

RADx Tech: 2-year update and future perspective

RADx Tech Webinars

May 31th, 2022

Bruce J. Tromberg, Ph.D.

Director

National Institute of Biomedical Imaging and Bioengineering

RADx Tech Program Leads @NIH: Jill Heemskerk, Tiffani Lash, Todd Merchak, Mike Wolfson, Doug Sheeley, David George, Bill Heetderks, Shawn Mulvaney, Matt McMahon, Felicia Qashu, Tony Kirilusha, Andrew Weitz, Krishna Juluru, Taylor Gilliland, Jennifer Jackson, Ray MacDougall, Patty Wiley, Chris Cooper, **@Deloitte:** Mark Snyder, Adrienne Lane, Michael Walker, Frances Fernando

RADx Tech: Looking Back



Francis Collins

April 16

Call with Sen Alexander

- Can we get more testing?
- Oh, a Shark Tank!

April 20

ZOOM with POCTRN

- Can everyone change direction?
- Deliver millions of tests by fall!

April 24

4th Congressional Supplement

- 1.5 Billion to NIH for testing
- Unusual Opportunity

April 29

Press conference, Funnel Open!

- 400 applications started in 24 hours
- The race begins

The Washington Post

Opinion: We need more covid-19 tests. We propose a 'shark tank' to get us there.

Opinion by **Lamar Alexander** and **Roy Blunt** Add to list

April 20, 2020 at 8:46 p.m. EDT

Lamar Alexander (R-Tenn.) is chairman of the Senate Health, Education, Labor and Pensions Committee. Roy Blunt (R-Mo.) is chairman of the Senate's health appropriations subcommittee.

There is no safe path forward to combat the novel coronavirus without adequate testing. To contain covid-19 and persuade

under this paragraph in this Act, not less than \$500,000,000 shall be transferred to the "National Institutes of Health—National Institute of Biomedical Imaging and Bioengineering" to accelerate research, development, and implementation of point of care and other rapid testing related to coronavirus: *Provided further*, That

134
 PUBLIC LAW 116-139—APR. 24, 2020
 this Act, not less than \$306,000,000 shall be transferred to the "National Institutes of Health—National Cancer Institute" to develop, validate, improve, and implement serological testing and associated technologies for the purposes specified under this paragraph in this Act: *Provided further*, That of the amount appropriated under this paragraph in this Act, not less than \$500,000,000 shall be transferred to the "National Institutes of Health—National

mental and non-governmental entities to research, develop, and implement the activities outlined in this proviso: *Provided further*, That funds in the preceding proviso may be transferred to the accounts of the Institutes and Centers of the National Institutes of Health (referred to in this paragraph as the "NIH") for the purposes specified in the preceding proviso: *Provided further*, That the transfer authority provided in the preceding proviso is in addition to all other transfer authority available to the NIH: *Provided further*, That of the amount appropriated under this paragraph in this Act, not less than \$1,000,000,000 shall be available to the Biomedical Advanced Research and Development Authority for necessary expenses of advanced research, development, manufacturing, production, and purchase of diagnostic, serologic, or other COVID-19 tests or related supplies, and other activities related to COVID-19 testing at the discretion of the Secretary: *Provided further*, That of the amount appropriated under this paragraph in this Act, \$22,000,000, shall be transferred to the "Department of Health and Human Services—Food and Drug Administration—Salaries and Expenses" to support activities associated with diagnostic, serological, antigen, and other tests, and related administrative activities: *Provided further*, That the amount appropriated

NIH National Institutes of Health
 Turning Discovery Into Health

EMBARGOED FOR RELEASE: 11:00 a.m. ET on Wednesday, April 29, 2020
Contact: NIH Office of Communications and Public Liaison
 NIH News Media Branch
 301-496-5787

NIH mobilizes national innovation initiative for COVID-19 diagnostics
Initiative aims to speed delivery of accurate, easy-to-use, scalable tests to all Americans

The National Institutes of Health today announced a new initiative aimed at speeding innovation, development and commercialization of COVID-19 testing technologies, a pivotal component needed to return to normal during this unprecedented global pandemic. With a \$1.5 billion investment from federal stimulus funding, the newly launched Rapid Acceleration of Diagnostics (RADx) initiative will infuse funding into early innovative technologies to speed development of rapid and widely accessible COVID-19 testing. At the same time, NIH will seek opportunities to move more advanced diagnostic technologies swiftly through the development pipeline toward commercialization and broad availability. NIH will work closely with the U.S. Food and Drug Administration, the Centers for Disease Control and Prevention and the Biomedical Advanced Research and Development Authority (BARDA) to advance these goals.

The stimulus investment supercharges NIH's strong research efforts already underway focused on prevention and treatment of COVID-19, including the recently announced planned [Accelerating COVID-19 Therapeutic Interventions and Vaccines](#) public-private partnership to coordinate the international research response to the pandemic.

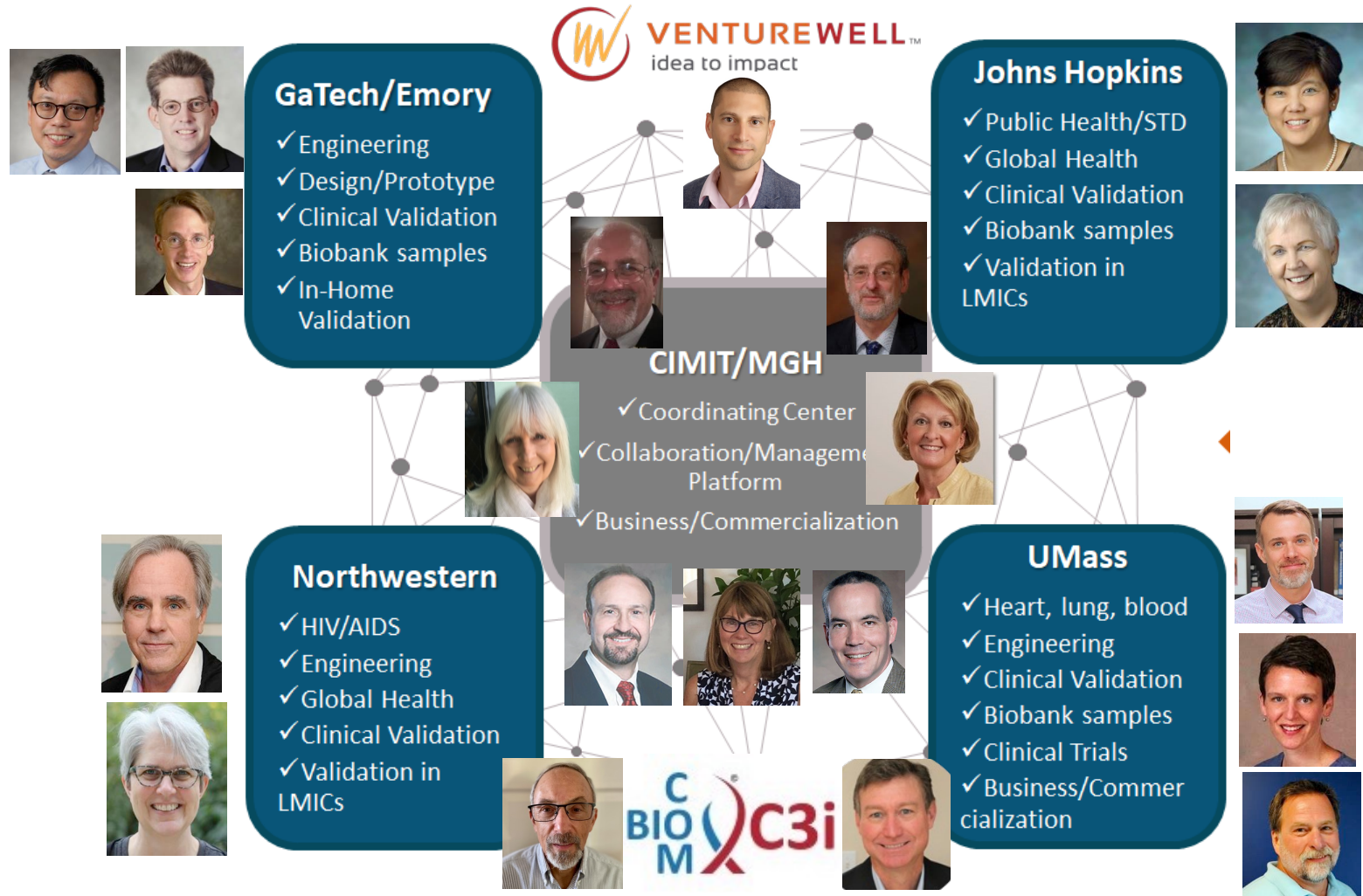
"We need all innovators, from the basement to the boardroom, to come together to advance diagnostic technologies, no matter where they are in development," said NIH Director Francis S. Collins, M.D., Ph.D. "Now is the time for that unmatched American ingenuity to bring the best and most innovative technologies forward to make testing for COVID-19 widely available."

As part of this initiative, NIH is urging all scientists and inventors with a rapid testing technology to compete in a national COVID-19 testing challenge for a share of up to \$500 million over all phases of development. The technologies will be put through a highly competitive, rapid three-phase selection process to identify the best candidates for at-home or point-of-care tests for COVID-19. Finalists will be matched with technical, business and manufacturing experts to increase the odds of success. If certain selected technologies are already relatively far along in development, they can be put on a separate track and be immediately advanced to the appropriate step in the commercialization process. The goal is to make millions of accurate and easy-to-use tests per week available to all Americans by the end of summer 2020, and even more in time for the flu season.

