Genomics and Population Health Action Collaborative
Leadership Meeting: Introduction

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Genomics/Precision Medicine, Implementation Science and Public Health: A Growing Intersection

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

Implementation Science
“Identify, understand, and develop to increase adoption, adaptation, integration, scale-up and sustainability of evidence-based interventions, tools, policies, and guidelines.”

Genomics & Precision Medicine
“Emerging approaches to disease treatment & prevention that takes into account information on genes, environment, & lifestyle”
### CDC Evidence-based Classification of Genomic Tests:
A Growing Number of Applications Ready for Health Impact Now!

<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>
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<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>
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<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>
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Multilevel Research and the Challenges of Implementing Genomic Medicine

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Advances in genomics and related fields promise a new era of personalized medicine in the cancer care continuum. Nevertheless, there are fundamental challenges in integrating genomic medicine into cancer practice. We explore how multilevel research can contribute to implementation of genomic medicine. We first review the rapidly developing scientific discoveries in this field and the nature of current applications that are ready for implementation in clinical and public health programs. We then define a multidisciplinary translational research agenda for successful integration of genomic medicine into policy and practice and consider challenges for successful implementation. We illustrate the agenda using the example of Lynch syndrome testing in newly diagnosed cases of colorectal cancer and cascade testing in relatives. We synthesize existing information in a framework for future multilevel research for integrating genomic medicine into the cancer care continuum.

The current state of implementation science in genomic medicine: opportunities for improvement

Megan C. Roberts, PhD¹, Amy E. Kennedy, PhD, MPH¹, David A. Chambers, DPhil¹ and Muin J. Khoury, MD, PhD²

Purpose: The objective of this study was to identify trends and gaps in the field of implementation science in genomic medicine.

Methods: We conducted a literature review using the Centers for Disease Control and Prevention’s Public Health Genomics Knowledge Base to examine the current literature in the field of implementation science in genomic medicine. We selected original research articles based on specific inclusion criteria and then abstracted information about study design, genomic medicine, and implementation outcomes. Data were aggregated, and trends and gaps in the literature were discussed.

Results: Our final review encompassed 283 articles published in 2014, the majority of which described uptake (35.7%, n = 101) and preferences (36.4%, n = 103) regarding genomic technologies, particularly oncology (35%, n = 99). Key study design elements, such as racial/ethnic composition of study populations, were underreported in studies. Few studies incorporated implementation science theoretical frameworks, sustainability measures, or capacity building.

Conclusion: Although genomic discovery provides the potential for population health benefit, the current knowledge base around implementation to turn this promise into a reality is severely limited. Current gaps in the literature demonstrate a need to apply implementation science principles to genomic medicine in order to deliver on the promise of precision medicine.

Key Words: dissemination; genomic medicine; implementation; precision medicine; translational research
1. Less than 2% of studies incorporated implementation science frameworks or theories. Perhaps as a result, studies often neglected contextual factors that drive implementation science theory.

2. The unit of analysis in >98% of published studies were the individual, rather than the provider or health system.

3. The majority of published studies occurred within an academic medical center setting.

4. Fewer than half of the included studies reported race/ethnicity data, challenging our ability to assess racial/ethnic disparities and the generalizability of study findings across subpopulations.

5. The majority of studies were in oncology, likely reflecting the current evidence base in the field. However, as evidence accrues, research in other disease areas will be needed.

6. Most studies were observational, many reporting barriers and facilitators for genomic medicine implementation.

7. Few studies reported the use of collaborative processes (e.g., key stakeholders) and sustainability indicators.
Vision for the Genomics and Population Health Action Collaborative

Objectives:

• Identify opportunities for genomics to improve population health now and in the near future
• Inform and communicate with population health policy makers and program officials
• Integrate evidence-based applications into practice at the clinical/public health interface

Action Collaborative Product – Year 1

• An online toolkit for states interested in integrating genomics into population health programs
Origins of the Genomics and Population Health Action Collaborative

- Collaboration of diverse stakeholders, including public health
- Development of tools, & resources, & implementation projects ("action")

Action Collaborative of the Roundtable on Genomics and Precision Health
Timeline of Activities To Date

**November 2015:** First in-person GPHAC meeting followed by a public workshop entitled, *Applying an Implementation Science Approach to Genomic Medicine,* and JAMA paper 2016 by D. Chambers et al.

