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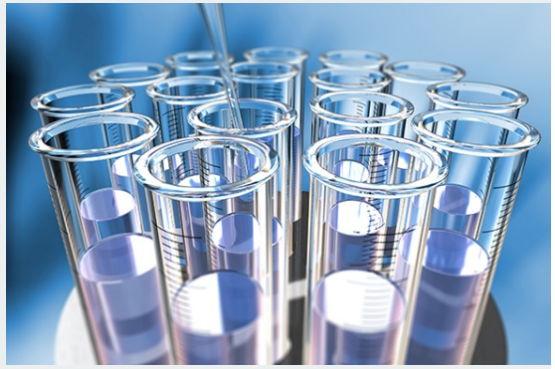


HA101: Demystifying SARS-CoV-2 Testing for COVID-19

Third Edition – Part 1: Updates and Trends

Health Advances LLC
BOSTON | SAN FRANCISCO | ZUG | HONG KONG
www.healthadvances.com

What to Expect from This Report

This Document Provides:

- Updates to our First and Second Editions on topics such as disease biology, test types, testing capacity, and test payment
- Exploration of the testing we need now and in the future to move to a “new normal”

What questions do you have regarding SARS-CoV-2/COVID-19 testing?

Please email additional questions to:
diagnostics@healthadvances.com

Agenda

- ***What has changed since the First and Second Editions?***
- What are the COVID-19 testing paradigm(s) of the future?
- Appendix

What We Still Don't Know About SARS-CoV-2: An Update

Updated 7/5/2020

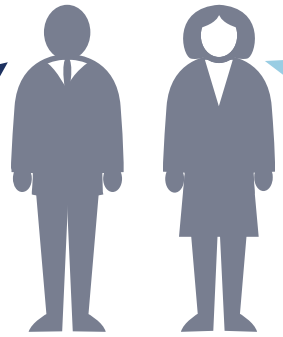
Research and clinical communities have made progress, but still have yet to answer many questions about SARS-CoV-2

Questions from First Edition (Early April)

Viral Characteristics
- How fast does the virus mutate?
- Will infections be seasonal?

Prognosis and Treatment
- What is the rate of asymptomatic cases?
- What are the mortality and morbidity rates?
- What measures can be taken to treat COVID-19?

Transmission
- How contagious is the virus (R_0)?
- To what extent can the virus be transmitted through passive material (e.g. mail, groceries, food delivery)?
- What measures can be taken to more effectively limit the spread of future outbreaks?
- Can asymptomatic and/or pre-symptomatic carriers spread the virus?



Immunity
- Does past infection provide immunity to future infection? If so, for how long?
- Which types and what levels of anti-virus antibody confer immunity?
- What are the titer levels in asymptomatic patients?

Progress Since First Edition

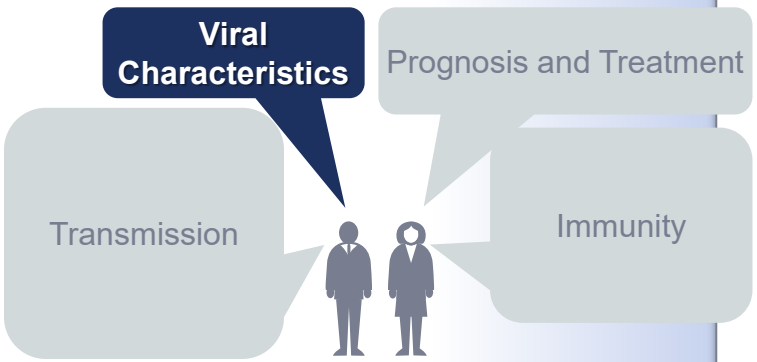
- Significant Progress
- Moderate Progress
- Limited Progress

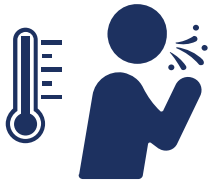
Note: R_0 = "R naught", the basic reproductive rate of an infection (i.e., the expected number of cases directly generated by one case in a population).
Original: See slide 9 in the 1st Edition.
Source: Health Advances analysis.

Transmission: General Update

Updated 7/5/2020

Scientists are honing in on how contagious SARS-CoV-2 is and how to avoid transmission. Ample testing and contact tracing will be critical in mitigating future outbreaks.





Degree of Contagion

- R_0 varies depending on the population studied
- CDC has settled on an R_0 of 2.5
- Compare to flu (1.3), Ebola (~2), MERS (~1)

Spread on Surfaces

- Virus survival time:
  - ~3 hours on printing paper
  - ~24 hours on cardboard packaging
  - ~4 days on paper money
  - ~7 days on plastic food packaging
- No reported cases from food products

Stopping Spread

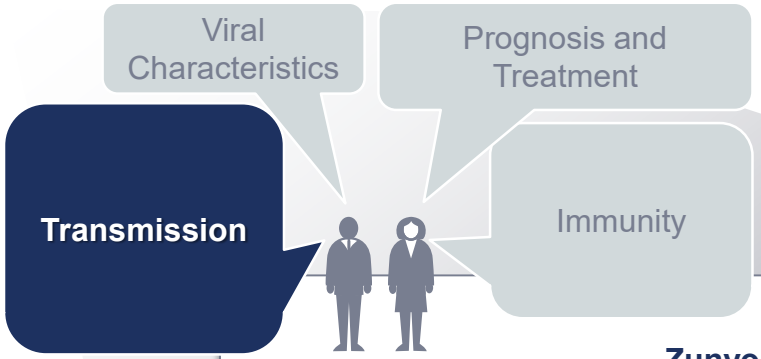
- Avoiding future outbreaks involves similar personal measures to what have already been implemented (i.e. masks, hand washing, distancing)
- Ample testing and contact tracing are critical to mitigate a second wave

Note: R_0 = "R naught", the basic reproduction rate of an infection (i.e., the expected number of cases directly generated by one case in a population).
Original: See slide 9 in the 1st Edition.
Source: Health Advances analysis, ABC News, SF Chronicle, CDC, NPR, Lancet, NEJM, Washington Post, Guardian, Bloomberg, NewsWeek.

Transmission: Asymptomatic Spread

New 7/5/2020

Studies suggest asymptotic infections can transmit SARS-CoV-2, but to what extent and how is not fully understood.



Zunyou, Apr 2020

- Transmission efficiency of asymptomatic patients is ~1/3 of confirmed cases
- Asymptomatic transmission accounts for 4.4% of infected persons

Huang, Jun 2020

- Strong infectivity during pre-symptomatic incubation period with rapid transmission in children

Less Infectious → **Publications Commenting on Asymptomatic Transmission** → *More Infectious*

Oran, Jun 2020

- 40-45% of those infected with SARS-CoV-2 will remain asymptomatic* and perhaps can transmit after 14 days

Lai, Jun 2020

- Viral load in asymptomatic patients was similar to that found in symptomatic patients

The World Health Organization made a statement at one point miscommunicating that asymptomatic transmission is “very rare,” but a day later retracted the statement, saying it had been intended to mean that there aren’t many studies following asymptomatic cases, and *asymptomatic transmission globally has not yet been determined.*

* Acknowledge results could include some pre-symptomatic patients due to lack of longitudinal data.

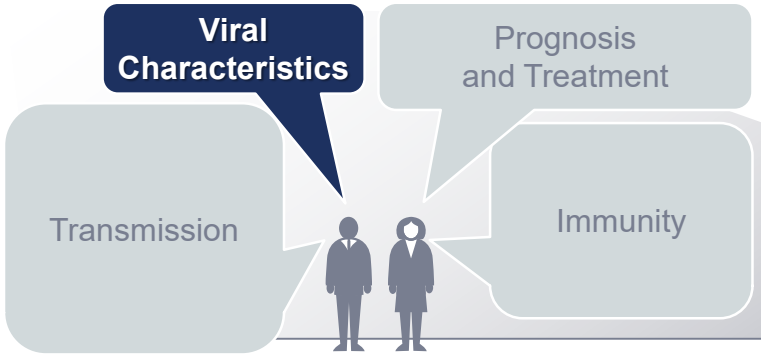
Original: See slide 9 in the 1st Edition.

Source: Health Advances analysis, Time, Annals of Internal Medicine, Chinese Journal of Epidemiology, Journal Microbiology, Immunology and Infection, Journal of Infection.

Viral Characteristics

Updated 7/5/2020

SARS-CoV-2 mutates slowly, raising hopes of long-term durability of either natural or vaccine-induced immunity. Researchers are also hopeful "rona" will become seasonal.



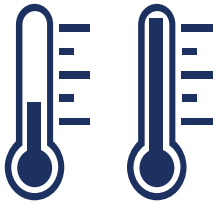
Mutation Rate

- <25 mutations per year
- About half the mutation rate of influenza

Implications

- ✓ Long-term natural immunity
- ✓ Potential for durable vaccine response*
- ✓ Tests remain useful for longer time

Seasonality



- No new info specific to SARS-CoV-2 is yet available
- 8-year study of non-novel coronaviruses shows a sharp winter seasonality
- If SARS-CoV-2 is similar, it will likely become a seasonal disease

* Assuming an effective vaccine becomes available.

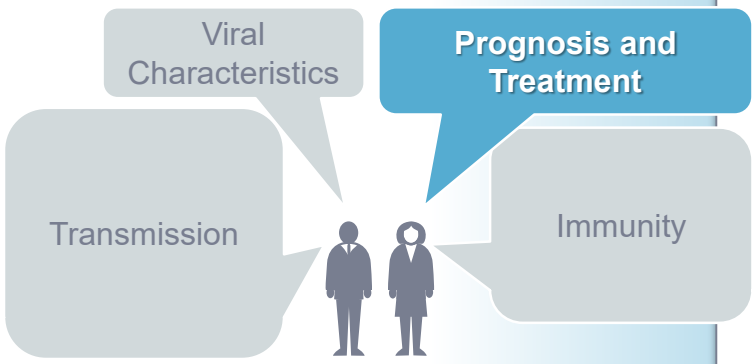
Original: See slide 9 in the 1st Edition.

Source: Health Advances analysis, NIH, Washington Post, Monto 2020 J Inf Dis, Healio.

Prognosis and Treatment

Updated 7/5/2020

The CDC estimates one third of COVID-19 cases to be asymptomatic. Mortality rates and effective treatment options have yet to be solidified.



Rate of Asymptomatic Cases

- Studies have shown varying rates (25%-80%)
- Newly released CDC planning guidelines indicate a best guess of 35%

Mortality Rates

- Still currently unknown
- CDC estimates a fatality ratio* of 0.4%, much lower than early estimates but still higher than the flu (0.1%)

Treatment Status

- No widely available treatments or vaccines for COVID-19 exist yet
  - Convalescent plasma and remdesivir have been approved for critical patients
  - Antivirals are currently under investigation
  - The FDA recommends against taking hydroxychloroquine and azythromycin

* Case fatality ratio represents the number of Covid-19 deaths divided by the number of confirmed cases.

Original: See slide 9 in the 1st Edition.

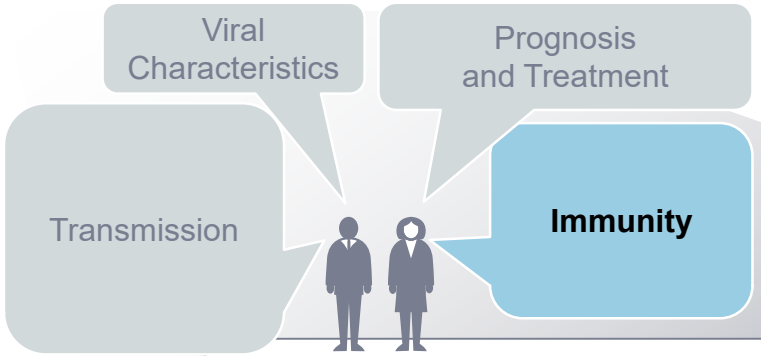
Note: The rate of asymptomatic cases was cited as 25-50% in slide five of our second edition. New data has since increased the upper bound to 80%. Similarly, case fatality rate was cited as 6% in slide seven of our first edition, but has since been revised by the CDC.

Source: Health Advances analysis, Healthline, CDC, Washington University website, CNN, John's Hopkins University, Ioannidis 2020 MedRxiv preprint.

Immunity

Updated 7/5/2020

Much is still unknown about acquired immunity to SARS-CoV-2. Although all reinfection cases have been debunked, new data suggests that some mild* patients lack antibodies.



Immunity Outlook

- Overall prevalence and durability of immunity among known infected patient remains unknown
- Reported cases of reinfection have been debunked

- A study in monkeys revealed acquired immunity through antibodies
- The role of T cells is also being debated

- Titer asymptomatic patients not yet solidified
- A recent study in China showed undetectable antibody titers in some patients with confirmed mild disease

* And likely asymptomatic patients.

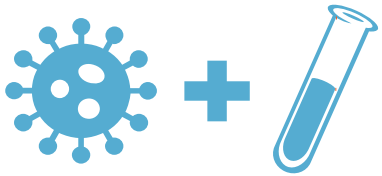
Original: See slide 9 in the 1st Edition.

Source: Health Advances analysis, Forbes, Guardian, Long 2020 Nature, Jacofsky 2020 J Arthroplasty, Wu 2020 MedRxiv preprint.

Which Organ Systems Does SARS-CoV-2 Affect?

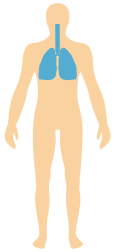
Updated 6/12/2020

SARS-CoV-2 was originally thought to be confined to the respiratory system, but new data reveals multi-system involvement in SARS-CoV-2 infection.

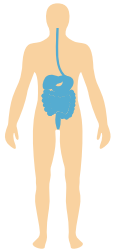


Infected Organ Systems

Sample with Potential for Testing

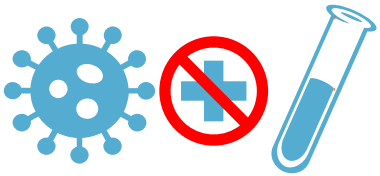


Respiratory



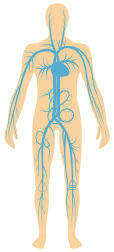
Digestive

(Not used for testing to date)

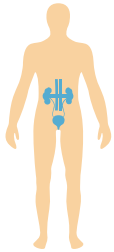


Infected Organ Systems

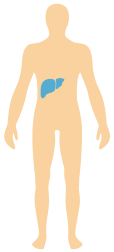
Not Relevant for Testing



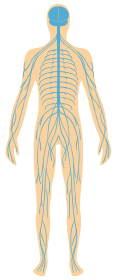
Cardiovascular



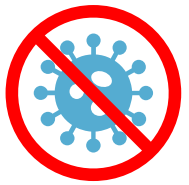
Urinary



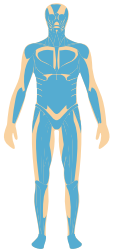
Hepatic



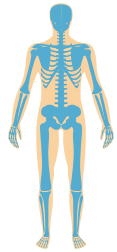
Nervous



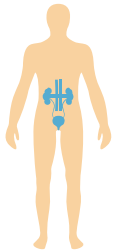
Low/Non-Infected Systems



Muscle



Skeletal



Reproductive

Original: See slide 5 in the 1st Edition.
Source: Health Advances analysis, Huang 2020 Lancet, Zaim 2020 Curr Probl Cardiol, Wang 2020 JAMA.

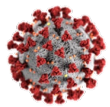
Most Commonly Used Tests Today in the US

Updated 6/12/2020

Since our first publication, molecular testing and antibody testing have become widely available, and antigen testing has started to emerge.

More Commonly Used

Less Commonly Used

Type of Test	Rationale for Frequency of Use to Date
 **Molecular Test for Viral RNA**	• Most accurate for identification of virus in a patient • Primary approach to diagnosis, which is the focus of current testing in the US
 **Anti-SARS-CoV-2 Antibody Immunoassays**	• Used in population surveillance to measure exposure rates • Increasing role in supporting diagnostic and screening paradigms in conjunction with viral testing to expand overall testing capacity • Approach to identify recovered patients who could provide blood with anti-virus antibodies to sick patients
 **Immunoassay for Viral Proteins (Antigens)**	• Not as accurate as molecular tests for virus detection • Harder to develop a test with an appropriate level of accuracy • ***First (and only) EUA granted for this method in May***

New Since First Publication

Original: See slide 16 in the 1st Edition.
Note: EUA = emergency use authorization by the FDA.
Source: Health Advances analysis.

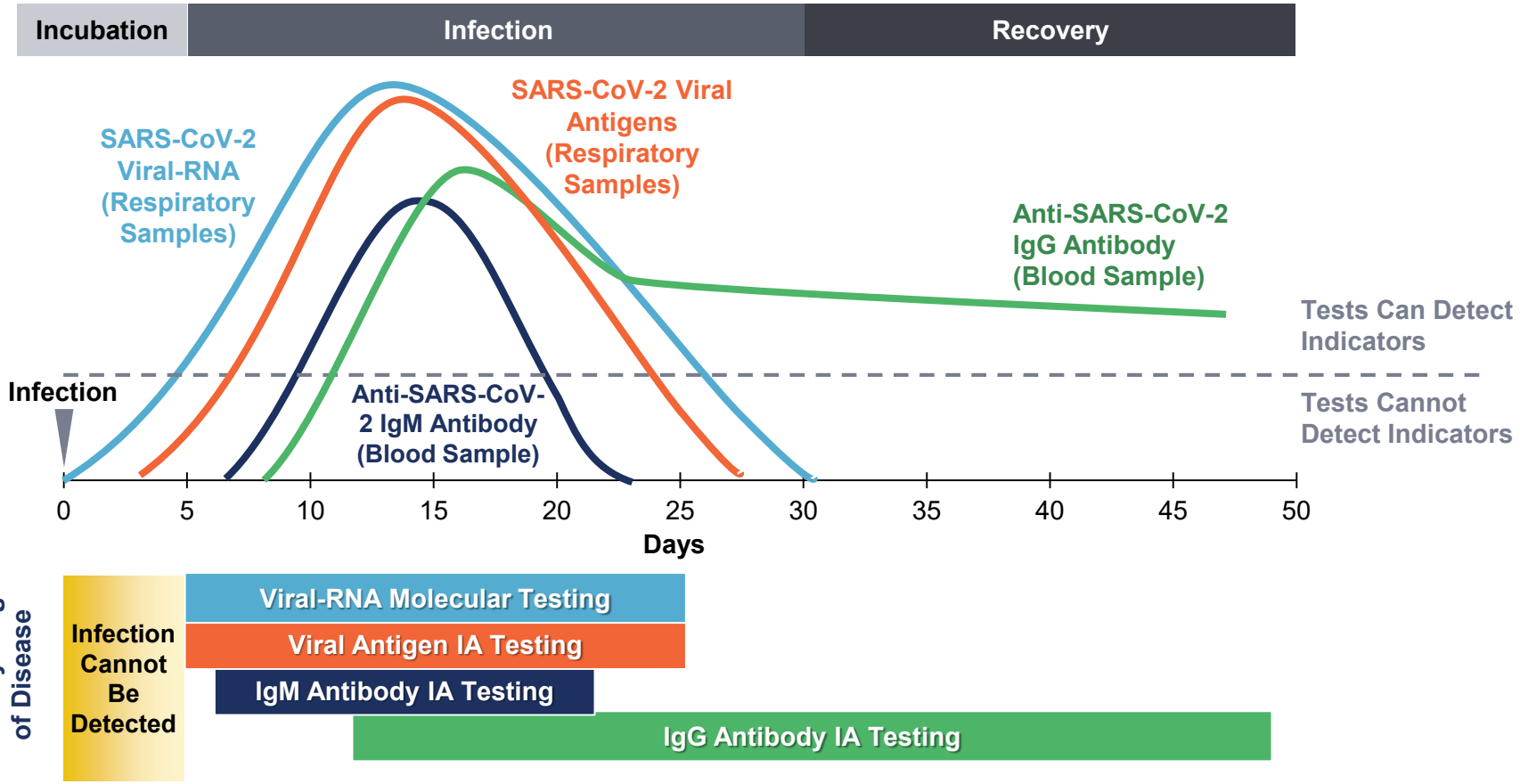
Biology of SARS-CoV-2 Infection

Updated 6/12/2020

Viral antigen tests are newly available since our last update. Viral antigen is detectable in a slightly narrower time window than viral RNA.

