Rapid Acceleration of Diagnostics: RADx Tech/ATP

Advisory Council to the Director, December 10, 2020

Bruce J. Tromberg, Ph.D.
Director
National Institute of Biomedical Imaging and Bioengineering

NIH National Institute of Biomedical Imaging and Bioengineering

NIH National Institute of Biomedical Imaging and Bioengineering

RADx Tech & ATP

NIH Office of the Director


Francis Collins


Rachael Fleurance


Larry Tabak


Tara Schwetz

April 24, 2020: $1.5B to NIH
$500 Million to NIBIB

RADx Tech – $500M
Highly competitive, rapid three-phase challenge to identify the best c… for at-home or point-of-care tests for COVID-19

April 29

RADx Advanced Technology Platforms (RADx-ATP) – $230M
Rapid scale-up of advanced technologies to increase rapidity and enhance and validate throughput – create ultra-high throughput machines and facilities

RADx Radical (RADx-Rad) – $200M
Develop and advance novel, non-traditional approaches or new applications of existing approaches for testing

RADx Underserved Populations (RADx-UP) – $500M
Interlinked community-based demonstration projects focused on implementation strategies to enable and enhance testing of COVID-19 in vulnerable populations


Jill Heemskerk.


Bruce Tromberg

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

$307 M Partnership with BARDA

Tech/ATP Team Leads: Tiffani Lash, Todd Merchak, Taylor Gilliland, Kate Egan, Mike Wolfson, Doug Sheeley, Gene Civillico

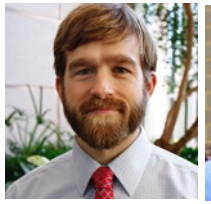
OASH FDA CMS CDC

https://www.nih.gov/research-training/medical-research-initiatives/radx;
Tromberg, Collins et al. NEJM, 2020

Point-of-Care Technologies Research Network (POCTRN)

NIBIB National Network: *5-6 years for new POC technologies*

Established 2007, Expanded 2020: >1,000 RADx experts & contributors




Todd Merchak Tiffany Lash

https://www.poctrn.org

VENTUREWELL idea to impact

GaTech/Emory
- ✓Engineering
- ✓Design/Prototype
- ✓Clinical Validation
- ✓Biobank samples
- ✓In-Home Validation

Johns Hopkins
- ✓Public Health/STD
- ✓Global Health
- ✓Clinical Validation
- ✓Biobank samples
- ✓Validation in LMICs

CIMIT/MGH
- ✓Coordinating Center
- ✓Collaboration/Management Platform
- ✓Business/Commercialization

Northwestern
- ✓HIV/AIDS
- ✓Engineering
- ✓Global Health
- ✓Clinical Validation
- ✓Validation in LMICs

UMass
- ✓Heart, lung, blood
- ✓Engineering
- ✓Clinical Validation
- ✓Biobank samples
- ✓Clinical Trials
- ✓Business/Commercialization

C BIO M C3i

Project Tech:

1) Review
2) Funding
3) Expertise
4) Testing

Validation Core

~50 projects complete, >2,000 participants

Clinical Studies Core

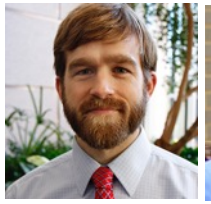
Standard Trial Design, Digital Health Platform, Single IRB, Center Network

Deployment Core

Supply chain, Manufacturing, User Community, End to end solutions

National Institute of Biomedical Imaging and Bioengineering

Point-of-Care Technologies Research Network (POCTRN)




