BCG

COVID-19

COVID-19 Diagnostics

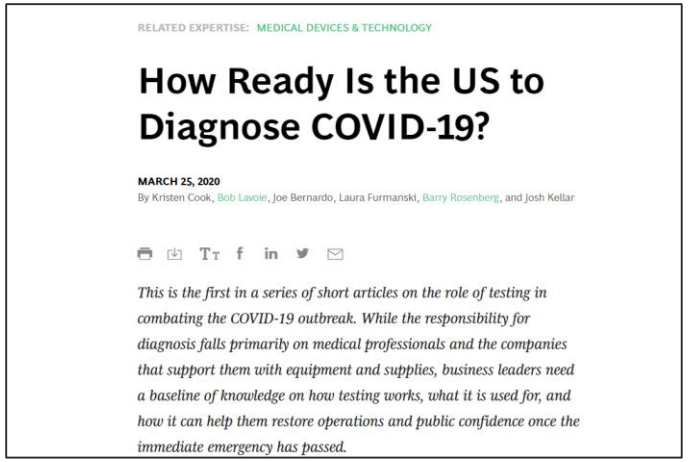
Evolving past Flatten into Fight

Updated as of May 18, 2020;
Please refer to BCG COVID-19 Microsite for updated materials

This is the third in a series of materials focused on COVID-19 diagnostic testing

These materials

How Ready is the US to Diagnose COVID-19?



RELATED EXPERTISE: MEDICAL DEVICES & TECHNOLOGY

How Ready Is the US to Diagnose COVID-19?

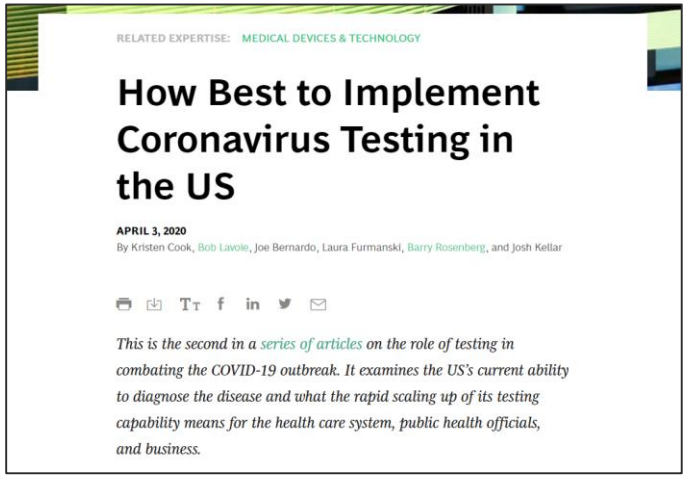
MARCH 25, 2020

By Kristen Cook, Bob Lavoie, Joe Bernardo, Laura Furmanski, Barry Rosenberg, and Josh Kellar

This is the first in a series of short articles on the role of testing in combating the COVID-19 outbreak. While the responsibility for diagnosis falls primarily on medical professionals and the companies that support them with equipment and supplies, business leaders need a baseline of knowledge on how testing works, what it is used for, and how it can help them restore operations and public confidence once the immediate emergency has passed.

Link to article here

How Best to Implement Coronavirus Testing in US



RELATED EXPERTISE: MEDICAL DEVICES & TECHNOLOGY

How Best to Implement Coronavirus Testing in the US

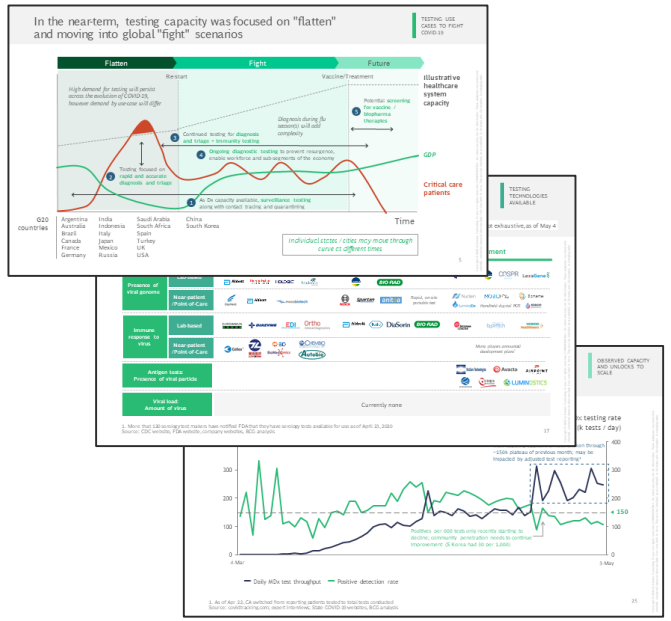
APRIL 3, 2020

By Kristen Cook, Bob Lavoie, Joe Bernardo, Laura Furmanski, Barry Rosenberg, and Josh Kellar

This is the second in a series of articles on the role of testing in combating the COVID-19 outbreak. It examines the US's current ability to diagnose the disease and what the rapid scaling up of its testing capability means for the health care system, public health officials, and business.

Link to article here

Evolving Past Flatten into Fight



COVID-19

This edition of Dx testing is intended to provide clarity on 4 topics

Testing use cases to fight COVID-19

What are the testing use cases as we fight COVID-19?

How do these change over time?

Testing technologies available/coming soon

What are the testing technologies (molecular, serological, etc.) available in the market?

What other new technologies are expected or possible?

What use cases are they most relevant for?

What tradeoffs for each technology need to be considered?

Testing capacity and considerations to scale

What is the estimated current capacity?

- US analysis example can serve as global blueprint

How much can we realistically scale?

What unlocks are needed to scale testing?

Global learnings from scaling testing

How have responses varied globally?

What are policy implications from the global experiences?

What are the US implications on entering the fight phase?

Important caveat and context for COVID-19 diagnostics current-state

Scientific understanding of the Covid-19 virus is dynamic and evolving rapidly

COVID-19 tests launched around the world have done so generally under emergency response oversight

- Given these conditions, test selection for use requires careful scrutiny and assessment

As tests are being deployed and scaled, real world clinical prospective trials are happening "real time"

- Independent clinical validation and QA recommended to ensure testing protocols/solutions implemented are robust

