AHA Rapid Response COVID–19 Research – What's Hot?

Mina Chung, MD

Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

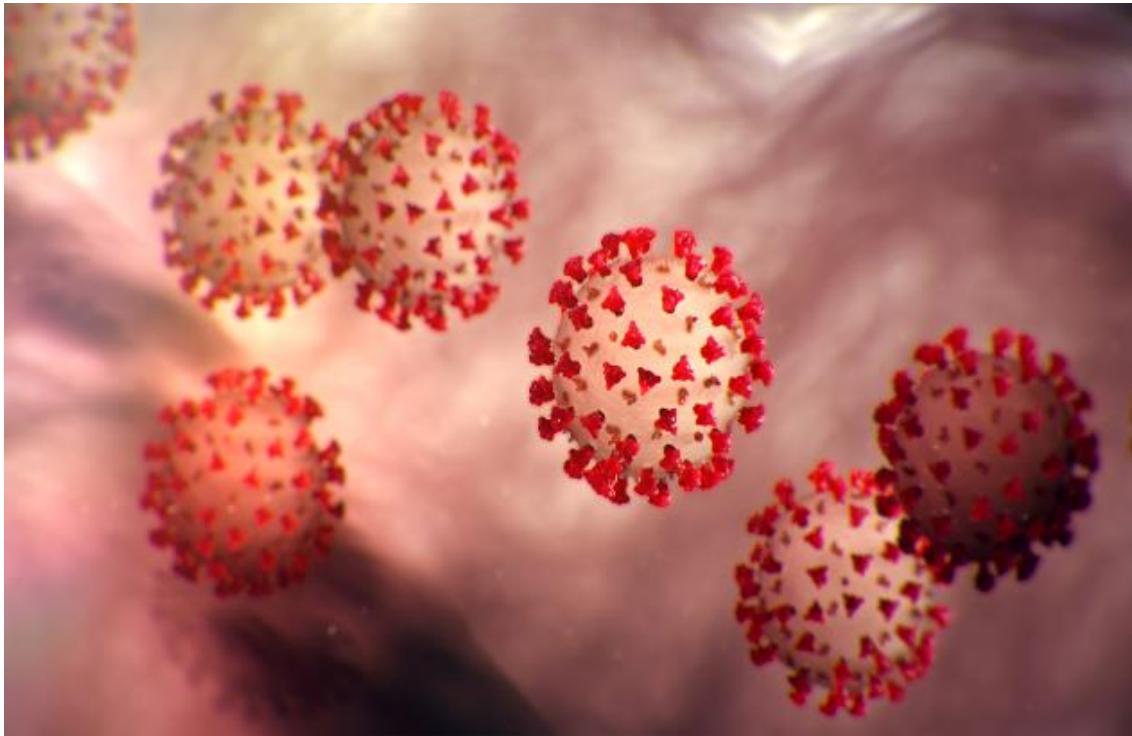Director, AHA COVID-19 Coordinating Center

Disclosures: Research funding: AHA, NIH

COVID-19

Funding for COVID-19 Initiatives

American Heart Association.

https://www.cdc.gov/media/dpk/diseases-and-conditions/coronavirus/images/outbreak-coronavirus-world-1024x506px.jpg

- AHA responded rapidly to COVID-19

- Over 750 Applications

- Over 150 AHA volunteer reviewers

- 16 individual awards

- 4 Health Tech and Innovation SFRN supplemental awards

- Coordinating Center

- June 1-July 1 start dates

COVID-19 Infection, African American Women and Cardiovascular Health

Michelle A. Albert, MD, MPH; Co-PI, Yvette C. Cozier ScD
University of California, San Francisco

American Heart Association.

UCSF University of California, San Francisco
advancing health worldwide

Boston University Slone Epidemiology Center
Black Women's Health Study

Health care disparities amplify the spread of COVID-19 to populations experiencing …

- Greater economic deprivation
- Dense, low-resource community environments
- Less access to quality health care despite a higher burden of underlying health conditions

Compared to women of other races/ethnicities, **black women** …

- Have the highest levels of cardiovascular disease
- Reside in lower socioeconomic status households
- More likely serve as caregivers for children and elderly relatives
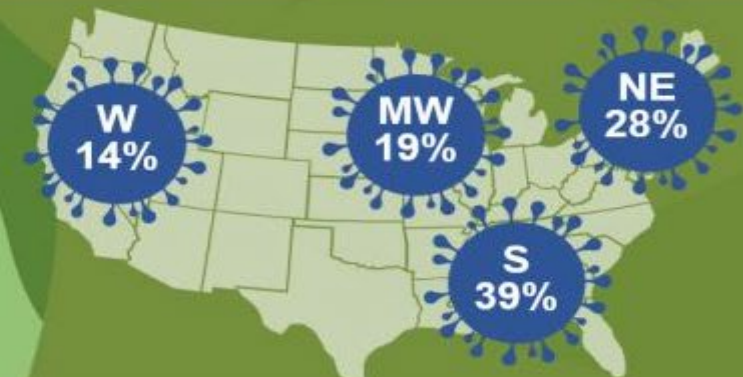- More frequently experience bias at all levels of society

Sample size = ~ 11,000 women

Age Range: **21–69**
Mean Age: **59.4 years**

STUDY AIMS

1. To document the experiences and perceptions of black women related to the COVID-19 pandemic in relation to infection risk, diagnostic testing accessibility, and perceived barriers to care

2. To examine the relation of COVID-19 infection and illness-related severity to cardiovascular health

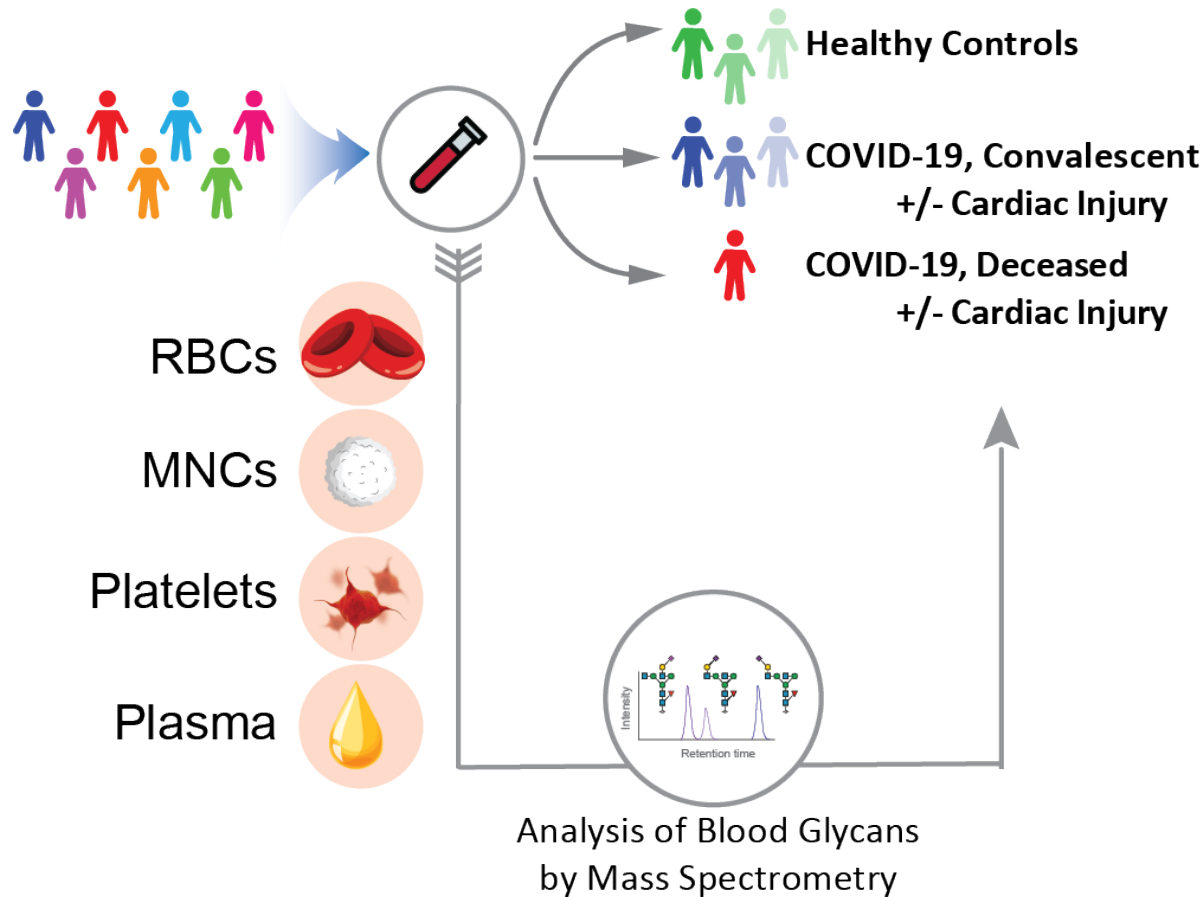3. To assess the relation of use of certain medications to COVID-19 infection and cardiovascular complications

