

Will Precision Medicine Improve Population Health?

Yes, But....

Muin J. Khoury MD, PhD

Office of Public Health Genomics

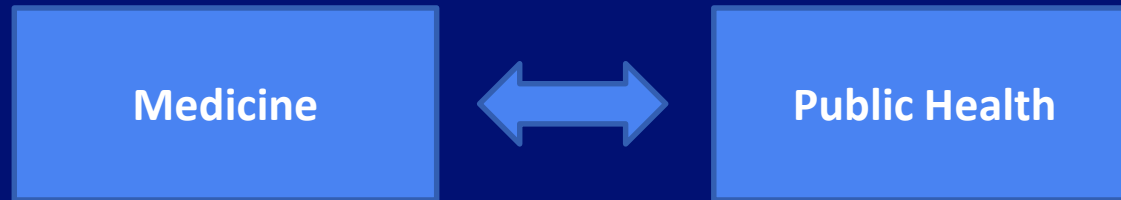
Centers for Disease Control and Prevention

Precision Medicine and Public Health

4 Themes

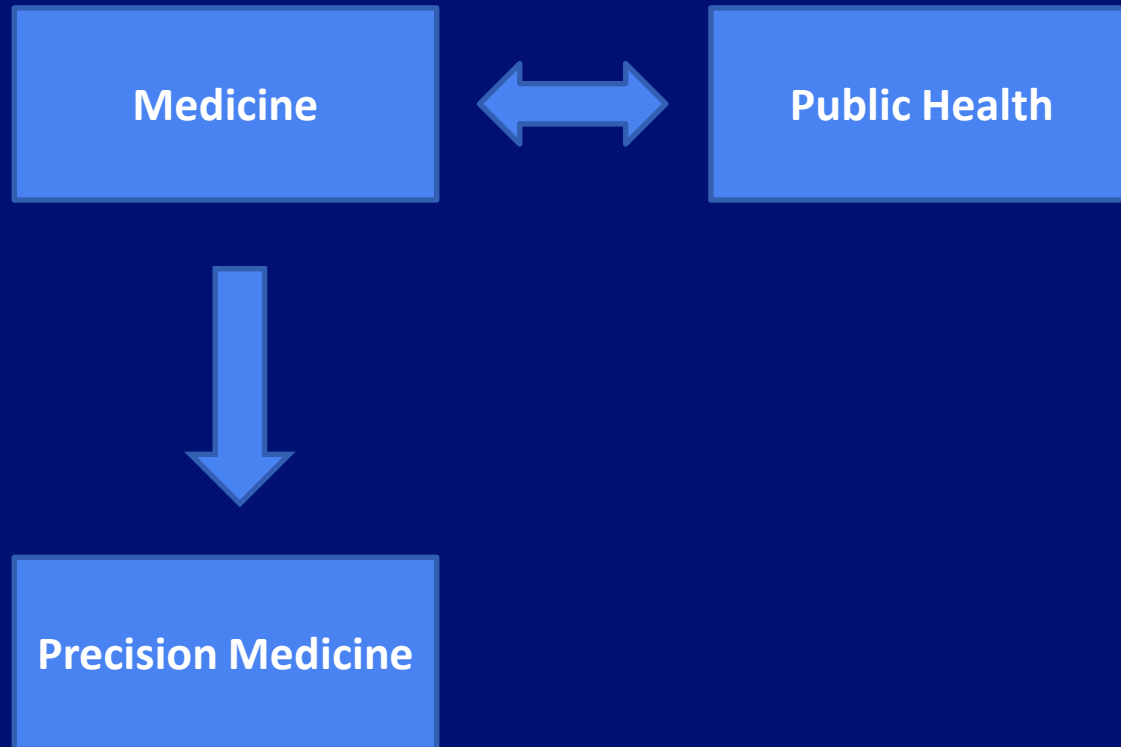
Medicine and Public Health:

Theme I. We Need Both to Improve Population Health



Precision Medicine and Public Health:

Theme I. We Need Both to Improve Population Health



What is Precision Medicine?

NATIONAL CANCER INSTITUTE PRECISION MEDICINE IN CANCER TREATMENT

Discovering unique therapies that treat an individual's cancer based on the specific genetic abnormalities of that person's tumor.



