# HEARTSHARE

**FNIH AMP® Heart Failure and
HeartShare Steering Committee Meeting**

**Gaylord National Resort & Convention Center, MD**
**September 29, 2022**
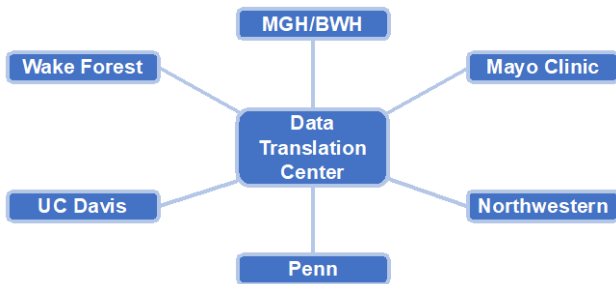
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HeartShare is an NHLBI-funded program to conduct large-scale analysis of phenotypic data, images, and omics from multiple existing datasets and from a new, prospective, multi-center cohort of patients with heart failure with preserved ejection fraction (HFpEF) and comparators without HFpEF. The goal of this study is to classify HFpEF into distinct phenotypes, characterize mechanisms of disease, and identify therapeutic targets for each HFpEF subtype. In 2017, NHLBI convened a working group to establish research priorities in HFpEF due to its growing prevalence and lack of effective treatments. One of the key opportunities identified by the working group was to create a comprehensive, multi-center, deeply phenotyped cohort of HFpEF patients with standardized protocols and a robust biorepository. In 2020, NHLBI created funding opportunities for a Data Translation Center (RFA-HL-21-016) and 6 clinical centers (RFA-HL-21-015). The HeartShare Data Translation Center at Northwestern University serves as the hub for coordinating the study and integrating all HeartShare data (existing datasets and prospective data). The 6 HeartShare Clinical Centers (Massachusetts General Hospital/Brigham and Women's Hospital, Mayo Clinic, Northwestern University, University of Pennsylvania, University of California-Davis, and Wake Forest University [**Figure 1**]), are conducting the prospective deep phenotyping part of the study (n=1000 participants) under the direction of the HeartShare Data Translation Center.

**Figure 1. Organization of HeartShare**



The **HeartShare Data Translation Center** consists of 4 cores: an Administrative and Outreach Core, a Cohort Core, a Data Portal Core, and a Data Management Core:

- The **Administrative and Outreach Core** oversees HeartShare program operations, the HeartShare research skills development (training) program, and the deep phenotyping prospective study. A key directive of the Administrative/Outreach Core is to ensure rapid and broad data sharing of clinical, imaging, and molecular data to promote the use and dissemination of all data that results from the HeartShare program (from both the parent study and all ancillary studies). The Administrative/Outreach Core also interfaces with each of the cores, the NHLBI, and the HeartShare Steering Committee (SC), External Advisory Committee (EAC), and Observational Safety Monitoring Board (OSMB).
- The **Cohort Core** is collecting and harmonizing data, images, and omics from previously conducted (extant) cardiovascular disease epidemiological cohorts, heart failure clinical trials, and heart failure registries (**Figure 2**). All data and images are being deposited into the NHLBI BioData Catalyst cloud resource for maximum data protection and dissemination to approved investigators for analysis. These data (including omics) and images are being analyzed using 2 approaches: (1) a hypothesis-driven approach to investigate pre-defined HFpEF subtypes and molecular pathways and (2) an unbiased approach (e.g., unsupervised machine learning) to identify novel HFpEF subtypes. Identified subtypes will then be validated and further studied in the prospective component of HeartShare.

**Figure 2. Cohort Core Scientific Approach**
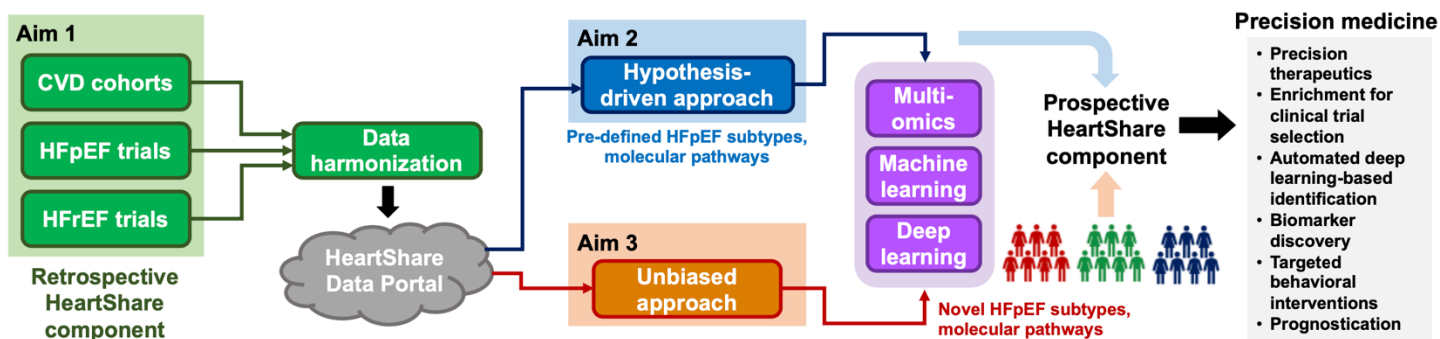


- The **Data Portal Core** serves as the hub for all data and images for HeartShare (from both existing datasets and the prospective, deep phenotyping component of the study) in concert with BioData Catalyst. The Data Portal Core is also responsible for supervising collection of EHR data from the 6 clinical centers and developing and maintaining the patient-facing Eureka HeartShare app, which is described in detail below.
- The **Data Management Core** oversees and ensures data quality, integration and harmonization of various data types, performs advanced analytics, coordinates biospecimen and imaging repositories and supports integration with the NHLBI TOPMed program for omics analyses.

Each of the cores are fully integrated with each other as shown in **Figure 3**, with the Data Portal and the NHLBI BioData Catalyst serving as the central hub for all HeartShare data.

**Figure 3. Organization of HeartShare Data Translation Center**
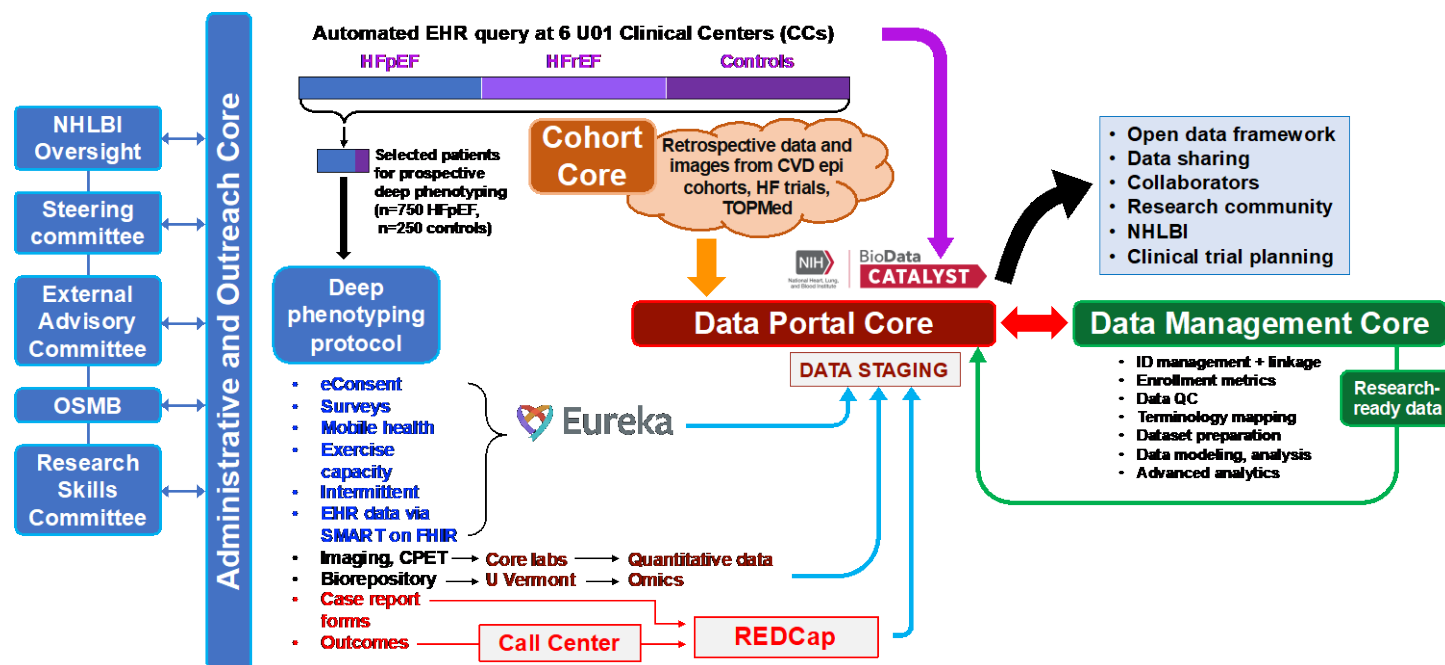
# HeartShare Aims and Study Design