W 14%
MW 19%
NE 28%
S 39%

Harnessing Glycomics to Understand Myocardial Injury in COVID-19

Rebekah L. Gundry, PhD, FAHA

Healthy Controls

COVID-19, Convalescent
+/- Cardiac Injury

COVID-19, Deceased
+/- Cardiac Injury

RBCs

MNCs

Platelets

Plasma

Analysis of Blood Glycans
by Mass Spectrometry

- Identify the glycan signatures that predict patients with **susceptibility** versus those with **protection** to **COVID-19 infection and post-viral myocardial injury**.

- Provide targets for **precision medicine** evaluation and **new mechanistic understanding** of how COVID-19 induces myocardial injury.
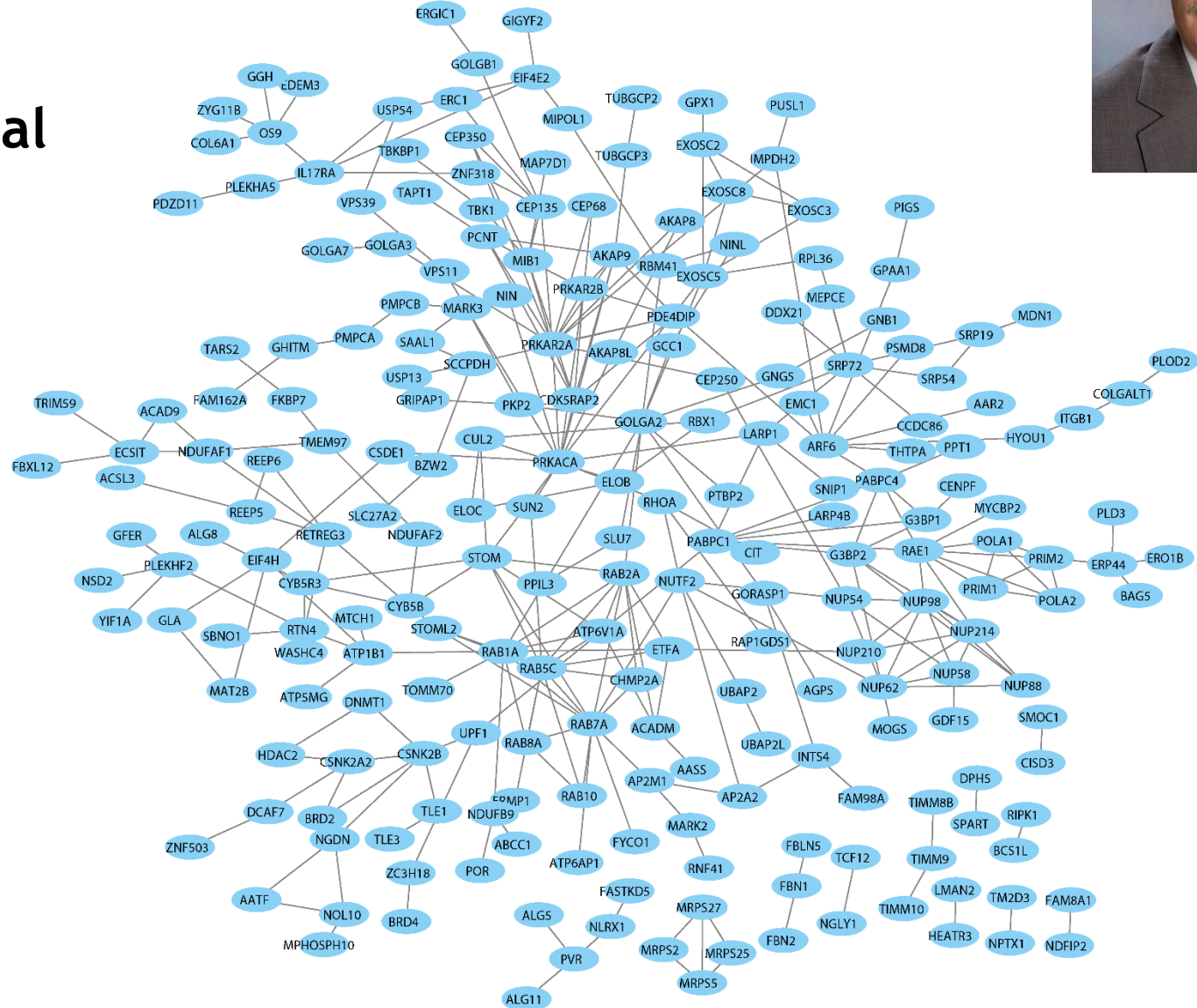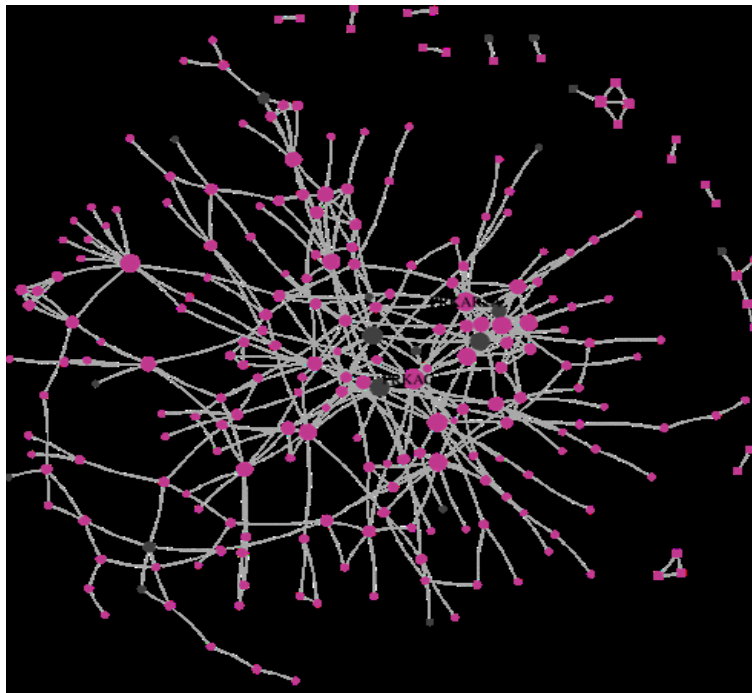
Repurposing Drugs for COVID–19