www.cancer.gov



Patient Partnerships



EHRs



Technologies



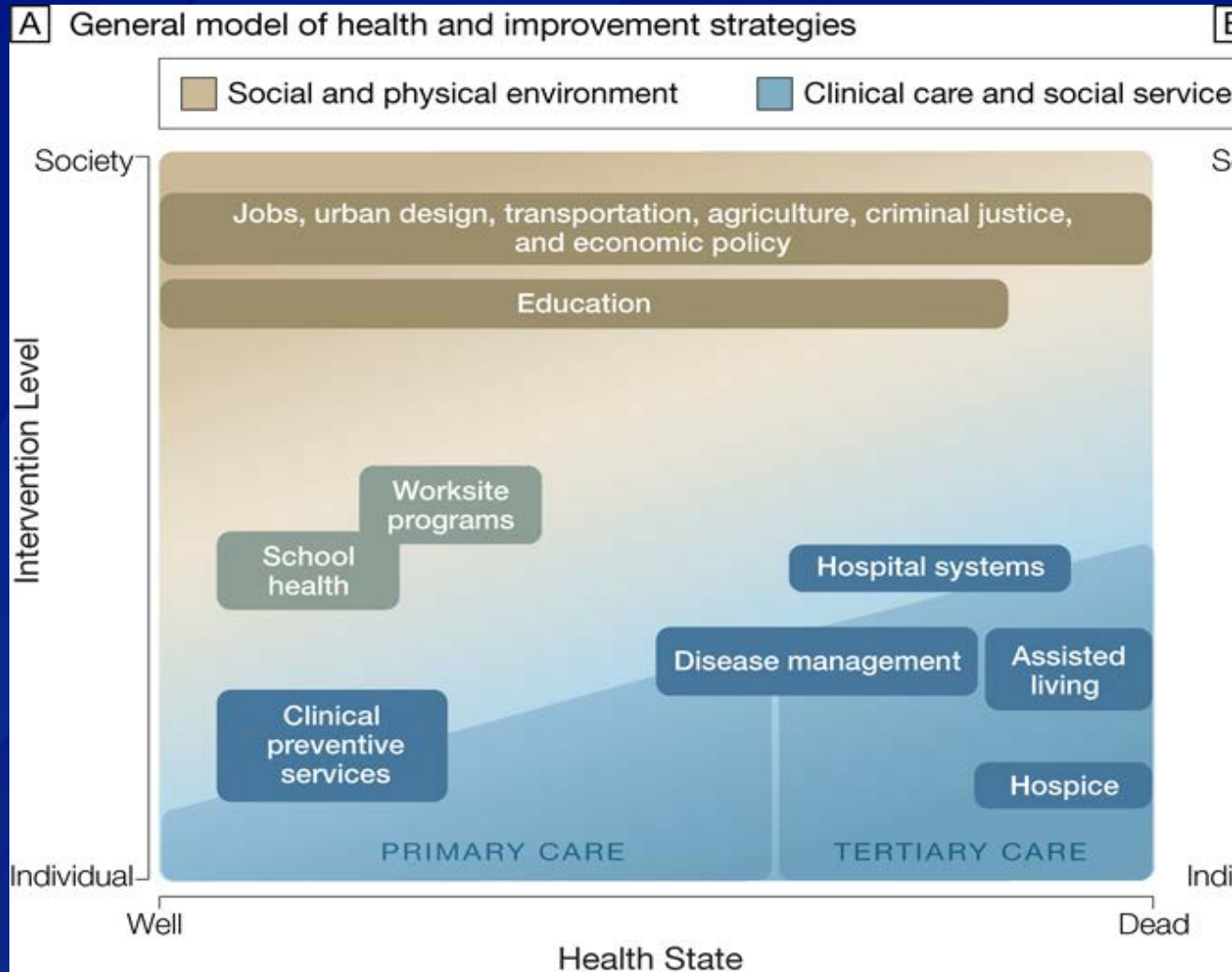
Genomics



Data Science

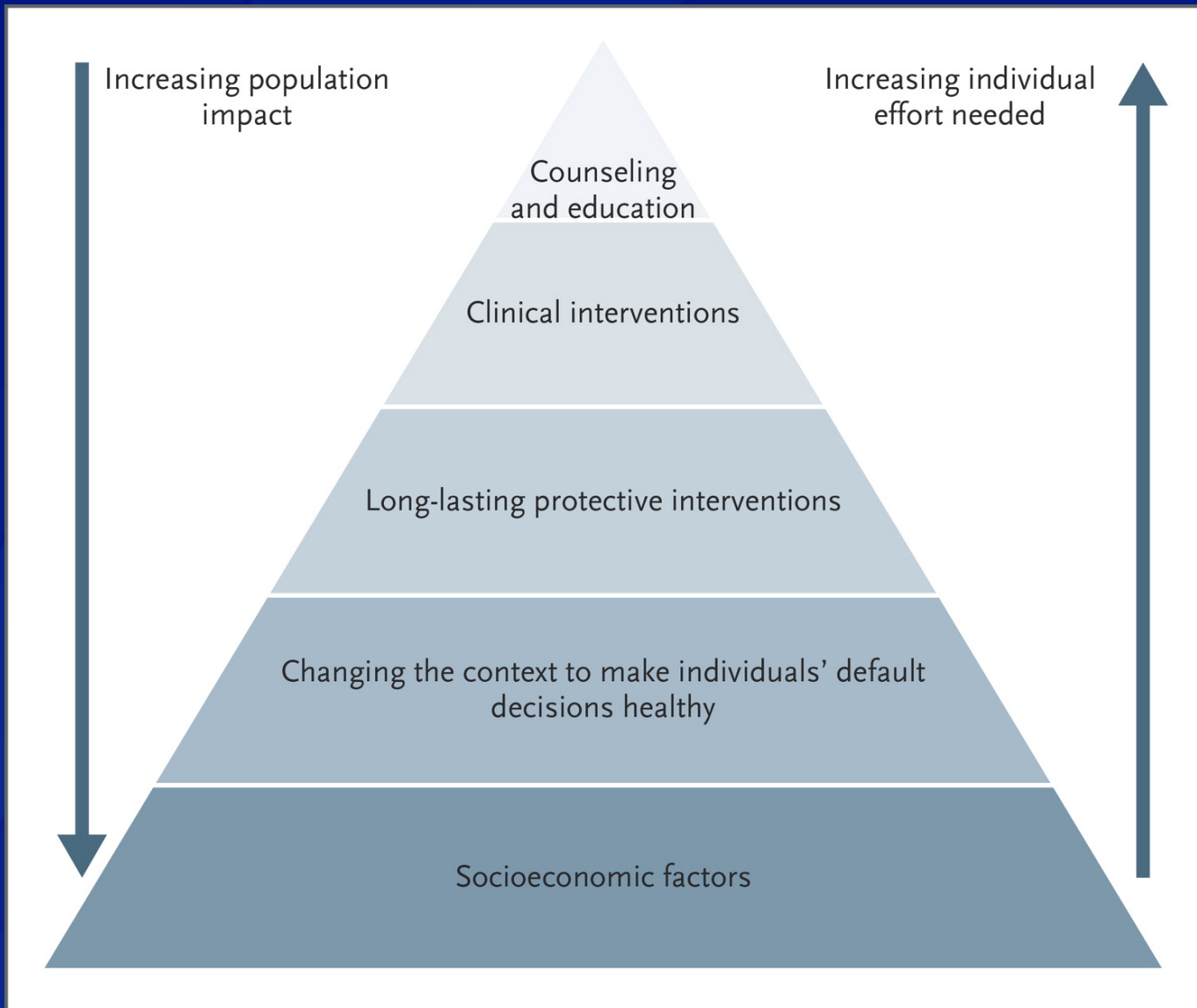
An emerging approach for disease prevention and treatment that takes into account variations in genes, environment, and lifestyle

Spectrum of Health & Strategies to Improve It: Individual and Population Approaches



Fielding, J. E. et al. JAMA 2011;305:2110-2111

The Health Impact Pyramid



Frieden TR. *N Engl J Med* 2015;373:1748-1754.

Precision Medicine and Public Health: We Need Both!

Precision Medicine vs. Public Health: a False Dichotomy?

Posted on September 28, 2015 by Ron Zimmern, PHG Foundation and Muin J. Khoury, Office of Public Health Genomics, Centers for Disease Control and Prevention

