Practical Approaches to Improving Diversity in Clinical Trials

Wednesdays
11AM –12noon ET

MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

LEANING IN: A WEBINAR SERIES

Disclaimer

The views and findings expressed in this document are those of the authors and do not imply endorsement or reflect the views or policies of the U.S. Food and Drug Administration or the affiliated organization or entity of any member who contributed to this work. Individuals have served in their individual capacity.

The MRCT Center is supported by voluntary contributions (www.MRCTCenter.org) and grants.


Practical Approaches to
Improving Diversity in Clinical Trials
Wednesdays
11AM –12noon ET
MULTI-REGIONAL
CLINICAL TRIALS
THE MRCT CENTER of
BRIGHAM AND WOMEN'S HOSPITAL
and HARVARD
LEANING IN: A WEBINAR SERIES
Recording available Community Awareness, Access, Knowledge
Recording available Workforce Development
Recording available Study Design, Eligibility, Site Selection & Feasibility
Recording available Study Conduct (Recruitment, Retention)
Recording available Data Standards and Analysis
Recording available Stakeholder Roles and Responsibilities
February 10, 2021 Role of Data in Diversity: Genetics & Real World Data

Today's topic

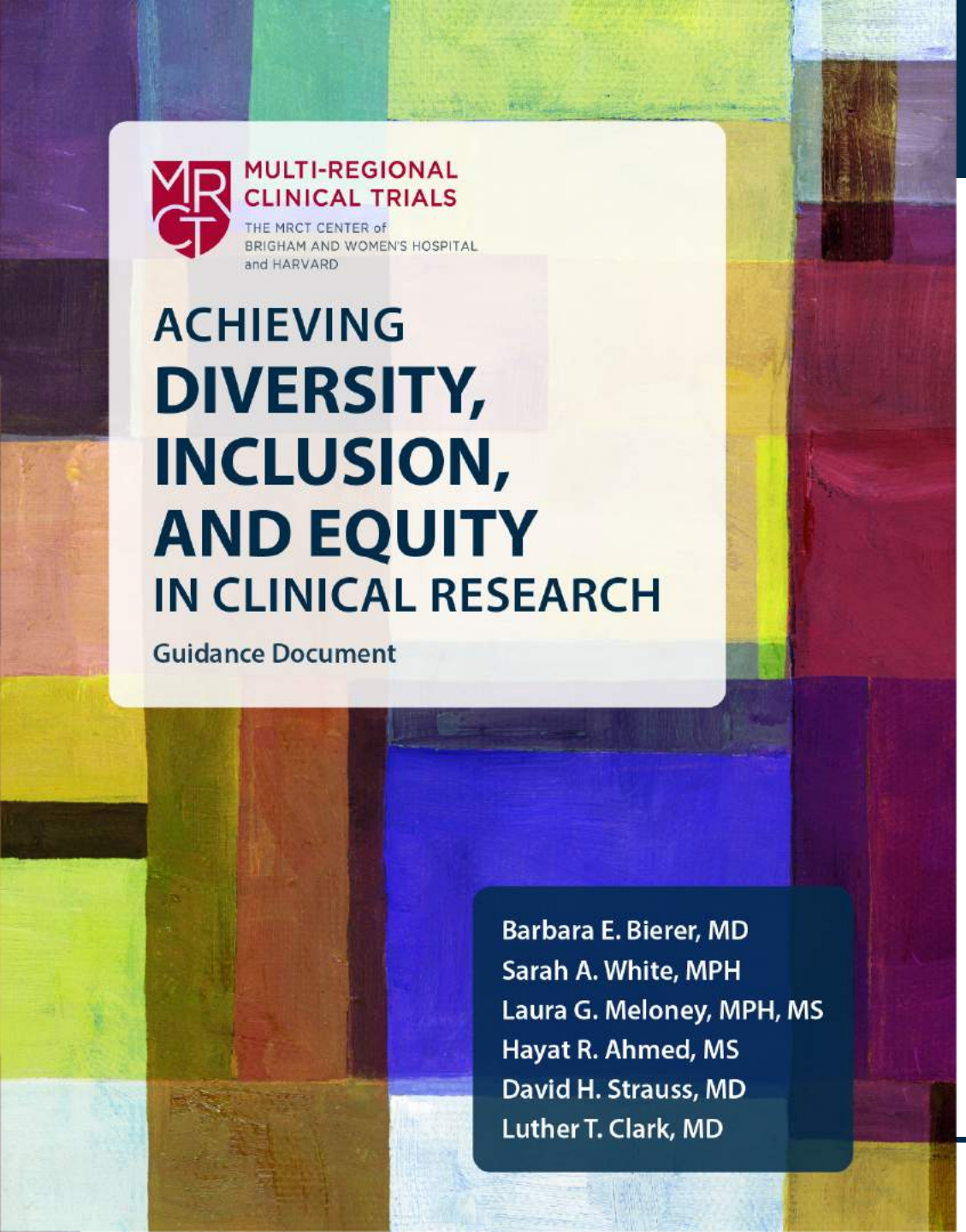
The Multi-Regional Clinical Trials Center (MRCT Center)

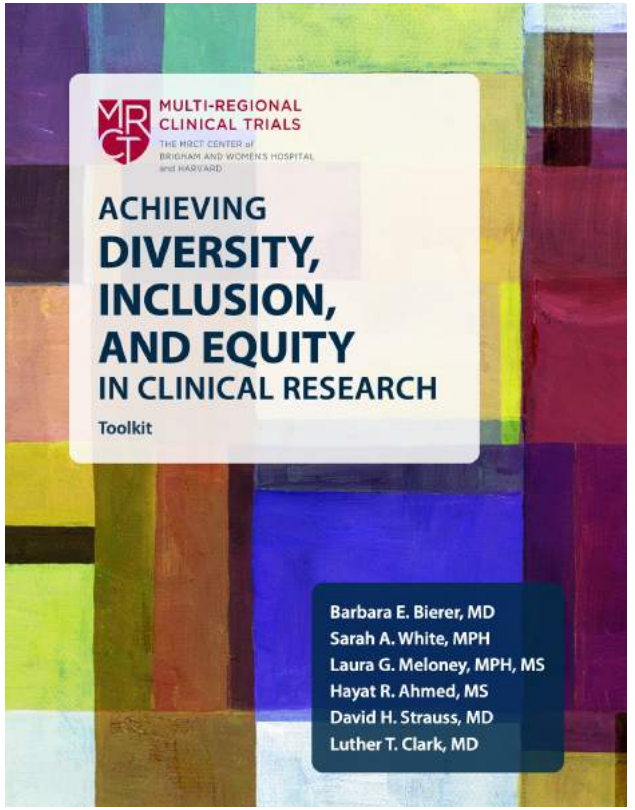
Our Vision

Improve the integrity, safety, and rigor of global clinical trials.

Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.





Achieving Diversity, Inclusion, Equity In Clinical Research

Guidance and Toolkit

mrctcenter.org/diversity-in-clinical-trials

Released 6 August 2020

Leadership

- RADM Richardae Araojo, PharmD, MS, U.S. FDA
- Barbara E. Bierer, MD, MRCT Center
- Luther T. Clark, MD, Merck & Co., Inc.
- Milena Lolic, MD, U.S. FDA
- David H. Strauss, MD, Columbia University
- Sarah White, MPH, MRCT Center

MRCT Center staff:

- Carmen Aldinger, PhD, MPH
- Hayat Ahmed, MS
- Laura Meloney, MS, MPH
- Joshua Smith-Sreen, MPH

And the invaluable contributions of >50 workgroup members, representing:

- Patients, Patient Advocates
- Academia
- Pharmaceutical companies
- CROs
- Non-profit organizations
- Trade associations
- Government agencies
- Research institutes

Each serving in their individual capacity.

Guidance Document

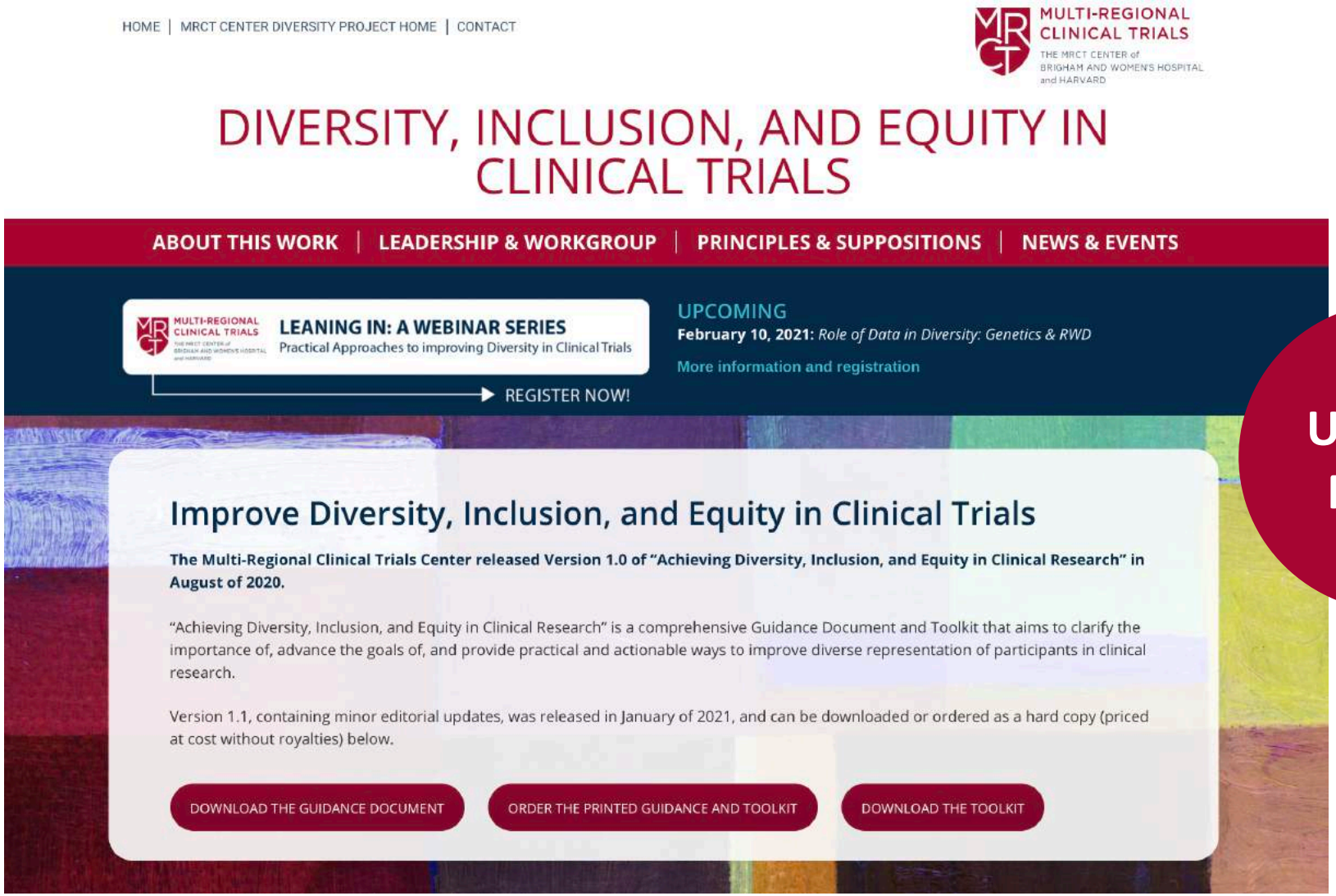
- Multi-stakeholder contributions and consensus
- Practical and actionable recommendations
- Accountability section considers how each stakeholder can change the paradigm
- Toolkit provides adaptable resources not easily found elsewhere

mrctcenter.org/diversity-in-clinical-trials

Starting in April!

STAY TUNED FOR UPCOMING WEBINAR DETAILS!

