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2016 UMass Center for Clinical and  
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May 20th, 9:00 AM

## Keynote Address: The Future of Cardiovascular Epidemiology: Current Trends?

Vasan S. Ramachandran  
*Boston University School of Medicine*

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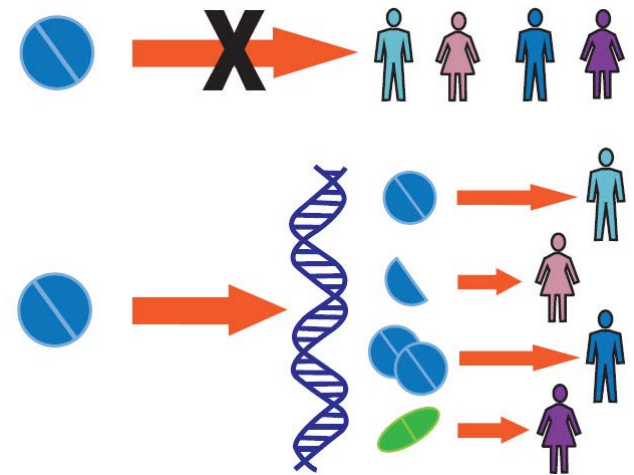
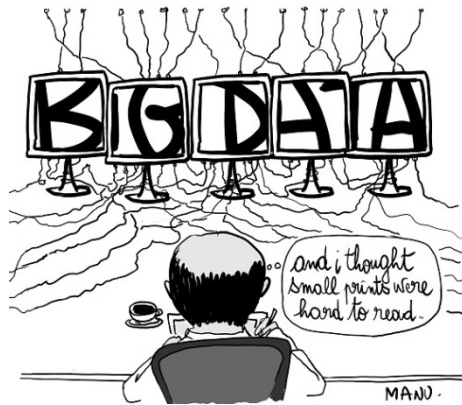
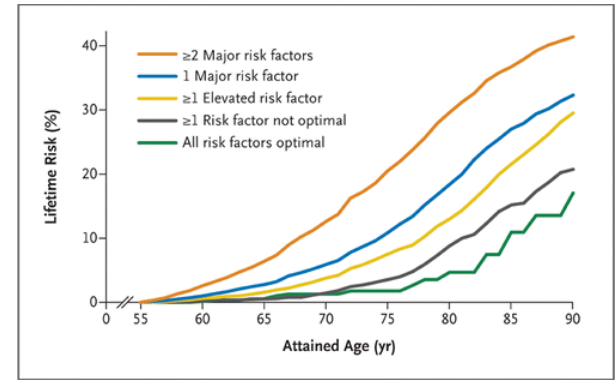
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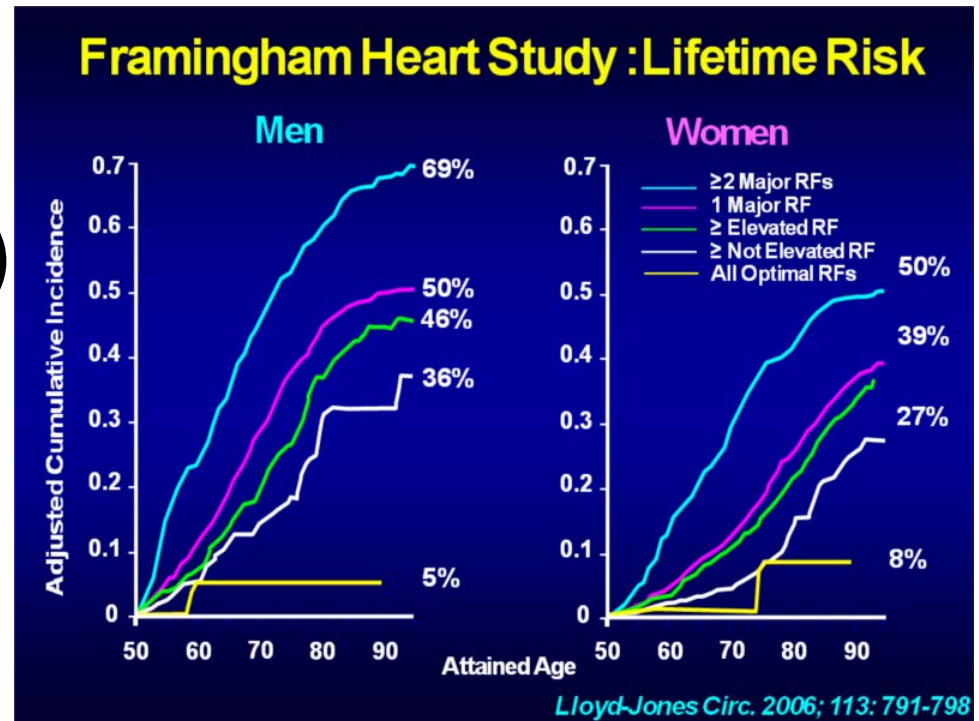
# Future of Cardiovascular Epidemiology

Vasan S. Ramachandran MD



# Future of Cardiovascular Epidemiology

- **Background**
- **Role of**
  - cHealth (community)
  - sHealth (social)
  - mHealth (mobile)
  - eHealth (electronic)
  - gHealth (genomic)
- **A synthesis**



# Time for a Creative Transformation of Epidemiology in the United States

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Michael S. Lauer, MD

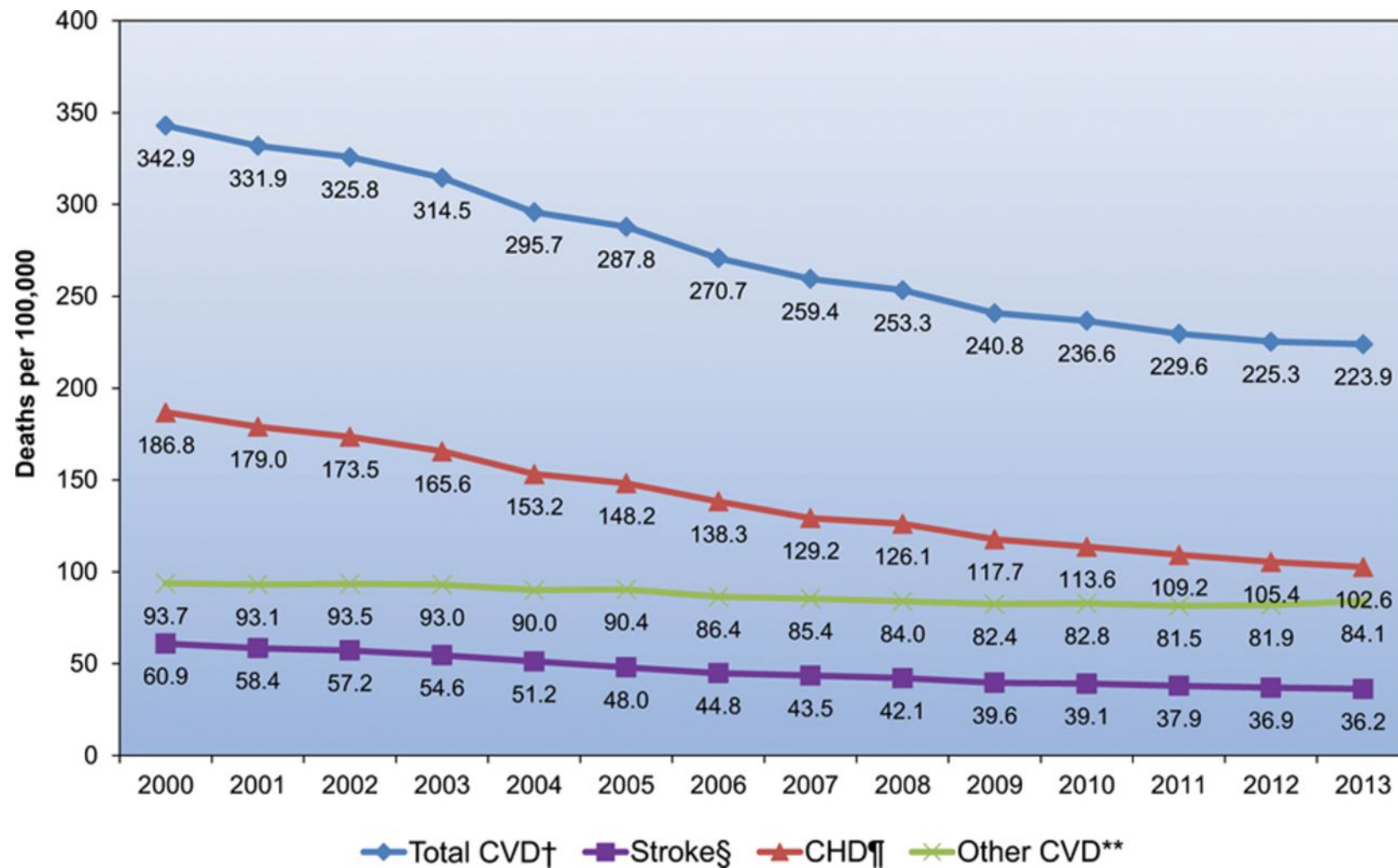
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JAMA, November 7, 2012—Vol 308, No. 17

What has epidemiology done for medical science lately?

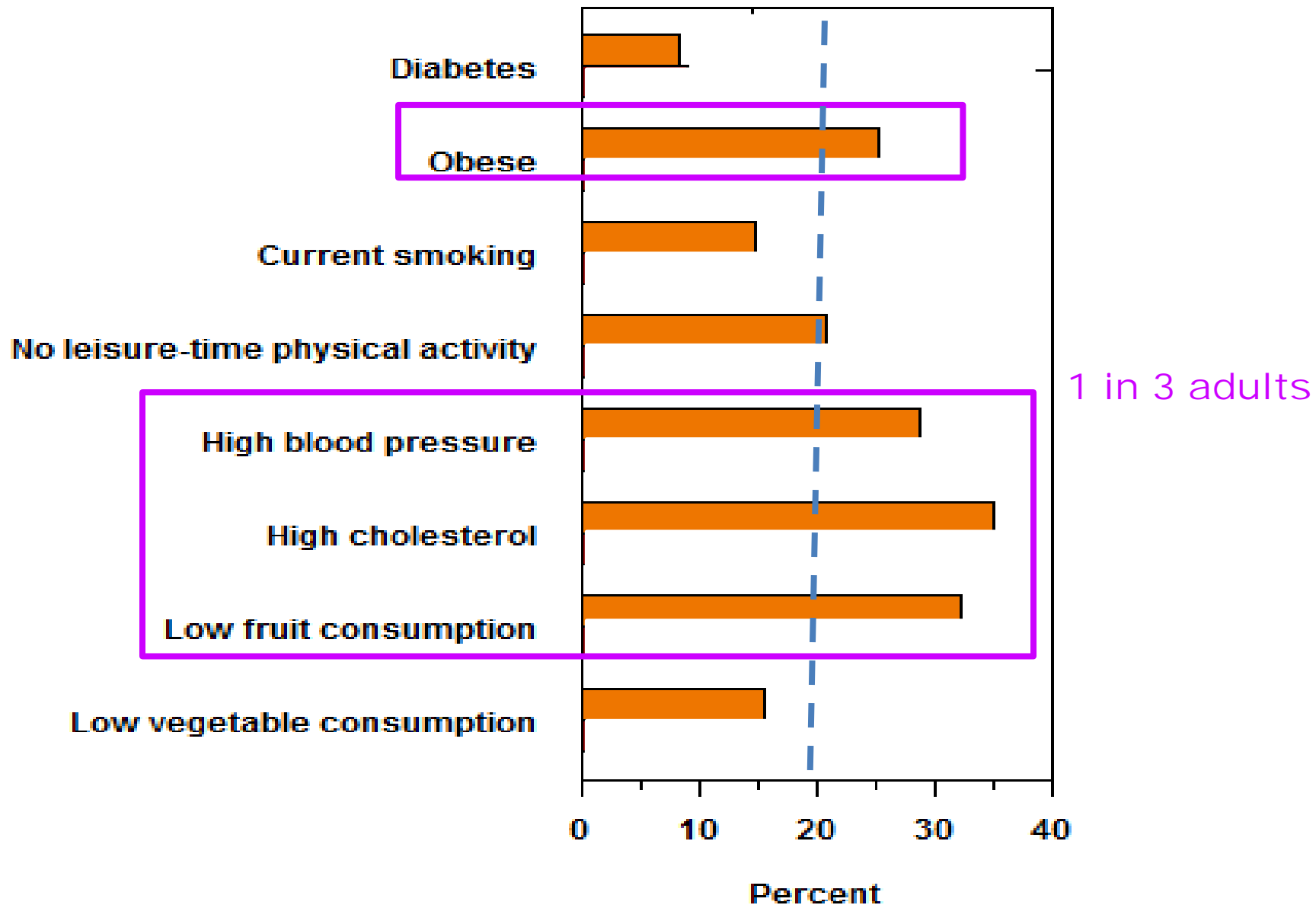
Answer: Much but not enough!