- To create a rich repository of data, omics, and images from multiple large scale cardiovascular disease epidemiology studies, multicenter heart failure clinical trials, and other studies (e.g., heart failure registries) to facilitate open data science for the investigation of HFpEF.
- To define subtypes of HFpEF and develop algorithms for identification of HFpEF subtypes.
- Discovery and prioritization of targets in mechanistic pathways for diagnosis, risk assessment, and development of new therapies for HFpEF.
- To establish a large, electronic health record (EHR)-based cohort of HF patients and age- and sex-matched comparators who will be enrolled in a registry for future studies.
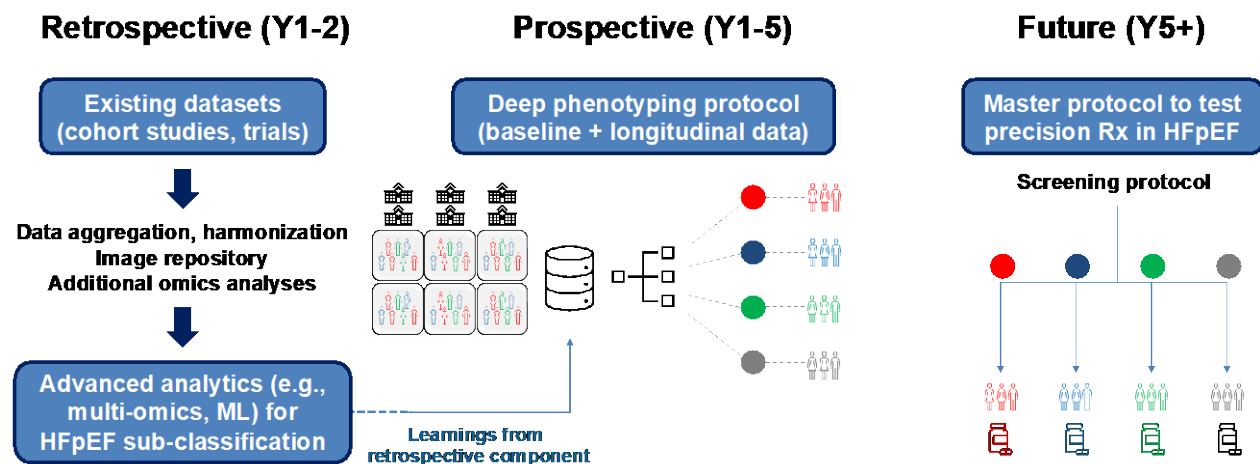- To establish a cohort of deeply-phenotyped HFpEF patients who can support target validation and facilitate proof-of-concept treatment trials for HFpEF.
- To train new heart failure data scientists proficient in multi-omics and machine learning techniques.

**Figure 4. HeartShare Study Design**



## BioData Catalyst

BioData Catalyst (https://biodatacatalyst.nhlbi.nih.gov) is the NHLBI's cloud-based platform for secure data sharing and analysis. It consists of a data ecosystem that is designed to be flexible, modular, and user-friendly, and contains 3 main components: Terra (genomic data), Seven Bridges (analysis workspaces), and Gen 3 (publicly available data). All HeartShare data and images are deposited into cloud buckets (e.g., Amazon Web Services [AWS]) that are connected to Seven Bridges analysis workspaces. The HeartShare Data Translation Center serves as the data steward and controls access and permissions for all users of HeartShare data in BioData Catalyst. **Figure 5** displays the flow of data and images from the various components of HeartShare into Seven Bridges where approved investigators can analyze HeartShare data and images.

**Figure 5. Data Flow from HeartShare Components to Seven Bridges in BioData Catalyst**
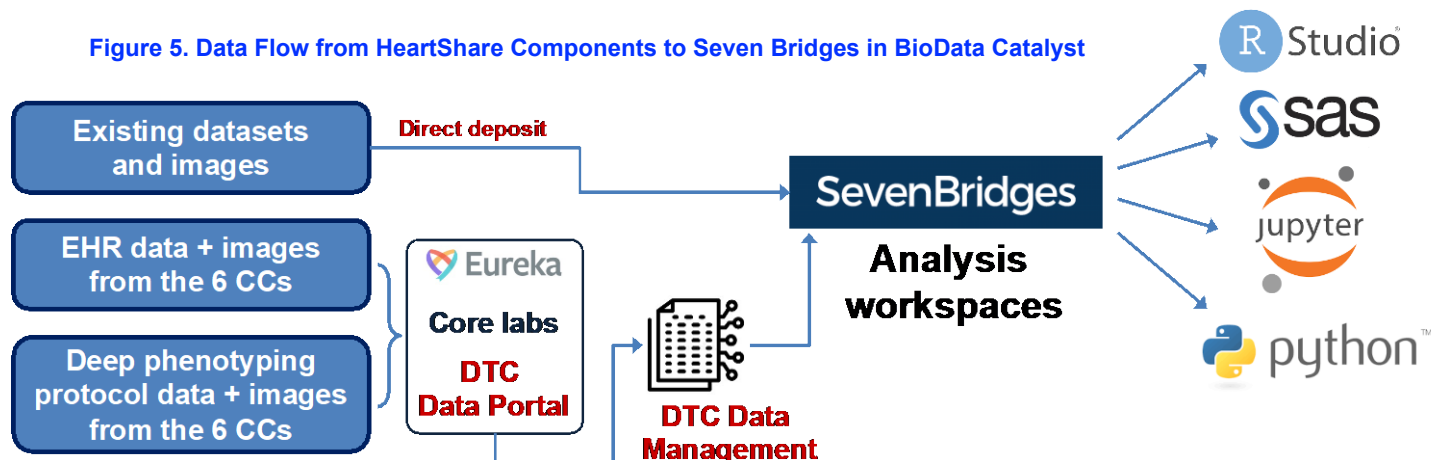
## Eureka Platform

The Eureka Platform creates a comprehensive patient engagement resource (web- and mobile-based platforms) to allow for (1) remote eConsents and surveys; (2) communication portal for participants; and data collection for home devices, sensors, and mobile apps. For more information, visit: https://info.eurekaplatform.org

**Patient engagement:** We will leverage the Eureka platform to create an interface for patient participants in the prospective component of HeartShare that allows eConsents and completion of forms and that facilitates communication with participants; collects mobile health (mHealth) data from home devices, sensors, and mobile apps; and seamlessly integrate with other data sources in BioData Catalyst. Eureka will allow HeartShare patients to engage in all phenotyping protocols. The Eureka platform, developed at UCSF with NIH-funding (U2CEB021881), is a direct-to-participant digital platform as a 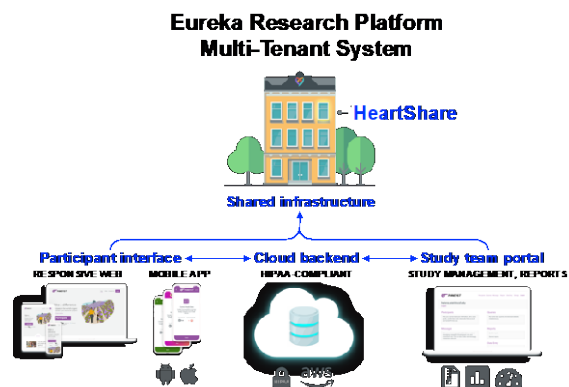resource for enabling efficient mHealth research. Detailed information about the Eureka Research Platform can be found at https://info.eurekaplatform.org. Building upon experience and technology developed by the UCSF team for the Health eHeart Study, >55 individual research studies have been launched on the Eureka platform, engaging over 500,000 participants and led by

**Figure 6. The Eureka platform for HeartShare**



researchers at multiple institutions across multiple disease areas. The Eureka Platform, which is available on the web and Eureka's native mobile apps (iOS and Android), is designed for scalability, cost-effectiveness and speed of study startup. The platform is architected with a robust backend that can host numerous studies, each with its own unique look and feel, study design, study activities and flow (**Figure 6**). The backend dynamically delivers content to a Eureka mobile app and/or web-based interface. **The Eureka architecture will allow for the rapid (and very cost-efficient) development of a HeartShare mHealth tracking and patient engagement resource without the need to develop a new app *de novo*.** Eureka can be

developed and deployed in 3-6 weeks. Eureka is a custom-built, HIPAA-compliant platform that runs on AWS, allowing scalability, and provides for redundancy, security, and data integrity. While Eureka is optimized for remote study participation, it is also equipped for in-person studies and hybrid studies with both remote and in-person components. Built as a national collaborative resource for mHealth research, Eureka is currently used for projects funded by NIH, PCORI, industry and others, including several large multi-center studies[1-4] (see Resources/Facilities for more detailed information and examples of studies that utilize Eureka). **Table 1** display the many functions provided by the Eureka platform, which are relevant to HeartShare.

**Table 1. Features of the Eureka Platform**

| Eureka function | Explanation |
| --- | --- |
| Cross-platform dynamic content delivery | Architecture allows dynamically deliver of study content and data collection via smartphone or web. on Android and iOS smartphones using the Eureka mobile app and on the web. Eureka app delivers all studies through our backend API |
| eConsent and study eligibility | Tested, IRB-approved approaches to obtaining remote consent, including HIPAA-authorization via an authenticated signature (Docusign integration) and checks complex eligibility criteria. |
| Patient engagement | robust messaging and reminder system using push notification, SMS texting, and email to improve compliance and longitudinal data collection. These messages can be triggered by any variety of triggers (e.g., time-based, completion of a particular survey or answer there-of) and can have automated escalation schema. |
| Survey tools and eVisits | Highly configurable and robust survey engine that delivers surveys, including complex triggering and skip logic within surveys and between surveys as well as real-time data validation during data entry. Supports eVisits (study activities that can open and close with time windows or can be triggered by events or previous activities). Custom trackers allow participants to granularly track symptoms (or other characteristics). |
| mHealth integration | Integration with multiple devices, sensors and apps, including Bluetooth-enabled BP cuffs, ECG monitors, and activity monitors. Supports integration with other apps and can pull data from phone sensors using standard approaches (e.g., OAuth2) as well as custom-built integrations. Allows integration for seamless user experiences and pulling of raw data into Eureka from devices and backend systems (e.g., Samsung, Apple HealthKit, Fitbit, Jawbone, Azumio, Omron, etc.) |
| Outcomes | Validated novel tools for measuring important outcomes, such as a home *mobile 6-Minute Walk Test*,[5] *screen-time* as a measure of sleep[6,7] and *geofencing* to detect hospitalizations[8]. In addition, we have developed novel markers from activity monitors as disease-specific outcomes, now in use in randomized trials on the platform.[9,10] |
| EHR integration | Direct access to the EHR via a FHIR API, allowing 2-way integration of research data with clinical data and workflows. |
| Study management portal | Allows study teams to manage consents, monitor participants' progress, and pull down reports and study data. Updated every 24 hours, password-protected (2-factor-authentication). Administrator and user accounts, with permission setting. |
| Proxy data entry | Study coordinators are able to complete surveys on behalf of participants (e.g., during an interview in-person or in a call-center); answers are logged as entered by the coordinator. Coordinator-specific CRFs provided for additional data entry. |
| Study messaging | Multiple options for messaging including automated and triggered messaging via email, SMS texting, or push notifications. Pinned messages can stay "on top" of the window in the app for instructions, status, or any other important and timely messages. Messages can be sent to individual participants or groups of participants. |

Through the ***Eureka Study Management Portal***, HeartShare personnel can export CSV-formatted files that are automatically updated overnight and thus up-to-date every 24 hours. For larger files (for example raw data from integrations), files (typically JSON formatted) will be uploaded and stored in an AWS S3 bucket for easy programmatic access HeartShare staff. Eureka data has been used for several AI and "big data" studies.[3,11-17] Eureka is also supported by a robust bio-signal processing platform using the AMPS CER-S software on a large server to ingest static ECG, continuous ambulatory ECG monitoring, continuous photoplethysmography (PPG) data, and other signals from wearables. The software has robust processing, enables custom algorithms, and has a system for adjudicating (or labeling) these signals.

