



**Wisconsin State
Laboratory of Hygiene**
UNIVERSITY OF WISCONSIN-MADISON



Update on COVID-19 Diagnostic Testing 09-02-20

Dr. Alana Sterkel

PhD, D(ABMM), SM(ASCP)^{CM}

Assistant Director

Erin Bowles

MT(ASCP)

WCLN Network Coordinator

Communicable Disease Division
Wisconsin State Laboratory of Hygiene



Notice

This information is subject to rapid change.

Please refer to our webpage for the most up to date guidance

<http://www.slh.wisc.edu/clinical/diseases/covid-19/>

The WSLH does not endorse products of any kind



Contents

- Pandemic update
- COVID reporting requirements
- What's new
- Antigen testing and positive predicative value



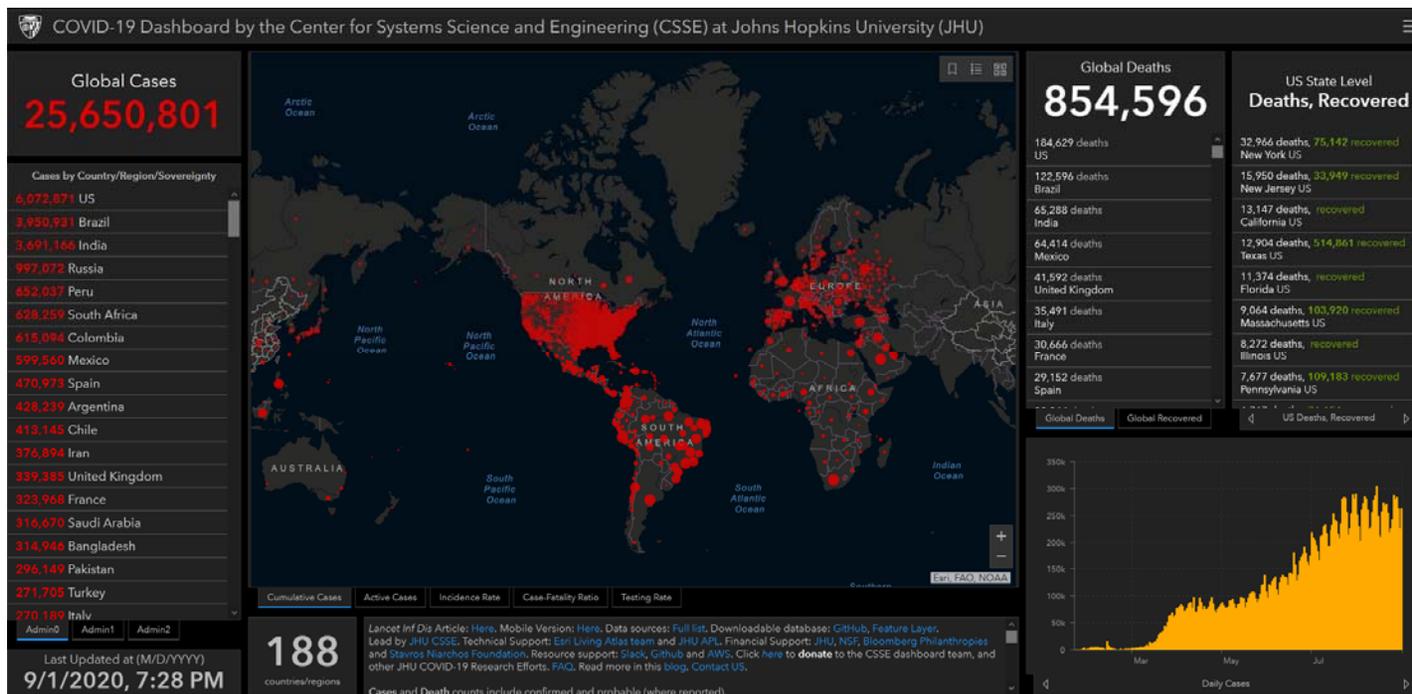




PANDEMIC UPDATE



Global Impact



In 2 months- twice the deaths, 2.7x the cases

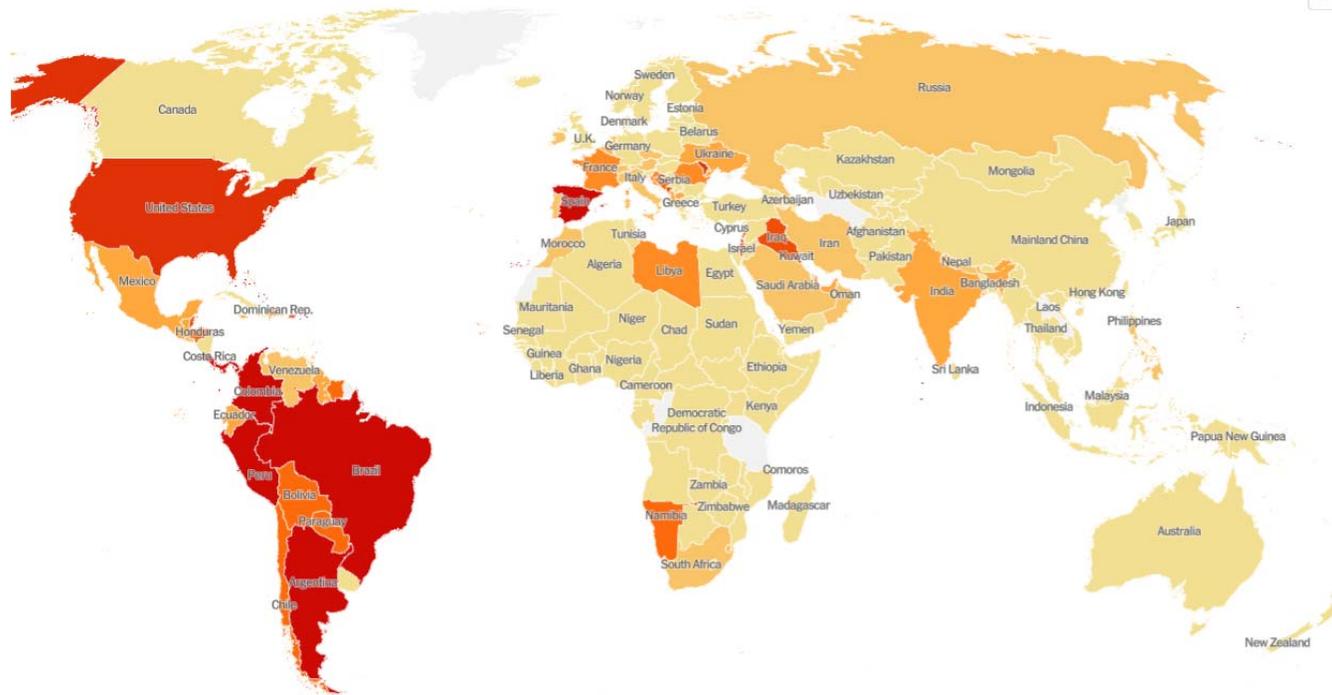
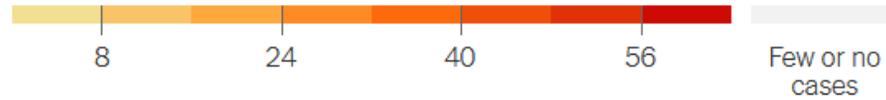
Johns Hopkins University Global Coronavirus Tracking:

