Electronic Supplementary Information (ESI) for:

Point-of-Care Diagnostics: Recent Developments in a Pandemic Age

Harshit Harpaldas[a]; Siddarth Arumugam[a]; Chelsey Campillo Rodriguez[a];

Bhoomika Ajay Kumar[a†]; Vivian Shi[a†]; Samuel K. Sia[a*]

[a] Department of Biomedical Engineering, Columbia University, New York, NY 10027, USA

[†] These authors contributed equally to this article.

* Corresponding author.

Data acquisition methods for figures in main text:

Figure 3:

Data on the number of over-the-counter (OTC) test approvals from 1990 to 2020 was obtained from the U.S Food and Drug Administration (FDA) Over the Counter database.[1] Data was collected for each year individually, by setting the effective date from January 1st to December 31st, exporting search results to a spreadsheet, and enumerating the list.

Figure 4:

All data in this figure was acquired as of September 26, 2021.

For Figure 4A, data on in vitro diagnostics (IVDs) that received emergency use authorization (EUA) in previous public health emergencies was compiled from the FDA website. Information on the current EUAs in place and the tests authorized for each can be found here.[2,3] Information on IVDs that have had their EUA revoked, including tests developed for H1N1 influenza (no current EUA in place), can be found here.[4] Tests were compiled and grouped under assay type (nucleic acid, antigen, antibody) in Microsoft Excel 2019, and graphed in GraphPad Prism 9. The "Other" category for SARS-CoV-2 IVDs includes laboratory developed nucleic acid tests, T-cell tests, and IVDs for management of COVID-19 patients (3 tests detecting Interleukin-6).[5]

For Figure 4B, data on current EUAs for SARS-Cov-2 IVDs was compiled from FDA databases covering the three main assay types (nucleic acid[6], antigen[7], antibody[8]). Data on the authorized setting was also compiled from the same databases. Non-POC designates tests authorized to be utilized in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high and moderate complexity tests (H,M). Tests that are categorized as N/A were also included in this category (e.g., collection kits). POC designates tests authorized to be utilized in patient care settings operating under a CLIA Certificate of Waiver (W). Home/OTC designates tests authorized for home-use and available OTC. Note, the home and OTC categories are grouped together as all tests currently approved for home-use are also available OTC. Additionally, all tests were categorized by their most restricted authorized setting, and only tests on the same platform that detect another target (e.g., includes Influenza) were counted more than once in the analysis. All data was compiled in Microsoft Excel 2019 and graphed in GraphPad Prism 9. For more information on the tests included in each category see **Supplementary Table 3.**

Figure 5:

All data in this figure was acquired as of July 15, 2021.

Data on the company founding date was collected from various web searches on google.com. In order to obtain the time (in months) for each company to receive an initial EUA from the FDA, the dates for the company's first FDA EUA were recorded using the FDA databases.[6–8] The time from the initial declaration of the EUA pathway by the FDA (February 4th, 2020) was then calculated and utilized in the analysis. Information on US federal funding was restricted to three sources, National Institutes of Health (NIH) Rapid Acceleration of Diagnostics (RADx)

initiative, Biomedical Advanced Research and Development Authority (BARDA), and the Department of Defense (DoD). For RADx, and BARDA numbers were taken from their respective websites which list funding given to various companies during the COVID-19 pandemic.[9,10] Information on DoD funding was obtained from various press releases from both the DoD and individual companies. Data was collected, and aggregated in Microsoft Excel 2019 and plotted using GraphPad Prism 9.

Figure 7:

All data in this figure was acquired as of September 26, 2021.

Using the FDA databases on IVDs that received EUA,[6–8] POC diagnostic platforms were grouped based on their use case (described in main text). The analysis done here was based solely on the platform, therefore platforms with multiple tests were only included once in the analysis. See **Supplementary Table 4** for a breakdown of the tests included in each category.

Supplementary Tables:

Supplementary Table 1: Company reported performance metrics for POC nucleic acids tests discussed in main text:

Test Name	Sensitivity (95% CI)	Specificity (95% CI)	Sample Type	Reported Limit of Detection (LOD)	Sample Type	LOD with FDA Reference Panel
Abbott ID NOW COVID-19	100% (83.9 -100%)	100% (88.7 -100%)	Contrived NP swabs	125 genome equivalents/mL	Purified RNA diluted in NP matrix	$3x\ 10^5$ NDU/mL
Mammoth Biosciences SARS-CoV-2 DETECTR kit	95% (83.5 - 98.6%)	100% (94.2 -100%)	Clinical NP swabs (prospective)	20 copies/µL (20,000 copies/mL)	AccuPlex Verification Panel Reference material diluted in NP matrix	$5.4x\ 10^5$ N DU/mL
Sherlock Biosciences Sherlock CRISPR SARS-CoV-2 kit	100% (83.9 -100%)	100% (88.6 -100%)	Contrived NP swabs	6.75 copies/µL (6,750 copies/mL)	Extracted RNA diluted in NP matrix	$0.6x10^4$ NDU/mL
Mesa Biotech Accula SARS-CoV-2 Test	95.8% (78.9 -99.9%)	100% (86.7 -100%)	Clinical nasal swabs (retrospective)	150 copies/mL	Heat inactivated virus diluted in nasal matrix	$4.75x\ 10^2$ NDU/mL
Visby Medical COVID-19 Point of Care Test	100% (89.0 -100%)	95.30% (87.1 -98.4%)	Clinical NP swabs (prospective)	435 copies/swab	Inactivated virus diluted in NP matrix	$5.4x\ 10^4$ NDU/mL
Roche cobas liat SARS-CoV-2 & Influenza A/B	100% (93.6 -100%)	100% (98.4 -100%)	Clinical NP swabs (prospective)	12 copies/mL	Heat inactivated virus diluted in NP matrix	$5.4x\ 10^3$ NDU/mL
Lucira Health CHECK-IT COVID-19 Test Kit	91.7% (85.6 - 95.8%)	98.2% (95.8 - 99.4%)	Clinical nasal swabs (prospective)	2700 copies/swab (900 copies/mL)	Heat inactivated virus diluted in nasal matrix	N/A
Cue Health COVID-19 Test	97.4% (86.5 -99.5%)	99.1% (96.9 – 99.8%)	Clinical nasal swabs (prospective)	1.3 genome copies/µL (1,300 copies/mL)	Viral RNA diluted in nasal matrix	$6\ x\ 10^4$ NDU/mL (Dry Swab)
Cepheid Xpert Xpress SARS-CoV-2	97.8% (88.4 – 99.6%)	95.6% (85.2 – 98.8%)	Clinical NP swabs (retrospective)	0.02 PFU/mL	Live virus diluted in NP swab matrix	$5.4x\ 10^3$ NDU/mL

BioFire Filmarray Respiratory Panel 2.1-EZ	98.40% (91.4 - 99.7%)	98.9% (97.5 – 99.5%)	Clinical NP swabs (prospective)	500 copies/mL	Heat inactivated virus diluted in NP swab matrix	6.0x 10^3 NDU/mL
Cepheid Omni SARS-CoV-2	97.6% (91.5 - 99.3%)	99.1% (94.8 - 99.8%)	Clinical NP swabs (prospective)	400 copies/mL	Heat inactivated virus diluted in NP swab matrix	N/A

Note: All performance metrics were obtained from Instruction for Use (IFU) documents from FDA EUA database. NDU stands for RNA NAAT detectable units and is further defined here on the FDA website.[11]

Supplementary Table 2: Company reported performance metrics for POC antigen tests discussed in main text:

Test Name	Sensitivity (95% CI)	Specificity (95% CI)	Sample Type	Reported Limit of Detection (LOD)	Sample Type
Quidel Sofia SARS Antigen FIA	96.70% (83.3 - 99.4%)	100% (97.9 -100%)	Clinical nasal swabs (prospective)	$1.13x10^2$ $TCID_{50}$/mL	Heat inactivated virus diluted in nasal swab matrix
Quidel QuickVue At-Home COVID-19 Test	83.5% (74.9 - 89.6%)	99.2% (97.2 -99.8%)	Clinical nasal swabs (prospective)	$1.91x10^4$ $TCID_{50}$/mL	Heat inactivated virus diluted in nasal swab matrix
Abbott BinaxNOW COVID-19 Ag Card Home Test	91.7% (73.0 - 98.9%)	100% (87.7 - 100.0%)	Clinical nasal swabs (prospective)	140.6 $TCID_{50}$/mL	Heat inactivated virus diluted in nasal swab matrix
Ellume COVID-19 Home Test	95% (82 - 99%)	97% (93 - 99%)	Clinical nasal swabs (prospective)	$10^{3.8}$ (6,310) $TCID_{50}$/mL	Heat inactivated virus diluted in NP swab matrix
Luminostics CLIP COVID Rapid Antigen Test	96.9% (83.8 - 99.9%)	100% (97.3 – 100%)	Clinical nasal swabs (prospective)	0.88×10^2 $TCID_{50}$/mL	Gamma irradiated virus diluted in nasal swab matrix
LumiraDx SARS-CoV-2 Ag Test	97.6% (91.6 - 99.3%)	96.6% (92.7 - 98.4%)	Clinical NP swabs (prospective)	32 $TCID_{50}$/mL	Gamma irradiated virus diluted in nasal swab matrix
BD Veritor System for Rapid Detection of SARS-CoV-2	84% (67 - 93 %)	100% (98 -100%)	Clinical nasal swabs (prospective)	$1.4x10^2$ $TCID_{50}$/mL	Gamma irradiated virus diluted in nasal swab matrix
BD Veritor At-Home COVID-19 Test	84.6% (70.3 - 92.8%)	99.8% (99 - 100%)	Clinical nasal swabs (prospective)	$1.87x10^5$ $TCID_{50}$/mL	Gamma irradiated virus diluted in nasal swab matrix

Note: All performance metrics were obtained from Instruction for Use (IFU) documents from the FDA EUA database.