SARS-CoV2 targets in cardiomyocytes: 230 proteins and 319 interactions

Joseph Loscalzo, MD, PhD

Brigham and Women's Hospital

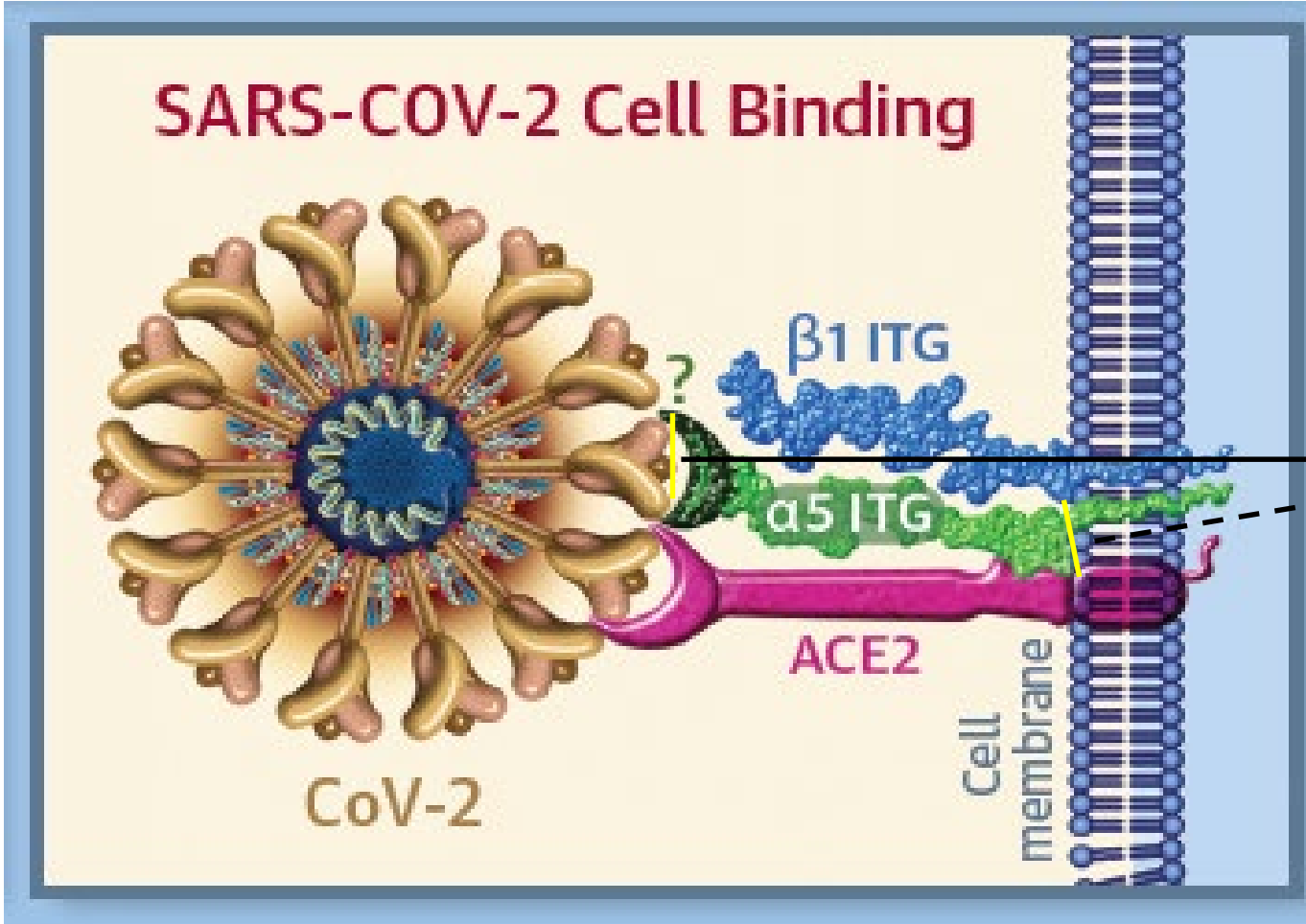**Harvard Medical School**

The COVIDOME

Myocardial Virus and Gene Expression in SARS CoV-2 Positive Patients with Clinically Important Myocardial Dysfunction

Michael Bristow, University of Colorado AMC

SARS-COV-2 Cell Binding

β1 ITG

α5 ITG

ACE2

Cell membrane

CoV-2

Integrin α5β1 facilitates CoV-2 binding and cell entry

Bristow MR et al, JBTS Sept 2020. DOI: 10.1016/j.jacbts.2020.06.007
Published online June 25, 2020

The Integrin Binding Peptide, ATN-161, as a Novel Therapy for SARS-CoV-2 Infection (in review, Greg Bix laboratory & BSL3 Core, Tulane SoM)

Gregory Bix, MD, PhD, FAHA gbix@tulane.edu
Director, Clinical Neuroscience Research Center, Tulane

ATN-161

(non RGD peptide derived from fibronectin, binds to α5β1 at an α5 ITG binding site). In VeroE6 cells:
– CoV-2 binds to α5β1
– ATN-161 prevents CoV-2 binding to α5β1, (nM affinity), and α5 binding to ACE2 (µM)
– **ATN-161 prevents CoV-2 cell infection (3.16 µM IC$_{50}$)**
https://doi.org/10.1101/2020.06.15.153387doi: bioRxiv preprint

# A Comprehensive Assessment of Arterial and Venous Thrombotic Complications in Patients with COVID-19

Sanjum Sethi, MD, MPH, Columbia University Irving Medical Center

The Relationship of D-Dimer and Deep Venous Thrombosis in COVID-19

Mahesh V. Madhavan, MD

Median peak D-Dimer levels were similar in patients with (N=186) and without (N=328) diagnosis of DVT (18.5 mg/dL [IQR: 6.4, 20.0] vs. 12.2 mg/dL [IQR: 3.7, 20], p = 0.83)

