An Introduction to CDC Information and Resources for Translation and Implementation in Genomic Medicine to Improve the Public’s Health

Muin J. Khoury

CDC Office of Public Health Genomics
Outline

- What is PHGKB?
- What is GPHAC?
- Healthcare-Public Health Collaboration
CDC Office of Public Health Genomics (OPHG)

Effective and responsible translation of genome-based discoveries into disease prevention and population health

https://www.cdc.gov/genomics

1. Identify evidence-based applications
2. Inform and communicate
3. Integrate into practice & programs
<table>
<thead>
<tr>
<th>WEEKLY UPDATE</th>
<th>GENETICS 101</th>
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<tbody>
<tr>
<td>Weekly summary of genomics and health impact information</td>
<td>Genetics basics explained including a glossary of genetic terms</td>
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<table>
<thead>
<tr>
<th>PHGKB</th>
<th>FAMILY HEALTH HISTORY</th>
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<tr>
<td>Online searchable knowledge base on genomics and health impact information</td>
<td>Family health history is known to be a risk factor for most diseases</td>
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<tr>
<th>AMD CLIPS</th>
<th>GENOMICS AND DISEASES</th>
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<tr>
<td>Weekly news and publications on pathogen genomics and bioinformatics</td>
<td>Genomics is important for many diseases of public health significance</td>
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<tr>
<th>IMPLEMENTATION</th>
<th>GENETIC COUNSELING</th>
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<tbody>
<tr>
<td>What public health can do now to save lives using genomics</td>
<td>Helping to inform individuals and families about genetic risks, testing and interventions</td>
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<thead>
<tr>
<th>REPORTS AND PUBLICATIONS</th>
<th>GENOMIC TESTING</th>
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<tr>
<td>CDC reports and publications in genomics</td>
<td>Genomic tests are used in many diseases</td>
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<tr>
<th>GENOMICS &amp; HEALTH IMPACT BLOG</th>
<th>PATHOGEN GENOMICS</th>
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<tbody>
<tr>
<td>A blog devoted to genomic issues in research, policy and practice</td>
<td>New tools are changing the landscape in the fight against infectious diseases</td>
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<tr>
<th>PODCASTS AND VIDEOCASTS</th>
<th>EPIDEMIOLOGY</th>
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Hot Topics of the Day

Last Posted: Feb-04-2018 10AM

Disparities

Integrating the Genetics of Race and Ethnicity Into Cancer Research: Trailing Jane and John Q. Public.
Newman Lisa A et al. JAMA surgery 2018 Jan

Study Finds Biological Differences in Lung Tumors of African Americans and Whites
NCl Blog. Jan 2018
Genomics & Health Impact Weekly Scan

This weekly update features emerging roles of human genomics, telomere biology, including birth defects, newborn screening, reproductive healthcare history, guidelines and recommendations. The weekly summary includes:

Advanced Molecular Detection Clips

Advanced Molecular Detection (AMD) clips are selected weekly from media. Special emphasis is given to the use of next-generation genomics for diagnostics and interventions. The collection is not comprehensive; authored articles are flagged.

CDC Information Database

This database includes general CDC public health information on genomics and health information from various CDC web pages. Users are also encouraged to explore the Ethics Library for ethical concerns.

CDC-Author Genomics Publications Database

This database contains CDC-authored scientific publications on genomics, newborn screening, birth defects, developmental disabilities, occupational health, laboratory methods, bioinformatics, and statistical methods.
CDC Information Database

Why did we build it?

- **Challenge:** Finding information about genomics- and family health history-related activities at CDC

- **Opportunity:** Provide a centralized, searchable, publicly available database for CDC resources related to genomics and family health history
CDC-Authorered Genomics Publications Database

Why did we build it?