Diversity in Clinical Trials Website: mrctcenter.org/diversity-in-clinical-trials



New Updates March 2021

Join us:

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

MRCTcenter.org

MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Genetics and Clinical Research Diversity: Implications of Recent Advances in Genetics and Genomics

Luther T. Clark, MD
Deputy Chief Patient Officer
Merck

February 10, 2021

Definitions

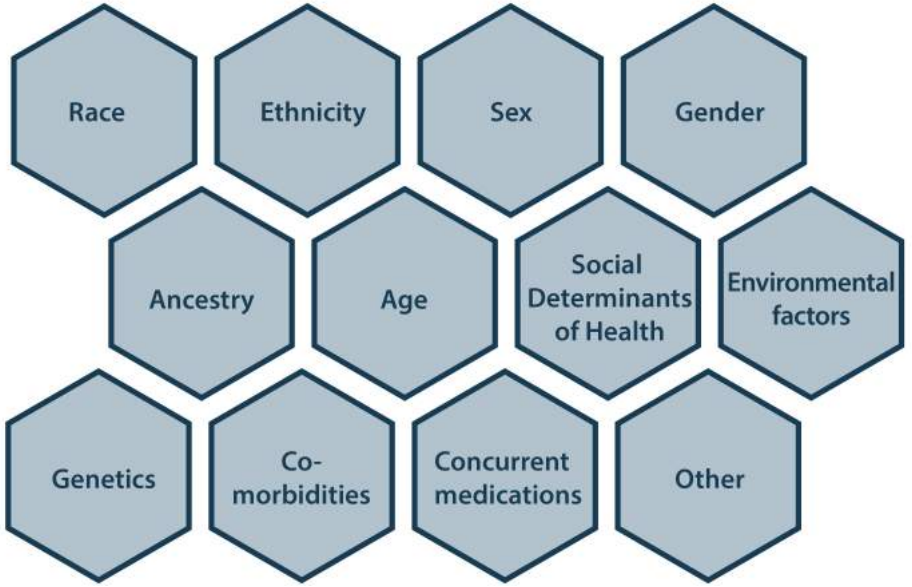
Genetics	Study of heredity; function and composition of single genes
Genomics	Study of genes, their functions, inter-relationships and related techniques
Pharmacogenomics	Study of how genes affect a person's response to particular drugs
Geographic Ancestry	Geographic locations of family origins
Genetic Ancestry	Method of quantifying ancestral background statistically by understanding genome history; different genomic segments may have their own ancestral history
Race	Sociocultural construct; not biologically distinct entities; genetically admixed populations
Precision Medicine	Identification of which approaches effective for which patients based on genetic, environmental, and lifestyle factors

Potential of Genetics & Genomic Medicine

Genetics, genomics, genomic technology

- Potential to improve health and health care by individual tailoring of prevention/treatment strategies
- Potential for wider adoption due to recent research and technological advances, and the decreasing cost of DNA sequencing

A broad definition of diversity



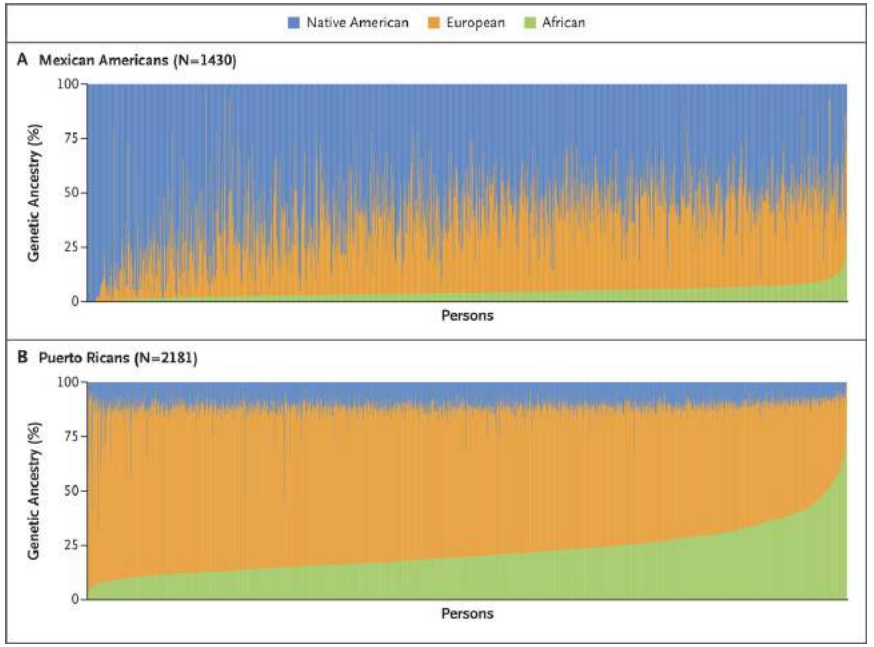
Approximately 20% of newly FDA approved molecular entities (NMEs) indicated differences in exposure and/or response across racial or ethnic groups that resulted in different prescribing recommendations for specific populations

- Ramamoorthy A, Pacanowski MA, Bull J, Zhang L. Racial/ethnic differences in drug disposition and response:eview of recently approved drugs. Clinical Pharmacology & Therapeutics. 2015 Mar;97(3):263-73.

Race, Ethnicity & Genetic Ancestry

- Self-identified race/ethnicity are crude social constructs; genetically admixed populations
- Geographical ancestry may correlate with race/ethnicity but does not predict an individual's genotype or response to drugs
- Genomics and precision medicine may advance our understanding of race, ethnicity and their utility in clinical practice and research.

Genetic Admixture in the Mexican American and Puerto Rican Populations.



LN Borrell, et al. Race and Genetic Ancestry in Medicine — A Time for Reckoning with Racism NE J Med 2021;384:474-480.

Differences in treatment response based on race, ethnicity, geographic ancestry, and genomics

CONDITION/ TREATMENT	GEOGRAPHIC/ ETHNIC ANCESTRY	SUMMARY
Clopidogrel (Anti-platelet therapy)	East Asians, Native Hawaiians	Genetic variation in expression of cytochrome (CYP) enzymes results in less efficacy of anti-platelet therapies in persons with CYP2C19*2 or CYP2C19*3 allele; frequencies of these genetic variations higher in East Asians, Native Hawaiians, other Pacific Islanders.
Carbamazepine (Treatment for Seizures)	Asians	HLA allele B*1502 marker for carbamazepine-induced Stevens–Johnson Syndrome and toxic epidermal necrolysis in Han Chinese; high frequency of this allele in many Asian populations; not found in Caucasian patients. FDA recommends genotyping Asians for the allele
NASH; NAFLD (nonalcoholic fatty liver disease)	Hispanics of Mexican, Dominican and Puerto Rican	Many Hispanics in U.S possess the PNPLA3 gene variation which has been associated with increased risk of NAFLD and NASH. Further studies needed to clarify differences in prevalence found among Hispanic subtypes living in the U.S.
Cystic Fibrosis	Northern European	Cystic fibrosis (CF) is a genetic disorder that is most common among people of Northern European ancestry; it is least common in Africans and Asians.

Differences in treatment response based on race, ethnicity, geographic ancestry, and genomics (Black, African Ancestry)

CONDITION/ TREATMENT	SUMMARY
BiDil (ISDN/Hydralazine)	Strong benefits in self-identified Blacks with heart failure; explanation unknown.
ACE Inhibitors	Individuals of African ancestry at greater risk for HBP; less responsive to ACE-I; greater risk for angioedema
PCSK9 Inhibitors	Blacks more likely to have the common PCSK9 gene variants associated with loss-of-function (LOF), lower LDL and decreased CVD risk than Whites. Identification of genetic variants and enriched polymorphisms important in discovery and development of PCSK9 inhibitors.
Sickle Cell trait and Disease	SS results from a mutation in the beta-chain gene resulting in an abnormal hemoglobin beta chain. This mutation is more common in individuals with African ancestry, it is frequently thought of as a disease that only affects those of African decent, though it is found in other ethnicities.

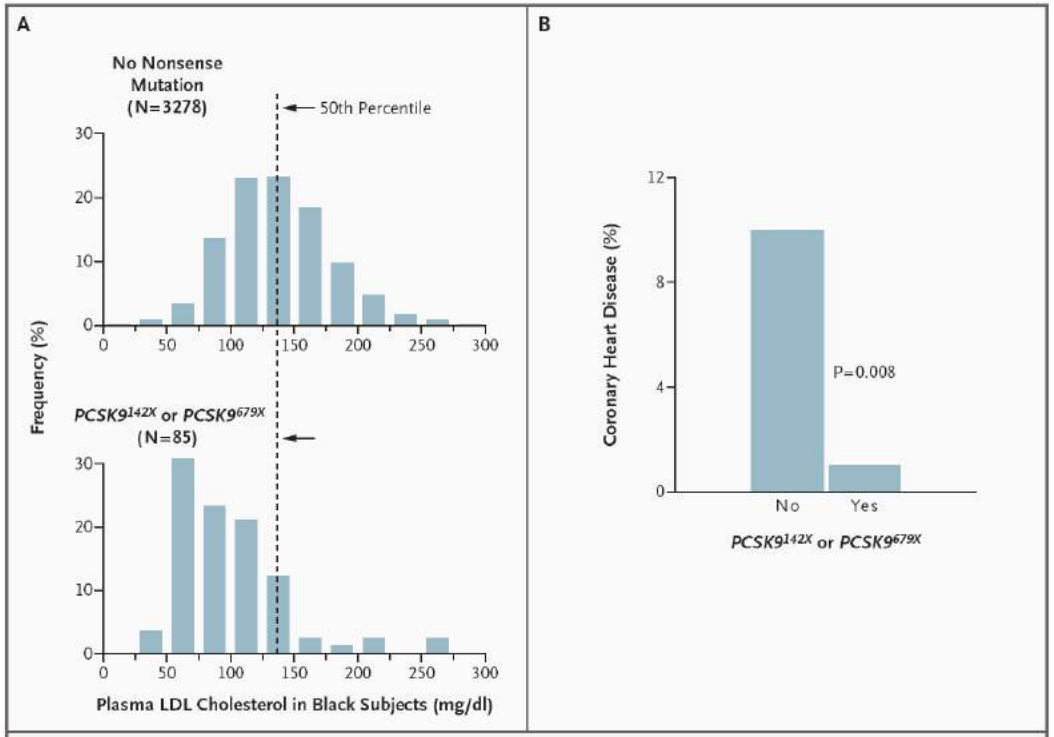


Figure 1. **Distribution of Plasma LDL Cholesterol Levels (Panel A) and Incidence of Coronary Heart Disease (Panel B) among Black Subjects, According to the Presence or Absence of a *PCSK9*^{142X} or *PCSK9*^{679X} Allele.**

In Panel A, the distribution of plasma LDL cholesterol levels at baseline among 3278 black subjects who did not have a *PCSK9*^{142X} or *PCSK9*^{679X} allele (top) is compared with the distribution of levels among the 85 black subjects who had one of these two alleles (bottom). Panel B shows the percentage of participants from these two groups who had no evidence of coronary heart disease at baseline and in whom coronary heart disease developed during the 15-year follow-up period. To convert values for LDL cholesterol to millimoles per liter, multiply by 0.02586.

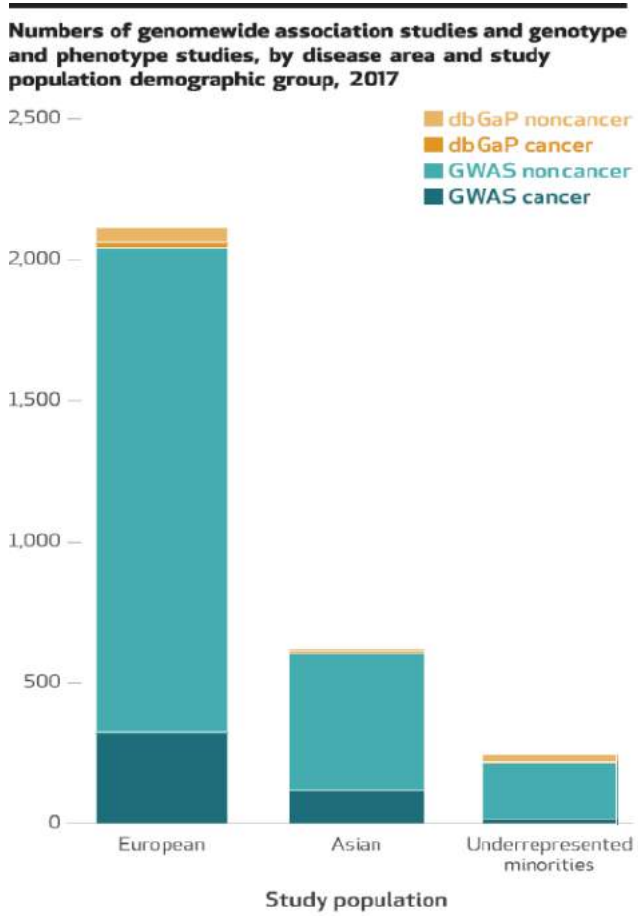
ARIC Study. Cohen *et al* 2006 NEJM

Hepatitis C: Interaction between viral genomics and host genomics

- Six major genotypes of the HCV that infect the liver that vary in prevalence (regional and ethnic/racial), disease severity, and response to treatment.
- Hepatitis C is potentially curable; treatment efficacy must be tested and demonstrated for each of the major viral genotypes – thus tested in the populations and regions where these are prevalent.
    - Genotype 1: most common in the U.S. ; more common in Blacks than others
    - Genotype 4: most prevalent in the Middle East and Africa;
    - Genotype 5: most prevalent in South Africa; and
    - Genotype 6: most prevalent in Southeast Asia

Genomics and Health Equity

- Genomics has the potential to improve health outcomes broadly but benefits may not be equitably available to all populations
- Racial and ethnic minorities underrepresented in genomic databases
- Lack of diversity in genomic research limits understanding of the relationships of genes and disease in unstudied populations
- Genomic databases need greater inclusion of diverse ancestral populations and ancestral information

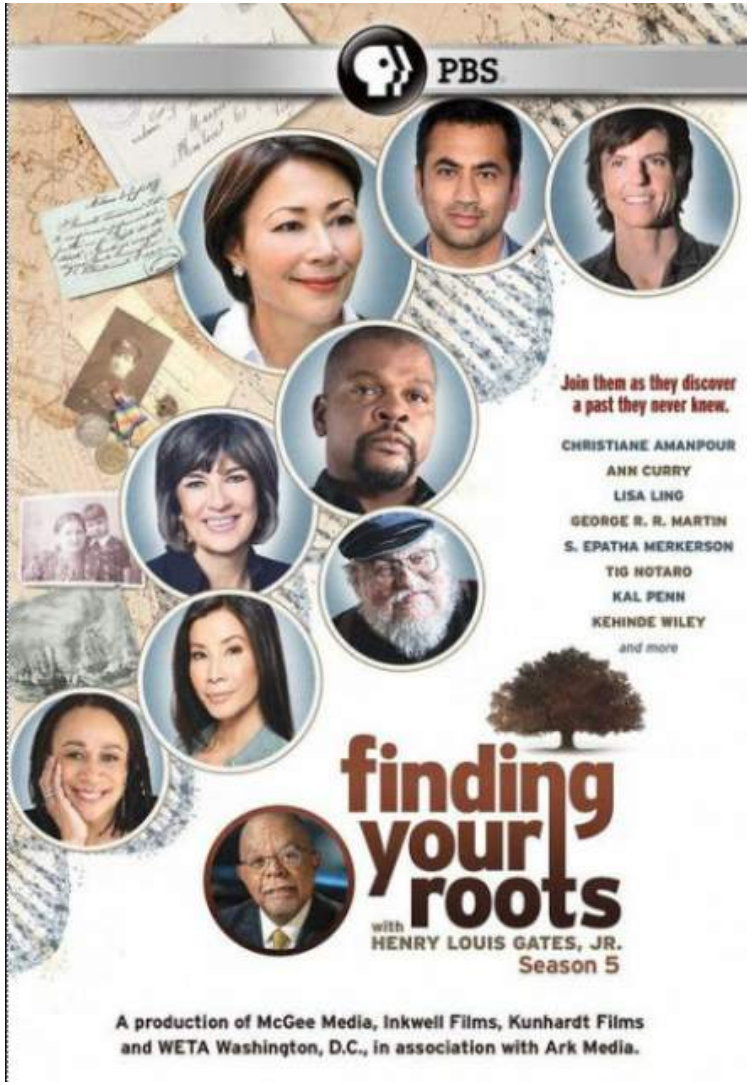


Landry LG, Ali N, Williams DR, Rehm HL, Bonham VL. Lack Of Diversity In Genomic Databases Is A Barrier To Translating Precision Medicine Research Into Practice. May 2018 37:5 Health Affairs 2018;37:5

