What is Precision Public Health and Where Does FH Fit in?

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Office of Genomics and Precision Public Health
Centers for Disease Control and Prevention

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

From Genomic Medicine to Precision Medicine

➢ **Increasing Number of genetic tests (from single genes to panels and NGS)**

➢ **Whole-genome sequencing as tool in clinical and public health practice**

➢ **Increasing public interest and proliferation of direct-to-consumer tests**

➢ **All of Us Research Initiative (1M person cohort)- genes and environments**
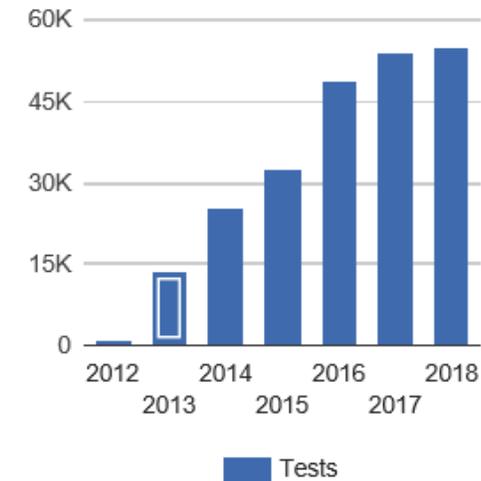
What is precision medicine?

"An emerging approach for disease prevention and treatment that takes into account people's individual variations in genes, environment, and lifestyle."

NIH Genetic Testing Registry Search September 15, 2019
59986 tests, 11995 conditions, 18629 genes, and 530 labs

CDC Office of Genomics and Precision Public Health

1. Identify
evidence-based applications

2. Inform
and communicate

3. Integrate
into practice & programs

- Selected "Tier 1" applications
- *BRCA1/2* Related Cancers, Lynch Syndrome
- Familial Hypercholesterolemia
- Collectively Affect >2 Million People in US and Most Don't know it.
- Implementation of existing evidence-based guidelines can prevent cancer & heart disease, & save thousands of lives every year!
- Toolkit for public health departments
- Working with CDC programs and external partners

https://www.cdc.gov/genomics

Will Precision Medicine Improve Population Health?

Will Precision Medicine Improve Population Health?

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Announcement of the precision medicine initiative has led to a variety of responses, ranging from enthusiastic expectations[1] to explicit skepticism,[2] about potential health benefits, limitations, and return on investment. This Viewpoint discusses whether precision medicine is unlikely or likely to improve population health, aiming to forge a consensus that bridges disparate perspectives on the issue. The potential of precision medicine to improve the health of individuals or small groups of individuals is not addressed here because it involves a different question with different metrics.

Precision Medicine Is Unlikely to Improve Population Health

There are 3 fundamental reasons that precision medicine might not improve the health of populations. First, disease pathogenesis, especially for common noncommunicable diseases, is extraordinarily complex. Abundant evidence has demonstrated this for the association between the multiplicity of specific genes and conditions, including obesity, hypertension, or certain cancers. Additionally, it is known that genetic associa-

health of its population. Over the past 30 years, the United States has fallen behind other high-income peer nations in health attainment on many metrics, including life expectancy and infant mortality, and there are persistent gaps in health outcomes by income and race/ethnicity.[4] The solution to these challenges is probably not an increased focus on the individual, but rather lies in focusing on the social, economic, and structural drivers of population health that are ubiquitous and inevitably linked to health achievement as a country. The centrality of the precision medicine effort to the US national health research agenda may distract from efforts to remedy the foundational causes of ill health such as poverty, obesity, and education. Without addressing these causes, there will be little, if any, success in reversing the trends of poor achievement in US population health.

Second, precision medicine could (and to some extent has) led to a shift from which projects are funded by health research agencies. Funding for grants with a population health or public health goal has declined over the past 10 years at the National Institutes of Health,

