NAACCR 2009 Conference
A New World in Cancer Surveillance
Public Health Genomics

Ralph J. Coates, PhD
Associate Director for Science
Office of Public Health Genomics, NCCDPHP
Centers for Disease Control and Prevention (CDC)
June 16, 2009, San Diego, CA
Outline

Context for Public Health Genomics

Phases of Translation Research in Genomics

Public Health Genomics – CDC/OPHG

Current Cancer Genomic Test Recommendations (Evidence-based)

Recent CDC Translation Initiatives

Some Potential Opportunities for Public Health Genomics in Cancer Surveillance
Potential applications from genomics research

Disease with Genetic Component

Identify Genetic Risk Variants

Diagnostics
Risk Appraisal
Screening

Pharmacogenomics

Understanding Biology

Drug Therapy
Gene Therapy
Diagnostics
Risk, Screening etc.

Policies & programs from gene-environment studies, nutrigenomics...
Diseases on Spectrum of Disorders by “Cause”
Nature vs. nurture

- Genetic dominant/fully penetrant
- Incompletely penetrant
- Polygenic
- Multifactorial, complex
- Environmental

Bomprezzi et al., 2003

CDC OPHG Focus
Research in Genomics Accelerating Including Genome Wide Association Studies with Common Diseases, Including Cancers

Celiac disease
Atrial fibrillation
Colorectal, breast & prostate cancers
Diabetes, Asthma
Gallstones
Multiple sclerosis
Rheumatoid arthritis
Crohn disease
Age-related macular degeneration

HuGENavigator, Jan 2009
Rapid Translation to Practice: “Road Map to Health?”

Navigenics

Welcome to Navigenics

Your genes offer a road map to optimal health

Welcome to 23andMe, a web-based service that helps you read and understand your DNA. After providing a saliva sample using an at...
Rapid Translation to Practice
e.g., Web-available Cancer-Related Testing

*G-nostic*: Smoking Cessation

*MyGenome*: Drug Metabolism/Sensitivities

*DNA Direct*:
  - Risk prediction/screening
  - Disease screening
Uncertainty in Process & Oversight for Genomic Test Development, Translation

Development process for diagnostics, markers, genomic tests, not well defined

Oversight of tests complex, many responsible parties with “significant gaps” that “could lead to harms”

IOM Cancer Biomarkers 2007
SACGHS. U.S. System of Oversight of Genetic Testing, April, 2008
What Consequences of Rapid Translation of Genetic Testing?

New England Journal of Medicine

Letting the Genome out of the Bottle — January, 2008
Will We Get Our Wish?
David J. Hunter, M.B., B.S., Sc.D., M.P.H., Muin J. Khoury, M.D., Ph.D., and Jeff

It may happen soon. A patient, perhaps one you have known for years, who is overweight and

Washington Post

What’s in Your Genes? You Don’t Want to Know -- Yet.
By H. Gilbert Welch and Wylie Burke
Sunday, May 11, 2008; Page B02

Editors.
November, 2008

My genome. So what?
Research is needed into the way individuals use their genomic information, and into protection from its abuse by others.

My genome. So what?

Vol 456 | Issue no. 7218 | 6 November 2008

EDITORIAL
1 My genome. So what?

NEWS
11 How to get the most from a gene test
Erika Check Hayden

CDC
Potentially Unanswered Questions about Genetic Tests in Translation

How valid and reliable are the genetic/genomic tests (analytic validity)
How well do they predict outcomes (clinical validity)
What are the benefits and harms, what actions to take (utility)
How should the medical community, public health, policy makers respond
What Information is Needed Before A Test is Implemented?

Jan 16, 2008 New Test to be Made Available

Jan 17, 2008 Publication: Prostate Ca Risk Increased 10-fold with 5 genetic variants
Testing for 5 Genetic Variants for Prostate Cancer?