Direct-to-Consumer Genetic Testing

23andMe MyHeritage FamilyTreeDNA

- Increasing popularity of DTC Genetic Testing
- Potential to support understanding of relationship between genetics, geography, ethnicity, interactions between biological and SDOH
- Individuals often have multiple geographic ancestries
- Genetic ancestries may be different from what individuals believe and how they self-identify



Key Takeaways

- The prevalence of genetic variants that impact disease can vary across populations.
- Increased diversity and inclusion of research participants in genomic and genetic research is necessary if the promises of genetic and genomic research are to benefit all
- Greater representation of underrepresented individuals and those from geographically-diverse populations will increase knowledge of genomic variants in population subgroups, geographic ancestry and the genetic and biological mechanisms linking SDOH to health and disease
- At present, self-identified race continues to have utility
  - correlates with geographic ancestry, a determinant of genomic variation (that can influence responses to drugs)
  - a proxy for other difficult to measure factors, i.e. SDOH (environment, health behaviors, effects of chronic bias, comorbidities, treatment seeking behavior and disease at presentation) that may impact treatment responses

Today's speaker

Latha Palaniappan, MD, MS,
Professor of Medicine
Stanford University School of Medicine

Role of Data in Diversity

Examples with Real World Data

Latha Palaniappan MD, MS

Professor of Medicine

Stanford University School of Medicine

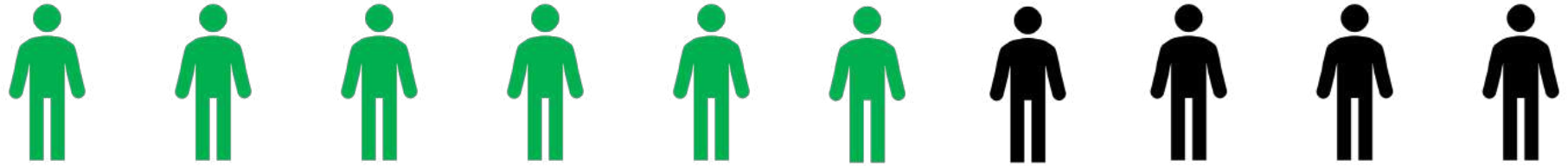
MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Stanford MEDICINE

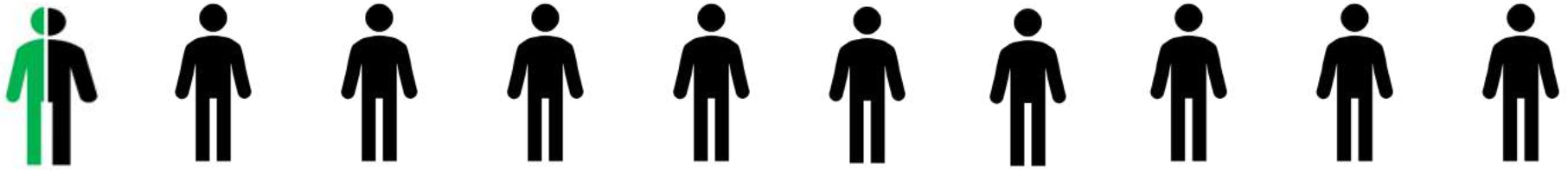
Role of Data in Diversity

- Real World Data for Diversity Research:
  - National Datasets
    - National Health Interview Survey (NHIS)
    - National Health and Nutrition Examination Survey (NHANES)
  - Electronic Health Records (EHR)
  - Mortality Data
- Clinical Implications
  - Culturally Competent Intervention Studies
  - Pharmacogenetic Differences
- Community Impact (CARE)

Stanford MEDICINE



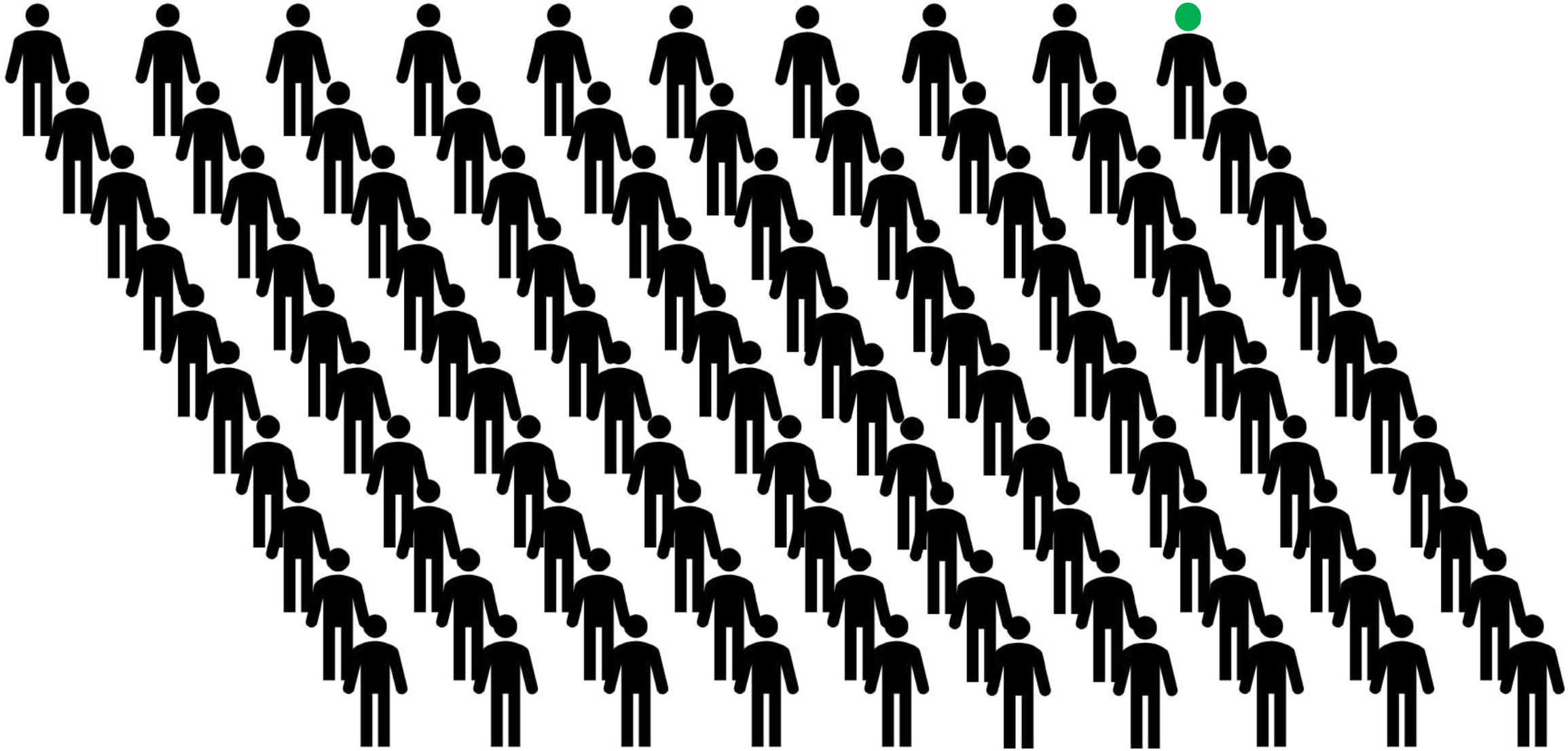
60% of the Globe



6% of the U.S.

30% of the Bay Area

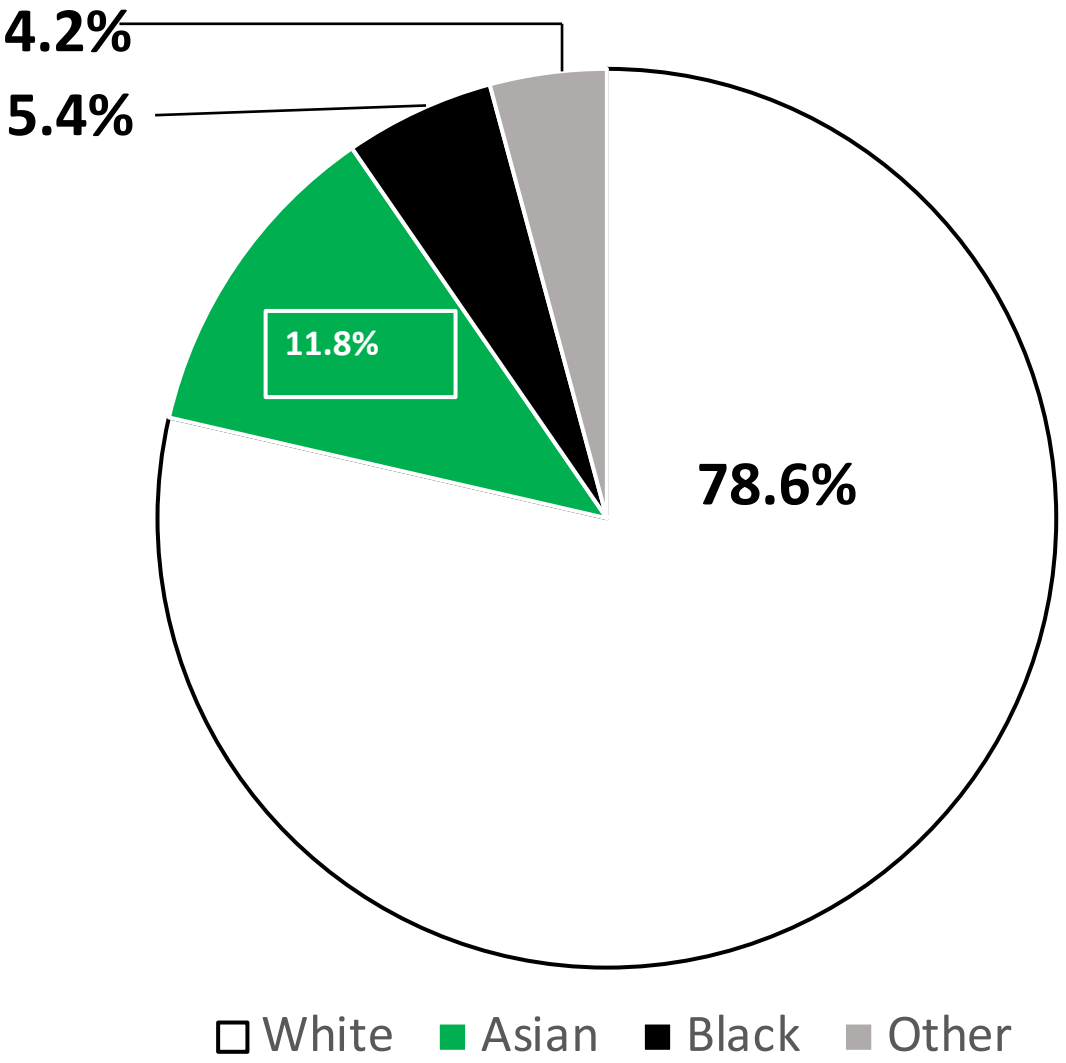
< 1% of NIH Funding



Decisions around Asian health are made using mainly non-Asian data.

