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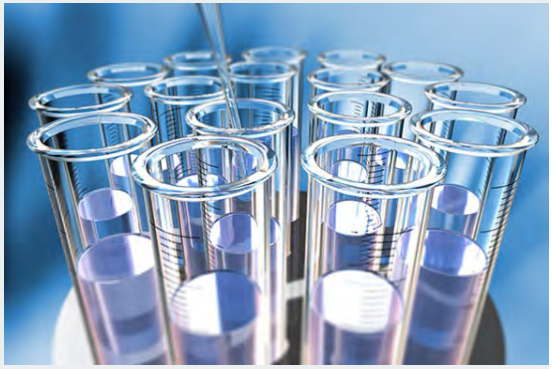


HA101: Demystifying SARS-CoV-2 Testing

Fourth Edition: The Long-Term Dx Industry Impact

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

What to Expect from This Report

This document provides:

- A review of how the diagnostic industry was affected by the COVID-19 pandemic
- Commentary on the pandemic's long-term impact on the diagnostic industry ecosystem, implications for established manufacturers, and the outlook for new entrants

For additional insights on COVID related testing please refer to previous additions of Demystifying SARS-CoV-2 Testing.

First Edition
Second Edition
Third Edition

AACC Reception

We cannot wait to further discuss the pandemic's long-term implications with you at Health Advances' AACC Reception. All are welcome.

HEALTH ADVANCES

Annual AACC
Cocktail Reception and Panel

Now What?

The Dx World Beyond COVID

Come Debate with Our Panelists . . .

- If the perception of Dx value and investment is sustainable
- How new players (in digital, point of care, lab and precision medicine) are reshaping the market
- Where COVID cash will be best invested
- *And many more topics*

Our panelists will be:

- Jeff Luber (Binx, CEO)
- Josh Pulido (LumiraDx, Director, Global Product Marketing)
- Valerie Dixon (Morgan Stanley, Managing Director)
- Yves Dubaquie (Perkin Elmer, Senior Vice President of Diagnostics)
- Fernando Chaves (Siemens, Global Head of Hematology)

LINK TO REGISTER

When:
Tuesday, July 26, 2022
Cocktails at 5:30PM CDT,
Panel at 6:30PM CDT

Where:
The Chicago Firehouse Restaurant

1401 S Michigan Ave
Chicago, IL 60605

We will also have a virtual attendance option. Details will follow for all registered guests.

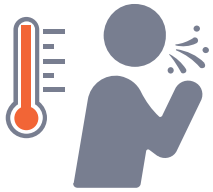
Agenda

- ***What new COVID-19 test types have emerged since the start of the pandemic?***
- What macro trends has the industry experienced? What changes in COVID testing are expected moving forward?
- How has the pandemic impacted established OEM activities and investment?
- What types of new entrants emerged during the pandemic and how will they fare long-term?
- What questions remain outstanding?

Original COVID-19 Testing Options

At the start of the pandemic, testing options for COVID-19 diagnosis, prognosis, exposure screening, and immune status monitoring were introduced.

Start of the Pandemic Testing Options



Patients with Suspected Active Infection

Diagnosis

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

Prognosis

- Assess COVID-19 disease severity and/or risk of progression
- May also be used to inform treatment decisions and predict response to therapy

Exposed Individuals and/or Those With Known Previous Infection

Screening

- Determine whether asymptomatic patients are infected and may pose transmission risk

Immune Status Monitoring

- Determine if an unvaccinated patient was previously infected with SARS-CoV-2
- Assess the presence of immunity based on presence of an anti-SARS-CoV-2 immune response*
- Track population epidemiology of SARS-CoV-2

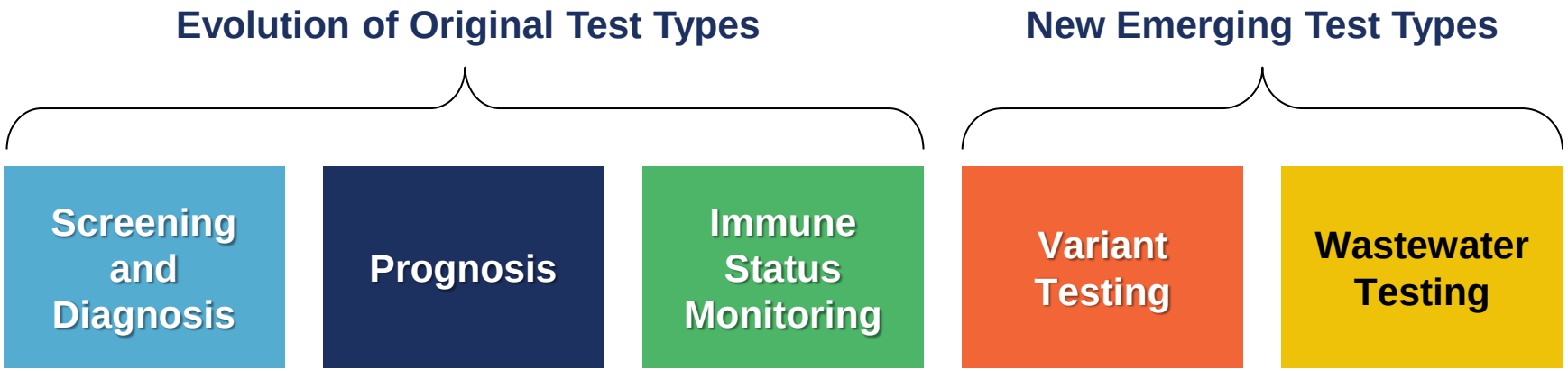
* Antibodies are a protein the body's immune system produces in response to an infection. Antibodies identify the infection as foreign and direct other parts of the immune system to attack and neutralize/destroy the infection. The presence of anti-virus antibodies does not necessarily mean a person is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

Original: Slide 11 in 1st Edition.

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

Changing Nature of COVID Test Types

As the pandemic has progressed, the use of original testing options has evolved. New test types for variant and wastewater assessment have also emerged.



Source: Health Advances analysis.

Screening/Diagnosis Test Types and Use Cases

Panel tests have emerged as an important test category to complement SARS-CoV-2 targeted testing. The breadth and composition of these panels varies.

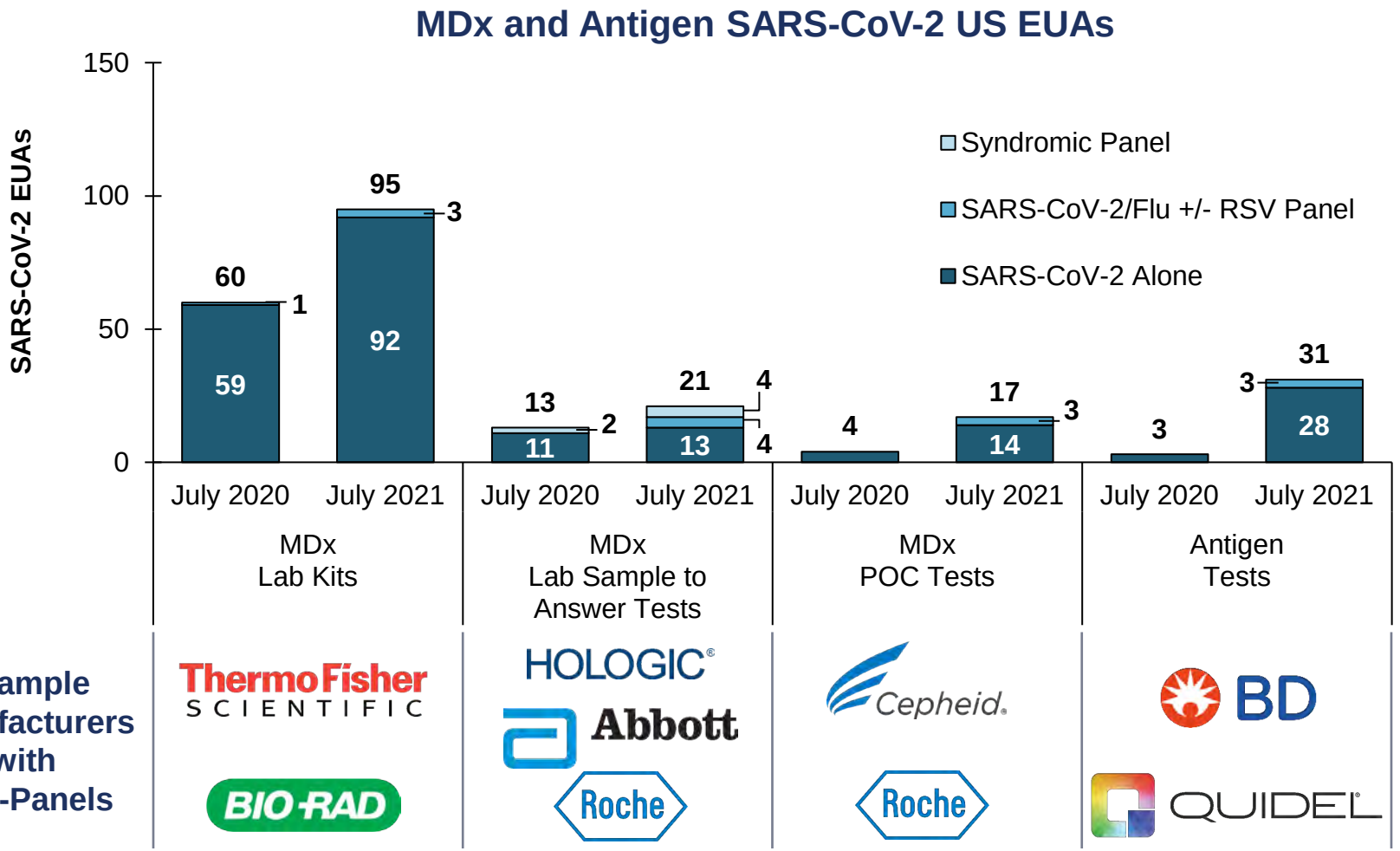
	Test Type	Launch	Primary Patient Populations
Targeted	**SARS-CoV-2 Only**	March 2020	• Confirm or disconfirm COVID in symptomatic patients or screen asymptomatic patients
Panels	**Syndromic Panel***	March 2020	• Identify pathogen of cause in severely symptomatic patients
	SARS-CoV-2 + Flu A/B Mini-Panel	July 2020	• Differentiate Flu and COVID in mild to moderately symptomatic patients
	SARS-CoV-2 + Flu A/B + RSV Mini-Panel	Sept. 2020	• Differentiate Flu, RSV, and COVID in mild to moderately symptomatic children

* For the purposes of this report, syndromic is any panel broader than Flu A/B + RSV + SARS-CoV-2.

Source: Health Advances analysis.

Introduction of Mini-Panels

Mini-panels have emerged as one notable panel category. Many manufacturers have added these mini-panels to menus to help manage the resurfacing of flu alongside COVID.

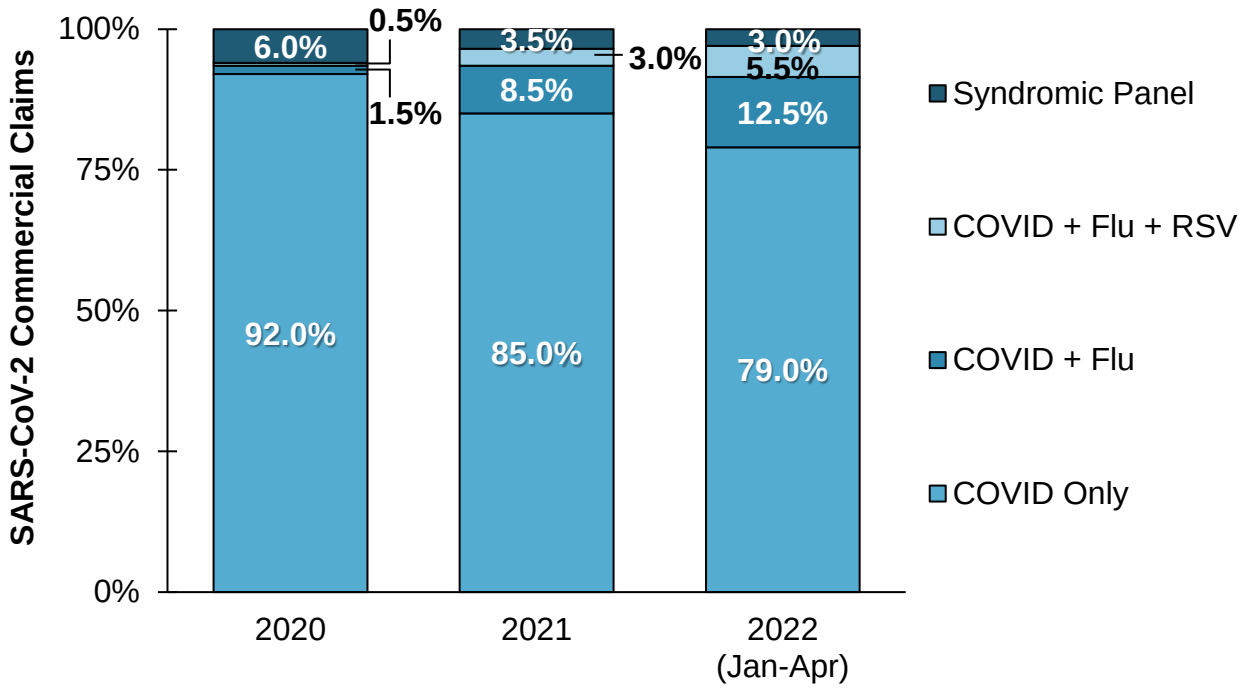


Note: EUA = Emergency Use Authorization.
Source: Health Advances analysis, FDA, 360Dx, FierceBiotech, FDA SARS-CoV-2 FAQ, company websites.

Use of Mini Multiplex Panels to Date

Against the backdrop of a slow return to normal societal behavior, use of mini-panels has steadily increased. Simultaneously, use of broader syndromic panels has decreased.

Symptomatic or Exposure Driven COVID-19 Testing by Panel Type Between 2020 and 2022*



- Mini-panel utilization has increased steadily since their introduction in 2020 while the use of syndromic panels has decreased
- The increase has been driven by the slow return of flu with the re-opening of society
- The decrease in syndromic panels is likely driven by their cost vs. alternative mini-panel options

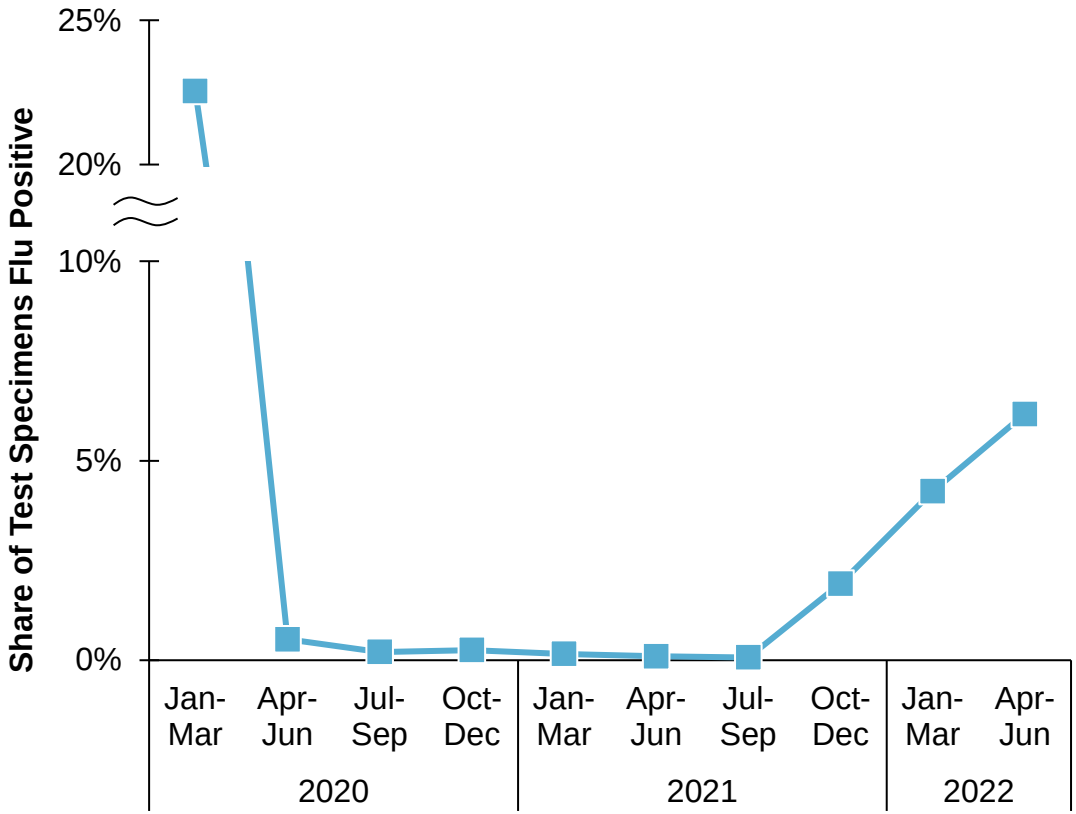
* Based on Definitive Healthcare data representing provider claims to commercial payers using the following codes 87635, 87636, 87637 and 87633.
Note: 2022 data is from January to April.
Source: Health Advances analysis, Definitive Healthcare, local community COVID-19 dashboards, media articles.

