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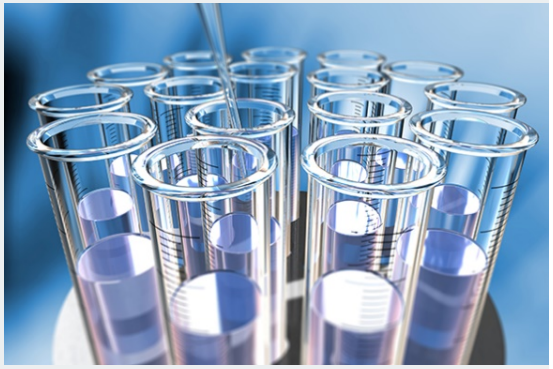


HA101: Demystifying SARS-CoV-2 Testing for COVID-19

First Edition

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

April 16, 2020

What to Expect from These Reports

This document provides a high level, easy to read review of:

- Background on SARS-CoV-2 and its associated disease, COVID-19
- Diagnostic testing approaches and relative availability and use in the US (and elsewhere)
- Answers to many other frequently asked questions with respect to SARS-CoV-2 testing

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

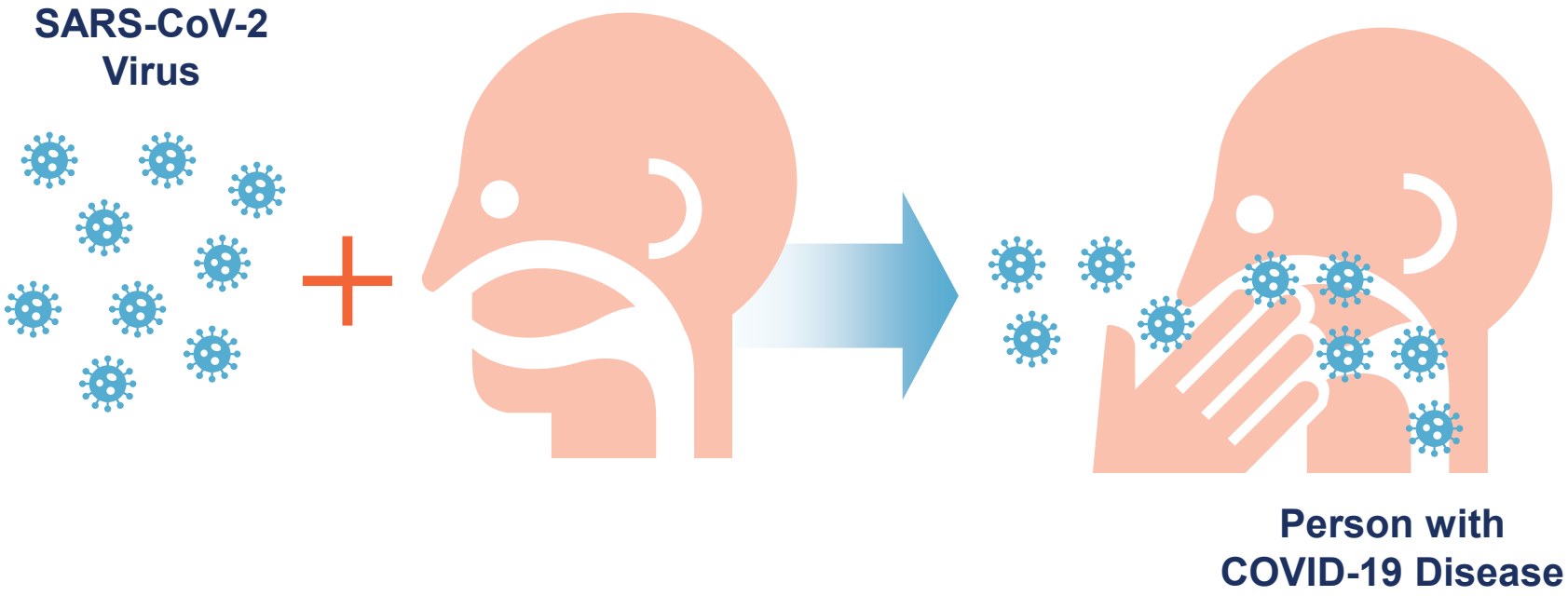
Please email additional questions to:
diagnostics@healthadvances.com

First Edition Agenda

- ***What are SARS-CoV-2 and COVID-19?***
- What types of tests are used for SARS-CoV-2/COVID-19 management?
- How is testing performed and where can I access testing?
- Appendix and Glossary

What is COVID-19?

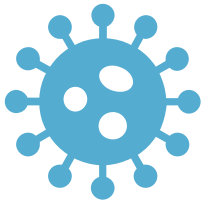
COVID-19 is a disease that is caused by a virus called SARS-CoV-2.

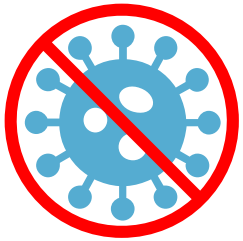


Source: Health Advances analysis, Seattle Times.

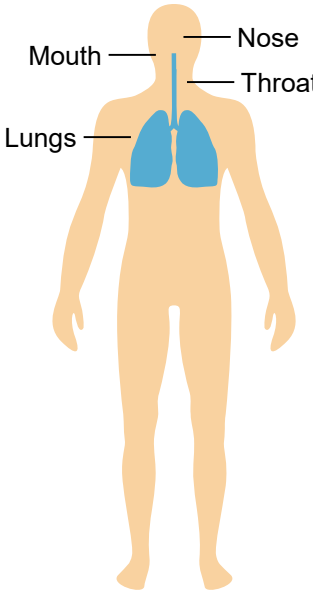
Where in the Body Does SARS-CoV-2 Infection Occur?

SARS-CoV-2 primarily infects the respiratory system and is not found in other parts of the body.





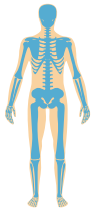
SARS-CoV -2 Primary Infection Locations



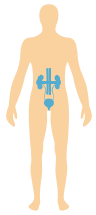
Respiratory

Low/Non-Infected Systems

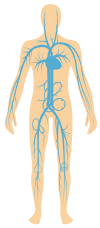
Muscle



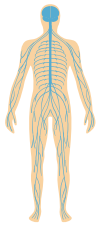
Skeletal



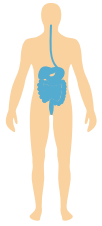
Reproductive and Urinary



Circulatory



Nervous



Digestive

Source: Health Advances analysis, Huang 2020 Lancet.

When to Suspect SARS-CoV-2 Infection

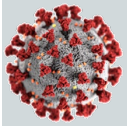
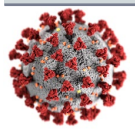
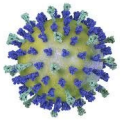
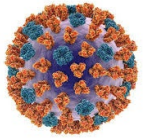
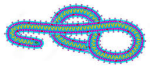
Mild forms of COVID-19 are similar to colds, flu and allergies. In other cases shortness of breath with high fever, aches and pains, and loss of smell can be indicators.

Symptom	Condition			
	COVID-19	Cold	Flu	Allergies
Fever				
Cough				
Shortness of breath				
Fatigue				
Aches and pains *(e.g., back pain)*				
Runny or stuffy nose				
Sore throat				
Loss of Smell/Taste				
Diarrhea				
Headaches				
Sneezing				
Itchiness				

Source: Health Advances analysis, JAMA, LA Times, WHO, CDC.

SARS-CoV-2 Compared to Other Common Viruses

SARS-CoV-2 may (we are still learning about the virus) have a higher infection and mortality rate as compared to seasonal influenza, the virus that causes the flu.