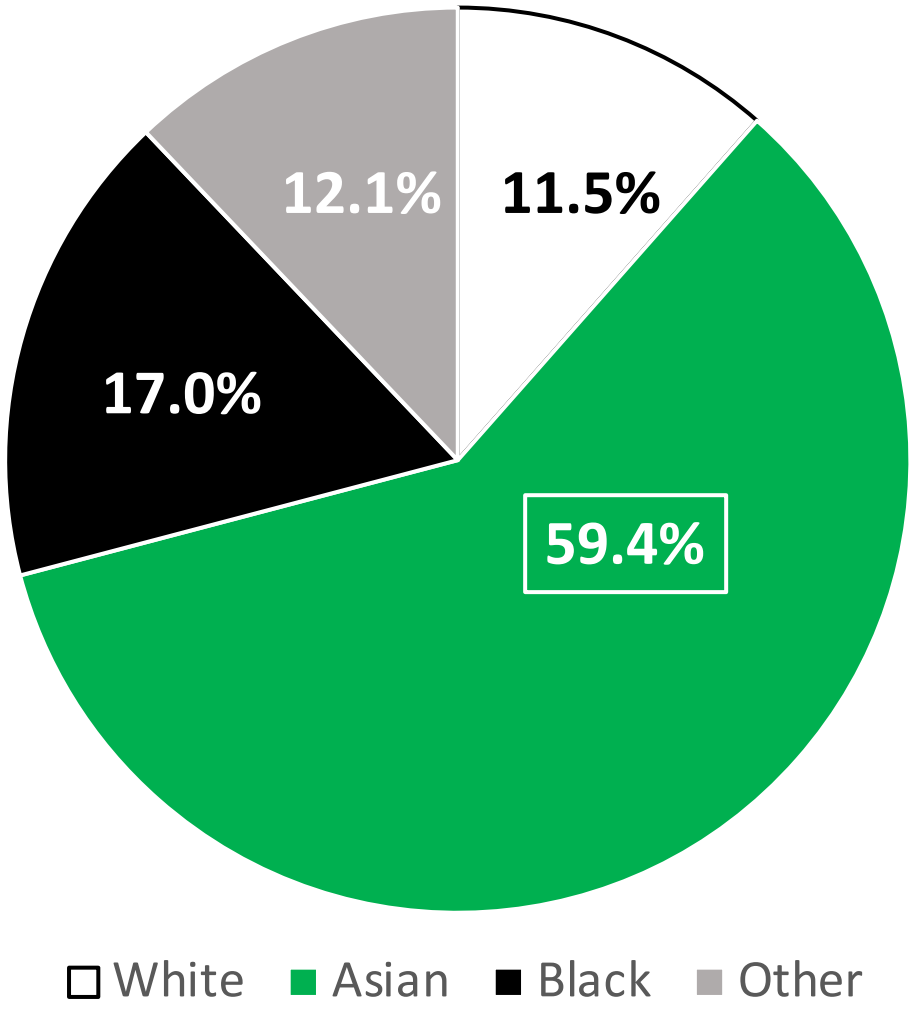
Global Racial Participation in Clinical Trials

Total Participants = 131,749



Global Population

Total Population = 7.8 billion

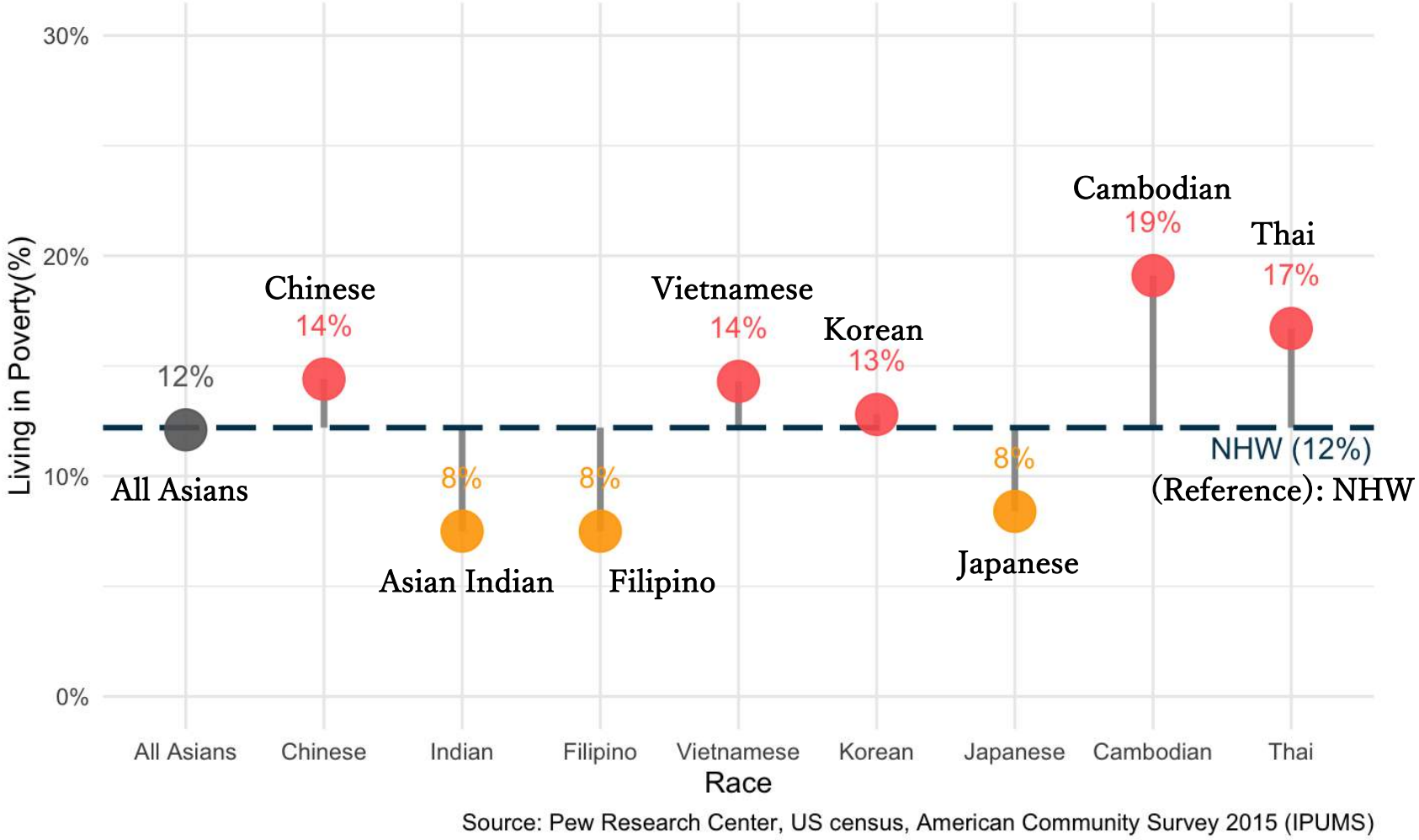


Source: U.S. Food & Drug Administration. FDA, 2016, p. 15, *2015 - 2016 GLOBAL PARTICIPATION IN CLINICAL TRIALS REPORT*.

Source: https://www.census.gov/popclock/world

Asian Americans

Income: % Living in Poverty



Source: Pew Research Center, US census, American Community Survey 2015 (IPUMS)

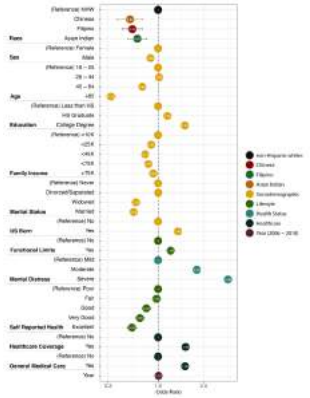
Stanford MEDICINE

Role of Data in Diversity

National Datasets: NHIS/NHANES

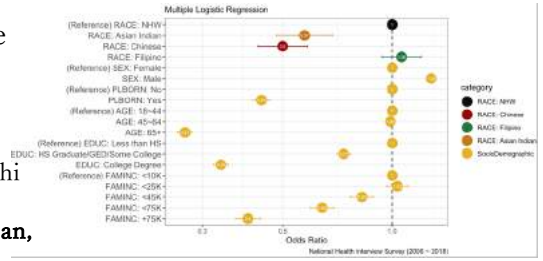
Psychological Distress and Mental Health Service Utilization Disparities in Disaggregated Asian American Populations, 2006~2018

Kaplana K. Balaraman, BS, Nicholas Ortega, Shozen Dan, Malathi Srinivasan, MD, **Latha Palaniappan, MD MS**, Jaiveer Singh, Sukyung Chung, PhD, and Shashank V. Joshi MD



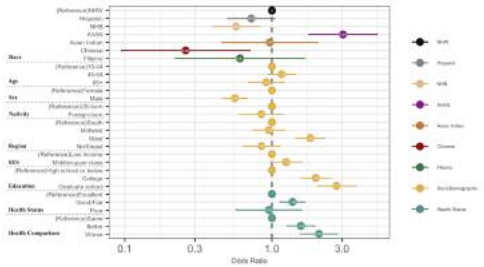
Disaggregated Asian American Cigarette and Alternative Tabacco Product Use: Results from the National Health Interview Survey (NHIS), 2006~2018

Manaeha Rao; Lilly Bar; Yunnan Yu; Sid Venkatraman; Malathi Srinivasan, MD; Arnab Mukherjea, DrPH, MPH; Jiang Li, PhD, MPH; Sukyung Chung, PhD**; Latha Palaniappan, MD MS**

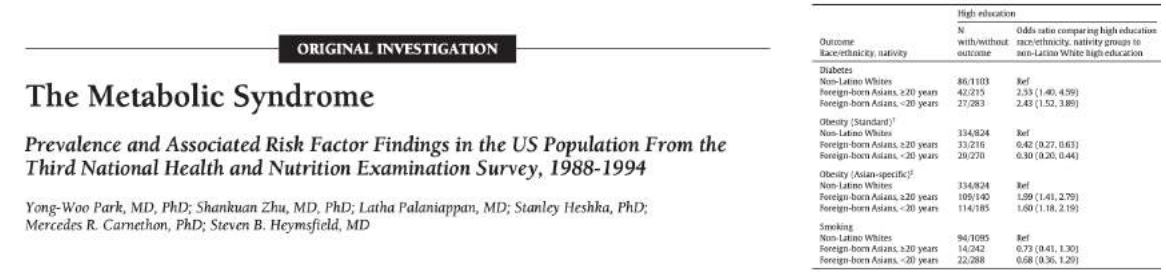


Effects of Ethnicity on Complementary Therapy Adoption over 10 Years, National Health Interview Survey 2007 and 2017

Yuelin He; Bridgette Han; Darynn Gayle Paragas; Nora Sharp; **Latha Palaniappan, MD MS**; Sukyung Chung, PhD; Randall S. Stafford, MD, PhD; Malathi Srinivasan, MD



N[Asian Americans] < 1,500



ORIGINAL INVESTIGATION

The Metabolic Syndrome

Prevalence and Associated Risk Factor Findings in the US Population From the Third National Health and Nutrition Examination Survey, 1988-1994

Yong-Woo Park, MD, PhD; Shankuan Zhu, MD, PhD; Latha Palaniappan, MD; Stanley Heshka, PhD; Mercedes R. Carnethon, PhD; Steven B. Heymsfield, MD

Outcome Race/ethnicity, nativity	N with/without outcome	Odds ratio comparing high education race/ethnicity, nativity groups to non-Latino White high education
	High education	
Diabetes		
Non-Latino Whites	86/1103	Ref
Foreign-born Asians, ≥20 years	42/215	2.33 (1.40, 4.59)
Foreign-born Asians, <20 years	27/283	2.43 (1.52, 3.89)
Obesity (Standard)[†]		
Non-Latino Whites	334/824	Ref
Foreign-born Asians, ≥20 years	33/216	0.42 (0.27, 0.63)
Foreign-born Asians, <20 years	29/270	0.30 (0.20, 0.44)
Obesity (Asian-specific)[‡]		
Non-Latino Whites	334/824	Ref
Foreign-born Asians, ≥20 years	109/140	1.99 (1.41, 2.79)
Foreign-born Asians, <20 years	114/185	1.60 (1.18, 2.19)
Smoking		
Non-Latino Whites	94/1095	Ref
Foreign-born Asians, ≥20 years	14/242	0.73 (0.41, 1.30)
Foreign-born Asians, <20 years	22/288	0.68 (0.36, 1.29)

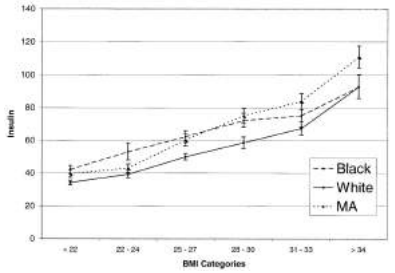
Epidemiology/Health Services/Psychosocial Research

ORIGINAL ARTICLE

Heterogeneity in the Relationship Between Ethnicity, BMI, and Fasting Insulin

LATHA P. PALANIAPPAN, MD, MS
MERCEDES R. CARNETHON, PHD
STEPHEN P. FORTMANN, MD

prevalence of type 2 diabetes was significantly greater in Mexican-American subjects than in white subjects, even when comparisons were made within obesity



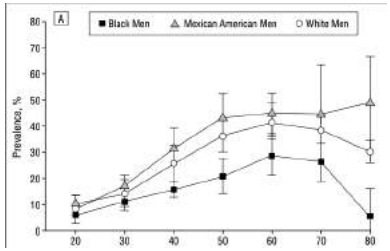
Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Social and clinically-relevant cardiovascular risk factors in Asian Americans adults: NHANES 2011–2014

Sandra E. Echeverria [a,*], Mehnaz Mustafa [b], Sri Ram Pentakota [c], Soyeon Kim [d], Katherine G. Hastings [e], Chioma Amadi [a], Latha Palaniappan [e]



Stanford MEDICINE

Role of Data in Diversity

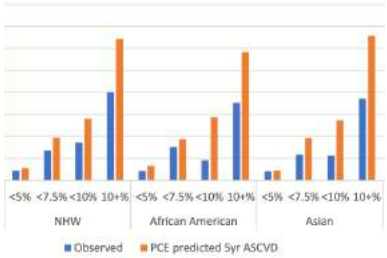
Electronic Health Records

ORIGINAL RESEARCH

American Heart Association

Atherosclerotic Cardiovascular Disease Risk Prediction in Disaggregated Asian and Hispanic Subgroups Using Electronic Health Records

Fatima Rodriguez, MD, MPH; Sukyung Chung, PhD; Manuel R. Blum, MD; Adrien Coulet, PhD; Sanjay Basu, MD, PhD; Latha P. Palaniappan, MD, MS



