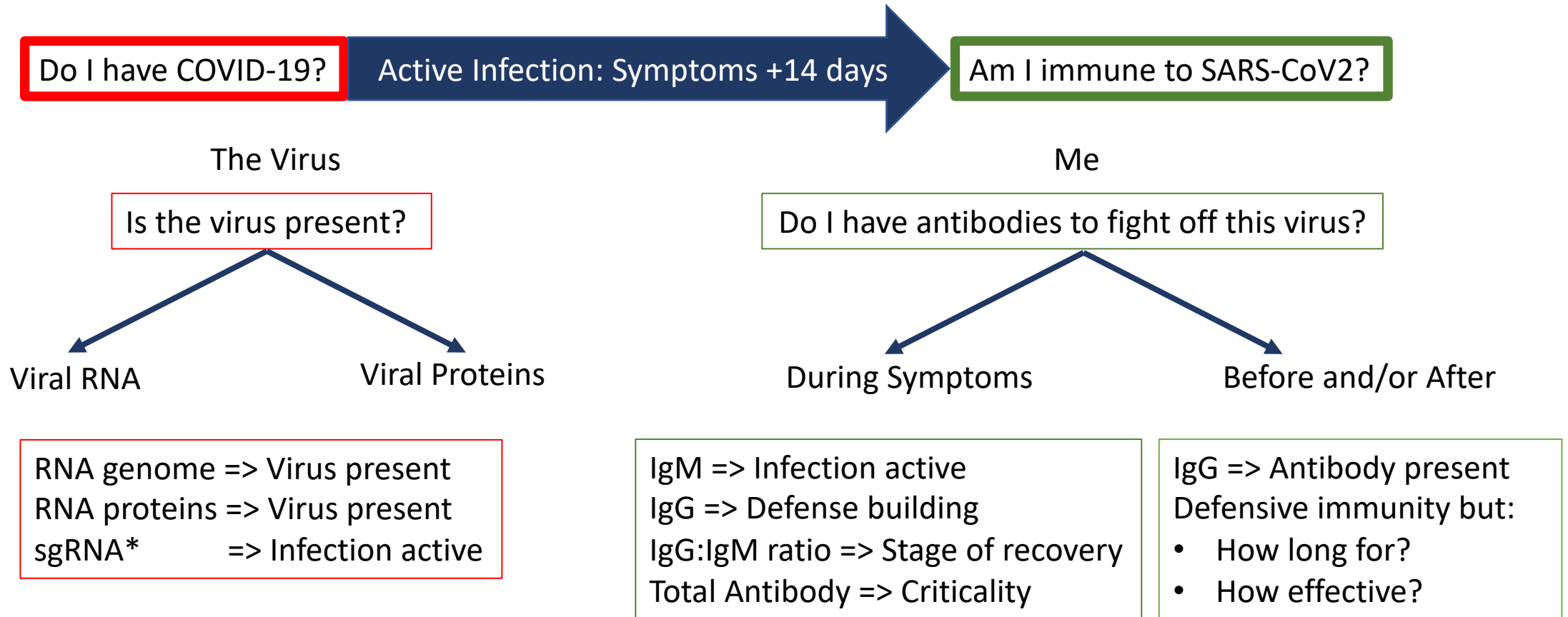


# Two Different Questions *require* Two Very Different Tests





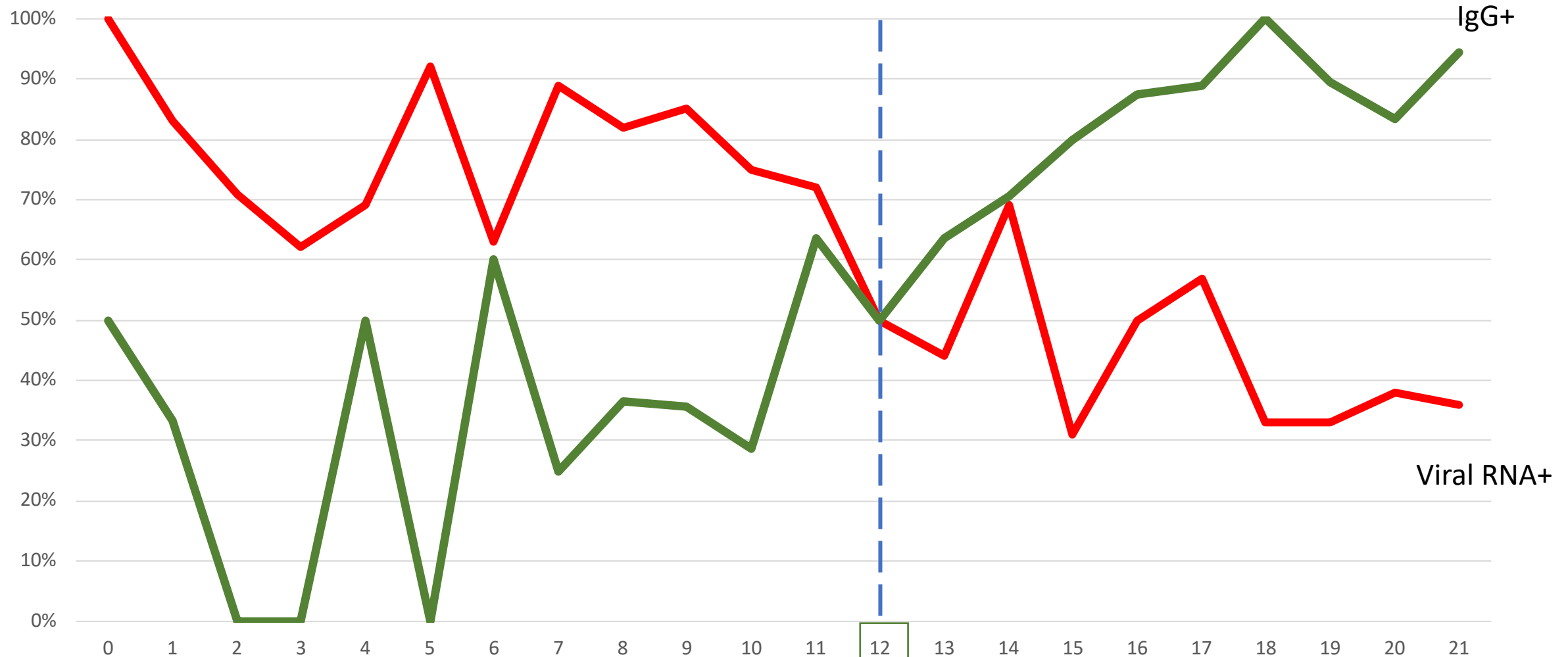
# Two Different Questions *require* Two Very Different Tests



\*sub genomic RNA: small messenger RNA's the virus forces the host cell to make to create essential Virus proteins (rarely clinically tested)



# In COVID-19: IgG rises slowly, Virus active longer



Note: Inpatient 2/6-2/14 PLA Central Command Hospital (n=238 symptomatic patients: 153 rtPCR+; 85 rtPCR-); total Ab stays high in all critically ill and terminal patients)

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# A wide range of technologies (examples)