Future Use of Mini-Panels

Looking forward, use of mini-panels will likely continue to increase as flu activity continues to slowly return to pre-pandemic levels.

US Influenza Activity Monitored by CDC

Reported to CDC by US Clinical Laboratories



- *"The symptom overlap is so high that as flu rates return to normal, it will be valuable to test for both." – PCP*
- *"We are already seeing flu return with the re-opening and, going forward, we anticipate more frequent use of the mini-panels to distinguish between them." – Lab Director*

Source: Health Advances analysis, CDC Influenza Activity Tracker.

Prognostic Testing Introduction

Given the variability in the severity of COVID-19 symptoms and the emergence of long hauler syndrome ("long COVID"), multiple use cases for prognostic testing have emerged.

Prognostic Testing Clinical Use Cases

	Pre-Infection Risk	Severity Prediction	Long-Hauler Diagnosis
Definition	• Identify individuals at high-risk of severe COVID-19 infection	• Predict probability of progressing to severe disease at time of diagnosis or later stages of infection/hospitalization	• Identify patients at risk of long-hauler syndrome and/or diagnose patients with persistent COVID related impacts
Rationale for Testing	• *Enable patients to feel more confident in managing their risk mitigation and social distancing activities*	• *Determine who should be hospitalized and optimize treatment among various patient groups to reduce morbidity and mortality*	• *Optimize acute infection and long-term treatment*

Source: Health Advances analysis.

Progress in Prognostic Testing

Commercial and clinical research efforts have focused on developing severity prediction as this is an urgent need for patient care. Tests for other use cases are still emerging.



	Pre-Infection Risk	Severity Prediction	Long-Hauler Diagnosis
Focus of Clinical Dx Research	• Some studies have identified potential genetic biomarkers for predisposition	• Several papers published on a variety of approaches to predict severity in patients	• Autoantibodies and other serum biomarkers are being explored by a small group of researchers*
Commercial Test Availability	• Several proprietary genetic tests available as LDTs	• CBC indexes and IL-6/IL-10 tests available • Proprietary test from MeMed is available in EU	• No commercial tests available to date

* No studies have been published or preprinted to date.
Note: LDT = laboratory developed test.
Source: Health Advances analysis, PubMed, medRxiv, bioRxiv, GenomeWeb/360Dx.

Limited to No Studies/ Tests Available ⟷ Several Studies/ Tests Available

Clinical Dx Research: Pre-Infection Risk

Research to determine risk factors for severe COVID-19 in healthy individuals remains early. Studies have demonstrated genetic correlation but not direct causation.

Select Pre-Infection Risk Studies

Publication or Posting	Year	N	Brief Description	Study Results and Implications
Ishak Gene	2022	N/A	• A systematic literature review on the association of COVID-19 susceptibility and severity with genetic risk factors found 60 relevant publications globally	• The review concluded that high-risk HLA variants and ACE polymorphisms increase susceptibility and severity of COVID-19
Hunter, bioRxiv	2021	80	• Blood samples of 80 COVID-19 patients with varying severity were used to derive an algorithm based on genomic loci to predict severity of COVID-19	• Applying the algorithm to the same cohort of 80 patients in a cross-validation study found an 86% positive predicative value for severe COVID-19 infection
Dite, medRxiv	2020	1,582	• UK biobanked samples of 1018 severe and 564 non-severe COVID-19 were used to develop a logistic regression model using clinical factors and 64 SNPs	• The model had 111% better discrimination of disease severity (AUC=0.786) than a model with just age and gender (AUC=0.635)

- Given the variability in SARS-CoV-2 response, genetics may be able to help predict the risk of severe infection
- Research is still early with limited validation of findings in large populations
- More studies are needed to confidently discern the genetic factors that drive variable virus responses

Note: SNPs = single nucleotide polymorphisms.
Source: Health Advances analysis, GenomeWeb, Hunter 2021 Preprint bioRxiv, Dite 2020 Preprint medRxiv.

Clinical Dx Research: Severity Prediction

Research studies on prognostic testing for severity prediction have yielded promising results and found many biomarkers to be useful, including CBC indices, IL-6, and IL-10.

Select Severity Prediction Studies

Publication or Posting	Year	N	Brief Description	Study Results and Implications
Mastboim, medRxiv	2021	394	• A study by MeMed of 394 COVID-19 patients with varying outcomes derived a score for predicting severity based on levels of TRAIL, IP-10, and CRP together	• In a cross-validation study with the same cohort the signature demonstrated a ROC curve AUC score of 0.86
Dhar, Heliyon	2021	2,157	• Meta-analysis of 18 studies measuring levels of 13 different cytokines in 2,157 COVID-19 patients determined cytokines to be associated with severity	• Measuring the standardized mean difference (SMD) of cytokine levels between severe and non-severe cases found IL-6 and IL-10 to have SMDs of .53 and .65 for severe cases
Fois, Molecules	2020	119	• A retrospective observational study of 119 patients was used to identify CBC-derived inflammation indexes for severity	• Neutrophil*platelet to lymphocyte ratio (systemic inflammation index) was significantly associated with severity with a hazard ratio of 1.0001
Andragie, JCI Insight	2021	138	• Prospective cohort study at Johns Hopkins patients to measure cfDNA levels including nuclear and mitochondrial cfDNA to determine link to COVID-19 and severity	• cfDNA levels 20-fold higher in COVID-19 than healthy individuals ($P < 0.0001$) • Nuclear cfDNA levels 4.5-fold higher in COVID-19 patients that died vs. those that recovered ($P < 0.0001$)

- A broad review of the clinical literature indicates that most research is focused on severity prediction of active cases
- CBC indices and IL-6/IL-10 are already being used to predict severity today, and newer biomarker approaches have promising study results

Note: Selected studies are representative to demonstrate research into multiple biomarker types ranging from inflammatory biomarkers to hematological indices to cell-free DNA.
Source: Health Advances analysis, Fois 2020 Molecules, Dhar 2021 Heliyon, Andragie 2021 JCI Insight, Mastboim 2021 Preprint MedRxiv.

Example Novel Commercial Prognostic Tests

Several novel commercial tests have emerged for prognosis to date. Most are pre-infection tests directed towards consumers; one aids clinicians with severity prediction.

Test Type	Company	Test Name	Description	Markers	Status	Data Summary
Pre-Infection Risk	OXFORD BIODYNAMICS	EpiSwitch COVID-19 Severity Test	• Blood-based qPCR test to predict severity of response	• Six epigenetic markers undisclosed	• LDT at specialty lab; on market in US / UK	• 96% Sens. • 86% Spec. • 92% PPV • 93% NPV
	Genetic Technologies SAMPLED VAULT	COVID-19 Risk Test	• Blood-based SNP test to predict severity of response[1]	• Clinical factors + 64 SNPs	• LDT at specialty lab; on market in US	• *Not available*
	SEQUENCING.COM OUTSMART YOUR GENES®	Coronavirus Health Report[2]	• Analyze raw genome data provided by patient	• Reviews status of 26 SNPs and haplotypes	• On market globally (un-regulated)	• *Not available*
Severity Prediction	MeMed	COVID-19 Severity Test	• POC serum test to predict likelihood of severe infection	• TRAIL, IP-10, and CRP	• CE Marked; on market in EU	• 86% Sens. • 98% Spec. • 91% NPV

[1] The technology used analyze the SNPs has not been disclosed.
[2] Four similar tests from other companies (SelfDecode, GeneInformed, LifeDNA, and Xcode) also provide a similar service.
Note: SNP = single nucleotide polymorphism, POC = point-of-care, NPV = negative predictive value, LDT = laboratory developed test
Source: Health Advances analysis, Forbes, company websites.

Use Cases for Immune Status Monitoring

Immune status monitoring is another tool to combat COVID-19 and enables insight on prior exposure, potential degree of immunity, and population surveillance for outbreaks.

Immune Status Monitoring Use Cases

	Prior Exposure	Immunity	Surveillance
Definition	• Determine if an unvaccinated person has been previously exposed to SARS-CoV-2	• Assess the current degree of immunity conferred from vaccination or previous infection if unvaccinated	• Understand how much of a population has been infected with and/or vaccinated from SARS-CoV-2
Testing Rationale	• Evaluate if lingering symptoms or exposure concerns have merit	• Understand if a patient possesses immunity to COVID-19	• Enable public health to track the epidemiology of SARS-CoV-2 infections

Source: Health Advances analysis.

Potential Value of Test Types

T-cell tests show greater potential value than antibody tests in the different use cases for immune status monitoring.

Potential Value for Immune Status Monitoring

Test Types	Description	Prior Exposure	Immunity	Surveillance
Antibody Tests	• Detect or measure levels of antibodies (IgA, IgG, IgM) against SARS-CoV-2	• Only useful within first few months due to declining antibody response	• Antibody titers and degree of immunity have not been determined yet	• Not reliable for long-term measurements due to antibody decay
T-cell Tests	• Detect or measure T cell-mediated immune response to SARS-CoV-2	• More reliable indicator due to longer-lasting response	• Theoretically useful, but studies have not proven connection to immunity conferred	• Longer-lasting T-cell response makes it a potentially useful tool for public health

Lower Potential Value ⟷ Higher Potential Value

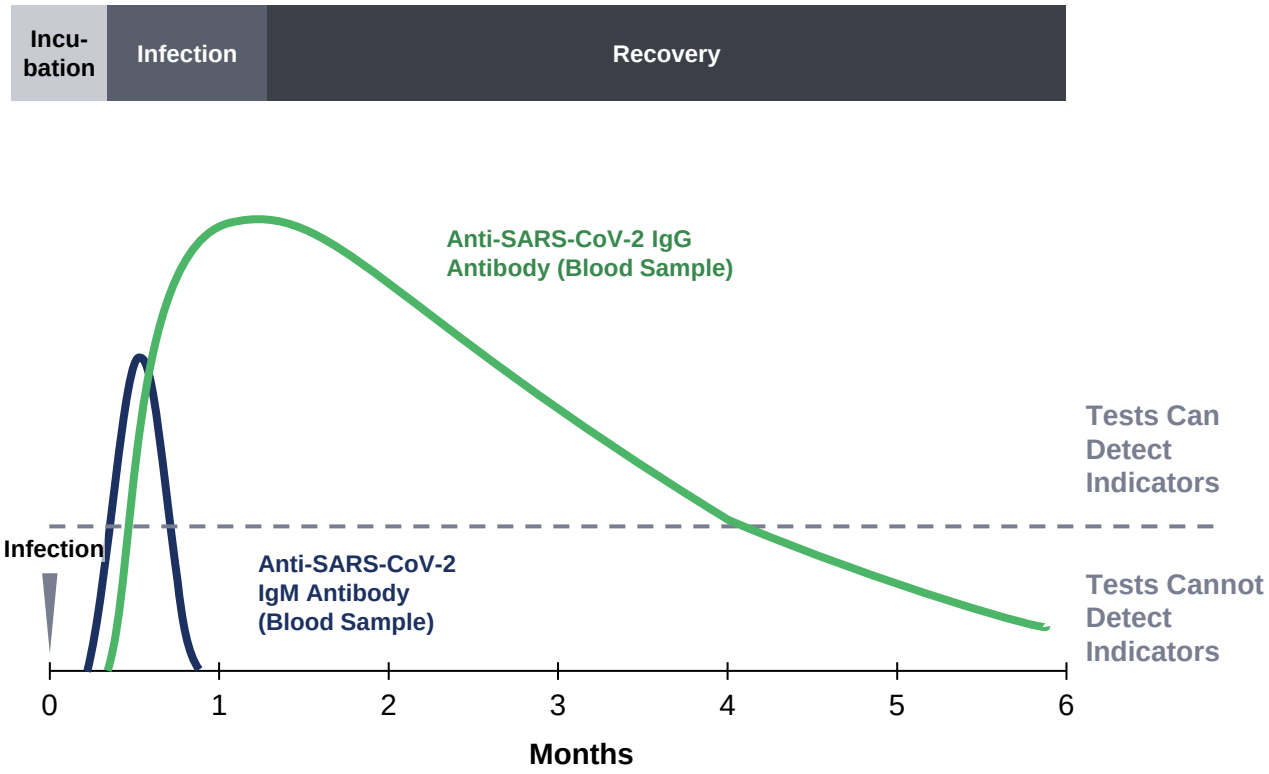
Source: Health Advances analysis. Hedges 2021 Vaccines, Ibarrando 2020 N Engl. J Med, Seow 2020 Nature Microbiology, Long 2020 Nature Medicine, Tan 2020 medRxiv, Spellberg 2020 JAMA Intern. Med, Wyllie 2021 medRxiv, Bert 2020 Nature, Peng 2020 Nature Immunology, Sekine 2020 Cell, Cox 2020 Nature Reviews.

Antibody Response to SARS-CoV-2

While antibody tests can indicate prior exposure soon after infection, their reliability wanes over time. Their ability to predict protection from reinfection is unknown.

Antibody Response to SARS-CoV-2 Infection

Illustrative Representation



- Antibody response deteriorates within months after infection
  - Antibody titers wane within 3-5 months after infection
  - 10-30% of patients may never develop antibodies
- The protection conferred by antibodies has not been determined
  - The protective titer of the neutralizing antibody and correlation of binding antibody titers to neutralization are under study

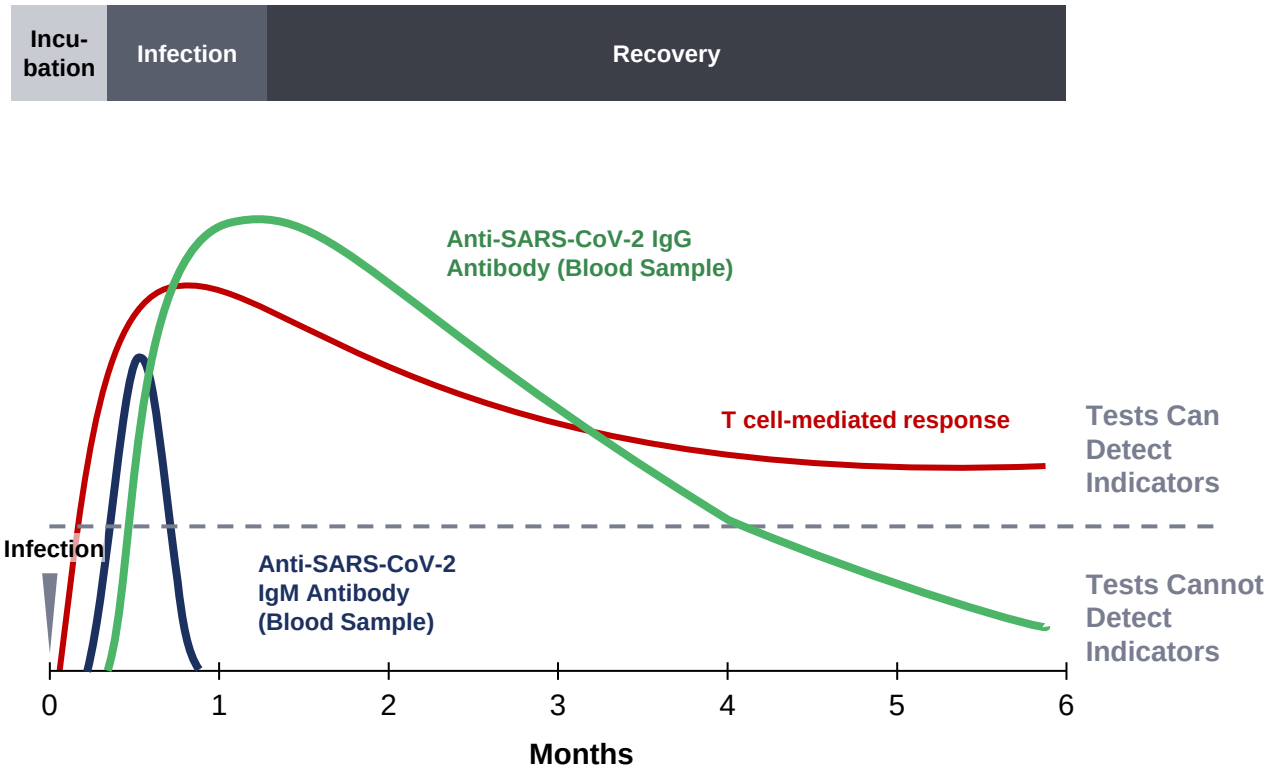
Source: Health Advances analysis. Hedges 2021 Vaccines, Ibarrando 2020 N Engl. J Med, Seow 2020 Nature Microbiology, Long 2020 Nature Medicine, Tan 2020 medRxiv, Spellberg 2020 JAMA Intern. Med.