Markers of Disease by Stage of SARS-CoV-2 Infection

Example Individual Response Based on Best Available Data as of 6/3/2020



Original: See slide 4 in the 2nd Edition.
Note: New data (Long 2020 Nature Medicine), not yet confirmed, suggests IgM may not always rise before IgG. IA = Immunoassay
Source: Health Advances analysis, National Academies of Science 2020, Guo 2020 Clin Inf Diseases, Okba 2020 Emerg Inf Disease, He 2020 MedRxiv, Lauer 2020 Annals of Int Med, Kai-Wang 2020 Lancet, Zhao 2020 Clin Infec Disease, Wolfel 2020 Nature.

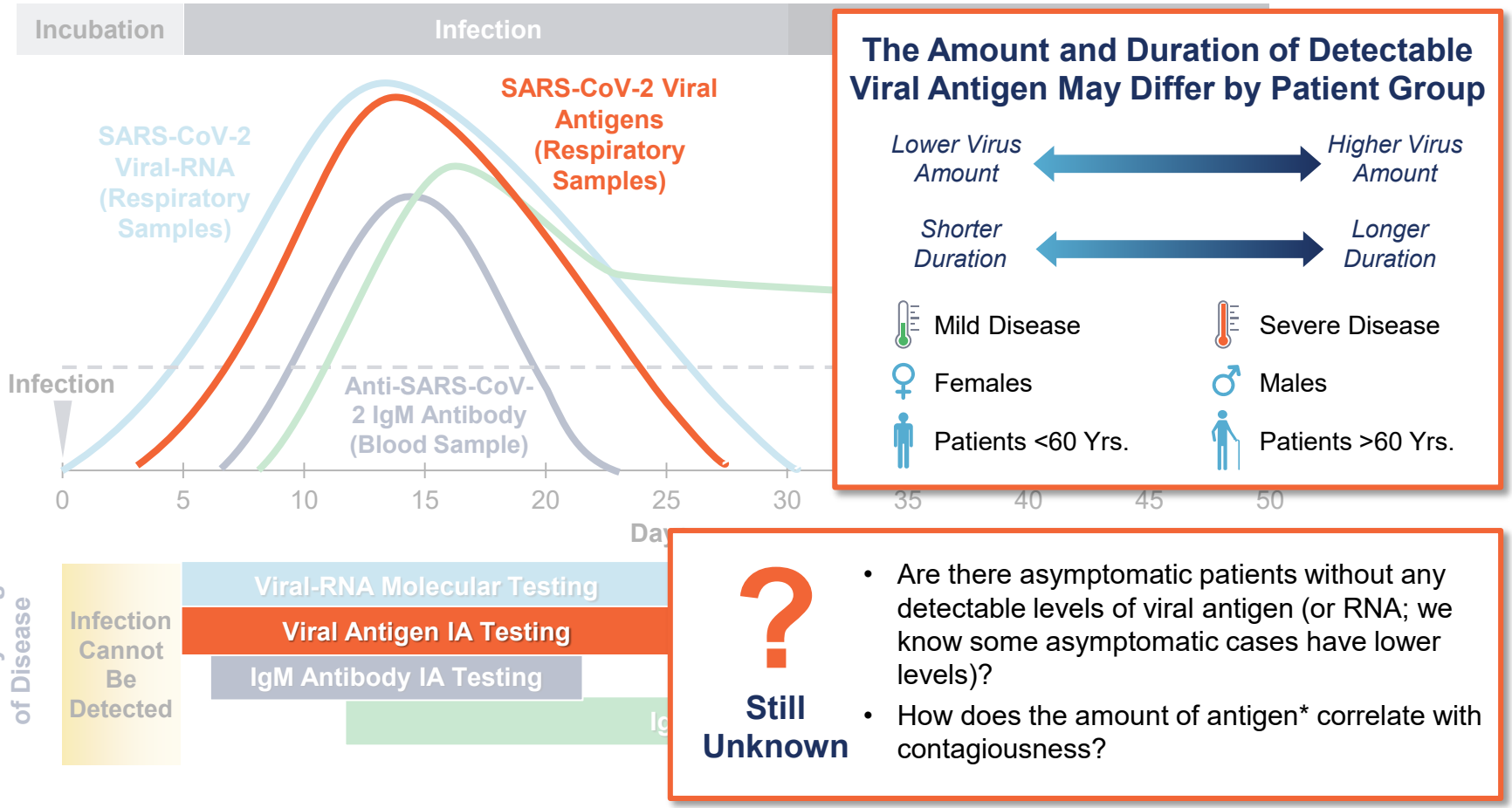
The Impact of Viral Antigen Detection on Infection Tracking

Updated 7/9/2020

IA for viral antigens can supplement molecular testing during acute infection; however, it is not completely clear whether all patient groups are detectable and for how long.

Markers of Disease by Stage of SARS-CoV-2 Infection

Example Individual Response Based on Best Available Data as of 6/3/2020



* Antigen indicates infectious virus while RNA can be detectable both in the presence or absence of live infectious virus.

Source: Health Advances analysis, Liu et al. 2020 MedRxiv, company websites.

Summary of Limitations for Each Test Type

Updated 7/9/2020

Although the scientific community now better understands SARS-CoV-2 testing, all tests still have unavoidable limitations.

Test	Type of Risk	Rationale and Other Limitations	
 **IA for IgM**	Missed Infections False Conclusion of Immunity		• Unlike many other viral infections, not all patients develop IgM at detectable levels • Not as sensitive or specific as molecular for diagnosis and less specific than IgG
 **IA for IgG**	False Conclusion of Immunity	• Not all patients have the same levels, timing or combination of antibody response • Tests available are still being validated and have mixed accuracy	• Unclear degree and length of immunity if antibodies present • Available tests measure antibodies for different parts of the virus (S vs. N) with potentially different clinical implications[1]
 **IA for IgA**			
 **IA for Total Ig**			• May be more sensitive but is complex to develop[2] • More costly
 **IA for Viral Antigens**	Missed Infections	• Negative isn't a guarantee of no infection – Viral load in some samples/patients may be below assay detection levels – Not all tests have the same sensitivity • Positive may not always mean infectious – Evidence of shedding for extended time periods, not all still infectious! – Capacity to perform these types of tests more limited than antibody testing	
 **Molecular for Viral RNA**	Missed Infection or Considered Infectious Longer than Necessary		

[1] Anti-N may be best for sensitivity of detecting past infection/exposure/contact tracing. Anti-S may be needed for detecting those who are immune.
[2] Particularly if all Igs reported separately as well as Total Ig.

Original: See slide 12 in the 2nd Edition.
Source: Health Advances analysis.

New Since First Publication

Summary of Considerations for Testing Based on Disease Biology

Updated 7/9//2020

What we do know is that no one test will be enough to manage the pandemic.

Test	Strongest Likely Use Case	Rationale
 **Molecular for Viral RNA**	• Use as primary testing tool for diagnosis, screening, surveillance, and tracing	• Least risk of missing an active infection
 **IA for Viral Antigens**	• Supplement molecular for diagnosis of symptomatic as well as screening, surveillance, and tracing	• May be less sensitive but cheaper, and (when supply increases) may be simpler/easier to access than molecular
 **IA for Total Ig**	• Supplement molecular for diagnosis of symptomatic as well as screening, surveillance, and tracing	• Sensitive serology option, but not as sensitive as molecular
 **IA for IgM and IgG Together**	• Supplement molecular for screening, surveillance, and contract tracing	
 **IA for IgG Alone**	• Now – supplement molecular for screening, surveillance, and contract tracing • Future – immune status monitoring	• Most consistent single Ig • Timing of presentation similar to IgM • Still unknown which antibodies are neutralizing and/or convey immunity
 **IA for IgM Alone**	• Follow-up test in highly suspicious symptomatic cases with negative molecular test	• Can be less specific than other Ig • Not sensitive enough to be a diagnostic on its own

Original: See slide 13 in the 2nd Edition.
Source: Health Advances analysis.

New Since First Publication

When Should I Consider Getting a Serology Test?

New 7/9//2020

While many caveats remain regarding the clinical impact of serology testing, there are some cases in which getting a serology test could be beneficial.

It May Be Worth Getting Tested If You…

Had a flu-like illness weeks or months ago

Have a household member, friend, coworker, etc. who was sick (diagnosed with COVID-19 or not)

Are planning to travel to a country that requires antibody testing

Are participating in research for COVID-19 surveillance

Are thinking of donating blood for convalescent therapy to help treat current patients

Caveats to Serology Testing

FDA standards for antibody tests are increasingly stringent, but CDC recommends confirming positive results with a secondary test

A positive result does not mean "immunity". Scientists are trying to understand whether antibodies actually provide any immunity, and for how long

A positive result only means you have been exposed to COVID-19 in the past few months

May need to pay out of pocket. Depending on health insurance, tests range from $5-$200

It is possible to have been exposed to SARS-CoV-2 and to not have developed antibodies

If you test negative, it does not rule out that you have an active infection

Source: Health Advances analysis, CDC, Hackensack Meridian Health, Abbot, Quest Diagnostics, HealthCARE Express.

Where Can POC Testing Be Performed?

Updated 7/5/2020

As state and workplaces reopen, we have already seen growth in the origins of testing demand and the locations where testing is performed.

POC Testing Locations	At-Home/ Patient Self Test	Physician Offices with CLIA-Waived Certificates	Clinics (e.g., Retail Clinics, Urgent Care)	Potential New Sites for Return to Work	Hospitals with CLIA-Waived Certificates
Common POC Tests Today	• Glucose monitoring for diabetes • hCG (pregnancy tests)	• Influenza • HbA1c • HIV	• Influenza • Strep • Lipids	• Some implementation of SARS-COV-2	• Influenza • Blood gases • Electrolytes • Hematocrit
SARS-CoV-2 Testing Today	X	✓	✓	✓	✓
Future SARS-CoV-2 Testing	✓	✓	✓	✓	✓
Examples Used Today	 Pregnancy Test  Glucose Meters	 Alere Influenza Rapid Test	 BD Veritor (Rapid Test Reader)	Mobile health clinics for SARS-COV-2 PCR testing	 Abbott i-Stat  Alere epoc

Original: See slide 23 in the 1st Edition.
Source: Health Advances analysis, company websites.

Update Since First Publication

Where Can You Access SARS-CoV-2 Testing Today?

Updated 7/5/2020

Testing for SARS-CoV-2 is now becoming more broadly available, though you should still call your personal doctor to determine the best option for you.

	Relative Access to SARS-CoV-2 Testing	Where You Can Go *(After Talking To Your Doctor)*
Lab Testing	Testing is now readily available in most states, either through your local provider or city/state health programs (if you exhibit ≥1 COVID-19 symptom)	1. Local Hospitals/ERs 2. Your Doctor's Office 3. Retail Clinics 4. Pharmacies(most states)
Point-of-Care	Call your doctor if you believe you are experiencing symptoms of COVID-19, as testing may be available at a local doctor's office or nearby testing site	
At-Home Patient Self Collection	Several companies are now authorized to send at-home sample kit collections (to then be mailed/tested in a lab)*	Company websites
At-Home Patient Self Test	! The FDA has not yet authorized use of at-home, self-testing methods for SARS-CoV-2 diagnosis Be wary of online vendors offering test kits, as these are likely fraudulent. Their use could pose public health risks !	

* Includes: Quest, LabCorp, Everlywell, P23 Labs, Vault Health, Hims&hers, and LetsGetChecked.

Original: See slide 27 in the 1st Edition.

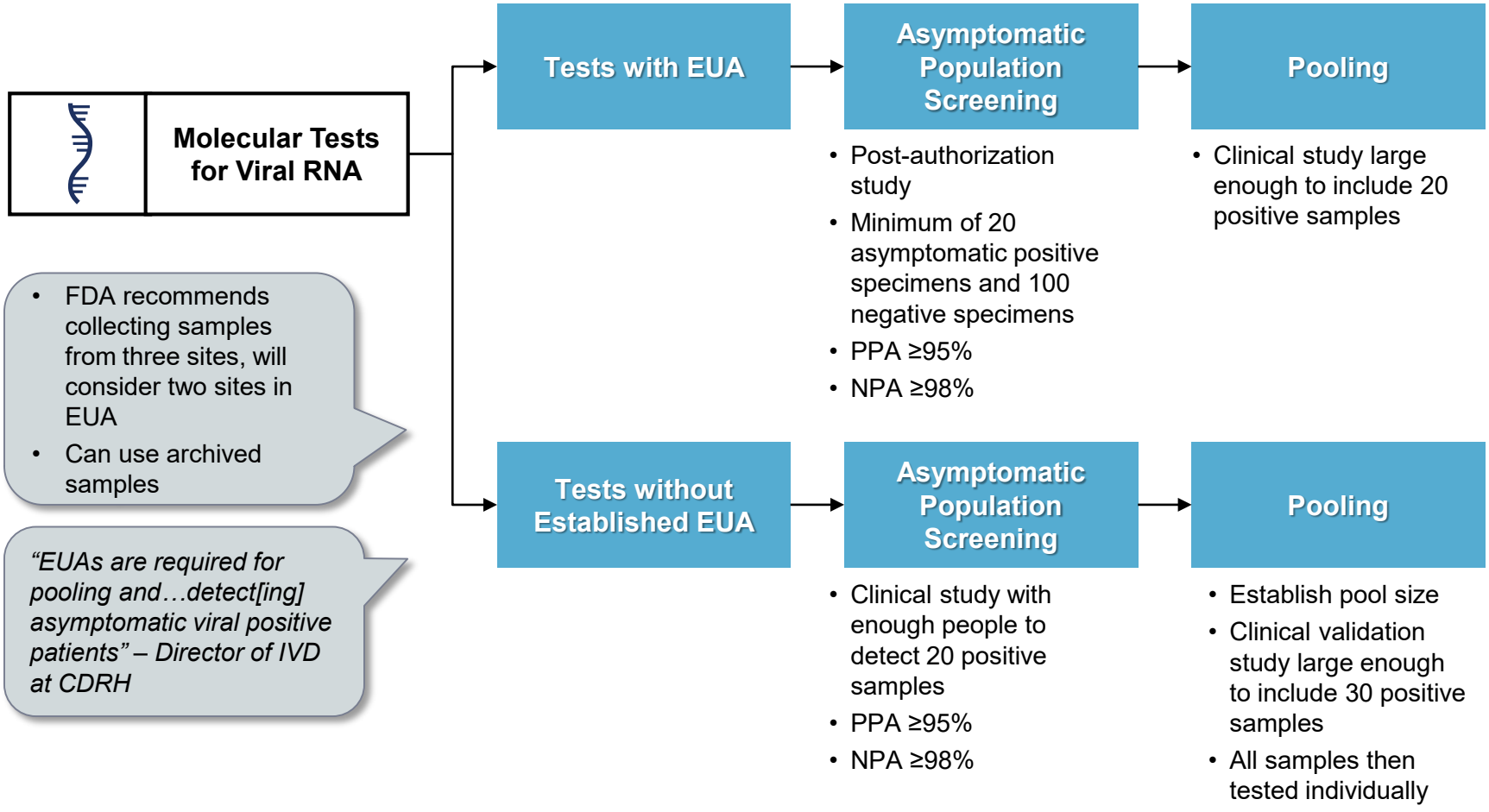
Source: Health Advances analysis, CDC, FDA.

Updated Since First Publication

Regulatory Requirements for Asymptomatic and Pooled Testing

New 7/5/2020

The FDA has released guidelines for test manufacturers looking to use SARS-CoV-2 tests to screen asymptomatic individuals or do pooled testing.



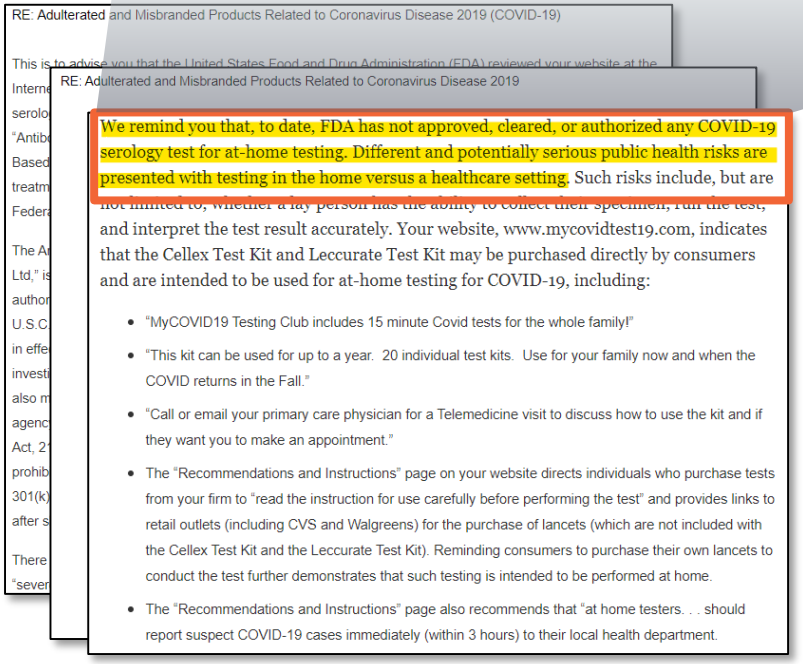
Note: PPA = positive percent agreement, NPA = negative percent agreement, IVD = *in vitro* diagnostics, CDRH = Center for Devices and Radiological Health, FDA.
Source: Health Advances analysis, FDA, Genome Web.

FDA Crackdown on Antibody Testing

New 7/5/2020

FDA has warned three companies against unlawfully selling antibody tests for at-home use and has revoked Chembio's EUA after discovering poor test performance.