For HeartShare participants who do not have access to internet or technology, and therefore cannot use the Eureka web- or smartphone-based apps, we will follow the ADAPTABLE clinical trial protocol and offer a non-internet enrollment pathway and survey completion via HeartShare

Clinical Center staff or the DTC call center staff, which will involve telephone follow-up with study coordinator data entry into Eureka directly.

**Figure 7. Overview of eVisit structure in Eureka.** "Triggered" surveys are only delivered to participants who meet criteria for the survey. The minimum number of questions per survey is indicated in parentheses.
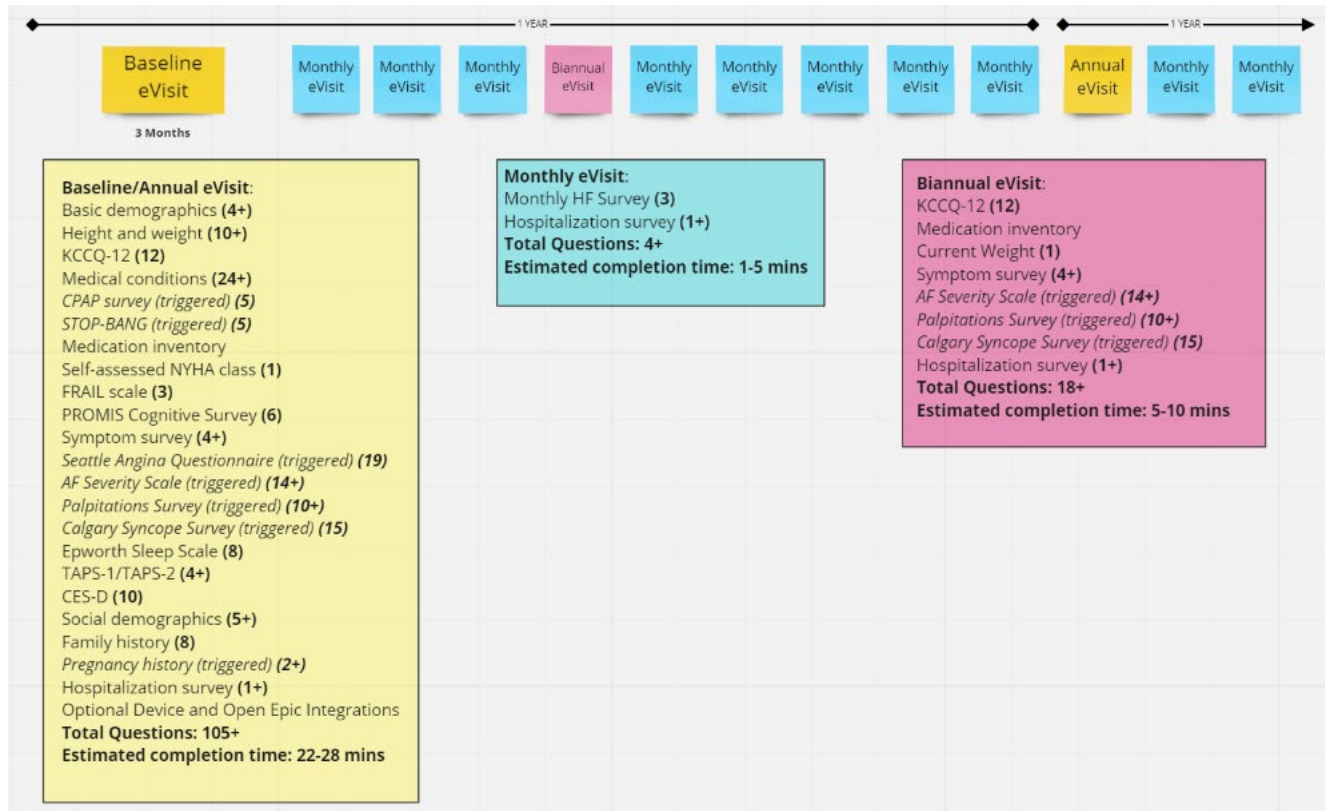


**Patient Experience**: Interested participants will be invited to sign up for Eureka on the iOS or Android mobile app or on the study website. They will create an account with an embedded Unique Participant Code that will be linked the patient's MRN. Upon account creation, they will be presented with an eligibility survey, and eligible participants will be prompted to sign the study eConsent. The Eureka platform will deliver surveys to the participant on a predetermined cadence. Each "batch" of surveys is called an eVisit, and these eVisits will be open for one month (except the baseline eVisit which will be open for 3 months) (**Figure 7**).

The Eureka platform will send regular reminders via Push Messages, SMS Messages, and emails to remind participants of their incomplete surveys. Once eVisit surveys are completed, the participant will no longer receive reminders until their next eVisit opens.

# Data Collection at the HeartShare Clinical Centers

There are 3 levels of data collection at the 6 HeartShare clinical centers. Level 1 involves retrospective and prospective de-identified EHR data and image collection of all living heart failure patients and age- and sex-matched comparators who have had contact with the health system at each clinical center from 2016 onwards. Level 2 is a prospective "low touch" registry that is a subset of level 1. Patients identified via the EHR query are invited to participate in HeartShare using the Eureka app, supplemented by outreach by clinical center staff to include underserved populations who may not have access to mobile phones or computers. Level 3, the prospective deep phenotyping study, is a subset of level 2 and is recruiting 1000 participants (750 HFpEF, 250 comparators). **Figure 6** illustrates the levels of data collection in HeartShare.

**Figure 6. Levels of Data Collection in HeartShare**
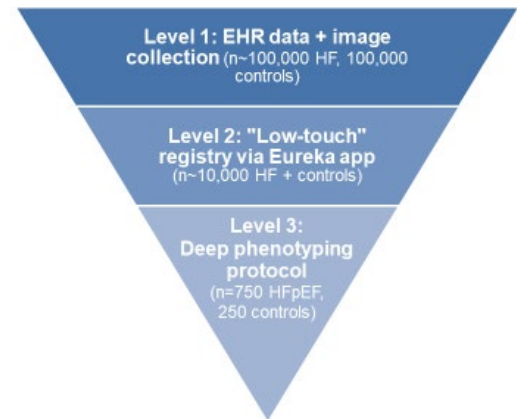


# HeartShare Committees and Core Labs

## Committees (and chair[s])

**Data Portal Committee**
Abel Kho, MD, Northwestern University
Firas Wehbe, MD, PhD, Northwestern University

**Deep Phenotyping Committee**
Barry Borlaug, MD, Mayo Clinic
Julio Chirinos, MD, PhD, University of Pennsylvania

**Eureka Working Group**
Jeff Olgin, MD, Eureka Platform, UCSF

**Extant Dataset Committee**
Alain Bertoni, MD, Wake Forest – Atrium Health
Laura Rasmussen-Torvik, PhD, Northwestern University
Margaret Redfield, MD, Mayo Clinic

**Extant Images Committee**
Sanjiv Shah, MD, Northwestern University
Scott Solomon, MD, Brigham and Women's Hospital

**Machine Learning/AI Committee**
Yuan Luo, PhD, Northwestern University

**Multi-omics/TOPMed Committee**
Nipavan Chiamvimonvat, MD, UC Davis
Denise Scholtens, PhD, Northwestern University

**Publications and Ancillary Studies Committee**
Sadiya Khan, MD, MSc, Northwestern University
Vandana Sachdev, MD, NHLBI

## Core Labs (and principal investigator[s])

**Adipose and Skeletal Muscle Biopsy**
Bret Goodpaster, PhD and Lauren Sparks, PhD, AdventHealth Research Institute
Mike Jensen, MD, Mayo Clinic
Jamie Justice, PhD, Wake Forest – Atrium Health

**Arterial Stiffness**
Julio Chirinos, MD, PhD, University of Pennsylvania

**Clinical Events**
Akshay Desai, MD, MPH, Brigham and Women's Hospital

**Cardiopulmonary Exercise Testing**
Greg Lewis, MD, Massachusetts General Hospital

**Computed Tomography**
Ashley Weaver, PhD and Leon Lenchik, MD, Wake Forest – Atrium Health

**Electrocardiography**
Elsayed Soliman, MD, MS and Oguz Akbilgic, PhD, Wake Forest – Atrium Health

**Echocardiography**
James Thomas, MD, Northwestern University

**Laboratory Testing**
Russell Tracy, PhD and Margaret (Peggy) Doyle, PhD, University of Vermont

**Microbiome**
Hariom Yadav, PhD, University of South Florida

**Magnetic Resonance Imaging**
Daniel Lee, MD, Northwestern

**Pulmonary Function Testing**
Charles Hardin, MD, PhD, Massachusetts General Hospital

## Layperson Summary of HeartShare

HeartShare is an innovative new program funded by the National Heart, Lung, and Blood Institute (NHLBI) of the US National Institutes of Health (NIH). HeartShare is a comprehensive study of heart failure, a common and serious medical condition which occurs when the heart is unable to keep up with the demands of the body, resulting in shortness of breath, fluid retention, and fatigue. Certain types of heart failure are difficult to treat because heart failure is a heterogeneous (varied) medical condition. HeartShare aims to better classify heart failure into subtypes to help develop more personalized treatments for patients, with the hope that this will

improve the lives of heart failure patients. To do this, HeartShare is bringing together a large amount of data (including images, such as heart ultrasounds and MRIs and molecular data from the blood, such as genetics) from previously conducted studies, electronic health records, and a new prospective study of heart failure enrolled in HeartShare. These data will be shared in a secure, online portal where researchers can use a variety of methods, including artificial intelligence and machine learning, to analyze the data and develop novel insights that will ultimately improve the health of heart failure patients.