Do I have COVID-19?

Active Infection: Symptoms +14 days

Am I immune to SARS-CoV2?

**Nucleic Acid Tests**  
(rtPCR primarily)

**Immunoassays**  
(Serology)



Central Lab automated

CDC-type rtPCR lab kit (manual)

Generic manual ELISA kit

Central Lab automated

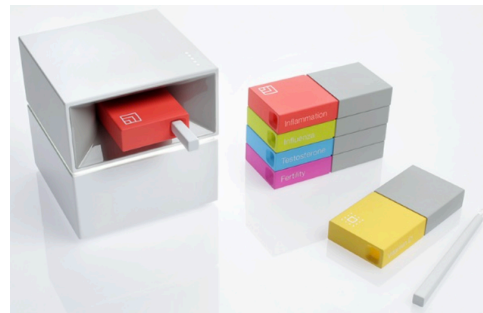


Point of Care Automated

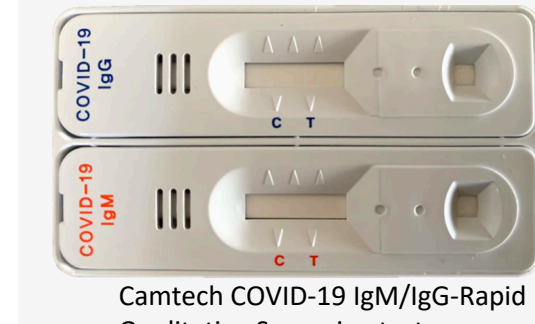
Fingerstick Point of Care

Point of Care Automated

Cepheid  
Gene Expert



Cue



Camtech COVID-19 IgM/IgG-Rapid  
Qualitative Screening test



Luminostics





# Pros and cons of the Different Tests

Do I have COVID-19?