Assuming analytic validity & successful replication
Adding test to age, region & family history > little better risk prediction (AUC from 0.61 to 0.63)
Limited ability to discriminate, predict
Clinical utility questionable:
chemoprevention? modifiable risk factors? cancer screening? harms may outweigh benefits
choose treatment? associated equally with aggressive & non-aggressive cancers

Should it be used?
Coates et al. Letter. NEJM 2008 358 (25):2738
1st Key Challenge for Public Health in Genomics

Premature Translation into Practice
2nd Key Challenge for Public Health Genomics: Lost in Translation

< 33% of patients with coronary artery disease are prescribed aspirin

“Let's be realistic: If we didn't do it with aspirin, how can we expect to do it with DNA?”

Lenfant NEJM 2003;349:868
Translation of genetic testing to practice in context of other health services in U.S.

Healthcare Spending High, Record $2.2 Trillion in 2007 ~16% of GDP

U.S. behind many advanced countries in health

~55% of Americans receive recommended care for acute or chronic conditions, ~50% receive recommended preventive care

~20%-30% receive contraindicated care

~30- 40% of dollars spent on overuse, underuse, misuse of services, etc.

Where does & how should genetic testing fit?

Translation in Context of Current Demands in Primary Care

For average primary care physician with average practice:
4.5 hrs./day spent on acute care
10.5 hrs. needed to do recommended chronic disease care
7.4 hrs. needed for recommended preventive care

Yarnell K et al. Am J Public Health 2003; 93:635
Lost in Translation After Recommendation: *BRCA 1,2*

*BRCA 1,2* only genetic test recommended by USPSTF (hereditary breast & ovarian cancers)

Sufficient evidence recommend, 2005

Women whose family history indicates increased risk of *BRCA* referred for counseling to make informed decision

2007 Cochrane Review

Too few studies to make conclusions about how best to deliver cancer genetic services

Further research needed

Similar statements in 2005 by USPSTF

Little Information on Implementation of BRCA 1,2 Recommendation

How commonly women who could benefit are not referred
women unlikely to benefit are tested
testing without quality risk assessment & counseling

What training & standards are needed for risk assessment & counseling

Why is translation to practice occurring as it is & how to improve
CDC-Proposed Translation Research Continuum in Genetics

T0 = gene discovery

T1 ↔ T2 ↔ T3 ↔ T4

Genetic Discovery to Candidate Health Application to Evidence-Based Guideline to Clinical & Public Health Practice in Communities

Practice to Impact on Health in Communities

Currently, Limited Research for Evaluation & Implementation

T0 T1 ↔ T2 ↔ T3 ↔ T4
Discovery to Application Guideline to Practice to Population
Application to Guideline Practice to Population
Health Impact

Bench to Bedside Continuum early phases only

↓ Population Health Benefit/Harm

97% of genetics research publications in T0 & T1

Need for More Translation Research & Programs

Torrent of basic research that dwarfs translational research, evaluation & oversight of genetics and genomics

Consequently no capacity or infrastructure to move these discoveries rationally into clinical application

Hudson K. Health Affairs 2008;27(6)1612-5.
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Emergence of “Public Health Genomics”

A multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technologies to improve population health

The path from genome-based research to population health: Development of an international public health genomics network

Wylie Burke, MD, PhD, Muin J. Khoury, MD, PhD, Alison Stewart, PhD, and Ronald L. Zimmern, MA, FPSPM

for the Bellagio Group

The health benefits of the Human Genome Project have been widely anticipated. Experts predict a new era of individualized disease prevention based on testing for genetic susceptibilities, and safer, more effective use of drugs based on

Which vision of the future should the prudent clinician believe: A cornucopia of healthcare innovations based on genomic research, or a stream of genetically-based interventions that fail to deliver value to the public? We argue that both visions are
CDC’s Public Health Genomics: Closing the Gene Discovery & Population Health Gap

Research/Discovery → Closing the Gap → Population Health

Population Studies
Evidence Syntheses
HuGE
EGAPP
Translation Research
Public Health Practice