Khoury MJ, et al. JAMA, 2017
Frieden TR, NEJM, 2015
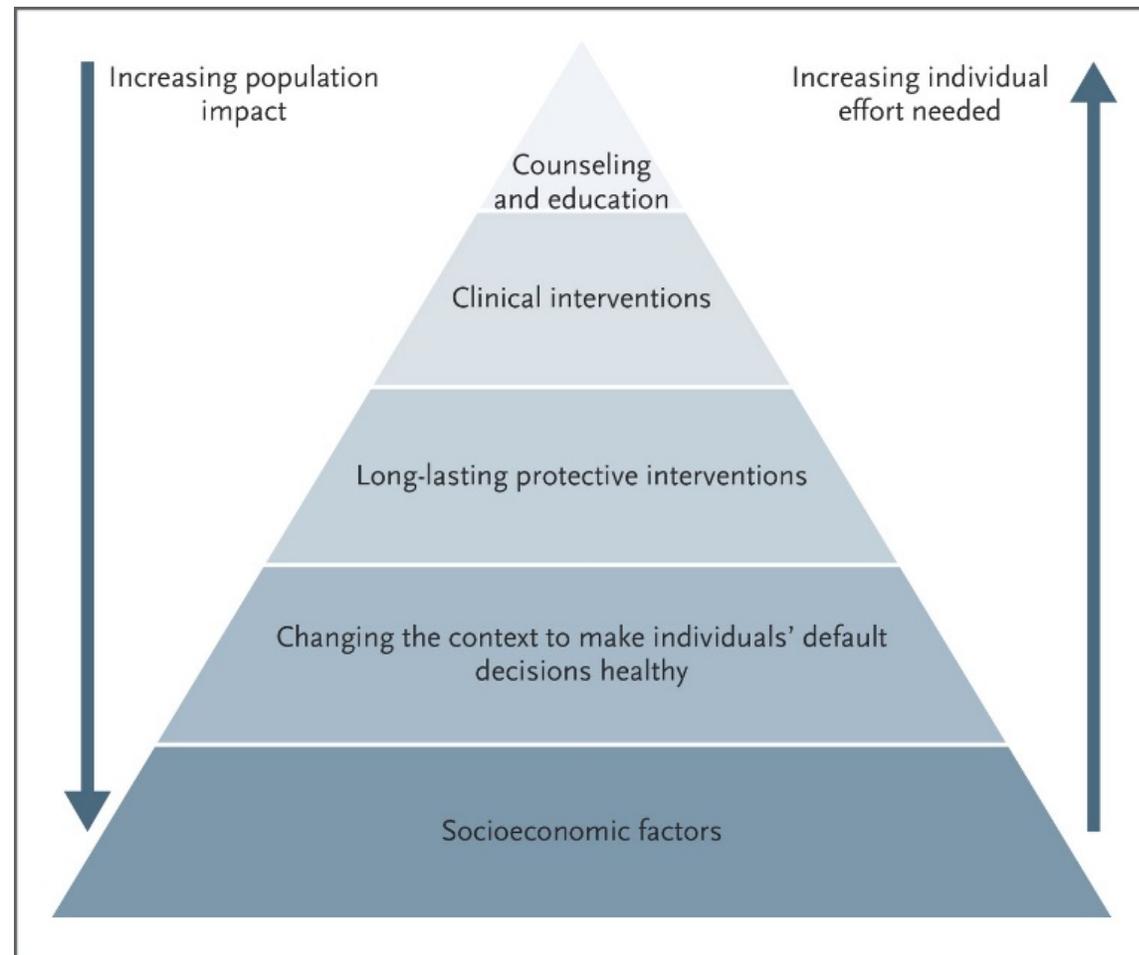
Precision Medicine and Precision Public Health: Two Peas in a Pod!
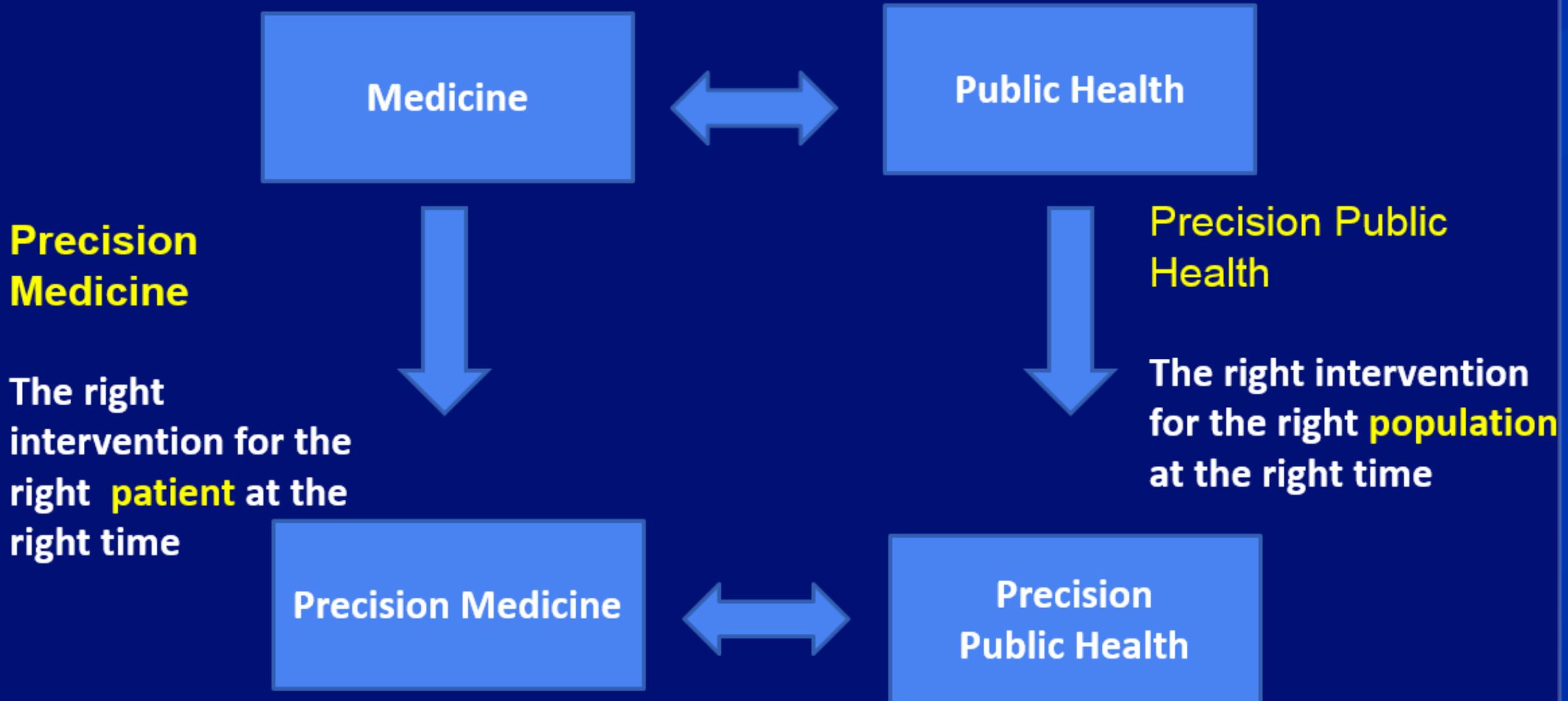
Beyond Public Health Genomics: Can Big Data and Predictive Analytics Deliver Precision Public Health?

