

Imagining The NHLBI at 75: Integrating Science and Public Service

Gary H. Gibbons, MD
Director
National Heart, Lung, and Blood Institute

Advisory Committee to the Director Meeting

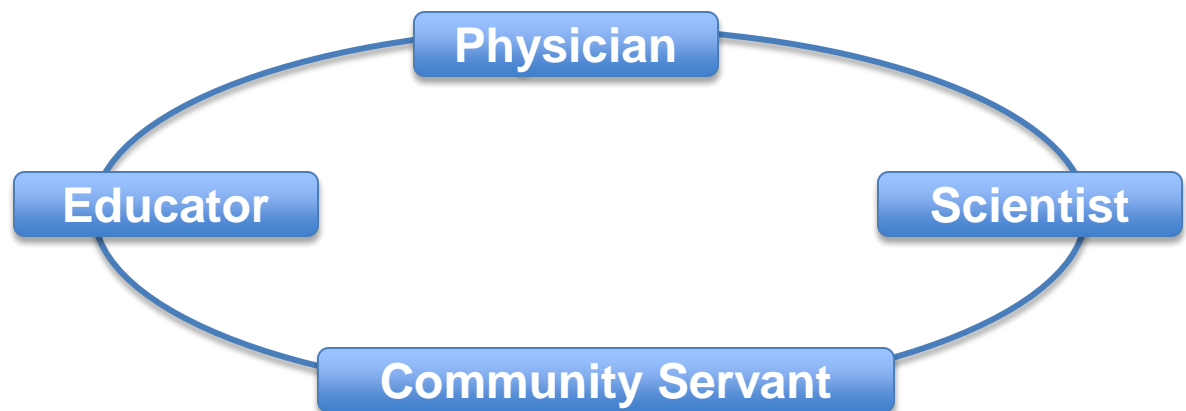
December 6, 2012



NHLBI Mission: Aligns with My Life's Purpose



Mission: Provide **global leadership** for research, training, and education programs to promote the **prevention and treatment** of heart, lung, and blood diseases and enhance the health of all individuals so that they can live longer and more fulfilling lives.



Joining the Legacy of Leadership Excellence



1948-1952
Cassius Van Slyke, M.D.



1952-1961
James Watt, M.D.,
D.P.H.



1961-1965
Ralph E. Knutti, M.D.



1965-1965
William H. Stewart, M.D.



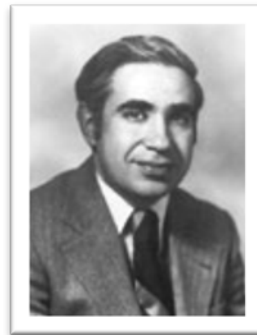
1966-1966
Robert P. Grant,
M.D.



1966-1968
Donald S. Frederickson, M.D.



1968-1974
Theodore Cooper, M.D., Ph.D.



1975-1981
Robert I. Levy,
M.D.



1982-2003
Claude Lenfant, M.D.

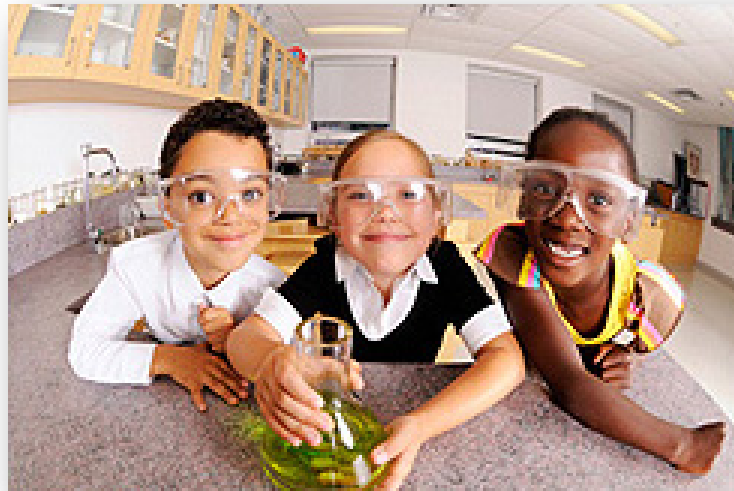


2005-2009
Elizabeth G. Nabel, M.D.

Being Accountable Stewards: Science and Scientists as Public Goods

“We do not inherit the land from our ancestors, we borrow it from our children. ”

Native American Proverb



Refining Our “Recipe” for Successful Stewardship: NHLBI Enduring Principles



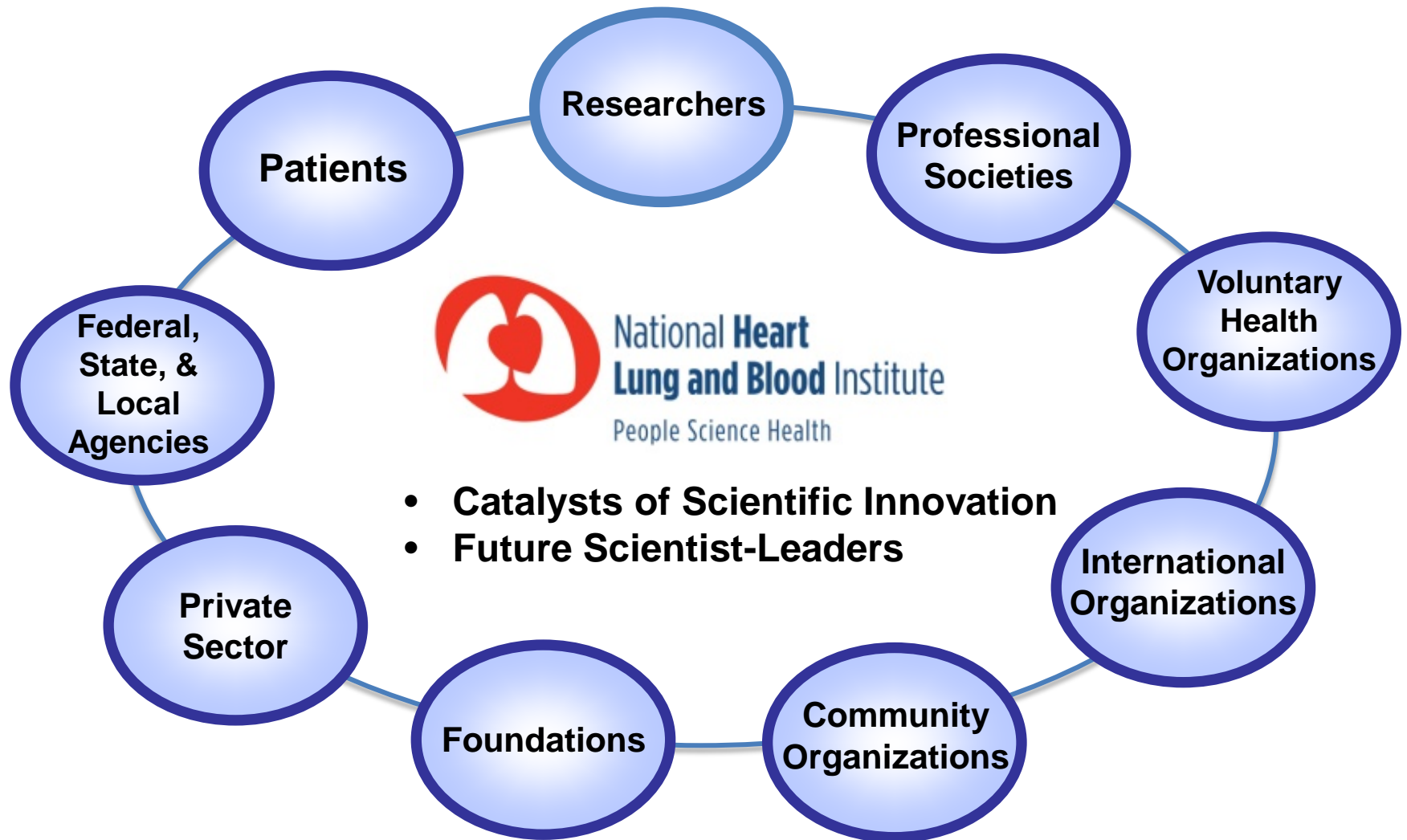
- Value and support investigator-initiated fundamental discovery science.
- Maintain a balanced, cross-disciplinary portfolio (basic, clinical, population science).
- Support implementation science that empowers patients and enables partners to apply knowledge that improves the health of the nation.

Refining Our “Recipe” for Success: NHLBI Enduring Principles



- Train and nurture a diverse new generation of leaders in science.
- Engage key thought-leaders to collectively identify and pursue high-yield opportunities that will advance the field.
- Value the health of all communities; elucidate and eliminate health inequities in the US and around the globe.

The NHLBI Community -- Circle of Partners Co-Stewards of Science as a Public Good



Towards a Diverse Biomedical Workforce: Disparities in NIH Funding Outcomes

Science

19 August 2011
Volume 333, 1015-9

Race, ethnicity and NIH research awards

Ginther DK, Shaffer WT, Schnell J,
Masimore B, Liu F, Haak LL, Kington R

The NIH Intramural Track Record on Diversity: The 'Glass House' Challenge

NIH Intramural Program Investigators (Race/Ethnicity)

	1993	2001	2005	2009	2011
Black	15	22	14	15	15
Hispanic	24	33	39	38	37
American Indian	2	3	1	1	1
Asian	98	115	147	194	201
White	1161	1090	999	968	945
Total	1302	1263	1210	1243	1223

