

COMPLIMENTARY ACCREDITED WEBINAR

THE UNPREDICTABLE RESPIRATORY SEASON: INFLUENZA AND COVID-19

September 21, 2021

11:00 a.m. – 12:00 p.m. ET / 5:00 – 6:00 p.m. CET

This webinar is sponsored by:



The speakers are presenting on behalf of Abbott.

The information presented is consistent with applicable FDA guidelines.

This program does not provide continuing medical education (CME) credits.

Disclosures

Receiving honorarium, Abbott

No conflicts

Learning Objectives

- Provide an update on influenza A&B and COVID-19 infections and variants
- Summarize steps healthcare systems are taking to prepare for the upcoming (and uncertain) respiratory season
- Describe use cases and testing scenarios for molecular and antigen testing - what works, when and where
- Apply practical experience and evidence to the use of rapid influenza (and COVID-19) testing in improving efficiencies of care, operations, and workflow

Polling Question #1

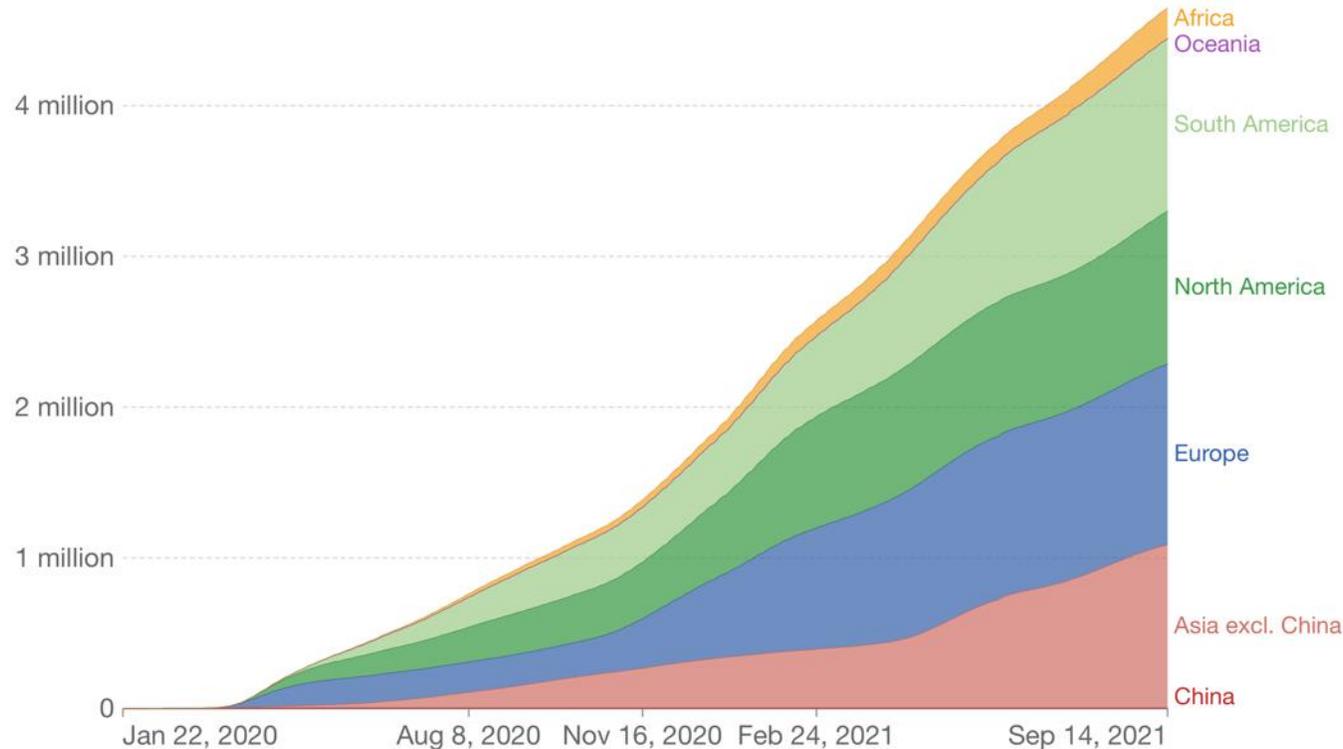
We CURRENTLY use **RAPID COVID-19 TESTING** in the following settings: (select all that apply)

- A. Emergency room
- B. Inpatient
- C. Pre-surgical
- D. Outpatient/Clinic
- E. Pharmacy
- F. Skilled Nursing/Long Term Care
- G. School
- H. Workplace
- I. Other
- J. None of our testing is rapid

COVID-19

Cumulative confirmed COVID-19 deaths

Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the actual number of deaths from COVID-19.



Source: Johns Hopkins University CSSE COVID-19 Data – Last updated 15 September, 18:03 (London time)
OurWorldInData.org/coronavirus • CC BY

- Global pandemic; began in Wuhan, Hubei Province, China, in late 2019.
- Caused by SARS-CoV-2 coronavirus.
- Has since spread worldwide, with > 4 million deaths so far.

Impact of COVID-19 Pandemic

• GLOBALLY

- Worst crash of global stock markets since 1987
- Jan – Feb 2020:
G20 economies fell 3.4% year-on-year
- April - June 2020:
International Labour Organization estimated that an equivalent of 400 million full-time jobs were lost across the world
- Jan – Sept 2020:
Global worker income earnings fell 10%, equivalent to a loss of over US\$3.5 trillion

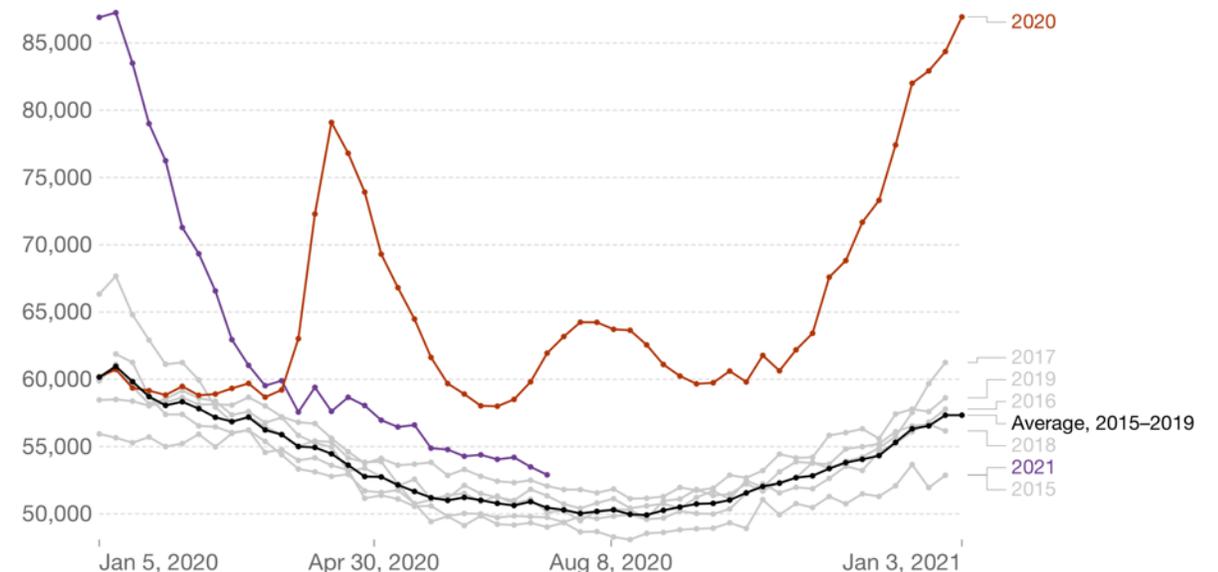
• U.S.

- 2020 GDP contracted at 3.5% annualized rate - biggest contraction since 1946, the first contraction since 2009

Excess mortality: Number of deaths from all causes compared to previous years, United States

Our World
in Data

Shown is how the number of weekly or monthly deaths in 2020–2021 differs from the number of deaths in the same period over the years 2015–2019. The reported number of deaths might not count all deaths that occurred due to incomplete coverage and delays in death reporting.



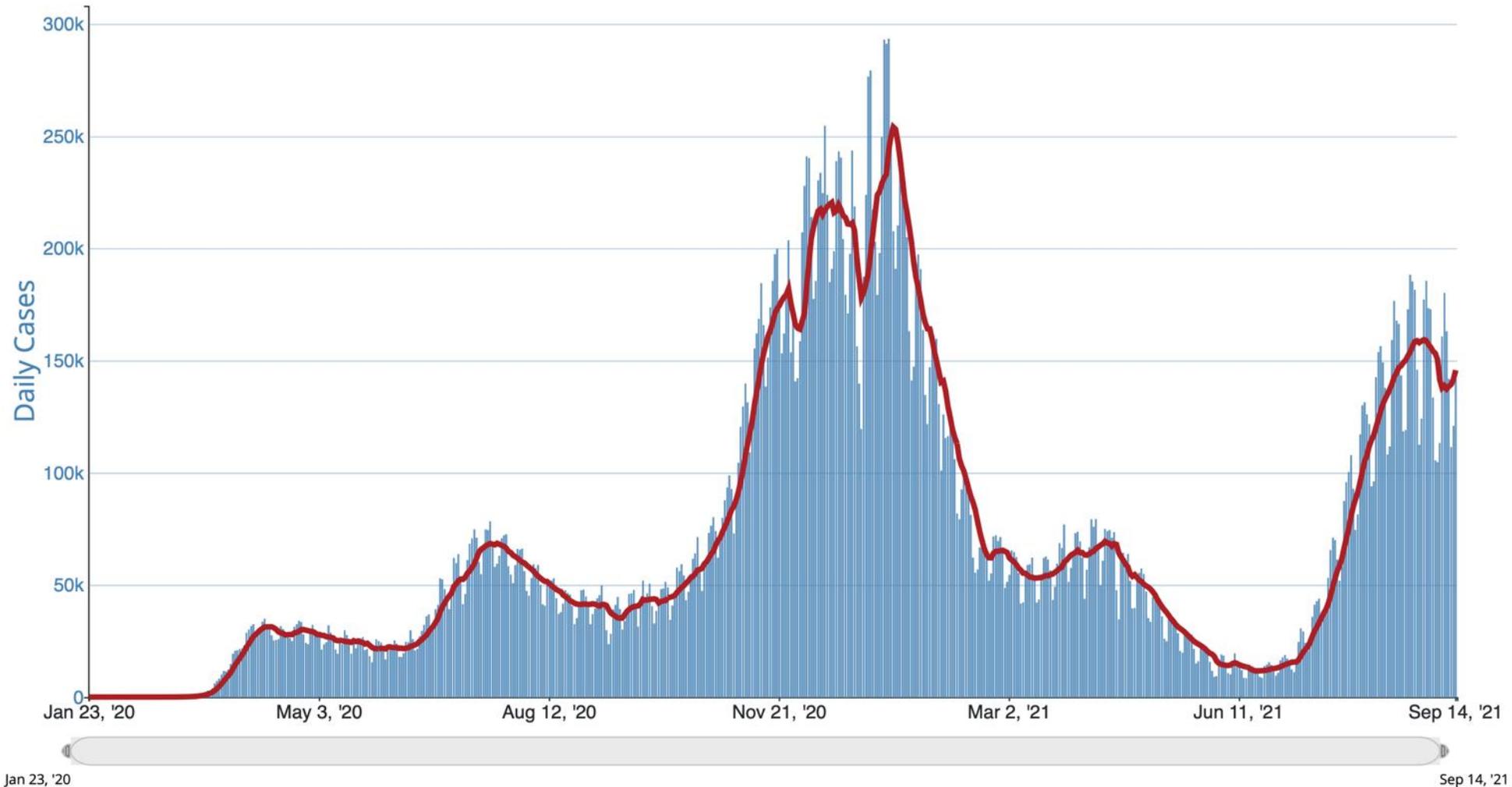
Source: Human Mortality Database (2021), World Mortality Dataset (2021)

OurWorldInData.org/coronavirus • CC BY

Note: Comparisons across countries are affected by differences in the completeness of death reporting. Details can be found at our Excess Mortality page.

COVID-19 Cases in the U.S.