	Virus	Virus Family	Disease	Years Active	Global Cases[1]	Global Deaths[1]
	**SARS-CoV-2**	Coronaviridae	COVID-19	2019 - Present	1.9M[2]	123K (~6%)[2]
	**SARS-CoV**	Coronaviridae	SARS	2002 - 2003	8K	800 (10%)
	**MERS-CoV**	Coronaviridae	MERS	2012 - Present	2K	800 (40%)
	**Influenza**	Orthomyxoviridae	Flu	400 BCE - Present	1B per year	300-650K per year (0.03%-0.065%)
	**HIV**	Retroviridae	AIDS	1983 - Present	75M	32M (43%)
	**Ebolaviruses**	Filoviridae	Ebola	1976 - Present	31K	13K (42%)

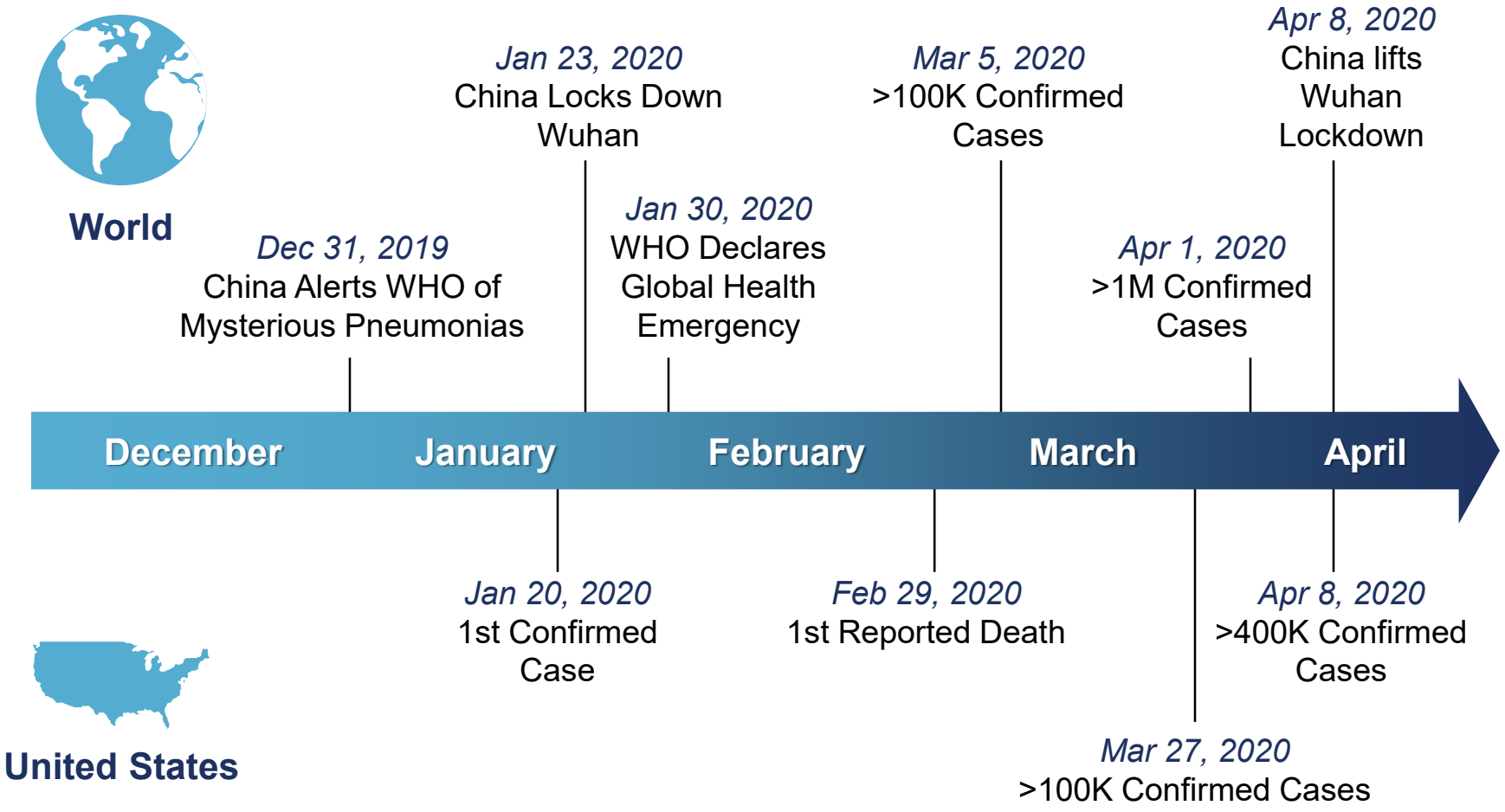
[1] Confirmed cases only. For SARS-CoV-2 this refers only to patients with an actual positive diagnostic test. Other diseases such as flu have been studied on an epidemiological basis and therefore may include estimates of unconfirmed (untested) cases.

[2] As of April 15, 2020; As the number of actual infections is unclear at this time, the death rate from SARS-CoV-2 is likely over estimated.

Source: Health Advances analysis, CDC, WHO.

The Spread of a Pandemic: SARS-CoV-2 and COVID-19 Timing

Starting with reports of a mysterious pneumonia in Wuhan, China in December, SARS-CoV-2 spread quickly to reach 1MM global confirmed cases by April.



Source: WHO, FDA, CDC, John Hopkins CSSE.

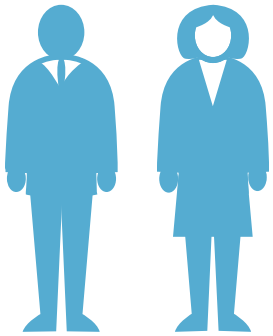
What We Still Don't Know, Though Some May Claim To Have the Answers

There is still a lot to learn about SARS-CoV-2. The global research and clinical communities, assisted by diagnostic testing, are working hard to address these questions.

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

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

- Does past infection provide immunity to future infection?
- If so, for how long?
- What level of anti-virus antibody confers immunity?



- 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?

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).
Source: Health Advances analysis.

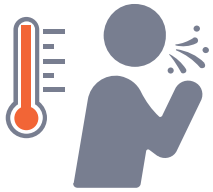
First Edition Agenda

- What are SARS-CoV-2 and COVID-19?
- ***What types of tests are used for SARS-CoV-2/COVID-19 management?***
- How is testing performed and where can I access testing?
- Appendix and Glossary

Reasons to Perform SARS-CoV-2 Testing

Multiple reasons do or could exist to perform testing for SARS-CoV-2.

Current and Potential Purposes of SARS-CoV-2 Testing



Patients with Suspected Active Infection

Diagnosis

- Confirm the presence of SARS-CoV-2 in patients with symptoms

Prognosis

- Assessment of COVID-19 disease severity and/or risk of progression

Exposed Individuals and/or Those With Known Previous Infection

Exposure Screening/ Infection History

- Determine if a patient was previously infected with SARS-CoV-2 (whether or not they had symptoms)
- Primarily for population surveillance by tracking cases (symptomatic and asymptomatic) and exposure of those close to known infections

***(Potential)* Immunity Status**

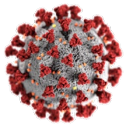
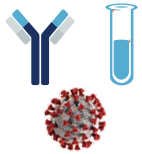
- Assess the presence of (potential) immunity due to previous infection based on presence and/or amount of anti-SARS-CoV-2 immune response (in the form of antibodies*)

* Antibodies are a protein the body's immune system produces in response to an infection. Antibodies identify the infection as foreign and direct other parts of the immune system to attack and neutralize/destroy the infection. The presence of anti-virus antibodies does not necessarily mean a person is immune to future infection. We are still learning about the SARS-CoV-2 immune response.

Source: Health Advances analysis, McKean, 2012 Principles and Practice of Hospital Medicine.

What Tests Measure

Diagnosis requires detecting the virus in the body, while screening for exposure and immunity status requires detection of anti-virus antibodies.

Clinical Reason for Testing		What the Test Measures
Diagnosis	 SARS-CoV-2 Virus	• To confirm[1] an ongoing/current infection, the virus itself must be detected in the body
Prognosis	 Combination of Virus, Antibody, and Health Tests	• To date, this is unclear • Likely a combination of virus, anti-virus immune response, and other parameters (e.g., # of blood cells)
Exposure Screening/ Infection History **Immunity Status**	 Anti-virus Antibodies[2]	• To determine prior infection or likelihood to be immune, a test looks for the presence of anti-virus antibodies produced by the immune system • The presence of anti-virus antibodies does not definitively indicate a person is immune

[1] Anti-virus antibody testing can also help with diagnosis, but should not be used alone for this purpose.
[2] Antibodies are a protein the body's immune system produces in response to an infection. Antibodies identify the infection as foreign and direct other parts of the immune system to attack and neutralize/destroy the infection.

Source: Health Advances analysis, Lab Tests Online.

What Testing are We Doing in the US Today?

The majority of testing today is for diagnosing an infection. Efforts are underway to begin widespread exposure screening to help us return to "normal."