Todd Merchak Tiffany Lash

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RADx UP

Duke/UNC CDCC RADx UP Coordinating Center

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C BIO M C3i

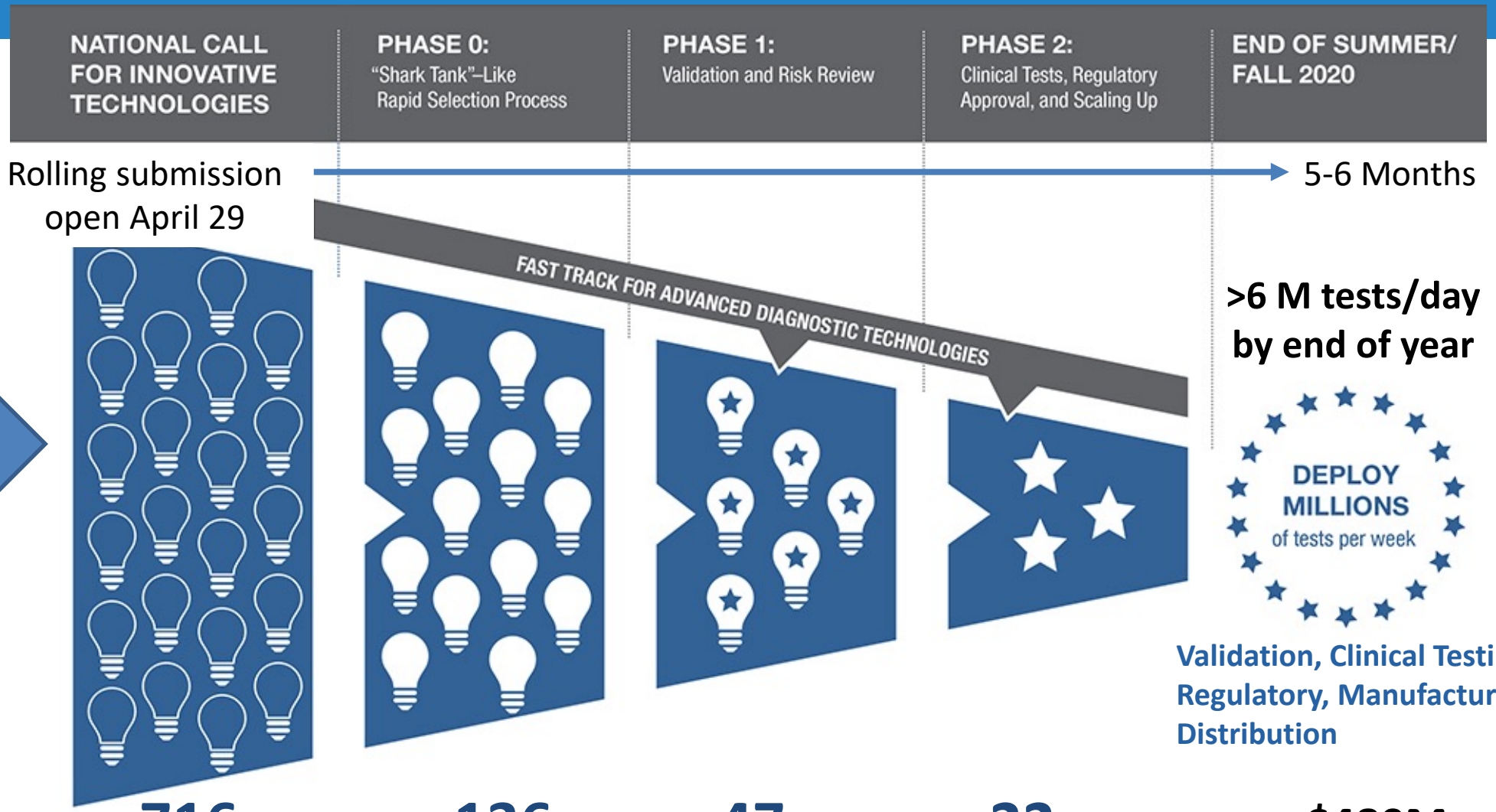
Validation Core

Clinical Studies Core

Deployment Core

National Institute of Biomedical Imaging and Bioengineering

RADx Tech/ATP Innovation Funnel



RADx Tech/ATP Innovation Funnel

Manufacturing Expansion Summary

- **Type:** 17 Nucleic Acid, 5 Viral Antigen
- **Setting:** 8 POC, 3 “between”, 11 Lab
- **Regulatory:** EUA → 8 lab, 3 POC
- **Impact:** ~1.5 M tests/day (Jan)

- **Pipeline:** 21 POC (9 NAT, 11 An, 1 VOC)
- **Impact:** >1 M LFA tests/day (Q1 2021)

22 (Tech + ATP) **~$480M**

22 Manufacturing Expansion

Innovation

1) Separation/concentration
2) µ-Fluidics
3) Chemistries, e.g. CRISPR, NGS
4) Labels, Reporters
5) Readout Tech
6) Miniaturization
7) Automation

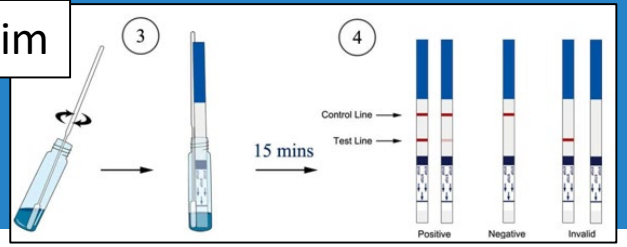
November
~590,000 tests/day sold;
~890,000 tests/day capacity

https://www.nibib.nih.gov/covid-19/radx-tech-program/radx-tech-phase2-awards

Visby Medical	Nucleic Acid: RTPCR	**POC**
MicroGEM International	Nucleic Acid: RTPCR	**POC**
Mesa Biotech, Inc.	Nucleic Acid: RTPCR	**POC**
Talis Biomedical Corp.	Nucleic Acid: Isothermal PCR	**POC**
MatMaCorp	Nucleic Acid: RTPCR	**Lab/POC**
Ubiquitome	Nucleic Acid: RTPCR	**Lab/POC**
Maxim Biomedical Inc	**Antigen: LFA dipstick**	**POC/home**
Luminostics, Inc.	**Antigen: LFA**	**POC/home**
Ellume USA LLC	**Antigen: LFA**	**POC/home**
Quidel Corp.	**Antigen: LFA**	**POC/home**
Quanterix	**Antigen/microbeads**	**Lab**
Mammoth Biosciences	Nucleic Acid: CRISPR	**Lab**
Flambeau Diagnostics	Nucleic Acid: Isothermal PCR	**Mobile Lab**
Ceres Nanosciences Inc	Nucleic Acid: Extraction	**Lab**
Fluidigm	Nucleic Acid: RTPCR	**Lab**
Broad Institute	Nucleic Acid: RTPCR	**Lab**
Illumina Inc	Nucleic Acid: NGS	**Lab**
Helix OpCo, LLC	Nucleic Acid: NGS	**Lab**
Ginkgo Bioworks	Nucleic Acid: NGS	**Lab**
Sonic Healthcare USA	Nucleic Acid: RTPCR	**Lab Network**
PathGroup	Nucleic Acid: RTPCR	**Lab Network**
Aegis Sciences	Nucleic Acid: RTPCR	**Lab Network**