Daily Trends in Number of COVID-19 Cases in The United States Reported to CDC

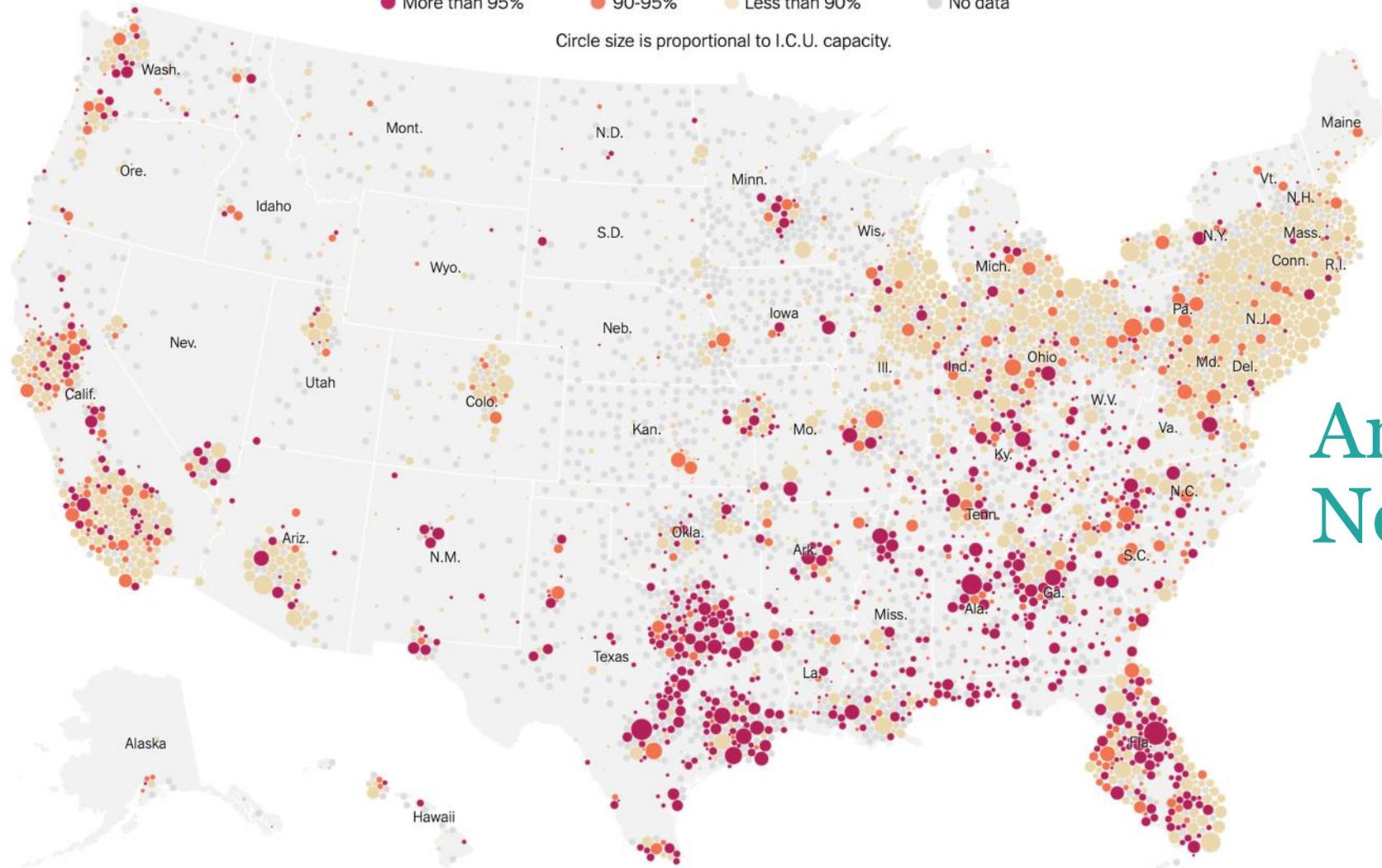


The New York Times

Share of I.C.U. beds occupied in each hospital

● More than 95% ● 90-95% ● Less than 90% ● No data

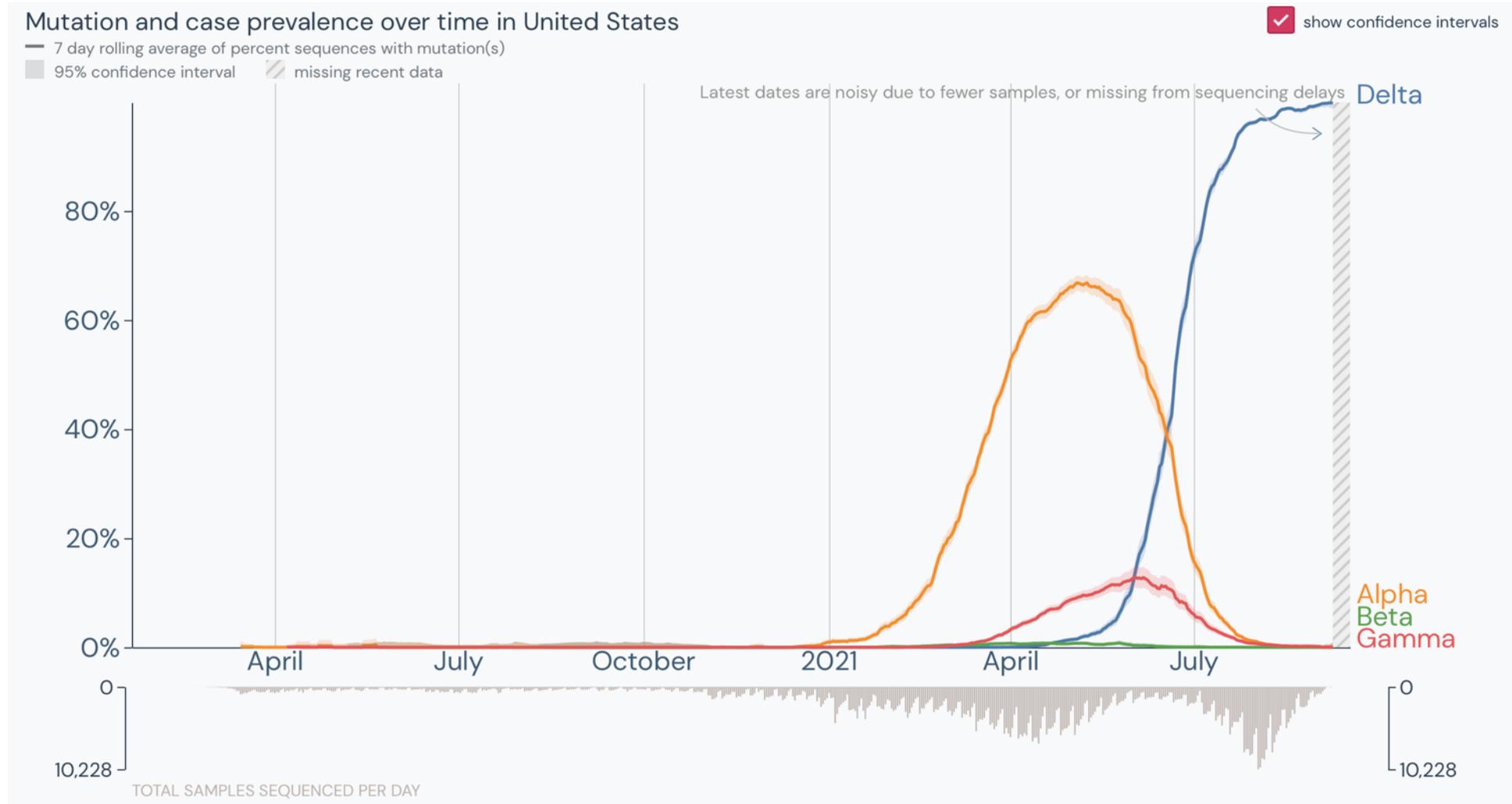
Circle size is proportional to I.C.U. capacity.



And In Your Neighborhood

Source: U.S. Department of Health and Human Services data. Notes: Some patient counts are not available because H.H.S. obscures weekly totals lower than four. Data is as of the week ending Sept. 9. Hospital locations are adjusted so that all hospitals are shown without overlapping.

The Rise of the Variants



COVID-19 WHO Variant Types

VARIANT OF INTEREST

A SARS-CoV-2 variant:

- ...with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape;
AND
- ...identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health.

VARIANT OF CONCERN

A SARS-CoV-2 variant that:

- ...meets the definition of a VOI and ...
- has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:
 - Increase in transmissibility or detrimental change in COVID-19 epidemiology; **OR**
 - Increase in virulence or change in clinical disease presentation; **OR**
 - Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.

Current Variants of Interest

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Eta	B.1.525	G/484K.V3	21D	Multiple countries, Dec-2020	17-Mar-2021
Iota	B.1.526	GH/253G.V1	21F	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21B	India, Oct-2020	4-Apr-2021
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021
Mu	B.1.621	GH	21H	Colombia, Jan-2021	30-Aug-2021

As of Sept 15, 2021

*includes all descendent lineages. The full list of Pango lineages can be found here: https://cov-lineages.org/lineage_list.html; for FAQ, visit: <https://www.pango.network/faqs/>

Current Variants of Concern

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Additional amino acid changes monitored ^o	Earliest documented samples	Date of designation
Alpha	B.1.1.7 #	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 [§]	G/478K.V1	21A	+S:417N	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

As of Sept 15, 2021

Where is Delta Now?

SARS-CoV-2 Variants by Country/Area

Variant

Delta (B.1.617.2)

Verification



Verified

Unverified

Total

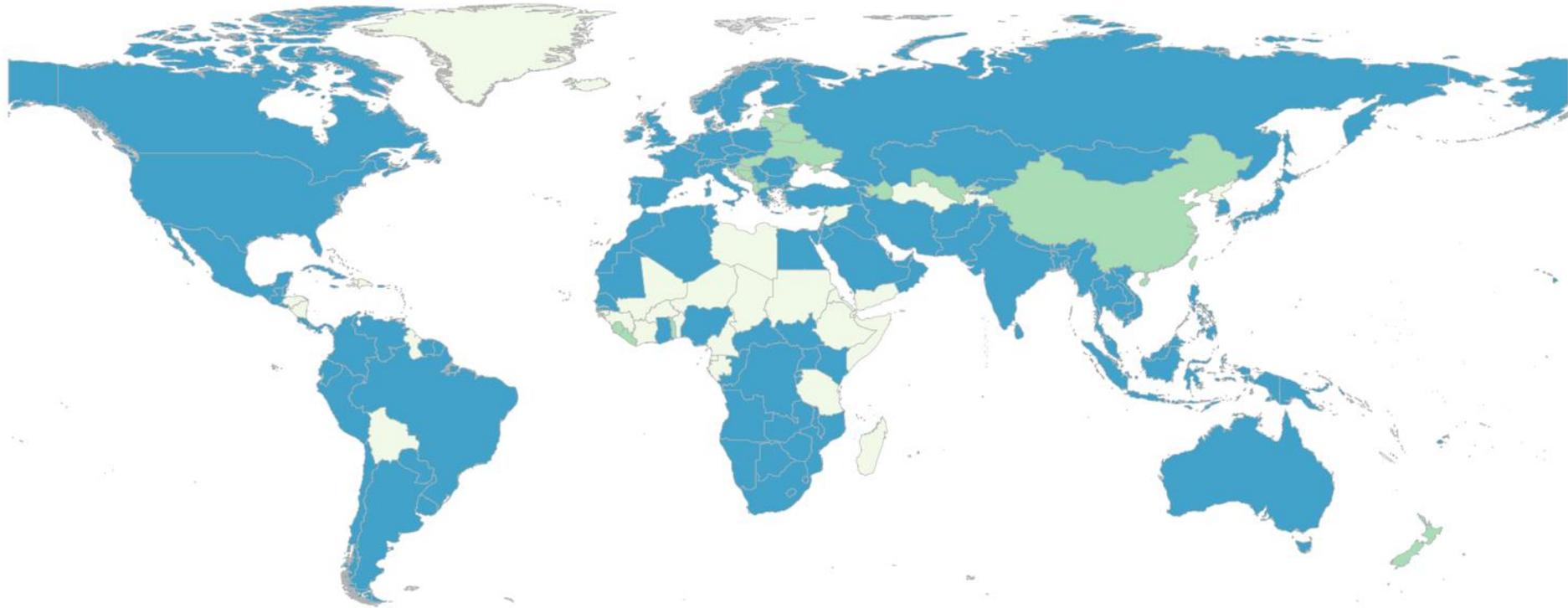
Number of Locations

143

27

170

The map shows which countries have reported variants of SARS-CoV-2, as defined by the World Health Organization (WHO). Country specific designations of notable variants may differ. Because of differences in detection and reporting, variants could be present in some countries that have not yet reported them. The lack of reporting does not indicate the variant is absent in that country. Labels assigned by [WHO](#) are presented. Variant names in parentheses are according to the dynamic nomenclature guidelines implemented in [Pango](#). Data were provided by the World Health Organization (WHO) Variant Tracker. For more information on variants, please see <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance.html>



Verification ● Not reported ● Unverified ● Verified

SARS-CoV-2 Genome

- SARS-CoV-2 has a linear, positive-sense, single-stranded RNA genome about 30,000 bases long.
- Encodes several different proteins.
- Spike protein responsible for cell binding and entry. Target of all current vaccines.
- Other proteins serve structural and non-structural roles.
- Mutations in all genes are found in different variants.
- Mutations in non-spike genes likely contribute to increased virulence and transmissibility of variants

The SARS-CoV-2 Genome



Alpha vs. Delta Mutations

ALPHA

First identified in United Kingdom

VARIANT OF CONCERN

List of mutations

Mutations in at least 75% of Alpha sequences ([read more](#))

[Compare to other lineages](#)

[View S-gene mutations](#)



DELTA

First identified in India

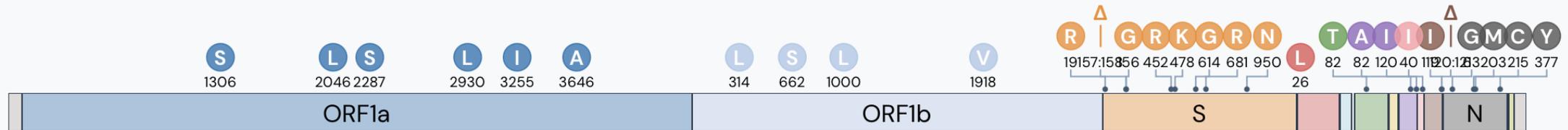
VARIANT OF CONCERN

List of mutations

Mutations in at least 75% of Delta sequences ([read more](#))

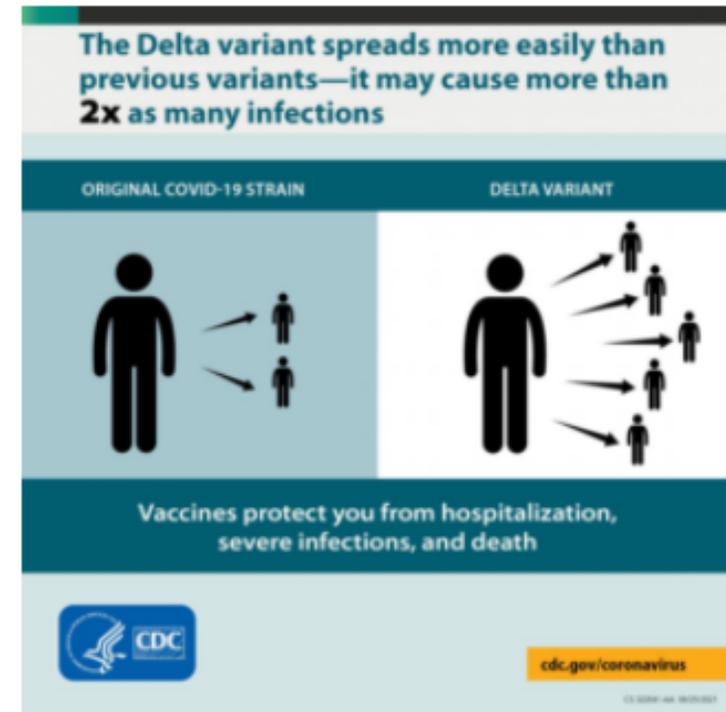
[Compare to other lineages](#)

[View S-gene mutations](#)



Delta Variant

- **The Delta variant is more contagious:** The Delta variant is highly contagious, more than 2x as contagious as previous variants.
- **Some data suggest the Delta variant might cause more severe illness than previous variants in unvaccinated people.** In two different studies from Canada and Scotland, patients infected with the Delta variant were more likely to be hospitalized than patients infected with Alpha or the original virus that causes COVID-19. Even so, the vast majority of hospitalization and death caused by COVID-19 are in unvaccinated people.
- **Unvaccinated people remain the greatest concern:** The greatest risk of transmission is among unvaccinated people who are much more likely to get infected, and therefore transmit the virus. Fully vaccinated people get COVID-19 (known as [breakthrough infections](#)) less often than unvaccinated people. People infected with the Delta variant, including fully vaccinated people with symptomatic breakthrough infections, can transmit the virus to others. CDC is continuing to assess data on whether fully vaccinated people with asymptomatic breakthrough infections can transmit the virus.
- **Fully vaccinated people with Delta variant breakthrough infections can spread the virus to others. However, vaccinated people appear to spread the virus for a shorter time:** For prior variants, lower amounts of viral genetic material were found in samples taken from fully vaccinated people who had breakthrough infections than from



[View Larger](#)

After Delta became the most common variant,*
fully vaccinated people had reduced risk[†] of...

INFECTION

5X

HOSPITALIZATION

>10X

DEATH

>10X

**Vaccination offers strong
protection against COVID-19**



bit.ly/MMWR91021

* June 20-July 17, 2021

[†] Compared with people not fully vaccinated

MMWR



Disclaimer: Early release articles are not considered as final versions. Any changes will be reflected in the online version in the month the article is officially released.

Volume 27, Number 10—October 2021

Dispatch

Breakthrough Infections of SARS-CoV-2 Gamma Variant in Fully Vaccinated Gold Miners, French Guiana, 2021

Nicolas Vignier¹✉, Vincent Bérot¹, Nathalie Bonnavé, Sandrine Peugny, Mathilde Ballet, Estelle Jacoud, Céline Michaud, Mélanie Gaillet, Félix Djossou, Denis Blanchet, Anne Lavergne, Magalie Demar, Mathieu Nacher, Dominique Rousset, and Loïc Epelboin

Author affiliations: Institut Pierre Louis d'Épidémiologie et de Santé Publique Inserm UMR1136, Paris, France (N. Vignier); Université Sorbonne Paris Nord, Bobigny, France (N. Vignier); Centre Hospitalier de Cayenne, Cayenne, French Guiana (N. Vignier, V. Bérot, N. Bonnavé, S. Peugny, E. Jacoud, C. Michaud, M. Gaillet, F. Djossou, D. Blanchet, M. Demar, M. Nacher, L. Epelboin); Centre d'Investigation Clinique Antilles Guyane Inserm 1424, Cayenne (N. Vignier, M. Nacher, L. Epelboin); Centre Hospitalier Ouest Guyanais, Saint Laurent du Maroni, French Guiana (V. Bérot); Agence Régionale de la Santé de Guyane, Cayenne (M. Ballet); Institut Pasteur de la Guyane, Cayenne (A. Lavergne, D. Rousset)

[Suggested citation for this article](#)

Abstract

An outbreak of severe acute respiratory syndrome coronavirus 2 caused by the Gamma variant of concern infected 24/44 (55%) employees of a gold mine in French Guiana (87% symptomatic, no severe forms). The attack rate was 60% (15/25) among fully vaccinated miners and 75% (3/4) among unvaccinated miners without a history of infection.