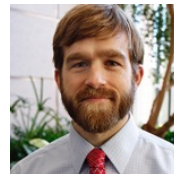
Point-of-Care Technologies Research Network (POCTRN)

NIBIB National Network: NHLBI, NIAID, NCCIH, FIC, OBSSR, OAR, ODP

Established 2007, Expanded 2020: >900 RADx experts & contributors



Tiffany Lash

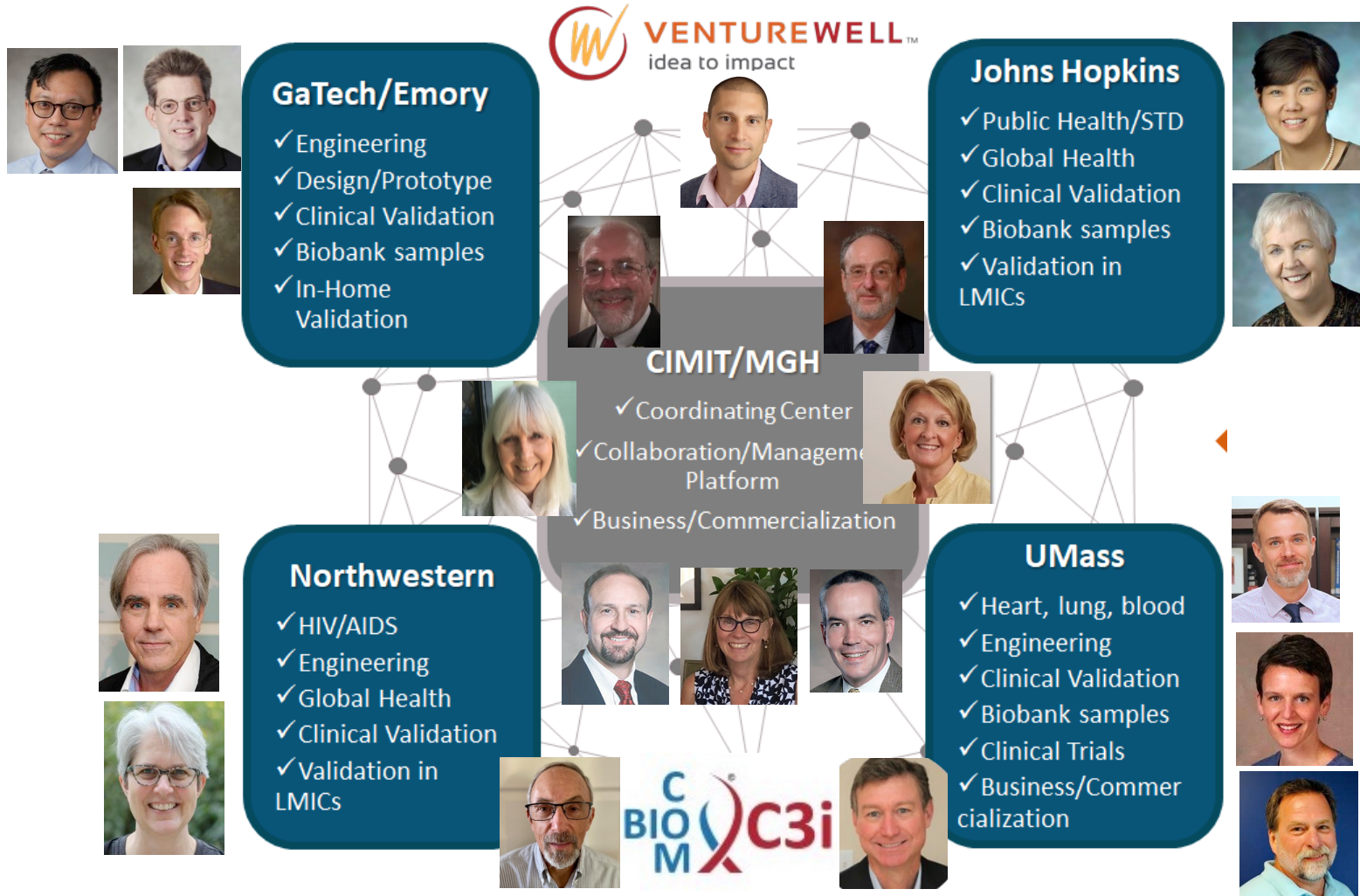


Todd Merchak

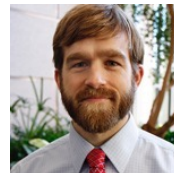
Rapid Acceleration of Diagnostics (RADx Tech)

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Todd Merchak



Rapid Acceleration of Diagnostics (RADx Tech)

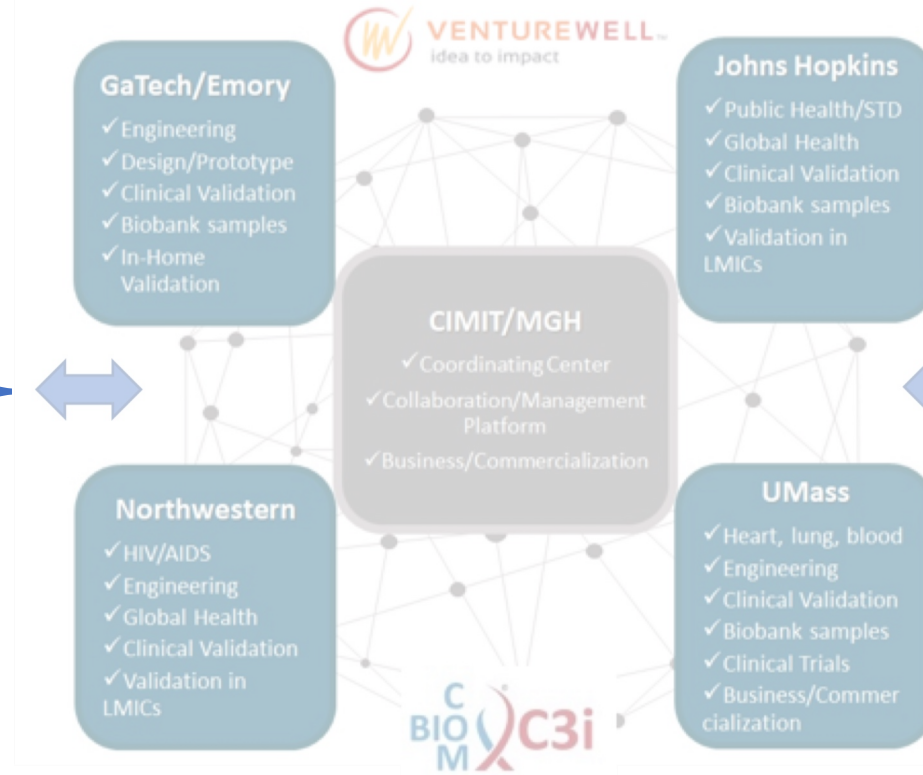
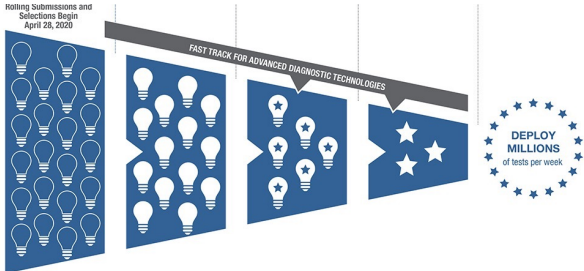
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Innovation, Manufacturing, Distribution, Guidance, Regulatory

Innovation Funnel

824 Applications, 50 phase 2 awards



<https://www.poctrn.org>



>100 projects complete,
>10,000 participants

Validation Core



Standard Trial Design, Digital Health Platform, Single IRB, Center Network

Clinical Studies Core



Supply chain, Manufacturing, User Community, *whentotest.org* My COVID Toolkit

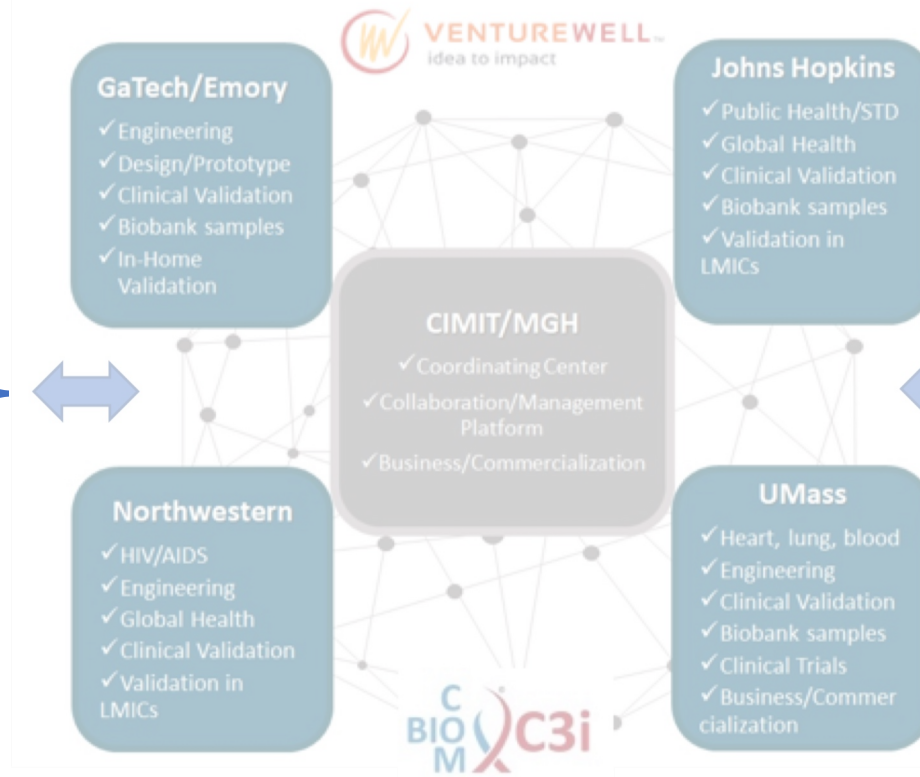
Deployment Core

Rapid Acceleration of Diagnostics (RADx Tech)

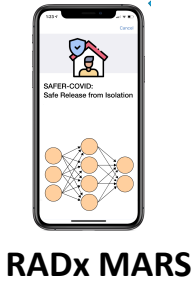
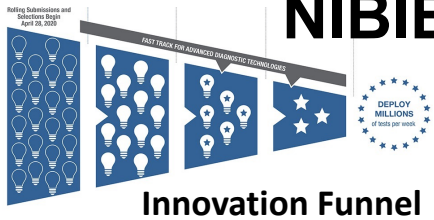
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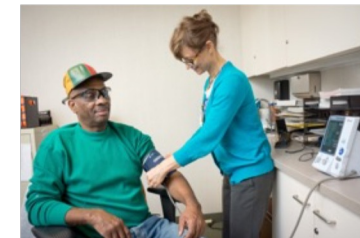