- **Challenge:** Finding CDC-authored publications on genomics and family health history
- **Opportunity:** Provide a centralized, searchable, publicly available database for these CDC publications
- **Challenge:** CDC’s work in genomics and family health history is not well known
- **Opportunity:** Showcase CDC publications to highlight work related to genomics and family health history
Genomics and Health Impact Scan Database

Why did we build it?

- **Challenge:** Keeping up with the latest developments in genomics and family health history relevant to public health
- **Opportunity:** Identify the latest publications and other resources on population-based applications of genomic discoveries
- **Challenge:** Addressing misconception that genomics applies only to research or clinical practice
- **Opportunity:** Highlight public health applications of genomics—and the role of public health at the health care interface
Genomics and Health Impact Scan Database

- Horizon Scan
  - Monitor Google Alerts, PubMed queries, key websites
  - Select news stories, blog posts, scientific articles, websites
  - Publish online in Weekly Update

- Categorized by
  - Translation and implementation studies
  - Evidence synthesis (systematic reviews, etc)
  - Guidelines
  - Tools/Methods
  - Reviews/Commentaries
Organizing Information for Public Health Genomics: “4 Phases of Translation”

T1: Bench

T2: Bedside

T3: Recommendations / Guidelines

T4: Practice / Programs

Outcomes
Organizing Information for Public Health Genomics: “4 Phases of Translation”

T1: Bench

T2: Recommendations / Guidelines

T3: Practice / Programs

“Implementation science”

Health services research
Organizing Information for Public Health Genomics: “4 Phases of Translation”

1. Bench
2. Bedside
3. Recommendations / Guidelines
4. Practice / Programs
5. Outcomes

Surveillance
Population Impact
Tier Table Database

Why did we build it?

- **Challenge:** The public and health care providers are bombarded with information on genomic tests, many with unproven utility

- **Opportunity:** Educate providers and the public about potential benefits and harms of genomic tests and the need for evidence

- **Challenge:** There is no widely agreed upon threshold level of evidence for determining whether genomic tests are ready for use

- **Opportunity:** Develop flexible method(s) for classification of tests by level of evidence to aid in research/evaluation and help define which aspects of evidence should be considered in developing thresholds
Tier Table Database

**Tier 1:**
- FDA label requires use of test to inform choice or dose of a drug
- CMS covers testing
- Clinical practice guideline based on systematic review supports testing

**Tier 2:**
- FDA label mentions biomarker*
- CMS coverage with evidence development
- Clinical practice guideline, not based on systematic review, supports use of test
- Clinical practice guideline finds insufficient evidence but does not discourage use of test
- Systematic review, without clinical practice guideline, supports use of test
- Systematic review finds insufficient evidence but does not discourage use of test
- Clinical practice guideline recommends dosage adjustment, but does not address testing

**Tier 3:**
- FDA label cautions against use
- CMS decision against coverage
- Clinical practice guideline recommends against use of test
- Clinical practice guideline finds insufficient evidence and discourages use of test
- Systematic review recommends against use
- Systematic review finds insufficient evidence and discourages use
- Evidence available only from published studies without systematic reviews, clinical practice guidelines, FDA label or CMS labels coverage decision

*Can be reassigned to Green or Red if one or more conditions in these categories apply
### Examples of Tier 1 Genomic Applications

<table>
<thead>
<tr>
<th>Disease/Disorder</th>
<th>Test to be Assessed</th>
<th>Intended Use</th>
<th>Tier Classified</th>
<th>Detail</th>
</tr>
</thead>
<tbody>
<tr>
<td>31 core conditions</td>
<td>Newborn screening panel</td>
<td>Screening</td>
<td>Tier 1&lt;sup&gt;①&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Parental history of hip fracture</td>
<td>Estimate fracture risk to inform osteoporosis screening</td>
<td>Tier 1&lt;sup&gt;①&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Familial hypercholesterolemia (FH)</td>
<td>DNA testing and LDL-C concentration measurement</td>
<td>Cascade testing of relatives of people diagnosed with FH</td>
<td>Tier 1&lt;sup&gt;①&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Hereditary breast and ovarian cancer</td>
<td>Family history of known breast/ovarian cancer with deleterious BRCA mutation</td>
<td>Risk prediction; referral to counseling for BRCA genetic testing</td>
<td>Tier 1&lt;sup&gt;①&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Lynch syndrome</td>
<td>Various strategies</td>
<td>Screening, cascade testing of relatives</td>
<td>Tier 1&lt;sup&gt;①&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>
State Public Health Genomics Programs Database

Why did we build it?