No ASSUMPTIONS on population modeling are made in these materials

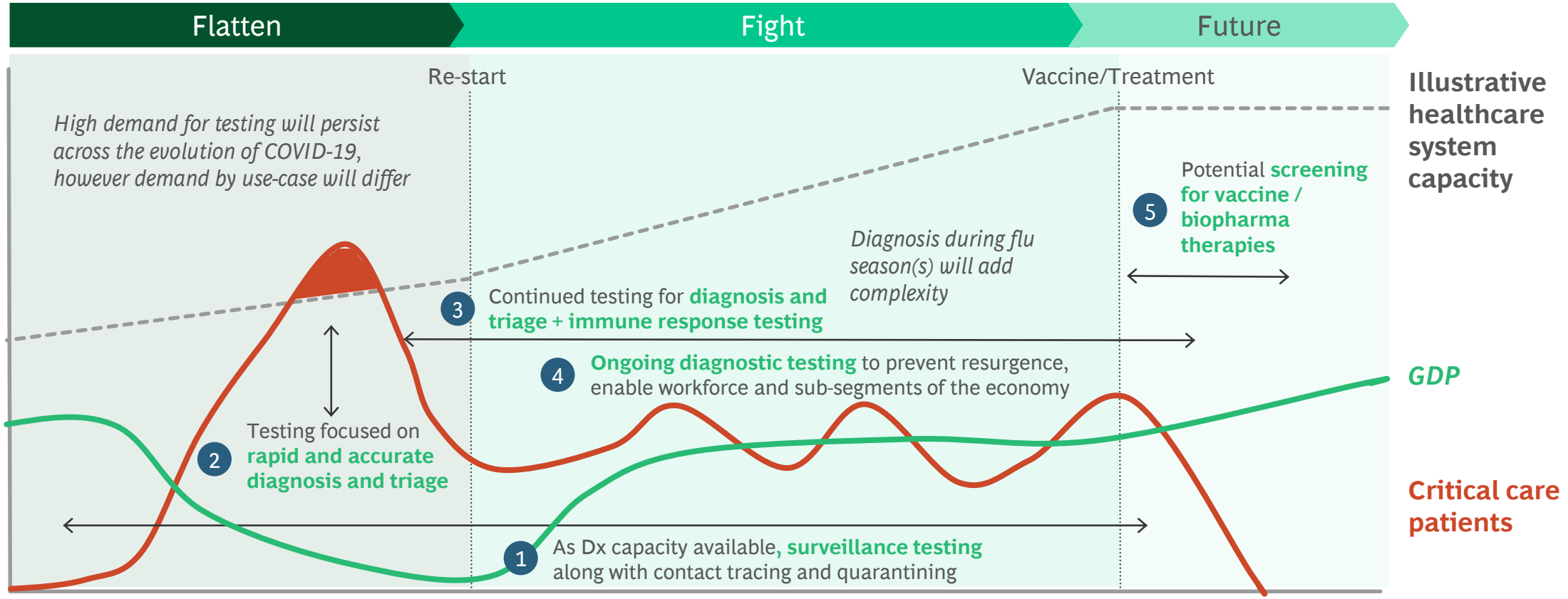
1 COVID-19 diagnostic testing use cases

2 Testing technologies available

3 Observed capacity and unlocks to scale

4 Global learnings from scaling COVID-19 testing

In the near-term, testing capacity was focused on "flatten" and moving into global "fight" scenarios



G20 countries

Argentina	India	Saudi Arabia	China
Australia	Indonesia	South Africa	South Korea
Brazil	Italy	Spain	
Canada	Japan	Turkey	
France	Mexico	UK	
Germany	Russia	USA	

Individual states / cities may move through curve at different times

Near-term, testing to focus on diagnosis and triage, immune response testing and workforce monitoring

Focus for the flatten and fight

1

Population health surveillance

Leverage testing as part of larger toolkit / strategy to continuously track and monitor spread and prevalence of disease in broad population

Target population: General population, suspected contacts of COVID-19 patients

2

Diagnose and triage symptomatic patients

Leverage installed base of diagnostic testing to quickly diagnose and triage symptomatic patients and inform clinical care

Target population: Symptomatic patients presenting at sites of care

3

Employer-contracted workforce testing and monitoring

Build testing programs with large employers to screen employees as they return to work

Target population: Employees upon return to work (identify potential immunity), ongoing monitoring of susceptible employees

4

Immune response testing in affected individuals

Identify if patients have antibodies that indicate prior viral exposure and potential immunity

Target population: Recovered patients to confirm potential immunity

General population to uncover asymptomatic patients

5

Screening for therapy and vaccine development

Screen potential patients for clinical testing of vaccines and drug therapies in development

Target population: Unexposed individuals (vaccine) and infected patients (therapy)

Summary | Different testing technologies/locations best-suited for use cases

1 Population health surveillance

Molecular diagnostic tests provide highly accurate results critical to avoiding false positives/negatives and detect disease earliest in progression

Potential considerations

- Needs to be combined with other measure (e.g., contact tracing)
- Testing capacity dependent on disease prevalence (testing early in curve = fewer tests)
- May be possible to supplement MDx with high-quality antigen testing

2 Diagnose and triage symptomatic patients

Molecular diagnostic (MDx) platforms as close to clinical care as possible (HT instruments in hospital labs, near-patient/ POC instruments) to provide highly accurate results

Potential considerations

- Ability to scale MDx limited by supply inputs (e.g., swabs) and installed base
- Sample-to-answer time is critical to inform care, so reference labs not ideal

3 Immune response testing in affected individuals

Serological tests (either high-quality lateral flow or high-throughput immunoassay instruments)

Potential considerations

- Can by deployed at variety of locations (timing less critical)
- Many lateral flow tests coming to market likely with mixed quality
- HT capacity likely ~1-6+ months away from deployment

4 Employer-cont. workforce testing and monitoring

Combination of immunoassay (serological antibody as well as antigen) tests and molecular diagnostics needed to find immune patients (serological antibody tests) and monitor un-infected population (MDx or antigen testing)

Potential considerations

- Can be deployed across variety of locations (timing less critical)
- Will need combined capabilities across testing types for complete offering
- Specific tests deployed (e.g., antigen vs. MDx) will depend on risk profile and availability of testing resources
- Quality issues for lateral flow (rapid) tests

5 Screening for therapy and vaccine development

High-quality MDx/serological (antibody and/or antigen) tests needed to determine whether someone has already been exposed to disease (and therefore not a candidate for trials / vaccines)

Potential considerations

- May eventually be deployed to many sites
- Quality issues for lateral flow tests; don't want to include patient who may taint results
- Potential good candidate for HT instruments since vaccine will come after HT capacity becomes available

Note: Antigen tests currently not available in the US; performance characteristics unknown for tests in development

US perspective: currently a wide range of estimates for COVID-19 testing demand (~2M-160M tests / week)

	American Enterprise Institute	Center for American Progress	Harvard Safra Center for Ethics	Paul Romer estimate
MDx demand estimate (per week)	2-3M (revised from initial 750K)	8.75M	35-140M	161M
Tracing approach & containment policies	Manual contact tracing Testing used primarily to diagnose and triage individuals Role of electronic tools to enforce quarantines Measures lifted on regional basis based on gating requirements	Use of wireless technologies to perform automatic contact tracing Goal to reach Korea-level testing coverage per case Isolation of infected and exposed individuals in designated facilities	Manual contact tracing Electronic tools for warning system and testing certificate Test all symptomatic patients and high risk groups and all contacts Only contacts that test positive req. to quarantine, those testing negative subject to regular testing throughout incubation period	No contact tracing nor surveillance Goal to keep quarantined population below 10% and infection rate below 20% Quarantines based solely on repeated testing 7% of population at random (entire population every 2 weeks)
Perspective on serological testing	Used to measure pop. level exposure, but utility limited by likely low level of exposure (<10%)	Used to inform who can safely return to work	Used to understand community-level prevalence and to determine who are safe to return to work (only in comb. with neg. PCR result)	Assumed all tests are MDx (but consistent with using IA for some patients if late enough in infection course)
	Manual contact tracing	*Automated digital contact tracing*	*Manual contact tracing*	*Testing only*

Automation and extent of contact tracing

Amount of testing required

Source: "National Coronavirus Response: A Road Map to Reopening", AEI; Dr. Scott Gottlieb interviews with Ezra Klein, CNBC; "A National and State Plan to End the Coronavirus Crisis", CAP; "Roadmap to pandemic resilience" white paper; Harvard Edmond J Safra Center for Ethics; Paul Romer Covid Simulations; BCG analysis