Mesa BioTech

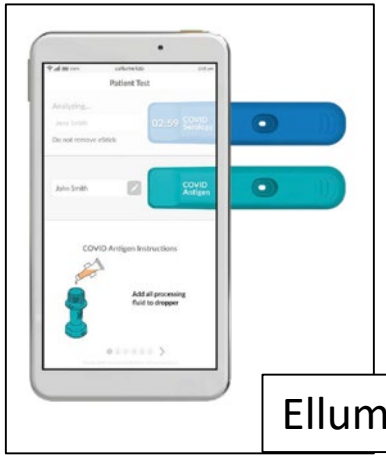
Maxim



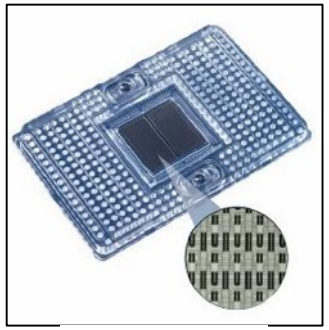
Quidel Sophia

Visby Medical

Ubiquitome



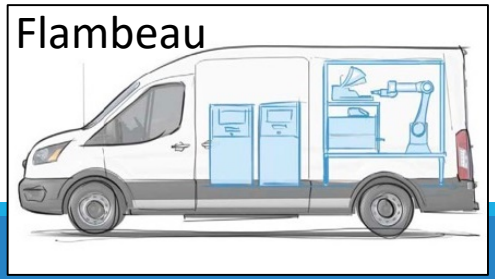
Ellume



Fluidigm

Luminostics

Flambeau



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Leveraging NIH Proof of Concept (PoC) Network

NIH SEED


Jodi Black


Matt McMahon

~50 early-stage RADx-tech projects

- Project Funding
- Industry Coaching and Mentoring
- Training and Resources

WASHINGTON ENTREPRENEURIAL RESEARCH EVALUATION & COMMERCIALIZATION HUB
WE-REACH
Bridge to Medical Impact

MBARC MIDWEST BIOMEDICAL ACCELERATOR CONSORTIUM

NCAI-CC NIH Center for Accelerated Innovations at Cleveland Clinic

CIMIT®
Consortia for Improving Medicine with Innovation & Technology

B-BIC: Translating Discoveries Into Products

SPARK IS NOW POWERED BY NIH REACH
SPARK REACH
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS | NATIONAL INSTITUTES OF HEALTH
COLORADO

NIH National Institutes of Health
Office of Extramural Research

RADx Test Validation Core (Emory-Gtech)

50 projects complete



Wilbur Lam Greg Martin. Oliver Brand

Feasibility

Ensure positive control (provided or commercial) is positive

Ensure negative matrix (i.e. saliva, patient sample or commercial) is negative

Ensure negative matrix spiked with live and/or inactivated SARS-CoV-2 virus is positive

Contrived samples

Verify the limit of detection (LOD) via live and/or inactivated SARS-CoV-2 virus by serial dilution using correct matrix

Test non-SARS-CoV-2 coronaviruses (test specificity/cross-reactivity)

Test different strains of SARS-CoV-2 (strain variation)

Patient samples

Test banked patient samples (adult and pediatric) with concomitant testing on reference method to determine concordance

Test prospective patient samples using collection sites

>2,000 participants

Calculate sensitivity, specificity, positive and negative predictive values with input from our biostatistical core

RADx Test Validation Core (Emory-Gtech)

50 projects complete

Feasibility

- Ensure positive control (provided or commercial) is po
- Ensure negative matrix (i.e. saliva, patient sample or c
- Ensure negative matrix spiked with live and/or inactiva

NIH score range: 1 (exceptional) to 9 (poor)

ACME POCT score: 2 (88% of respondents)

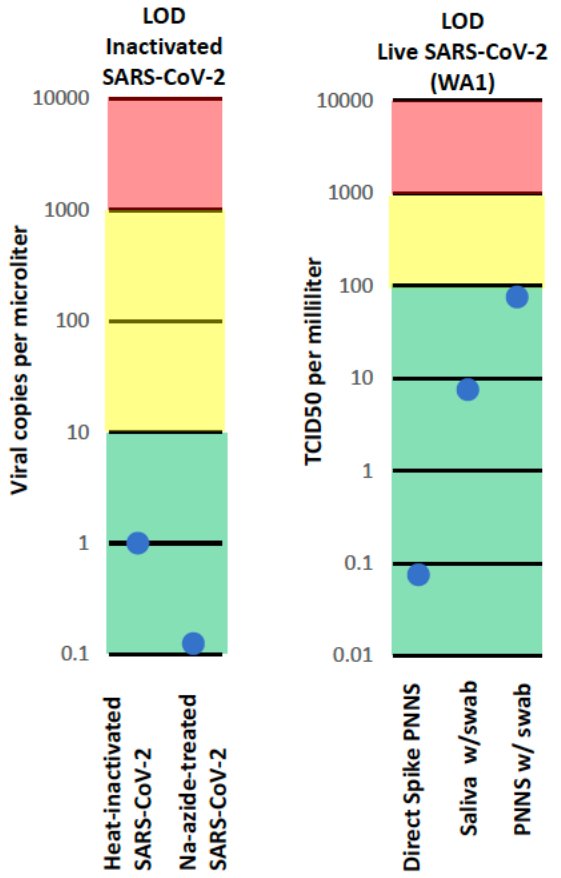
RADx Test Verification Core Recommendation: Proceed to WP2

Resume and Summary of Discussion: the RADx ACME POCT convened an internal study section on July 9th, 2020 to discuss the RADx Test Verification Core's analysis of Project #2244 in which the criteria for evaluation included: LOD, Sensitivity, Specificity, Repeatability, and Usability. The testing of this COVID-19 point-of-care (POC) PCR diagnostic test comprised of 1) LOD testing at several of our sites, including our Emory BSL-3 facility, Children's Healthcare of Atlanta clinical pathology laboratory, and laboratories in

Patient samples

- Test banked patient samples (adult and pediatric) wit
- Test prospective patient samples using collection sites
- Calculate sensitivity, specificity, positive and negative

OVERALL SUMMARY OF RESULTS ACROSS ACME POCT SITES



Specificity	
Virus Type	Lack of Cross-Reactivity?
OC43 seasonal coronavirus	✓
MERS (heat inactivated)	✓