## DESCRIPTIONS OF HEARTSHARE COMMITTEES

## Data Portal Committee

The HeartShare Data Portal Committee is the forum for design and implementation of workflows and interrelated platforms for integrating the diverse datasets and data resources applicable to HeartShare. Working closely with informatics and data science professionals across the consortium and with the Deep Phenotyping Committee, the Data Portal Committee ensures that the processes for acquiring and integrating data –such as cohort, clinical trial, multi-omics, EHR, research testing, biomarkers, and imaging data –are sound, secure, effective, and adherent with the research protocols of HeartShare.

## Deep Phenotyping Committee

The HeartShare Deep Phenotyping Committee is tasked with the design and development of the deep phenotyping protocol for HeartShare. This committee has at least one representative from each of the clinical centers and works collaboratively to ensure HeartShare captures data that will be integral to furthering HFpEF research. The Deep Phenotyping Protocol Committee works with the Data Portal Committee to ensure all data is captured and to plan how data will be integrated across HeartShare.

The Deep Phenotyping Committee completed the HeartShare Deep Phenotyping Study protocol (which includes the HeartShare Registry and the HeartShare Deep Phenotyping Cohort) IRB review at Northwestern in August. Northwestern will act as the central IRB for the study. The current versions of the protocol, registry consent, and deep phenotyping consents can be accessed via Dropbox.

## Extant Datasets Committee

The HeartShare Extant Dataset Committee determines which existing studies to include in HeartShare and works on harmonizing the data between these studies. Current studies under consideration for inclusion can be found in Table 1.  The Extant Datasets committee also interfaces with the various coordinating centers of these existing studies and applies for access to data and images from these studies.

**Table 1. Studies under consideration for inclusion into HeartShare**

| Study name | Number of participants at inception | Coordinating center location | What data is available online? | Data on BioLINCC? |
|---|---|---|---|---|
| **Studies included in C4R (Collaborative Cohort of Cohorts for COVID-19 Research)** | | | | |
| Atherosclerosis Risk in Communities (ARIC) | 15,792 | University of North Carolina at Chapel Hill, NC | Data available for request include ARIC v1-v6 examination cycles, collated annual follow-up communication data for contact years 2-29, and follow-up for mortality, heart disease, and stroke events through 2017. Also included are data from ancillary studies. | Yes |
| Jackson Heart Study (JHS) | 5,306 | Jackson State University, Jackson, MS | Data available for request include Jackson Heart Study visit 1-3 examination cycles, collated annual follow-up communication data through 2016, and follow-up for mortality, heart disease, and stroke events through 2014. | Yes |
| Coronary Artery Risk Development in Young Adults (CARDIA) | 5,115 | University of Alabama at Birmingham | Available data for request include exam data through Year 30 and follow-up data through 2016. | Yes |
| Genetic Epidemiology of COPD (COPDGene) | 10,198 | Brigham and Women's Hospital, Boston MA | | No |
| Framingham Heart Study | 5,124 | Framingham Heart Study, Framingham, MA | Data available for request include Framingham Offspring examination data from the first 9 clinical exams and selected ancillary data and event follow-up through 2018. Also included are the first 4 exams from the OMNI 1 cohort. | Yes |
| Framingham Heart Study (FHS-G3) | 4,095 | Framingham Heart Study, Framingham, MA | Data available for request include Framingham Generation 3 examination data from the first 2 clinical exams, selected ancillary data and event follow-up through 2018. Also included are the OMNI 2 and New Offspring (NOS) cohorts. | Yes |
| Hispanic Community Health Study/Study of Latinos (HCHS/SOL) | 16,415 | University of North Carolina at Chapel Hill, Chapel Hill, NC | Data available for this study were updated on 5/06/2022. The data package now includes baseline and visit 2 data from the main HCHS-SOL study as well as four ancillary studies: the Sociocultural ancillary study, the Sueno ancillary study, the SOLNAS ancillary study, and the Youth ancillary study. | Yes |
| Mediators of Atherosclerosis in South Asians Living in America (MASALA) | 1,164 | University of California, San Francisco, CA | Baseline Exam 1: October 2010-March 2013 <br> Social Networks: September 2014-March 2018 <br> Exam 2: September 2015-March 2018 <br> Exam 1A: March 2017-March 2018 (new wave of recruitment) | No |
| Multi-Ethnic Study of Atherosclerosis (MESA) | 6,814 | Collaborative Health Studies Coordinating Center (CHSCC) University of Washington, Seattle, WA | Data available for request include data from exam 1 through exam 5 and events data updated through calendar year 2015. Also included are data from several ancillary studies. | Yes |

| | | | | |
|---|---|---|---|---|
| Northern Manhattan Study (NOMAS) | 4,400 | Columbia University,New York, NY | | No |
| Prevent Pulmonary Fibrosis (PrePF) | 15,241 | | | No |
| REasons for Geographic and Racial Differences in Stroke (REGARDS) | 30,239 | The University of Alabama at Birmingham, Birmingham, AL | | No |
| Severe Asthma Research Program (SARP) | 700 | Penn State University, Hershey, PA | | No |
| Strong Heart Study (SHS) | 3,516 | University of Oklahoma, Oklahoma City, OK | | No |
| SubPopulations and InteRmediate Outcome Measures in COPD Study (SPIROMICS) | 2,983 | University of North Carolina at Chapel Hill, Chapel Hill, NC | Data available for request include SPIROMICS I main study data as well as SPIROMICS Bridge phone call follow-up period data (period between SPIROMICS I NIH contract and SPIROMICS II grant). | Yes |
| **Subtotal** | **127,102** | | | |
| **Observational Cohorts** | | | | |
| Framingham, FHS (non-BioLINCC) | 14,975 | Framingham Heart Study, Framingham, MA | Phenotypic Data and Summary Table of Past Exams, Genetics Data, Omics Data, Noninvasive and Biomarker Protocols | No |
| Framingham Heart Study-Cohort (FHS-Cohort) | 5,209 | Framingham Heart Study, Framingham, MA | The data now include examination data from the first 32 clinical exams, selected ancillary data, and event follow-up through 2018. | Yes |
| CHS | 5,888 | Collaborative Health Studies Coordinating Center (CHSCC)  University of Washington, Seattle, WA | The BioLINCC CHS data package was last updated in June of 2016 and includes follow-up data through year 24, events data through 12/31/2011, and several ancillary studies. | Yes |
| WHI | 161,808 | Fred Hutchinson Cancer Research Center, Seattle, WA | Data are available from the following: the multi-component clinical trial (CT), the observational study (OS), the extension studies (ES), and the ancillary memory study (MS). | Yes |
| **Subtotal** | **188,158** | | | |
| **Clinical Trials** | | | | |
| TOPCAT | 3,445 | PIs: New England Research Institutes, Inc., Watertown, MA  Brigham and Women's Hospital, Boston, MA | https://biolincc.nhlbi.nih.gov/studies/topcat/#available-biospecimens-panel-title | Yes |
| ALLHAT | 42,448 | PI:University of Texas | Study Datasets only, not otherwise specified | Yes |

| | | | | |
|---|---|---|---|---|
| ACCORD | 10,251 | PI :Wake Forest University, Winston-Salem, NC | Data available for request include the ACCORD main study data and the ACCORDION ancillary study data. | Yes |
| Look AHEAD | 5,145 | Wake Forest University Health Sciences, Winston-Salem, NC | This article is a good summary: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2613279/ | No |
| SPRINT | 9,361 | Wake Forest University Health Sciences, Winston-Salem, NC | The available data include all elements of the previously released SPRINT Primary Outcome Paper (SPRINT-POP) data, the full SPRINT clinical data including the MRI and MIND data, and select ancillary study data (Ambulatory Blood Pressure Monitoring, APOL1, Acute Kidney Injury). | Yes |
| RELAX | 216 | PI: Duke Clinical Research Institute, Durham, NC | Study Datasets only, not otherwise specified | Yes |
| NEAT | 110 | PI: Duke Clinical Research Institute, Durham, NC | Study Datasets only, not otherwise specified | Yes |
| CARRESS | 188 | PI: Duke Clinical Research Institute, Durham, NC | Study Datasets only, not otherwise specified | Yes |
| DOSE (DOSE-AHF) | 308 | PI: Duke Clinical Research Institute, Durham, NC | Study Datasets only, not otherwise specified | Yes |
| EXACT (EXACT HF) | 253 | PI: Duke University, Durham, NC | Study Datasets only, not otherwise specified | Yes |
| ROSE | 360 | PI: Duke University, Durham, NC | Study Datasets only, not otherwise specified | Yes |
| **Subtotal** | **72,085** | | | |
| **TOTAL** | **387,345** | | | |

# Publications and Ancillary Studies Committee

The HeartShare Publications and Ancillary Studies (PAS) Committee has the following goals:
- To encourage publication submissions – particularly collaborative works involving multiple HeartShare sites.
- To ensure and expedite orderly and timely presentations to the scientific community of all pertinent data resulting from HeartShare studies.
- To ensure scientifically accurate presentations and papers from HeartShare investigators.
- To maintain a complete up-to-date list of HeartShare presentations and publications, and to distribute such lists to all HeartShare investigators on a regular basis.
- To support submission of Ancillary Studies that are aligned with HeartShare objectives for extramural funding.