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PHG, 2019

Abstract
The field of public health genomics has matured in the past two decades and is beginning to deliver genomic-based interventions for health and health care. In the past few years, the terms precision medicine and precision public health have been used to include information from multiple fields measuring biomarkers as well as environmental and other variables to provide tailored interventions. In the context of public health, "precision" implies delivering the right intervention to the right population at the right time, with the goal of improving health for all. In addition to genomics, precision public health can be driven by "big data" as identified by volume, variety, and variability in biomedical, sociodemographic, environmental, geographic, and other information. Most current big data applications in health are in elucidating pathobiology and tailored drug discovery. We explore how big data and predictive analytics can contribute to precision public health by improving public health surveillance and assessment, and efforts to promote uptake of evidence-based interventions, by including more extensive information related to place, person, and time. We use selected examples drawn from child health, cardiovascular disease, and cancer to illustrate the promises of precision public health, as well as current methodologic and analytic challenges to big data to fulfill these promises.   © 2019 S. Karger AG, Basel

Introduction

The term "precision" is increasingly used in medicine [1] and public health [2]. Precision medicine is often used synonymously with genomic medicine, and precision public health has been equated with applications of precision medicine in populations [3]. Applications of precision medicine (e.g., cancer genomics) are unlikely to lead to improved population health, as targeted interventions benefit only a small subset of the population. Nevertheless, as we and others have discussed, there is a bigger role for precision in public health beyond genomics [4]. Precision public health can be viewed as the delivery of the right intervention to the right population at the right time, and includes consideration of social and environ-

Put at its simplest, precision public health is about using the best available data to target more effectively and efficiently interventions of all kinds to those most in need."

