Genomic Medicine Implementation in Diverse Healthcare Settings and Populations

A Public Health Perspective

Muin J. Khoury MD, PhD

CDC Office of Public Health Genomics
Outline

- Exploring the Intersection of Genomic (and Precision) Medicine, Implementation Science, and Public Health

- Public Health Genomics and Cancer: Case Study

- The Genomics and Population Health Action Collaborative (of the NASEM Roundtable on Genomics & Precision Health)
Epidemiology, Implementation Science and Precision Medicine: A Growing Intersection

Public Health

Genomics & Precision Medicine

Implementation Science

“What we as a society do collectively to assure the conditions in which people can be healthy.”

“Emerging approach to disease treatment & prevention that takes into account information on genes, environment & lifestyles”

“Identify, understand, and develop to increase adoption, adaptation, integration, scale-up and sustainability of evidence-based interventions, tools, policies, and guidelines”
Numerous Genomic Tests are Available

- 78,973 Tests
- 4,539 Disorders
- 5,386 Genes
- 680 Laboratories
- 1,067 Clinics

Updated March 30, 2016
An Expanded Genomics Translation Cycle (<1% of Publications are T2+)

Knowledge Integration

Discovery

Application

Population Health

Effectiveness & Outcomes Research

Health care & Prevention Programs

Basic, Clinical & Population Sciences T0

T1

Development

Evaluation T2

Evidence based Recommendation or Policy

Implementation Science T3

Khoury MJ et al, AJPH, 2012
**Horizon scanning for translational genomic research beyond bench to bedside**

Mindy Clyne, MHS\(^1,2\), Sheri D. Schully, PhD\(^2\), W. David Dotson, PhD\(^3\), Michael P. Douglas, MS\(^4,4\), Marta Gwinn, MD, MPH\(^3,4\), Katherine Kolor, PhD\(^2\), Anja Wulf \(^3,5\), M. Scott Bowen, MPH\(^3\) 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 scanning literature.

**Results:** Most articles (62%) addressed a specific genomic test or other health application; almost half of these (n = 180) were related to cancer. We estimate that these publications account for 0.5% of reported human genomics and genetics research during the same time.

![Bar chart showing applications of genomic research](chart.png)
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## CDC Evidence-based Classification of Genomic Tests: A Growing Number of Applications Ready for Prime Time

<table>
<thead>
<tr>
<th>Tier 1</th>
<th>Supported by a base of synthesized evidence for implementation in practice</th>
<th>e.g., Newborn Screening, HBOC, Lynch syndrome, Familial Hypercholesterolemia</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>
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*List of applications by level of evidence on CDC Public Health Genomics Knowledge Base website: https://phgkb.cdc.gov/GAPPKB/topicStartPage.do*
CDC Selected Emerging Tier 1 Genomic Applications

- Familial Hypercholesterolemia, Hereditary Breast and Ovarian Cancer, Lynch Syndrome
- 2 million people in the US
- Many don’t know they have it
- Effective interventions reduce mortality
- Evidence-based recommendations
  - Familial Hypercholesterolemia
    - NICE Cascade screening
  - Hereditary Breast and Ovarian Cancer
    - USPSTF high risk approach
  - Lynch Syndrome
    - EGAPP universal colorectal cancer screening
Cancer and Family History: Using Genomics for Prevention

Tuesday, April 19, 2016 at 1 pm EDT

The risk factors for cancer are many and varied, and inherited genetic mutations play a major role in 5 to 10% of all cancers. When these mutations are identified early, patients are able to work with their healthcare providers to take crucial steps toward care and treatment. Many of those affected by genetic cancer syndromes don't know that genetic testing is an option.
The USPSTF recommends that primary care providers screen women who have family members with breast, ovarian, tubal, or peritoneal cancer with one of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (BRCA1 or BRCA2). Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. Grade: **B Recommendation**.