T-Cell Response to SARS-CoV-2

Researchers have postulated that T-cells could be a better predicator of prior exposure and immunity than antibodies. Early data indicates this may be true.

T-cell and Antibody Response to SARS-CoV-2 Infection

Illustrative Representation



- Robust T-cell response is maintained at 6 months following infection
  - A study of 100 individuals with SARS-CoV-2 infection found all retained T cell responses at 6 months following infection
- T-cell counts have shown early association with COVID-19 protection
  - Additional studies are required to validate this hypothesis
  - A prospective study of 2,826 participants found those with higher T-cell responses did not develop COVID-19 during a median 118 days follow-up; those with lower T-cell responses did develop COVID-19 in the same time period

Source: Health Advances analysis, Zuo 2021 T cell immunity Nature Immun, Wyllie T cell protection medRxiv.

Immune Status Summary Outlook

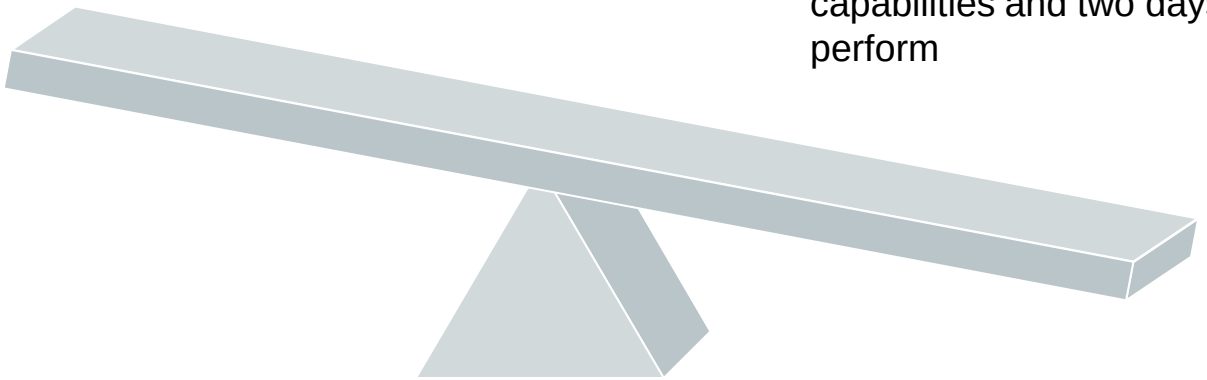
We anticipate T-cell tests will become the gold standard for assessing long-term immunity to COVID-19 given their more reliable measure of immune response vs. antibodies.

Antibody Tests

- ✓ Simple to perform and widely available across labs
- ✓ Can confirm prior exposure in initial months after infection
- ✘ Not reliable as some patients do not produce antibodies
- ✘ Correlation of titers to immunity not understood

T-Cell Tests

- ✓ More reliable measure of immune response compared to antibodies
- ✓ Longer-lasting response that can be measured
- ✓ Possible correlation between T-cell counts and degree of immunity
- ✘ Requires specialized testing capabilities and two days to perform



Source: Health Advances analysis.

Dynamics Influencing Variant Emergence

Widespread SARS-CoV-2 transmission and increasing vaccination are applying strong selective pressure and leading to variant emergence, thus creating need for variant tests.

Mutation Rate

- SARS-CoV-2 mutates at about half the rate of influenza (<25 mutations per year) with the spike protein region mutating the fastest

Viral Spread

- As restrictions wane, spread of SARS-CoV-2 will continue and provide more opportunity for variant emergence

Vaccination Rate

- Transmission in vaccinated individuals selectively favors more transmissible and vaccine-evading variants

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

Key SARS-CoV-2 Variants

Many variants have emerged over the course of the pandemic. The most notable variants of concern have high transmissibility and have included the Delta and Omicron variants.

Mutations and Emergence of Variants

The SARS-CoV-2 Genome

- As important regions such as the spike protein mutate, the virus's ability to replicate and attach to human cells changes and thus these regions are closely monitored for changes.

Variants of Concern *(proven high transmissibility and/or high severity)*

Alpha (Sep 2020)
- S: 484K
- ↑ transmissibility, potential ↑ severity

Beta (May 2020)
- S: 417N, 484K, 501Y
- ↑ transmissibility

Delta (Oct 2020)
- S: 452R
- ↑ transmissibility

Gamma (Nov 2020)
- S: 417T, 484K, 501Y

Omicron* (Nov 2021)
- S: E484A, N501Y
- ↑ transmissibility

Earliest Documentation and Classification from WHO

Variants of Interest *(predicted or known to affect transmission and/or severity with known high spread)*

Epsilon (Mar 2020)
- S: 13I, 152C, 452R

Zeta (Apr 2020)
- S: 484K, 614G, 1176F

Kappa (Oct 2020)
- S: 452R, 484Q, 681R

Iota (Nov 2020)
- S: 484K

Eta (Dec 2020)
- S: 484K

Lambda (Dec 2020)
- S: 452Q

Mu (Jan 2021)
- Y144S

Theta (Jan 2021)
- S: E484K, N501Y, D614G, P681H

* The WHO has classified multiple Omicron lineages under monitoring.

Note: Mutations of therapeutic concern are listed. S: 417N indicates a mutation in the spike protein at amino acid 417 to asparagine (N).

Source: Health Advances analysis, WHO, CDC.

Impact of Variants on Diagnostic SARS-CoV-2 Tests

To date, variants have had minimal impact on the performance of tests used to screen for or diagnose a SARS-CoV-2 infection because most tests include multiple targets.

Type of Test	Impact from Variants	Rationale
 **Molecular**	**Minimal**	• Vast majority of molecular tests target 2-3 regions of the SARS-CoV-2 genome (e.g., ORF1/2 and N regions), which are highly conserved • This limits the risk from mutations in any one region • FDA identified only 2 out >250 molecular tests with potential concerns due to target regions being impacted by variant mutations
 **Antigen**	**Minimal**	• Limited concern; antigen tests target 1 region of N gene, which is highly conserved • Mutations in new variants have predominantly occurred in the S gene that codes for the spike protein
 **Serology**	**None**	• Limited risk as serology tests measure the host's antibodies rather than the virus itself; a small concern is if the antibodies being formed are not detected due to antigenic mutations in the virus
 **Prognostic**	**None**	• Generally, no risk as they rely on the host's genetic and/or protein biomarkers, which are not directly impacted by variants

Source: Health Advances analysis, company websites, FDA.

Guidelines on Variant Monitoring

WHO and regional health organizations recommend continued vigilance and continued variant monitoring within each country's national health systems.

World Health Organization

- Encourages countries to deposit sequences in public database
- Refrains from specific guidance due to varying sequencing infrastructure by country

Pan American Health Organization

- Recommends ≥50 samples sequenced per month
- Implemented 8 regional sequencing labs network to support in-country testing

AFRICA CDC
Centres for Disease Control and Prevention
Safeguarding Africa's Health

- Advises member states to include genomic surveillance as part of disease surveillance
- Few specific details

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

- Provides target of ≥500 samples or ≥10% of cases sequenced per week
- Relies upon countries to implement programs

Source: Health Advances analysis, WHO, ECDC, Africa CDC, PAHO.

Technologies for Variant Monitoring

Multiple approaches are available to monitor the emergence and spread of variants. The most common approach is sequencing-based genomic analysis.

Technologies for Variant Monitoring

Technique	Frequency of Use	Description	Example Products
Sequencing-based Methods		• Primary method for tracking existing variants and identifying new variants • Required cost and time limits the number of samples analyzed in this manner	 Illumina MiSeq System  Ion Torrent Genexus System
NAAT		• Most tests cannot distinguish variants • Some tests can serendipitously detect certain variants	 ThermoFisher TaqPath COVID-19 PCR  Roche Variant Set 1 (RUO)

Note: NAAT = nucleic acid amplification test.
Source: Health Advances analysis, WHO Methods for Variant Detection

General Approach to Variant Monitoring

Several archetypes of variant monitoring are observable, which are differentiated by the degree of centralization in decision making and processing.

Decision-Making

- Decision-makers such as central and/or local governments and public health institutions guiding variant monitoring policies and funding

Testing Method and Location

- Method by which variant monitoring is being accomplished and where the testing is performed

Results Aggregation and Reporting

- How results are reported to GISAID (Global Initiative on Sharing All Influenza Data)

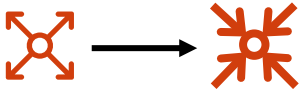
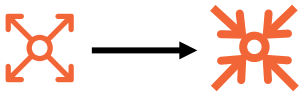
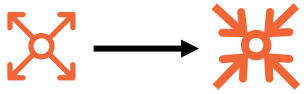
Each approach further varies by degree of centralization:

Source: Health Advances analysis.

Variant Monitoring in the US

The US started with a highly decentralized approach where each state determined its own method of monitoring. Eventual federal funding created a more centralized approach.

US

	Decision-Making	Testing Approach and Infrastructure	Results Aggregation and Reporting
Description	• In the beginning each state's public health agency organized its own surveillance programs and behaved differently • Federal funding in 2021 resulted in the CDC eventually coordinating a national surveillance program	• Multi-layer approach is used – Public health labs send CDC samples weekly – CDC contracts with labs to sequence samples – Additional sequences are submitted by various labs – CDC collaborates with universities for surveillance research	• Each lab that performs testing submits results to GISAID* • Initially there was no coordination for reporting, but the CDC recently established a public report for tracking variants
Centralization vs. Decentralization			
Results	• The US has published the second most genomic sequences to GISAID after the UK, but ranks low in of the percent of cases sequenced		

* GISAID provides open access to genomic data of influenza viruses and coronaviruses. It plays a critical role as a central global repository for SARS-CoV-2 sequences.

Note: GISAID = Global Initiative on Sharing Avian Influenza Data CDC = Centers for Disease Control and Prevention.

Source: Health Advances analysis, CDC, Abbasi 2021 J Am Med Assoc, Maxmen 2021 Nature, Washington Post, Furuse 2020 Intl J Infec. Dis.

Variant Monitoring in the UK

The UK has a highly centralized approach to variant monitoring, resulting in one of the highest percentages of cases sequenced and making it a global leader in surveillance.

UK

	Decision-Making	Testing Approach and Infrastructure	Results Aggregation and Reporting
Description	• Govt. funding allocated to the COG-UK to coordinate surveillance	• Samples sent to the Sanger Institute and 4 Public Health England labs for sequencing	• Central data collection and analysis by COG-UK with other epidemiologic and clinical information before submitting to GISAID
Centralization vs. Decentralization			

Results

- The UK has uploaded over 2MM SARS-CoV-2 sequences accounting for 25% of sequences shared globally and sequenced samples from >10% of all UK-based COVID-19 cases
- This is attributed to a strong focus and funding on sequencing from the start of the pandemic from a centralized decision-making authority

Note: COG-UK = COVID-19 Genomics UK, which is a consortium of National Health Services, Public Health England, Wellcome Sanger Institute, and academic institutions.
Source: Health Advances analysis, COG-UK, PHE, Furuse 2021 Intl J Infec. Dis, AP News, UK Govt.

Variant Monitoring in Germany

Germany's surveillance program is a hybrid of centralization and decentralization. Variant monitoring traditionally lagged, but new funding and attention increased utilization.

DE

	Decision-Making	Testing Approach and Infrastructure	Results Aggregation and Reporting
Description	• Central government reimburses local and state-level diagnostic labs for sequencing 5-10% of positive samples	• Local and state authorities collect sequence data and patient metadata from predesignated labs and submit to the RKI • Testing is divided across state and local levels	• RKI performs final analyses with sequence and epidemiological data
Centralization vs. Decentralization			

Results

- Germany was initially less active in variant sequencing, but eventual govt. funding of 200MM Euros for variant sequencing and new requirements for labs to sequence have led to a marked increase in sequencing

 **Centralized**  **Decentralized**

Note: RKI = Robert Koch Institut.
Source: Health Advances analysis, RKI, Furuse 2020 Intl J Infec. Dis, Reuters.

Strategies for Monitoring Variants

Different approaches to monitoring variants each have pros and cons. Overall, centralized approaches reap greater benefits of coordination and standardization across a country.

Strategies for Monitoring Variants

	Decentralized		Hybrid		Centralized	
Pros/Cons	✓ Easier to initiate ✓ Less bureaucracy ✓ Ability to customize	✗ Inconsistent execution ✗ Lack of accountability ✗ Unpredictable outcomes	✓ Flexibility to adapt as needed	✗ Confusion on authority and rules to follow	✓ Organized ✓ Predictable results ✓ Higher accountability	✗ Time/effort to organize ✗ Requires consensus
Impact on Variant Monitoring	*Lack of oversight and organization ultimately results in weaker monitoring*		*Potential to benefit from both approaches or can create confusion depending on execution*		*Upfront effort results in better execution and strong monitoring for variants*	

Source: Health Advances analysis.

Wastewater Testing

Research has shown that wastewater testing can effectively monitor overall disease burden and COVID-19 incidence in local communities.