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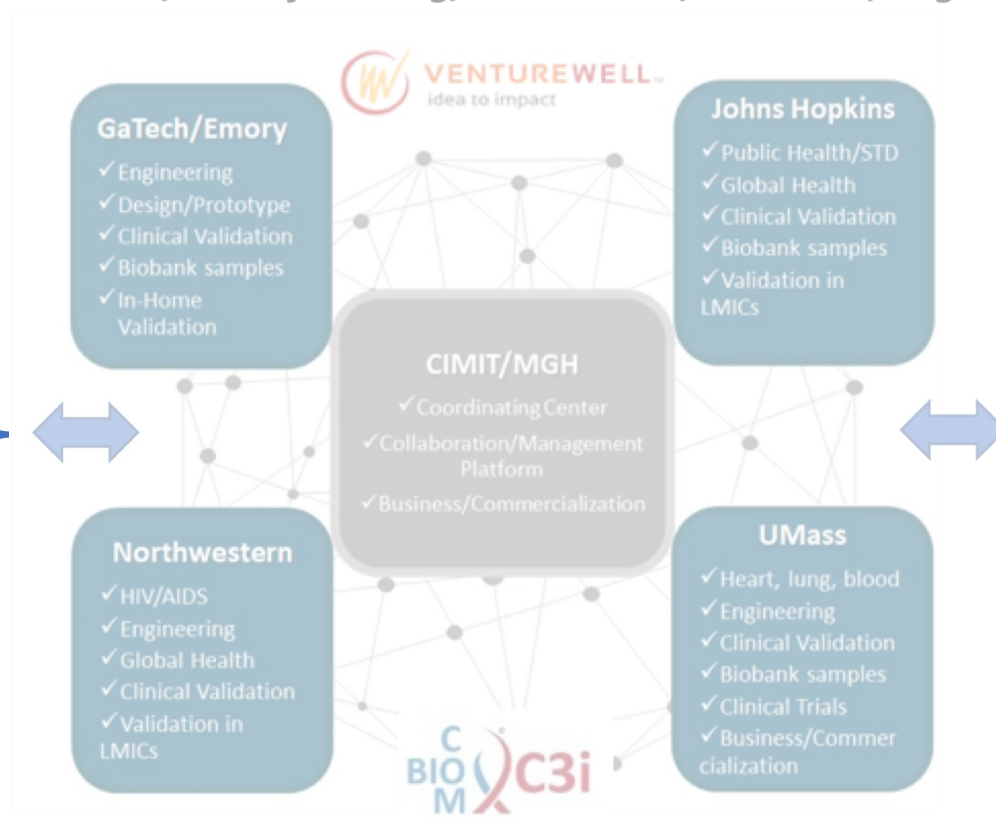
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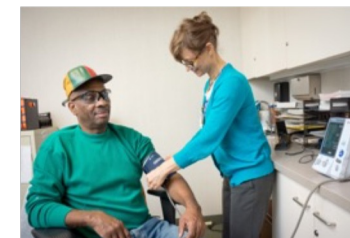
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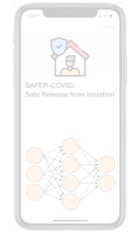
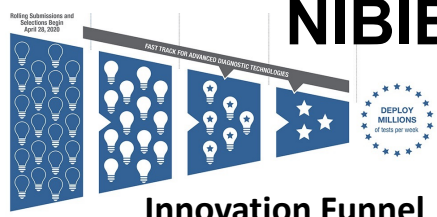
Clinical Studies Core

Standard Trial Design, Digital Health Platform, Single IRB, Center Network

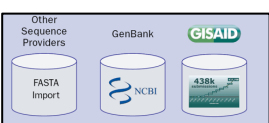


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RADx MARS



Variant Task Force Project Rosa



Independent Test Assessment (ITAP)

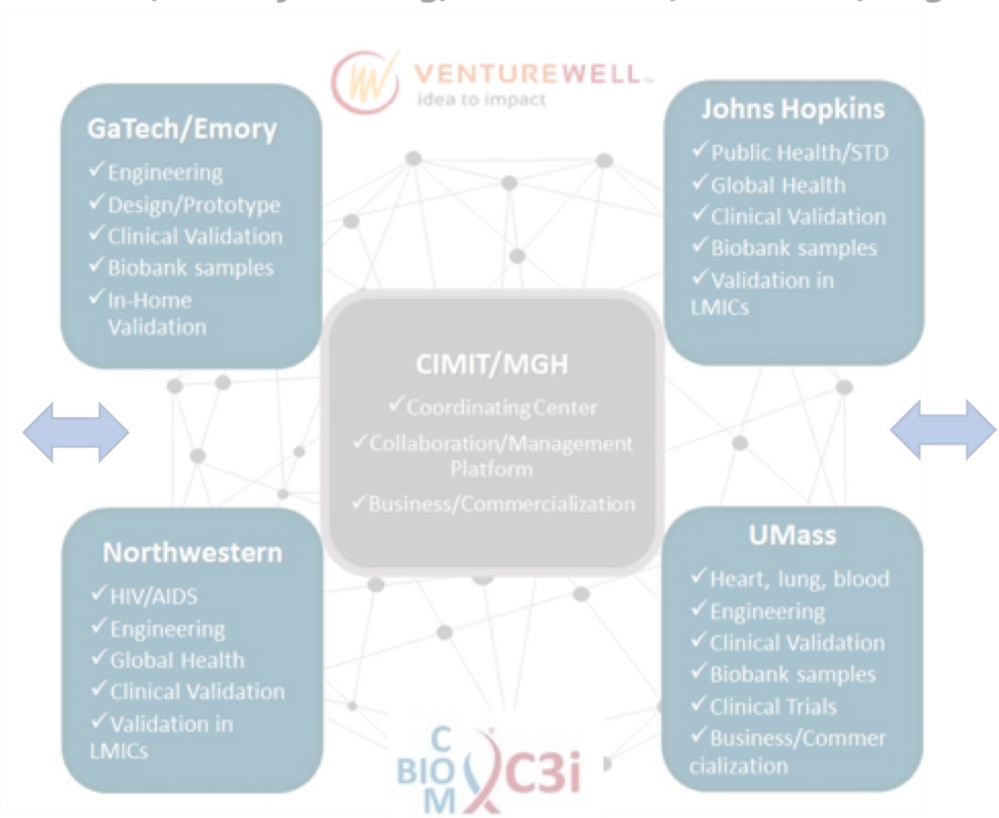
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Innovation Funnel



RADx MARS



Variant Task Force Project Rosa



Independent Test Assessment (ITAP)