Prospective Clinical Results

DiaSorin RT-PCR

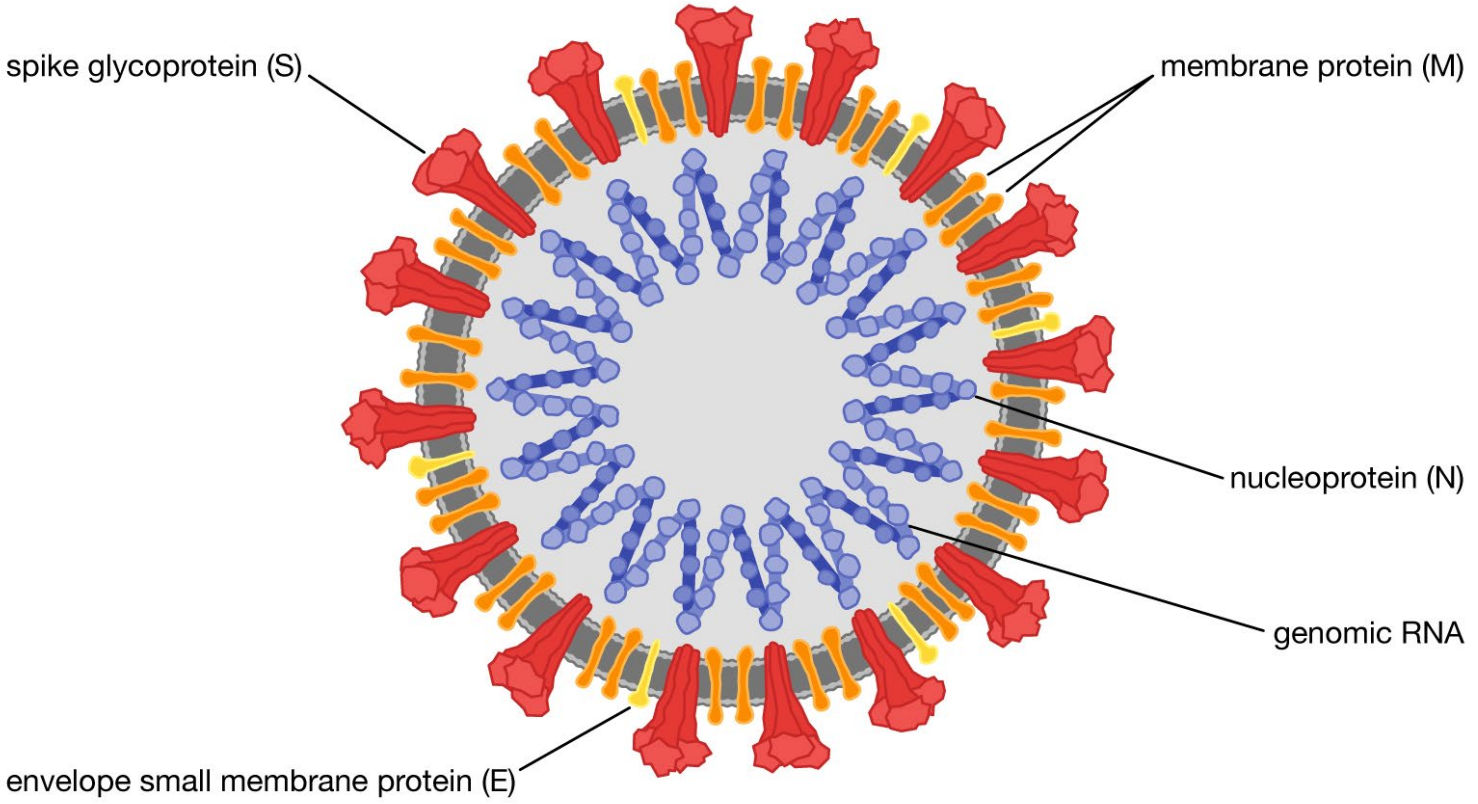
2244	+	-
+	4	0
-	0	48

Sensitivity: 100%
Specificity: 100%

* PNNS, pooled negative nasal swab

RADx Test Validation Core (Emory-Gtech)

Challenge: *Compare NAT and Antigen Test Performance*



Viral Antigen Test
Lateral Flow Assay (LFA)
LOD: $TCID_{50}$/mL ~10^3-10^4/mL

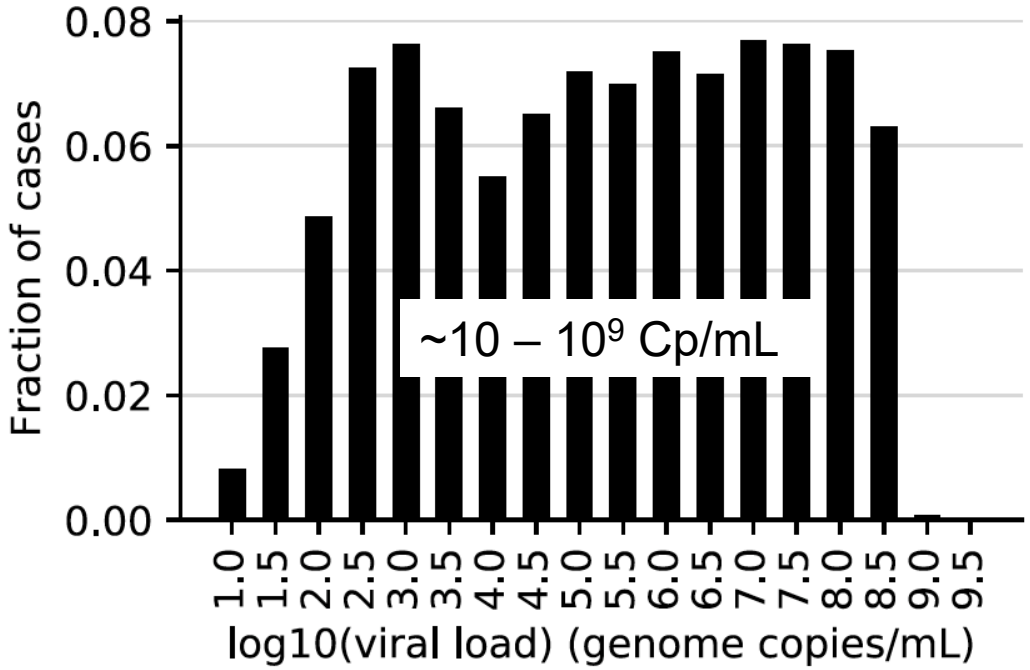
Copies/$TCID_{50}$?