Important Wastewater Studies

Study	Journal	# of Citations	Findings on Wastewater Testing
First Detection of SARS-CoV-2 in Wastewater in Australia	*Sci. Total Environ*	1125	• First study that reported the detection of SARS-CoV-2 in wastewater
SARS-CoV-2 RNA in Wastewater Tracks Infection Dynamics	*Nature Biotech.*	426	• Wastewater provides notice of infections in community days ahead of patient testing
Analysis of SARS-CoV-2 Surveillance by Wastewater: Feasibility, Economy, Opportunities and Challenges	*Sci. Total Environ*	369	• One infected individual theoretically is detectable among 100 to 2,000,000 persons

Implications

- The number of COVID-19 cases in a community correlates with the SARS-CoV-2 RNA concentration in that community's wastewater
- SARS-CoV-2 RNA concentrations can be found several days in advance of positive SARS-CoV-2 test results
- Wastewater testing is cost-effective method for monitoring epidemiology

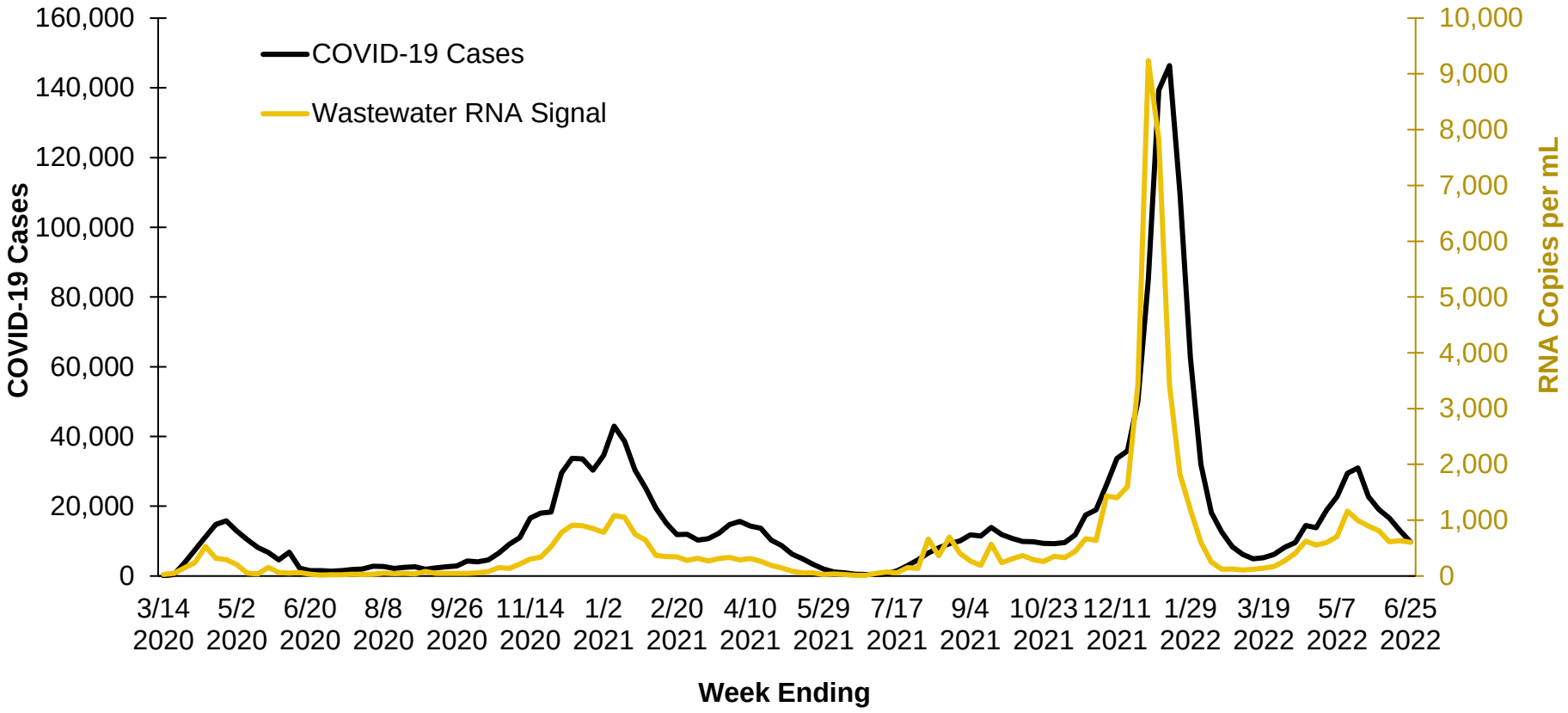
Source: Health Advances analysis, Ahmed, W., 2020 Sci Tot. Environ, Peccia, j., 2020 Nature Biotech, Hart, O., 2020 Environ. Sci. Technol.

Value to Identify Real-Time Case Rates

For example, Massachusetts reports its wastewater testing and uses these results as an early predicator of outbreaks and to contextualize potential underreporting of cases.

Massachusetts Wastewater COVID-19 Tracking

*COVID-19 Cases and Viral RNA Signal in Wastewater by Date**



* Cases and viral RNA signal is based on the running 7-day average at the represented date. Data accounts for the individual North and South Water Systems being monitored by MA.

Source: Health Advances interviews and analysis, Massachusetts Water Resources Authority, JHU.

Current Utilization of Wastewater Testing

Thus far, the US, Europe, and Australia have been at the forefront of implementing wastewater testing to monitor case rates and identify potential outbreaks.

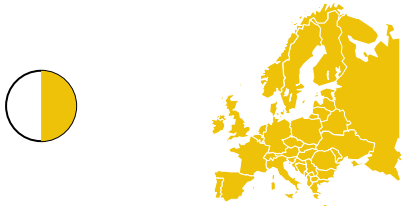
Utilization of Wastewater Testing

As Indicated by Publications and/or Media Reports

US

- CDC has provided guidance and a voluntary program for municipalities to submit wastewater to labs, followed by CDC data analysis and result reporting back to health departments
- Lack of national or state-level policies has resulted in sporadic use
- Wastewater testing has highest adoption in the Midwest, Northeast and West coast regions

Europe



- The European Commission recommended EU members establish a common systematic surveillance approach for SARS-CoV-2 in EU wastewater
- EU member states have responded, with France, Belgium, Netherlands, Spain, and Austria leading the way with the most waste treatment plants under regular surveillance

ROW

- Australia established a national program sewage surveillance program that at its peak can test 90% of the population's wastewater to aid COVID-19 response
- Lack of national policies or guidelines to monitor wastewater suggests limited use elsewhere

Source: Health Advances analysis, Politico, European Union Website.

Future of Wastewater Testing

Looking forward, as unreported self-testing grows and/or the general rate of testing wanes, wastewater testing will become essential for measuring COVID trends.

Unreported Self-Testing

- With the growing utilization of rapid over-the-counter tests, reported cases of COVID-19 will become a less reliable measure of prevalence

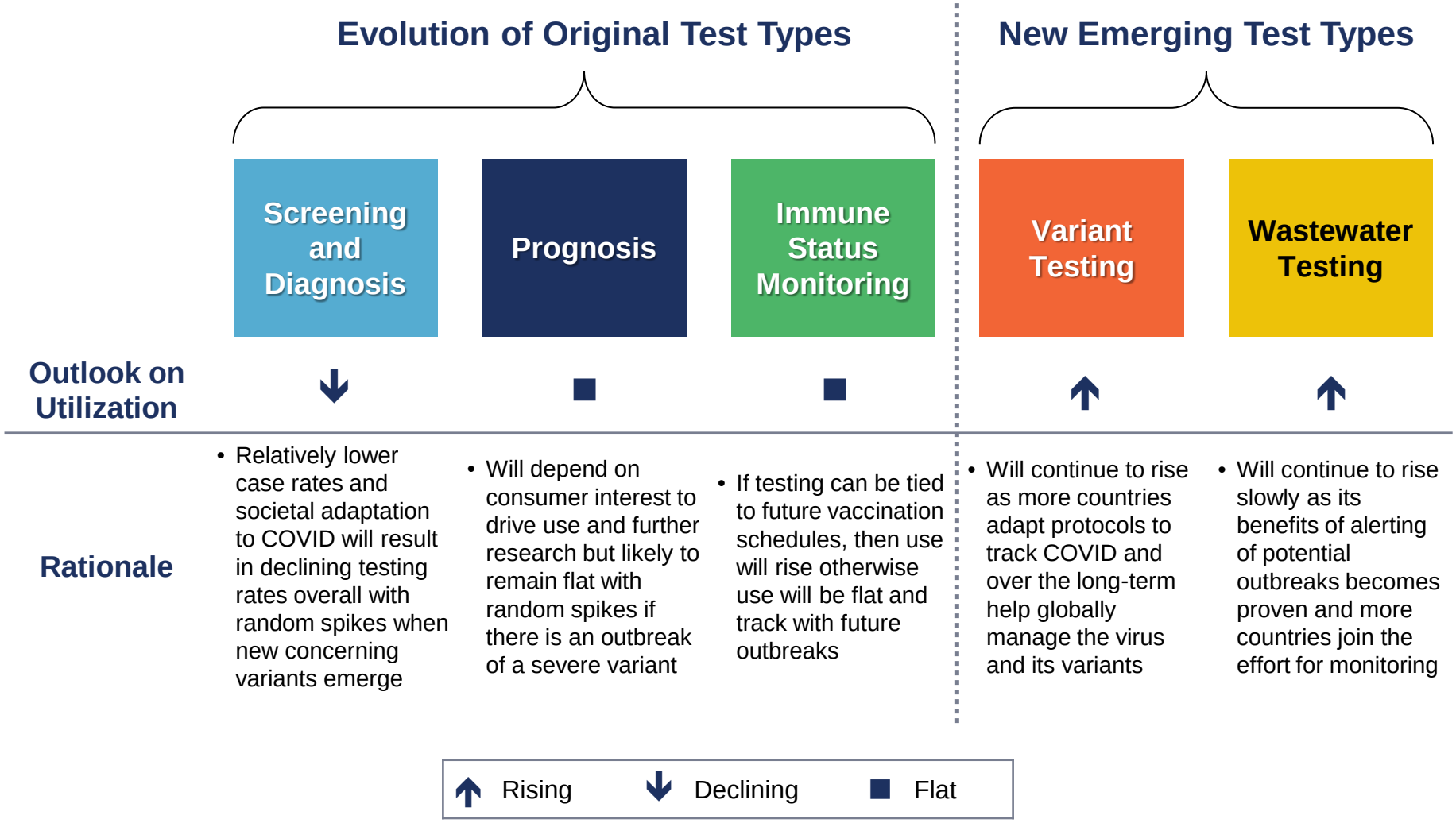
Lower Rates of Testing

- As milder strains of COVID-19 emerge and the public inches towards a new normal, individuals will be less likely to test themselves unless they are severe or concerned, resulting in underestimating prevalence

Source: Health Advances analysis, Mara Aspinall COVID Newsletter Dec 2021.

Future Outlook for Test Types

Screening and diagnosis of COVID-19 will continue to wane as normal societal behavior prevails, while other test types will either stay flat or rise as we shift to preventing outbreaks.



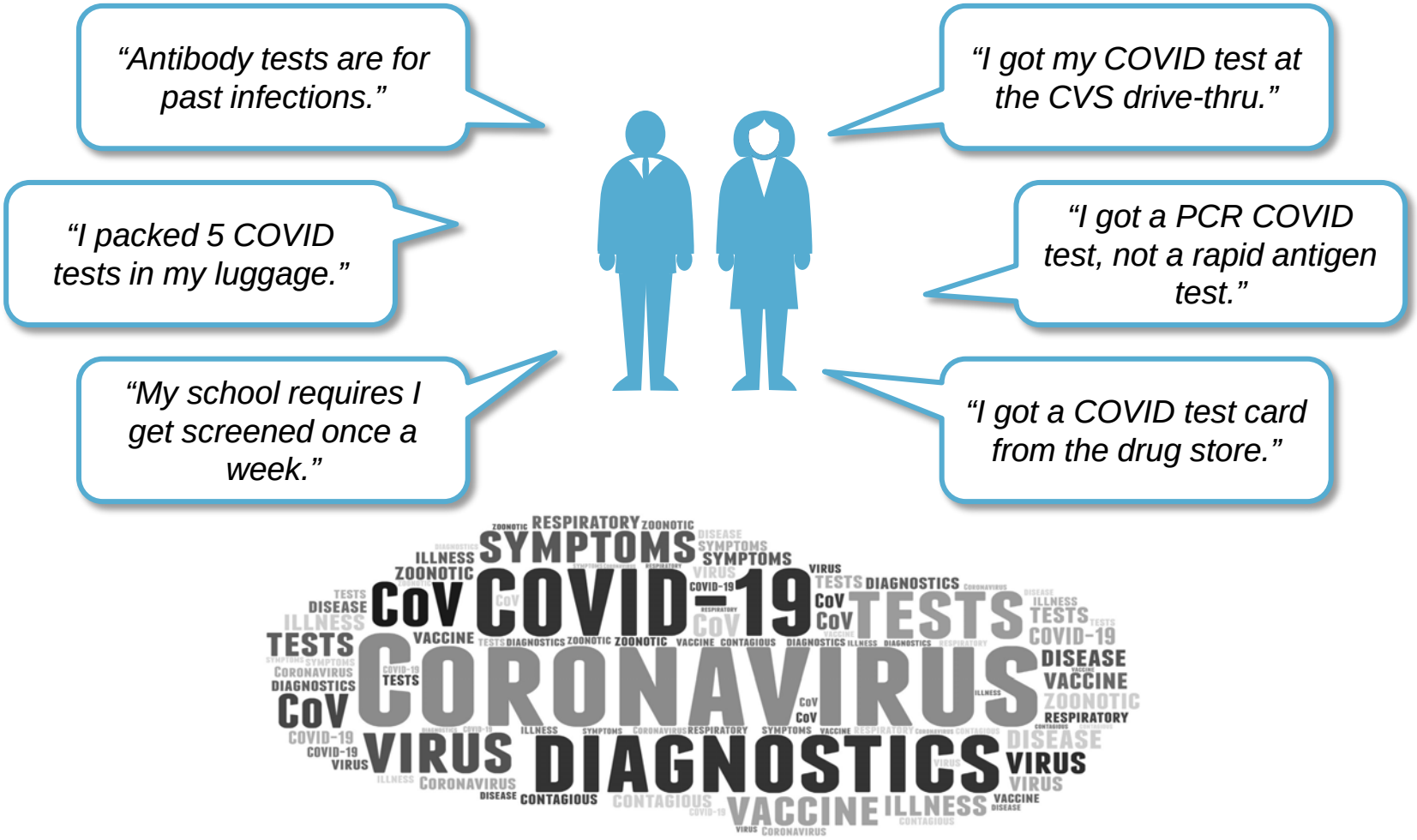
Source: Health Advances analysis.

Agenda

- What new COVID-19 test types have emerged since the start of the pandemic?
- ***What macro trends has the industry experienced? What changes in COVID testing are expected moving forward?***
- How has the pandemic impacted established OEM activities and investment?
- What types of new entrants emerged during the pandemic and how will they fare long-term?
- What questions remain outstanding?

Elevation of Diagnostics in the Public Conversation

The COVID pandemic put the diagnostics industry "on the map" and extended broad public awareness of testing around the globe.



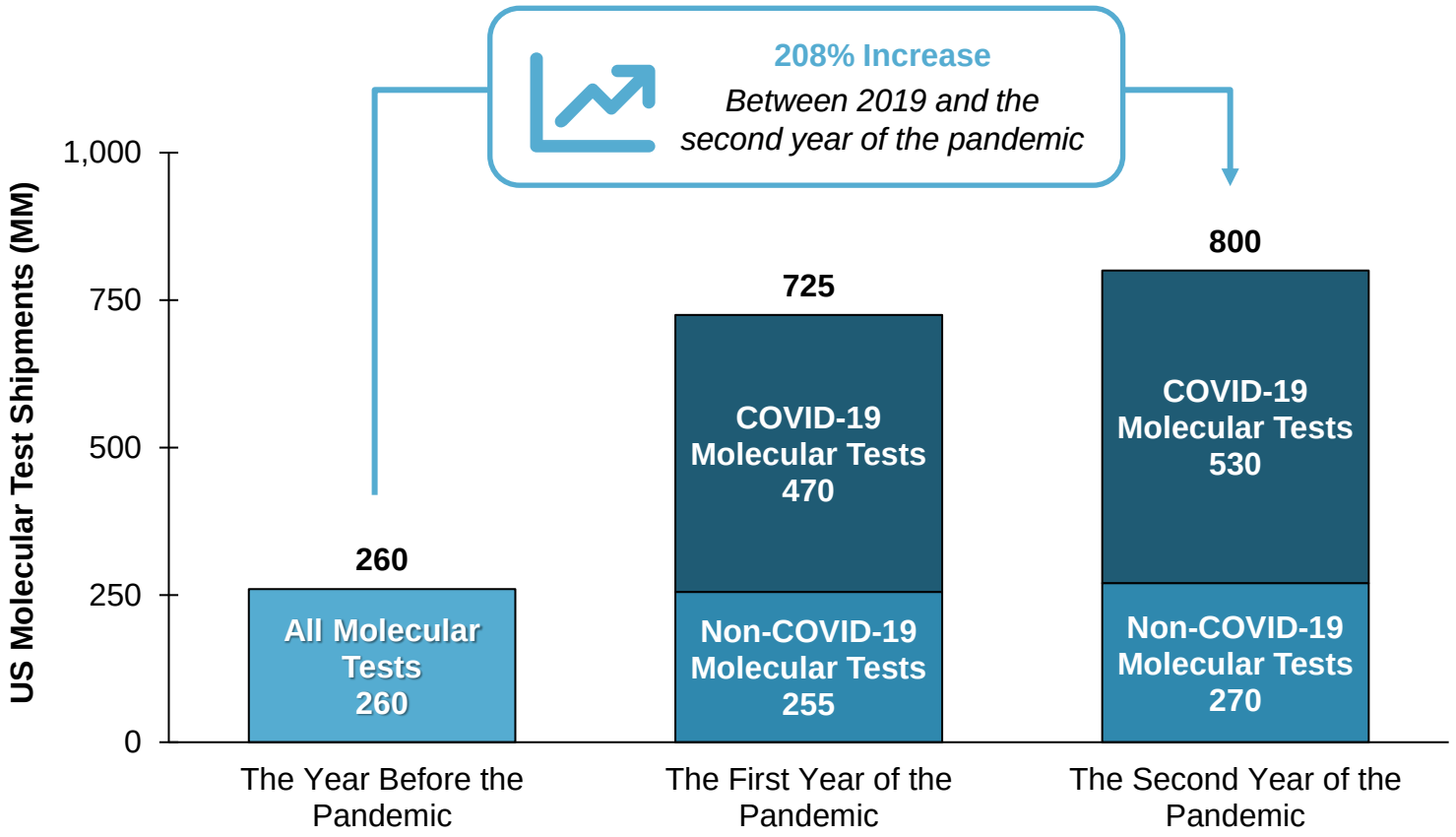
Note: Dx=Diagnostics; The diagnostics industry is defined, for the purposes of this publication, as test reagent and instrumentation manufacturers.
Source: Health Advances analysis.