Active Infection: Symptoms +14 days

Am I immune to SARS-CoV2?

**Nucleic Acid Tests**  
(rtPCR primarily)

**Immunoassays**  
(Serology)



- Swabs are non-invasive
- Exquisitely sensitive and specific
  - ~100 viral copies when positive swabs have 300,000+ copies
- But:
- Sampling Hard - Virus is primarily in the lung
  - Nasal and Oral swabs may not reach deep enough
  - Saliva collects more material but is virus captured?
  - Sputum is good, but patients rarely have wet cough
- Cross-patient contamination at sampling will yield false positives
- Central Lab takes a minimum of 24 hours mostly longer
- Inflammatory storm cannot be detected this way and may occur after viral load declines

- Needs blood serum tube or a fingerstick for POC tests
- Sampling technique variation not an issue

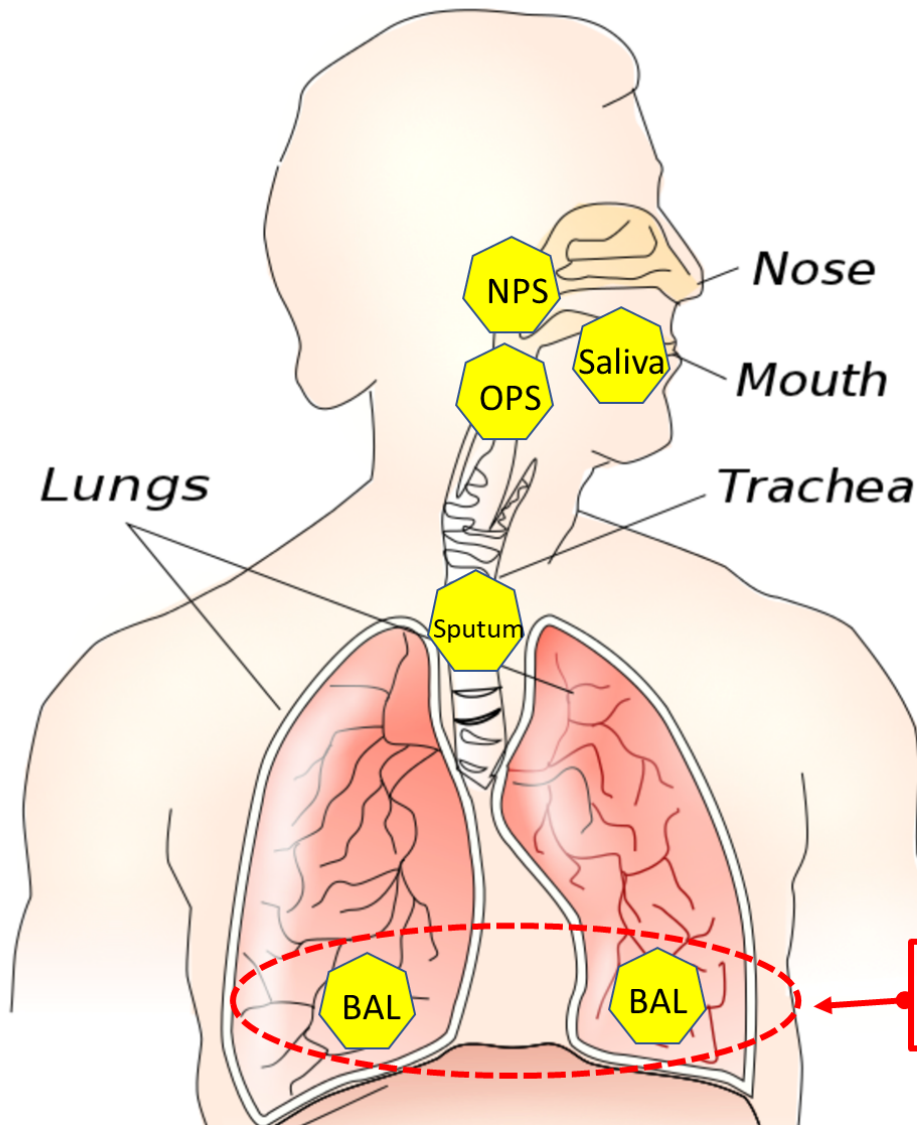
But:

- Antibody design is both an art and a science
  - Vast range of effectiveness for different tests
  - Few companies disclose scientific details
  - 40-90% accuracy
- Cross-reactivity to similar prior diseases can result in false claims of immunity (IgG is present for years)
- False positives dangerous, especially for health care workers
- Immunity value of IgG is unknown (time & effectiveness)



# Effective Sample Taking is Critical

Do I have COVID-19 now?



