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ICTR COVID-19 Clinical Research Center Town Hall

Wednesday December 9, 2020

Town Hall Agenda

- Updates on current research activity
- Outpatient Research Presentations:
  - —RADx – Yukari Manabe, MD
  - —Plasma – David Sullivan, MD
  - —ACTIV-2 – Kelly Dooley, MD, PhD
  - —PROTECT – Mark Sulkowski, MD
  - —Astra-Zeneca Vaccine – Anna Durbin, MD
  - —HOPE Registry – Cassie Lewis-Land, MS, CCRP

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ICTR COVID-19 Clinical Research Center

https://ictr.johnshopkins.edu/covid-research-center

COVID-19 Steering Committee

- Capital Region Research @ Sibley, Suburban, and HCGH
- Recruitment Innovation Unit
- Research Coordinator Support Service

COVID-19 Outpatient Clinical Research Units

COVID-19 Clinical Research Coordinating Committee

COVID-19 And Data Research Evaluation Committee (CADRE)

COVID-19 Biospecimen Repository Committee

Updates on Current Research Activity

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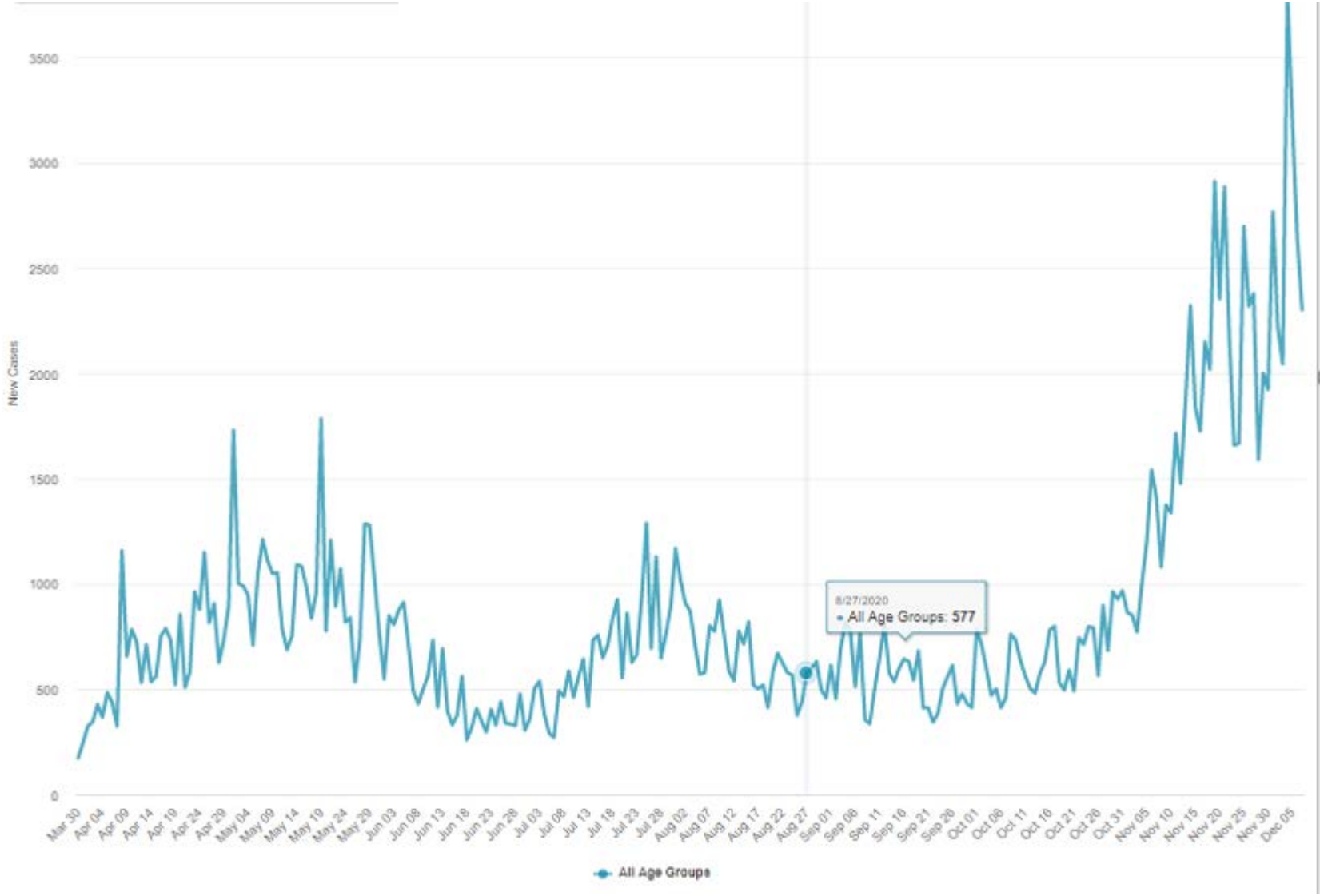
COVID-19 Research Updates: Recent completion of study enrollment

- A Randomized Placebo-Controlled Safety and Dose-Finding Study for the Use of the IL-6 Inhibitor Clazakizumab in Patients with Life-Threatening COVID-19 Infection
  - —Investigators: Drs. Nada Alachkar, Russell Wesson and Mark Landrum
  - —Johns Hopkins Hospital and Howard County General Hospital
  - —Enrollment, 67 patients (180 overall)
- CRITICAL: CRIzanlizumab for Treating COVID-19 vAscuLopathy
  - —Investigators: Drs. Charles Lowenstein and Thorsten Leucker
  - —Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center
  - —Enrollment, 50 patients (JHU study)

Maryland COVID-19 Data Dashboard: Daily new cases of SARS-CoV-2 infection



<u>December 9</u>
MD daily COVID-19 positive: 2,692
7-day average: 7.74%

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NIH COVID-19 Treatment Guidelines Panel: Recommendation for Pharmacologic Management

COVID-19 Severity	Panel's Recommendation
Non-hospitalized or hospitalized but not requiring supplemental oxygen	• **At this time, there are insufficient data to recommend either for or against the use of bamlanivimab or casirivimab + imdevimab for the treatment of outpatients with mild to moderate COVID-19.** • **Do not use dexamethasone (AI)**
Prevention and Prophylaxis of SARS-CoV-2 infection	
Pre-exposure	**The Panel recommends against the use of any agents for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pre-exposure prophylaxis (PrEP), except in a clinical trial (AIII)**
Post-exposure	**The Panel recommends against the use of any agents for SARS-CoV-2 post-exposure prophylaxis (PEP), except in a clinical trial (AIII).**

Strength of recommendation: A, Strong; B, Moderate; C, Optional
Quality of Evidence: I, One or more randomized trials with clinical outcomes and/or validated lab endpoints; II, One or more well-designed, nonrandomized trials or observational cohort studies; III, Expert opinion

https://www.covid19treatmentguidelines.nih.gov; accessed December 9, 2020

Updates on Clinical Research for Ambulatory Patients with or at risk for SARS-CoV-2 infection

