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

Medicine ↔ Public Health
Precision Medicine and Public Health:
Theme I. We Need Both to Improve Population Health
What is Precision Medicine?

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

Increasing population impact

Counseling and education

Clinical interventions

Long-lasting protective interventions

Changing the context to make individuals’ default decisions healthy

Socioeconomic factors

Increasing individual effort needed

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

- Medicine
- Public Health
- Precision Medicine
A Public Health Perspective on a National Precision Medicine Cohort
Balancing Long-term Knowledge Generation With Early Health Benefit

Muin J. Khoury, MD, PhD
Office of Public Health Genomics, Centers for Disease Control and Prevention, Atlanta, Georgia.

The new US precision medicine initiative 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 benefit. 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 nicotine 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

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

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

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

BRCA testing in young women with breast cancer: underutilization in Black and Hispanic women

Probability of BRCA testing (Hazard Ratio)

Race/ethnicity

White
Black
Hispanic
Asian
Other/unknown

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

- Medicine
- Public Health
- Precision Medicine
A Vision for the Future of Medicine
Why We Need Public Health Sciences?

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

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

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

Collins FC, NEJM 1999

A 23 year old man named John
How Often Should You Get A Mammogram?
Screening standards, by organization

Optional screen every 2 years
Screen every 2 years

American Cancer Society (2015)
Optional yearly screen
Screen yearly
Screen every 2 years, until <10 years of life expectancy

National Health Service (U.K., 2012)
Screen every 3 years

Source: Journal of the American Medical Association
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

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

Mavaddat et al. JNCI 2015: 107(5): djv036 From N Pashayan
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

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

- General socioeconomic, cultural and environmental conditions
- Living and working conditions
- Social and community influences
- Individual lifestyle factors

Determinants of Health
- Income and social status
- Social support networks
- Employment and working conditions
- Physical environments
- Biological and genetic endowment
- Healthy child development
- Education
- Health services
- Personal health practices and coping skills
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

**Human Disease**
- Genetic variation

**Behavioral & Environmental Factors**

**What Environments?**
- Infection
- Chemicals
- Physical agents
- Diet
- Behavioral
- Social

*Mayo Clinic Blog*
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?

Google Trend search
Blue: “Precision medicine”
Red: “Personalized medicine”
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, Michael F. Iademarco, MD, MPH, William T. Riley, PhD

The Precision Medicine Initiative 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. Public health experts are concerned about the disproportionate emphasis on genes, drugs, and disease, while neglecting strategies to address social determinants of health. Collecting information for gene sequencing is logistically challenging and lacks an 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 diverse populations requires a public health approach.

Khoury MJ, et al. AJPM, December 2015
# Pathogen Genomics: Precision Medicine for Public Health

## Advanced Molecular Detection (AMD)

**Unlocking the promise of technology to protect Americans from microbial threats**

<table>
<thead>
<tr>
<th>Application</th>
<th>Patient care</th>
<th>Public health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogen identification</td>
<td>Rapid diagnosis</td>
<td>Outbreak detection</td>
</tr>
<tr>
<td>Antibiotic selection</td>
<td>Proper treatment</td>
<td>Effective antibiotic use guidelines</td>
</tr>
<tr>
<td>Vaccines</td>
<td>Better protection</td>
<td>Reduced burden of disease</td>
</tr>
</tbody>
</table>
**Listeria Cluster Metrics Pre/Post WGS**

- **No. of clusters detected**
  - Pre-WGS (Sept 2012–Aug 2013): 14
  - WGS Year 1 (Sept 2013–Aug 2014): 19
  - WGS Year 2 (Sept 2014–Aug 2015): 21

- **No. of clusters detected sooner or only by WGS**
  - Pre-WGS: 0
  - WGS Year 1: 6
  - WGS Year 2: 6

- **No. of outbreaks solved (food source identified)**
  - Pre-WGS: 1
  - WGS Year 1: 4
  - WGS Year 2: 9

- **Median no. of cases per cluster**
  - Pre-WGS: 6
  - WGS Year 1: 4
  - WGS Year 2: 3

- **No. of cases linked to food source**
  - Pre-WGS: 6
  - WGS Year 1: 16
  - WGS Year 2: 93

From R. Khabbaz
“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.”

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”