On This Page

[The Study](#)

[Conclusions](#)

[Suggested Citation](#)

Figures

[Figure](#)

Tables

[Table](#)

One more US Designation

VARIANT OF HIGH CONSEQUENCE

In addition to the possible attributes of a variant of concern

- **Impact on Medical Countermeasures (MCM)**

- Demonstrated failure of diagnostic test targets
- Evidence to suggest a significant reduction in vaccine effectiveness, a disproportionately high number of vaccine breakthrough cases, or very low vaccine-induced protection against severe disease
- Significantly reduced susceptibility to multiple Emergency Use Authorization (EUA) or approved therapeutics
- More severe clinical disease and increased hospitalizations

A variant of high consequence would require notification to WHO under the International Health Regulations, reporting to CDC, an announcement of strategies to prevent or contain transmission, and recommendations to update treatments and vaccines.

Currently, there are no SARS-CoV-2 variants that rise to the level of high consequence.

Polling Question #2

We would like/plan to expand **RAPID COVID-19 TESTING** into the following settings:
(select all that apply)

- A. Emergency room
- B. Inpatient
- C. Pre-surgical
- D. Outpatient/Clinic
- E. Pharmacy
- F. Skilled Nursing/Long Term Care
- G. School
- H. Workplace
- I. Other
- J. None of our testing is rapid

Vaccine and Transmission

NEJM, August 19, 2021, Effect of Vaccination on Household Transmission of SARS-CoV-2 in England

Table 1. Numbers of Household Contacts and Secondary Cases of Covid-19, According to Vaccination Status of Index Patient, and Adjusted Odds Ratios.*

Vaccination Status of Index Patient	Household Contacts	Secondary Cases	Adjusted Odds Ratio (95% CI)
	<i>no.</i>	<i>no. (%)</i>	
Not vaccinated before testing positive	960,765	96,898 (10.1)	Reference
Vaccinated with ChAdOx1 nCoV-19 vaccine ≥21 days before testing positive	3,424	196 (5.7)	0.52 (0.43–0.62)
Vaccinated with BNT162b2 vaccine ≥21 days before testing positive	5,939	371 (6.2)	0.54 (0.47–0.62)

* Odds ratios were adjusted for the age and sex of the index patient and their household contact, geographic region, calendar week of the index case, and an index of multiple deprivation and household type and size. CI denotes confidence interval, and Covid-19 coronavirus disease 2019.

Vaccine and Transmission

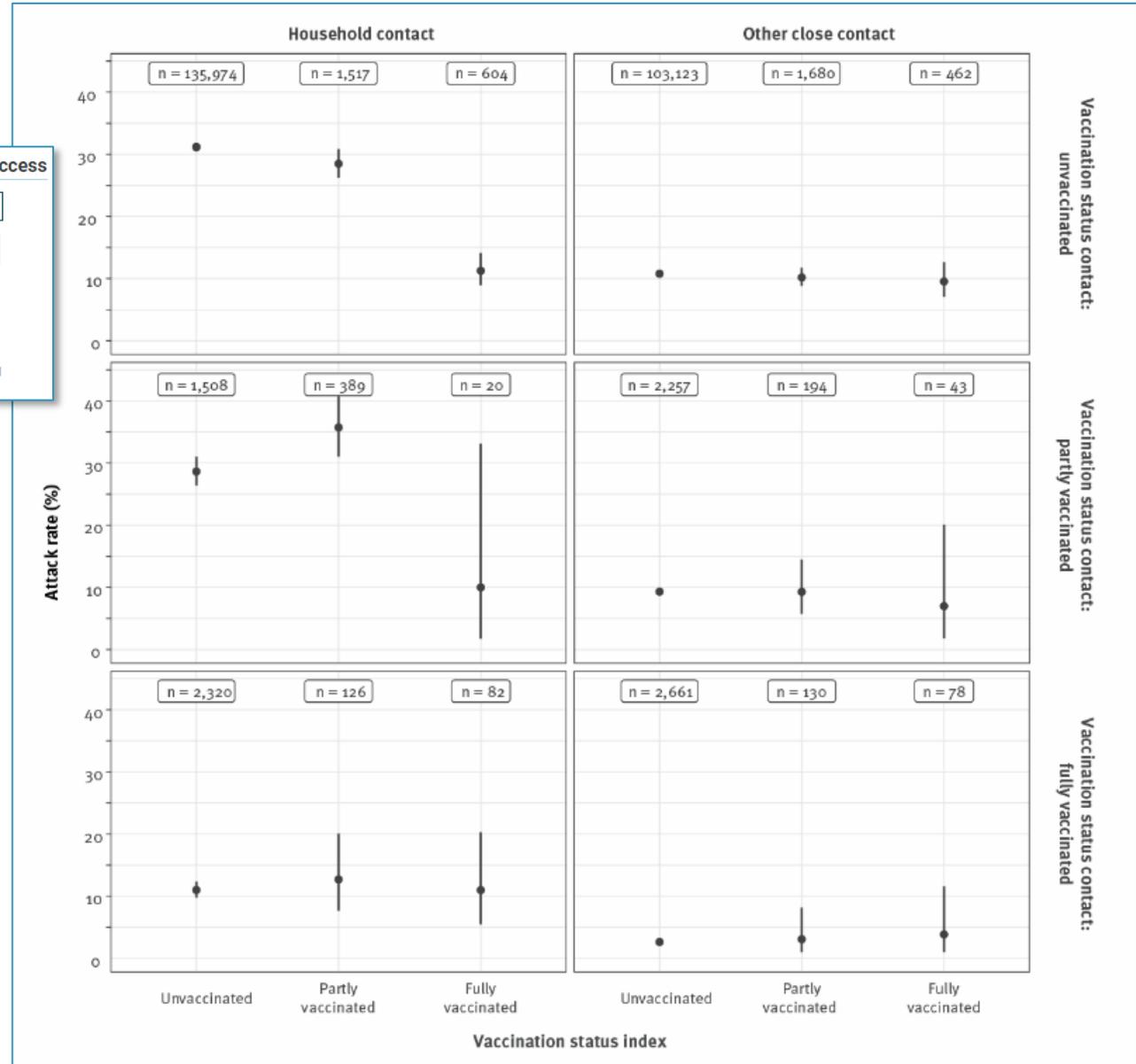
Rapid communication

Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021 | [Open Access](#)

[Check for updates](#)

Brechje de Gier¹, Stijn Andeweg¹, Rosa Joosten¹, Ronald ter Schegget², Naomi Smorenburg¹, Jan van de Kasstelee¹, RIVM COVID-19 surveillance and epidemiology team^{1,3}, Susan JM Hahné¹, Susan van den Hof¹, Hester E de Melker¹, Mirjam J Knol¹

de Gier B, Andeweg S, Joosten R, et al. Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021. *Euro Surveill.* 2021;26(31):2100640.



Sustained Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Associated Hospitalizations Among Adults — United States, March–July 2021

Summary

What is already known about this topic?

COVID-19 mRNA vaccines provide strong protection against severe COVID-19; however, the duration of protection is uncertain.

What is added by this report?

Among 1,129 patients who received 2 doses of a mRNA vaccine, no decline in vaccine effectiveness against COVID-19 hospitalization was observed over 24 weeks. Vaccine effectiveness was 86% 2–12 weeks after vaccination and 84% at 13–24 weeks. Vaccine effectiveness was sustained among groups at risk for severe COVID-19.

What are the implications for public health practice?

mRNA vaccine effectiveness against COVID-19–associated hospitalizations was sustained over 24 weeks; ongoing monitoring is needed as new SARS-CoV-2 variants emerge. To reduce hospitalization, all eligible persons should be offered COVID-19 vaccination.

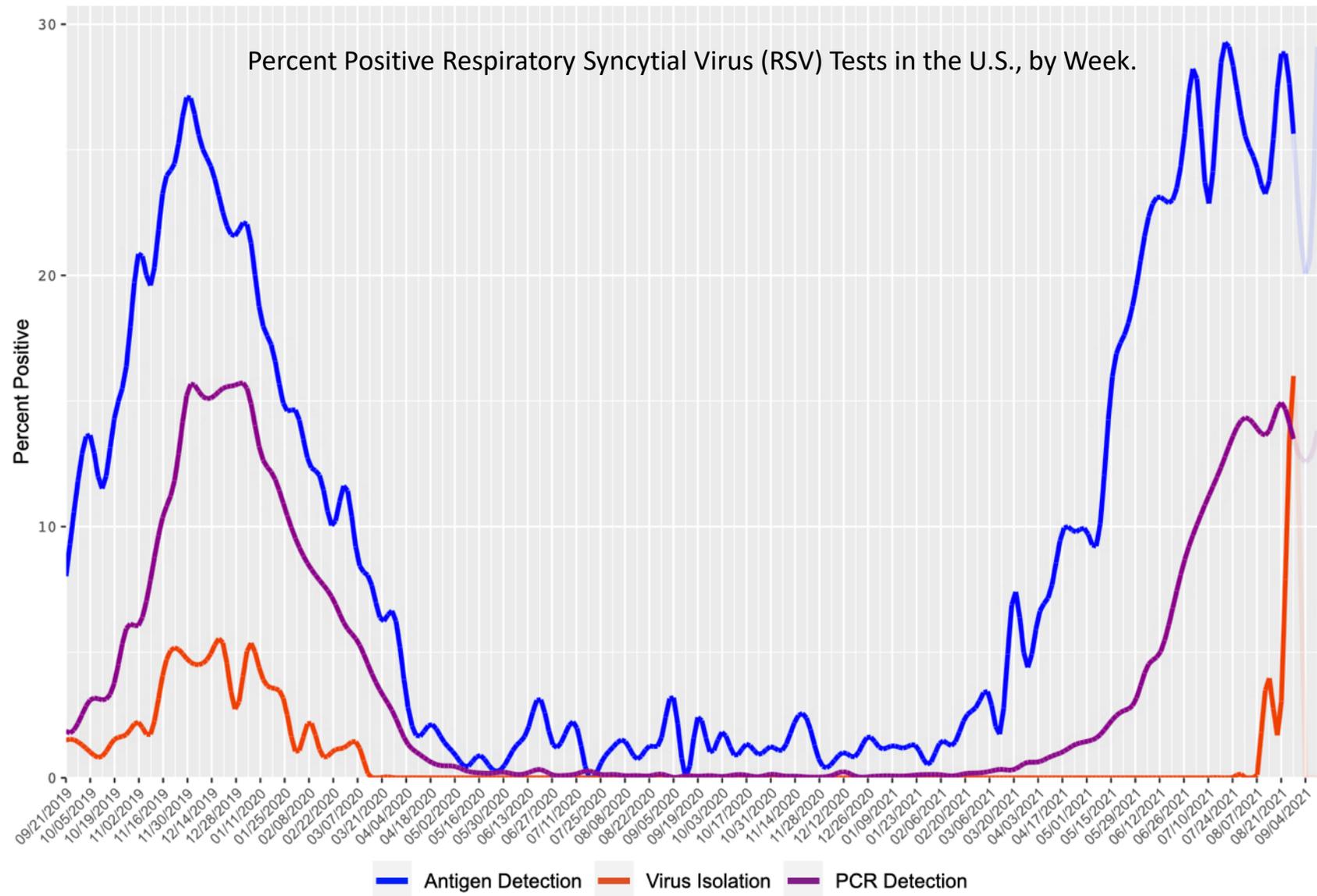


**RESPIRATORY
SYNCYTIAL
VIRUS (RSV)**

INFLUENZA

Other Viruses

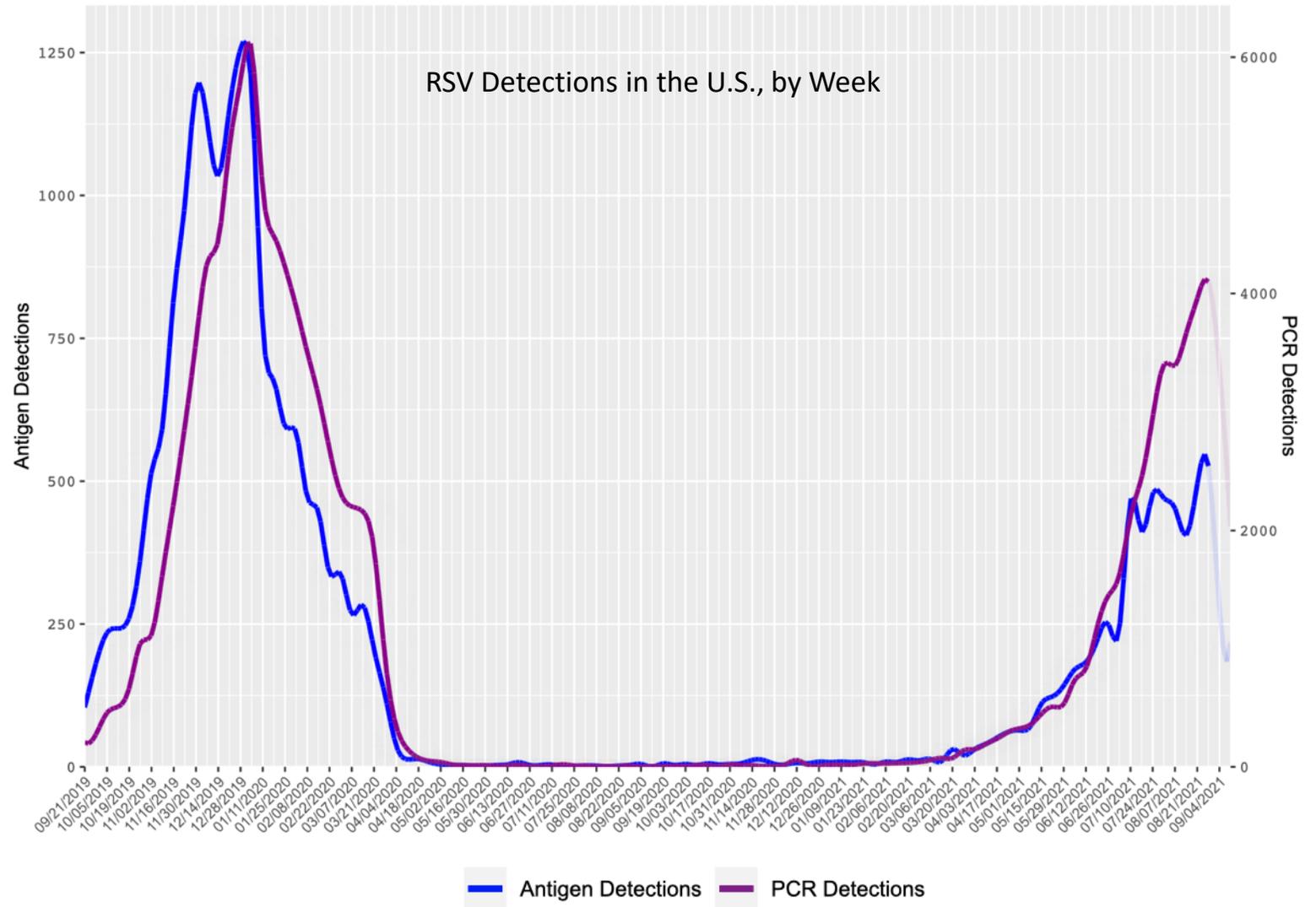
Because It's Not All About COVID-19
(I Know That's Hard To Believe)