GAPPNet
www.cdc.gov/genomics
Gene Variants and Risk of Disease: Evaluating, Synthesizing the Evidence

Global collaboration
hundreds of people,
dozens of organizations,
10 journals,
to assess relations between genomics & health, evaluate literature, improve methods
HuGE Navigator Genopedia

MTHFR

418 disease terms (MeSH) have been reported with MTHFR gene.

hugenavigator.net/ (May 13, 2009)
National Profile of Genome Variation

NHANES: representative cross sectional surveys of U.S. population
Extensive phenotypic data, risk factors, biological markers
Prevalence of genetic variants
Genotype-phenotype studies

From 100 genetic variants to >1,000,000 variants

www.cdc.gov/genomics
Public Health Investigations: Genomics

Human genomics:
- Understand variation in disease susceptibility, outcomes
- Characterize environmental exposures
- Improve public health interventions
  - Vaccines; chemoprophylaxis
  - Exposure reduction
  - Health promotion

Pathogen genomics
Family History Study

Develop tools for collecting and assessing family history, stratifying on risk and guiding prevention efforts

Evaluate whether family history based strategies work to increase use of preventive clinical services or increase healthy behavior

www.cdc.gov/genomics
Genomic tests, ready for use?

Evaluation of Genomic Applications in Practice and Prevention

Purpose:
Establish & test a systematic, evidence-based process for evaluating genetic tests and other applications of genomic technology in transition from research to practice

www.egappreviews.org/
cdc.gov/genomics/gtesting/
Evolution of EGAPP

Development shaped by a number of U.S. & International meetings & reports

1994  US IOM  *Assessing Genetic Risks*

1997-2008  US HHS Advisory Committees on genomics & health  

2003-2008  EU & OECD meetings & reports on evaluation & quality assurance
EGAPP

Non-regulatory CDC-supported initiative
Develop process for evaluation
Evidence-based, transparent, publicly accountable
Integrate existing processes for evaluation
Minimize conflicts of interest
Independent multidisciplinary Work Group composed of non-federal experts to develop methods, make recommendations
Steering Committee of federal agencies
Stakeholder Group for consultation, evaluation

cdc.gov/genomics/gtesting/
EGAPP Approach: Expanding on other processes, methods

U.S. Preventive Services Task Force
www.ahrq.gov/clinic/uspstf07/methods/benefit.htm

Centre for Evidence-Based Medicine
http://www.cebm.net/

Agency for Healthcare Research & Quality
Evidence-based Practice Center Program
www.ahrq.gov/clinc/epc/

Guide to Community Preventive Services
www.thecommunityguide.org/

FDA, others
www.cdc.gov/genomics/gtesting/

Teutsch SM et al. Genetics In Medicine 2009;11:3-14
Common Procedures for Evidence-based Recommendations, USPSTF & EGAPP

Published, transparent methods & procedures

Recommendations based on scientific evidence, not expert opinion

Use of analytic frameworks to link pathway from health service to health outcomes & to link direct & indirect evidence to key questions in pathway

Comprehensive, systematic, & objective search for & review of evidence with grading of evidence quality

Transparent, explicit linkage of evidence to recommendation

Gen Med 2009;11:3-14
Common Procedures for Evidence-based Recommendations, USPSTF, EGAPP (2)

Technical experts primarily as consultants & reviewers, not decision-makers

Peer review of evidence reviews & of recommendations by experts & stakeholders

Final evaluation & recommendations from independent panel, experts in evidence-based processes, minimize conflicts of interest

Recommendation based on overall evaluation of benefits & harms; strength of recommendation based on evidence quality

AJPM 2001;20(s3):21-35; AJPM 2000;18(1s):35-91
Gen Med 2009;11:3-14
EGAPP Evaluation

Careful, explicit, specific definitions of disorder, genetic test & clinical setting

Evaluation of accuracy & reliability in detecting genomic markers of interest (analytic validity)

Evaluation of accuracy & reliability of test in predicting disorder or phenotype of interest (e.g., drug response) (clinical validity)

*Gen Med* 2009;11:3-14
EGAPP Evaluation

Evaluation of evidence of improved health outcomes from test & interventions, utility in decision-making (clinical utility)

Assessment of contextual factors, such as alternative approaches, costs

Overall assessment of benefits & harms

*Gen Med* 2009;11:3-14
Evaluation Issues in Risk Assessment

“Prediction is very difficult, especially about the future.”