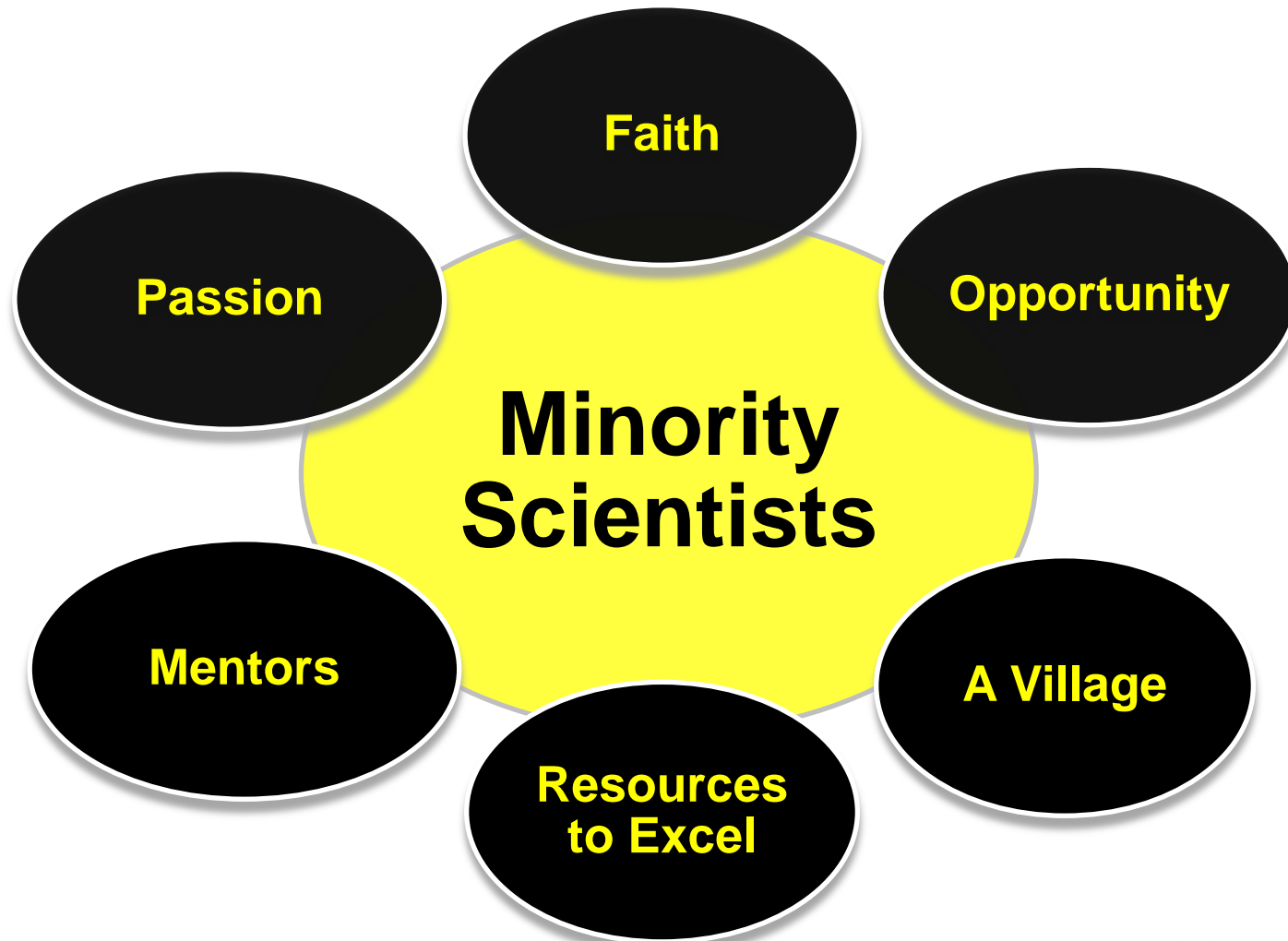
Transformational Leaders ‘Have a Dream’ -- Moving Forward : A Diverse Biomedical Workforce Reflecting a Diverse Nation

“ It ain’t easy being green”

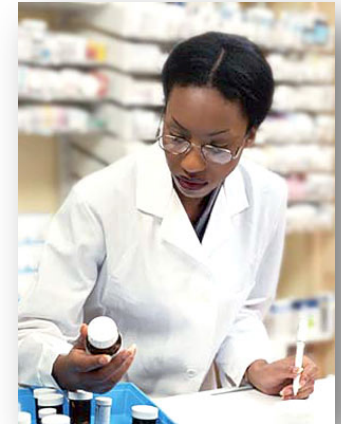
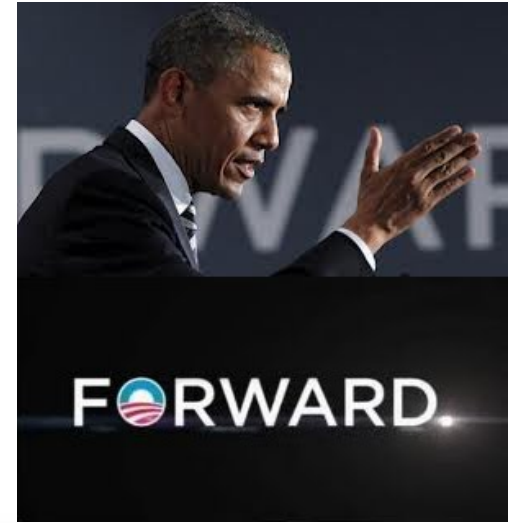
-- Kermit the Frog



Promoting Diversity in the Next Generation: Leading the Biomedical Community



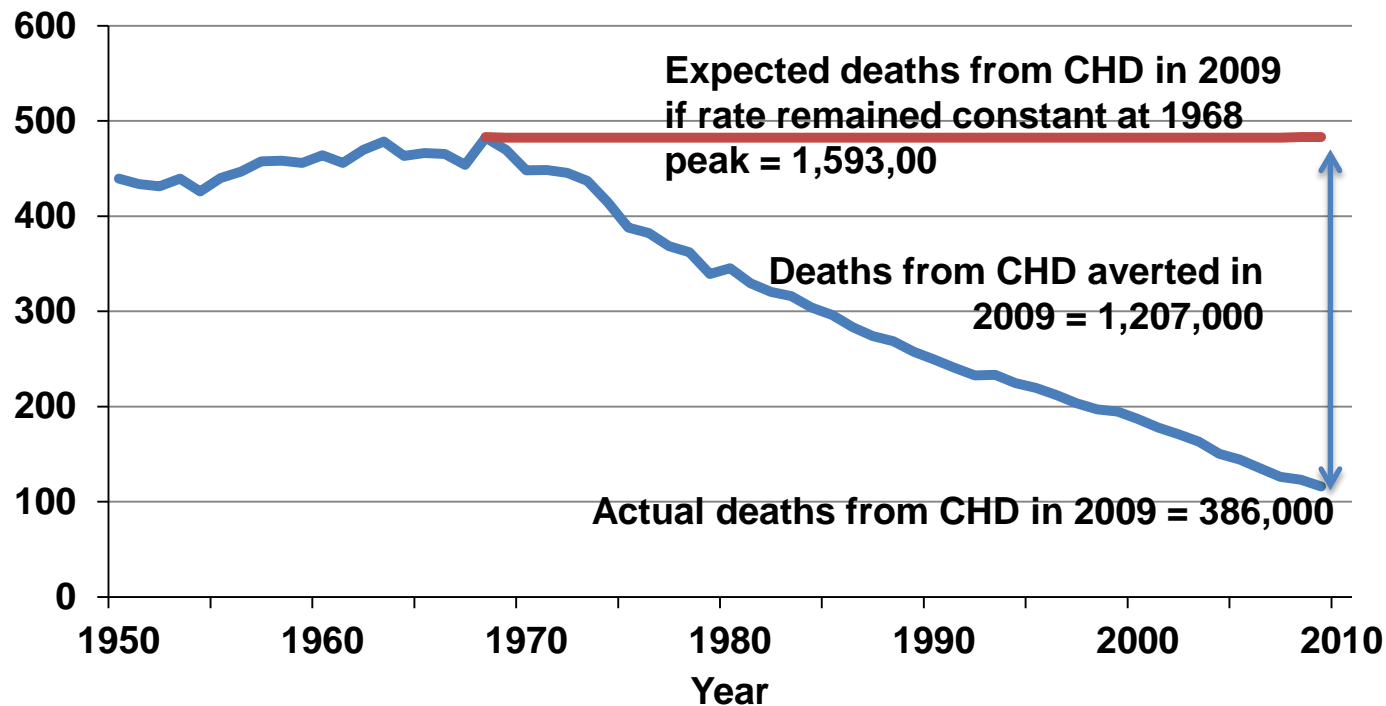
A Diverse Nation's Next Generation: Investing in **ALL** of the available talent



An Inheritance Built on a Legacy of Good Stewardship: Today's Investments for Tomorrow's Breakthroughs

“We do not inherit the land from our ancestors, we borrow it from our children.”

Native American Proverb



Building Upon a Legacy of Excellence: Lessons of One NHLBI Success Story



Framingham Risk Factors



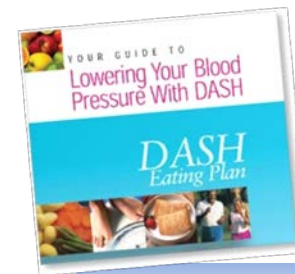
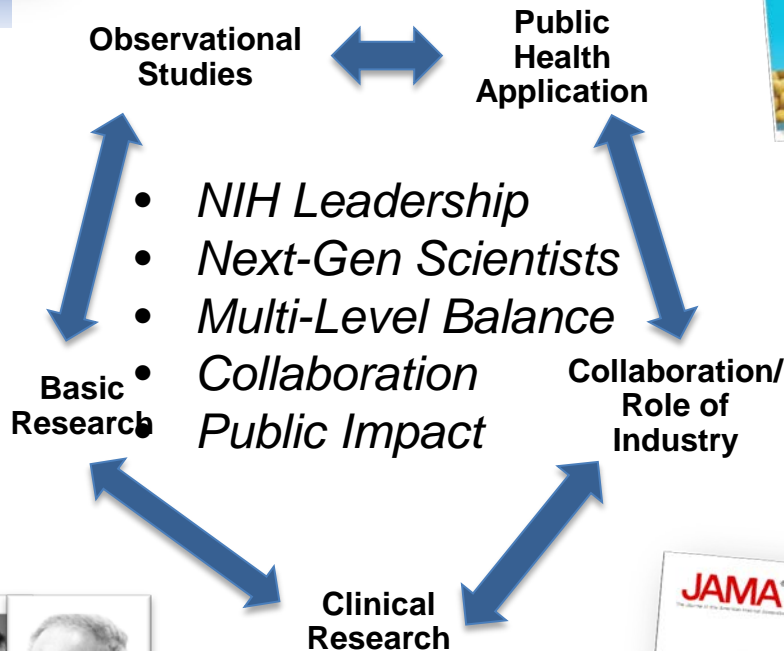
Intramural Research Program: Frederickson, Stadtman



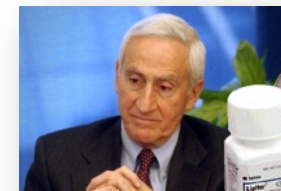
Clinical Research: Tangier's Disease (HDL Cholesterol)



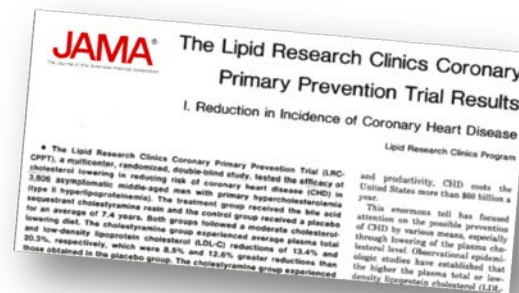
Brown and Goldstein: Nobel Prize (LDL Cholesterol)