<https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>

WISCONSIN STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN



Average daily cases per 100,000 people in the past week

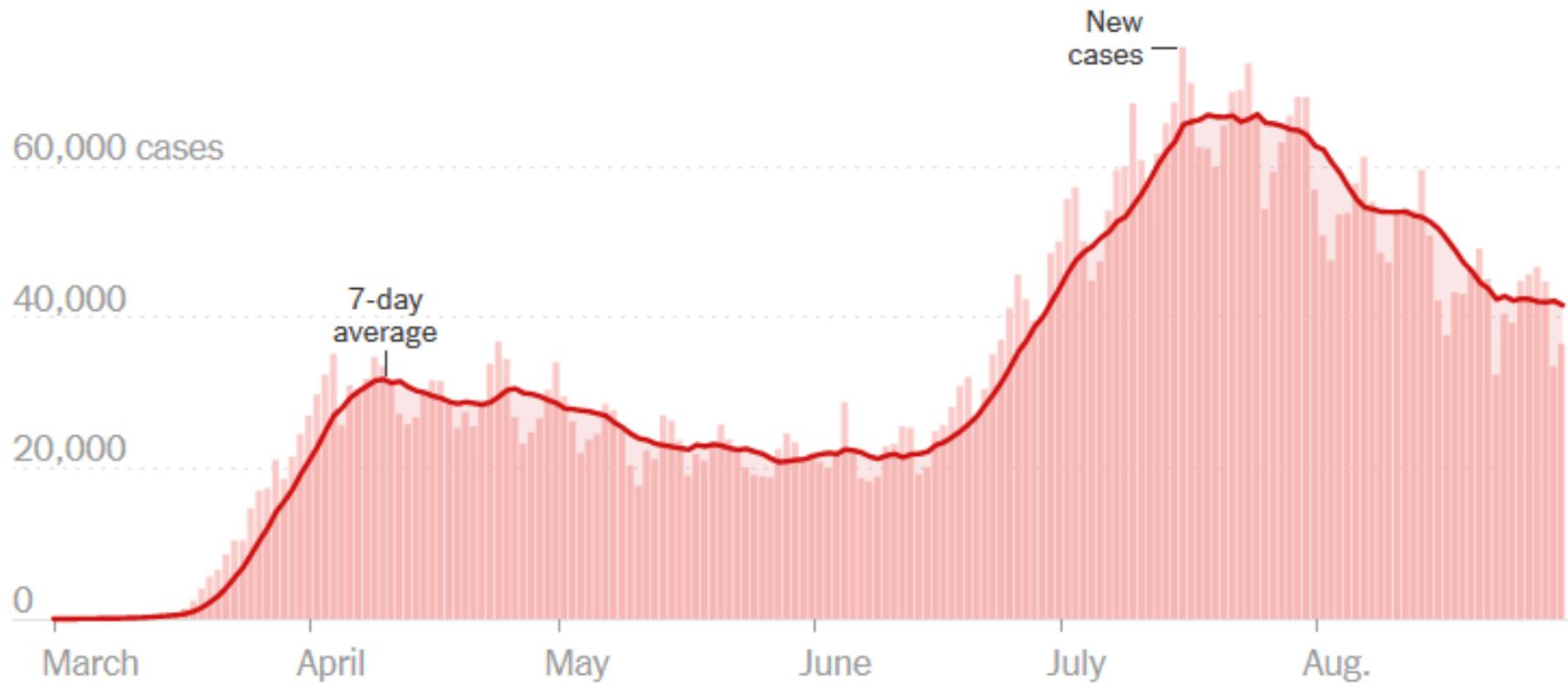


<https://www.nytimes.com/interactive/2020/world/coronavirus-maps.html>

WISCONSIN STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN



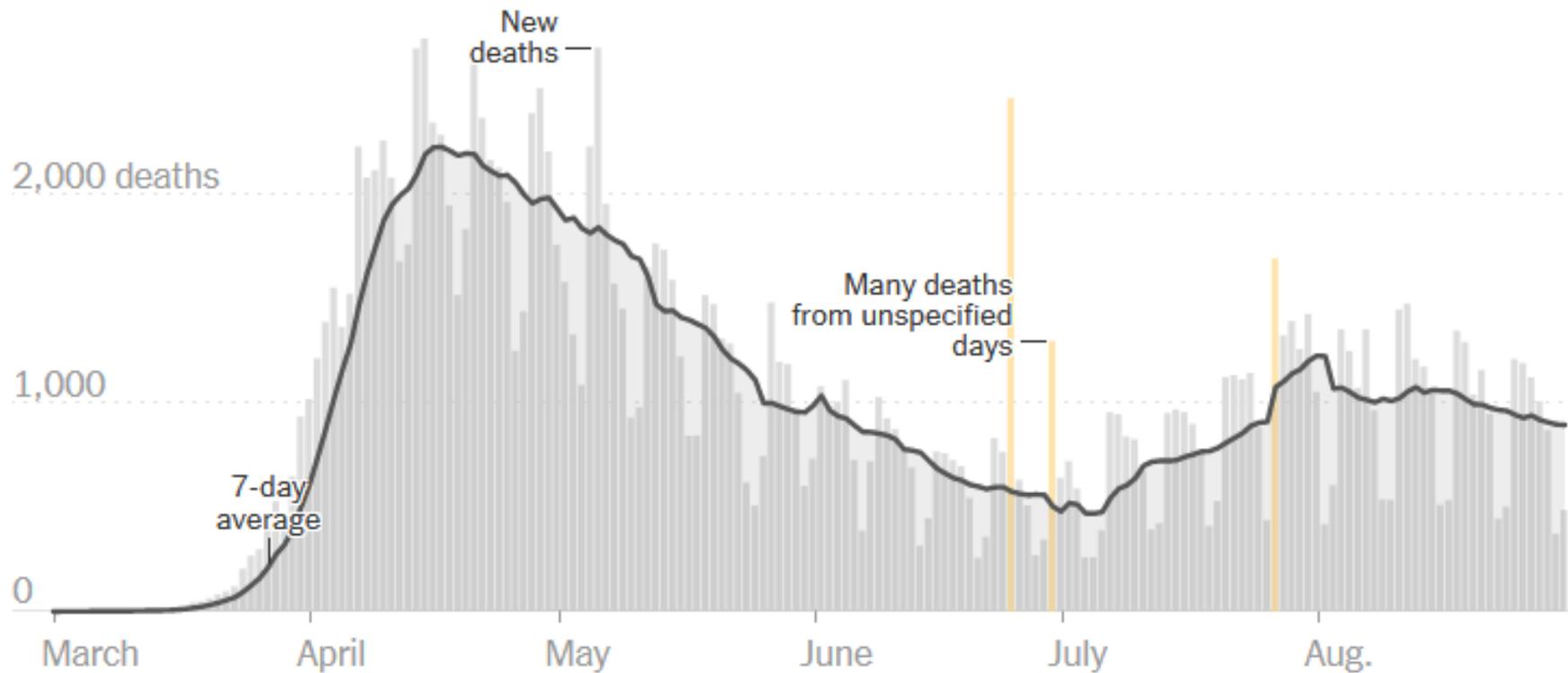
New reported cases by day in the United States



<https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html#map>



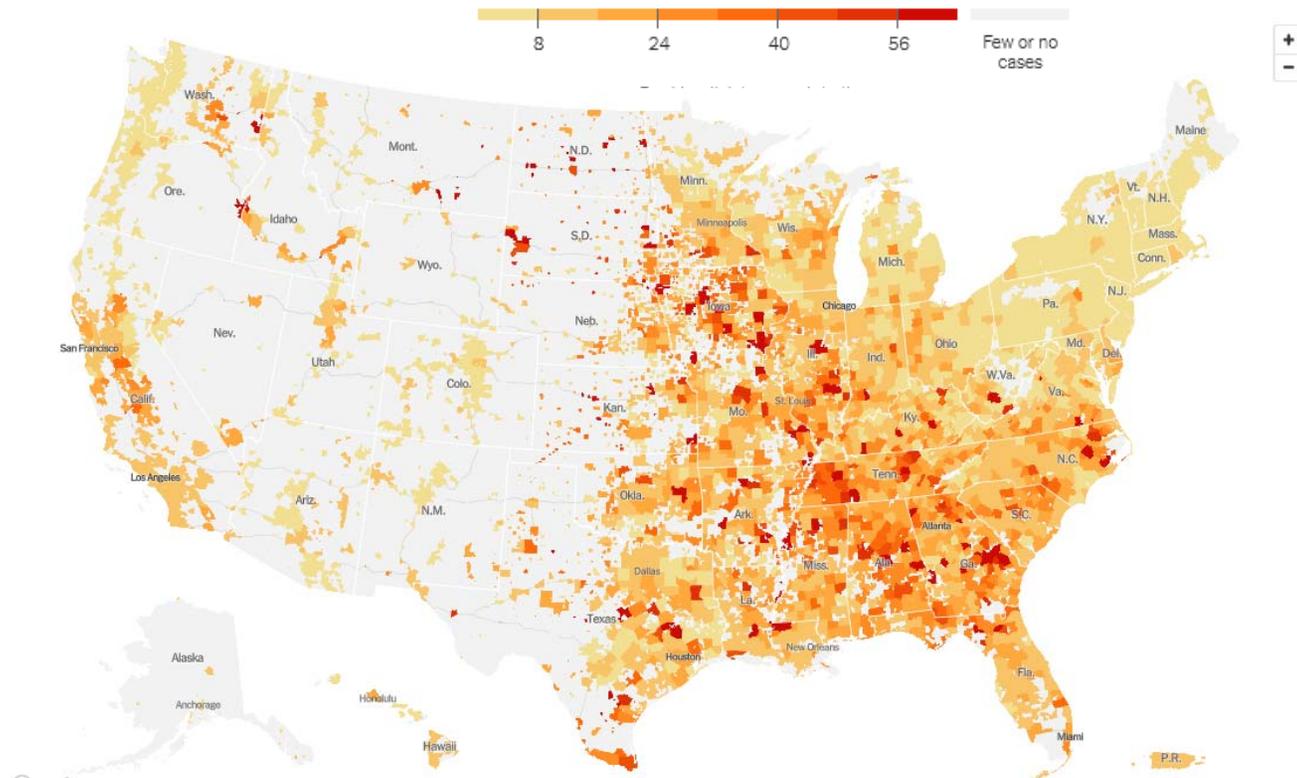
New reported deaths by day in the United States



<https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html#map>



US Hot Spots



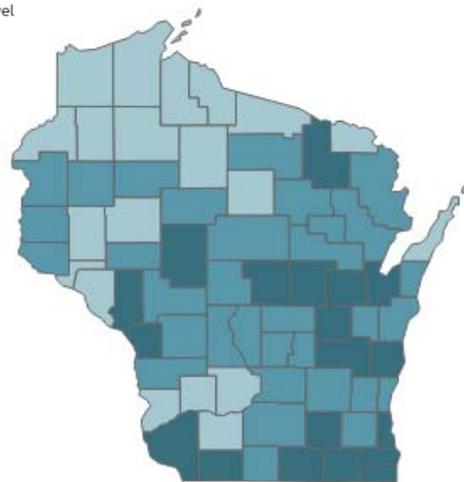
<https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html>



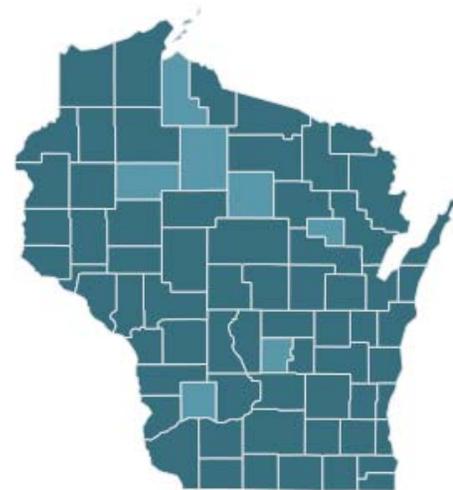
DHS COVID-19 Activity Level Data Dashboard

Consists of maps and tables that toggle between counties and Healthcare Emergency Readiness Coalition (HERC) regions.