Clinical Reason for Testing	Frequency of Testing*		Reasons
	Today	Future Trend	
Diagnosis		↑	• First priority has been diagnosing the most severe symptomatic patients • Control of the current outbreak, a return to normal, and future "flu" and "covid" seasons will require this testing
Exposure Screening/ Infection History		↑↑	• Needed for a return to "normal" to enable current and future contact tracing as well enhancing our understanding of population exposure levels
Immunity Status		Unknown	• As antibody tests become available use is focused on determining exposure as it is not known if antibodies confirm immunity and or at what level (titer)
Prognosis		Unknown	• We do not yet know the best combination of tests to inform prognostic assessment

↑ Increasing ■ Stable ↓ Declining Low ○ ⟷ ● High

* Based upon current events and indications from government authorities.

Source: Health Advances analysis, press releases.

Research Initiatives for SARS-CoV-2: NIH 'Serosurvey'

The NIH recently initiated a study to quantify undetected cases of SARS-CoV-2 infection. The study is using at-home blood collection to test 10,000 volunteers for their antibody status.

National Institute of Allergy and Infectious Diseases

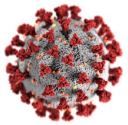
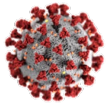
https://www.niaid.nih.gov/news-events/nih-begins-study-quantify-undetected-cases-coronavirus-infection

Study Purpose	• To determine how many adults in the US without a confirmed SARS-CoV-2 infection have antibodies to the virus which indicates a prior infection and support creation of epidemiological models to better understand how the disease spreads
Study Design	• Blood samples collected from 10,000 volunteers • Testing for anti-SARS-CoV-2 IgG and IgM antibodies using a test developed by NIAID & NIBIB
Who is Eligible to Participate?	• Healthy volunteers over the age of 18 from anywhere in the US • Individuals with a confirmed history or current symptoms of COVID-19 are not eligible
How will Samples be Collected?	• Blood samples (80 microliters) will be collected at-home using a new blood collection technology from Neoteryx • Samples are shipped back in a tamper-proof pouch with no risk of transmission to mail carriers
When Will Study Results be Available?	• Results reported to federal public health authorities on rolling basis • Identities of volunteers will remain private
Can I Find Out My Results if I Participate?	• Yes, but results will not be with rapid turnaround as investigators will provide information only after weeks-months of analysis to confirm the tests accuracy

Source: Health Advances analysis, NIAID, NIH.

Types of Tests that Measure SARS-CoV-2 Virus and Immune Response

Multiple measurement types, called molecular tests and immunoassays (IA), can be used to detect virus. Immune system response requires IA to detect anti-virus antibodies.

What the Test is Measuring		Type of Test
Diagnosis	 Virus	 **Molecular Test for Viral RNA[1]**
		 **Immunoassay for Viral Proteins[2]**
Exposure Screening/ Infection History	 Anti-Virus Antibodies	 **Immunoassays for Anti-SARS-CoV-2 Antibody**
Immunity Status		

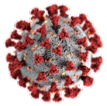
[1] RNA stands for ribonucleic acid. Coronaviruses RNA is the genetic information that enables the virus to replicate.
[2] Viral proteins refers to any protein part of the virus itself that can be detected via an immunoassay.
Source: Health Advances analysis, Lab Tests Online.

Most Commonly Used Tests Today in the US

Today, in the US, molecular tests are the most widely used due to higher accuracy for diagnosis. Other types of testing are just emerging.

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**	• Emerging use to help assess population based exposure and track infection • Needed to help identify recovered patients that could provide blood with anti-virus antibodies to ICU patients • Can help confirm diagnosis but cannot be (should not be) used for diagnosis alone
 **Immunoassay for Viral Proteins**	• Not as accurate as molecular tests for virus detection • No tests yet available by this method (likely due to focus on other types of tests and harder development processes)

Source: Health Advances analysis.

Why Do Some Patients' Test Results Change Over Time?

Testing is not perfect. Individual results can change over time due to disease progression and/or be impacted by less optimal tests and testing practices.

Why do some patients test negative, but eventually become positive, and
Why are some "recovered" patients testing positive again?
When are tests most accurate?

Test Timing

- A first test may happen when a patients is not yet shedding virus or enough virus to be detected
- Virus is present in many patients for several days to a week after symptoms resolve

Test Quality

- Testing is not 100% accurate, every test (for SARS-CoV-2 or other) has an error rate
- Even for the same method (e.g., molecular) performance can vary between test manufacturers and labs

Clinical Skill

- For example, sample collection is challenging; skills can vary between clinical staff

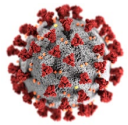
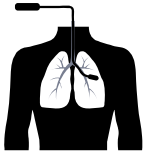
The Unknown

- Details of the full disease course are not well understood yet
- In particular, we don't know
  - The timing and amount of virus shed overtime or by severity
  - How antibody-mediated immunity develops over time

Source: Health Advances analysis.

Sample Types for SARS-CoV-2 Testing

Diagnostic testing to detect the actual virus requires samples from the respiratory tract. Anti-virus antibodies require a blood sample from your finger or vein.

Clinical Reason	What Needs to be Detected by the Test	Relevant Sample Types				
Diagnosis	 **Virus** (either RNA or viral particle protein)	 Saliva or Sputum	 Throat Swab	 Nasal Swab	 Nasopharyngeal (NP) Swab	 Bronchial Lavage
		• Easier to collect • Higher chance of missing virus due to less virus content in sample			• Intrusive • Takes training to collect well • High virus amount; best sample type	• Complex • Can only be performed in hospital
Exposure Screening/ Infection History	 **Anti-Virus Antibodies**	 Finger Stick			 Whole Blood, Serum or Plasma	
		• Simpler to collect, but more difficult to quantify antibody amounts			• Potentially more painful for some, but provides enough sample to quantify antibody amounts	

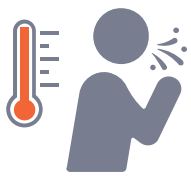
Source: Health Advances analysis, CDC.

Summary of SARS-CoV-2/COVID-19 Testing

SARS-CoV-2 testing is performed for a variety of clinical purposes. Today testing is focused on diagnosis via the most widely available method, which is molecular viral RNA.

Clinical Purposes of SARS-CoV-2 Testing

Relevant Test Type



Patients with Suspected Active Infection

Diagnosis

- Confirm the presence of SARS-CoV-2 in a symptomatic patients

Molecular Test for Viral RNA | **Immunoassay for Viral Proteins**

Prognosis

- Assessment of potential COVID-19 disease severity/disease progression

Combination of Virus, Immunity and Health Tests

Exposed Individuals and/or Those With Known Previous Infection

Exposure Screening/ Infection History

- Determine if a patient was previously infected with SARS-CoV-2 (whether or not they had symptoms)

Immunoassay for Anti-SARS-CoV-2 Antibody

Immunity Status

- Predict the ability of a previously infected patient to resist future infection based on presence of anti-SARS-CoV-2 antibodies

Immunoassay for Anti-SARS-CoV-2 Antibody

Widespread Use Today | Limited Use Today

Source: Health Advances analysis.

