The Future of Personalized
Cardiovascular Medicine A
Practical Reality or a Dream Not
Economical Feasible?

Robert M Califf MD

Vice Chancellor for Health Data Science

Duke University

Advisor, Verily Life Sciences

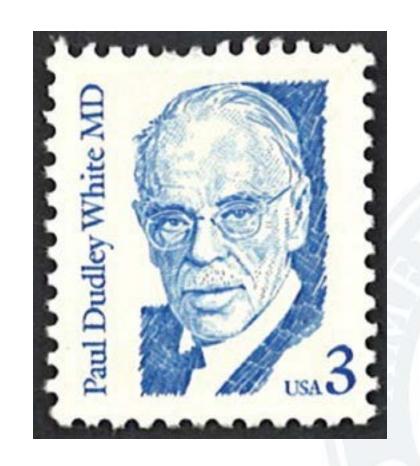
NY CVS

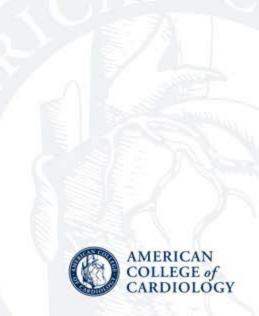
December 2017



Paul Dudley White

- Caring for the average person and the famous and wealthy
- Prevention by developing habits
- Diagnostic gadgets (the ECG)
- Keeping orderly records over time
- These are contributions worth emulating!



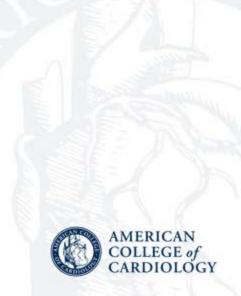


At the height of his career, White became an ardent promoter of habits conducive to good health, including those that improved mental and physical wellness. Following the Eisenhower case. White wrote an article on preventing heart attacks, which appeared on the front page of *The New York Times* and other newspapers. The article was said to have reached an audience of over 50 million readers. White presented a philosophy for a healthy way of life that included three main elements: optimism, regular physical activity and work.

SYTan, Singapore Medical Journal 2016; 57(4): 215-16



We know from our clinical experience in the practice of medicine that in diagnosis, prognosis, and treatment, the individual and his background of heredity are just as important, if not more so, as the disease itself. Paul Dudley White



A vigorous five-mile walk will do more good for an unhappy but otherwise healthy adult than all the medicine and psychology in the world.

I wish we could do something useful with tobacco, like make fertilizer out of it.



Asymptotic Goal

People should have access to clear, understandable information about the benefits and risks of medical products, medical interventions and major decisions about their health.

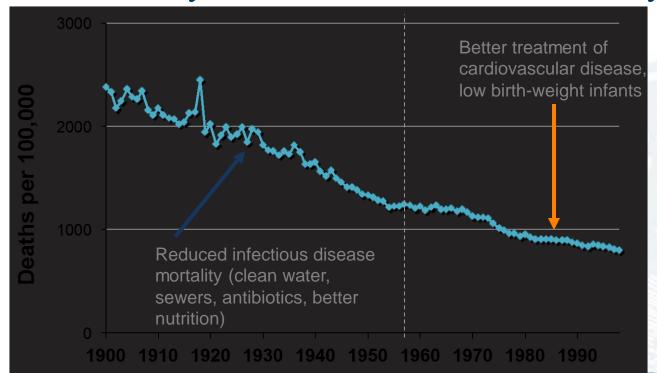


Premise

There is no technological limitation to developing clear, understandable information about the benefits and risks of medical products, healthcare delivery practices and major decisions about people's health and to giving them access to it.



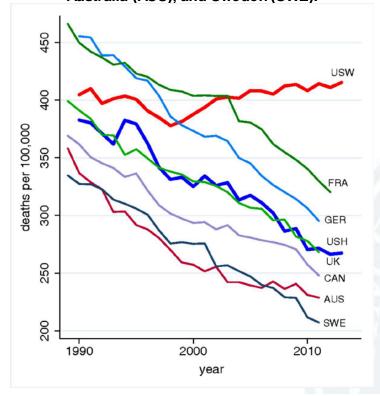
Mortality in the 20th Century



AMERICAN COLLEGE of CARDIOLOGY



All-cause mortality, ages 45-54 for US White non-Hispanics (USW), US Hispanics (USH), and six comparison countries: France (FRA), Germany (GER), the United Kingdom (UK), Canada (CAN), Australia (AUS), and Sweden (SWE).