## US age-standardized death rates\* attributable to cardiovascular diseases, 2000 to 2013.



Dariush Mozaffarian et al. *Circulation*. 2016;133:e38-e360

# CVD Risk Factors in US: 2016



# Eight Americas: Investigating Mortality Disparities across Races, Counties, and Race-Counties in the United States

Christopher J. L. Murray<sup>1,2,3</sup>, Sandeep C. Kulkarni<sup>2,4</sup>, Catherine Michaud<sup>2,3</sup>, Niels Tomijima<sup>3</sup>, Maria T. Bulzacchelli<sup>3</sup>, Terrell J. Iandiorio<sup>3</sup>, Majid Ezzati<sup>1,2\*</sup>

PLoS Medicine September 2006 | Volume 3 | Issue 9 | e260

- 1 Asian
- 2 Northland low-income rural white
- 3 Middle America
- 4 Low-income whites in Appalachia and the Mississippi Valley
- 5 Western Native American
- 6 Black Middle America
- 7 Southern low-income rural black
- 8 High-risk urban black

Males

Females

Gap in life expectancy in US of up to 14 years

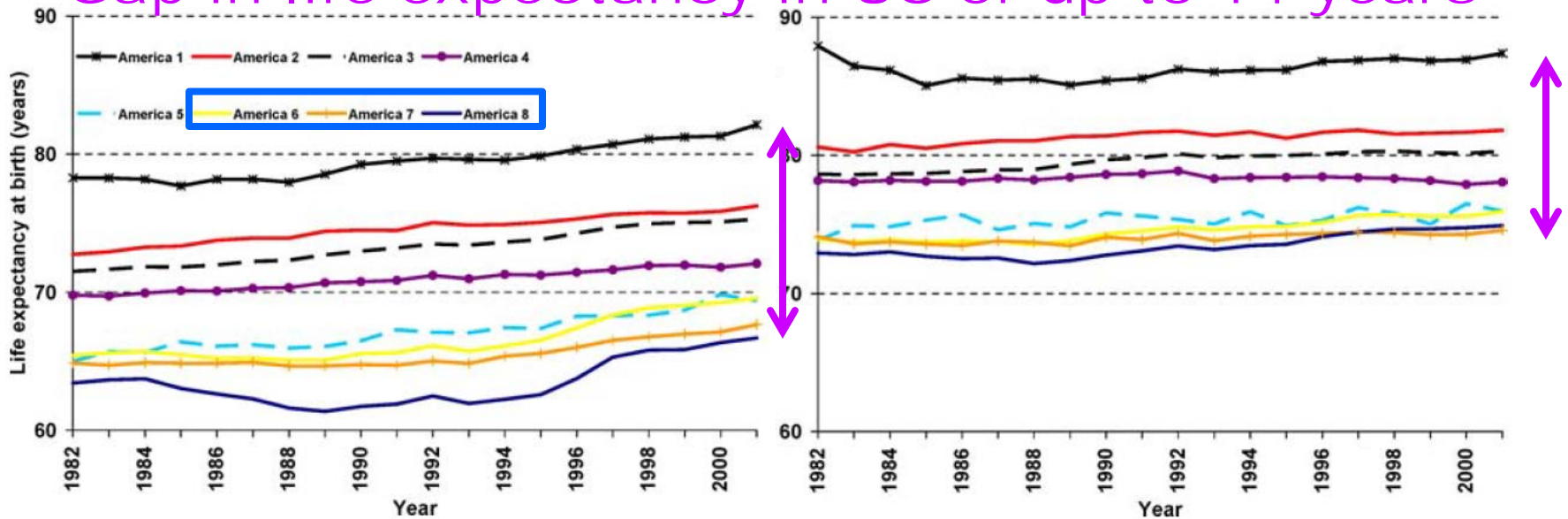
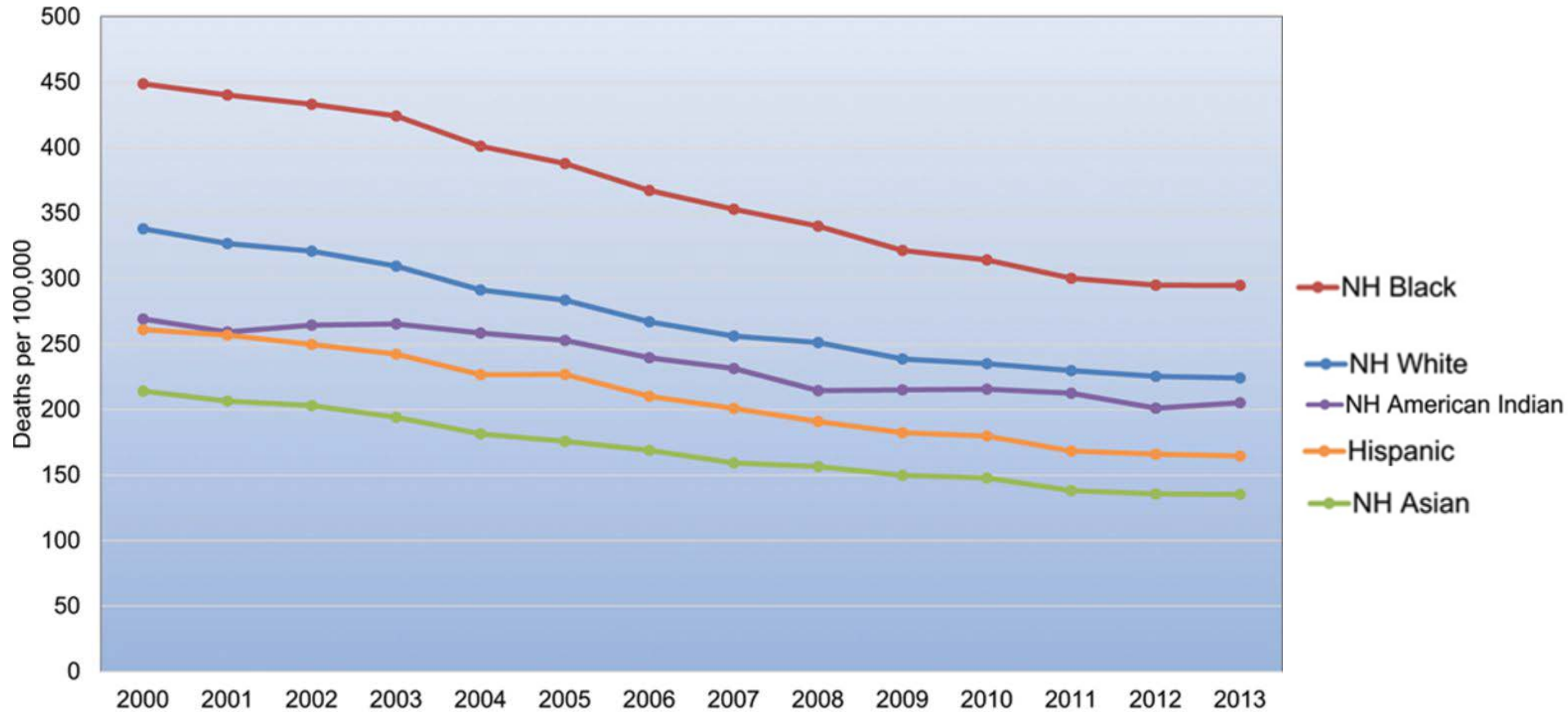


Figure 3. Life Expectancy at Birth in the Eight Americas (1982–2001)

## US age-standardized death rates\* attributable to cardiovascular disease (CVD) by race/ethnicity, 2000 to 2013.



Dariush Mozaffarian et al. *Circulation*. 2016;133:e38-e360



# AHA Policy Statement

## Forecasting the Future of Cardiovascular Disease in the United States

### A Policy Statement From the American Heart Association

Paul A. Heidenreich, MD, MS, FAHA, Chair; Justin G. Trogon, PhD; Olga A. Khavjou, MA;  
Javed Butler, MD, MPH, FAHA; Kathleen Dracup, RN, DNSc;  
Michael D. Ezekowitz, MBChB, DPhil, FRCP, FAHA; Eric Andrew Finkelstein, PhD, MHA;  
Yuling Hong, MD, PhD, FAHA\*; S. Claiborne Johnston, MD, PhD, FAHA; Amit Khera, MD, MSc;  
Donald M. Lloyd-Jones, MD, MSc, FAHA; Sue A. Nelson, MPA;  
Graham Nichol, MD, MPH, FRCP(C), FAHA; Diane Orenstein, PhD\*;  
Peter W.F. Wilson, MD, FAHA; Y. Joseph Woo, MD, FAHA; on behalf of the American Heart Association

*Circulation. 2011;123:933-944*

**Table 1. Projections of Crude CVD Prevalence (%), 2010–2030 in the United States**

Year	All CVD*	Hypertension	CHD	HF	Stroke
2010	36.9	33.9	8.0	2.8	3.2
2015	37.8	34.8	8.3	3.0	3.4
2020	38.7	35.7	8.6	3.1	3.6
2025	39.7	36.5	8.9	3.3	3.8
2030	40.5	37.3	9.3	3.5	4.0
% Change	9.9	9.9	16.6	25.0	24.9

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# cHealth: Health of Communities

International Journal of Epidemiology  
© International Epidemiological Association 1985

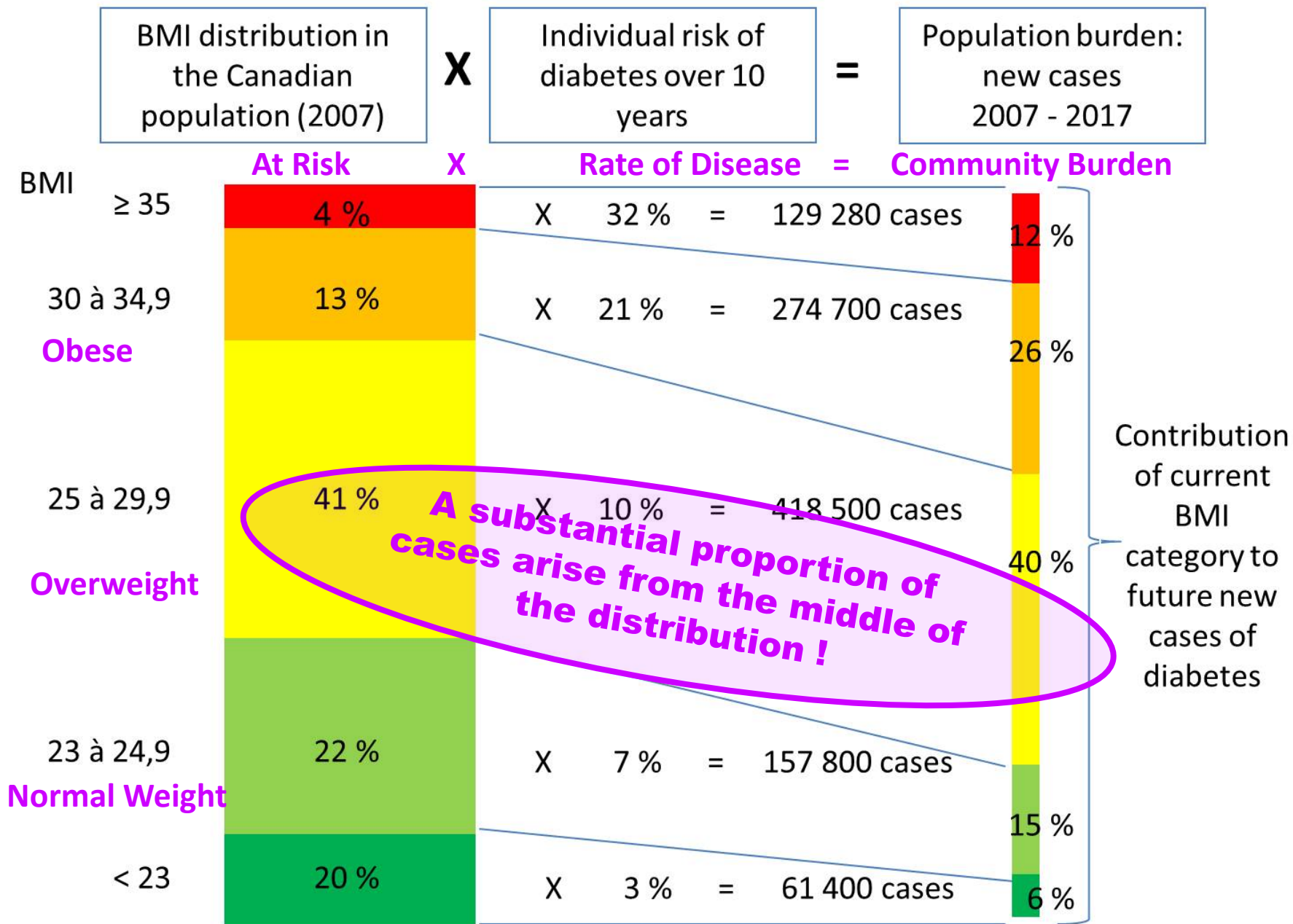
Vol. 14, No. 1  
Printed in Great B

## Sick Individuals and Sick Populations

GEOFFREY ROSE



Aetiology confronts two distinct issues: **the determinants of individual cases, and the determinants of incidence rate.** If exposure to a necessary agent is homogeneous within a population, then case/control and cohort methods will fail to detect it: they will only identify markers of susceptibility. The corresponding strategies in control are the 'high-risk' approach, which seeks to protect susceptible individuals, and the population approach, which seeks to control the causes of incidence. The two approaches are not usually in competition, but the prior concern should always be to discover and control the causes of incidence.