1 COVID-19 diagnostic testing use cases

2 Testing technologies available

3 Observed capacity and unlocks to scale

4 Global learnings from scaling COVID-19 testing

Several underlying technologies that detect different aspects of the COVID-19 pathogen/human immune response

Immunoassays

Available and scaling across multiple platforms, others anticipated

Molecular diagnostics:
Detection of presence of viral genetic material

- Direct detection of viral nucleic acids (RNA or DNA)
- Requires molecular testing

Technologies
- PCR (various platforms on market)
- LAMP[1] (methods published)
- NGS-based[2] (being pursued)
- CRISPR-based[3] (EUA approved)

Several rapid and lab-based options available

Serological (antibody) tests:
Development of immune response to virus in patients

- Indirect detection of virus by measuring immune response (may be prior exposure or current infection)
- Requires validated antibody

Platforms
- Lab-based (high throughput)
- Rapid (lateral flow)

First rapid test available, additional tests expected in 1-5 months

Antigen tests:
Presence of viral particle

- Direct detection of proteins making up the viral “head”
- Requires validated antibody against virus

Platforms
- Lab-based (high throughput)
- Rapid (lateral flow)

Not currently available

Viral load:
Quantitative amount of virus

- Quantitation of amount of viral genome in patient samples
- Requires large amount of data to link test result and patient outcomes

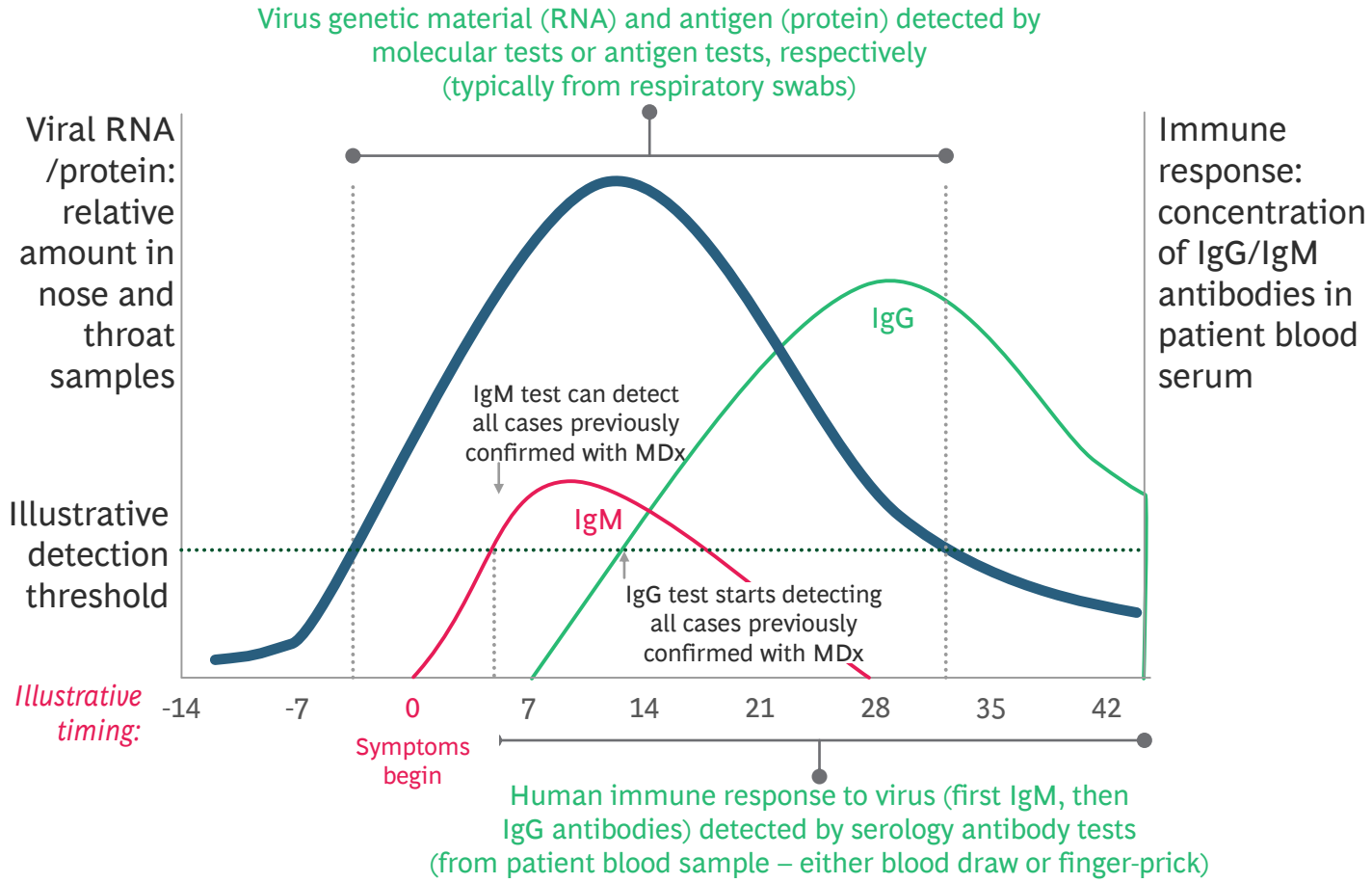
Diagnostic imaging and other clinical tests (heart, liver, kidney enzyme assays etc.) are an important factor in both managing individual patients and allocating resources, but not discussed in this document; timelines approximate and directional

1. Loop-mediated isothermal amplification; 2. Next-generation sequencing; 3. Clustered Regularly Interspaced Short Palindromic Repeats (DNA sequence that is the basis of a genetic sequence targeting system)

Global

Molecular and antigen tests may detect virus genetic material prior to symptoms and Serology IgG/IgM antibody tests detect immune response after a week

TESTING TECHNOLOGIES AVAILABLE



1. Current tests detecting presence of viral genome are qualitative and are not meant to measure absolute amount or viral genome present (i.e., viral load)

Note: Curves of viral RNA and protein condensed for simplification, likely not identical values in practice

Source: Wang et al., JAMA (2020); IgG/IgM product insert materials; Expert interviews; BCG analysis

Observations and indications

Molecular and antigen tests detect the virus itself and provide the earliest detection window (may detect slightly before symptoms begin)

Immune response tests (serology antibody tests) are useful to understand past exposure and population-level disease prevalence, but do not detect disease early enough for diagnosis/tracing