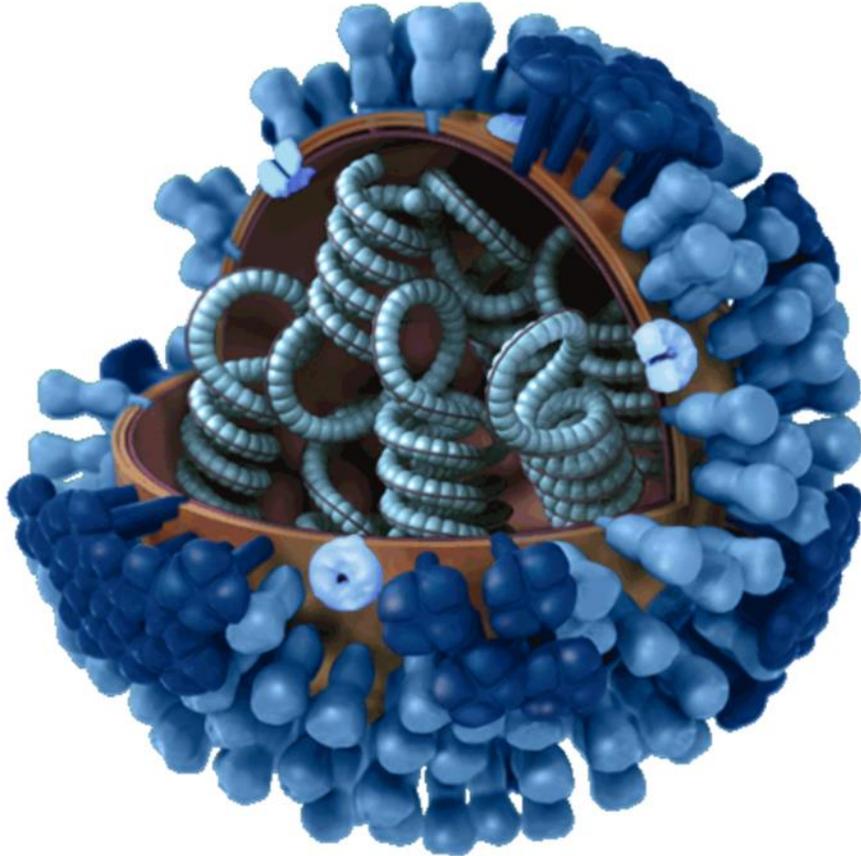
A Summer RSV Spike!!

RSV Absolute Numbers

May reflect changes in testing practice as well as incidence.



Influenza – It's not Just 'the Flu'



- **In the U.S., 5-20% of the population gets influenza each year¹**
 - 200,000 hospitalizations, 12,000 – 79,000 deaths²
- **Worldwide, 3-5 million severe cases³**
 - 290,000-650,000 deaths per year^{3,4}
- **That's an average; a pandemic would greatly increase these numbers**
 - And, also drives us all berserk with no notice as in April-May 2009.
 - But you know that now.

CDC, Influenza Virus.

<https://www.cdc.gov/flu/resource-center/freeresources/graphics/images.htm>

1. CDC. Key facts about influenza. <https://www.cdc.gov/flu/about/keyfacts.htm>, accessed Sept 15, 2021.

2. CDC, Frequently Asked Questions about Estimated Flu Burden. <https://www.cdc.gov/flu/about/burden/faq.htm#hospitalizations>, accessed Sept 15, 2021.

3. WHO launches new global influenza strategy. <https://www.who.int/news/item/11-03-2019-who-launches-new-global-influenza-strategy>, accessed Sept 15, 2021.

4. CDC. Seasonal flu death estimate increases worldwide. <https://www.cdc.gov/media/releases/2017/p1213-flu-death-estimate.html>, accessed Sept 15, 2021.

Last Year Was Just Strange

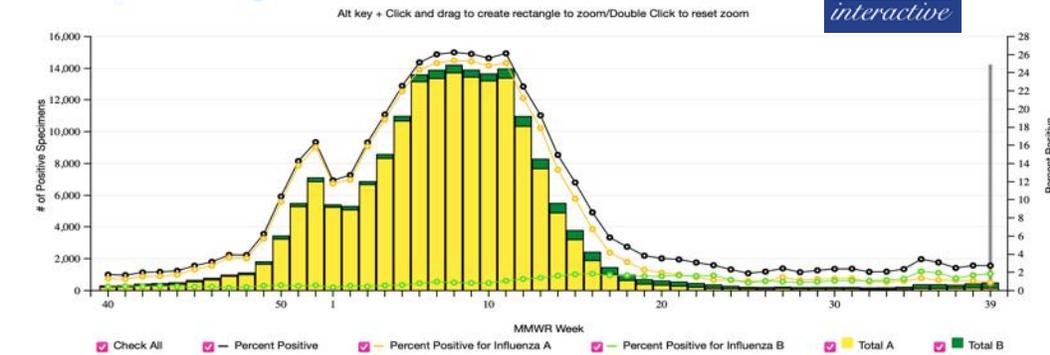
- At first glance these three graphs appear similar; with peak levels of influenza early in the year.
- The abrupt ending in 2019-20 is remarkable; a combination of societal shutdown ending the season abruptly and all of us stopping flu testing to devote resources to COVID.
- But...look at the Y axes.

2018-19

Influenza Positive Tests Reported to CDC by Clinical Laboratories, National Summary, 2018-19 Season, week ending Sep 28, 2019
Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet

[Download Image](#) [Download Data](#)

FLUVIEW
interactive

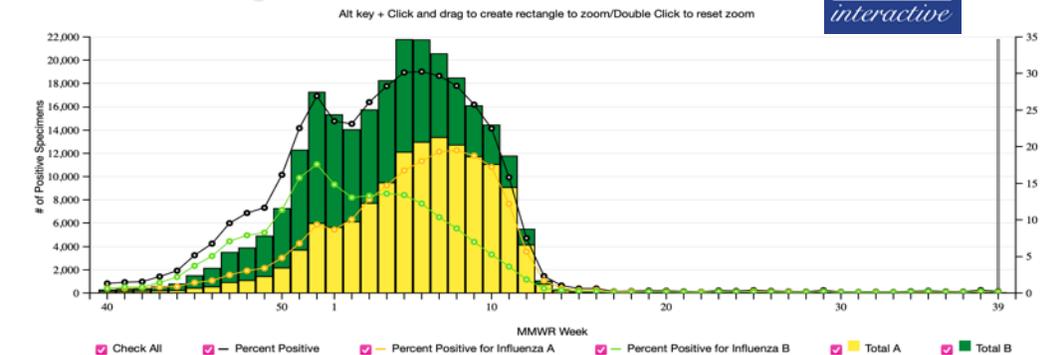


2019-20

Influenza Positive Tests Reported to CDC by Clinical Laboratories, National Summary, 2019-20 Season, week ending Sep 26, 2020
Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet

[Download Image](#) [Download Data](#)

FLUVIEW
interactive

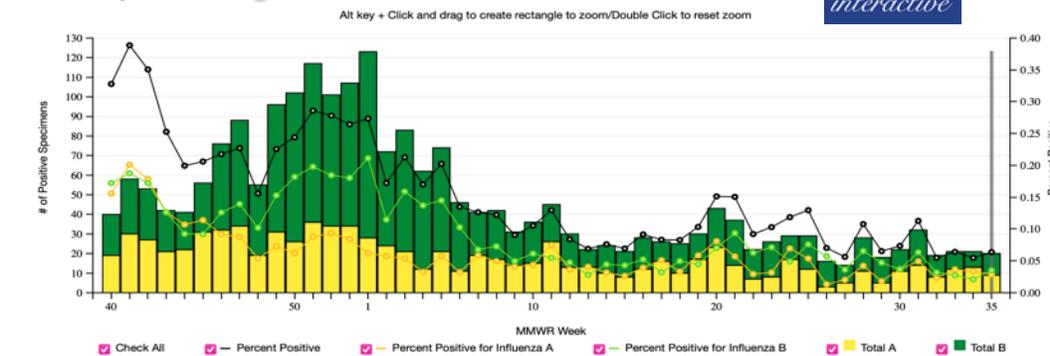


2020-21

Influenza Positive Tests Reported to CDC by Clinical Laboratories, National Summary, 2020-21 Season, week ending Sep 04, 2021
Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet

[Download Image](#) [Download Data](#)

FLUVIEW
interactive



Last Year Was Just Strange

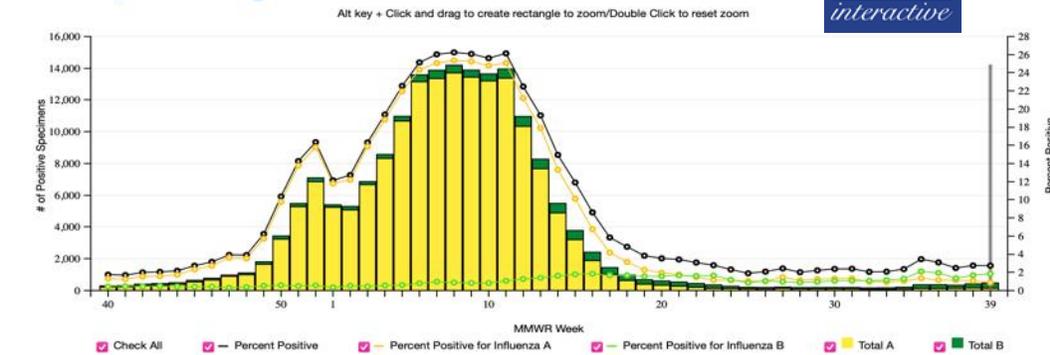
- At first glance these three graphs appear similar; with peak levels of influenza early in the year.
- The abrupt ending in 2019-20 is remarkable; a combination of societal shutdown ending the season abruptly and all of us stopping flu testing to devote resources to COVID.
- But...look at the Y axes.

2018-19

16,000

Influenza Positive Tests Reported to CDC by Clinical Laboratories, National Summary, 2018-19 Season, week ending Sep 28, 2019
Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet

[Download Image](#) [Download Data](#)

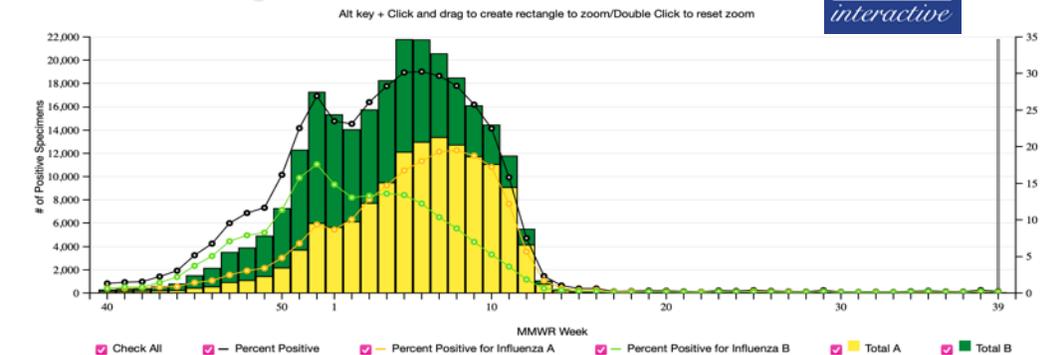


2019-20

22,000

Influenza Positive Tests Reported to CDC by Clinical Laboratories, National Summary, 2019-20 Season, week ending Sep 26, 2020
Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet

[Download Image](#) [Download Data](#)

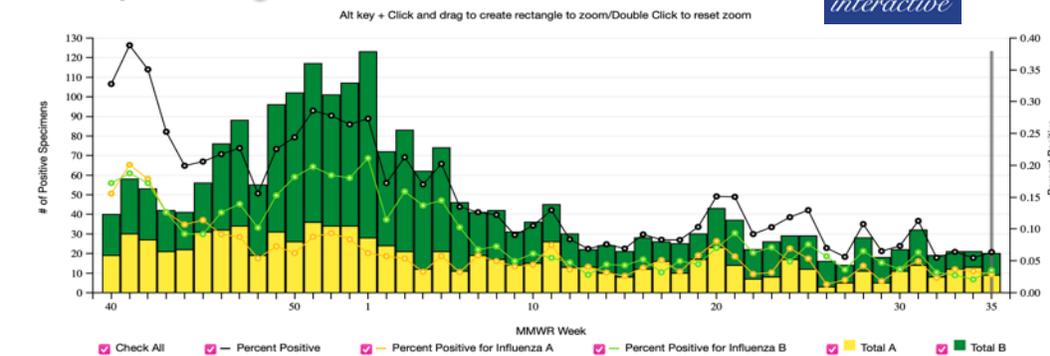


2020-21

130

Influenza Positive Tests Reported to CDC by Clinical Laboratories, National Summary, 2020-21 Season, week ending Sep 04, 2021
Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet

[Download Image](#) [Download Data](#)



Why?

