Redefining CVD Prevention and Patient Care: The New Era of Big Data, Precision Medicine, and Digital Health

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Chair, Department of Medicine

Stanford University

Acknowledgements and thanks

- Elliott Antman
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- Nigam Shah

Outline

- Historical context for “big data” and computers in cardiovascular medicine
- Contemporary evidence for cardiovascular clinical care
- Precision health and precision medicine: broad concepts
- Examples of precision health/medicine in cardiology
  - Extreme data collection (phenotype, genotype, and beyond)
  - Data mining in FH
  - Mobile technology for data collection, aggregation, analysis
  - Precision in traditional epidemiology research
  - (Very large) Pragmatic clinical trials

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"Chronic, multifactorial disease problems can be studied, but not by the methods of the present or past. If one wishes to create useful information… computer technology must be exploited."

—Eugene Stead, MD

(1908-2005)

The Doctor and the Computer

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"In summary, the Seattle project represents an implementation of an approach that illustrates how doctors and patients can gain from carefully collected and computerized clinical experience. Predictions were that many such projects would be flourishing by 1980. The time course has been slower because of the difficulty of characterizing the complexity of chronic illness rather than because of problems with computer technology. **In the future, data banks will provide a reference library for each patient with chronic disease. Proper interpretation and use of computerized data will depend as much on wise doctors as any other source of data in the past."**

ROBERT M. CALIFF, MD

ROBERT A. ROSATI, MD

Duke University Medical Center

THE WESTERN JOURNAL OF MEDICINE

October 1981

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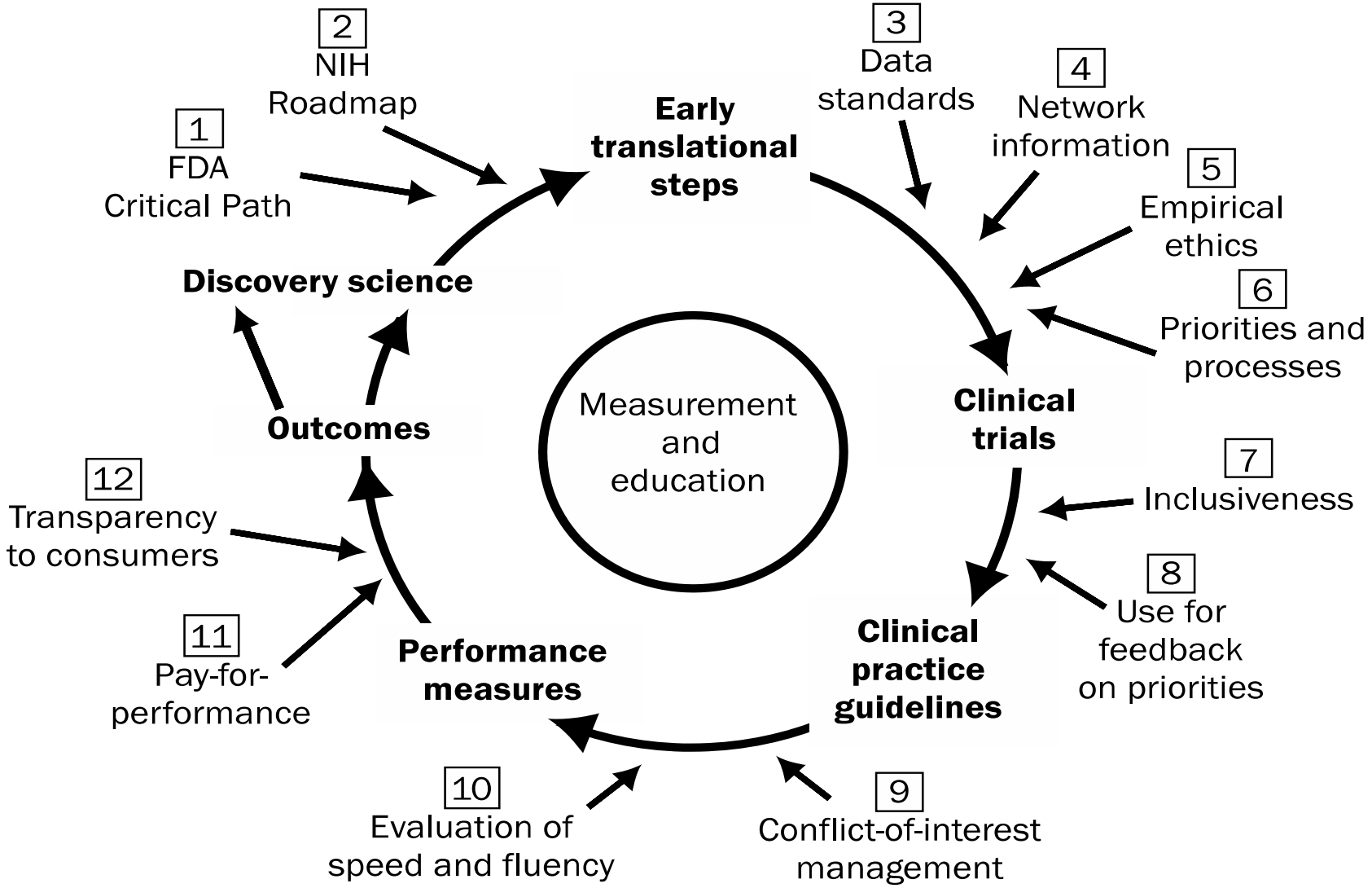
Curbing The Cardiovascular Disease Epidemic: Aligning Industry, Government, Payers, And Academics

A model for connecting scientific innovation with measurement of effectiveness and the effective delivery of proven technologies.

by Robert M. Califf, Robert A. Harrington, Leanne K. Madre, Eric D. Peterson, Deborah Roth, and Kevin A. Schulman

ABSTRACT: Despite decades of progress in the diagnosis, treatment, and prevention of cardiovascular disease, its prevalence continues to grow in both developed and developing countries. We have constructed a model, the "cycle of quality," which connects the innovation of initial scientific discovery with validated methods of translating research into effective delivery. This model can serve as a basis for evaluating proposed efforts to improve interactions among private and public aspects of health care to accelerate development and appropriate adoption of new treatments, and to achieve greater penetration of effective behavioral therapies and established technologies, resulting in major improvements in cardiovascular health. [*Health Affairs* 26, no. 1 (2007): 62–74; 10.1377/hlthaff.26.1.62]

The Cycle Of Quality: Twelve Steps



Califf et al. Health Affairs. 2007;26:62-74.

Six Medical Therapies Proven to Reduce Death in CV Disease

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Therapy	Indication	# pts	Reduction in deaths Relative	Absolute	C/E
Aspirin	MI	18,773	23%	2.4%	+++++
Fibrinolytics	MI	58,000	18%	1.8%	++++
Beta blocker	MI	28,970	13%	1.3%	++++
ACE inhibitor	MI	101,000	6.5%	.6%	+
Aspirin	2nd prev	54,360	15%	1.2%	+++++
Beta blocker	2nd prev	20,312	21%	2.1%	++++
Statins	2nd prev	17,617	23%	2.7%	++++
ACE inhibitor	2nd prev	9,297	17%	1.9%	++++
ACE inhibitor	CHF	7,105	23%	6.1%	+++++
Beta blocker	CHF	12,385	26%	4%	+++++
Spironolactone	CHF	1,663	30%	11%	+++++

—Adapted from Granger CB and McMurray JJV. JACC 2006;48:434.

“Datafication”

- Render virtually anything into data
- “Like other infrastructural advances it will bring fundamental changes … different mindset”
- OK to re-use data
- N = All

Mayer-Schonberger V, Cukier K, Houghton Mifflin, 2013

The “Tapestry” of Data

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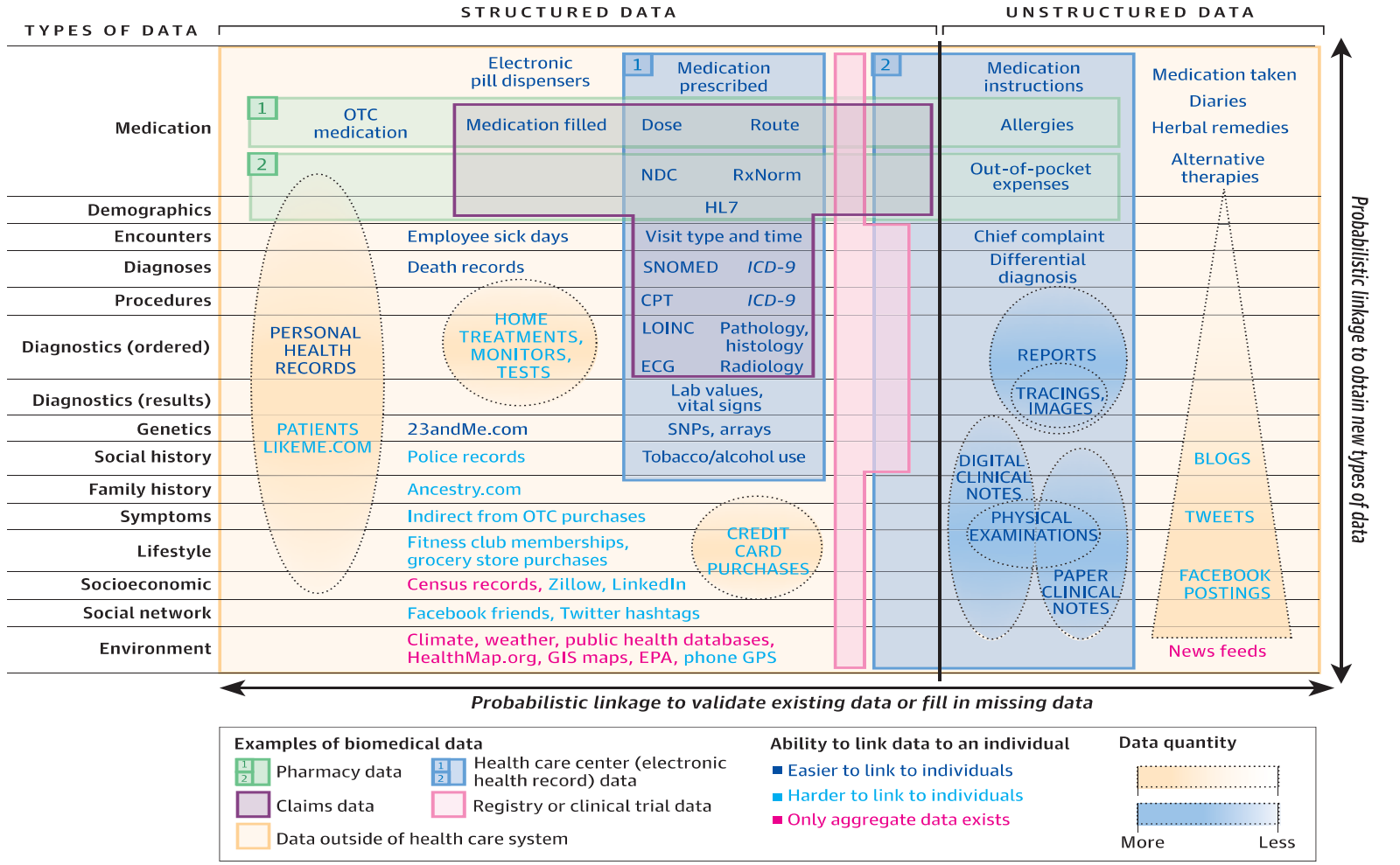
Figure. The Tapestry of Potentially High-Value Information Sources That May be Linked to an Individual for Use in Health Care



Weber GM et al. JAMA 2014;311:2479-80.