Anne Case, and Angus Deaton PNAS 2015;112:15078-15083



MERICAN



From: Inequalities in Life Expectancy Among US Counties, 1980 to 2014Temporal Trends and Key Drivers

JAMA Intern Med. Published online May 08, 2017. doi:10.1001/jamainternmed.2017.0918

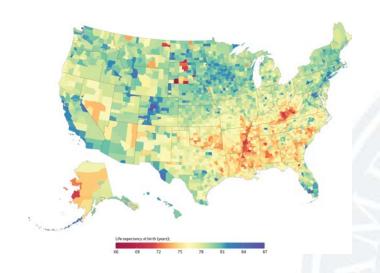


Figure Legend:

Life Expectancy at Birth by County, 2014Counties in South Dakota and North Dakota had the lowest life expectancy, and counties along the lower half of the Mississippi, in eastern Kentucky, and southwestern West Virginia also had very low life expectancy compared with the rest of the country. Counties in central Colorado had the highest life expectancies.

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From: Inequalities in Life Expectancy Among US Counties, 1980 to 2014Temporal Trends and Key Drivers

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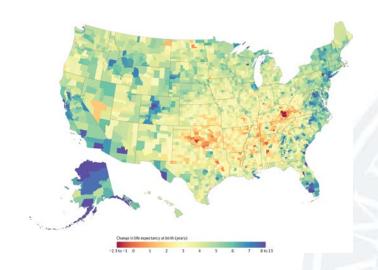


Figure Legend:

Change in Life Expectancy at Birth by County, 1980 to 2014Compared with the national average, counties in central Colorado, Alaska, and along both coasts experienced larger increases in life expectancy between 1980 and 2014, while some southern counties in states stretching from Oklahoma to West Virginia saw little, if any, improvement over this same period.

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From: Inequalities in Life Expectancy Among US Counties, 1980 to 2014Temporal Trends and Key Drivers

JAMA Intern Med. Published online May 08, 2017. doi:10.1001/jamainternmed.2017.0918

| Variable | Summary Statistics, Mean (SD) [Range] | Bivariate Regression Results | |
|---|--|-------------------------------------|----------------|
| | | Coefficient (SE) | R ² |
| Socioeconomic and race/Ethnicity factors | | | |
| Population below the poverty line, % | 16.3 (6.4) [3.1-62.0] | -0.24 (0.005) | 0.47 |
| Median household income, log \$ | 10.6 (0.2) [9.8-11.6] | 6.06 (0.130) | 0.41 |
| Graduates, age ≥25 y, % | | | |
| High school | 83.7 (7.2) [46.3-98.6] | 0.20 (0.004) | 0.42 |
| College | 19.2 (8.6) [4.2-72.0] | 0.15 (0.004) | 0.34 |
| Unemployment rate, age ≥16 y, % | 9.1 (3.2) [2.1-27.4] | -0.29 (0.011) | 0.18 |
| Black population, % | 9.4 (14.7) [0-85.8] | -0.07 (0.002) | 0.24 |
| American Indian, Native Alaskan, and Native Hawaiian population, % | 2.3 (7.9) [0-97.2] | -0.06 (0.005) | 0.04 |
| Hispanic population, % | 8.1 (13.1) [0-95.9] | 0.02 (0.003) | 0.01 |
| Behavioral and metabolic risk factors, % | | | |
| Obesity prevalence, age ≥20 y | 37.0 (4.3) [18.0-52.0] | -0.39 (0.006) | 0.54 |
| No leisure-time physical activity prevalence, age ≥20 y | 27.0 (5.2) [11.7-47.2] | -0.34 (0.005) | 0.62 |
| Cigarette smoking prevalence, age ≥18 y | 24.7 (4.1) [7.7-42.1] | -0.40 (0.007) | 0.54 |
| Hypertension prevalence, age ≥30 y | 39.5 (3.6) [27.9-56.4] | -0.49 (0.007) | 0.62 |
| Diabetes prevalence, age ≥20 y | 14.0 (2.4) [8.1-25.5] | -0.72 (0.011) | 0.59 |
| Health care factors | | | |
| Insured population, age <65 y, % | 81.7 (5.7) [57.3-96.7] | 0.15 (0.007) | 0.14 |
| Quality index | 70.1 (11.5) [0-100] | 0.10 (0.003) | 0.28 |
| Physicians per 1000 population, No. | 1.1 (1.0) [0-4.4] | 0.53 (0.039) | 0.06 |

