



Fifty Shades of COVID-19 Testing & the Need for Speed

**Matt Modleski, Executive VP of Business Development
Orchard Software Corporation
September 24, 2020**

Learning Objectives

1. Describe the history and progression of COVID-19 testing from PCR through POCT.

2. Define COVID-19 testing challenges and roadblocks.

3. Evaluate the importance of rapid results in disease management (e.g., contact tracing, prevention, containment).

4. Identify the role of integrated POCT in the COVID-19 pandemic response.

5. Recognize the laboratory's vital role and its future outlook.

COVID-19 Fluidity

- Mention of specific vendors is not meant as an endorsement, only as an informational resource
- COVID-19 tests listed do not represent an all-inclusive list; new tests are added daily

A Little COVID History



A Novel Virus

- 1918 H1N1 pandemic produced the greatest pandemic mortality in history
 - ~ 500 million people (1/3 of the world's population) were infected & ~ 50 million died
- Flu kills 12,000 - 61,000 annually in the US (since 2010)
 - Globally, flu kills 290,000 - 650,000 people each year

- SARS-CoV-2 is a novel virus that causes the coronavirus disease 2019 (COVID-19).
- 3rd serious coronavirus outbreak in < 20 years
 - SARS in 2002
 - MERS in 2012

It's not 1918, but not the typical flu

- Globally, total confirmed cases > 29M; > 6M in US
- Worldwide, cases continue to rise
 - US, Brazil, & India the top 3 most affected countries
- Deaths continue to rise
 - > 920,000 globally;
 - > 194,000 in the US

2020 Goes Awry

Dec. 2019
– First case detected in Wuhan, China

Jan 30th –
WHO declares global PH emergency

March 11th
- COVID-19 classified as pandemic

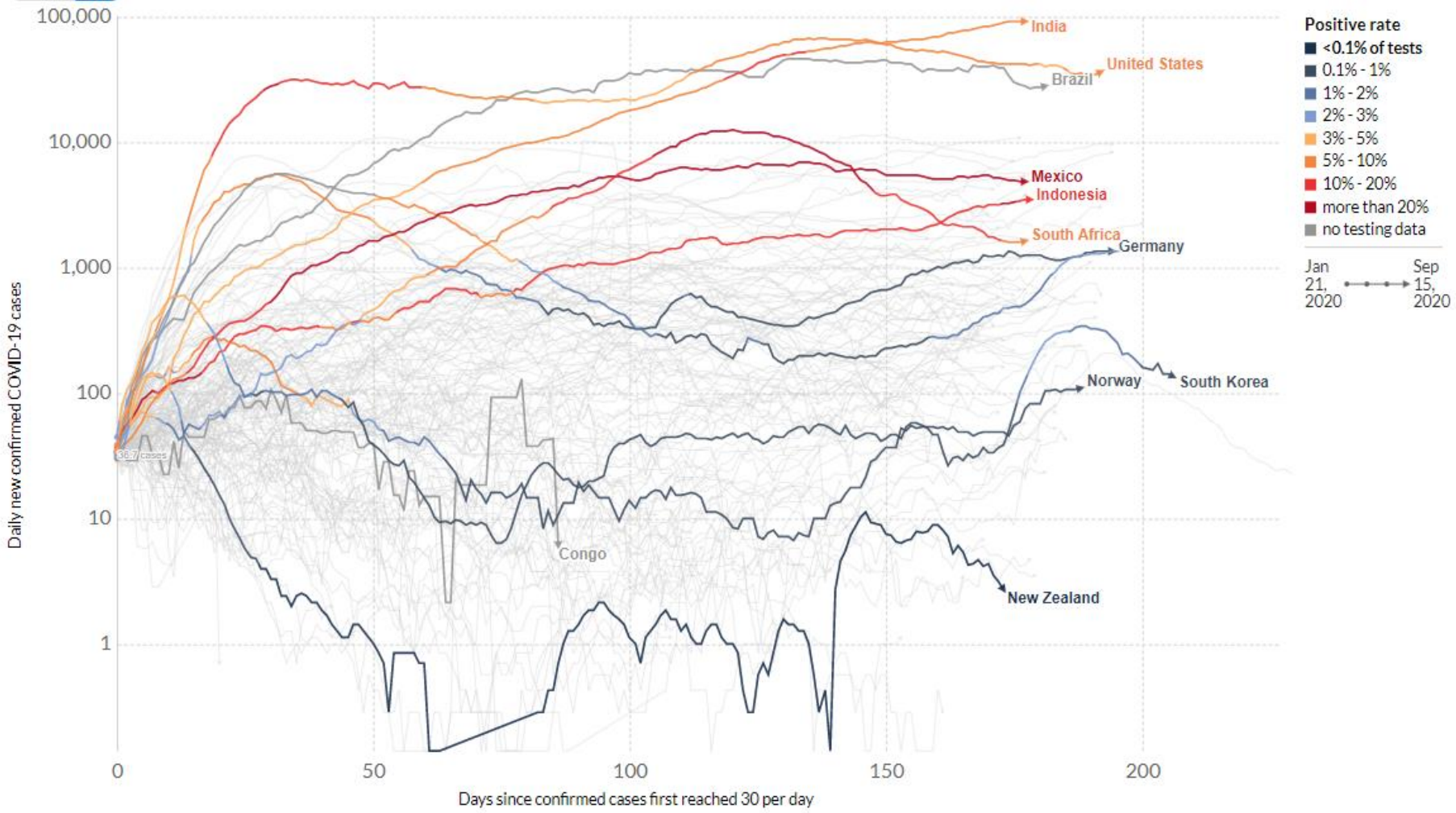
May 28th –
US death toll surpasses 100,000

June 10th –
US cases reach 2 million

Daily new confirmed COVID-19 cases

Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.