Quality of Care:
Institute of Medicine (IOM) Definition

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Timely: Rapid identification and treatment

Effective: with right drugs / procedures

Equitable: in all eligible pts

Safe: at right dose and / or done right

Cost-effective: avoiding over-treatment

Patient centered: But considering the risks and benefits for the individual patient

Moving Towards Precision Health

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Health care today		Precision Health tomorrow
after-the-fact	→	predictive and preventive
one-size-fits-all	→	personalized
fragmented	→	patient-centered
uninvolved	→	participatory
low value	→	preeminent

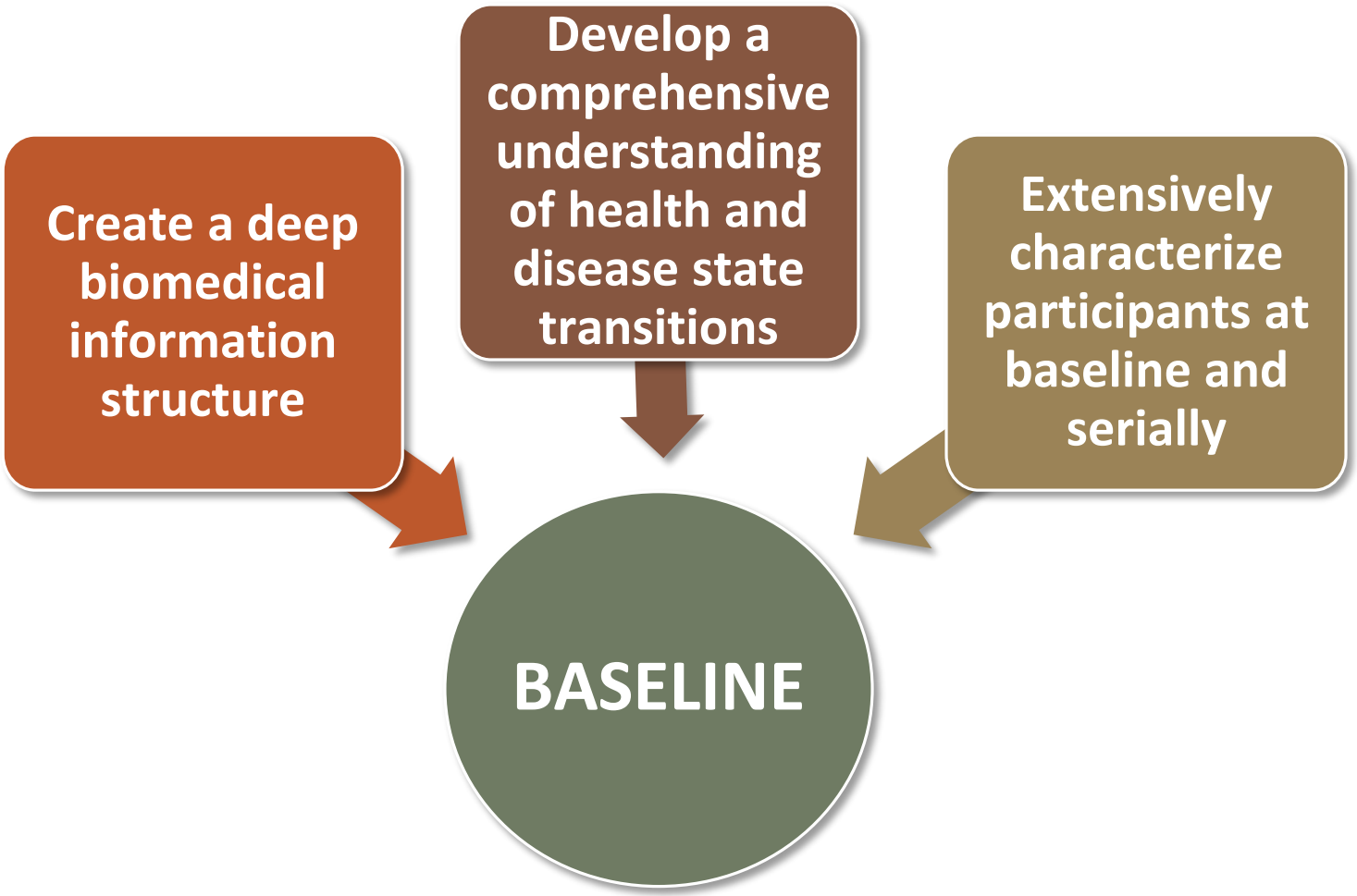
BASELINE STUDY

A COLLABORATION AMONG DUKE, STANFORD, AND GOOGLE TO DEVELOP AN INTEGRATED UNDERSTANDING OF HUMAN HEALTH

Study Goals

Baseline

Duke UNIVERSITY | Stanford MEDICINE | Google



Overall Objectives

Baseline

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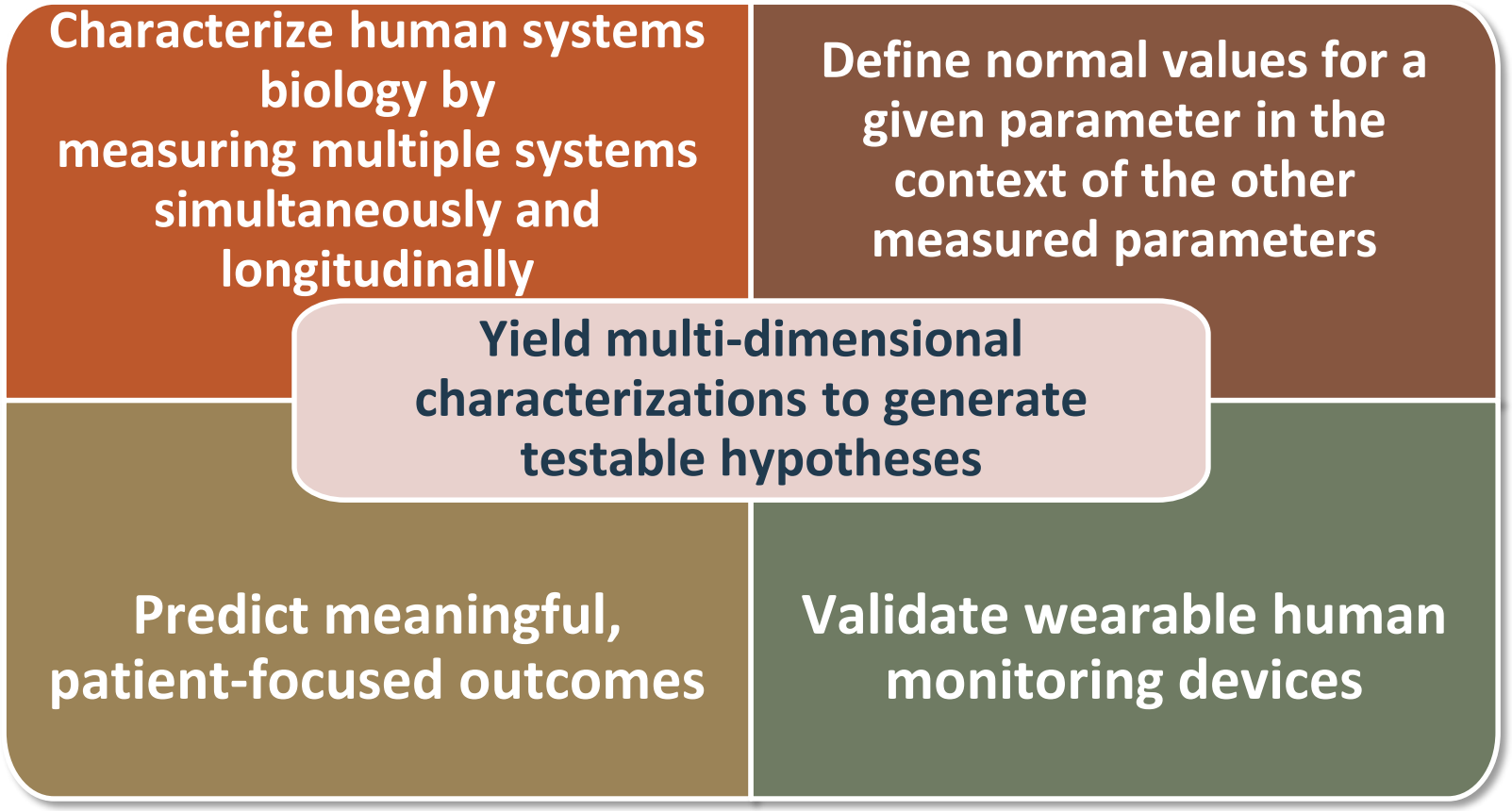


Study Cohorts

Baseline

Duke UNIVERSITY | Stanford MEDICINE | Google

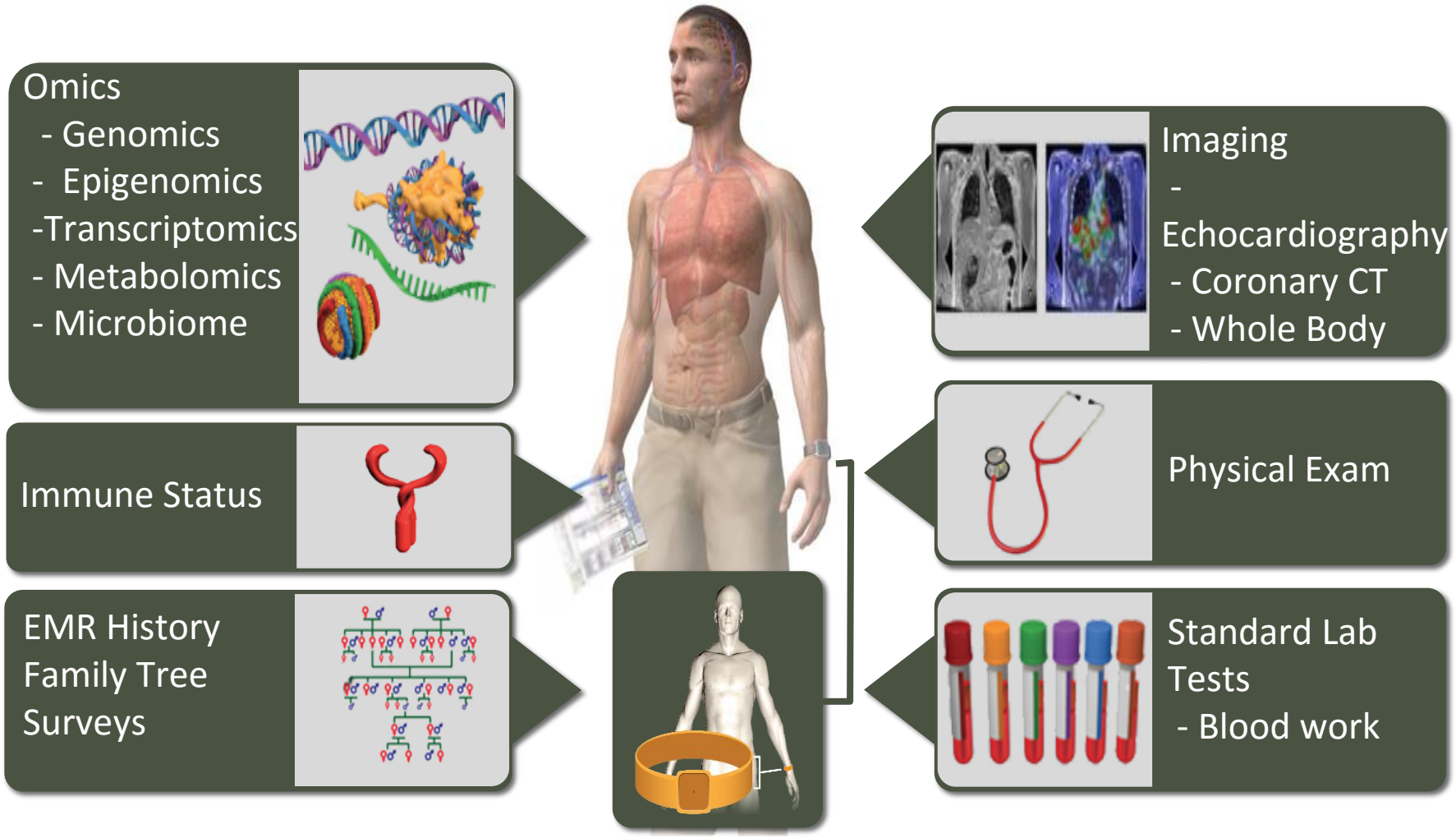
The study will enroll and characterize cancer and cardiovascular disease risk cohorts who are at specific points along the continuum of disease state and risk at inception