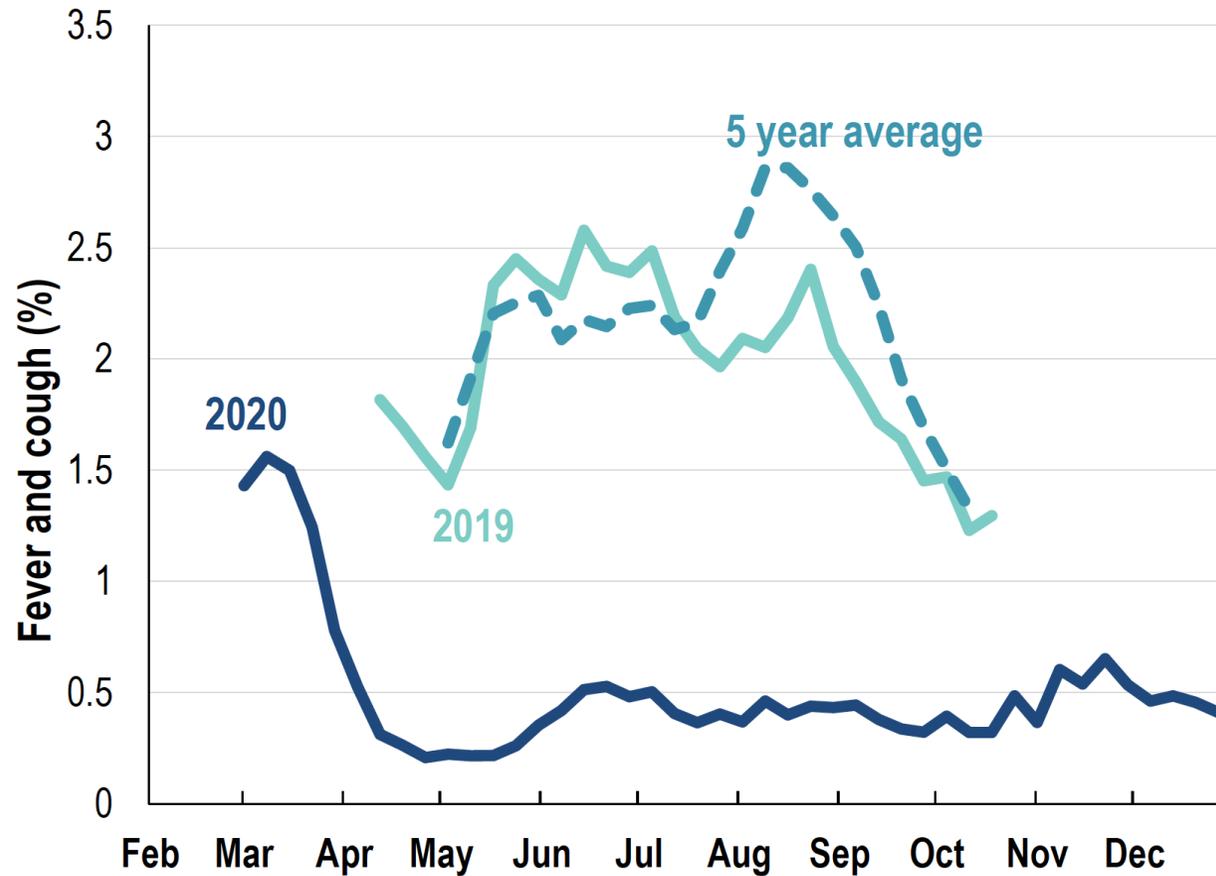
- Decreased transmission due to masks and social distancing?
- Decreased testing; due to competition for resources with COVID, decreased likelihood of seeking care for minor illnesses?
- Some sort of biological competition with SARS-CoV-2?
- Increased vaccine coverage
(probably not, since preliminary numbers suggest 55% in adults)¹

1. <https://www.cdc.gov/flu/fluview/dashboard/vaccination-adult-coverage.html>

We Were Warned, Though

Influenza-like illness activity:

Fever and cough: 0.4% this week (flu-like illness activity is historically low)



*5 year average is calculated using 2015, 2016, 2017, 2018 and 2019 data

^ Data are age standardised in this chart

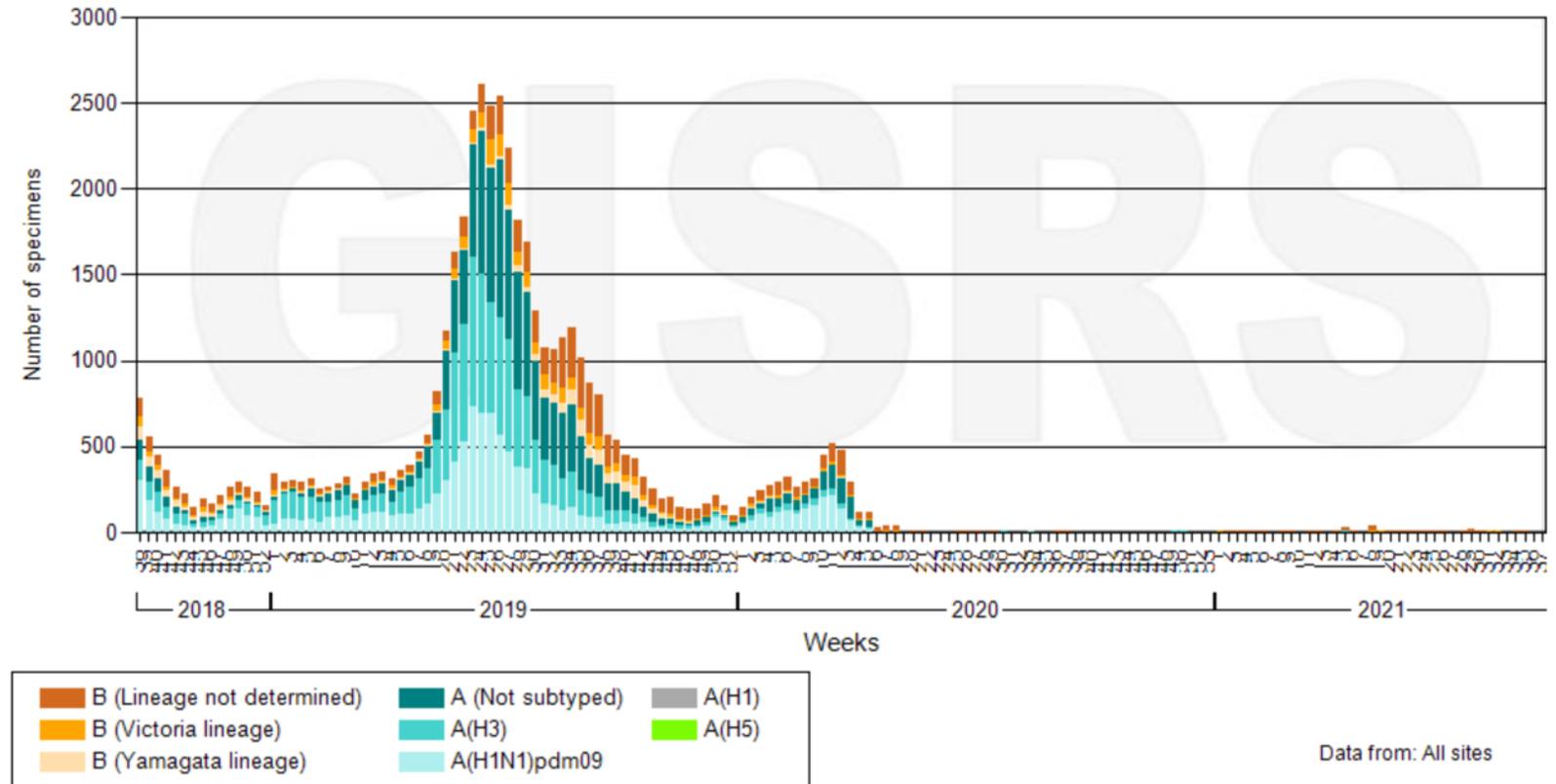
This Year Looks Similar

Southern Hemisphere data from WHO FluNet

But, maybe we can't bet on it. Could it be partly due to changes in testing resources?

Southern hemisphere

Number of specimens positive for influenza by subtype



Data source: FluNet (www.who.int/fluNet), GISRS

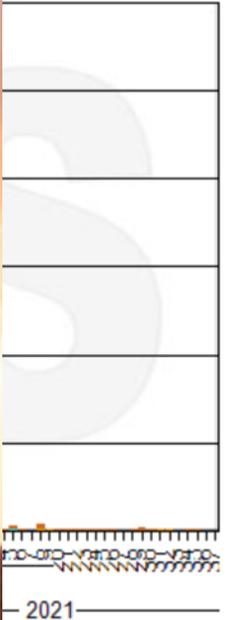
© World Health Organization 2021

This Year
Similar

Southern
data from
WHO FL

But, may
bet on it
partly d
in testin

THE CALM BEFORE THE STORM?



Data from: All sites
World Health Organization 2021

Polling Question #3

How important will a COVID-19/influenza differential diagnosis be during flu season?

- a) Very Important
- b) Important
- c) Indifferent
- d) Unimportant
- e) Very unimportant



Testing for COVID-19; Why and How and When and All That

Because I'm a Diagnostics Guy at Heart...

Why Test for SARS-CoV-2 in our Health System?

“ WHAT A STUPID QUESTION, CAMPBELL! IT’S THE BIGGEST THING THIS CENTURY. ”

3 (SOMEWHAT CONFUSING AND OCCASIONALLY-OVERLAPPING, BUT STILL USEFUL) BINS:

Diagnostic

Symptomatic, high-risk exposure, or otherwise high suspicion of active infection

Screening

Asymptomatic, tested related to a discrete event (e.g., admission, high-risk procedure)

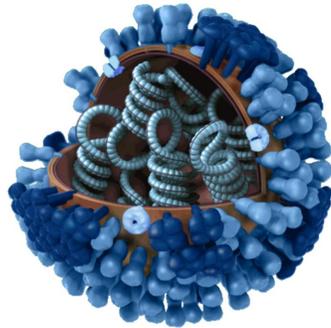
Monitoring

Pre-, a-, or paucisymptomatic; used periodically, at intervals, for all eligible members (or a sample) of a defined population

WHAT TEST DO YOU USE FOR WHICH? DECISION DRIVEN BY:

- **Clinical Question:** presence of pathogen or infectivity?
- **Test Characteristics:** sensitivity/specificity
- **Operational Issues:** turnaround time, labor, cost, reagent availability

Types of COVID Tests



DIRECT TESTS FOR VIRUS

- Antigen tests
- NAAT: RT-PCR and other molecular tests



SEROLOGICAL TESTS

- Antibody tests (IgG, IgM)
- Neutralizing antibody tests

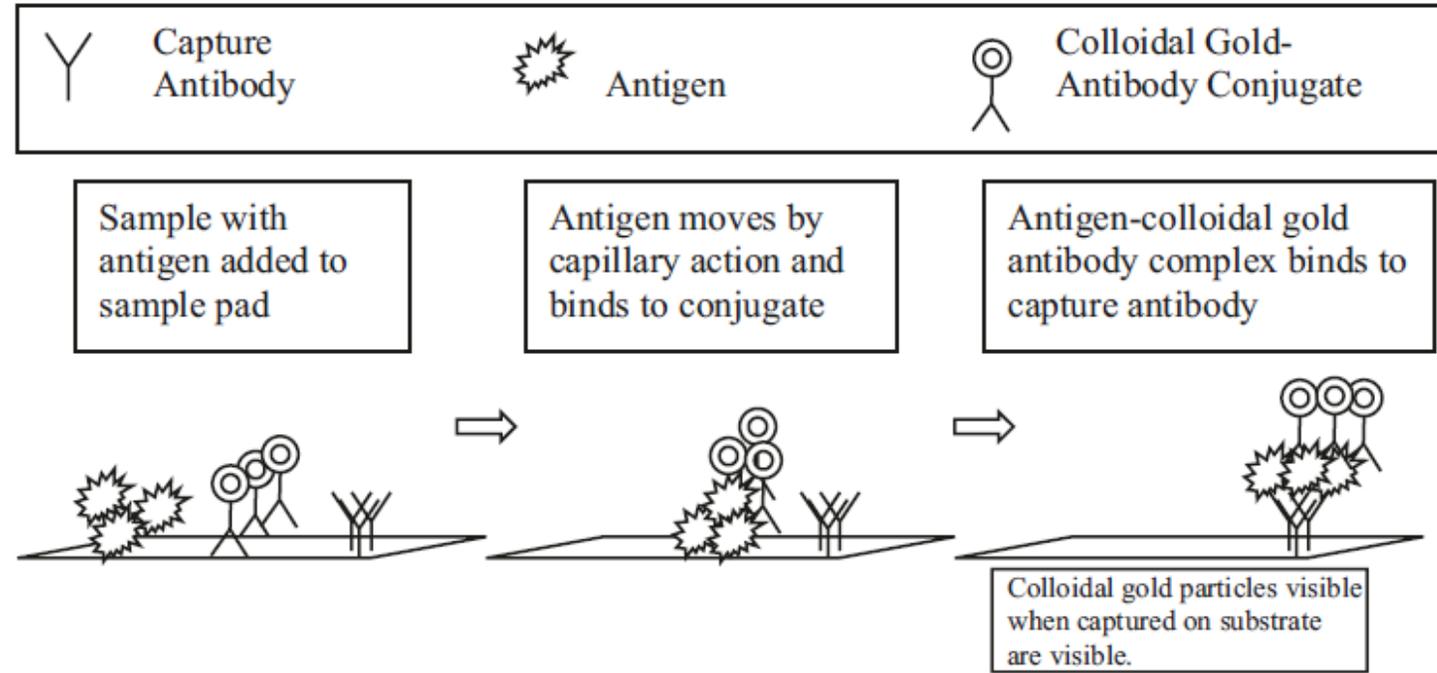


DIRECT TEST FOR VIRUS

Antigen or Molecular?

Antigen (“Lateral Flow”) Tests – Immunoassays

React antigen with antibody and detect the reaction.

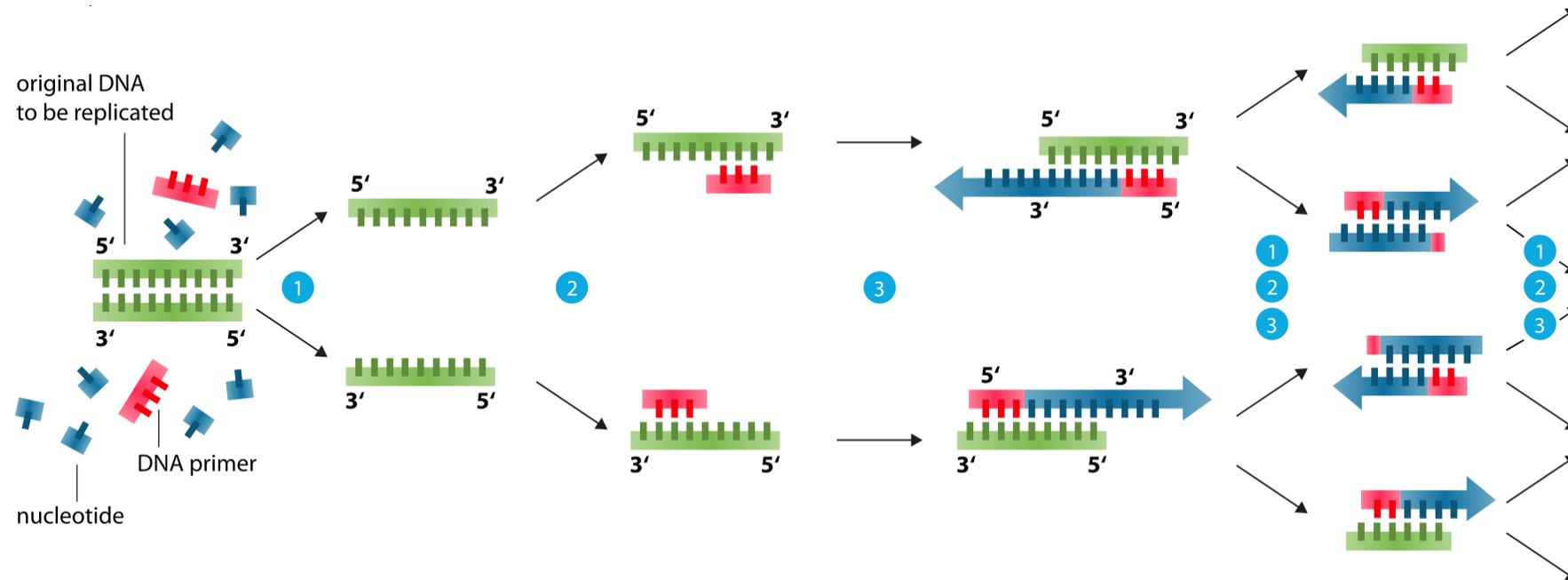


Depending on format, detect microbes (by looking for their antigens) or specific antibodies.