LINEAR LOG



Source: European CDC - Situation Update Worldwide - Last updated 15 September, 10:36 (London time), Official data collated by Our World in Data

CC BY



Source: ourworldindata.org/coronavirus

COVID-19 Testing



Early Testing Timeline

Late March: EUA issued for first diagnostic POCT & Early April: EUA issued for first antibody tests

Demand increases rapidly, causing backlogs of testing - supplies of reagents and PPE are strained

March: Labs that are properly equipped to perform biohazardous, highly-complex molecular testing develop approved tests

Early March: US commercial labs began testing - LabCorp & Quest announce RT-PCR tests available

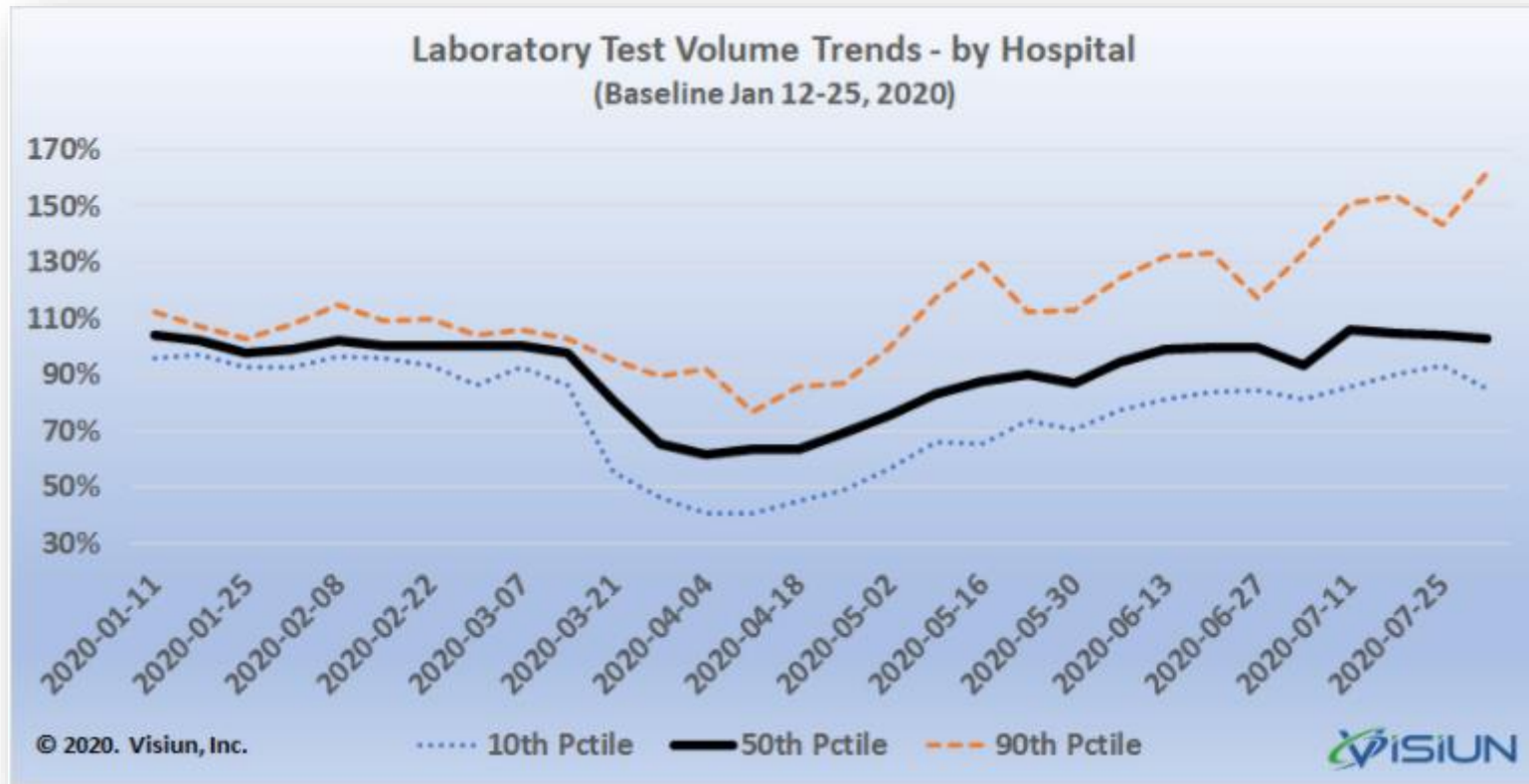
Early March: State & local laboratories permitted to begin testing - problems encountered with CDC's test reagent

Feb 2020: testing only performed at CDC allowing < 100 samples/day to be processed

FDA enacted Emergency Use Authorization (EUA) to allow labs to start COVID-19 testing without going through the full FDA approval process.

Currently there are > 200 FDA EUA-approved COVID-19 tests available with varying reliability.