A summary of available and emerging testing technologies

TESTING TECHNOLOGIES AVAILABLE

Tools to detect active, acute infection

Tools to detect immune response

	MDx (PCR)	LAMP[1]	CRISPR[2]-based	NGS[3]-based	Antigen	Serological (IgG/IGM)
What is detected	Viral genetic material (RNA)	Viral genetic material (RNA)	Viral genetic material (RNA)	Viral genetic material (RNA)	Viral protein	Patient immune response to virus
Sample type(s)	Respiratory swabs, saliva (LDT only)	Respiratory swabs, saliva	Respiratory swabs, saliva	Respiratory swabs, saliva	Respiratory swabs, saliva	Finger prick or venipuncture
Platform format(s)	HT and semi-automated lab-based, near-patient, POC (equipment)	HT lab-based, portable/ POC (equipment)	Near-patient lab-based, POC (lateral flow)	HT lab-based	HT and semi-automated lab-based, POC (lateral flow)	HT and semi-automated lab-based, POC (lateral flow)
Throughput	HT platforms 500-1k+/ day, near-patient and POC platforms 20-90/day, semi-automated variable	HT platforms 300-1k/day, POC platforms variable (dependent on production vol and distr)	Near-patient platforms 15-20/day, POC platforms variable (dependent on production vol and distr)	Up to 750k/day per machine	HT platforms 500-4k+/day, POC platforms variable (dependent on production vol and distr)	HT platforms 500-4k+/day, POC platforms variable (dependent on production vol and distr)
Turnaround time	1-2 days for ref lab, same-day for in-house, <45 min for near-patient, <15 min for POC	1-2 days for ref lab, same-day for in-house, <30 min for POC	1-2 days for ref lab, same-day for in-house, <30 min for POC	1-3 days	1-2 days for ref lab, same-day for in-house, <15 min for POC	1-2 days for ref lab, same-day for in-house, <15 min for POC
Sensitivity	Lab tests >98%, lower for POC	>95% for both lab and POC tests	>95%	>99%	Lab tests >90%, POC tests variable from 50-80%	Lab tests 80-90+%, POC tests highly variable
Specificity	Lab tests >98%, lower for POC	Lab tests >95%, POC tests >90%	>95%	>99%	>95%	Lab tests >95%, rapid tests highly variable
Major benefits	Gold standard diagnostic tool, large install base	More rapid than PCR, visual readout, isothermal amplification	More rapid than PCR, visual readout, accessible lateral flow format	Massively scalable as instruments configured to run many samples in parallel	Can be run on same platforms as serological tests	Massive capacity, limited sample processing required
Major challenge/ drawback	Currently capacity constrained	New install base required to scale	Technology has not been previously used at-scale	Logistics needed to collect large volume of samples and relay results to patients	Low sensitivity of POC tests	Cannot be used to detect acute infections

Emerging MDx technologies

First tests appearing

1. Loop-mediated isothermal amplification; 2. Clustered Regularly Interspaced Short Palindromic Repeats; 3. Next-generation sequencing

US

How we test | current landscape of molecular diagnostic tests

TESTING TECHNOLOGIES AVAILABLE

	Individual LDTs	High-throughput IVD MDx[1]	Rapid "near-patient" IVD MDx[1]	PoC IVD MDx[1]
Examples (not exhaustive)	LabCorp, Quest Diagnostics, Johns Hopkins Medicine, Stanford Health Care	Roche, Hologic	Cepheid	Abbott
Description	MDx tests developed and used in-house at academic and private labs	Large, high-volume automated MDx platforms	Moderately portable (~30-40 lbs) automated near-patient MDx platforms	Portable (<10 lbs) platforms that can be used at various sites of care
What is detected	Viral genome	Viral genome	Viral genome	Viral genome
What technologies	PCR	PCR Not yet available: LAMP[2], TMA[3]	PCR Not yet available: CRISPR-based	PCR, isothermal amplification Not yet available: LAMP, CRISPR-based
Where deployed	Local academic medical centers and large reference labs	Hospitals and large reference labs	Clinical or field-based settings	Multiple clinical and field-based settings
Turnaround time	Wide variability depending on location (same-day for in-house, 2-3 days for reference lab)	Logistics and batching workflows imply 1-2 days	<45 mins	~5-15 minutes
Throughput and scalability	Throughput variable depending on platform used, but as a whole cannot be scaled effectively	Highly scalable due to high throughput (~500-1000+ samples per day) and pre-existing install base	Low throughput: 15-25 per day; moderate scalability based on current and potentially new install base	Moderate throughput: 60-90 per day; moderate scalability based on current and potentially new install base
Accuracy	MDx testing typically has high accuracy but can vary from lab-to-lab	High (98%+ specificity and sensitivity)	High (98%+ specificity and sensitivity)	Moderate (lower than high-throughput and near-patient MDx platforms)
Sample type	Respiratory swab, saliva	Respiratory swab	Respiratory swab	Respiratory swab

1. MDx = Molecular diagnostic; 2. LAMP = Loop-mediated isothermal amplification; 3. TMA = Transcription-mediated amplification

US

How we test | Current landscape of immunoassay tests

TESTING TECHNOLOGIES AVAILABLE

			Available in US in next 1-2+ months	First tests appearing
	Serological IgG/IgM (in lab)	**Serological IgG/IgM POC**	**Antigen/Immunoassay (in lab)**	**Antigen/Immunoassay POC**
Examples (not exhaustive)	Manual/semi-automated: Icahn School of Medicine at Mount Sinai; EDI Epitope Diagnostics, Inc. Automated/high throughput: Ortho Clinical Diagnostics; Diazyme	BD; BioMedomics; Cellex™	High-throughput lab-based tests not yet available as of 5/12/20	QUIDEL
Description	Various formats of ELISA[1] to qualitatively detect Abs in blood using colorimetric assay	Handheld "lateral flow" devices to qualitatively detect Abs in blood (sign of immune responses)	Various formats of ELISA to qualitatively detect viral protein using colorimetric assay	Portable "lateral flow" devices to qualitatively detect viral proteins using man-made Abs
What is detected	Patient's antibodies	Patient's antibodies	Viral proteins	Viral proteins
What technologies	Lab-based immunoassays	Lateral flow immunoassays	Lab-based immunoassays	Lateral flow immunoassays
Where deployed	Local academic medical centers, large reference labs, most large hospitals	Hospital ERs/ICUs, doctor's offices, community or retail clinics, at-home	Local academic medical centers and large reference labs	Hospitals ERs/ICUs, doctor's offices, community or retail clinics, at-home
Turnaround time	Wide variability depending on location (same-day for in-house, 2-3 days for reference lab)	5-15 minutes	Wide variability depending on location (same-day for in-house, 2-3 days for reference lab)	~5-15 minutes
Throughput and scalability	Depends on workflow, automated high throughput (~500-4000+ tests per day), manual/semi-automated flexible for low sample volumes	Low throughput (60-100 per day) but high scalability as tests can be distributed widely	Depends on workflow, automated high throughput (~500-4000+ tests per day), manual/semi-automated flexible for low sample volumes	Low throughput (60-100 per day) but high scalability as tests can be distributed widely
Accuracy	Moderate to very high (from ~80-90% sensitivity, ~95% specificity[2] to >95% for both)	Highly variable as many tests are sold without usual regulatory review Typically lower accuracy compared to lab-based assays	Varies depending on protein being detected, typically moderate to high	Highly variable, typically lower accuracy compared to lab-based assays (50-80% sensitivity)
Sample type	Venipuncture	Primarily finger prick (some venipuncture)	Patient sample TBD; likely nasal swab, saliva	Patient sample TBD; likely nasal swab, saliva

1. Enzyme-linked immunosorbent assay; 2. Diazyme DZ-Lite self-reported accuracy

Need to evaluate tests along several key dimensions

Speed

Time from "sample to answer", including sample collection, logistics to send out the sample, sample processing, time to run and interpret test

Sensitivity

Ability to detect Covid-19 in all patients who have the disease (avoiding false negative results for ill/infectious patients)

Specificity

Ability to distinguish Covid-19 from other similar viruses, avoiding false positive results for patients who do not have the disease

Together, these metrics provide the accuracy of the test

Cost

Cost per test, driven by the reagents (chemical ingredients) needed, as well as the labor to collect and process samples

Throughput

Rate of tests that can be analyzed (e.g., per day, per week)

Sample type

Type of clinical sample, e.g., oral or nasal swab, blood sample, lower respiratory swab. Implications for access, supplies needed, cost, and accuracy

No diagnostic test is perfect!