Molecular (NAAT) Testing

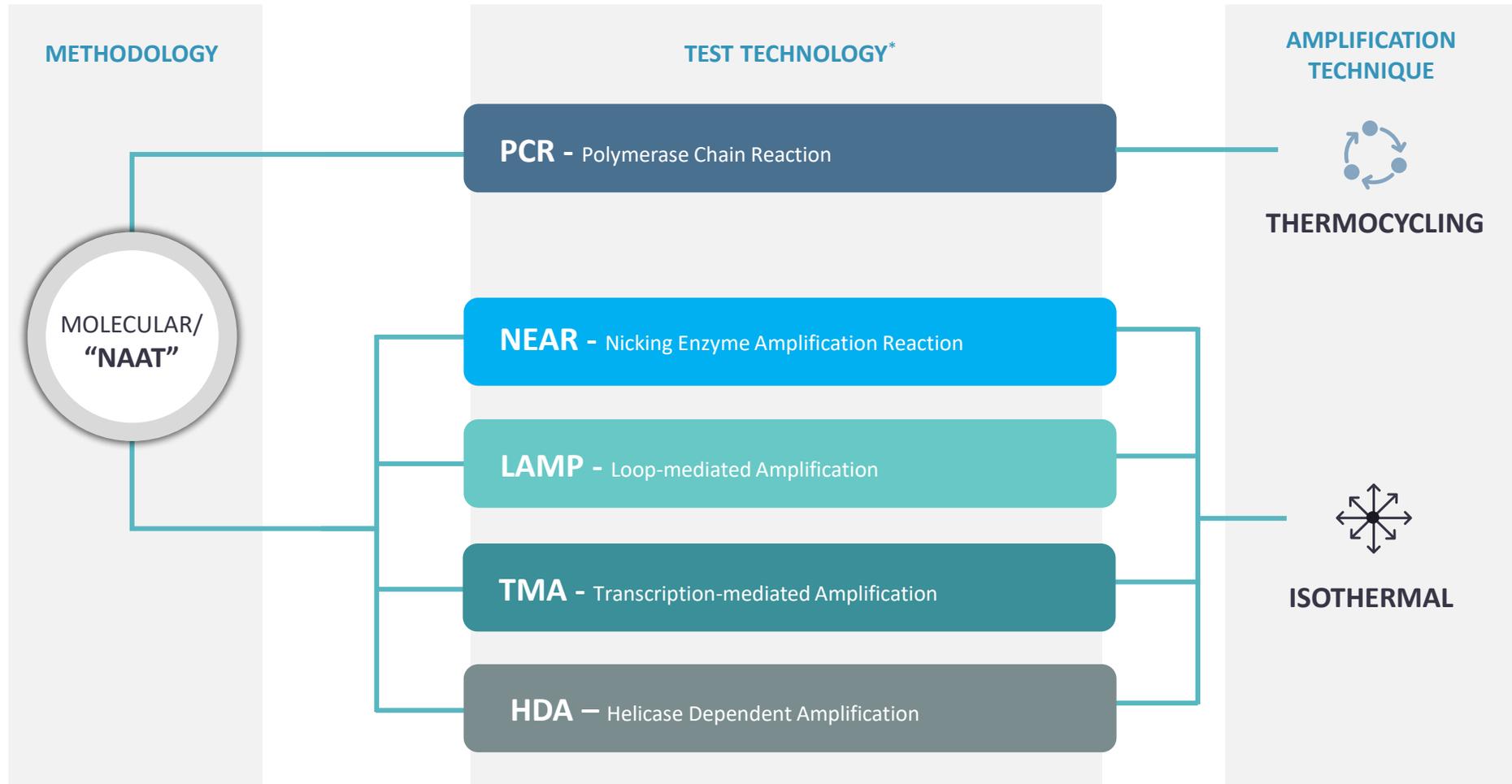
IT ALL STARTED WITH
POLYMERASE CHAIN REACTION (PCR)...

Basically, you pick a target sequence out of a bunch of other DNA and make a jillion copies of it, then detect those copies.



BUT THERE ARE MANY OTHER AMPLIFICATION TECHNOLOGIES.

Molecular (NAAT) COVID-19 Tests (By Methodology)



NAAT, nucleic acid amplification test.

*Multiple NAATs amplify nucleic acids, not a comprehensive list.

CDC, [Nucleic Acid Amplification Tests \(NAATs\)](#), updated June 16, 2021. Accessed July 21, 2021.

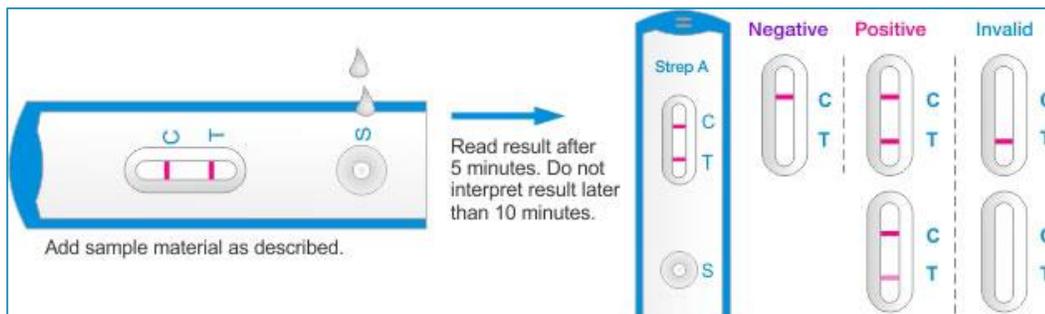
Antigen vs. Molecular

Antigen/Immunoassay

- Rapid; typically minutes
- May not need instrumentation (though some do)
- Usually highly specific; tend to lack sensitivity vs gold standard methods
- Usually relatively inexpensive

Molecular/NAAT

- Rapid; minutes to 1h or so, or batched
- Require instrumentation
- Can be highly sensitive and specific
- Detect only target nucleic acid, not host response
- Relatively costly



How Sensitive are Molecular Tests for Diagnosis?

All highly sensitive; can detect smallish numbers of viral copies

FDA lists limit of detection with standard materials for many assays:¹

These numbers (for most tests 180-18,000 copies/ml but occasionally *much* higher) don't translate well to clinical sensitivity.

SARS-CoV-2 Reference Panel Comparative Data

[Share](#) [Tweet](#) [LinkedIn](#) [Email](#) [Print](#)

The FDA SARS-CoV-2 Reference Panel allows for a more precise comparison of the analytical performance of different molecular in vitro diagnostic (IVD) assays intended to detect SARS-CoV-2. The Reference Panel contains common, independent, and well-characterized reference material that is available to developers of SARS-CoV-2 nucleic acid-based amplification tests (NAATs) for which Emergency Use Authorization (EUA) was requested.

Content current as of:
12/07/2020

Regulated Product(s)
Medical Devices

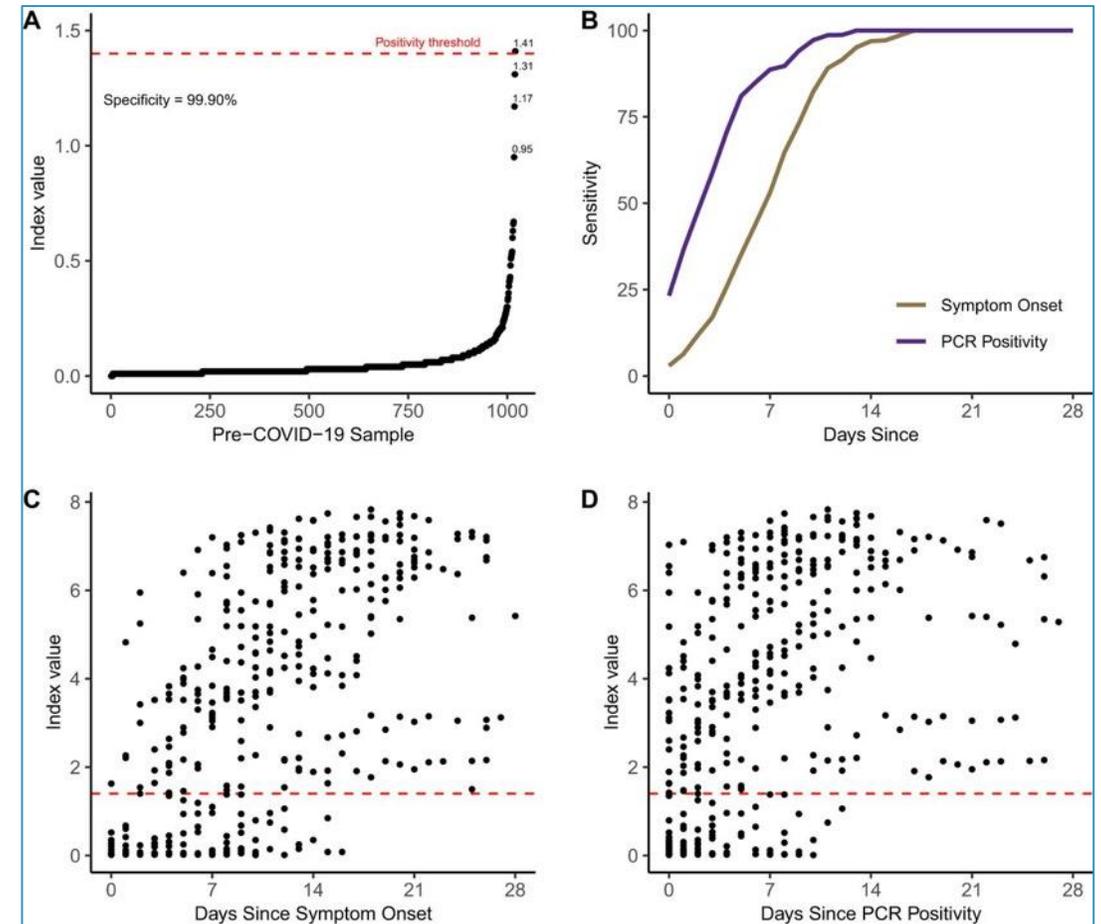
Clinical sensitivity: In symptomatic patients, sensitivity of a single RT-PCR test is well under 100%, but I haven't seen a well-conducted study saying what it is.

- Keep testing 'till you get the answer you want...that's what everyone else does.
- **Just kidding...sort of.**

1. <https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data>

SARS-CoV-2 Serology

- **Antibody response to SARS-CoV-2 infection**
 - Generally turns positive within 7-14d of symptom onset.
- **Two types of tests:**
 - Spike-protein antibody
 - Will be positive after vaccination, and after natural infection
 - Nucleocapsid antibody
 - Will only be positive after natural infection
- **Can be used to discriminate between vaccine and infection**



Bryan A, et al. Performance Characteristics of the Abbott Architect SARS-CoV-2 IgG Assay and Seroprevalence in Boise, Idaho. J Clin Microbiol. 2020 Jul 23;58(8):e00941-20.

Testing Scenarios

EARLY OUTBREAK (SPRING 2020)

‘We have six patients in the **ED** with fever and respiratory distress, **how long ‘till the COVID tests are done?’**

EARLY RE-OPENING (SUMMER-FALL 2020)

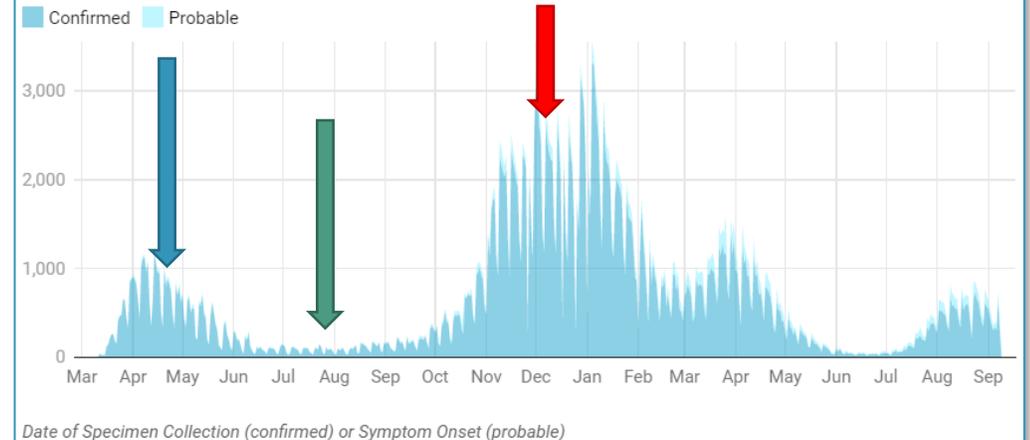
‘How many COVID tests can you do in a day? We’re trying to re-open the **colonoscopy** service. And can you turn them around **within 30 minutes** of the patient arriving?’

RESURGENCE (WINTER-2020)

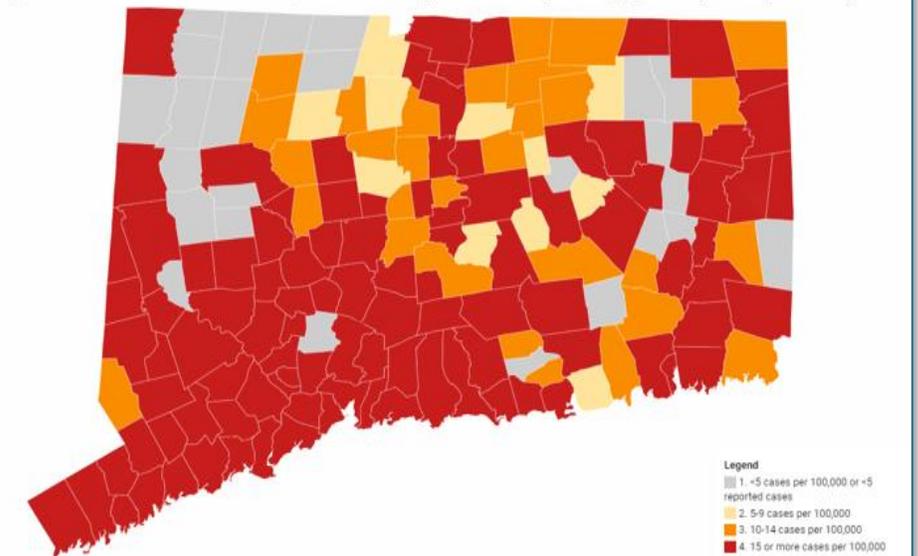
‘We have six patients in the **ED** with fever and respiratory distress and twelve in the **MICU** and we need to repeat four of those, and also the **nursing home** wants to test their entire population and staff **twice a week** and they really need those **within an hour** of collection. And the pulmonary people are doubling their outpatient **bronchoscopies**, too. And we’re opening a new **community drive-through testing site**, can you work out the transportation?’

Number of Confirmed and Probable COVID-19 Cases by Date

Test results may be reported several days after the result. Data are incomplete for the most recent days. Data from previous dates are routinely updated.



Town Map Average Daily Rate of COVID-19 Cases Among Persons Living in Community Settings per 100,000 Population By Town



This map shows the average daily rate of new cases of COVID-19 by town during the past two weeks. Only cases among persons living in community settings are included in this map; the map does not include cases among people who reside in nursing home, assisted living, or correctional facilities.
Map: Ver 12.1.2020 • Source: CT Department of Public Health • Get the data • Created with Datawrapper

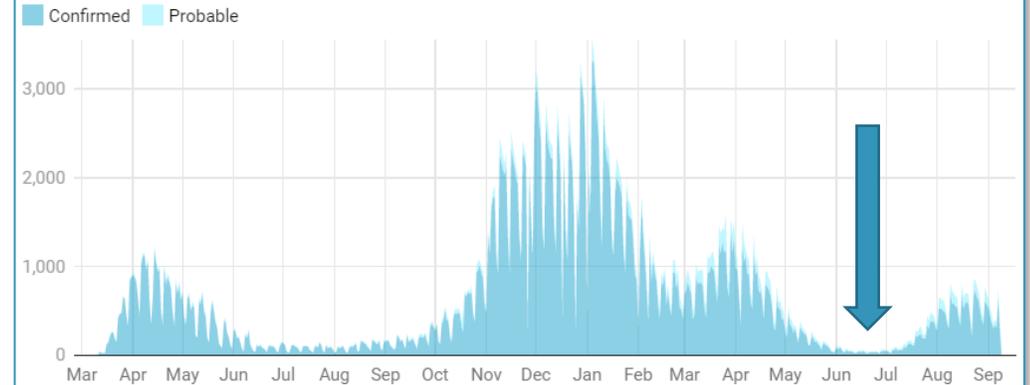
Case from Last June...