Nucleic Acid Test
RTPCR (Isothermal PCR)
LOD: Cp/mL ~10^2-10^3/mL

Understanding Screening/Surveillance Performance

Impact of LOD and Population Viral Load on Performance

Population Viral Loads from Ct values *(n = 4774)*



- Wide range of viral loads in population
- Generally higher with time after onset
- Levels not correlated with infectiousness

Ramy Arnaout, James E. Kirby, et al., **SARS-CoV2 Testing: The Limit of Detection Matters**
bioRxiv 2020.06.02.131144; doi: https://doi.org/10.1101/2020.06.02.131144

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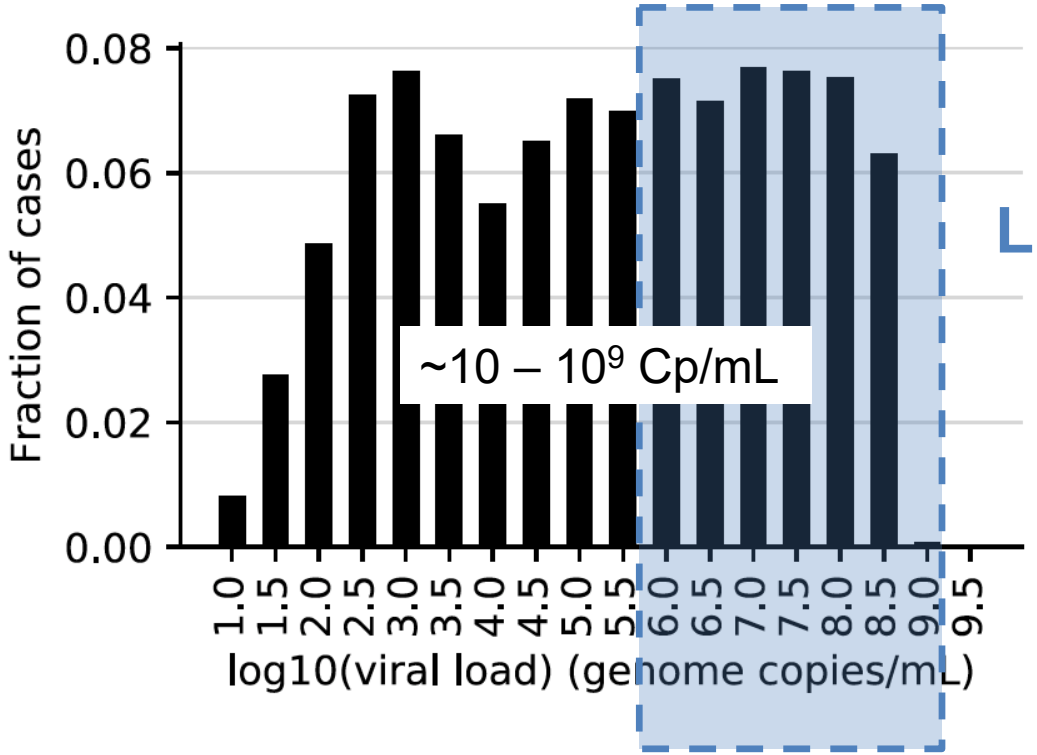

LFA → Typical LOD ~10^6 Copies/mL
Sensitivity ~40% vs. RTPCR for all (symptomatic + asymptomatic)

Vs.

Sens/Spec ~90/95% for symptomatic population (EUA: ~5 days post-onset)

Ramy Arnaout, James E. Kirby, et al., **SARS-CoV2 Testing: The Limit of Detection Matters**
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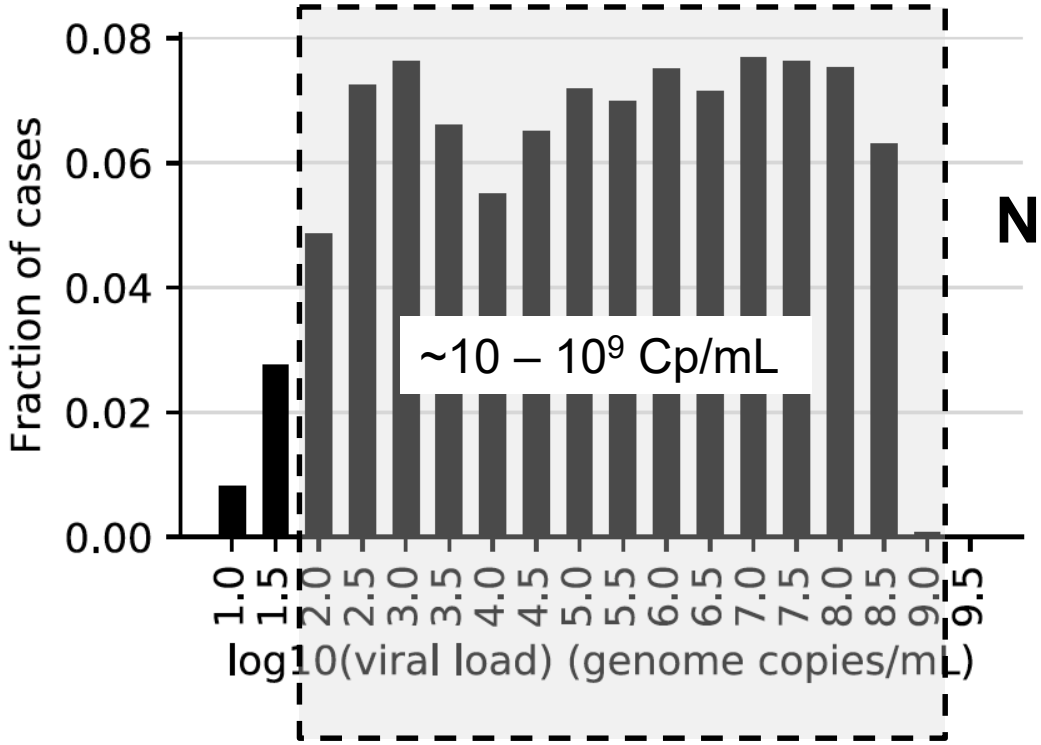