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Outpatient Research: RADx

Yukari Manabe, MD

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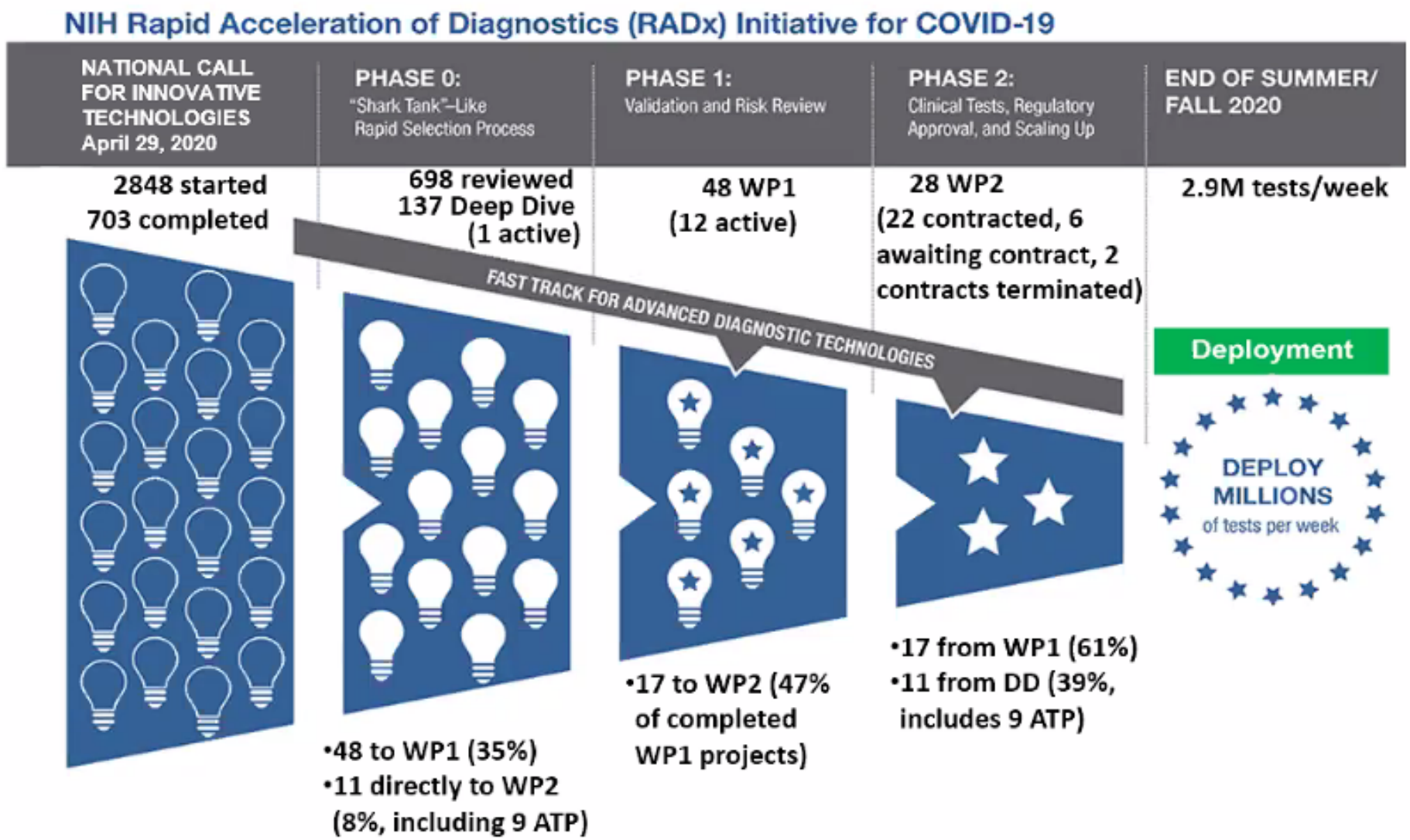
NIH National Institutes of Health
Turning Discovery Into Health

Rapid Acceleration of Diagnostics (RADx) Projects Overview

The NIH has launched several programs to accelerate innovation in, development and commercialization of, and implementation of COVID-19 testing. RADx-ATP is one of these programs.

Project	Description
 RADx Tech (RADx-Tech)	*Highly competitive, rapid three-phase challenge to identify the best candidates for at-home or point-of-care tests for COVID-19*
 RADx Underserved Populations (RADx-UP)	*Interlinked community-engaged demonstration projects focused on implementation strategies to enable and enhance testing of COVID-19 in underserved and/or vulnerable populations*
 RADx-Radical (RADx-Rad)	*Develop and advance novel, non-traditional approaches or new applications of existing approaches for testing*
 RADx Advanced Testing Program (RADx-ATP)	*Rapid scale-up of advanced POC technologies to increase rapidity and enhance and validate throughput – and support of ultra-high throughput machines and facilities*
 Data Management Support	Build an infrastructure for and support coordination of the various data management needs of many of the COVID-19 efforts

RADx Tech Projects by Phase
11/25/20



Study Rationale

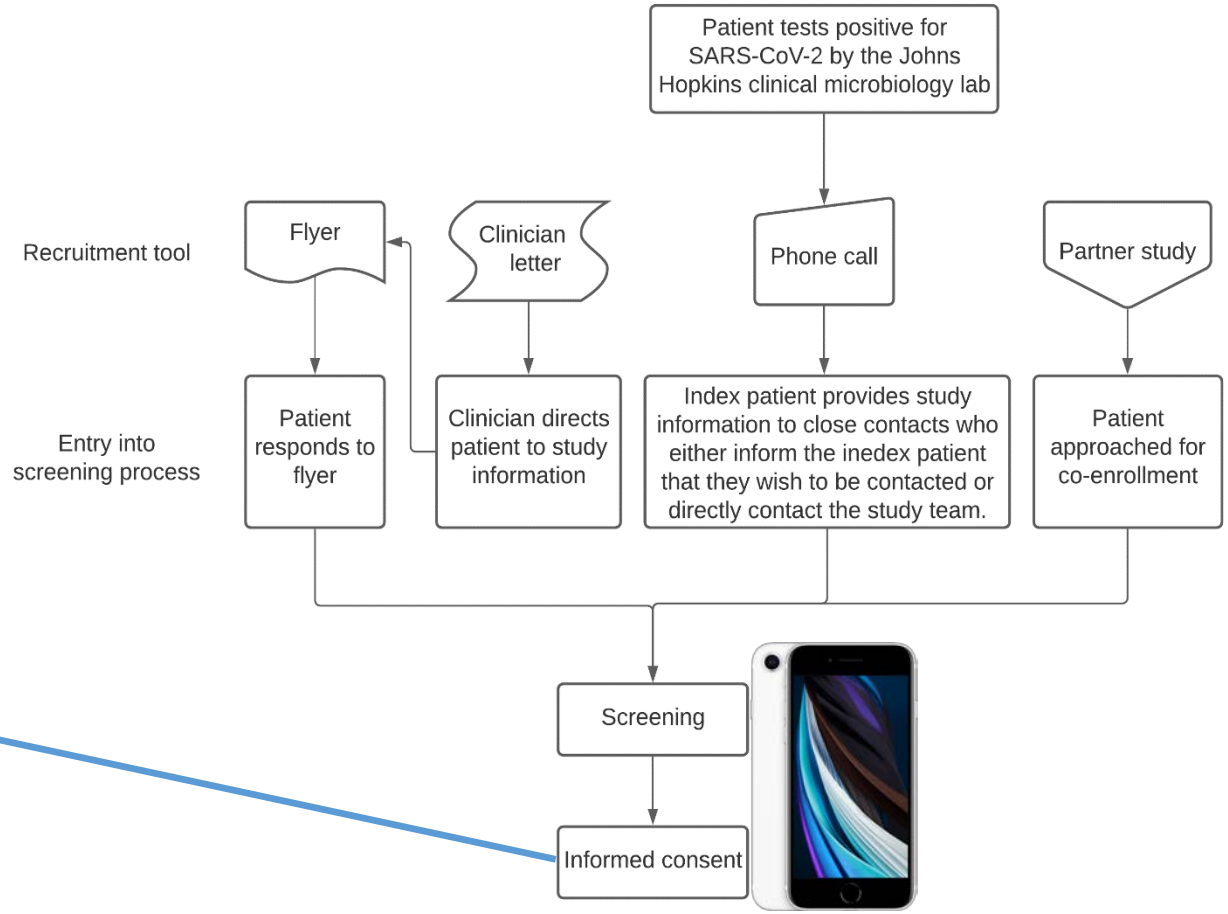
- Demand for SARS-CoV-2 exceeds current testing capacity.
- Identify low cost and easily scalable diagnostic tests that directly detect SARS-CoV-2.
- Find suitable replacements for NP samples, such as: midturbinate or saliva.
- Bridge the evidence gap in performance of NAT and antigen test in different sample types: NP, MT and Saliva.