COVID-19 activity level
Low
Medium
High



6/24/20



8/28/20

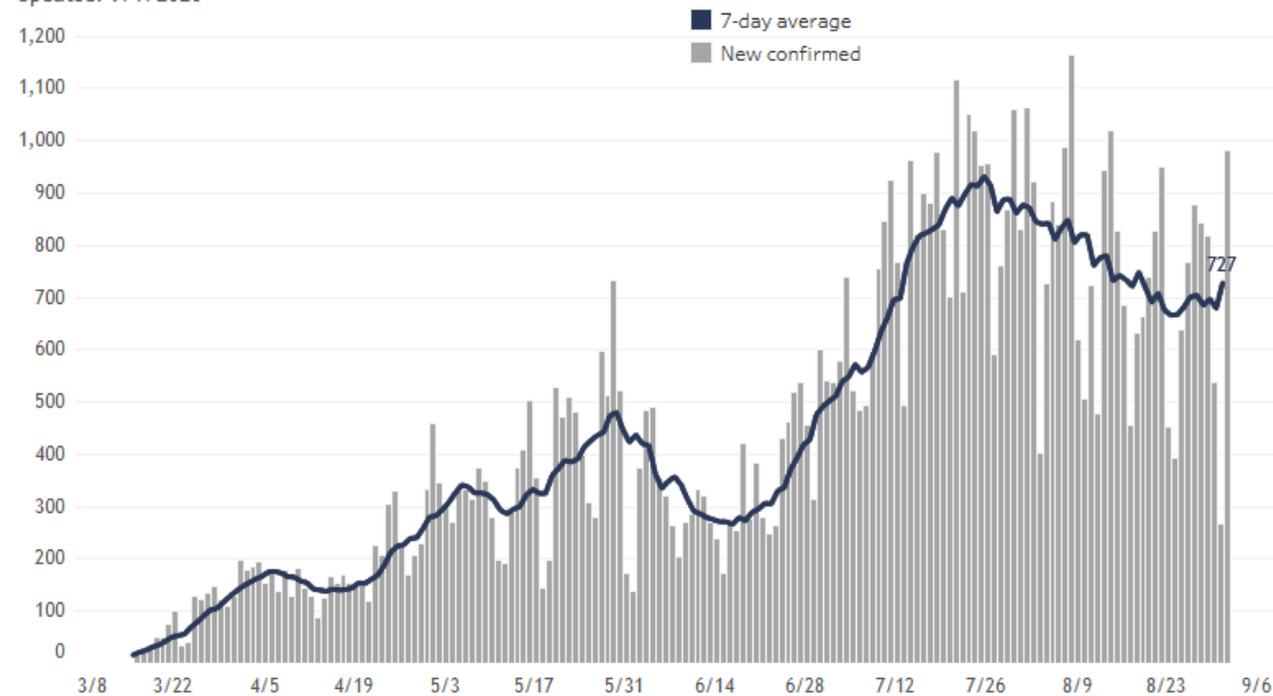
<https://www.dhs.wisconsin.gov/covid-19/local.htm>



WI Cases

New confirmed COVID-19 cases by date confirmed, and 7-day average

Updated: 9/1/2020



<https://www.dhs.wisconsin.gov/covid-19/data.htm>

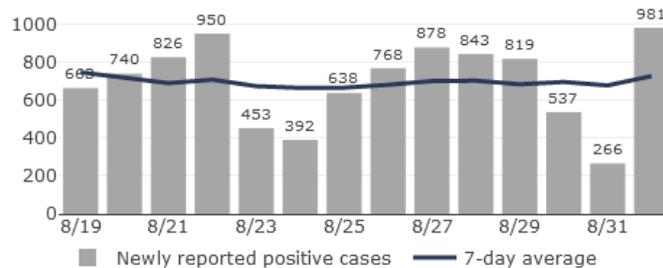


Wisconsin

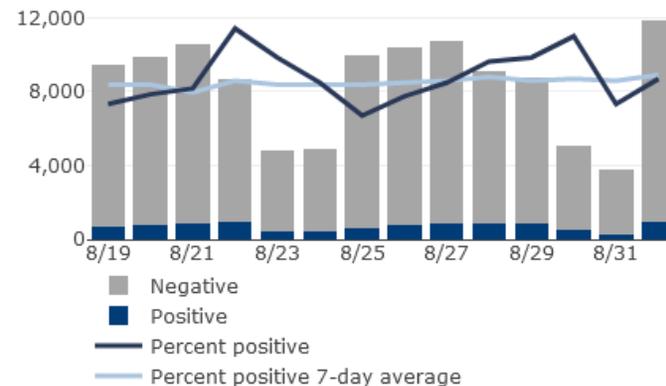
Total people tested: 1,260,301 (+11,844 from prior day)
 Positive (Confirmed Case): 76,584 (+981)
 Negative: 1,183,717 (+10,863)

Recovery Status	Deaths	Hospitalizations
Recovered: 67,902 (88.7%) Active: 7,534 (9.8%)	Deaths: 1,130 (+8) Percent who died: 1.5%	Ever hospitalized: 5,878 (+61) Percent ever hospitalized: 7.7%

Updated: 9/1/2020



Updated: 9/1/2020



<https://www.dhs.wisconsin.gov/outbreaks/index.htm>



How Close Are We to Herd Immunity?

- 1.3% of Wisconsinites have had a positive test
- ~2% have antibodies against SARS-CoV-2
- Herd Immunity likely needs to be >85%
- We've detected about 65% of cases



Vaccine

Operation Warp Speed

Operation Warp Speed (OWS) aims to deliver 300 million doses of a safe, effective vaccine for COVID-19 by **January 2021**, as part of a broader strategy to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics (collectively known as countermeasures). More information on Operation Warp Speed [here](#).

Volunteers Needed: Volunteers interested in participated in a COVID-19 prevention clinical trial can find more information and register [here](#).



REPORTING REQUIREMENTS



Reporting COVID-19 Results

- **HHS** [requires](#) that **ALL** SARS-CoV-2 test results are reported along with patient specific information.
- **CMS** [requires](#) that you report all diagnostic test results and the method used
- **WI State Public Health** [requires](#) that you report (WEDSS)
 - Positive and negative Molecular test results
 - Positive antibody results
 - Positive antigen results



Electronic Lab Reporting (ELR)

- WSLH reports to CDC/HHS, and WEDSS using HL7 messaging when you report via
 - Web-based Lab Reporting (WLR)
 - Electronic Lab Reporting (ELR)
- **IMPORTANT**- If you report directly into WEDSS, WSLH is unable to forward your reports
- Contact Mary Wedig if you have questions or want to get set-up. mary.wedig@slh.wisc.edu



HHS Reporting

General reporting guidance can be found on several websites, including [HHS](#) and [CDC](#). Guidance for *hospital reporting* can be found in a HHS [FAQ](#).