Abbreviation: SE, standard error.

Table Title:

Variables Included in the Regression Analysis With Summary Statistics and Bivariate Regression Results





From: Income Disparities in Absolute Cardiovascular Risk and Cardiovascular Risk Factors in the United States, 1999-2014

JAMA Cardiol. 2017;2(7):782-790. doi:10.1001/jamacardio.2017.1658

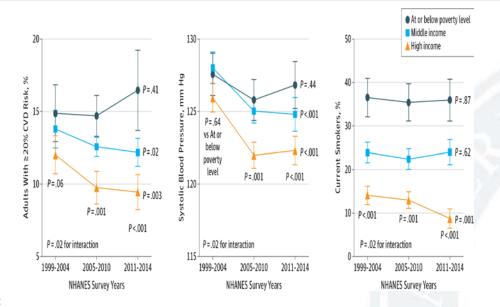


Figure Legend:

Trends in 10-Year Predicted Absolute Cardiovascular Disease (CVD) Risk, Mean Systolic Blood Pressure, and Smoking by Income StrataThere was a statistically significant interaction between survey year and income strata; therefore, individual tests for trends were conducted for each income group separately and between-group differences were assessed at each survey year. Expressional Figure 195% Cls. NHANES indicates National Health and Nutrition Examination Survey.

CARDIOLOGY

Data Scientist:

The Sexiest Job of the 21st Century

Meet the people who can coax treasure out of messy, unstructured data. by Thomas H. Davenport and D.J. Patil

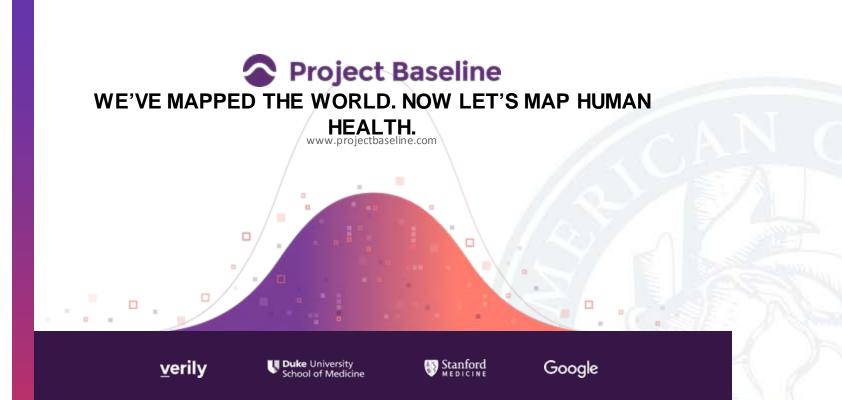
hen Jonathan Goldman arrived for work in June 2006
at LinkedIn, the business
networking site, the place still
felt like a start-up. The company had just under 8 million
accounts, and the number was
growing quickly as existing members invited their friends and colleagues to join. But users weren't

seeking out connections with the people who were already on the site at the rate executives had expected. Something was apparently missing in the social experience. As one LinkedIn manager put it, "It was like arriving at a conference reception and realizing you don't know anyone. So you just stand in the corner sipping your drink—and you probably leave early."