R Horton, Lancet 2018

Can we Conduct Public Health Functions With More "Precision"?

❑ **Assessment**

➤ More "precision" in measuring population health problems

❑ **Policy Development**

➤ Developing the right intervention for the right population at the right time

❑ **Assurance**

➤ More "precision" in delivering interventions & addressing health disparities

AJPM, 2016

Precision Public Health for the Era of Precision Medicine

Muin J. Khoury, MD, PhD,[1,2] Michael F. Iademarco, MD, MPH,[1,3] William T. Riley, PhD[2]

The Precision Medicine Initiative[1] promises a new healthcare era. A proposed 1 million–person cohort could create a deeper understanding of disease causation. Improvements in quality of sequencing, reduction in price, and advances in "omic" fields and biotechnology promise a new era, variably labeled personalized or precision medicine. Although genomics is one driver of precision health care, other factors may be as important (e.g., health information technology).

Both excitement and skepticism met the announcement.[2] Public health experts are concerned about the disproportionate emphasis on genes, drugs, and disease, while neglecting strategies to address social determinants

evidentiary foundation for use. The following are examples of priority areas.

Role of Multidisciplinary Public Health Sciences

Though precision medicine focuses on individualized care, its success truly requires a population-based approach. To learn what interventions work for whom, data on each individual need to be compared with data from large, diverse numbers of people to identify population subgroups likely to respond differently to interventions. In addition, collecting information from

Using Big Data in Public Health Requires Complex Analytics, By Person, Place and Time
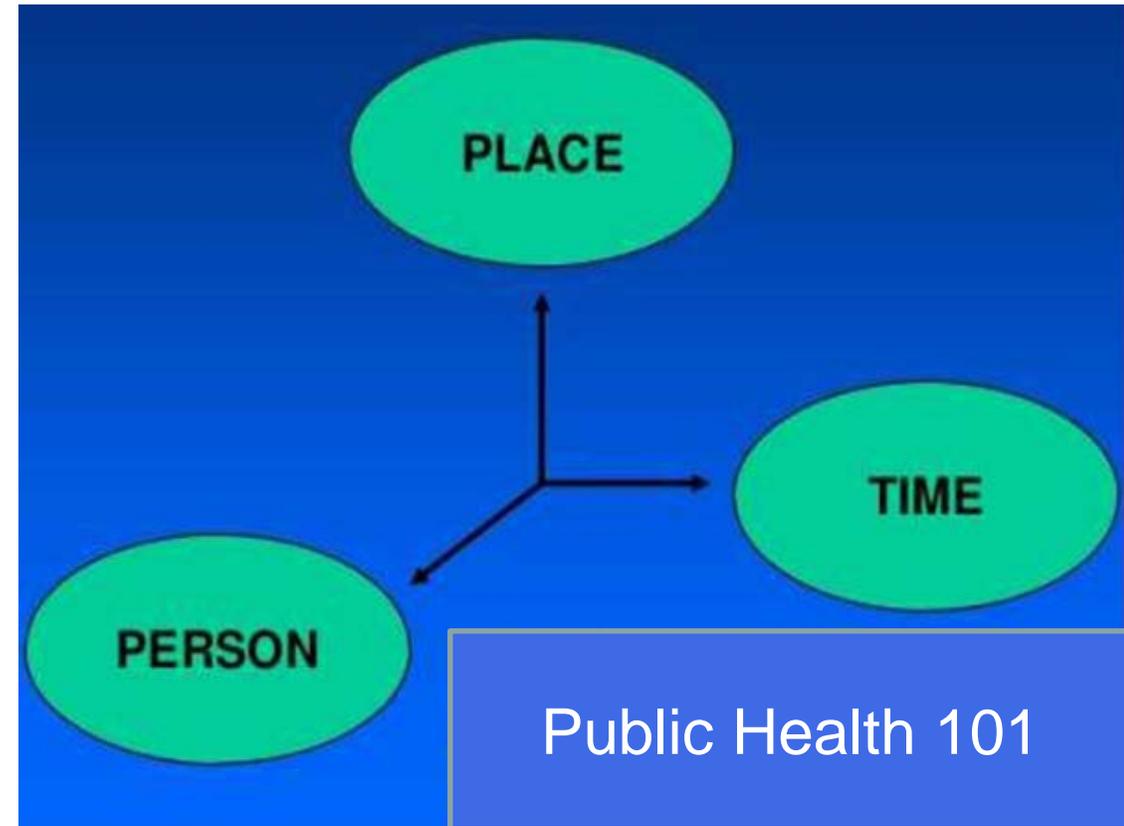
❑ Person