‘Patient tested positive pre-procedure. They were vaccinated in March. Can you investigate?’

WHAT WOULD YOU DO?

Number of Confirmed and Probable COVID-19 Cases by Date

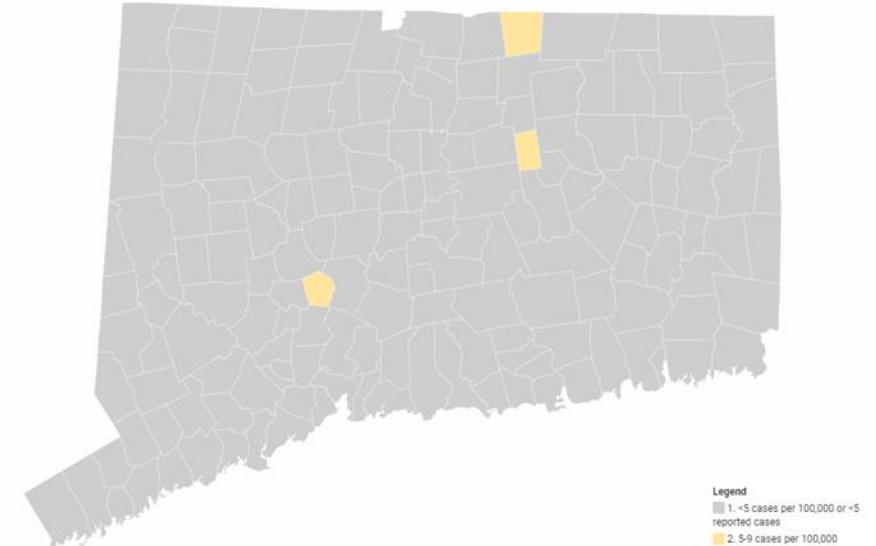
Test results may be reported several days after the result. Data are incomplete for the most recent days. Data from previous dates are routinely updated.



Date of Specimen Collection (confirmed) or Symptom Onset (probable)

Town Map

Average Daily Rate of COVID-19 Cases Among Persons Living in Community Settings per 100,000 Population By Town



This map shows the average daily rate of new cases of COVID-19 by town during the past two weeks. Only cases among persons living in community settings are included in this map; the map does not include cases among people who reside in nursing home, assisted living, or correctional facilities.

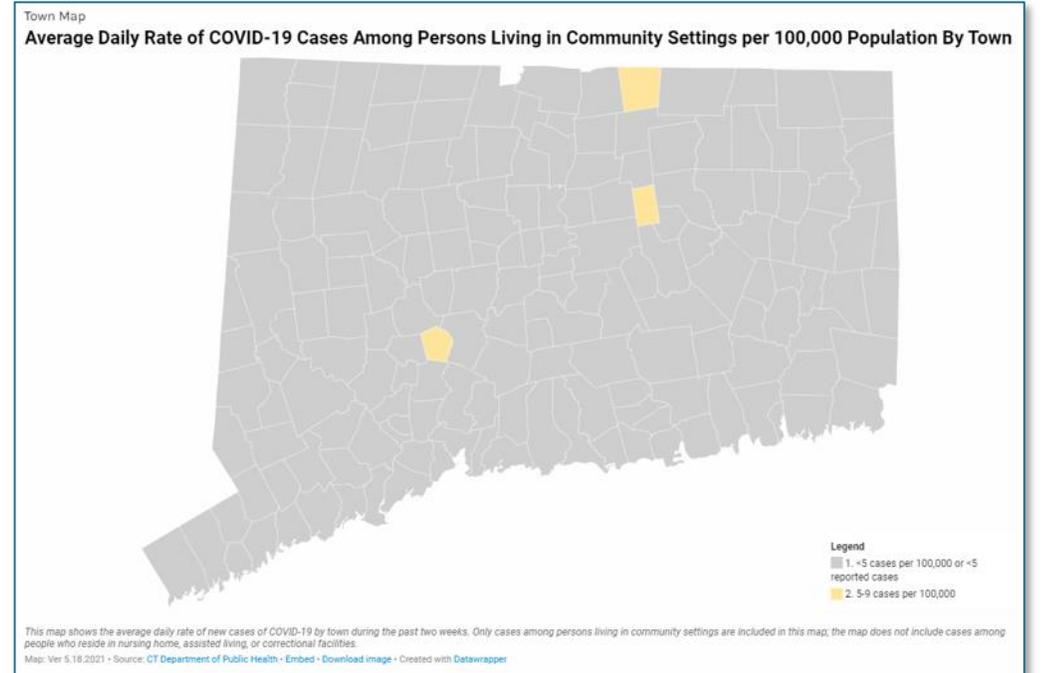
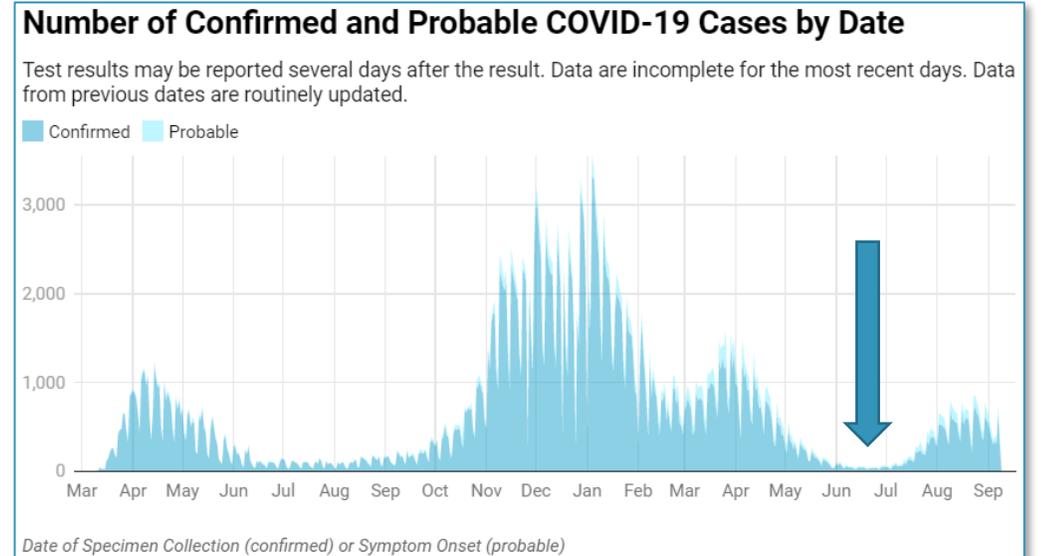
Map: Ver 5.18.2021 • Source: CT Department of Public Health • Embed • Download image • Created with Datawrapper

Case from Last June...

‘Patient tested positive pre-procedure. They were vaccinated in March. Can you investigate?’

WHAT WOULD YOU DO?

- Note community case rates
 - 200 tests/d, 0-2 positives.
- Check Ct value
 - High (note no number here)
- Re-test on same platform
 - Negative
- Re-test x2 on another (good) platform:
 - Negative



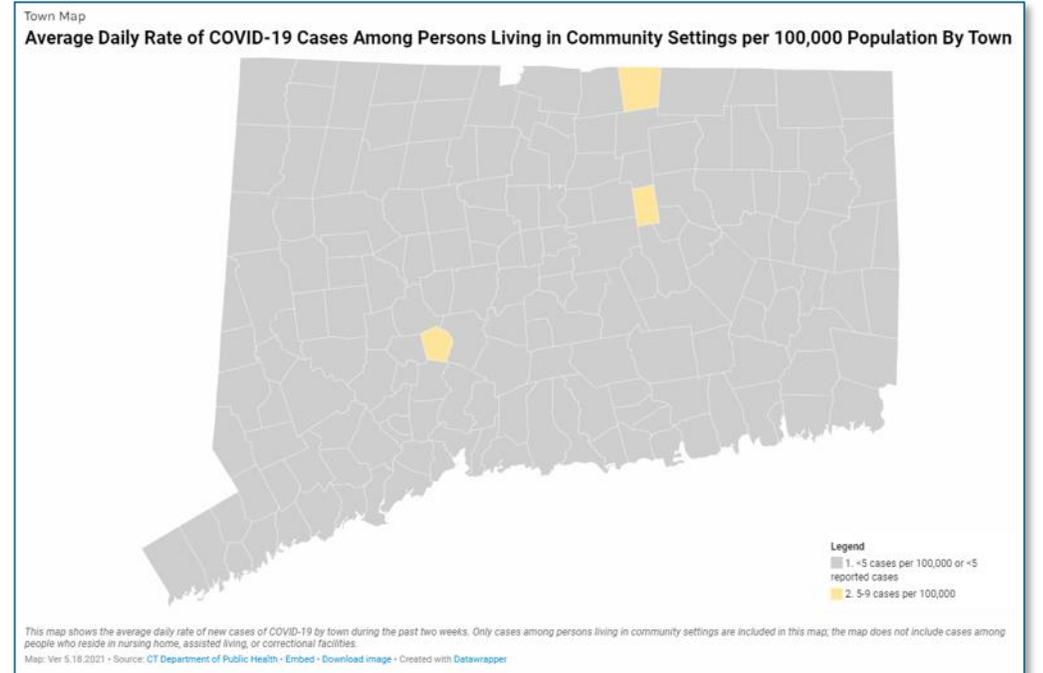
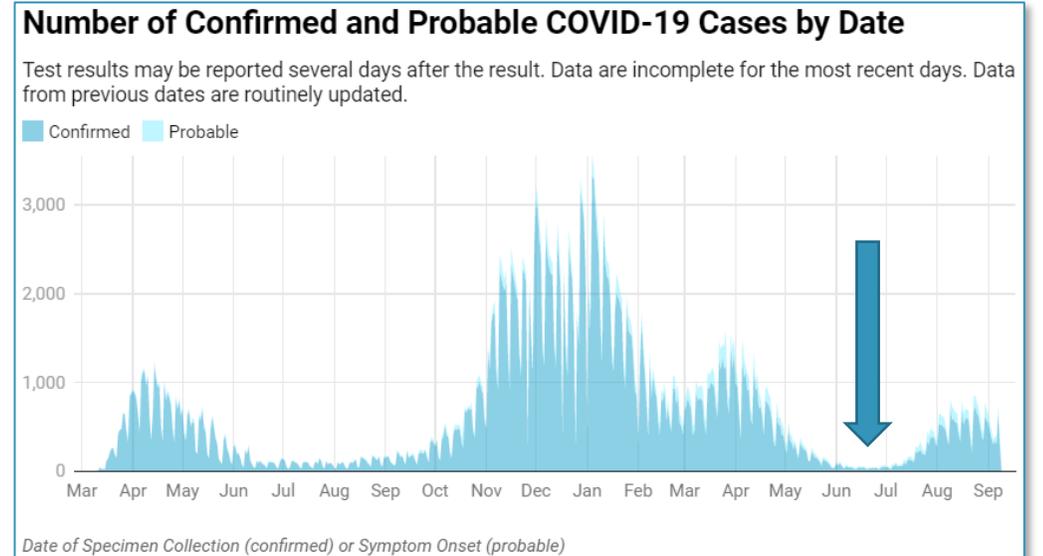
Case from Last June...

‘Patient tested positive pre-procedure. They were vaccinated in March. Can you investigate?’

WHAT WOULD YOU DO?

- Note community case rates
 - 200 tests/d, 0-2 positives.
- Check Ct value
 - High (note no number here)
- Re-test on same platform
 - Negative
- Re-test x2 on another (good) platform:
 - Negative

NOW WHAT? CONSIDER:



Case from Last June...

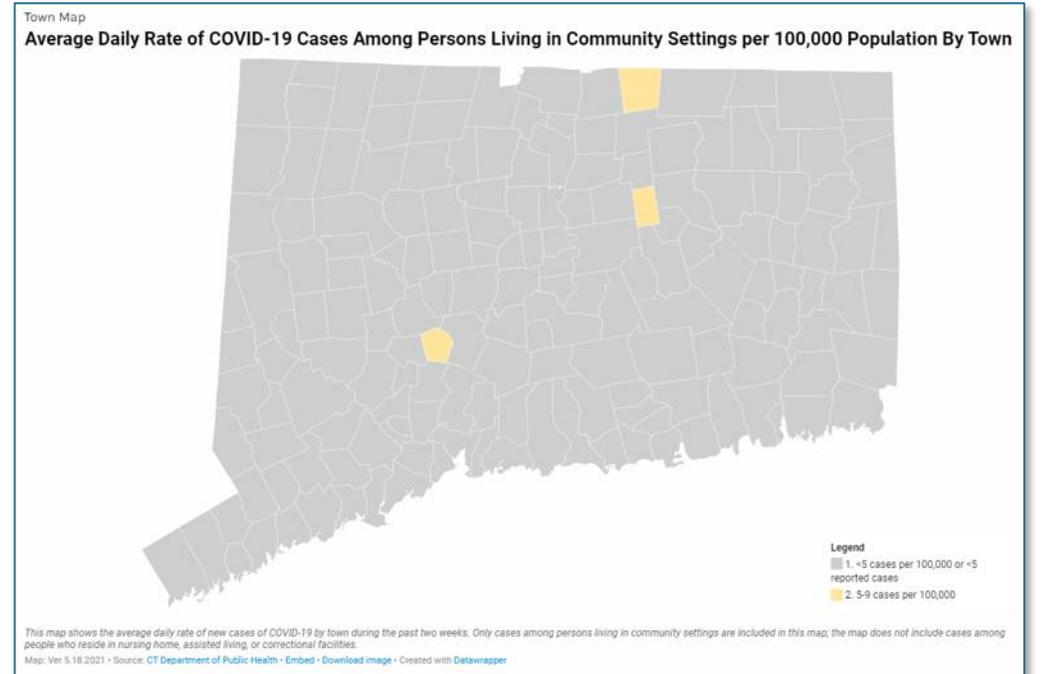
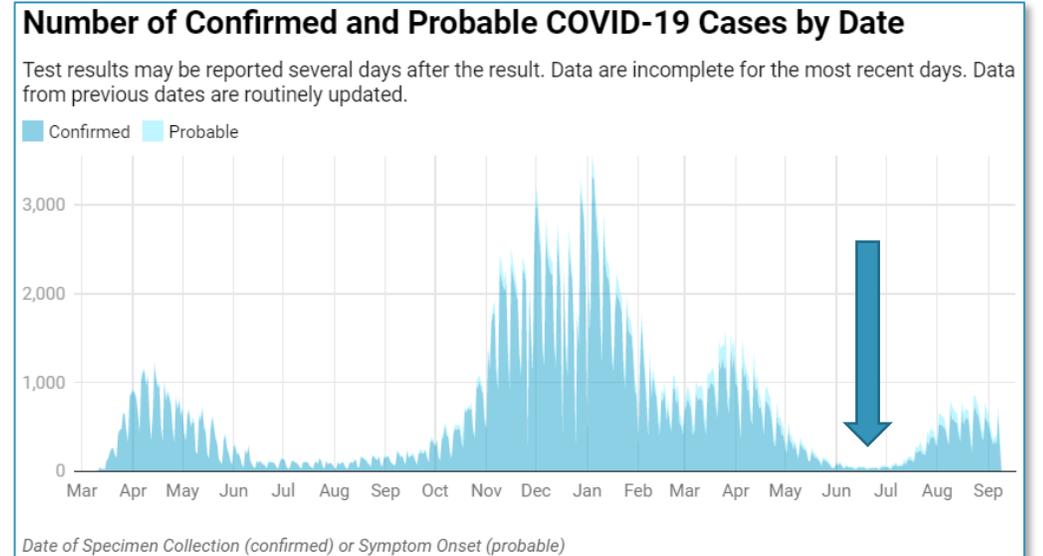
‘Patient tested positive pre-procedure. They were vaccinated in March. Can you investigate?’