IMPROVE COVID
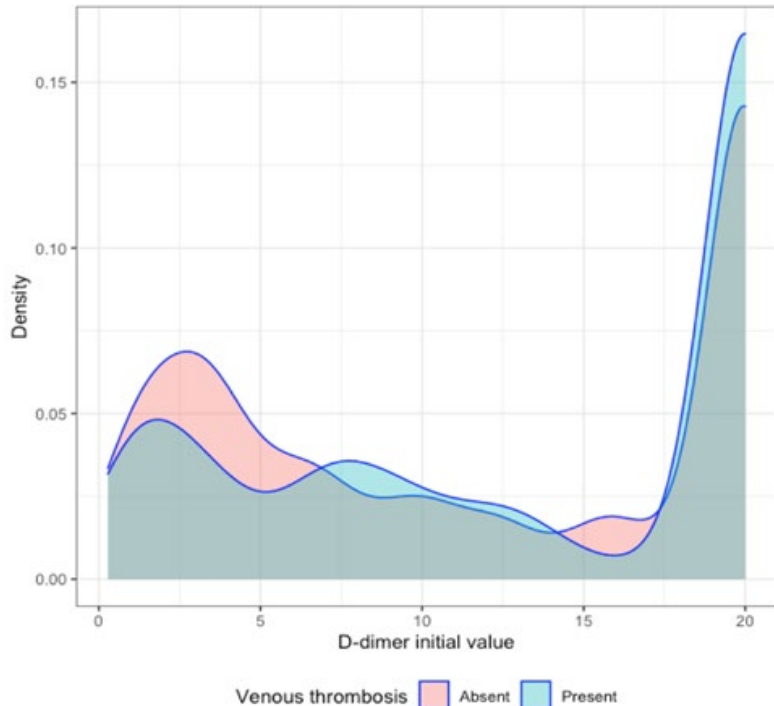
Intermediate or Prophylactic-Dose Anticoagulation for Venous or Arterial Thromboembolism in Severe COVID-19: A Cluster Based Randomized Selection Trial

NCT04367831

From the Frontlines of the Pandemic: Best of COVID-19 Clinical Research
Friday, November 13, 2020, 9:00 am - 10:00 am

7

Pathogenesis of Cardiac Inflammation During COVID-19

Daniela Cihakova, Department of Pathology, Johns Hopkins University, Baltimore

Objective: We will determine changes of cardiac stroma cells and infiltrating immune cells phenotypes induced by COVID-19 infection by comparing heart autopsy samples of COVID-19 and non-CIVID-19 patients by immunohistochemistry, multiparameter flow cytometry, and scRNA sequencing.

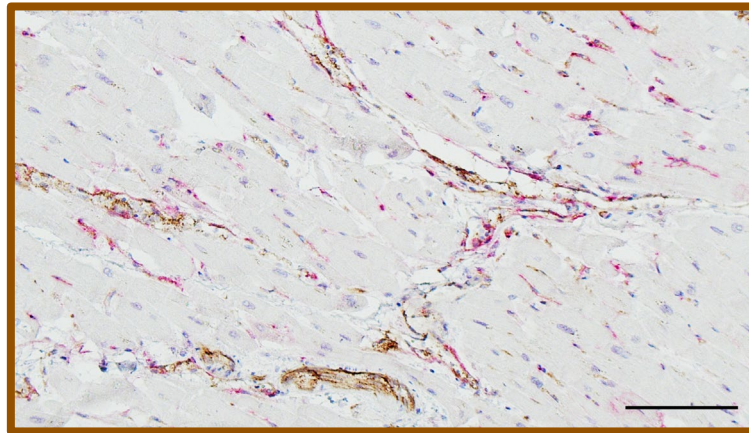Dr. Daniela Cihakova (PI)   Dr. Taejoon Won
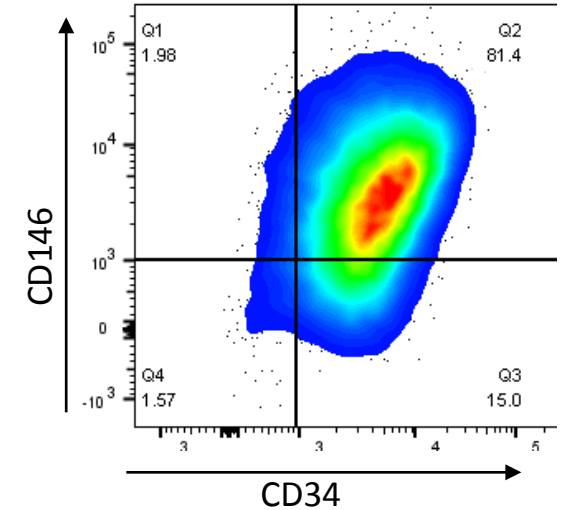
Monica Talor   Megan Wood   David Hughes

ACE2 expression in endothelial cells as seen via IHC

Endothelial cells in SARS-CoV-2 infected heart

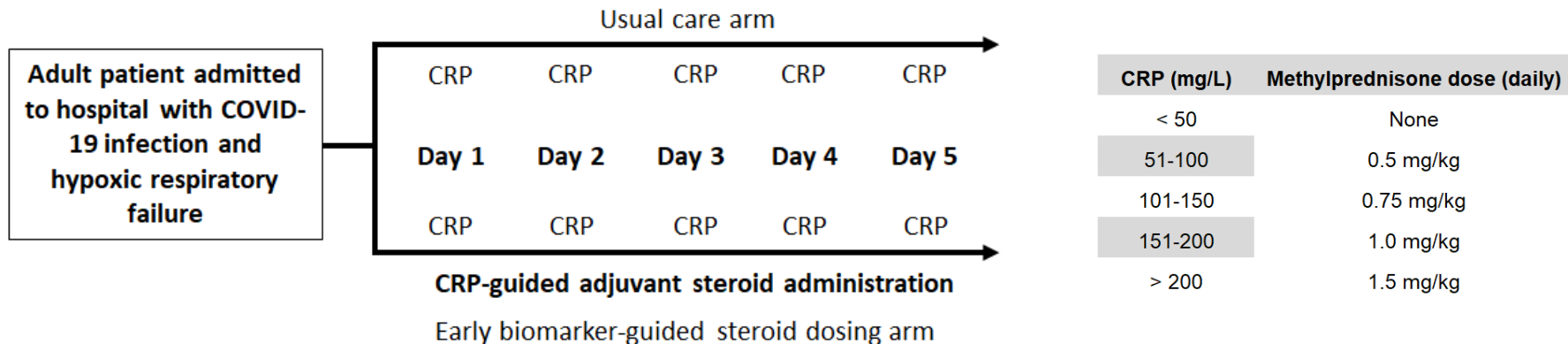OPEN TO COLLABORATION!

Come see our website: http://labs.pathology.jhu.edu/cihakova/about/lab-members/

Cardiovascular Outcomes and Biomarker Titrated Corticosteroid Dosing for SARS COV-2 (COVID-19): A Randomized Controlled Trial
SMART-COVID Trial

Yewande Odeyemi, MD; Ognjen Gajic, MD, MS, Jacob C Jentzer, MD, Hemang Yadav, MD. Mayo Clinic

- **Feasibility** of individualized-dosing (based on CRP) for adjuvant steroids

- **Comparison of individualized-dosing** to:
  - Fixed dose / one-size-fits-all (dexamethasone 6mg for 10 days)
  - No steroids

- **Secondary CV Outcomes** : arrhythmias, pressor requirement, evidence of myocardial injury (daily troponin)


Usual care arm

Adult patient admitted to hospital with COVID-19 infection and hypoxic respiratory failure

CRP	CRP	CRP	CRP	CRP
Day 1	Day 2	Day 3	Day 4	Day 5
CRP	CRP	CRP	CRP	CRP

CRP-guided adjuvant steroid administration

Early biomarker-guided steroid dosing arm

CRP (mg/L)	Methylprednisone dose (daily)
< 50	None
51-100	0.5 mg/kg
101-150	0.75 mg/kg
151-200	1.0 mg/kg
> 200	1.5 mg/kg