NAT → Typical LOD > ~10^2 Copies/mL
Sensitivity >~90% for all population
(symptomatic + asymptomatic)

Ramy Arnaout, James E. Kirby, et al., **SARS-CoV2 Testing: The Limit of Detection Matters**
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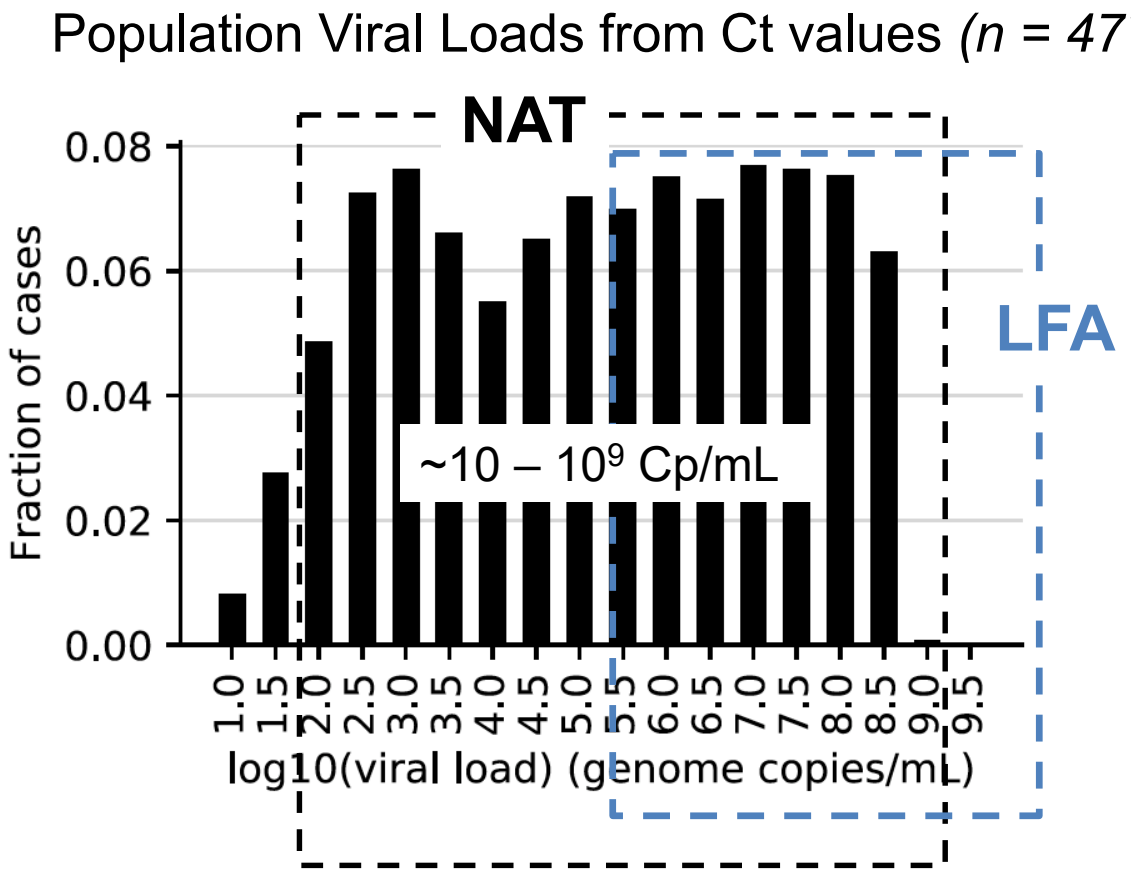
Understanding Screening/Surveillance Performance

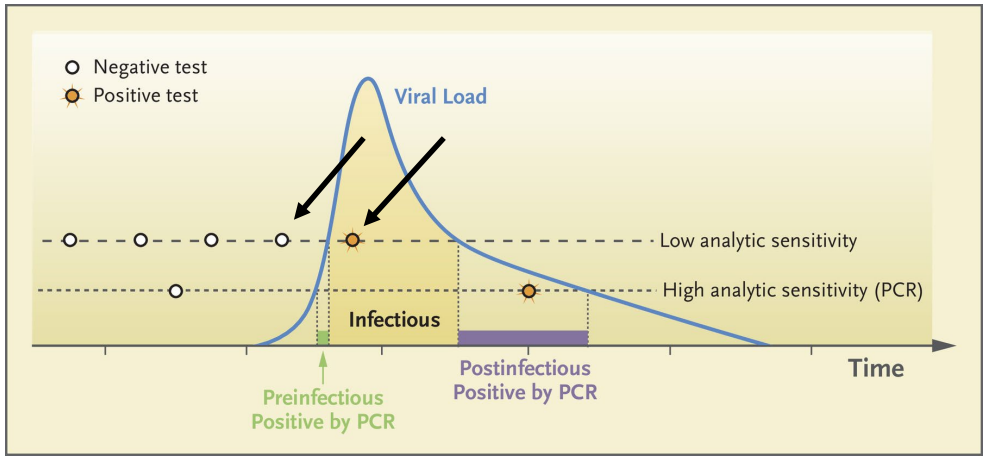
Implications: NAT (PCR) vs LFA (An)



1) Use LFA within ~5-7 days of symptoms
   - Elevated viral load (>90% sens, spec)

2) "Off Label" LFA in Asymptomatics:
   - Backup PCR w/positive in low prevalence
   - Backup PCR w/negative recently exposed

3) Sequential LFA tests



M. Mina et al, NEJM, DOI: 10.1056/NEJMp2025631

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RADx Clinical Studies Core (UMass)

Mission: Evaluate RADx platforms that advance to Phase 2 in rigorous clinical studies w/ diverse populations and settings.