70 Harvard Business Review October 2012









CONTINUOUS MONITORING THROUGH **PASSIVE SENSORS**



Study watch

Investigational wrist-worn sensor for continuous recording of physiological and environmental data



App

Mobile interface for self-reported and passive data acquisitions



Sleep sensor

Commercially available, placed under mattress to passively monitor multiple physiologic data parameters



Study hub

Safely sends device data to secure, encrypted Baseline database







From: Digital PhenotypingTechnology for a New Science of Behavior

JAMA. Published online September 21, 2017. doi:10.1001/jama.2017.11295

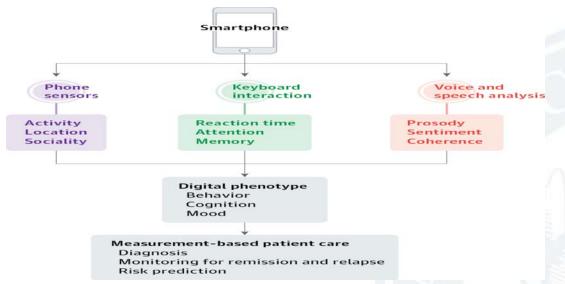
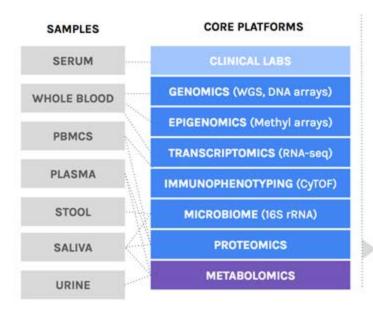


Figure Legend:

The Process of Digital Phenotyping Digital phenotyping involves collecting sensor, keyboard, and voice and speech data from smartphones to measure behavior, cognition, and mood.