- **Challenge**: State, local, and territorial health departments need practical information that they can use to integrate genomics and family health history into their activities

- **Opportunity**: Provide a searchable database of available resources categorized by resource type, disease, and state so that health departments can find new resources and learn from other states

- **Challenge**: State, local, and territorial public health departments and policymakers want to know about genomic and family health history activities in their state and communities

- **Opportunity**: Activities can be searched by state and can also be identified through the clickable map
Click on a state to find information on public health genomics activities in that state. States have implemented genomics applications for Hereditary Breast and Ovarian Cancer syndrome, Lynch Syndrome, Familial Hypercholesterolemia, newborn screening, and more. Find relevant information from your own state or learn about what’s been accomplished in other states. You can filter results by condition and resource type (data, programs, education, policy, tools, and general information). Please let us know about new efforts so that we can keep the information current!
State Public Health Genomics Programs Database

*CDC Funding to States Over Time*

- 2003-2008: Michigan, Minnesota, Oregon, and Utah
- 2008-2011: Michigan and Oregon
- 2011-2014: Georgia, Michigan, and Oregon
  - Enhancing Cancer Genomic Best Practices through *Education, Surveillance, and Policy*
  - Goal: Provide leadership and build capacity for cancer genomics activities in state public health departments
State Public Health Genomics Programs Database

**CDC Tier 1 Priorities and Toolkit**

- Hereditary Breast and Ovarian Cancer (*BRCA1/2*)
- Hereditary Nonpolyposis Colorectal Cancer (Lynch Syndrome)
- Familial Hypercholesterolemia
- **Collectively Affect ~3 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**
Challenge: The translation pathway from genome discoveries to improved health requires funding. It is not clear what translational research and implementation science is been funded and by whom?

Opportunity: Provide a searchable database of available grant information connected with PHGKB related publications. Grant information can be searched by disease/condition, environmental risk factors, or gene of study and other free text.

Still work in progress- Currently connecting to NIH reporter and other sources
Specialized PHGKB Databases: Cancer, HLBS, Infectious Diseases and MyPHGKB

Public Health Genomics Knowledge Base (v4.0)

- About
- MyPHGKB
- Specialized PHGKB
- Cancer PHGKB
- Infectious Diseases PHGKB
- HLBS-PopOmics
- Genomics (A-Z)
- Office of Public Health Genomics
- State Public Health Genomics Programs Map
- Genomics & Health Impact Weekly Scan (Current Edition)
- Advanced Molecular Detection Weekly Clips (Current Edition)
- All Databases
- DataSet Download Center
- Release Note
- Contact Us

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**What’s New**

Last Posted: Aug 02, 2018

- The case for population screening for BRCA, Lynch Syndrome, and FH
  - Color Genomics, YouTube, June 2018
- No Difference in Colorectal Cancer Incidence or Stage at Detection by Colonoscopy Among 9 Countries With Different Lynch Syndrome Surveillance Policies
  - Engel Christoph et al. Gastroenterology 2018 Jul
- Predictors for High Microsatellite Instability in Patients with Colorectal Cancer Fulfilling the Revised Bethesda Guidelines
- Routine molecular analysis for Lynch syndrome among adenomas or colorectal cancer within a national screening program
  - Goeberde A et al. Gastroenterology 2018 Jul
- Would Routine Genomic Testing For Cancer And Heart Risk Make Economic Sense?
  - A Weintraub, Forbes, July 30, 2018
- Inherited gynaecological cancers
  - George Angela et al. Current opinion in oncology 2018 Jul
- Lower gastrointestinal neuroendocrine neoplasms associated with hereditary cancer syndromes: a case series
  - Kidanli Trilskesh Dut et al. Familial cancer 2017 Oct 16(4) 537-543
MyPHGKB – A Special Informatics Tool in PHGKB