2020 Test Volumes



Source: covid19briefings.com/visiun-2/

Types of SARS-CoV-2 Assays

1	Molecular	diagnose active infection	Reverse transcription polymerase chain reaction (RT-PCR)
2	Antigen*	diagnose active infection	Lateral flow, others; *Negative results should be confirmed with molecular test
3	Serological (Antibody)	exposure history/ immune status	Lateral flow, ELISA, Chemiluminescent immunoassay, others

- Each category has different: clinical utility, specimen types, characteristics, and limitations
- All are available as a POCT

POC COVID-19 Molecular Testing

Cepheid Xpert SARS CoV-2

- PCR
- 98.3% positive agreement & 100% negative agreement
- TAT ~ 30 minutes
- CLIA-waived



Abbott ID Now SARS CoV-2

- PCR
- 87.7% positive agreement & 100% negative agreement
- TAT ~ 5-13 minutes
- CLIA-waived



Abbott ID NOW Statement

“While we understand no test is perfect, test outcomes depend on a number of factors including patient selection, specimen type, collection, handling, storage, transport and conformity to the way the test was designed to be run.”



POC COVID-19 Antigen Testing

Quidel Sofia POC SARS CoV-2 Antigen Test

- 80% positive agreement & 100% negative agreement
- TAT ~15 minutes
- CLIA-waived



BD Veritor System for Rapid Detection of SARS-CoV-2

- 84% positive agreement & 100% negative agreement
- TAT ~ 15 minutes
- CLIA-waived



POC COVID-19 Antigen Testing

LumiraDX SARS CoV-2 POC Antigen Test

- 97% positive agreement & 97% negative agreement
- TAT ~12 minutes
- CLIA-waived



Abbott BinaxNow Covid-19 Ag Card Rapid Test

- 97% sensitivity & 98% specificity
- TAT ~ 15 minutes
- CLIA-waived



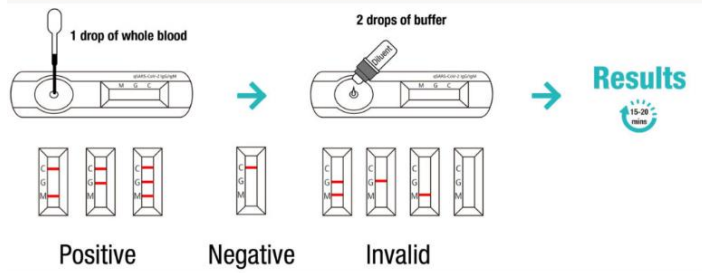
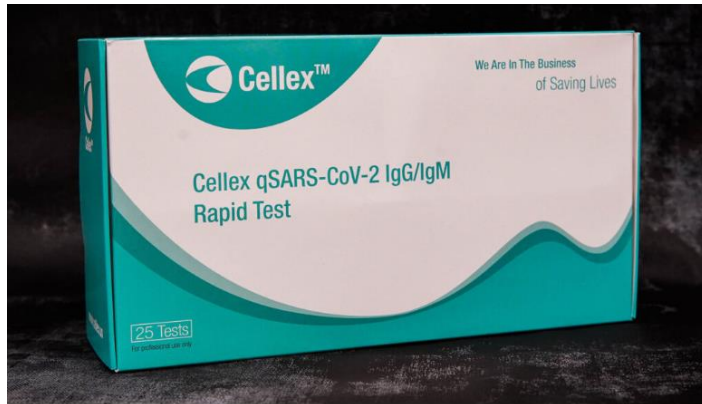
Source: www.lumiradx.com/us-en/what-we-do/diagnostics/test-technology/antigen-test
Source: <https://abbott.mediaroom.com/2020-08-26-Abbotts-Fast-5-15-Minute-Easy-to-Use-COVID-19-Antigen-Test-Receives-FDA-Emergency-Use-Authorization-Mobile-App-Displays-Test-Results-to-Help-Our-Return-to-Daily-Life-Ramping-Production-to-50-Million-Tests-a-Month>

HHS Awards \$760M for Abbott BinaxNOW COVID-19 Ag Card

- 150 million dx POCT
- uses nasal swabs
- Cost ~ \$5
- Includes NAVICA app

“to expand strategic, evidence-based testing in the U.S.”