Cohort	Cancer	Cardiovascular Disease
Cohort 1	Low Risk	Low Risk
Cohort 2	High Risk	High Risk
Cohort 3	High Risk for Recurrence	High Risk for Recurrence

Assessments

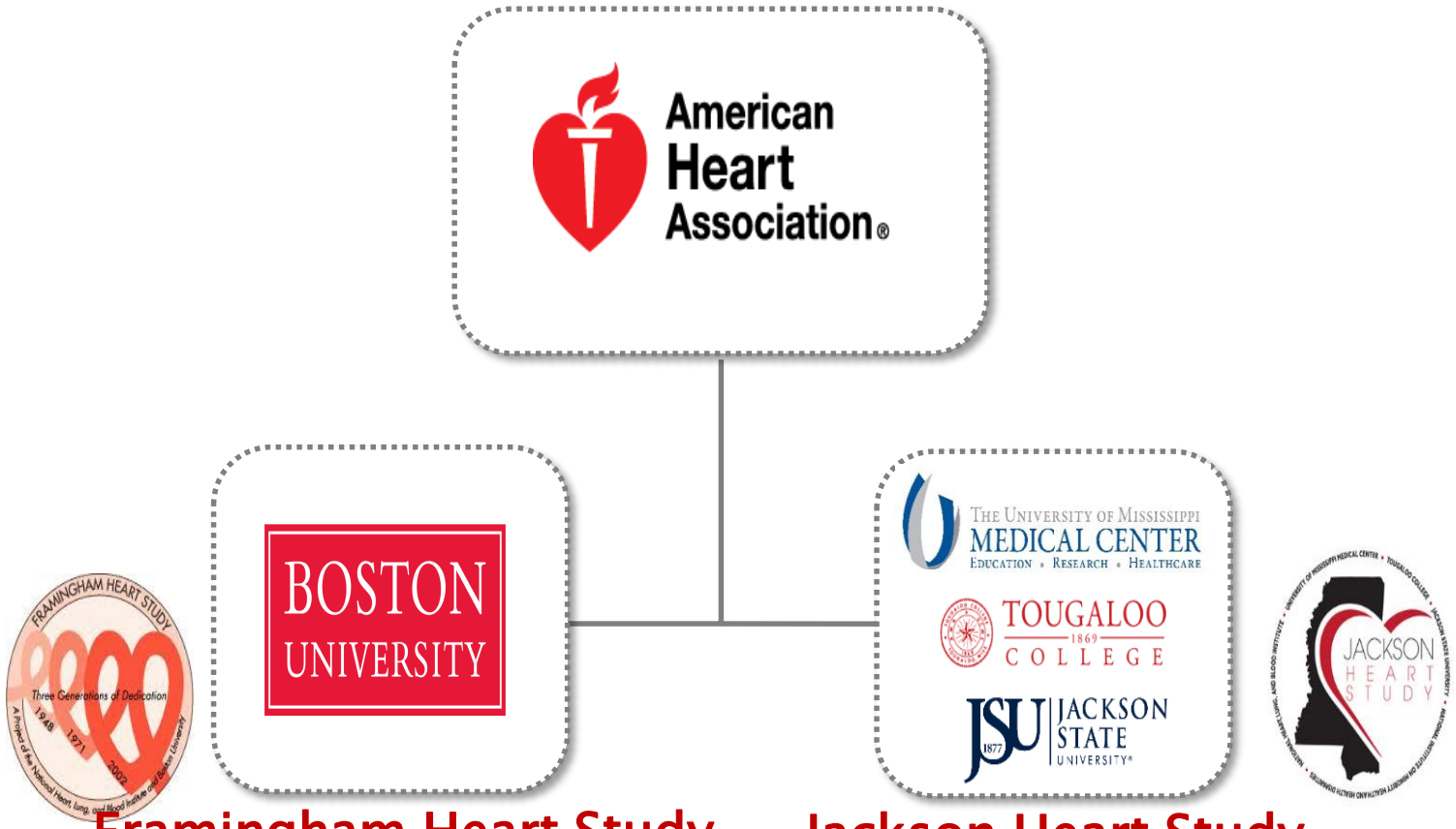
Baseline

Duke UNIVERSITY | Stanford MEDICINE | Google



CVGPS™

The Cardiovascular Genome-Phenome Study



Framingham Heart Study

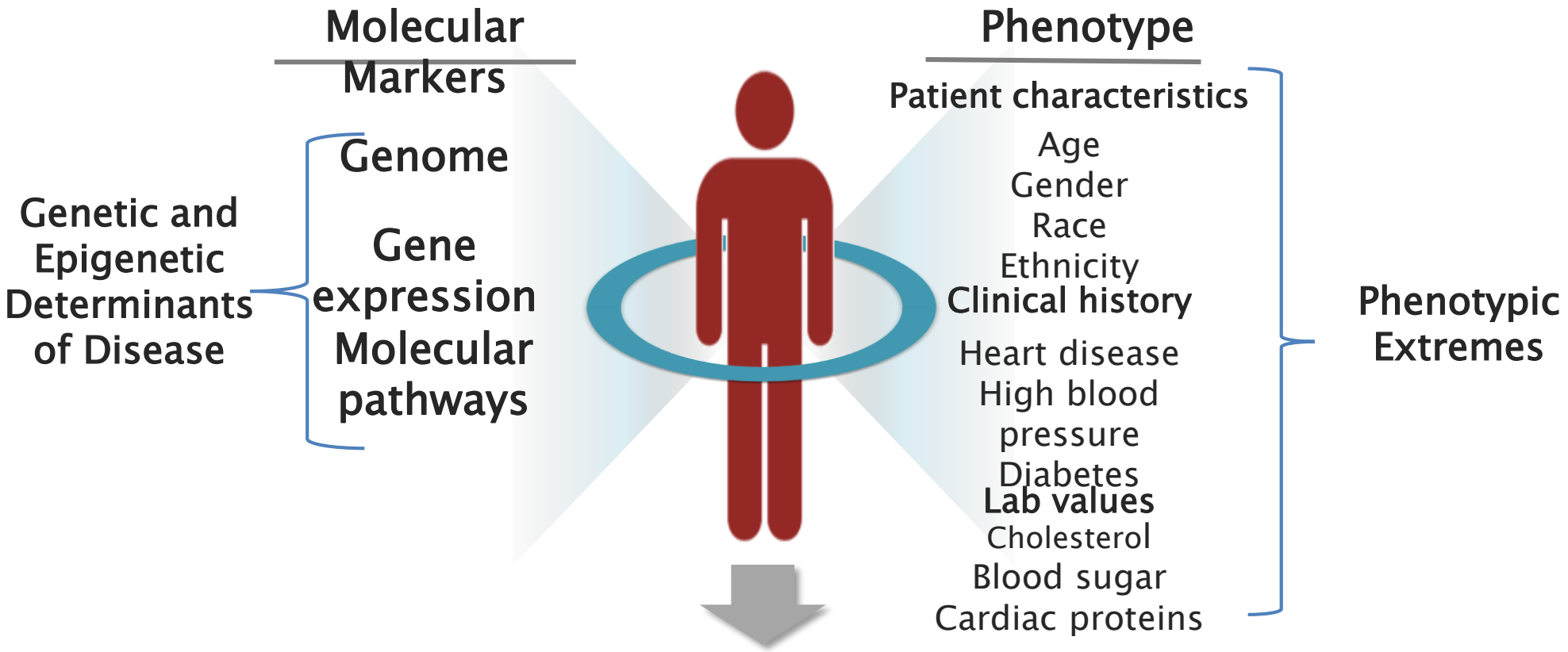
The nation's longest-running heart research program

Jackson Heart Study

The largest research effort focused on African-Americans

360 ° Look at Cardiovascular Health

CVGPS™
The Cardiovascular Genome-Phenome Study



Deeper knowledge and understanding of an individual's CV health and treatment response across ethnicities

American Heart Association. | SCIENTIFIC SESSIONS 2014

ONE BRAVE IDEA™

ABOUT · THE AWARD · SUBMISSIONS

DO YOU HAVE AN IDEA BRAVE ENOUGH TO END CORONARY HEART DISEASE?

SUBMISSIONS >

ONE TEAM. ONE VISION. ONE CURE.

The FIND FH™ Initiative

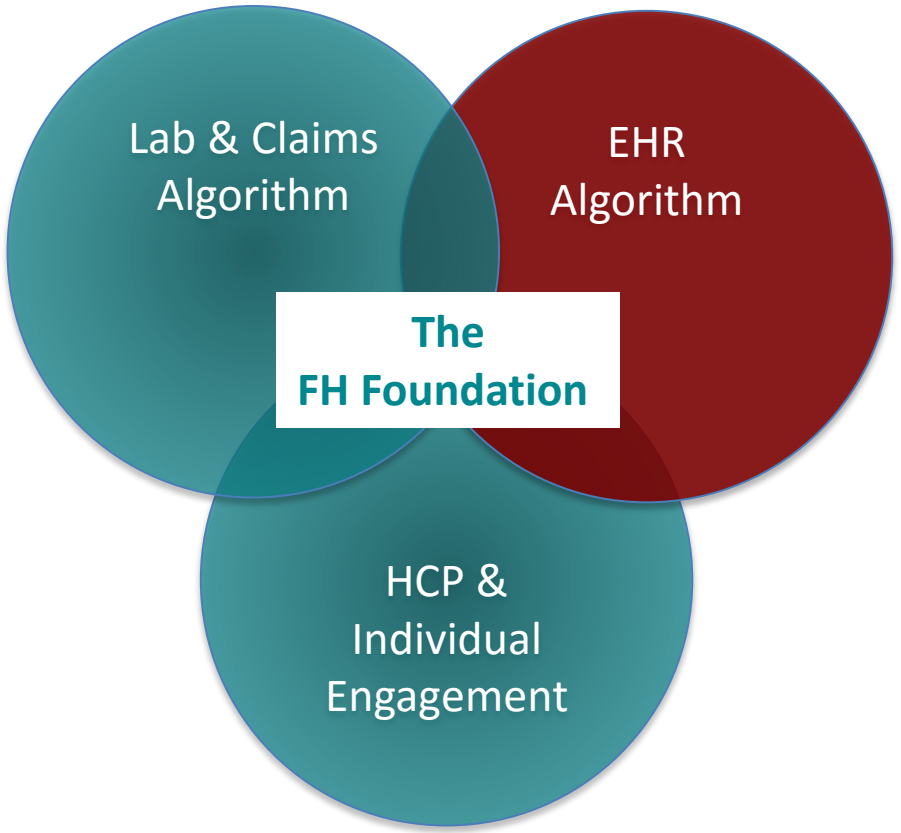
Finding Undiagnosed Familial Hypercholesterolemia Patients in the U.S.