## Success Rate in Confirmed Patients\*:

- OPS (OroPharangeal Swab): 32%
- NPS (NasalPharangeal Swab): 63%
- Sputum: 90% **BUT** need productive cough
- BAL (Broncho-Alveolar Lavage): 100% **BUT** invasive
- Saliva ?

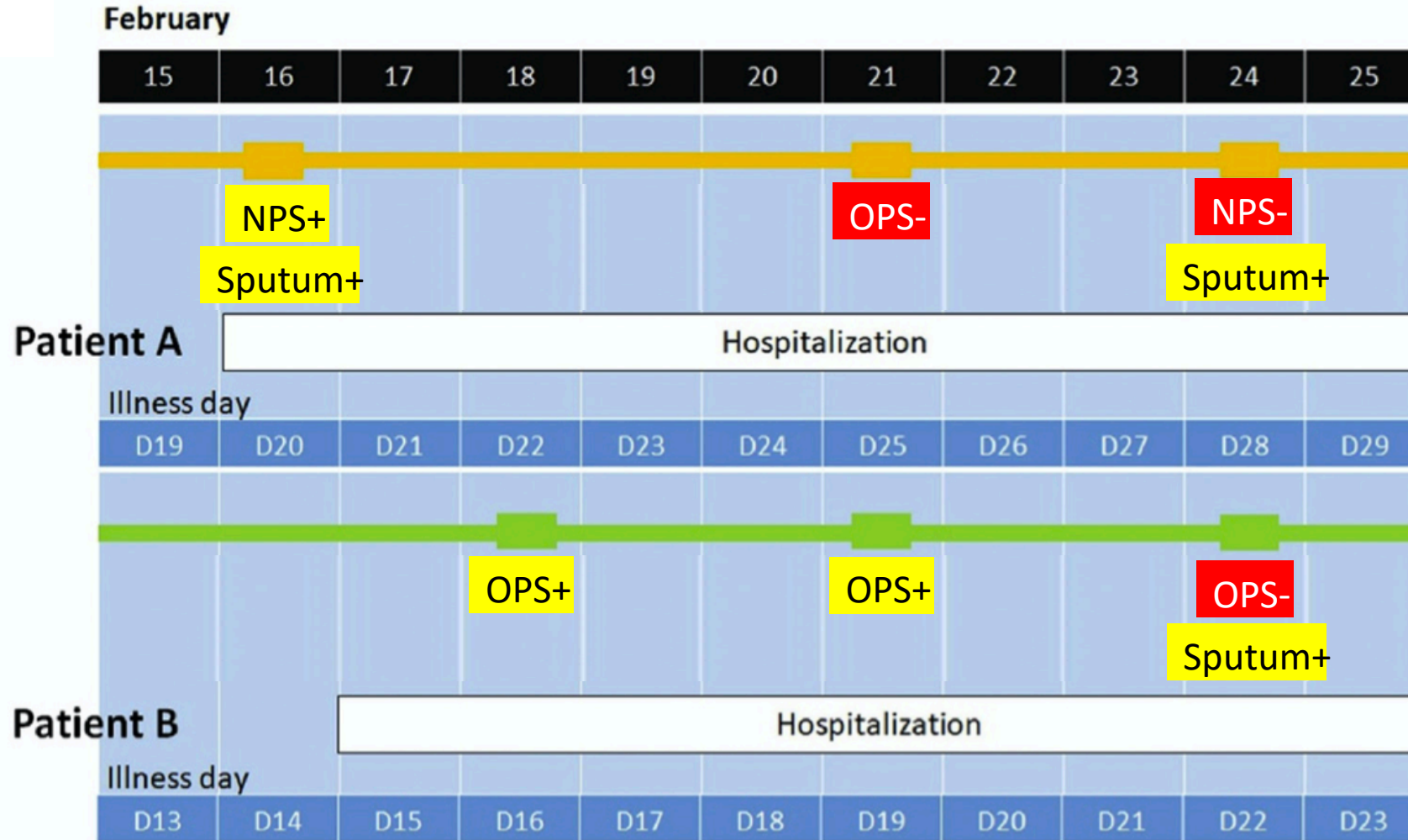
Covid-19 is primarily a Lower Respiratory Infection