Research Goal

- Determine the accuracy of novel SARS-CoV-2 assays against a NP swab gold standard
- Compare the performance of antigen tests in saliva and nasal samples to the current standard RT-PCR test.
- Setup biorepository for future testing and research collaboration.
- Study findings will be shared with NIH-supported RADx Clinical Studies Core in their recommendation to device manufacturers and the NIH.

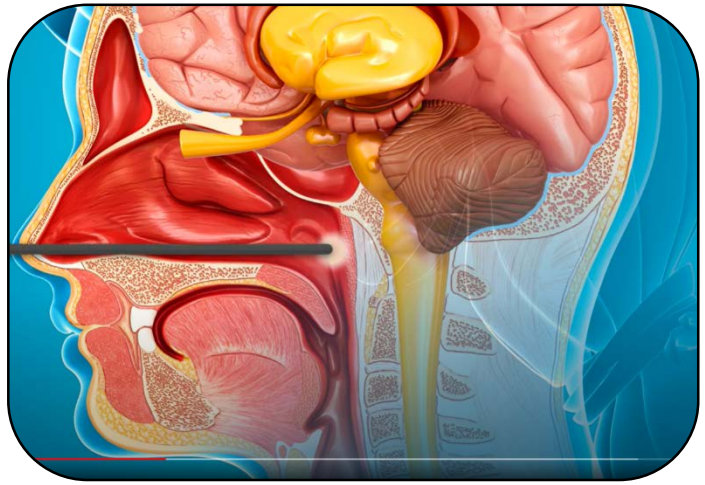
Recruitment

- Recruitment
  - Letters to Providers
  - Flyers
  - Phone call (Index pt provides study information to close contacts)
  - Partner study
  - HOPE Registry
- **Participant (≥18 years)**
  - **Symptomatic**
  - **Asymptomatic**
- **Study Location: ICTR-CRU**
  - **—Bayview**
  - **—Green Spring Station**



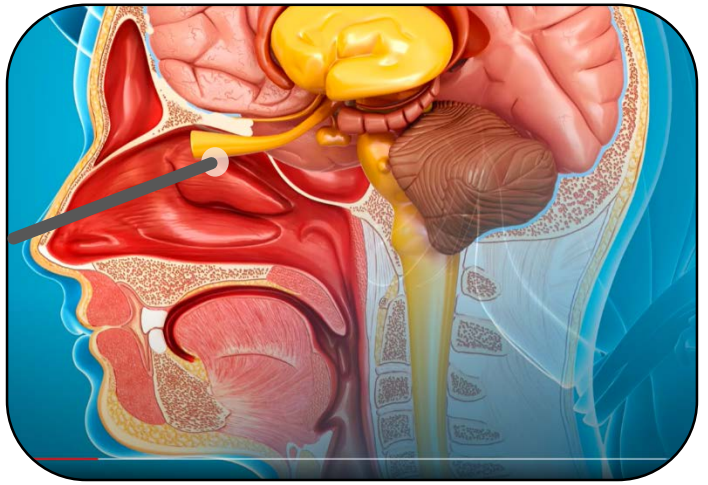
*An asymptomatic close contact is defined as a person who has none of the above COVID-19 symptoms but who was within 6 feet of an infected person for at least 15 minutes starting from 2 days before illness onset or 2 days prior to specimen collection of a positive specimen.

Sample Collection



NP Swab

- Nares to the pharynx
- Swabs into VTM



MT

- Dry sample

Saliva

- Spit/passive drool (~ 2ml)

If you're sick and think you might have COVID-19, or if you're a close contact of someone who tested positive, you may qualify for a Johns Hopkins study on easier COVID-19 tests.

Get tested.

Call today to find out if you're eligible: 443-301-8572

Researchers at Johns Hopkins are seeking volunteers to participate in a clinical research study to identify easier approaches for COVID-19 testing. The potential participants will be eligible for the study if they are either: A symptomatic person suspected of having COVID-19 or an asymptomatic close contact of a person diagnosed with COVID-19. Participation in the study requires phone screening, informed consent and visit to the testing site for samples collection. Benefits: 1) All study participants will undergo the gold standard testing for COVID-19. 2) Participant will receive test results within 48 hours. 3)Participants will be reimbursed for time and travel.

Principal Investigator: Yukari Manabe, M.D. IRB00264304

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MEDICINE

Outpatient Research: Plasma

David Sullivan, MD

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Convalescent Plasma Randomized Clinical Trials for SARS-CoV-2 Prophylaxis and Early COVID-19 Treatment are Foundational for Subsequent Hyperimmune Globulin and Vaccines

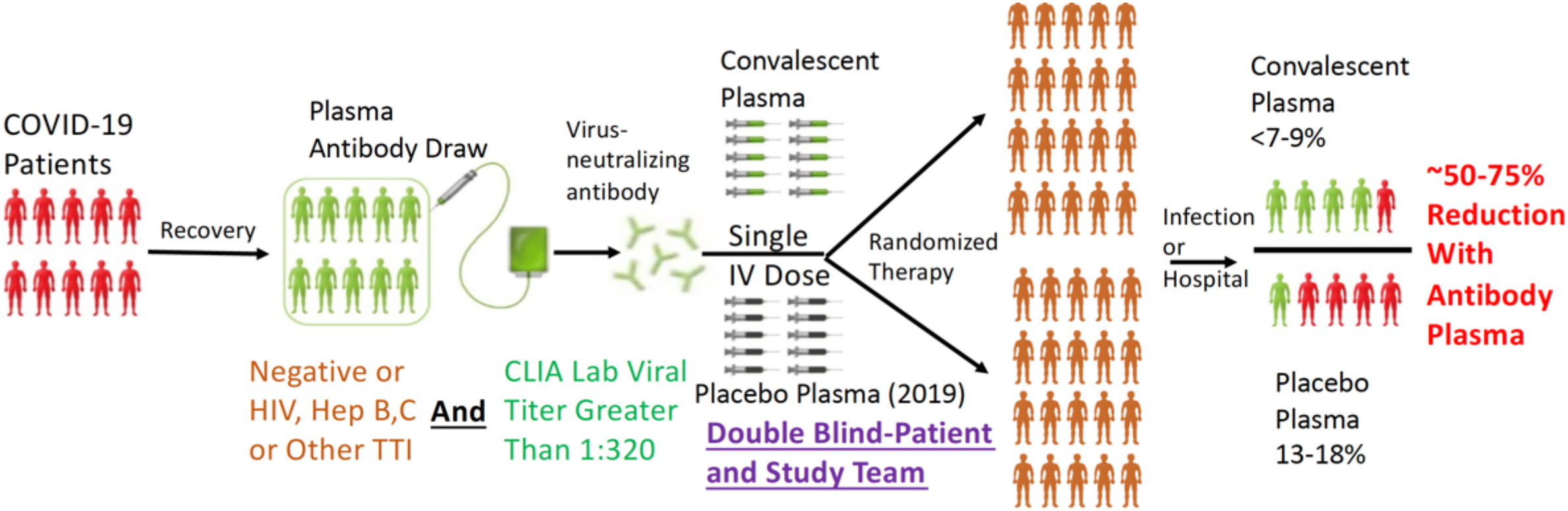
- David Sullivan, Shmuel Shoham, Kelly Gebo
- Dan Hanley, Arturo Casadevall and Bryan Lau