We remind you that, to date, FDA has not approved, cleared, or authorized any COVID-19 serology test for at-home testing. Different and potentially serious public health risks are presented with testing in the home versus a healthcare setting. Such risks include, but are



RE: Adulterated and Misbranded Products Related to Coronavirus Disease 2019 (COVID-19)

This is to advise you that the United States Food and Drug Administration (FDA) reviewed your website at the

RE: Adulterated and Misbranded Products Related to Coronavirus Disease 2019

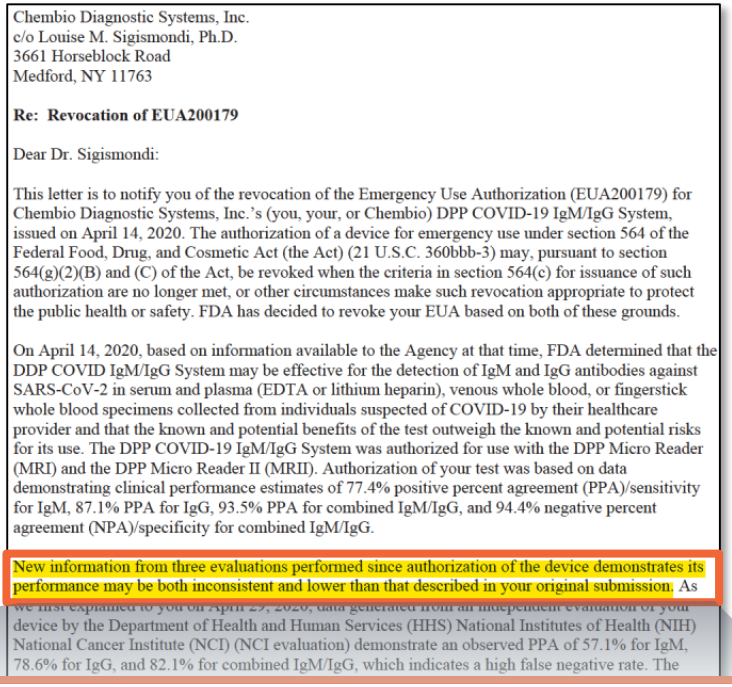
We remind you that, to date, FDA has not approved, cleared, or authorized any COVID-19 serology test for at-home testing. Different and potentially serious public health risks are presented with testing in the home versus a healthcare setting. Such risks include, but are

and interpret the test result accurately. Your website, www.mycovidtest19.com, indicates that the Cellex Test Kit and Leccurate Test Kit may be purchased directly by consumers and are intended to be used for at-home testing for COVID-19, including:

- "MyCOVID19 Testing Club includes 15 minute Covid tests for the whole family!"
- "This kit can be used for up to a year. 20 individual test kits. Use for your family now and when the COVID returns in the Fall."
- "Call or email your primary care physician for a Telemedicine visit to discuss how to use the kit and if they want you to make an appointment."
- The "Recommendations and Instructions" page on your website directs individuals who purchase tests from your firm to "read the instruction for use carefully before performing the test" and provides links to retail outlets (including CVS and Walgreens) for the purchase of lancets (which are not included with the Cellex Test Kit and the Leccurate Test Kit). Reminding consumers to purchase their own lancets to conduct the test further demonstrates that such testing is intended to be performed at home.
- The "Recommendations and Instructions" page also recommends that "at home testers. . . should report suspect COVID-19 cases immediately (within 3 hours) to their local health department.

FDA Warning Letters to Companies Selling Antibody Tests for At-Home Use

FDA Revocation of Chembio's SARS-CoV-2 Serology Test EUA Due to Concerns about Sensitivity and Specificity



Chembio Diagnostic Systems, Inc.
c/o Louise M. Sigismondi, Ph.D.
3661 Horseblock Road
Medford, NY 11763

Re: Revocation of EUA200179

Dear Dr. Sigismondi:

This letter is to notify you of the revocation of the Emergency Use Authorization (EUA200179) for Chembio Diagnostic Systems, Inc.'s (you, your, or Chembio) DPP COVID-19 IgM/IgG System, issued on April 14, 2020. The authorization of a device for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3) may, pursuant to section 564(g)(2)(B) and (C) of the Act, be revoked when the criteria in section 564(c) for issuance of such authorization are no longer met, or other circumstances make such revocation appropriate to protect the public health or safety. FDA has decided to revoke your EUA based on both of these grounds.

On April 14, 2020, based on information available to the Agency at that time, FDA determined that the DDP COVID IgM/IgG System may be effective for the detection of IgM and IgG antibodies against SARS-CoV-2 in serum and plasma (EDTA or lithium heparin), venous whole blood, or fingerstick whole blood specimens collected from individuals suspected of COVID-19 by their healthcare provider and that the known and potential benefits of the test outweigh the known and potential risks for its use. The DPP COVID-19 IgM/IgG System was authorized for use with the DPP Micro Reader (MRI) and the DPP Micro Reader II (MRII). Authorization of your test was based on data demonstrating clinical performance estimates of 77.4% positive percent agreement (PPA)/sensitivity for IgM, 87.1% PPA for IgG, 93.5% PPA for combined IgM/IgG, and 94.4% negative percent agreement (NPA)/specificity for combined IgM/IgG.

New information from three evaluations performed since authorization of the device demonstrates its performance may be both inconsistent and lower than that described in your original submission. As

device by the Department of Health and Human Services (HHS) National Institutes of Health (NIH) National Cancer Institute (NCI) (NCI evaluation) demonstrate an observed PPA of 57.1% for IgM, 78.6% for IgG, and 82.1% for combined IgM/IgG, which indicates a high false negative rate. The

New information from three evaluations performed since authorization of the device demonstrates its performance may be both inconsistent and lower than that described in your original submission. As

Source: Health Advances analysis, GenomeWeb, FDA.

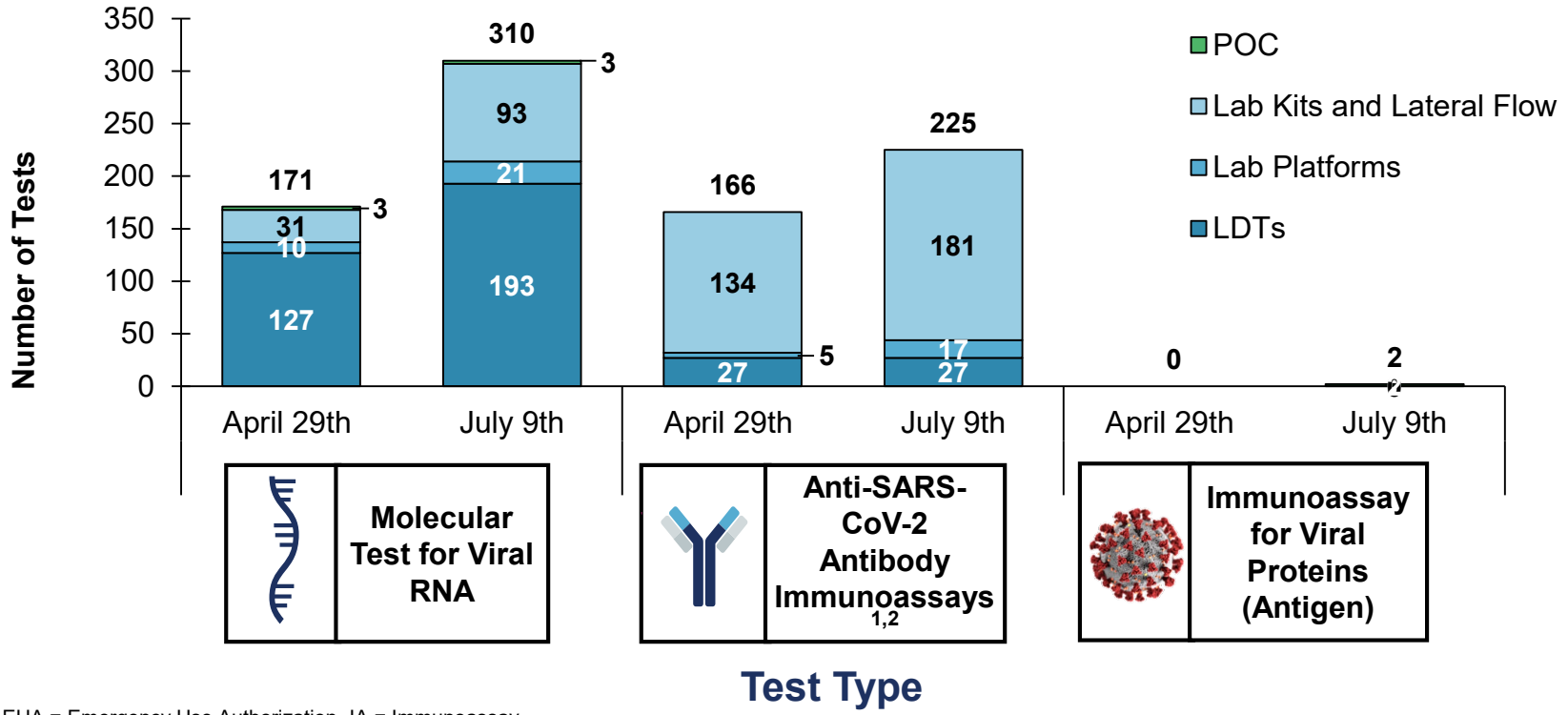
Status of SARS-CoV-2 Tests in the US

Updated 7/9/2020

To date, over 500 tests for SARS-CoV-2 have been developed for use in the US, many more than previously available just two months ago.

Commercially Available SARS-CoV-2 Tests in the US[1,2]

EUA-Approved, EUA-Exempt or FDA-Notified (n=538)



Note: EUA = Emergency Use Authorization. IA = Immunoassay.

[1] As of the date of this analysis, no antibody (serology) tests have received an EUA for CLIA-waived testing (POC). Two viral antigen tests (for diagnosis) have received EUA.

[2] All antibody (serology) tests that have notified the FDA under "Policy D" must submit EUA will have 10 business days to submit EUA. During these 10 days they are still commercially available, but "if an EUA request is not submitted within a reasonable period of time, or if significant problems are identified with a test and cannot be or have not been addressed in a timely manner, FDA intends to remove the manufacturer and test from this list, would expect the manufacturer to suspend distribution of the test, and may take additional actions as appropriate." Thus far FDA has put 64 tests on the "do not distribute" list, available on the website's FAQ page.

Original: See slide 41 in the 2nd Edition.

Source: Health Advances analysis, FDA, GenomeWeb, FierceBiotech, FDA SARS-CoV-2 FAQ, company websites.

New Entrants in Sars-CoV-2 Testing: At-Home Collection (1 of 2)

New 7/9/2020

Since our second addition, the FDA has granted EUA for several additional at-home, self-collection kits*.

Company	EUA Received	Sample Type	OOP Cost	Turnaround Time
pixel by LabCorp	4/19	Nasal	$119	1-2 days
Quest Diagnostics	4/28	Nasal	Unknown	1-3 days
Rutgers	5/8	Saliva	$150	5-8 days
everlywell	5/15	Nasal	$109	<48 hours after lab receives sample
P23 Labs	5/21	Saliva	Unknown	Unknown
Picture By Fulgent Genetics	5/21	Nasal	$119	1-2 days

* These sample collection kits are primarily for use with molecular tests for viral RNA.

Source: Health Advances analysis, FDA, Quest Diagnostics, PR Newswire, Lassauniere 2020 MedRxIV, Kruttgen 2020 J Clin Virology, MedTechDive, GenomeWeb, company websites.

New Entrants in Sars-CoV-2 Testing: At-Home Collection (1 of 2)

New 7/9/2020

Since our second addition, the FDA has granted EUA for several additional at-home, self-collection kits*.

Company	EUA Received	Sample Type	OOP Cost	Turnaround Time
LetsGet Checked	5/28	Nasal	$129	<24 hours after lab receives sample
GRAVITYDIAGNOSTICS	6/1	Nasal	Unknown	~ 2 days
Phosphorus	6/4	Saliva	$108	~3 days
KAISER PERMANENTE	6/13	Nasal	Unknown	Unknown
Kroger health	6/30	Nasal	Free for employees	Unknown

* These sample collection kits are primarily for use with molecular tests for viral RNA.

Source: Health Advances analysis, FDA, Quest Diagnostics, PR Newswire, Lassauniere 2020 MedRxIV, Kruttgen 2020 J Clin Virology, MedTechDive, GenomeWeb, company websites.

New Entrants in Sars-CoV-2 Testing: Product Companies

New 7/5/2020

Several product companies are using novel approaches to develop tests for SARS-CoV-2.

Company	Technology	SARS-COV-2 Test Name	Test Type	TAT	Data to Date	Development Status	Description	Value Proposition
SHERLOCK BIOSCIENCES / binx	CRISPR (Sherlock) and POC (binx)	Sherlock CRISPR SARS-CoV-2 kit	Molecular	One hour	100% specificity and sensitivity for 2,000 tests	EUA approval May 6, 2020	Cas-13a-based system that cleaves SARS-CoV-2 RNA into fluorescent fragments	Low cost POC test
Genalyte	Multi-antigen serology panel	Maverick SARS-CoV-2 Multi-Antigen Serology Panel	Serology	<48 hours	100% specificity, >87% sensitivity	Awaiting EUA approval	Distinguishes five SARS-CoV-2 antibodies from SARS-CoV, MERS, and flu antibodies	High specificity
MeMed	Immune Status Profiling	MeMed BV™ and MeMed Key™	Other Protein Biomarkers	15 minutes	Prelim data shows detection of pre-symptomatic and asymptomatic patients	In development; US launch planned for 2021	Measures biomarker levels in a blood sample to distinguish between bacterial and viral infections and predict disease severity	Fast detection of bacterial vs viral infection to inform antibiotic use
illumina	NGS	Illumina COVIDSeq Test	Molecular	24 hours	Limit of detection is 1,000 copies per mL	EUA approval June 10, 2020	High-throughput molecular test using next generation sequencing (NGS)	Massively parallel processing of samples(1,000s per lan) through barcoding capability

Note: WGS = whole genome sequencing. NGS = next generation sequencing. Limit of detection is the number of viral RNA copies needed to yield reliable detection. TAT = turnaround time.
Source: Health Advances interviews and analysis, GenomeWeb, FierceBiotech, Cannacord, FDA, company websites.

New Entrants in Sars-CoV-2 Testing: Specialty Labs

New 7/5/2020

Several specialty labs are venturing into the infectious disease space with SARS-CoV-2 tests. Some are taking novel approaches.

Company	Technology	SARS-COV-2 Test Name	Test Type	TAT	Data to Date	Development Status	Description	Value Proposition
GUARDANT	Oncology	NGS	N/A	Molecular	24-36	Not available	In development	High-throughput RT-PCR
color	Cancer and Cardio-vascular	RT-PCR	LAMP technology	Molecular	<24	100% accuracy on 543 samples	FDA notified, EUA not required	High-throughput RT-PCR with loop-mediated isothermal amplification
EXACT SCIENCES	Colorectal Cancer	RT-PCR	SARS-CoV-2 (N gene detection) Test	Molecular	Unknown	Not available	EUA approval April 20, 2020	RT-PCR test that runs on Thermo Fisher's 7500 Fast Dx instrument
sema4	Women's Health and Oncology	WGS	N/A	Molecular	<24	95% sensitivity, 100% specificity	N/A	Combines Sema4 molecular test with WGS to build predictive modeling for clinical outcomes

Source: Health Advances interviews and analysis, GenomeWeb, FierceBiotech, Cannacord, FDA, company websites.

New Entrants in Sars-CoV-2 Testing: Academic Institutes

New 7/10/2020

A number of academic institutes are also joining the effort to increase testing capacity and support for Sars-CoV-2. Examples are shown below.

Institution*	Technology	SARS-COV-2 Test Name	Test Type	Turn-around Time (hrs)	Data to Date	Development Status	Description
BROAD INSTITUTE	RT-PCR	CRSP Sars-CoV-2 RT-PCR Assay	Molecular	24 hrs	100% accuracy with lower limit of detection 0.2 copies/µl on 153 samples	CLIA certified	Named a MA state reference lab, processing 35,000 tests per day as of June 5, 2020
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center	RT-PCR	MD Anderson High-throughput SARS-CoV-2 RT-PCR Assay	Molecular	Not available	Not available	EUA approval June 25, 2020	Performed at MDACC Molecular Diagnostics Laboratory
COLUMBIA UNIVERSITY	RT-PCR	Triplex CII-CoV-1 RT-PCR Test	Molecular	Not available	Not available	EUA approval May 13, 2020	Performed at Columbia's Laboratory of Personalized Genomic Medicine

Other Academic Institutions Supporting Testing

MAYO CLINIC

Hackensack Meridian Health
Hackensack University Medical Center

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

RUTGERS
THE STATE UNIVERSITY OF NEW JERSEY

* List is not comprehensive.

Source: Health Advances interviews and analysis, GenomeWeb, FierceBiotech, FDA, company websites.

New Entrants in Sars-CoV-2 Testing: High Throughput Approaches

New 7/10/2020

A number of academic institutes and companies are working toward high-throughput methods to support Sars-CoV-2 testing capacity. Examples are shown below.

Institution*	Test Name	Development Status	Description	Value Proposition
BROAD INSTITUTE	LAMP-Seq	In development	• Reverse-transcription loop-mediated isothermal amplification of parts of the viral genome • Sample-specific barcodes, followed by sequencing of pooled samples	• No RNA extraction, costs under $7/sample • Scalable to 100K's samples per day per facility
OCTANT	SwabSeq	In development	• Multiplex isothermal RT-PCR for NGS, not requiring RNA extraction • Octant has made the protocol freely available and is working with several other academic and commercial labs to refine the test	• Scalable up to 10,000 samples per day without automation or 100,000 with automation • Cost effective
GINKGO BIOWORKS™	Not yet named	In development	• Repurposing Ginkgo NGS capacity for scaled Sars-Cov-2 testing • Ginkgo is seeking CLIA approval for its laboratory and filed pre-EUA	• Focused on scaling testing for schools and businesses as part of new service called Cocentric

* List is not comprehensive.

Source: Health Advances interviews and analysis, GenomeWeb, FierceBiotech, FDA, company websites.

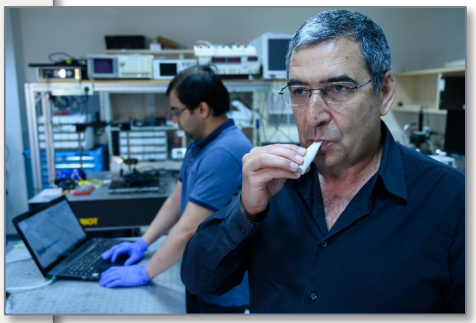
New Market Participants

A number of novel approaches to Sars-CoV-2 are in development.