US SARS-CoV-2 Test Volumes

SARS-CoV-2 US molecular test shipments ramped quickly, reaching ~470MM in the first year and continued to account for 2/3 of the 800MM molecular tests the next year.

US Molecular Test Shipments Before and During the Pandemic

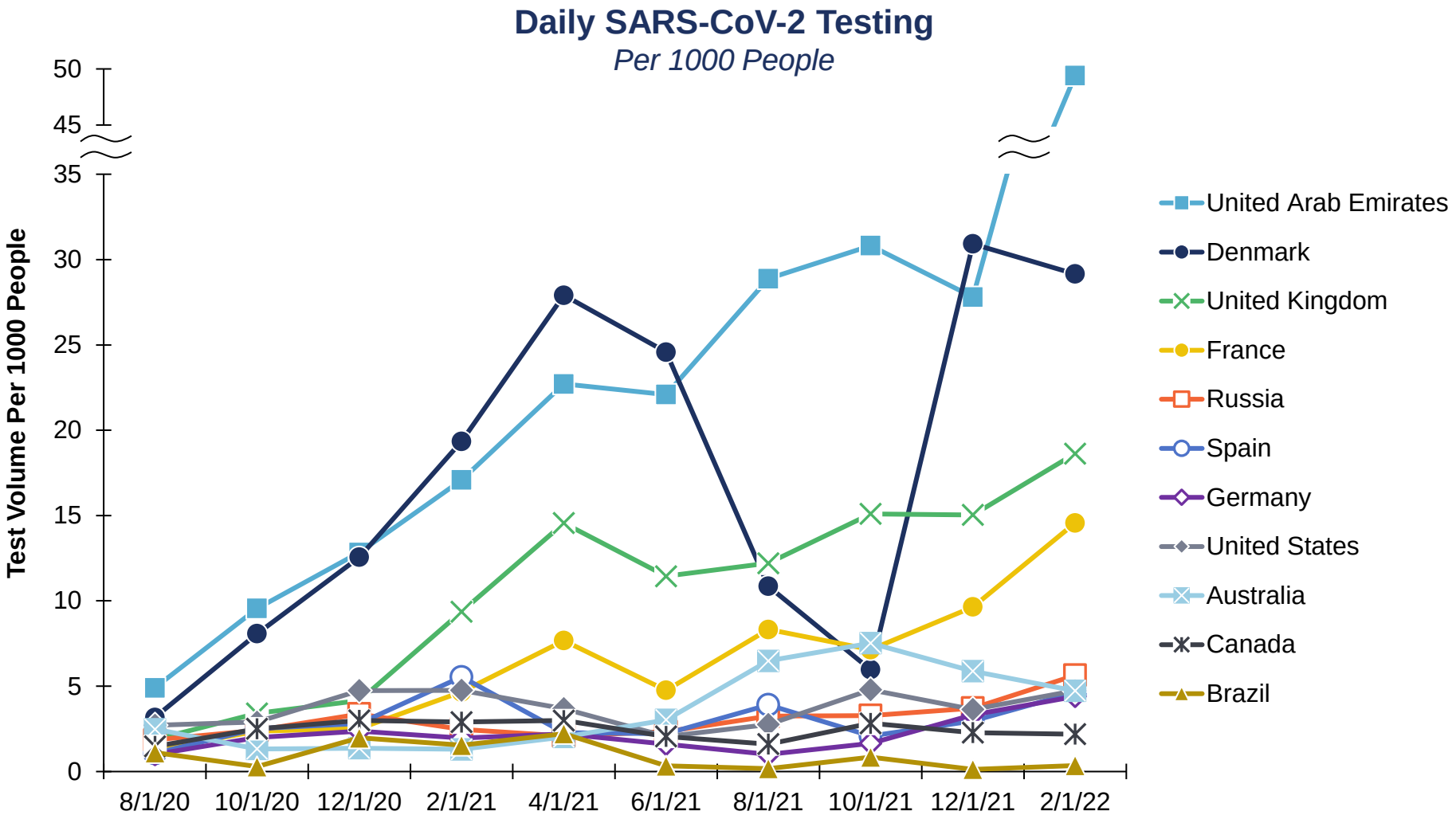
Millions (MM)



Source: Health Advances analysis, AdvaMedDx COVID Testing Supply Retrospective Report 2022.

WW SARS-CoV-2 Test Volumes

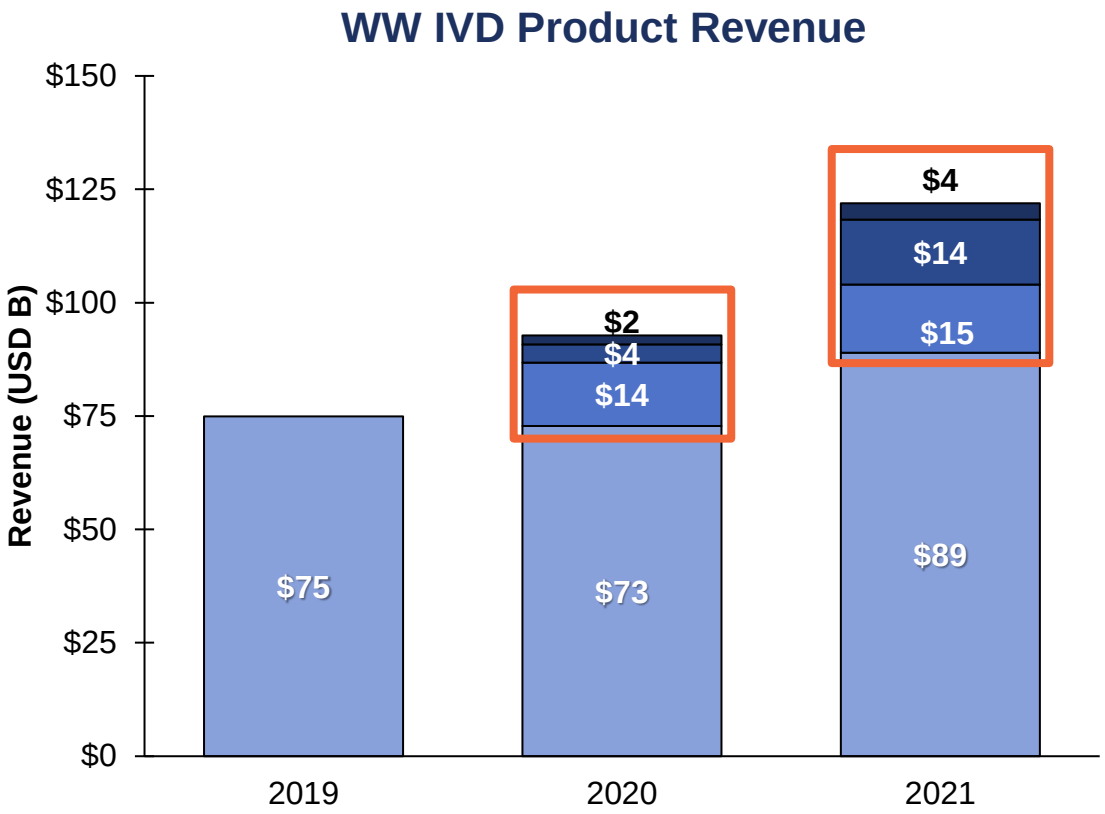
Testing rates have similarly remained at high rates throughout the world.



Note: Selected countries out of the top 25 by daily SARS-CoV-2 daily tests per 1000 people on Aug 1, 2020, are presented.
Source: Health Advances analysis, Our World in Data.

WW IVD Revenues

As a result, the overall diagnostics industry has grown significantly over the pandemic despite temporary declines in non-COVID testing segments.



	2019-2021 CAGR
SARS-CoV-2 Serology	N/A
SARS-CoV-2 Antigen	N/A
SARS-CoV-2 Molecular	N/A
Non-SARS-CoV-2	9%
Total	28%

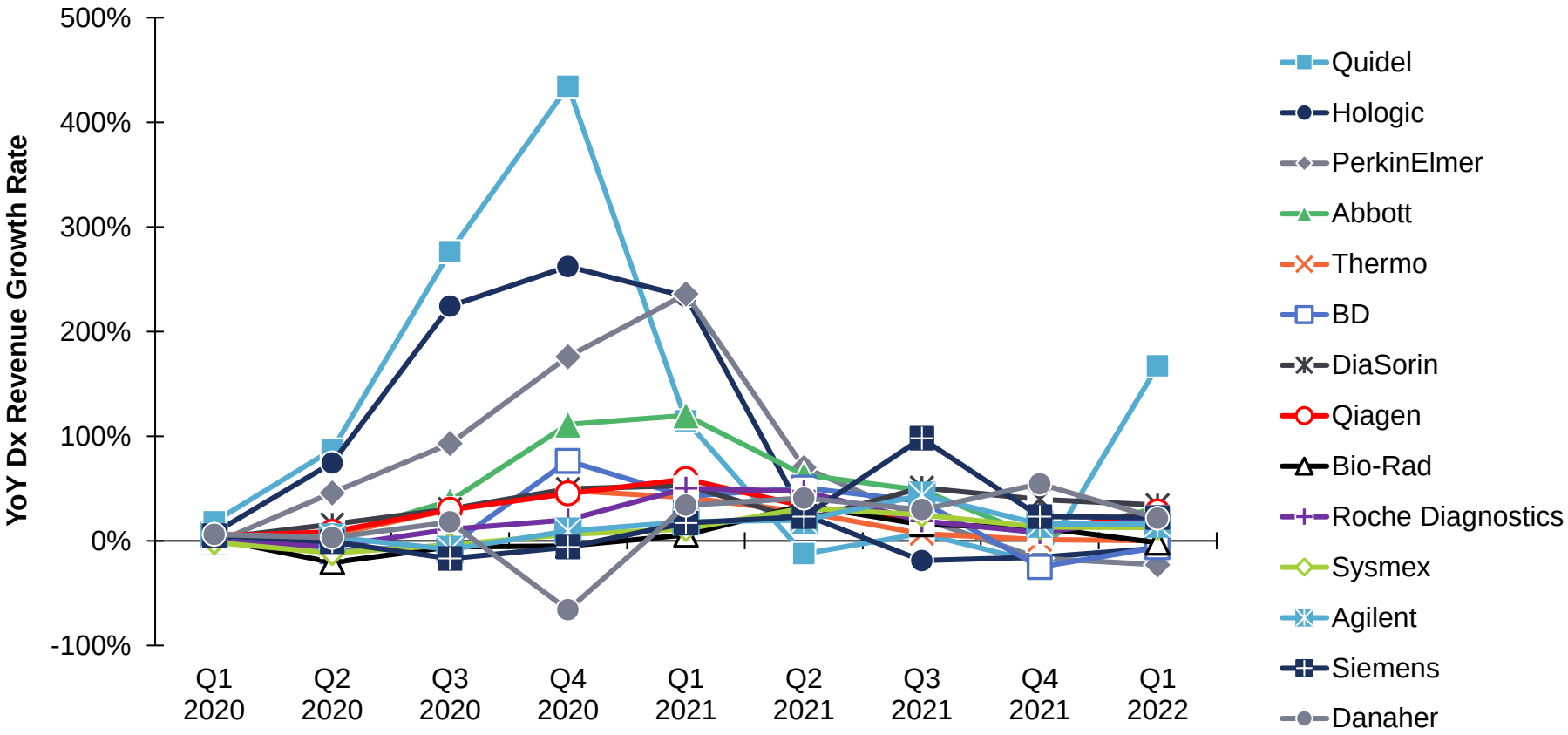
SARS-CoV-2 Tests

Source: Health Advances analysis, Kalorama.

Major OEM Growth

Major diagnostics OEMs observed very high YoY growth rates throughout 2020, with the highest growth rates among Quidel, Hologic, and PerkinElmer, with strong MDx portfolios.

Revenue Growth of Leading Dx Product Companies



Note: Companies shown are the largest companies by worldwide diagnostics revenue in 2019, except companies with no published quarterly revenues. YoY= year over year, Dx=Diagnostics, OEM= original equipment manufacturer, CY=Calendar Year.
Source: Health Advances analysis, company SEC filings.

Blockbuster Sales by Major OEMs

Several companies achieved COVID-driven blockbuster sales of >$1B for some of their diagnostic platforms and assays in 2020.

Selected Blockbuster Dx Products

			CY20 Annual Revenue*
ThermoFisher SCIENTIFIC	COVID Related Products		$6.6 B
HOLOGIC	Panther Assays		$2.3 B
Abbott	Alinity m Assays		$1.3 B
Seegene / BIO-RAD	CFX96 Assays		$0.7B

			CY20 Annual Revenue*
Abbott	BinaxNOW™		$6.1 B *(All Rapid Diagnostics)*
	ID NOW™		
QUIDEL	Sofia® Assays		$1.2 B
BD	Veritor™		$1.2 B
PerkinElmer For the Better	COVID Related Products		$1 B

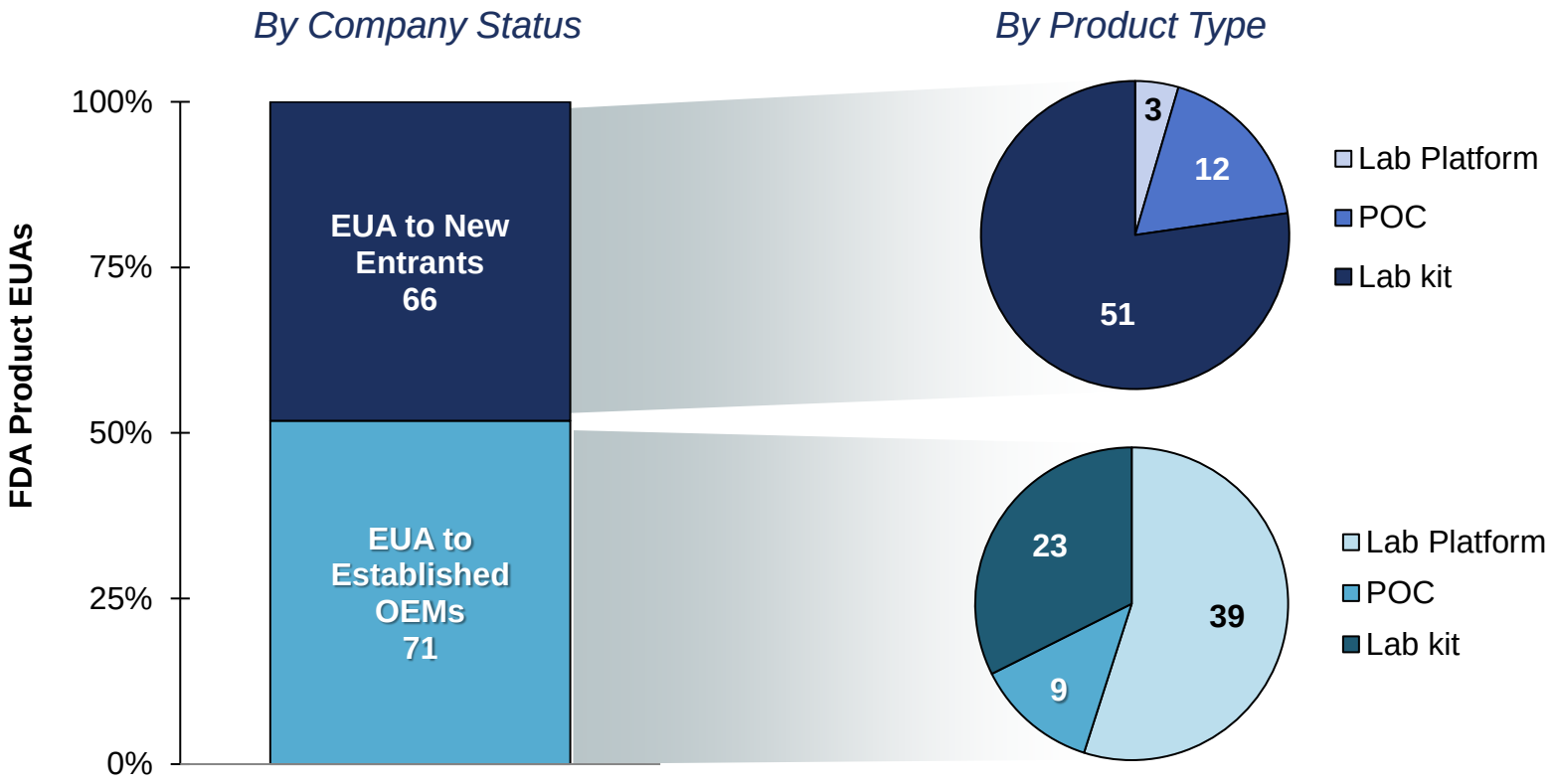
* Revenue from Q2 2020-Q1 2021, CY=Calendar Year.
Source: Health Advances analysis.