POC COVID-19 Antibody Testing



Cellex serologic POC qSARS-CoV-2 IgG/IgM Rapid Test

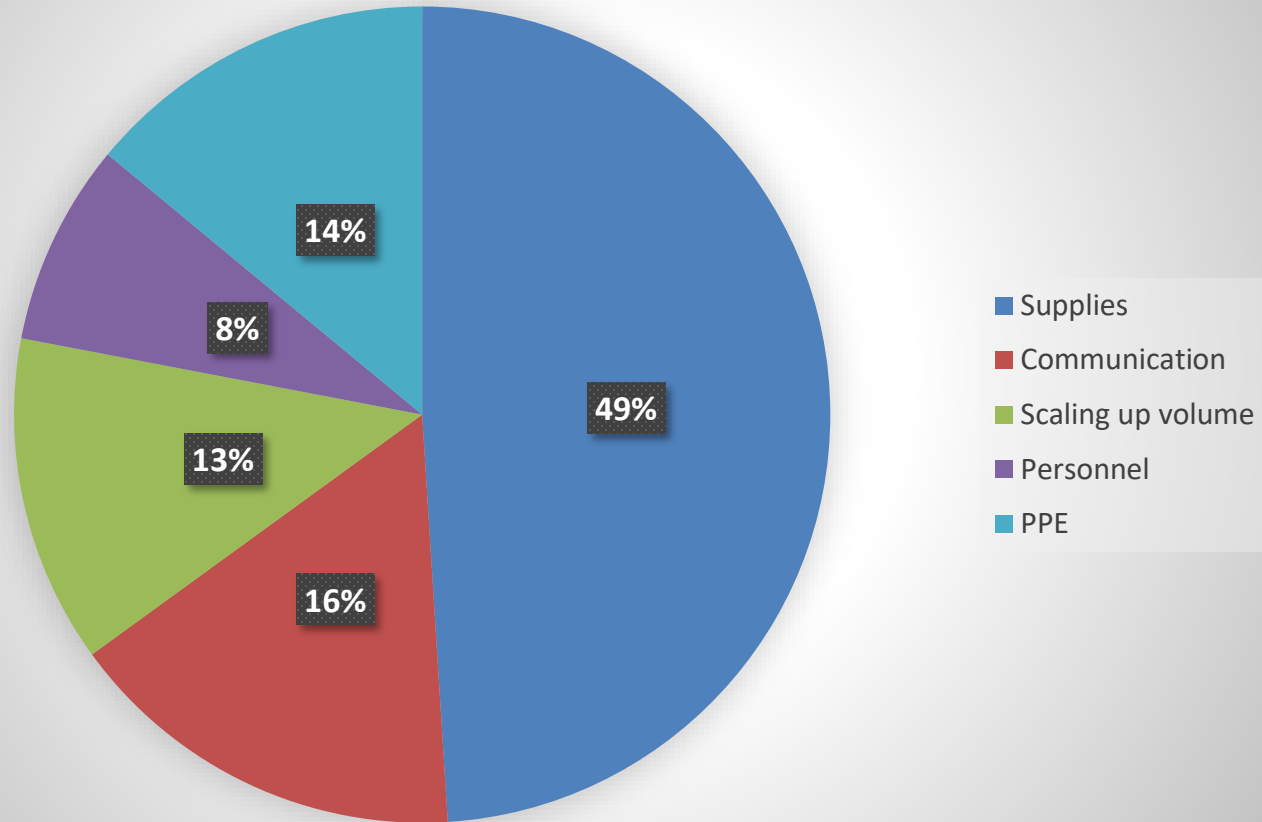
- Lateral flow immunoassay - qualitatively detects IgM and/or IgG antibodies from whole blood specimens
- 94 % positive agreement & 96% negative
- TAT ~ 15-20 minutes
- CLIA license required (moderately complex)

Source: <https://cellexcovid.com/>

COVID-19 Testing Challenges & Roadblocks



Biggest COVID Testing Challenges



Source: <https://www.mlo-online.com/disease/infectious-disease/article/21142733/covid19-testing-despite-supply-chain-issues>

CARES Act

June
4th

Coronavirus Aid, Relief, and Economic Security (CARES) Act

- requires “every laboratory that performs or analyzes a test that is intended to detect SARS-CoV-2 or to diagnose a possible case of COVID-19” to report the results from each such test to HHS
- data should be sent to state or local public health departments using existing reporting channels ... to ensure rapid initiation of case investigations...

Difficult decisions govern the provision of care with limited resources & supplies

- Since the beginning of the pandemic, the US has been plagued by testing problems.
- As demand has increased, backlogs & choke points occur at many steps along the testing chain.
 - spot shortages of many different items

In addition to > 190,000 Deaths...

- Pandemic has taken a toll on mental health as well
 - 1/3 of US adults report stress, anxiety, & sadness
 - Unemployment- as high as 16%; comparable to the Great Recession

- Caused unknown # of missed or delayed diagnoses for non-COVID conditions
 - patients are unwilling/ unable to access medical attention due to fear of COVID-19
- Many HCOs report higher # of cardiac arrests
 - patients are waiting too long to seek cardiac care

How the Pandemic has Impacted Lab Revenue



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Reimbursements

- Labs spend ~ \$40 to \$150 per test
- CMS reimburses ~ \$51 for a standard PCR assay and \$100 for a high-throughput test
- Reimbursements barely cover costs of test kits
 - Does not cover overhead (e.g., rent, salaries, PPE)



CPT Code	Code Description	Reimbursement
87635	Infectious agent detection by nucleic acid (DNA or RNA);severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19]), amplified probe technique	\$51.31
86769	Antibody; severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19])	\$42.13
86328	Immunoassay for infectious agent antibody(ies), qualitative or semiquantitative, single-step method (e.g., reagent strip); severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19])	\$45.23

Source: <https://revcycleintelligence.com/news/cms-releases-medicare-payment-rates-for-covid-19-test-cpt-codes>



HCPCS Code	Code Description	Reimbursement
U0003	Infectious agent detection by nucleic acid (DNA or RNA); severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19]), amplified probe technique, making use of high throughput technologies as described by CMS-2020-01-R.	\$100
U0004	2019-nCoV Coronavirus, SARS-CoV-2/2019-nCoV (COVID-19), any technique, multiple types or subtypes (includes all targets), non-CDC, making use of high throughput technologies as described by CMS-2020-01-R.	\$100

Neither HCPCS code U0003 nor U0004 should be used for tests that detect COVID-19 antibodies.