Typical tradeoffs that exist in diagnostic testing

- Speed vs. sensitivity/specificity
- Cost vs. sensitivity/specificity
- Cost vs. throughput

Accuracy of testing has critical implications for effective medical response and containment; molecular and serological tests are the current options in US

TESTING TECHNOLOGIES AVAILABLE

	Sensitivity	Specificity	For 100k tests administered[1] and assumed disease prevalence of 5% Sick patients (5K) False Negative Patients (sick patient mis-diagnosed negative)	Healthy patients (95K) False Positive Patients (healthy patients mis-diagnosed positive)	Use cases by disease state Disease-naïve	Symptomatic	Recovered
Molecular "gold standard" May detect ~2-4 days before onset	98%	99%	100	950	1 Pop. health surveillance 4 Workforce testing & monitoring	2 Diagnose and triage symptomatic patients	
Molecular POC May detect ~2-4 days before onset	90%	95%	500	4,750			
Rapid antigen tests[2] May detect virus on similar timing as molecular testing	80%	99%	1000	950			
"Gold standard" serology Detection ~6-10 days after symptom onset	95%	95%	250	4,750			3 Immune response testing for recovered patients
Rapid finger-stick serology "high quality" Detection ~6-10 days after symptom onset	75%	95%	1,250	4,750			
Rapid finger-stick serology "low quality"[3] Detection ~6-10 days after symptom onset	30%	60%	3,500	38,000			

1. Roughly equivalent to US nationwide daily throughput as of March 31, 2020 2. Estimated using Quidel antigen test; while the specificity of that test was reported as 100% from 84 samples, 99% was used here as 100% specificity in unlikely in a large patient sample 3. The Guardian ("Coronavirus test kits withdrawn in Spain over poor accuracy rate", March 27, 2020)

Source: Expert interviews, Popular press articles, Product specifications, BCG analysis

1 COVID-19 diagnostic testing use cases

2 Testing technologies available

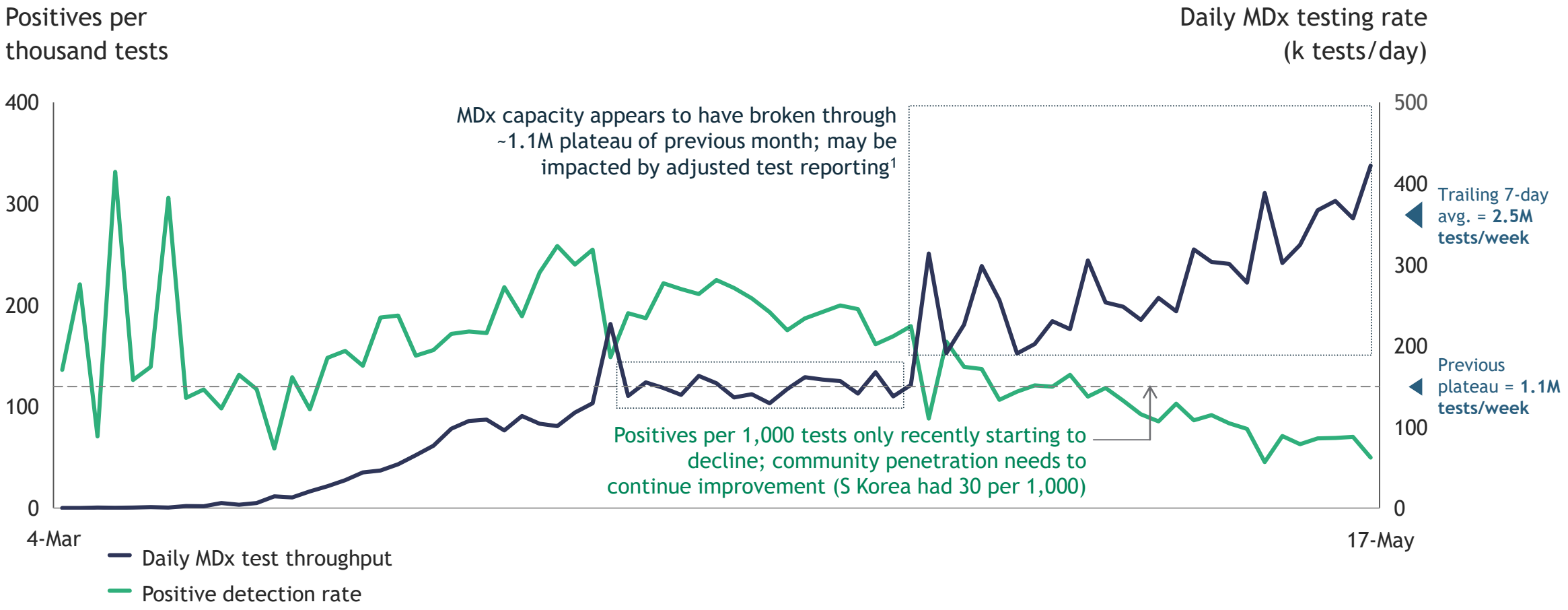
3 Observed capacity and unlocks to scale

4 Global learnings from scaling COVID-19 testing

Observed MDx capacity has broken through previous plateau of ~1.1M tests/week and has now reached >2.5M tests/week

OBSERVED CAPACITY AND UNLOCKS TO SCALE

As of 5/17/20



1. As of Apr 22, CA, OK and FL switched from reporting patients tested to total tests conducted; VA currently combines serological and MDx test results; reported numbers also likely impacted by large reporting backlog being cleared

Source: covidtracking.com; expert interviews; State COVID-19 websites, The Atlantic: "How Virginia Juked Its COVID-19 Data", May 13, 2020; The Richmond Times-Dispatch; BCG analysis

US, MDx (PCR)

Molecular diagnostics: US currently processing ~200-350K tests/day, or ~40-70% of its pragmatic installed base potential

OBSERVED CAPACITY AND UNLOCKS TO SCALE

Theoretical max platform capacity[1]

~2.7M tests/day

×

Set up, maintenance, workflow downtime, regional volume imbalances, running other essential tests

Pragmatic installed base potential[2]

~500K tests/day

×

Sample collection and processing, reagent shortages[4], lag between approval to going live in labs etc.

Currently observed throughput[3]

~200-350K tests/day

Daily MDx volume increased from ~150K plateau observed in April

- Aggregate platform capacity nationwide is not limiting testing in US today
- Regional workload imbalances (i.e., some labs with backlogs while others with unfilled capacity), sample collection and RNA extraction reagent shortages are key limitations
- Addressing reagent shortages and balancing workload among labs are the best ways of boosting capacity in the short term

1. Assuming continuous operation of all instruments compatible with COVID-19 tests approved to date in the US over 16 hrs shift 2. Net set up and maintenance time mandated by instrument safe operation procedures, downtime inherent in workflows 3. Trailing 7 day average as of May 10, 2020, stable since late April 2020 4. Excl. testing kits themselves which are not considered limiting
Note: MDx = Molecular diagnostics. Numbers shown reflect number of people tested (not number of PCR reactions run)
Source: BCG analysis, Company SEC filings, investor communications and public announcements; CDC website