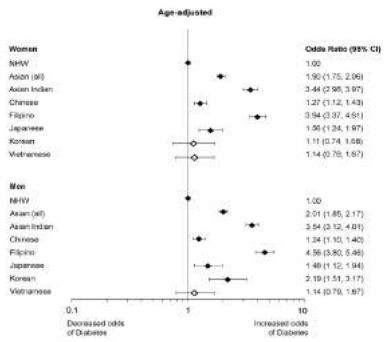
DIABETES RESEARCH AND CLINICAL PRACTICE 93 (2011) 248–254

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation



Type 2 diabetes: Identifying high risk Asian American subgroups in a clinical population

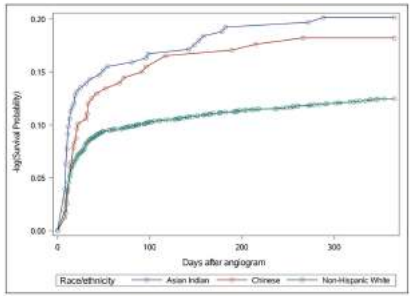
Elsie J. Wang[a], Eric C. Wong[a], Anjali A. Dixit[b], Stephen P. Fortmann[c], Randolph B. Linde[d], Latha P. Palaniappan[a,*]

[a] Palo Alto Medical Foundation Research Institute, Department of Health Policy Research, Palo Alto, CA, United States
[b] Columbia University, Mailman School of Public Health, United States
[c] Kaiser Permanente Center for Health Research, United States
[d] Palo Alto Medical Foundation, Palo Alto, CA, United States

Journal of the American Heart Association

ORIGINAL RESEARCH

Heterogeneity of Treatment and Outcomes Among Asians With Coronary Artery Disease in the United States



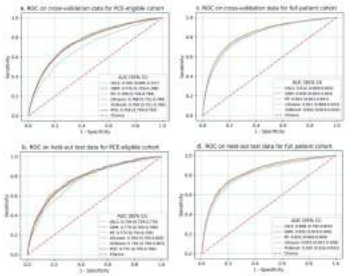
npj | Digital Medicine

www.nature.com/npjdigitalmed

ARTICLE OPEN

Machine learning and atherosclerotic cardiovascular disease risk prediction in a multi-ethnic population

Andrew Ward[1,7], Ashish Sarraju[2,7], Sukyung Chung[3,4], Jiang Li[3], Robert Harrington[2], Paul Heidenreich[2], Latha Palaniappan[3,4], David Scheinker[5,6,8] and Fatima Rodriguez[2,8]

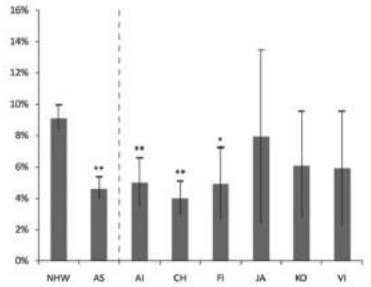


JOGNN

RESEARCH

Clinically Identified Postpartum Depression in Asian American Mothers

Deepika Goyal, Elsie J. Wang, Jeremy Shen, Eric C. Wong, and Latha P. Palaniappan



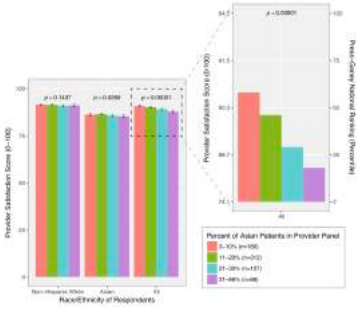
Liao et al. BMC Health Services Research (2020) 20:678
https://doi.org/10.1186/s12913-020-05534-6

BMC Health Services Research

RESEARCH ARTICLE Open Access

The association between Asian patient race/ethnicity and lower satisfaction scores

Lillian Liao[1,2,3*], Sukyung Chung[4], Jonathan Altamirano[5], Luis Garcia[5], Magali Fassiotto[5], Bonnie Maldonado[5], Paul Heidenreich[2] and Latha Palaniappan[2]



N[Asian Americans] = 250,000

Stanford MEDICINE

Role of Data in Diversity

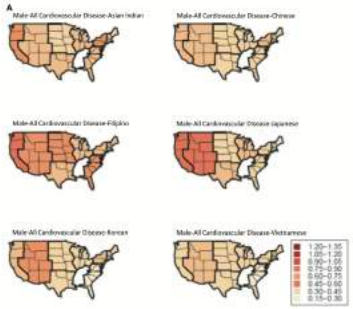
Mortality Records

ORIGINAL RESEARCH

American Heart Association | American Stroke Association

Geographic Variations in Cardiovascular Disease Mortality Among Asian American Subgroups, 2003–2011

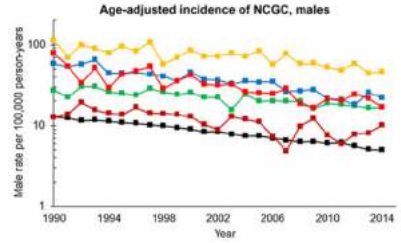
Jia Pu, PhD; Katherine G. Hastings, MPH; Derek Boothroyd, PhD; Powell O. Jose, MD; Sukyung Chung, PhD; Janki B. Shah, MD; Mark R. Cullen, MD; Latha P. Palaniappan, MD, MS; David H. Rehkopf, ScD, MPH



CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION | RESEARCH ARTICLE

One Size Does Not Fit All: Marked Heterogeneity in Incidence of and Survival from Gastric Cancer among Asian American Subgroups

Robert J. Huang[1], Nora Sharp[2], Ruth O. Talamoa[2], Hanlee P. Ji[3], Joo Ha Hwang[1], and Latha P. Palaniappan[4]

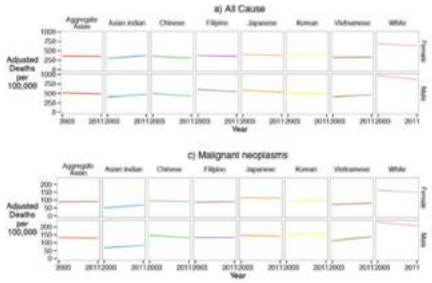


PLOS ONE

RESEARCH ARTICLE

Leading Causes of Death among Asian American Subgroups (2003–2011)

Katherine G. Hastings[1], Powell O. Jose[2], Kristopher I. Kapphahn[1], Ariel T. H. Frank[3], Benjamin A. Goldstein[1], Caroline A. Thompson[4], Karen Eggleston[5], Mark R. Cullen[1], Latha P. Palaniappan[1]*



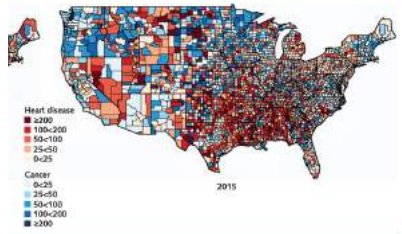
ORIGINAL RESEARCH

Annals of Internal Medicine

Socioeconomic Differences in the Epidemiologic Transition From Heart Disease to Cancer as the Leading Cause of Death in the United States, 2003 to 2015

An Observational Study

Katherine G. Hastings, MPH; Derek B. Boothroyd, PhD; Kristopher Kapphahn, MS; Jiaqi Hu, MPH; David H. Rehkopf, ScD, MPH; Mark R. Cullen, MD; and Latha Palaniappan, MD, MS

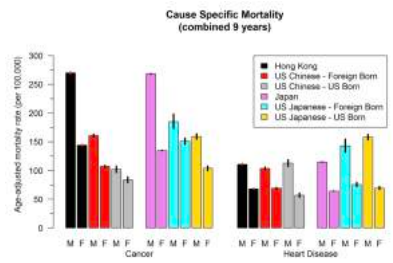


Open Access | Research

BMJ Open

Mortality outcomes for Chinese and Japanese immigrants in the USA and countries of origin (Hong Kong, Japan): a comparative analysis using national mortality records from 2003 to 2011

Katherine G Hastings,[1] Karen Eggleston,[2] Derek Boothroyd,[3] Kristopher I Kapphahn,[3] Mark R Cullen,[4] Michele Barry,[5] Latha P Palaniappan[1]

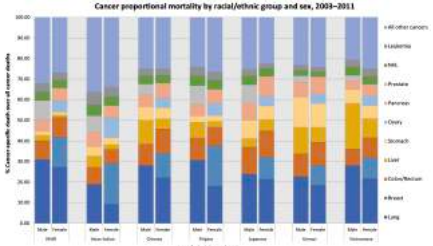


Research Article

Cancer Epidemiology, Biomarkers & Prevention

The Burden of Cancer in Asian Americans: A Report of National Mortality Trends by Asian Ethnicity

Caroline A. Thompson[1,2], Scarlett Lin Gomez[3,4,5], Katherine G. Hastings[6], Kristopher Kapphahn[7], Peter Yu[8], Salma Shariff-Marco[3,4,5], Ami S. Bhatt[9,10], Heather A. Wakelee[5,11], Manali I. Patel[11,12], Mark R. Cullen[6,13], and Latha P. Palaniappan[6]



Stanford MEDICINE

Role of Data in Diversity
Examples with Real World Data

Uncovering Consistent Signals on Health

National Datasets

ORIGINAL INVESTIGATION

The Metabolic Syndrome

Prevalence and Associated Risk Factor Findings in the US Population From the Third National Health and Nutrition Examination Survey, 1988-1994

Yong-Woo Park, MD, PhD; Shankuan Zhu, MD, PhD; Latha Palaniappan, MD; Stanley Heshka, PhD; Mercedes R. Carnethon, PhD; Steven B. Heymsfield, MD

Epidemiology/Health Services/Psychosocial Research

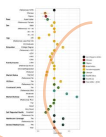
Heterogeneity in the Relationship Between Ethnicity, BMI, and Fasting Insulin

Preventive Medicine

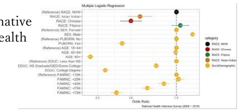
Social and clinically-relevant cardiovascular risk factors in Asian Americans adults: NHANES 2011–2014

Psychological Distress and Mental Health Service Utilization Disparities in Disaggregated Asian American Populations, 2006~2018

Kaplana K. Balaraman, BS, Nicholas Ortega, Shozen Dan, Malathi Srinivasan, MD, Latha Palaniappan, MD MS, Jaiveer Singh, Sukyung Chung, PhD, and Shashank V. Joshi MD

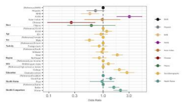


Disaggregated Asian American Cigarette and Alternative Tabacco Product Use: Results from the National Health Interview Survey (NHIS), 2006~2018



Effects of Ethnicity on Complementary Therapy Adoption over 10 Years, National Health Interview Survey 2007 and 2017

Yuelin He; Bridgette Han; Darynn Gayle Paragas; Nora Sharp; Latha Palaniappan, MD MS; Sukyung Chung, PhD; Randall S. Stafford, MD, PhD; Malathi Srinivasan, MD



Electronic Health Records

Dyslipidemia in Special Ethnic Populations

Jia Pu, Robert Romanelli, Beinan Zhao, Kristen M.J. Azar, Katherine G. Hastings, Vani Nimbal, Stephen P. Fortmann, Latha P. Palaniappan

"All of Those Things We Don't Eat": A Culture-Centered Approach to Dietary Health Meanings for Asian Indians Living in the United States

Christopher J. Koenig, Mohan J. Dutta, Namratha Kandula, Latha Palaniappan

JOGNN

Paediatric and Perinatal Epidemiology

Racial/Ethnic Differences in Gestational Diabetes Prevalence and Contribution of Common Risk Factors

ORIGINAL RESEARCH

Atherosclerotic Cardiovascular Disease Risk Prediction in Disaggregated Asian and Hispanic Subgroups Using Electronic Health Records

Journal of the American Heart Association

ORIGINAL RESEARCH

Heterogeneity of Treatment and Outcomes Among Asians With Coronary Artery Disease in the United States

RESEARCH

Clinically Identified Postpartum Depression in Asian American Mothers

Diabetes Research and Clinical Practice

Type 2 diabetes: Identifying high risk Asian American subgroups in a clinical population

npj Digital Medicine

ARTICLE OPEN

Machine learning and atherosclerotic cardiovascular disease risk prediction in a multi-ethnic population

BMC Health Services Research

RESEARCH ARTICLE Open Access

The association between Asian patient race/ethnicity and lower satisfaction

ORIGINAL ARTICLE

Clocks Moving at Different Speeds

Cultural Variation in the Satisfaction With Wait Time for Outpatient Care

Mortality Records

American Journal of Epidemiology

Practice of Epidemiology

A Multiple-Imputation "Forward Bridging" Approach to Address Changes in the Classification of Asian Race/Ethnicity on the US Death Certificate

Caroline A. Thompson, Derek B. Boothroyd, Katherine G. Hastings, Mark R. Cullen, Latha P. Palaniappan, and David H. Rehkopf

ORIGINAL RESEARCH — Annals of Internal Medicine

Socioeconomic Differences in the Epidemiologic Transition From Heart Disease to Cancer as the Leading Cause of Death in the United States, 2003 to 2015

An Observational Study

CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION | RESEARCH ARTICLE

One Size Does Not Fit All: Marked Heterogeneity in Incidence of and Survival from Gastric Cancer among Asian American Subgroups

Robert J. Huang, Nora Sharp, Ruth O. Talamoa, Hanlee P. Ji, Joo Ha Hwang, and Latha P. Palaniappan

Cardiovascular Disease Mortality in Asian Americans

PLOS ONE

RESEARCH ARTICLE

Leading Causes of Death among Asian American Subgroups (2003–2011)

ORIGINAL RESEARCH

Geographic Variations in Cardiovascular Disease Mortality Among Asian American Subgroups, 2003–2011