- DoD OTA-W911QY2090012
- Bloomberg Philanthropy, NIAID, The Moriah Fund, The Mental Wellness Foundation, Octapharma

Study Rationale

- Antibodies work for the SARS-CoV-2 vaccine
- Antibodies decrease death in the hospital
- Infection prevention and outpatient early treatment has not been validated for FDA approval
- Drugs are not coming to the rescue. We have only antibodies for therapy.
- Passive immunization is an established approach to prevention and treatment of viral infections (e.g. rabies immune globulin (RIG), hepatitis B immune globulin (HBIG), RSV monoclonal antibody
- Convalescent plasma has now been used as TREATMENT for severe COVID-19 in over 250,000 hospital patients
- Convalescent plasma has proven success for hemorrhagic fevers, influenza, Ebola, bacterial and other viral diseases

How it Works


COVID-19 Patients
Recovery
Plasma Antibody Draw
Negative or HIV, Hep B,C or Other TTI
And
CLIA Lab Viral Titer Greater Than 1:320
Virus-neutralizing antibody
Convalescent Plasma
Single IV Dose
Placebo Plasma (2019)
Double Blind-Patient and Study Team
Randomized Therapy
Infection or Hospital
Convalescent Plasma <7-9%
Placebo Plasma 13-18%
~50-75% Reduction With Antibody Plasma

Recruitment

Infection Prevention **Subjects:** 500 subjects

- —**Inclusion:** ≥ 18 years old, high risk exposure to COVID+ person in past 120 hours at home at work at play).
- —30 minute screen day -1, 1 hour transfusion day 0, swab follow up day +1, 7, 14, 28 & 90 (15 minutes

Early Treatment **Subjects:** 1344 subjects

- —**Inclusion:** ≥ 18 years old, COVID-19 infection, well enough to not require hospitalization, symptom onset <8 days
- —30 minute screen day -1, 1 hour transfusion day 0, follow up day 14, 28 and 90 (15 minutes

- —**Design:** blinded; 1:1 randomization; 1 unit of convalescent plasma (ELISA titer ≥ 1:320) vs. normal plasma

COVID-19 PLASMA TRIALS
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Randomizations are at 543, Transfusions 489, plasma dispensed at 505 Infection Prevention 109 (20% of 500) Early Treatment ~434 (72% of 600) (33% of 1344)

Study recruitment over time

Dec 4 IP-109 ET-434=543 +45
Nov 28 IP-104 ET-394=498 +36
Nov 21 IP-98 ET-364=462 +75
Nov 14 IP-82 ET-305=387 +59
Nov 7 IP-75 ET-253=328 +34
Oct 31 IP-66 ET-228=294 +40
Oct 24 IP-58 ET-196=254 +23
Oct 17 IP-52 ET-179=231 +20
Oct 3 IP-45 ET-134 = 179 +27
Sept 19 IP-34 ET-102 = 136 +17
Sept 12 IP-30 ET-89 = 119 +12
Aug 29 IP-26 ET-65 = 91 +12
Aug 15 IP-23 ET-45 = 68 +11

Table 2: Cumulative Randomization by Trial and Site (As of 05 December 2020, 21:00 EDT)

Site	CSSC-001 Post Exposure Prophylaxis			CSSC-004 Outpatient Early Treatment		
	Randomized, N (%)	Transfused, N (%)	Plasma Dispensed, N (%)	Randomized, N (%)	Transfused, N (%)	Plasma Dispensed, N (%)
AAMC	4 (3.7)	3 (3.0)	3 (2.9)	11 (2.5)	8 (2.1)	11 (2.7)
BCM	0 (0.0)	0 (0.0)	0 (0.0)	8 (1.8)	8 (2.1)	5 (1.2)
JHSPH-Shiprock	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.3)	1 (0.2)
JHSPH-Whiteriver	0 (0.0)	0 (0.0)	0 (0.0)	10 (2.3)	10 (2.6)	10 (2.5)
JHU	36 (33.0)	35 (35.0)	35 (34.0)	147 (33.9)	120 (30.8)	134 (33.3)
L/B: RIH	8 (7.3)	7 (7.0)	8 (7.8)	24 (5.5)	23 (5.9)	23 (5.7)
MS-Georgetown	10 (9.2)	10 (10.0)	10 (9.7)			
MS-Washington				45 (10.4)	42 (10.8)	42 (10.4)
NorthShore	1 (0.9)	1 (1.0)	1 (1.0)	48 (11.1)	45 (11.6)	41 (10.2)
UAB	0 (0.0)	0 (0.0)	0 (0.0)	41 (9.4)	41 (10.5)	41 (10.2)
UCinci	2 (1.8)	1 (1.0)	2 (1.9)	17 (3.9)	13 (3.3)	16 (4.0)
UC-Irvine	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	2 (0.5)	2 (0.5)
UCLA	7 (6.4)	5 (5.0)	7 (6.8)	15 (3.5)	11 (2.8)	13 (3.2)
UCSD	21 (19.3)	19 (19.0)	18 (17.5)			
UMass	2 (1.8)	2 (2.0)	2 (1.9)	14 (3.2)	14 (3.6)	12 (3.0)
UR	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	3 (0.8)	3 (0.7)
Utah	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.4)	6 (1.5)	6 (1.5)
UTHealth	3 (2.8)	3 (3.0)	3 (2.9)	21 (4.8)	21 (5.4)	21 (5.2)
VBMC	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.9)	4 (1.0)	4 (1.0)
WCHN-Danbury	2 (1.8)	2 (2.0)	2 (1.9)	6 (1.4)	6 (1.5)	6 (1.5)
WCHN-Norwalk	1 (0.9)	1 (1.0)	1 (1.0)	1 (0.2)	1 (0.3)	1 (0.2)
WSU	12 (11.0)	11 (11.0)	11 (10.7)	10 (2.3)	10 (2.6)	10 (2.5)
Total	**109 (100.0)**	**100 (100.0)**	**103 (100.0)**	**434 (100.0)**	**389 (100.0)**	**402 (100.0)**

Note: Number of transfused is based on data entered in CSSC-001, and CSSC-004 system; number of blood dispensed is based on data from LOCATOR system; both may be subject to late data entry.
For CSSC-001, **3** randomized subjects was confirmed not getting transfusion; for CSSC-004, **11** subjects were confirmed not getting transfusion.

COVID-19 PLASMA TRIALS
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We Need Your Help

- If you have an infected or an exposed patient that you think would be interested in these trials- reach out to us.