More detail technical explanation available [here](#)

For technical assistance, laboratories and testing sites should contact eocevent405@cdc.gov



SEOC SURVEY AND DATA



SEOC Survey

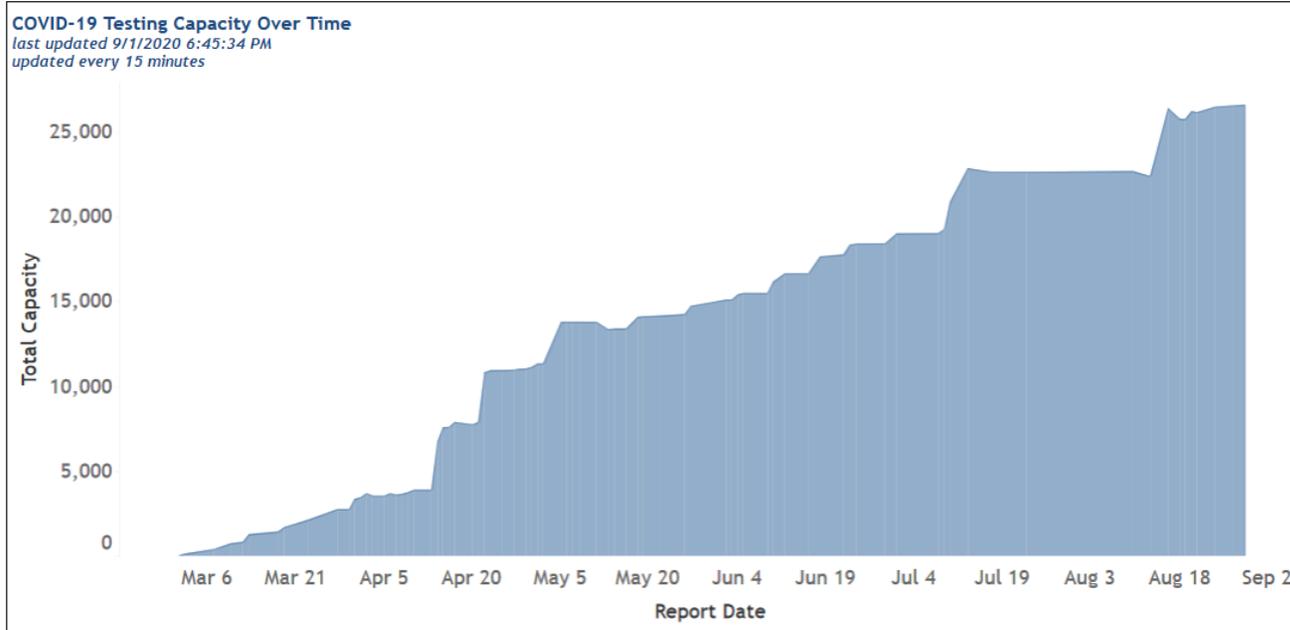
PLEASE, Update the SEOC Survey!

- Start testing
- Change in testing methods
- Change in capacity
- To report a supply shortage
- To remove a supply shortage report



Wisconsin COVID-19 Molecular Testing Capacity

Laboratories actively testing 86	Laboratories planning to test 25	Current state capacity (tests/day) <i>Last Updated: 9/1/2020 6:45:24 PM</i> 26,591
---	---	--



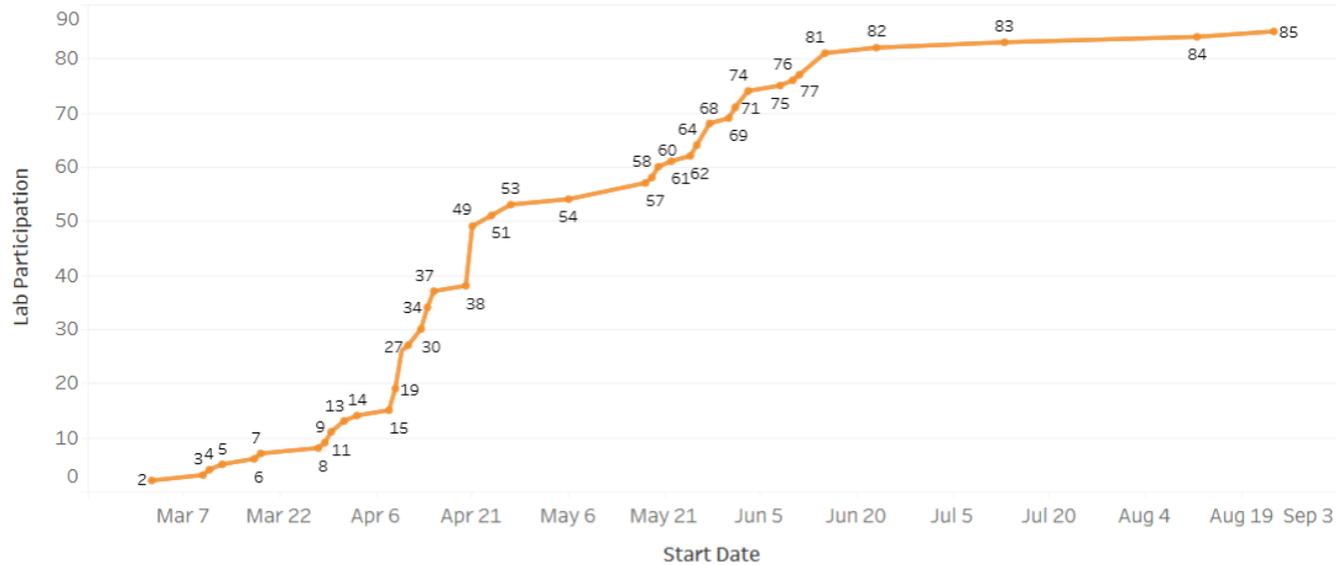
https://bi.wisconsin.gov/t/COVID19_Analytics/views/LabDashboards/PublicDashboard?:origin=card_share_link&:embed=y&:isGuestRedirectFromVizportal=y



Wisconsin COVID-19 Testing Laboratories

Laboratories actively testing	Laboratories planning to test	Current state capacity (tests/day) <i>Last Updated: 9/1/2020 6:45:24 PM</i>
86	25	26,591

COVID-19 Lab Participation Rate Over Time
last updated 9/1/2020 6:45:34 PM
updated every 15 minutes



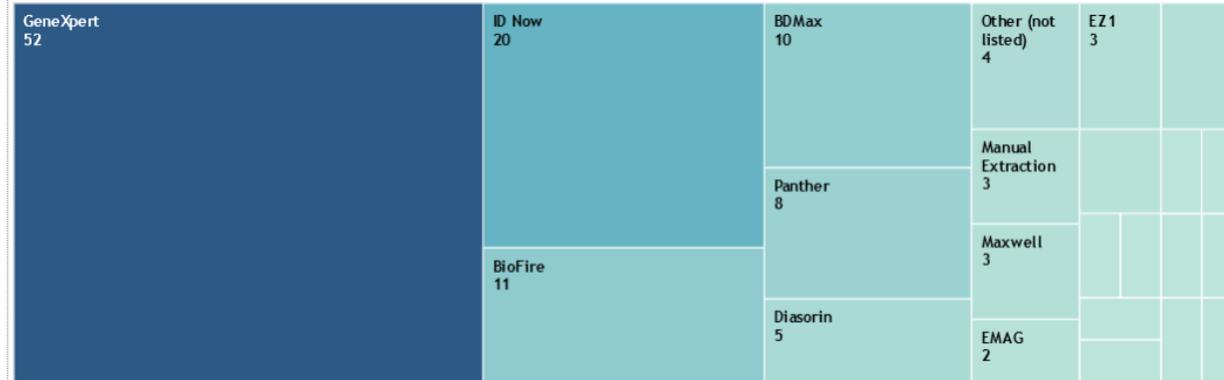
https://bi.wisconsin.gov/t/COVID19_Analytics/views/LabDashboards/PublicDashboardLabs?isGuestRedirectFromVizportal=y&embed=y



Wisconsin Clinical Laboratory COVID-19 Test Methods

(Last updated 9/1/2020 6:45:28 PM)

Active Test Methods Statewide



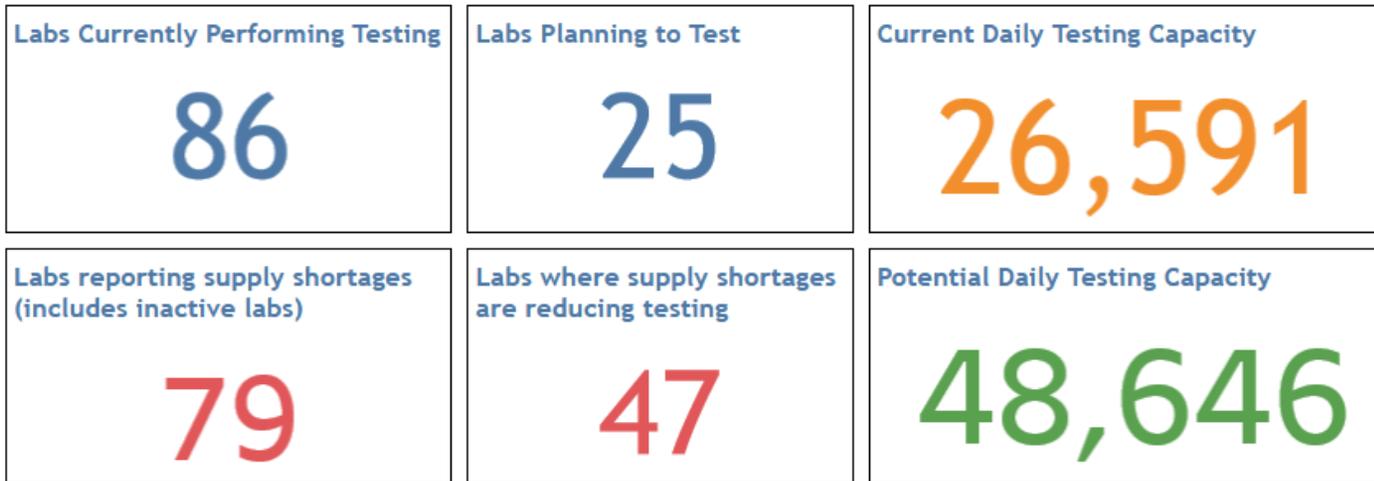
Current and Planned Methods



https://bi.wisconsin.gov/t/DHS/views/InternalLabCapacityDashboards_15941441982880/TestingMethods?:iid=1&:isGuestRedirectFromVizportal=y&:embed=y