\*Source: Wang et al, JAMA March 11, 2020



# Not just which test but how the sample is taken

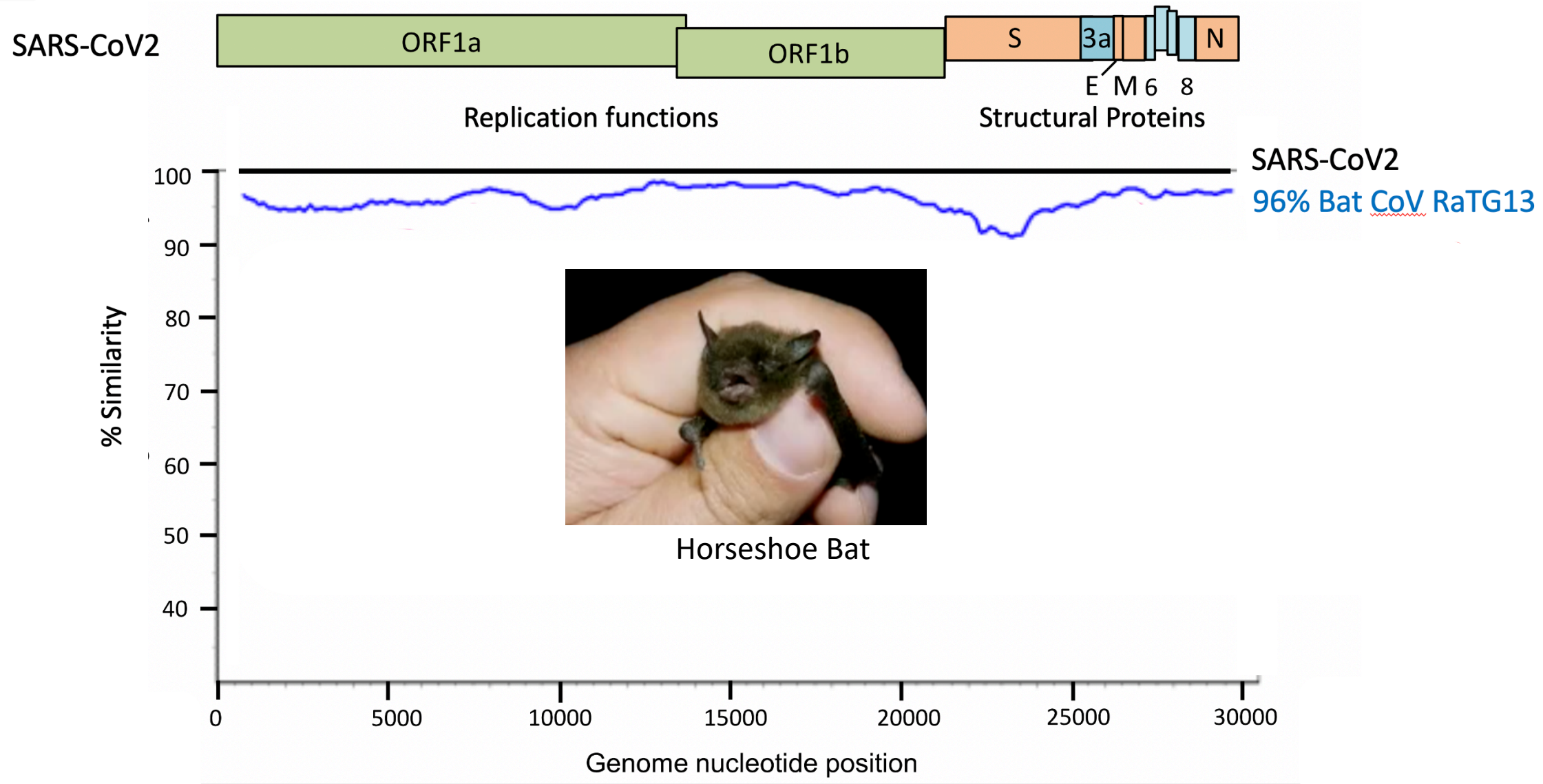
Do I have COVID-19?