## Ancillary Studies Proposals Approved to Date (Funding Pending)

*ECG-AI Based Detection and Phenotyping of HFpEF*
O. Akbilgic, Wake Forest University

*A Novel Phenomics Analysis Framework for Bioprofiling*
M. Cadeiras, University of California Davis

*Novel therapeutic targets for HFpEF*
N. Chiamvimonvat, University of California Davis

*Integrated Proteomic and Metabolomic Determinants of Left Atrial Dysfunction*
R. Patel, Northwestern University

*Digital Biomarkers of HFpEF Phenotypes and Progression*
J. Olgin, University of California San Francisco

*Familial and Genetic Patterns of HFpEF in HeartShare*
L. Rasmussen-Torvik, Northwestern University

*Biomarker Relationships in Alzheimer's and Imaging Neuropathology (HeartShare-BRAIN)*
C. Schaich, Wake Forest University

*Microbiome/Leaky gut/Inflammation Axis in HFpEF Patients*
H. Yadav, University of South Florida

## Ancillary Studies Under Review

*Characteristics and Implications of Sleep and Sleep Disruption in HFpEF*
V. Somers, Mayo Clinic

*A Multi-modal Platform for Deep Phenotyping of HFpEF Using Raw, Widely-available Data and Artificial Intelligence Algorithms*
G. Tison, University of California San Francisco

## Publications

Shah SJ, Butler J, Shah SH, Kamphaus TN, Sachdev S. Accelerating therapeutic discoveries for heart failure: a new public–private partnership. *Nat Rev Drug Discov* 2022 (in press).
Rationale and Design of the HeartShare Study Data Portal and Electronic Health Record Repository (manuscript in progress)
Rational and Design of the HeartShare Deep Phenotyping Study (manuscript in progress)

## Publications Policy

The HeartShare Publications Policy is currently in development.

## Ancillary Studies Policy

The HeartShare Ancillary Studies Policy can be viewed here. All ancillary study proposals must be submitted for review by using the form available at https://redcap.link/mt2wj4i7.

## Research Skills Program

The HeartShare Research Skills Program is a 1-year, full-time research fellowship intended for post-doctoral trainees interested in gaining clinical research skills in data science. The program includes an intensive 3-month bootcamp led by the Northwestern Computer Science Department in which trainees receive hands-on training in data management, programming, and application of machine learning and artificial intelligence approaches to clinical research in data science. The remaining 9 months are dedicated to completing a mentored research project related to HFpEF, using the approaches they learned in the data science bootcamp. Fellows are paired with one clinical mentor and one data science mentor and attend monthly virtual work-in-progress and career development meetings, as well as HeartShare committee meetings relevant to their proposed research project. Fellows have access to extant datasets/images and EHR data compiled for HeartShare to use for their research project and are immersed in the HeartShare research environment. The co-chairs of the Research Skills Committee are Dr. Jordana Cohen and Dr. Phil Greenland.



**Jordana Cohen, MD, MSCE**
**Research Skills Committee Co-chair**
Dr. Jordana Cohen is an Assistant Professor of Medicine and Epidemiology in the Renal-Electrolyte and Hypertension Division and Department of Biostatistics, Epidemiology, and Informatics at the University of Pennsylvania, Perelman School of Medicine. She went to medical school at Rutgers and completed her Internal Medicine residency at Boston University and her Nephrology fellowship at the University of Pennsylvania. She is the principal investigator of multiple NIH grants in which she leads translational studies evaluating the

pharmacologic management and physiologic characteristics of hypertension in multimorbid patients. In addition to her role in HeartShare, she currently serves as Vice Chair of the American Heart Association Hypertension Science Committee, Co-Chair of the CRIC Study Blood Pressure Working Group, and Co-Chair of the American Medical Association's Blood Pressure Validated Device Listing.

**Phil Greenland, MD**
**Research Skills Committee Co-chair**
Dr. Phil Greenland is the Harry W. Dingman Professor of Cardiology and Professor of Preventive Medicine at Northwestern University's Feinberg School of Medicine and a Senior Editor for JAMA. He held previous positions as Department Chair of Preventive Medicine at Northwestern, Executive Associate Dean for Clinical and Translational Research, and Director of Northwestern's Clinical and Translational Sciences Institute. He has been actively engaged as a cardiovascular epidemiologist in the MESA Study, the CARDIA Study, the Women's Health Initiative, the Chicago Heart Association Detection Project in Industry, and the Chicago Western Electric Study. He is a longstanding member of the NHLBI Observational Study Monitoring Board for the Framingham Heart Study and was a long-term member of the Board of External Experts of the NHLBI. Dr. Greenland's research has helped to shape cardiovascular care guidelines around the world. His work, which has been cited thousands of times, was among the first to reveal that women are more likely to die from heart attacks than men, and his studies illustrated that major risk factors almost always precede heart attacks, overcoming the "50% myth." He has also contributed to enhanced diagnostic and preventive care, showing the importance of coronary calcium scanning for cardiovascular disease risk prediction. He has been recognized multiple times as a Thomson Reuters Highly Cited Researcher in clinical medicine.  He is an elected member of the Association of American Physicians and an elected Fellow of the Royal College of Physicians (London). He is also an elected Fellow of the American Heart Association, the American College of Cardiology, and the European Society of Cardiology.  He has received distinguished national awards for his research, his teaching, and his mentoring from the Association of American Medical Colleges, American College of Physicians, National Institutes of Health, Society for Cardiovascular Computed Tomography, American Society for Preventive Cardiology, and the American Heart Association.

**Ahmed Fayyaz, MD**

Dr. Ahmed U. Fayyaz is a postdoctoral fellow in Dr. Margaret M. Redfield's laboratory, and a second-year Ph.D. student in Clinical and Translational Science, with a particular focus on contemporary biology and machine-learning tools, at Mayo Clinic, Rochester MN. Immediately after graduating from medical school in his native Pakistan, Dr. Fayyaz came to Mayo Clinic as research trainee in cardiovascular pathology division and learned basic cardiovascular and autopsy pathology from distinguished Mayo cardiovascular pathologists, Drs. William D. Edwards, and Joseph J. Maleszewski. At the completion of this appointment, Dr. Redfield hired Dr. Fayyaz to head a collaborative project regarding human pulmonary vascular remodeling in pulmonary hypertension related to heart failure. During his postdoctoral training at Dr. Redfield's lab and collaborating with Dr. Barry A. Borlaug and Dr. Surendra Dasari, Dr. Fayyaz continues to learn and gain expertise in tissue research, spatial omics technologies, bioinformatics and computational biology, machine-learning, generating translational large animal models, and circulatory hemodynamics. His work has resulted in publications related to pulmonary hypertension, cardiac amyloidosis and HFpEF in peer-reviewed journals: *Circulation*, *JAMA Cardiology* and *Cardiovascular Research* etc. Currently Dr. Fayyaz is working on delineating the pathobiology of development of HFpEF and pulmonary vascular remodeling secondary to pulmonary hypertension due to left heart diseased using both human cardiopulmonary tissue and experimental translational animal models through spatial multi-omics technologies and hopes to find therapeutic targets for further translational research.



**Hanna Gaggin, MD, MPH**

Dr. Hanna Gaggin is a general cardiologist, educator and clinical investigator at Massachusetts General Hospital and Harvard Medical School. She is interested in single and multi-center clinical trials to evaluate heart failure with a focus on heart failure with preserved ejection fraction and cardiac amyloidosis phenotypes. She is a member of the Cardiovascular Medicine Section Leadership Council in the Cardiology Division and the Subspecialty Core Educator for the Internal Medicine residency at Massachusetts General Hospital. Dr. Gaggin graduated from the Eastern Virginia Medical School in 2003. She completed her Internal Medicine residency at the University of Virginia Health System, followed by an MPH at Harvard School of Public

Health with a concentration in Quantitative Methods in 2007. She completed her clinical cardiology fellowship at the University of Pittsburgh Medical Center and clinical research fellowship at MGH and joined the faculty at Massachusetts General Hospital and Harvard Medical School in 2012.



**Adrienne Kline, MD, PhD**
Dr. Adrienne Kline is a postdoctoral fellow in the Department of Preventative medicine at Northwestern University. Prior to this, she completed her Ph.D. in biomedical engineering, an M.D. in medicine, preceded by a B.Sc. in electrical engineering. Her interests lie at the intersection of medicine and engineering, specifically in leveraging algorithmic decision-making (machine learning/artificial intelligence) support for translational applications to medicine. Her work has led to the development of novel methods for handling missing data, innovative metrics for evaluating the reliability of machine learning predictions, and information fusion of multimodal data streams. With an emphasis on structural data, computer vision, reinforcement learning and generative algorithms, she hopes to change the efficiency and reliability with which medicine is practiced.



**Praneet Mylavarapu, MD**
Dr. Praneet Mylavarapu is a current HeartShare fellow and M.S. in Artificial Intelligence candidate at Northwestern University as a member of Northwestern's Bluhm Cardiovascular Institute Fellowship Program in Artificial Intelligence in Cardiovascular Disease. He recently graduated from internal medicine residency at the University of California, San Diego and plans to enter a cardiology fellowship upon completion of his HeartShare fellowship. He is interested in applying machine learning and artificial intelligence for cardiovascular disease classification and treatment. His project on using machine learning to predict atrial fibrillation ablation outcomes earned the Young Investigator Award at Heart Rhythm Society 2021. Currently, he is working on computer vision for echocardiography and ECG analysis to better understand HFpEF.

**Oday Salman, MD**
Dr. Oday Salman received his BS degree with distinction in biology from the American University of Beirut (AUB) in 2016, followed by his MD in 2020. Following graduation, he worked for 2 years at AUB medical center, one of the largest and most capable tertiary care facilities in the Middle East – North Africa region, in the emergency department as a research scholar and moonlighter. He subsequently joined Dr. Julio Chirinos's core lab in March 2022 at the University of Pennsylvania as a postdoctoral research fellow where he started working on multiple projects involving proteomics and genomics. He plans to hone his skills in machine learning in hopes of leading an impactful HFpEF-related research project that integrates machine learning models as part of the HeartShare fellowship curriculum.