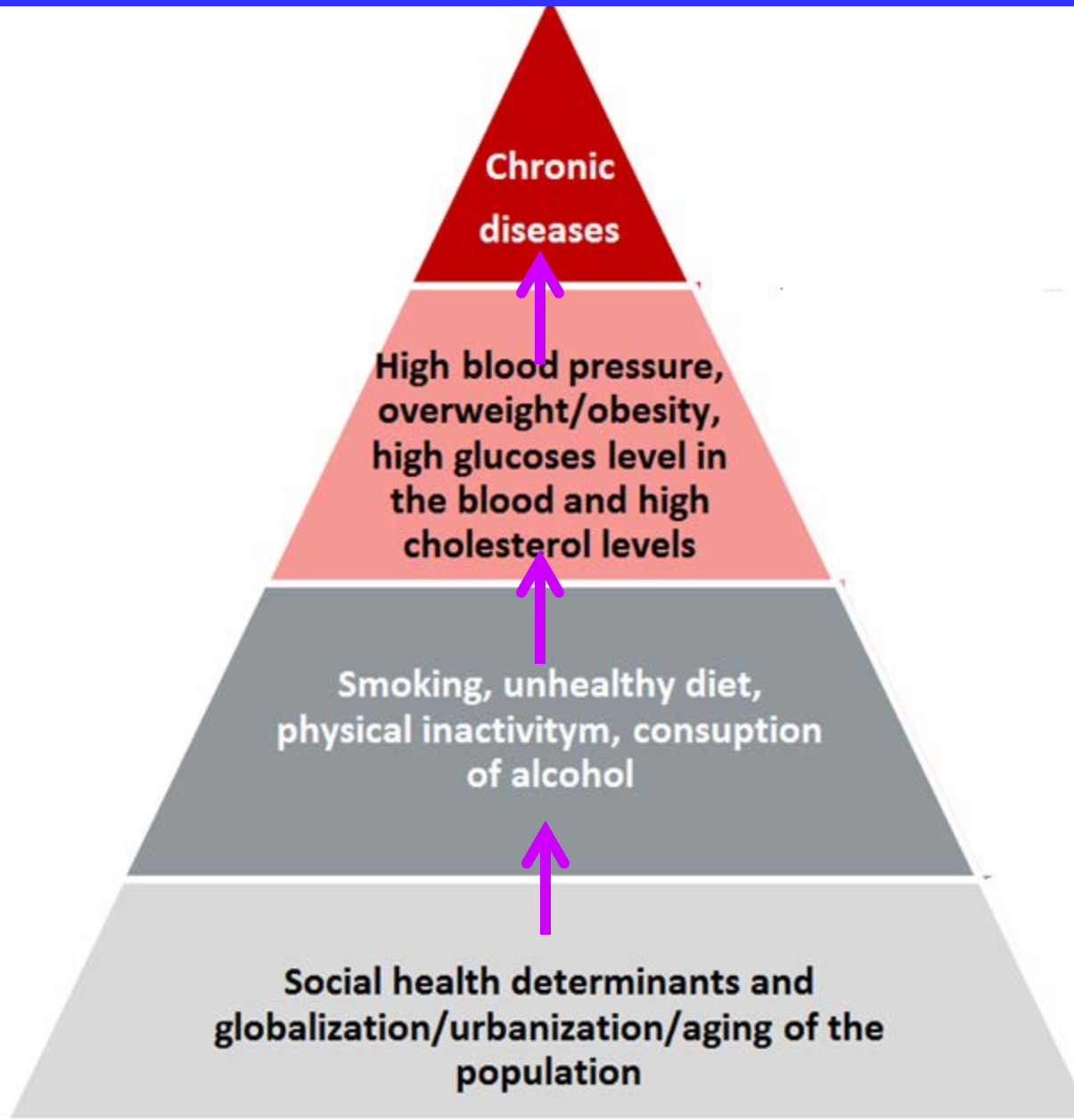
## **American Heart Association Guide for Improving Cardiovascular Health at the Community Level, 2013 Update A Scientific Statement for Public Health Practitioners, Healthcare Providers, and Health Policy Makers**

Thomas A. Pearson, MD, PhD, FAHA, Co-Chair; Latha P. Palaniappan, MD, MS, FAHA, Co-Chair;  
Nancy T. Artinian, PhD, RN, FAHA; Mercedes R. Carnethon, PhD, FAHA;  
Michael H. Criqui, MD, MPH, FAHA; Stephen R. Daniels, MD, PhD, FAHA;  
Gregg C. Fonarow, MD, PhD, FAHA; Stephen P. Fortmann, MD; Barry A. Franklin, PhD, FAHA;  
James M. Galloway, MD, FAHA; David C. Goff, Jr., MD, PhD, FAHA;  
Gregory W. Heath, DHSc, MPH, FAHA; Ariel T. Holland Frank; Penny M. Kris-Etherton, PhD, RD;  
Darwin R. Labarthe, MD, MPH, PhD, FAHA; Joanne M. Murabito, MD, ScM;  
Ralph L. Sacco, MD, MS, FAHA; Comilla Sasson, MD, MS; Melanie B. Turner, MPH;

***Circulation. 2013;127:1730-1753.***

# cHealth

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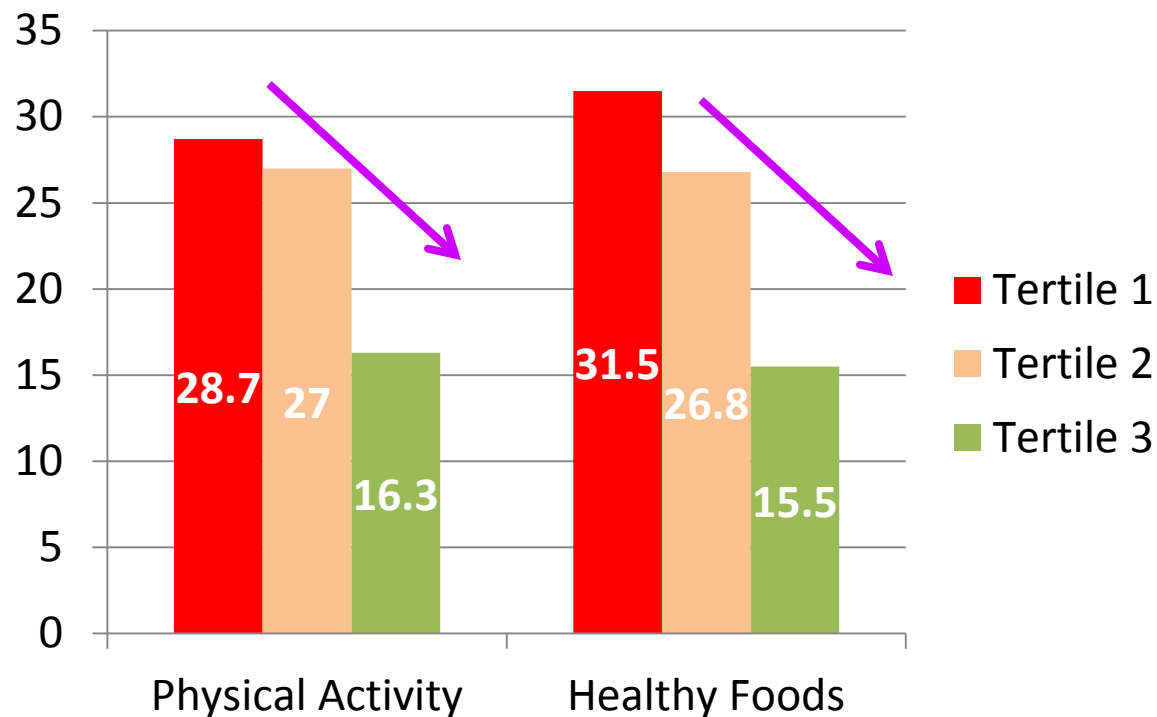


# cHealth: Impact of Built Environment

## Neighborhood Resources for Physical Activity and Healthy Foods and Incidence of Type 2 Diabetes Mellitus

*The Multi-Ethnic Study of Atherosclerosis*

Amy H. Auchincloss, PhD, MPH; Ana V. Diez Roux, MD, PhD; Mahasin S. Mujahid, PhD, MS; Mingwu Shen, MS; Alain G. Bertoni, MD, MPH; Mercedes R. Carnethon, PhD



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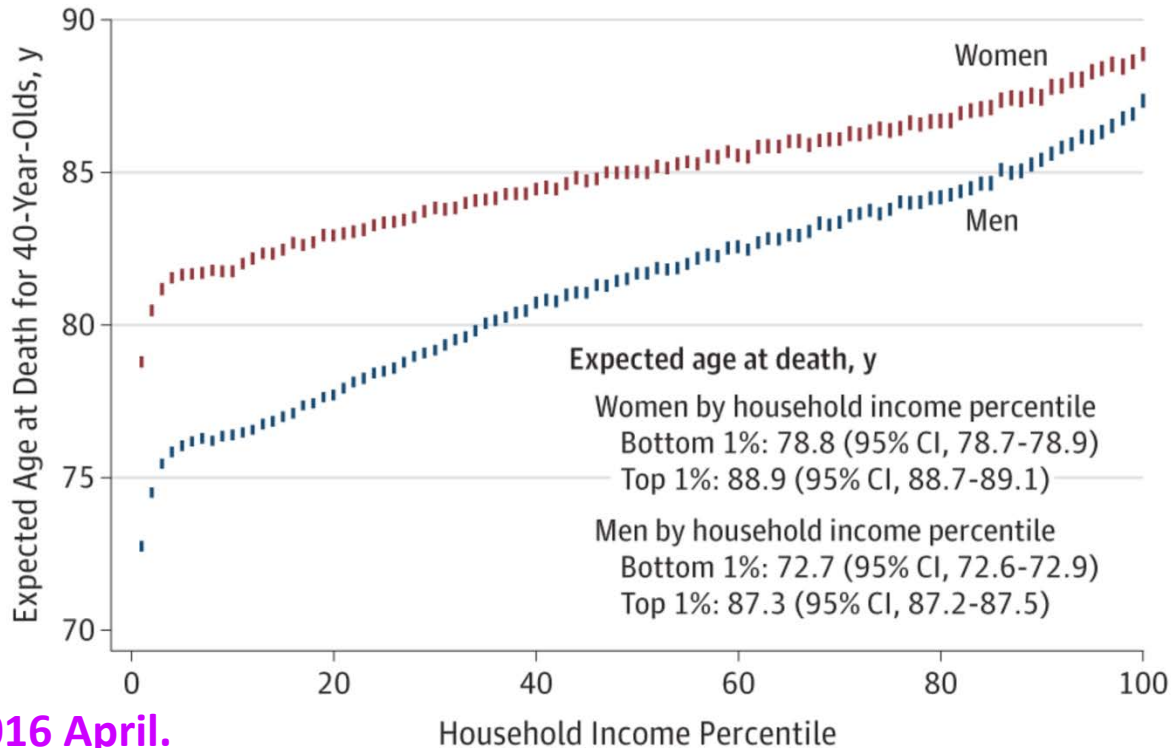


# sHealth

## Public Health Classics

### Economic and social determinants of disease

Michael Marmot<sup>1</sup>



Chetty R. JAMA 2016 April.

Mean household income  
in thousands, \$<sup>a</sup>

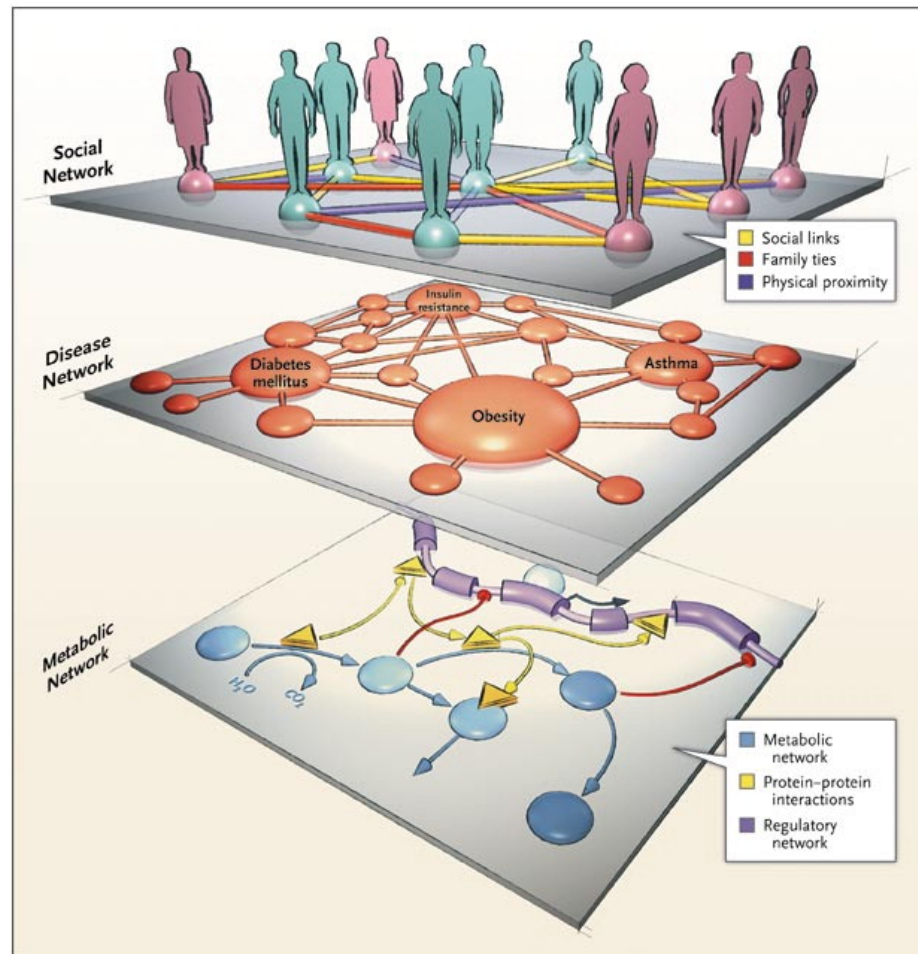
Women	24	45	71	112	1.9 million
Men	26	50	77	119	2.0 million

# sHealth

## Public Health Classics

### Economic and social determinants of disease

Michael Marmot<sup>1</sup>



FAT FRIENDS FOREVER!