Value of Lifestyle Interventions

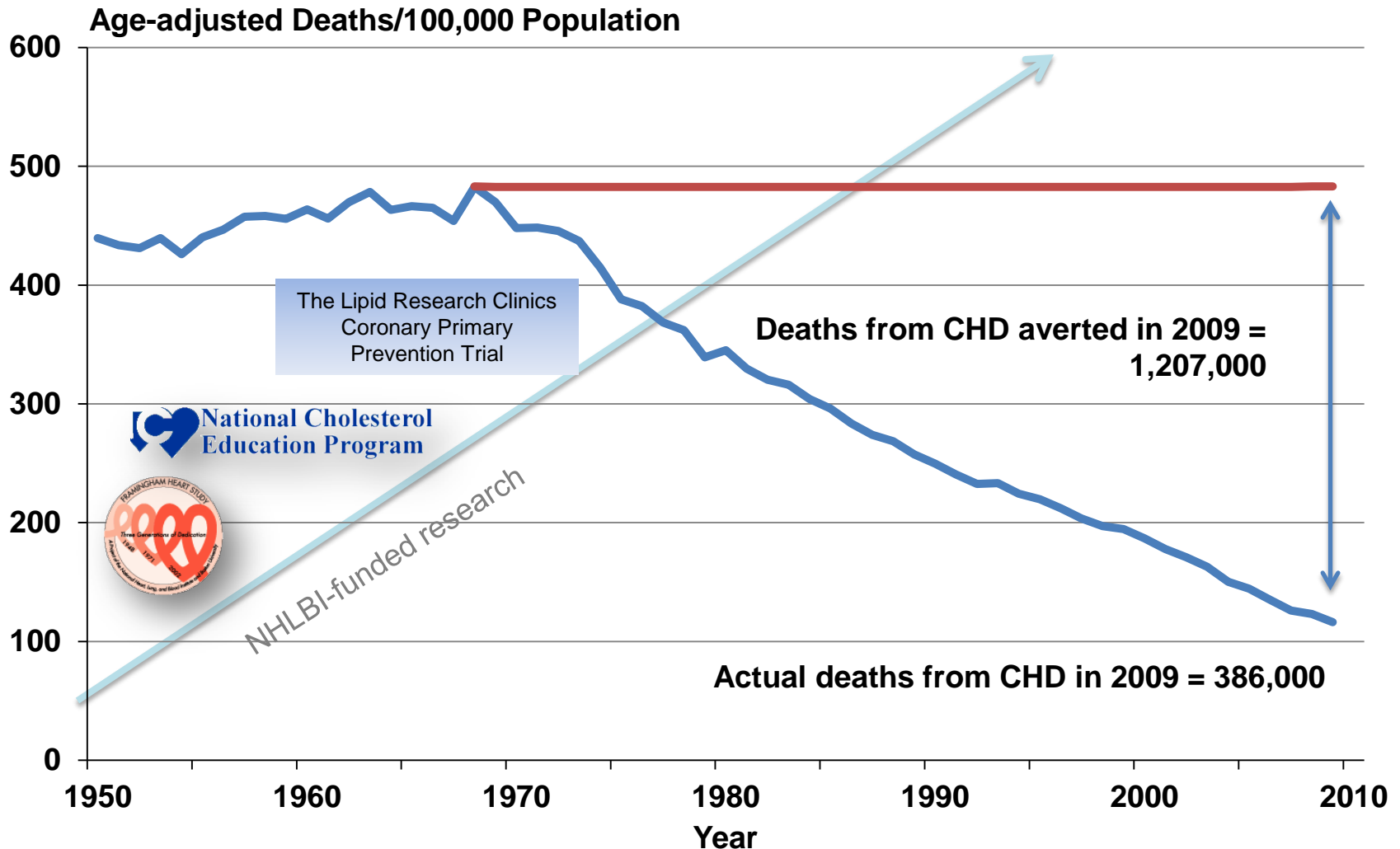


Roy Vagelos: Statins



NHLBI Trial: Lowering Cholesterol Cuts CHD Risk

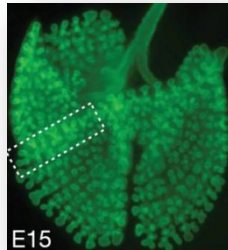
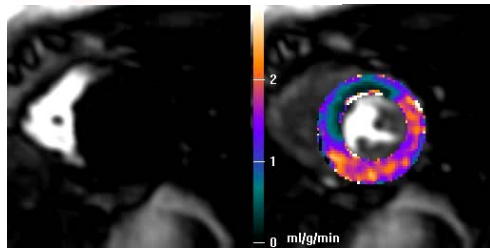
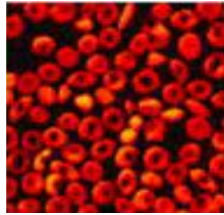
Research to Results – NHLBI at 75: How do we continue to ‘Bend the Curve’?



A Legacy of Catalyzing Transformational Change: Applying New Knowledge in All Communities



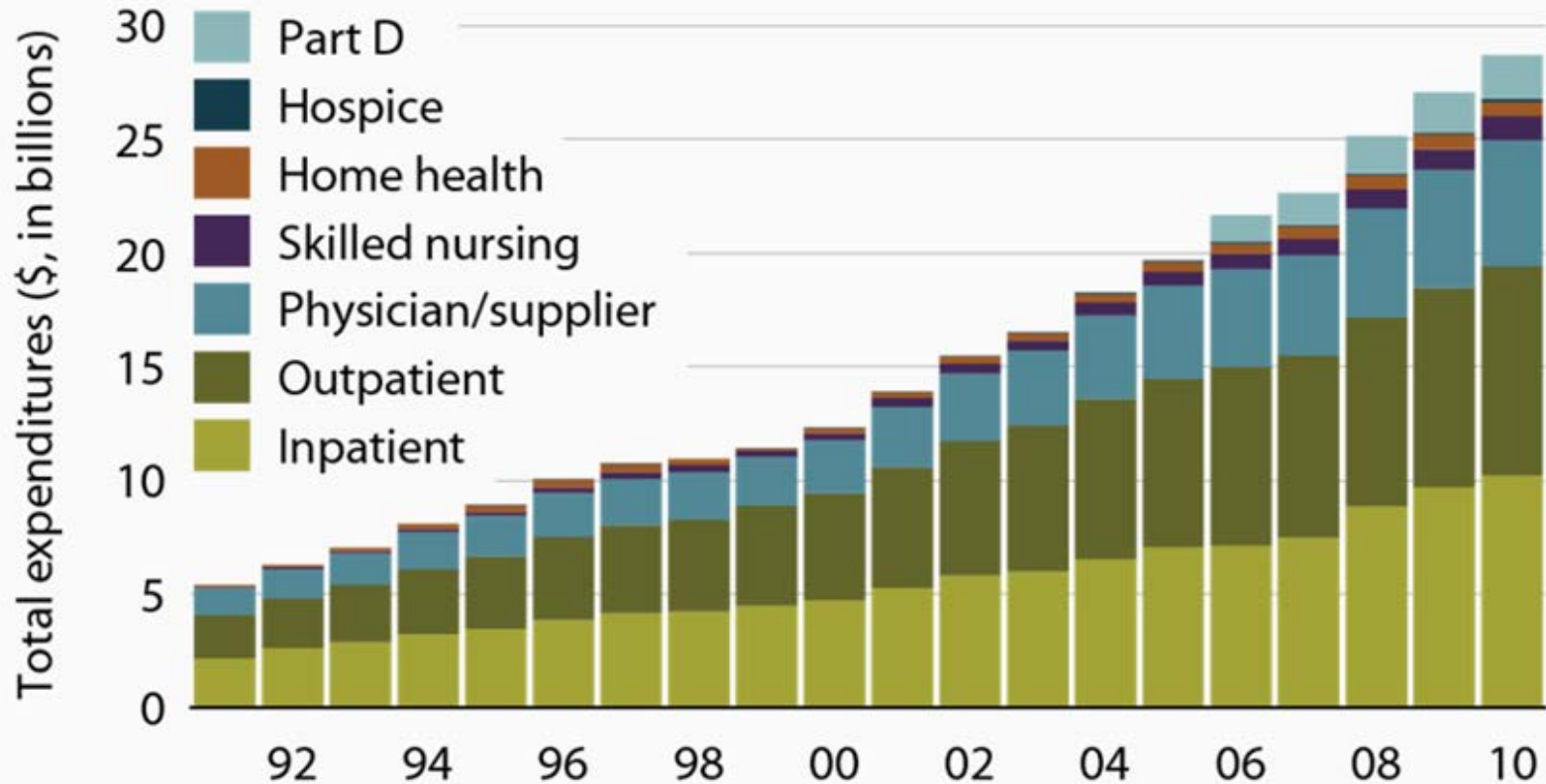
Creating Our Collective Future – NHLBI at 75: 21st Century, Unprecedented Opportunities



- Systems biology/medicine
- Reparative biology/medicine
- Predictive health; Pre-emption Trials
- Health Inequities (local & global)
- New tools and platforms
 - ‘Omics’
 - Imaging
 - Informatics / Computational Modeling
 - Stem cells
 - Nanotechnology/bioengineering
 - Collaborative Knowledge-Intervention Networks

Transformational Change and Chronic Diseases: The Science that 'Bends the Curve' -- An Economic Imperative

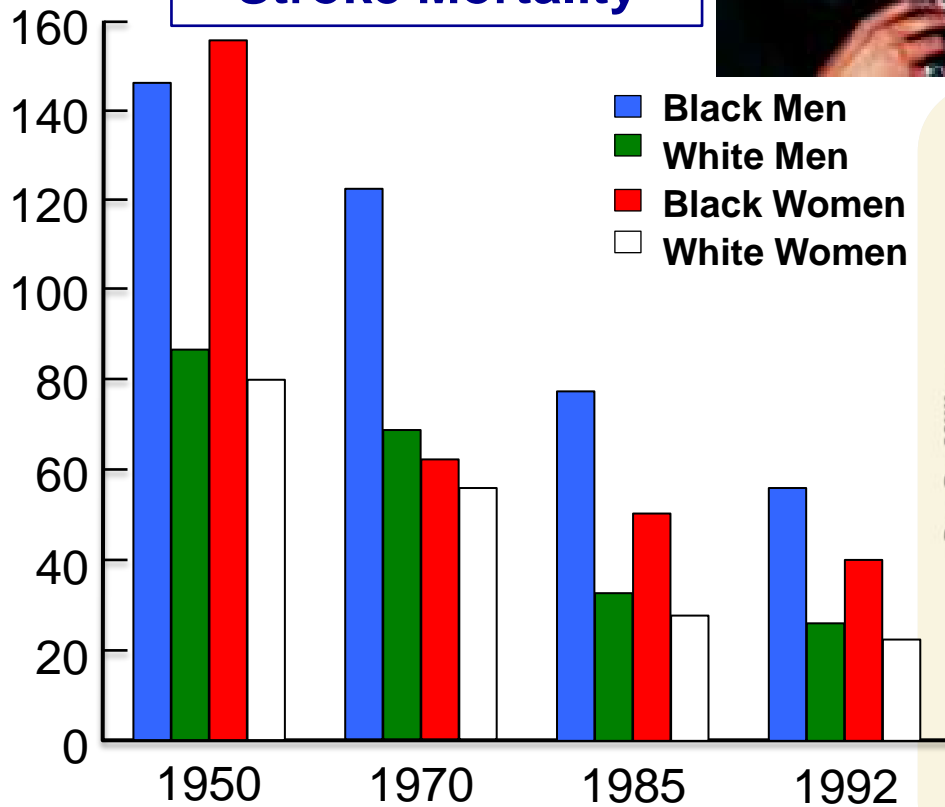
Medicare Expenditures for Chronic Kidney Disease



