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

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Duke University
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NY CVS
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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.

SY Tan, 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.

Paul Dudley White
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

- Better treatment of cardiovascular disease, low birth-weight infants
- Reduced infectious disease mortality (clean water, sewers, antibiotics, better nutrition)
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

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Life Expectancy at Birth by County, 2014

Counties 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.
Change in Life Expectancy at Birth by County, 1980 to 2014

Compared 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.
### Table 1. Variables Included in the Regression Analysis With Summary Statistics and Bivariate Regression Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Summary Statistics, Mean (SD) [Range]</th>
<th>Bivariate Regression Results</th>
<th>Coefficient (SE)</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Socioeconomic and race/Ethnicity factors</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Population below the poverty line, %</td>
<td>16.3 (6.4) [3.1-62.0]</td>
<td>-0.24 (0.005)</td>
<td>0.47</td>
<td></td>
</tr>
<tr>
<td>Median household income, log $</td>
<td>10.6 (0.2) [9.8-11.6]</td>
<td>0.66 (0.130)</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Graduates, age ≥25 y, %</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>High school</td>
<td>83.7 (7.2) [46.3-98.6]</td>
<td>0.20 (0.004)</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>19.2 (8.6) [4.2-72.0]</td>
<td>0.15 (0.004)</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>Unemployment rate, age ≥16 y, %</td>
<td>9.1 (3.2) [2.1-27.4]</td>
<td>-0.29 (0.011)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Black population, %</td>
<td>9.4 (14.7) [0-85.8]</td>
<td>-0.07 (0.002)</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>American Indian, Native Alaskan, and Native Hawaiian population, %</td>
<td>2.3 (7.9) [0-51.2]</td>
<td>-0.06 (0.005)</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Hispanic population, %</td>
<td>8.1 (13.1) [0-95.9]</td>
<td>0.02 (0.003)</td>
<td>0.01</td>
<td></td>
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<tr>
<td><strong>Behavioral and metabolic risk factors, %</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Obesity prevalence, age ≥20 y</td>
<td>37.0 (4.3) [18.0-52.0]</td>
<td>-0.19 (0.006)</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>No leisure-time physical activity prevalence, age ≥20 y</td>
<td>27.0 (5.2) [11.7-47.2]</td>
<td>-0.34 (0.003)</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking prevalence, age ≥18 y</td>
<td>24.7 (4.1) [7.7-42.1]</td>
<td>-0.40 (0.007)</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>Hypertension prevalence, age ≥30 y</td>
<td>39.5 (3.6) [27.9-56.4]</td>
<td>-0.49 (0.007)</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>Diabetes prevalence, age ≥20 y</td>
<td>14.0 (2.4) [8.1-25.5]</td>
<td>-0.72 (0.011)</td>
<td>0.59</td>
<td></td>
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<tr>
<td><strong>Health care factors</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Insured population, age ≥65 y, %</td>
<td>81.7 (5.7) [57.3-96.7]</td>
<td>0.15 (0.007)</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Quality index</td>
<td>76.1 (11.5) [0-100]</td>
<td>0.10 (0.003)</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Physicians per 1000 population, No.</td>
<td>1.1 (1.0) [0-4.4]</td>
<td>0.53 (0.039)</td>
<td>0.06</td>
<td></td>
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</tbody>
</table>

**Abbreviation:** SE, standard error.
Trends in 10-Year Predicted Absolute Cardiovascular Disease (CVD) Risk, Mean Systolic Blood Pressure, and Smoking by Income Strata

There 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. Error bars represent 95% CIs. NHANES indicates National Health and Nutrition Examination Survey.
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

When 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.”
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CONTINUOUS MONITORING THROUGH PASSIVE SENSORS

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

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

App
Mobile interface for self-reported and passive data acquisitions.

Study hub
Safely sends device data to secure, encrypted Baseline database.
The Process of Digital Phenotyping
digital phenotyping involves collecting sensor, keyboard, and voice and speech data from smartphones to measure behavior, cognition, and mood.

Figure Legend:
The Process of Digital Phenotyping...
DEEP MOLECULAR PROFILING

SAMPLES
- SERUM
- WHOLE BLOOD
- PBMCS
- PLASMA
- STOOL
- SALIVA
- URINE

CORE PLATFORMS
- CLINICAL LABS
- GENOMICS (WGS, DNA arrays)
- EPGENOMICS (Methyl arrays)
- TRANSCRIPTOMICS (RNA-seq)
- IMMUNOPHENOTYPING (CyTOF)
- MICROBIOME (16S rRNA)
- PROTEOMICS
- METABOLIMICS

AUTOMATION
- ~6TB data per subject
  - External/at clinic site
  - In-house
  - External
Learning health care systems

In a learning health care system, research influences practice and practice influences research.

**Implement**: Apply plan in pilot and control settings.

**Evaluate**: Collect data and analyze results to show what works and what doesn’t.

**Design**: Design care and evaluation based on evidence generated here and elsewhere.

**Adjust**: Use evidence to influence continual improvement.

**Disseminate**: Share results to improve care for everyone.

**Internal and External Scan**: Identify problems and potentially innovative solutions.
National System Paradigm Shift

Passive Surveillance: Challenging to find right pre/post market balance without confidence in post-market data.

Active Surveillance to better protect patients: Leverage RWE to support regulatory decisions throughout TPLC.

Current: Parallel track to clinical practice.

Inefficient one-off studies.

National System: Embedded in Health Care System (collect data during routine clinical care).

Shared system to inform the entire Ecosystem (patients, clinicians, providers, payers, FDA, Device Firms).
PCORnet® embodies a "network of networks" that harnesses the power of partnerships

20 Patient-Powered Research Networks (PPRNs) + 13 Clinical Data Research Networks (CDRNs) + 1 Coordinating Center = A national infrastructure for people-centered clinical research
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 Network**
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 Network for All (CENA)**
Genetic Alliance, Inc.

**COPD Patient Powered Research Network**
COPD Foundation

**DuchenneConnect Registry Network**
Parent Project Muscular Dystrophy

**Health eHeart Alliance**
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**
Accelerated Cure Project for Multiple Sclerosis

**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

**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”

PCORnet represents:
~122 million patients
who have had a medical encounter in the past 5 years

*some individuals may have visited more than one Network Partner and would be counted more than once
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

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 outreach-based 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.
1 in 20 of over 3 billion Google searches per day are health related.
Our Mission:

Make health information universally accessible and useful.
### Measles

**About**

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

**Symptoms**

- Fever
- Dry Cough
- Runny nose
- Rash

**Treatments**

- Treatable by a medical professional

**Very rare**

645 US cases in 2014

- Preventable by vaccine
- 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 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

**Card Creation**
PRODUCT OVERVIEW: What is PHQ-9?

PHQ-9 is a Patient Health Questionnaire, with 9 questions, that is used to measure depression severity.
Google partners with VA, National Alliance on Mental Illness to offer PTSD screening

by Dave Muoio
December 05, 2017
SHARE 42

When 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.
Actual and inferred voting patterns.
Data Activation and Testing Outcomes

What Impacts Behavior?

A  B
CONTROL  VARIATION
Digital Transformation

2010
- Individual Productivity
- IT Silos
- Data on premise, hard to access, analyze and use
- Productivity tools built for individual, local usage
- IT focusing on where it computes

2020
- Collective Intelligence
- Distributed Computing
- 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.

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THE WESTERN JOURNAL OF MEDICINE October 1981