Human iPSCs and Organ Chips Model SARS-CoV-2-Induced Viral Myocarditis
Clive Svendsen and Arun Sharma, Cedars-Sinai Medical Center
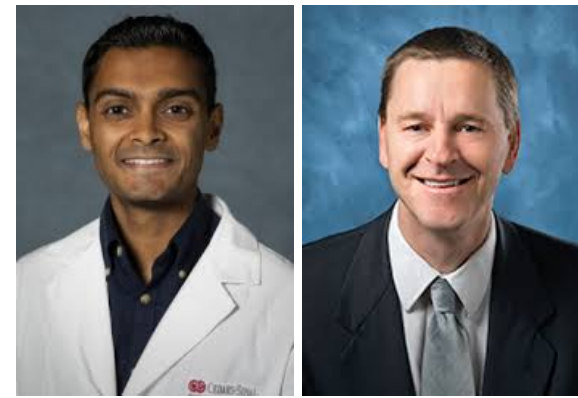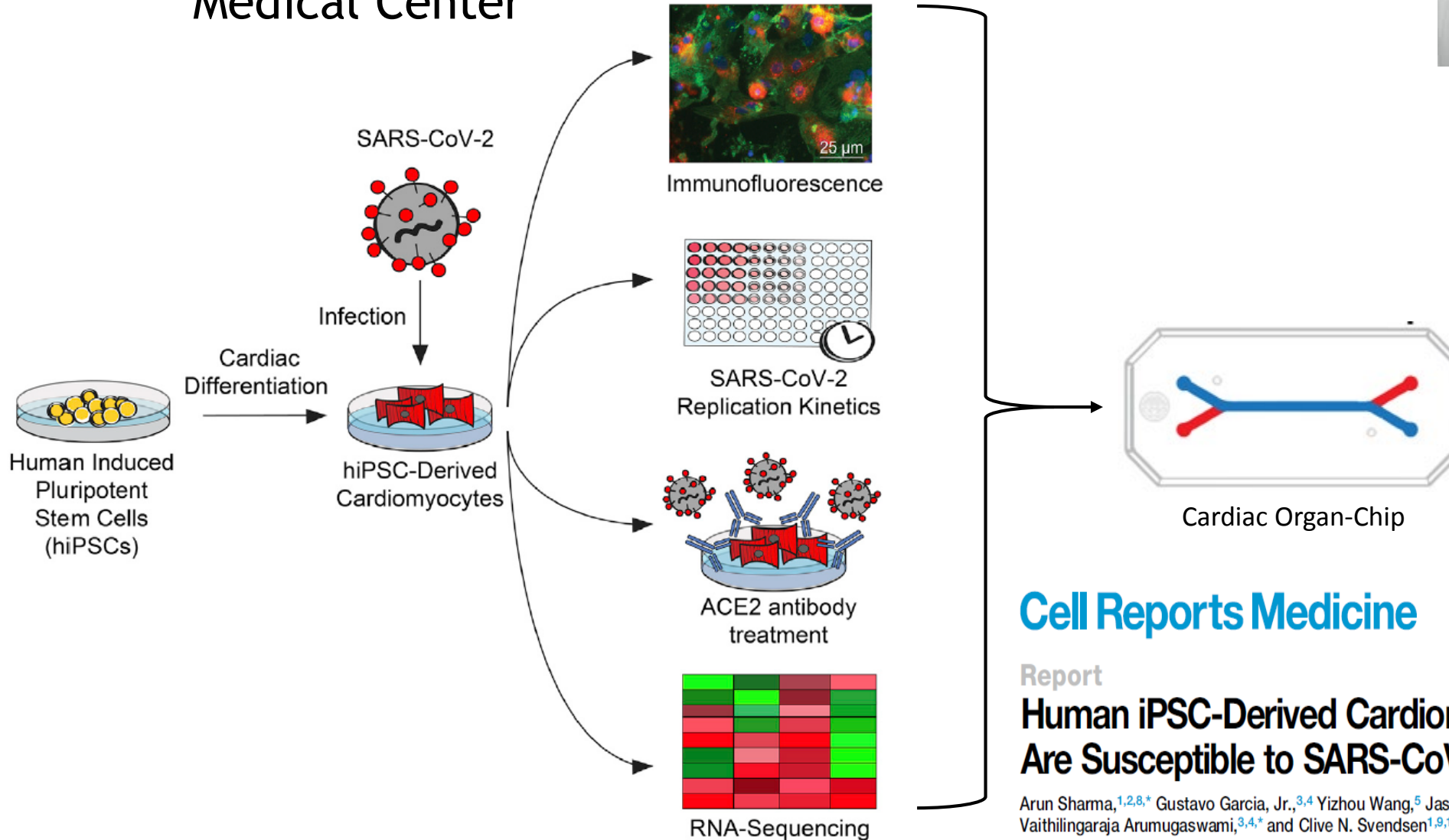
Cell Reports Medicine