New Entrants

New entrants were also able to join the market, enabled by the favorable regulatory environment. More than 40% of EUAs were awarded to new Dx product companies.

FDA Molecular and Antigen Product EUAs

March 2020-Aug 2021



Note: Data included here are as of Aug 20, 2021. New Entrants are defined as companies for which the COVID EUA represents a first US regulatory approved/reviewed product. Lab platforms are defined as products that include both reagents and instrumentation to perform testing. Lab kits are defined as reagents only (for use on open systems). POC represents any form of point of care product defined as those with CLIA waiver for professional or home use. Additional FDA EUAs not counted here include 29 home sample collection kits and 125 single site lab tests.

Source: Health Advances analysis, FDA.

Changed Market Dynamics

Against the backdrop of this growth, the pandemic changed fundamental market dynamics.

Source: Health Advances analysis.

Heightened Dx Valuation and Investment

The diagnostics industry has traditionally played second fiddle to biopharma. COVID was a turning point that has significantly increased available capital for investment in diagnostics.

Increased Appreciation of the Value of Diagnostics across many stakeholders

Greater Investor Interest in the Diagnostic Sector

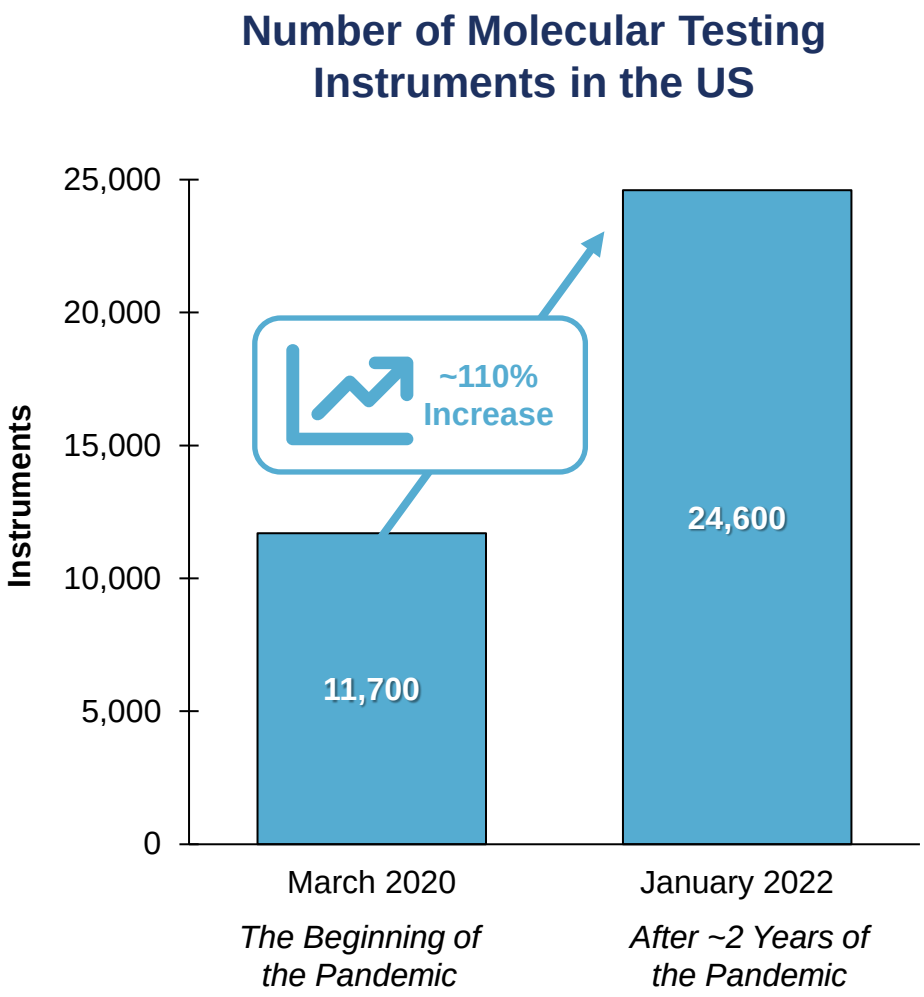
Cash Windfall for Strategic OEMs, especially those with pandemic exposure via MDx and antigen portfolios

Elevated perception and pandemic-driven revenue performance has led to **increased capital for diagnostics investment** available from both investors and strategic OEMs

Source: Health Advances analysis.

MDx Installed Base Expansion

The MDx installed base increased by ~110% to meet the urgent need for testing, disrupting capital purchasing cycles and broadening testing placement settings.



During the Pandemic, Labs Were Seeking to Add New Instruments to Support Demand

- **Disruption in Purchasing Cycles**
- **Expanded Placement Settings for MDx Testing**
- **Slowdown in Platform Consolidation within the Lab**
- **Purchasing of Back-Up Options to Keep TAT for Results Short**

The Next Several Years Will Be Affected By a Ripple Effect in Customer Purchasing Decisions

However, these instruments have seen very high utilization and may be replaced on shorter than traditional lifecycles

Source: Health Advances analysis, AdvaMedDx COVID Testing Supply Retrospective Report 2022.

Accelerating Consumerization of Testing (1 of 2)

Simultaneously, COVID-19 self-testing has gained significant traction driving demand for other, consumer-friendly workflows like remote sample collection and for other indications.

COVID-19 Has Accelerated Demand for Rapid Accessible Testing

Self Test

- Widespread access at-home COVID-19 testing
- Increased consumer familiarity with self-testing workflow
- Self-testing menus expected to expand to include other respiratory pathogens, STIs

Remote/Home Sample Collection

- Enables moderate and high complexity testing combined with ease of consumer sample collection
- May also ride tailwinds of increasing consumer familiarity with self-testing workflows

Professional POC

- Enables rapid results within the physician office, urgent care, retail and other settings

More Consumer-Driven ⟷ *More Clinician-Driven*

Source: Health Advances analysis.

Accelerating Consumerization of Testing (2 of 2)

Ellume, Everlywell, and Abbott have built large businesses based on the success of consumer-focused workflows and will likely see continued growth as offerings expand.

Example Companies Offering Consumerized Testing

Self Test

Abbott

- BinaxNow major contributor to Abbott Rapid Dx revenue growth
- $1B+ contract to provide rapid COVID-19 testing to US federal government

ellume

- Broad distribution deals with CVS, Walmart, Everlywell, Qiagen

Remote/Home Sample Collection

everlywell

- $2.9B valuation following acquisition of PWNHealth and Home Access Health
- Offers 35+ home testing kits

QuestDirect™

labcorp pixel by LabCorp

- Large menus of tests for direct purchase
- Partnerships with major retail settings (e.g., Quest & Walmart, LabCorp & Walgreens)

Professional POC

WW POC Installed Base Expansion
(000s)

		2019	Δ	2021
ID NOW	Abbott	19	+395%	75
Sofia	QUIDEL	18[1]	+390%	71
Liat	Roche	3.6	+39%	5.0[2]

[1] Installed base not reported in 2019. 2018 installed base was 17,500 systems.
[2] Installed base not reported in 2021. 2020 installed base was 5,000 and has likely grown significantly.

Source: Health Advances analysis, FDA, press releases, SEC filings.

Supply Chain Disruption

Supply chain disruptions—both pandemic and Ukraine/Russia-related—have and are continuing to lead to pressure on price, supplier selection, and labs as the end-customer.

Laboratory Supply Shortages Are Impacting COVID-19 and Non-COVID Diagnostic Testing
American Society for Microbiology, 2020

'Another year of crazy hiccups': Russia and China pose new threats to global supply chain
The Washington Post, 2022

- Shipping & raw materials costs increasing, transportation disruptions to continue through the year
- Impacting businesses broadly, including the diagnostics sector

OEMs Must Continue to Navigate Supply Chain Issues in Face of Global Uncertainties

- Uncertain macroeconomic conditions driven by ongoing pandemic and geopolitical conflict in Russia and Ukraine
- OEMs face decisions to increase prices to maintain margins across their portfolios
- Labs and hospitals face staffing shortages and lack of reliable access to testing products, driving changes to supplier selection decisions

Source: Health Advances analysis, Washington Post, GenomeWeb, ASM.

SARS-CoV-2 Test Volume Outlook

Looking towards the future, SARS-CoV-2 is expected to become endemic and evolve slowly, potentially with seasonal fluctuations like the flu.

Estimated Demand for COVID-19 Testing

Today → **3-5 Years** → **5-10+ Years**

COVID-19 Broadly Expected to Become Endemic

- Timeline to endemic state likely to vary by country, based on vaccination status, prior exposure, and emergence of novel variants

Demand for COVID-19 Testing, Including Differential Diagnosis, Expected to Continue

- Testing volume will likely decline to level of flu testing in 3-5 years
- Demand for testing that enables differential diagnosis between COVID-19, flu, and/or RSV likely to remain attractive
- Testing will continue to decentralize away from the lab as POC and home testing grow; POC antigen and POC molecular testing will battle each other for share competing on price and accuracy with molecular likely winning in developed countries and antigen winning in emerging countries

Total Test Volume in 3-5 Years	Relative Share by Test Type in 3-5 Years		
	Molecular	Antigen	Serology
↓	■ /↓	■ / ↑	■

Source: Health Advances analysis, analyst reports.

Market Dynamics Outlook

Regardless of future SARS-COV-2 test volume, many of the shifted market dynamics of COVID will persist and have ramifications for the segments with future market growth.

Tailwinds: Elevation of the Diagnostics Sector

- Widespread appreciation of the value of diagnostics
- Significant market growth and expansion
- Increased access to testing and resulting new customer channels

Headwinds: Ramifications of "Endemic Phase"

- Supply chain disruptions
- Lower overall demand for COVID testing

Outstanding Questions

- *What is the outlook for valuations of diagnostic companies?*
- *What demands will new customer types (e.g., consumers) put on diagnostic companies for products and services?*
- *Which technology(s) will win for COVID testing?*
- *How will companies that have found initial success in COVID testing stay relevant?*

Source: Health Advances analysis.

Agenda

- What new COVID-19 test types have emerged since the start of the pandemic?
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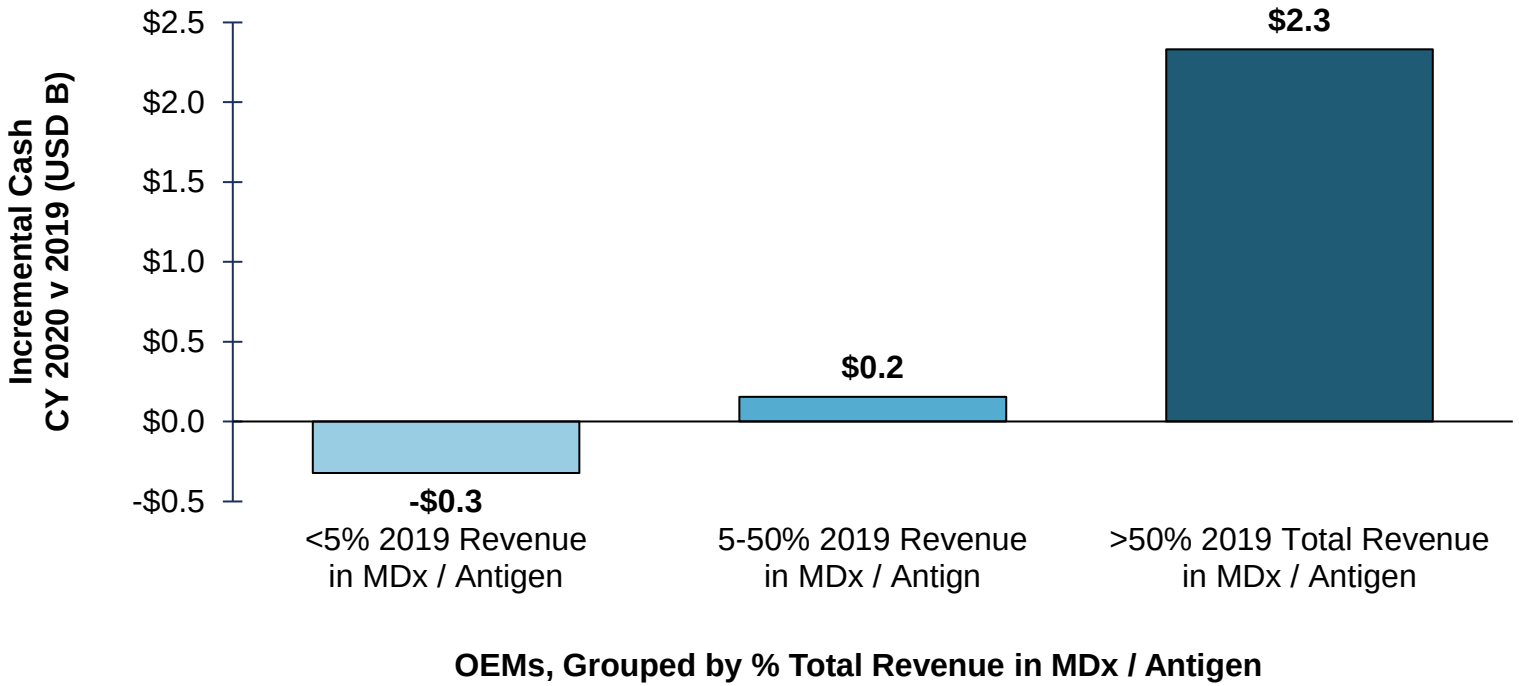
COVID Cash Investment Opportunity

Many OEMs with significant MDx and antigen portfolios have had and continue to have an unparalleled opportunity to invest in their businesses with COVID cash.

Avg. Incremental Cash Among OEMs

*2020 vs. 2019, Large Dx Companies**
By % Total Revenue in MDx / Antigen



Note: CY=Calendar Year.
* Companies and divisions included are listed here. <5% 2019 Revenue in MDx / Antigen: Siemens Healthineers (Diagnostics), Ortho Clinical Diagnostics, Sysmex. 5-50% 2019 Revenue in MDx / Antigen: Qiagen, DiaSorin, Agilent, Bio-Rad. >50% 2019 Revenue in MDx / Antigen: Abbott (Dx), BD (IDS), PerkinElmer (Dx), Thermo (Specialty Dx), Hologic, Quidel, Seegene, Danaher, Roche.
Source: Health Advances interviews and analysis, company SEC filings.

OEM Investment Priorities

As OEMs consider how to invest, priorities include disciplines with heightened importance post-COVID, such as MDx menu and POC. Other portfolio areas also remain key.