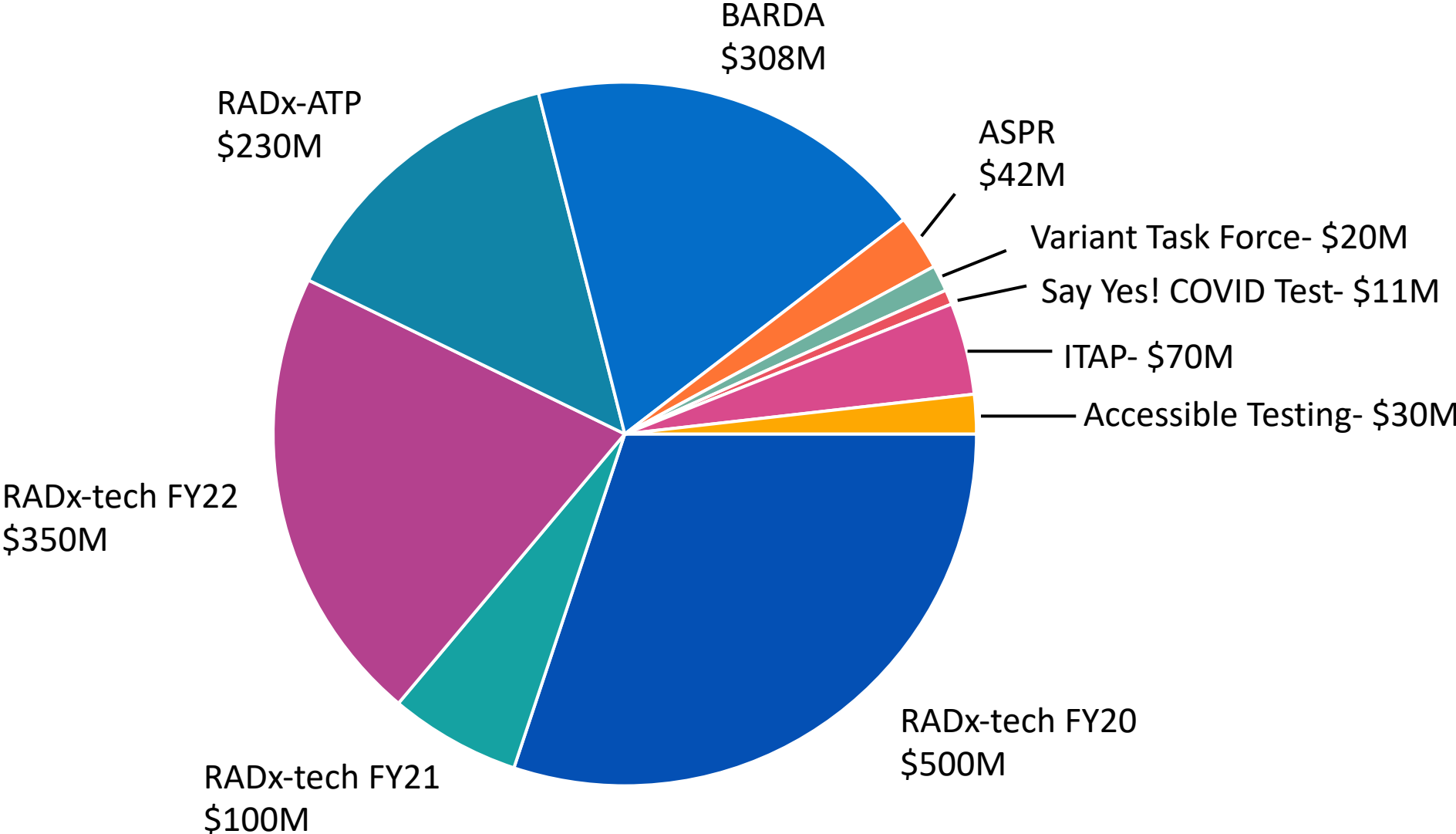


My COVID Toolkit Whentotest.org



Test Accessibility

RADx Funding: \$500M → \$1.7 Billion

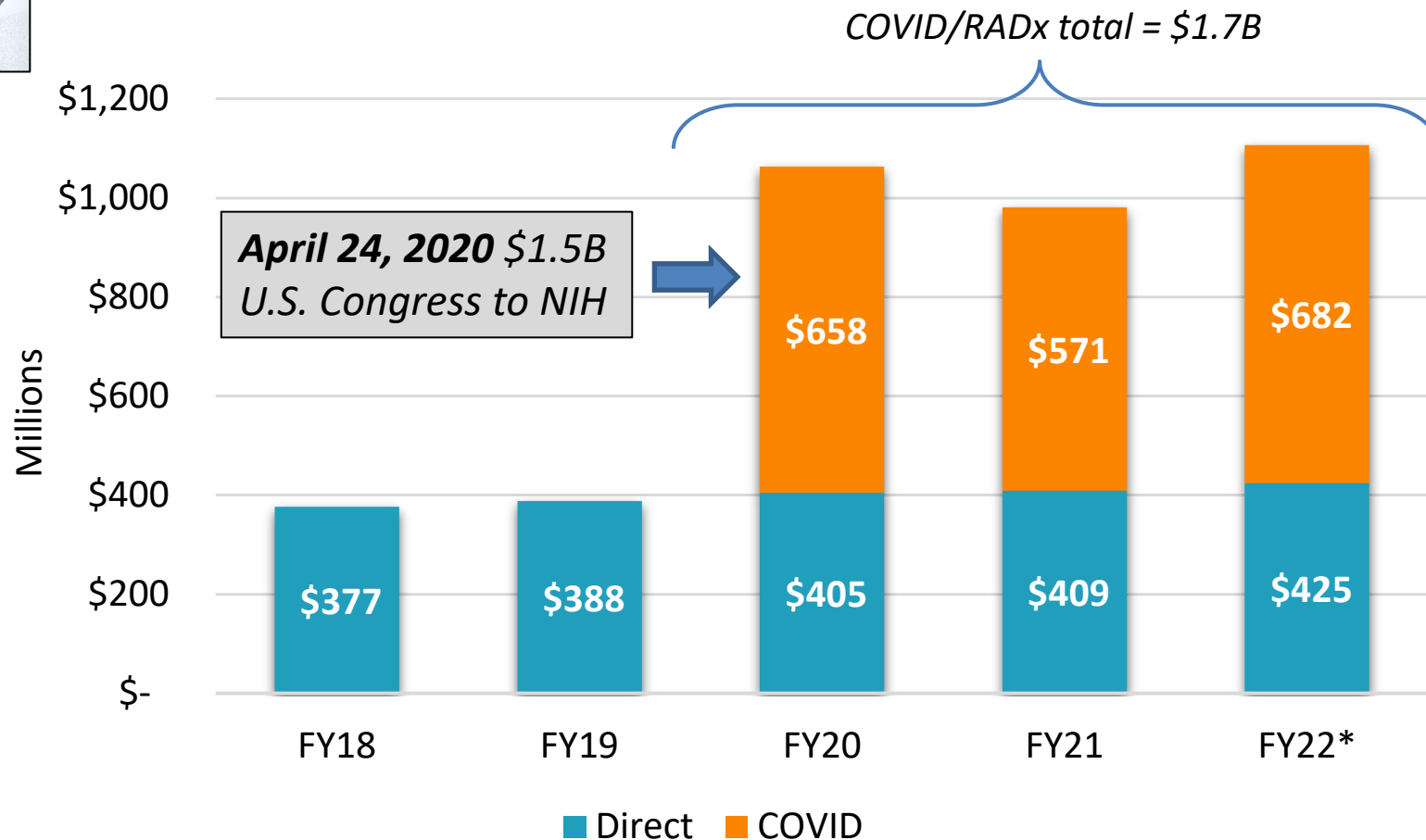


NIBIB Impact



NIBIB team:

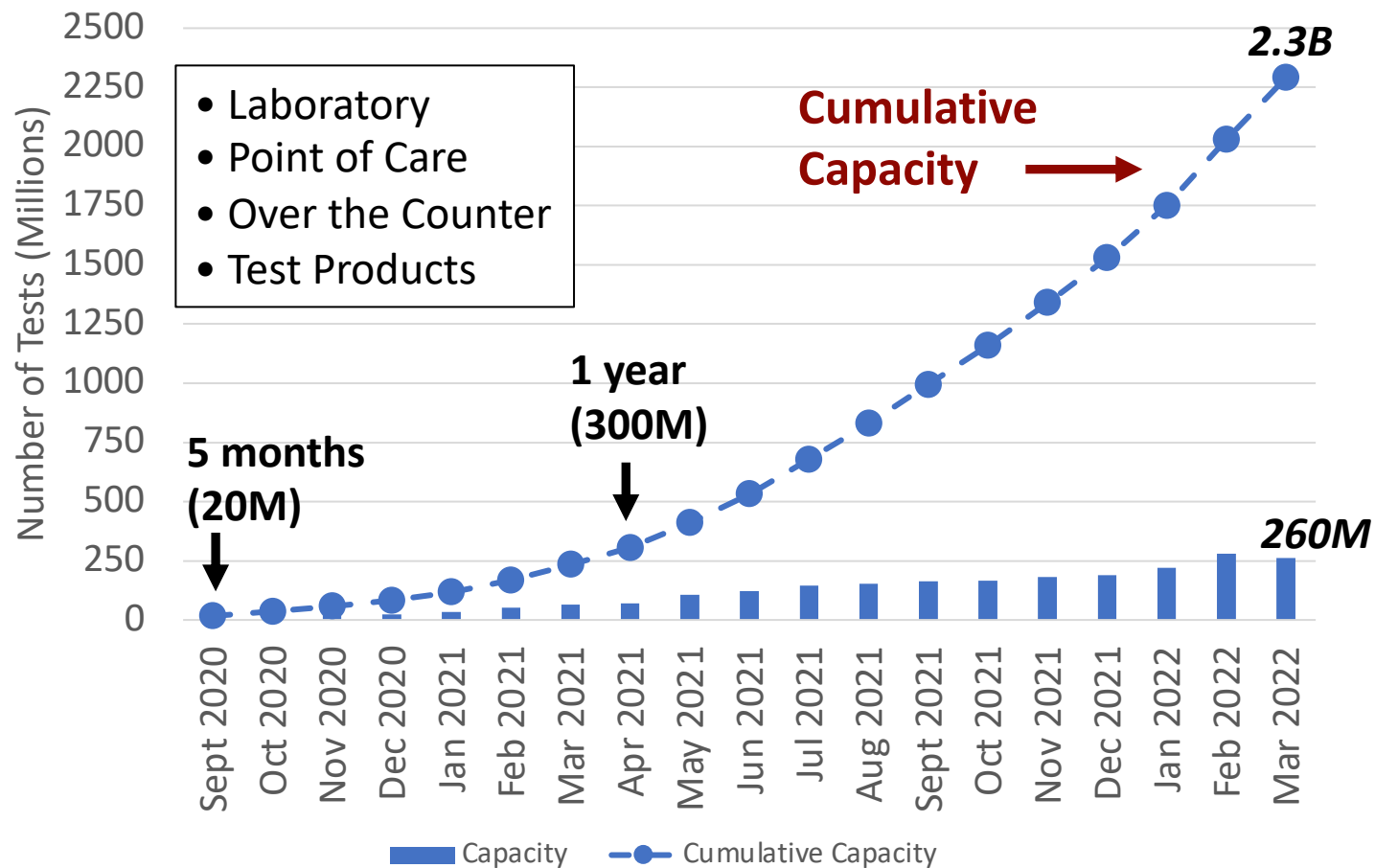
Jill Heemskerk,
David George,
Jason Ford,
Deb Kelly,
Admin, Budget,
Grants
Management,
Communications,
Program,...



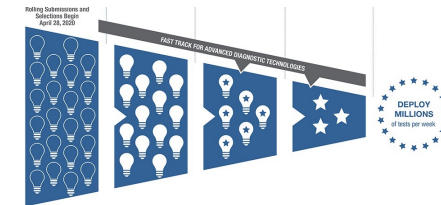
*projected

RADx Tech Impact: *Capacity thru March 2022*

Cumulative EUA Tests + Test Products



824 applications
~50 phase 2 awards



Innovation Funnel & ITAP

- **2.3B** tot capacity thru March 2022
- **~260 M** tests & products Mar 2022
- **44 EUAs**: 9 "OTC": 8 An, 1 RT-LAMP

Paradigm Shift

Lab >> POC → POC, OTC >> Lab (~12%)

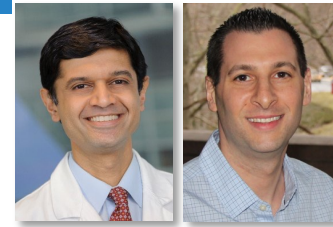
April 2020 <8M tests

Feb 2022 >1.1B tests w/~1B OTC

<https://www.nibib.nih.gov/covid-19/radx-tech-program/radx-tech-dashboard>

RADx MARS (Mobile Application Reporting Standards)

<https://www.nibib.nih.gov/covid-19/radx-tech-program/mars>

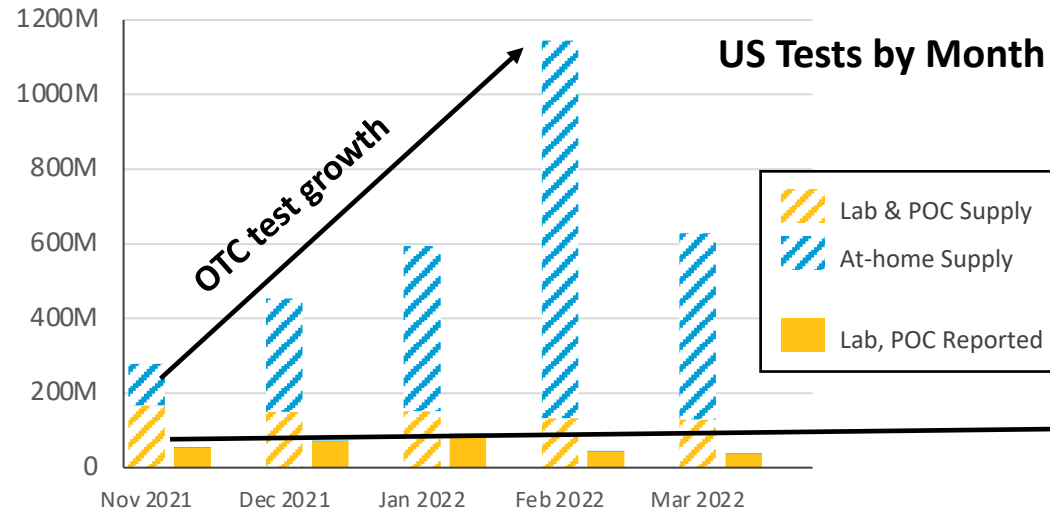


Krishna Juluru

Andrew Weitz

OTC Paradigm Shift Challenges:

- 1) Reporting Cases
- 2) Use & Interpret Antigen Tests



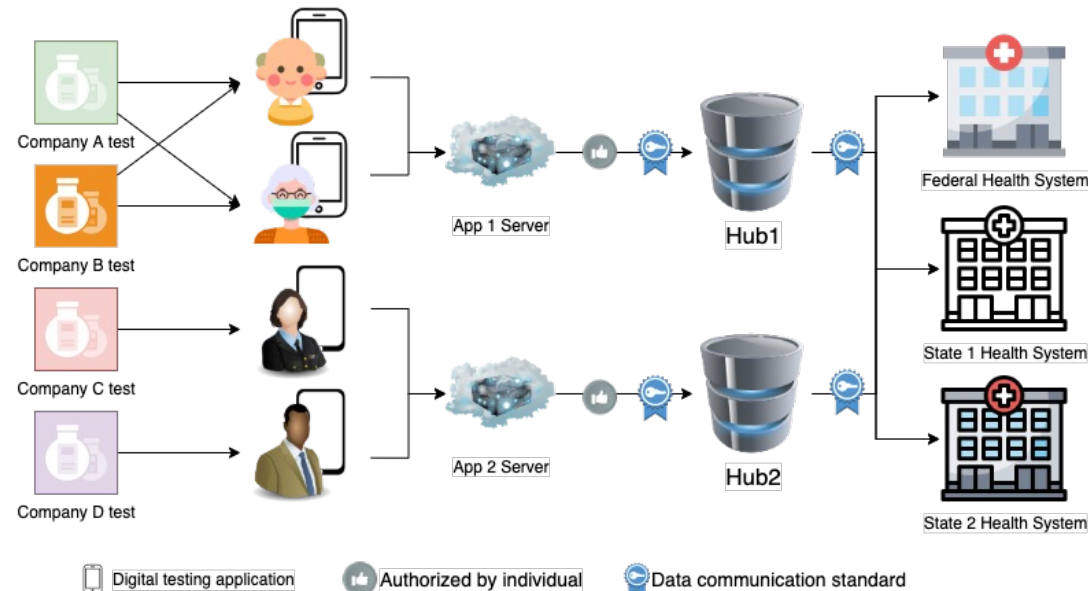
tests reported <100M/mo

Establish **common standard** for over-the-counter (OTC) test results (iHealth 1st)