Report

**Human iPSC-Derived Cardiomyocytes Are Susceptible to SARS-CoV-2 Infection**

Arun Sharma,[1,2,8,*] Gustavo Garcia, Jr.,[3,4] Yizhou Wang,[5] Jasmine T. Plummer,[5] Kouki Morizono,[6,7] Vaithilingaraja Arumugaswami,[3,4,*] and Clive N. Svendsen[1,9,10,*]
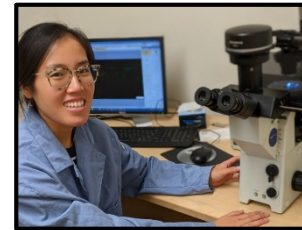
Rapid COVID-19-on-A-Chip to Screen Competitive Targets for SARS-CoV-2 Spike Binding Sites
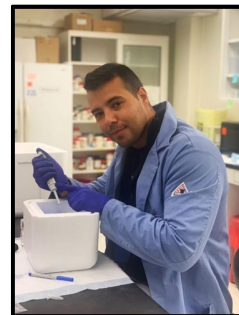## Tzung Hsiai, MD, PhD, University of California, Los Angeles
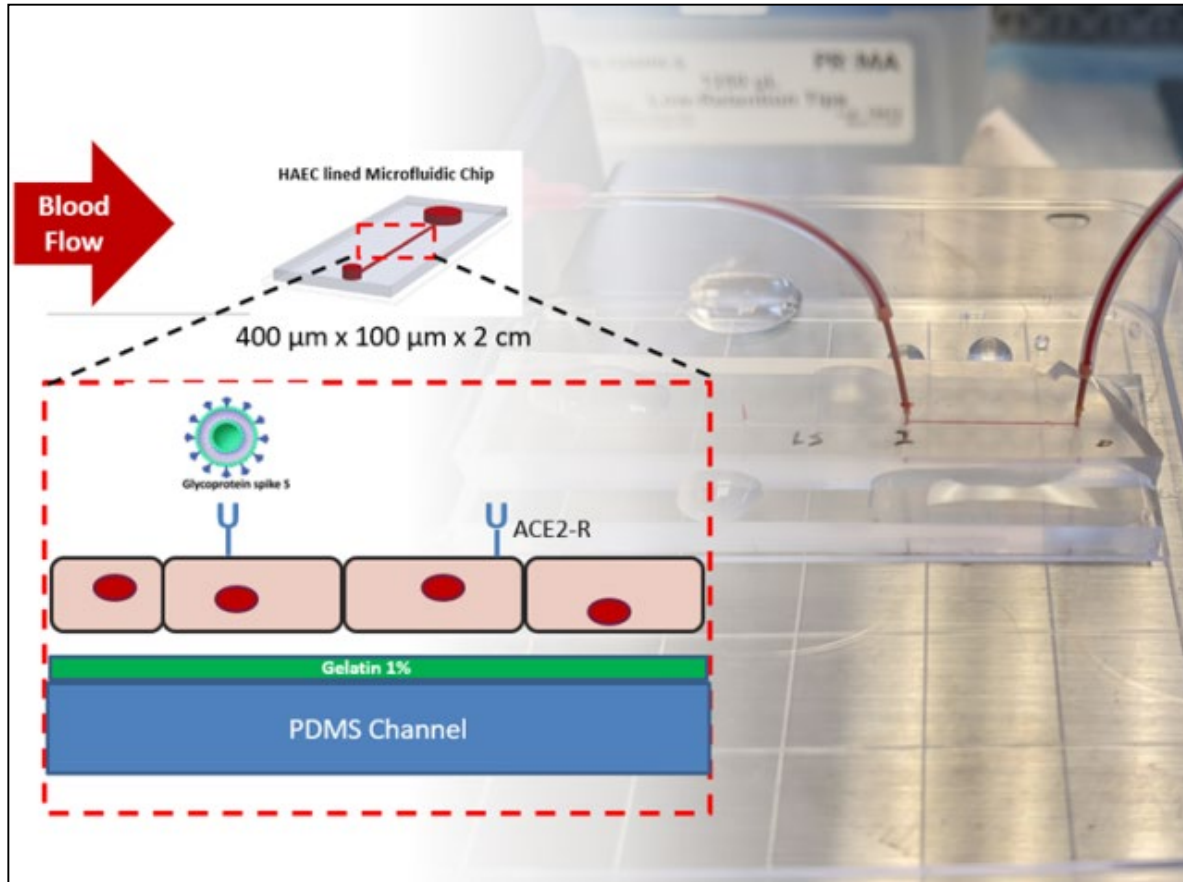
Angela Lai, et al. Rapid Liposome Mimicking SARS-CoV-2 to Elucidate Thrombosis in Endothelialized Microfluidic Chip
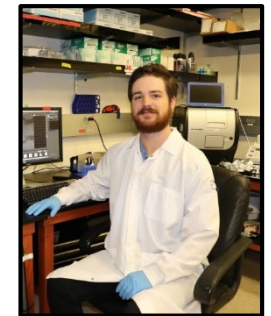
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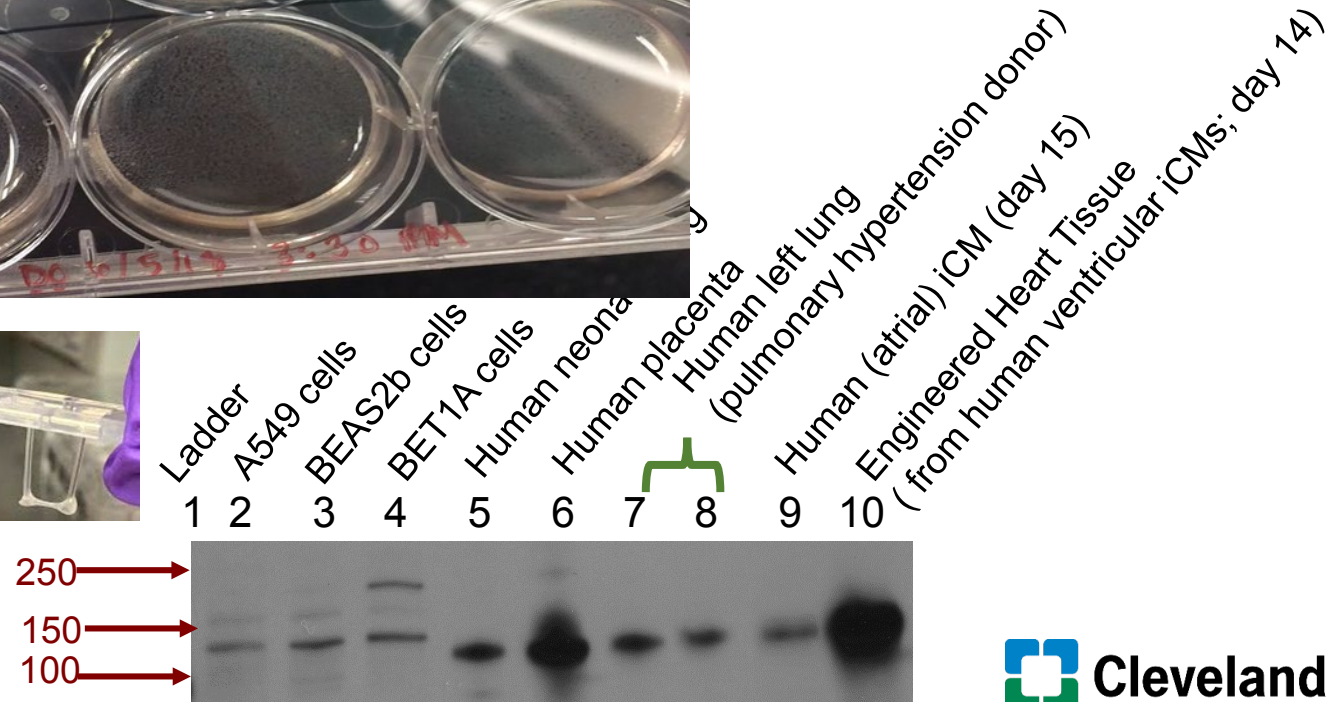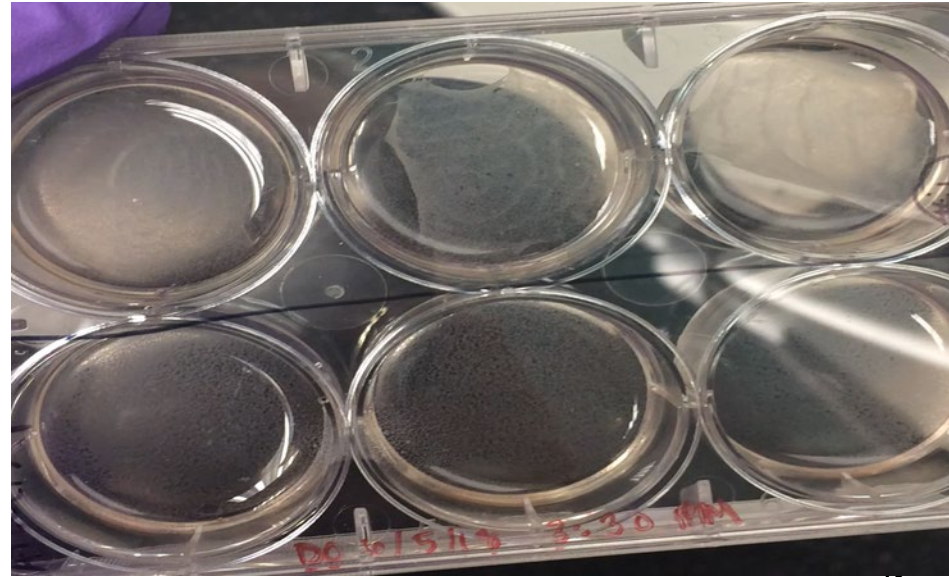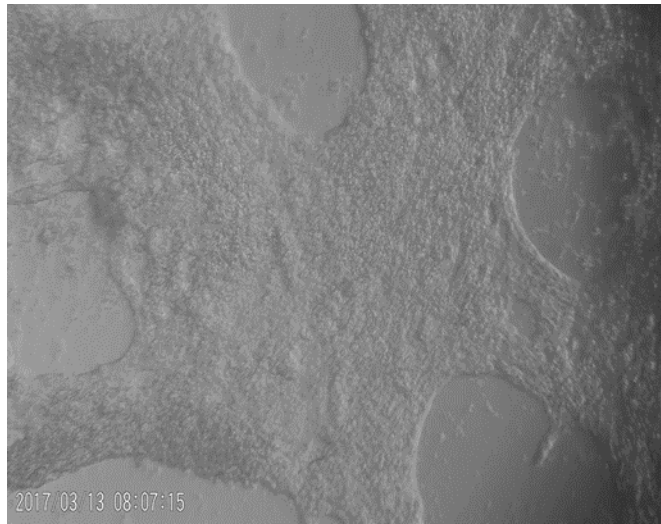
Sandro Satta, PhD