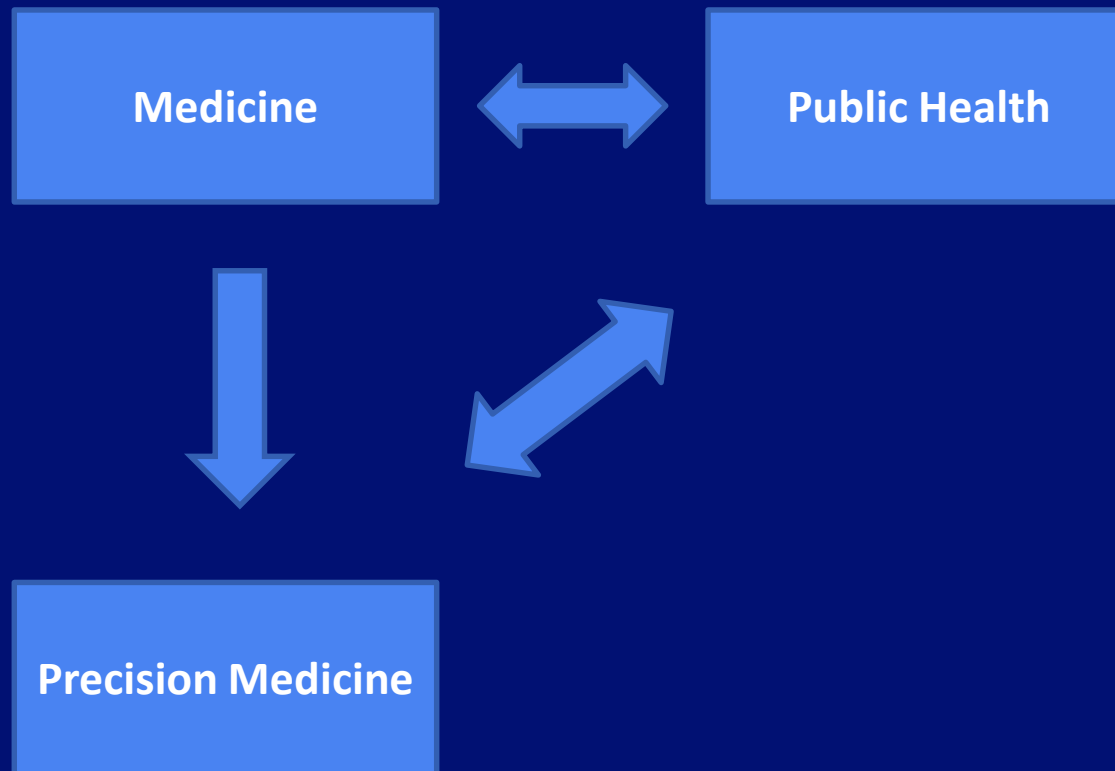


The recent focus on precision medicine has attracted criticism from the [public health community](#) that firmly believes that health is determined by far more than health care, and that more sophisticated medical technologies may not adequately address important determinants of population health. There is no argument that a focus on the wider environmental, structural and social determinants of health is of the greatest importance for improving the health of populations and addressing health disparities. However, we wonder whether a contrast between public health practice and precision medicine is a false dichotomy. Improving the health of populations requires a multifaceted approach that includes access to quality health care and diverse disease prevention efforts. Already public health programs are using the power of genomics and molecular tools in the [investigation and control of infectious disease outbreaks](#). For common chronic diseases, evidence is accumulating for targeting [preventive actions that incorporate genomics](#).



Precision Medicine and Public Health:

Theme II. Implementing What We Already Know



VIEWPOINT

A Public Health Perspective on a National Precision Medicine Cohort

Balancing Long-term Knowledge Generation With Early Health Benefit

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The new US precision medicine initiative¹ has been made possible by improvement and price reduction in genome sequencing, as well as advances in multiple sectors of biotechnology. The initiative includes 2 components: a focus on cancer intended to spur development of new targeted cancer treatments, and a proposal for establishing a national cohort of at least 1 million people to explore genetic and environmental determinants of health and disease. The success of this initiative requires a public health perspective to help ensure generalizability, assess methods of implementation, focus on prevention, and provide an appropriate balance between generation of long-term knowledge and short-term health gains.

Although precision medicine focuses on individualized

enefit. For example, improving access to smoking cessation assistance is a component of the highly successful public health efforts that have resulted in reductions in smoking over the past few decades. Recent data suggest that using genetically informed biomarkers of the speed with which people metabolize nicotine² could lead to personalized smoking cessation. Another example of precision prevention is changes in recommended screening schedules for people at increased risk of cancer, identified either by acquisition of family health history or through detection of those individuals who carry pathogenic mutations in high-risk cancer genes.

The proposed long-term investment in precision medicine comes at a time of increasing fiscal restraint and widespread recognition that the US health care system

CDC Evidence-based Classification of Genomic Tests

Tier 1	Supported by a base of synthesized evidence for implementation in practice	e.g., HBOC, Lynch syndrome, newborn screening
Tier 2	Synthesized evidence is insufficient to support routine implementation in practice; may provide information for informed decision making	e.g., many pharmacogenomic tests
Tier 3	Evidence-based recommendations against use, or no relevant synthesized evidence identified; not ready for routine implementation in practice	e.g., direct-to-consumer personal genomic tests

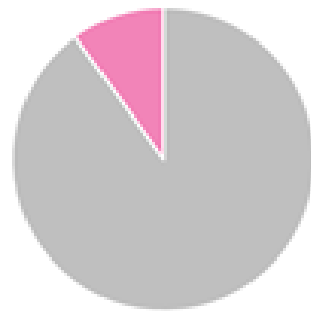
Dotson WD, Douglas MP, Kolor K, et al. Clin Pharmacol Ther. 2014 Apr; 95(4): 394–402.

List of applications by level of evidence on CDC Public Health Genomics Knowledge Base website:

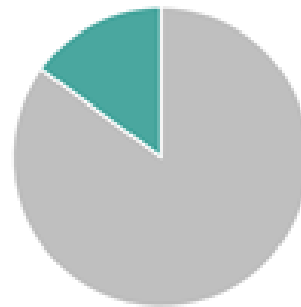
<https://phgkb.cdc.gov/GAPPKB/topicStartPage.do>

Selected Cancers Associated with Hereditary Syndromes

HBOC Syndrome

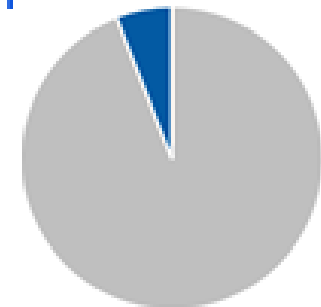


Up to 10% or approximately
22,000 cases of
breast cancer each year



15% or approximately
3,000 cases of ovarian
cancer each year

Lynch Syndrome



Up to 3-5% or approximately
4,000 cases of
colorectal cancer each year

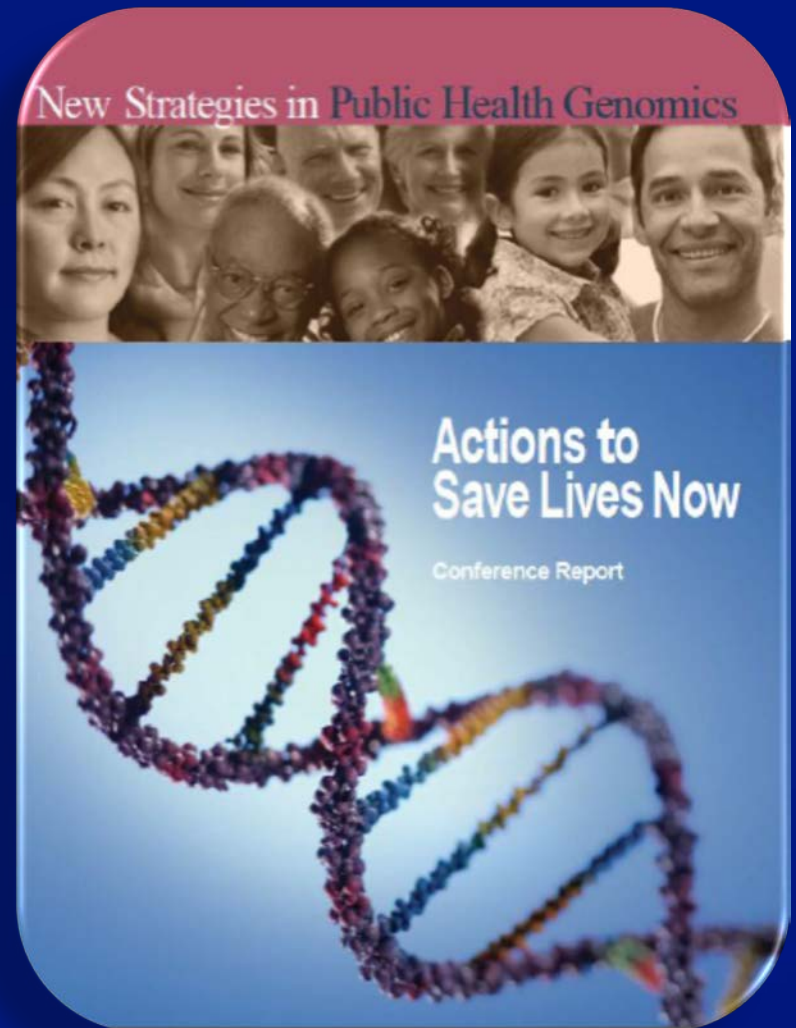
Campeau PM, Foulkes WD, Tischkowitz MD. Human Genetics 2008; 124(1):31-42.