- Customize the user interface display for your MyPHGKB home page.
- Customized search result based on your own preference on information sources.
- Automatic email alerts for the information you are interested based on your preference on topics and information sources.
Searching PHGKB: An Example

What’s New

Last Posted: Aug 02, 2018

- The case for population screening for BRCA, Lynch Syndrome, and FH
  Color Genomics, YouTube, June 2018

- No Difference in Colorectal Cancer Incidence or Stage at Detection by Colonoscopy Among 3 Countries With Different Lynch Syndrome Surveillance Policies
  Engel Christoph et al. Gastroenterology 2018 Jul

- Predictors for High Microsatellite Instability in Patients with Colorectal Cancer Fulfilling the Revised Bethesda Guidelines
  Arakawa Keiichi et al. Anticancer research 2018 Aug 38(8):4871-4876

- Routine molecular analysis for Lynch syndrome among adenomas or colorectal cancer within a national screening program
  Goverdie A et al. Gastroenterology 2018 Jul

- Would Routine Genomic Testing For Cancer And Heart Risk Make Economic Sense?
  A Weinstein, Forbes, July 30, 2018

- Inherited gynaecological cancers
  George Angela et al. Current opinion in oncology 2018 Jul

- Lower gastrointestinal neuroendocrine neoplasms associated with hereditary cancer syndromes: a case series

- Modified capture-recapture estimates of the number of families with Lynch syndrome in Central Ohio
### Information in Various Databases

<table>
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<tr>
<th>CDC Information (3)</th>
<th>NIH Resources (4)</th>
<th>CDC-Authored Publications (9)</th>
<th>State Public Health Genomics Programs (83)</th>
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<tr>
<td>Tier Table (11)</td>
<td>Epidemiologic Studies (319)</td>
<td>Translation/Implementation Studies (287)</td>
<td>Evidence Synthesis (44)</td>
</tr>
<tr>
<td>Reviews/Commentaries (175)</td>
<td>Tools/Methods (13)</td>
<td>Ethical/Legal and Social Issues (4)</td>
<td>Guidelines (25)</td>
</tr>
<tr>
<td>Genetic Testing (GTR)</td>
<td>Genetic Disease (OMIM)</td>
<td>PubMed Review</td>
<td>PubMed Clinical Queries</td>
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From **CDC Information Database**
This database includes general CDC public health information on specific diseases and health related topics. When available, the database displays genomic information from various CDC web pages. Users are also encouraged to conduct searches of CDC website for additional information.

- **Listen to a CDC podcast about Genetic Testing for Lynch syndrome**
- **Colorectal Cancer Awareness**
- **Genetic Testing for Hereditary Colorectal Cancer**

[Go to CDC Information Database](#)
An overview of grant information associated with 3 CDC tier 1 genomic applications, by country, agency and associated publications

* Analysis conducted using grants database on March 6, 2018
Outline

- What is PHGKB?
- What is GPHAC?
- Healthcare-Public Health Collaboration

Genomics and Population Health Action Collaborative
NASEM Roundtable on Genomics and Precision Health
Goal

- Explore ways to integrate evidence-based genomic applications into population health programs at the health care/public health interface

Focus on Lynch syndrome, HBOC and FH as prototypes (CDC Tier 1s)

Output/Deliverables

- 2018: Add to PHGKB Online guide/toolkit for states interested in implementing PH genomics
- 2019: Extend collaborations to health systems
Genomics and Population Health
Action Collaborative - 2018