  —Early Treatment
  - dsulliv7@jhmi.edu
  - 443-690-2496 (David Sullivan cell phone)
  - kgebo@jhmi.edu
  - 443-794-6757 (Kelly Gebo cell phone)

  —Infection Prevention
  - sshoham1@jhmi.edu
  - 202-215-6760 (Shmuel Shoham cell phone)

Outpatient Research: ACTIV-2

Kelly Dooley, MD, PhD

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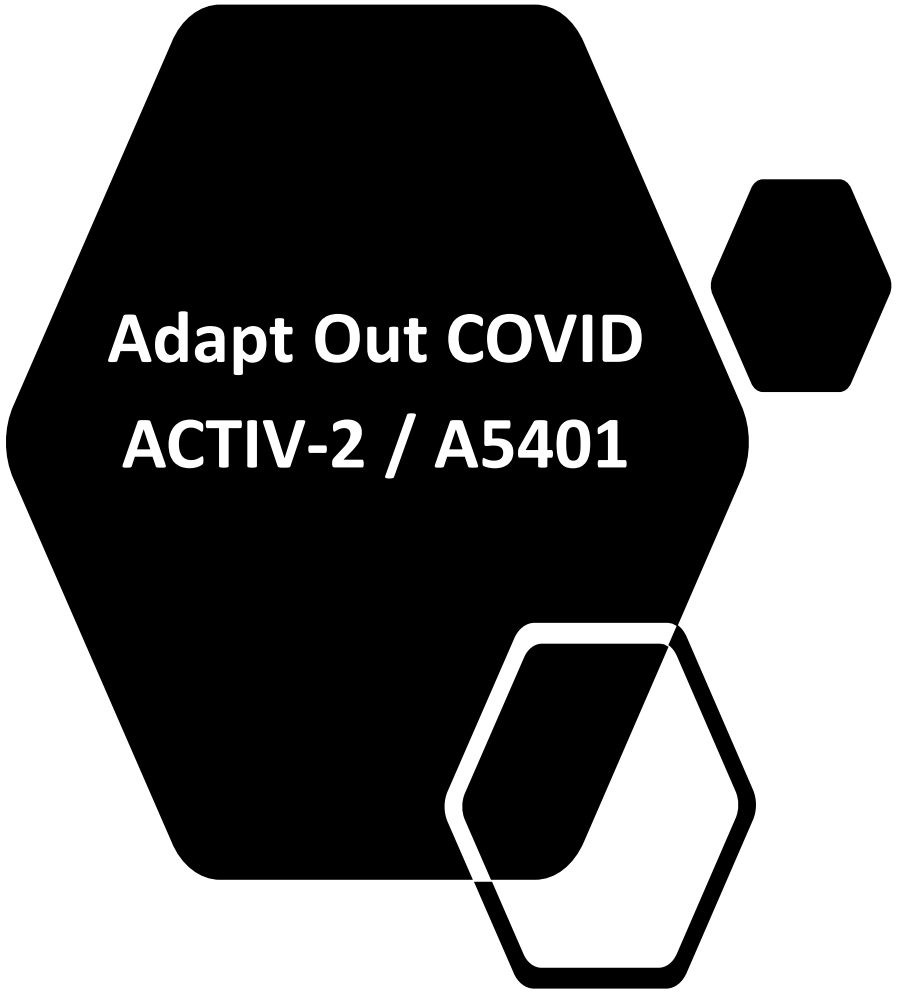
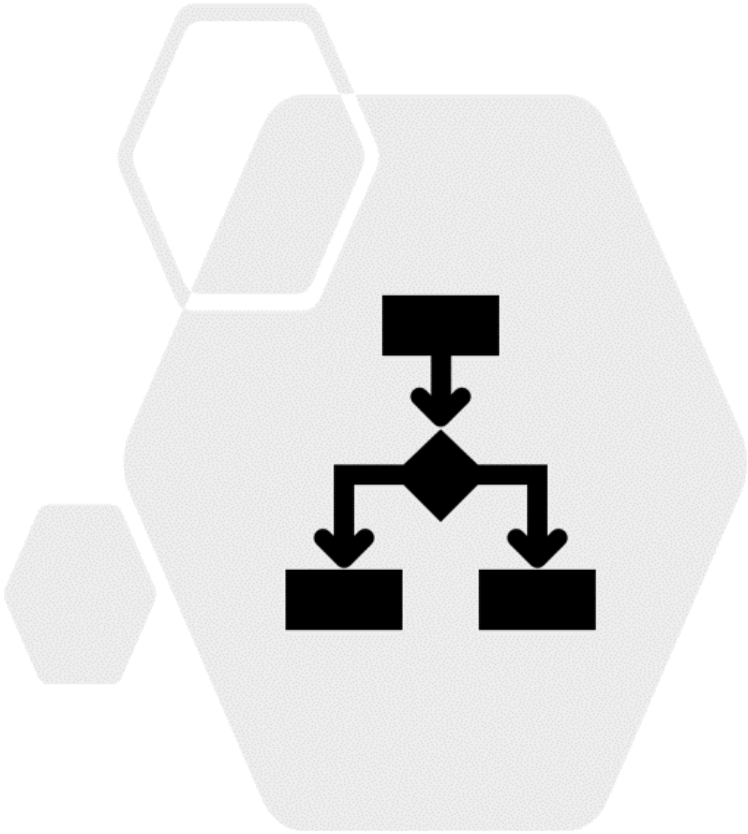
Adaptive Platform Treatment Trial for Outpatients with COVID-19



A Multicenter Trial of the AIDS Clinical Trials Group (ACTG) and the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership

Trial Design

- Randomized, blinded, controlled platform
- Allows agents to be added and dropped during study for efficient testing of new agents
- Begins with a phase II, followed by a transition into a larger phase III evaluation for promising agents.
- When two or more agents are being tested concurrently, the same placebo will be used, if feasible.



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Study Eligibility

- Ambulatory Adult (≥18 years)
- Active CoV-2 infection ≤7 days prior to Entry
- At least one COVID-19 symptom for ≤10 days prior to Entry, plus one the following symptoms present <48 hours of entry:
  - —Fever or feeling feverish, cough, shortness of breath at rest or with activity, sore throat, body or muscle pain, fatigue, headache, chills
- Tailored per study agent

Phase II Objectives

- Determine safety and efficacy of an agent to reduce the duration of COVID-19 symptoms and nasopharyngeal SARS-CoV-2 RNA detection through 28 days after study entry.

Phase II Graduation

Virology: NP Swabs

- Proportion negative by ≥20%
- Decrease of ≥1 log10 copies/mL
- Reduction in median AUC

Symptoms: Diary

- Relative reduction of ≥20%

Oxygen saturation: Pulse ox

- Proportion oxygen saturation of >=96%

Other considerations:

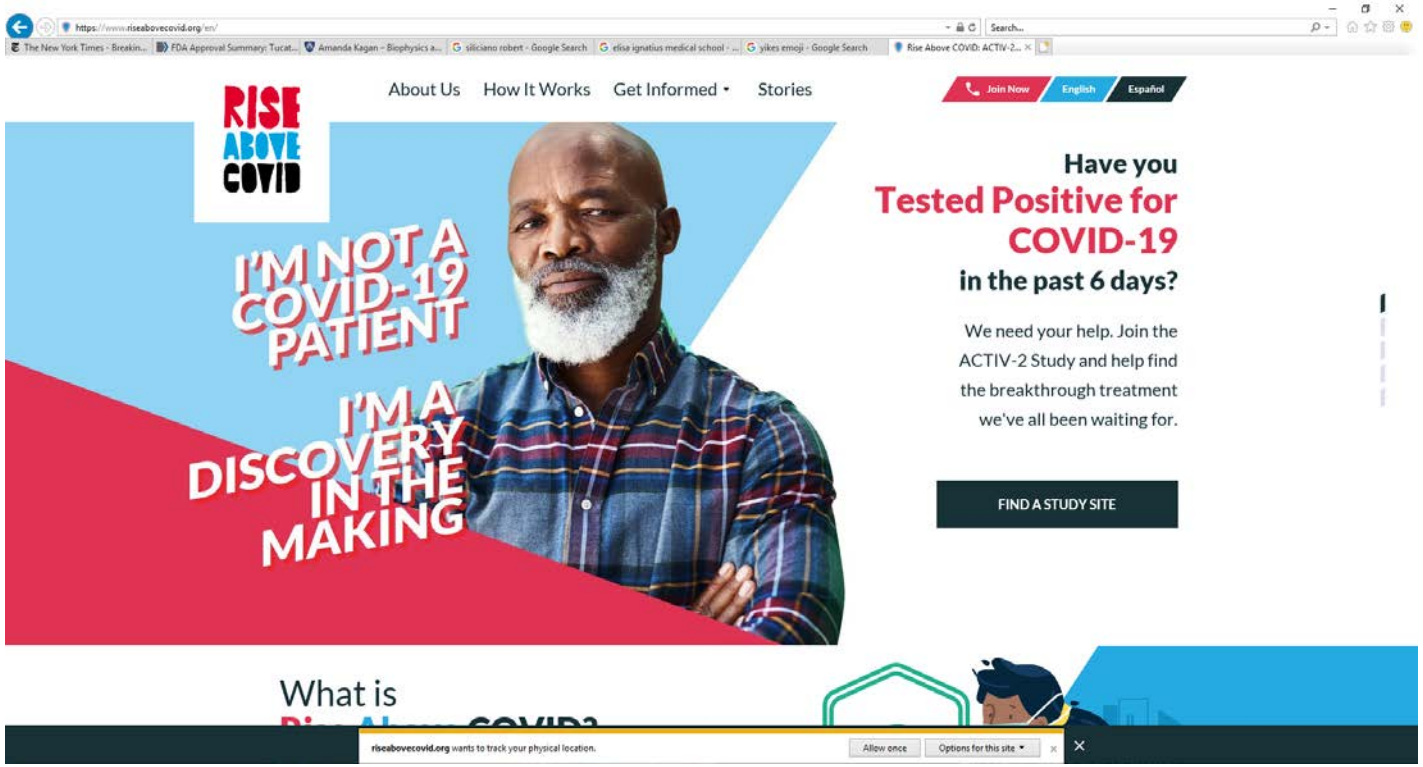
- Safety
- Dynamics of virology and symptoms
- Viral rebound

Phase III Objectives & Endpoint

- **Objective**: Determine if an agent will prevent the composite endpoint of either hospitalization or death through 28 days after study entry.
- **Endpoint:** Death from any cause or hospitalization through 28 days after study entry.
  - —Hospitalization defined as requiring ≥24 hours of acute care in a hospital or similar acute care facility.

Thank you

More information:
www.riseabovecovid.org



Referrals:

Rennisse McKinley, MHSA
Health Educator II/Recruiter
410 955-7127 or
410 955-2898 - rmckinl2@jhmi.edu

Outpatient Research: PROTECT Study

Mark Sulkowski, MD

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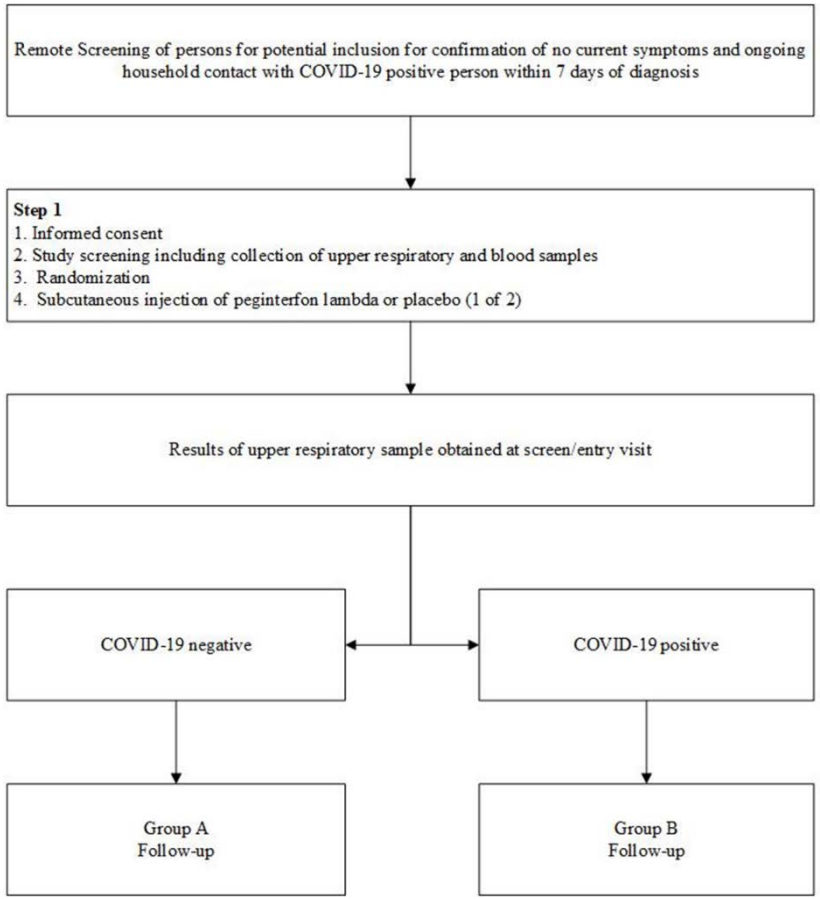
Lambda interferon for prevention and early treatment of SARS-CoV-2 infection

- Type 3 interferon
  - — IFNs are antivirals
  - —Lambda receptors are largely restricted to epithelial cells
  - —Once weekly pegylated interferon lambda has been extensively studied for viral hepatitis B and C with less side effects than IFN alfa or beta
  - —Not FDA approved for any indication

- Household contacts are at high risk for SARS-CoV-2 infection
- CDC MMWR 11/6/2020
  - —Prospective study of household transmission of SARS-CoV-2 in Nashville, Tennessee and Marshfield, Wisconsin
  - —April–September 2020
  - —Rate of secondary from index patients (n=101):
    - 53% (102/191 at risk persons)

Peginterferon lambda-1a for the prevention and treatment of SARS-CoV-2 infection: The PROTECT Study

- Household contacts of persons with confirmed COVID-10
  - ≥ 18 years old
  - ≤ 7 days of exposure and no symptoms
  - Oxygen saturation ≥ 95%
- PegIFN lambda or placebo – one SC injection
  - —Participants dosed with pending NP swab results
- Location: Greenspring Station COVID-19 CRU



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Peginterferon lambda-1a for the prevention and treatment of SARS-CoV-2 infection: The PROTECT Study

Phone 410-314-1142
Email PROTECT-study@jhmi.edu
https://www.covidprotectstudy.org/

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Outpatient Research: Astra-Zeneca Vaccine