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Testing Approaches

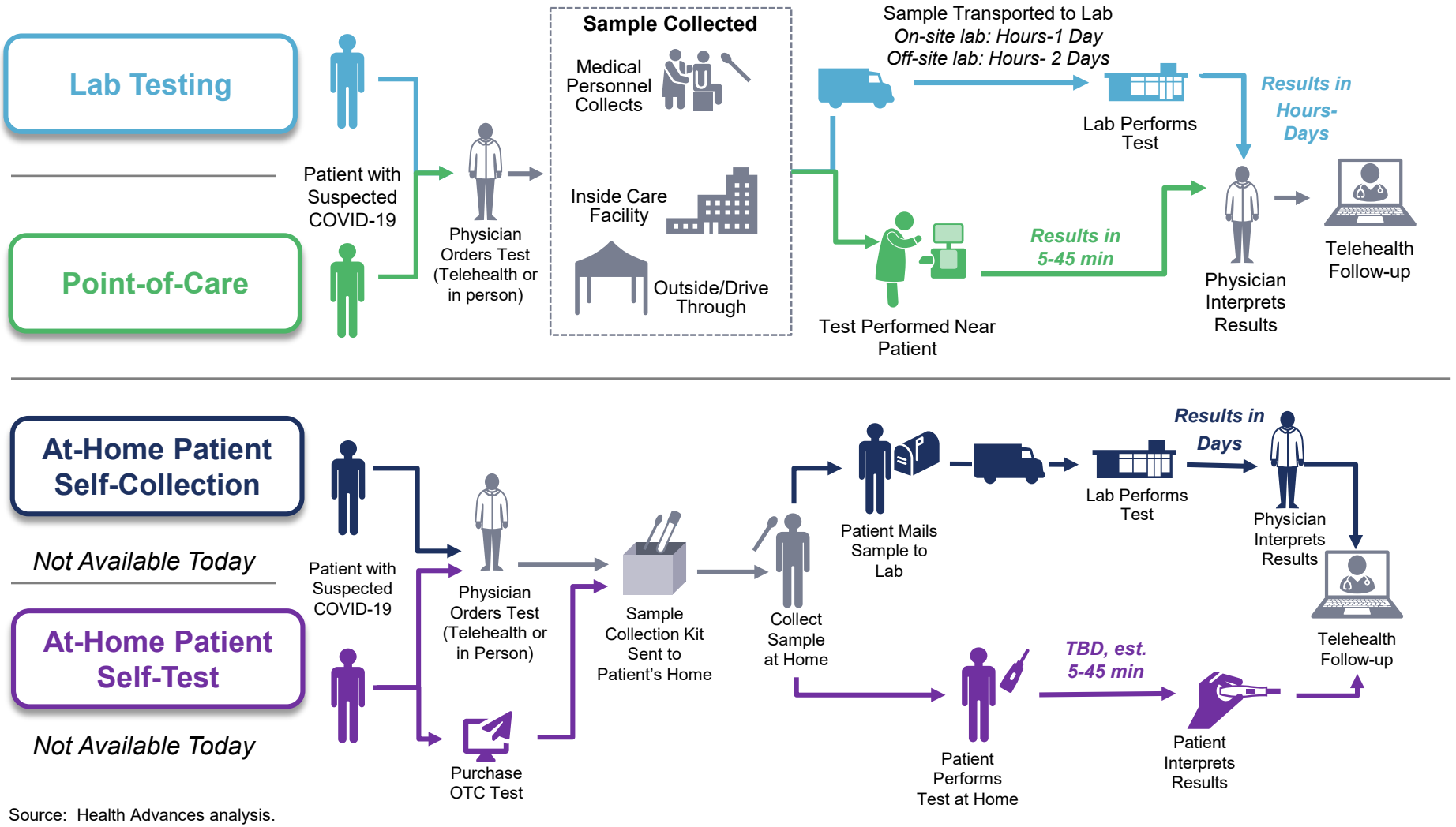
Testing can be supported by various formats, which differ primarily by 1) Where and by whom the sample to be tested is collected, and 2) Where the testing is conducted.

Testing Approach	Where the Sample is Collected	Who Collects the Sample	Where the Testing is Done	Examples You Might Recognize:
Lab Testing	 Doctors office or hospital	 Medical staff	 At a laboratory, by certified lab personnel	• Testing performed when you get your blood drawn from your arm (e.g. cholesterol, etc.)
Point-of-Care	 At (or near) a doctors office or hospital	 Medical staff	 Location of sample collection, by medical staff	• Getting tested for flu or strep at a CVS MinuteClinic
At-Home Patient Self-Collection	 Patient's home	 Patient	 At a laboratory, by certified lab personnel	• 23andme or AncestryDNA kits • Cologuard for colorectal cancer screening
At-Home Patient Self-Test	 Patient's home	 Patient	 By patient at-home	• Pregnancy tests • Glucose tests for diabetics

Source: Health Advances analysis.

SARS-CoV-2 Testing Journey by Test Approach

A patient's experience with SARS-CoV-2 testing varies depending on the testing approach used.



Source: Health Advances analysis.

Where Can POC Testing Be Performed?

POC tests for SARS-CoV-2 can be performed at physician offices and hospitals with CLIA waived certificates. In the future, it may be performed at your home or even your workplace.

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	• Potential new sites; no testing yet	• Influenza • Blood gases • Electrolytes • Hematocrit
SARS-CoV-2 Testing Today	X	✓	X	X	✓
Future SARS-CoV-2 Testing	✓	✓	✓	✓	✓
Examples Used Today	 Pregnancy Test  Glucose Meters	 Alere Influenza Rapid Test  BD Veritor (Rapid Test Reader)			 Abbott i-Stat  Alere epoc

Source: Health Advances analysis.

Current US Testing Approaches for SARS-CoV-2

Currently, only lab and POC tests are available for SARS-CoV-2 in the US, though some companies are developing at home self-collection or self-testing options.

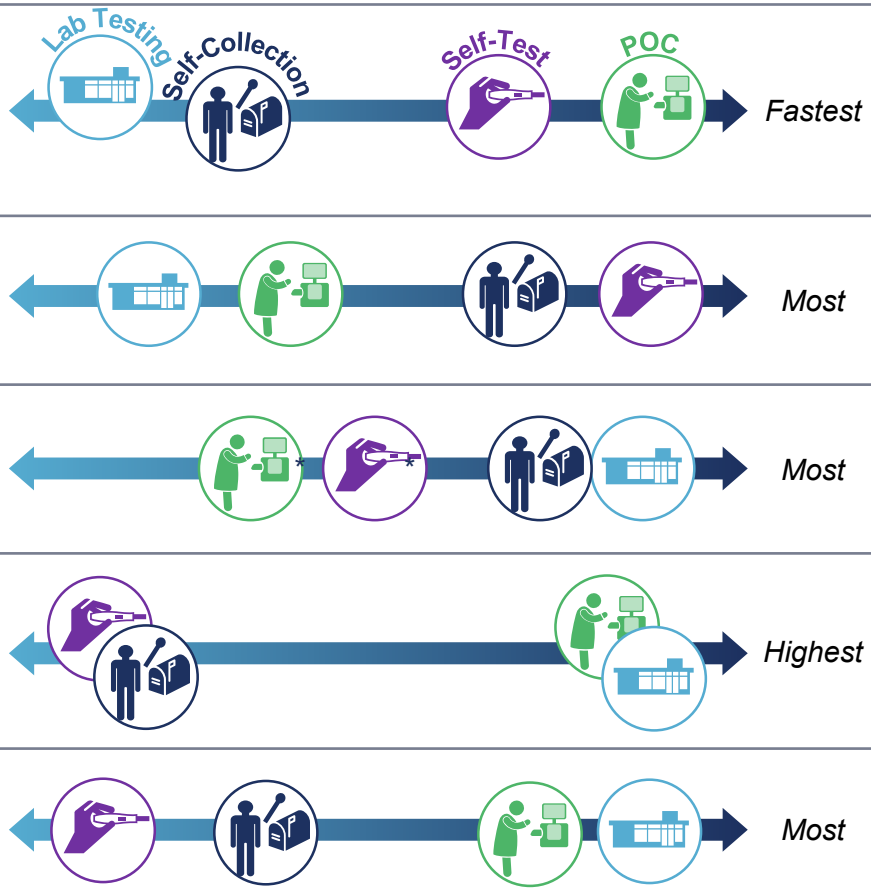
Test Approach	Current Use for SARS-CoV-2	
	Diagnosis	Exposure Screening/ Infection History
Lab Testing	 Vast majority of testing (molecular testing)	 Still early days of use (serology testing)
Point-of-Care (POC)	 Beginning to be used early-April	 No tests yet authorized by FDA
At-Home Patient Self-Collection	*"At this time, the FDA has not authorized any test that is available to purchase for testing yourself at home for COVID-19…We are actively working with test developers in this space." – FDA, March 20, 2020*	
At-Home Patient Self-Test		

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

SARS-CoV-2 Test Formats: Advantages and Disadvantages

No single test format offers the perfect approach for SARS-CoV-2 testing.

Test Feature/Impact	Degree to Which Each Test Format Meets Test Feature				Rationale
	Worst			Best	
Fast Time to Test Results (From Patient Presentation)	*Slower*	Lab Testing, Self-Collection, Self-Test, POC		*Fastest*	• At-home methods provide immediate results, but require time to ship the collection kit or test to the patients' home
Help with Social Distancing	*Least*			*Most*	• Unknown if there is potential for an at-home collection kit sent to a lab to increase spread through couriers/mail
Tests per Hour	*Least*			*Most*	• Laboratory platforms support automated high-throughput, upwards of 30-50x the tests/hour of point-of-care
Sample Quality	*Lowest*			*Highest*	• Some sample types currently being used are difficult for patients to reliably collect at home (e.g., nasopharyngeal swab)
Accurate Interpretation of Results	*Least*			*Most*	• Concern over ensuring patients accurately interpret at home test results and follow-up with doctors



* If the POC or over the counter test requires an instrument to read the results, tests per hour are limited by the TAT of the test as only one test can be run per instrument at a time. If there is no instrument reader, tests per hour are essentially unlimited though could only scale based on the number of tests available and timing of sample collection.