HRSA Funding for COVID-19 Testing

Awarded ~ \$2B to health centers to address COVID-19, including testing and related services

Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020	prevent, prepare for, and respond to COVID-19
Coronavirus Aid, Relief, and Economic Security (CARES) Act	detect coronavirus, prevent, diagnose, and treat COVID-19, and maintain current health center capacity and staffing levels
Paycheck Protection Program and Health Care Enhancement Act	support purchasing, administering, and expanding organizations' capacity for testing to monitor and suppress COVID-19

COVID-19 Claims Reimbursement to Health Care Providers & Facilities for Testing and Treatment of the Uninsured Program

provides reimbursements directly to eligible providers for claims that are attributed to the testing and treatment of COVID-19 for uninsured individuals

Families First Coronavirus Response Act (FFCRA) Relief Fund

funds received from the Public Health and Social Services Emergency Fund, appropriated in the FFCRA & the Paycheck Protection Program and Health Care Enhancement Act (PPHCEA); each appropriated \$1B to reimburse for COVID-19 testing for the uninsured

Provider Relief Fund

appropriated in the CARES Act & the PPHCEA to reimburse providers for treating uninsured individuals with a COVID-19 diagnosis

COVID-19 Testing Reimbursement Challenges

- with the need for rapid TAT, labs do not hold up testing for billing purposes → may cause large # denials
- verifying insurance eligibility and demographic information on patients at emergency testing sites
- with higher test volumes, missed charges can have a serious effect on a HCO's finances
- PCR testing on instruments can be costly
 - important to batch & run confirmatory tests wisely
 - conserve reagent and QC materials to keep costs in check

Source: www.mlo-online.com/management/rcm/article/21138310/covid19-testing-and-the-revenue-cycle

- Registering, documenting & creating instrument-ready labels at drive-thru testing sites
- Creating interfaces to exchange test and result information to fill orders from external organizations
- Sending testing data daily to state DOH & HHS

New pandemic-related workflows require modifications to standard electronic lab processes



Variations in Normal Revenue Sources

- 59% reported significant impact from COVID-19 pandemic
 - declines in almost all testing categories, with histology & oncology experiencing the biggest hit
 - greatest concern for labs during the pandemic is their people, with ~ 2/3 concerned about hiring, reducing, & maintaining staff
 - Kalorama Information survey (April)
- Initial drop in revenues up to 50%, whether or not offering COVID-19 testing
 - attributed to lockdown policies & reduction in scheduled tests/procedures
 - furloughs + increased stress & burnout
 - CAP Survey (May)

COVID-19 Testing TAT Problems



Testing Delays “Hobble” Effective Response



Source: www.washingtonpost.com/health/long-delays-in-getting-test-results-hobble-coronavirus-response/2020/07/12/d32f7fa8-c1fe-11ea-b4f6-cb39cd8940fb_story.html

Unacceptable TATs

- National Reference Labs
 - Up to 3-5 days
- Other labs
 - Up to 10-14 days

- Limited # of tests can be performed within the established TAT
- Some labs accept all tests that are sent, but TATs then increase to unreasonable levels
- Other labs cap the # of tests accepted to protect the TAT

Source: www.washingtonpost.com/health/long-delays-in-getting-test-results-hobble-coronavirus-response/2020/07/12/d32f7fa8-c1fe-11ea-b4f6-cb39cd8940fb_story.html

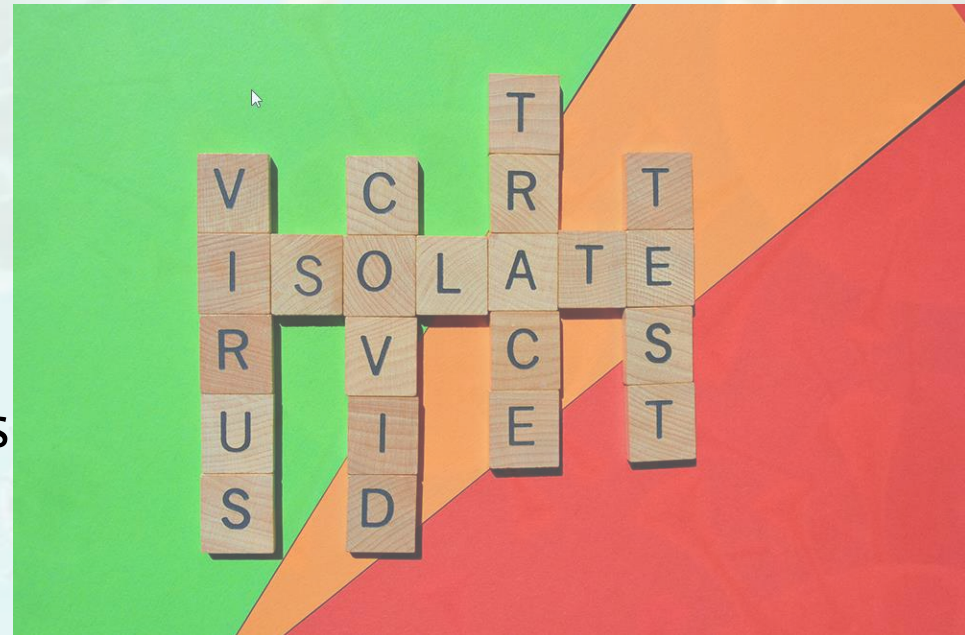
Factors Influencing Increased Demand

- increasing spread of the virus
- testing for pre-op patients
- testing in FQHCs, nursing homes, & prisons
- orders from drive/walk through community events
- organizations bringing employees back to work

Delays in testing mean public health workers are not able to notify the contacts of people who test positive, so people unwittingly continue to spread the virus.

TAT is Imperative

- Objective is isolating sick people
- **the rate of testing must be ramped up, employing multiple strategies**
- long TATs are making it impossible for the US to replicate the strategy used by other countries to effectively contain the virus — **test, trace, and isolate**
- lagging test times could discourage people from getting tested & practicing social distancing



Concerns about national COVID-19 lab testing capacity and supply chain distribution methods are growing.