## SCIENTIFIC PRESENTATIONS SPEAKERS



**Bret Goodpaster, PhD, Scientific Director at the Translational Research Institute, AdventHealth Research Institute**
Dr. Bret Goodpaster is a Senior Investigator and Scientific Director at the AdventHealth Translational Research Institute (TRI). Dr. Goodpaster's primary research is in the pathophysiology of human obesity, insulin resistance, and diabetes, and to help decipher biological mechanisms underlying the health benefits of exercise. He has received a number of awards and honors for his work, including the Nathan Shock Award from the National Institute of Aging in 2008, for his work investigating the role of muscle fat infiltration in aging and muscle quality. He is particularly well known for "the athlete's paradox" which has shifted the paradigm in Type 2 diabetes research to investigate, how and why does fat accumulation in muscle cause insulin resistance in some subjects but not others? Dr. Goodpaster has published over 270 peer-reviewed papers, review articles and book chapters, and his papers have received more than 34,000 citations (h-index 91). He has served on Editorial Boards for Diabetes, the American Journal of Physiology, and the Journals of Gerontology, and served as Associate

Editor for both Obesity and Diabetologia. He has also served on several NIH grant review panels as well as the American Diabetes Association. Dr. Goodpaster obtained a B.S. in Biology from Purdue, and after completing a Pre-doctoral Fellowship at Maastricht University in the Netherlands, received his Ph.D. in Human Bioenergetics from Ball State University in 1995.



**Jamie Justice, PhD, Assistant Professor, Gerontology and Geriatric Medicine, Wake Forest University**



**Lauren Sparks, PhD, Associate Investigator at the Translational Research Institute for Metabolism and Diabetes, AdventHealth Research Institute**



**Anna Hemnes, MD**
**Associate Professor of Medicine, Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University**

Dr. Anna Hemnes is a translational physician-scientist with a research focus on the role of altered metabolism in pulmonary vascular disease. Her basic research is on the effect of BMPR2 mutation on insulin-mediated intracellular signaling in the pulmonary vasculature and the right ventricle. Her clinical research interests include the role of insulin resistance and metabolic syndrome in human pulmonary vascular disease with a focus on genetic susceptibility to these conditions, and deep molecular phenotyping of pulmonary vascular disease. This interest in molecular phenotypes of pulmonary vascular disease has led to her prior work demonstrating an Omic signature of vasodilator-responsive pulmonary arterial hypertension, one of the earliest publications demonstrating the feasibility of precision medicine in an ultra-rare pulmonary vascular disease. Dr. Hemnes' lab is now actively investigating novel blood-based Omic predictive strategies for FDA-approved therapies for pulmonary arterial hypertension. She actively see patients in the Vanderbilt Center for Pulmonary Vascular Disease and have effectively worked with this population to recruit into clinical studies for pulmonary vascular disease, including the treatment of pulmonary hypertension, diagnostic modalities in pulmonary vascular disease and novel classification of pulmonary vascular disease. Her lab has a unique and powerful capacity to study molecular mechanisms of pulmonary vascular disease and right heart dysfunction in studies spanning cell culture and rodent models through human translational studies and clinical trials.



**Alanna Morris, MD, Associate Professor of Medicine, Emory University**



**Leighton T. Izu, PhD**
**Professor of Pharmacology, University of California, Davis**

Dr. Leighton T. Izu was born and raised on a coffee farm in Hawaii and studied hard to avoid needing to pick coffee for the rest of his life. He is now Professor of Pharmacology at UC Davis and Faculty in the Graduate Group in Applied Mathematics. He now picks coffee only when he chooses to. He became interested in human behavior in high school so he majored in psychology and math at the University of Hawaii. There he used linear algebra to decompose behavior into simpler components, the eigenbehaviors. In graduate school at SUNY Buffalo he realized humans were too complex so he worked on something simpler, the heart. Dr. Izu's research has been primarily on understanding the calcium control system of the heart first in isolation and more recently when it interacts with the contractile system. While preparing math lectures on the singular value decomposition (SVD) he realized how he can use it to understand how parts are coordinated in a complex system such as hearts, wines, and human diseases. The Functional Connectome, which grew out of these lectures, will be used to analyze data from HeartShare to answer the question: How do subclasses of HFpEF differ? The Functional Connectome is eerily similar to Dr. Izu's analysis of human behavior done as an undergraduate.

## HEARTSHARE STEERING COMMITTEE MEMBERS

## HeartShare Data Translation Center



**Sanjiv J. Shah, MD**
**Principal Investigator, Data Translation Center**
Dr. Sanjiv J. Shah is the Stone Endowed Professor; Director of Research for the Bluhm Cardiovascular Institute; Director, Center for Deep Phenotyping and Precision Medicine in the Institute for Augmented Intelligence in Medicine; and Director of the HFpEF Program at Northwestern University Feinberg School of Medicine. Dr. Shah's clinical expertise and research program are focused HFpEF, and in 2007, he started the world's first dedicated HFpEF program at Northwestern University; this program has served as a model for several other similar programs in the United States and throughout the world. Dr. Shah has been continuously funded by grants from the AHA and the NIH since 2008. He directs a laboratory that investigates the pathogenesis of HFpEF; conducts multicenter clinical trials of novel therapeutics for heart failure, pulmonary hypertension, and cardiac amyloidosis; and develops novel techniques for machine learning and AI for the classification, diagnosis, and tracking of cardiovascular diseases. His research, which has spans basic research in animal models, clinical physiologic studies, human clinical trials, and population-based epidemiology studies, has highlighted the heterogeneity of the HFpEF syndrome, and has improved the understanding of the risk factors, pathogenesis, and pathophysiology of HFpEF. Dr. Shah has served as the international principal investigator, executive committee member, or steering committee member for >35 multicenter randomized clinical trials and studies in heart failure. He has

published >450 peer-reviewed scientific publications, a textbook on cardiovascular genetics, and handbooks on internal medicine and cardiovascular disease.



**Abel Kho, MD**
**Co-PI, Data Translation Center**
Dr. Abel Kho is an Internist and Professor of Medicine and Preventive Medicine in the Northwestern University Feinberg School of Medicine where he is the Founding Director of both the Center for Health Information Partnerships (2015) and the Institute for Augmented Intelligence in Medicine (2020). His research focuses on developing regional Electronic Health Record (EHR) enabled data sharing platforms for a range of health applications including high throughput phenotyping, cohort discovery, estimating population level disease burden, and quality improvement. He has served as Principal Investigator for over $80M in external funding, published over 100 manuscripts, and mentored numerous students and trainees. He is an internationally recognized expert in privacy preserving record linkage, having published the first large scale real-world application of this method for which he was assigned a patent, and co-founded a startup which was subsequently acquired by Datavant. He is an elected Fellow of the American College of Medical Informatics and recipient of the Donald A.B. Lindbergh Award for Innovation in Informatics.



**Yuan Luo, PhD**
**Co-PI, Data Translation Center**
Dr. Yuan Luo is currently Associate Professor at Department of Preventive Medicine, at Feinberg School of Medicine in Northwestern University. He is Chief AI Officer at Clinical and Translational Sciences Institute (NUCATS) and Institute for Augmented Intelligence in Medicine. Dr. Luo earned his PhD degree from MIT EECS with a math minor. He is a Fellow of American Medical Informatics Association (AMIA). He won the American Medical Informatics Association (AMIA) New Investigator Award in 2020. Dr. Luo has been developing a novel suite of accurate, interpretable and generalizable models to integrate multi-modal health data (e.g., clinical and insurance claims data) for improving health care practice and advancing medical knowledge. He

has been leading major research initiatives with >$10M in grant support, and has published over 100 peer-reviewed papers. His publications appear in leading journals including Nature Medicine, JAMA, AJRCCM, Circulation: Heart Failure, JAMIA, JBI etc. He has published in and/or served as PC members for top AI and informatics conferences including AAAI, KDD, CVPR, ACL etc. He has also been invited to give more than 50 keynotes and guest lectures at many top universities, think tanks, societies, industry labs.



**Denise Scholtens, PhD**
**Co-PI, Data Translation Center**
Dr. Denise Scholtens is Chief of the Division of Biostatistics and Director of Northwestern University Data Analysis and Coordinating Center (NUDACC). She is interested in the design and conduct of multicenter, prospective observational studies and clinical trials and serves as the data coordinating center director and lead statistician for multiple large-scale, ongoing studies. She is particularly interested in the integration of high-dimensional data analyses into these settings.



**Lauren Balmert-Bonner, PhD**
**Core Leader, Data Management Core**
Dr. Lauren Balmert-Bonner is an Assistant Professor in the Department of Preventive Medicine, Division of Biostatistics, whose research interests lie in clinical trial design and analysis, connecting methodological developments with clinical applications. As a member of the Biostatistics Collaboration Center (BCC) and Northwestern University Data Analysis and Coordinating Center (NUDACC), she facilitates and promotes scientific research as a collaborative biostatistician across a range of clinical fields including HIV maternal child health, gastroenterology, and pediatric medicine.  She currently serves as the lead biostatistician for several studies: a cluster randomized trial assessing the effectiveness of a walking intervention on reducing frailty; a phase II pharmacodynamic study in patients with critical COVID19 pneumonia; and two concurrent trials comparing interventions for pediatric arm fractures. For the HeartShare Network, she serves as Data Management Core PI within the Data Translation Center.

**Firas Webhe, MD, PhD**
**Core Leader, Data Portal Core**
Dr. Firas Wehbe is the Medical Director of the Center for AI in Bluhm Cardiovascular Institute at Northwestern Medicine, specializing in building, deploying, and evaluating AI-enabled infrastructure and systems in support of cardiovascular research and care. He is a co-investigator of the HeartShare DTC primarily involved in the Data Portal Committee. His prior roles include associate professor of preventive medicine, division of health and biomedical informatics and of pathology, and Chief Research Informatics Office at the Feinberg School of Medicine at Northwestern University. He received his medical doctorate from the American University of Beirut and his PhD in biomedical informatics from Vanderbilt University. He has been co-investigator with core leadership roles on multiple large NIH-funded initiative including the International Epidemiological Databases to Evaluate AIDS (IeDEA) [NIAID], Electronic Medical Records and Genomics (eMERGE) [NHGRI], Northwestern's Alzheimer's Disease Core Center [NIA], the Robert H. Lurie Comprehensive Cancer Center [NCI], the All of Us Research Program [NIH], the Vanderbilt Institute for Clinical and Translational Research (VICTR) [NCATS], the Northwestern University Clinical and Translational Science Institute (NUCATS) [NCATS].