Niels Bohr
Danish physicist (1885 - 1962)

Evaluation of clinical validity for risk assessment, screening (diagnosis)

**Validation or Replication**

**Calibration**: degree to which prediction correct in observed data

**Risk Distribution**

**Ability to discriminate**: ROC Curve, AUC, sensitivity, specificity, predictive values

**Absolute Risk Prediction**

**Reclassification**: ability to classify individuals for clinical guidelines

Adapted with permission from Janssens C, Erasmus University: Personal Genomics, 10/08, Bethesda, MD; Janssens et al. AJHG 2008; Alonzo, Pepe: Development, evaluation of classifiers. Methods Molec Biol vol 404 Ambrosius WT (ed).
Calibration

Important esp. when predictions based on models: e.g., multiplicative assumption correct? effects independent?

Gail Model for breast cancer risk prediction (AUC = 0.61 without age in model) Calibrated in Nurses Health Study Cohort Concordance: 0.58

From Janssens Personal Geomics; Elmore JG, Fletcher SW, JNCI 2006;98:1673; Gail MH, JNCI 2008;100:1037-41
Calibration & Generalizability

Do estimates apply to a given population?

Accuracy of prediction depend on disease risk, genotype frequencies, risk ratios; all of which may vary from group to group.

Study of candidate genes in sample representative of the U.S. adult population:

Frequencies gene variants differed by race/ethnicity for 88 of 90 variants studied.

Chang MH Am J Epidemiol 2009 Jan 1;169(1):54
Janssens AJGH 2008;82:593
Discriminating among those at increased risk and those not

Higher AUC generally reflects greater sensitivity, specificity, predictive values, & ability to discriminate between groups. AUC good summary of overlaps in distributions. Other characteristics add important information.

Alonzo, Pepe: Development, evaluation of classifiers
Janssens AC. Genet Med 2007;9(8):528-535
Ware JH. NEJM 2006;355(25):2615-2617
Adding Genomics to Traditional Breast Cancer Risk Factors, Little Added Discrimination (Gail Model)

Model                          AUC  
4 risk factors                0.61  
7 SNPS                        0.57  
4 R.F.s & 7 SNPs              0.63  

Clinically Useful?            

Gail MH. JNCI 2008;200:1037
Women diagnosed with breast cancer who meet specific criteria (may differ by test) → Gene expression pattern $\rightarrow$ Recurrence Score $\rightarrow$ Predicted recurrence risk and need for chemotherapy $\rightarrow$ Informed management decisions $\rightarrow$ Patient Outcomes
- Morbidity/mortality
- Quality of life
- Avoiding adverse effects of chemotherapy

Potential Harms
# Breast Cancer GEP Evidence Overview

<table>
<thead>
<tr>
<th>Test</th>
<th>Analytic Validity</th>
<th>Clinical Validity</th>
<th>Clinical Utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncotype DX</td>
<td>Adequate Evidence</td>
<td>Adequate Evidence (assoc. of recurrence score with recurrence &amp; response to chemotherapy)</td>
<td>Inadequate Evidence</td>
</tr>
<tr>
<td>Mamma Print</td>
<td>Inadequate Evidence</td>
<td>Adequate Evidence (association with future metastases)</td>
<td>No evidence</td>
</tr>
<tr>
<td>H:I Ratio Test</td>
<td></td>
<td>Inadequate Evidence (to assess added value to standard risk stratification)</td>
<td>No evidence</td>
</tr>
</tbody>
</table>
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Phases of Translation Research in Genomics

