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

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WISCONSIN STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN
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
“And I thought it was a nasal swab.”

Covid Testing In The Rear
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
Average daily cases per 100,000 people in the past week

Few or no cases

COVID-19 in the US

In 2 months- 60,000 new deaths, 2x the cases

Johns Hopkins University Global Coronavirus Tracking:
https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6
DHS COVID-19 Activity Level Data Dashboard

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

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 STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN
Wisconsin

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

<table>
<thead>
<tr>
<th>Recovery Status</th>
<th>Deaths</th>
<th>Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovered: 67,902 (88.7%)</td>
<td>Deaths: 1,130 (+8)</td>
<td>Ever hospitalized: 5,878 (+61)</td>
</tr>
<tr>
<td>Active: 7,534 (9.8%)</td>
<td>Percent who died: 1.5%</td>
<td>Percent ever hospitalized: 7.7%</td>
</tr>
</tbody>
</table>

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
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 Testing Laboratories

<table>
<thead>
<tr>
<th>Laboratories actively testing</th>
<th>Laboratories planning to test</th>
<th>Current state capacity (tests/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>86</td>
<td>25</td>
<td>26,591</td>
</tr>
</tbody>
</table>

**COVID-19 Lab Participation Rate Over Time**

*Last updated 9/17/2020 6:43:34 PM*

Updated every 15 minutes

[https://bi.wisconsin.gov/t/COVID19_Analytics/views/LabDashboards/PublicDashboardLabs?isGuestRedirectFromVizportal=y&embed=y](https://bi.wisconsin.gov/t/COVID19_Analytics/views/LabDashboards/PublicDashboardLabs?isGuestRedirectFromVizportal=y&embed=y)
## COVID-19 Lab Capacity in Wisconsin

<table>
<thead>
<tr>
<th>Labs Currently Performing Testing</th>
<th>Labs Planning to Test</th>
<th>Current Daily Testing Capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>86</td>
<td>25</td>
<td>26,591</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Labs reporting supply shortages (includes inactive labs)</th>
<th>Labs where supply shortages are reducing testing</th>
<th>Potential Daily Testing Capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>47</td>
<td>48,646</td>
</tr>
</tbody>
</table>

### Top 6 Lab Products in Short Supply

<table>
<thead>
<tr>
<th>Shortage Reason</th>
<th>Labs Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>GeneXpert cartridges</td>
<td>58</td>
</tr>
<tr>
<td>Collections Kits (NP swab and/or VTM)</td>
<td>18</td>
</tr>
<tr>
<td>Panther supplies</td>
<td>14</td>
</tr>
<tr>
<td>Abbott ID Now cartridges</td>
<td>12</td>
</tr>
<tr>
<td>BD Max supplies</td>
<td>10</td>
</tr>
<tr>
<td>BioFire supplies</td>
<td>6</td>
</tr>
</tbody>
</table>

### Impact of Shortages

- Labs without shortages: 32
- Labs with shortages: 79

### Severity of Shortages

- Low: 13%
- Moderate: 44%
- Severe: 44%
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
COVID-19 Testing


*Not all labs reporting to WSLH
Other Respiratory Pathogens

<table>
<thead>
<tr>
<th>Resp. Pathogen PCR</th>
<th># Tested</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinovirus/ Enterovirus</td>
<td>832</td>
<td>6.6</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>117,551</td>
<td>5.0</td>
</tr>
<tr>
<td>Influenza</td>
<td>905</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td>861</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td>855</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>37</td>
<td>0</td>
</tr>
<tr>
<td>RSV</td>
<td>874</td>
<td>0</td>
</tr>
<tr>
<td>Seasonal coronaviruses</td>
<td>37</td>
<td>0</td>
</tr>
<tr>
<td>B. pertussis</td>
<td>399</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

% 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

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

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

Using Tests Off-Label?!


“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
POSITIVE PREDICTIVE VALUE AND ANTIGEN TESTING
Point-of-care (POC) tests

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

<table>
<thead>
<tr>
<th>Test</th>
<th>Method</th>
<th>Run time</th>
<th>Swab types</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott ID NOW</td>
<td>Molecular</td>
<td>5-13 min</td>
<td>NP, nasal, OP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cepheid GeneXpert</td>
<td>Molecular</td>
<td>40 min</td>
<td>NP, OP, nasal, mid-turbinate, nasal wash</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accula</td>
<td>Molecular</td>
<td>30 min</td>
<td>Nasal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cue</td>
<td>Molecular</td>
<td>25 min</td>
<td>Nasal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quidel Sofia</td>
<td>Antigen</td>
<td>17 min</td>
<td>NP and nasal</td>
<td>96.7</td>
<td>100</td>
</tr>
<tr>
<td>BD Veritor</td>
<td>Antigen</td>
<td>15 min</td>
<td>Nasal</td>
<td>84.0</td>
<td>100</td>
</tr>
<tr>
<td>LumiraDx</td>
<td>Antigen</td>
<td>15 min</td>
<td>Nasal</td>
<td>97.6</td>
<td>96.6</td>
</tr>
<tr>
<td>BinaxNOW</td>
<td>Antigen</td>
<td>15 min</td>
<td>Nasal</td>
<td>97.1</td>
<td>98.5</td>
</tr>
</tbody>
</table>
It’s it easy to tell them apart?