Source: Health Advances analysis.

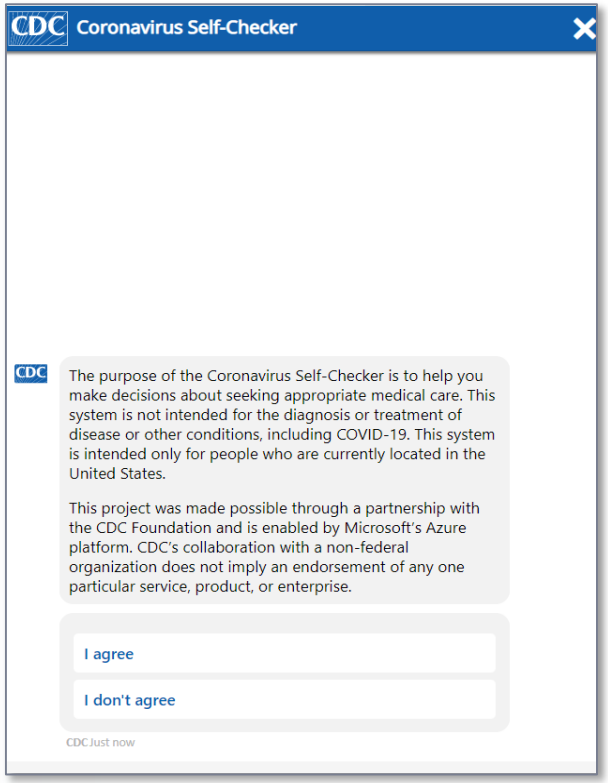
What Should I Do If I'm Having COVID-19 Symptoms?

Consult the CDC and your local doctor for medical advice if you, or anyone in your care, is experiencing symptoms.

https://www.cdc.gov/coronavirus/2019-ncov/

CENTERS FOR DISEASE CONTROL AND PREVENTION

The CDC's online Self-Checker can help you make decisions to seek appropriate medical care for you and anyone in your care



Call your doctor: If you think you have been exposed to COVID-19 and develop a fever and symptoms, such as cough or difficulty breathing, call your healthcare provider for medical advice.

Source: Health Advances analysis, CDC.

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

Because testing for SARS-CoV-2 is not broadly available today, to determine where you can personally go to get tested, if needed, start by calling your personal doctor.

	Relative Access to SARS-CoV-2 Testing	Where You Can Go *(After Talking To Your Doctor)*
Lab Testing	Per CDC guidelines, testing is only recommended for priority cases and not yet broadly available due to limited testing capacity (though expansion is happening quickly)	1. Local Hospitals/ERs 2. Your Doctor's Office 3. Retail Clinics 4. And Soon Pharmacies
Point-of-Care	Call your Doctor if you believe you are experiencing symptoms of COVID-19	
At-Home Patient Self-Collection	The FDA has not yet authorized use of at-home sample collection or testing methods for SARS-CoV-2 diagnosis	
At-Home Patient Self-Test	! Be wary of online vendors offering test kits, as these are likely fraudulent Their use could pose public health risks !	

Source: Health Advances analysis, CDC, FDA.

How Sars-CoV-2 Testing is Paid For

The CARES Act, signed March 27, provides funding for uninsured patients to receive testing and requires private insurers to cover the test at negotiated prices.

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	• CDC test = $36 • Non-CDC Test = $100*	$20-$40	$0	• CMS announced they will cover SARS-CoV-2 testing for all Medicare and Medicaid patients
Private Insurance	• Negotiated Price or Cash Price on Website	$20-$40	$0	• The CARES Act forces private insurance companies to cover all eligible SARS-CoV-2 tests at the negotiated or listed price • This requirement is in effect until the end of the public health emergency
Uninsured	• CDC test = $36 • Non-CDC Test = $51	$20-$40	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

Future Steady-State of Reimbursement

- Reimbursement for future SARS-CoV-2 molecular assays will likely be similar to molecular flu test reimbursement today with a price between $90-$100 and wide coverage from both CMS and private insurers

* On April 14th, CMS announced that Medicare will pay a higher amount of $100 for COVID-19 Dx tests using high-throughput technologies (>200 samples/day), lower-throughput testing will remain at the $51 per test rate.

Note: CMS = Centers for Medicare and Medicaid.

Source: Health Advances analysis, news reports, CARES Act, CMS.

Second Edition Agenda

Our next edition will address the following questions:

- **What does it take to operationalize testing?**
- **What tests are available for SARS-CoV-2 testing in the US today? In other geographies?**
- **What went well and what didn't in establishing US testing?**
- **What is the future testing outlook?**

First Edition Agenda

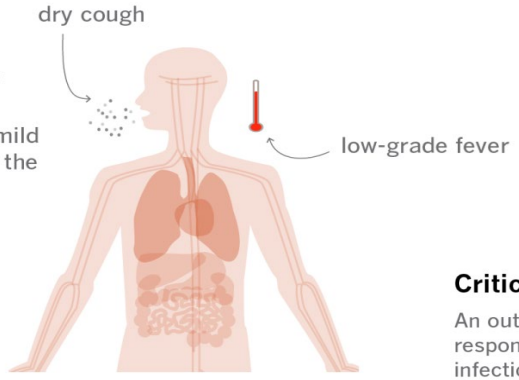
- What are SARS-CoV-2 and COVID-19?
- What types of tests are used for SARS-CoV-2/COVID-19 management?
- How is testing performed and where can I access testing?
- ***Appendix and Glossary***

Symptoms of SARS-CoV-2/COVID-19

Mild forms of COVID-19 have symptoms similar to the seasonal flu while severe forms have more intense respiratory symptoms or even septic shock.

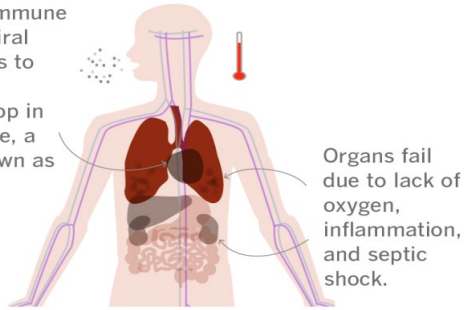
Mild

Most cases of coronavirus infection are mild and resemble the flu.



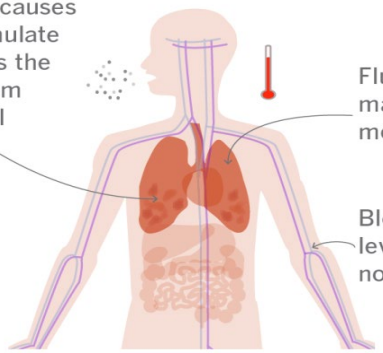
Critical

An outsized immune response to viral infection leads to sepsis and a dangerous drop in blood pressure, a condition known as septic shock.