“It [long TAT] makes contact tracing almost useless. By the time a person is getting results, they already have symptoms, their contacts may already have symptoms and have gone on to infect others.”

- Crystal R. Watson, PH Expert, Johns Hopkins University

Source: www.washingtonpost.com/health/long-delays-in-getting-test-results-hobble-coronavirus-response/2020/07/12/d32f7fa8-c1fe-11ea-b4f6-cb39cd8940fb_story.html

“If you're going to do contact tracing and the test comes back in five to seven days, you might as well not do contact tracing because it's already too late.”

- Dr. Anthony Fauci, National Institute of Allergy and Infectious Diseases

“Nationally, we'd likely save tens of thousands of lives if test turnaround times were shortened.”

- Jaline Gerardin, Disease modeling expert, Northwestern University

Source: www.wsj.com/articles/wait-times-grow-for-covid-19-test-results-as-infections-rise-sharply-11594287001

Source: www.washingtonpost.com/health/long-delays-in-getting-test-results-hobble-coronavirus-response/2020/07/12/d32f7fa8-c1fe-11ea-b4f6-cb39cd8940fb_story.html

Role of Integrated POCT in COVID-19 Response

I feel the need—
the need for
speed!

Peter “Maverick” Mitchell, played
by Tom Cruise in **Top Gun**



Harvard Study

- ~ 4.3 million people would have to be tested daily to suppress the US outbreak and begin to get back to normal
- 16 states have reached the mitigation benchmark, and of those 4 are doing enough testing to suppress the virus

Source: www.npr.org/sections/health-shots/2020/06/30/883703403/as-coronavirus-surges-how-much-testing-does-your-state-need-to-subdue-the-virus

POCT Steps in to Fill the Gap

“...fast point-of-care tests can help solve the problem of overburdened laboratories and could aid in the reopening of schools and businesses ...”

- ADM Brett P. Giroir, M.D., Assistant Secretary for Health (ASH)

Source: <https://www.npr.org/sections/health-shots/2020/07/14/891116538/despite-shortfalls-and-delays-u-s-testing-czar-says-efforts-are-mostly-sufficien>

“POC tests are a useful component of the diagnostic strategy in response to the SARS-CoV-2 (COVID-19) outbreak.”

- Office of the Asst Secretary for Health SARS-CoV-2 Fact Sheet

- nucleic acid amplification (molecular) tests
 - detect the presence of a pathogen
- antigen tests
 - detect the presence of a pathogen
- serological tests
 - determine if an individual has immunological evidence of exposure to a pathogen

July 14th

POCT in SNF

- HHS announced large-scale procurement of FDA-authorized rapid diagnostic POCT to be distributed to nursing homes
 - COVID-19 hotspots
 - on-site testing for nursing home residents & staff
 - to help prevent the spread of SARS-CoV-2

Source: www.hhs.gov/about/news/2020/07/14/trump-administration-announces-initiative-more-faster-covid-19-testing-nursing-homes.html

CDC Recommendations for NHs

- > 216,000 COVID-19 cases & > 53,000 deaths among NH residents as of August 30th
- CDC recommends that baseline testing of all residents and staff
 - regular screening and surveillance to detect potential outbreak situations early and reduce morbidity and mortality

“Access to rapid point-of-care testing in nursing homes will further protect our Nation’s most vulnerable patients.”

- ADM Brett P. Giroir, M.D., Assistant Secretary for Health

Source: www.hhs.gov/about/news/2020/07/14/trump-administration-announces-initiative-more-faster-covid-19-testing-nursing-homes.html

Source: <https://data.cms.gov/stories/s/COVID-19-Nursing-Home-Data/bkwz-xpvg/>





“ This new [POC] testing initiative is critical for keeping vulnerable older adults safe while delivering the quality of life they deserve. It gives nursing homes the ability to swiftly identify residents that need to be isolated and mitigate the spread of the virus. As one more tool in the toolbox, it represents an important step toward the long-awaited reunion of residents with their loves ones.”

- Seema Verma, CMS Administrator

Compared to a Thermometer...

Research by University
of Colorado at Boulder
& Harvard University

“test frequency and
turnaround time is
more important than
accuracy when it comes
to broad disease
surveillance”

Trade-off Between Speed & Accuracy

- POCT yields much speedier results but there are concerns about false negatives and lower sensitivity
- POCT can correctly identify positive cases in minutes
- Negative results may need to be confirmed with a high-sensitivity molecular test
- PCR testing is accurate on day of disease; **testing is a snapshot in time**

“Coronavirus tests administered outside lab settings are considered useful in fighting the pandemic even if they miss 20% of positive cases.”

– Senior FDA Official

Source: www.npr.org/sections/health-shots/2020/07/14/891116538/despite-shortfalls-and-delays-u-s-testing-czar-says-efforts-are-mostly-sufficien

Source: www.darkdaily.com/abbott-labs-id-now-covid-19-rapid-molecular-test-continues-to-face-scrutiny-over-false-negatives/

Efforts to Increase Testing & Reduce TAT



How Labs Are Adapting?

What clinical processes did you adapt for COVID-19 in-house testing?