Laura Gibson, MD

David McManus, MD

Standard Trial Design: Master protocols, powered studies (~250 subjects), device-specific amendments, accelerate regulatory review

Eureka Digital Health Platform mobile app and website, participants enter own data

Data Safety Board and Single IRB for oversight and safety monitoring

Robust Research Center Network: POCTRN core center network for enrollment (w/Practice Based Research Network and Centers for Clinical and Translational Science assisting)

COVID-19 Test US

Clinical Study Partners

UMassMemorial Health Care

UCSF Health

Northwestern Medicine

Eureka

Participant ID & Enrollment

JOHNS HOPKINS MEDICINE

EMORY HEALTHCARE

The CTSA Trial Innovation Network

Connecting: NIH Institutes, Industry, Researchers, and Participants

Investigators at CTSA Hubs across the U.S.

Trial Innovation Centers (TICs)

Request Support and Advice for Success

Recruitment Innovation Centers (RICs)

RADx Clinical Studies Core (UMass)

Mission: Evaluate RADx platforms that advance to Phase 2 in rigorous clinical studies w/ diverse populations and settings.

Laura Gibson, MD

David McManus, MD

- 2 Technologies tested (>500 subjects)
- 3 in progress (Quidel, MicroGem, Quanterix) w/~1000 subjects
- Quidel Multisite study: *UMass, UIUC, JHU*
  - Longitudinal sequential Lateral Flow Assay (LFA) assessment (2 weeks)
  - RTPCR, saliva, + viral infectiousness assay
- LFA home testing in design phase
  - Self sampling, digital health platforms, break chain of transmission?

COVID-19 Test US

Clinical Study Partners

UMassMemorial Health Care

UCSF Health

Northwestern Medicine

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+

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RADx Deployment Core (CIMIT)

Bridging NIH/USG, non-profit Foundations, Academia, and Industry

Mission

Provide support for successful commercialization and deployment of COVID-19 solutions in unique communities.

- Members: 32
- Nancy Gagliano, MD, Core Lead
- Brian Walsh, Commercialization Lead
- Sreeram Ramakrishnan, Data Solutions Lead
- Susan Moreira, Deployment Lead

Nancy Gagliano, MD

www.poctrn.org
RADx webinars, tools

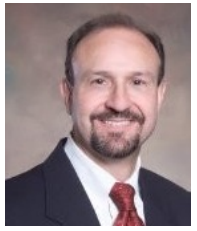
https://whentotest.org/

"When-to-Test" modeling tool: Match tests w/needs; evaluate impact of risk reducing activities.

Current Highlights

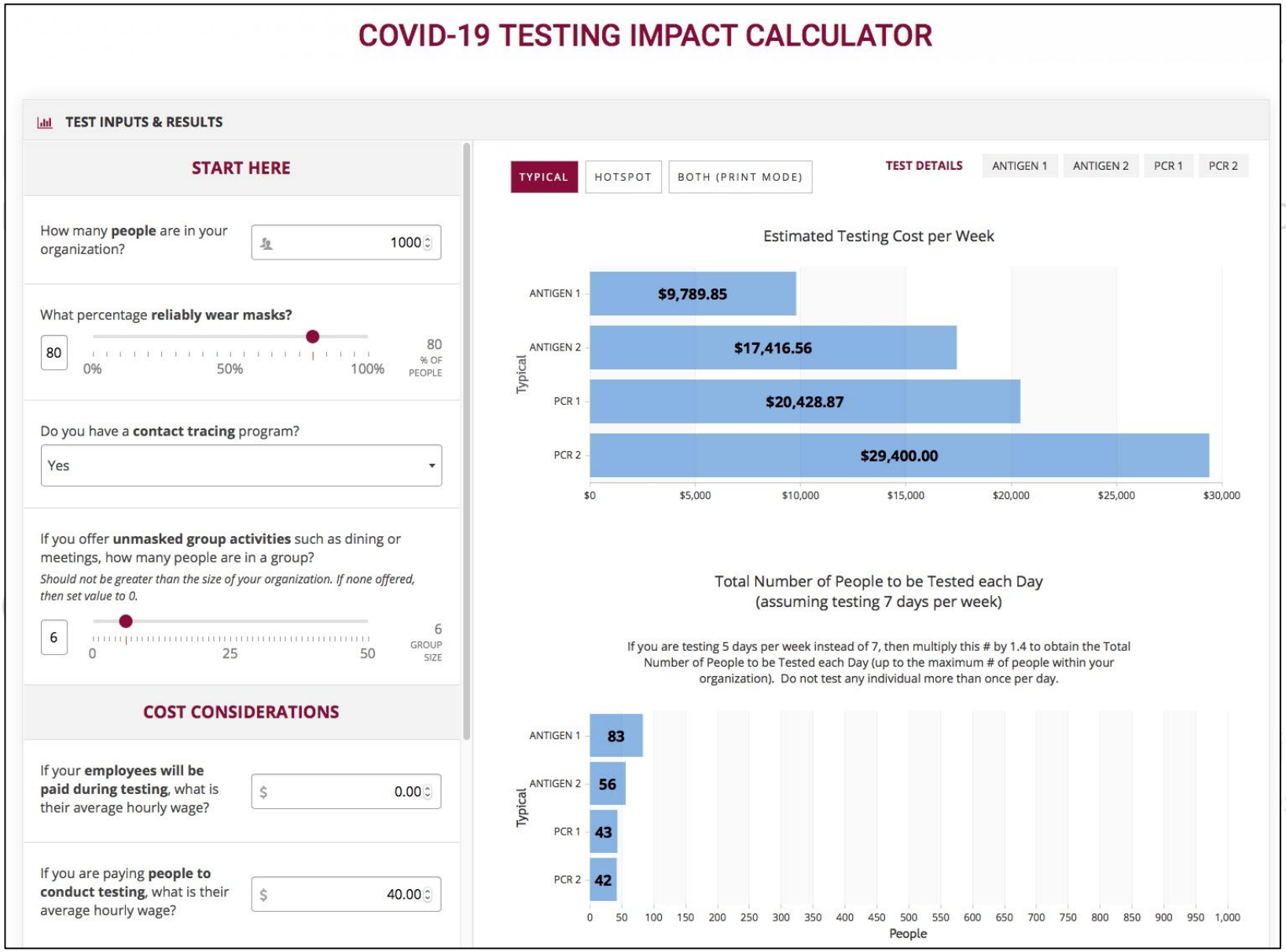
- Supply Chain continues to be core challenge
- Development of Testing Model has received international recognition
- User communities need end-to-end solutions to deploy COVID testing
- Design-a-thon scheduled to develop data solutions