Douchy,  
YOUR KILLIN'  
ME!

YEAH  
YEAH  
YEAH

...NEAS



Heenan  
2016

# EATING HABITS ARE CONTAGIOUS

how the people around us influence what we eat



OUR FRIENDS INFLUENCE THE HEALTHINESS\*  
OF WHAT WE CHOOSE TO EAT BY 34.5%

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# Big Data and the Internet of Things



Big data will become valuable to healthcare in what's known as the internet of things (IoT).

SAS describes the IoT as:

“a growing network of everyday objects from industrial machines to consumer goods that can share information and complete tasks while you are busy with other activities, like work, sleep, or exercise.

# THE QUANTIFIED SELF:

*Fundamental Disruption in Big Data Science  
and Biological Discovery*



## 40 ZETTABYTES

[ 43 TRILLION GIGABYTES ]  
of data will be created by 2020, an increase of 300 times from 2005

6 BILLION PEOPLE have cell phones

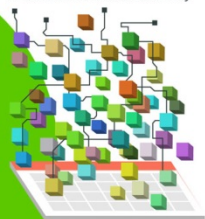


WORLD POPULATION: 7 BILLION

## Volume SCALE OF DATA



It's estimated that **2.5 QUINTILLION BYTES** [ 2.3 TRILLION GIGABYTES ] of data are created each day



Most companies in the U.S. have at least **100 TERABYTES** [ 100,000 GIGABYTES ] of data stored

The New York Stock Exchange captures **1 TB OF TRADE INFORMATION** during each trading session



## Velocity ANALYSIS OF STREAMING DATA

By 2016, it is projected there will be **18.9 BILLION NETWORK CONNECTIONS** — almost 2.5 connections per person on earth



Modern cars have close to **100 SENSORS** that monitor items such as fuel level and tire pressure



# The FOUR V's of Big Data

From traffic patterns and music downloads to web history and medical records, data is recorded, stored, and analyzed to enable the technology and services that the world relies on every day. But what exactly is big data, and how can these massive amounts of data be used?

As a leader in the sector, IBM data scientists break big data into four dimensions: **Volume, Velocity, Variety and Veracity**

Depending on the industry and organization, big data encompasses information from multiple internal and external sources such as transactions, social media, enterprise content, sensors and mobile devices. Companies can leverage data to adapt their products and services to better meet customer needs, optimize operations and infrastructure, and find new sources of revenue.

By 2015 **4.4 MILLION IT JOBS** will be created globally to support big data, with 1.9 million in the United States



As of 2011, the global size of data in healthcare was estimated to be

**150 EXABYTES** [ 161 BILLION GIGABYTES ]



**30 BILLION PIECES OF CONTENT** are shared on Facebook every month



## Variety DIFFERENT FORMS OF DATA



By 2014, it's anticipated there will be **420 MILLION WEARABLE, WIRELESS HEALTH MONITORS**

**4 BILLION+ HOURS OF VIDEO** are watched on YouTube each month



**400 MILLION TWEETS** are sent per day by about 200 million monthly active users



**1 IN 3 BUSINESS LEADERS** don't trust the information they use to make decisions



in one survey were unsure of how much of their data was inaccurate

## Veracity UNCERTAINTY OF DATA



Poor data quality costs the US economy around **\$3.1 TRILLION A YEAR**

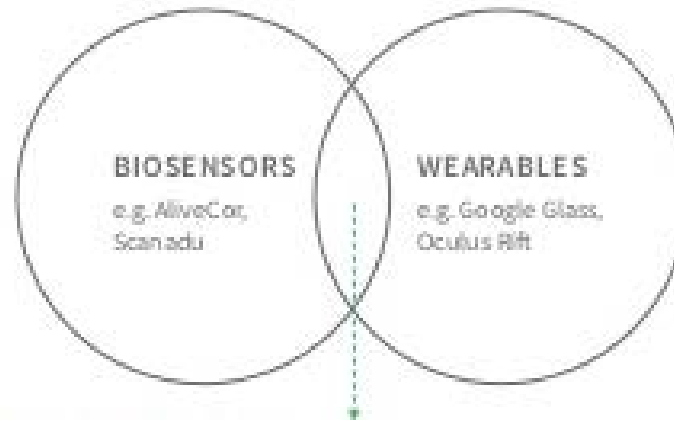


# mHealth: personally generated health data (PGHD)

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*Biosensing wearables allow continuous physiological monitoring in a wide range of form factors*

**Biosensors** are devices that convert a biological recognition element into a signal output



**Wearables** are on- or in-body accessories that enhance the user experience

**Biosensing Wearables**



# mHealth/quantitative sensor data

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- wrist-based accelerometers in the Centers for Disease Control and Prevention National Health and Nutrition Examination Survey (NHANES) and the UK Biobank
- Health eHeart Study (a PCORnet Patient Powered Research Network)
- Apple's ResearchKit, MyHeart Counts
- Extensive "physiome" data through wearable sensors are planned for a Baseline Study coordinated by Stanford, Duke University, and Google Inc
- mobile health data also planned for the NIH's Precision Medicine Initiative cohort

# mHealth Advantages/Opportunities

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- new knowledge about living with and managing health and illness.
- Increase compliance with meds
- ‘hovering’ to promote healthy behavior
- Use predictive analytics and behavioral economics

# mHealth: Pitfalls & Challenges

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- Few measurements from wearable sensors have been validated relative to existing metrics
- continuous ambulatory data that do not directly match the tests done in the clinic
- data quality can be dependent on individual participants and their level of engagement
- accepting trade-offs in precision for more frequent, scalable measures
- selection bias from the participants who “opt in” and who have sufficient technological knowledge and access
- privacy and security of the data are critical

# mHealth: Pitfalls and Challenges

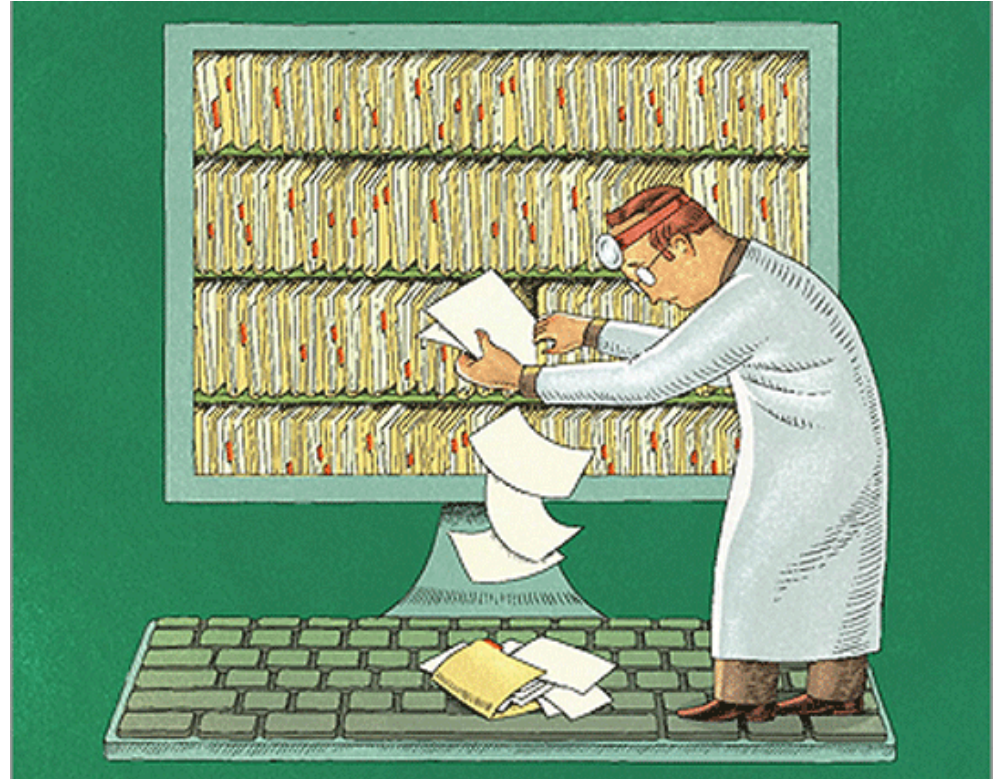
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- Technology necessary but not sufficient to induce health choice
- Adherence to use of mhealth technology unclear
- Must be integrated into clinical practice
- Applicability of approaches across diverse populations unknown
- Reach people when they are not patients

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# How Big Data will change science

Here's how medical research traditionally works:



**1** Come up with a question or hypothesis.



**2** Design an experiment to test it. Wait for new data to come in.



**3** Form your conclusion.

# Big Data: EMR

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- Enactment of the Patient Protection and Affordable Care Act of 2010 → hospitals and clinics received a mandate for electronic medical records (EMRs).
- Digitization of patients' past histories & complaints, treatments, and outcomes → clinical research
- Lack of standardized data elements and definitions limits interoperability
- National standards have been promulgated, and EMRs are slowly mapping to these standards.

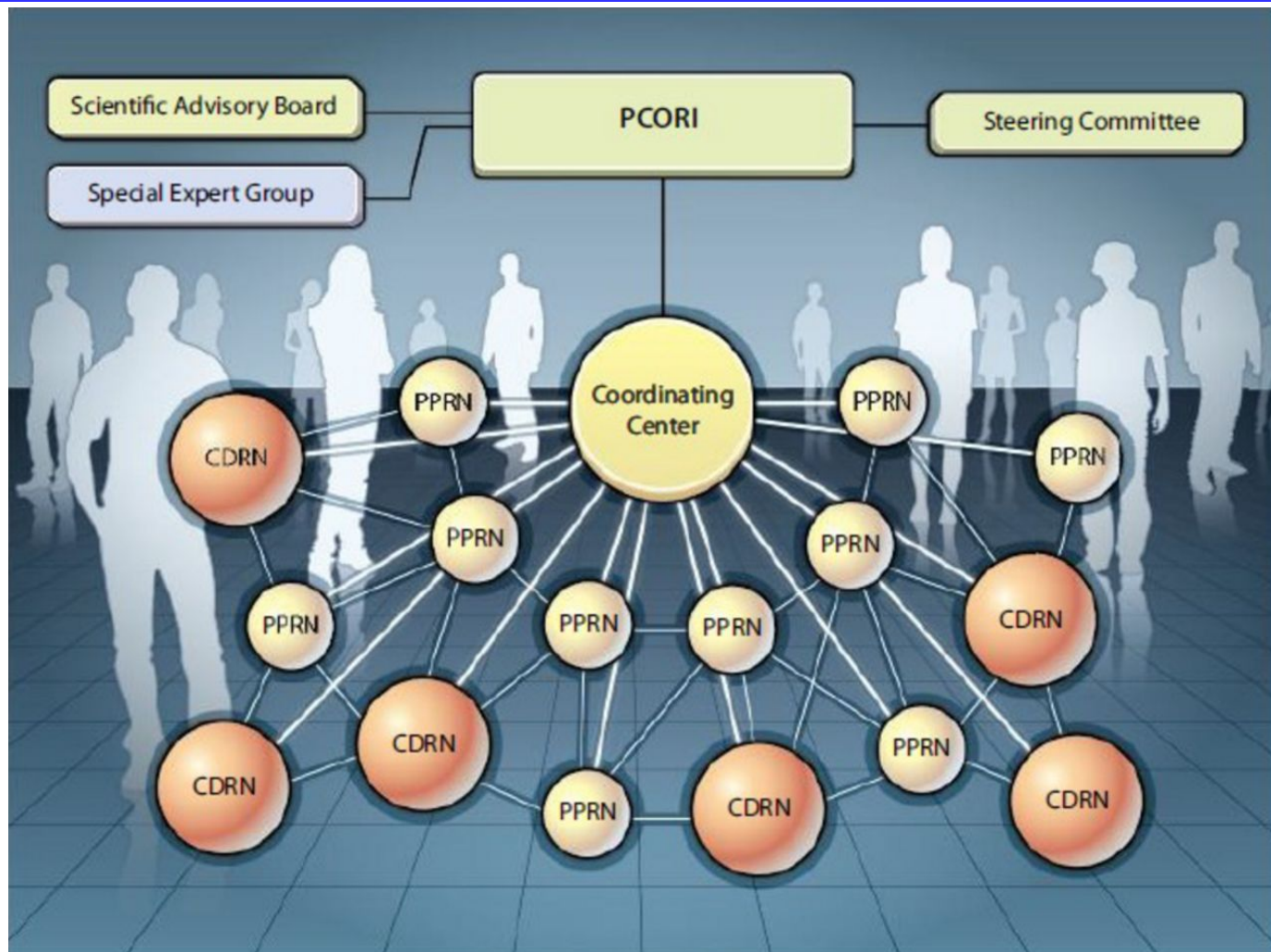
# Big Data: EMR

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- Infrastructure projects such as the National Institutes of Health (NIH) Collaboratory and the National Patient-Centered Clinical Research Network (PCORnet) facilitated linking of EMR data across multiple large health systems
- Large-scale post-market surveillance studies
- Recruit patients and collect information in practical clinical trials
- Incorporate quality improvement systems into the flow of clinical care.