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**Current Cancer Genomic Test Recommendations (Evidence-based)**

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Some Potential Opportunities for Public Health Genomics in Cancer Surveillance
USPSTF BRCA1,2 Recommendation

Referral for genetics counseling for women whose family history of breast &/or ovarian cancer indicates increased risk of BRCA1,2 (recommendation for counseling, not testing)

Evaluation of family history as first step

Counseling by a trained professional to assist women in making informed decisions for testing & for any follow up clinical procedures

Evidence for identification of disease risks & for benefits of counseling, testing, & treatment

Woman’s decision based on values, benefits, harms  *Ann Internal Med* 2005;143:355-61 & 362-379
USPSTF *BRCA1,2* Recommendation (2)

Against routine referral for counseling & possible testing for women without high risk family history

Potential harms outweigh benefits, given low risk of having a *BRCA1,2* mutation & potential harms from referral or testing

BRCA Counseling & Testing
Potential Population Health Benefit

~ 93,000,000 U.S. women aged 18-64 (2005)
Many could benefit from taking family history, evaluating history for risk

~ 1.8 million (2%) with positive family history could benefit from medical consult & referral for counseling

~ 280,000 (0.3%) are likely to be BRCA positive, would benefit from counseling on options

Risk reduced by > 85% with surgery

U.S. Census 2006;
USPSTF Recommendations on Fecal DNA Testing for Colorectal Cancer

Concludes that the evidence is insufficient to assess the benefits and harms of fecal DNA testing as a screening modality for colorectal cancer

Balance of benefits & harms cannot be determined

Ann Internal Med 2008;149:627-637 & 638-658
Recent EGAPP Recommendations
Genetics in Medicine January 2009

EGAPP Recommendation Statement

Recommendations from the EGAPP Working Group: can tumor gene expression profiling improve outcomes in patients with breast cancer?
Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group*

Recommendations from the EGAPP Working Group: can UGT1A1 genotyping reduce morbidity and mortality in patients with metastatic colorectal cancer treated with irinotecan?
Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group*

Recommendations from the EGAPP Working Group: genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives
Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group*

www.egappreviews.org/
Breast Cancer Gene Expression Profiles

Application: Prognostic, Used in Treatment Decisions

Population: Women with stage I or II, node negative breast cancer (estrogen receptor status variable, depending on test)

Summary Statement: The EGAPP Working Group found insufficient evidence to make a recommendation for or against the use of tumor gene expression profiles to improve outcomes

UGT1A1 Genotyping

Application: Pharmacogenomic

Population: Patients with metastatic colorectal cancer to be treated with irinotecan

Summary Statement: The EGAPP Working Group found that evidence is insufficient to recommend for or against routine use of UGT1A1 genotyping in patients with the intent of modifying the dose as a way to avoid adverse drug reactions (severe neutropenia)

Testing for Lynch syndrome in individuals with newly diagnosed colorectal cancer

Application: Diagnostic

Population: Individuals with newly diagnosed colorectal cancer (CRC)

Summary Statement: The EGAPP Working Group found sufficient evidence to recommend offering genetic testing for Lynch syndrome to newly diagnosed individuals to reduce morbidity and mortality in relatives, but insufficient evidence to recommend a specific genetic testing strategy among the several examined

Counseling & Testing for Lynch Syndrome Potential Population Health Benefit

~ 142,000 individuals diagnosed with colorectal cancer (CRC) each year

~ 4,250 (3%) of CRC patients with Lynch syndrome

~ 17,000 relatives of Lynch syndrome CRC patients (4 per Lynch CRC patient)

~ 8,500 relatives with Lynch (50% with mutation)