Anette Hosoi
MIT



Paul Tessier,
CIMIT/MGH

RADx Deployment Core (CIMIT)



ademia, and Industry

-19 solutions in unique communities.

www.poctrn.org
RADx webinars, tools

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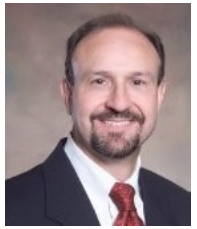
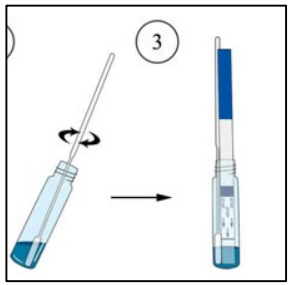


Paul Tessier,
CIMIT/MGH

POC/Home Challenges: *Digital Health*

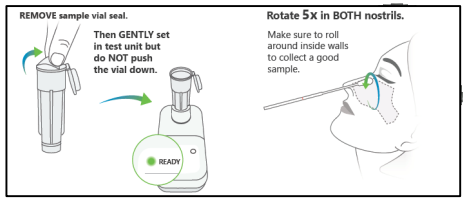
RADx POC Test

PCR



LFA

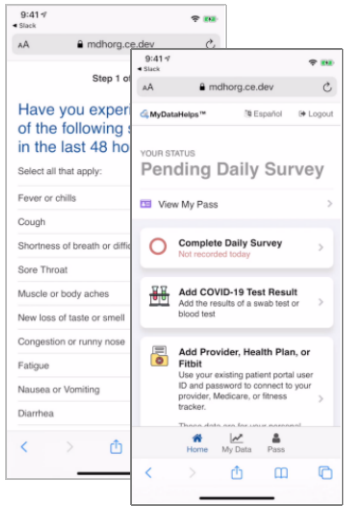
How to Use

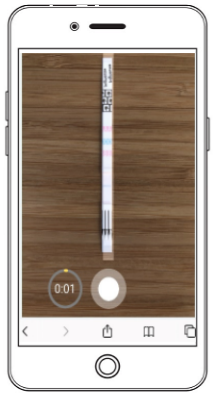


Wearables

Digital Contact Tracing

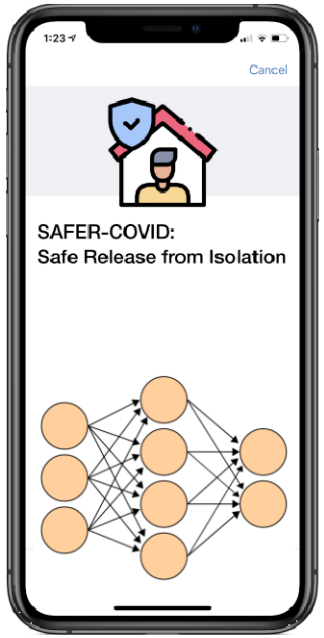
Symptom Surveys





Cell Phone Reader

e.g. OpenRDT (Audere)



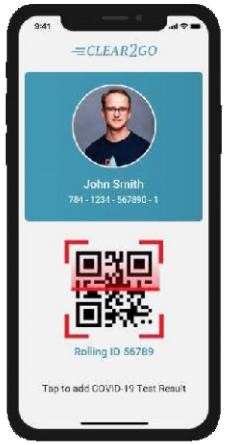
EHR & Claims

SYNC FOR SCIENCE

HL7 FHIR

Blue Button Download My Data

Proof of Health Status



GATES foundation

NIH National Institute of Biomedical Imaging and Bioengineering

NIH NATIONAL CANCER INSTITUTE

https://www.nibib.nih.gov/news-events/newsroom/nih-awards-contracts-develop-innovative-digital-health-technologies-covid-19

RADx Tech/ATP: *Summary*

Implementation Challenges:

- *Screening/Surveillance: assess +/- of disease in asymptomatic populations*
- *Create "at home" use path: prescription, OTC*
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RADx Clinical Studies for Guidance:

- *Can sequential LFA tests provide equivalent info to PCR for "infectiousness"?*
- *Can frequent, inexpensive LFA tests at home break chain of transmission?*