Susana Cavallero, PhD

Cayden Williamson, PhD student

Testing of SARS-CoV-2 Infectivity and Antiviral Drug Effects in Engineered Heart Tissue, Microglial Cell Models, and COVID-19 Patient Registries Mina Chung, MD; Mitali Das, PhD, Cleveland Clinic

A new way to study COVID-19 and test drugs
iPSCs⇒Cardiomyocytes⇒Engineered Heart Tissues

COVID–19 (C19)

Health Tech SFRN supplements

Andrea Beaton, Cincinnati Children's Hospital

- Ejection Fraction as Sixth Vital Sign in C19 Patients: Improved triage using point-of-care echo

David Newman-Toker, Johns Hopkins University

- In-Home Diagnostic Triage via Smartphone Video Virtual Check-In for Potential Stroke Symptoms During Pandemic: Novel Approach to Improving CV Health Equity & Long-Term Prevention

Paul Wang, Stanford University

- Digital C19 Patient Tracking & Reporting Tool Kit Focused on CV Complications & Disease

Brahmajee Nallamothu, University of Michigan

- C19 Health Eval & CV Complications Study: Using mHealth to Track Physiological & CV Consequences
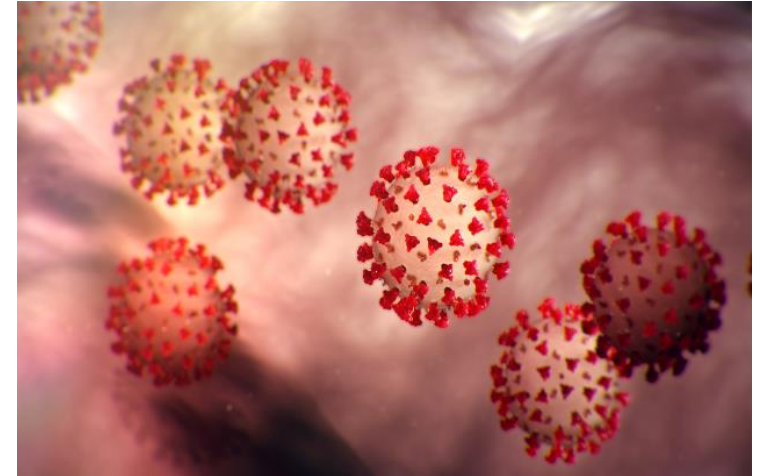
Ejection Fraction as the Sixth Vital Sign for Patients with COVID: *Improved triage using point-of-care echocardiography*

American Heart Association.

Andrea Beaton, Cincinnati Children's Hospital

- Access to echo is limited in many situations
- Rapid scale up of non-expert echo has challenges
- Navigational guidance provides a technology solution
- Conserves resources, improves access to diagnosis, change outcomes
- Prediction tool will be built to include LVEF

Quality Meter

Prescriptive Guidance

Reference Image

Probe Positioning Diagram

AutoCapture

Save Best Clip
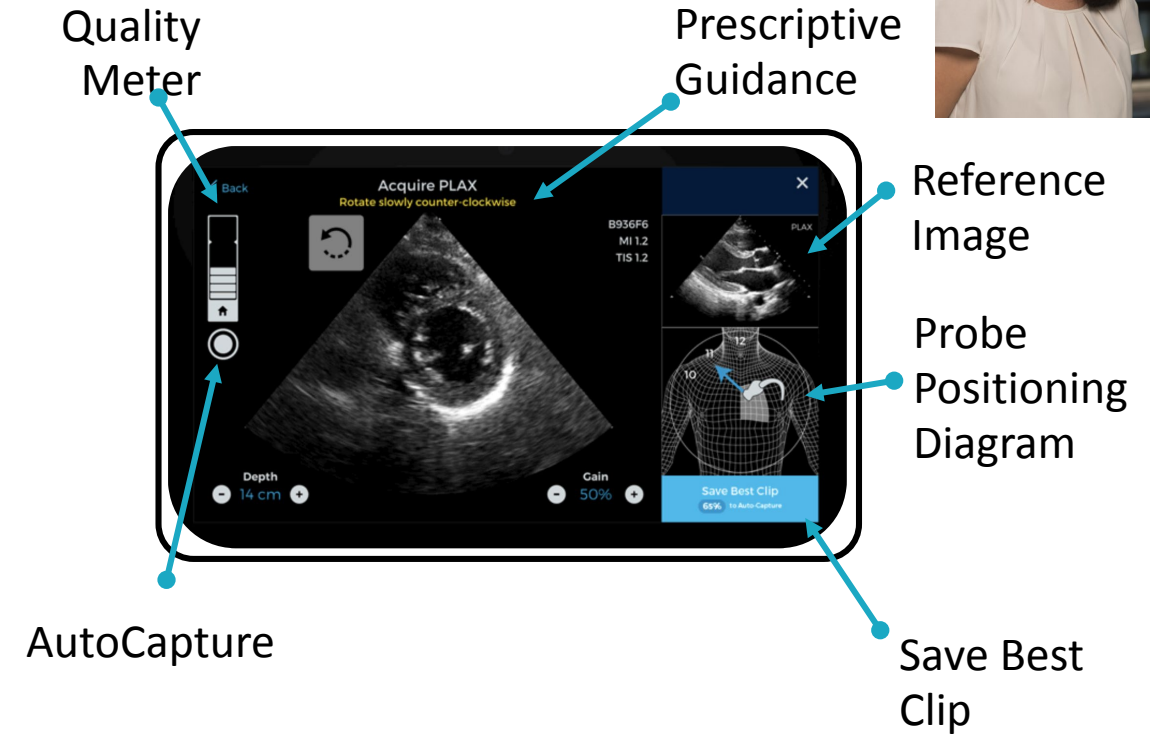
Real time feedback given on probe position and diagnostic quality

AHA COVID-19 GET WITH THE GUIDELINES® STEPPED WEDGE TRIAL

Paul J Wang, MD (Stanford); Mintu Turakhia, MD, MAS (Stanford); Ying Lu, PhD (Stanford); Ashish Sarraju , MD (Stanford); Fatima Rodriguez, MD, MPH (Stanford), Connor O'Brien, MD (UCSF)

AHA SFRN Funded Research

CAN DATA EXTRACTION FACILITATE DATA ENTRY?