Colonoscopy reduces risk by > 30%

[www.cdc.gov/cancer/]
Stakeholder Response to EGAPP
Generally Positive

“HHS should create and fund a sustainable public/private entity of stakeholders to assess the clinical utility of genetic tests (e.g. building on CDC’s Evaluation of Genomic Applications in Practice and Prevention [EGAPP] initiative).”
Response: The MEDCAC consensus is that the desirable characteristics of evidence for diagnostic genetic testing are not different from the desirable characteristics of diagnostic testing in general. The panel felt that the evidence should be rigorous, and noted that genetic testing has potential harms as well as potential benefits, and that the public is served by robust evidence. The panel also noted that, as with other diagnostic testing, determining the acceptable level of evidence may be interpreted within the context of specific diseases, specific treatments and specific tests. The MEDCAC consensus is that the EGAPP-identified ACCE (Analytic and Clinical validity, Clinical utility and associated Ethical, legal, and social implications) criteria are a desirable framework for this use. See Teutsch SM et al. (2009), in particular Tables 3 and 4 from that article. Note: EGAPP is the Evaluation of Genetic Applications in Practice and Prevention working group, supported by the Centers for Disease Control and Prevention’s National Office of Public Health Genomics.
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CDC’s Public Health Genomics: Closing the Gene Discovery & Population Health Gap

Research/Discovery → Closing the Gap → Population Health

Population Studies
Evidence Syntheses
HuGE
EGAPP
Translation Research
Public Health Practice

GAPPNet

www.cdc.gov/genomics
Increasing Communications to Improve Translation

Clinical, Public Health, & Community Practice

Evidence Based Recommendations

Translation Programs

Network of Stakeholders

Knowledge Synthesis

Translation Research

Research to fill Knowledge Gaps

Determining & sharing what is known & not known & how it’s known

Linking Evidence to Practice Guidance in a Transparent & Credible Way

Genomic Applications In Practice & Prevention Network (GAPPNet)
Networking Stakeholders
NIH/CDC Personal Genomics Workshop

Agreement on Broad Recommendations:
Development of standards for assessment
Multidisciplinary research to fill knowledge
gaps on validity, utility
Credible knowledge synthesis & dissemination
to researchers, clinicians, public
Linkage of science to evidence-based
recommendations
Assessment, evaluation of criteria for personal
utility in addition to clinical utility

Khoury Genetics in Medicine 2009 In Review
NCI-CDC Collaborative Examination

NCI Cancer Genomics Research Funding

Where are NCI Genomics Funds Allocated?

T0  T1  ↔  T2  ↔  T3  ↔  T4

Discovery to Application  ↔  Application to Guideline  ↔  Guideline to Practice  ↔  Practice to Population Health Impact

Bench to Bedside Continuum early phases only

↑ Population Health Benefit

97% of genetics research publications in T0 & T1

Schully SD, Khoury MJ, Pub Health Genomics Submitted
Recent NIH/NCI Funding Opportunity in Translation

NCI Guidelines for ARRA Research and Research Infrastructure Grand Opportunities: Comparative Effectiveness Research in Genomic and Personalized Medicine

Announcement Number: RFA-OD-09-004

Areas of Scientific Priority:

Advances in cancer genomics and the recent progress in identifying susceptibility genes for a wide variety of cancers are ushering in a new era of personalized cancer care and prevention. Using pharmacogenomic testing, we expect that cancer drugs could become tailored by genetic backgrounds to minimize adverse effects and increase treatment effectiveness. Moreover, stratification of cancer risk using biological markers such as genetic variants and protein markers are expected to increase early detection and primary prevention efforts. Gene expression profiles in tumors may become prognostic markers that could direct personalized chemotherapies and other interventions. Several examples of genetic risk on stratification for treatment and prevention are already available in breast cancer, colorectal cancer, prostate cancer and leukemias. Nevertheless, to date, there has been no systematic research conducted to compare the clinical effectiveness and cost-effectiveness of cancer care and prevention based on genomic tools and markers compared to existing standards of care and prevention that do not use genome-based approaches. Without such research, the promise of genomics and personalized medicine may not be fulfilled.
CDC Translation Research Announcement