  ➢ Disease subtypes using biomarkers

  ➢ Disease susceptibility (e.g. genetics)

❑ Place

  ➢ Geographic and environmental data

  ➢ Health systems

❑ Time

  ➢ Wearables

  ➢ Social Media

PLACE

TIME

PERSON

Public Health 101

Khoury MJ et al, Public Health Genomics, 2019

ARTICLE

https://doi.org/10.1038/s41467-018-08082-0   OPEN

Improved state-level influenza nowcasting in the United States leveraging Internet-based data and network approaches

Fred S. Lu[1], Mohammad W. Hattab[2], Cesar Leonardo Clemente[3], Matthew Biggerstaff[4] & Mauricio Santillana[1,5]

In the presence of health threats, precision public health approaches aim to provide targeted, timely, and population-specific interventions. Accurate surveillance methodologies that can estimate infectious disease activity ahead of official healthcare-based reports, at relevant spatial resolutions, are important for achieving this goal. Here we introduce a methodological framework which dynamically combines two distinct influenza tracking techniques, using an ensemble machine learning approach, to achieve improved state-level influenza activity estimates in the United States. The two predictive techniques behind the ensemble utilize (1) a self-correcting statistical method combining influenza-related Google search frequencies, information from electronic health records, and historical flu trends within each state, and (2) a network-based approach leveraging spatio-temporal synchronicities observed in historical influenza activity across states. The ensemble considerably outperforms each component method in addition to previously proposed state-specific methods for influenza tracking, with higher correlations and lower prediction errors.