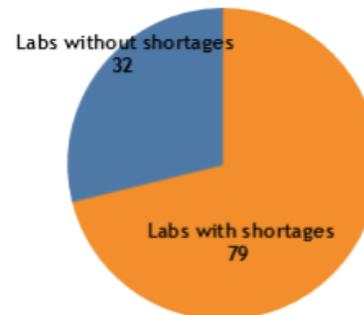
COVID-19 Lab Capacity in Wisconsin (Last Updated 9/1/2020 1:45:57 PM)



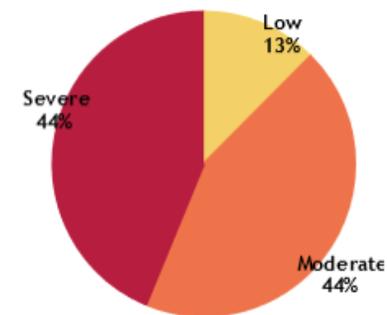
Top 6 Lab Products in Short Supply

Shortage Reason	Labs Reporting ..
GeneXpert cartridges	58
Collections Kits (NP swab and/or VTM)	18
Panther supplies	14
Abbott ID Now cartridges	12
BD Max supplies	10
BioFire supplies	6

Impact of Shortages



Severity of Shortages





SEOC Supplies

- Healthy supply of collection materials, order through the SEOC web portal if needed

<https://covid19supplies.wi.gov/Testing>

- “Flash offering” of unusual supplies in recent lab message.
 - Still a lot left, second offering expected soon



Local Collection Kits

Stable stored at room temp for
5 months
and counting!

Package inserts for WVDL and Gentueri will be
updated on WSLH and SEOC webpages

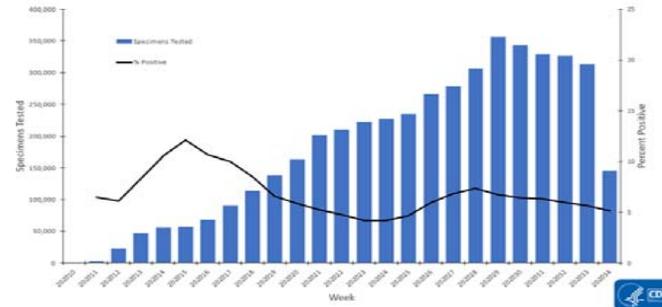
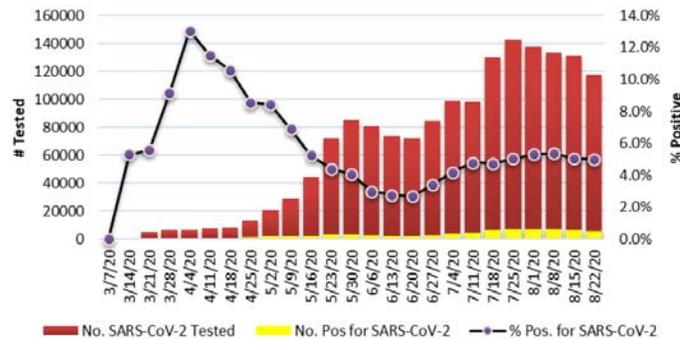


WHAT'S NEW



COVID-19 Testing

**% Positive SARS-CoV-2 by PCR (Wisconsin),
Week Ending August 22, 2020**



<http://www.surveymoz.com/s3/389222/Wisconsin-Laboratory-Surveillance-Reporting>

<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html>

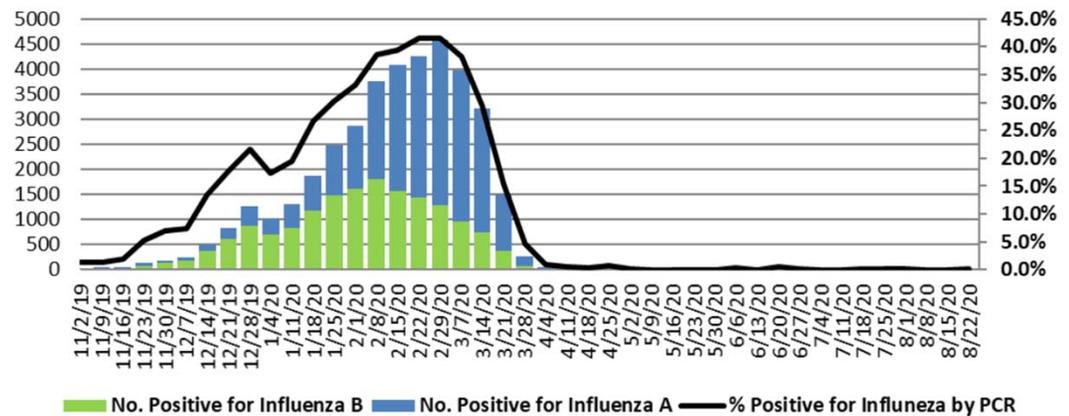
*Not all labs reporting to WSLH



Other Respiratory Pathogens

Week Ending August 22, 2020		
Resp. Pathogen PCR	# Tested	% Positive
Rhinovirus/ Enterovirus	832	6.6
SARS-CoV-2	117,551	5.0
Influenza	905	<1
Human metapneumovirus	861	<1
Parainfluenza	855	<1
Adenovirus	37	0
RSV	874	0
Seasonal coronaviruses	37	0
<i>B. pertussis</i>	399	<1

% Positive for Influenza by PCR (Wisconsin), Week Ending August 22, 2020



Please send **all positive influenza specimens** for further characterization.



Flu

- No asymptomatic testing
- Most accurate during flu season
- If you can't multiplex, test for flu second until flu is more prevalent than COVID-19



SalivaDirect

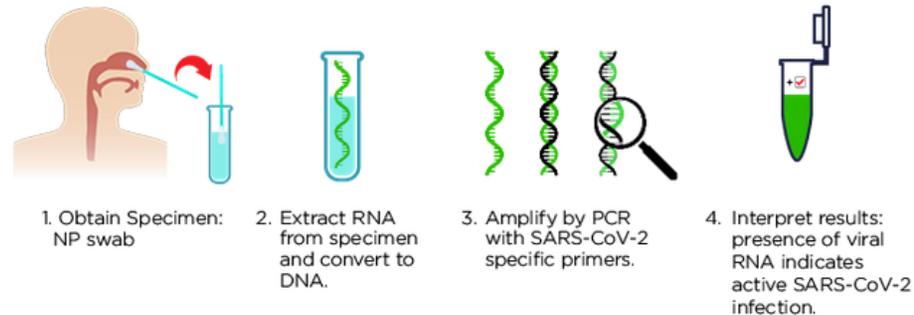
Pro:

- No swab/VTM
- No extraction step saves reagents, cost, and time

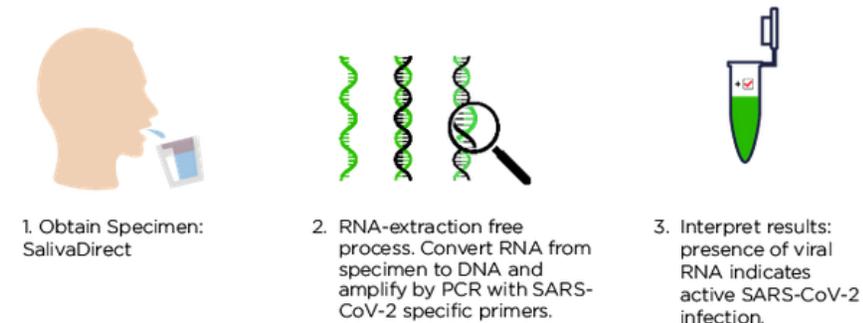
Con:

- More variable/less sensitive sample type
- Removing extraction step reduces sensitivity

Molecular Tests (Nucleic Acid Detection)



SalivaDirect Test



<https://asm.org/Articles/2020/August/What-is-the-COVID-19-SalivaDirect-Test>



FDA updates

FDA Approved Tests: To date, the FDA has currently authorized 221 tests under EUAs; these include 179 molecular tests, 39 antibody tests, and 4 antigen tests.

LumiraDx

SARS-CoV-2 Ag test (LumiraDx)



97.6% Sensitivity, 96.6% Specificity



BinaxNOW

COVID-19 Ag card (Abbott)



97.1% Sensitivity, 98.5% Specificity

<https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas>



EUA no Longer Required?!