Promote **data hubs** to reduce complexity of reporting channels

Free for companies to report OTC test results

Help OTC app developers **navigate** reporting

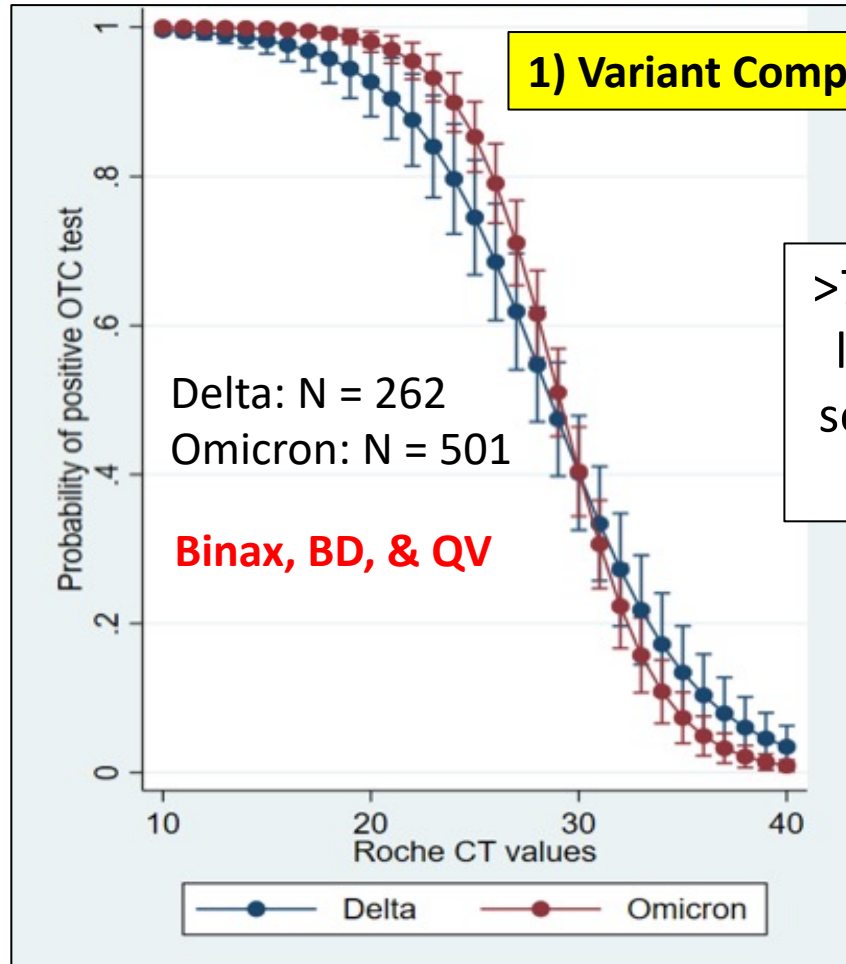


Challenge: Use & Interpret An Tests

ROC Curves

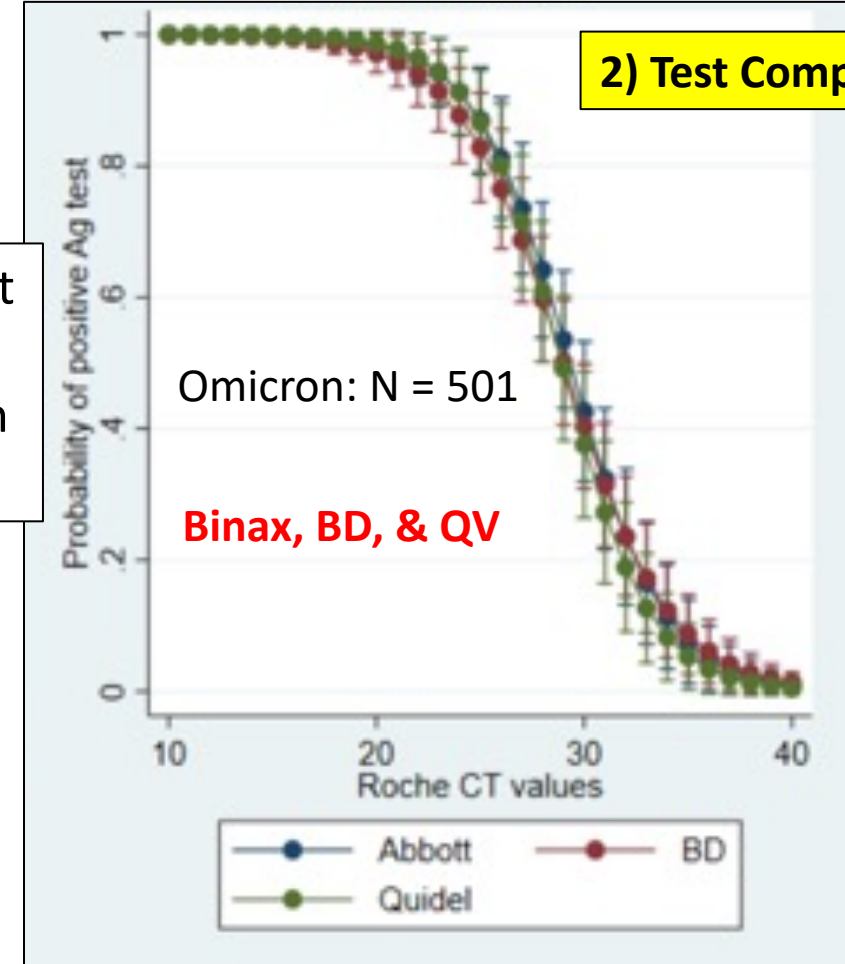
BD, Binax, Quidel QV vs. Roche COBAS RTPCR

1) Variant Comparison

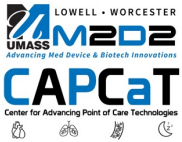


>7000 subject
longitudinal
serial antigen
test study

2) Test Comparison



UMass



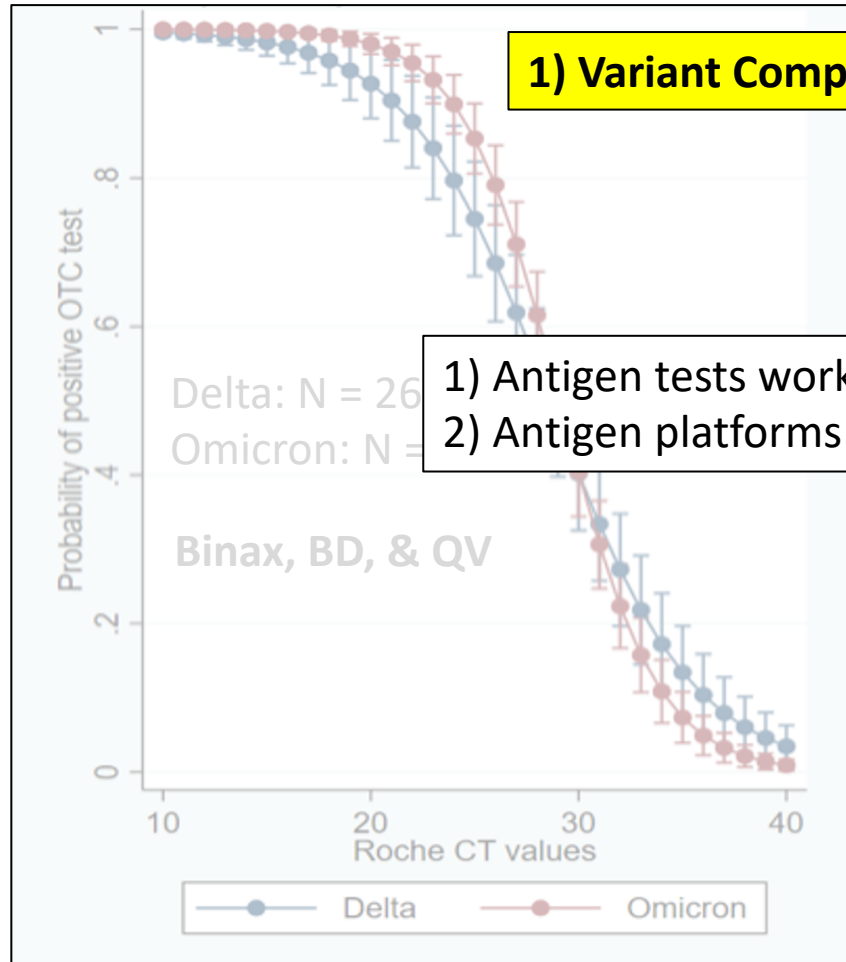
A. Soni, et al.,
RADx Clinical
Studies Core
team and Test
Us At Home
Investigators

Antigen Test Performance: Variants and Platforms

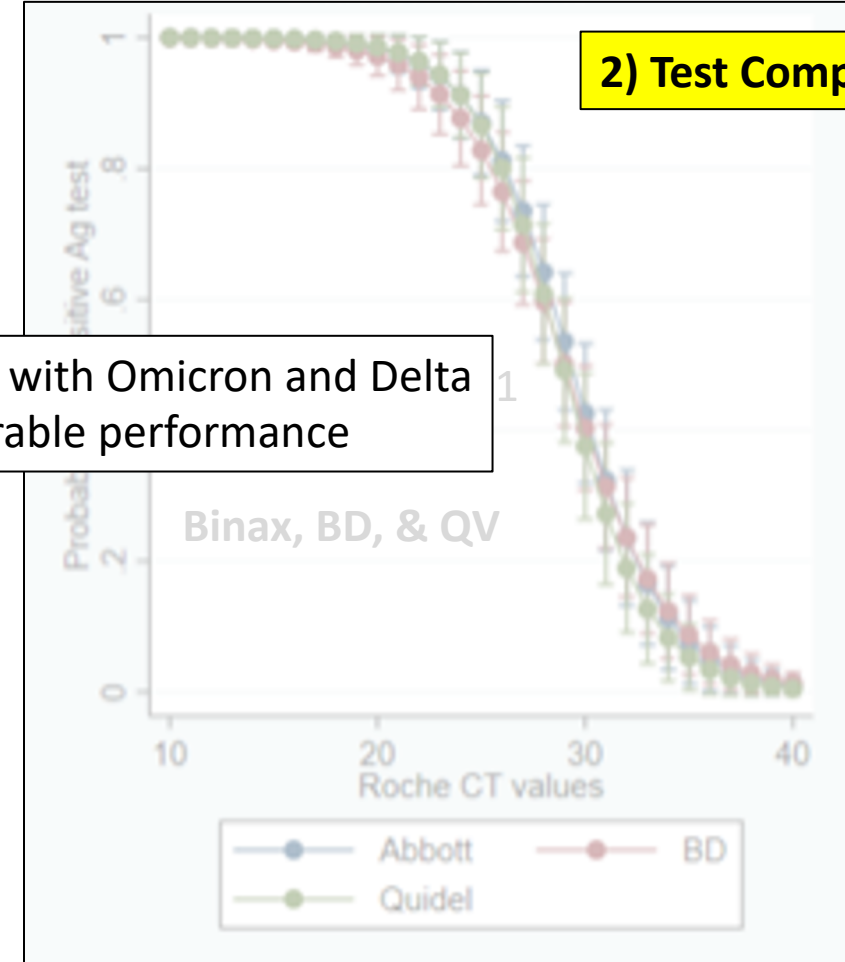
ROC Curves

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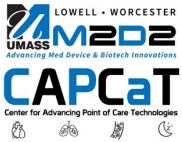