OEM Investment Priority		Rationale
MDx Menu Expansion		• Utilize expanded MDx installed base and capacity • Reach parity with MDx competitors
POC		• Capture growth of consumer-friendly workflows • Capitalize on pandemic growth of lateral flow
COVID Portfolio Mgmt.		• Extend SARS-CoV-2 revenues as long as possible • Ensure test options align with evolving epidemiology of respiratory pathogens
Ancillary Testing Components and Workflows		• Refocus on components, like pipet tips, that proved to be critical in pandemic testing supply chain • Improve workflows and sample types to differentiate in crowded field
Other Key Portfolio Areas		• Diversify and solidify competitive advantage in other portfolio areas that are critical for long-term growth

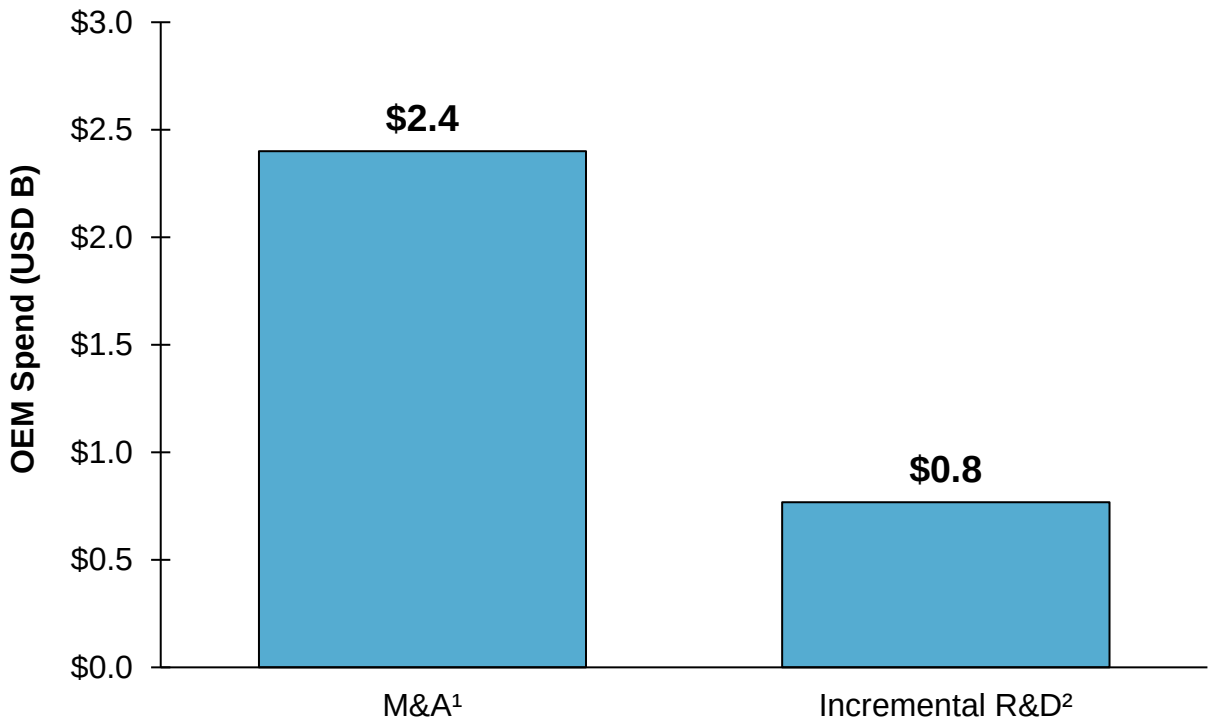
Source: Health Advances interviews and analysis.

Focus on COVID Cash M&A

OEMs have largely chosen to invest in these areas with M&A as the primary mechanism, rather than internal R&D.

Incremental R&D vs. M&A Spend

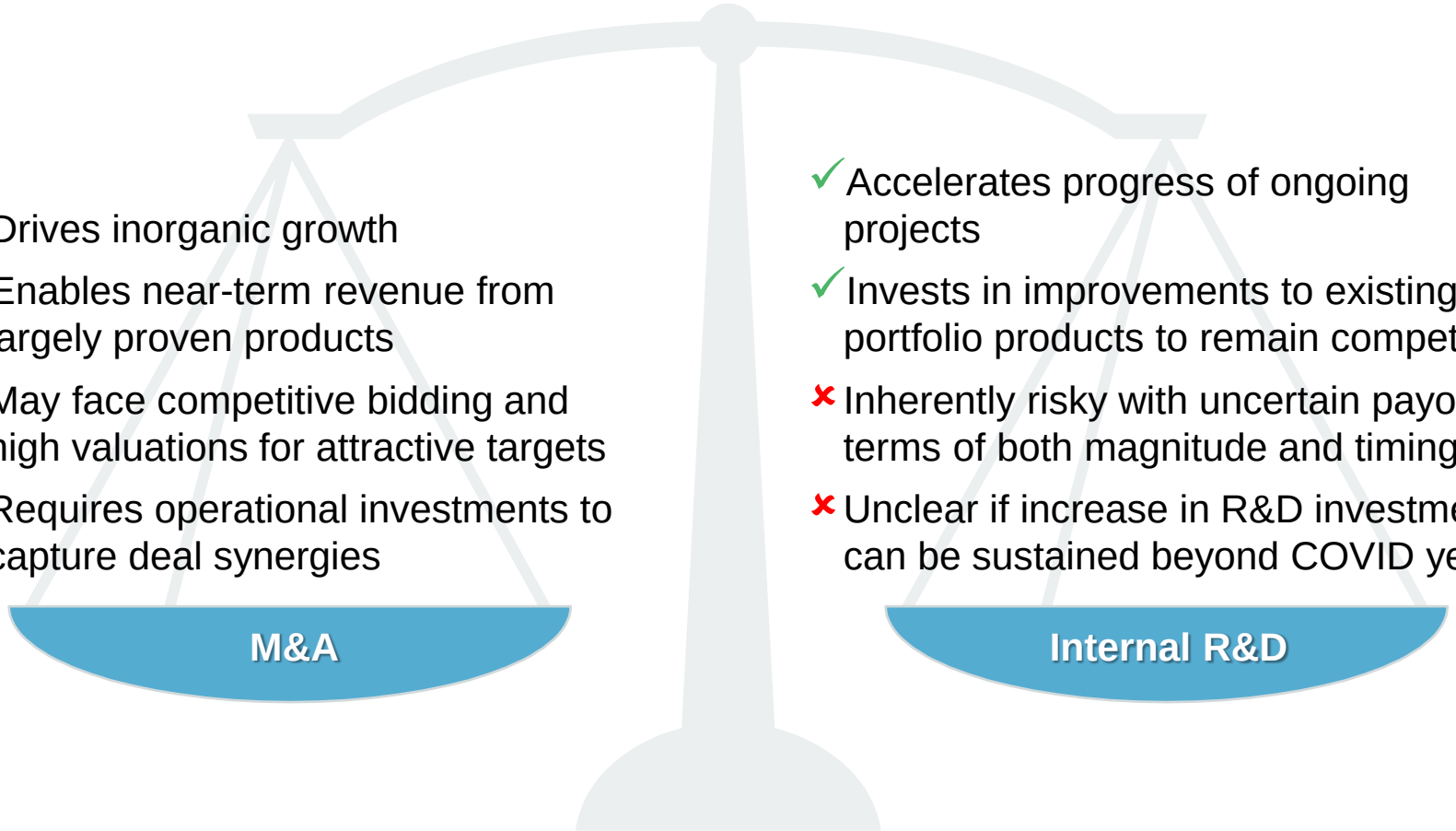
H1 2021, Large Dx OEMs with >50% 2019 Revenue in MDx / Antigen



[1] M&A is the total Dx related deal value between Jan 1, 2021-Jun 30, 2021 among OEMs with >50% 2019 revenues in MDx / Antigen.
[2] Incremental R&D is H1 2021 Dx R&D expense minus H1 2020 Dx R&D expense for the OEMs with >50% 2019 revenues in MDx / Antigen.
Note: CY=Calendar Year
Source: Health Advances analysis, company filings and reports.

M&A vs. Internal R&D Trade-Offs

M&A offers the advantage of enabling rapid inorganic growth with investment in more proven products, while internal R&D is inherently riskier with uncertain returns.



Source: Health Advances interviews and analysis.

Key M&A Segments

Some OEMs have invested heavily through M&A in their portfolio beyond Dx, like both Thermo and PerkinElmer. Other M&A has highlighted continued interest in POC and MDx.

Acquirer	Target	POC	MDx	Other Portfolio	Deal Value	Target Portfolio
ThermoFisher SCIENTIFIC	PPD			✓	$17.4B	• Contract clinical research and lab services for drug development
PerkinElmer	BioLegend®			✓	$5.25B	• Antibodies and related reagents
DiaSorin	Luminex		✓		$1.8B	• Protein and molecular multiplexing instruments and reagents for research and clinical Dx testing
Roche	GenMark Dx		✓		$1.8B	• Syndromic testing • Respiratory pathogen detection • Order to reporting workflow
HOLOGIC	MOBIDIAG A Hologic Company	✓	✓		$795M	• Infectious disease molecular diagnostics
ThermoFisher SCIENTIFIC	MESA BIOTECH	✓	✓		$550M	• Rapid POC PCR detection of infectious diseases
HOLOGIC	BIO THERANOSTICS		✓		$230M	• PCR-based early-stage breast cancer dx • PCR-based all metastatic cancer dx

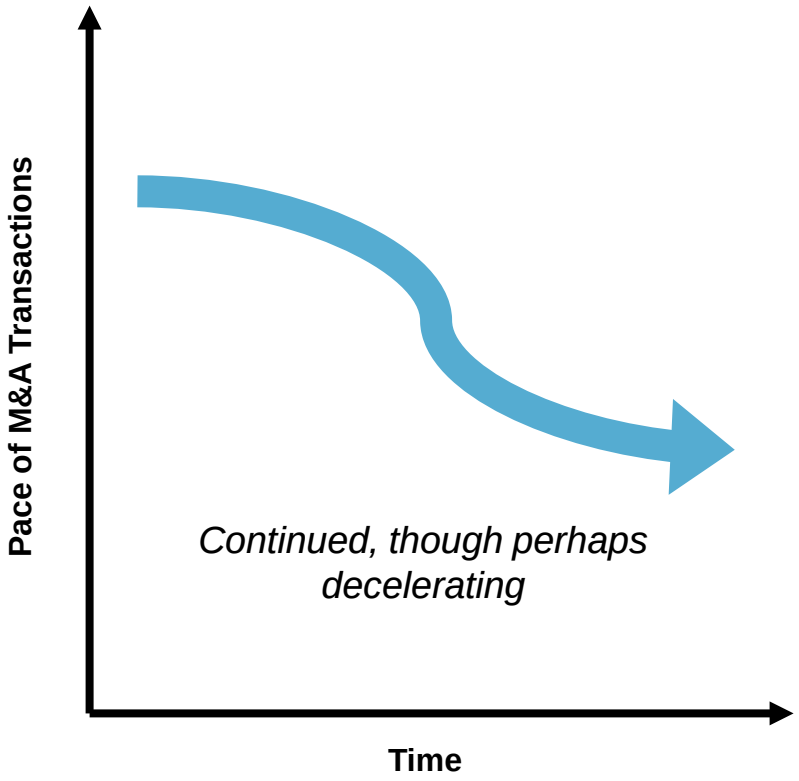
Multiples of 5X-15X of 2020 revenue

Note: CY=Calendar Year
Source: Health Advances interviews and analysis, BioMed Tracker, company websites.

Outlook for Continued M&A

M&A will likely continue under the current financial conditions, though perhaps at a slower pace.

Pace of M&A Transactions
Forward-Looking



- Established OEMs continue to have high capital availability with large amounts of cash persisting on their balance sheets
- These companies are experiencing pressure from boards to reduce cash and make inorganic growth investments
- In addition, the IPO market is no longer a promising exit strategy for new entrants, thus creating an M&A opportunity for OEMs
  - M&A is more attractive exit option for new entrants given recent fall in public market valuations
  - As a result, potential deal/transaction values have also decreased and thus become more attractive to the larger OEM buyers

Source: Health Advances interviews and analysis, company financials, conference call transcripts.

Potential Buyers and Targets

Many of the large diagnostics OEMs represent key potential buyers for continued M&A. Large companies as well as midsize and new entrants may be targets.

Potential Buyers

Abbott
BD
Roche
DANAHER
PerkinElmer
ThermoFisher SCIENTIFIC
HOLOGIC
LGC
illumina
Agilent Technologies
QUIDEL
QIAGEN
BIOMÉRIEUX

☐ OEM has Pursued >$2B+ M&A Since Pandemic Onset*

Potential Targets

Big Dx
Did not benefit from COVID

SIEMENS Healthineers
sysmex

Midsize Dx
Some COVID cash, but may pursue M&A due to high valuations

Meridian Bioscience, Inc.
Seegene
SEKISUI
OraSure Technologies, Inc.
Copan
ELITechGroup
STRECK

New Entrants
Non-exhaustive list

PlexBio
LUCIRA
lumiraDx
cue
SEASUN BIOMATERIALS
CO-DIAGNOSTICS INC.
Quanterix
1DROP DIAGNOSTICS
ellume
visby medical
Oxford NANOPORE Technologies
GENCURIX
BillionToOne

* Accounts for M&A deals of PerkinElmer/BioLegend, ThermoFisher Scientific/PPD, and Quidel/OrthoClinical Diagnostics.
Source: Health Advances interviews and analysis.

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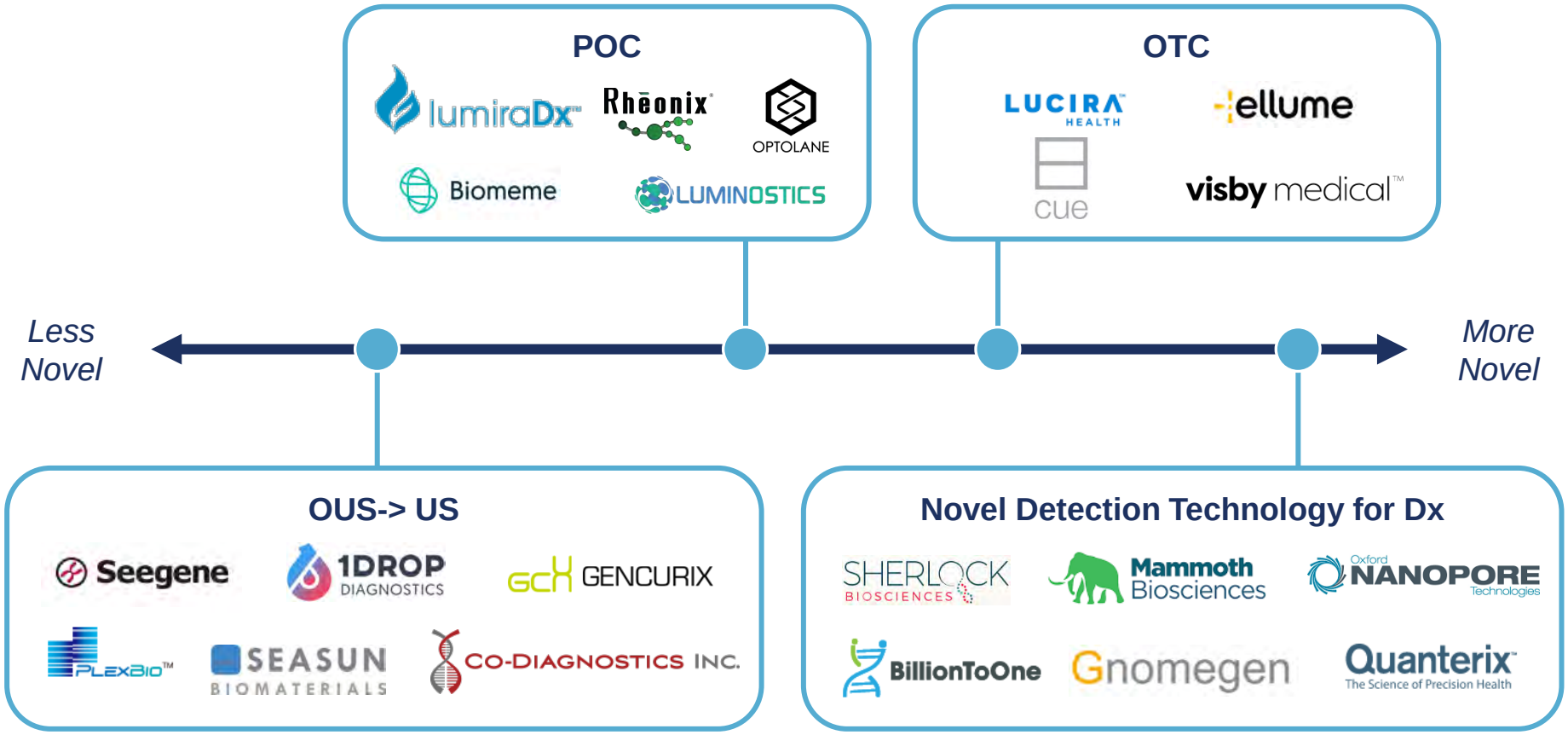
- What questions remain outstanding?