Joshua W. Knowles, MD, PhD
Stanford University and the FH Foundation
knowlej@stanford.edu

Kelly D. Myers
The FH Foundation
KM@theFHfoundation.org

FIND FH®

A multiyear screening and engagement initiative to identify and encourage the diagnosis and treatment of FH



Lab & Claims Data Mining

- Healthcare Encounter Data on 89 Million Americans with Cardiovascular Disease
- Data from a significant majority of clinical practices

EHR Data Mining

- Comprehensive EHR data from two academic centers
- Expanding to key integrated health systems

HCP & Individual Engagement

- Multichannel tools to engage health systems and individual HCPs
- Tools for clinicians and individuals with FH

FIND FH® Lab & Claims Algorithm

- **Goal:**
  - Identify high-probability FH patients on a national scale
- **Challenges:**
  - "True Positive" FH patients are not known in national claims/lab data
    - No ICD9 code for FH
    - Family History not available in claims data
  - FH is a heterogeneous condition
- **Approach:**
  - Build a machine learning model using True Positive and True Negative patients and validate with Stanford and UPenn
  - The resulting machine learning model can predict probable FH patients from national claims/data

Health Technology

Smartphone fitness apps enable researchers to gather health data from large numbers of people.

MOBILE DATA

Made to measure

Wearable sensors and smartphones are providing a flood of information and empowering population-wide studies.

BY NEIL SAVAGE

For decades, doctors around the world have been using a simple test to measure the cardiovascular health of patients. They ask them to walk on a hard, flat surface and see how much distance they cover in six minutes. This test has been used to predict the survival rates of lung transplant candidates, to measure the progression of muscular dystrophy, and to assess overall cardiovascular fitness.

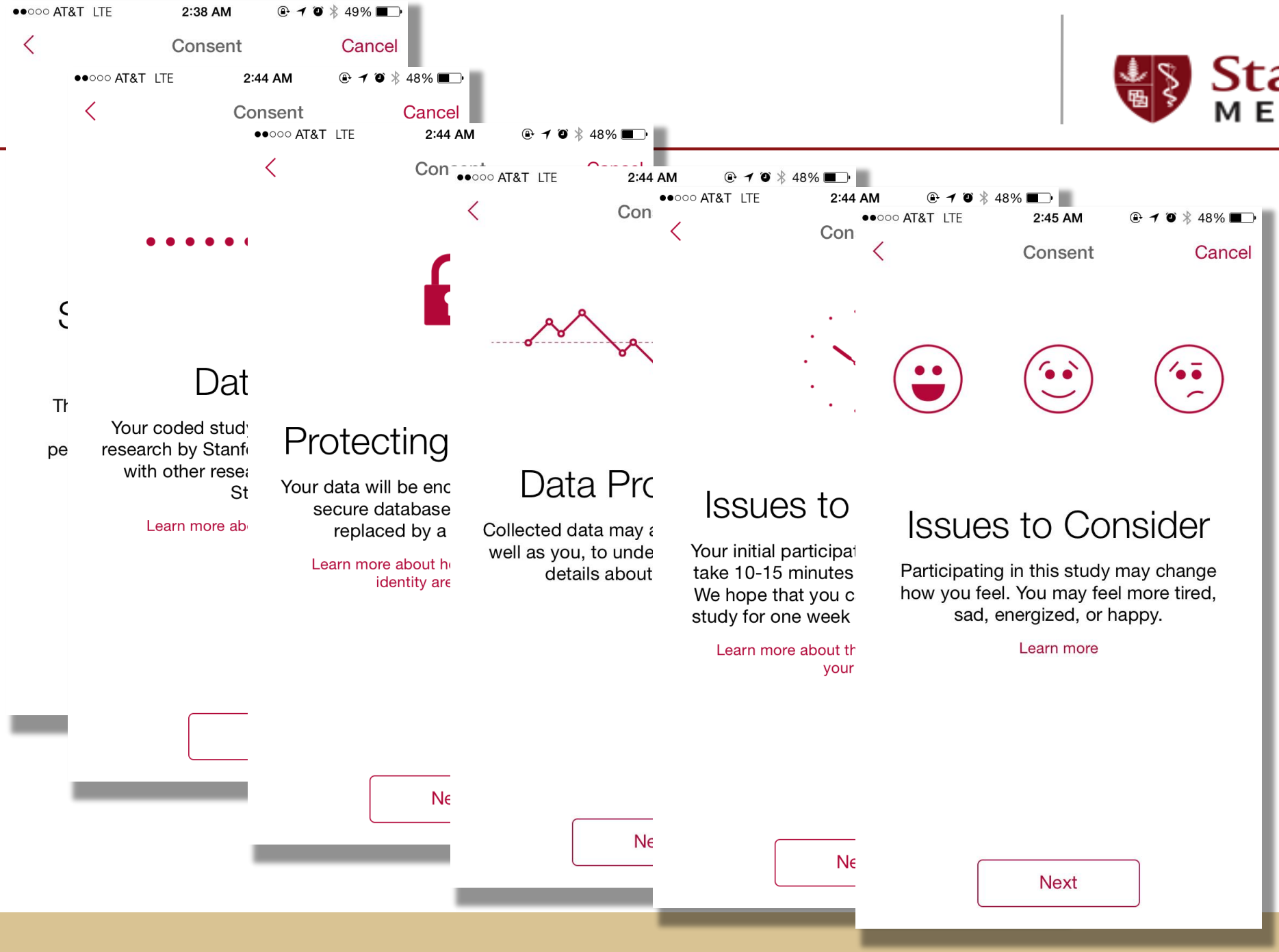
The walk test has been studied in many trials, but even the biggest rarely top a thousand participants. Yet when Euan Ashley launched a cardiovascular study in March 2015, he collected test results from 6,000 people in the first two weeks. "That's a remarkable number," says Ashley, a geneticist who heads Stanford University's Center for Inherited Cardiovascular Disease. "We're used to dealing with a few hundred patients, if we're lucky."

Numbers on that scale, he hopes, will tell him a lot more about the relationship between physical activity and heart health. The reason they can be achieved is that millions of people now have smartphones and fitness trackers with sensors that can record all sorts of physical activity. Health researchers are studying such devices to figure out what sort of data they can collect, how reliable those data are, and what they might learn when they analyse measurements of all sorts of day-to-day activities from many tens of thousands of people and apply big-data algorithms to the readings.

By July, more than 40,000 people in the United States had signed up to participate in


9:41 AM
100%
Messages
Calendar
Photos
Camera
Weather
Clock
Maps
Videos
Notes
Reminders
Stocks
Game Center
Newsstand
iTunes Store
App Store
iBooks
Health
Passbook
Settings
MyHeart
Phone
Mail
Safari
Music
9:41 AM
100%
Step 9 of 9
Done
Heart Age Results
Comparison of your actual age and your heart age.
62
Your Age
60
Your Heart Age
10-Year Risk Estimate
According to your answers, your calculated risk of developing Heart Disease or Stroke within 10 years is:
6%
Calculated Risk
7%
Optimal Risk Factors
Heart Age Summary
10-Year Risk Score: In general a 10-year risk > 7.5% is considered high and warrants discussion with your doctor. There may be other medical or family history that can increase your risk and these should be discussed with your doctor.


Cardiovascular Disease
MyHeart Counts
Stanford Medicine
University of Oxford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Protecting
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secure database
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Learn more about h
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take 10-15 minutes
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study for one week
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your
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Consent
Cancel
Issues to Consider
Participating in this study may change how you feel. You may feel more tired, sad, energized, or happy.
Learn more
Next

HEALTH & FITNESS SOFTWARE apple, ios, researchkit, healthkit, iphone

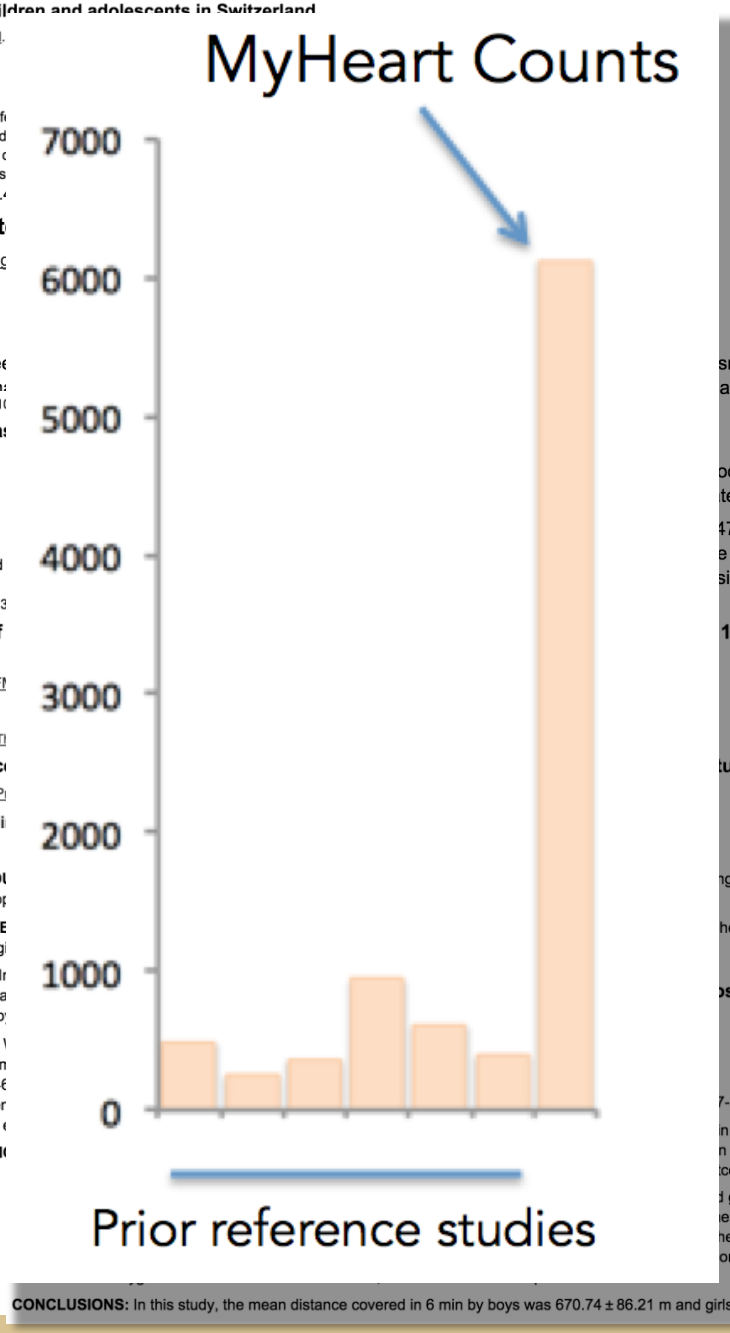
Stanford's ResearchKit app gained more users in 24 hours than most medical studies find in a year

Ian Paul | *@ianpaul*
ian@ianpaul.net, Macworld

Mar 12, 2015 7:51 AM

Apple's attempt to revolutionize medical studies appears off to a strong start. Just one day after the company released the first five apps using the new ResearchKit framework, 11,000 iPhone users signed up for one of the studies.

Stanford Researchers were amazed at the response for the MyHeart Counts app that studies heart health by measuring a user's daily activity, fitness level, and other factors. "To get 10,000 people enrolled in a medical study normally, it would take a year," Alan Yeung, medical director of Stanford Cardiovascular Health, told Bloomberg Business.