Anna Durbin, MD

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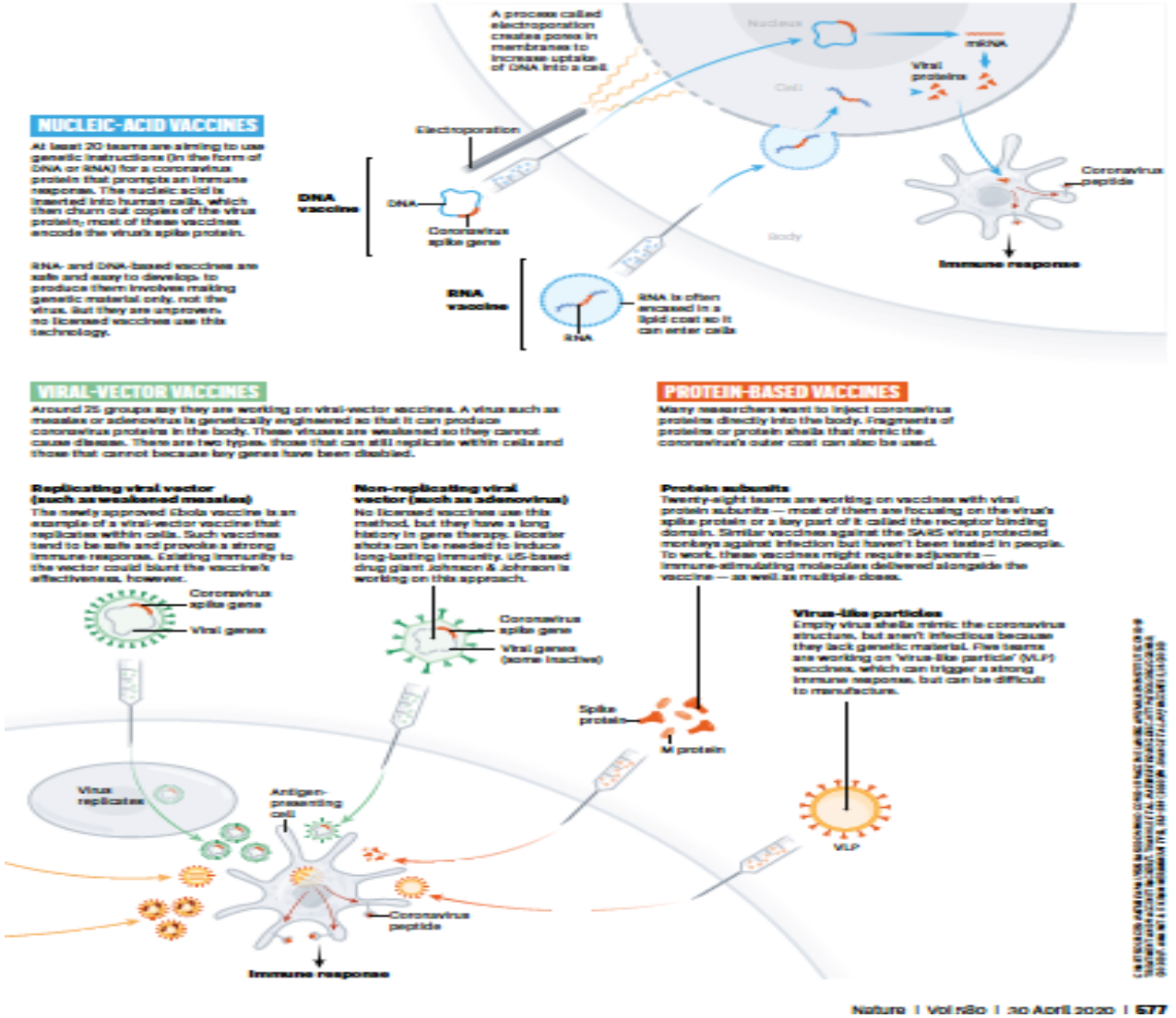
Vaccine Platforms

- mRNA vaccines
  - —Moderna & **Pfizer**
- Virus vectored vaccines
  - —**Astra Zeneca ChAdOx1**
  - —Janssen Ad26
  - —Merck VSV-vectored
  - —**Merck measles virus-vectored**
- Sub-Unit Protein
  - —Novavax
  - —**Sanofi**



Callaway Nature 30 April 2020

Pfizer mRNA vaccine (BNT162b2)

- Modified RNA to dampen innate immune sensing and increase mRNA translation
- Now in Phase 3 clinical trial (30 µg dose)
  - —>30,000 randomized 1:1; 2 doses given 21 days apart
  - —Fully enrolled at JHU
- ***Interim efficacy results announced Nov. 9: >90% efficacy***
- **EUA filed Nov. 20, 2020**
- **JHU will participate in pediatric trial to begin Q2 2021 (K. Talaat, PI)**

AZD-1222

- ChAdOx1 vector expressing the Spike protein of SARS-CoV-2 protein
- Enroll 44,000 subjects ≥18 years of age
- Randomized 2:1 vaccine to placebo
- Goal is to enroll a diverse population of subjects; those who have borne the major burden of COVID
  - —Persons living with HIV are eligible (CD4 ≥ 200)
- JHU **currently enrolling** (A. Durbin, PI)
  - —Included JHU CRNs: Tidal Health, Anne Arundel, and Tower Health)
  - —Utilized the Hope registry, Fraility registry, and the CoVPN registry
  - —Collaborated with Kathleen Page, Father Bruce at Sacred Heart for outreach to the Latinx com

Future studies

- Sanofi Pasteur
  - —Sub-unit protein vaccine given with GSK adjuvant
  - —Projected enrollment to begin mid-late January 2021
- Merck & Co
  - —Measles virus-vectored vaccine
  - —Enrollment expected to begin April 2021

Outpatient Research: HOPE Registry

Cassie Lewis-Land, MS, CCRP

JOHNS HOPKINS
INSTITUTE for CLINICAL & TRANSLATIONAL RESEARCH

Recruitment Innovation Unit HOPE Registry

Cassie Lewis-Land, MS, CCRP
Program Administrator
Recruitment Innovation Unit

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Objective of HOPE Registry and Outreach

The registry is designed to be patient centric allowing potential participants:

- to stay informed of study opportunities that they may be eligible to join related to COVID-19 research
- ability to choose a study or studies that best fits their personal preferences and gives them autonomy in choosing
- Ability to spread the word about research opportunities within their networks

MYCHART MESSAGES

E-MAILS

TEXT MESSAGES

PHONE CALLS

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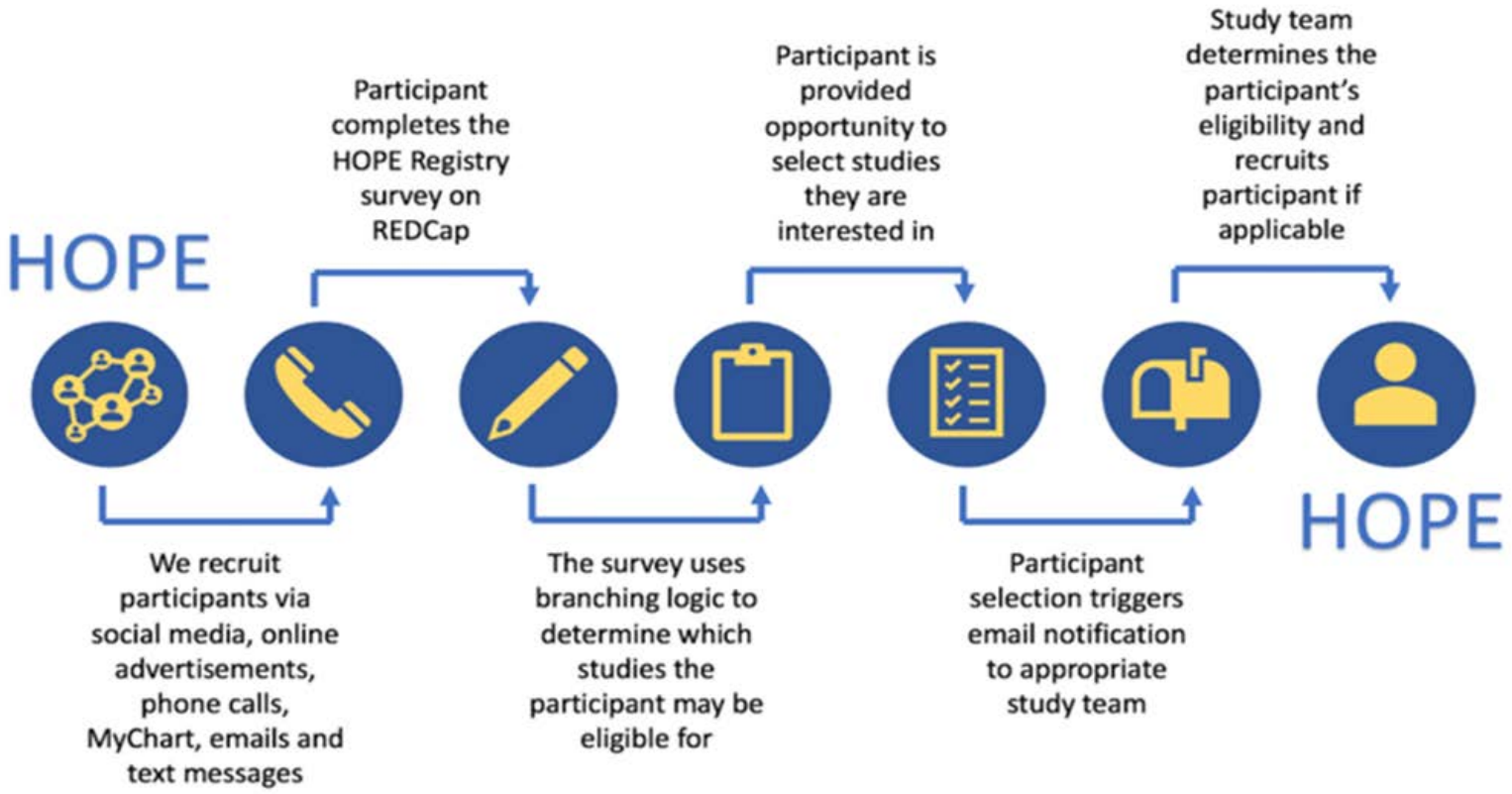
How it HOPE Registry Works