2) Test Comparison



1) Antigen tests work equally well with Omicron and Delta
2) Antigen platforms have comparable performance

UMass



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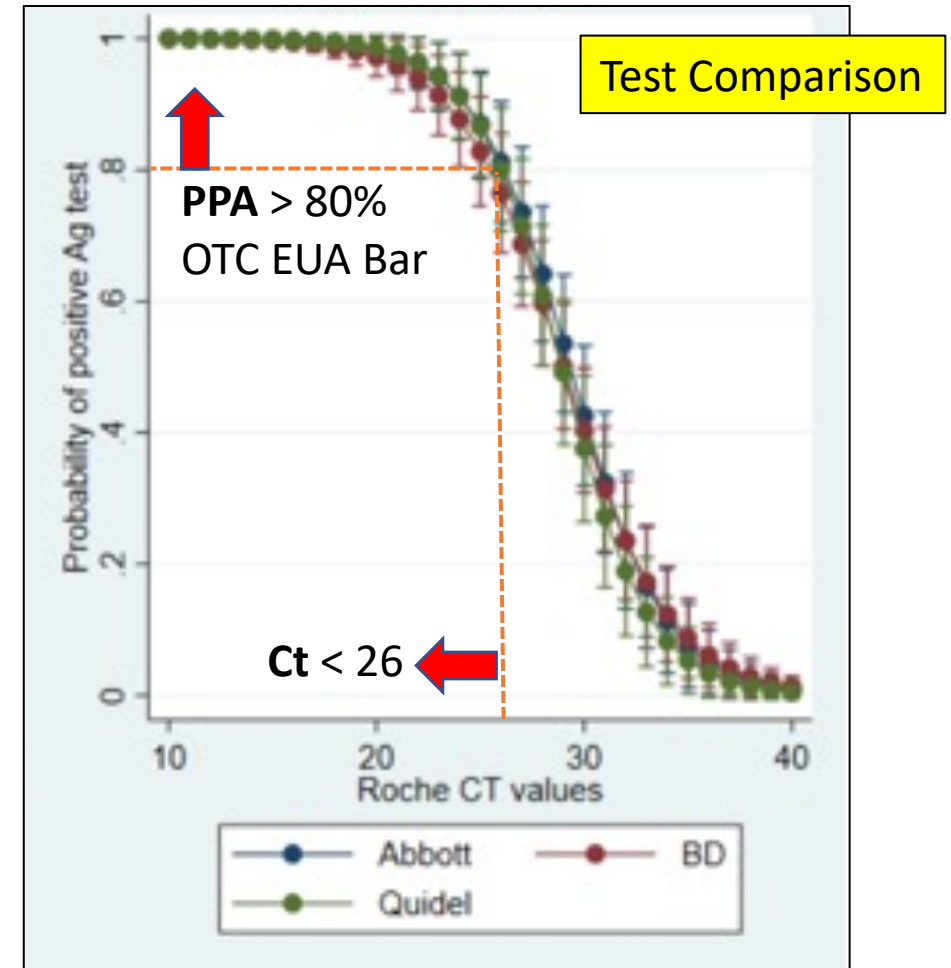
Antigen Test Performance: *Platform PPA*

ROC Curves

BD, Binax, Quidel QV vs. Roche COBAS RTPCR

For *high* viral loads, e.g. Ct < ~26 ($\sim 10^6$ Cp/mL)

- Antigen PPA $\geq 80\%$
- Large changes in Ct, modest changes in PPA



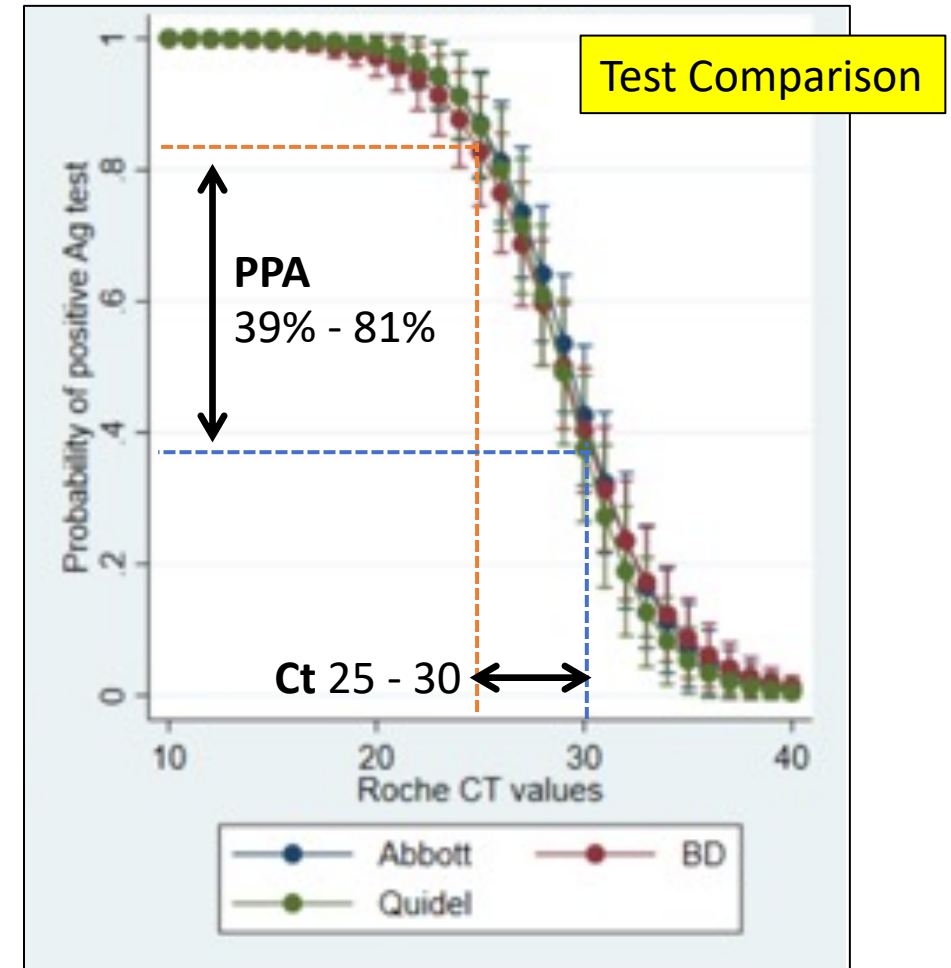
Antigen Test Performance: *Platform PPA*

ROC Curves

BD, Binax, Quidel QV vs. Roche COBAS RTPCR

For *intermediate* viral loads, e.g. Ct ~25 - 30

- Antigen PPA 31% - 81%
- Small changes in Ct = large changes in PPA



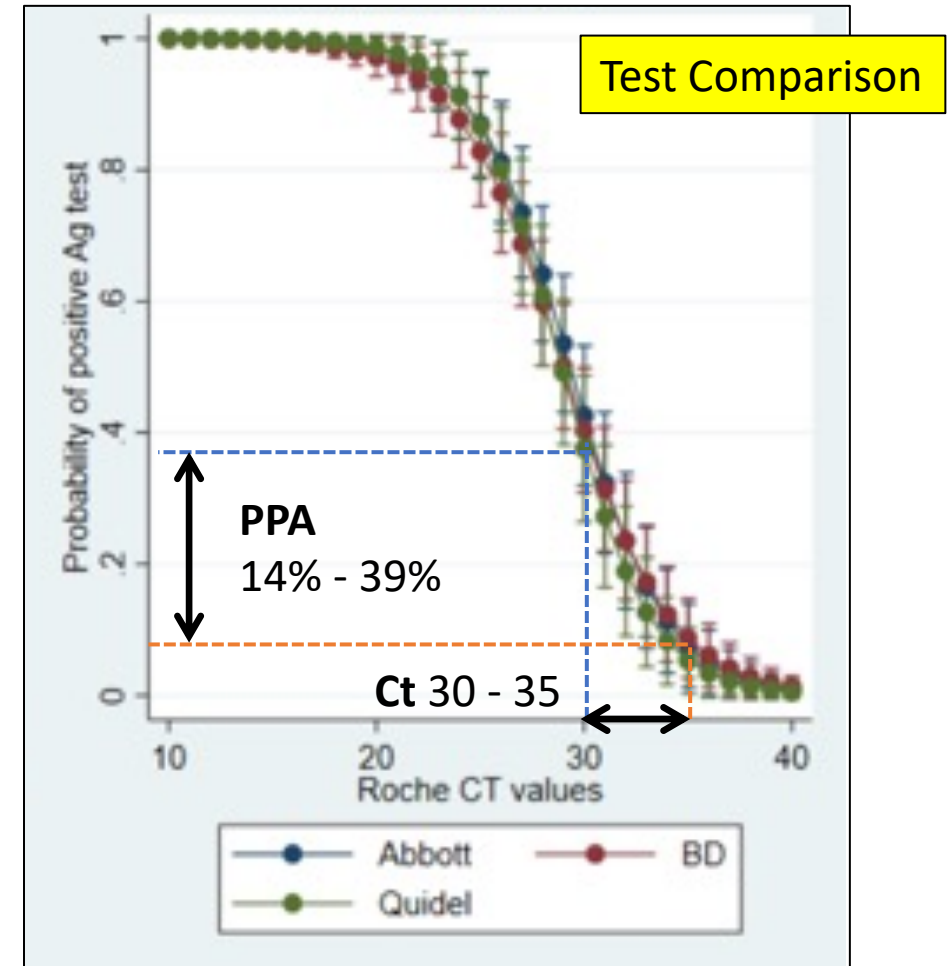
Antigen Test Performance: *Platform PPA*

ROC Curves

BD, Binax, Quidel QV vs. Roche COBAS RTPCR

For *low viral loads*, e.g. Ct 30 - 35 (weak positive)