ISRAELI INNOVATION

Israel invents one-minute coronavirus breath test

The invention of an instant COVID-19 breathalyser could have enormous implications for air travel, with borders able to be re-opened and passengers mandatorily tested before flying



Test	POC Breath test for Sars-CoV-2
Developer/ Company	**Ben-Gurion University, Israel**
Status	In development, seeking FDA approval
Description	Hand-held device contains chip with densely packed sensors to capture virus particles in breath, spectroscopy instrument reads result in ~20 seconds
Value Proposition	Rapid Low cost Easily distributed Non-invasive sample type

Sars-CoV-2 Reimbursement: Serology

New 7/5/2020

Since our last edition, coverage policies have now been set for serology tests. No specific coverage has been released for viral antigen tests.

Insurance Type	Test Reimbursement *(Paid from Insurer to a Lab)*	Cost of Test *(Paid from Lab to Manufacturer)*	Patient Cost-Sharing/Out of Pocket Cost	Details
Medicare/ Medicaid	• Multi-Step = $42 • Single-Step = $45	Estimated $5-10	$0	• CMS announced they will cover SARS-CoV-2 serological testing for all Medicare and Medicaid patients
Private Insurance	• Negotiated Price or Cash Price on Website	Estimated $5-10	$0	• The CARES Act forces private insurance companies to cover all eligible SARS-CoV-2 serological tests at the negotiated or listed price • This requirement is in effect until the end of the public health emergency
Uninsured	• Multi-Step = $42 • Single-Step = $45	Estimated $5-10	Most Likely $0	• HHS Secretary, Alex Azar claims part of the $100B in funding for hospitals and HCPs will go to paying for testing and treatment of uninsured patients

- Reimbursement rates have not yet been determined for antigen tests.
- This is the first time a single-step test (generally POC format) garners a higher reimbursement rate than multi-step tests. This higher rate seems to recognize the clinical value of the rapid TAT of this approach.

* The April 14th CMS announcement that Medicare will pay a higher amount of $100 for COVID-19 Dx tests does not apply to serological tests, just molecular tests.

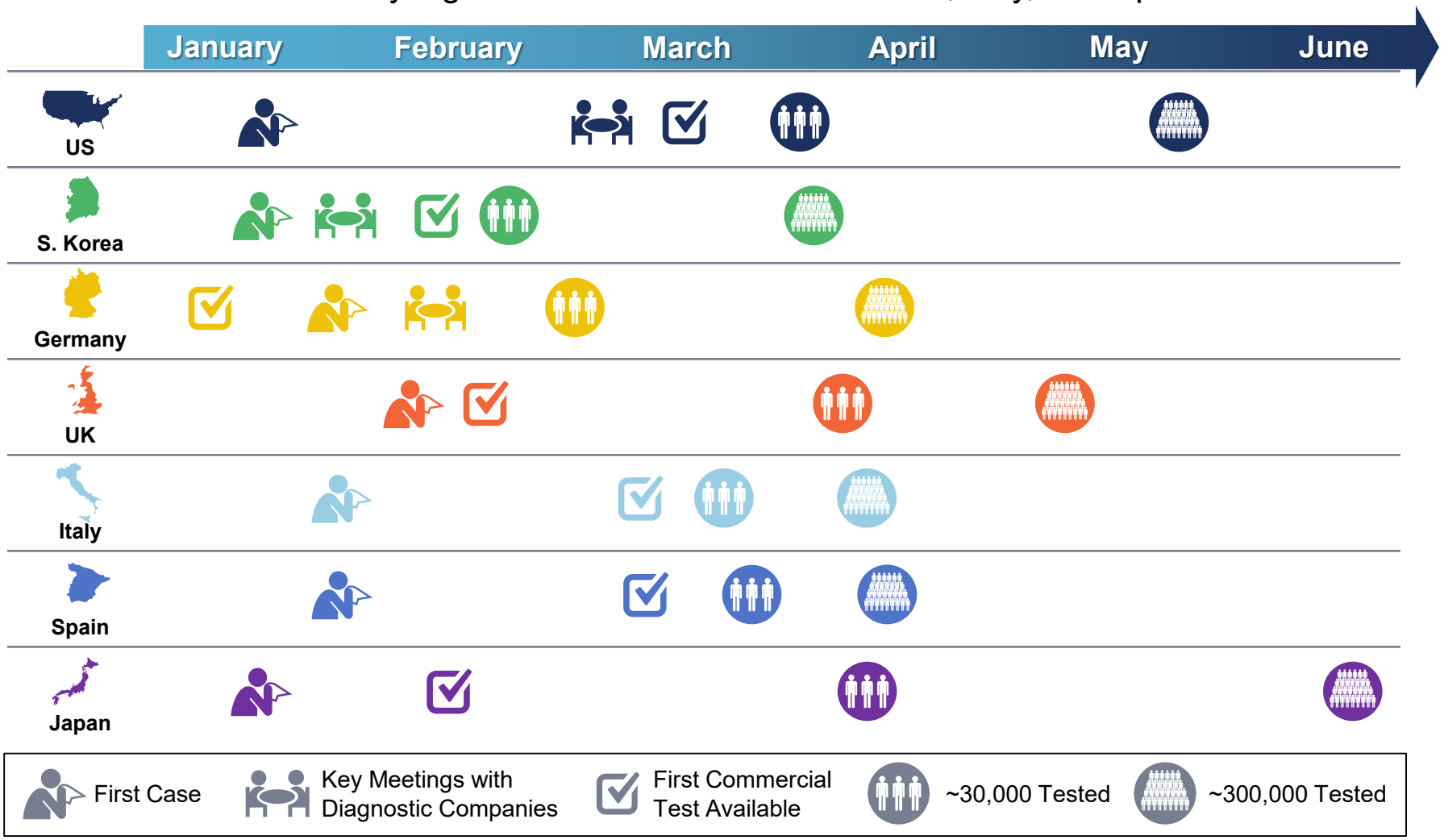
Note: CMS = Centers for Medicare and Medicaid. See Slide 28 of our first edition for the status of COVID test reimbursement at that time. Cost of test is primarily based on instrumented immunoassay costs rather than lateral flow costs, which are cheaper. HHS = Department of Health and Human Services. HCP = health care provider.

Source: Health Advances analysis, news reports, CARES Act, CMS, Yetisen 2013 Lab on a Chip.

Differences in SARS-CoV-2 Testing Response Timelines

Updated 7/5/2020

The US has had a noticeably delayed response to the COVID-19 pandemic, even compared to countries with relatively high infection rates such as the UK, Italy, and Spain.



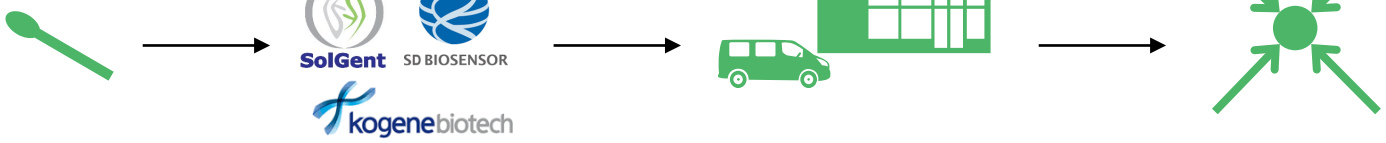
Note: See slide 24 of the 2nd Edition. Current research suggests the UK, Italy, and Spain did not publicly engage with private diagnostic companies during this timeframe.
Source: Health Advances analysis, WHO, FDA, CDC, KCDC, Robert Koch Institute, John Hopkins CSSE.

Developed Country Initial Testing Strategies (1 of 3)

Presented 5/7/2020

Ex-US developed countries have implemented a mix of centralized and decentralized approaches.

The South Korean Centralized Approach



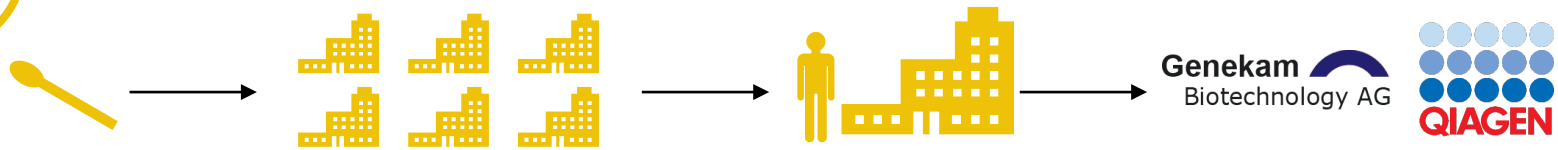
WHO Validated Test Kit

South Korea Government engaged with four manufacturers in Jan. 2020 to replicate the WHO kit

Set up drive-through and walk-in clinics to enable access to testing in Jan 2020

Directed test kits to hotspots within the country

The German Decentralized Approach



WHO Validated Test Kit

In Jan 2020, Germany authorized hundreds of labs to develop LDTs, implementing virology expertise to replicate the WHO kit

Patients could access the closest hospital for testing

Germany then authorized commercial testing kits for scale-up in early Feb 2020

Note: LDT = laboratory developed test.
Source: Health Advances analysis.

Developed Country Initial Testing Strategies (2 of 3)

New 7/5/2020

Japan implemented limited testing, focused more on cluster-identification than individual diagnosis, while UK had a slow, haphazard scale-up of testing.

The Japanese Limited Approach

NIID-Developed Test

Limited testing only for cluster identification and tracing, conducted at a mix of NIID labs, local public health labs, and private labs

Approval of commercial test for diagnostic use for patients displaying severe symptoms

Approval of rapid antigen test and more molecular tests, as well as slight relaxation of criteria to qualify for testing

The UK's Expanding Approach

PHE-Developed Test

Small number of centralized government labs, tests administered only at hospitals

Slow expansion to include additional government labs, hospital labs, and newly constructed large COVID-centric labs. Addition of CE-marked and locally-developed tests

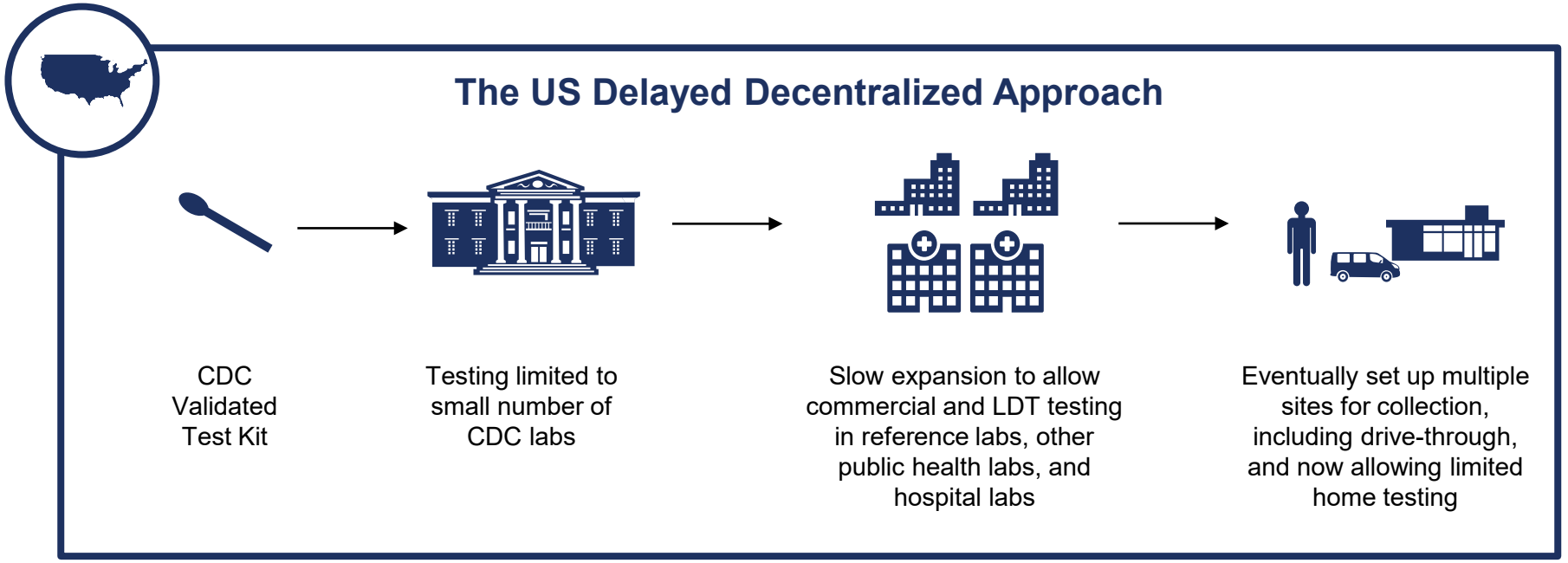
Eventually set up multiple sites for collection, including drive-through, and implemented limited home testing

Note: NIID = National Institute for Infectious Disease, PHE = Public Health England.
Source: Health Advances analysis.

Developed Country Initial Testing Strategies (3 of 3)

Presented 5/7/2020

Building SARS-CoV-2 diagnostic testing capacity was a slow process in the US, initially due to CDC testing limitations and FDA red tape.



Source: Health Advances analysis.

Developed Country Initial Isolation and Testing Outcomes

New 7/9/2020

Outcomes for each of the countries have varied, largely due to the timing of when testing was implemented and the extent to which testing has been available.





	UK	Germany	South Korea	US	Japan
First Known Case	Jan 29	Jan 27	Jan 20	Jan 20	Jan 15
Start of Testing Implementation[2]	Mar 13	Feb 22[1]	Feb 24	March 14	Mar 31
Testing Delay[2] (Days)	44	26	36	53	76
Total Cases[3] (Per Million)	4,227	2,360	260	9,230	159
Total Deaths[3] (Per Million)	656	108	6	400	8
Rationale for Outcome	Delayed expansion of testing	Successfully deployed early testing	Successfully deployed early testing	Delayed expansion of testing	Testing focused on cluster identification

[1] Start of testing in Germany was estimated by conducting data analysis on the available testing data beginning in March.
[2] The start of testing implementation is defined as the date when 30,000 total diagnostic tests have been processed in the country. Testing delay is defined as the number of days between the first confirmed case and the day 30,000 tests were processed.
[3] As of July 9, 2020.

Source: Health Advances analysis, JHU, CNN, NY Times, WHO, Bohmer 2020 Lancet, CDC, OWID.

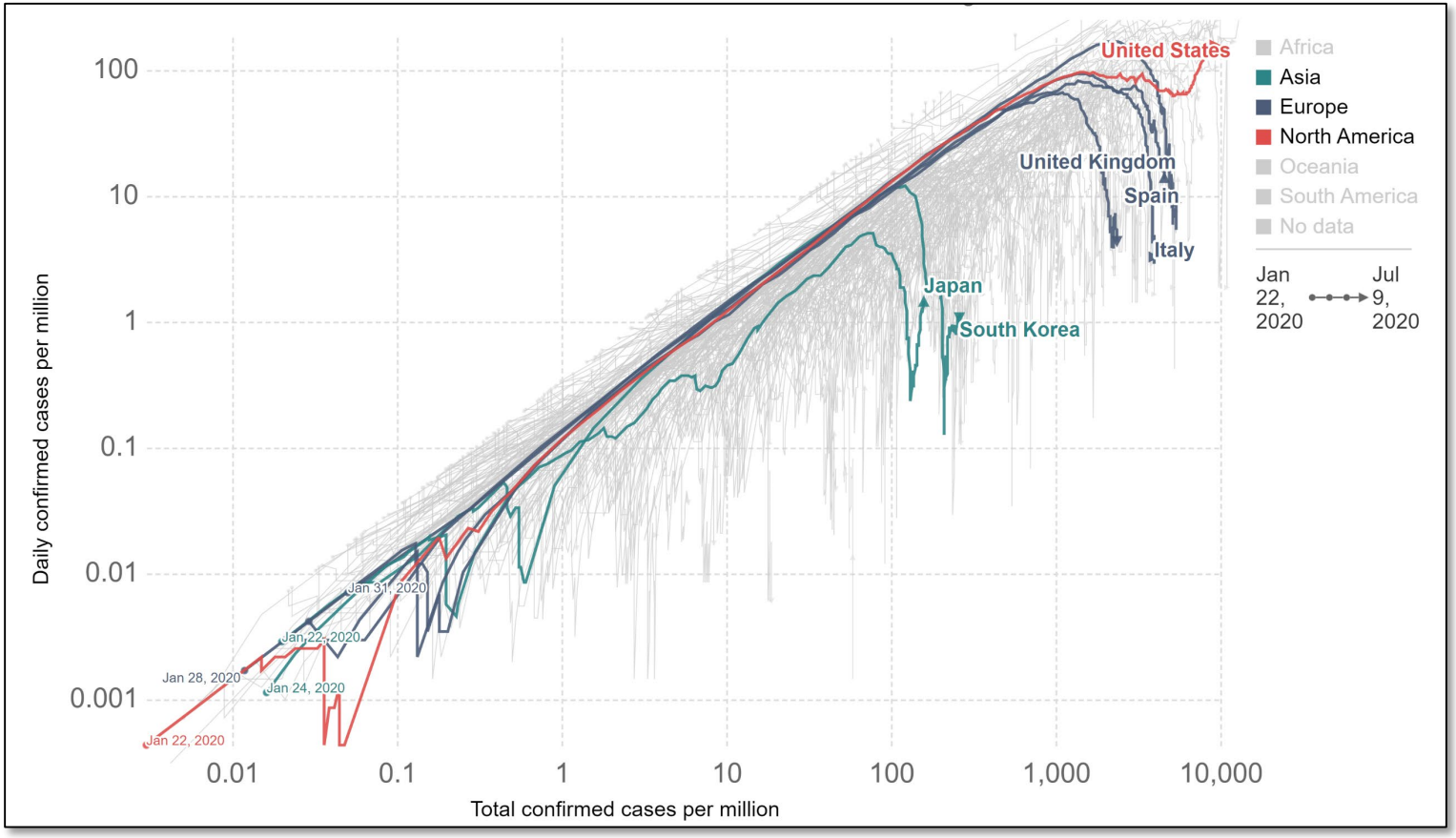
Developed World Trends

New
7/9/2020

As a result of fairly aggressive testing and containment strategies in the developed world, most countries are seeing a decline in new COVID-19 cases, except in the US.

Daily vs. Total Confirmed COVID-19 Cases per Million

Jan 22- July 9, 2020



Note: Daily confirmed cases is the 7-day rolling average of confirmed COVID-19 cases per million people.
Source: Health Advances analysis, Our World in Data, CDC, European CDC.

Emerging Country Testing Strategies (1 of 3)

New 7/5/2020

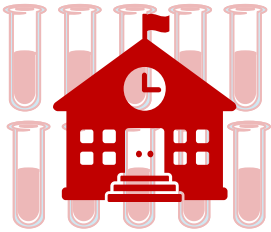
China suffered test shortages like many other countries, but maximized the few tests available by complementing them with extreme isolation measures.