Implementation
Deb Duquette and David Chambers, Co-Chairs

Project 1: Perform information gathering interviews of state public health officials

Project 2: Develop outcome measures for genomics programs at state public health departments

Project 3: Explore health disparities related to genomic screening for Tier 1 conditions

Population Screening
Jim Evans and Mike Murray, Co-Chairs

Project: Addressing Important Questions about Genomic-Based Screening Programs in Health Care Systems

• Which genes should be screened?
• In what setting should screening take place?
• What is the optimal age for screening?
• What’s the best way to communicate/engage with participants?
• What are the ethical concerns?
• Are these programs cost effective?

Cascade Screening
Heather Hampel and Katherine Wilemon, Co-Chairs

Project 1: Literature review of past cascade screening work

Project 2: Considerations for future cascade screening pilot projects

Project 3: Policies and ELSI issues surrounding cascade screening

Project 4: Patient perspectives on cascade screening
GPHAC Public Health Genomics Implementation: Outcome Metrics

Proposed outcomes measures for state public health genomic programs

Debra Lochner Doyle, MS, LCGC, Mindy Clyne, MHS, CGC, Juan L. Rodriguez, MPH, MS, Deborah L. Cragun, PhD, MS, Laura Senier, MPH, PhD, Georgia Hurst, Kee Chan, PhD and David A. Chambers, DPhil

Purpose: To assess the implementation of evidence-based genomic medicine and its population-level impact on health outcomes and to promote public health genomic interventions, in 2015 the Roundtable on Genomics and Precision Health of the National Academies of Sciences, Engineering, and Medicine formed an action collaborative, the Genomics and Public Health Action Collaborative (GPHAC). This group engaged key stakeholders from public/population health agencies, along with experts in the fields of health disparities, health literacy, implementation science, medical genetics, and patient advocacy.

Methods: In this paper, we present the efforts to identify performance objectives and outcome metrics. Specific attention is placed on measures related to hereditary breast ovarian cancer (HBOC) syndrome and Lynch syndrome (LS), two conditions with existing evidence-based genomic applications that can have immediate impact on morbidity and mortality.

Results: Our assessment revealed few existing outcome measures. Therefore, using an implementation research framework, 38 outcome measures were crafted.

Conclusion: Evidence-based public health requires outcome metrics, yet few exist for genomics. Therefore, we have proposed performance objectives that states might use and provided examples of a few state-level activities already under way, which are designed to collect outcome measures for HBOC and LS.

Genet Med advance online publication 4 January 2018

Key Words: hereditary breast and ovarian cancer; implementation science; Lynch syndrome; outcome measures; public health genomics

Figure 1 The implementation framework developed by Proctor et al.2
State Semi-structured interviews

- 11 states
- States
- with diverse funding arrangements

- Prior experiences
- Funding
- Legislation
- Staffing resources
- Influencers/champions (internal and external)
- Interest
- Training/education
- Tools/resources
- Evaluations
- Approaches/frameworks
ABSTRACT Cascade screening is the process of contacting relatives of people who have been diagnosed with certain hereditary conditions. The purpose is to identify, inform, and manage those who are also at risk. We conducted a scoping review to obtain a broad overview of cascade screening interventions, facilitators and barriers to their use, relevant policy considerations, and future research needs. We searched for relevant peer-reviewed literature in the period 1990–2017 and reviewed 122 studies. Finally, we described 45 statutes and regulations related to the use and release of genetic information across the fifty states. We sought standardized best practices for optimizing cascade screening across various geographic and policy contexts, but we found none. Studies in which trained providers contacted relatives directly, rather than through probands (index patients), showed greater cascade screening uptake; however, policies in some states might limit this approach. Major barriers to cascade screening delivery include suboptimal communication between the proband and family and geographic barriers to obtaining genetic services. Few US studies examined interventions for cascade screening or used rigorous study designs such as randomized controlled trials. Moving forward, there remains an urgent need to conduct rigorous intervention studies on cascade screening in diverse US populations, while accounting for state policy considerations.
A Guide for Considering Genomics-Based Screening Programs