New technologies can unlock additional MDx capacity

Technology	Platforms	Description	Impact on MDx capacity
LAMP[1]	High-throughput, portable/POC	• Method to amplify genetic material at a single temperature (isothermally) more rapidly than PCR • Can be performed in a single tube and result can be visually detected	• Can utilize/repurpose existing capacity of all MDx equipment • Can also utilize other simpler equipment (heat block, water bath) to run tests (in addition to MDx instruments)
NGS-based[2]	High-throughput	• Method to detect specific viral sequences after initial amplification step • Can run many patient samples in parallel	• Can add significant capacity at national scale • Would need to use existing install base of MDx instruments at labs with sequencing equipment
CRISPR-based[3]	Near-patient, POC	• After isothermal amplification, CRISPR-mediated targeting of viral genetic material leads to activation of readout signal that can be detected on a lateral flow device or reader	• New capacity with new equipment • Incremental to current installed base • Additional capacity from lateral flow POC tests

1. Loop-mediated isothermal amplification; 2. Next-generation sequencing; 3. Clustered repeating interspaced short palindromic repeats (DNA sequence that is the basis of a nucleic acid-targeting system)

Like molecular tests, antigen tests can also be used to detect the presence of the virus; tradeoffs between speed/ease and sensitivity

OBSERVED CAPACITY AND UNLOCKS TO SCALE

	Molecular (PCR) tests	Antigen tests[2]
What is being detected	Genetic material (RNA) that is specific to the virus	A specific antigen (often a protein or part of a protein) on the surface of the virus
Sample type	Nasal/nasopharyngeal swabs, saliva	Nasal/nasopharyngeal swabs, saliva
Detection method	Virus-specific RNA fragments are amplified via PCR[1]; instrument detects if/when signal is above threshold	Specific antibodies are used to detect if viral antigen is present in sample; readouts are either visual for rapid tests or fluorescent/chemiluminescent for lab-based tests
Platforms	Lab-based or near-patient/POC platforms (equipment required for all)	Rapid POC lateral-flow assays or lab-based tests (equipment required for lab-based only)
Major benefit(s)	• More accurate (>90% sensitivity, >95% specificity)	• Increased scalability: Higher capacity on high-throughput instruments • POC tests require either no or less complex equipment
Major drawback	• Currently capacity strained	• Less accurate (50-90% sensitivity, higher for POC tests with automated readers or tests on high-throughput instruments)

1. Polymerase chain reaction; 2. Only 1 antigen test with EUA approval for COVID-19 available, based on other antigen tests for other diseases/conditions (e.g. influenza, HIV, hepatitis)
Source: Ghebremedhin B et al, J Med Microbiol, 2009; MIT Technology Review; CDC; BCG analysis

Antigen tests can be a valuable diagnostic tool, but need to understand risks and implications

When MDx testing capacity is unavailable, limited, or needed for higher priority use cases, antigen tests can be used to diagnose acute infections by detecting presence of viral antigen (protein) …

… however, lower sensitivity will lead to >10x more false negative results compared to gold standard MDx tests, which is exacerbated in populations with higher disease prevalence …

… therefore, need to understand underlying disease prevalence and consider risk tolerance of population to use antigen tests in an informed manner

Rapid and automated immunoassays (antibody and antigen tests)

Basic sense-check needed to screen products entering market with limited regulatory oversight

- Has the product received Emergency Use Authorization (EUA) from the US FDA?
  - If not, has the manufacturer at least notified the FDA under the policy outlined in Section IV.D?
    - notifying the FDA does NOT mean that the FDA reviewed the product; check fda.gov for latest info on both
- Does the product come with a product insert?
- Does it have clearly described testing and result read-out directions?

Was test accuracy evaluated on real patient samples?

- Does the insert clearly state what samples were used for the study?
- Is it clear at what stage in the infection those samples were taken? Does this approximate population that you intend to test?

- Was the number of samples used in the study high enough?
  - At least 250 positive and 125 negative or more
- Does the insert include information on test accuracy?
  - Are both sensitivity and specificity clearly stated? If IgM and IgG antibody responses are both tested, are separate accuracy data listed for each?
  - Is the accuracy high enough for intended use (i.e., Is the no. of false positives and false negatives acceptable)? Does the test claim to have 100% accuracy and specificity (not possible for a serological, or any other test)? Clinical Dx tests for a disease like COVID-10 likely need >90% sensitivity/>95%specificity

Independent technical validation, QA/QC is then needed to implement testing

Initial study of rapid serology tests reveals wide variability in test performance

		Sensitivity					
Days since symptom onset:		1-5	6-10	11-15	16-20	>20	Specificity
IgM Indicative of earlier point in infection	BioMedomics	27%	61%	74%	76%	82%	88%
	Bioperfectus	41%	74%	80%	76%	100%	97%
	DecomBio	32%	67%	85%	70%	91%	91%
	DeepBlue	44%	78%	80%	76%	91%	84%
	Innovita	15%	33%	38%	29%	17%	96%
	Premier	37%	71%	80%	76%	91%	98%
	Sure-Bio	11%	43%	63%	67%	73%	100%
	UCP Biosciences	26%	58%	74%	71%	91%	98%
	VivaDiag	29%	63%	84%	71%	90%	95%
	Wondfo	N/A					
IgG Indicative of later point in infection or potential long-term immunity	BioMedomics	23%	53%	68%	67%	82%	96%
	Bioperfectus	26%	66%	77%	67%	90%	98%
	DecomBio	28%	67%	85%	70%	91%	92%
	DeepBlue	22%	50%	60%	71%	82%	99%
	Innovita	26%	47%	76%	64%	67%	100%
	Premier	22%	51%	63%	67%	82%	99%
	Sure-Bio	19%	54%	71%	67%	91%	100%
	UCP Biosciences	26%	50%	71%	67%	82%	98%
	VivaDiag	29%	63%	81%	67%	90%	96%
	Wondfo	N/A					
Overall (IgM and/or IgG)	BioMedomics	31%	64%	77%	81%	82%	87%
	Bioperfectus	41%	77%	86%	81%	100%	95%
	DecomBio	32%	67%	85%	70%	91%	90%
	DeepBlue	44%	78%	80%	81%	91%	84%
	Innovita	26%	56%	76%	64%	83%	96%
	Premier	37%	71%	83%	81%	91%	97%
	Sure-Bio	19%	54%	71%	71%	91%	100%
	UCP Biosciences	26%	58%	77%	71%	91%	98%
	VivaDiag	29%	63%	84%	71%	90%	95%
	Wondfo	40%	67%	82%	81%	82%	99%

Observations and indications

Test performance improves the longer you wait to test after symptom onset; limits utility for timely population monitoring

Generally, IgG detection is more specific than IgM detection

Combining results for IgM and IgG improves detection sensitivity[1]

There is a trade-off between sensitivity and specificity

More studies are needed to evaluate new tests as they enter the market prior to widespread use

Note: High sensitivity implies low false negatives while high specificity implies low false positives

>90% 80-89% <80%

1. Wondfo's test reports single band for both IgM and IgG

Source: COVID Testing Project and pre-print manuscript ("Test performance evaluation of SARS-CoV-2 serological assays") by UCSF, UC Berkeley, Chan Zuckerberg Biohub, Innovative Genomics Institute researchers

US, Immunoassay

High-throughput immunoassay testing: total pragmatic platform capacity in US ~10x higher than that for mdx tests

None of these tests are currently run, expected in weeks to 2 months

OBSERVED CAPACITY AND UNLOCKS TO SCALE

Theoretical platform capacity[1]

~28 M tests/day

- 96% razor-razor blade[5]
- 4% open platform[6]

×

Set up, maintenance, workflow downtime, regional volume imbalances, running other essential tests

Total installed base pragmatic platform capacity[2]