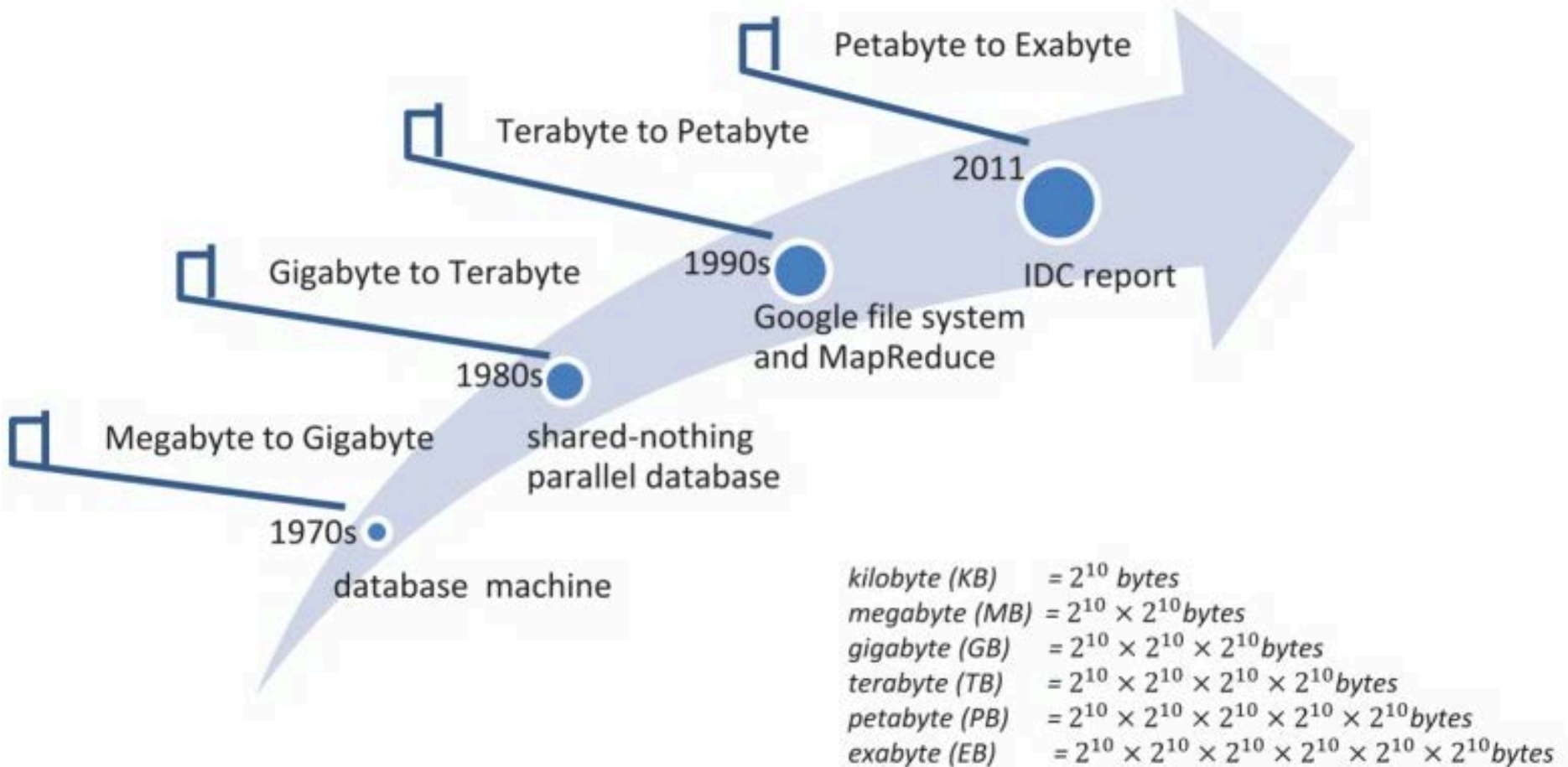


# PCORnet: clinical research and patient engagement on a large scale.



CDRNs indicates Clinical Data Research Networks;  
PCORI, Patient-Centered Outcomes Research Institute;  
PCORnet, National Patient-Centered Clinical Research Network;  
PPRNs, Patient Powered Research Networks.

# Growth of Big Data in Health Care



## Goals of Big Data Science in Medicine

Facilitating **discovery science**: avoiding duplication, ensuring reproducibility

Increasing **understanding of human disease**

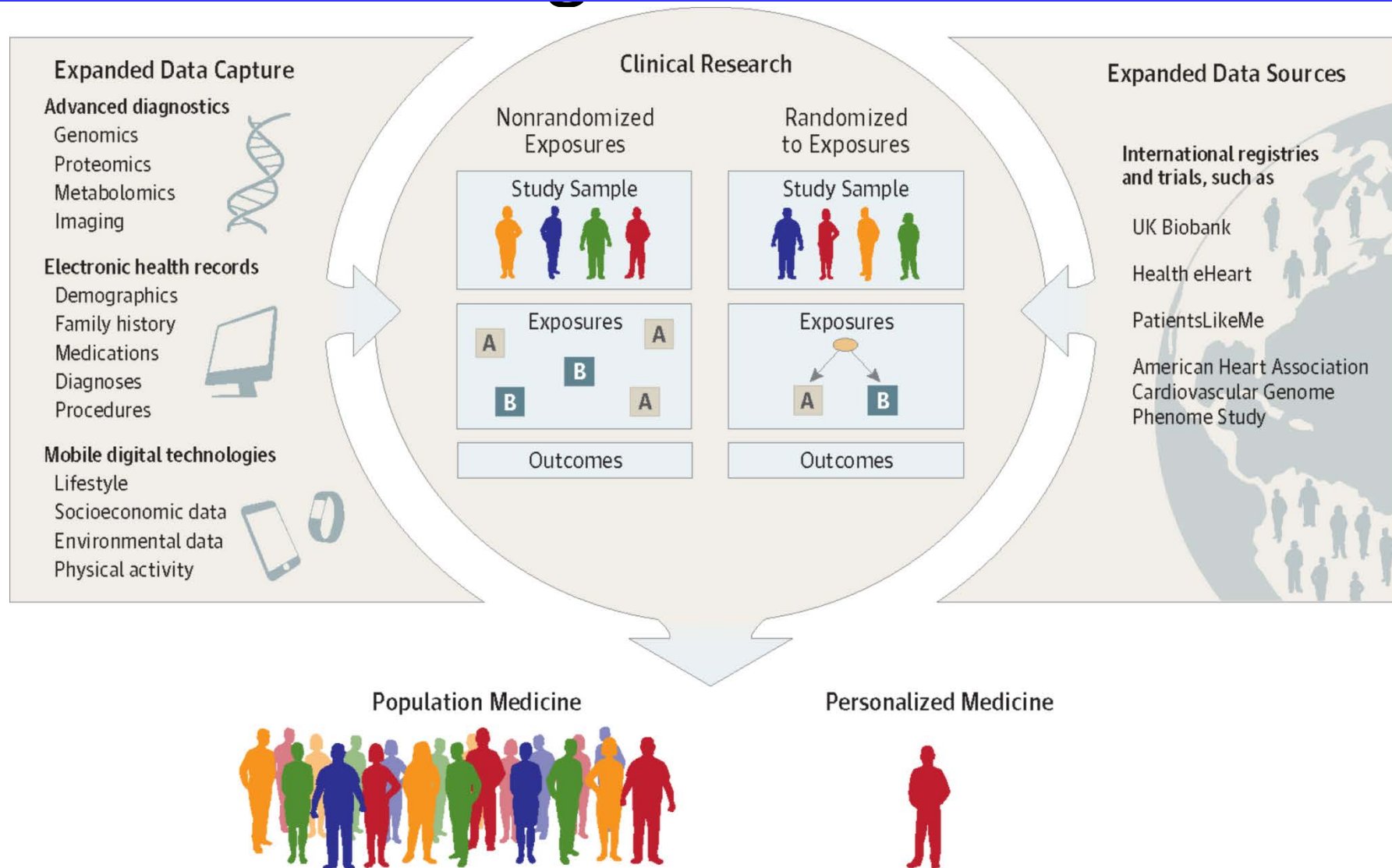
Improving the design, efficiency, and quality of **clinical trials**

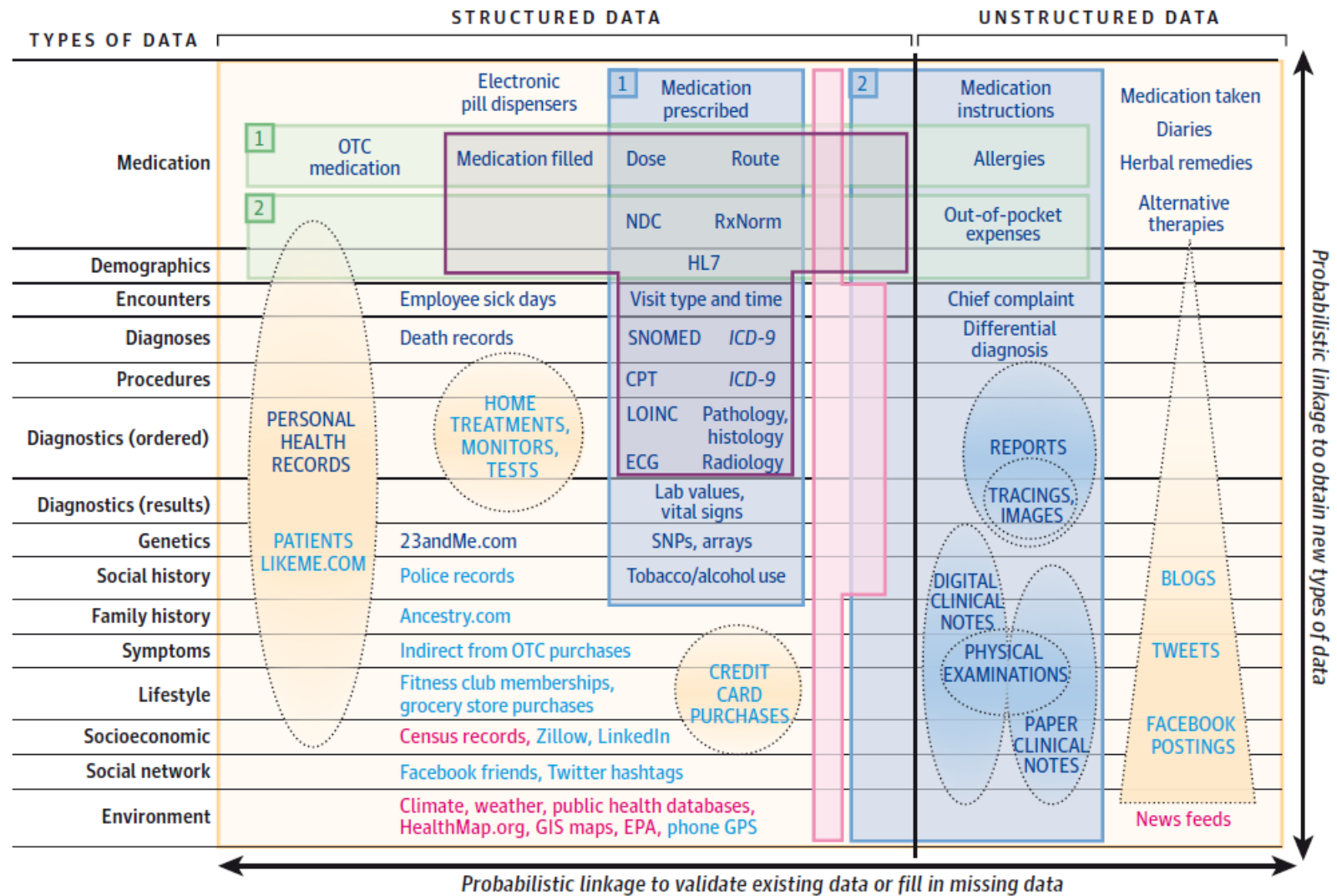
Improving the quality of **care in clinical settings**











Increasing the effectiveness of **prevention**

Translation to **public**

# Kinds of big data in Medicine





Examples of biomedical data		Ability to link data to an individual	Data quantity
 Pharmacy data	 Health care center (electronic health record) data	 Easier to link to individuals	 More
 Claims data	 Registry or clinical trial data	 Harder to link to individuals	 Less
 Data outside of health care system		 Only aggregate data exists	