James Evans, UNC Chapel Hill; Michael Murray, Yale University; Misha Angrist, Duke University; Kee Chan, University of Illinois at Chicago; Wendy Uhlmann, University of Michigan; Debra Lochner Doyle, Washington State Department of Health; Malia Fullerton, University of Washington; Ted Ganiats, AHRQ; Jill Hagenkord, Color Genomics; Sara Imhof, North Carolina Biotechnology Center; Sun Hee Rim, Centers for Disease Control and Prevention (CDC); Leonard Ortmann, Centers for Disease Control and Prevention (CDC); Nazneen Aziz, Kaiser Permanente; Dave Dotson, Centers for Disease Control and Prevention (CDC); Ellen Matloff, MyGene Counsel; Kristen Young, Northwestern University; Jillian Huang, UT Southwestern Simmons Comprehensive Cancer Center; Kimberly Kaphingst, University of Utah; Cat Davis Ahmed, The FH Foundation; Angela Bradbury, University of Pennsylvania; Joan Scott, Health Resources & Services Administration (HRSA); Catharine Wang, Boston University; Ann Zauber, Memorial Sloan Kettering Cancer Center; Marissa Levine, USF College of Public Health; Bruce Korf, University of Alabama at Birmingham; Debra Leonard, University of Vermont; Cathy Wicklund, Northwestern University; George Isham, HealthPartners; Muin Khoury, Centers for Disease Control and Prevention (CDC)

“The central idea of early disease detection and treatment is essentially simple. However, the path to its successful achievement (on the one hand, bringing to treatment those with previously undetected disease, and, on the other, avoiding harm to those persons not in need of treatment) is far from simple though sometimes it may appear deceptively easy.”—Wilson and Jungner, Principles and Practice of Screening for Disease
Roundtable-GPHAC Inspired Essay on Population Screening, Implementation Science and Learning Health Systems

ESSAY
A collaborative translational research framework for evaluating and implementing the appropriate use of human genome sequencing to improve health

Muin J. Khoury1, W. Gregory Feero5, David A. Chambers2, Lawrence E. Brody4, Nazneen Aziz2, Robert C. Green6, A. Cecile J.W. Janssen1, Michael F. Murray1, Laura Lyman Rodriguez2, Joni L. Rutter2, Sheri D. Schulzy10, Deborah M. Winn5, George A. Mensah11

1 Office of Public Health Genomics, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, 2 Maine-Dartmouth Family Medicine Residency Program, Augusta, Maine, United States of America, 3 Division of Cancer Control and Population Sciences, National Cancer Institute, NIH, Rockville, Maryland, United States of America, 4 National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland, United States of America, 5 Kaiser Permanente, Oakland, California, United States of America, 6 Brigham and Women’s Hospital, Broad Institute and Harvard Medical School, Boston, Massachusetts, United States of America, 7 Rollins School of Public Health, Emory University, Atlanta, Georgia, United States of America, 8 Yale School of Medicine, New Haven, Connecticut, United States of America, 9 All of Us Research Program, National Institutes of Health, Bethesda, Maryland, United States of America, 10 Office of Disease Prevention, National Institutes of Health, Bethesda, Maryland, United States of America, 11 Center for Translation Research and Implementation Science, National Heart, Lung, and Blood Institute, NIH, Bethesda, Maryland, United States of America

OPEN ACCESS

* M&I @cdc.gov
Outline

- What is PHGKB?
- What is GPHAC?
- Healthcare-Public Health Collaboration

- A natural partnership around translation and implementation
- Healthcare –public health interface
- Sharing tools and resources
- Collaborative analyses to explore gaps and needs
- Training and technical assistance
Last but Not Least,

Surgeon General’s My Family Health Portrait is NOW Housed at CDC/PHGKB