Pal T, Permuth-Wey J, Betts JA, et al. Cancer 2005; 104(12):2807-16.

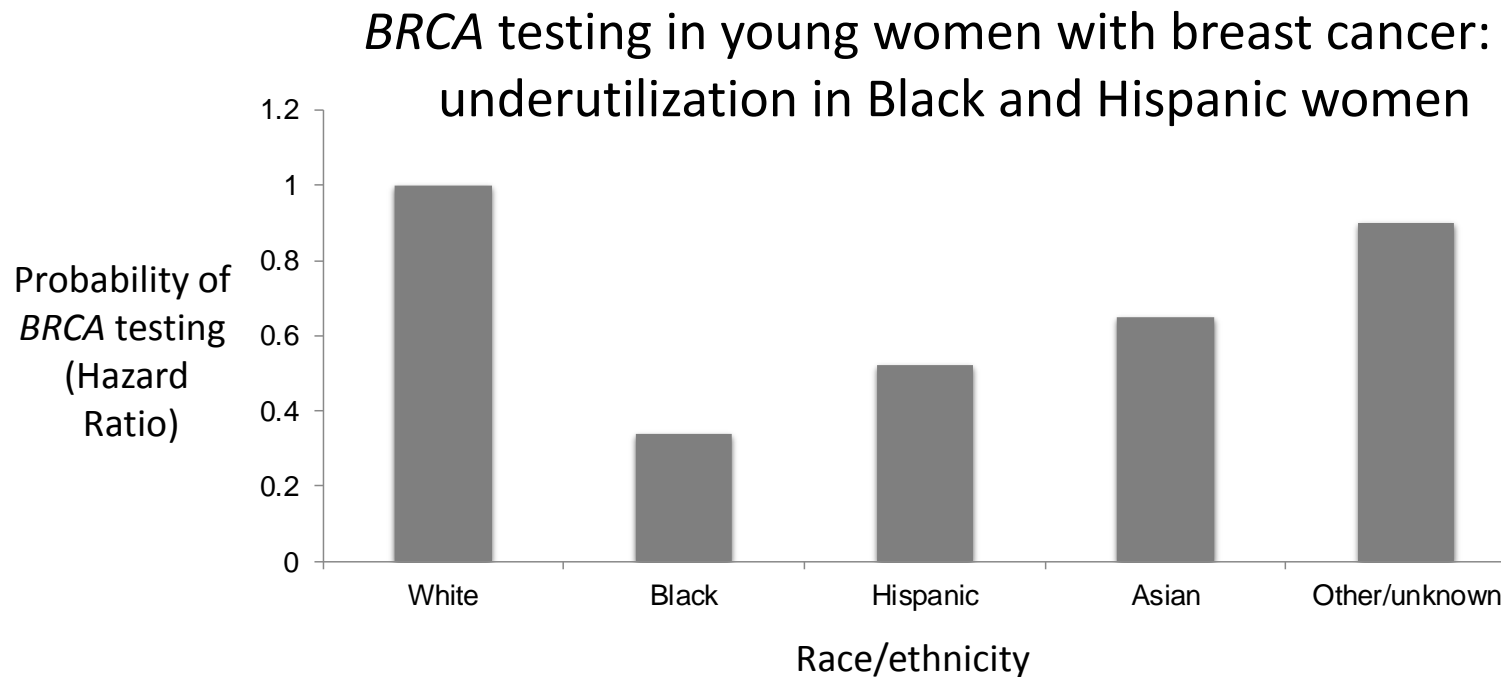
Hampel H, Frankel WL, Martin E, et al. J Clin Oncol 2008; 26 (35): 5783-8.

Selected Tier 1 Cancer Genomic Applications:

- Autosomal dominant disorders with adult onset
- Relatively common (collectively >1 million people in the US)
- Most people not ascertained or managed by health care
- Evidence of disparities
- Effective interventions that reduce mortality
- Involves family history and cascading interventions
- Can be integrated into public health programs with strong healthcare collaborations



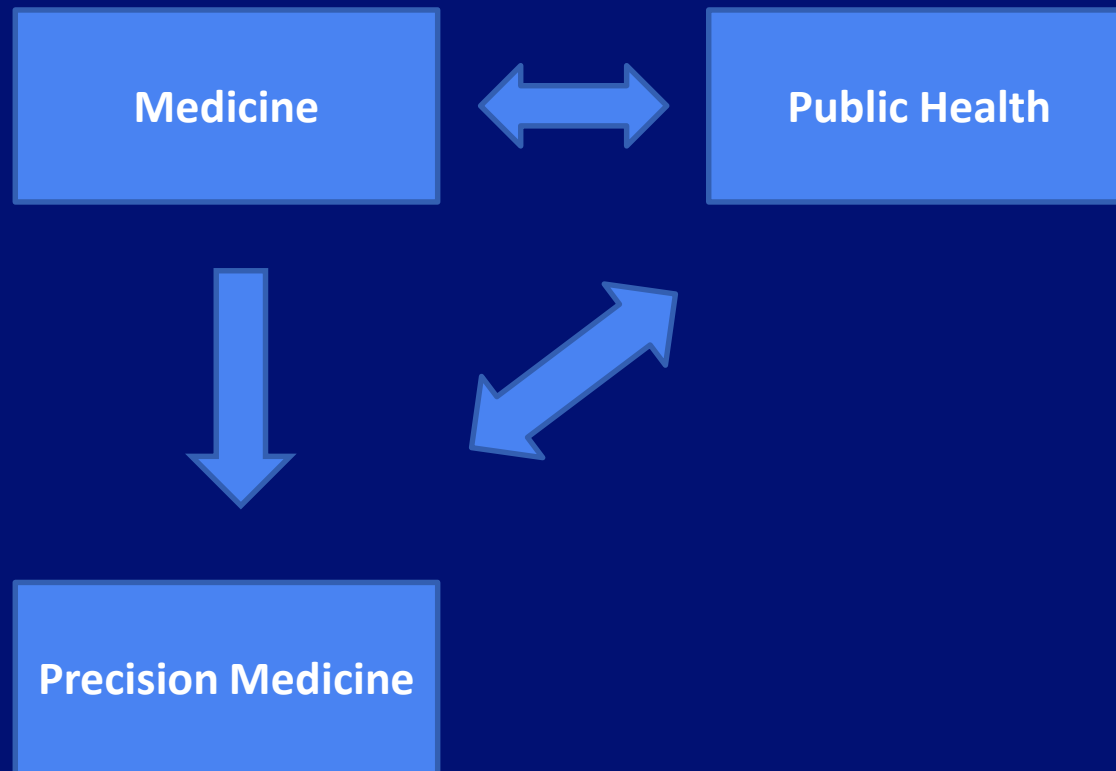
Disparities in Implementation of BRCA Testing



Levy DE, Byfield SD, Comstock CB, et al. *Genet Med*. 2011 Apr;13(4):349-55.

Precision Medicine and Public Health:

Theme III. Role of Public Health Sciences in Developing and Implementing New Knowledge



A Vision for the Future of Medicine

Why We Need Public Health Sciences?

**TABLE 1. RESULTS OF GENETIC TESTING
IN A HYPOTHETICAL PATIENT IN 2010.**

A 23 year old man named John

CONDITION	GENES INVOLVED*	RELATIVE Risk	LIFETIME Risk (%)
Reduced risk			
Prostate cancer	<i>HPC1, HPC2, HPC3</i>	0.4	7
Alzheimer's disease	<i>APOE, FAD3, XAD</i>	0.3	10
Elevated risk			
Coronary artery disease	<i>APOB, CETP</i>	2.5	70
Colon cancer	<i>FCC4, APC</i>	4	23
Lung cancer	<i>NAT2</i>	6	40

Collins FC, NEJM 1999

Where do we get these numbers? (hint, epidemiology)
What do we do with these numbers?