You can make a COVID-19 lab developed test (LDT) and use it without applying for EUA from FDA [link](#)

- Cannot receive Prep Act funds
- Still subject to CLIA

“The Trump Administration is committed to combating COVID-19, to ensuring that the American people are protected against future pandemics, and to keeping duplicative regulations and unnecessary policies from interfering with those efforts. . . . the department has determined that the Food and Drug Administration ("FDA") will not require premarket review of laboratory developed tests ("LDT") ” - HHS

<https://www.hhs.gov/coronavirus/testing/recission-guidances-informal-issuances-premarket-review-lab-tests/index.html>



Using Tests Off-Label?!

You can use POC tests off label for asymptomatic screening [link](#)

“If highly sensitive tests are not feasible, or if turnaround times are prolonged, health care providers may consider use of less sensitive point of care tests, even if they are not specifically authorized for this indication (commonly referred to as "off label")” - FDA

https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/pooled-sample-testing-and-screening-testing-covid-19?utm_campaign=2020-08-21%20Pooled%20Sample%20Testing%20and%20Screening%20Testing&utm_medium=email&utm_source=Eloqua



POSITIVE PREDICTIVE VALUE AND ANTIGEN TESTING



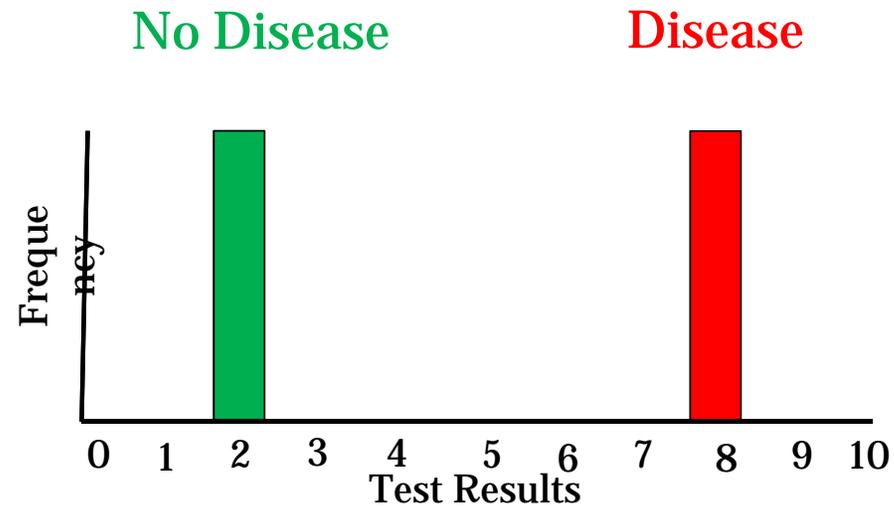
Point-of-care (POC) tests

Test	Method	Run time	Swab types	Sensitivity	Specificity
Abbott ID NOW	Molecular	5-13 min	NP, nasal, OP		
Cepheid GeneXpert	Molecular	40 min	NP, OP, nasal, mid-turbinate, nasal wash		
Accula	Molecular	30 min	Nasal		
Cue	Molecular	25 min	Nasal		
Quidel Sofia	Antigen	17 min	NP and nasal	96.7	100
BD Veritor	Antigen	15 min	Nasal	84.0	100
LumiraDx	Antigen	15 min	Nasal	97.6	96.6
BinaxNOW	Antigen	15 min	Nasal	97.1	98.5

- Allow for rapid, actionable results
- Veritor and Sofia being provided to LTCFs with a CLIA waiver
- Being used at universities, businesses, clinics

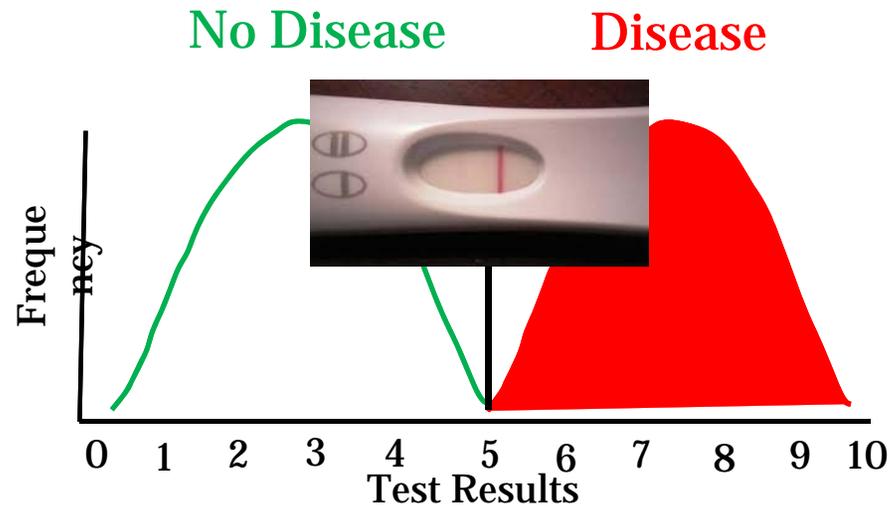


It's it easy to tell them apart?





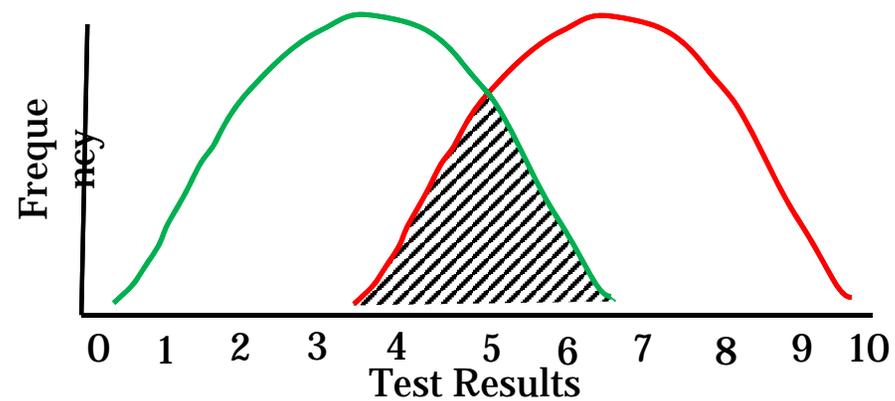
Biology Means Diversity





There's a Gray Zone

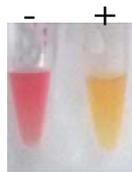
No Disease Disease





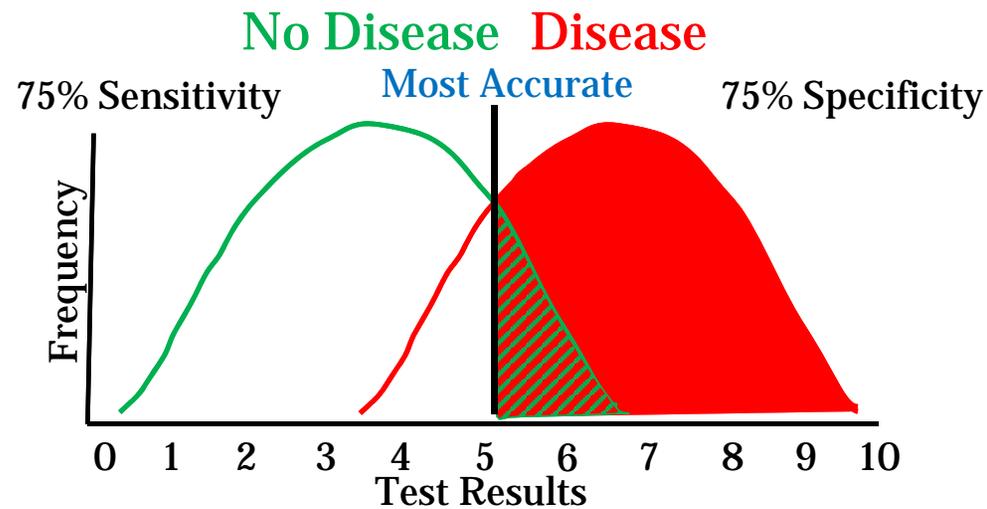
What Causes the Overlap?

- Human error
 - Improper collection
 - Improper transport
 - Mix-up in the lab
 - Contamination
 - Using the test on pets
 - Not following instructions
- Defective testing supplies or broken equipment
- Interfering substances (nose spray, antibiotic gel)
- Error is intrinsic in the test itself





Back to Basics

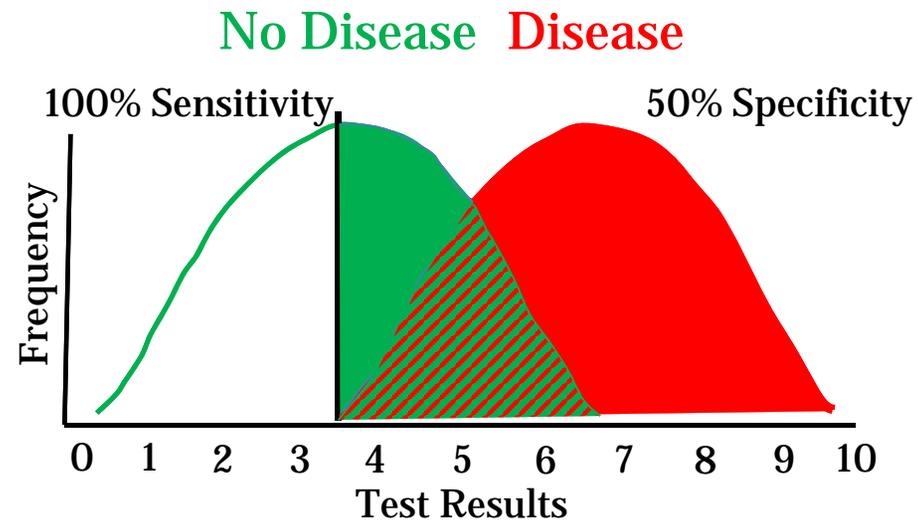


Sensitivity- How good is the test at detecting positives?