DEEP MOLECULAR PROFILING



AUTOMATION





External/at clinic site

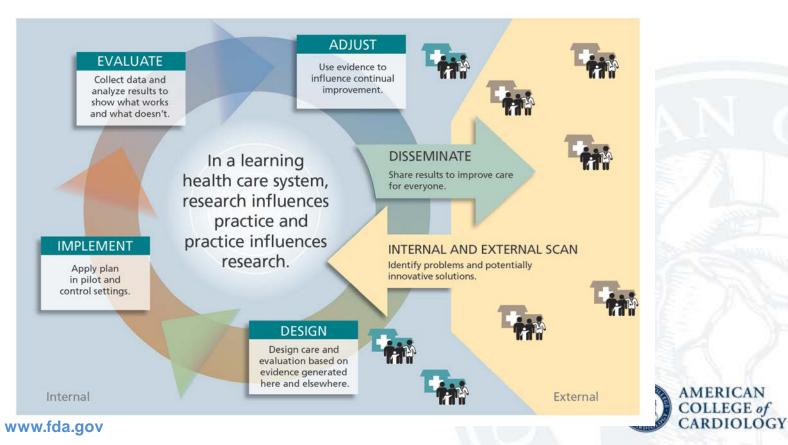
In-house

External



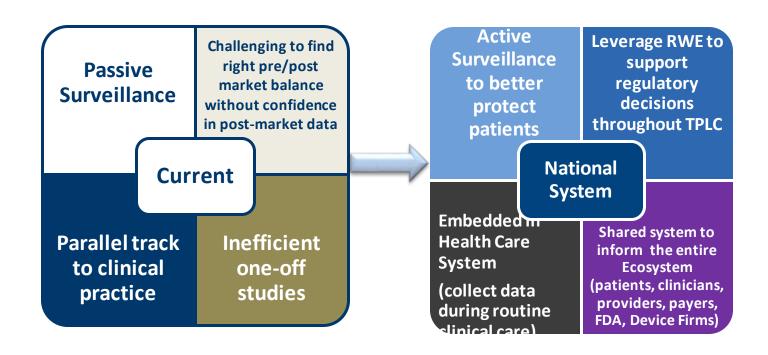


Learning health care systems





National System Paradigm Shift

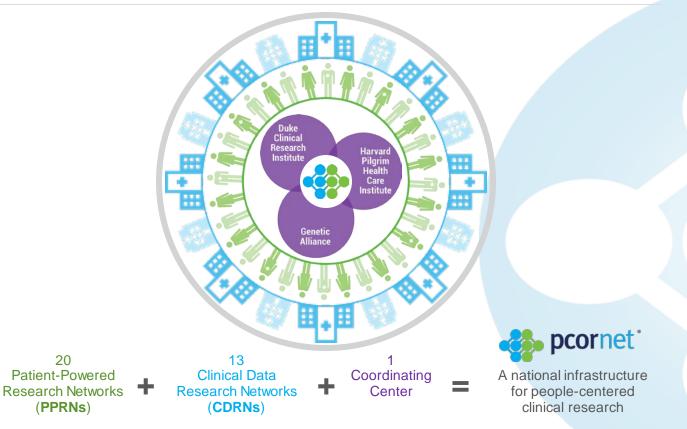




PCORnet® embodies a "network of networks" that harnesses the power of partnerships

20

(PPRNs)





PPRNs



American BRCA Outcomes and Utilization of Testing Patient-Powered Research Network (ABOUT Network)

University of South Florida



ARthritis patient Partnership with comparative Effectiveness Researchers (AR-PoWER PPRN) Global Healthy Living Foundation



CCFA Partners Patient Powered Research

Crohn's and Colitis Foundation of America



Collaborative Patient-Centered Rare Epilepsy Network (REN) **Epilepsy Foundation**



Community and Patient-Partnered Centers of Excellence for Behavioral Health University of California Los Angeles



Community-Engaged Networkfor All (CENA)
Genetic Alliance, Inc.



COPD Patient Powered Research Network COPD Foundation

DuchenneConnect DuchenneConnect Registry Network Parent Project Muscular Dystrophy



University of California, San Francisco (UCSF)



ImproveCareNow: A Learning Health System for Children with Crohn's Disease and Ulcerative Colitis Cincinnati Children's Hospital Medical Center



Interactive Autism Network Kennedy Krieger Institute



Mood Patient-Powered Research Network Massachusetts General Hospital



Multiple Sclerosis Patient-Powered Research Network





National Alzheimer's and Dementia Patient and Caregiver-Powered Research Network Mayo Clinic



NephCure Kidney International
Arbor Research Collaborative for Health



Patients, Advocates and Rheumatology Teams Network for Research and Service (PARTNERS) Consortium Duke University



Phelan-McDermid Syndrome Data Network Phelan-McDermid Syndrome Foundation



PI Patient Research Connection: PI-CONNECT Immune Deficiency Foundation



Population Research in Identity and Disparities for Equality Patient-Powered Research Network (PRIDEnet)



University of California San Francisco



Vasculitis Patient Powered Research Network University of Pennsylvania





CDRNs



Accelerating Data Value Across a National Community Health Center Network (ADVANCE)

Oregon Community Health Information Network (OCHIN)



Chicago Area Patient Centered Outcomes Research Network (CAPriCORN)

The Chicago Community Trust



Greater Plains Collaborative (GPC)
University of Kansas Medical Center



Kaiser Permanente & Strategic Partners
Patient Outcomes Research To Advance
Learning (PORTAL) Network

Kaiser Foundation Research Institute



Research Action for Health Network (REACHnet)

Louisiana Public Health Institute (LPHI)



Mid-South CDRN Vanderbilt University



National PEDSnet: A Pediatric Learning Health System

The Children's Hospital of Philadelphia



New York City Clinical Data Research Network (NYC-CDRN)

Weill Medical College of Cornell University



OneFlorida Clinical Data Research Network

University of Florida



Patient-Centered Network of Learning Health Systems (LHSNet) Mayo Clinic



Patient-oriented SCAlable National Network for Effectiveness Research (pSCANNER) University of California, San Diego (UCSD)