Severe

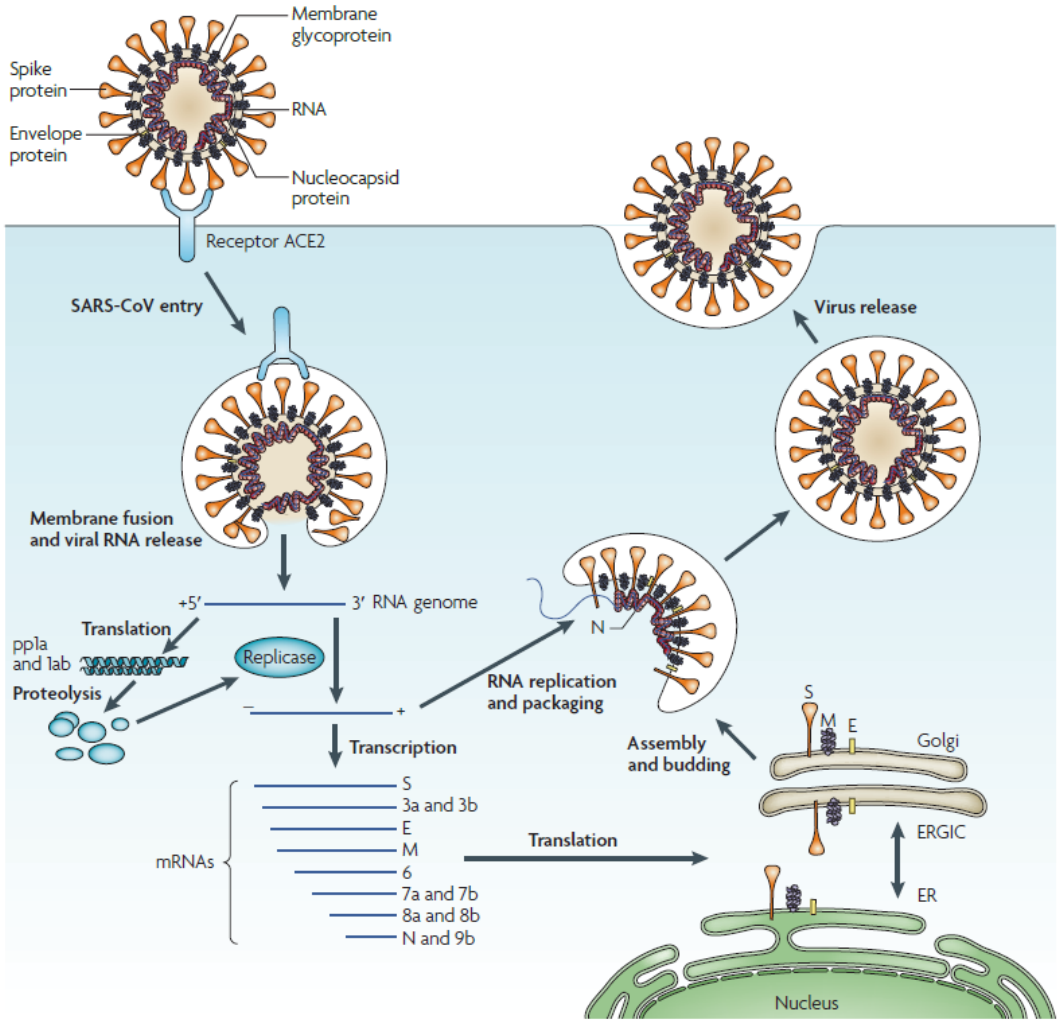
Inflammation causes fluid to accumulate in the lungs as the immune system fights the viral infection.



Source: Health Advances analysis, LA Times.

SARS-CoV-2 Life Cycle

Similar to SARS-CoV (the virus that causes the disease SARS), SARS-CoV-2 enters human respiratory cells to produce new viral particles that are then released to infect other cells.



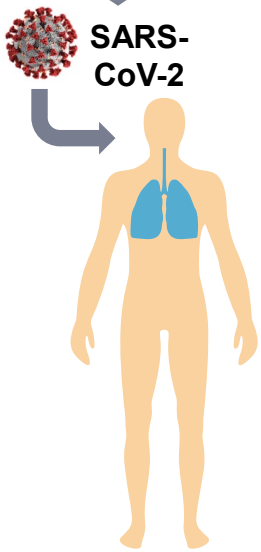
Source: Health Advances analysis, Du Nat Rev Micro 2009.

Understanding the Immune Response and Response (Antibody) Testing

Immunity to viruses develops through a complex chain of events that leads to antibodies. Whether or not SARS-CoV-2 antibody provides immunity at all or that will last is not known.

Overly Simplified Representation of the Antibody Immune Response

Initial Infection



SARS-CoV-2

Days to Week+

IgM Antibodies

- Body forms initial antibodies that circulate in the body and help fight the virus
- Presence of IgM antibodies in a test indicate a recent or active infection

Week+

IgG Antibodies

- Over time the body develops memory cells that produce antibodies faster in case of future infection
- IgG antibodies in a test indicate a previous infection and possible immunity

Months to Years

Possible Immunity

- Ability to form immunity varies by pathogen
- In some cases viruses quickly mutate making existing immunity irrelevant
- In other cases antibody levels naturally decline or viruses have mechanisms to evade antibody based immunity
- We do not know how SARS-CoV-2 immunity will progress

Source: Health Advances analysis, Johns Hopkins Health Medicine.

NIH SARS-CoV-2 Epidemiology Research Study

The NIH recently initiated a study to quantify undetected cases of SARS-CoV-2 infection. The study is using at-home blood collection to test 10,000 volunteers for their antibody status.

> NIH Begins Study to Quantify Undetected Cases of Coronavirus Infection
>
> Blood Samples from Healthy Volunteers Needed to Inform Public Health Decision Making
>
> April 10, 2020

Study Design

10,000 healthy volunteers from throughout the US. To be eligible, you cannot have a confirmed history of COVID-19 nor currently have symptoms consistent with COVID-19

Enrolled participants will have a **virtual clinic visit** with the NIH, complete a health assessment questionnaire and provide basic demographic information

Participants will self-collect their blood-sample using Neoteryx's home blood collection kit and ship back to the NIH for testing

NIH will analyze the blood samples for anti-SARS-CoV-2 **antibodies IgG and IgM** using an ELISA assay developed by researchers at the NIAID and NIBIB

Study results will be reported to federal public health authorities on a rolling basis to support **epidemiological modeling efforts** to inform public decision making

Results upon request will be provided back to participants. Participants should not expect rapid turnaround, as it will only be provided after **weeks or months of analysis to confirm the test's accuracy**

Note: NIAID= National Institute of Allergy and Infectious Diseases. NIBIB= National Institute of Biomedical Imaging and Bioengineering (NIBIB).
Source: Health Advances analysis, NIAID, NIH.

Glossary

Term	Definition
Academic	A noncommercial research environment, focused on the goal of advancing our collective scientific knowledge base.
Assay	The procedure used for conducting a diagnostic test.
Analyte	Entity or target that is being analyzed. Can be an ion, a protein, a cell, a molecule, etc.
Automation Line	A track system moving samples between instruments as opposed to a “sneaker network” which is technicians moving samples through the lab.
Biomarker	A biological marker of disease. Technically all diagnostics are measuring biomarkers but in market terminology this refers to novel markers linked to personalized medicine.
CLIA Waiver	Tests receiving a CLIA waiver are low complexity and can be performed by a healthcare worker with no diagnostic training or experience or by the patient themselves. CLIA waivers are a requirement for POC or NPT and apply to the US only.
Clinical Laboratory Improvement Amendments (CLIA)	CLIA of 1988 created quality standards for all US laboratory testing to ensure accuracy, reliability and timeliness regardless of where the test was performed. Each specific laboratory test system, assay, and examination is graded for level of complexity by assigning scores of 1, 2, or 3 (1 indicates the lowest level of complexity, and 3 indicates the highest level) for each of the following seven criteria: Knowledge; Training and experience; Reagents and materials preparation; Characteristics of operational steps; Calibration, quality control, and proficiency testing materials; Test system troubleshooting and equipment maintenance; Interpretation and judgment. High complexity tests are performed in specialty laboratories. Moderate complexity tests are performed in hospital, reference or physician office laboratories by trained laboratory technicians. Low or CLIA waived tests are typically performed at the point of patient care and can be performed by untrained personnel or even by the patient.

Source: Health Advances analysis.

Glossary

Term	Definition
Companion Diagnostics (CDx)	(HA definition) Diagnostic tests which are used in combination with a specific therapy in order to guide treatment decisions. (FDA definition) *In vitro* diagnostic device or imaging tool that provides information that is essential for the safe and effective use of a corresponding therapeutic product. The joint application of the diagnostic test and therapeutic are explicitly described in the product labels.
Core Lab	Hospital laboratory staffed by minimally trained lab technicians performing high volume, moderately complex tests on highly automated instruments.
Cost per Reportable	A method of financing the cost of an instrument and reagents. Total laboratory costs for running an assay divided by the number of results obtained. This spreads out the cost of "non-reportable" results (caused by either sample or analysis error) over all of the useful results.
Emergency Room (ER)	Emergency room (ER) is the area in a hospital where patients present, are evaluated, and are often treated in an emergency situation.
(FDA) IVD	• The mark given to *in vitro* diagnostic (IVD) products indicating that the product has been cleared (510k) or approved (PMA) for use as a diagnostic product in the US • Manufacturers can market these products to labs for the specific claims included in the product label
Grant/Research Grant	Non-repayable funding provided by an agency, foundation, trust, or other entity. Typically provided to fund a specific project or objective as outlined in a grant proposal. See R01.
Hospital Near Patient Testing (NPT)	Testing performed outside of the laboratory, near to the patient in a hospital. These tests are rapid and include both handheld readers and benchtop analyzers.
Immunoassay (IA)	A discipline of clinical laboratory medicine in which antibodies are used to detect target analytes from body fluids primarily blood. A number of different IA methods are available. IA is typically performed on highly automated instrumentation.
Industry	A commercial research environment, focused on the goal of developing new products or services which enhance health but also generate financial returns.
Information Technology (IT)	Technology that encompasses the computer systems and software that control instrumentation as well as results reporting and connections of the lab instruments to the laboratory information system (LIS) and hospital information system (HIS).
Installed Base	Total number of actively used instruments of a particular type among a group or multiple groups of customers.