~6.5 M tests/day

- Available for both antibody and antigen testing

Pragmatic capacity for announced antibody tests[3]

~5 M tests/day

*only smaller instruments)

Roche	(46%)	Abbott	(4%)
Beckman Coulter	(30%)	Open platforms /LDTs	(4%)
Ortho Clinical Diagnostics	(15%)	Diazyme	(1%)

Pragmatic capacity for antigen tests[4]

No high-throughput lab-based tests announced yet, expected in 1-2 months

- Aggregate platform capacity nationwide is not limiting testing in US today
- Regional workload imbalances (i.e., some labs with backlogs while others with unfilled capacity), sample collection and RNA extraction reagent shortages are key limitations
- Addressing reagent shortages and balancing workload among labs are the best ways of boosting capacity in the short term

1. Assuming continuous operation of all currently installed immunoassay instruments over 16 hrs shift 2. Net set up and maintenance time mandated by instrument safe operation procedures, downtime inherent in workflows 3. Not accounting for availability of kits themselves which are expected to be limiting 4. Proportion of capacity used for antigen testing will depend on development timeline and relative demand5. Can only run tests for which manufacturer has assays available on their menu 6. Can run "home-brew" assays and compatible assays by other manufacturers

Source: Company SEC filings, investor communications and public announcements; CDC website; BCG analysis

1 COVID-19 diagnostic testing use cases

2 Testing technologies available

3 Observed capacity and unlocks to scale

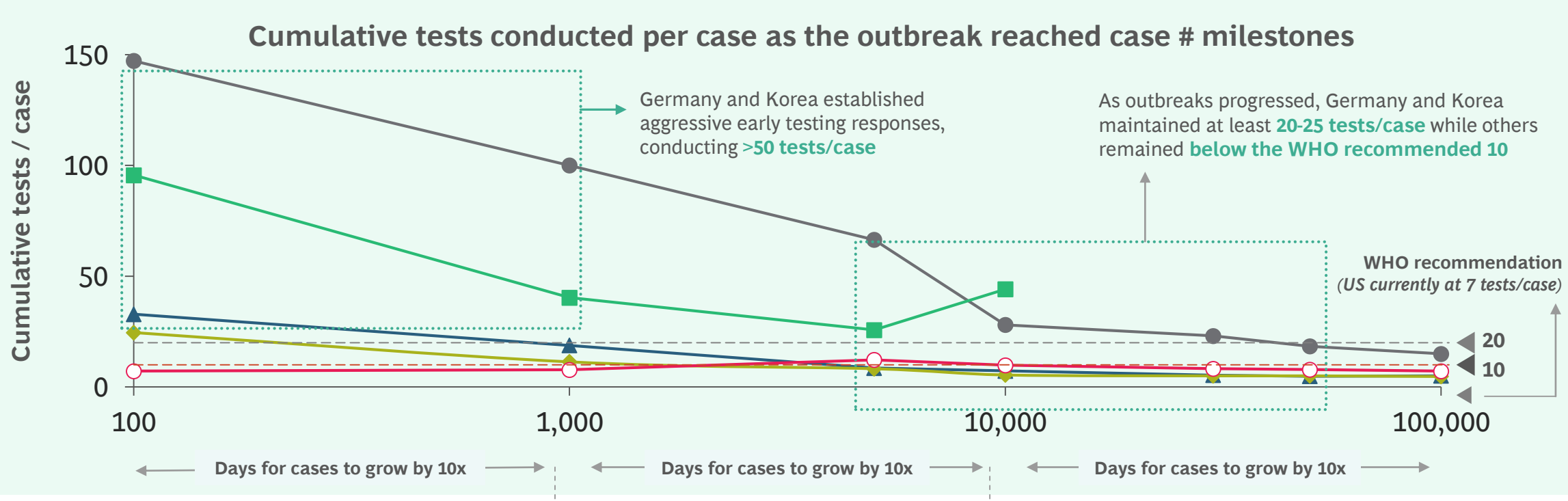
4 Global learnings from scaling COVID-19 testing

Varied testing and containment responses by different countries have corresponded with a range of outcomes

	Aggressive testing + contact tracing	Aggressive testing + delayed lockdown	Limited testing + earlier lockdown	Limited testing + delayed/partial lockdown
Examples (non-exhaustive)	S. Korea	Germany	Italy & France	USA
Description	• Quick test validation and widespread use • Very robust, automated contact tracing system • Targeted isolation and quarantining	• Quick test validation and widespread use • Strict national social distancing guidelines with some states in lockdown when national cases were ~18K	• Slow testing ramp-up • Gradual or non-uniform implementation of national containment measures • Lockdowns implemented when national cases were ~7-8K	• Slow testing ramp-up • Non-uniform implementation of containment measures (some states still not in lockdown) • 30 states in lockdown when national cases were ~150K
Outcomes[1]	• New cases have slowed to ~15/day • Cumulative cases plateaued at ~11K (210/1M people)	• New case rate has slowed from ~6K/day at its peak to ~350/day currently • Cumulative case growth slowing, currently at ~170K (2K/1M people)	• New case rates have slowed from ~6-8K/day at their peaks to <1K/day currently • Cumulative case growth slowing, currently at ~140-220K (2.1-3.6K/1M people)	• New case rates have plateaued at ~25K/day • Cumulative cases continue to grow, currently at 1.5M (4.6K/1M people)

1. As of May 18, 2020
Sources: "Coronavirus Disease (COVID-19) – Statistics and Research". OurWorldInData.org; BCG analysis

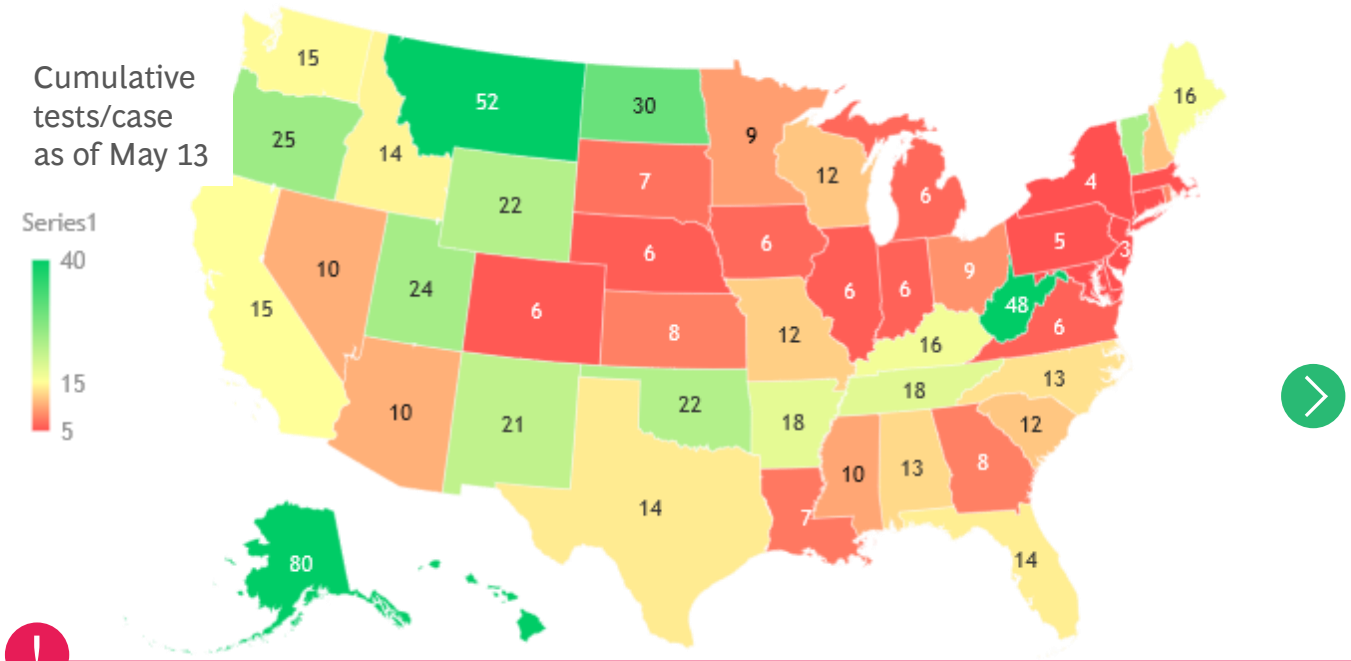
Global testing coverage varies across the globe; countries beginning to re-open economies with testing ratios of ~20+ tests/confirmed case