PaTH: Towards a Learning Health System University of Pittsburgh

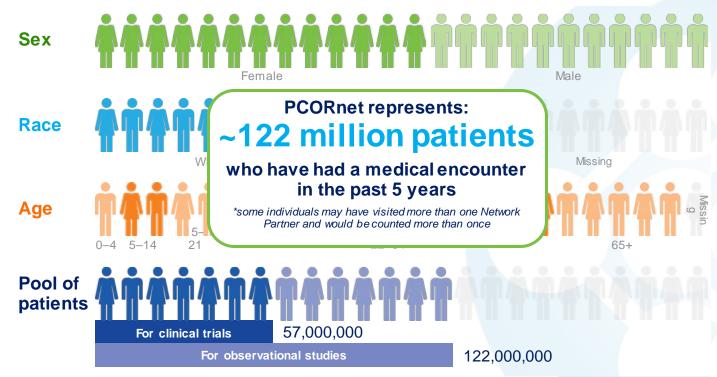


Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS) Harvard University





Resulting in a national evidence system with "research readiness"





ADAPTABLE

Study Design

Patients with known ASCVD + ≥ 1 "enrichment factor"

Patients identified by Clinical Data Research Networks (CDRNs) through EHR searches using a computable phenotype that classifies inclusion/exclusion criteria

Patients provided with trial information and link to e-consent on a web portal;†
Randomized treatment assignment provided directly to patient

ASA 81 mg QD

ASA 325 mg QD

Electronic patient follow -up: Every 3 or 6 months Supplemented with searches of EHR/CDM/claims data

Duration: Enrollment over 24 months; maximum follow -up of 30 months

Primary endpoint:

Composite of all-cause mortality, hospitalization for MI, or hospitalization for stroke

Primary safety endpoint:

Hospitalization for major bleeding

† Participants without internet access will be consented and followed via a parallel system

ClinicalTrials.gov: NCT02697916

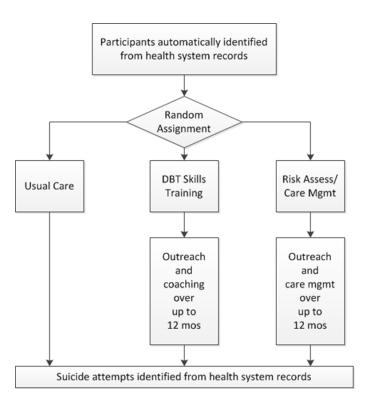


Suicide Prevention Outreach Trial summary

- Demonstration project of the NIH Healthcare Systems Research Collaboratory
- Pragmatic trial of two outreach interventions to reduce long-term risk of suicide attempt
- Automatically enroll health system patients who report frequent thoughts of death or self-harm
- Randomly assign to continued usual care or to one of two outreachbased interventions
- Examine risk of suicide attempt over 12-18 months after randomization
- Planned sample size = 19,500 (6500 per group)



Intervention Research: Pragmatic trial of population-based selective prevention programs (funded by NIH Collaboratory)

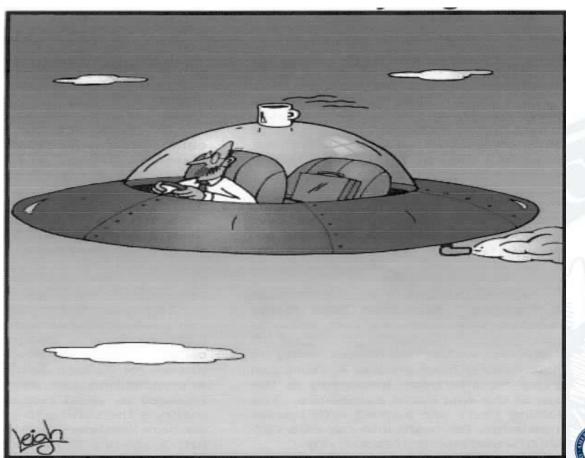


Ongoing at four MHRN sites:

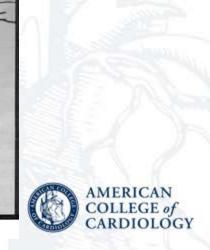
- KP Washington
- HealthPartners
- KP Colorado
- KP Northwest