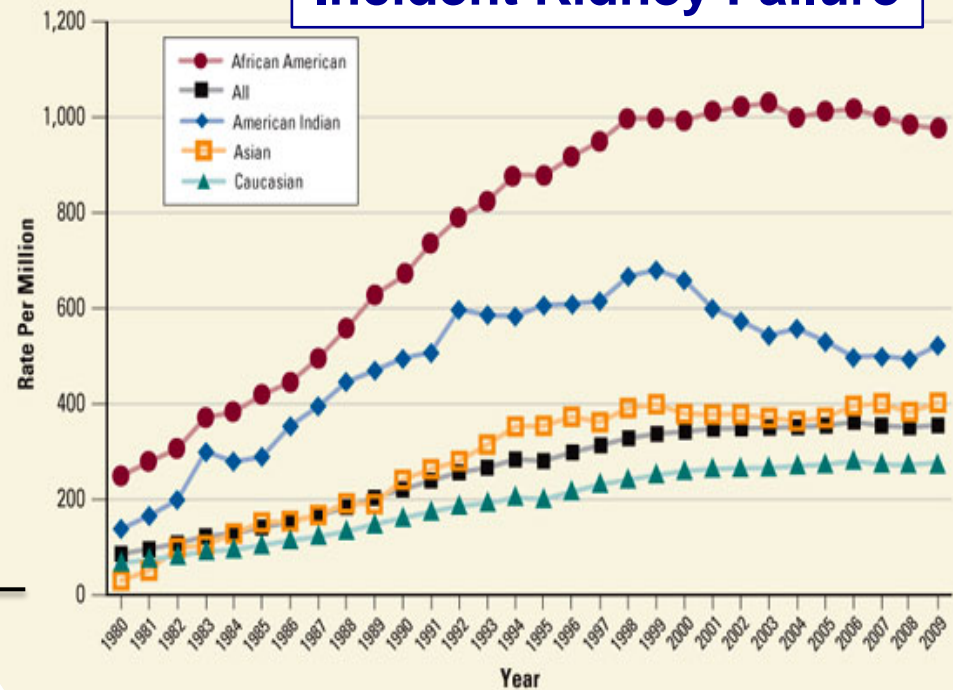
Racial Inequities in Health: Integrating Science and Public Service



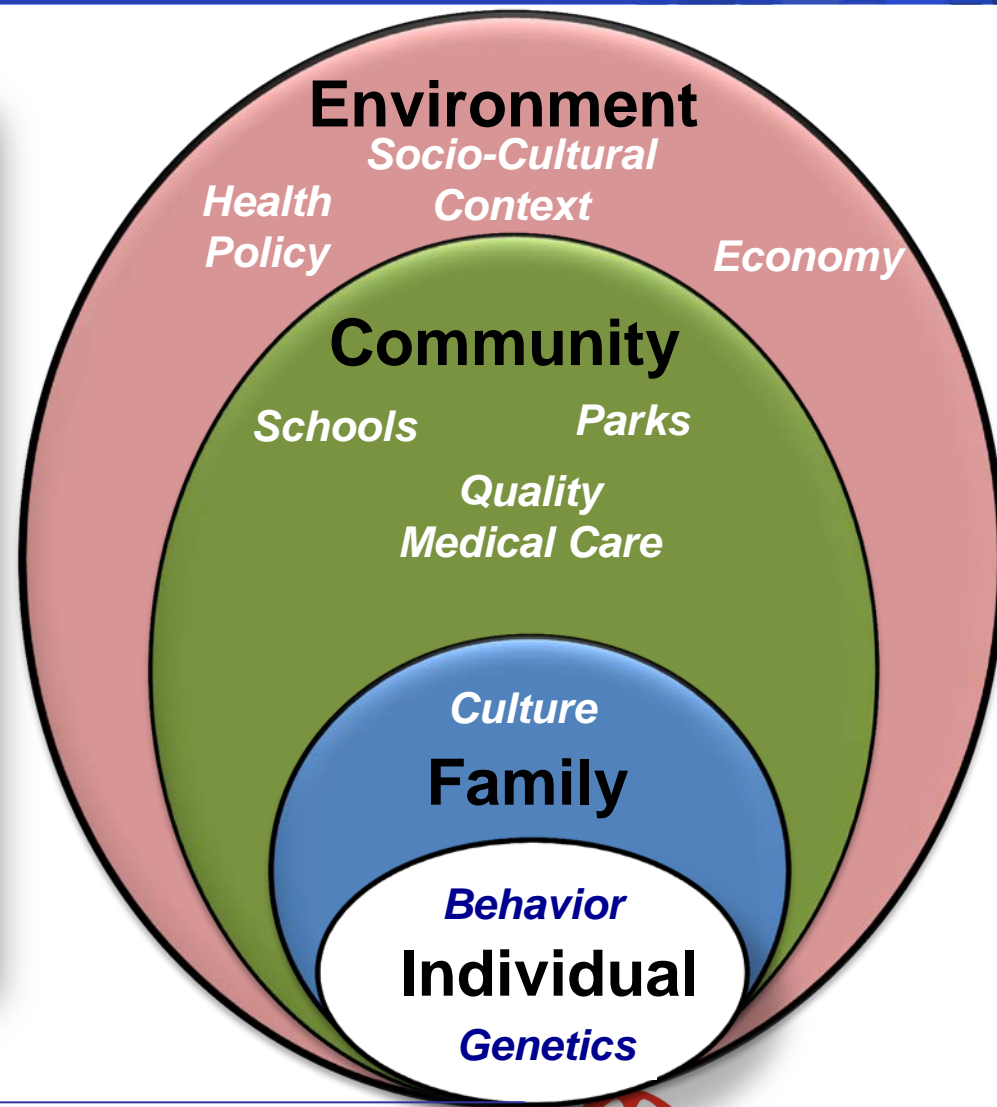
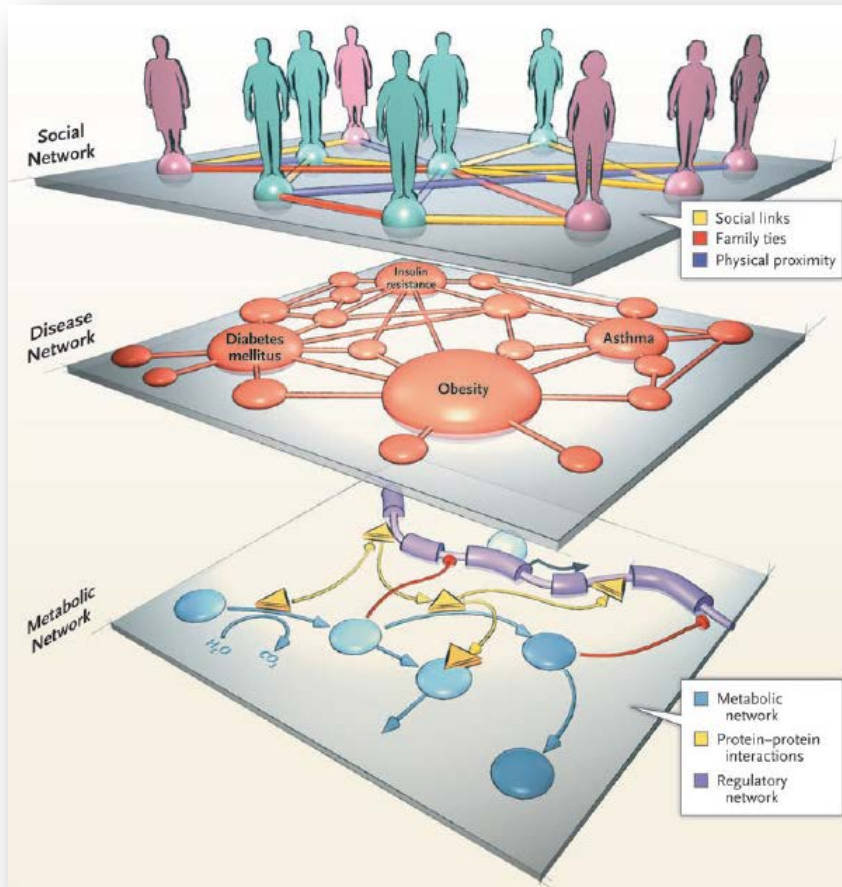
Stroke Mortality



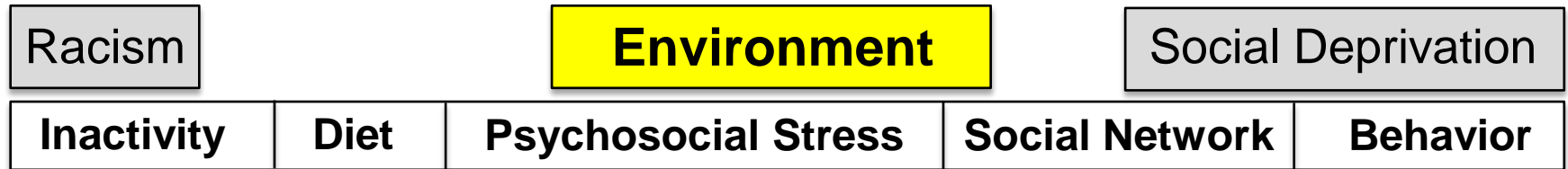
Incident Kidney Failure



Health Inequities: A Complex, Multi-Level, Systems Problem



The Etiologies of Cardiovascular Health Inequities: Multi-Level, Bio-Social Determinants



The Bio-Social Interface

Microbiome

Immune System

Epigenome

Biological Systems

Genetic Variation

Population History

Obesity

Diabetes

Hypertension

Stroke
Kidney Failure

The Ying-Yang of Transformational Change: Integrating New and Traditional Approaches

Classical Research Approach	Systems Medicine Approach
Reductionist	Holistic/Systems-level
Uni-dimensional data	Multi-dimensional data requiring integration
Single-discipline laboratories	Multidisciplinary collaborative teams
Focus on individual molecules	Focus on pathways and networks
Descriptive modeling	Predictive modeling
Largely qualitative	Increasingly quantitative
Low-throughput assays	High-throughput assays
Uni-scalar analysis in individual projects	Multi-scalar, integrative analysis in individual projects
Molecules <u>OR</u> Cells <u>OR</u> Tissues/Organs /Organism <u>OR</u> Populations	Molecules <u>AND</u> Cells <u>AND</u> Tissues/Organs/Organism <u>AND</u> Populations <u>AND</u> Society