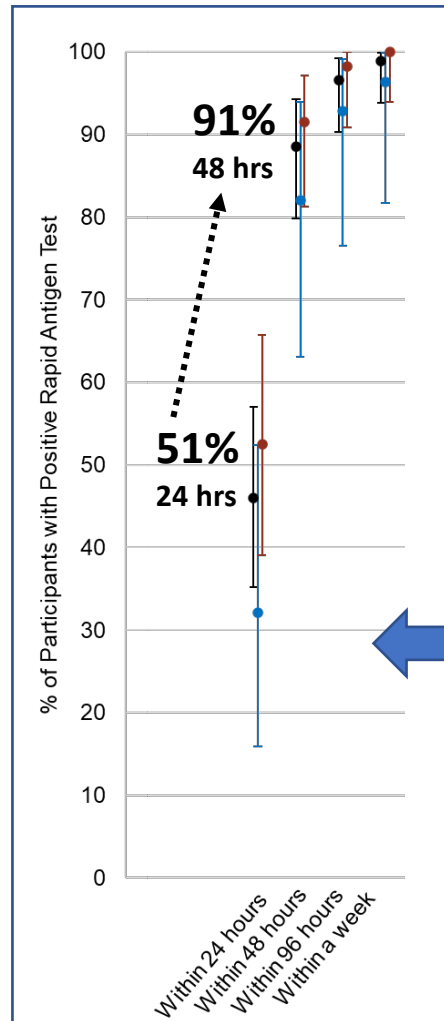
- Antigen PPA 14% - 39%
- Small changes in Ct = modest changes in PPA



Antigen Test Performance: Platform PPA

ROC Curves

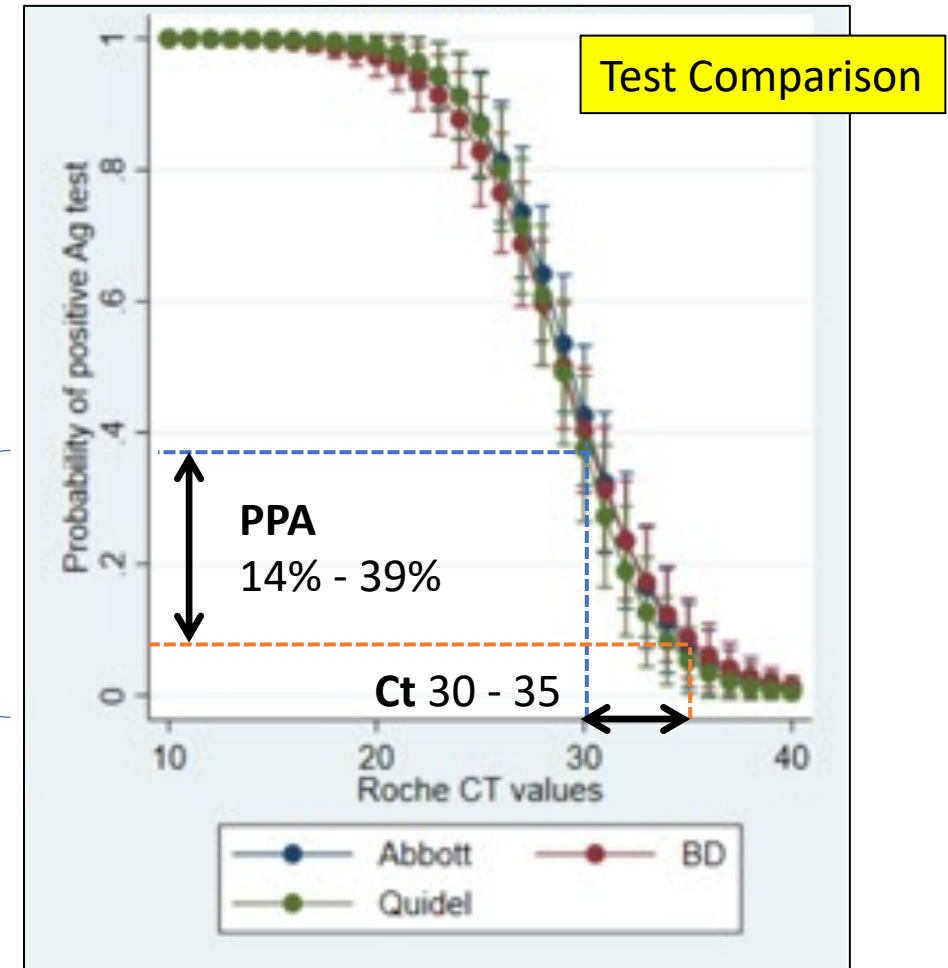
BD, Binax, Quidel QV vs. Roche COBAS RTPCR



- Omicron
- Delta
- Ave.

Serial Testing


Probability of turning An+ after weak RTPCR+



FDA Antigen Performance: *Is there a difference?*

- 1) EUA for serial testing
- 2) EUA PPA depends on study population

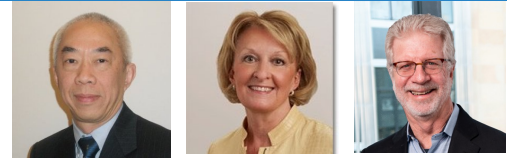
FDA IFU for Boson

Primary Analysis					
	10% Low Positive	12.5% Low Positive	15% Low Positive	17.5% Low Positive	20% Low Positive
High Positive Samples	52	52	52	52	52
Low Positive Samples	6	8	10	12	13
Total Comparator Positive for PPA Calculation	58	60	62	64	65
Total Test Positives for PPA Calculation	48	48	48	48	48
 PPA (%)	82.7%	80.0%	77.4%	75.0%	73.8%
95% CI (XX% - XX%)	71.1% - 90.4%	68.2% - 88.2%	65.6% - 86.0%	63.2% - 84.0%	62.0% - 83.0%
NPA (%)	99.1% (112/113)				
95% CI (XX%-XX%)	95.2%-99.8%				

When all study participants are included, the PPA is 67.1% and the NPA is 99.1% with the 95% confidence interval bounds of 55.7% to 76.8% for the PPA and 95.2% to 99.8% for the NPA, respectively

Date EUA Issued or Last Updated	Entity	Diagnostic (Most Recent Letter of Authorization) and Date EUA Originally Issued	Attributes	Authorized Setting(s) ¹	Authorization Documents ²	PPA
04/07/2022	Xiamen Boson Biotech Co., Ltd.	Rapid SARS-CoV-2 Antigen Test Card 04/06/2022	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Testing, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test)	82.7
04/06/2022	OSANG LLC	OHC COVID-19 Antigen Self Test 04/06/2022	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Testing, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test)	82.9
04/04/2022	SD Biosensor, Inc.	Pilot COVID-19 At-Home Test 12/24/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test)	95.3
04/04/2022	iHealth Labs, Inc.	iHealth COVID-19 Antigen Rapid Test 11/05/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test)	95.3
04/04/2022	Abbott Diagnostics Scarborough, Inc.	BinaxNOW COVID-19 Antigen Self Test 03/31/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, Individuals, IFU, IFU (Home Test)	91.7
03/30/2022	Maxim Biomedical, Inc.	MaximBio ClearDetect COVID-19 Antigen Home Test 01/19/2022	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test)	86.9
03/25/2022	Becton, Dickinson and Company (BD)	BD Veritor At-Home COVID-19 Test 8/24/2021	Lateral Flow, Digital Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, Individuals, IFU, IFU (Home Test)	84.6
03/25/2022	Access Bio, Inc.	CareStart COVID-19 Antigen Home Test 08/02/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test)	87.0
03/23/2022	Celltrion USA, Inc.	Celltrion DiaTrust COVID-19 Ag Home Test 10/21/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening, Multiple Targets	Home, H, M, W	HCP, IFU, IFU (Home Test)	86.7
03/23/2022	Siemens Healthineers	CLINITEST Rapid COVID-19 Antigen Self-Test 12/29/2021	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test)	86.5
03/18/2022	Ellume Limited	Ellume COVID-19 Home Test 12/15/2020	Lateral Flow, Fluorescence, Instrument Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test), FAC	96.0
03/16/2022	PHASE Scientific International, Ltd.	INDICAID COVID-19 Rapid Antigen At-Home Test 03/16/2022	Lateral Flow, Visual Read, Over the Counter (OTC) Home Testing, Serial Screening, Single Target	Home, H, M, W	HCP, IFU, IFU (Home Test)	81.7

FDA Antigen Performance: *Is there a difference?*



FDA antigen team, ITAP team

Eric Lai Pam Miller Richard Creager

PPA

82.7

82.9

95.3

95.3

91.7

86.9

84.6

87.0

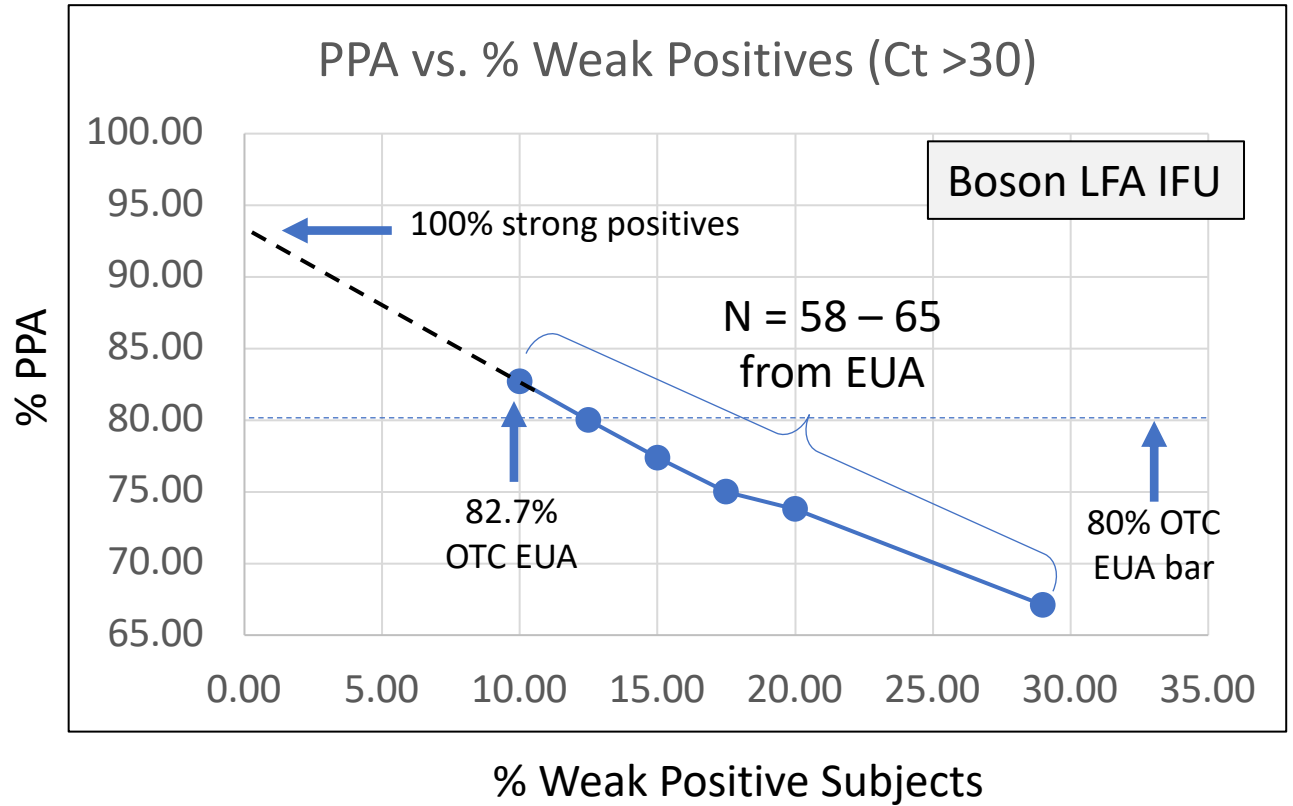
86.7

86.5

96.0

81.7

EUA PPA depends on clinical study population



RADx Tech Performance Challenges

Lab RTPCR



ABL 7500

POC RTPCR

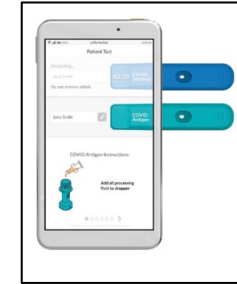


Mesa BioTech

POC An (LFA/reader)