12,000 enrolled as of 10/1/2017





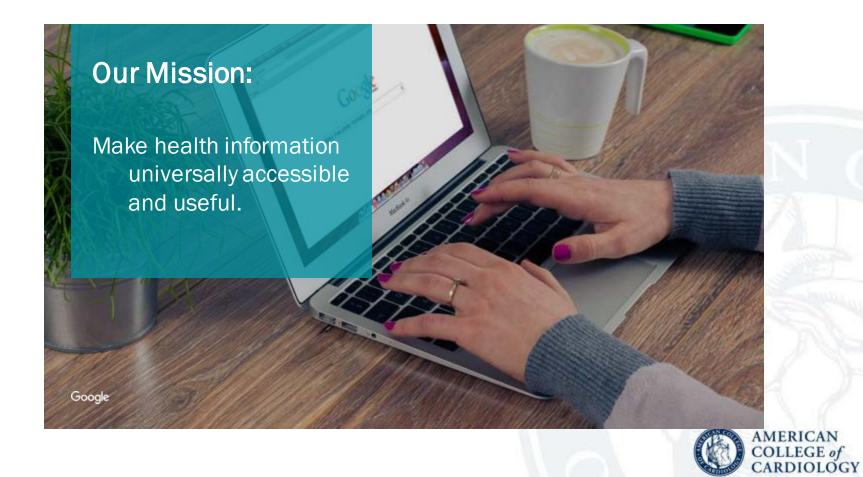
Technology advances; people stay the same.











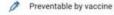
Information structure



A viral infection that's serious for small children but is easily preventable by a vaccine.



645 US cases in 2014



- Treatable by a medical professional
- Requires a medical diagnosis
- Lab tests or imaging often required
- Spreads easily
- Short-term: resolves within days to weeks

Measles symptoms don't appear until 10 to 14 days after exposure. They include cough, runny

Measles
Also called: rubeola

ABOUT SYMPTOMS TREATMENTS

Requires a medical diagnosis

Measles symptoms don't appear until 10 to 14 days after exposure. They include cough, runny nose, inflamed eyes, sore throat, fever, and a red, blotchy skin rash.

People may experience:

Pain areas: in the muscles

Cough: can be dry or severe

Whole body: fatigue, fever, loss of appetite, or malaise

Nasal: redness, runny nose, or sneezing

Skin: rashes or red spots

Also common: eye irritation, headache, pink eye, sensitivity to light, sore throat, or swollen lymph nodes



Measles

Also called niheola

INIT SYMPTO

TREATMENTS

Treatable by a medical professional

There's no treatment to get rid of an established measles infection, but over-the-counter fever reducers or vitamin A may help with symptoms.

Prescription

Vitamin A

Self-treatment

Pain reliever: Acetaminophen (Tylenol)

Also common

MMR vaccine

Specialists

Primary care provider (PCP): Prevents, diagnoses, and treats diseases.

Infectious disease doctor: Treats infections, including those that are tropical in nature.

Pediatrician: Provides medical care for infants, children, and teenagers.

Consult a doctor for medical advice -Sources: Mayo Clinic and others.





PRODUCT OVERVIEW: What is PHQ-

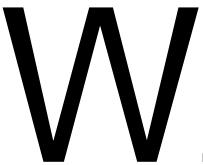
is a Patient Health Questionnaire, with 9 questions, that is used to measure depression severity

| PATIENT HEALTH QUESTIONNAIRE-9 | | | | | | | |
|--|---|-----------------|----------------------------------|------------------------|--|--|--|
| Over the <u>last 2 weeks</u> , how often have you been bothered by any of the following problems? | | Several days | More than half the days | Nearly every day | | | |
| Little interest or pleasure in doing things | 0 | 1 | 2 | 3 | | | |
| 2. Feeling down, depressed, or hopeless | 0 | 1 | 2 | 3 | | | |
| 3. Trouble falling or staying asleep, or sleeping too much | 0 | 1 | 2 | 3 | | | |
| Feeling tired or having little energy | 0 | 1 | 2 | 3 | | | |
| 5. Poor appetite or overeating | 0 | 1 | 2 | 3 | | | |
| Feeling bad about yourself — or that you are a failure or have let yourself or your family down | 0 | 1 | 2 | 3 | | | |
| Trouble concentrating on things, such as reading the newspaper or watching television | 0 | 1 | 2 | 3 | | | |
| Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual | 0 | 1 | 2 | 3 | | | |
| Thoughts that you would be better off dead or of hurting yourself in some way | 0 | 1 | 2 | 3 | | | |