WE WILL CONDUCT A STEPPED WEDGE CLUSTER RANDOMIZED TRIAL IN WHICH DATA EXTRACTION IS INTRODUCED

Possible Barriers to Data Entry:

- Add to stress to providers and health care system
- May prevent low resource centers from participating, undermining attempts to get data from diverse populations
- May result in incomplete data entry
- May result in selective non-consecutive entry of patients

Month 1   Month 2   Month 3   Month 4
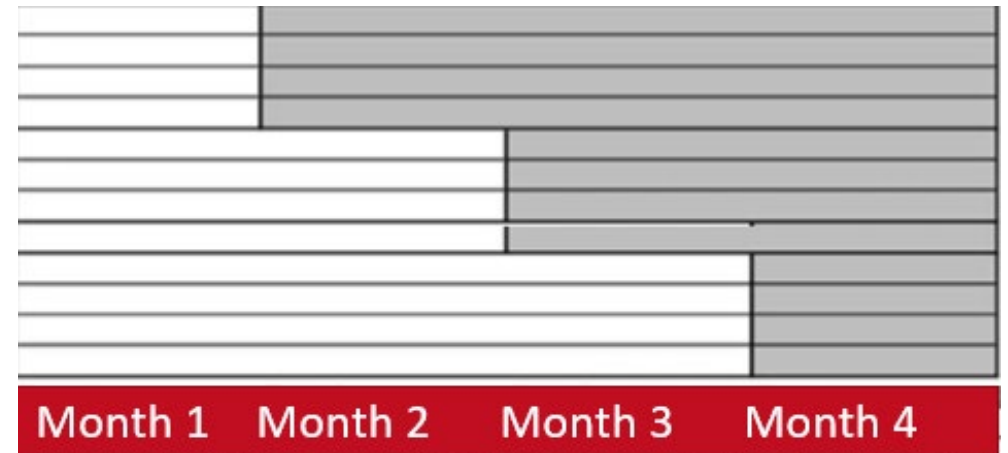
The AHA Health Technologies and Innovation SFRN

AHA COVID-19 Health Evaluation & Cardiovascular Complications (CHECC) Study: Using mHealth to Track Physiological & CV Consequences

Brahmajee Nallamothu, University of Michigan

Hypothesis

COVID 19 pandemic has resulted in an adverse change of **activity measures**, such as step count and exercise; **physiologic measures**, such as blood pressure and heart rate; and **other health measures**, such as stress and mood levels

Vision

To develop interventions to maintain activity, control BP, and modulate stress and mood levels.

Our Approach

Use Apple Watch to understand changes in activity as well as heart rate

Use Omron blood pressure cuff to measure changes in blood pressure over time

Distribute COVID survey, with questions on COVID related symptoms, diagnosis, testing, exposures, and treatment

Baseline, weekly and quarterly distribution intervals

Next Steps

Complete analysis on step count, HR, mood, stress

Recruit small cohort of participants in UM community with documented COVID 19 to understand recovery trajectory using wearable device

Step counts of participants by week across COVID pandemic
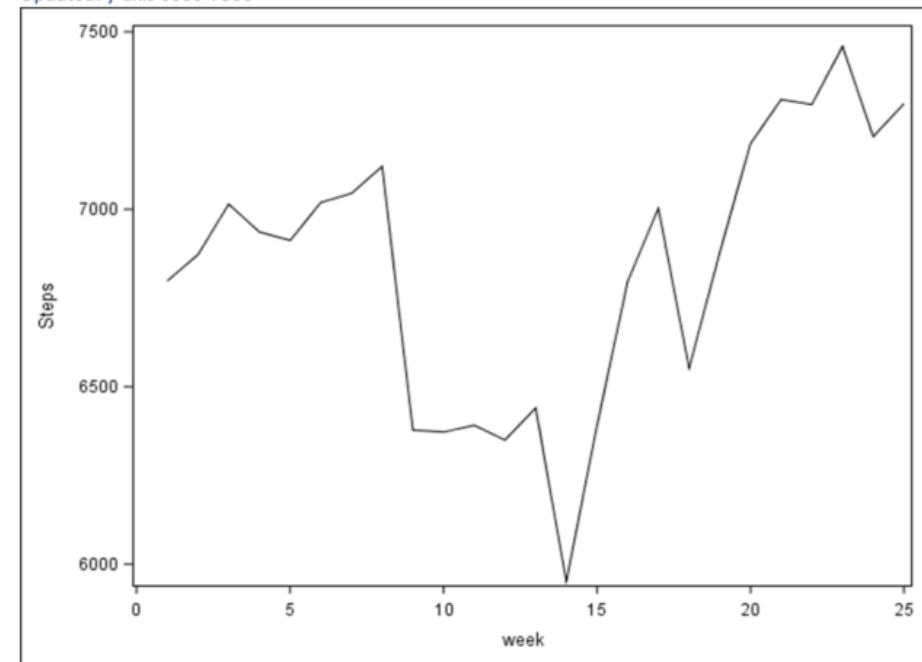
AHA COVID–19 Coordinating Center

- Website

    https://professional.heart.org/en/research-programs/aha-rapid-response-grant-covid19

Thank You.

AHA Rapid Response Grants

COVID-19 and Its Cardiovascular Impact

Michelle Albert, University of California, San Francisco
- COVID-19 Infection, African American Women and Cardiovascular Health

Anand Prasad, University of Texas Health Science Center at San Antonio
- SARS-CoV-2 Infection and the Development of Cardiac Dysfunction

Jaejin An, Kaiser Permanente Southern California
- Risk of Severe Morbidity and Mortality of Coronavirus Disease 2019 (COVID-19) Among Patients Taking Antihypertensive Medications

Paul Heidenreich, Stanford University
- Outcomes for Patients with Hypertension, Diabetes and Heart Disease in the Coronavirus Pandemic: Impact of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers Treatment

Michael Lu, Massachusetts General Hospital
- Deep learning using chest radiographs to predict COVID-19 cardiopulmonary risk

AHA Rapid Response Grants

COVID-19 and Its Cardiovascular Impact

Rebekah Gundry, University of Nebraska Medical Center
- **Harnessing Glycomics to Understand Myocardial Injury in COVID-19**

Michael Bristow, University of Colorado AMC
- **Myocardial Virus and Gene Expression in SARS CoV-2 Positive Patients with Clinically Important Myocardial Dysfunction**

Joseph Loscalzo, Brigham and Women's Hospital and Harvard Medical School
- **Repurposing Drugs for Treatment of Cardiomyopathy Caused by SARS-CoV-2**

AHA Rapid Response Grants

COVID-19 and Its Cardiovascular Impact

Sanjum Sethi, Columbia University Irving Medical Center
- A Comprehensive Assessment of Arterial and Venous Thrombotic Complications in Patients with COVID-19

Jane Freedman, University of Massachusetts Medical School
- The Role of the Platelet in Mediating Cardiovascular Disease in SARS-CoV-2 Infection

Emily Tsai, Columbia University Vagelos College of Physicians & Surgeons
- Elucidating the Pathogenesis of COVID-19 Cardiac Disease: Histopathological and snRNA-Seq Analyses of Human Myocardium

Daniela Cihakova, Johns Hopkins
- Pathogenesis of Cardiac Inflammation During COVID-19

AHA Rapid Response Grants

COVID-19 and Its Cardiovascular Impact

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