For Example

How Often Should You Get A Mammogram?

Screening standards, by organization

U.S. Preventive Services Task Force (2015)



American Cancer Society (2015)



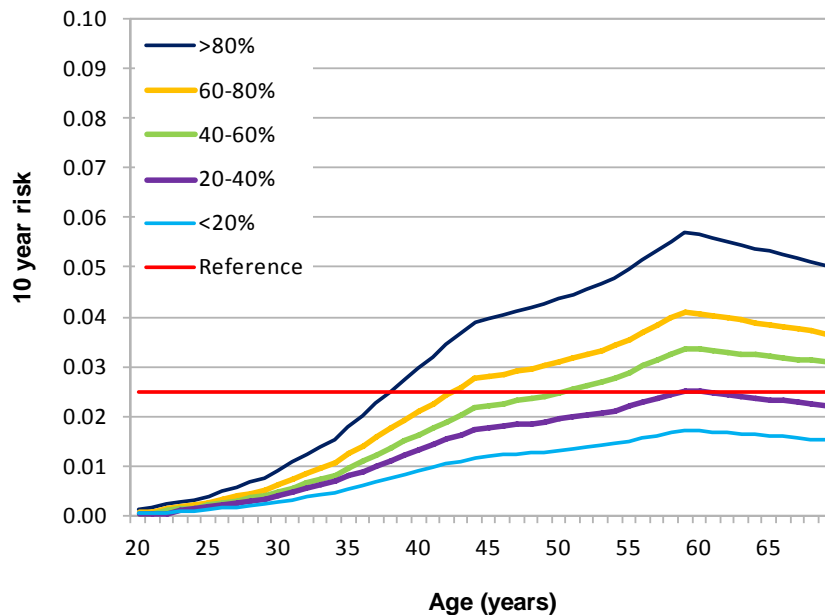
National Health Service (U.K., 2012)



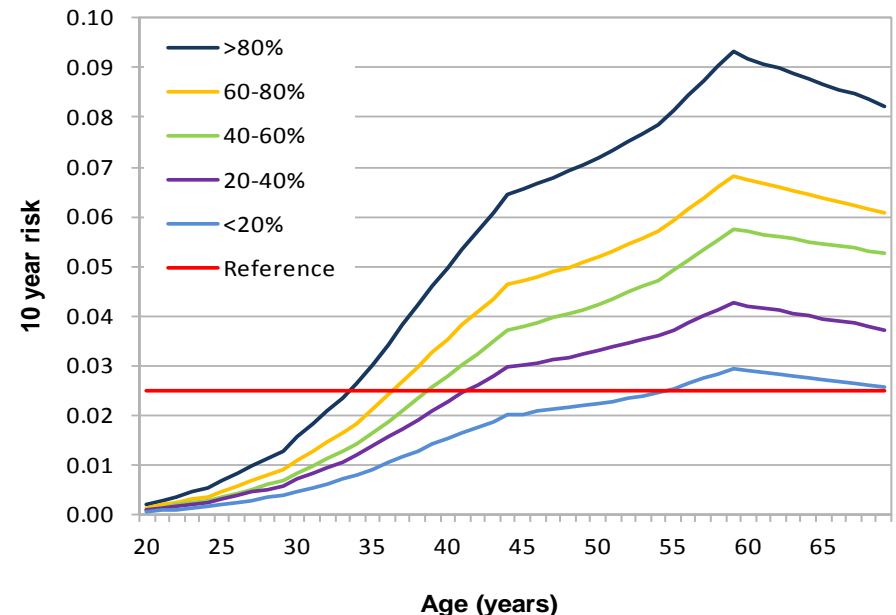
Can We Use Age and Polygenic Score in Breast Cancer Screening?

10-year absolute risk of developing breast cancer for women with and without family history by polygenic risk percentiles

Women without Family History



Women with Family History



Reference: 2.5% 10-year absolute risk for developing breast cancer corresponds to risk of UK women aged 47, i.e. age of invitation to the UK NHS Breast Screening programme

Public Health Sciences Needed to Fulfill Promise of Precision Medicine

- **Epidemiology**
- **Behavioral, Communication and Social Sciences**
- **Health Care Delivery Research**
- **Implementation Science**
- **Economic Analysis: Cost Effectiveness & Beyond**
- **ELSI**
- **And many others**

Investments in Public Health Genomic Sciences Beyond “Bench to Bedside” Are Limited

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ORIGINAL RESEARCH ARTICLE

Genetics
inMedicine

Horizon scanning for translational genomic research beyond bench to bedside

Mindy Clyne, MHS^{1,2}, Sheri D. Schully, PhD², W. David Dotson, PhD², Marta Gwinn, MD, MPH^{3,4}, Katherine Kolor, PhD³, Anja Wulf, PhD³, and Muin J. Khoury, MD, PhD^{2,3}

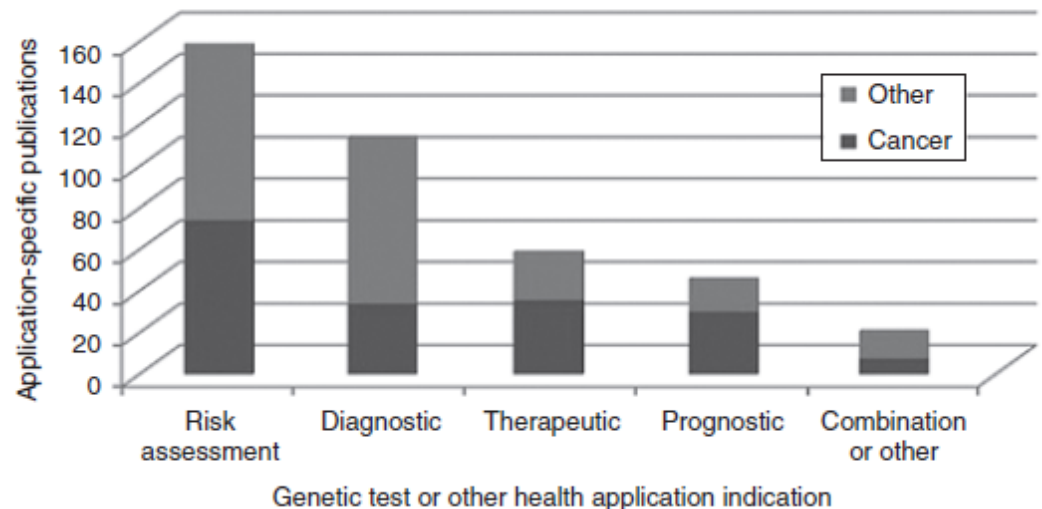
Purpose: The dizzying pace of genomic discoveries is leading to an increasing number of clinical applications. In this report, we provide a method for horizon scanning and 1 year data on translational research beyond bench to bedside to assess the validity, utility, implementation, and outcomes of such applications.