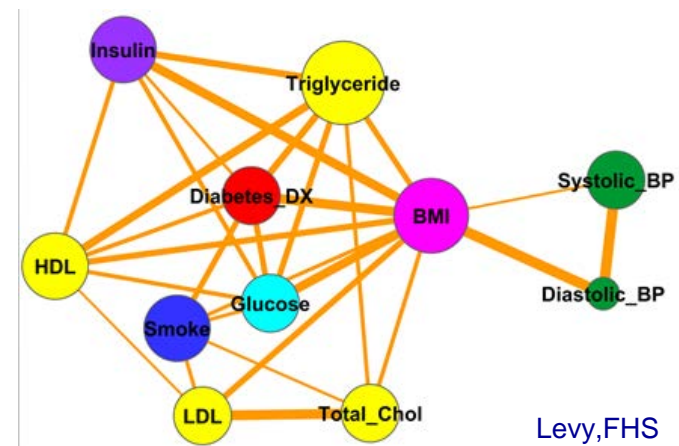
META-Health Study (Atlanta): Racial Difference in CVD Risk Profile

African-American

- Age = 49
- **BMI** = 32
- **SBP** = 125 mmHg
- **Hx of Diabetes** = 13 %
- Framingham Risk = 6.0
- **Low physical activity**
- **Low fruit/vegetable diet**

White

- Age = 51
- BMI = 28
- SBP = 119 mmHg
- Hx of Diabetes = 5 %
- Framingham Risk = 6.0



Levy, FHS

MOREHOUSE & EMORY TEAM UP TO



ELIMINATE CARDIOVASCULAR HEALTH DISPARITIES
M.E.T.A-Health Study

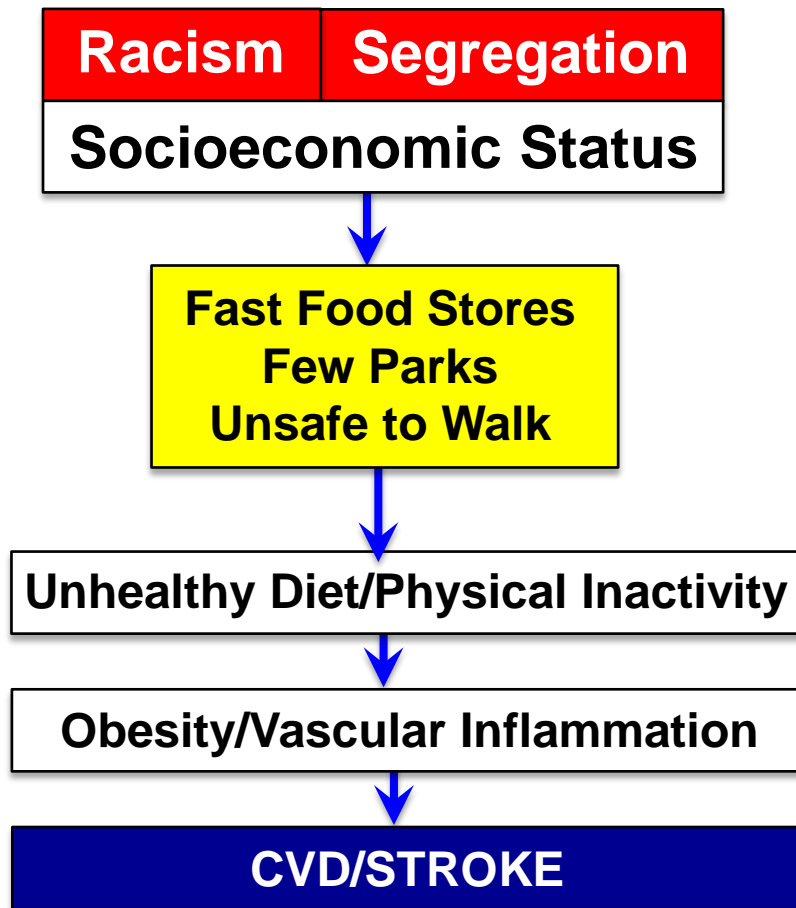
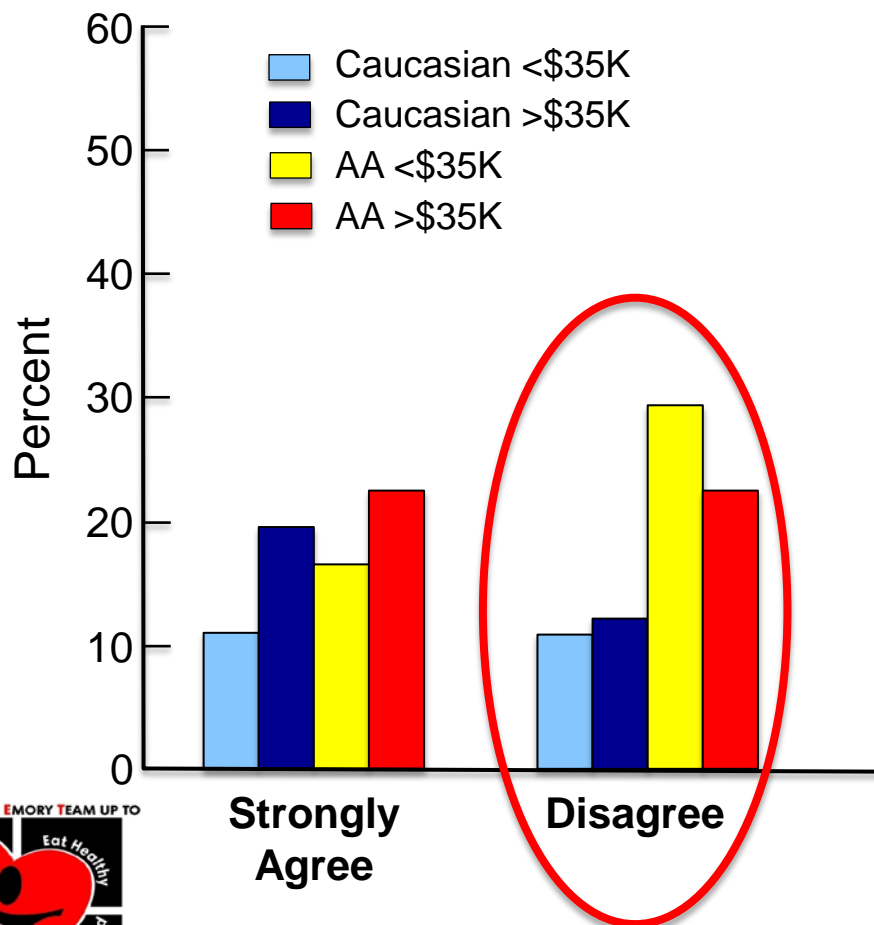
Din, Vaccarino, Gibbons, Quyyumi 2009



National Heart
Lung and Blood Institute

META-Health Study – The Social Determinants of Health: Where you live, work and play matters

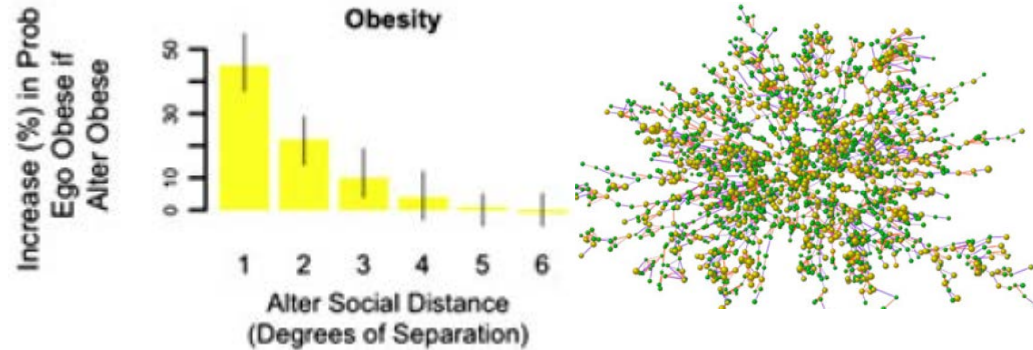
My neighborhood offers many opportunities to be physically active”



Din, Vaccarino, Gibbons, Quyummi 2009



'Social Contagion' of Cardiovascular Disease: Interplay of Social and Biological Systems



Racism **Segregation**

Socioeconomic Status

Social Network

Unhealthy Community
Unhealthy Diet

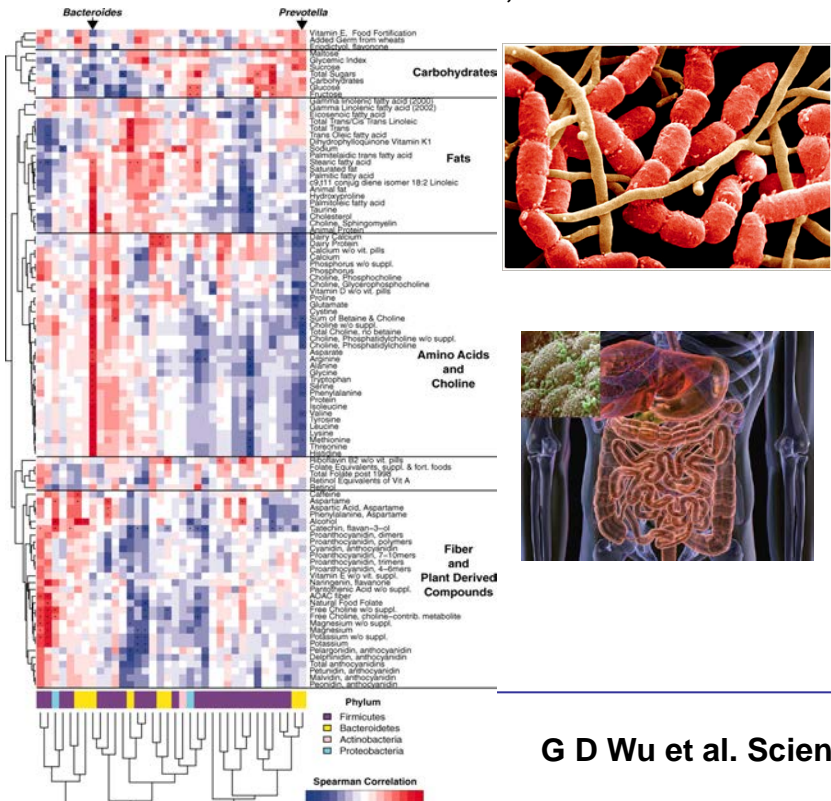
Bio-Social Interface

Digestive System - Microbiome

Immune System Activation

Vascular Dysfunction/Disease

Christakis Nicolas NEJM 2007;357:370-9.