**January - February 2016:** National Academies staff begins recruiting stakeholders to join GPHAC.

**March 2016:** Two working groups are formed – Evidence and Implementation. Monthly conference calls begin.

**April 2016:** Group decides to focus the first year’s work on state public health systems and 2 hereditary cancers (Lynch syndrome and HBOC)
Genomics and Population Health Action Collaborative

**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

**Leader:** Dave Dotson

**Work Stream 2:**
- Explore potential population health impact of implementing genomic applications in public health programs including modelling, population data and existing evidence

**Leader:** Sheri Schully

**Work Stream 3:**
- Examine health disparities related to hereditary cancer.
- Outline possible approaches for public health genomics programs to alleviate health disparities.

**Leader:** Georgia Hurst

**Implementation Working Group**

**Chair:** Deb Duquette

**Work Stream 1:**
- Assess what factors determine ‘genomics readiness’ of states
- Perform qualitative interviews of state public health officials

**Leaders:** Laura Senier and Ridgely Fisk Green

**Work Stream 2:**
- Using principles of implementation science, design a set of outcome metrics for public health genomics programs.

**Leaders:** David Chambers and Debra Lochner Doyle

**Work Stream 3:**
- Using case studies (BRCA1/2 and Lynch syndrome) consider how genomic applications can reach ‘Tier 1’ level
Timeline of Activities To Date (continued)

May-December 2016:

Evidence Working Group members:
  • Wrote a series of background pieces on horizon scanning and evidence assessment

Implementation Working Group members:
  • Created a table of outcome measures for state programs
  • Began interviewing state health officials to learn about barriers and challenges to implementation
  •Outlined two publications on hereditary cancer-associated health disparities
What’s Next?

February 2017:
• Finalize products of the Evidence and Implementation Working Groups
• Post to Action Collaborative & CDC websites
• Meet in person to discuss strategy for the second year of GPHAC and launching of 2 new Working Groups (screening and cascading) in addition to the Implementation Working Group

March 2017:
• Engage with members and ask for volunteers/collaborators for new working groups
• Begin monthly conference calls and projects
Extending the Reach of the Action Collaborative in Years 2-3

- Expand to look at other high-impact ‘Tier 1’ genetic tests/screens
  - Familial Hypercholesterolemia (FH), Lynch syndrome, and HBOC.
  - Collectively impact ~2-3 million Americans
- Engage and include health care delivery systems in addition to state public health departments
  - Emphasize importance of partnerships
  - Develop collaborations and protocols for pilot projects and demonstration of health impact
Reducing the Burden of BRCA, Lynch Syndrome and FH in the Population:

• Current Recommendations (will miss a lot of cases)

• Cascade Screening (extended)

• Population Screening?
  – Actual (not recommended yet)
  – “Opportunistic”
Can the action collaborative develop methods, approaches and pilot projects for “cascade screening” for selected genomic applications via a public health-health care collaboration model?
Population Screening


- ~3.5% of sequenced participants harbored one or more pathogenic or expected pathogenic variants in a list of 76 ‘actionable’ genes
- FH Prevalence: 1/256, 24% w/clinical dx, 58% on statins, 37% w/high intensity statin use

Opportunistic Screening

- Many issues/open questions
  - Prevalence/penetrance of variants in unselected populations
  - Analytic needs
  - Return of results – positive and negative
  - Implementation issues
  - Economics

Opportunistic Screening

- We screen newborns, don’t we?: realizing the promise of public health genomics
  - James P. Evans, MD, PhD¹, Jonathan S. Berg, MD, PhD¹, Andrew F. Olshan, PhD,² Terry Magnuson, PhD¹ and Barbara K. Rimer, DrPH²

Actual Screening

Center of Excellence in Genomics & Society (CEGS) at UNC-Chapel Hill

GeneScreen

The CGS has one overarching research project, GeneScreen. This project explores a wide range of ELSI issues raised by the prospect of applying a DNA sequencing technology to identify rare but clinically significant genetic variants in the general adult population.

GeneScreen arises from recent advances in genomic sequencing technology.
Reducing the Burden of BRCA, Lynch Syndrome and FH: Prototype for “Precision Public Health”

- Implementing Current Recommendations (will miss a lot of cases)
- Implementing Extended Cascade Screening
- Evaluating Population Screening (not ready)
  - Actual
  - “Opportunistic”
Goals for Today’s Meeting

– Review progress from Evidence and Implementation Working Groups

– Consider perspectives from various stakeholders

– Discuss potential ACTIONS for 3 revised working groups in Year 2 (implementation, cascade screening and population screening)

– Identify additional stakeholders/collaborators

– Discuss next steps