Supplementary Table 3: SARS-CoV-2 POC IVDs that have received EUA, grouped by their authorized setting (Figure 4B)

Test Type	Authorized Setting	Test Name
Nucleic Acid	CLIA waived laboratories (POC)	Visby Medical COVID-19 Point of care Test
		Mesa Biotech Accula SARS-CoV-2 Test
		Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV
		Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV plus
		Cepheid Xpert Xpress SARS-CoV-2 test
		Cepheid Xpert Omni SARS-CoV-2
		Cepheid Xpert Xpress SARS-CoV-2 DoD
		BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ)
		Roche cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System
		Roche cobas SARS-CoV-2 Nucleic Acid Test for use on the cobas Liat System
		Abbott ID Now COVID-19
	Home/OTC	Lucira CHECK-IT COVID-19 Test Kit
		Cue Health Cue COVID-19 Test
Antigen	CLIA waived laboratories (POC)	BD Veritor System for Rapid Detection of SARS-CoV-2
		BD Veritor System for Rapid Detection of SARS-CoV-2 & Flu A+B
		LumiraDx SARS-CoV-2 Ag Test
		Luminostics Clip COVID Rapid Antigen Test
		Quidel Sofia SARS Antigen FIA
		Quidel Sofia 2 Flu + SARS Antigen FIA
		Access Bio CareStart COVID-19 Antigen test
		Princeton BioMeditech Status COVID-19/Flu
		Celltrion DiaTrust COVID-19 Ag Rapid Test
		Salofa Oy Sienna-Clarity COVID-19 Antigen Rapid Test Cassette
		InBios SCoV-2 Ag Detect Rapid Test
		Ellume Lab COVID Antigen Test
		GenBody COVID-19 Ag Test
		PHASE Scientific INDICAID COVID-19 Rapid Antigen Test
	Home/OTC	Quidel QuickVue At-Home OTC COVID-19 Test
		Ellume COVID-19 Home Test
		Abbott BinaxNOW COVID-19 Ag Card Home Test
		BD Veritor At-Home COVID-19 Test
		Access Bio CareStart COVID-19 Antigen Home Test
		Orasure InteliSwab COVID-19 Rapid Test
Antibody	CLIA waived laboratories (POC)	Nirmidas Biotech MidaSpot COVID-19 Antibody Combo Detection Kit
		ADVAITE RapCov Rapid COVID-19 Test
		Salofa Oy Sienna-Clarity COVIBLOCK COVID-19 IgG/IgM Rapid Test Cassette
		Hangzhou Biotest Biotech RightSign COVID-19 IgG/IgM Rapid Test Cassette

		Assure Tech Assure COVID-19 IgG/IgM Rapid Test Device
		Sugentech SGTi-flex COVID-19 IgG
		Megna Health Rapid COVID-19 IgM/IgG Combo Test Kit
		NOWDiagnostics ADEXUSDx COVID-19 Test
		InBios SCov-2 Detect IgG Rapid Test
		Access Bio CareStart COVID-19 IgM/IgG
		Diabetomics CovAb SARS-CoV-2 Ab Test
		LumiraDx SARS-CoV-2 Ab Test
		Access Bio CareStart EZ COVID-19 IgM/IgG

Supplementary Table 4: POC IVD platforms that have received EUA for a SARS-CoV-2 test, grouped by their most appropriate use case (Figure 7)

Assay Type	Use Case	Company Name/POC Platform
Nucleic Acid	Premium Clinic	Biofire FilmArray 2.1
		Roche cobas Liat
	Premium/Economy Clinic	Cepheid GeneXpert*
	Economy Clinic	Cepheid GeneXpert Omni
		Mesa Biotech Accula
		Abbott ID NOW
	Premium Field	Visby Medical
		Cue Health
		Lucira Health
Antigen	Economy Clinic	LumiraDx
		BD Veritor Plus
		Quidel Sofia 2
		Qorvo Biotechnologies Omnia
		Celltrion Sampinute
		Ellume Lab
	Premium Field	Ellume
		Luminostics Clip
	Economy Field	Abbott BinaxNOW
		Quidel QuickVue
		Salofa Oy
		Celltrion Diatrust
		InBios International
		Princeton Biomeditech
		Access Bio CareStart
		BD Veritor At Home
		Orasure InteliSwab
		Genbody
		Phase Scientific INDICAID
Antibody	Economy Clinic	QIAGEN QIAreach
		LumiraDx
	Economy Field	NOWDiagnostics ADEXUSDx
		ADVAITE RapCoV
		Sugentech SGTI-flex
		Megna Health
		Access Bio CareStart
		Nirmidas Biotech
		Beijing Wantai Biological Pharmacy Enterprise Co. WANTAI
		Salofa Ou Sienna-Clarity
		Hangzhou Biotest Biotech Co. RightSign
		ACON Laboratories
		Hangzhou Laihe Biotech Co. LYHER
		Innovita
		Jiangsu Well Biotech Co. Orawell

		Xiamen Biotime Biotechnology Co., BIOTIME
		Biohit Healthcare
		Assure Tech
		TBG Biotechnology Corp.
		Biocan Diagnostics Tell Me Fast
		Cellex
		Healgen Scientific
		InBios
		Access Bio
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