Figure 2. Actual Obesity Prevalence and Cross-Validated Model Estimates of Obesity Prevalence in High-Prevalence Areas
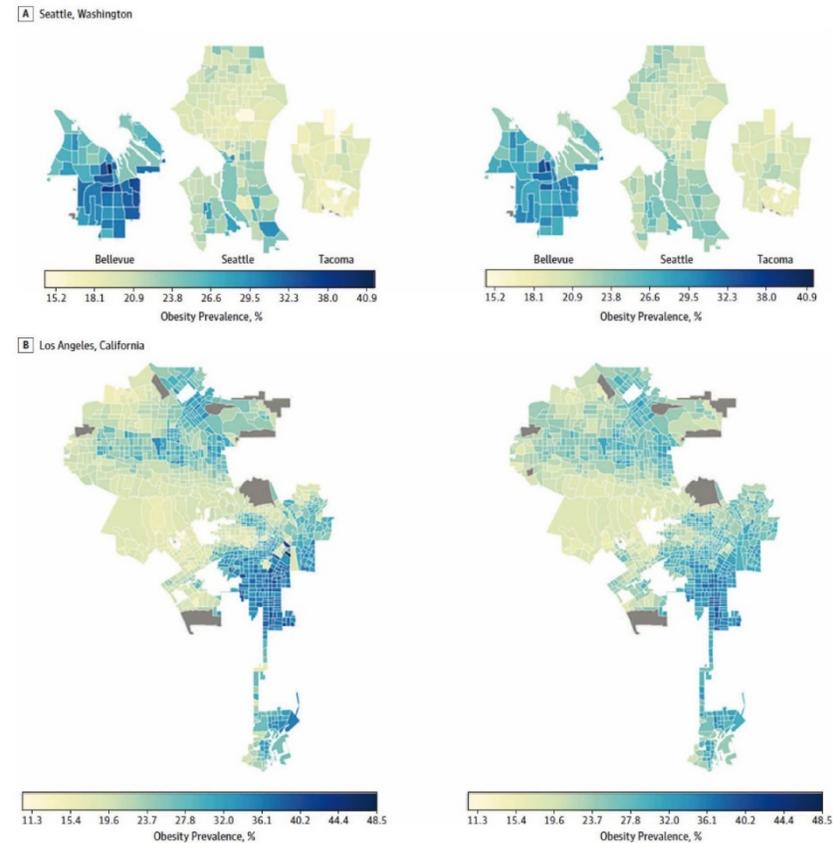
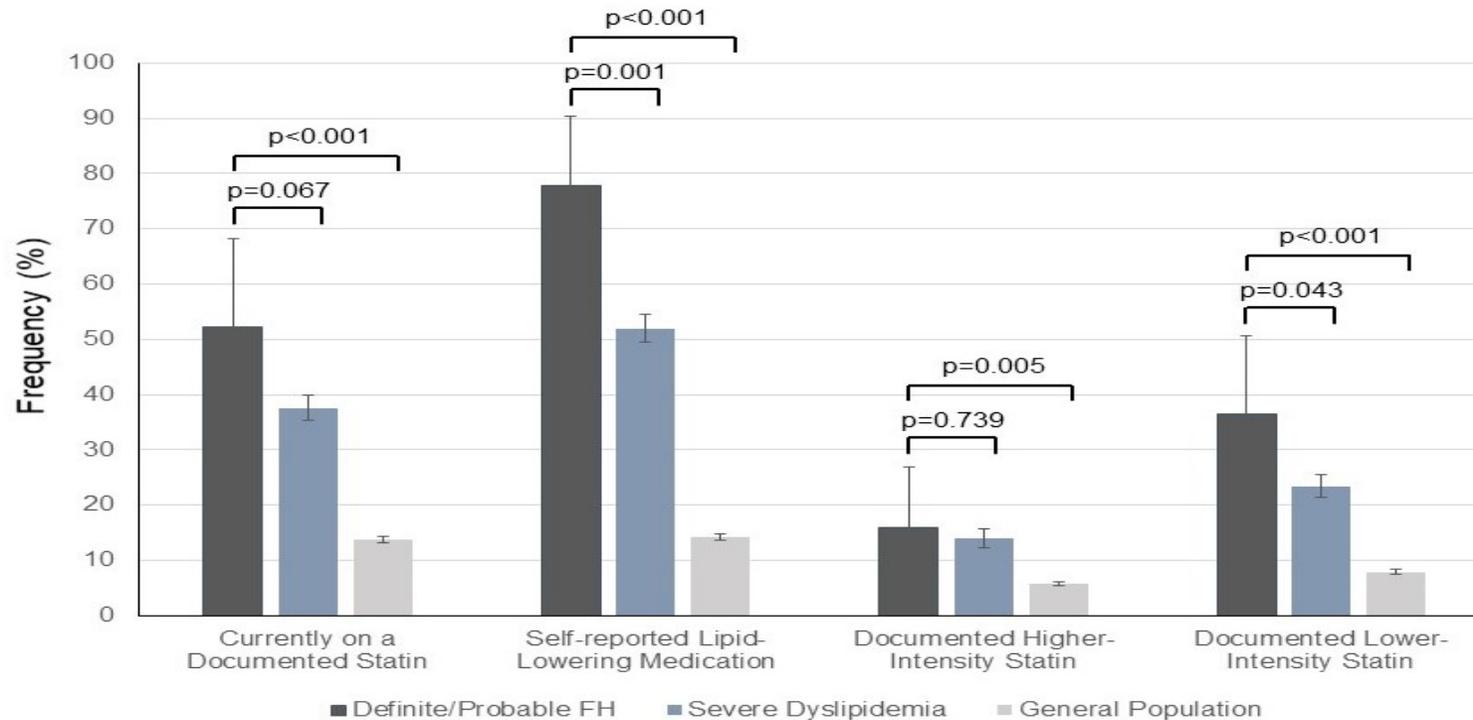# Familial Hypercholesterolemia