Am I immune to SARS=CoV2?

# Need Test that is Unique & Essential to SARS-CoV2

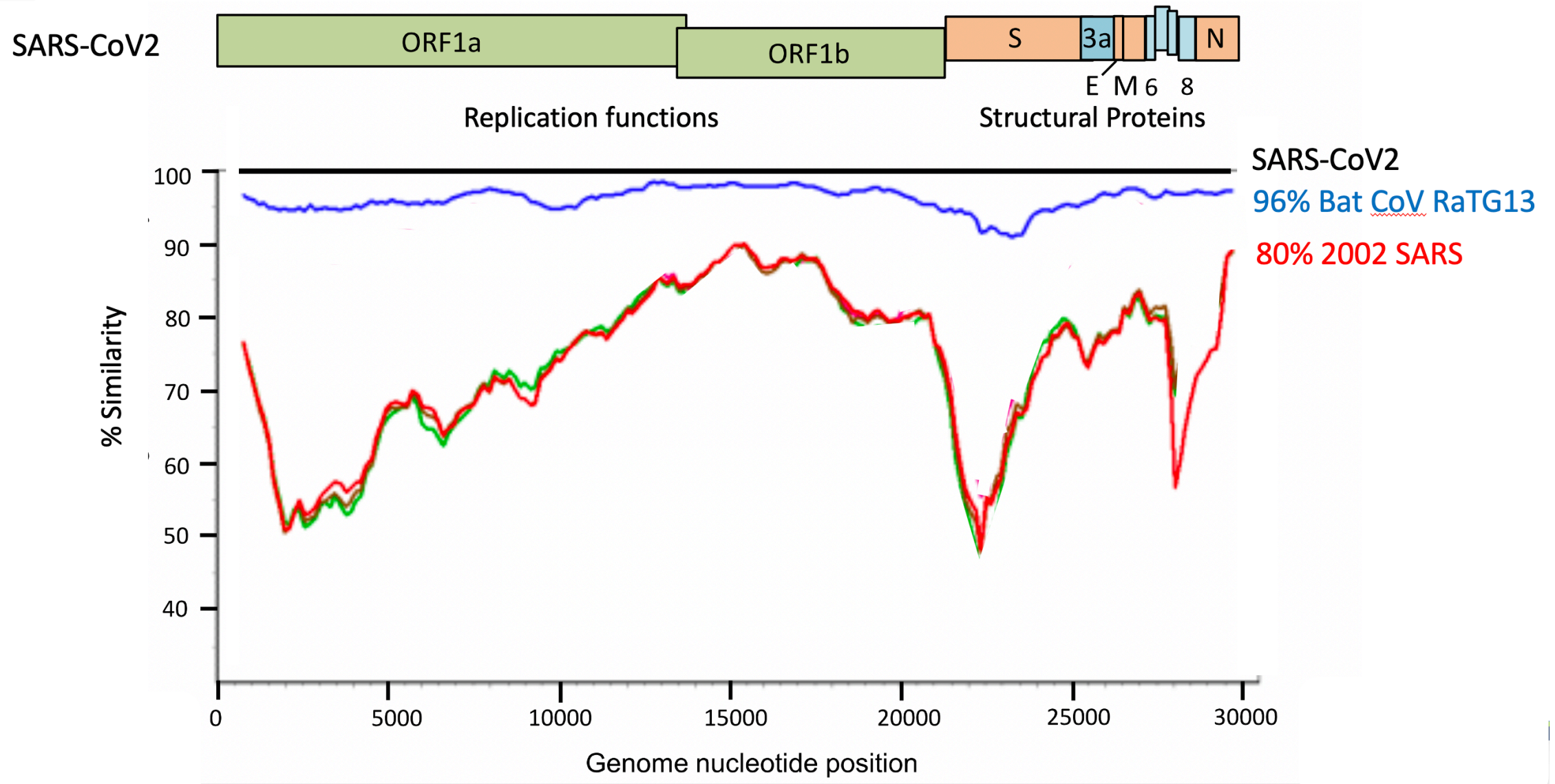






Am I immune to SARS-CoV2?