Germany	9	Implemented aggressive tracing and quarantining	10	20	National lockdown at ~18k cases
Korea	5		37	*N/A*	
Italy	6		10 Nat'l lockdown at ~8k cases	21	
France	8		11 Nat'l lockdown at ~7k cases	27	
US	8		9	9	**30 states were in lockdown at ~150K cases**

Sources: "Coronavirus Disease (COVID-19) – Statistics and Research". OurWorldInData.org; BCG analysis

Variation in testing coverage suggests that re-opening should happen regionally with additional assessment of other containment measures in place



- Each state's tests/case ratio is highly dependent on **where they are along the epidemiological curve**, which varies from state-to-state (a high ratio will drop as cases grow if testing capacity is not expanded)
- State-by-state **test reporting may vary** (e.g. VA counting serological tests along with MDx tests)
- While a ratio of ~20 tests/case may be sufficient for a state under lockdown, **an "open" state will need higher testing coverage** to perform sufficient surveillance testing and contact tracing as disease incidences increase

Key implications

Some states/regions observed to have higher test coverage, a key component to re-open the economy

Beyond testing coverage, other measures and factors are critical for determining when and how to re-open specific regions

- Contact tracing
- Enforced social distancing policies
- Symptom monitoring
- Self-isolation and quarantining
- Capacity to expand testing upon resurgences

With more of the above measures in place, a lower test/case ratio may be sufficient

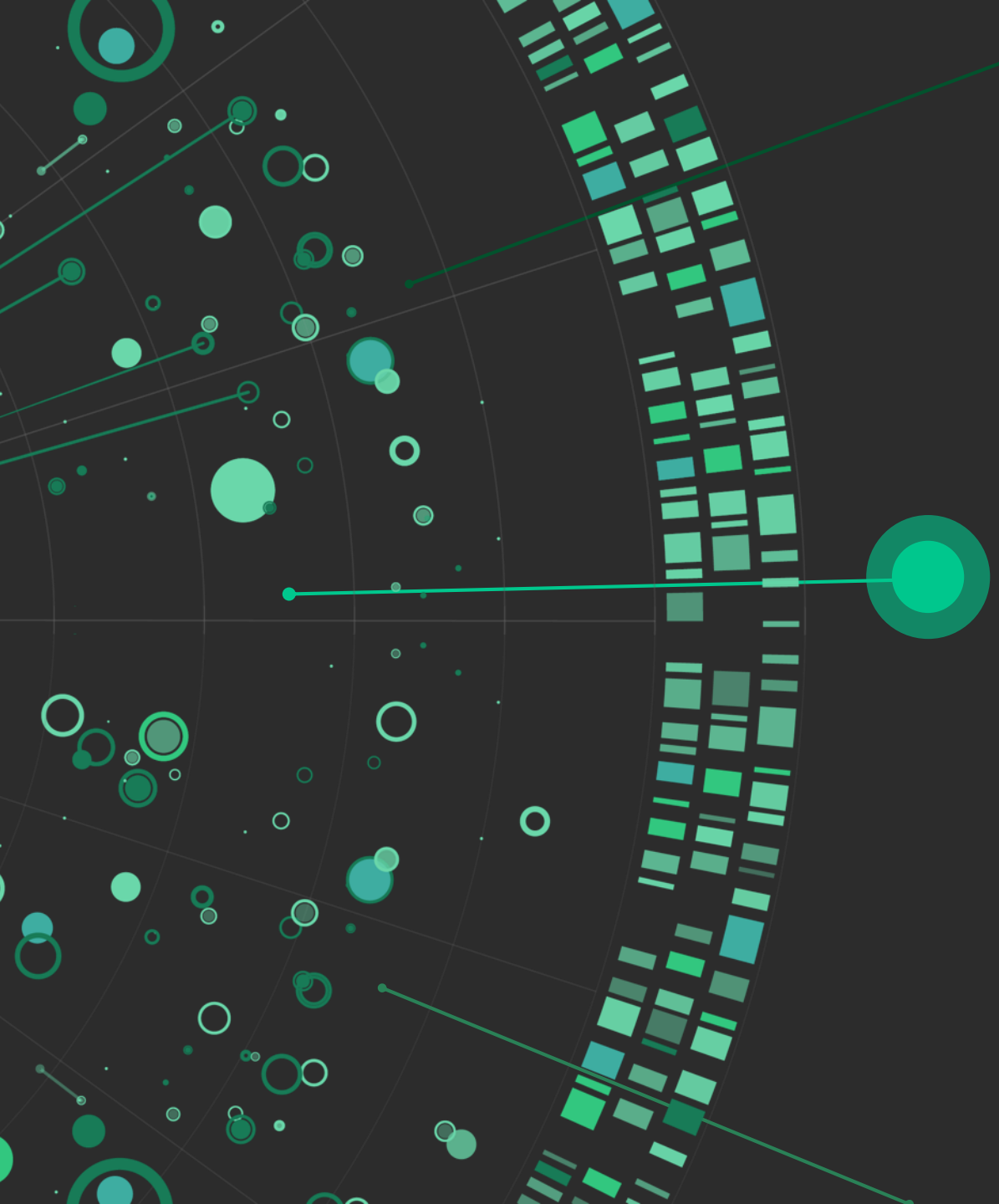
Sources: COVIDtracking.org (data as of May 13); The Atlantic article: "How Virginia Juked Its COVID-19 Data"; BCG analysis

Testing more per case enables informed decision making and implementation of effective outbreak containment measures

	Flatten	Fight
	~5-10 tests per case (US currently at ~7[1])	~20+ tests per case
Who is being tested?	• Only symptomatic patients (including those with similar conditions but not COVID-19)	• Symptomatic patients • Direct contacts of confirmed cases • Some high-risk populations
Implications	• Limited understanding of actual disease prevalence • Asymptomatic cases go undetected and can unknowingly spread disease • Inability to trace second-order contacts of positive case without testing of direct contacts	• Improved tracking of disease prevalence • Some asymptomatic cases caught via contact tracing • Informed isolation and treatment of direct contacts as well as second-order contact tracing from any discovered positive cases

Additional testing required beyond ~20 tests/case for additional monitoring and surveillance (e.g., expanded high-risk populations, workforce testing, broad population sampling)

Sources: 1. "Coronavirus Disease (COVID-19) – Statistics and Research". OurWorldInData.org (data as of May 13); BCG analysis



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