<table>
<thead>
<tr>
<th>Frequency</th>
<th>No Disease</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>4</td>
<td>75</td>
</tr>
<tr>
<td>10</td>
<td>610</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>9</td>
<td>10</td>
</tr>
</tbody>
</table>
Biology Means Diversity

No Disease  Disease

Test Results

Frequency

0 1 2 3 4 5 6 7 8 9 10
There’s a Gray Zone

No Disease  Disease

![Graph showing frequency of test results for no disease and disease, with a shaded area representing the gray zone between the two distributions.](image-url)
What Causes the Overlap?

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

<table>
<thead>
<tr>
<th>Test Results</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>75</td>
</tr>
<tr>
<td>75</td>
<td>102</td>
</tr>
<tr>
<td>610</td>
<td>89</td>
</tr>
</tbody>
</table>

Most Accurate 75% Specificity

Sensitivity - How good is the test at detecting positives?
Specificity - How good is the test 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

<table>
<thead>
<tr>
<th>Disease</th>
<th>No Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Results</td>
<td>Frequency</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

100% Specificity

50% Sensitivity

Test Results

100% Specificity
Most Often the Disease is Rare

<table>
<thead>
<tr>
<th>Test Results</th>
<th>Disease</th>
<th>No Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

75% Sensitivity, 75% Specificity

96% Sensitivity, 99% Specificity
## Calculating Test Performance
### Understanding the Chart

<table>
<thead>
<tr>
<th>Test Results</th>
<th>Truth</th>
<th>Patients with Disease</th>
<th>Patients without Disease</th>
<th>Total test results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive Test</strong></td>
<td>True positive</td>
<td>False positive</td>
<td></td>
<td>Total positive tests</td>
</tr>
<tr>
<td><strong>Negative Test</strong></td>
<td>False negative</td>
<td>True negative</td>
<td></td>
<td>Total negative tests</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>Total people with disease</td>
<td>Total people without disease</td>
<td>Total People tested</td>
<td></td>
</tr>
</tbody>
</table>

- **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)

- **PPV**
  - (% of positive result in people with disease)

- **NPV**
  - (% of negative result in people without disease)
## Calculating Test Performance

<table>
<thead>
<tr>
<th></th>
<th>Patients with Disease</th>
<th>Patients without Disease</th>
<th>Total test results</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive Test</strong></td>
<td>A % sensitivity x E</td>
<td>B (1-% specificity) x F</td>
<td>A+B</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Negative Test</strong></td>
<td>C (1-% sensitivity) x E</td>
<td>D % specificity x F</td>
<td>C+D</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>E % prevalence x G</td>
<td>F (1-% prevalence) x G</td>
<td>G # of people tested</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- PPV: $\frac{A}{(A+B)} \times 100$
- NPV: $\frac{D}{(C+D)} \times 100$
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?

<table>
<thead>
<tr>
<th></th>
<th>Patients with Disease</th>
<th>Patients without Disease</th>
<th>All Patients</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.8</td>
<td>9.7</td>
<td>12.5</td>
<td>22.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>False positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Negative Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>314</td>
<td>314.5</td>
<td>99.8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>False negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3.28</td>
<td>324.72</td>
<td>328*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A test is only as good as the population tested

85% Sensitivity
97% Specificity
1% Prevalence

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

<table>
<thead>
<tr>
<th></th>
<th>Patients with Disease</th>
<th>Patients without Disease</th>
<th>All Patients</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive Test</strong></td>
<td>27.88</td>
<td>8.86</td>
<td>36.74</td>
<td>76%</td>
<td>98%</td>
</tr>
<tr>
<td></td>
<td><strong>False positive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Negative Test</strong></td>
<td>4.92</td>
<td>286.34</td>
<td>291.26</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>False negative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>32.8</td>
<td>295.2</td>
<td>328*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A test is only as good as the population tested

85% Sensitivity  
97% Specificity  
10% Prevalence  

*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 oversights. However, individual patient results cannot be communicated to the patient or used for medical treatment.

Antigen Testing Strategy


Please Type Your Questions in the Question Box!