496 participants

259 participants

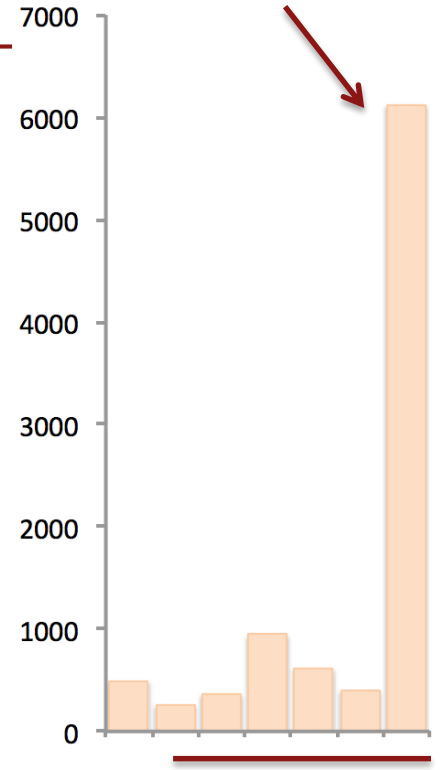
370 participants

949 participants

617 participants

400 participants

MyHeart Counts

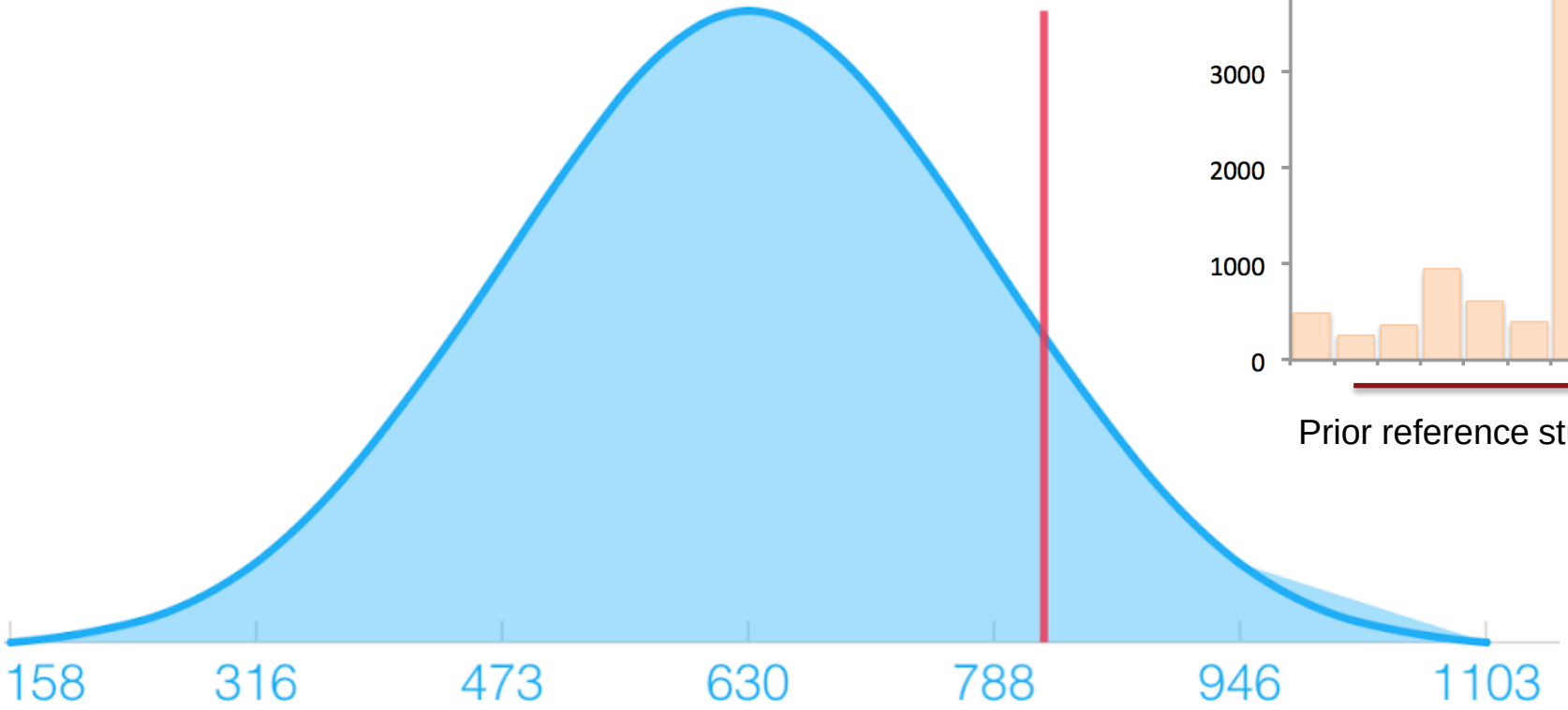


Prior reference studies

6-Minute Walk Test Comparison

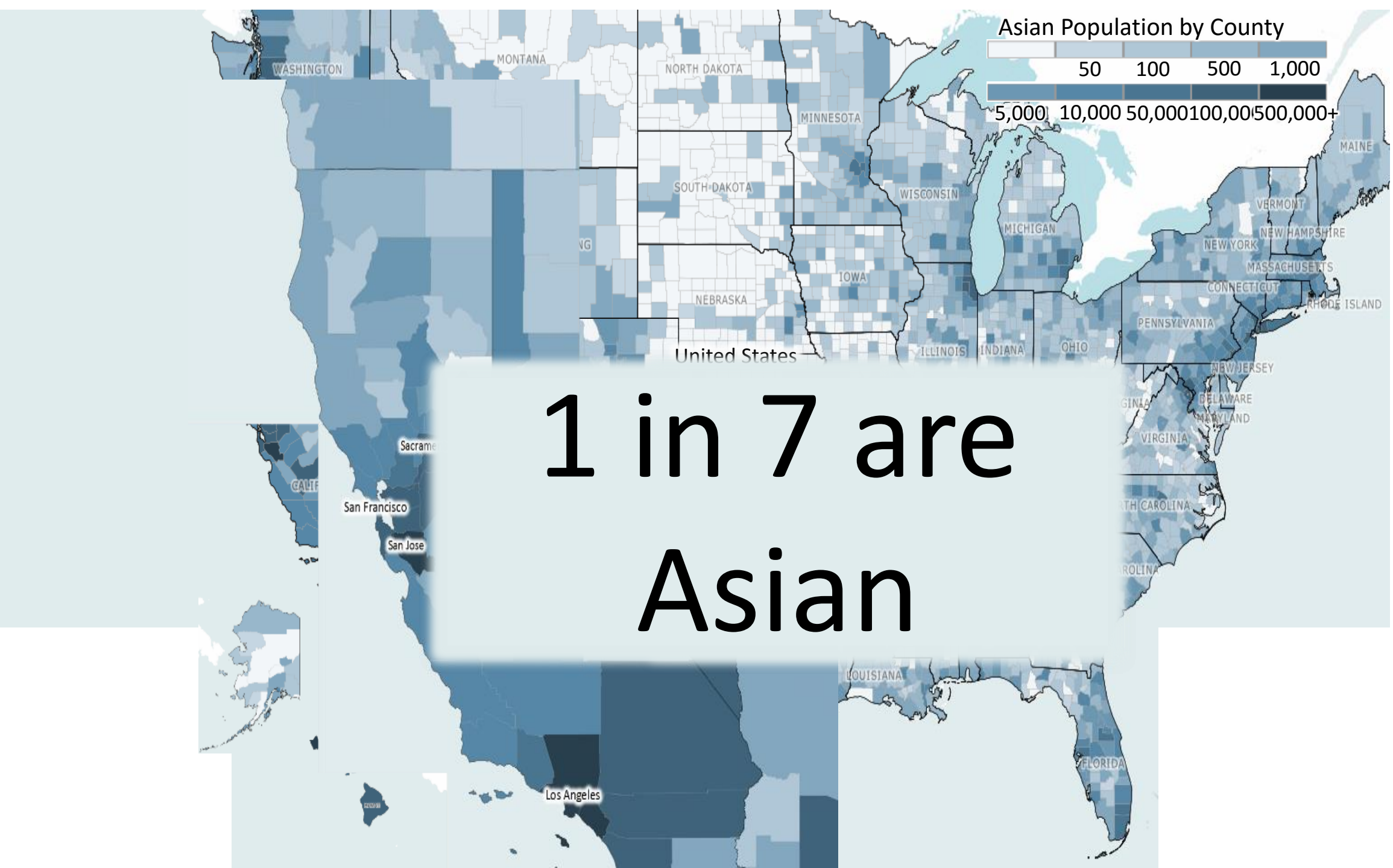
You vs Others

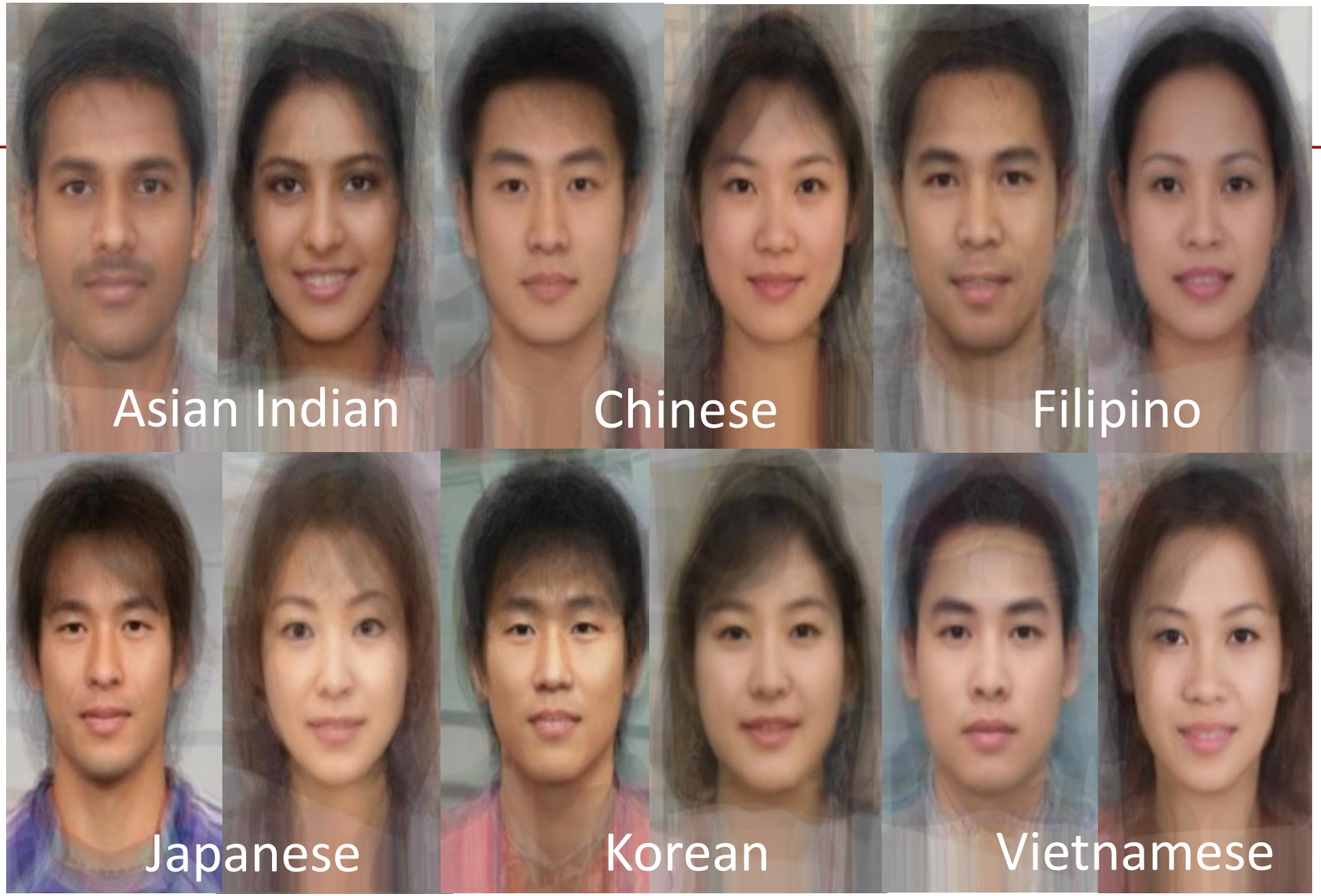
820 yards



Asian American Health – Learning from Diversity

Latha Palaniappan, MD, MS


Asian Population by County
50
100
500
1,000
5,000
10,000
50,000
100,000
500,000+
WASHINGTON
MONTANA
NORTH DAKOTA
MINNESOTA
SOUTH DAKOTA
WISCONSIN
MICHIGAN
MAINE
VERMONT
NEW HAMPSHIRE
NEW YORK
MASSACHUSETTS
CONNECTICUT
RHODE ISLAND
IOWA
NEBRASKA
PENNSYLVANIA
ILLINOIS
INDIANA
OHIO
NEW JERSEY
DELAWARE
MARYLAND
VIRGINIA
San Francisco
San Jose
Los Angeles
LOUISIANA
FLORIDA
1 in 7 are
Asian