Methods: We compiled cross-sectional results of ongoing horizon

Results: Most articles had a health application; almost all were in cancer. We estimate that 1% of human genomics and

Conclusion: These data suggest that the evolving knowledge of genomics is

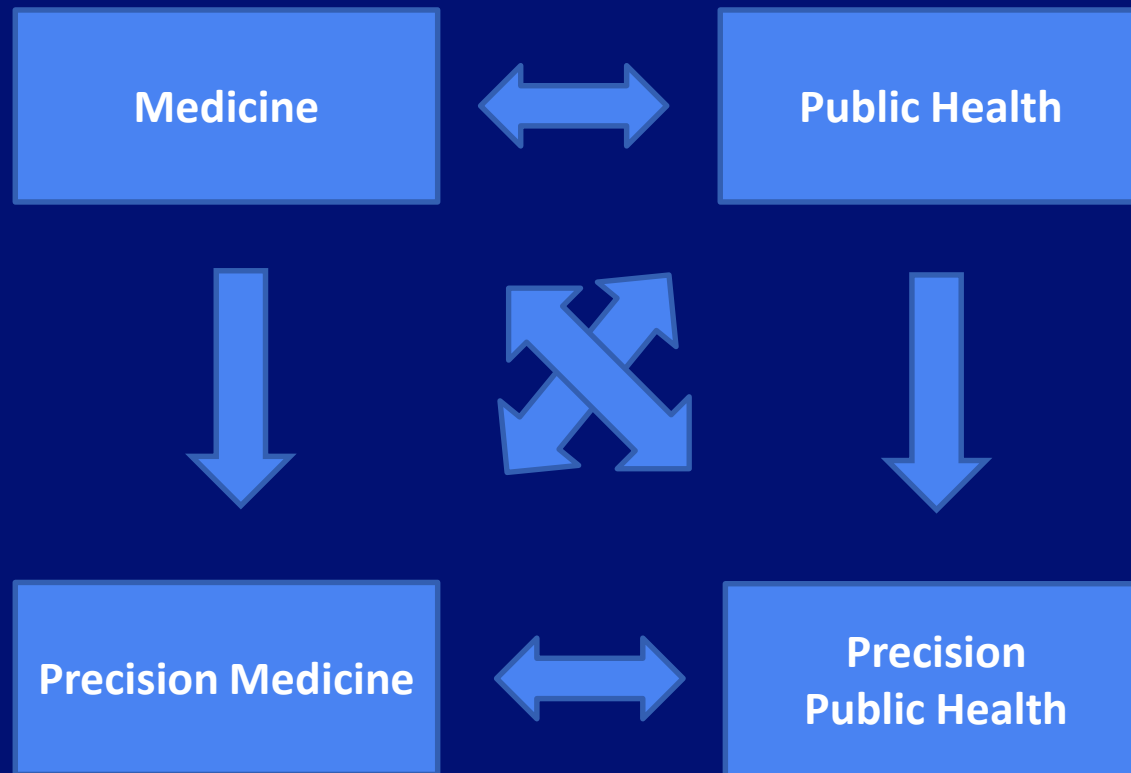
Clyne, M et al, 2014



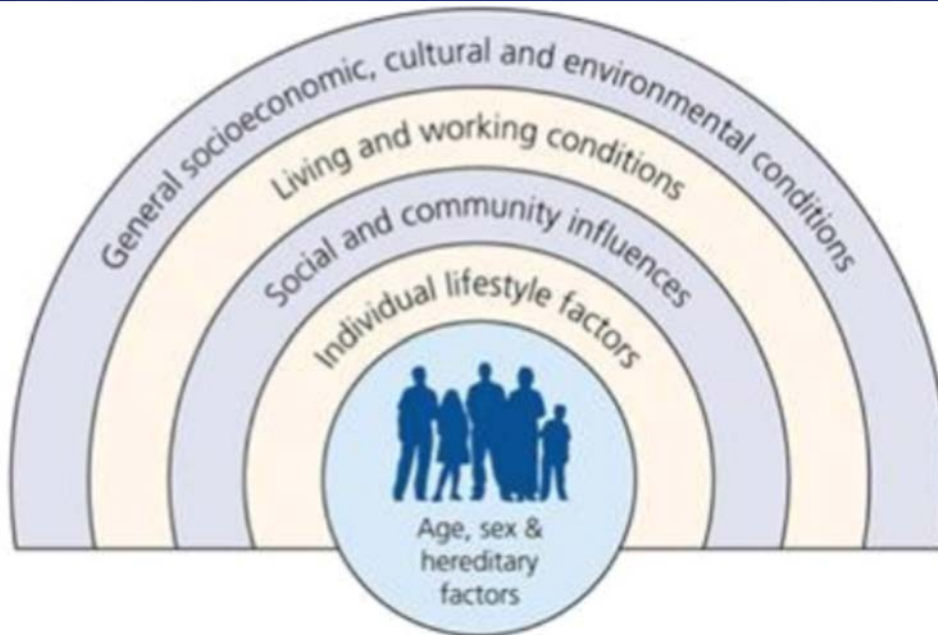
<1% of published genomics research is beyond “bench to bedside” and half of it is in cancer

Precision Medicine and Public Health:

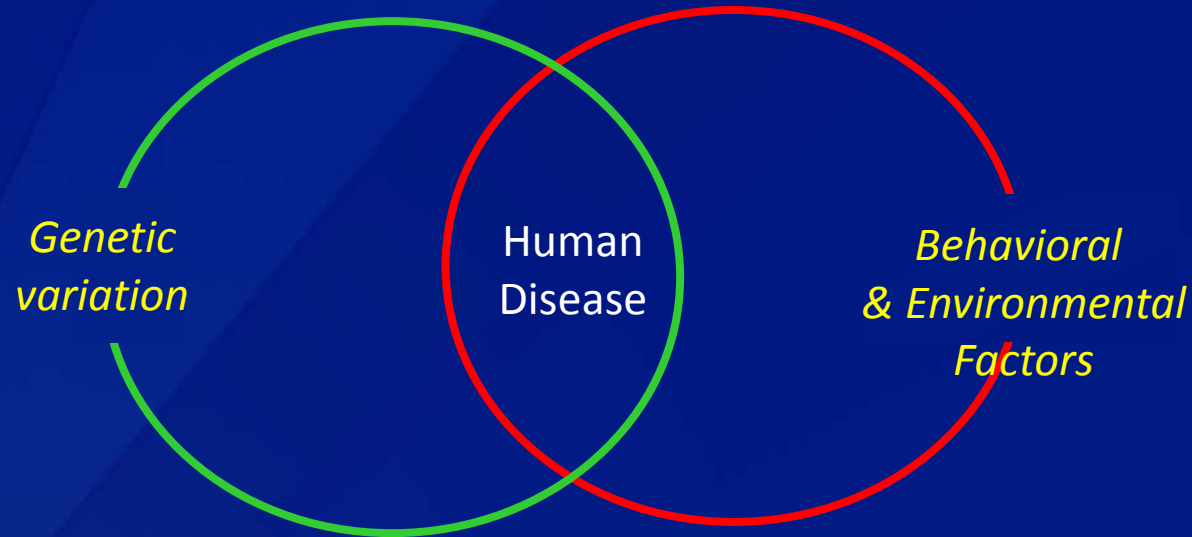
Theme IV. A New Era of “Precision Public Health”



Multi Level Determinants of Health



Genes, Behavior, Environment and Human Disease



Genetic Diseases: Mendelian disorders-PKU Example, 5000+ conditions, 5%-10% of human disease