WHAT WOULD YOU DO?

- Note community case rates
 - 200 tests/d, 0-2 positives.
- Check Ct value
 - High (note no number here)
- Re-test on same platform
 - Negative
- Re-test x2 on another (good) platform:
 - Negative

NOW WHAT? CONSIDER:

- S and NC antibodies
- Recollect tomorrow

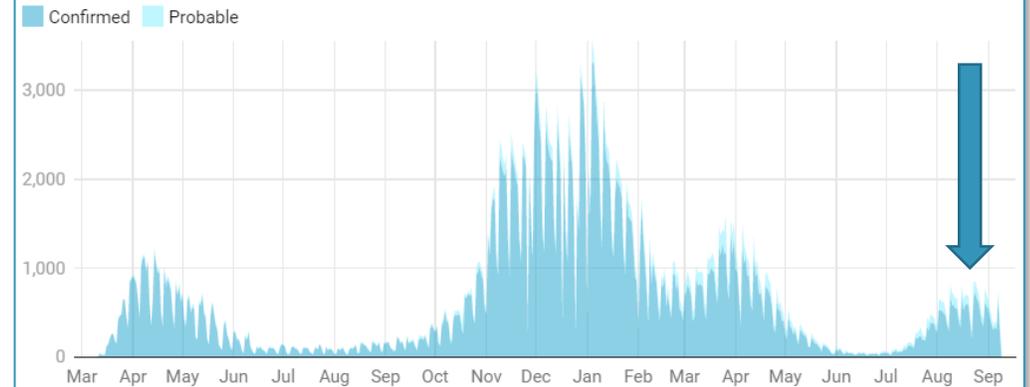


And Now...

MAYBE, ALL OF THE ABOVE?

Number of Confirmed and Probable COVID-19 Cases by Date

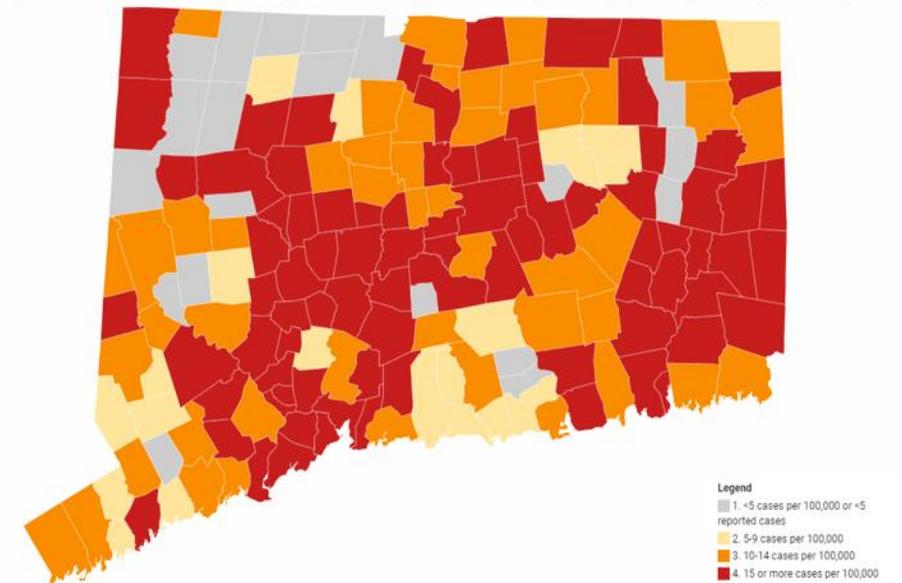
Test results may be reported several days after the result. Data are incomplete for the most recent days. Data from previous dates are routinely updated.



Date of Specimen Collection (confirmed) or Symptom Onset (probable)

Town Map

Average Daily Rate of COVID-19 Cases Among Persons Living in Community Settings per 100,000 Population By Town



This map shows the average daily rate of new cases of COVID-19 by town during the past two weeks. Only cases among persons living in community settings are included in this map; the map does not include cases among people who reside in nursing home, assisted living, or correctional facilities.

Polling Question #4

We plan to use rapid COVID-19 and influenza testing for asymptomatic patients during respiratory season:

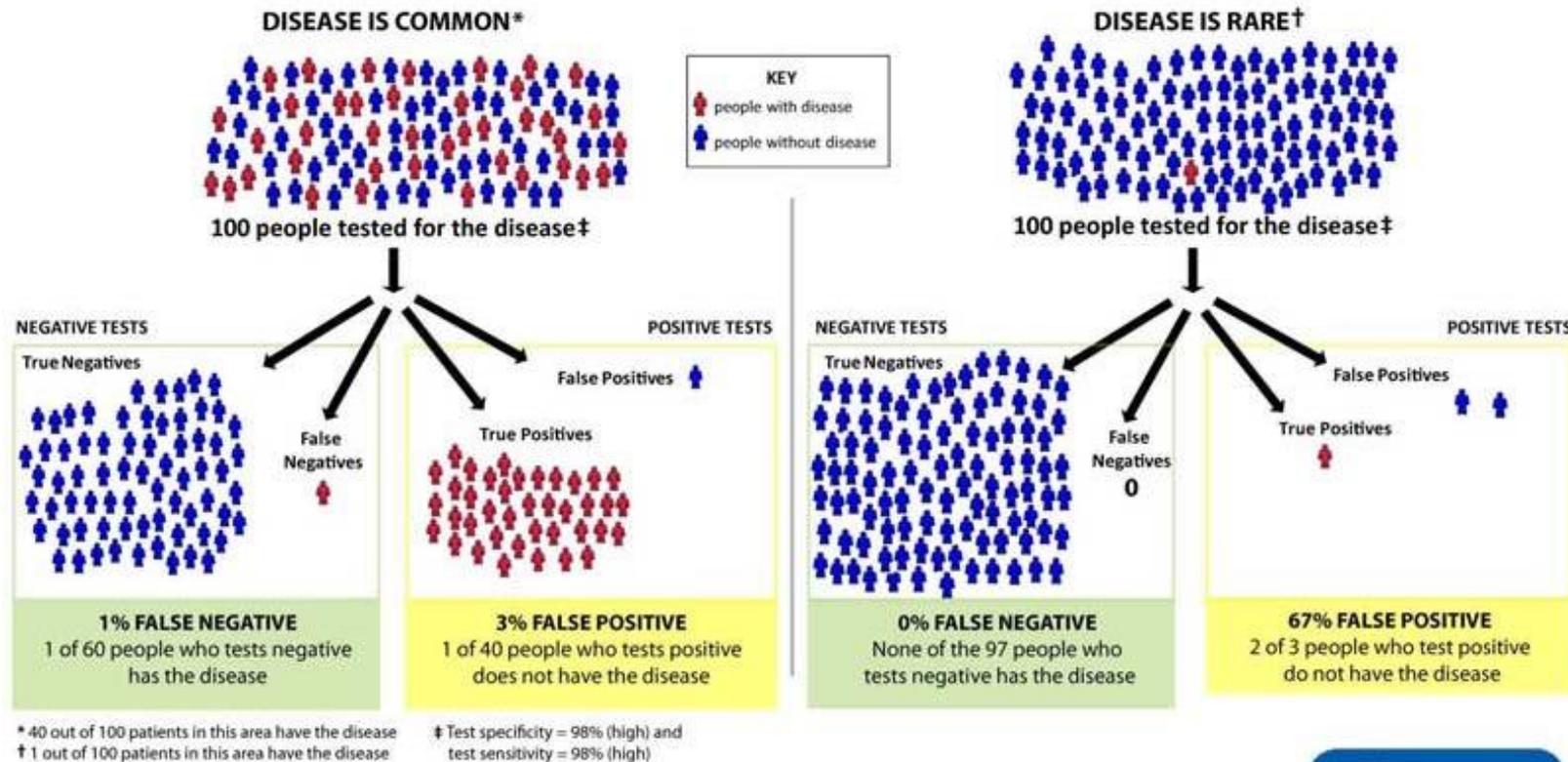
- a) Routinely
- b) Only when flu is circulating
- c) No rapid asymptomatic testing
- d) Protocol not yet established for asymptomatic patients
- e) Don't know

Understanding Test Results for Infectious Diseases

Consider the likelihood of disease *before* performing Laboratory testing

The likelihood that a patient has a disease depends on many factors:

- Has the patient been in an area where the disease is found?
- Does the patient have signs and symptoms typical of the disease?
- Does the patient have risk factors for contracting or developing the disease?



Why Use What Test?

MOLECULAR (NAAT - PCR OR ISOTHERMAL)

Expensive, highly-sensitive.
Test of choice for diagnosis of
symptomatic patients.

ANTIGEN

Cheap(er), less sensitive.
Is it an adequate test
for infectivity?

SEROLOGY

NOT (currently) a marker for
protection. Useful as
adjunct diagnostic marker.

An Argument For Widespread Antigen Testing

CORONAVIRUS

Test sensitivity is secondary to frequency and turnaround time for COVID-19 screening

Daniel B. Larremore^{1,2*}, Bryan Wilder³, Evan Lester^{4,5}, Soraya Shehata^{5,6}, James M. Burke⁴, James A. Hay^{7,8}, Milind Tambe³, Michael J. Mina^{7,8,9,*†}, Roy Parker^{2,4,6,10,*†}

The COVID-19 pandemic has created a public health crisis. Because SARS-CoV-2 can spread from individuals with presymptomatic, symptomatic, and asymptomatic infections, the reopening of societies and the control of virus spread will be facilitated by robust population screening, for which virus testing will often be central. After infection, individuals undergo a period of incubation during which viral titers are too low to detect, followed by exponential viral growth, leading to peak viral load and infectiousness and ending with declining titers and clearance. Given the pattern of viral load kinetics, we model the effectiveness of repeated population screening considering test sensitivities, frequency, and sample-to-answer reporting time. These results demonstrate that effective screening

Copyright © 2021 The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works. Distributed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC).

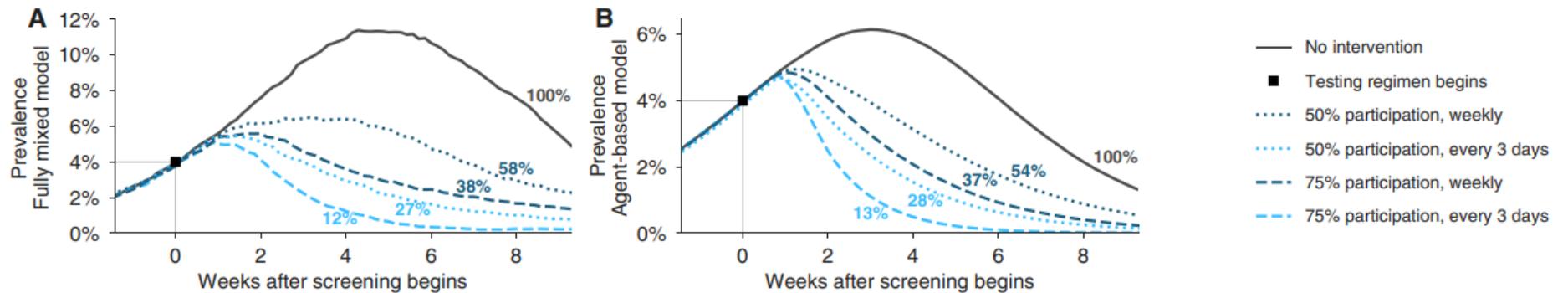
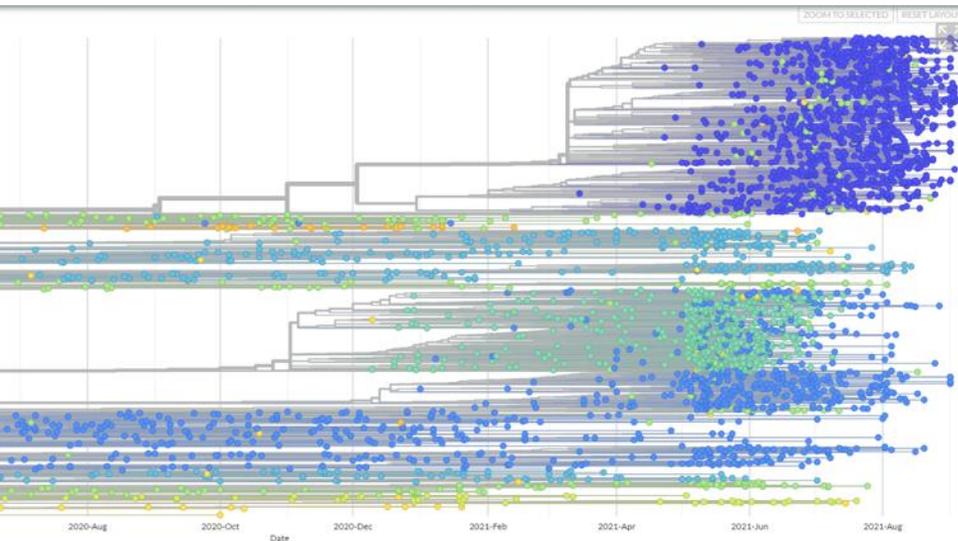


Fig. 6. Repeated population screening suppresses an ongoing epidemic. Widespread testing and isolation of infected individuals drive prevalence downward for both (A) the fully mixed compartmental model and (B) the agent-based model. Time series of prevalence, measured as the total number of infectious individuals, are shown for no intervention (solid) and population screening scenarios (various dashed lines; see legend) for individual stochastic simulations. Screening began only when prevalence reached 4% (box), and time series are shifted such that testing begins at $t = 0$. Scenarios show the impact of a test with LOD 10^5 , no delay in results, and with 10% of samples assumed to be incorrectly collected (and therefore negative) to reflect decreased sensitivity incurred at sample collection in a mass testing scenario. Annotations show total number of post-intervention infections, as a percentage of the no-intervention scenario, labeled as 100% (see fig. S8 for identical simulations using a test with LOD 10^6).



The Reality

- COVID has proven an adaptive, resilient, dangerous pathogen.
- Human beings are complex entities.
- Human societies are even more complex entities.



When You Drive Your Car, Do You...?

- **Maintain the car so the steering and brakes work?**
- **More-or-less obey traffic laws and signs?**
- **Wear your seat belt?**





COVID-19 Risk Reduction is Similar

- **WE ASK PEOPLE TO:**
 - Get vaccinated
 - Wear masks and social distance
 - Test as needed, for symptoms or screening
- **IT'S NOT ONE OR THE OTHER; IT'S ALL OF THE ABOVE**

Summary

Tests include antigen, nucleic acid, and serology, each testing slightly (or markedly) different things, each with specific characteristics, even within a methodology.

Reasons to test include diagnosis, screening, and monitoring.

Test strategy and interpretation may vary not only with test type and clinical question, but by background epidemiology.

Be available for consultation and recommendations.