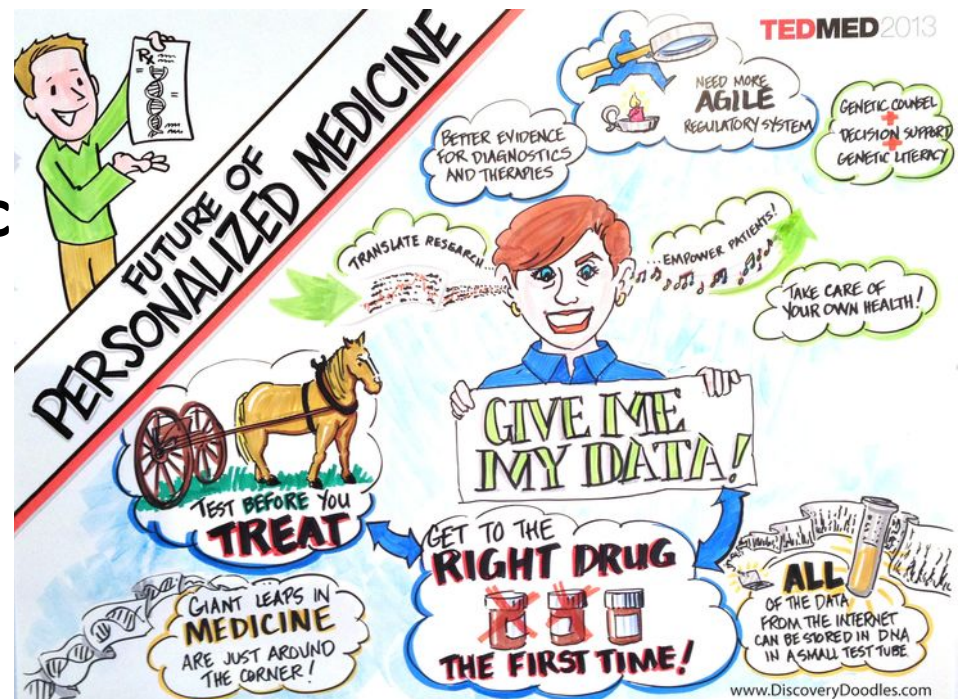
# Challenges

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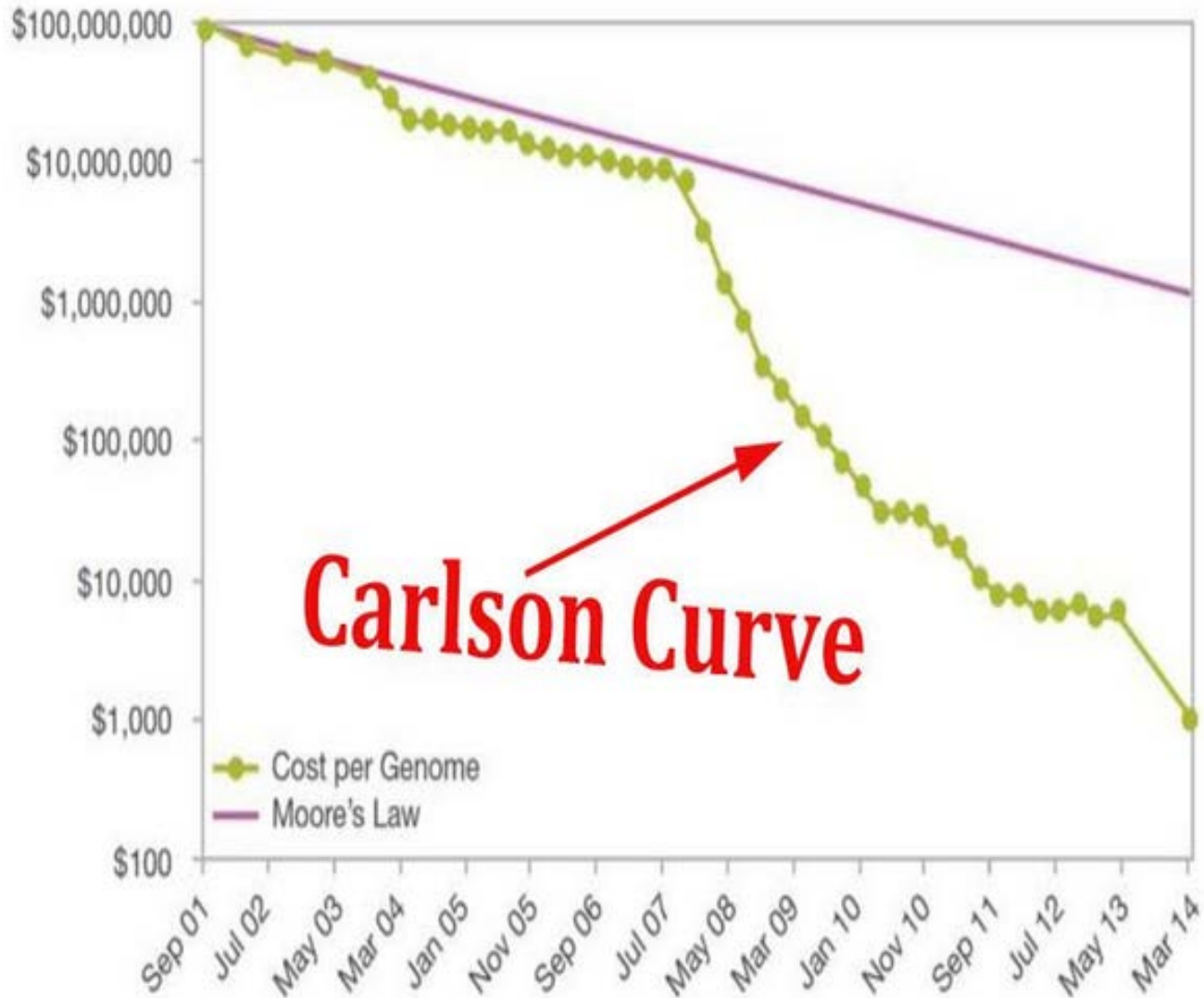
- integrating large data sets, but it is imperative that this is not uncoupled from biological investigation
- Longitudinal datasets: connect the large clinical data sets with an abundance of preclinical data,
- pharma companies externalizing and partnering on research

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# Big data: The \$1000 Genome





# Big Data in Genomics Era

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- deCODE Genetics: history records with genome data from 150,000 Icelandic people (including 15,000 whole-genome sequences).
- United Kingdom launched the 100,000 Genomes Project
- Geisinger-Regeneron collaboration launched 250,000 genomes
- PMI (US) and BGI (China): 1,000,000 genomes

# The Precision Medicine Initiative 2015

## THE PRECISION MEDICINE INITIATIVE



### WHAT IS IT?

**Precision medicine** is an emerging approach for disease prevention and treatment that takes into account people's individual variations in genes, environment, and lifestyle.

The Precision Medicine Initiative will generate the scientific evidence needed to **move the concept of precision medicine into clinical practice.**

### WHY NOW?

The **time is right** because of:

Sequencing of the human genome



Improved technologies for biomedical analysis



New tools for using large datasets



### NEAR TERM GOALS

Intensify efforts to apply precision medicine to **cancer.**

Innovative **clinical trials** of targeted drugs for adult, pediatric cancers



Use of **combination therapies**



Knowledge to overcome **drug resistance**



### LONGER TERM GOALS

Create a research cohort of **> 1 million American volunteers** who will share genetic data, biological samples, and diet/lifestyle information, all linked to their electronic health records if they choose.



Pioneer a **new model for doing science** that emphasizes **engaged participants, responsible data sharing, and privacy protection.**

Research based upon the cohort data will:

- Advance **pharmacogenomics**, the right drug for the right patient at the right dose
- Identify new targets for **treatment and prevention**
- Test whether **mobile devices** can encourage healthy behaviors
- Lay **scientific foundation** for precision medicine for **many diseases**

# Precision Medicine

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- Better taxonomy of disease
- Better ontology of phenome
- Better predictive & prognostic biomarkers
- Multidimensional phenotypic/omic data
- Machine learning
- Better disease modeling, trajectory and time series
- Data lakes

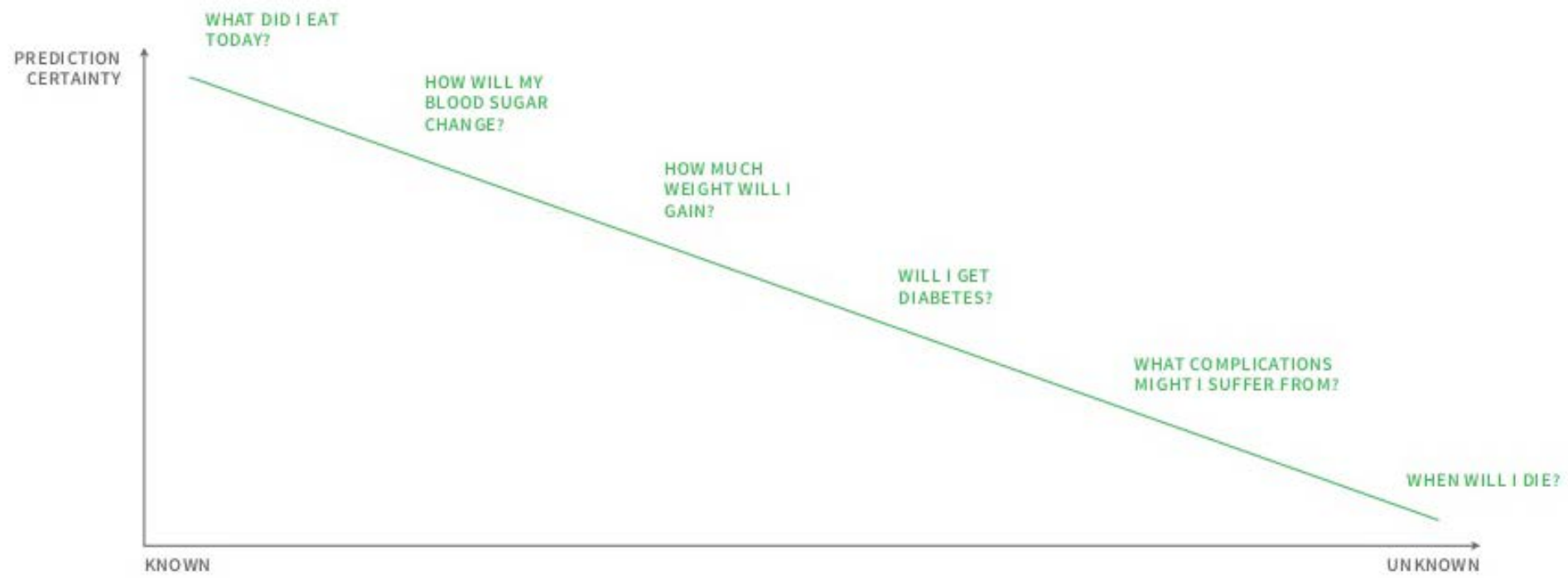
# Precision Medicine

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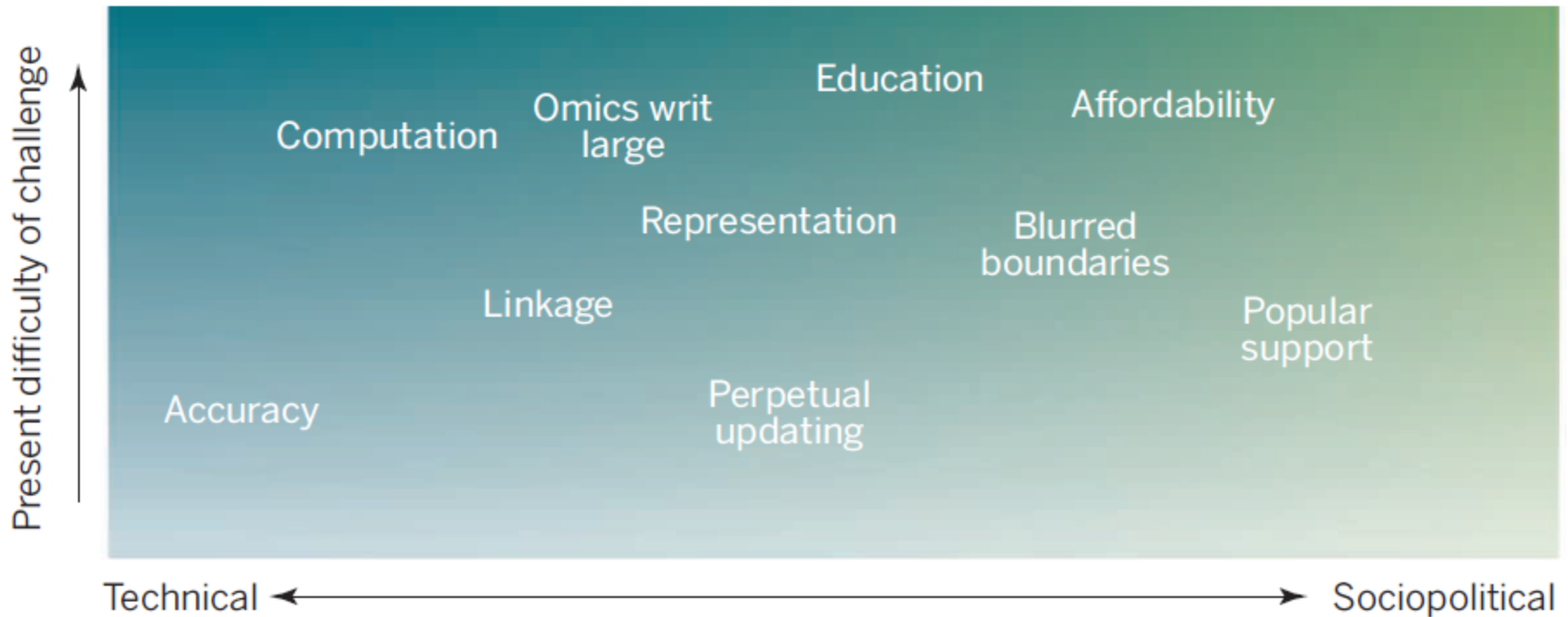
- Requires an understanding of the **precise relationship between gene and phenotype, and the stratification of diseases into subtypes** according to their underlying biological mechanisms
- Functions of most genes unknown, and what is known limited to a few cell types, tissues or physiological contexts.
- Descriptions of disease phenotypes often fail to capture the diverse manifestations of common diseases or to define subclasses of those diseases that predict the outcome or response to treatment.
  - Phenotype descriptions are typically “sloppy or imprecise”

---

*The goal of predictive analytics in any field is to reliably predict the unknown*



# Challenges for PMI



**Moving toward precision medicine.** Ten challenges for achieving precision medicine are qualitatively ordered on the x axis by how much they are intrinsically technical versus sociopolitical challenges. The y axis qualitatively orders the difficulty each challenge currently presents if we are to attain the widely articulated goals for precision medicine.