Wuhan Approach

Facing shortage, testing in Hubei reserved for patients sick enough to seek treatment

Extreme distancing measures paired with door-to-door testing and tracing

China orders re-testing of recovered patients in Wuhan and increases screening of asymptomatic patients



Tested 6.5MM Wuhan residents in two weeks via mobile testing centers (i.e. schools), with a plan to test all 11MM

Overall China Approach

Government approval of a handful of kits in late January

Testing efforts limited amongst reagent shortage, unavailable for many patients

WHO-China Joint Mission published, China to establish body that fast tracks tests

China implements strict isolation and molecular screening of all international travelers

China's health authority calls for stronger nationwide isolation and testing

China starts mass testing 90,000 people in response to Beijing outbreak

Source: Health Advances analysis, SCMP, New York Times, USA Today.

Emerging Country Testing Strategies (2 of 3)

New 7/5/2020

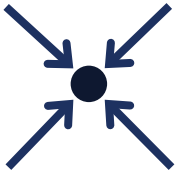
India and Brazil have relied on test shipments from other countries rather than building internal production, which has ultimately led to delayed testing and high numbers of cases.

The Indian Approach

Heavy reliance on insufficient/delayed antibody tests ordered from China and Europe

Delay from regulatory bodies such as DCGI and ICMR slows rapid kit approvals and molecular testing

Facing critical shortage, Indian government approves many local molecular and serology manufacturers



Indian government orders widespread free molecular testing, targeting hotspots and slums

The Brazilian Approach

Brazil's sanitary body approves first eight diagnostic tests (mix of molecular and serology) in late March

First shipment of serological tests (useless for diagnosis) ordered from China in late March, seemingly few efforts to expand internal production

Government allows drug stores to perform testing in late April

Limited efforts to implement widespread testing, as president has dismissed urgency of COVID-19

Note: NIV = National Institute of Virology.
Source: Health Advances analysis, Scroll.in, Forbes, BBC, India Times, Reuters, Agencia Brazil, USA Today.

Emerging Country Testing Strategies (3 of 3)

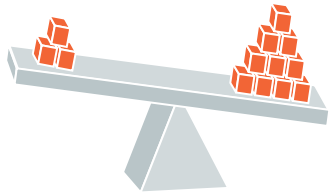
New
7/5/2020

Africa's prolonged inability to access test reagents may force them to rely on locally manufactured antibody tests, which are essentially useless in diagnosing SARS-CoV-3 infection.

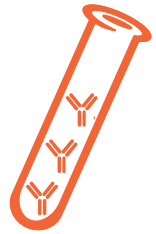
Approaches in Africa

Only two laboratories – Senegal and South Africa – originally had the reagents for testing

The WHO sends testing kits to over 20 African countries in mid-February



Unequal global allocation of reagents has left African countries – even those with enough money – with test shortages



Africa plans to ramp up and rely on cheaper in-house serological tests

Source: Health Advances analysis, New Humanitarian, South China Morning Post.

Ex-US Developing Country and Region Outcomes

New 7/9/2020

India and Africa were the slowest ex-US developing countries to start testing, but Brazil is facing by far the highest case and death rates.




	China	India	Brazil	Africa
First Known Case	Dec 31[1]	Jan 30	Feb 26	Feb 13
Start of Testing Implementation*	Unknown	Mar 27	Mar 16[2]	Mar 27[3]
Testing Delay* (Days)	Unknown	57	19	43
Total Cases (Per Million)	59	556	8,060	60
Total Deaths (Per Million)	3	15	320	0.6
Rationale for Outcome	Shutdown of Hubei, immediate implementation of testing and tracing	Insufficient total tests relative to other countries, only ~3 tests per 1,000 people	Insufficient total tests relative to other countries, government dismissal of pandemic	Limited access to reagents, limited internal testing capabilities

[1] December 31 was the day Chinese authorities confirmed that they were treating pneumonias of unknown causes, which would later be deemed COVID-19. The date of the very first case in China is unknown.
[2] Start of testing in Brazil was estimated by conducting data analysis on the available testing data beginning in March.
[3] Start of testing in Africa is estimated using testing data from Ethiopia, Morocco, Senegal, South Africa, and Tunisia. Total cases and deaths per 100K is a weighted average of African countries except Burundi, DR of Congo, Eritrea, Gambia, Guinea, Lesotho, Namibia, Rwanda, Seychelles, and Uganda.

Note: The start of testing implementation is considered the date when 30,000 total diagnostics tests have been processed in the country. Testing delay is defined as the number of days between the first confirmed case and the day 30,000 tests were processed. Testing data for China is not publicly available at this time. Total cases and deaths are as of June 1

Source: Health Advances analysis, JHU, CNN, NY Times, WHO, Bohmer 2020 Lancet, CDC, The Hill, OWID.

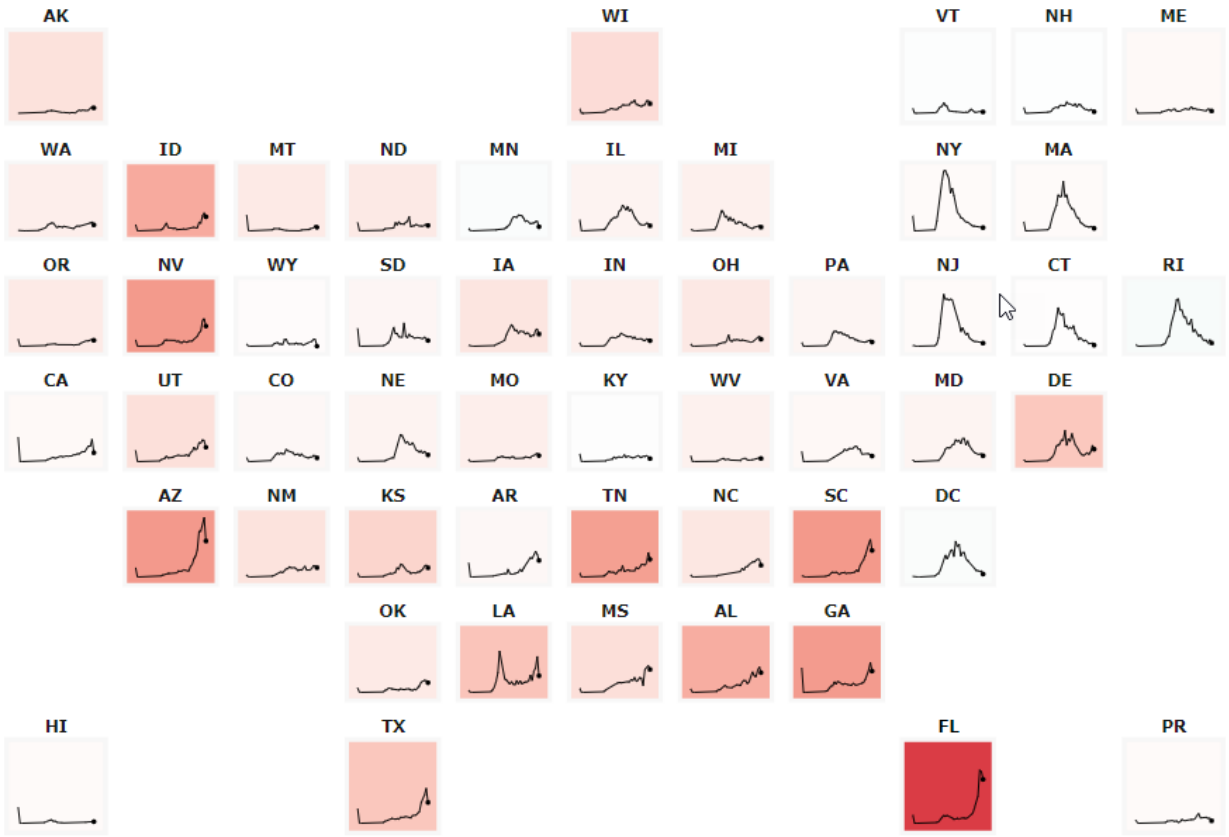
US Statistical Snapshot

New
7/5/2020

The John's Hopkins University of Medicine Coronavirus Resource Center is tracking daily trends in cases across all 50 states. The update below is from July 4th.

Daily New Cases per 100k People

Data Shown from 1/22/20 to 7/4/20



Line shows 3-day moving average of ***new cases per day*** in this state. Dot corresponds to most recent day.

The ***greener*** the background, the bigger the ***downward trend*** of new case in this state.

The ***redder*** the background, the bigger the ***upward trend*** of new case in this state.

Source: JHU Coronavirus Resource Center.

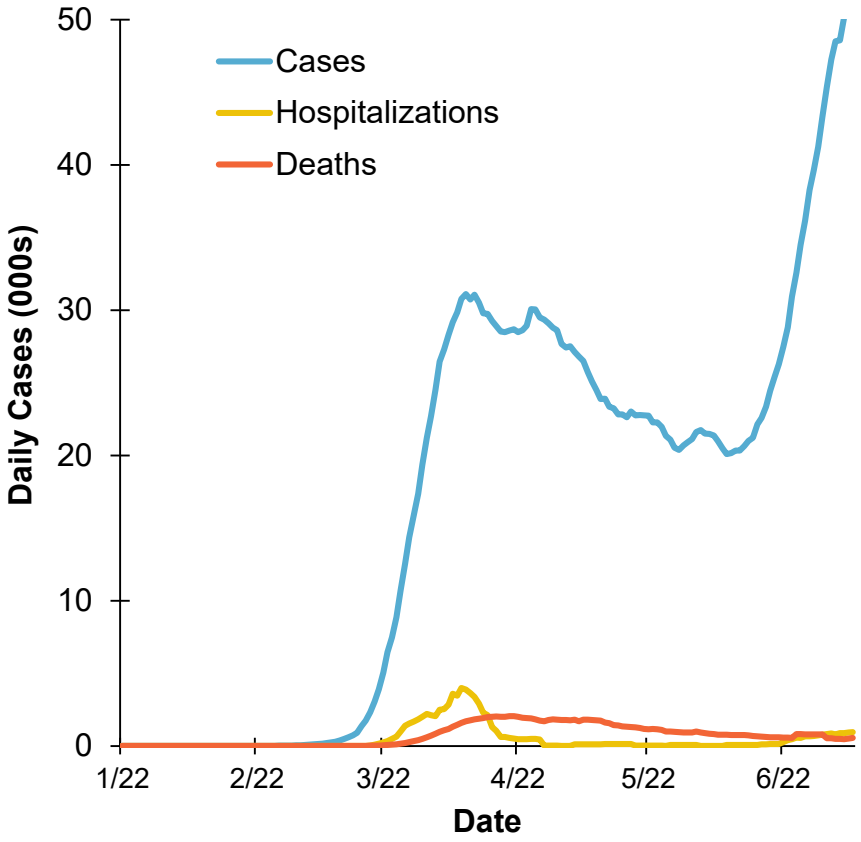
US COVID-19 Pandemic Response and Trends

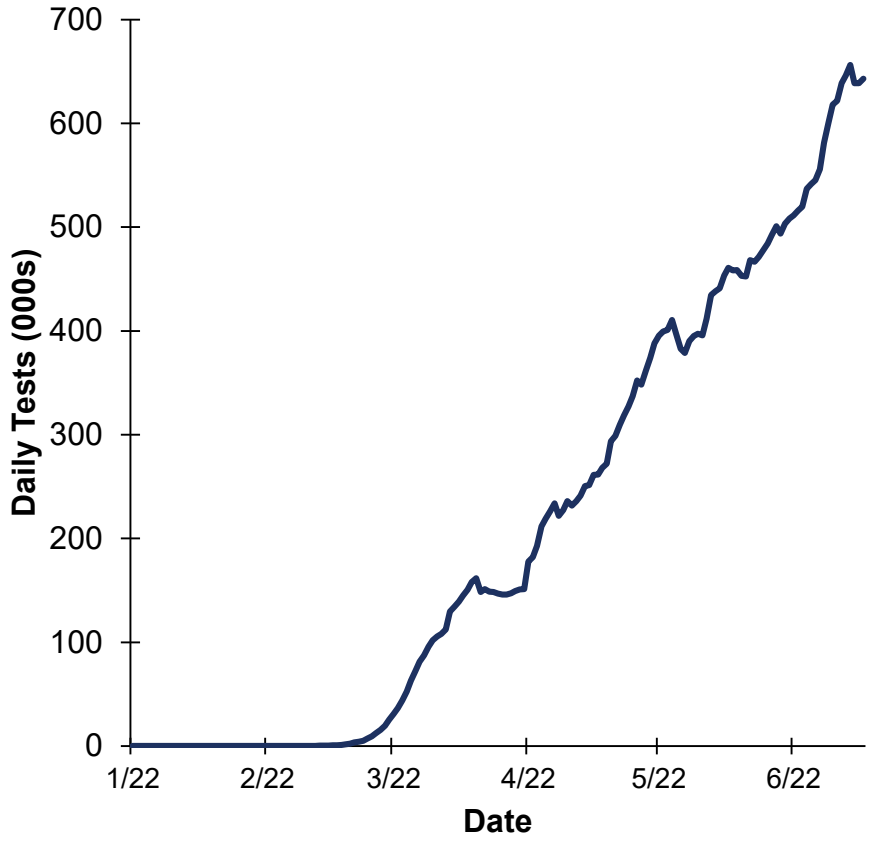
New
7/8/2020

The slow containment of COVID-19 in the US caused cases and deaths to slowly increase in March and April. Early re-opening has caused a spike in cases over the last month.

US COVID-19 7-Day Moving Average Statistics

January 22 – July 8, 2020



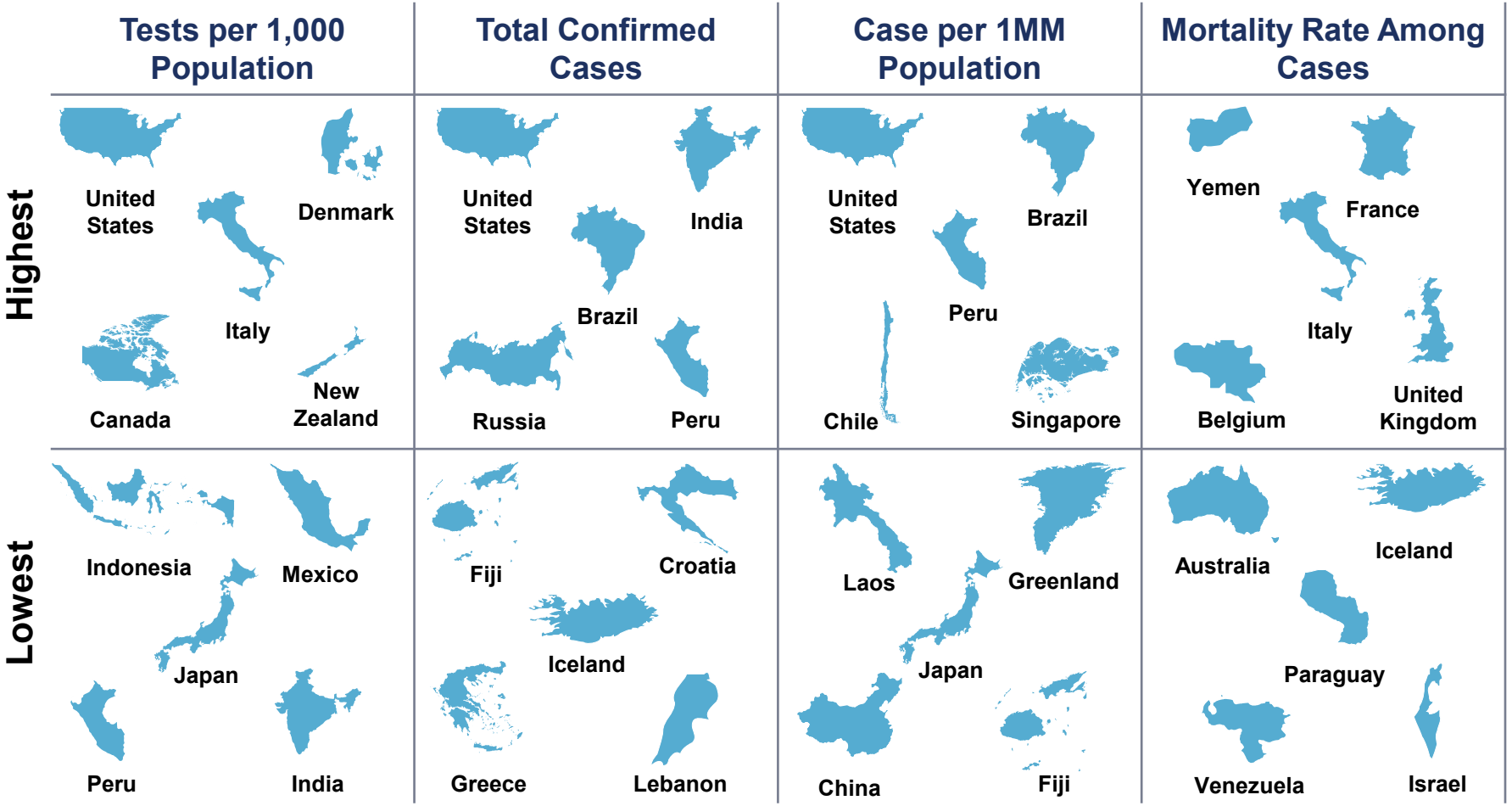


Note: 7-day average was used, as data is inherently noisy on a day-to-day basis. Past 7-day average shows better reflection of trend.
Source: Health Advances analysis, CDC, The COVID Tracking Project, Holshue et al. 2020 NEJM.

Global Statistical Snapshot: Top and Bottom 10

New
7/5/2020

The US has the greatest number of cases, and one of the highest case rates per 1MM population, globally.



Source: JHU Coronavirus Resource Center, Wikipedia.

Agenda

- What has changed since the First and Second Editions?
- ***What are the COVID-19 testing paradigm(s) of the future?***
- Appendix

Pandemic Management Options

New 7/5/2020

Globally, most nations elected a containment strategy to reduce healthcare strain and minimize mortality.

	Herd Immunity	Containment
Pros	• Life could largely return to normal • It is possible that natural immunity is more protective than vaccine-acquired immunity	• Containment has proven effective at reducing cases and deaths (e.g. South Korea) • Distancing measures keep hospitals from being overwhelmed • Can more easily restore social isolation if cases/deaths rise
Cons	• It is unknown if immunity can be developed to this virus • A population needs ~70% immunity (currently 2-20% seropositivity in US), which would result in ~918,000 deaths* in the US • Viral mutation could render herd immunity useless	• Slower economic recovery • Containment measures must last until a vaccine is available (at least 12-18 months)

* Deaths are calculated using a case fatality rate of 0.4%, the most recent CDC estimate.

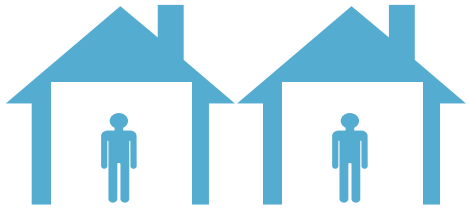
Source: Health Advances analysis, JHU, NYT, The Guardian, University of Michigan, UC Berkeley, KFF, CDC.