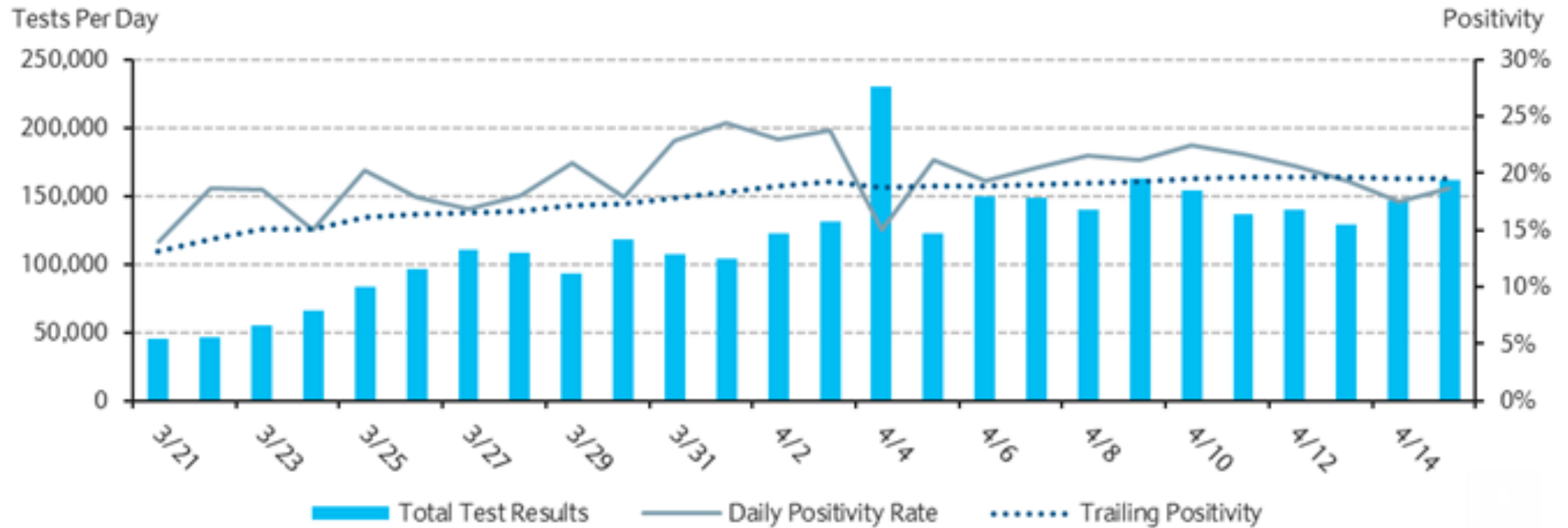
# Need Test that is Unique & Essential to SARS-CoV2





# Tests per Day and Positivity Rate

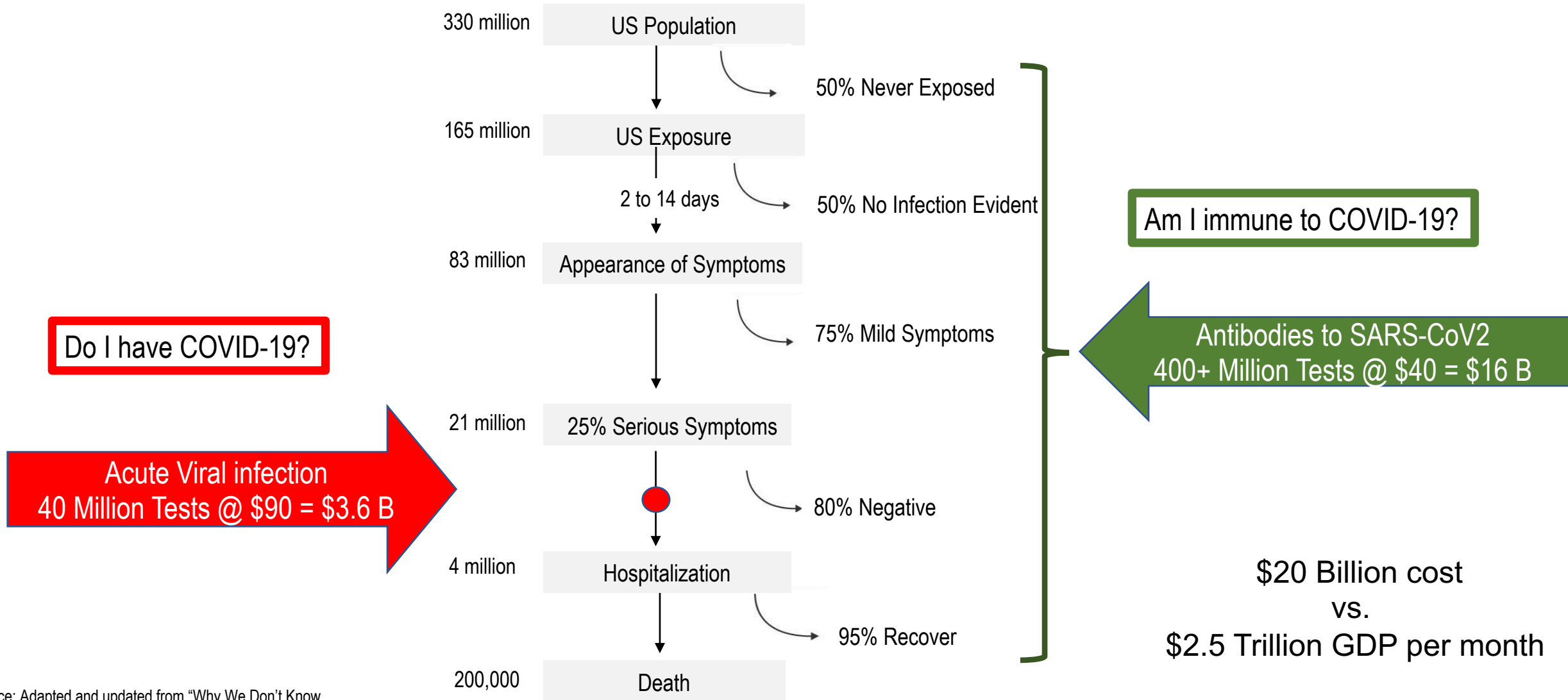
United States: Tests Run Per Day and Positivity Rate