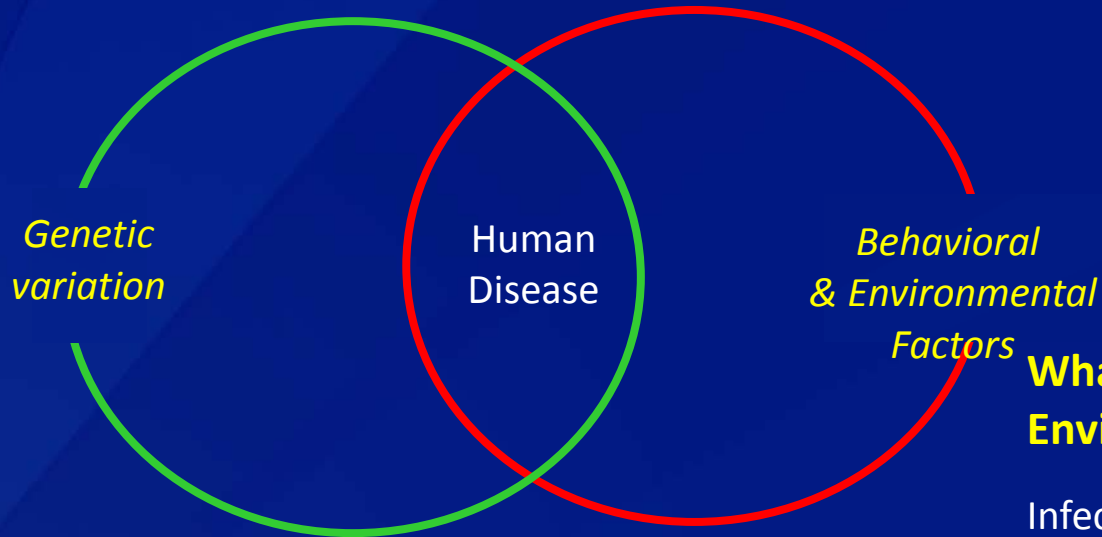
“Complex” Diseases: heart disease, cancer, diabetes, environmental , behavioral & infectious agents – 90%-95% of human disease

Interactions Getting More Complex

What Genomes?

What Genome?

Inherited (germ)
Acquired (somatic)
(e.g. cancer)
Symbiotic
(microbiome)
Vectors



What Environments?

Infection
Chemicals
Physical agents
Diet
Behavioral
Social



Interaction Getting Even More Complex

Epigenetics: Life Course & Intergenerational

What Genome?

Inherited (germ)
Acquired (somatic)
(e.g. cancer)
Symbiotic
(microbiome)
Vectors

*Genetic
variation*

Human
Disease

*Behavioral
& Environmental
Factors*

What Environments?

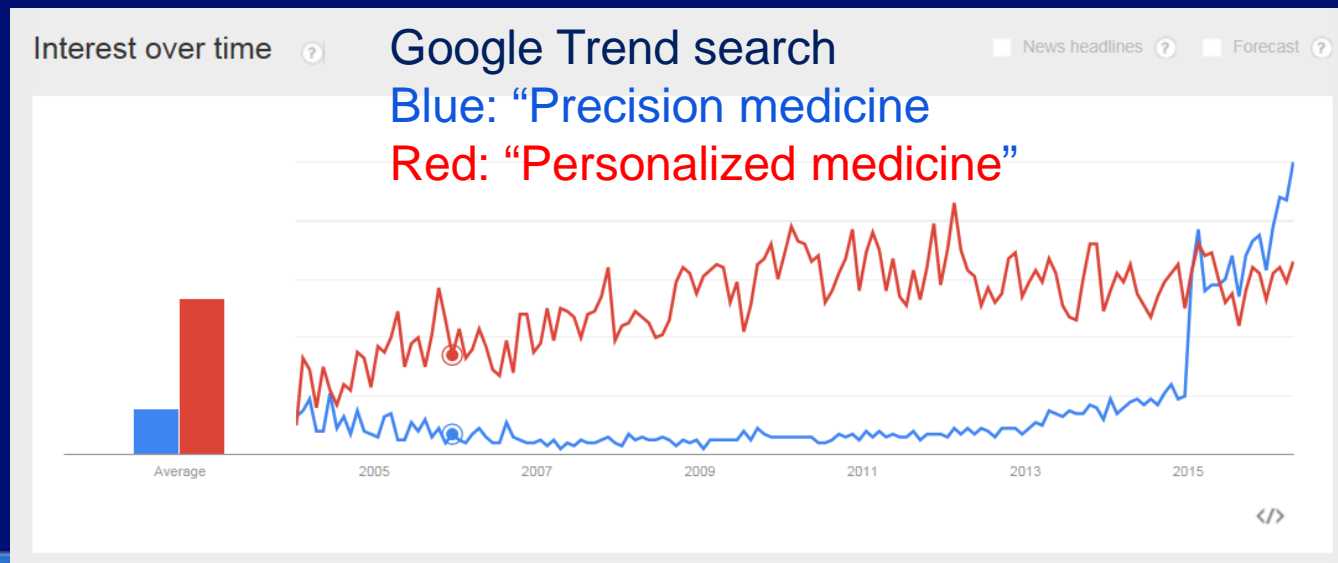
Infection
Chemicals
Physical agents
Diet
Behavioral
Social

*Epigenetic and
post-genomic
modification*



From Personalized Medicine to Precision Medicine & Precision Public Health: Words Matter

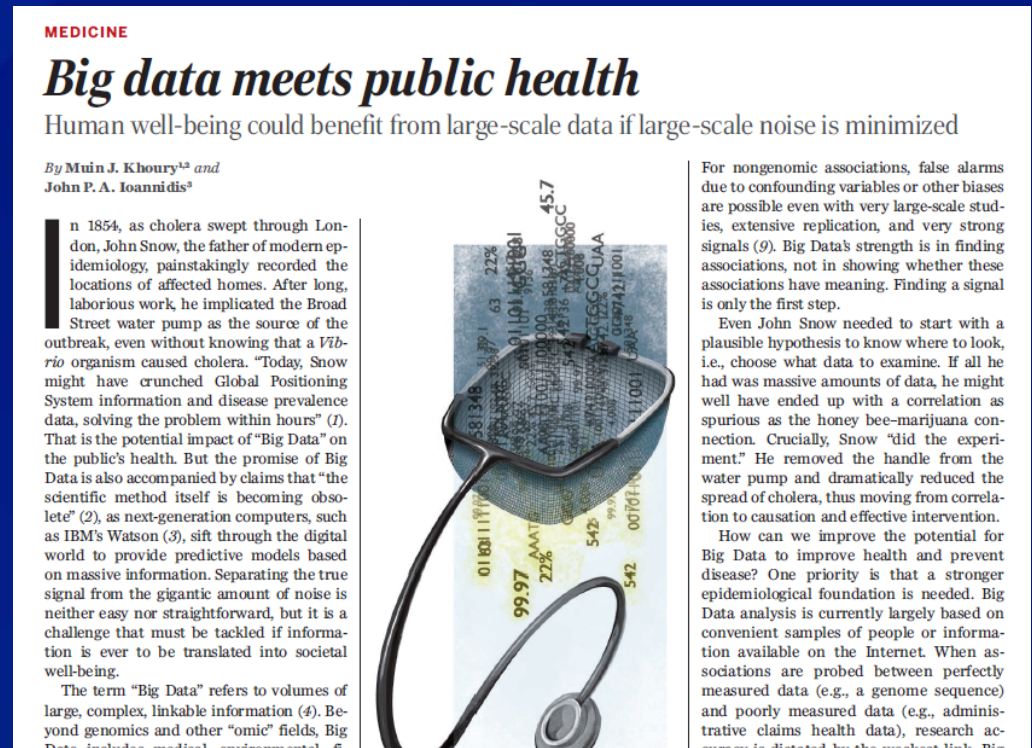
- Personalized Medicine: individualized but can be imprecise (e.g DTC genetic tests)
- Precision Medicine: provides biological & Environmental insights but its applications may be population-wide (e.g. statins)
- Can we use ALL determinants of health (from the micro to the macro) to develop analytic approaches to population health?