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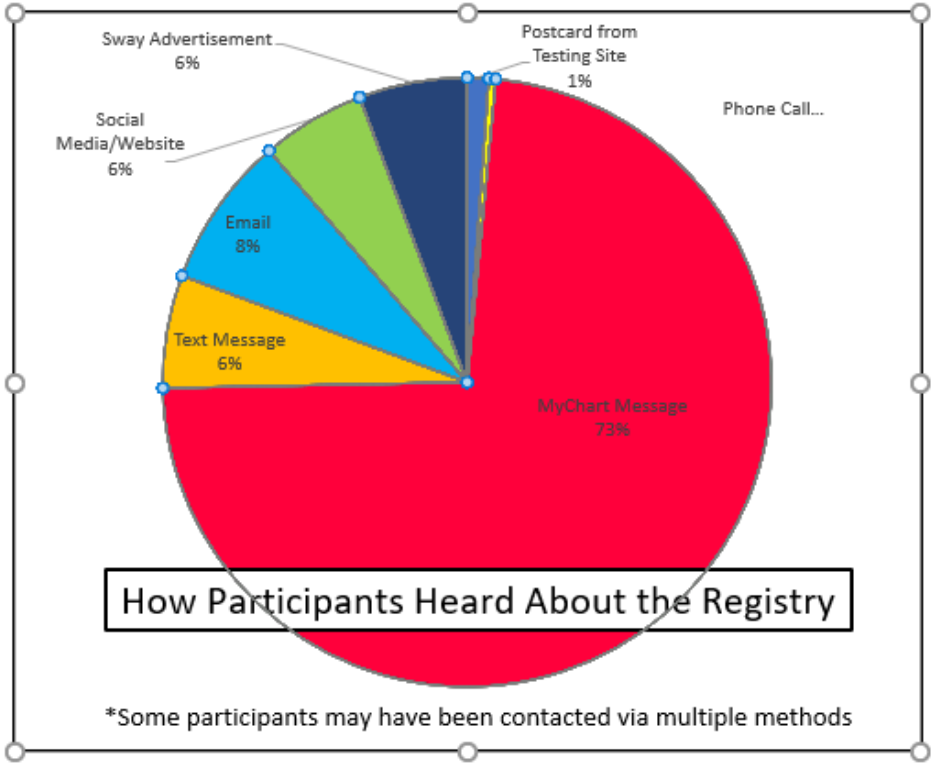
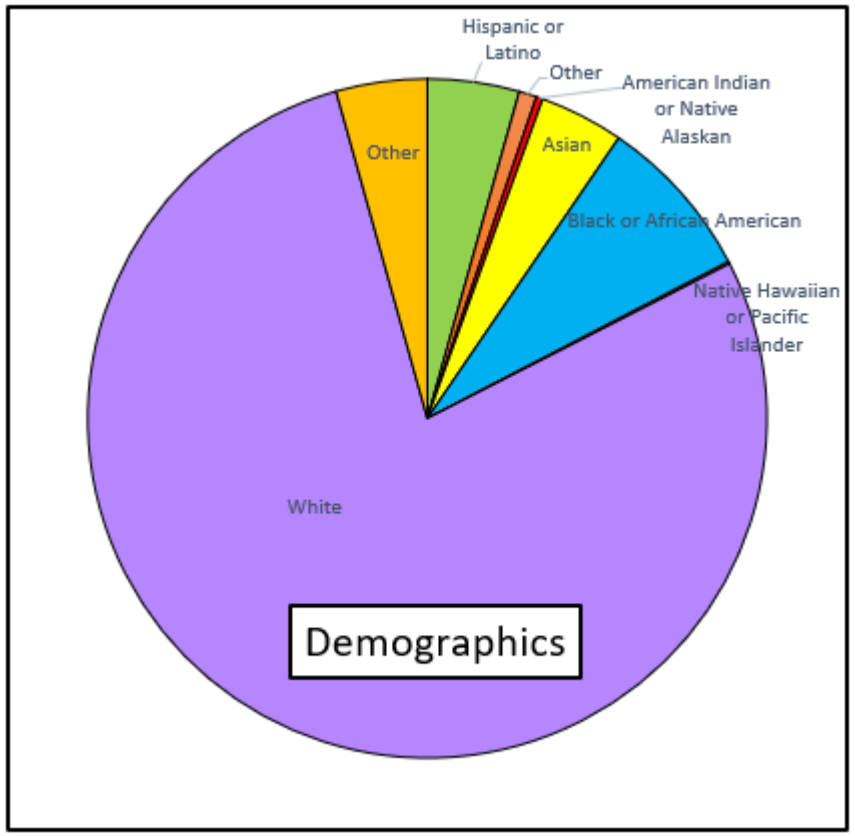
HOPE Registry Enrollment

Hope Registry Dashboard

Total Participants: 7246





Race	Number	Percent
American Indian or Native Alaskan	18	0.50%
Asian	226	4.50%
Black or African American	441	8.80%
Native Hawaiian or Pacific Islander	6	0.10%
White	4404	81.10%
Other	244	5.00%

Mean Age: 53.53

COVID Positive: 14.20%

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How to join HOPE Registry

Study Teams wanting to join can contact RIU HOPE team:

- we can help you submit a Change in Research (CIR) to IRB to utilize the registry
- build branching logic to identify enrollees in registry whom meet study inclusion criteria

Interested in joining the registry as a participant:

- hoperegistry@jhu.edu
- Website johnshopkinshope.org
- Text “HOPKINSHOPE” to 474747
- Call 410-314-1334

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COVID-19 Clinical Research Center

How to work with us

- Ask questions
  - —COVID19ResearchCtr@jhmi.edu
- Start at the ICTR COVID-19 CRC website
  - —https://ictr.johnshopkins.edu/covid-research-center
  - —Re-design underway to provide step-by-step guidance for human subjects and non-human subject research
- Join our monthly Town Hall Meetings

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Questions

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