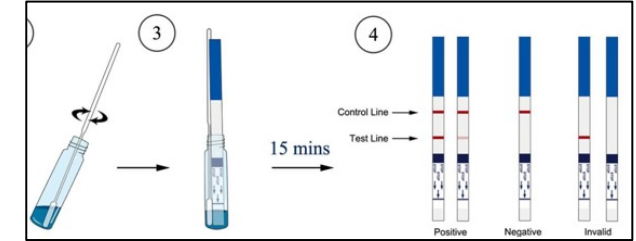


Quidel Sophia



Ellume

OTC An (LFA/visual)



Dipstick LFA

Tech to Bridge the Gap?

Cost	\$\$\$\$	\$\$\$		\$\$	\$
Speed	hours	~30 min		<15 min	
Sens/Spec	>90/95	>90/95		>90/95	
LOD	<10 ³ Cp/mL	<10 ³ Cp/mL		>10 ⁶ Cp/mL	

RADx Tech: *Better Performance*

Isothermal PCR (OTC)

Cue



Lucira



RT PCR (POC)

Mesa/Thermo



Antigen w/PCR LOD

Qorvo



Detect



Uh-Oh Labs



Visby

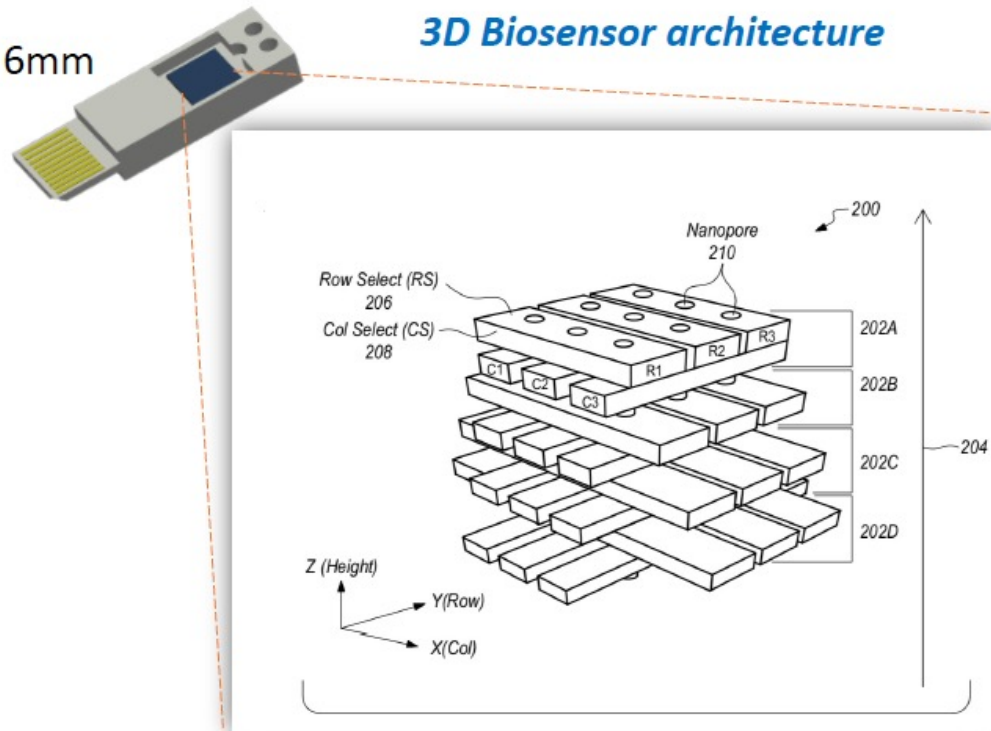


Quanterix



3D Nano-electronic Biosensor

3D Biosensor architecture

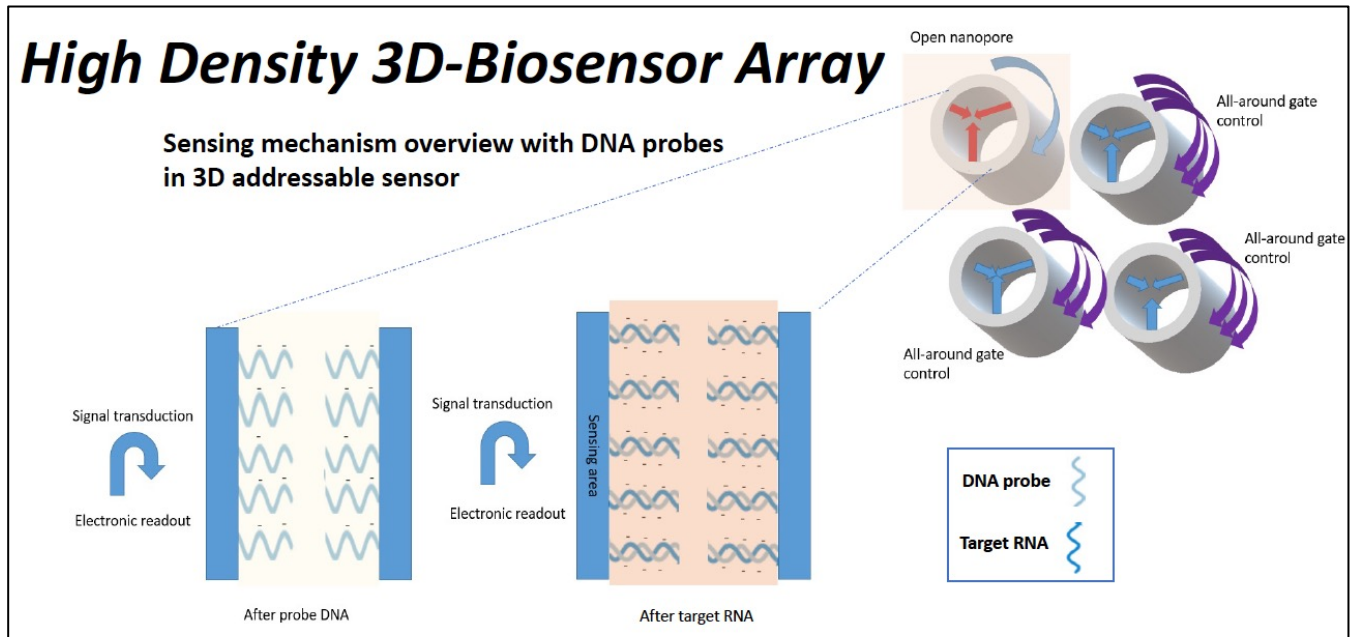


3D Flash Memory (V-NAND)

DNA Probes, Parallel Nucleic Acid Detection

High Density 3D-Biosensor Array

Sensing mechanism overview with DNA probes in 3D addressable sensor



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Ongoing Challenges

1) Improve Performance and Information Content

- **Accessibility:** *vision, fine motor, cognitive impairments, etc.*
- **Next gen performance:** *POC/home tests w/lab performance; multiplex + variant capabilities; host response; Standard designs?*

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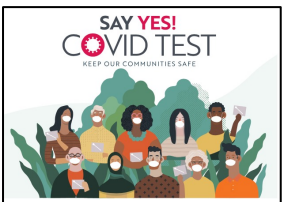
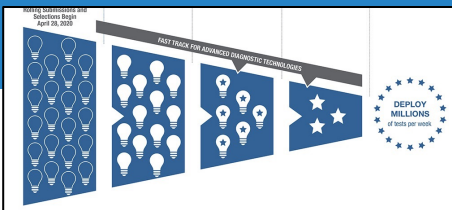
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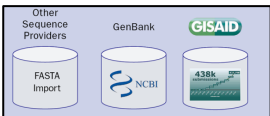
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4) Impact: **Process:** *RADx-ification at NIBIB/NIH;*
Practice: *OTC “Test to Treat” for diagnostic-led precision medicine*

Thank You! National Policy Impact



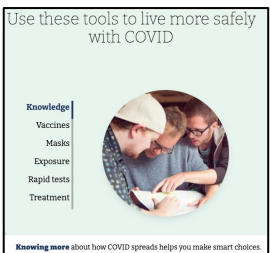
RADx MARS



Variant Task Force
Project Rosa



Independent Test
Assessment (ITAP)



My COVID ToolKit
Whentotest.org



Test Accessibility

POLITICS

Biden administration to launch website for free 500 million COVID-19 testing kits on Wednesday



Courtney Subramanian
USA TODAY

Published 2:55 p.m. ET Jan. 14, 2022 | Updated 5:02 p.m. ET Jan. 14, 2022



President Biden promises 'free' N95 masks and more at-home COVID tests

President Biden also announced that 1,000 military medical personnel will begin deploying to help overwhelmed medical facilities. STAFF VIDEO, USA TODAY

WASHINGTON – The Biden administration on Wednesday will launch a website where Americans can order up to four free COVID-19 testing kits per person, according to a senior administration official.

The New York Times

Biden announces 500 million more tests will be purchased for Americans.



President Biden said his administration would double its previous purchase of coronavirus tests to be distributed for free to Americans and deploy additional medical personnel to states hard-hit by the Omicron variant. Doug Mills/The New York Times



By Michael D. Shear

Jan. 13, 2022

WASHINGTON — President Biden on Thursday stepped up his administration's response to a coronavirus surge driven by the Omicron variant, sending what he said is urgently needed help to overwhelmed hospitals and pledging to provide Americans with free tests and masks as the country enters the pandemic's third year.