The USPSTF recommends against routine genetic counseling or BRCA testing for women whose family history is not associated with an increased risk for potentially harmful mutations in the BRCA1 or BRCA2 genes. Grade: **D Recommendation**.
“The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group found **sufficient evidence to recommend offering genetic testing for Lynch syndrome to individuals with newly diagnosed colorectal cancer (CRC) to reduce morbidity and mortality in relatives.**
Partnerships Needed to Address Challenges in Genomics Implementation

- Provider and public education
- Healthcare system limitations
- Evidence-based policy
- Population health impact data
- Laboratory quality
- Health disparities

Know:BRCA
An interactive web resource with unique areas for consumers and healthcare providers
Launched in 2014
Using State Cancer Registries for Surveillance of Cancer Genetic Services & Outcomes

Genomics Goal

- Increase availability of cancer-related genetic information to the Michigan public and decrease barriers to risk-appropriate services
- Examine potential cases at risk for HBOC or Lynch syndrome
- Disseminate data to healthcare systems and providers to reinforce educational messages
# Multi-Level & Multidisciplinary Partners

## National Health Partners:
- CDC DCPC
- CDC OPHG
- NCCN Experts
- ASHG/Jackson Laboratory
- LSSN
- Kintalk.org/UCSF

## Local Health Partners:
- BCBSM
- Priority Health
- Other health plans
- WSU Genetic Counseling Program
- Grand Valley State University
- Local cancer registrars

## Providers of individuals at risk or with HBOC/LS:
- Primary Care Providers Workshop Participants
- Providers who care for cancer patients and cancer survivors
- Providers who care for family members of cancer patients

## Michigan residents at risk for or with HBOC/LS

## State Health Partners:
- MDHHS Cancer Genomics
- MDHHS Cancer Prevention & Control
- Michigan Cancer Surveillance Program & Vital Records
- Michigan Medicaid
- MIBRS
- Michigan Cancer Consortium
- Michigan Association of Health Plans
- Michigan Cancer Genetics Alliance

## Clinical Practices:
- BRCA Clinical Network
- Health systems/clinical practices that diagnose cancer
- Health systems that perform universal/routine LS screening
- Health systems/practices that collect family history

## Family members at risk for HBOC/LS

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*Taplin et al, Multilevel Intervention Clinical-Public Health Collaboration, 2011*
Michigan Population Data Related to BRCA Counseling Access and Referrals

- Black women less likely than other women to use cancer genetic services
Cascade genetic testing in Lynch syndrome: room for improvement

Kory Jaspersen

Genetic testing in relatives of individuals with Lynch syndrome is of utmost importance for targeted screening and prevention. A recent systematic review suggests that the uptake of testing in at-risk relatives is inadequate and therefore the cost-effectiveness of Lynch syndrome testing is questionable. The results...

The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group (EWG) in 2009 established that there was "sufficient evidence to recommend offering genetic testing for Lynch syndrome to individuals with newly diagnosed colorectal cancer."

Population-Based Universal Screening for Lynch Syndrome: Ready, Set... How?

Joanne Ngeow and Charis Eng, Cleveland Clinic Genomic Medicine Institute, Cleveland, OH

See accompanying article on page 2554

Although the fields of health care and public health have many evidence-based innovations, the failure to implement health interventions that have been rigorously demonstrated to be cost effective hampers health care delivery. The identification of individuals who are at increased risk of hereditary cancer allows for the possibility of heightened surveillance and early cancer detection, resulting in decreased disease-specific mortality. Such data-driven identification and risk stratification to guide management is one of the foundations of value-based health care delivery. However, it is not always easy to identify those in the general population who may be at increased risk of developing colorectal cancer. Lynch syndrome, defined as the presence of microsatellite instability (MSI) or loss of MMR protein expression (detected via immunohistochemistry [IHC]), which are the cellular hallmarks of this disorder. Ward et al. explored a population-based approach by including all incident CRCs that were identified within their catchment area of 1.2 million residents in New South Wales, Australia. The study consisted of two phases. In the first phase, without obtaining patient consent, they identified all MMR-deficient cancers by IHC and assigned an a priori likelihood for LS as either low (both MLH1 loss and BRAF mutation) or high (all other cancers). Recommendations were sent to the treating...
Implementing screening for Lynch syndrome among patients with newly diagnosed with colorectal cancer: Summary of a public health/clinical collaborative meeting

Cecelia A. Bellcross, PhD, MS¹,², Sara R. Bedrosian, BA, BFA¹, Elvan Daniels, MD, MPH³, Debra Duquette, MS⁴, Heather Hampel, MS⁵, Kory Jasperson, MS⁶, Djenaba A. Joseph, MD, MPH⁷, Celia Kaye, MD, PhD⁸, Ira Lubin, PhD⁹, Laurence J. Meyer, PhD, MD¹⁰, Michele Reyes, PhD, MS¹, Maren T. Scheunert, MD, MPH¹¹, Sheri D. Schully, PhD¹², Leigha Senter, MS⁵, Sherri L. Stewart, PhD⁷, Jeanette St. Pierre, MA, MPH¹, Judith Westman, MD⁵, Paul Wise, MD¹³, Vincent W. Yang, MD, PhD¹⁴, and Muin J. Khoury, MD, PhD¹