Testing to Reopen

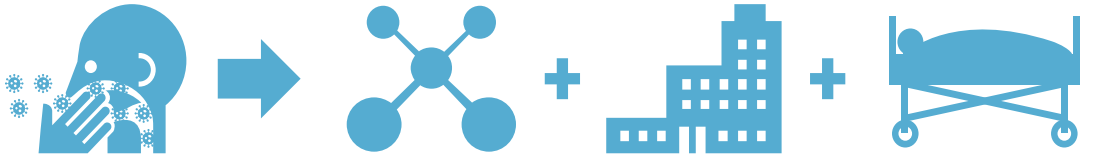
New
7/5/2020

Social isolation, when adhered to, has worked. High-volume screening and aggressive testing/tracing would complement ongoing social distancing and other safety measures.

Containment Stage



Social Isolation



Re-Opening Stage

High Volumes of Testing

We know how and what type of testing we need to do.
The question remains, when will we have the capability to do high-volume testing?

Source: Health Advances analysis, CDC, John's Hopkins University, Nature, New York Times, UPI.

Ex-US Reopening Case Study: South Korea

New 7/9/2020

South Korea reopening has seen only small spikes in cases due to thorough contact tracing, strict quarantining, and continuous testing.

May 6

- Events allowed to take place and businesses and entertainment (zoos, nightclubs, sports games) to reopen
- Small spike in cases after this phase, some places reclosed

May 20

- (Originally planned for May 13th) Some schools reopened with social distancing and prevention measures
- Reclosed due to a few cases reported in classrooms

Future

- Goal is to begin to slowly attain normalcy while monitoring the disease

Testing Approach

- Centralized
- Free testing to all, asymptomatic included
- >10,000 tests a day, even as cases decline
- Contact tracing app urges those who come into contact to get tested

Results Thus Far

- Small spikes traced back to a bar and school after reopening
- Have been able to actively monitor cases and re-close when necessary
- Had been under 50 cases for over a month until May 28th, still under 100 now

Key Learnings

- Consistently high testing, strict quarantine regulations with fines, and accurate and reliable contact tracing are essential to reopening and staying open

Source: Health Advances analysis, Our World in Data, Foreign Policy, CNN, Washington Post, ABC News.

Ex-US Reopening Case Study: Hong Kong

New 7/5/2020

Hong Kong has successfully reopened. The city is performing 2,000 tests per day, with plans to scale up, and is screening all incoming travelers.

May 5-8
- Theaters, gyms, bars, massage parlors, and gaming parlors reopen with restrictions
- Gatherings of up to eight people allowed

May 27
- Secondary schools begin reopening

June 8
- Eases travel for executives

June 15
- Primary schools begin reopening

End of June
- Masks mailed to every household

Apr | May | Jun | Jul

Testing Approach

- 2,000 tests/day with plans to increase to 7,500
- Aggressive, mandatory testing and contact tracing
- Testing all incoming airport passengers
- Home testing options, including at-home sample pickup, reduces testing burden

Results Thus Far

- Both the first wave and second wave suppressed
- <10 daily new cases
- Total case count has reached 1,100

Key Learnings

- Full lockdown may not be necessary with sufficient voluntary distancing, targeted testing, contact tracing, and isolation of known positive and high-risk people

Source: Health Advances analysis, South China Morning Post, ABC News, Bloomberg News, Fortune.

Ex-US Reopening Case Study: Germany

New 7/9/2020

Germany implemented aggressive testing and contact tracing to move towards reopening. That approach kept R_0 <1, however a recent flare up has set back the reopening effort.

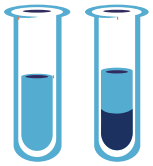
April 30
- Shops, schools, and other public spaces open
- Hygiene practices (i.e. 1.5m distance) remain
- Visiting limited to two households

May 15
- Football league Bundesliga opened to play behind closed doors

Jun 15
- Germany opens borders to European travelers

Jun 25
- A spike of 1500 cases within days led to the first regional lockdown since May and set back reopening efforts

Aug 31
- Large gatherings, such as concerts, banned until Aug 31



Testing Approach

- Antibody testing of 3,000 households to inform reopen plan
- Plans to conduct >140,000 tests/day
- >500 *Gesundheitsämter* (health officials) and >500 *Kontaktmanagers* (civilian tracers) for contact tracing

Results Thus Far

- An R_0 <1 and daily new infections <1,000 allowed initial reopening
- R_0 remained <1 and daily cases dropped to a few hundred until late June when a spike in cases occurred in slaughterhouses and crowded low-income housing causing a regional lockdown

Key Learnings

- Strong government leadership and subsequent trust in the government, along with aggressive testing and tracing lead to success, however vigilance is key as outbreaks can quickly set back reopening momentum

Source: Health Advances analysis, CNN, NY Times, BBC, DW News, Financial Times.

Ex-US Reopening Case Study: Japan

New 7/9/2020

Japan just recently reopened. Its very limited testing has allowed only the most at-risk to get tested, which has been surprisingly successful in preventing high death rates.

May 25
- State of emergency lifted

May 26
- Museums, libraries, and other cultural institutions reopen

June 1
- Movie theaters, gyms, and entertainment with no history of clustering infections reopen

June 12
- Almost all business closures lifted including arcades, pachinko parlors, restaurants, and bars

July 1
- Tokyo Disneyland and Disneysea reopened after four-month closure as part of Japan's gradual reopening

May — Jun — Jul

Testing Approach

- Only tested 0.185% of population
- Early on, testing was limited to those who likely needed hospitalization
- Later, private facilities also became available for testing, and expanded criteria to any older people who were seriously ill

Results Thus Far

- Despite limited testing, the death rate has been extremely low
- Only 920 total deaths, or 7.27 per million, as of June 11 th
- Testing capacity has now increased and reached 24,000 tests per day

Key Learnings

- Public health experts warn against drawing conclusions from Japan's experience. Numbers could be underestimated, as there might be a large number of asymptomatic cases who were not tested
- Limited testing was able to prevent the medical system from becoming overwhelmed early on, potentially helping lower the death rate

Source: Health Advances analysis, Our World in Data, Foreign Policy, New York Times, Japan Times.

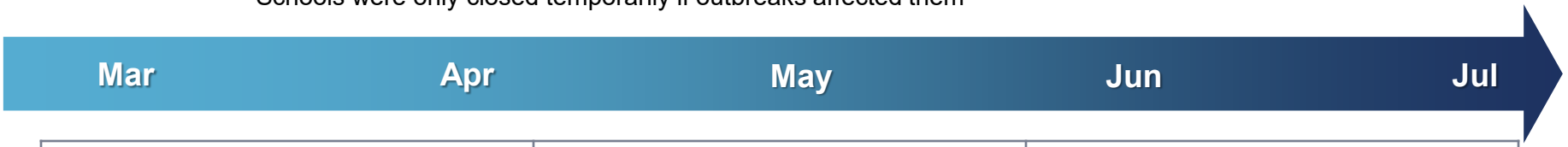
Ex-US Reopening Case Study: Sweden

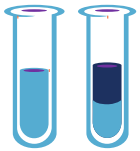
New 7/9/2020

Sweden never went into lockdown,which minimized the effect on the economy and healthcare system, but resulted in high death tolls compared to other countries.

Sweden never fully went into lockdown, and therefore has not needed to reopen in phases

- Restaurants were required to implement social distancing, but all businesses were kept open
- Schools were only closed temporarily if outbreaks affected them





Testing Approach

- Started testing early for symptomatic and asymptomatic patients
- Later changed approach, now only testing the most vulnerable
- Only 0.9% of the population has been tested, or only 5X the number of cases, compared to 280X in Norway, 110X in Denmark, and 18X in Italy

Results Thus Far

- Total deaths in Sweden are higher than other Nordic countries
- Outbreaks in schools, teachers have died
- Disease transmission still remains high,19.35/100,000 compared to Denmark, Finland and Norway <2

Key Learnings

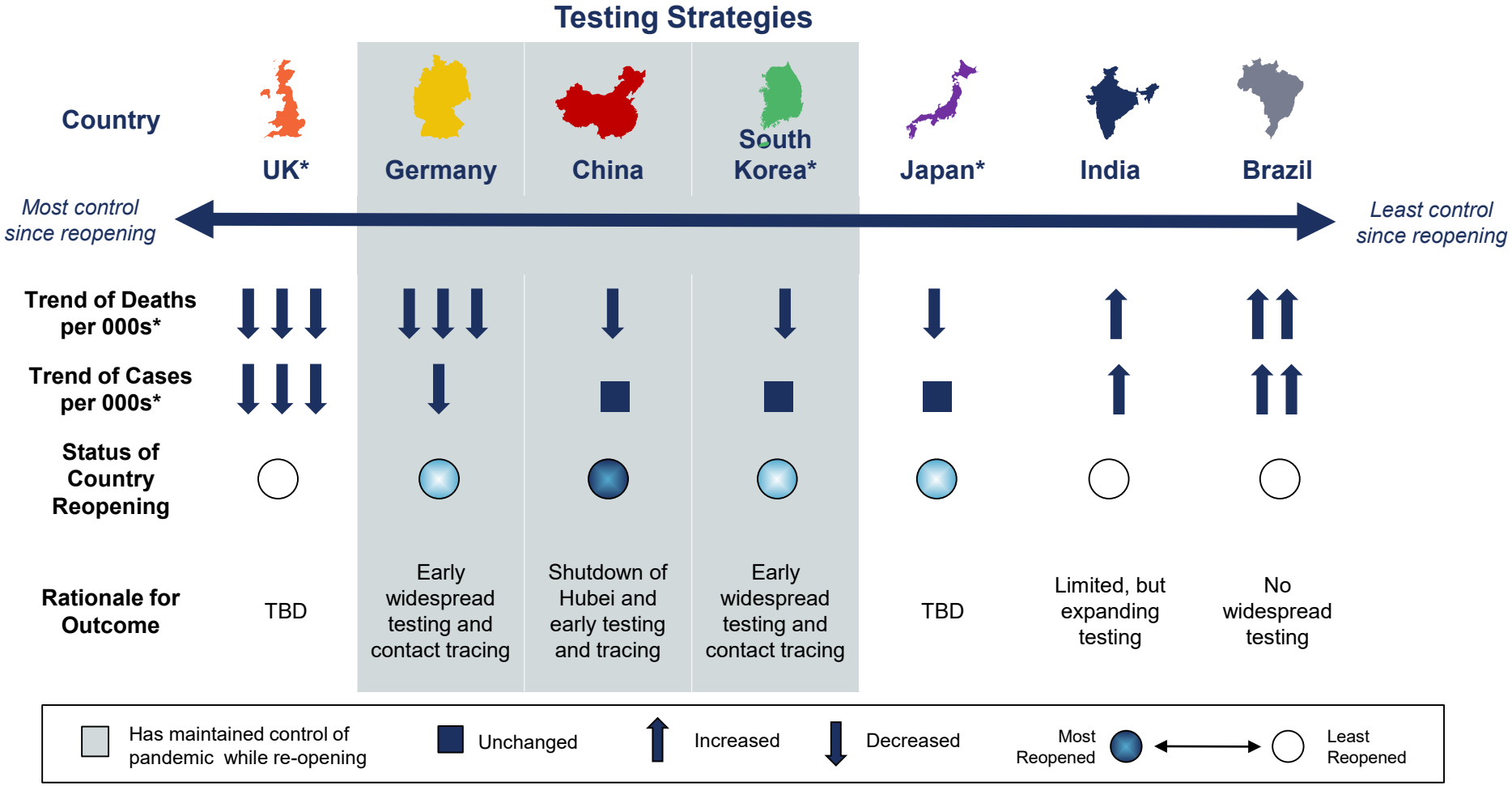
- Relaxed lockdown minimized shortages in hospitals, but caused a high death rate and did not protect at-risk groups
- Prevented detrimental effect on economy, but they have still had increases in unemployment
- Did not successfully build substantial herd immunity, only 7% seropositivity in Stockholm

Source: Health Advances analysis, Think Global Health, CNBS, The Local, Science Magazine, CNN, New York Times.

Ex-US Testing Strategic Impact On-reopening Success

New 7/9/2020

A combination of intense contact tracing and widespread testing has helped some ex-US countries reduce the scale of the pandemic and allowed for successful reopening.



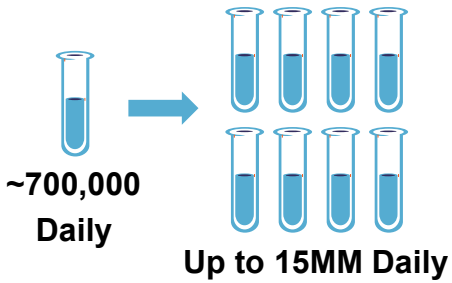
* Japan and the UK have begun reopening, but it is too early to judge success. Trends of deaths and cases per MM are based on an average of June 3rd to June 17th data relative to peak numbers in each country. Although South Korea has not drastically reduced deaths or cases, its numbers remain consistently low relative to other countries.

Source: Health Advances analysis, Our World in Data.

US Testing Actions Needed to Support Reopening

Despite the severe outbreak in the US, a well-defined and executed plan could be successful in managing the outbreak over the coming months and years.

High Testing Capacity



- Estimated to need 3-6MM per day for high risk and guideline recommended testing and up to 15MM to truly control the spread in the US

Well Defined Testing Protocols

- Test protocols must be in place to ensure consistent, widespread testing

Multiple Points of Access to Testing

- Must be fast, easy, and convenient
- POC tests, drive-thru testing centers, and retail clinics

Contact Tracing

- Critical for containing asymptomatic and pre-symptomatic spread

Rapid diagnosis of infected patients – both symptomatic and asymptomatic – is crucial to maintain low R_0.

Source: Health Advances analysis, New Yorker.

Ability to Achieve Testing Goals

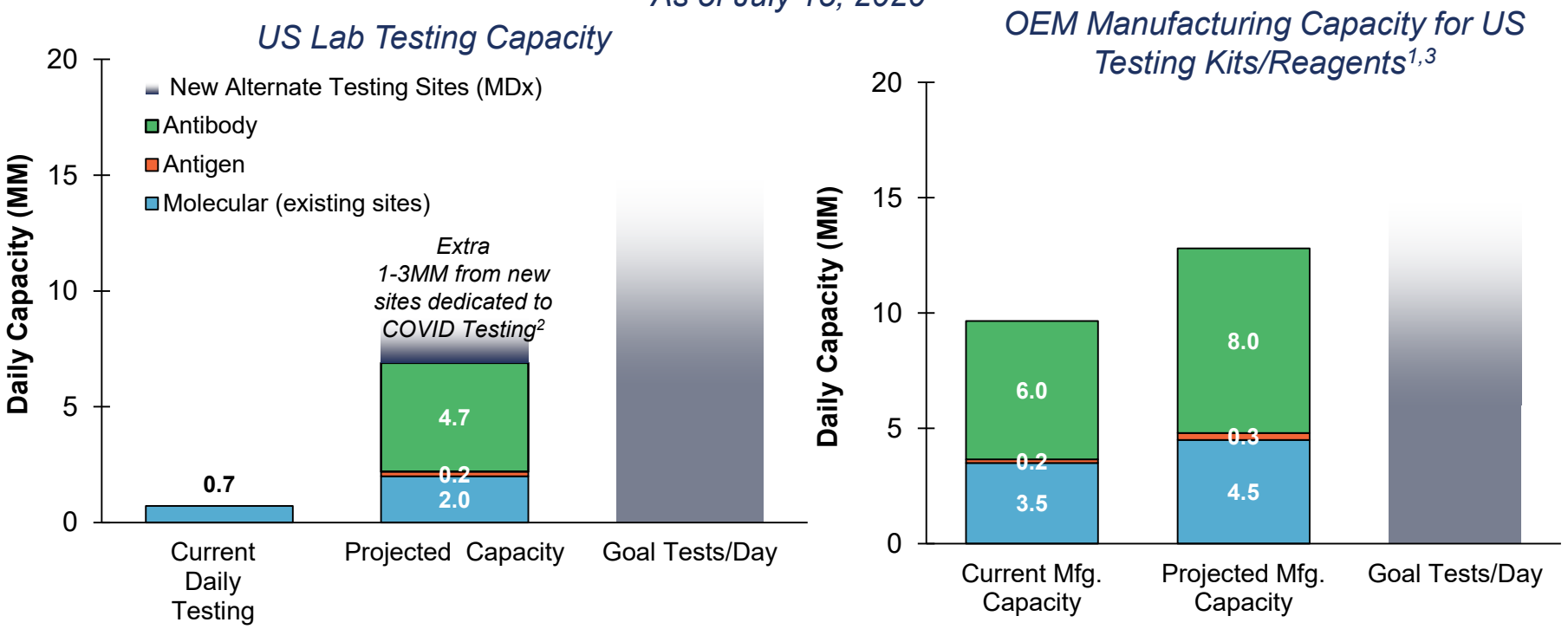
Updated 7/15/2020

Multiple Points of Access

Given current and anticipated testing capacity, the US will need to rely on a mix of molecular and immunoassay tests, rather than primarily on molecular.

US Current and Projected Daily Testing Capacity

As of July 15, 2020



[1] Projection considers the next several months as a time frame. [2] The extra 1-3MM capacity is based on other new locations (not current clinical labs) for testing expected to become available, such as employer-based testing; research lab capacity shifts, additional commercial specialty lab capacity conversions, etc. [3] Projection will ramp quickly over the next few months, but not fully reach these numbers until end of 2020.

Note: All projections are compiled from the combined stated numbers for larger labs and manufactures with scaling based on Health Advances analysis of relative capacity among smaller players and the number of labs and OEMs offering or projected to offer testing or manufacturing. OEM manufacturing capacity for RNA and immunoassay tests considers all manufacturers that have notified the FDA and made their tests available for purchase in the US. This manufacturing capacity represents only what we estimate will be available in the US, and not global manufacturing capacity. The goal tests number of 15MM per day combines the use cases of diagnostic testing and immune monitoring (via antibody tests).

Source: Health Advances analysis, company websites, press releases, COVID Tracking Project.

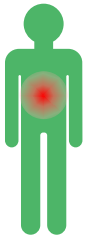
Challenges with Mandatory Testing

New 7/9/2020

Well Defined Testing Protocols

Testing everyone would be collectively beneficial, but the implications on individual freedoms will prevent ubiquitous testing in the US. Other protocols will therefore be needed.

Mandatory Testing Challenges

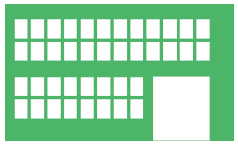


Patients

- Patient desire for privacy
- Unequal access to testing
- May create an inappropriate incentive for individuals to seek out infection (for "immunity passports")

Healthcare Providers (HCPs)

- HIPAA, data security
- Data sharing protocols
- Without sufficient resources, HCPs will be forced to prioritize patients for testing



Employers

- HIPAA, data security
- Data sharing protocols
- Right to work policy challenges
- Potential for employee discrimination

Government

- Societal stratification may encourage stigma and discrimination
- Increased monitoring and policing, creating higher risk of profiling, and harm for marginalized groups

Source: Health Advances analysis, Kofler 2020 Nature, Gibson Dunn, The Lancet, Miller 2020 Rueters, NS Tech.