Specificity- How good is the tests at distinguishing true positives from false positives?

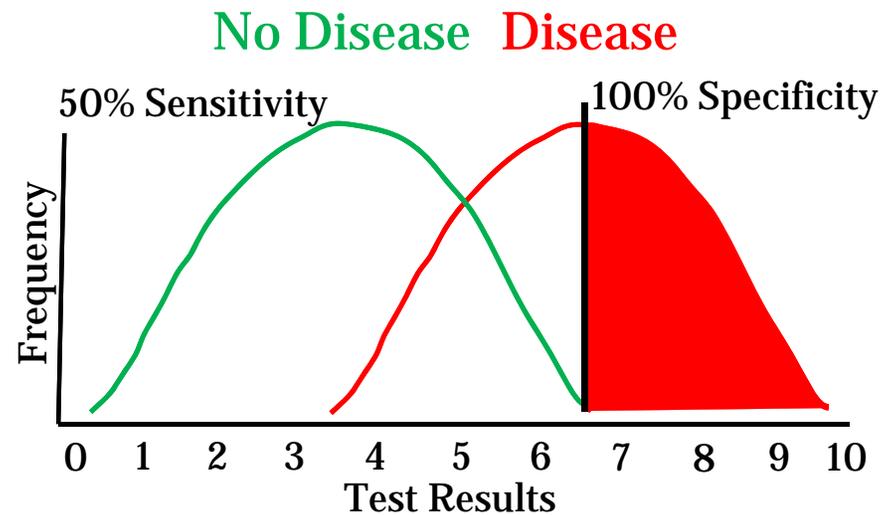


If it's most important to
not miss any positives



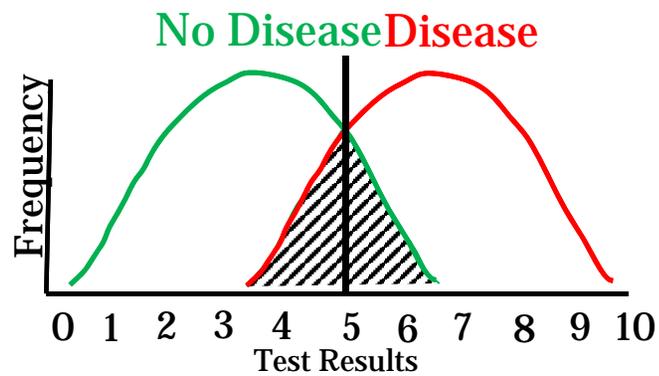


If it's most important to have no false positives

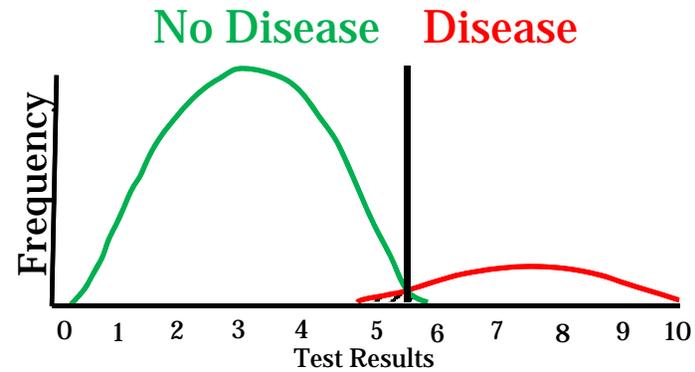




Most Often the Disease is Rare



75% Sensitivity, 75% Specificity



96% Sensitivity, 99% Specificity



Calculating Test Performance

Understanding the Chart

		<u>Truth</u>		Total test results	
		Patients with Disease	Patients without Disease		
<u>Test Results</u>	Positive Test	True positive	False positive	Total positive tests	PPV=% of positive result in people with disease
	Negative Test	False negative	True negative	Total negative tests	NPV=% of negative result in people without disease
Total		Total people with disease	Total people without disease	Total People tested	

Sensitivity
(% of people with disease that have a positive test)

Specificity
(% of people without disease that have a negative test)

Prevalence= % of people tested that have disease



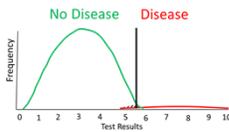
Calculating Test Performance

	Patients with Disease	Patients without Disease	Total test results	
Positive Test	A % sensitivity x E	B (1-% specificity) x F	A+B	PPV $\frac{A}{(A+B)} \times 100$
Negative Test	C (1-% sensitivity) x E	D % specificity x F	C+D	NPV $\frac{D}{(C+D)} \times 100$
Total	E % prevalence x G	F (1-% prevalence) x G	G # of people tested	



Let's Test Everyone in America!

- All 328 Million Americans get tested **Once** . . .
- About 1% of Americans are actively infected with COVID-19
- Antigen test with a sensitivity of 85% and specificity of 97%.



What if we mass test everyone in the US?

	Patients with Disease	Patients without Disease	All Patients	
Positive Test	2.8	9.7 <i>False positive</i>	12.5	PPV 22.2%
Negative Test	0.5 <i>False negative</i>	314	314.5	NPV 99.8%
Total	3.28	324.72	328*	

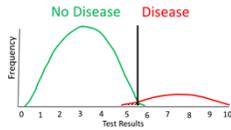
85%
Sensitivity

97%
Specificity

1% Prevalence

A test is only as good as the population tested

*numbers in millions



What if we mass test everyone in the US, but there is 10x more disease?

	Patients with Disease	Patients without Disease	All Patients	
Positive Test	27.88	8.86 <i>False positive</i>	36.74	PPV 76%
Negative Test	4.92 <i>False negative</i>	286.34	291.26	NPV 98%
Total	32.8	295.2	328*	

85%
Sensitivity

97%
Specificity

10% Prevalence

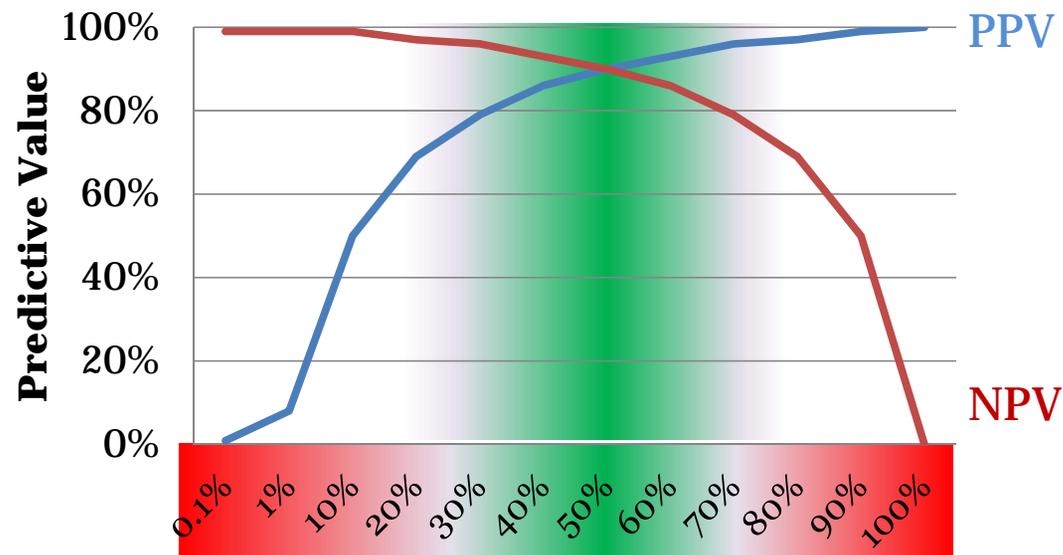
**A test is only as
good as the
population
tested**

*numbers in
millions



What prevalence can you test?