Abstract: Lynch syndrome is the most common cause of inherited colorectal cancer, accounting for approximately 3% of all colorectal cancer cases in the United States. In 2009, an evidence-based review process conducted by the independent Evaluation of Genomic Applications in Practice and Prevention Working Group resulted in a recommendation to offer genetic testing for Lynch syndrome to all individuals with newly diagnosed colorectal cancer, with the intent of reducing morbidity and mortality in family members. To explore issues surrounding implementa-

Lynch syndrome can potentially serve as a model to facilitate the development and implementation of population-level programs for evidence-based genomic medicine applications involving follow-up testing of at-risk relatives. Such endeavors will require multilevel and multidisciplinary approaches building on collaborative public health and clinical partnerships. Genet Med 2011;XX(X):000–000.

Key Words: genetic screening, colorectal cancer, Lynch syndrome, HNPCC, genetic testing
Making Universal Screening for Lynch Syndrome a Reality: The Lynch Syndrome Screening Network

Categories: colorectal cancer, genomics

March 22nd, 2012 11:35 am ET - Guest Blogger

Deb Duquette, MS, CGC, Sarah Mange, MPH- Michigan Department of Community Health
Cecelia Bellcross, PhD, MS- Emory University
Heather Hampel, MS, CGC- The Ohio State University
Kory Jasperson, MS, CGC- Huntsman Cancer Institute

Authors are all from the Lynch Syndrome Screening Network (LSSN) Founding Board of Directors

Every day, about 400 people in the United States are diagnosed with colorectal cancer. Approximately twelve of them have Lynch syndrome, a hereditary condition that increases the risk of colorectal cancer and other cancers. Identifying people with Lynch syndrome could have substantial health
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The Road Ahead

Hybrid studies that examine effectiveness & implementation measures may reduce the amount of time it takes to integrate a research discovery in the clinic

Within existing implementation efforts, gather useful knowledge from case studies of “exceptional implementation” and failures

Leveraging existing health systems and networks, such as those at the state level, may be useful during implementation
Convergence of Implementation Science, Precision Medicine, and the Learning Health Care System
A New Model for Biomedical Research

Figure. Contributions of Implementation Science, Learning Health Care System, and Precision Medicine

Key Areas of Synergy
- Evolution of evidence base for precision medicine and implementation science
- Recognition of underuse and overuse of interventions
- Management of abundance of data

Optimal use of genomics and behavioral data to drive clinical and patient decision making
- Ongoing development of genomics evidence base
- Personalized and population impact

Key Areas of Synergy
- Refresh cycle of evidence base
- Determination of degree of achievable personalization of care

Use of ongoing data to drive health system improvement
- Focus on iterative and ongoing learning
- All stakeholders participate

Optimal integration of effective diagnosis, prevention, and treatment
- Understanding of multilevel context
- Theories and strategies to drive health care improvement

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

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James P. Evans, MD, PhD
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The new US precision medicine initiative\(^1\) 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\(^2\) 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

Khoury MJ et al, JAMA, 2015
Implementation Science & Precision Medicine Cohort
“Tier 1” 56 Genes and their Variants

American College of Medical Genetics and Genomics

ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing

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Genomics and Population Health Action Collaborative of the NASEM Roundtable on Genomics & Precision Health

**Work Product:** Develop an online guide/toolkit for states interested in integrating genomics into population health programs.

**Evidence Working Group**
- **Chair:** Ned Calonge
  - **Work Stream 1:** Using case studies (BRCA1/2 and Lynch syndrome) consider how genomic applications can reach ‘Tier 1’ level

**Implementation Working Group**
- **Chair:** Deb Duquette
  - **Work Stream 1:** Assess what factors determine ‘genomics readiness’ of states
  - **Work Stream 2:** Explore potential population health impact of implementing genomic applications in public health programs including modelling, population data and existing evidence
  - **Work Stream 1:** Using principles of implementation science, design a set of common outcome metrics for public health genomics programs that are implementing genomic applications

NEW ADDITION: TOOL KIT FOR HEALTH SYSTEMS-IGNITE COLLABORATION
Summary

- A Widening Intersection Among Genomics (and Precision) Medicine, Implementation Science, and Public Health

- Cancer Continues to Serve as a Main Driver for Public Health Genomics Beyond Newborn Screening.

- Current Field is Still limited and We Need More Robust Collaboration at the Interface of Public Health & Healthcare