Cross-national comparisons of increasing suicidal mortality rates for Koreans in the Republic of Korea and Korean Americans in the USA, 2003–2012

CEBP FOCUS

Patient and Provider Characteristics Associated with Colorectal, Breast, and Cervical Cancer Screening among Asian Americans

BMJ Open

Mortality outcomes for Chinese and Japanese immigrants in the USA and countries of origin (Hong Kong, Japan): a comparative analysis using national mortality records from 2003 to 2011

Research Article

The Burden of Cancer in Asian Americans: A Report of National Mortality Trends by Asian Ethnicity

Stanford MEDICINE

Role of Data in Diversity

Culturally Competent Intervention Studies

Open Access Research

BMJ Open Diabetes Research & Care

Engaging South Asian women with type 2 diabetes in a culturally relevant exercise intervention: a randomized controlled trial

Alamelu Natesan,[1] Vani C Nimbal,[2] Susan L Ivey,[1] Elsie J Wang,[3] Kristine A Madsen,[1] Latha P Palaniappan[3]

Asia Pac J Clin Nutr 2008;17 (4):669-671 669

Short Communication

Clinical experience with a relatively low carbohydrate, calorie-restricted diet improves insulin sensitivity and associated metabolic abnormalities in overweight, insulin resistant South Asian Indian women

Andrea C Backes BA, Fahim Abbasi MD, Cindy Lamendola RN, Tracey L McLaughlin MD, Gerald Reaven MD, Latha P Palaniappan MD

ELSEVIER

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

STRONG-D: Strength training regimen for normal weight diabetics: Rationale and design

Lida Faroqi[a,*], Saniya Bonde[a], Daniella Tatianna Goni[a], Chi Wai Wong[a], Myo Wong[a], Khalil Walai[a], Saron Araya[a], Sayed Azamey[a], Gabriella Schreiner[a], Monica Bandy[a], Sonia Sunita Raghuram[a], Anuva Mittal[a], Aishee Mukherji[a], Tenzin Wangdak[a], Ruth Talamoa[a], Katherine Vera[a], Carla Nacif-Coelho[a], Leah Groppo CDE[c], Mary Christensen[b], Neil Johannsen[c], Francois Haddad[d], Minal Moharir[a], Latha Palaniappan[a]

Stanford MEDICINE

Role of Data in Diversity

Pharmacogentic Differences

Cardiology

Rosuvastatin Calcium

Warfarin

Clopidogrel (Plavix)

Oncology

Irinotecan

Tamoxifen

Infectious Disease and Rheumatology

Atazanavir

Voriconazole

Stanford MEDICINE

Role of Data in Diversity

Community Impact

Stanford MEDICINE | CARE
Center for Asian Health Research and Education

Mission Statement

CARE seeks to improve the health of Asians by increasing knowledge, empowering education and positively impacting their clinical care.

Promotional Video
https://vimeo.com/504220633

Research

- Heart Risk factors among Asian Imimigrants
- Asian Americans and COVID-19 Deaths
- The dissaggregation of Asian American Health Data

Education

- Courses on minoriy health
- CARE Scholars Program
- Chi Li Pao Hong Kong University (HKU) Enrichment Year, 2021-2022

Stanford MEDICINE

Role of Data in Diversity

Contacts

lathap@stanford.edu

Stanford MEDICINE

Today's speaker

Nicole Richie, PhD
Global Head
Health Equity and Population Science
Genentech Roche

Race/Ethnicity vs Ancestry vs Geographic Origin

Ancestry is driven by genetics, whereas race and ethnicity are social constructs

Race

Self-reported or physician-reported:

- American Indian or Alaska Native
- Asian
- Black or African American
- Native Hawaiian or other Pacific Islander
- White

These categories have been historically used in the United States. Hispanic or Latino is sometimes asked together with Race

Ethnicity

Self-reported or physician-reported:

- Hispanic or Latino

Other ethnic groups include cultural (e.g. Romani), religious (e.g. Jews), language, or nationality groups (e.g. Puerto Ricans)

Ancestry

Calculated by genetic information compared to continental-level information:

- AFR (African)
- AMR (Native American, all continent)
- EUR (European)
- EAS (East-Asian)
- SAS (South Asian)

Borderline/fringe cases are difficult to assess (e.g. middle-eastern, admixed populations, Pacific-islanders)

Geographic Origin

Belonging to or characteristic of a **particular region**:

- North Africa
- East Africa
- Central Africa
- West Africa
- Southern Africa
- etc.

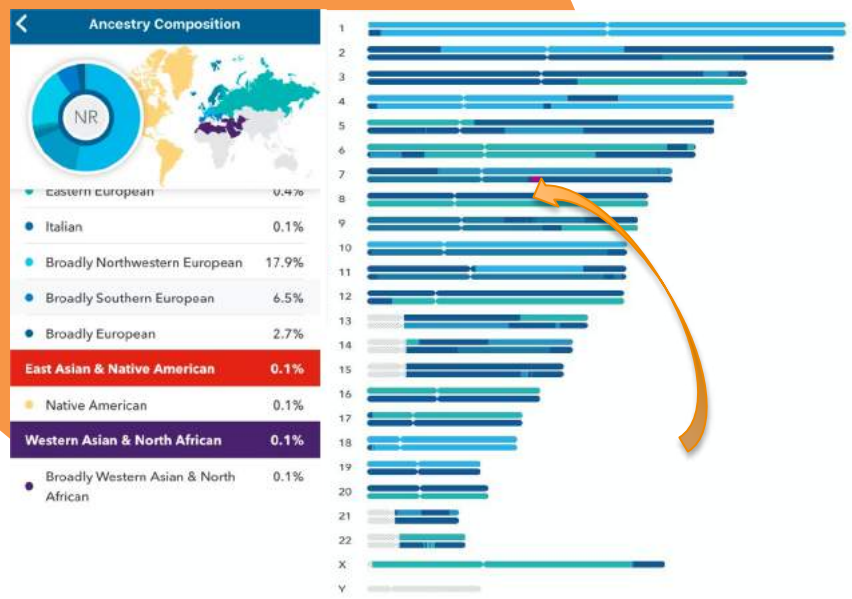
Geographic distance may be an excellent predictor of genetic differentiation within a region.

The Utility of Data Elements

Ancestry and self reported race/ethnicity

Ancestry

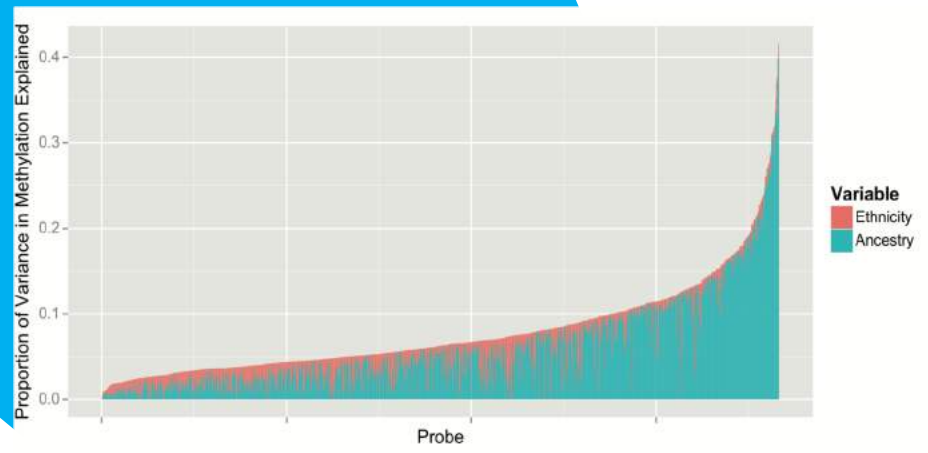
Genetic Construct



- Ancestry is a way of categorizing genes
- Clinical relevance of ancestry: understanding if variant associated with pathology vs variant associated with ancestry
- Relevance contingent upon understanding biology- requires more diverse genomic data

Self Reported Race

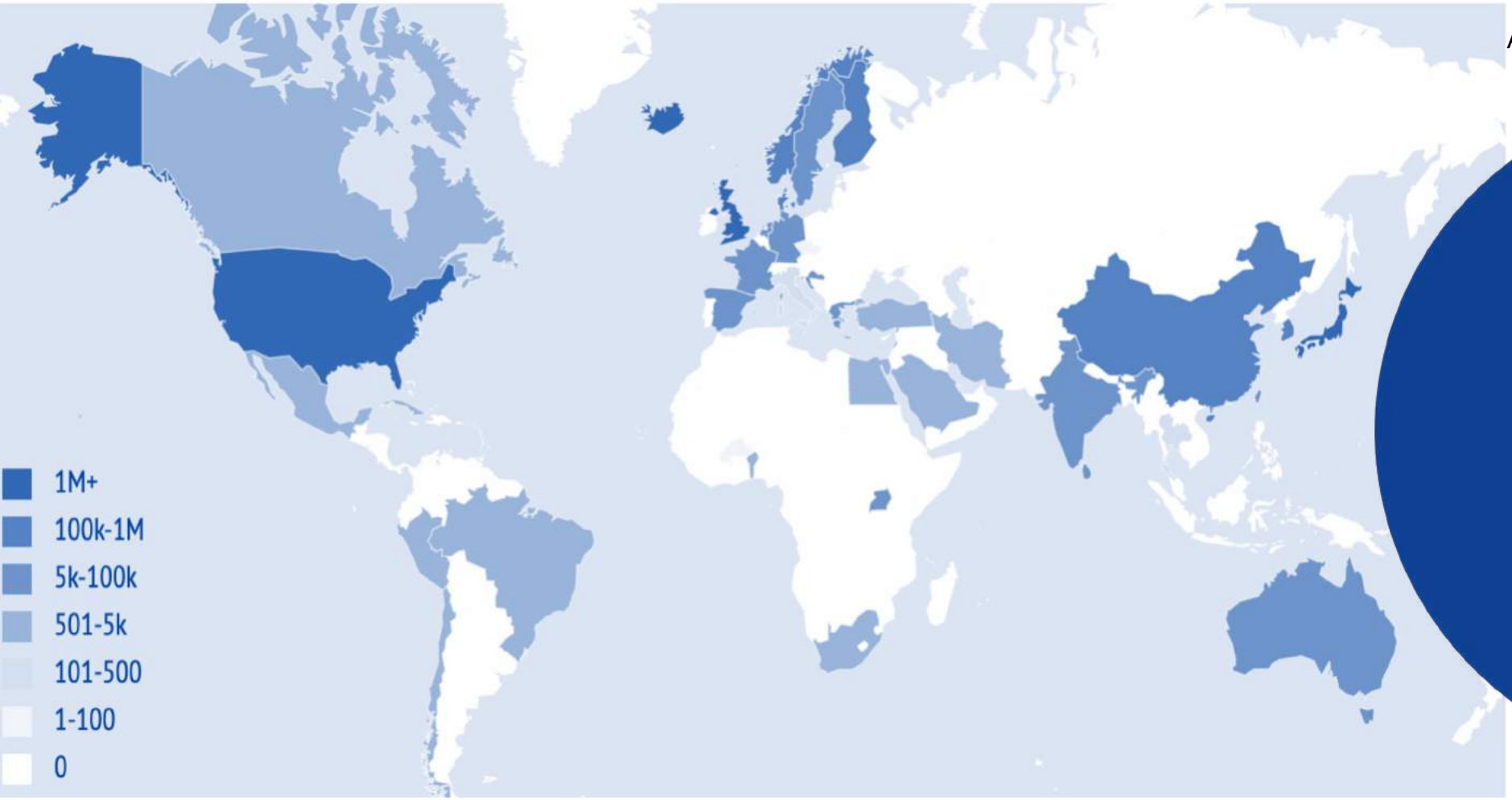
Social Construct

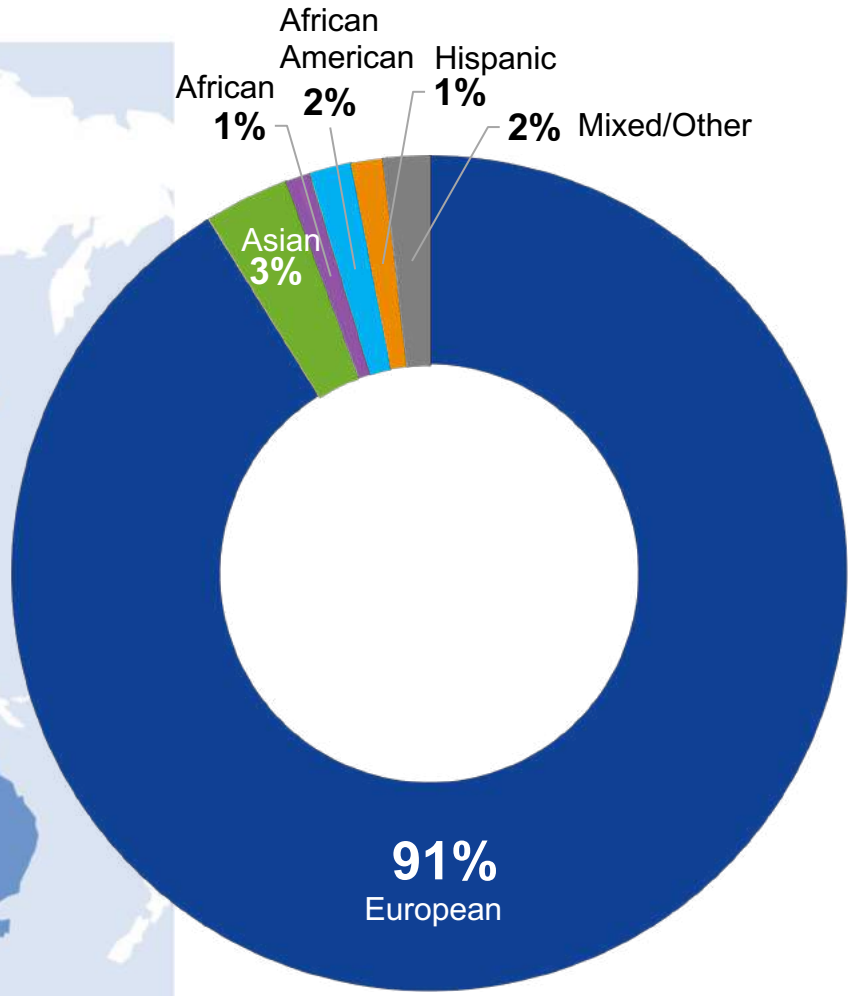


- Self reported race can provide relevant environmental information on risk and response measurable by epigenetics