Testing Protocol Case Study: CDC

New 7/9/2020

Well Defined Testing Protocols

CDC recommends viral tests for symptomatic and asymptomatic individuals, and antibody testing only for those with elevated likelihood of previous exposure.

What Type of Test

Viral Tests
(for acute diagnosis)

Antibody Tests
(for determining previous exposure only)

Who is Tested

Symptomatic Individuals

Asymptomatic at Higher Risk

Asymptomatic in Close Contact with Infected Persons

Test Performance Data Needed

For Antibody Testing, You Need:

High Specificity
Preferably ≥99.5%

Focus on People with High Pre-Test Probability of Having Had the Virus

Orthogonal Testing
(persons initially tested positive are tested with a second, but different, test)

When and Where

Routine testing (e.g., weekly) for vulnerable asymptomatic populations

Community, Outpatient, and Hospital-Based Practices

Homes or Workplaces Where People Are at Risk for Severe Disease
(i.e. nursing homes or factories)

Source: Health Advances analysis, CDC.

Testing Protocol Case Study: Washington DOH

New 7/9/2020

Well Defined Testing Protocols

The Washington State Department of Health recommends PCR testing for symptomatic and specific asymptomatic patients. Serology is actively discouraged.

What Type of Test

PCR Tests Preferred

Antibody Tests Not Recommended

Several Respiratory Methods Approved for Specimen Collection

Who is Tested and When

Symptomatic Individuals are the priority

Hospitalized patients, those at risk for adverse outcomes, and pregnant women are prioritized if resources are limited

Asymptomatic Individuals (every 2 weeks) in close contact with infected persons, living in congregate settings, or from racial and ethnic minority groups affected by adverse outcomes; as supply allows, high-risk employment or living conditions

Test Performance Data Needed

High Sensitivity and Fewer False Negatives

Where

Specimens Should Be Sent to Commercial Laboratories

Can Only Be Sent to Public Health Laboratories if for healthcare workers, residents in long-term care facilities, or those without health insurance

Source: Health Advances analysis, Washington State Department of Health.

Testing Protocol Study: NY State DOH

New 7/9/2020

Well Defined Testing Protocols

New York State has expanded testing capabilities to provide thousands of free tests per day to symptomatic and asymptomatic patients who meet the criteria.

What Type of Test

Molecular Test on Nasopharyngeal, Saliva or Self-Nasal Swabs including self collection. Developed by NY's Wadsworth Lab

Where

Authorized 28 Public and Private Labs for Testing, includes manual, semi-automated, and automated

Free Testing Available at Any Site Run by New York State
Can also go to test sites operated by local government or private company, but tests may not be free

Who is Tested*

Symptomatic Individuals

Those over 70 y/o, with Compromised Immune Systems, or Underlying Conditions

Those in Close Contact to Infected Persons, Healthcare and Essential Workers, Those Attending Protests, Returning to Work in Phase 1, and other factors deemed relevant by NYSDH criteria; students and others 7-14 days before arrival

* Frequency of asymptomatic screening not explicitly stated.
Source: Health Advances analysis, NY State Department of Health.

Testing Protocol Case Study: Amazon

New 7/9/2020

Well Defined Testing Protocols

Amazon is piloting at a small-scale testing warehouse workers through its own lab and protocol. Amazon has not committed to expanding this pilot at this time.

What Type of Test

Nasal Swabs for Molecular Testing

Looking into Other Tests
Including temperature checks and pulse oximetry (measures oxygen levels in the blood, which some scientists suspect can detect respiratory symptoms)

When and Where

Workers Will Collect Samples Themselves Every Two Weeks
using video guidance, with a clinical professional supervising

Setting Up Diagnostic Labs at Work Sites

Refer Positive Patients Out to Third Party, Grand Rounds, for telehealth consultations

Who is Tested and When

Workers in Their Fulfillment Centers and Warehouses (every 2 weeks)

Might Include Testing More Employees in the Future
(e.g., corporate)

Source: Health Advances analysis, CNBC.

Testing Protocol Case Study: Schools

New 7/9/2020

Well Defined Testing Protocols

Several public and private universities across the US have started piloting their own SARS-CoV-2 testing protocols to prepare for expanded testing for school reopening in the fall.

Harvard University Decision for 2020-21 Academic Year

July 6, 2020

"Those guidelines […] will include, among other features, the requirement that ***students and residential staff*** participate in a viral testing program that will **begin with an initial *screening upon arrival, followed by testing for the virus every three days while in residence.*** The frequency of testing may increase or decrease depending on the prevalence of infection within the Harvard community and the region."

UC San Diego's "Return to Learn" Program

June 2020

UCSD launched its "Return to Learn" program May 11, an effort to broadly test students, faculty and staff.

*"Over a three-week period, more than **1,500** resident undergraduate and graduate students took part in self-administered COVID-19 testing. The ultimate goal is to broaden the scope to **test 60-90% of UC San Diego's on-campus population** for the virus **on a recurring basis**."*

*"All students who reside on campus will be expected to participate in **daily symptom screening** and will be offered **free SARS-CoV-2 testing** as part of the move-in process."*

BU to Set Up COVID-19 Testing for Students, Faculty, and Staff

May 21, 2020

*"BU's testing protocols most likely will involve **distributing testing kits for self sampling** and could require people to spit their **saliva** into a cup, or possibly **swab inside their nostrils...** The samples would be tested for the coronavirus at a lab […] and results of the tests would be delivered to people electronically…"*

Source: Health Advances analysis, universities and schools news releases.

Testing Protocol Case Study: Nursing Homes

New 7/9/2020

Well Defined Testing Protocols

Massachusetts represents an example of a state-sponsored nursing home testing program supported by a collaboration between government and private testing providers.

Mass.gov COVID-19 Testing Guidance

Mobile Testing at Long Term Care and Assisted Living Residences

On March 31st, the ***Massachusetts National Guard*** was activated to temporarily support COVID-19 testing in ***nursing homes, assisted living residences and rest homes*****,** allowing for safe, onsite, sample collection by trained personnel. It will conclude testing on June 15th. Facilities are eligible and encouraged to schedule testing for:

- ***All symptomatic residents*** and staff, as well individuals who are close contacts of positive COVID-19 cases
- ***One-time facility-wide testing of residents and staff.*** If your facility has already completed facility-wide baseline testing, the National Guard is available to retest all staff only

Options for On-Site LTC Testing

Provider	Type(s) of Specimen Collection	Who Collects the Specimen
Fallon EMS	Nasopharyngeal	Fallon
Brewster Ambulance	Nasopharyngeal	Brewster Ambulance
Quest	Nasopharyngeal and blood (antibody testing)	Employer must provide/identify medical staff
LabCorp	Nasopharyngeal and blood (antibody testing)	Employer must provide/identify medical staff
Orig3n	Nasopharyngeal and anterior nasal swabs	Orig3n or employer-provided medical staff
PhysicianOne Urgent Care	Nasopharyngeal and blood (antibody testing)	PhysicianOne Urgent Care

MassLive: Most Massachusetts Nursing Homes Met the State's Coronavirus Testing Criteria

May 27, 2020

*"Nearly all of the **360 nursing homes** in Massachusetts who had to submit testing data **met the coronavirus testing criteria** set under a state program […] all but nine received positive marks for achieving the baseline testing threshold for residents and staff."*

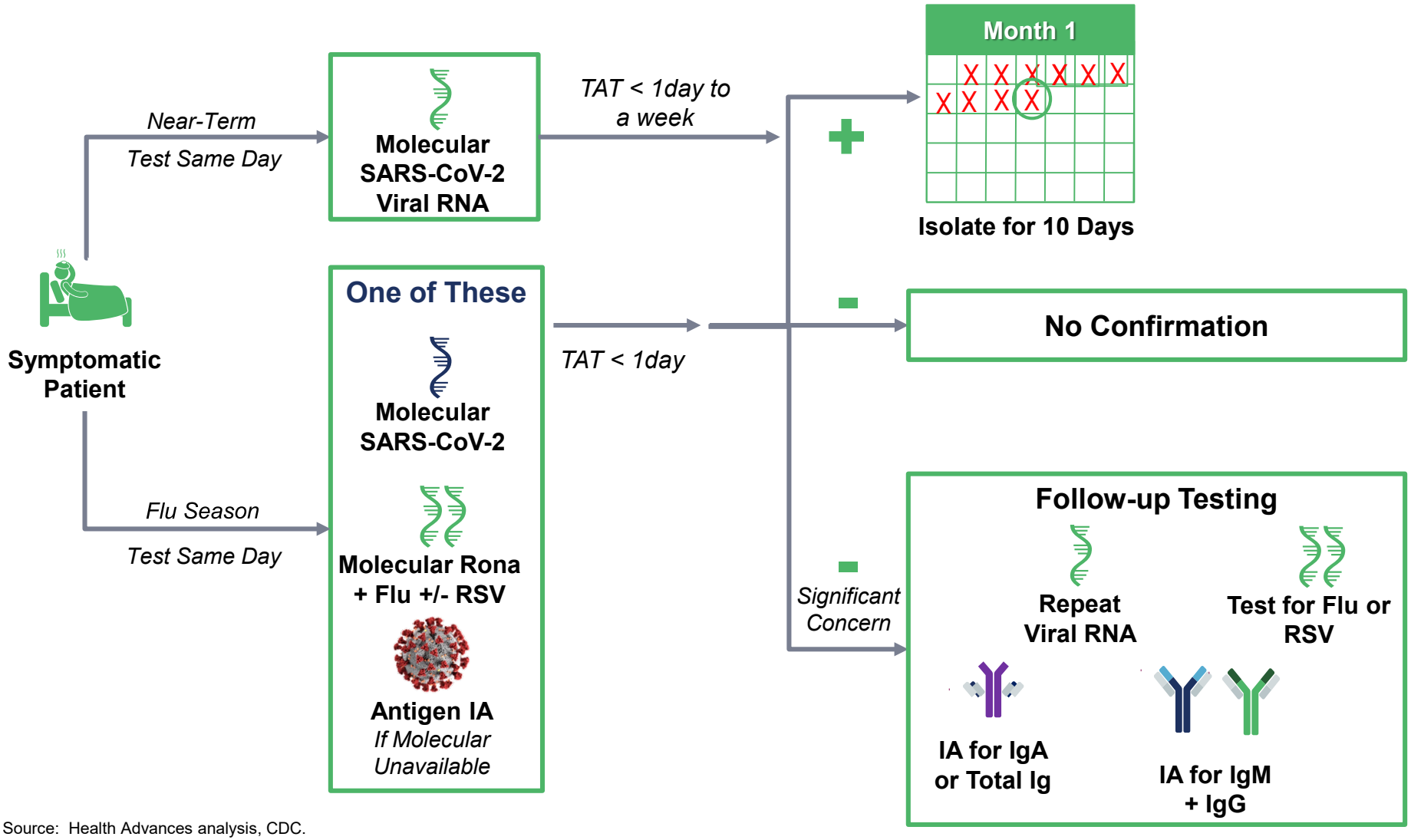
Note: LTC = long term care.
Source: Health Advances analysis, Mass.gov, MassLive.

Likely US Testing Protocols: Symptomatic Patients

New 7/9/2020

Well Defined Testing Protocols

Ideally, moving forward all symptomatic patients, regardless of severity will have access to molecular testing supplemented with antigen and antibody testing as needed.



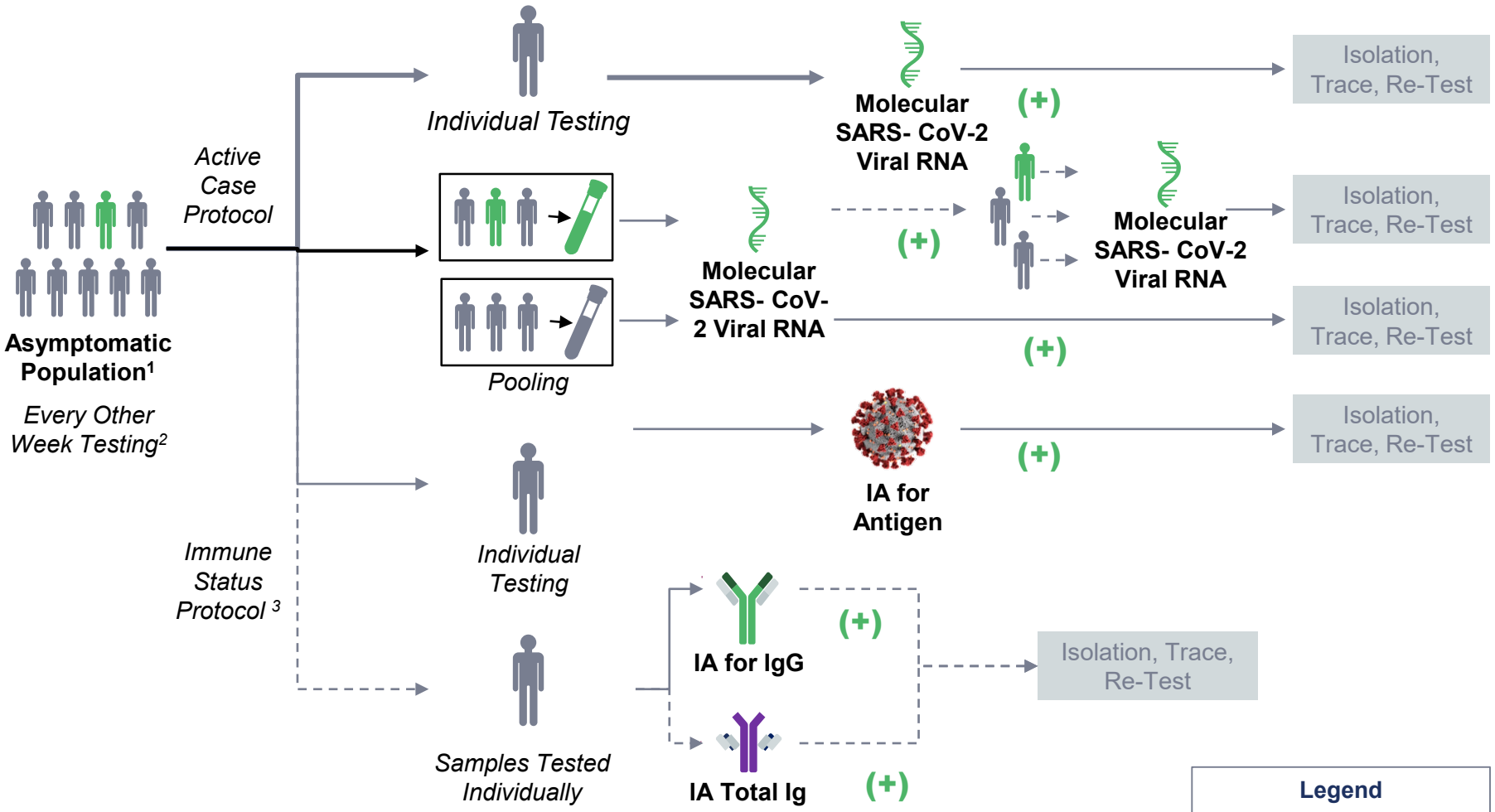
Source: Health Advances analysis, CDC.

Likely US Testing Protocols: Asymptomatic Patients

New 7/9/2020

Well Defined Testing Protocols

Given cost and access challenges, screening of asymptomatic/pre-symptomatic infections will likely leverage a combination of molecular, pooling, and antigen assays.



[1] Includes schools, certain large employers, and those in close living quarters (e.g., nursing homes).
[2] Asymptomatic screening has only been implemented in limited circumstances to date. Actual frequency will depend on availability of testing and testing costs as well as who pays for testing.
[3] Based on assumption that antibodies do indicate at least some level of immunity.

Source: Health Advances analysis, Treibel 2020 The Lancet, Eberhart 2020 J. Clin. Virology.

Testing Access Points

New 7/9/2020

Multiple Points of Access to Testing

Testing will need to be accessible in multiple locations and through multiple pathways.

Symptomatic

Asymptomatic/Pre-symptomatic

Sample Access Point

Hospitals

Retail/ Urgent Clinic, Primary Care

Drive Thru

At Home

Retail/ Urgent Clinic, Primary Care

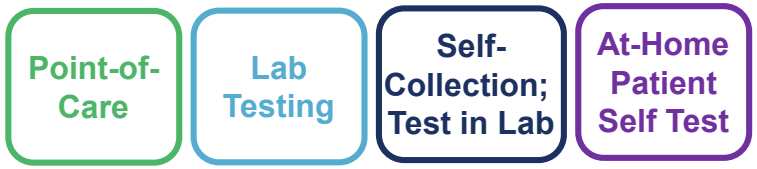
Drive Thru

At Home

Congregate Care*

Schools/ Employers

Location of Testing



Note: Congregate Care refers to places such as jails, nursing homes, assisted living, summer camps, and dorms.
Source: Health Advances analysis.

Dynamics of Testing for Employers

New 7/9/2020

Multiple Points of Access to Testing

Employers need safe and productive workplaces, but generally lack experience and control in determining the design and implementation of testing programs

Employer Decisions on COVID-19 Testing	Employer Expertise	Employer Control
Is testing required?	○	◑
Which employees will be tested?	○	◑
What testing will be done?	○	◑
How frequently will testing occur?	○	◑
Where will testing be done?	◕	●
Is testing run by company or contracted to 3rd party?	◕	●
What is required for data management and privacy?	◔	◑
Who pays for testing?	◔	◑
What liability does the employer have for employee lost work time, wages, and disability or death in the presence or absence of testing programs?	◔	◑

Less ○ ⟷ ● More

Source: Health Advances analysis, EEOC guidance documents, CDC guidance documents.