**Faraz Ahmad, MD, MS**
**Co-investigator, Data Portal Core**
Dr. Faraz Ahmad is an Assistant Professor of Medicine-Cardiology and Preventive Medicine-Health and Biomedical Informatics and the Associate Director of the Bluhm Cardiovascular Institute Center for Artificial Intelligence at Northwestern Medicine. Dr. Ahmad's research interests are in the application of data science and digital health technologies to improve quality of care and patient-centered outcomes for patients with heart failure and other cardiovascular diseases. His work has received support from multiple organizations, including the National Heart, Lung, and Blood Institute, the American Heart Association, the Patient-Centered Outcomes Research Institute, the Heart Failure Society of America, and the Centers for Disease Control and Prevention. Dr. Ahmad is a practicing heart failure cardiologist who cares for

patients across the spectrum of heart failure. He has a particular clinical interest in the diagnosis and management of patients with heart failure with preserved ejection fraction and with cardiac amyloidosis.

## HeartShare Steering Committee Co-chairs



**Javed Butler, MD, MPH, MBA**
**Steering Committee Co-chair**
Dr. Javed Butler is the President of the Baylor Scott and White Research Institute and Senior Vice President for the Baylor Scott and White Health. He is also the Distinguished Professor of Medicine at University of Mississippi in Jackson, MS. Prior to joining Baylor Scott and White Health, he served as the Patrick H. Lehan Chair in Cardiovascular Research, and Professor and Chairman of the Department of Medicine at the University of Mississippi, where he was also Professor of Physiology. Prior to joining the University of Mississippi, he was Charles A. Gargano Professor and Director of the Division of Cardiovascular Medicine and Co-Director of the Heart Institute at Stony Brook University, New York. He had served as the director for heart failure research at Emory University and director of the heart and heart-lung transplant programs at Vanderbilt University prior to that. He received his medical degree from the Aga Khan University and then completed residency training at Yale University, cardiology fellowship and advanced heart failure and transplant fellowships at Vanderbilt University, and cardiac imaging fellowship at the Massachusetts General Hospital at the Harvard Medical School. He has completed Master of Public Health degree from Harvard University and an MBA from the Emory University. Dr. Butler's research interests focus on clinical trials in patients with heart failure. He serves on several national committees for the American College of Cardiology, American Heart Association, National Institutes of Health, and the Heart Failure Society of America. He is the recipient of the Simon Dack Award by the American College of Cardiology as well as the Time, Feeling, and Focus Award by the American Heart Association. Dr. Butler has authored more than 875 peer-reviewed publications. He serves on the editorial board of several peer reviewed cardiovascular journals. He has been cited numerous times in America's Best Doctors list.

**Svati Shah, MD, MHS**
**Steering Committee Co-chair**
Dr. Svati Shah is a physician scientist and Vice-Chief of Translational Research in the Division of Cardiology, Department of Medicine, and a faculty member and Co-Director of Translational Research in the Duke Molecular Physiology Institute (DMPI) and Duke Clinical Research Institute (DCRI). Her research focus is on metabolic and genetic pathways of cardiometabolic diseases, integrating diverse genomic, metabolomic and proteomic techniques for identification of novel mechanisms of disease and biomarkers. Her multidisciplinary molecular epidemiology lab within the DMPI has quantitative and molecular components and leverages several large cardiovascular biorepositories on which she is PI or co-I to perform discovery studies using omics technologies, with subsequent functional validation for mechanistic insight. Dr. Shah also collaborates closely with the DCRI for biomarker discovery in biospecimens from clinical trials and she is the Duke PI for the Verily Project Baseline study. Dr. Shah is also Director of the Duke Adult Cardiovascular Genetics Clinic where she cares for patients and their families who have, or at risk of, cardiovascular genetic disorders. Her training includes receiving a M.H.S. in epidemiology from Johns Hopkins School of Public Health, a Master's degree in Medical Genomics from Duke University.

## Clinical Center Leadership

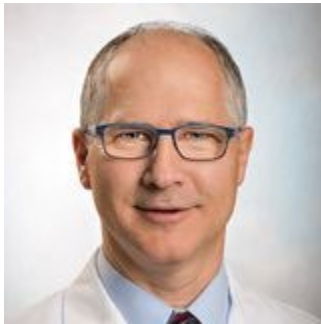### Mass General Brigham



**Greg Lewis, MD**
**Principal Investigator, Mass General Brigham Clinical Center**



**Akshay Desai, MD, MPH**
**Co-PI, Mass General Brigham Clinical Center**

Dr. Akshay Desai is the Director of the Cardiomyopathy and Heart Failure Program in the Advanced Heart Disease Section of the Cardiovascular Division, Brigham and Women's Hospital and an Associate Professor of Medicine at Harvard Medical School (both in Boston, Massachusetts). He received his undergraduate education at Princeton University, where he graduated Summa Cum Laude in 1992 with an A.B. in Public and International Affairs. He was subsequently awarded a Rhodes Scholarship for study at Oxford University, where he completed an M. Phil. in European Politics and Society at Balliol College in 1994. Following on this, he began his medical training at Harvard Medical School where he was awarded the M.D. degree in 1998. He completed his internship and residency in Internal Medicine at Brigham and Women's Hospital in 2001 and subsequently elected to pursue fellowship training in Cardiovascular Medicine at the same institution. During the final years of subspecialty training in cardiology, he completed additional fellowship training in Heart Failure and Transplantation under the direction of Dr. Lynne Stevenson. Concurrently, he conducted translational research in vascular medicine and diastolic heart failure under the supervision of Dr. Mark Creager. He was awarded an M.P.H. in 2004 from the Harvard School of Public Health. He currently divides his time between clinical care of patients with advanced heart disease and clinical research in cardiovascular clinical trials, with an emphasis on the pathophysiology, pharmacologic treatment, and ambulatory management of patients with heart failure.



**Michael Givertz, MD**
**Co-PI, Mass General Brigham Clinical Center**



**Scott Solomon, MD**
**Co-PI, Mass General Brigham Clinical Center**
Dr. Scott D. Solomon is the Edward D. Frohlich Distinguished Chair, Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, where he directs the Clinical Trials Outcomes Center and the Cardiac Imaging Core Laboratory. His research interests have focused on cardiac structure and function following myocardial injury and heart failure, modifiers of risk and outcomes in heart failure, and cardiovascular imaging.  He is a world-renowned clinical trialist, having led numerous phase 2 and phase 3 clinical trials in heart failure, including

the PARAGON-HF and DELIVER trials in heart failure with mildly reduced and preserved ejection fraction. He has published more than 950 peer-reviewed articles, three textbooks of echocardiography, and serves as Editor for *Braunwald's Heart Disease*.

## Mayo Clinic



**Barry Borlaug, MD**
**Principal Investigator, Mayo Clinic Clinical Center**
Dr. Barry Borlaug is Professor of Medicine and Director of Circulatory Failure Research in the Department of Cardiovascular Medicine at Mayo Clinic in Rochester, MN. He is an active clinical investigator interested in the fields of heart failure and pulmonary hypertension, with particular interest on the hemodynamic underpinnings of cardiac disease and exercise physiology. He is currently working to better understand the causes and mechanisms of heart failure and pulmonary vascular disease, and is active in a number of clinical trials developing and testing novel medical and device based therapies to improve outcomes for people with heart failure.



**Margaret Redfield, MD**
**Co-PI, Mayo Clinic Clinical Center**
Dr. Margaret Redfield is a heart failure cardiologist and has devoted her research career to the study of HFpEF epidemiology, pathophysiology and therapeutics in human subjects and animal models. She has performed large scale, prospectively enrolled, mechanistic cohort studies. Dr. Redfield designed and served as national PI on randomized clinical trials of therapy in HFpEF. Under her leadership, Mayo led enrollment in both funding cycles (12 years) of the NIH-sponsored Heart Failure Clinical Research Network and proposed and led 5 of the trials (3 in HFpEF) performed in the Network. She has served on the scientific advisory board/steering committees for large industry-sponsored trials in HFpEF (PARAGON, CAPACITY). She has performed extensive studies of biomarkers in community and HF cohorts, studied inflammatory mediators in HFpEF, analyzed large complex data sets and used artificial intelligence to

discover HFpEF phenogroups. She has unique expertise in pathological studies on human and animal HFpEF tissues. More recently, Dr. Redfield has used mass spectroscopy-based proteomics and bioinformatics approaches to study mechanisms underpinning pulmonary arterial and pulmonary venous remodeling in HFpEF with pulmonary hypertension. She has served on the major HFpEF working groups, including the most recent NIH working group identifying the key research priorities in HFpEF.

## Northwestern University



**Sadiya Khan, MD, MSc**
**Principal Investigator, Northwestern University Clinical Center**
Dr. Sadiya Khan received her medical degree from the Feinberg School of Medicine at Northwestern University in 2009 as part of the Honors Program in Medical Education. She completed her internship and residency in Internal Medicine at Northwestern University Feinberg School of Medicine in Chicago, IL in 2012 and then served as Chief Medical Resident from 2012-2013. She also obtained her master's degree in Clinical Investigation from the Northwestern University Graduate School in 2014. Dr. Khan completed her fellowship in cardiovascular diseases at Northwestern in 2016 followed by a post-doctoral fellowship in cardiovascular epidemiology in 2017 before joining the Northwestern faculty. She has received multiple awards for excellence in research, teaching, and patient care.



**Laura Rasmussen-Torvik, PhD, MPH**
**Co-PI, Northwestern University Clinical Center**
Dr. Laura Rasmussen-Torvik is a genetic epidemiologist interested in the identification of genetic risk factors for chronic diseases and the implementation of genomics into clinical care. She is also interested in the use of electronic health records in clinical and epidemiological research.   She has worked extensively with multiple large observational cohort studies including MESA and CARDIA.  She is one of the PI of the Northwestern center of the NHGRI-

funded eMERGE network which conducts genetic discovery and implementation research using biorepositories linked to electronic health record data.