Added precautions to ensure safety 30%

Created standard workflows 23%

Physical segmentations of instruments 16%

Added module(s) to LIS system 13%

None 12%

Source: www.mlo-online.com/disease/infectious-disease/article/21142733/covid19-testing-despite-supply-chain-issues

COPCP Case Study

- Overview

- Perform 4 million tests/yr
- 3 patient draw centers

Problem

- Trouble getting reagents & NG swabs
- Took weeks to months to purchase new platforms because supply struggled to meet demand

Solution

- Performing SARS-CoV-2 testing on multiple vendors' platforms
 - had Cepheid GeneXpert; added DiaSorin Molecular Liaison MDX & Abbott ID Now
- Added SARS-CoV-2 POCT
- With the 3 platforms, ramped up capacity to 90 tests/day

7 states band together to secure rapid COVID testing

- Virginia, Louisiana, Massachusetts, Michigan, Ohio, Maryland, & NC
 - goal = show private companies that there is significant demand to scale up production of POCT that deliver results in 15-20 mins
 - Becton Dickinson & Quidel

“With severe shortages and delays in testing..., the states are banding together to acquire millions of faster tests to help save lives and slow the spread of COVID-19.”

- Larry Hogan, Governor of Maryland

Source: <https://thehill.com/policy/healthcare/510552-six-states-band-together-to-secure-rapid-covid-testing/> <https://covid19briefings.com/2020/08/20/order-for-3-5-million-poc-sars-cov-2-antigen-tests-may-decrease-need-for-clinical-lab-based-pcr-testing/>

“Shark Tank” Approach

- NIH’s [Rapid Acceleration of Diagnostics \(RADx\)](#) initiative
 - awarded contracts to 7 biomedical diagnostic companies
 - support new lab and POCT to increase the number, type and availability of tests by millions per week
 - September 2020
- these technologies are expected to make a significant contribution to expanding the nation’s testing capacity

Source: www.nih.gov/news-events/news-releases/nih-delivering-new-covid-19-testing-technologies-meet-us-demand

COVID-19

coronavirus

Test

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HHS Actions to Reduce Testing TATs

- **Accelerating Technology and Authorizations**
 - commercial laboratories have received EUA to use pooled samples
- **Surge Testing**
 - temporary federal surge testing sites are being set up in communities experiencing outbreaks
- **Expanding Capacity**
 - commercial labs and government partners to expand testing capacity
- **Point-of-Care**
 - sending POCT to nursing homes in the US
 - 2,400 POCT devices will be sent in the first 4 weeks

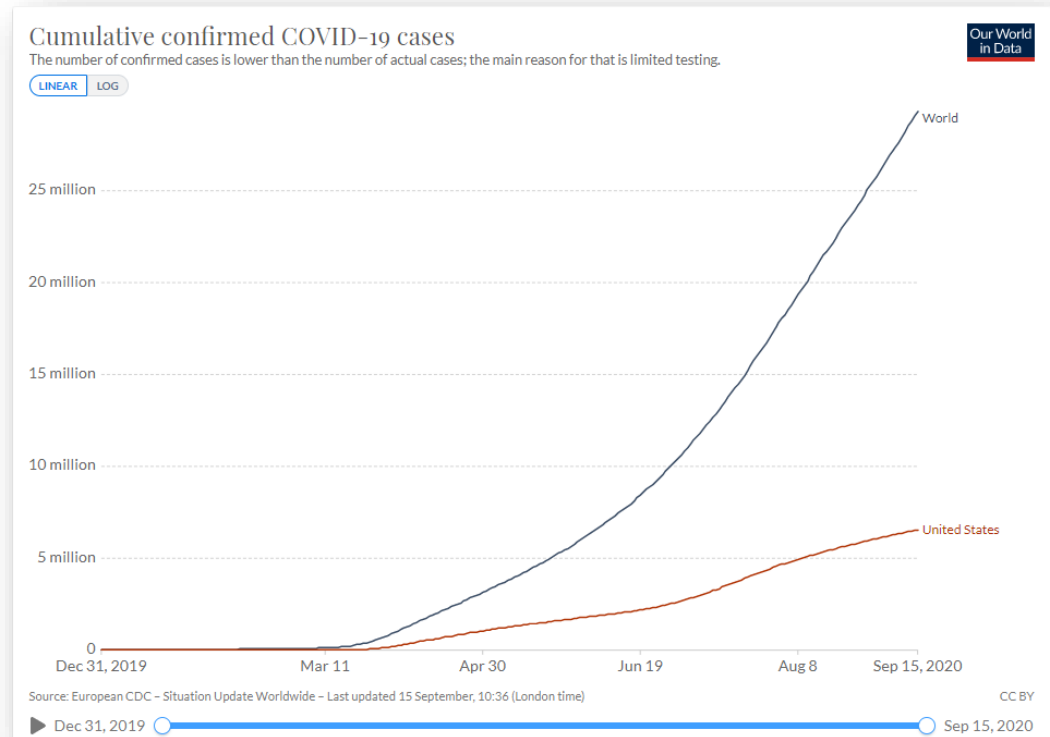
The Lab's Vital Contribution



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Without Testing There is No Data

- Testing is crucial to understand the spread of the pandemic & respond appropriately
- No country knows the total # of people infected
 - we know the infection status of those who have been tested
 - counts of confirmed cases depend on amount of testing



Testing is our window into the pandemic and how it is spreading.