Understudied Populations

Biased Genetic Discoveries





Available genomic data and medical research is predominantly based on **European ancestry**, leaving significant amounts of **world wide genotypic and phenotypic variation undiscovered**

Source GWAS participants by country and ancestry (2019), GWAS Diversity Monitor. https://gwasdiversitymonitor.com/ (Accessed March 13. 2020)

Genomic Based Healthcare is becoming the Norm

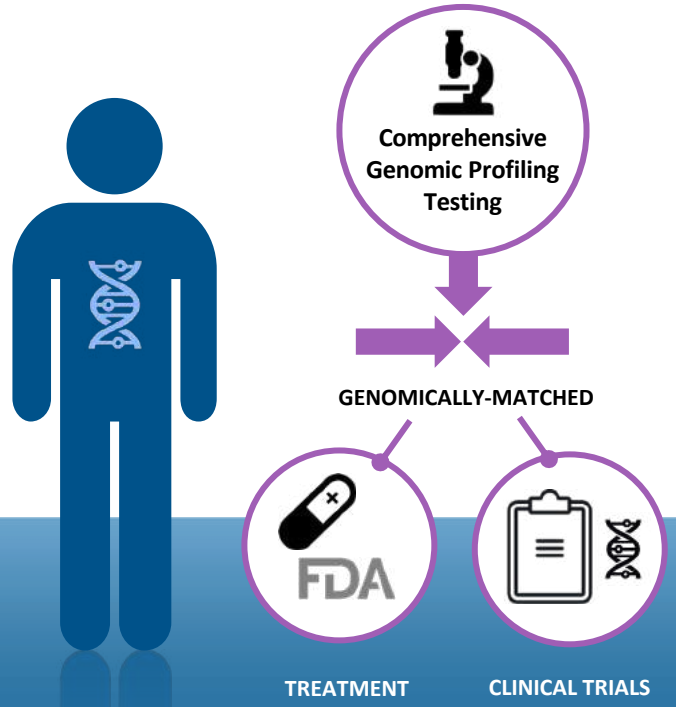
Without conscious effort, existing inequities will be exacerbated over time, contributing to a widening gap in access to innovation.

Molecular Profiling is Guideline Recommended

Broad molecular profiling to inform genomically-matched therapy is recommended by NCCN Guidelines

NCCN National Comprehensive Cancer Network®

"NCCN believes that the best management for any patient with cancer is in a clinical trial. ***Participation in clinical trials is especially encouraged****."*



References:
NCCN – National Comprehensive CancerNetwork
1. IQVIA Institute. Global Oncology Trends 2018. https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/global-oncology-trends-2018.pdf. Published May 2018.

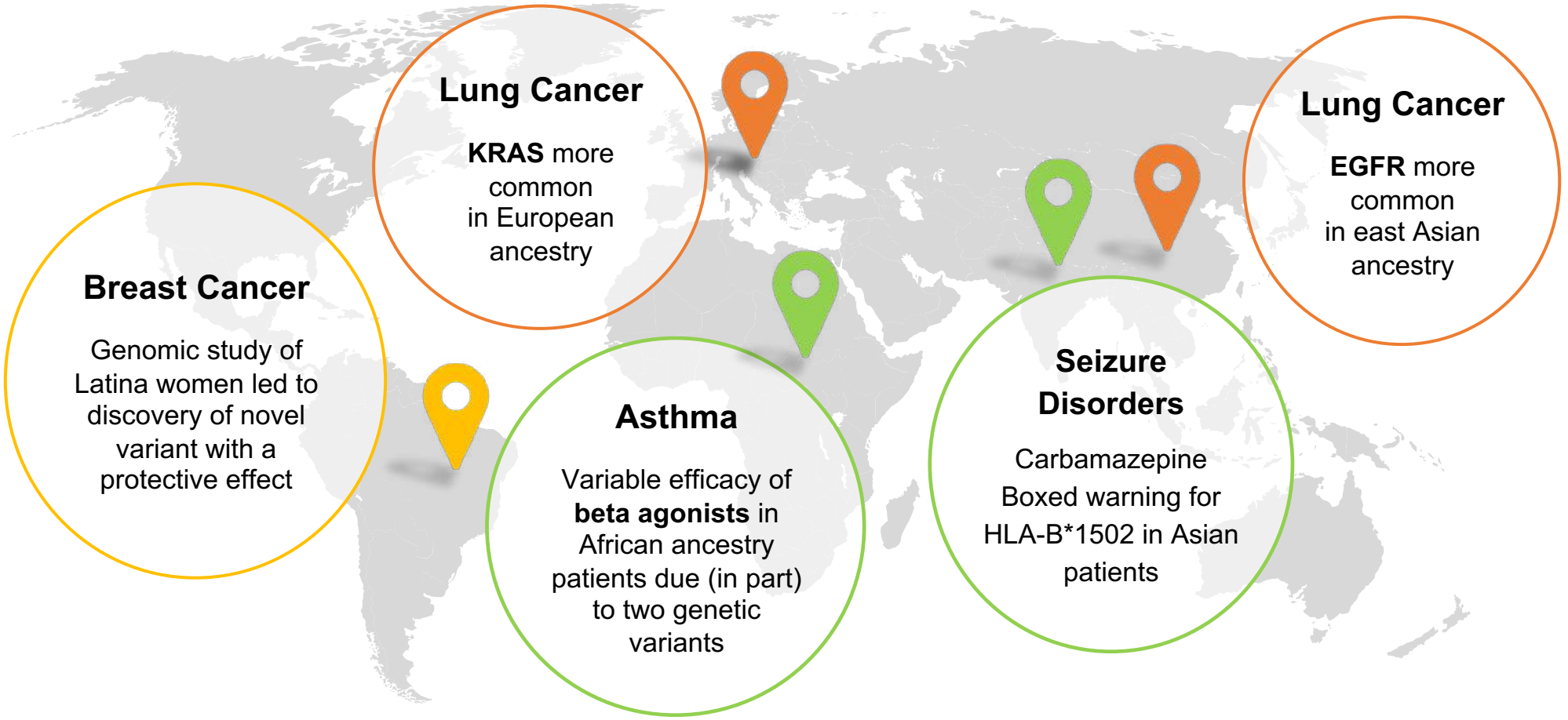
Clinical Importance

Disease pattern, clinical presentation, and therapeutic response can vary dramatically by race/ethnicity and ancestral background

Biomarker Prevalence

Differences in Safety/Efficacy

Scientific Discovery

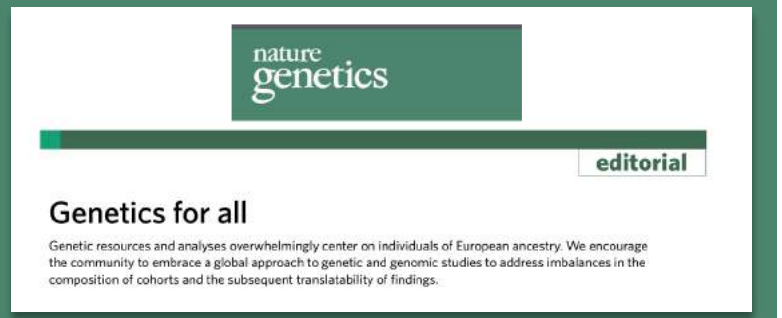


Genomic data helps us understand how patients react and respond to medicines

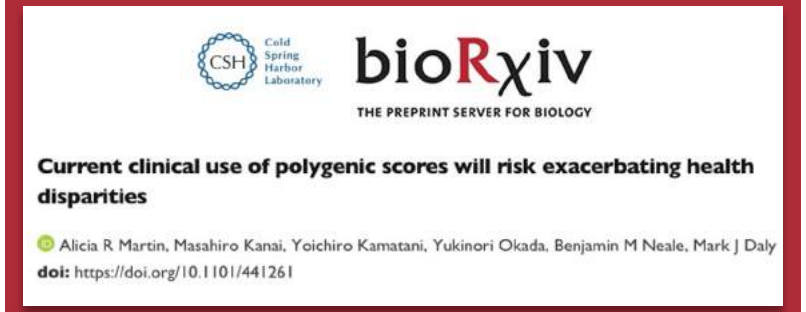
Global Health Equity & Population Science

Scientific Importance

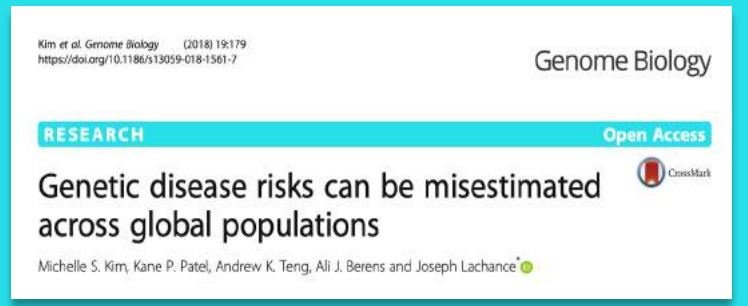
Rare variants tend to be population specific and disproportionately important in predicting disease risk and drug response



Robust, powerful genome sequencing enables greater **understanding** of disease **biology**, identification of **novel targets**



Single-ancestry genome-wide association studies (GWAS) **limits clinical utility**[1,2]



Inferences derived **from single-ancestry** may be **incomplete or inaccurate**[3-6]

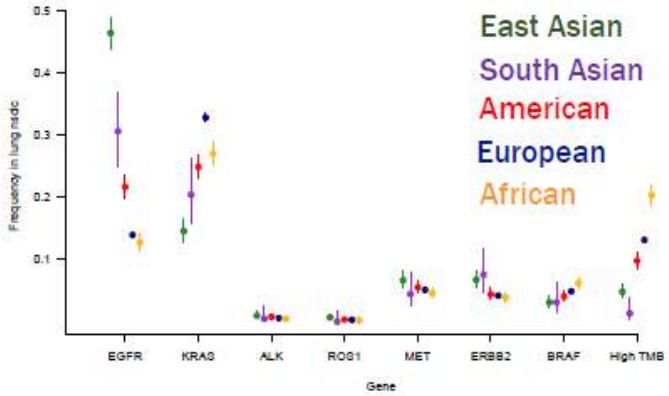
- Misdiagnosis of pathogenic hypertrophic cardiomyopathy in African Americans
- Population-enriched GWAS identified novel variants (AD, CRC, RA)

Global Health Equity & Population Science

Sources:1) Genetics for all. https://www.nature.com/articles/s41588-019-0394-y.pdf (Access March 2020)
2) Genetic disease risks can be misestimated across global populations https://genomebiology.biomedcentral.com/articles/10.1186/s13059-018-1561-7 (Access March 2020)
3) Genetic Misdiagnoses and the Potential for Health Disparities https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5292722/ (Access March 2020)
4) The more from East-Asian, the better: risk prediction of colorectal cancer risk by GWAS-identified SNPs among Japanese. https://rd.springer.com/content/pdf/10.1007%2Fs00432-017-2505-4.pdf (Access March 2020)
5) A Comprehensive Genetic Association Study of Alzheimer Disease in African Americans https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3356921/pdf/nihms375246.pdf (Access March 2020)
6) A Common DIO2 Polymorphism and Alzheimer Disease Dementia in African and European Americans. https://www.ncbi.nlm.nih.gov/pubmed/29481662 (Access March 2020)

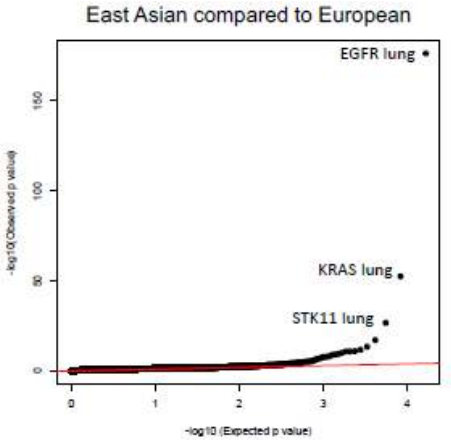
Prediction of actionable targets can vary based on Ancestry

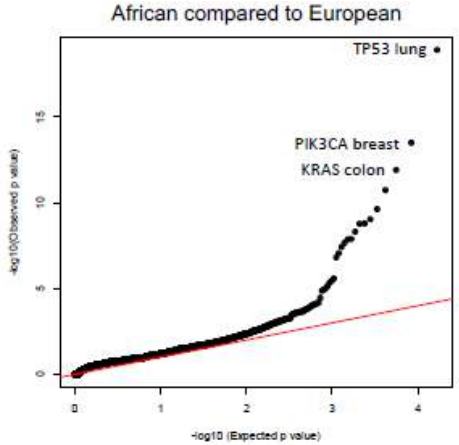
Frequency of somatic alterations in driver genes in non-small cell lung cancer by SNP-inferred ancestry group [1)]