G D Wu et al. Science 2011;334:105-108

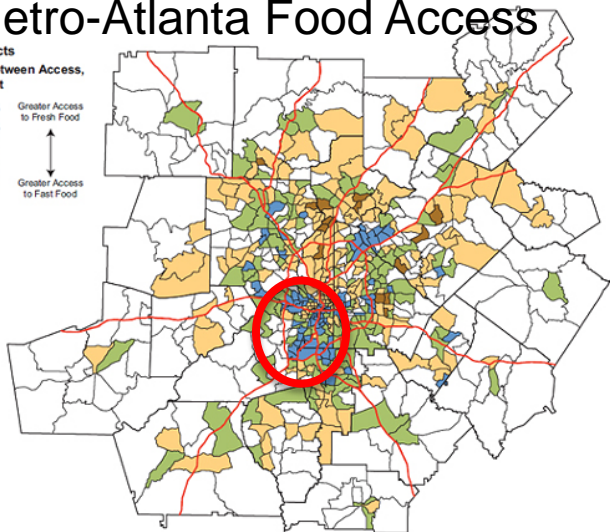
Social Determinants of Heart Disease: Interplay of Social and Biological Systems

Metro-Atlanta Food Access

Census Tracts
Difference Between Access,
Fresh vs. Fast

- 5.3 - -2.5
- 2.4 - -0.5
- 0.4 - 0.5
- 0.6 - 2.9
- 3.0 - 5.2

Greater Access to Fresh Food
↑
↓
Greater Access to Fast Food



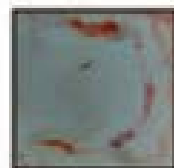
Control



Cy-3-G



PCA



Cy-3-G + PCA



Control + Abx



Cy-3-G + Abx



PCA + Abx



Cy-3-G + PCA + Abx

Racism

Segregation

Socioeconomic Status

Social-Environment

**Food Desert
Unhealthy Diet**

Bio-Social Interface

Microbiome

Immune System Activation

Vascular Dysfunction/Disease

The Etiologies of Cardiovascular Health Inequities: Multi-Level, Bio-Social Determinants



The Bio-Social Interface

Microbiome

Immune System

Epigenome

Biological Systems

Genetic Variation

Population History

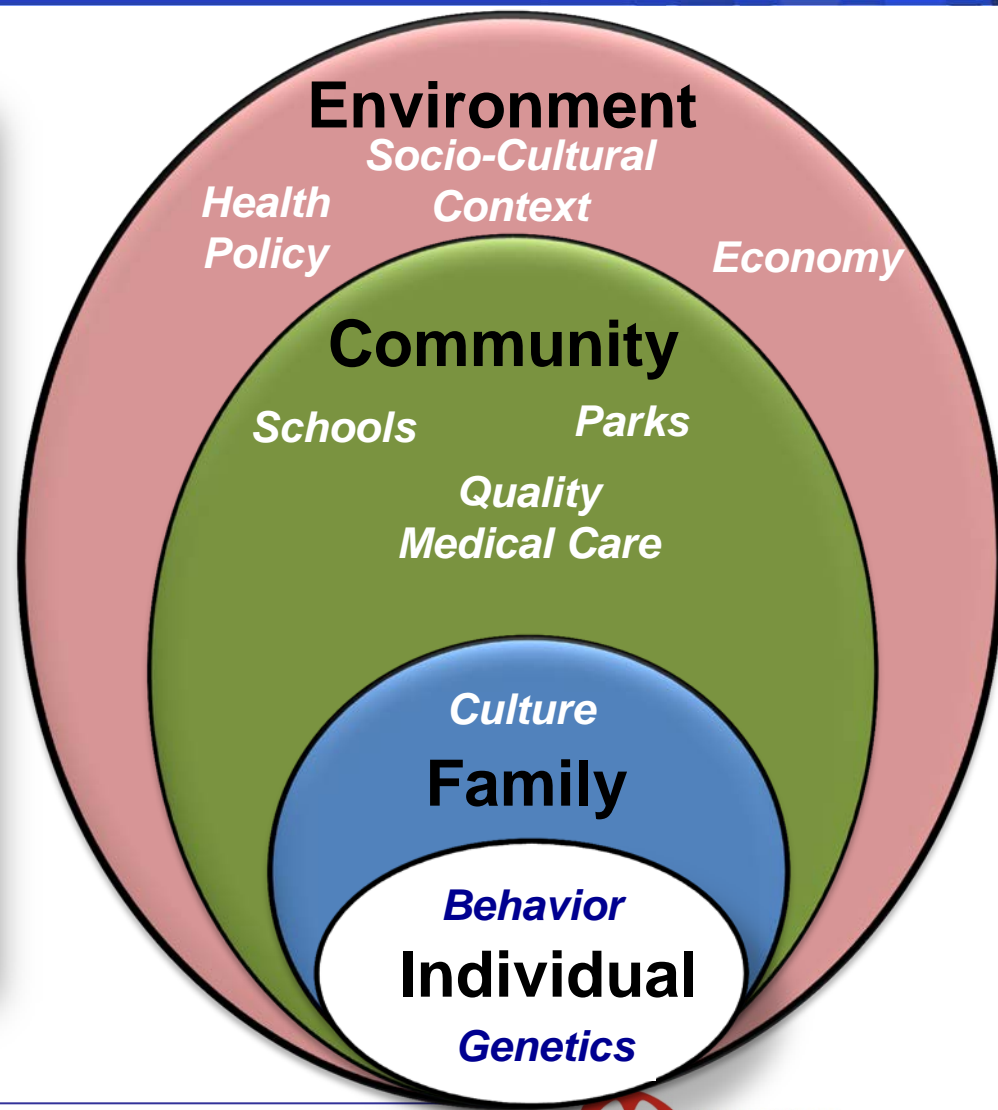
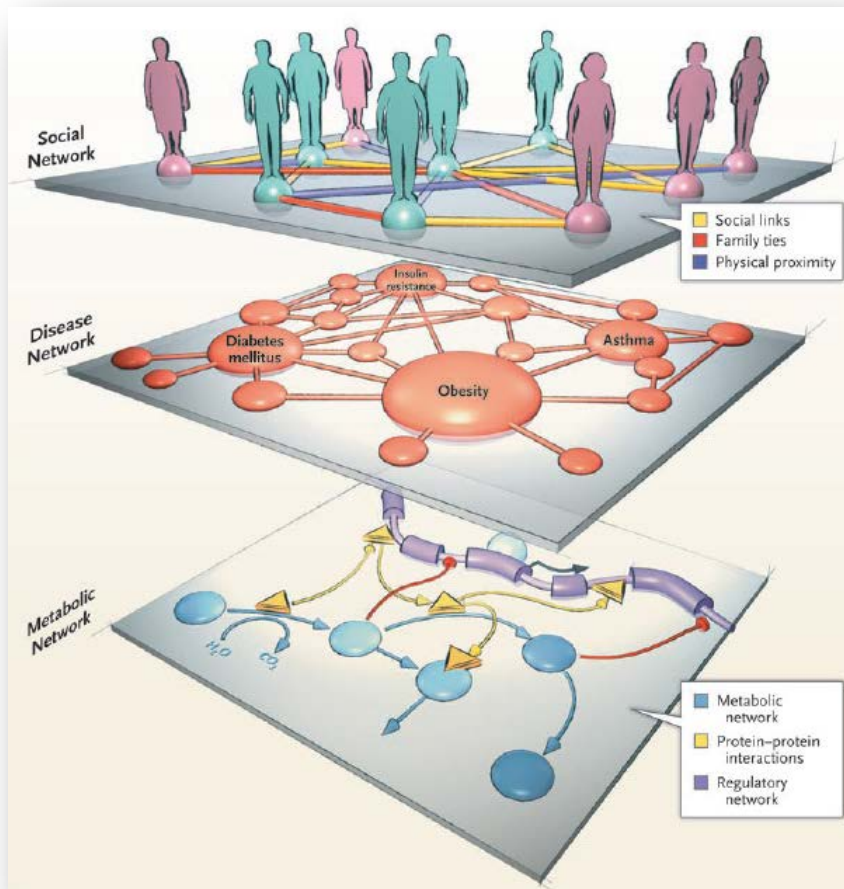
Obesity

Diabetes

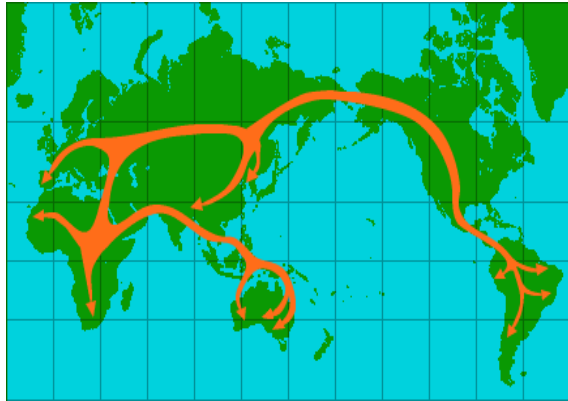
Hypertension

Stroke
Kidney Failure

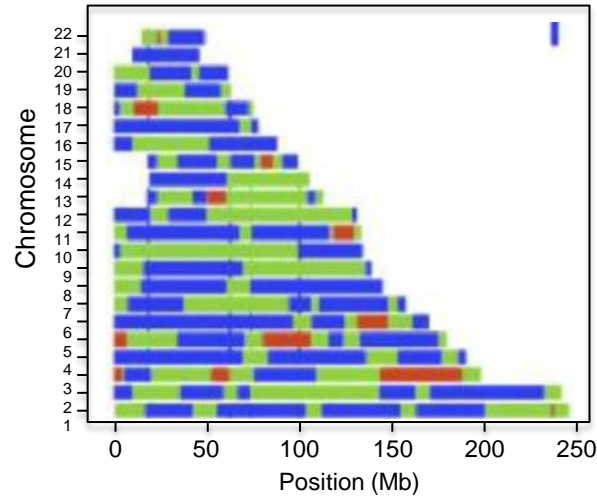
Addressing Health Inequities: Toward a, Multi-Level, Systems Approach



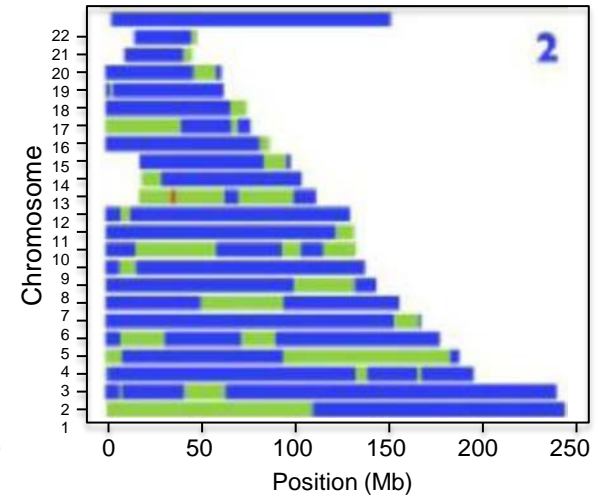
Racial Health Disparities & Genomic Variation: Footprints of Population History and Admixture