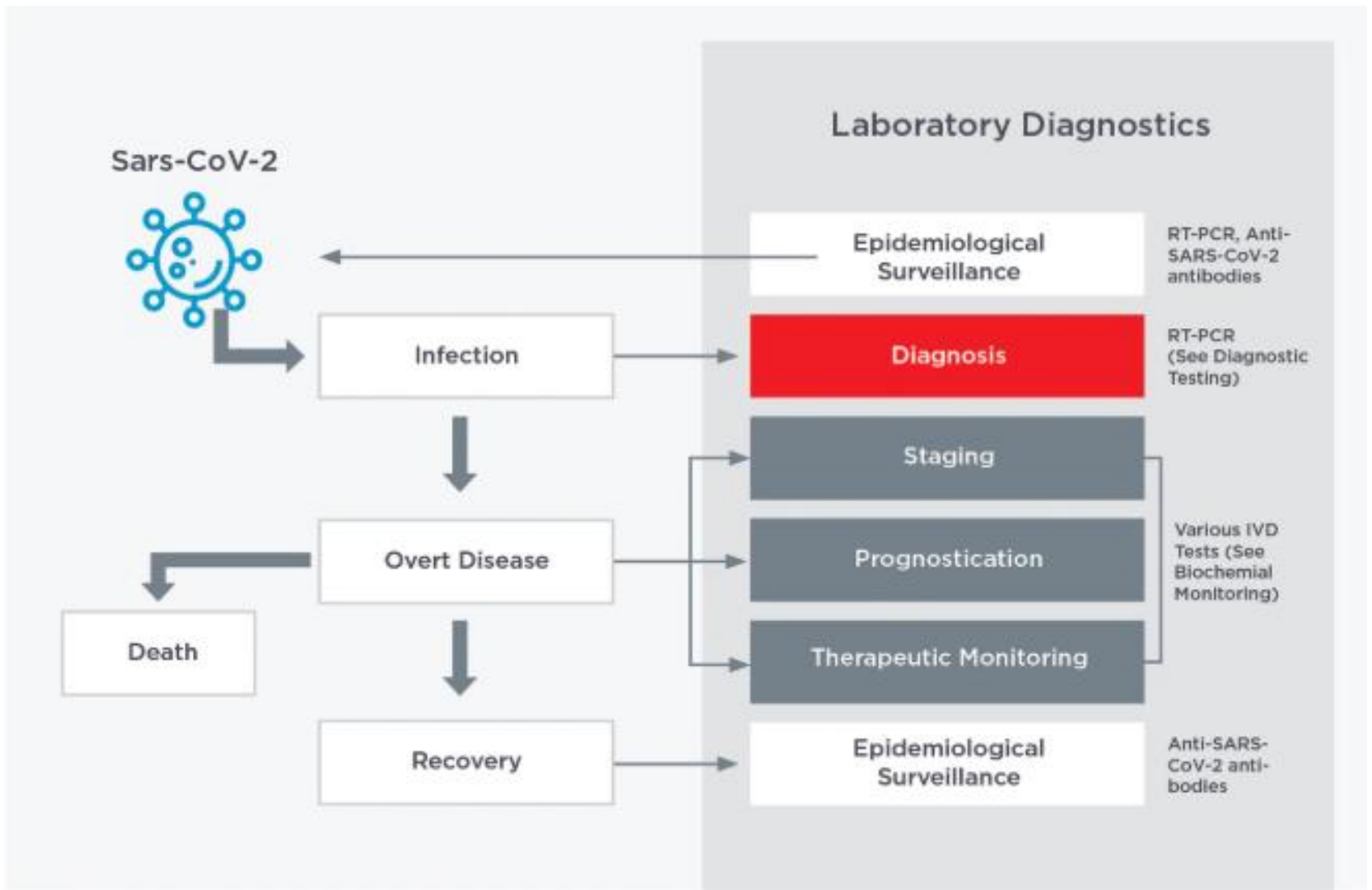



Figure 1. The critical role of laboratory medicine in COVID-19 (Modified from Lipi et al, PMIC: 32191623).

Source: www.mlo-online.com/disease/infectious-disease/article/21142491/navigating-through-crisis-in-a-pandemic-event



Clinical laboratories are often the first line of defense in a pandemic response

- perform diagnostic testing
- may be the first to identify the causes of illnesses in communities
- important for laboratories to maintain pandemic preparedness protocols

TriCore- “Higher Regard for POCT”

“Although the public now has eyes on the lab, there is still much that people don’t know, such as the limitations of antibody and other testing. **We need to be better educators, for the benefit of colleagues, as well as patients.**”

- Kathleen David, MT (ASCP), Manager, Point-of-Care Testing, TriCore Reference Laboratories

Source: poct.groupsite.com/file_cabinet/files/997548/download/KD-COVID%20paper-7.30-FINAL.pdf?m=1596210912



“The hidden profession saving lives”



Source: <https://www.cNBC.com/video/2020/08/09/the-hidden-profession-saving-lives.html#:~:text=In%20the%20midst%20of%20this,testing%20is%20in%20high%20demand.>

Paradigm shift of lab embracing POCT as powerful tool in the right places when speed is critical

- Not perfect but trade-off is worth it in specific scenarios
- Needs to be integrated/ automated reflex testing
- When speedy results can positively impact patient care

Key Lessons Learned

Early availability of diagnostic testing is of great value for patient management & public health.

Development, validation, scale-up, & distribution of diagnostic tests should be a key priority in early preparation during an emerging infectious disease outbreak.

Multiple testing methodologies/venues, including rapid POCT are beneficial to meet demand.

Laboratory medicine needs an integrated approach.

We need laboratory professionals leading this effort.

Thank you!