Goal: Support research needed for evidence-based clinical and public health practice in genomics

Focus: Fill Evidence Gaps identified by EGAPP & USPSTF reviews & recommendations
Research Project: Clinical Utility

University of Washington
Evaluate the clinical utility (improved health outcomes, value in clinical decision making) of:
- Warfarin pharmacogenomics
- Gene expression profiling for treatment of early stage breast cancer
- Factor V Leiden testing for pregnant women
Collaborative process with stakeholders
CDC Translation Program Announcement

Goal: Promote evidence-based clinical and public health practice in genomics
Focus: EGAPP, USPSTF reviews, recommendations
Supported activities: education, policy, surveillance
4 funded projects
CDC Translation Program Announcement: Surveillance

Use of counseling and testing for BRCA1 & 2
Use of family medical history tools for CHD, stroke, diabetes, and/or 3 cancers
Use of genomic tests under consideration by EGAPP Work Group
Knowledge and attitudes of the public and/or clinical practitioners with regard to the use of BRCA1 & 2 or genomic tests under consideration by the EGAPP Work Group
Funded Statewide Intervention

Michigan Department of Community Health
Multi-faceted, state-wide comprehensive program
Surveillance, health education, & policy
With State CCC Coalition
Translation of USPSTF *BRCA* recommendations into practice
Translation of EGAPP recommendations on Lynch syndrome, breast cancer gene expression profiling
Evaluate effectiveness in changing knowledge, test use, insurance coverage
Michigan Cancer Genomics Surveillance

Established surveillance system on
Use of counseling for BRCA 1 & 2
Knowledge and attitudes of the public on use of BRCA 1 & 2, MMR (Lynch), and tumor gene expression profiling
Use of BRCA 1 & 2, MSI, IHC, MMR, Oncotype DX, MammaPrint, and H:I ratio testing
Provide surveillance reports to the public and practitioners
Funded: State-wide Surveillance

Oregon Public Health Division
Cancer genomics surveillance program of State’s adult population & healthcare providers
Monitor use of cancer-specific genomic tests & family history
Focus on tests identified by EGAPP & USPSTF related to breast, colorectal, & ovarian cancers
Evaluate: information completeness, quality & usefulness of information to others
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T4
Health Practice to Health Impact

Define outcomes of interest
Identify/develop appropriate metrics
Implement surveillance; outcomes research
Re-evaluate benefits & harms
Re-evaluate guidelines and policies → Identify needed changes

Improved population health

Health practice

Courtesy: W. Burke
Based on Khoury et al. Genet Med 2007
Surveillance Needs

Improved Ability to Conduct Surveillance on Genomics

Lack of Infrastructure

e.g., No CPT Codes for specific tests

AHRQ.gov/: Report No. 08-EHC012
Surveillance Opportunities: OPHG Priorities

Use of counseling and testing for BRCA1 & 2
Use of family medical history tools for colorectal, breast, ovarian cancers
Use of cancer-related genomic tests under consideration by EGAPP Work Group
Knowledge and attitudes of the public and/or clinical practitioners with regard to the use of BRCA1 & 2 or cancer genomic tests under consideration by the EGAPP Work Group
Information from Medical Records Reportable to Registries?

BRCA 1 & 2 testing
- Subset of women newly diagnosed with breast cancer
MSI, IHC, MMR, BRAF testing
- Men & women newly diagnosed with colorectal cancer
Oncotype DX, MammaPrint, or H:I ratio testing
- Women newly diagnosed with specific types of breast cancer
UGT1A1 testing
- Men & women newly diagnosed with metastatic colorectal cancer when irinotecan treatment considered
Use of Tests Identified by EGAPP

![Image of EGAPP website](www.egappreviews.org/workingrp/topics/)