Source: Health Advances analysis.

Glossary

Term	Definition
Integrated Hospital Network (IHN; IDN)	A group or system of hospitals and clinics operating jointly to serve their patients. Buying decisions are often made for the entire system at once to provide power in price negotiations with vendors and standardize equipment and products used across the system. These relatively small groups typically drive compliance more effectively than GPOs. Alternatively called an Integrated Delivery Network (IDN).
Intended Use/Indications for Use	Device classification depends on the intended use of the device and also upon indications for use. For example, a scalpel's intended use is to cut tissue. A subset of intended use arises when a more specialized indication is added in the device's labeling such as, "for making incisions in the cornea". Indications for use can be found in the device's labeling, but may also be conveyed orally during sale of the product. the term intended use means the general purpose of the device or its function, and encompasses the indications for use. The term indications for use, as defined in 21 CFR 814.20(b)(3)(i), describes the disease or condition the device will diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended.22
Integrated Platform	An automated analyzer that has the capability to run both clinical chemistry and immunoassay tests.
Intensive Care Unit (ICU)	Intensive care unit (ICU) is the area in a hospital where patients in critical conditions are treated and monitored.
In-Vitro Diagnostics (IVD) or Clinical Diagnostics Market	*In Vitro* Diagnostics Services or products including instruments and reagents that utilize a variety of methods and formats to perform tests on human samples outside the body in order to assess disease risk, diagnose a condition, or monitor a patient's health
IVDMIA	In Vitro Diagnostics Multivariate Index Assays: Use multiple molecular and non-molecular markers to produce a diagnostic, prognostic and/or predictive index (value) for a patient. *Example IVDMIA: Agendia's Mammaprint, a 70-gene, tissue-based assay to determine the risk of breast cancer recurrence post surgery*
IVD Supplies Market	Revenues derived by vendors from sale of instruments, reagents, and service provided to clinical laboratories for IVD purposes.

Source: Health Advances analysis.

Glossary

Term	Definition
(FDA) IVD	The mark given to *in vitro* diagnostic (IVD) products indicating that the product has been cleared (510k) or approved (PMA) for use as a diagnostic product in the US. Manufacturers can market these products to labs for the specific claims included in the product label
Kit	A set of reagents manufactured and packaged together for a specific purpose or to detect a specific analyte. Kits can come in RUO or IVD form. These are sold to labs that perform the testing.
Laboratory Developed Test (LDT)	A test that is developed and validated within a single laboratory and is not sold as a diagnostic kit for other labs to perform. These tests are not approved by the FDA, but rather, are regulated by CLIA (for accuracy, precision, test sensitivity and specificity). These tests may utilize CE and FDA IVD marked products or RUO products to perform the test. In the US, labs must be CLIA certified to perform such testing.
Laboratory Testing Market	Revenues derived from laboratories performing tests (includes hospital and reference laboratories as well as certified physician office laboratories; does not include near-patient or patient self-testing). By definition, these tests are performed by trained lab personnel and are not CLIA waived. The costs (IVD Supplies Market Revenue) are inherently captured in this revenue.
Microbiology	A discipline of clinical laboratory medicine used to detect the presence of pathogens in bodily tissues. Performed in a specialty laboratory with a low level of automation. Testing involves slow culture-based (measurement of pathogen growth over time) testing methods.
Molecular Diagnostics (MDx)	A discipline of laboratory medicine involving the use of testing procedures to measure **DNA and/or RNA** Despite being measures of molecules, other testing disciplines that assess proteins etc. are NOT considered to be MDx by standard industry terminology. For example, if you ask a lab director if they perform molecular testing, if they are not doing DNA or RNA analysis they will say no. In addition, molecular labs perform only or mostly DNA/RNA analysis methods
Multi-analyte Test	Type of multiplexing in which multiple analytes are measured and each analyte measured corresponds to one distinct diagnostic answer.

Source: Health Advances analysis.

Glossary

Term	Definition
Multi-analyte Technology	A single platform, instrument, box, or technology that can measure more than one type of analyte at a time with analytes defined as nucleic acids, proteins, lipids, ions, cells, etc.
Multiplexed Test/Technology	Technical definition: Simultaneous measurement of multiple target analytes in a single reaction vessel. Broader market definition: In the marketplace, some technologies that take a single sample input and split that sample (via automation or microfluidics) into individual reaction vessels to perform multiple tests are also considered to be “multiplex” technologies.
Near-Patient Testing (NPT) Market	Revenues derived by vendors from sale of IVD supplies outside the laboratory within the hospital setting. This does not include point-of-care (POC) testing in the physician office. Tests performed in this setting are rapid and must be CLIA waived. They are performed by nurses and physician rather than by trained laboratory professionals.
National Institute of Health (NIH)	A US government agency dedicated to medical innovation. The largest public funder of biomedical research in the world.
Novel Content	Newly discovered analytes or biomarkers.
Patient Self Testing (PST)	Test performed by the patient. Most PST is performed for glucose monitoring at home. All are CLIA waived.
Physician Office Laboratory (POL)	Laboratory associated with large physician practices performing non-CLIA waived tests. POC testing can also be performed in a physician office but this is not considered laboratory testing.
Point-of-Care (POC) Market	Revenues derived by vendors from sale of IVD supplies to be used outside of the laboratory. The POC market includes professional POC and patient self testing revenues. Tests are performed either by a healthcare worker or patient. All are CLIA waived.

Source: Health Advances analysis.

Glossary

Term	Definition
Pre- and Post- Analytic Automation	Pre-analytic automation is instrumentation which automates single or multiple steps in the preparation of a sample for testing, including sample sorting, centrifugation, de-capping, and aliquotting. Post-analytic automation is instrumentation which automates single or multiple steps in the processing of a sample after testing, including re-sorting, storage, and retrieval.
Professional POC	Testing performed at the point of patient care by trained healthcare worker. This includes hospital near patient testing and physician office POC testing. (POL testing is included in the Laboratory Testing Market)
R01	The most common type of grant awarded by the NIH. Used to support a specific investigator and research program for 3-5 years. Awarded for research which represents the investigators' specific interests and competencies and that falls within the mission of the participating NIH Institutes and Centers.
Random Access Instrumentation	Ability to add samples to an instrument at any time without disrupting on-going testing. Each sample can be tested in its own way: Number of tests, type of test (single analyte or multiplex), and specific test(s) performed. Instrument software prioritizes which samples get what test in what order to maximize instrument throughput and minimize TAT.
Random Manual Assays	Tests which due to low volume and esoteric nature will never be automated and will always be performed manually.
Reference Lab	Commercial service organizations offering routine and esoteric laboratory services to physician offices, clinics, and hospitals.

Source: Health Advances analysis.

Glossary

Term	Definition
Research Group	Two or more investigators of any tenure or level of experience using shared resources and funding in support of a common mission and goal. Colloquially referred to as a “lab”.
Research Use Only (RUO)	A mark given to products indicating that product has NOT been given clearance or approval to be used for clinical purposes. In the US, manufacturers cannot market these products to clinical labs or help them develop tests in their labs that use these products.
Sample to Result Automation/Processing	A fully automated instrument which allows the operator to input a sample and walk away. The instrument returns a result with no further intervention.
Specialty CLIA Lab	A term used for two purposes: (More common) to describe a service organization performing proprietary tests (e.g. OncotypeDx) but not performing routine testing. (Less common) to describe divisions of the hospital laboratory performing complicated testing requiring highly trained laboratory technicians. Specialty labs within the hospital include: anatomical pathology labs, microbiology, molecular and blood banks.
Turnaround Time (TAT)	The time it takes to return a result, either within the context of an instrument or of the whole laboratory procedure, beginning with the sample being loaded onto the instrument and ending with the result being recorded on the instrument. This can also be called the time to result. An alternative definition, not used in this presentation, is the total time it takes from sample acquisition to the time the result reaches the ordering physician.

Source: Health Advances analysis.