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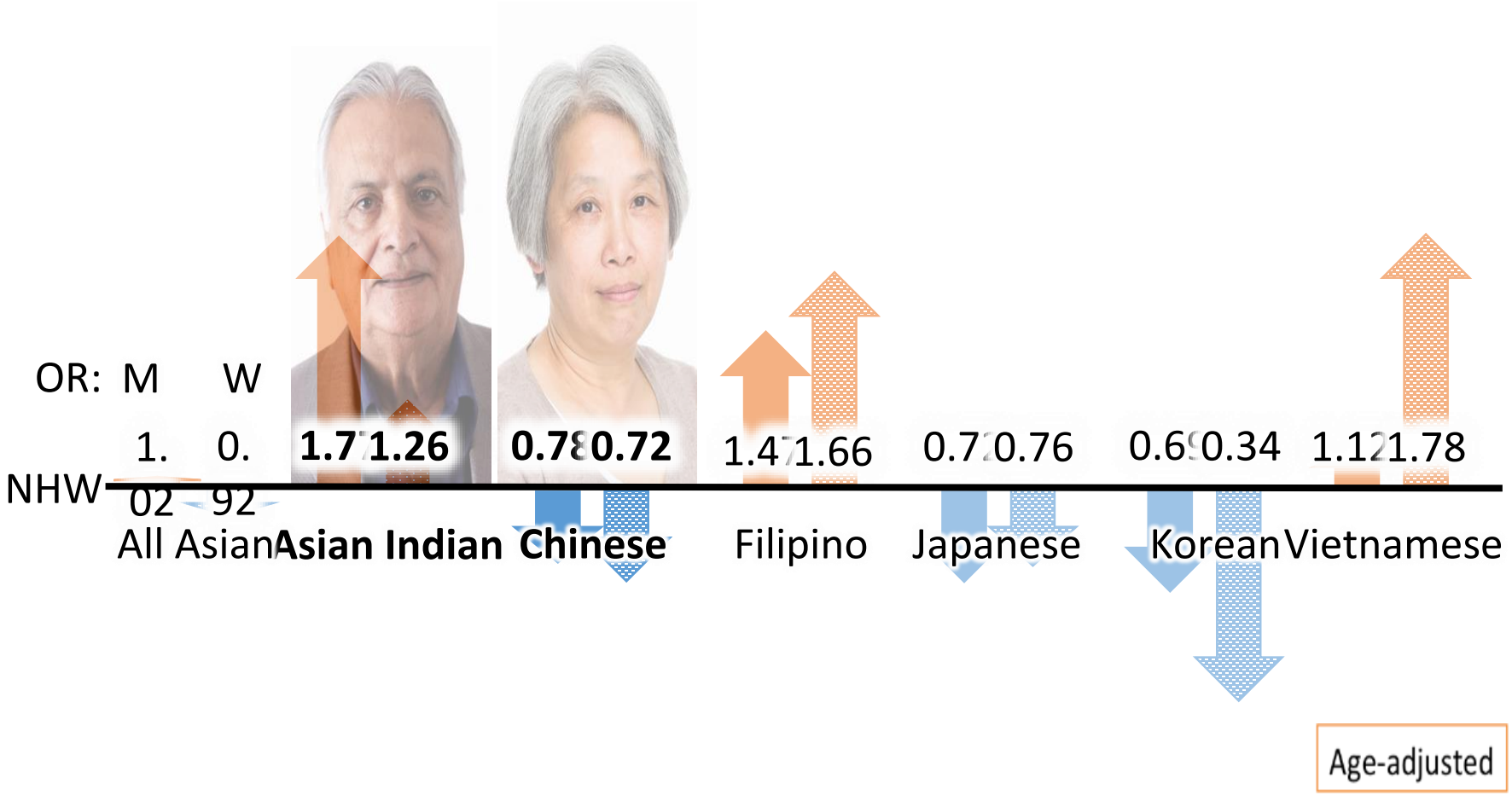
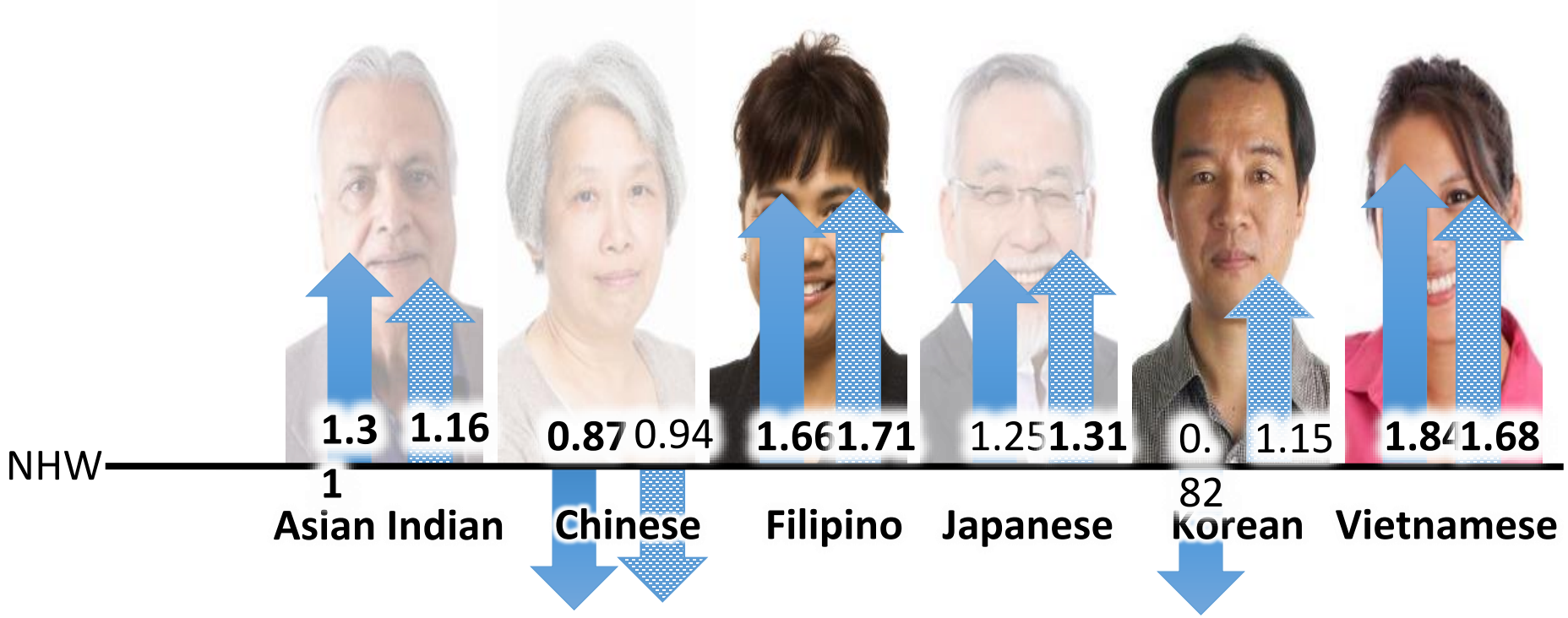
Coronary Artery Disease, Disaggregated Asians:



Holland AT, Wong EC, Lauderdale DS, Palaniappan LP. Annals of Epidemiology. 2011;21(8):608-14. PMID: 21737048.

High LDL-C Prevalence (OR)



Adjusted for: Age, BMI, Primary Insurance, and Smoking Status

Frank et al. Circulation. 2014;129:570-9.

SSATHI

Stanford South Asian Translational Heart Initiative

*"Discover & Deliver **Evidence-based**, **Ethnic-specific,** **Personalized, Comprehensive** Cardiac Care"*

Precision Medicine Approach to South Asian Heart Health:

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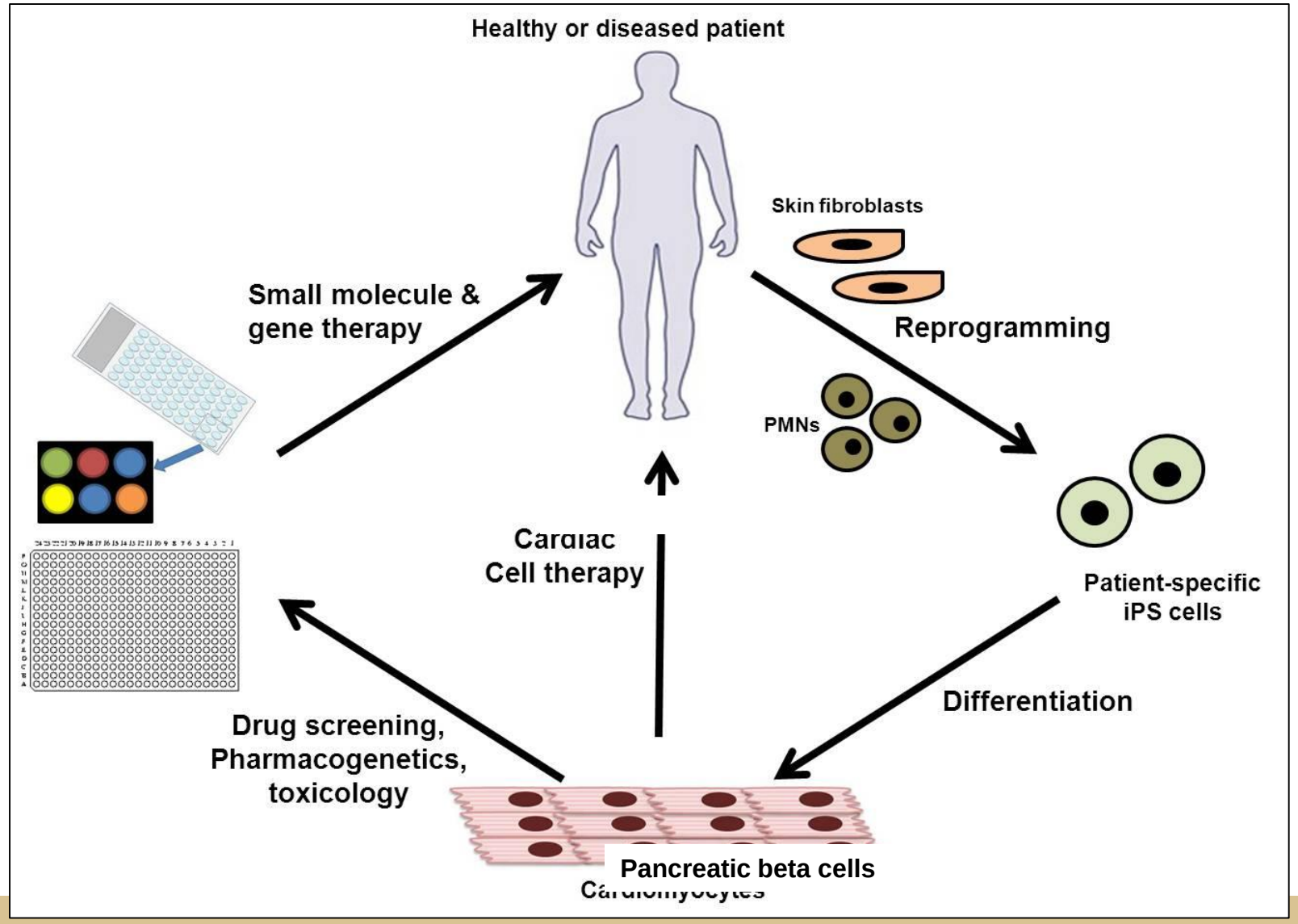
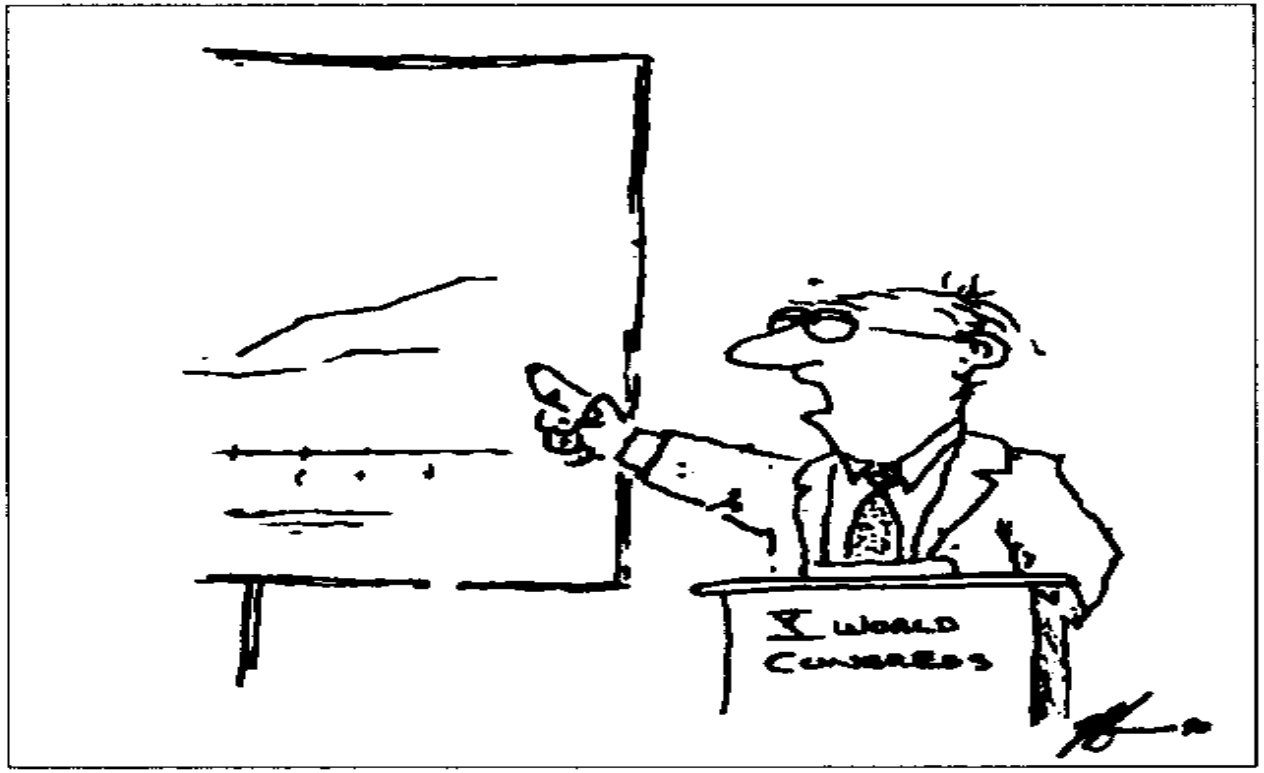
- 3 visit, 6 month program
- **Precisely Define** - Personal Cardiovascular Risk:

TRADITIONAL:	**Lipids, HTN, DM, Obesity, Tobacco, Family History**
NON-TRADITIONAL:	**Inflammation, Pre-Diabetes, Insulin Resistance, Body Composition**

- **Aggressively Reduce Each Individual's Personalized Risk Profile:**
  - **Lifestyle Goals**
  - **Dietary Goals**
  - **Early Follow-up for Goal Re-Assessment and Re-Focusing**

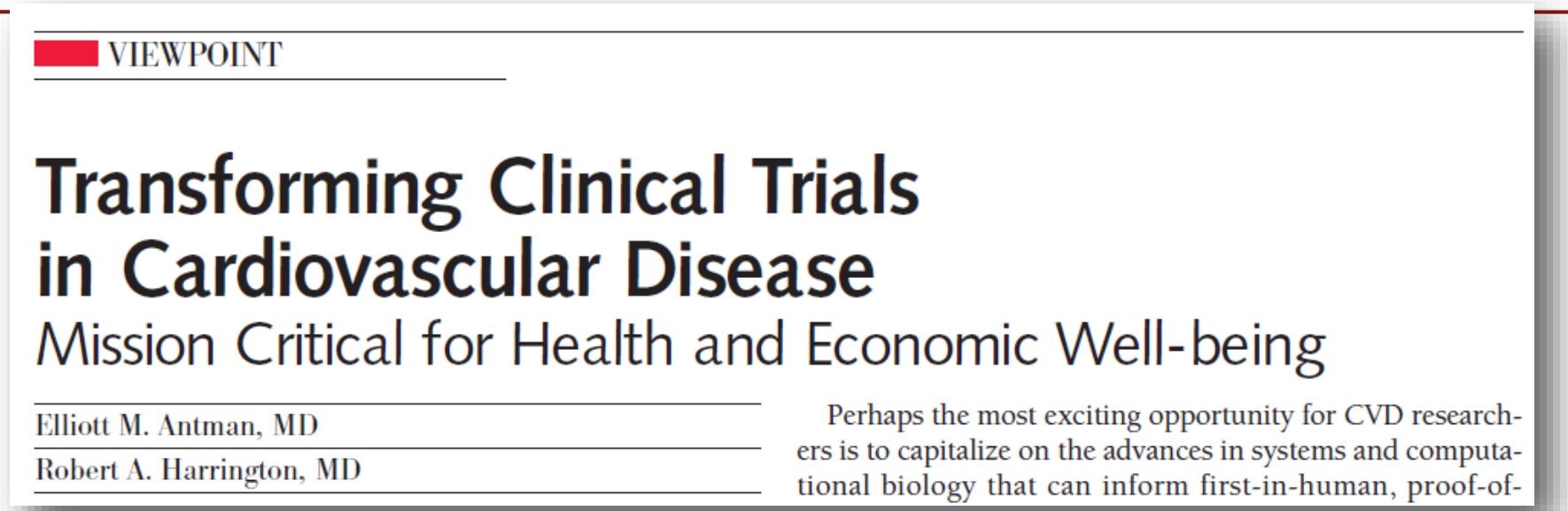
iPSC Modeling of Insulin Hyposecretion





"This randomized, double-blind trial involving over 20,000 patients was conducted over a 10 year period. Unfortunately we've forgotten why."

Current State of Clinical Trials



VIEWPOINT

Transforming Clinical Trials in Cardiovascular Disease

Mission Critical for Health and Economic Well-being

Elliott M. Antman, MD
Robert A. Harrington, MD

Perhaps the most exciting opportunity for CVD research-ers is to capitalize on the advances in systems and computa-tional biology that can inform first-in-human, proof-of-

"As large trials became popular…the original simplicity was lost…leading to increasingly complex trials. The unintended consequence has been to threaten the very existence of RCTs, given the operational complexities and insuring costs. An ideal opportunity would be to embed randomization in the EMR… introducing randomization into registries sponsored by societies."

-Antman E, Harrington RA. JAMA. 2012;338:1743-4.

Selecting Revascularization Strategies in Patients with Coronary Disease

Robert A. Harrington, M.D.

The treatment of patients with coronary artery disease includes risk-factor modification (e.g., treatment of hypertension, hyperlipidemia, and diabetes) and some combination of medical therapies and coronary revascularization.[1] For patients for whom revascularization is deemed to be appropriate, a decision must be made between percutaneous coronary intervention (PCI) and coronary-artery bypass grafting (CABG). In direct comparisons, CABG has been shown to be associated with fewer repeat revascularizations than PCI. However, questions have been raised about incremental improvements in stent technologies that might narrow the outcome gap be-

N ENGL J MED 372;13 NEJM.ORG MARCH 26, 2015

The New England Journal of Medicine

ISCHEMIA Overview

International Study of Comparative Health Effectiveness with Medical and Invasive Approaches

Stanford MEDICINE

Chair - Judith Hochman, Co-Chair/PI - David Maron

Co-PIs William Boden, Bruce Ferguson, Robert Harrington, Gregg Stone, David Williams

- Patients: stable, at least moderate ischemia (core lab)
- Primary Aim: to determine whether an initial invasive strategy of cath and revascularization (PCI or CABG) + OMT is superior to a conservative strategy of OMT alone, with cath reserved for OMT failure
- Composite Primary Endpoint: CV death or MI
- Major Secondary Endpoint: angina-related QOL
- Sample Size: 8,000
- Follow-up: average ~4 years

National Heart Lung and Blood Institute

ISCHEMIA Jan 2014

What Is a Quality Clinical Trial?

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1. Relevant question being addressed
2. A protocol that is clear, practical, focused
3. Adequate number of events to answer question with confidence
4. In a general practice setting to make results generalizable
5. With proper randomization
6. With reasonable assurance that patients receive (and stay on) assigned treatment
7. With reasonably complete follow-up and ascertainment of primary outcome (and other key outcomes such as death)
8. With a plan for ongoing measurement, feedback, improvement of quality measures during trial conduct
9. With safeguards against bias in determining clinically relevant outcomes
10. With protection of rights of research patients

-Slide courtesy LG Berdan

Engaging the Public in a Truly Large Simple Randomized Clinical Trial

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CLINICAL TRIALS *HISTORY* *Clinical Trials* 2004; **1**: 122–130

The Salk Polio Vaccine Trial of 1954: risks, randomization and public involvement in research

Liza Dawson

The year 2004 marks the fiftieth anniversary of the celebrated 1954 Salk polio vaccine trial. This enormous clinical trial, involving 1.8 million children, was carried out with the co-operation and assistance of hundreds of thousands of lay volunteers, along with medical professionals and local health departments throughout the USA. While the trial was an impressive public health achievement, firmly establishing the efficacy of the killed virus vaccine and paving the way for eradication of the disease, it was not without controversy. This article recounts the story of this important early clinical trial and how the social and political conditions at the time affected its

The NEW ENGLAND JOURNAL of MEDICINE

Stanford MEDICINE

ORIGINAL ARTICLE

Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

Ole Fröbert, M.D., Ph.D., Bo Lagerqvist, M.D., Ph.D., Göran K. Olivecrona, M.D., Ph.D., Elmir Omerovic, M.D., Ph.D., Thorarinn Gudnason, M.D., Ph.D., Michael Maeng, M.D., Ph.D., Mikael Aasa, M.D., Ph.D., Oskar Angerås, M.D., Fredrik Calais, M.D., Mikael Danielewicz, M.D., David Erlinge, M.D., Ph.D., Lars Hellsten, M.D., Ulf Jensen, M.D., Ph.D., Agneta C. Johansson, M.D., Amra Kåregren, M.D., Johan Nilsson, M.D., Ph.D., Lotta Robertson, M.D., Lennart Sandhall, M.D., Iwar Sjögren, M.D., Ollie Östlund, Ph.D., Jan Harnek, M.D., Ph.D., and Stefan K. James, M.D., Ph.D.