- **Common autosomal dominant condition associated with premature death from heart disease (> 1M affected in US)**
- **Evidence-based recommendation for aggressive cholesterol reduction and cascade screening in relatives**
- **Highly underdiagnosed and undertreated**
- **Racial and ethnic disparities in diagnosis and management**
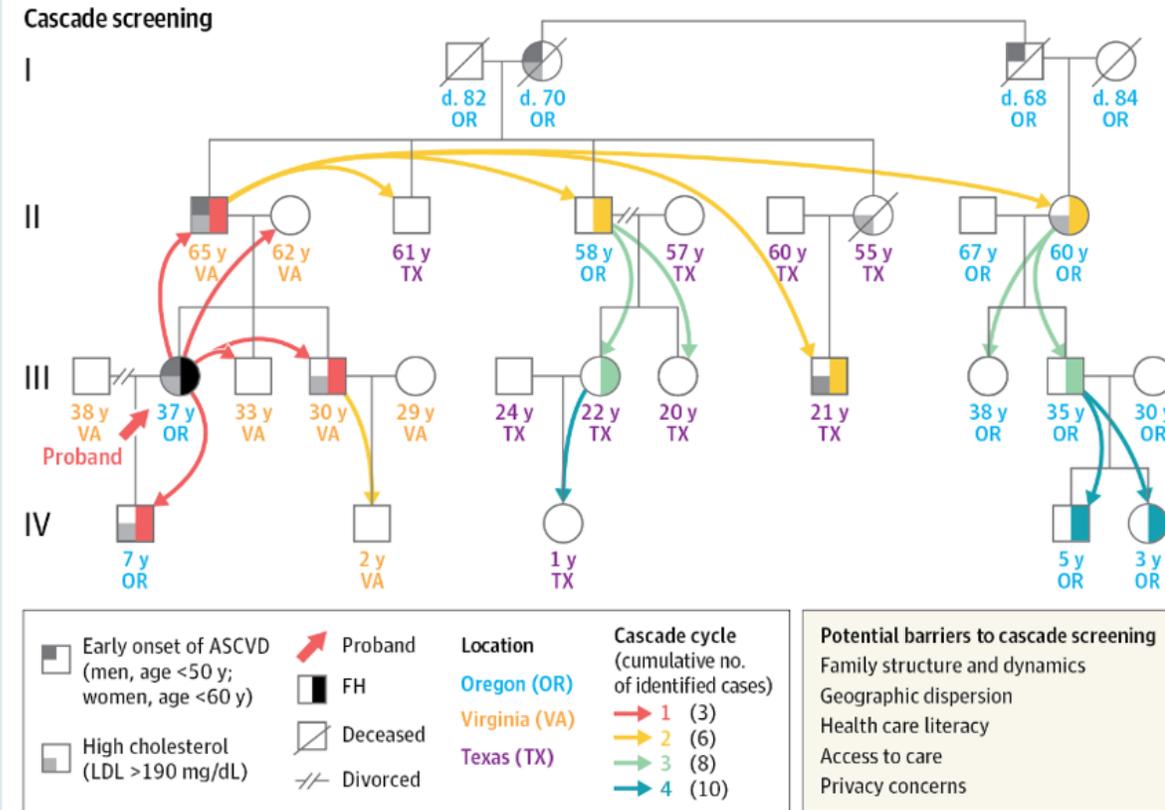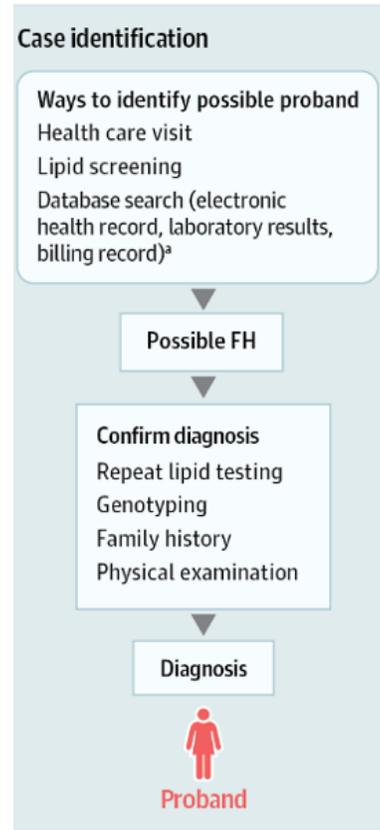
JW Knowles et al, JAMA, 2017

Familial Hypercholesterolemia is Common and Undertreated in the United States

Prevalence of documented statin and self-reported lipid lowering medication use

Young and uninsured patients are at the highest risk for under treatment

Bucholz, EM et al. Prevalence and predictors of cholesterol screening, awareness, and statin treatment among U.S. adults with familial hypercholesterolemia or other forms of severe dyslipidemia (1999-2014). Submitted.