Source: Barclays Research, <https://covidtracking.com/data/us-daily>



# The Immense Dx Challenge



Source: Adapted and updated from "Why We Don't Know How Many Americans Are Infected With Coronavirus—and Might Never Know". WSJ 4/4/20



# What should be done going forward?

1. Testing must increase 10-fold from current levels
  - Widely available tests with validation data with active CDC/FDA policing for defective or misleading claims
  - All testing must be free to all
  - Consumer Viral and Antibody self sampling and full at home kits needed ASAP
2. Effective treatment protocols established
  - Nationwide data collection on current hospital practices - integration with implications rapidly disseminated
  - Adaptive clinical trials (like NCI MATCH basket trials) with Phase IV type data collected
3. Effective case and positive contact tracing
  - Isolation based on comprehensive contact tracing (Smart Phone enabled)
4. Intelligent, focused quarantine & isolation practices
  - Patient segmentation (recovered, immune, age, existing co-morbidities)
  - SMSA / County specific
5. Hospitals to be re-engineered for adaptability to infectious disease surges



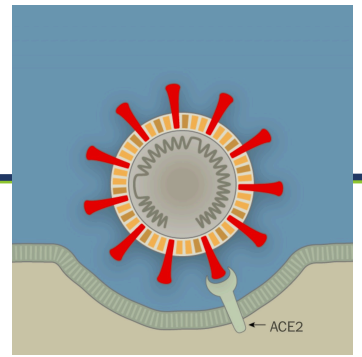
**Thank you**

**Mara G. Aspinall**

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# Simplified COVID-19 pathology



Immunity

Day 1 Virus Binds  
epithelial cell  
ACE2 receptor

Lack of ACE2  
constricts  
blood vessels

Blood pressure rises  
to compensate

Cell no longer  
able to  
transport  $O_2$

Heart stressed to  
increase  $O_2$  delivery

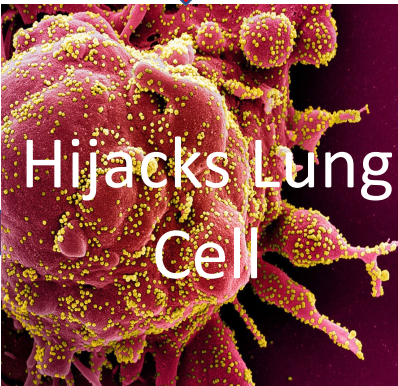
Exhausted Cell dies  
12-24 hours later

Immune system  
over-reacts

Heart  
Failure

Multiple  
organ failure

Death



Hijacks Lung  
Cell

1-10,000  
Virions  
released to  
local tissue

pinall

t Permission