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

Unmet Aspirations — Where To Now for Cathete
Thrombectomy?

Robert A. Byrne, M.B., B.Ch., Ph.D., and Adnan Kastrati, M.D.

Perspective

The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research?

Michael S. Lauer, M.D., and Ralph B. D'Agostino, Sr., Ph.D.

The randomized trial is one of the most powerful tools clinical researchers possess, a tool that enables them to evaluate the effectiveness of new (or established) therapies while accounting for

United States and abroad have collected vast amounts of data from patients with acute coronary syndromes, stable coronary disease, and heart failure, as well as

Aspirin Dosing:
A Patient-Centric Trial Assessing Benefits and Long-term Effectiveness (ADAPTABLE) Trial

PCORnet's First Pragmatic Clinical Trial

pcornet

The National Patient-Centered Clinical Research Network

ADAPTABLE Study Design

Patients with known coronary artery disease (MI or CAD or Revasc) + ≥1 "enrichment factor"*

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Identified through EHR with direct pt. eConsenting in clinics and hospitals (CDRNs)

Pts. contacted electronically with trial information and eConsent; Treatment assignment will be provided directly to patient

ASA 81 mg QD

ASA 325 mg QD

Electronic F/U Q 4 months; supplemented with EHR/CDM/claims data

Duration: Enrollment over 24 months; maximum f/u of 30 months

Primary Endpoint: Composite of all-cause mortality, nonfatal MI, nonfatal stroke

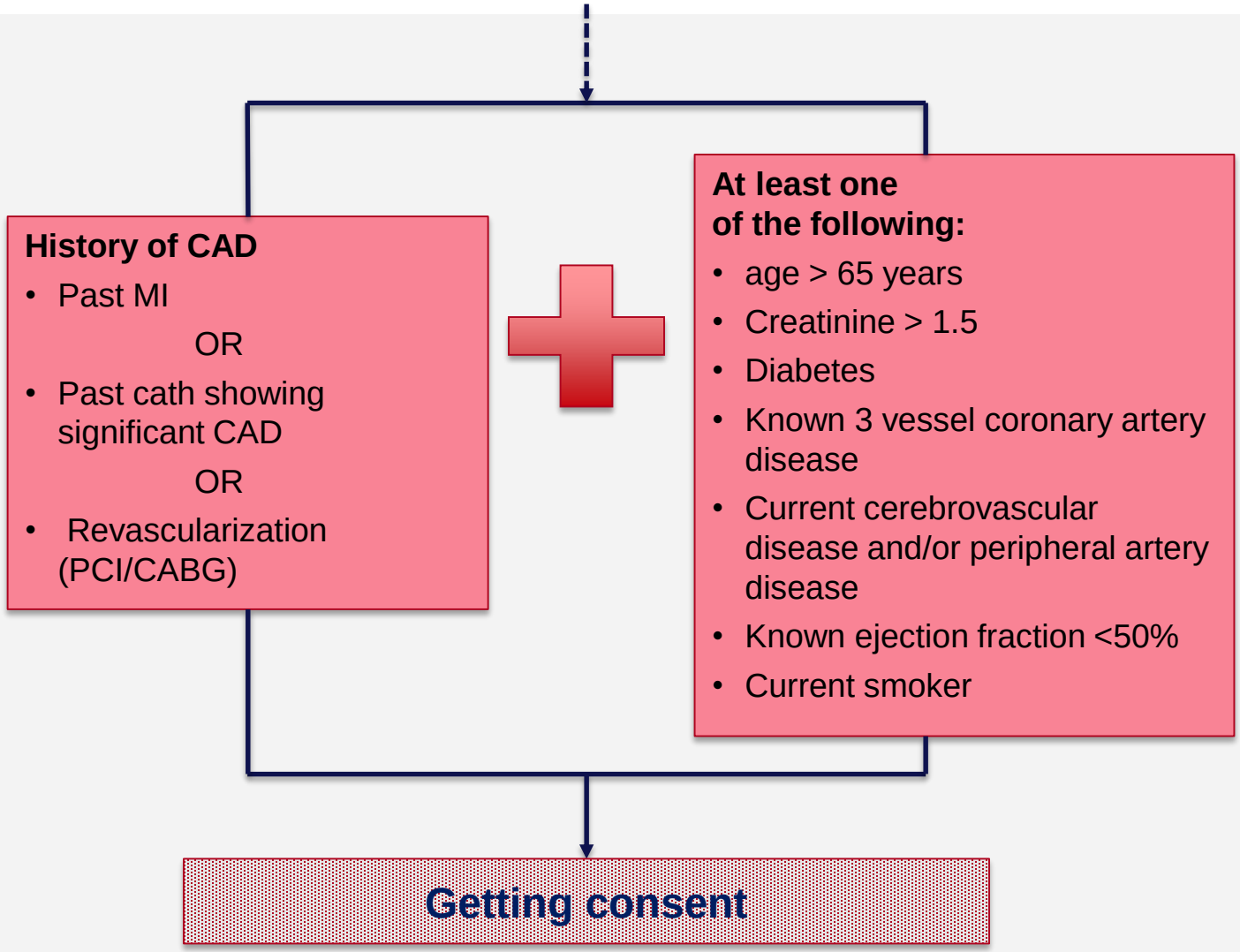
Primary Safety Endpoint: Major bleeding complications

***Enrichment factors**

- age > 65 years
- creatinine > 1.5
- diabetes
- known 3-vessel coronary artery disease
- current cerebro-vascular disease and/or peripheral artery disease,
- known ejection fraction <50%
- current smoker

Adaptable

Computable Phenotype



Endpoint Ascertainment - Centralized Follow-Up

20,000 CV Patients

R

(ASA 81mg vs. 325mg)

ADAPTABLE Enrollee

Baseline Data

Health eHeart™

OR

HeH FOLLOW-UP
- *Patient Reported Outcomes*
- *Medication use*
- *Health outcomes*

DCRI FOLLOW-UP
- *Patient Reported Outcomes*
- *Medication use*
- *Health outcomes*

4 — 8 — 12 — 16 — 20 …. 30

PCORNet Coordinating Center FOLLOW-UP
- *Via Common Data Model*
- *Longitudinal health outcomes*

CMS and private health plans FOLLOW-UP
- *Longitudinal health outcomes*

National Death Index

pcornet

"OUR STATISTICIAN WILL DROP IN AND EXPLAIN WHY YOU HAVE NOTHING TO WORRY ABOUT."

RAPID-LEARNING AGENDA

By Harlan M. Krumholz

Big Data And New Knowledge In Medicine: The Thinking, Training, And Tools Needed For A Learning Health System

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ABSTRACT **Big data in medicine—massive quantities of health care data accumulating from patients and populations and the advanced analytics that can give those data meaning—hold the prospect of becoming an engine for the knowledge generation that is necessary to address the extensive unmet information needs of patients, clinicians, administrators, researchers, and health policy makers. This article explores the ways in which big data can be harnessed to advance prediction, performance, discovery, and comparative effectiveness research to address the complexity of patients, populations, and organizations. Incorporating big data and next-generation analytics into clinical and population health research and practice will require not only new data sources but also new thinking, training, and tools. Adequately utilized, these reservoirs of data can be a practically inexhaustible source of knowledge to fuel a learning health care system.**

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American Heart Association | American Stroke Association

Clinician Innovator: A Novel Career Path in Academic Medicine

A Presidentially Commissioned Article From the American Heart Association

Maulik D. Majmudar, MD; Robert A. Harrington, MD; Nancy J. Brown, BS; Garth Graham, MD, MPH; Michael V. McConnell, MD, MSEE

The practice of medicine is transforming substantially and a pivotal driver of this change has been the accelerating pace of technology innovation. Traditional healthcare innovation has focused on the development of new diagnostics, drugs, and devices for use in hospitals and clinics, with more recent expansion to include quality-improvement and cost-containment efforts. The explosion of digital health technologies, centered around smartphones and connected devices, and enabled by advanced low-cost, miniaturized electronics, presents significant opportunities for clinicians, researchers, and healthcare administrators.[1] This is coinciding with the rapid growth of personal and population "big data"—from genome to physiome—that can help us diagnose and treat illness more effectively and efficiently, including in heart disease and stroke care. As these advances in healthcare accelerate, academic medical centers should play an active role in collaborating with industry in championing innovation, including implementation of technology-enabled healthcare solutions. More than ever before, innovators in academic medicine need to be trained and appropriately supported in their career path to meet the needs of a changing, and challenging, healthcare system.

The American Heart Association (AHA) recently convened clinicians, scientists, engineers, and entrepreneurs at the first Heart Tech Forum in Austin, Texas to inspire and increase collaboration and innovation toward AHA's 2020 goal of reducing heart disease and stroke.[2] A key component of the meeting was discussion and promotion of career development in this rapidly emerging area. Academic medicine has always been a significant contributor to innovation, with the advances in basic research providing the foundation of healthcare innovation. However, as we continue to witness unprecedented change in technology and health care, there is a need for academic medicine to promote, educate, and support trainees for a career at the convergence of basic and translational research, healthcare delivery and implementation science, and emerging digital health technologies. The growing number of digital health tools and other novel forms of technology require new training paradigms and thinking to understand their appropriate place and value in clinical practice. Additionally, young trainees and faculty are needed in this area and may require career paths that incorporate new analytical or technological tools, including connected devices, behavior change, and social media.

Cardiovascular Care and Innovation

The major advances in the diagnosis and treatment of cardiovascular disease and stroke have revolutionized how we approach the No. 1 and No. 5 causes of death in the United States, respectively. From 2001 to 2011, death rates from cardiovascular disease declined 31%, while the actual number of cardiovascular deaths per year declined by 15.5%.[3] Similarly, during the same time period, the relative rate of stroke death fell by 35.1% and the actual number of stroke deaths declined by 21.2%.[3] From 1999 to 2010, Medicare data also show significant improvements in the care of patients hospitalized with acute myocardial infarction or stroke. One-year mortality declined 23.4% for myocardial infarction and 13.1% for ischemic stroke.[4]

Despite the progress, management of chronic diseases continues to dominate the healthcare system. In 2012, roughly half of all adults had 1 or more chronic health conditions.[5] The number and financial burden of individuals with chronic conditions is likely to grow as the population ages—roughly 20% of Medicare beneficiaries account for 80% of Medicare costs. It is important to note that technology innovation has played an instrumental role in improving and

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Outline

- Historical context for “big data” and computers in cardiovascular medicine
- Contemporary evidence for cardiovascular clinical care
- Precision health and precision medicine: broad concepts
- Examples of precision health/medicine in cardiology
  - Extreme data collection (phenotype, genotype and beyond)
  - Data mining in FH
  - Mobile technology for data collection, aggregation, analysis
  - Precision in traditional epidemiology research
  - (Very large) Pragmatic clinical trials


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