# Concept of Deep Phenotyping

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- exhaustive examination of the discrete components of a phenotype that goes beyond what is typically recorded in medical charts
- There are a hundred ways to be “diabetic” involving different processes in the pancreas, liver, muscle, brain and fat
- Genetic studies lose statistical power by looking at a conglomeration of underlying causes.

# Concept of Deep Phenotyping

---

- Different genes are responsible for particular subtypes of diabetes, so mixing them together obscures the reasons why people with the same genetic mutation respond differently to the same treatment
- studying 'outbred' mice better mirrors human diversity in diseases such as diabetes that have many genetic contributors.



# Concept of Deep Phenotyping

---

- New human cell models of complex diseases.
- induce skin cells to form stem cells, and can differentiate them into self-assembled clusters of cells called organoids, so they can study the connections between phenotypes, genomics and related biological data

# Genomic Big Data

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- Harvesting genomes or even exomes at the population scale produces a vast amount of data, perhaps up to 40 petabytes (40 million gigabytes) each year
- Storage is not a problem
- Computational scales increase linearly
- Processing power is a limiting factor: no longer a desk top game!
- Cloud based architecture and hosting

# Sharing Genomic Big Data

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- A multinational coalition, the **Global Alliance for Genomics and Health**, developed the Framework for Responsible Sharing of Genomic and Health-Related Data.
- The Framework includes guidelines on privacy and consent, & on accountability and legal consequences for those who break the rules.
- Data-transfer agreements

# Integrating genomics into electronic health records

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- The NIH launched the Electronic Medical Records and Genomics (eMERGE) Network in 2007 to define best practices
- The issue there is, how do you take a practitioner who has 12 minutes per patient and about 45 seconds of time allocated for prescribing drugs, and influence their practice in a meaningful way?”
- Genome is only part of story...other omes!
- Each patient may become a big-data producer

# Systematic comparison of phenome-wide association study of electronic medical record data and genome-wide association study data

Joshua C Denny<sup>1,2</sup>, Lisa Bastarache<sup>2</sup>, Marylyn D Ritchie<sup>3</sup>, Robert J Carroll<sup>2</sup>, Raquel Zink<sup>2</sup>, Jonathan D Mosley<sup>1</sup>, Julie R Field<sup>4</sup>, Jill M Pulley<sup>4,5</sup>, Andrea H Ramirez<sup>1</sup>, Erica Bowton<sup>4</sup>, Melissa A Basford<sup>4</sup>, David S Carrell<sup>6</sup>, Peggy L Peissig<sup>7</sup>, Abel N Kho<sup>8</sup>, Jennifer A Pacheco<sup>9</sup>, Luke V Rasmussen<sup>10</sup>, David R Crosslin<sup>11</sup>, Paul K Crane<sup>12</sup>, Jyotishman Pathak<sup>13</sup>, Suzette J Bielinski<sup>14</sup>, Sarah A Pendergrass<sup>3</sup>, Hua Xu<sup>15</sup>, Lucia A Hindorff<sup>16</sup>, Rongling Li<sup>16</sup>, Teri A Manolio<sup>16</sup>, Christopher G Chute<sup>13</sup>, Rex L Chisholm<sup>17</sup>, Eric B Larson<sup>6</sup>, Gail P Jarvik<sup>11,12</sup>, Murray H Brilliant<sup>18</sup>, Catherine A McCarty<sup>19</sup>, Iftikhar J Kullo<sup>20</sup>, Jonathan L Haines<sup>21</sup>, Dana C Crawford<sup>21</sup>, Daniel R Masy<sup>22</sup>, David M Denny<sup>1,23</sup>

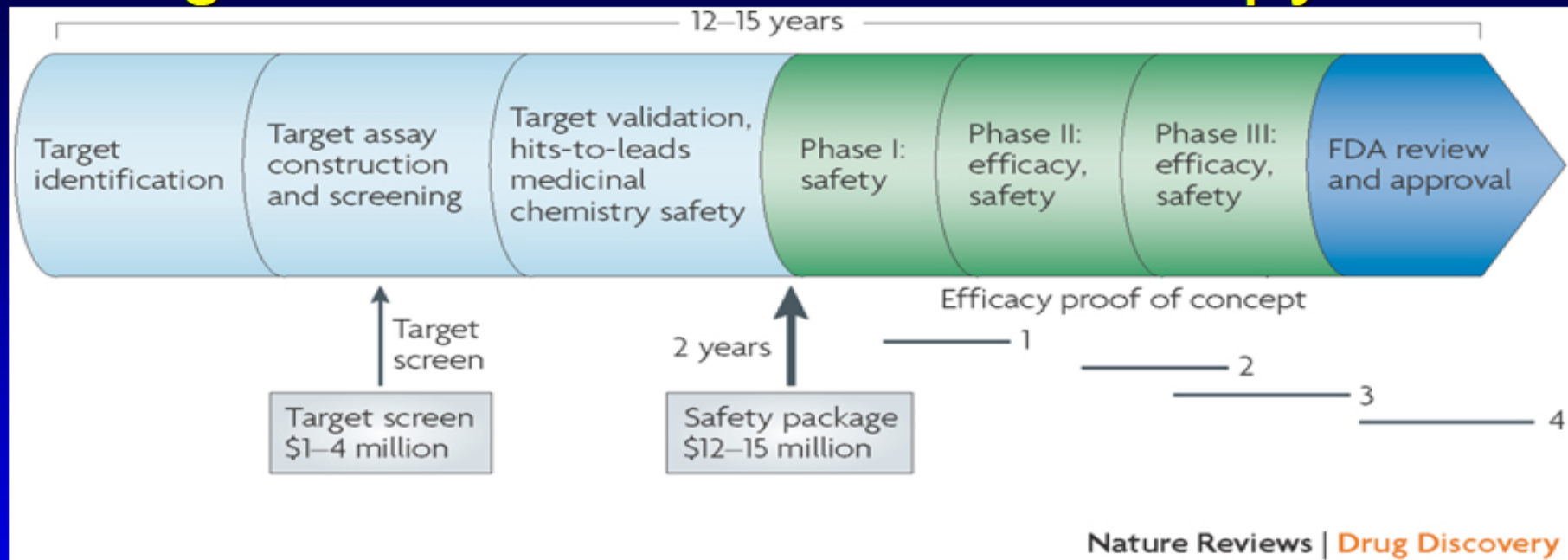
VOLUME 31 NUMBER 12 DECEMBER 2013 **NATURE BIOTECHNOLOGY**

# PheWAS

**Table 1 NHGRI Catalog associations replicated by PheWAS**

	PheWAS phenotype	Cases	Region	Nearest gene	SNP	Odds ratio (95% CI)	P-value	NHGRI Catalog disease(s)
Autoimmune	Psoriasis	327	6p21.33	<i>HLA-C</i>	rs10484554	1.71 (1.41, 2.08)	6.2E-08	Psoriasis
			6p21.33	<i>HCP5</i>	rs2395029	2.38 (1.74, 3.26)	2.0E-08	Psoriasis
	Rheumatoid arthritis	398	6p21.32	<i>C6orf10</i>	rs6910071	1.50 (1.27, 1.76)	1.5E-06	Rheumatoid arthritis
			6p21.32	<i>HLA-DRB1</i>	rs660895	1.56 (1.33, 1.84)	6.7E-08	Rheumatoid arthritis
Hypothyroidism <sup>a</sup>	2,042	9q22.33	<i>FOXE1</i>	rs7850258	0.77 (0.71, 0.83)	1.1E-11	Hypothyroidism	
Hematologic	Iron metabolism disorder	40	6p22.2	<i>SLC17A1</i>	rs17342717	6.84 (4.36, 10.7)	5.3E-17	Serum ferritin
			6p22.2	<i>HFE</i>	rs1800562	12.3 (7.64, 19.7)	3.4E-25	Serum transferrin
			6p22.1	<i>HIST1H2BJ</i>	rs13194491	7.80 (4.76, 12.8)	3.8E-16	Serum transferrin
Neoplastic	Melanoma	268	16q24.3	<i>MC1R</i>	rs4785763	1.52 (1.27, 1.81)	2.8E-06	Melanoma
	Nonmelanoma skin cancer	1,931	6p25.3	<i>EXOC2</i>	rs12210050	1.32 (1.20, 1.45)	6.0E-09	Basal cell carcinoma
	Prostate cancer	848	8q24.21	Intergenic	rs1447295 <sup>b</sup>	1.61 (1.34, 1.92)	2.8E-07	Prostate cancer
Circulatory	Myocardial infarction	1,382	9p21.3	<i>CDKN2BAS</i>	rs4977574	1.28 (1.17, 1.40)	4.0E-08	Myocardial infarction
	Coronary atherosclerosis	3,499	9p21.3	<i>CDKN2BAS</i>	rs4977574 <sup>b</sup>	1.26 (1.18, 1.34)	1.0E-12	Coronary heart disease
	Atrial fibrillation	1,950	4q25	Intergenic	rs2200733	1.52 (1.34, 1.72)	1.5E-10	Atrial fibrillation
Endocrine / metabolic	Type 1 diabetes	615	6p21.32	<i>HLA-DQB1</i>	rs2647044	1.42 (1.24, 1.61)	2.0E-07	Type 1 diabetes
	Type 2 diabetes	3,122	10q25.2	<i>TCF7L2</i>	rs7903146 <sup>b</sup>	1.31 (1.23, 1.40)	8.3E-16	Type 2 diabetes
	Hypercholesterolemia	4,518	1p13.3	<i>CELSR2</i>	rs646776	0.77 (0.70, 0.85)	1.0E-07	LDL & total cholesterol
			2p24.1	<i>APOB</i>	rs693	0.78 (0.73, 0.85)	7.4E-10	LDL & total cholesterol
			19p13.2	<i>LDLR</i>	rs6511720	0.74 (0.65, 0.84)	2.5E-06	LDL cholesterol
			11q23.3	<i>APOA5</i>	rs12272004	2.24 (1.70, 2.95)	7.2E-09	Triglycerides
	Hyperglyceridemia	492	11q23.3	<i>ZNF259</i>	rs964184	2.22 (1.78, 2.75)	5.8E-13	Hypertriglyceridemia
			4p16.1	<i>SLC2A9</i>	rs16890979	0.67 (0.59, 0.78)	5.1E-08	Serum urate
	Gout	769			rs13129697 <sup>b</sup>	0.72 (0.63, 0.81)	2.4E-07	Gout, Serum urate
			4p16.1	Intergenic	rs4698036	0.68 (0.60, 0.79)	7.8E-08	Serum urate
			4q22.1	<i>ABCG2</i>	rs2231142	1.72 (1.48, 1.99)	1.0E-12	Serum urate
	Hyperbilirubinemia	46	2q37.1	<i>UGT1A1</i>	rs887829 <sup>b</sup>	33.8 (14.5, 78.5)	3.2E-16	Serum bilirubin
			2q37.1	<i>HEATR7B1</i>	rs2361502	7.74 (4.72, 12.7)	4.2E-16	Serum bilirubin
Other	Alzheimer's disease	737	19q13.32	<i>TOMM40</i>	rs157580	0.70 (0.62, 0.80)	8.6E-08	Alzheimer's disease
					rs2075650	2.41 (2.06, 2.82)	5.2E-28	Alzheimer's disease
	Age-related macular degeneration	749	1q31.3	<i>CFH</i>	rs1329428	0.51 (0.45, 0.59)	7.2E-20	Age-related macular degeneration
			6p21.33	<i>SKIV2L/C2/CFB</i>	rs429608	0.57 (0.46, 0.70)	4.8E-08	Age-related macular degeneration
Fuchs' dystrophy	108	18q21.2	<i>TCF4</i>	rs613872	2.61 (1.90, 3.58)	2.9E-09	Fuchs' dystrophy	

# Genomics/'Omics over the Translational Stages of Cardiometabolic Therapy R&D



## Harnessing Genomics/'Omics for Optimal Patient Care and Population Prevention

Target discovery & identification:  
Effect direction  
Effect size  
Correct tissue