Health Advances Diagnostics Leadership Team

Donna Hochberg, PhD

Partner

- Donna Hochberg joined Health Advances in 2005 and leads the firm's Diagnostics and Life Science Tools Practice.
- Her work includes application prioritization, launch strategy, corporate strategy, deal diligence, and international and domestic market analysis using both qualitative and quantitative approaches. Her clients offer products and services in personalized medicine, point-of-care, mainstream clinical diagnostic, and life science tools and range from small diagnostics and tools start-ups to the largest public companies and non-profit institutions in the industry.
- Prior to joining Health Advances, Donna worked as a scientist at One Cell Systems and Iquum developing diagnostics for oncology and infectious diseases. She received her Bachelors degree in Biology from the University of Illinois at Urbana-Champaign and her Ph.D. in Immunology from the Sackler School of Biomedical Sciences at Tufts University

Gary Gustavsen

Partner and Managing Director

- Gary Gustavsen came to Health Advances in 2005 and leads the Personalized Medicine Practice at Health Advances. His work focuses on commercialization strategy, indication prioritization, pricing and reimbursement strategy, system economics, and business development opportunities for both diagnostic and therapeutic clients.
- Prior to joining Health Advances, Gary was a researcher at Brookhaven National Lab evaluating a proprietary line of synthetic growth factors. Gary also worked in the Cell & Tissue Technologies group at Becton Dickinson, the Exploratory Cancer Research group at OSI Pharmaceuticals, and most recently the Corporate Strategy group at Millennium Pharmaceuticals. Gary received his Bachelors degree in Biomedical Engineering from Duke University and his Masters degree in Biomedical Engineering from Stony Brook University.

Health Advances Diagnostics Leadership Team

Kristen Amanti, PhD

Vice President

- Kristen Amanti joined the Health Advances team in 2010 and is a leader in the Reproductive and Genomic Health practice and Personalized Medicine practice. She has deep experience in commercialization strategy, business development opportunity assessment, deal diligence, international and domestic market assessment, corporate strategy, and is a seasoned workshop facilitator. She has content expertise in companion diagnostics, reproductive and prenatal health, genomic health, cancer screening, tumor genetics and oncology.
- Prior to joining Health Advances, Kristen received her PhD in Cancer Pharmacology from Dartmouth College where her research focused on the development of novel targeted cancer therapeutics. She received her Masters degree in Cell and Molecular Biology and Bachelors degree in Biology from the University of Vermont.

Peter Origenes

Vice President

- Peter Origenes brings over 30 years of healthcare experience to Health Advances, including as a corporate executive, principal investor, and strategy consultant across diagnostics, life science research products, medical devices, and biopharmaceuticals.
- Prior to joining Health Advances, Peter held executive positions at Becton Dickinson, GE Healthcare, and Ortho Clinical Diagnostics. Prior to that, he was a partner at Radius Ventures, and a consultant with The Wilkerson Group and Bain.
- Peter holds a Master of Science in Industrial Administration from the Tepper School at Carnegie Mellon University, and Bachelor's degrees in Genetics and History from the University of California, Berkeley.

Kristine C. Mechem PhD

Vice President

- Kristine Mechem has over 15 years of life science experience across diagnostics, medical devices and therapeutics. Her experience spans the full continuum of commercial activities from market planning to sales force effectiveness. She has expertise in portfolio prioritization, product requirements, asset opportunity assessments and launch planning.
- Most recently she was the commercial head of a micro-cap molecular diagnostic company. At OncoCyte, she helped to take the company public, served as a corporate officer and led the development of the commercial plan. She has also held positions at Abbott, Genentech and The Zitter Group
- Kristine received her PhD in Sociology from the University of Chicago. She is an active member of Women In Bio.

Health Advances Diagnostics Leadership Team

Arushi Agarwal
Vice President

- Arushi Agarwal joined the Health Advances team in 2011 and spends the majority of her time working in the Diagnostics and Life Sciences Practice. She has expertise in M&A due diligence and global commercialization strategies for diagnostics. Arushi's specific areas of focus include companion diagnostics, point-of-care diagnostics and liquid biopsy testing.
- Prior to joining Health Advances, Arushi received her Masters in Biomedical Engineering from Columbia University and Bachelors in Biology from the Massachusetts Institute of Technology.

Daniela Hristova-Neeley, PhD
Director

- Daniela is an experienced team leader with expertise in opportunity assessment, global commercialization strategy, market access, and business model evaluation across diagnostics and life sciences products. Daniela's diverse experience in the diagnostics and life sciences tools space provides a strong base to help generate actionable growth strategies for clients.
- Prior to joining Health Advances, Daniela helped clients in the healthcare industry optimize their value proposition and global market access strategies to enable product adoption.
- Daniela earned her PhD in Chemistry, summa cum laude, from the University of Basel, Switzerland and her MBA from Johnson Graduate School of Management at Cornell University.

Health Advances Diagnostics Team

Ravi Amin
Engagement Manager

- Ravi Amin joined Health Advances in 2014 and is an experienced team leader in the firm's Diagnostics and Life Science Tools Practice.
- His experience includes opportunity assessment, commercialization strategy, and market analysis using both qualitative and quantitative approaches. He also has experience developing strategies for companies ranging in size from start-ups to large public companies.
- Prior to joining Health Advances, Ravi worked at Beckman Coulter in a variety of roles across corporate strategy and strategic marketing. He received his Bachelors in Genetics from the University of Georgia and his Master of Business and Science at the Keck Graduate Institute of Applied Life Sciences

Kelsey Taylor, PhD
Engagement Manager

- Kelsey Taylor joined the Health Advances team in 2016 and is an experienced team leader across Health Advance' Diagnostics, Biopharma, and Precision Medicine Practices.
- Kelsey's experience includes opportunity assessment, business model evaluation, and commercialization strategy development for novel diagnostics.
- Prior to Health Advances, Kelsey received her PhD in Biological and Biomedical Sciences at Harvard University and Bachelors in Biochemistry, Cellular and Molecular Biology from Connecticut College.

Emily Kong
Consultant

- Emily Kong joined Health Advances in 2016 and is a team leader across firm's Diagnostics, Digital Health, and Precision Medicine Practices
- Her experience includes development and commercialization strategy, competitive assessment, market sizing, and revenue forecasting with a content focus in several areas including oncology, precision medicine, traditional laboratory diagnostics, and rare diseases
- Prior to joining Health Advances, Emily received her Bachelors in Biology and Economics from Dartmouth College

Health Advances Diagnostics Team

John Latimer
Senior Analyst

- John Latimer joined Health Advances in 2018 and works primarily in the firm's Diagnostics and Life Sciences practice.
- He has experience in strategy development, international and domestic market analysis, M&A diligence, and opportunity assessment of emerging technologies.
- Prior to joining Health Advances, John graduated from Stanford University with a B.S. in Biology. He held several research positions during his time at Stanford including as a clinical researcher in the Department of Cardiovascular Medicine.

Aaron Dy, PhD
Senior Analyst

- Aaron Dy joined Health Advances in 2019 and works across healthcare practices, with a particular focus in the Diagnostics and Life Sciences Tools practice.
- His experience includes competitive assessment, commercial strategy, product positioning strategy, survey design, and revenue forecasting.
- Prior to Health Advances, Aaron received his Bachelors degree in Applied Physics from Indiana University and his PhD in Biological Engineering from the Massachusetts Institute of Technology.

Emily Berghoff, PhD
Senior Analyst

- Emily Berghoff joined Health Advances in 2020 and works across the firm's Diagnostic, MedTech, and BioPharma practices.
- Her experience includes opportunity assessment, commercialization strategy, market analysis, and revenue forecasting.
- Prior to Health Advances, Emily worked at Exosome Diagnostics developing assays for oncology. She received her PhD in Biological Sciences from Columbia University and her Bachelors degree in Chemistry from Colby College.

Alexis Froistad
Analyst

- Alexis Froistad joined Health Advances in 2019 and works across healthcare practices, with a focus in the Diagnostics and Life Sciences Tools practice.
- Her experience includes product positioning strategy, franchise development strategy, market analysis, and survey design.
- Prior to Health Advances, Alexis graduated from Stanford University with a B.S. in Human Biology. She held a long-term research position in the Stanford Parker Center for Allergy and Asthma Research studying pulmonary arterial hypertension.

Contact Information

HEALTH ADVANCES

Donna Hochberg, PhD
Partner
dhochberg@healthadvances.com

Gary Gustavsen
Partner
ggustavsen@healthadvances.com

Kristen Amanti, PhD
Vice President
kgamanti@healthadvances.com

Arushi Agarwal
Vice President
aagarwal@healthadvances.com

Kristine Mechem, PhD
Vice President
kmechem@healthadvances.com

Peter Origenes
Vice President
porigenes@healthadvances.com

Health Advances LLC
275 Grove Street
Suite 1-300
Newton, MA 02466

781-647-3435
www.healthadvances.com