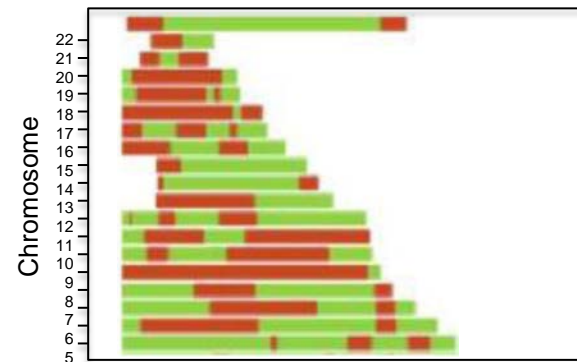
Representative African American



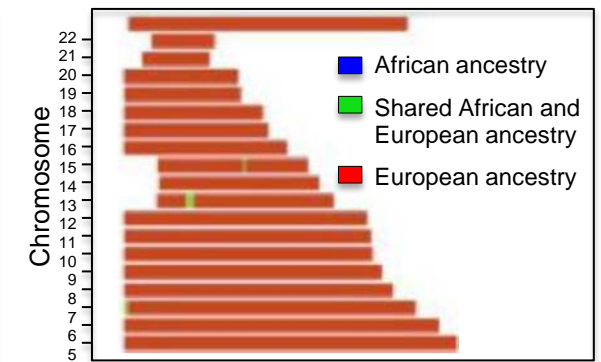
Recent admixture



Recent European ancestry



High degree of European ancestry



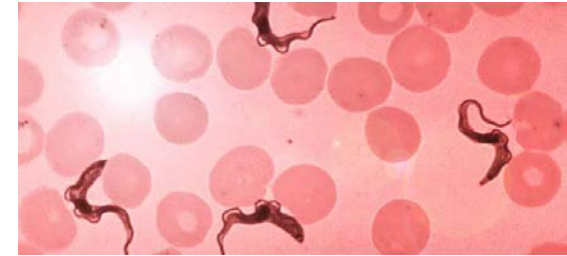
Science

13 August 2010
Volume 329, Issue 5993

Association of Trypanolytic ApoL1 Variants with Kidney Disease in African- Americans

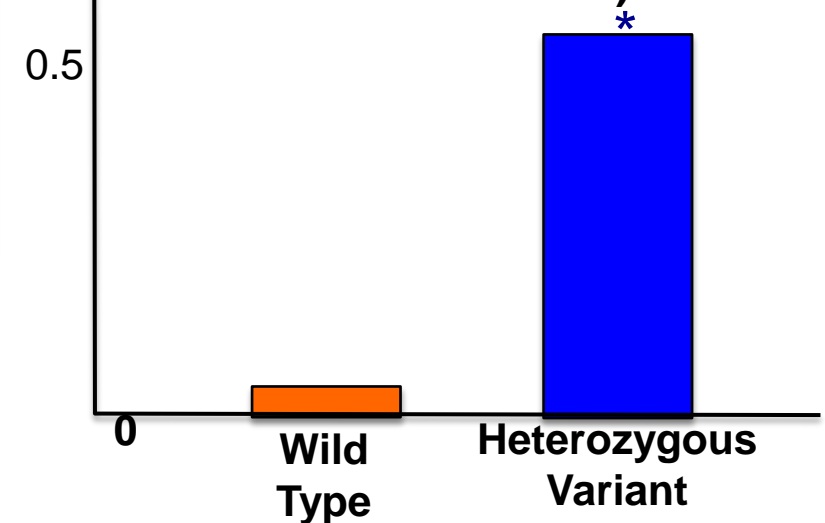
G Genovese, DJ Friedman...JB
Kopp, E Pays, MR Pollack

- Variant > 5-fold increased risk of ESKD
- Hypertension, HIV, SCD
- 12% of AA have 2 risk alleles (G1/G2)



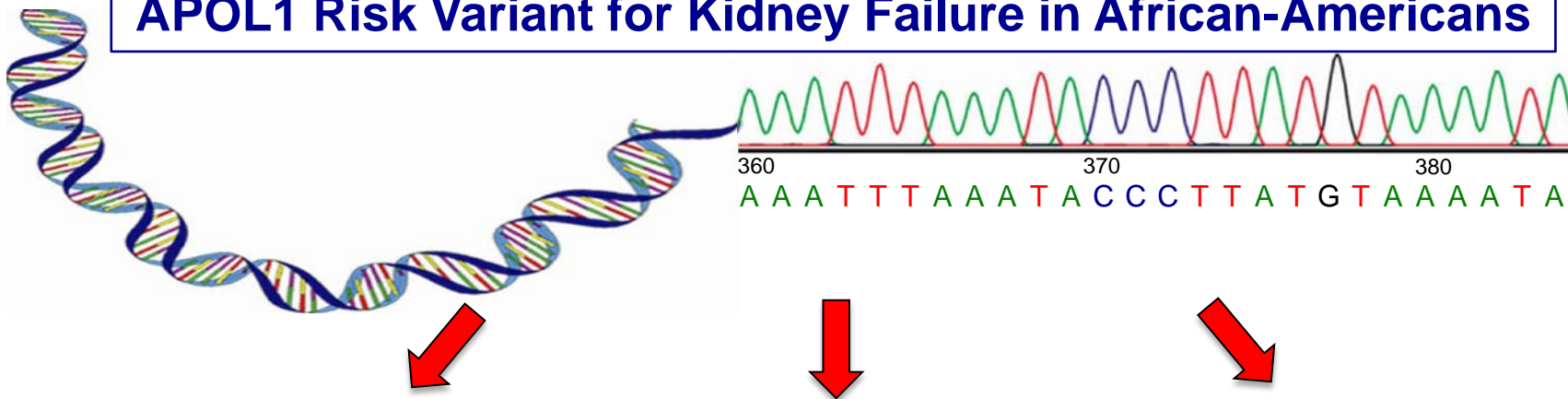
1.0
0.5
0

APOL1 Trypanolytic Activity (HDL; Immune Cells Vascular Cells)



WHAT IF : APOL1-Based Genomic Medicine Therapeutic Strategy to Reduce Racial Inequities in CKD

APOL1 Risk Variant for Kidney Failure in African-Americans



Risk prediction

DEA # GD000000 Lic # ME 0000000

M. F. Doe, M.D.
Associates in Internal Medicine
9000 Medical Center Drive, Suite 300
East Orange, NJ 90314
Tel: (301) 712-6699 FAX: (301) 712-8094

Name: _____ Age: _____

Rx Start anti-hypertensive treatment at lower goal of 130/80 in at-risk APOL1 carriers

Label Refill 0 12 24 Signature _____

Pharmacogenomics

DEA # GD000000 Lic # ME 0000000

M. F. Doe, M.D.
Associates in Internal Medicine
9000 Medical Center Drive, Suite 300
East Orange, NJ 90314
Tel: (301) 712-6699 FAX: (301) 712-8094

Name: _____ Age: _____

Rx Angiotensin Blockers in African-Americans with high-risk APOL1 genotype

Label Refill 0 12 24 Signature _____

New therapies

DEA # GD000000 Lic # ME 0000000

M. F. Doe, M.D.
Associates in Internal Medicine
9000 Medical Center Drive, Suite 300
East Orange, NJ 90314
Tel: (301) 712-6699 FAX: (301) 712-8094

Name: _____ Age: _____

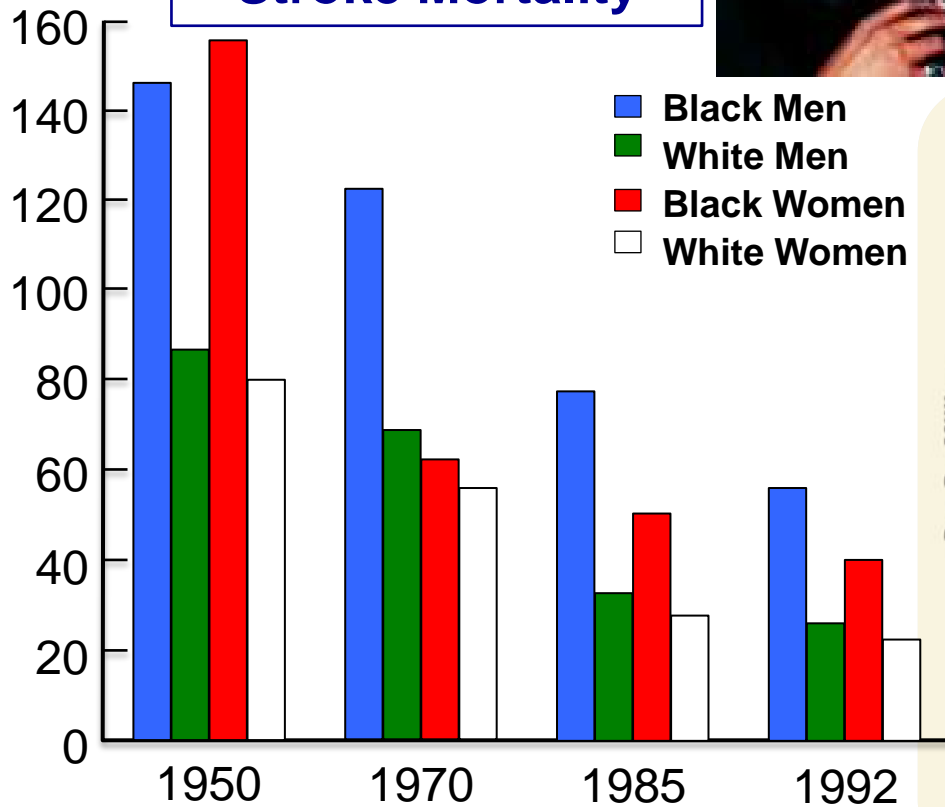
Rx New drugs targeting mediators downstream of APOL1 to prevent kidney failure

Label Refill 0 12 24 Signature _____

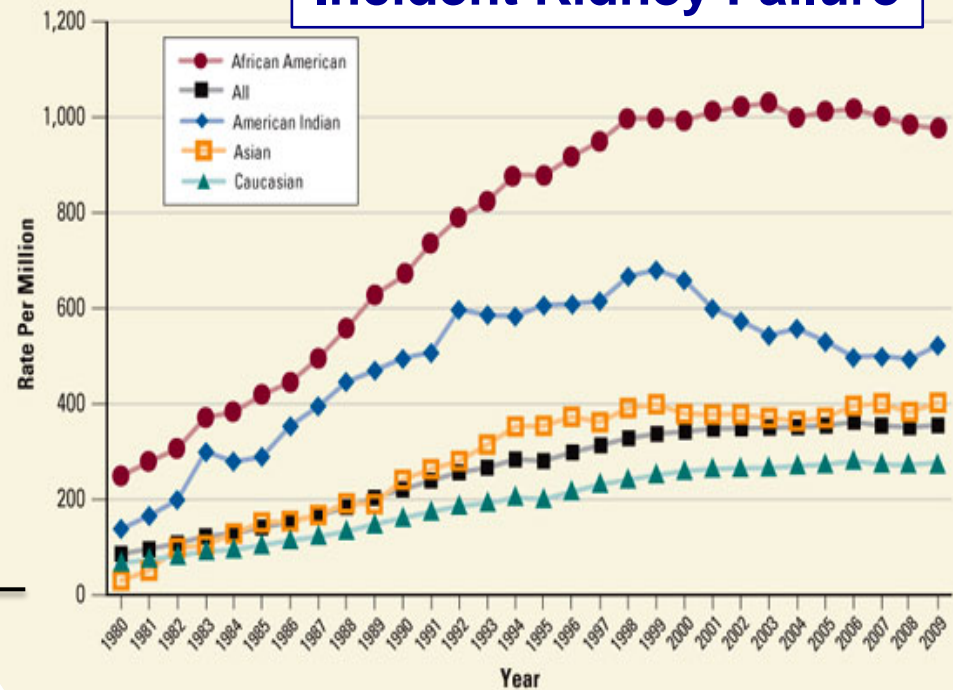
Prediction, Pre-emption and Remission of Chronic Diseases: ‘Bending the Curves’ of Racial Inequities in Health:



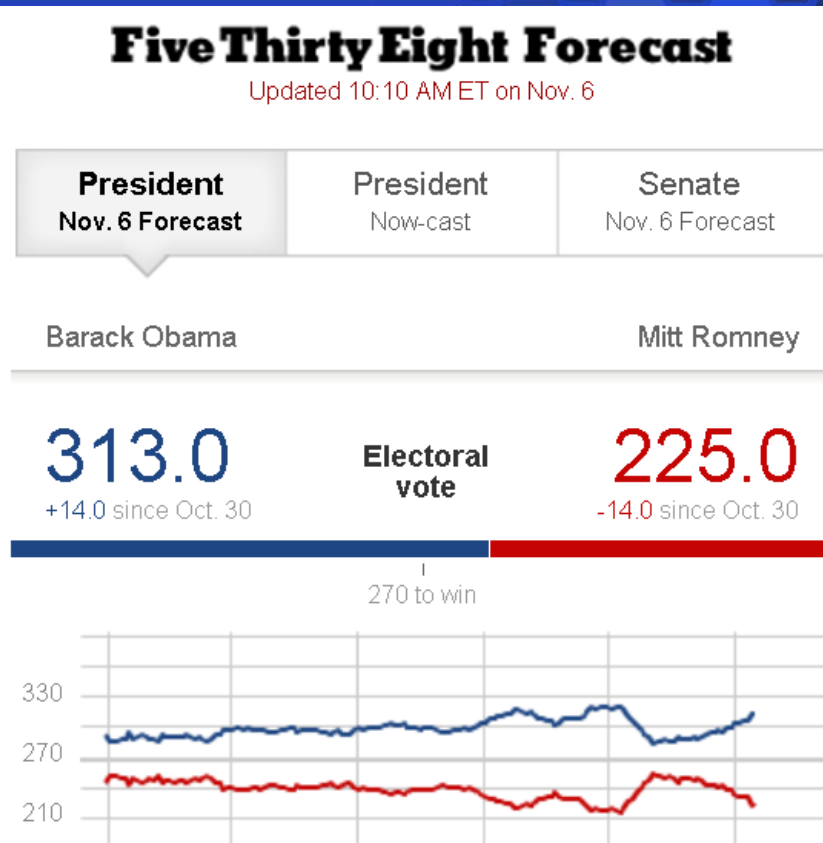
Stroke Mortality



Incident Kidney Failure

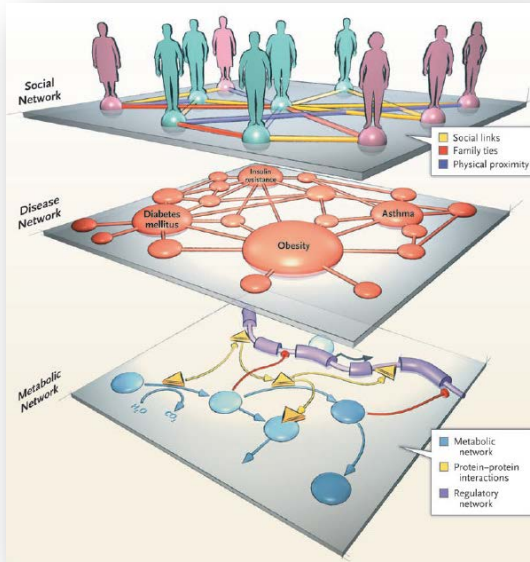


Transforming 'Big Data': Towards Predictive Health and Systems Medicine



Nate Silver

A Systems Approach to the NHLBI Portfolio: Synergy with Scientific Community Resources:



“Scientific Commons”

Diverse Cohort Study Datasets

Clinical Research
Registry-Biobanks

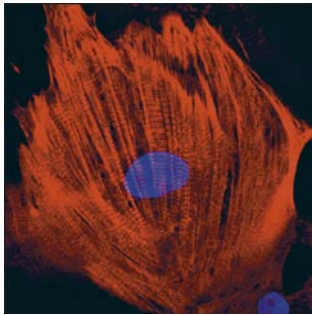
Phenomics:
Ontologies

Bioinformatic Tools;
Computer Modeling

Open ‘Omic’ Data
Repositories

Schadt EE. Nature 2009;461:218-23; Barabasi A. NEJM 2007;357:404-7

Imagine the Future: The NHLBI at 75



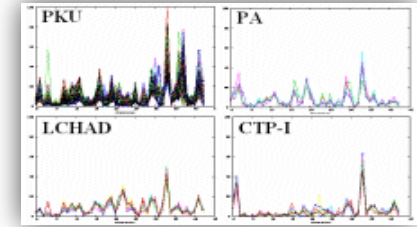
iPSCs



Astute Clinicians



Cohort Datasets



Proteomics/Metabolomics

**From 'Bench-to-Bassinet':
Phenomics Atlas of
Congenital Heart Disease**



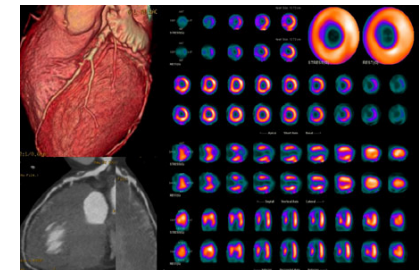
Genomics



Big Data- Ontologies
Computational Models



Biorepositories

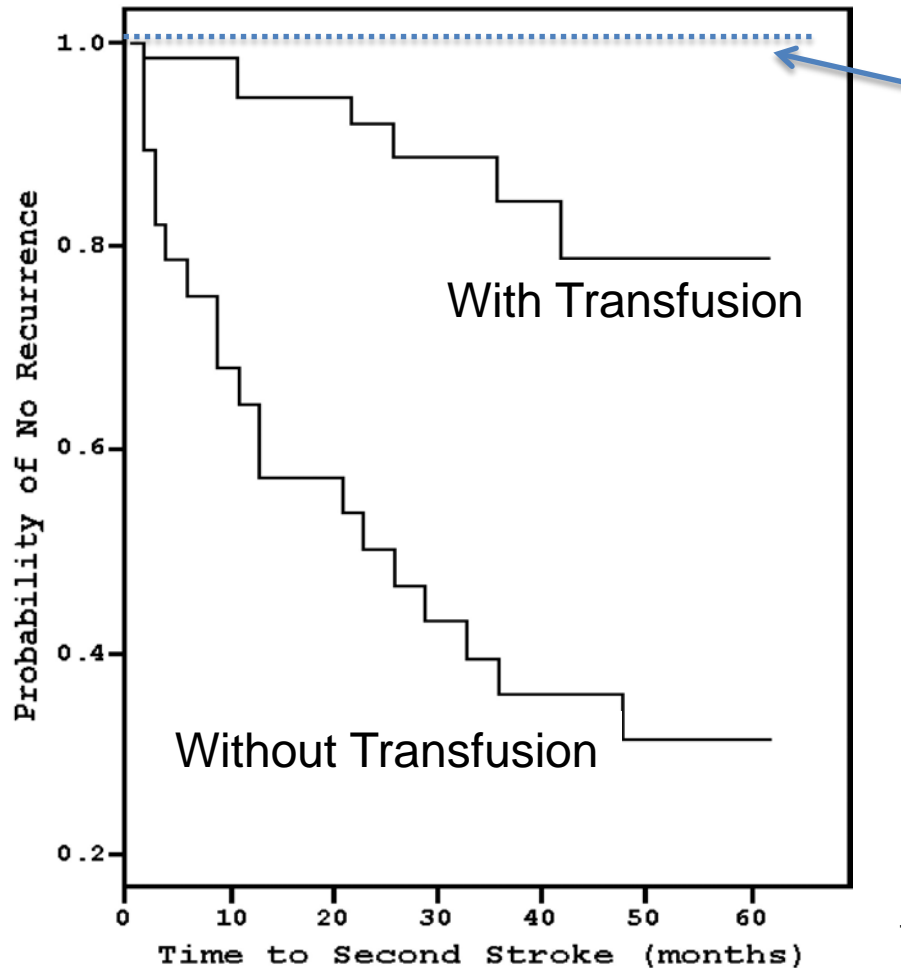


Rubidium PET Scan
Rubidium PET scan demonstrating apical infarction, with comparative CTA images revealing soft plaque in LAD.

Imaging

“What If” Unprecedented Opportunities: Eliminating Stroke and Cognitive Impairment in Sickle Cell Disease?

Recurrent Stroke



What if

- *Modifier genes?*
- *Vasculopathy targets?*



Stroke recurrence with chronic blood transfusions compared with historical controls.

A Systems Approach to the NHLBI Portfolio: Catalyzing Scientific Community Connectivity



Knowledge Networks

**Community-based
Networks**

Diverse Cohort Study Networks

Clinical Trial Networks

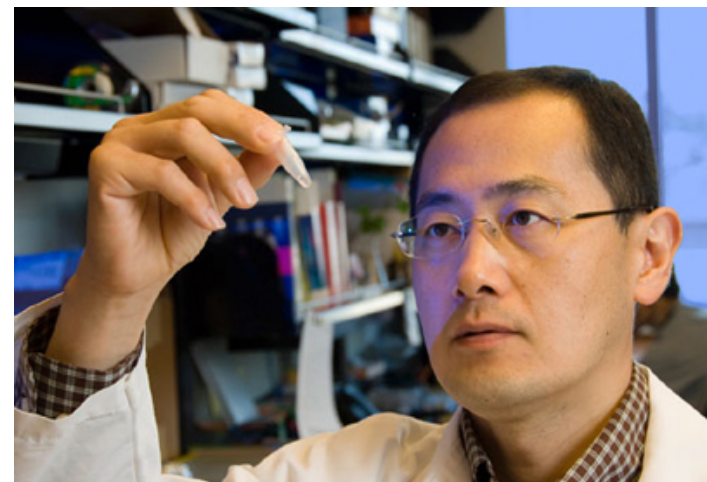
**Genomic Medicine
Networks**

**System Biology
Networks**

**Diverse, Cross-
Disciplinary Trainees**

An Exciting Legacy of Excellence

Recent NHLBI-Funded Nobel Prize Winners



Being Accountable Stewards: Science and Scientists as Public Goods

“We do not inherit the land from our ancestors, we borrow it from our children. ”

Native American Proverb