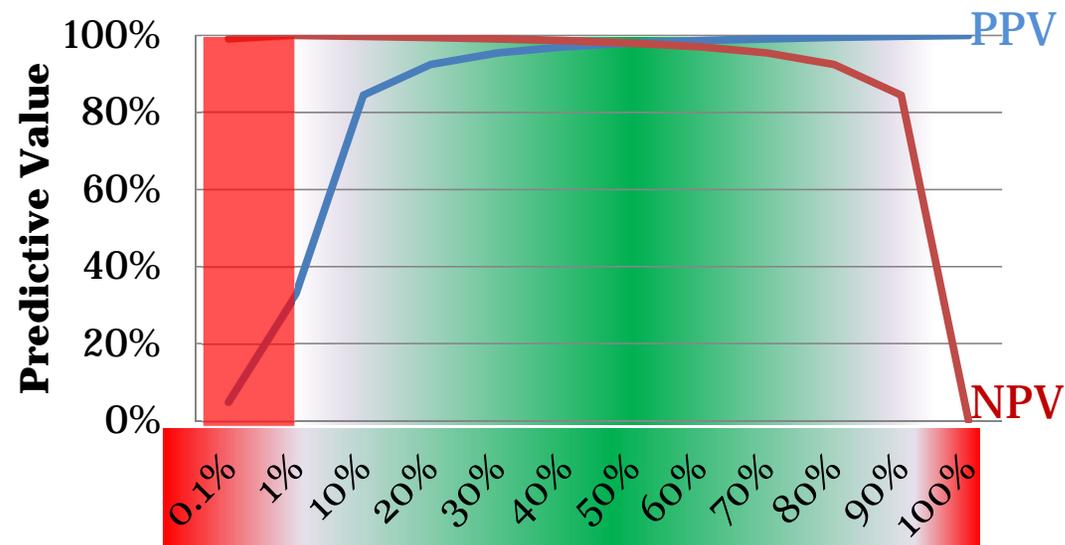
90% Sensitivity and 90% Specificity





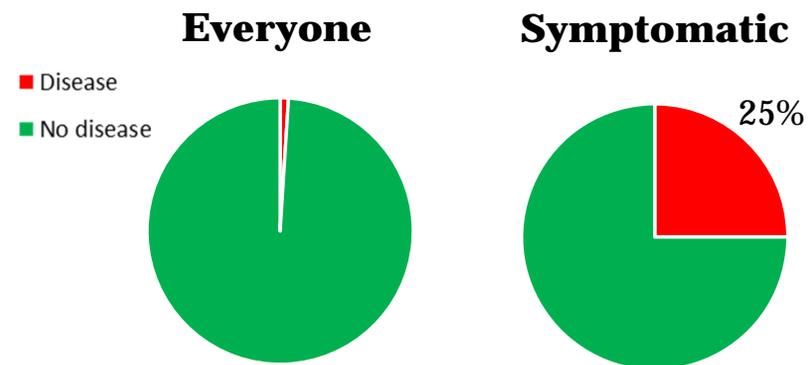
What prevalence can you test?

98% Sensitivity and 98% Specificity at 98%





How can you test when the prevalence is low?

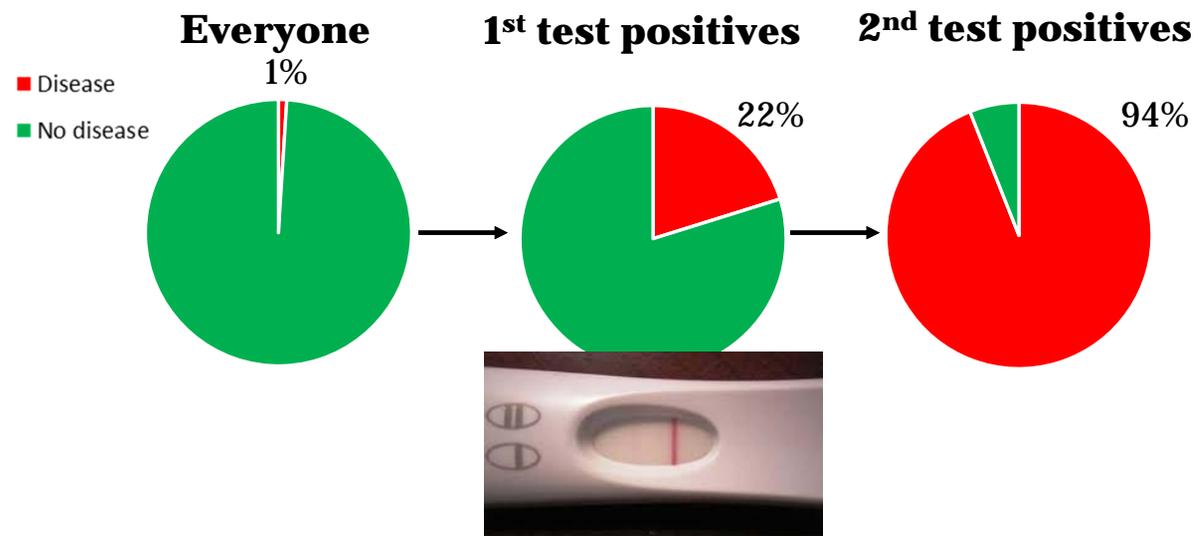


If the prevalence of a disease is low

1. The positive predictive value can be increased by only testing symptomatic or high risk patients.
2. Confirming results by a second test



Two Tiered Testing to Improve Predictive Value



Pro tip: If you use a 2 tiered testing system the first test should be the most sensitive, the second should be highly specific.



Definitions

Diagnostic Testing: intended to identify current infection in individuals and is performed when a person has signs or symptoms consistent with COVID-19, or when a person is asymptomatic but has recent known or suspected exposure to SARS-CoV-2. It is reportable and must be done in a CLIA regulated environment.

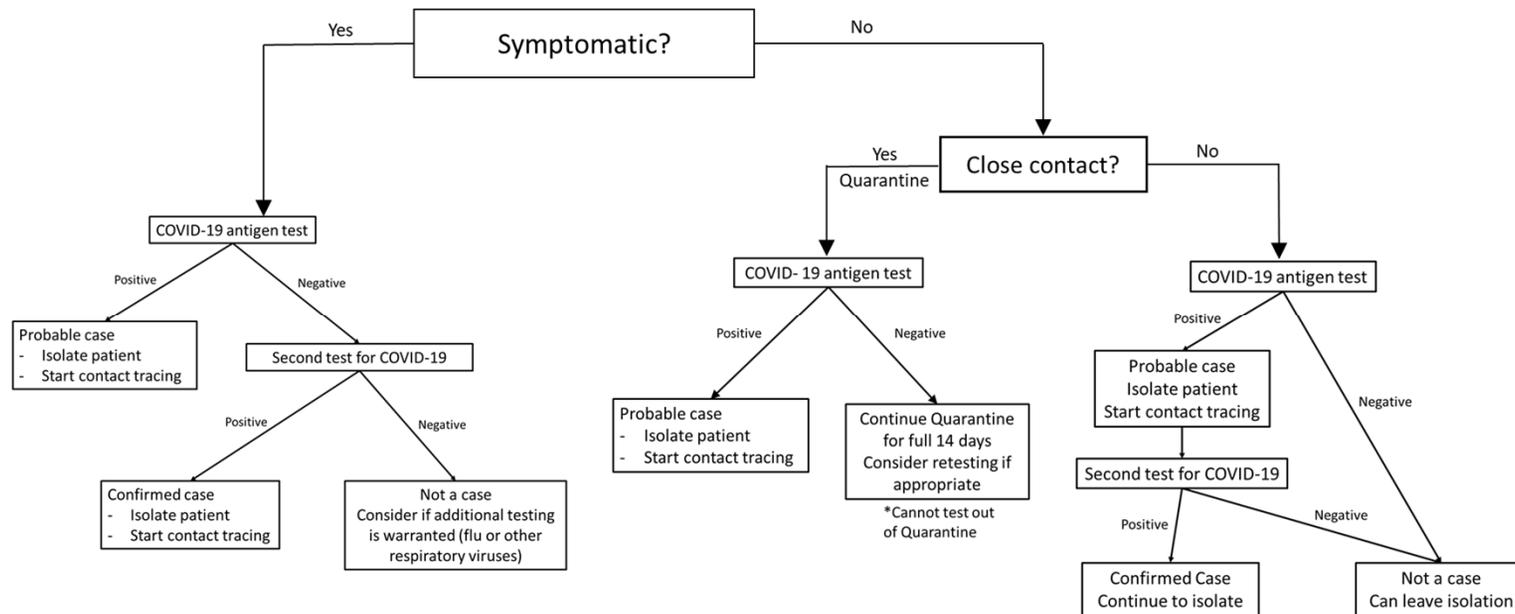
Screening Testing: intended to identify infected persons who are asymptomatic and without known or suspected exposure to SARS-CoV-2. It is reportable and must be done in a CLIA regulated environment.

Surveillance Testing: intended to monitor for a community- or population-level infection and disease, or to characterize the incidence and prevalence of disease. It is not reportable and does not require CLIA oversight. However, individual patient results cannot be communicated to the patient or used for medical treatment.

https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html?deliveryName=USCDC_2067-DM35559



Antigen Testing Strategy



CDC 2 tiered testing guidance- https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html?deliveryName=USCDC_2067-DM35559

CDC decision tree for LTCFs <https://www.cdc.gov/coronavirus/2019-ncov/downloads/hcp/nursing-home-testing-algorithm-508.pdf>

FDA Guidance for “off-label” antigen testing- https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/pooled-sample-testing-and-screening-testing-covid-19?utm_campaign=2020-08-21%20Pooled%20Sample%20Testing%20and%20Screening%20Testing&utm_medium=email&utm_source=Eloqua



Please Type Your Questions in the Question Box!