Can We Conduct Public Health Functions with More “Precision”?

3 Core Public Health Functions

- Assessment
 - More “precision” in measuring population health problems
- Policy Development
 - Developing the right intervention for the right population
- Assurance
 - More “precision” in delivering interventions



Khoury & Ioannidis, Science 2014

Precision Public Health: Examples of Immediate Applications to Improve Population Health

Pathogen Genomics

Modernizing
Surveillance,
Informatics,
Tracking (Data
Science)

Targeting Prevention
Efforts (beyond
Genomics)

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, PhD²

The Precision Medicine Initiative¹ 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

Khoury MJ, et al. AJPM, December 2015

Pathogen Genomics: Precision Medicine for Public Health



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™



CDC A-Z INDEX ▾

Advanced Molecular Detection (AMD)

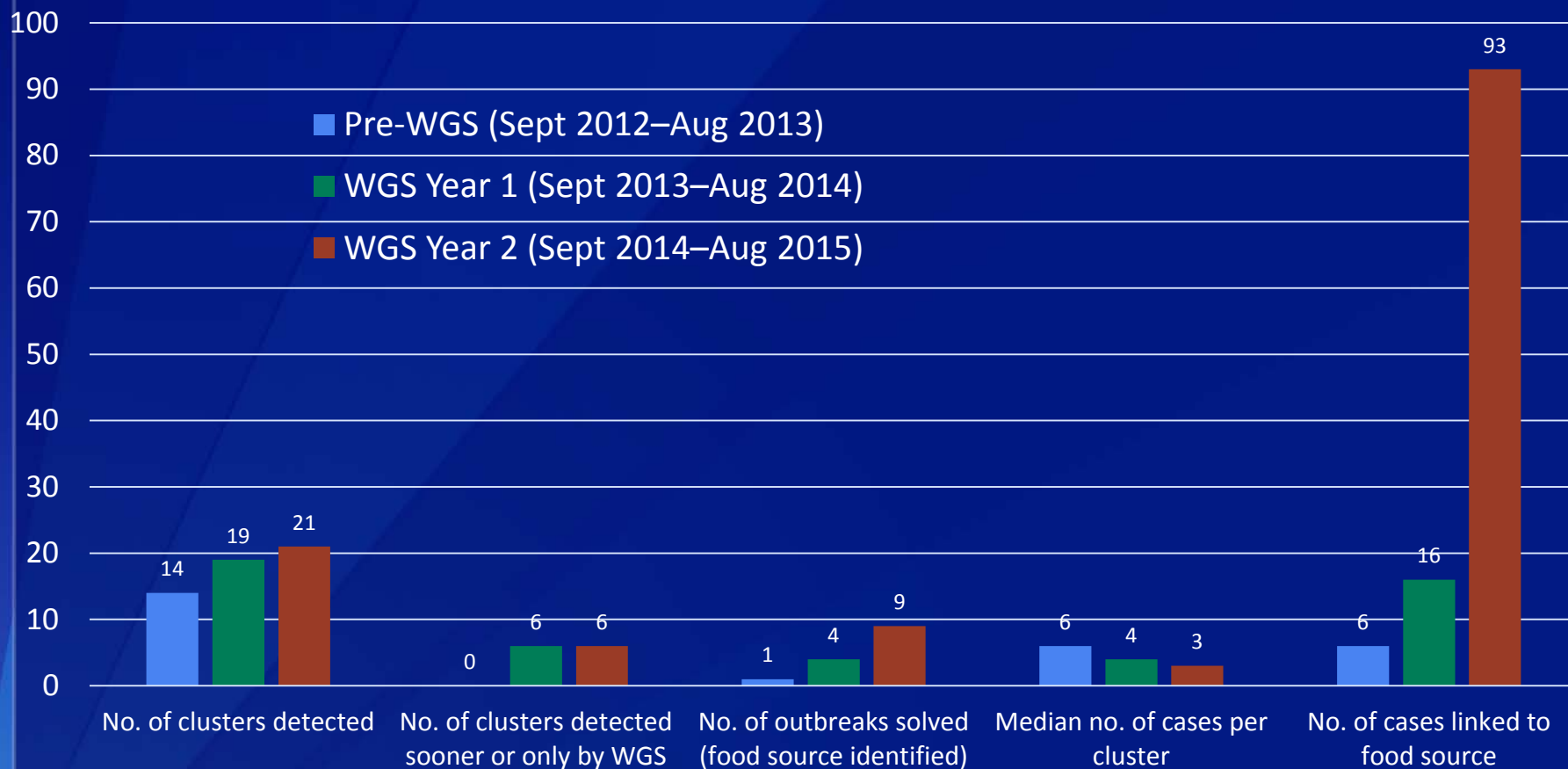


Unlocking the
promise of technology
to protect Americans
from microbial threats

Using molecular technologies to counter infections in patients and populations

Application	Patient care	Public health
Pathogen identification	Rapid diagnosis	Outbreak detection
Antibiotic selection	Proper treatment	Effective antibiotic use guidelines
Vaccines	Better protection	Reduced burden of disease

Listeria Cluster Metrics Pre/Post WGS



From R. Khabbaz

From WGS to GPS

“As cholera swept through London in the mid-19th century, a physician **named John Snow** painstakingly drew a paper map indicating clusters of homes where the deadly waterborne infection had struck. In an iconic feat in public health history, he implicated the Broad Street pump as the source of the scourge—a founding event in modern epidemiology. Today, Snow might have crunched GPS information and disease prevalence data and solved the problem within hours”



[http://www.hsph.harvard.edu/news/magazine/big-datas-big-visionary/?utm_source=SilverpopMailing&utm_medium=email&utm_campaign=Kiosk%2009.25.14_academic%20\(1\)&utm_content](http://www.hsph.harvard.edu/news/magazine/big-datas-big-visionary/?utm_source=SilverpopMailing&utm_medium=email&utm_campaign=Kiosk%2009.25.14_academic%20(1)&utm_content)

What is Precision Public Health?

- “As a cancer doctor, I was part of this new targeted therapy, getting the right medicine to the right patient. So today, I’m interested in something I’d call precision public health. Can we bring that same innovation, that speed, that ability to use big data to the problems we’re trying to solve? That is not a one-cause passion. That is my wish: To bring all of this intellectual data, understanding and tracking of diseases to bear for things that affect the poor every bit as much as we have traditionally done for the rich.”



S. Desmond-Hellman, CEO Gates Foundation, Aspen Institute, December 2015

Conclusions

Precision Medicine and Precision Public Health- Two Peas in a Pod!

- We need both (precision) medicine and public health to improve population health
- Public health-medicine partnerships are needed to implement what we already know in precision medicine to save lives and reduce health disparities
- Public health sciences are needed to generate and implement new knowledge in precision medicine
- We are entering a new era of precision public health that is not just about “genes, drugs, and diseases”