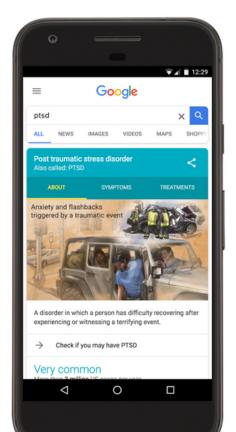
Google partners with VA, National Alliance on Mental Illness to offer PTSD screening

ву <u>Dave Muoio</u> December 05, 2017 SHARE 42



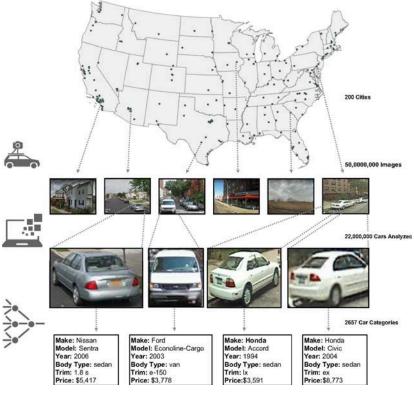
hen mobile users perform a Google search for PTSD or a related query on their mobil

The effort — a partnership between Google, the Na





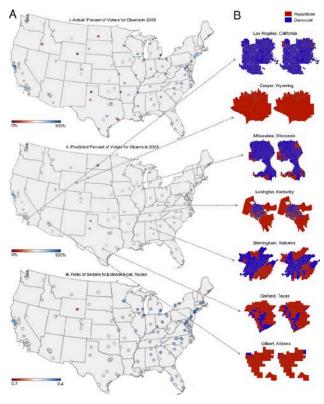
We perform a vehicular census of 200 cities in the United States using 50 million Google Street View images.



Timnit Gebru et al. PNAS doi:10.1073/pnas.1700035114

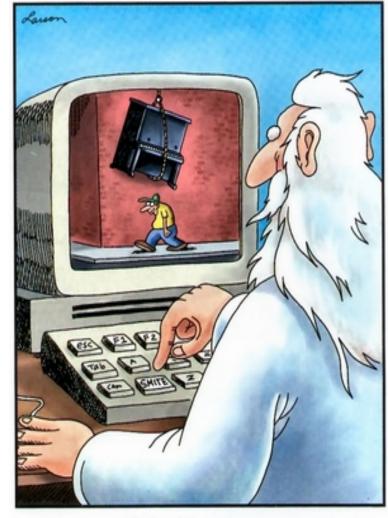


Actual and inferred voting patterns.



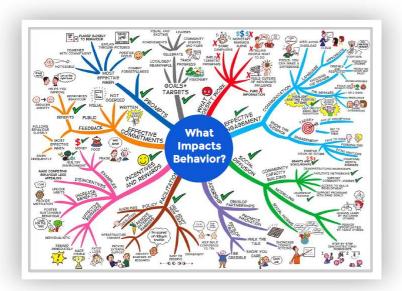
Timnit Gebru et al. PNAS doi:10.1073/pnas.1700035114

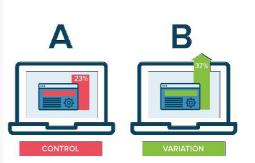
©2017 by National Academy of Sciences



God at His computer

Data Activation and Testing Outcomes







Verily |

Digital Transformation



- Data on premise, hard to access, analyze and use
- Productivity tools built for individual, local usage
- IT focusing on where it computes

- Data stored in cloud, simple to query
- Collaborative, cloud based productivity applications
- Machine learning drives deep, actionable insights
- IT changing how it computes



The Doctor and the Computer

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

ROBERT M, CALIFF, MD
ROBERT A. ROSATI, MD
Cardiovascular Division, Department of Medicine
Duke University Medical Center
Durham, North Carolina
THE WESTERN JOURNAL OF MEDICINE October 1981