Social Media

Heat Maps

Finding Missed Cases of Familial Hypercholesterolemia in Health Systems Using Machine Learning

B) Evaluation by chart review

Flagged by classifier

35,562 potential cases at **Stanford**

0.60-0.69 (n = 10)	0.70-0.79 (n=16)	0.80-0.89 (n=18)	0.90-0.99 (n=56)
10%	56%	50%	84%

Percentage of correct cases per DLNC or MEDPED criteria on chart review of 100 predictions across different predicted probability levels

197 FH cases

6,590 non-FH controls (age and sex matched)

Classifier for FH
PPV = 0.88
sensitivity = 0.75
specificity = 0.99

A) Internal Validation

Geisinger 71 cases

4,970 non-cases

PPV = 0.85
sensitivity = 0.68
specificity = 0.99

The 71 cases are a random sample of the full 466 FH cases found at Geisinger. This sampling was done 10 times

C) External Validation

Banda JM et al, NPJ Digital Medicine 2019

CASCADE FH REGISTRY
Longitudinal Follow-Up Analysis

Heterozygous FH Patients (N=1900): 56 years of age, 61% Female, Untreated LDL-C 249 mg/dl

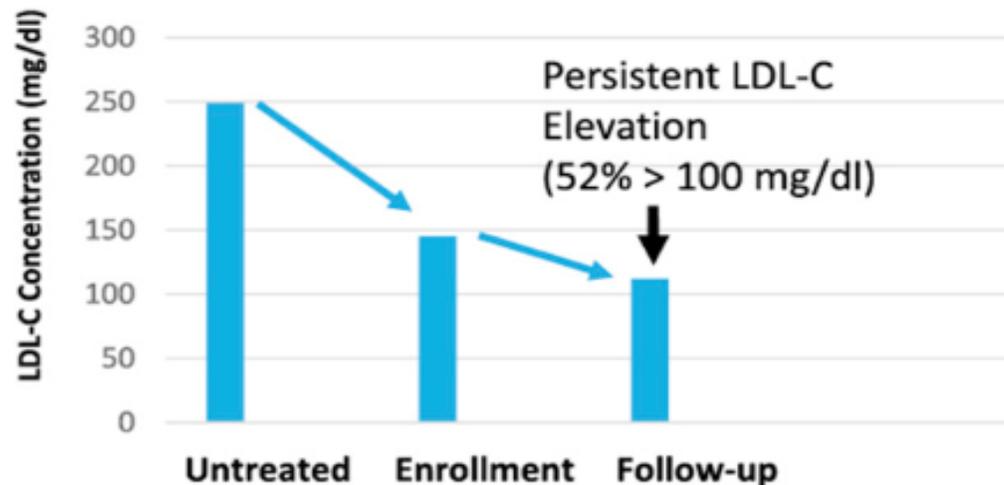**High Rate of Prevalent ASCVD at Enrollment**

1196 without ASCVD (63%) →

704 with ASCVD (37%) →

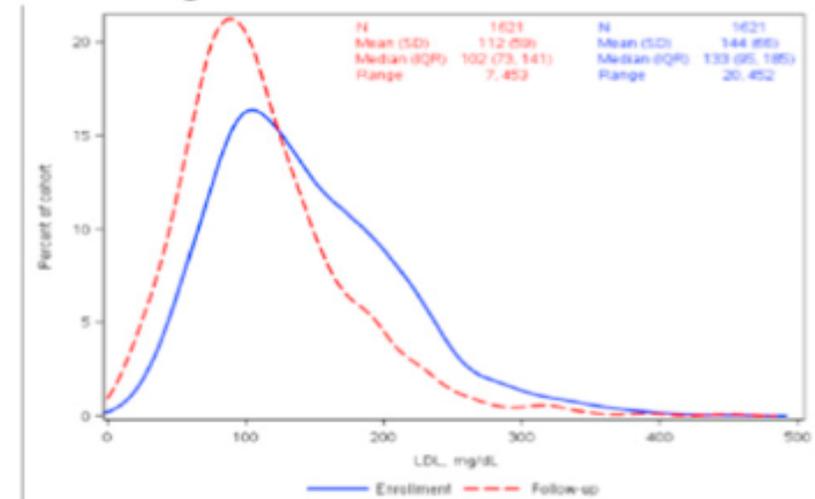**High Rate of Incident ASCVD Events During 20 months F/U**

16 new ASCVD events **(0.8/100 patient years)** (estimated 8.2% 10-year risk)

53 new ASCVD events **(4.6/100 patient years)** (estimated 45.7% 10-year risk)

Mean LDL-C Results Over Time

Persistent LDL-C Elevation (52% > 100 mg/dl)

LDL-C Concentration (mg/dl): Untreated, Enrollment, Follow-up

Change in LDL-C After Enrollment

FH in the Era of Precision Public Health