US Workplace Return Plans

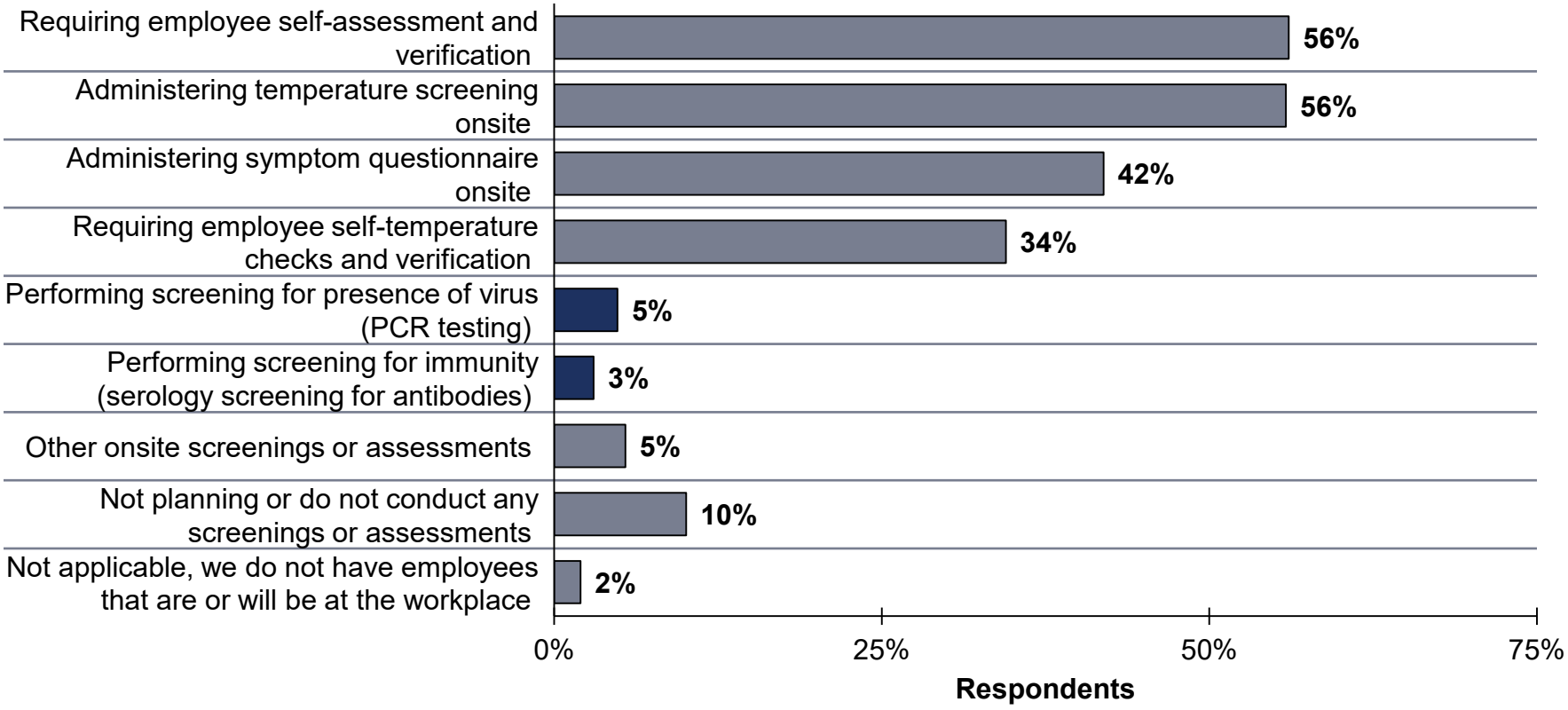
Updated 7/8/2020

Multiple Points of Access to Testing

Only a small percentage (<10%) of US employers are planning to deploy SARS-CoV-2 testing as the US slowly returns to the workplace.

Employer-Sponsored SARS-CoV-2 Screening/Assessments for Returning to the Workplace

n = 496 as of July 8



Note: Survey data of ongoing survey as of July 8, 2020.
Source: Health Advances analysis, Mercer Global Survey.

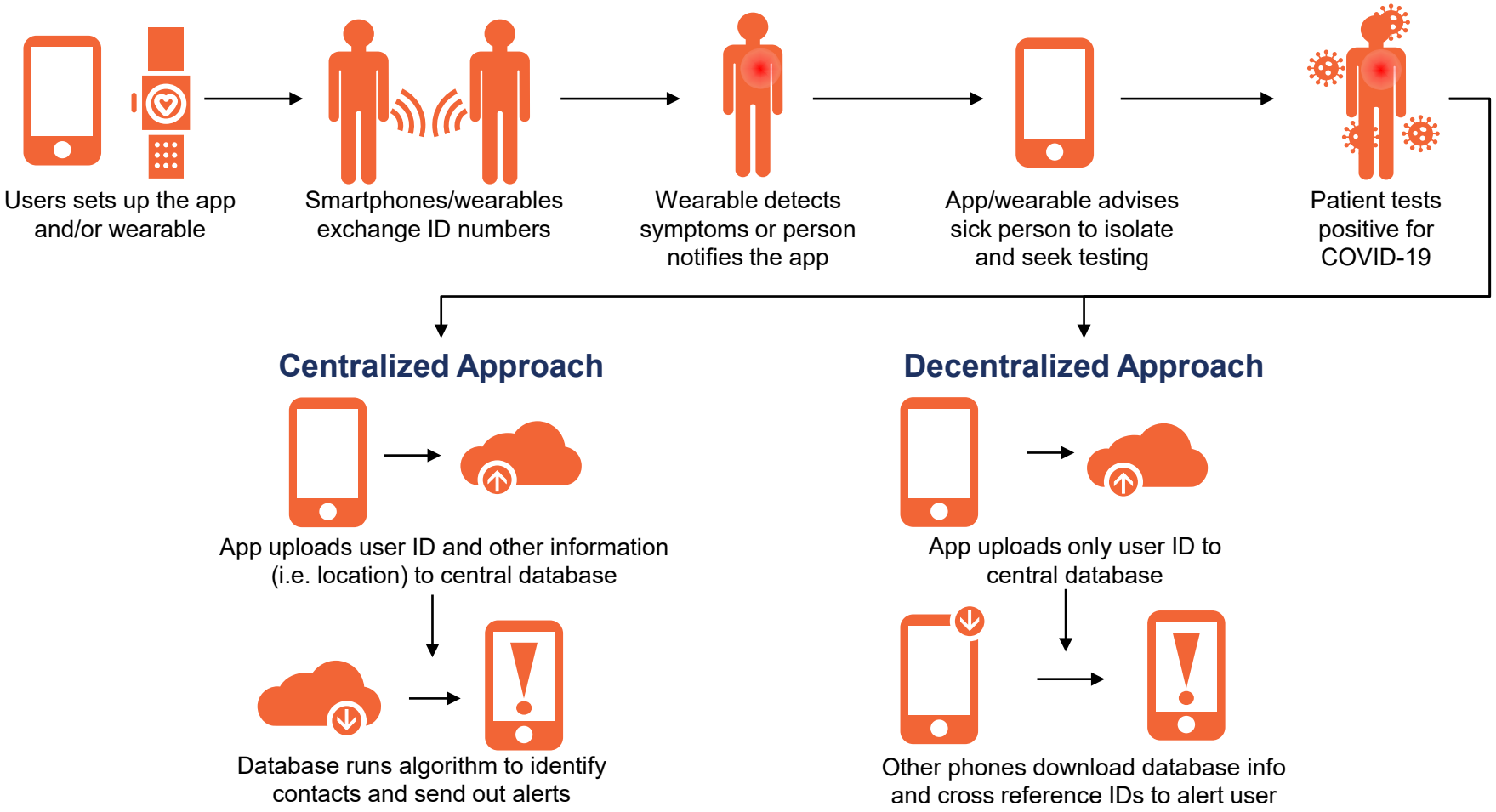
Contact Tracing Technologies

New
7/9/2020

Contact Tracing

Nationwide contact tracing will require the use of novel technologies like phone apps and wearables that may help with early detection and provide automated contact alerts.

Example Tracing Technology Workflow



Source: Health Advances analysis, BBC, CBC, Zastrow 2020 Nature.

Contact Tracing Status

New 7/9/2020

Contact Tracing

Most states are attempting to conduct some degree of contract tracing for COVID-19. However, approaches vary based on the spread in each state and available resources.

Contact Tracing Approaches in the US

Based on United States of Care Monitoring of Contact Tracing Situation

Hiring or reassigning government employees

- WA, UT, AL, CA, TN, and MO have all started initiatives to hire or reassign govt. employees

Contracting with outside vendors

- MA, OH, IN, and MY have signed agreements with healthcare organizations to implement tracing

Deploying the National Guard

- WA, RI, WV, IA, and ND are activating the National Guard to help

Recruiting volunteers

- OK, ND, KS, MI, and AZ are taking creative approaches to recruit recent graduates and others to volunteer for help

Utilizing technology

- CA, RI, CO, ND, SD, UT, KS, VT have announced building databases and/or using cell phone data to track patients

Key Challenge

- Lack of alignment between state needs and capabilities
  - For example, MA launched a large scale program in collaboration with Partners in Health and budgeted $44MM to hire over 1,000 employees, however it recently downscaled the program due to lack of need, while other states like FL do not have an adequate program in place considering its population size and recent outbreaks

Source: Health Advances interviews and analysis, United States of Care, Boston Globe.

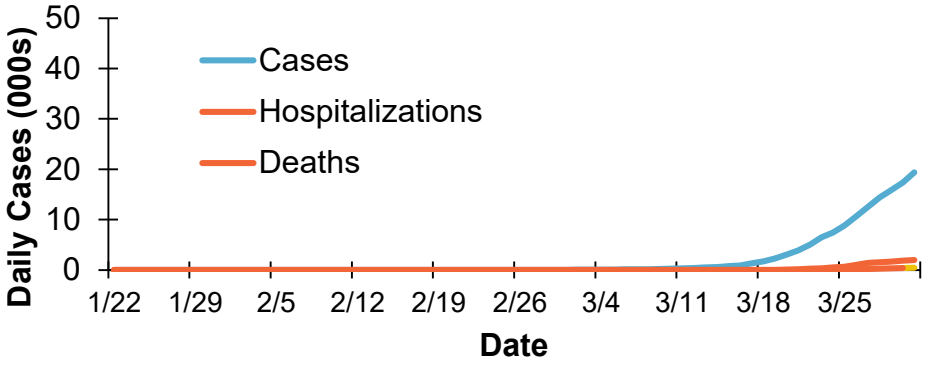
Agenda

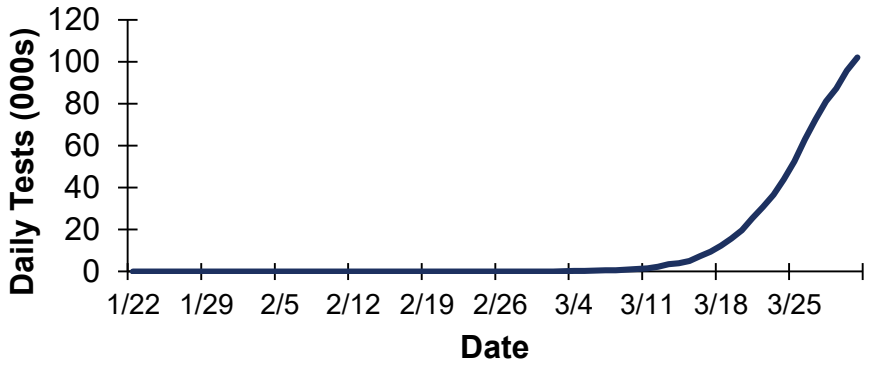
- What has changed since the First and Second Editions?
- What are the COVID-19 testing paradigm(s) of the future?
- ***Appendix***

US COVID-19 Pandemic Response: January - March

From January to March, the US was slow to ramp up testing. As a result, cases continued to spread, forcing nearly all states to issue stay-at-home orders by end of March.

US COVID-19 7-Day Moving Average Statistics





January

- 1/20: First US case reported
- 1/31: US DHHS declares public health emergency, mandatory 14-day quarantine for visitors of Hubei Province

February

- 2/6: CDC ships defective tests to state labs, first COVID-19 death in CA
- 2/15: US evacuates US nationals from Diamond Princess in Japan, several cases confirmed
- 2/26: First case of community transmission confirmed in CA

March

- 3/6: Multiple states report first cases
- 3/11: WHO classifies COVID-19 as pandemic
- 3/12: Several states announce school closures, sports leagues suspend seasons
- 3/16: President Trump recommends against gatherings of >10 people and restricts discretionary travel
- 3/17-24: Multiple states issue stay-at-home orders

April

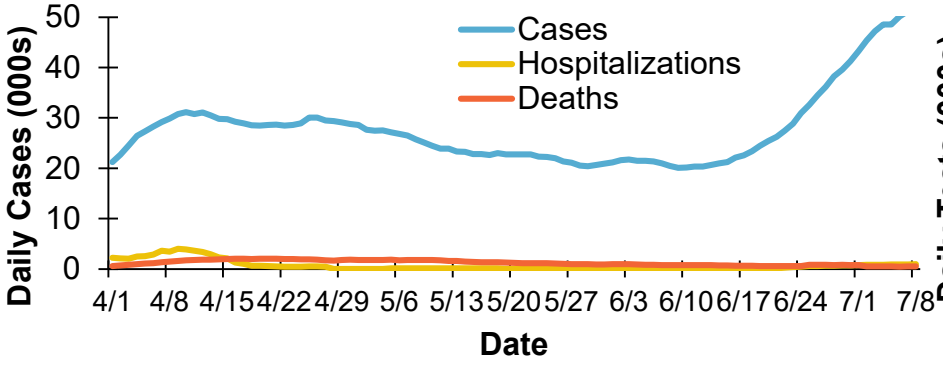
- 3/25: Congress passes $2T coronavirus stimulus bill

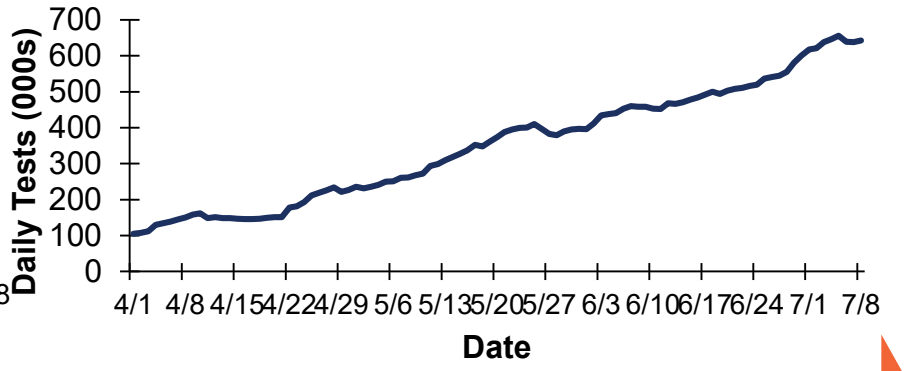
Note: 7-day average was used as data is inherently noisy on a day-to-day basis. Past 7-day average shows better reflection of trend.
Source: Health Advances analysis, CDC, The COVID Tracking Project, Holshue et al. 2020 NEJM.

US COVID-19 Pandemic Response: April - July

While the US was largely shuttered for most of April, by mid May most states had begun to ease social distancing restrictions, often without sufficient testing programs.

US COVID-19 7-Day Moving Average Statistics





April

- 4/1-4/8: More states announce shelter-in-place orders through end of April
- 4/14: Dr. Fauci declares that the US does not yet have critical testing and tracing procedures needed to reopen the economy
- 4/16: Trump administration unveils federal guidelines outlining a 3-phase approach to reopening, leaving it up to states to decide phases and timelines

May

- 4/20-4/27: Multiple states announce partial reopening plans
- 5/1: Protests against stay-at-home orders held across the country

June

- 5/20: All 50 states have begun easing restrictions, most without meeting guidelines and without consistent programs to test, trace, and isolate cases
- 6/1-6/8: Uptick in COVID-19 cases, likely caused by eased restrictions and social gatherings around Memorial Day
- 6/20-7/1: Continued uptick in cases, particularly in hotspots of CA, AZ, FL, and TX

July

- 7/3-7/8: States begin to reclose public areas as cases continue to spike

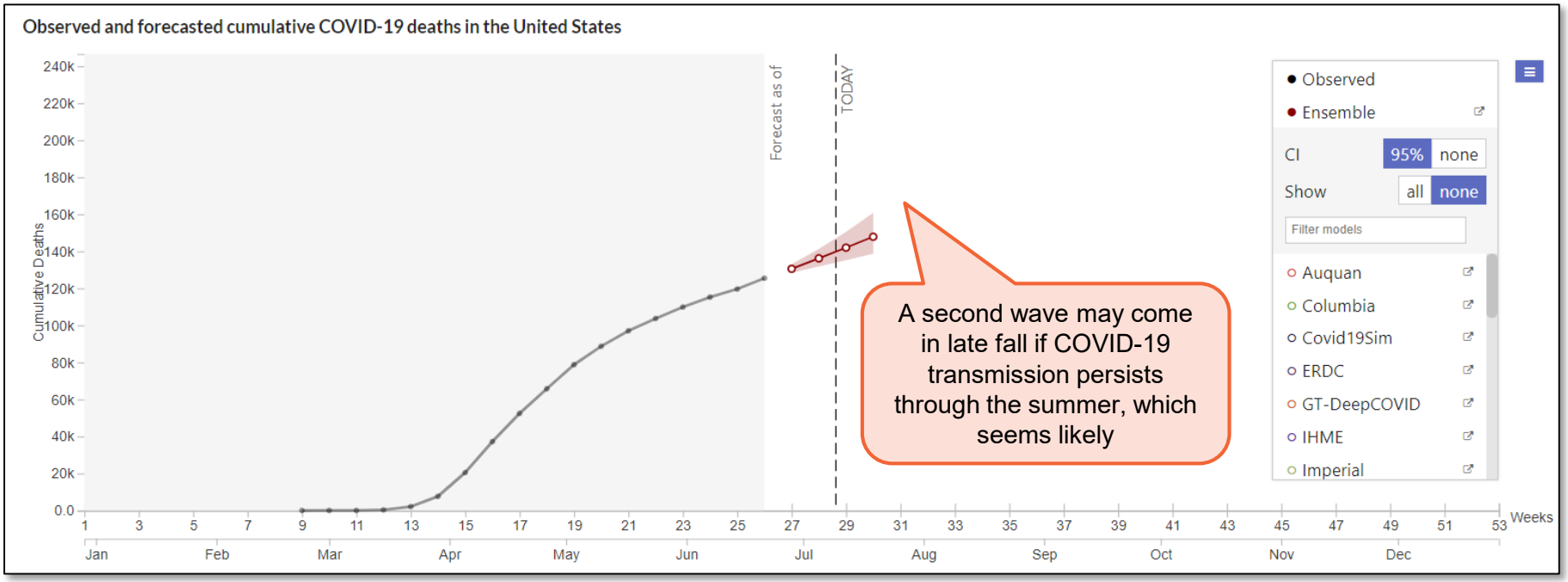
Note: 7-day average was used as data is inherently noisy on a day-to-day basis. Past 7-day average shows better reflection of trend.
Source: Health Advances analysis, CDC, The COVID Tracking Project, Holshue et al. 2020 NEJM.

Impact of Reopening during COVID-19 Pandemic

The CDC anticipates ~148,000 total reported COVID-19 deaths by July 25th; however, this may significantly increase if reopening plans continue without adequate testing and tracing protocols.

Observed and Forecasted Cumulative COVID-19 Deaths in the US

Forecasted as of July 9, 2020



Note: Forecast models make various assumptions about the levels of social distancing and other interventions, which may not reflect recent changes in behavior. ERDC = US Army Engineer Research and Development Center. GT-DeepCOVID = Georgia Institute of Technology. IHME = Institute of Health Metrics and Evaluation. ISU = Iowa State University. JHU = Johns Hopkins University. LANL = Los Alamos National Laboratory. MIT = Massachusetts Institute of Technology. MOBS = Northeastern University. UA = University of Arizona. UCLA = University of California Los Angeles. UT = University of Texas Austin. YYG = Youyang Gu (COVID-Projections).

Source: Health Advances analysis, CDC.