- Recapitulate known EGFR differences
  - East Asian: alteration rate 0.46 (0.44- 0.49)
  - European: alteration rate 0.14 (0.13-0.14 95% CI)
  - $p<2.2 \times 10^{-16}$
- Recapitulate known KRAS differences
  - East Asian: 0.14 (0.13-0.16)
  - European: 0.32 (0.32-0.33)
  - $p<2.2 \times 10^{-16}$

Genes with significantly different alteration frequency between samples of different inferred ancestry groups [1)]





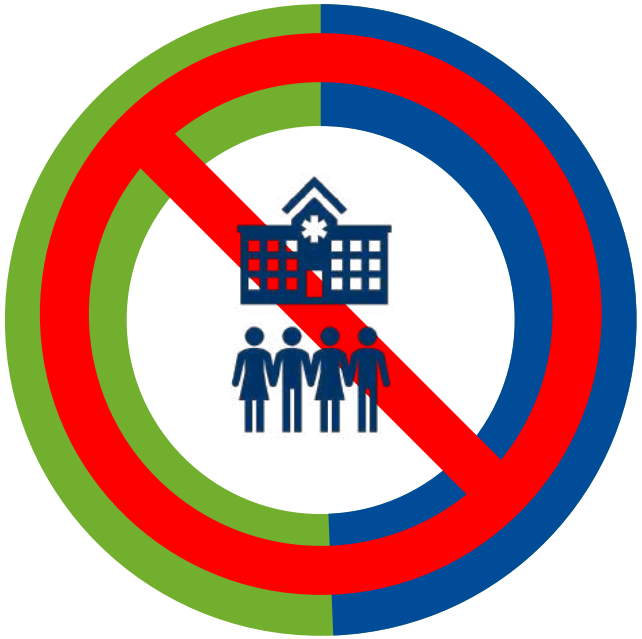
Genes with significantly different alteration frequency between samples of African inferred ancestry compared to European inferred ancestry [1)]

Gene	Disease ontology	P value	African alteration frequency	European alteration frequency	Odds Ratio	Odds Ratio 2.5% CI	Odds Ratio 97.5% CI
TP53	lung adenocarcinoma	1.23×10^{-19}	0.684	0.565	0.601	0.536	0.673
PIK3CA	breast carcinoma (nos)	1.23×10^{-12}	0.234	0.360	1.834	1.540	2.192
KRAS	colon adenocarcinoma (crc)	1.82×10^{-11}	0.596	0.498	0.671	0.596	0.755
TP53	breast invasive ductal carcinoma (idc)	2.33×10^{-10}	0.732	0.607	0.566	0.471	0.680
PTEN	uterus endometrial adenocarcinoma (nos)	9.06×10^{-10}	0.255	0.512	3.024	2.069	4.491
VHL	kidney renal cell carcinoma	1.61×10^{-9}	0.092	0.465	7.433	3.331	19.547
KRAS	lung adenocarcinoma	1.66×10^{-9}	0.319	0.398	1.406	1.255	1.576
BRAF	colon adenocarcinoma (crc)	4.85×10^{-9}	0.052	0.100	1.990	1.549	2.590
RBM10	lung adenocarcinoma	1.29×10^{-6}	0.045	0.085	1.937	1.513	2.514
APC	colon adenocarcinoma (crc)	1.34×10^{-6}	0.826	0.757	0.658	0.564	0.764
TP53	breast carcinoma (nos)	2.18×10^{-6}	0.623	0.516	0.649	0.555	0.757
PIK3CA	breast invasive ductal carcinoma (idc)	8.66×10^{-6}	0.220	0.321	1.668	1.374	2.033
TP53	uterus endometrial adenocarcinoma (nos)	1.54×10^{-7}	0.696	0.473	0.397	0.273	0.571

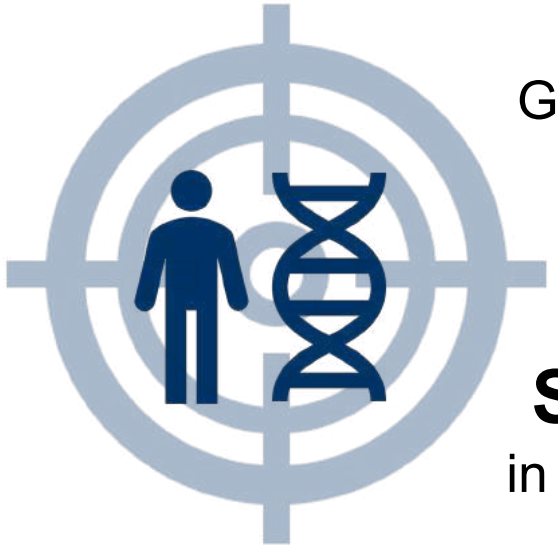
Source: 1) Conelly et al., 2018, AACR abstract □ data sets to be updated based on actual case volume

Data Inclusive of Worldwide Genetic Variation Increases The Ability to Successfully Develop New Drugs for Patients

Value of Broadening Population Specific Data in Early Research and Discovery



50%
of clinical trials fail



Genetically supported targets have

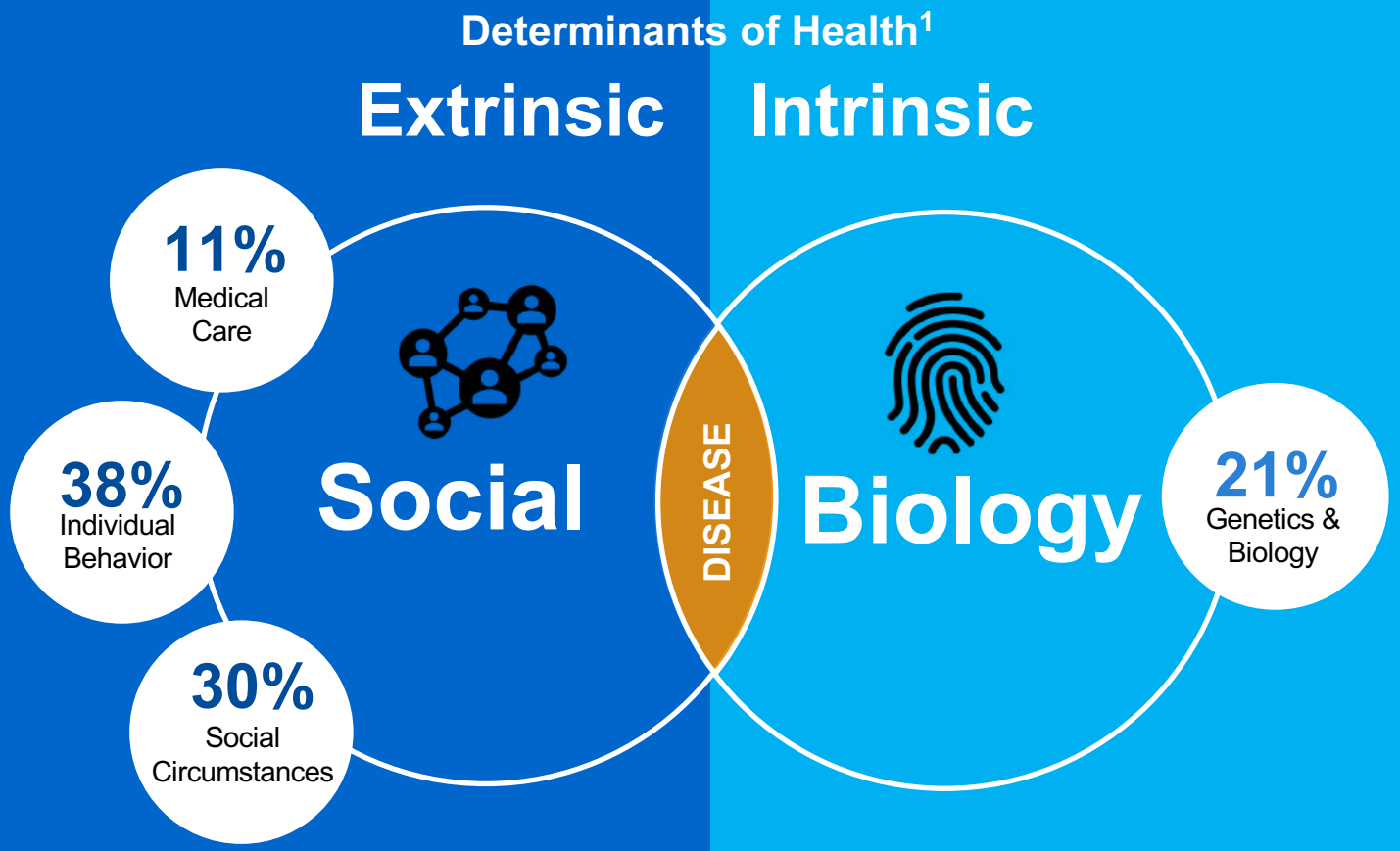
>2X

Success Rate
in clinical development

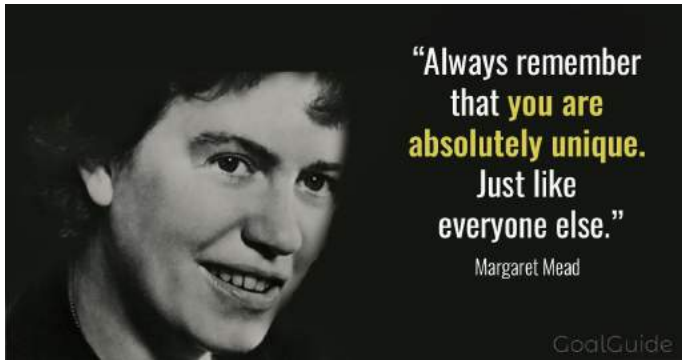
GENOMIC DATA INCREASES CLINICAL RESEARCH SUCCESS RATE

Source: https://www.nature.com/articles/ng.3314

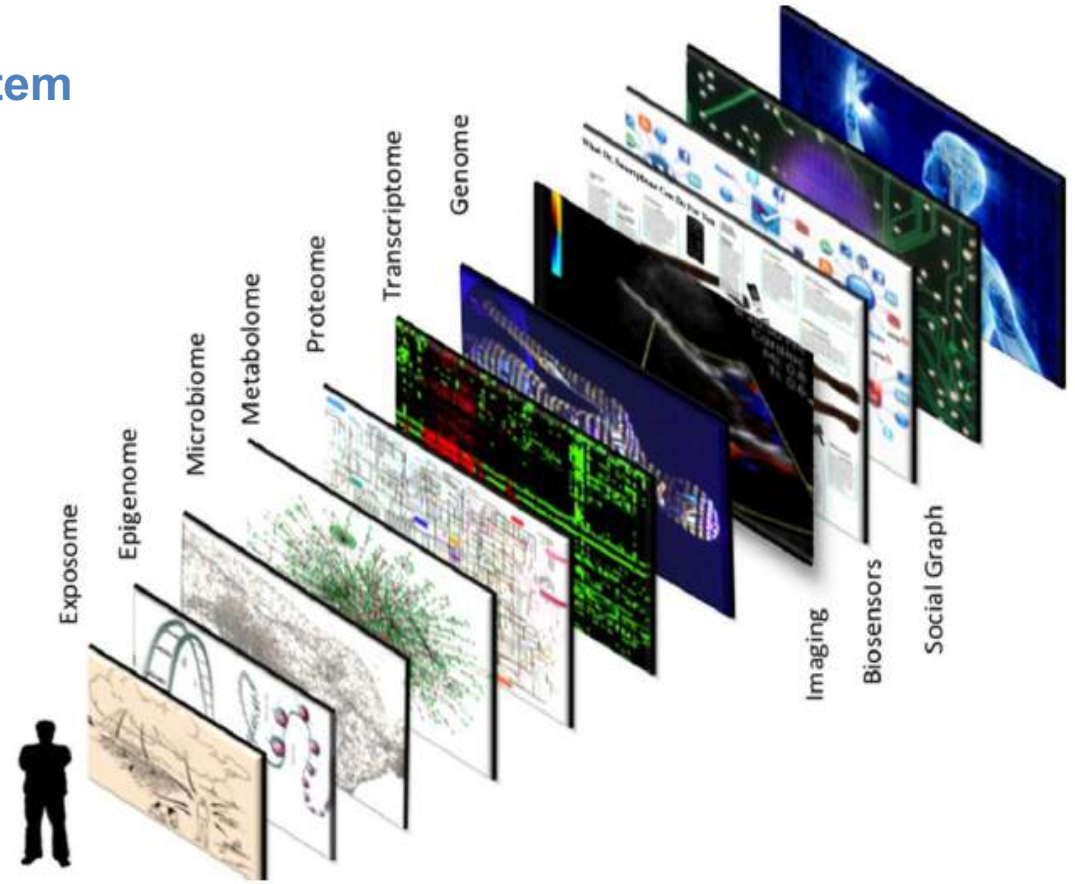
Ability to Develop Personalized Healthcare Requires Understanding Biologic and Social Determinants



Source
1) Edwin Choi, Juhan Sonin 2016, http://www.informationisbeautifulawards.com/showcase/1720-determinants-of-health



Individualized Human Information System



Adapted from Topol Cell 2014

Global Health Equity & Population Science

Takeaway

With greater and more refined technology and scientific capabilities there is an unprecedented opportunity to realize the promise of personalized healthcare.

Diversity in genomic and clinical data is fundamental to this notion and must be included throughout the full lifecycle of drug discovery, development, and clinical practice

MULTI-REGIONAL
CLINICAL TRIALS

THE MRCT CENTER of
BRIGHAM AND WOMEN'S HOSPITAL
and HARVARD

Discussion and Questions