COVID Dx New Entrants

A wide range of companies gained early market entry thanks to COVID EUAs.

Spectrum of Technical Innovation Among New Entrants



Note: EUA=emergency use authorization.
Source: Health Advances interviews and analysis, company websites.

Expanded Capabilities and Presence

New entrants also obtained new manufacturing capabilities, new capital, new partners, or expanded to new markets due to increased investor interest and strong market demand.

New Funding

- cue: Closed $235M financing round
- LUCIRA: IPO with $176M proceeds
- Oxford NANOPORE Technologies: IPO with £350M proceeds
- lumiraDx: Achieved public listing through merger with a SPAC*

Build Out of Manufacturing Capacity

- ellume: Built New 180K sq ft mfg facility in Maryland
- cue: Built new capacity to supply 6MM tests / month
- LUCIRA: Built new facility in Dominic Republic
- lumiraDx: Built new facility in Glasgow to product 28MM COVID tests / month

New Partners

- SHERLOCK BIOSCIENCES / IDT INTEGRATED DNA TECHNOLOGIES: Sherlock established strategic partnership with IDT to manufacture CRISPR SARS-CoV-2 Diagnostic
- Oxford NANOPORE Technologies: Nanopore partners with UK government to roll out sequencing based COVID testing
- ellume / QIAGEN: Ellume extended strategic partnership with Qiagen to build COVID antibody test on QIAreach™ platform

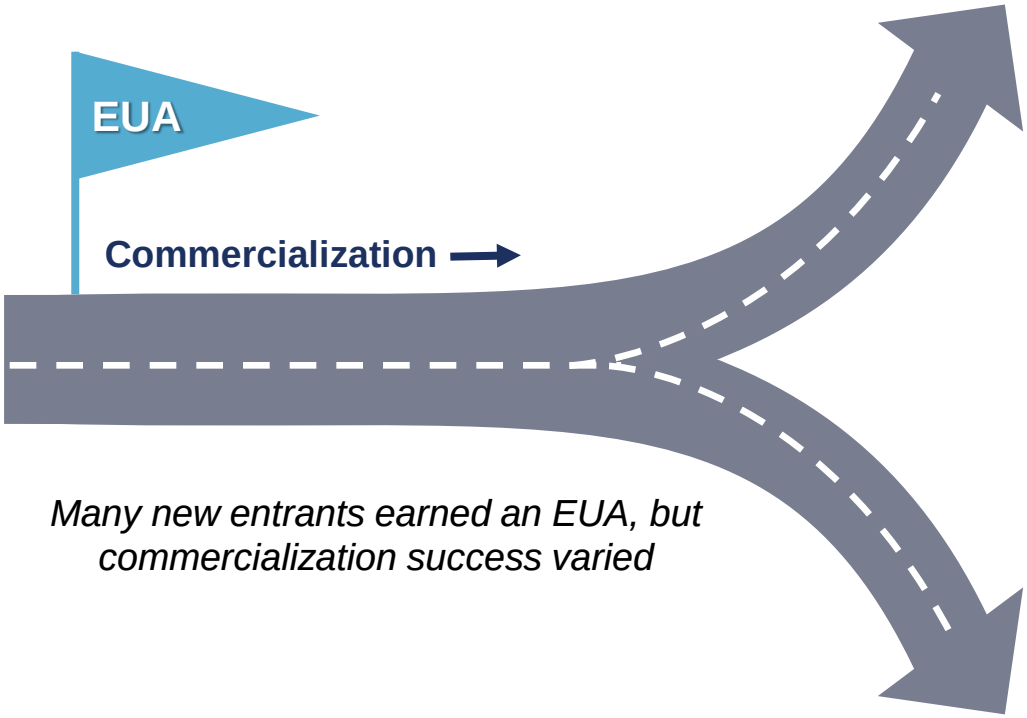
Geographic Expansion

- GENETRON 泛生子: Cancer Dx company obtained EUA to claim "international recognition" on website
- GCX GENCURIX: GCX obtained first regulatory clearance with FDA through its SARS-CoV-2 Test
- Seegene: Seegene secured multi-million deals in public tenders in Italy, Scotland and Germany

Note: HTP=high throughput. SPAC: special purpose acquisition company.
Source: Health Advances analysis, company website and press releases.

Mixed Outcomes

Despite receiving an EUA, many new entrants did not gain significant traction in commercialization or struggled to scale manufacturing/logistics.



Many new entrants earned an EUA, but commercialization success varied

More Successful New Entrants

- Strong volume uptake was the experience of outlier new entrants, not the majority
- These entrants often marketed a disruptive product directly to consumers, rather than incumbent clinical Dx customers
- Some that were regarded as successful, like Cue, are now pursuing layoffs

Less Successful New Entrants

- EUA demonstrated basic regulatory capabilities, but many faced challenges scaling operations and supply chains
- After EUA and launch, lack of subsequent press releases documenting sales suggests minimal uptake

Source: Health Advances interviews and analysis, 360Dx, company websites and press releases.

Headwinds for New Entrants

Today, these new entrants face many long-term headwinds, which create challenging market conditions, operating capabilities, and access to capital.

Wide Availability of COVID Tests Across Markets

- Lab, POC, OTC, Home Sample Collection

HOLOGIC, QUIDEL, Abbott, LabCorp, Roche, LUCIRA, binx

Rising Customer Requirements

- Menu, Pricing, Reimbursement

Declining Covid Test Demand

- Future endemic testing rate <20% of peak test demand

Investment in Broader Company Capabilities

- Manufacturing, regulatory, logistics, sales

Difficult Macro-Economic Environment

- Inflation and CPI
- Supply Chain
- Tight labor supply

Capital Markets Pressure

- Access to capital for public and private companies

Source: Health Advances interviews and analysis.

Headwinds Impact

These headwinds are causing many entrants to revert to pre-COVID long-term strategies. More successful entrants are seeking to use COVID as a springboard for future growth.

- Menu expansion with CE Marks for NT-proBNP, D-Dimer, HbA1c
- *"R&D efforts to expand our test menu for 30+ diagnostic tests for common health conditions gives us confidence in our opportunities for non-COVID growth for many years"* – Lumira Dx CEO

- De Novo submission for COVID-19 FDA IVD approval
- *"Together with BioReference, Cue can empower healthcare providers with the tools and insights they need to make better-informed care decisions together with their patients, today and into the future" – Cue Health CEO*

- Website now focused on Unity™ cfDNA testing for prenatal genetic testing with no mention of COVID-19

- Expanding offering of tests and digital services
- *"Everlywell launches new food and celiac disease testing" – PR Newswire, June 27, 2022*
- *"Everlywell, a leading digital health company, has acquired PWNHealth and Home Access Health Corporation and formed parent company Everly Health" – PR Newswire, March 24, 2022*

Source: Health Advances interviews and analysis.

Exit Strategy and Long-Term Planning

Exit strategy planning has become a more acute question given changing access to capital and deflating public IPO markets.

IPO

Unfavorable market conditions may require companies to delay pursuit of IPO in favor of alternative strategies

M&A

Position company for acquisition by strategic or institutional buyer

Fundraising from Private Investors

Wait out current market conditions until situation improves

Source: Health Advances interviews and analysis.

M&A as Exit Strategy

For many new entrants, M&A is a promising exit strategy as potential acquirers are motivated by significant cash on hand and more favorable valuations.

Large Cash Reserves

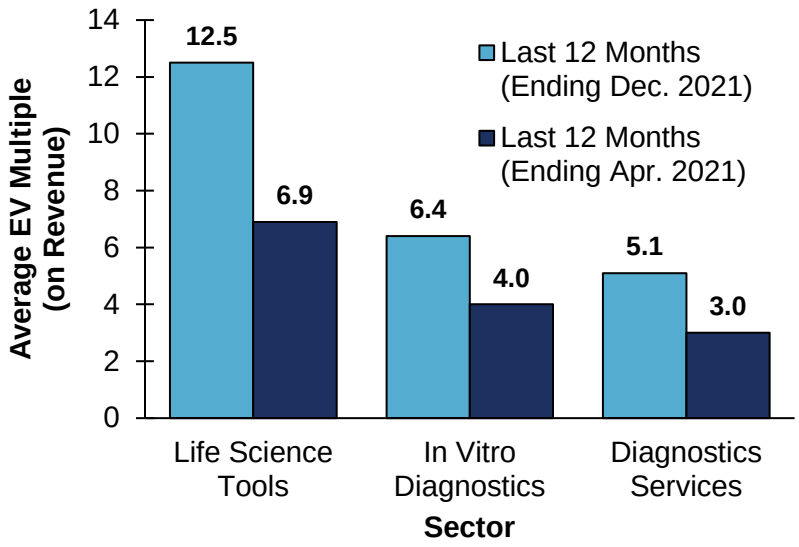
Recent Acquisition Activity

HOLOGIC®	Closed five acquisitions in 2021, including Mobidiag for $795MM
Roche	Acquisition of Genmark ($1.8B)
QUIDEL	Acquisition of Ortho-Clinical Diagnostics ($6B)

"With mergers worth more than $22B currently awaiting close, and plenty of big medtechs sitting on Covid-based fortunes, the sector could make another very strong showing in 2022" – Elizabeth Cairns, Evaluate Vantage

Lower Valuations

Average Dx EV Multiples on Revenue



Source: Health Advances analysis, Evaluate Vantage January 2022, Crosstree Capital Diagnostics & Tools Blue Book.

M&A Positioning

New entrants can make themselves attractive to potential acquirers by bolstering internal capabilities and articulating a compelling story on product value and quality.

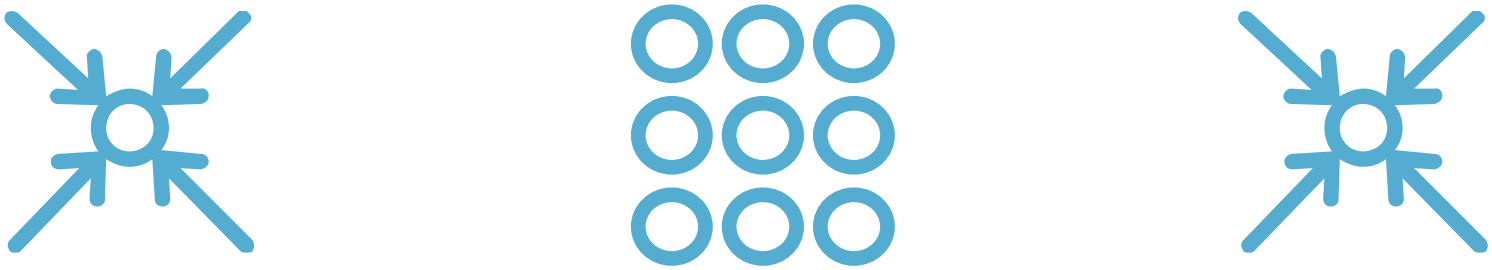
Factor	Key Considerations
Internal Capabilities and Expertise	• Plan for key talent retention • Acknowledge and plan for key risks
Value Proposition and Differentiation	• Articulate realistic product launch roll-out strategy and planning • Show clear differentiation of core business from potential acquirer • Highlight how strategy is niche, focused, and reasonable
Product Quality	• Demonstrate mitigated regulatory risk for full FDA approvals • Show robust manufacturing QC controls (e.g., no risk of product recalls)

Source: Health Advances interviews and analysis.

Outlook for New Entrants

If new entrants can navigate the increasingly competitive M&A environment, the trend towards consolidation is likely to continue.

Pre-Pandemic → *Pandemic* → *Endemic*



- Initially consolidated market with a handful of dominant players

- Many new entrants leveraging the pandemic for long-term success
- Some have succeeded in establishing a competitive position, while others have failed due to growing competitive intensity

- Return to consolidation as new entrants position successfully for acquisition

Source: Health Advances interviews and analysis.

Agenda

- What new COVID-19 test types have emerged since the start of the pandemic?
- What macro trends has the industry experienced? What changes in COVID testing are expected moving forward?
- How has the pandemic impacted established OEM activities and investment?
- What types of new entrants emerged during the pandemic and how will they fare long-term?
- ***What questions remain outstanding?***

Outstanding Questions

When will the pandemic end and the endemic phase begin?

What is the future for COVID testing itself?

Is the current perception of the value that diagnostics provide sustainable?

Is the current level of diagnostic investment sustainable?

How will COVID cash best be invested going forward?

What have we learned as an industry over the course of the pandemic?

Source: Health Advances interviews and analysis.

AACC Reception

We cannot wait to further discuss the pandemic's long-term implications with you at Health Advances' AACC Reception. All are welcome.

HEALTH ADVANCES

Annual AACC
Cocktail Reception and Panel

Now What?
The Dx World Beyond COVID

Come Debate with Our Panelists . . .

- If the perception of Dx value and investment is sustainable
- How new players (in digital, point of care, lab and precision medicine) are reshaping the market
- Where COVID cash will be best invested
- *And many more topics*

Our panelists will be:

- Jeff Luber (Binx, CEO)
- Josh Pulido (LumiraDx, Director, Global Product Marketing)
- Valerie Dixon (Morgan Stanley, Managing Director)
- Yves Dubaquie (Perkin Elmer, Senior Vice President of Diagnostics)
- Fernando Chaves (Siemens, Global Head of Hematology)

LINK TO REGISTER

When:
Tuesday, July 26, 2022
Cocktails at 5:30PM CDT,
Panel at 6:30PM CDT

Where:
The Chicago Firehouse Restaurant

1401 S Michigan Ave
Chicago, IL 60605

We will also have a virtual attendance option. Details will follow for all registered guests.

Experienced Diagnostics and Life Science Research Tools Leadership

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 PhD in Immunology from the Sackler School of Biomedical Sciences at Tufts University.

Gary Gustavsen
Partner

- 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.

Kristen Amanti, PhD
Partner

- 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.

Daniela Hristova-Neeley, PhD, MBA
Vice President

- 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.

Experienced Diagnostics and Life Science Research Tools Leadership

Peter Origenes
Vice President

- Peter joined Health Advances in 2019 bringing over 30 years of healthcare experience including corporate executive, principal investor and strategy consulting positions across diagnostics, life science research products, medical devices and biopharmaceuticals. With an integrated view of technology commercialization, medical markets and corporate capability,
- Prior to joining Health Advances, Peter held executive positions at Becton Dickinson, GE Healthcare and Ortho Clinical Diagnostics. Previously, was a Partner with Radius Ventures, a consultant with The Wilkerson Group and Bain, and held business development, marketing and sales positions with Schering-Plough, Genentech and Roche Laboratories, respectively.
- Peter holds a Master of Science in Industrial Administration from the Tepper School at Carnegie Mellon University, and Bachelors degrees in Genetics and History from the University of California at 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.

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.

Chris Karras
Vice President

- Over the past 25 years, Chris has worked closely with leading companies across the diagnostics and biopharma industries on a broad array of strategy issues. He brings diverse insights from his experience to help leaders make tough decisions in the face of uncertainty.
- Prior to joining Health Advances, Chris served as a Director in Global Strategic Marketing in the Rapid Diagnostics Division of Abbott Laboratories.
- Chris's work focuses developing strategies
- Prior to Abbott, Chris spent 15 years in management consulting, primarily with Arthur D. Little as a Principal in their Healthcare and Strategy Practices. Chris also served as a Director in Strategy Development at Pharmacia (now Pfizer) and was an Equity Analyst at Prudential covering the specialty pharmaceuticals sector.
- Chris holds a BBA degree from the University of Iowa and an MBA from the Booth School of Business at the University of Chicago.