## University of California Davis



**Nipavan Chiamvimonvat, MD**
**Principal Investigator, UC Davis Clinical Center**



**Martin Cadeiras, MD**
**Co-PI, UC Davis Clinical Center**



**Javier Lopez, MD**
**Co-PI, UC Davis Clinical Center**

## University of Pennsylvania

**Julio Chirinos, MD, PhD**
**Principal Investigator, University of Pennsylvania Clinical Center**
Dr. Julio A. Chirinos is the Director of the Core Laboratory and an Associate Professor of Medicine at the University of Pennsylvania Perelman School of Medicine. Dr. Chirinos directs an established extramurally funded research program at Penn, focused on the non-invasive assessment of cardiac and arterial structure and function using a combination of imaging modalities (including echocardiography and cardiac MRI), in patients with or at risk for heart failure. The lab has particular expertise in assessing arterial stiffness and its impact on target organs, particularly the left ventricle. Dr. Chirinos also studies the effects of interventions to attenuate left ventricular hypertrophy, fibrosis and dysfunction. We have particular interest/experience in assessing the mechanistic effects of novel treatments for Heart Failure with Preserved Ejection Fraction. Dr. Chirinos has published over 150 scientific papers, chapters, reviews, and editorials. He has also participated in various working groups and guideline Committees for the American Heart Association, the European Society of Cardiology, the American Society of Hypertension, the American Society of Echocardiography, and the European Association of Cardiovascular Imaging.

## Wake Forest – Atrium Health



**Dalane Kitzman, MD**
**Principal Investigator, Wake Forest – Atrium Health Clinical Center**
Dr. Dalane W. Kitzman is a Professor of Cardiovascular Medicine and Geriatrics/Gerontology at Wake Forest School of Medicine, and the Kermit G. Phillips II Endowed Chair in Cardiovascular Medicine. His career focus is understanding and treating the severe physical dysfunction associated with cardiovascular disease in older persons, particularly heart failure with preserved ejection fraction (HFpEF). He published one of the earliest descriptions of HFpEF and one of the first mechanistic phenotyping studies in the disorder. His work has contributed significantly to advancing our understanding of the pathophysiology and treatment of HFpEF, particularly the pivotal outcome of the severe exercise intolerance experienced by these patients. His team

reported the first randomized controlled trials of exercise training and dietary weight loss in HFpEF, which remain among the few proven interventions for exercise intolerance in HFpEF.

Dr. Kitzman has received many awards for his original research, including the prestigious MERIT award from NIH, and the Michael L. Pollack Established Investigator Award from AACVPR. He has served in key/leadership positions for >30 clinical trials, most of them focussed on HF, contributed to 5 large, NIH-funded population studies, and served on and chaired many NIH and other national committees. Dr. Kitzman is Associate Editor for JAGS and Consulting Editor for JACC:HF, has authored nearly 500 peer-reviewed publications, and successfully mentored ~30 early career investigators toward independence.



**Alain Bertoni, MD, MPH**
**Co-PI, Wake Forest – Atrium Health Clinical Center**
Dr. Alain Bertoni trained at Johns Hopkins for his MD and MPH. He completed internal medicine residency at the Johns Hopkins Hospital. He is a board-certified general internist and epidemiologist whose primary research interests are in the areas of type 2 diabetes, metabolism, and obesity and their relationship to cardiovascular diseases, including heart failure. He has been at Wake Forest School of Medicine since 2001 and currently is Professor and Associate Director of Public Health Sciences. He has experience working on cohort studies (ARIC, Jackson Heart Study, and the Multi-Ethnic Study of Atherosclerosis (MESA)) as well as clinical trials. He is the current field center PI for MESA, and is a co-investigator for HeartShare, and the REHAB-HFpEF randomized trial.

## Eureka Platform



**Jeff Olgin, MD**
**Principal Investigator, Eureka Platform**
Dr. Jeff Olgin is Chief of Cardiology and the Gallo-Chatterjee Distinguished Professor of Medicine at UCSF. He is a practicing electrophysiologist and cardiologist and a cardiovascular

researcher. He has been involved in leading clinical trials and clinical research for over 30 years. He is one of the Principal Investigator of the Health eHeart Study and one of the creators and Principal Investigator of the Eureka Research Platform. In addition to basic research and clinical trials focused on arrhythmia mechanisms, prediction, detection and prevention, he has a robust research program in digital health and developing novel technology for digitally-enabled clinical research and trials.

## SUGGESTED READING

Click here to download full text PDFs of these papers.

1. Dolgin E. Massive NIH–industry project opens portals to target validation. *Nat Rev Drug Disc* 2019;18:240-242. DOI: 10.1038/d41573-019-00033-8. *This paper describes the FNIH Accelerating Medicines Partnership Program.*

2. Heinzel FR, Shah SJ. The future of heart failure with preserved ejection fraction. *Herz* 2022;47:308-323. DOI: 10.1007/s00059-022-05124-8. *This recent paper highlights a variety of methods for subphenotyping HFpEF, many of which will be used in HeartShare.*

3. Hemnes AR, et al. PVDOMICS: A Multi-Center Study to Improve Understanding of Pulmonary Vascular Disease Through Phenomics. *Circ Res*. 2017;121(10):1136-1139. doi: 10.1161/CIRCRESAHA.117.311737. *This paper describes the NHLBI PVDOMICS program, which is akin to HeartShare, but targeted towards pulmonary hypertension and pulmonary vascular disease.*

4. Shah SJ, Borlaug B, Kitzman DW, et al. Research Priorities for Heart Failure with Preserved Ejection Fraction: National Heart, Lung, and Blood Institute Working Group Summary. *Circulation* 2020;141(12):1001-1026. doi: 10.1161/CIRCULATIONAHA.119.041886. *This white paper is a summary of a 2017 working group on HFpEF conducted at the NIH to provide suggestions on research priorities for HFpEF. It is a comprehensive review of unanswered questions in the field and provides rationale for studies like HeartShare.*

# REFERENCES

1.  Pletcher MJ, Fontil V, Carton T, et al. The PCORnet Blood Pressure Control Laboratory: A Platform for Surveillance and Efficient Trials. Circ Cardiovasc Qual Outcomes 2020;13(3):e006115. DOI: 10.1161/CIRCOUTCOMES.119.006115.

2.  Pereira NL, Avram R, So DY, et al. Rationale and design of the TAILOR-PCI digital study: Transitioning a randomized controlled trial to a digital registry. Am Heart J 2020;232:84-93. DOI: 10.1016/j.ahj.2020.10.069.

3.  Marcus G, Olgin JE, Peyser N, et al. Predictors of Incident Viral Symptoms Ascertained in the Era of Covid-19. medRxiv 2020.

4.  Lowe DA, Wu N, Rohdin-Bibby L, et al. Effects of Time-Restricted Eating on Weight Loss and Other Metabolic Parameters in Women and Men With Overweight and Obesity: The TREAT Randomized Clinical Trial. JAMA Intern Med 2020. DOI: 10.1001/jamainternmed.2020.4153.

5.  Brooks GC, Vittinghoff E, Iyer S, et al. Accuracy and Usability of a Self-Administered 6-Minute Walk Test Smartphone Application. Circ Heart Fail 2015;8(5):905-13. DOI: 10.1161/CIRCHEARTFAILURE.115.002062.

6.  Christensen MA, Bettencourt L, Kaye L, et al. Direct Measurements of Smartphone Screen-Time: Relationships with Demographics and Sleep. PLoS One 2016;11(11):e0165331. DOI: 10.1371/journal.pone.0165331.

7.  Christensen MA, Dixit S, Dewland TA, et al. Sleep characteristics that predict atrial fibrillation. Heart Rhythm 2018;15(9):1289-1295. DOI: 10.1016/j.hrthm.2018.05.008.

8.  Nguyen KT, Olgin JE, Pletcher MJ, et al. Smartphone-Based Geofencing to Ascertain Hospitalizations. Circ Cardiovasc Qual Outcomes 2017;10(3). DOI: 10.1161/CIRCOUTCOMES.116.003326.

9.  Block VJ, Bove R, Zhao C, et al. Association of Continuous Assessment of Step Count by Remote Monitoring With Disability Progression Among Adults With Multiple Sclerosis. JAMA Netw Open 2019;2(3):e190570. DOI: 10.1001/jamanetworkopen.2019.0570.

10. Block VJ, Lizee A, Crabtree-Hartman E, et al. Continuous daily assessment of multiple sclerosis disability using remote step count monitoring. J Neurol 2017;264(2):316-326. DOI: 10.1007/s00415-016-8334-6.

11. Whitman IR, Pletcher MJ, Vittinghoff E, et al. Perceptions, Information Sources, and Behavior Regarding Alcohol and Heart Health. Am J Cardiol 2015;116(4):642-6. DOI: 10.1016/j.amjcard.2015.05.029.

12. Tison GH, Avram R, Kuhar P, et al. Worldwide Effect of COVID-19 on Physical Activity: A Descriptive Study. Ann Intern Med 2020;173(9):767-770. DOI: 10.7326/M20-2665.

13. Rosenthal DG, Vittinghoff E, Tison GH, et al. Assessment of Accelerometer-Based Physical Activity During the 2017-2018 California Wildfire Seasons. JAMA Netw Open 2020;3(9):e2018116. DOI: 10.1001/jamanetworkopen.2020.18116.

14. Avram R, Olgin JE, Kuhar P, et al. A digital biomarker of diabetes from smartphone-based vascular signals. Nat Med 2020;26(10):1576-1582. DOI: 10.1038/s41591-020-1010-5.

15. Zheng Y, Sereika SM, Burke LE, et al. Temporal patterns of self-weighing behavior and weight changes assessed by consumer purchased scales in the Health eHeart Study. J Behav Med 2019;42(5):873-882. DOI: 10.1007/s10865-018-00006-z.

16. Tison GH, Sanchez JM, Ballinger B, et al. Passive Detection of Atrial Fibrillation Using a Commercially Available Smartwatch. JAMA Cardiol 2018;3(5):409-416. DOI: 10.1001/jamacardio.2018.0136.

17. Avram R, Tison GH, Aschbacher K, et al. Real-world heart rate norms in the Health eHeart study. NPJ Digit Med 2019;2:58. DOI: 10.1038/s41746-019-0134-9.