Target validation and biomarkers:  
Patient subsets  
Risk prediction  
Genomic strata  
Biomarker strata

Drug indication selection & repositioning  
RCT patient Stratification and enrichment

In era of WGS, optimal patient treatment guided by genome + adjunctive tests

# Federalist principles for healthcare data networks

Kenneth D Mandl & Isaac S Kohane

VOLUME 33 NUMBER 4 APRIL 2015 NATURE BIOTECHNOLOGY

## Instrumented health system study versus traditional trial or registry

	Traditional clinical trial or registry	Instrumented health system study
Data source	All data generated during and for the trial	Electronic health records, bio-specimen banks, laboratory information systems, payor claims, e-prescribing data, inpatient pharmacy data
Data specifications	Data formats fully specified but traditionally specific to the particular study rather than universal	Highly varied clinical data formats, with federal specification by the CMS and other agencies slowly increasing
Data acquisition	Data meticulously collected by trained personnel according to well-specified standard operating procedures	Data collected during the course of routine care by nonstandardized systems, including the 'free text' dictation of physician notes
Study design	Study design fully specified, including data types acquired	No preexisting nationwide standard of data from laboratory systems, or for annotations such as clinical notes
Study hypotheses	Small number of hypotheses tested—e.g., is drug A superior to drug B; often no secondary analysis is planned	Myriad questions to be asked and hypotheses to be tested in the future, not specified at the time of data acquisition
Cost	High cost for data standardization and collection	Low cost for acquisition, but variable cost for transformation and transmission



# Principles of engagement in federated networks

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- Transparency
- Representation
- Local benefit
- Right to reassert
- Cost neutrality
- Access
- Parsimony of data storage standards

# Cloud Computing

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- access a shared pool of data in an environment equipped with extensive and **elastic computing resources** and a sophisticated model for **access control**
- allows researchers to **rent a data center** under a **pay-as-you-go** model
- also a paradigm for writing algorithms to enable massive parallelization, allowing for **scalable on-demand** “supercomputers.”
- Because genomic computations are easily parallelized by genomic locus, they are ideally suited

# Computational health care

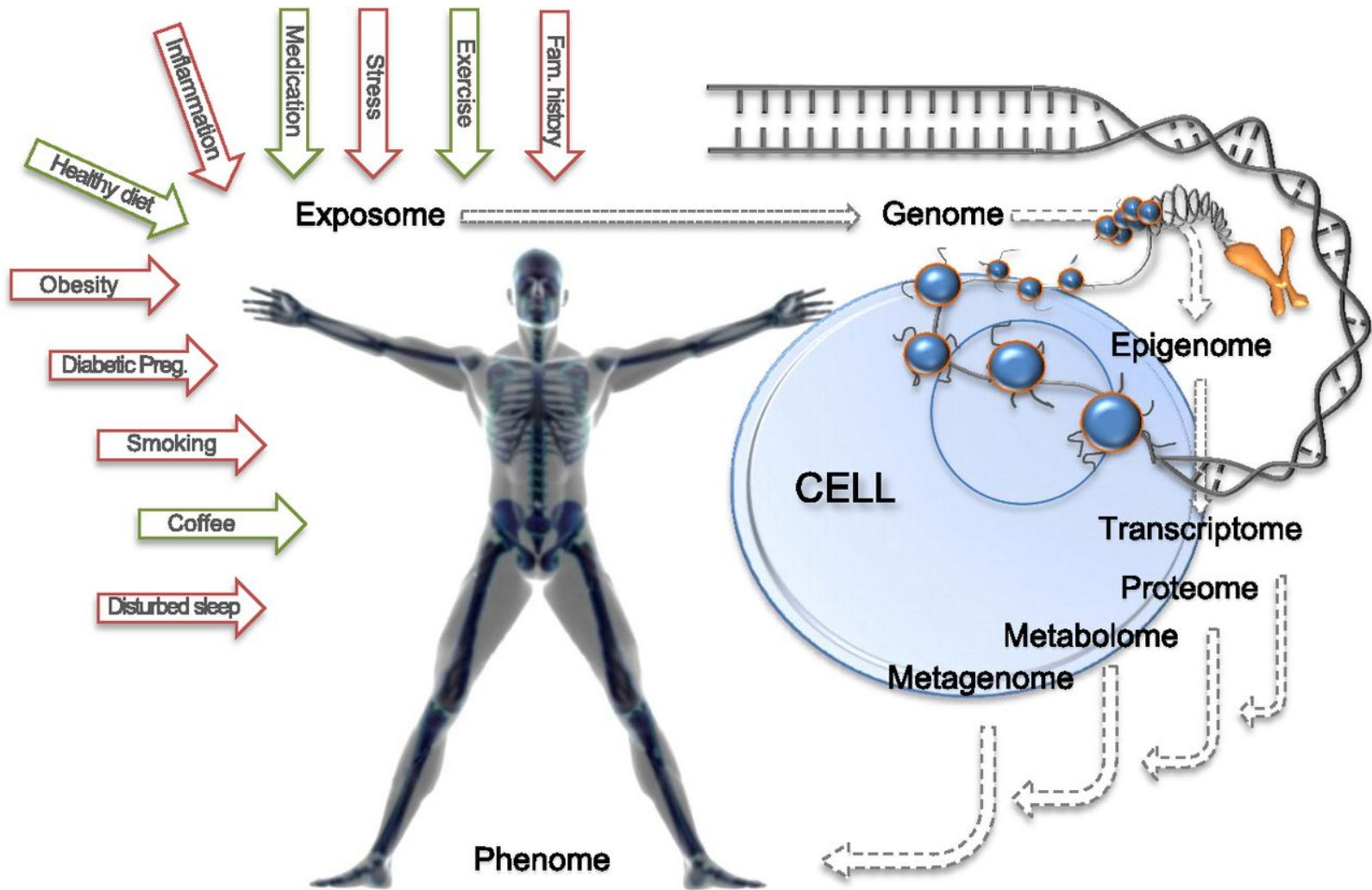
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- **60% of data are exogenous** (eg, behavioral, socioeconomic, environmental) and are rarely captured as part of EMR systems.
- data are generated in **uncontrolled environments** (ie, no hospital or supply-side control), which create highly fragmented value chains that need a neutral entity that can collect, store, manage, curate, and analyze data for insights
- To implement behavior modification in clinical care, it will be important to study the **biometrics, medication usage patterns, stress levels, sleep patterns, and social interactions** of individual patients

# Future of Cardiovascular Epidemiology

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- **Background**
- **Role of**
  - **cHealth (community)**
  - **sHealth (social)**
  - **mHealth (mobile)**
  - **eHealth (electronic)**
  - **gHealth (genomic)**
- **A synthesis**

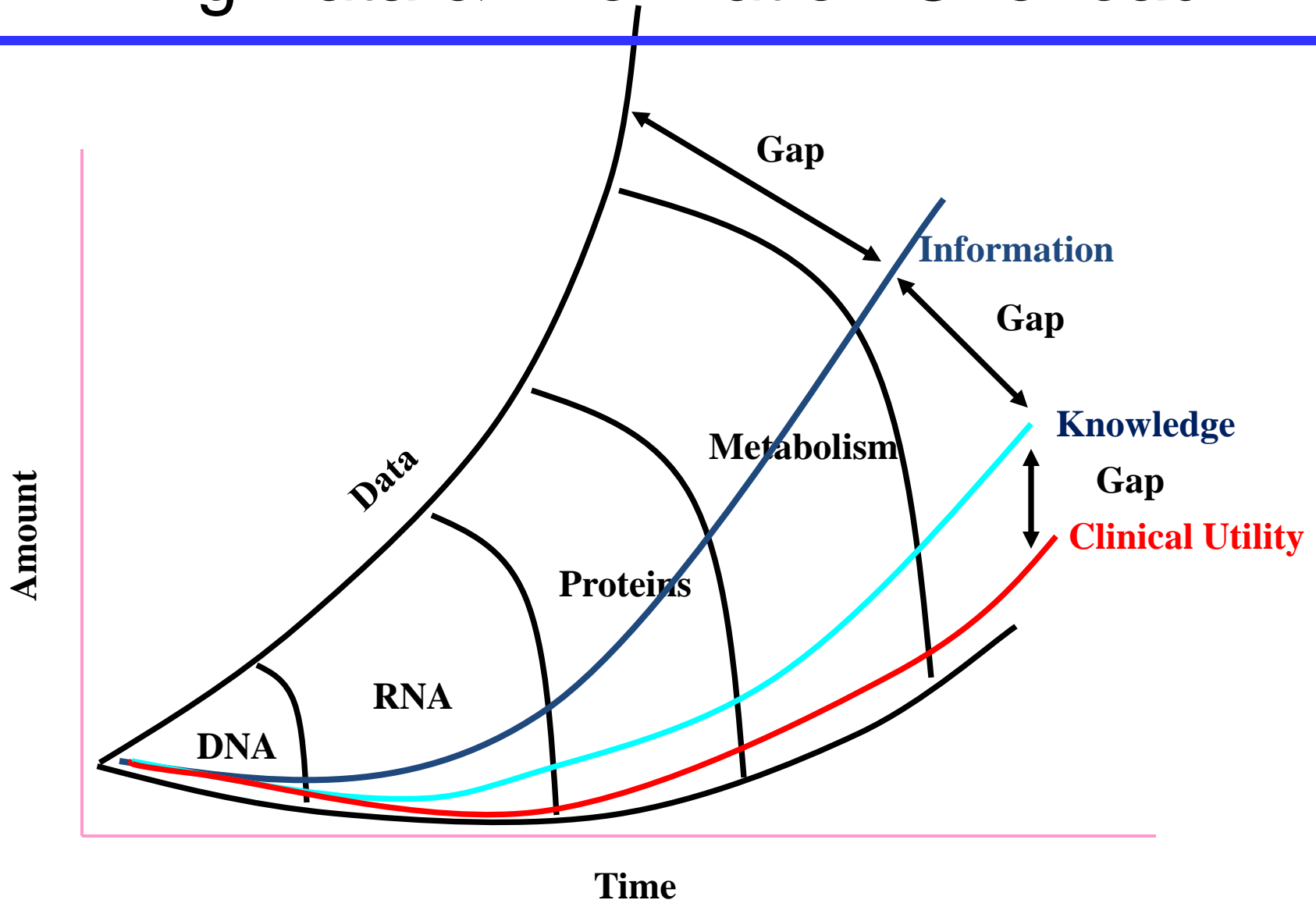


Paul W. Franks et al. Dia Care 2013;36:1413-1421

# Future of CV Epidemiology: Summing up



# Big Data & Information Overload



“It’s hard to tell who’s swimming naked until the tide goes out.”

Warren Buffet

# Time for a Creative Transformation of Epidemiology in the United States

Michael S. Lauer, MD

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JAMA, November 7, 2012—Vol 308, No. 17

What has epidemiology done for medical science lately?

Answer: much but not enough!

Suggests:

1. Refocused scientific questions
2. Centralized and integrated governance
3. Different types of exposures and outcome measures
4. Embedded clinical and policy trials



# Disease Mx and Behavior Change?

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- Opportunities to improve disease management and treatment may exist through context-aware data acquisition, medication/dosage and comorbidity management, and patient education and engagement
- behavior change and prevention can be addressed by using behavior models to develop recommendation services and by understanding habit-formation cycles to design new service models, incentives, and touch-point modifications

# Personalized Medicine vs. Personalized Health Care

## PERSONALIZED MEDICINE

Right

Deterministic

Treatment (through drugs)

Molecular



"Figuring out how to get the right drug to the right person at the right dose at the right time."

**DR. FRANCIS COLLINS**

DIRECTOR, NATIONAL INSTITUTES OF HEALTH

MANTRA

MODEL

FOCUS

DATA

## PERSONALIZED HEALTH CARE

Best

Probabilistic

Prevention, intervention, and treatment

Demographic, social, administrative, clinical, molecular, patient-generated/reported

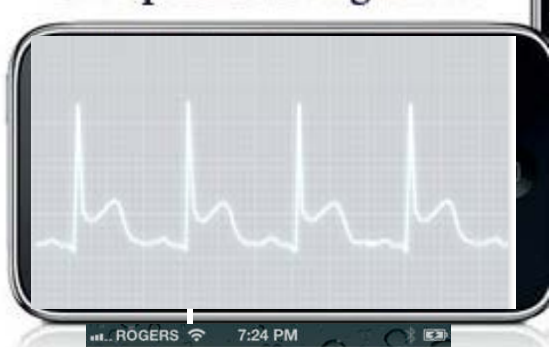
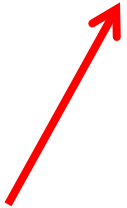


"If I wanted to be a doctor today I'd go to math school not to medical school."

**VINOD KHOSLA**

VENTURE CAPITALIST

# THE WORLD IN 2025



... ROGERS 7:24 PM

911

Emergency Call — calling...



mute



keypad



speaker



add call

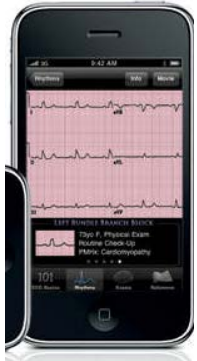


FaceTime



contacts

End



# Thank You!