### Topics Identified

<table>
<thead>
<tr>
<th>Disorder/Effect</th>
<th>Test to be Used*</th>
<th>Clinical Scenario</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne</td>
<td>G6PD</td>
<td>Target Population: Individuals prior to treatment for acne</td>
</tr>
<tr>
<td>Acute Lymphoblastic Leukemia (ALL)</td>
<td>TPMT</td>
<td>Target Population: Individuals prior to treatment for ALL</td>
</tr>
<tr>
<td>Acute Myeloid Leukemia (AML)</td>
<td>FLT3</td>
<td>Target Population: Individuals prior to treatment for AML</td>
</tr>
<tr>
<td>Atrial Fibrillation and Stroke</td>
<td>Chromosome 4q25</td>
<td>Target Population: General Population</td>
</tr>
<tr>
<td>Alzheimer's Disease (AD)</td>
<td>ApoE</td>
<td>1) Dementia patients; 2) Individuals with a family history of dementia; and 3) General population</td>
</tr>
</tbody>
</table>

[www.egappreviews.org/workingrp/topics/](www.egappreviews.org/workingrp/topics/)
# Use of Tests Identified by EGAPP (2)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Gene</th>
<th>Description</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory Bowel Disease</td>
<td>TPMT</td>
<td>Individuals diagnosed with Inflammatory Bowel Disease</td>
<td>Treatment with Azathiopurine</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>GSTM1</td>
<td>Individuals with clinical suspicion of lung cancer</td>
<td>Predictive testing/risk assessment</td>
</tr>
<tr>
<td>Lung Cancer, Non-Small Cell (NSC)</td>
<td>EGFR, KRAS</td>
<td>Individuals prior to treatment for NSC lung cancer</td>
<td>Treatment with tyrosine kinase inhibitor (TKI) drugs (gefitinib, erlotinib)</td>
</tr>
<tr>
<td>Malignant Hyperthermia</td>
<td>RYR1</td>
<td>High risk individuals prior to surgery</td>
<td>Management in surgery</td>
</tr>
<tr>
<td>Melanoma / Pancreatic Cancer</td>
<td>p16</td>
<td>General population</td>
<td>Predictive testing/risk assessment</td>
</tr>
<tr>
<td>Myelodysplastic Syndromes</td>
<td>Hemescan MDS</td>
<td>Individuals with refractory anemia and clinical suspicion of leukemia</td>
<td>Risk Assessment and management</td>
</tr>
<tr>
<td>Myeloproliferative disorders</td>
<td>JAK2</td>
<td>Individuals with clinical suspicion of myeloproliferative disorders</td>
<td>Confirm diagnosis</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>CDKN2A/2B</td>
<td>General Population</td>
<td>Risk assessment</td>
</tr>
<tr>
<td>Multiple disorders</td>
<td>Multigene Panels</td>
<td>General Population</td>
<td>Risk Prediction</td>
</tr>
<tr>
<td>Pain Management</td>
<td>CYP450</td>
<td>Individuals treated for chronic or acute pain</td>
<td>Treatment with codeine and derivative drugs</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>LRRK2</td>
<td>Individuals with clinical suspicion or family history of Parkinson’s disease</td>
<td>Diagnosis and treatment of individuals and family members</td>
</tr>
</tbody>
</table>
Evaluation of Use, Therapies, Outcomes
e.g., Oncotype DX, MammaPrint, or H:I ratio

Breast cancer gene expression profiling: use with stage I or II, node negative breast cancer (ER status specific for each test)

What cancers are being tested? Is chemotherapy based on risk score? What are the recurrence rates, other outcomes among women stratified by risk score & by therapy Effectiveness same as efficacy?
Evaluation of Use, Therapies, Outcomes
e.g., HER2 & Herceptin

Recommended by ASCO, NCCN

Are guidelines followed?
  Is testing conducted prior to use of Herceptin?
  Is Herceptin used in women who are HER2 negative?
What are the outcomes of treatment?
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Public Health Genomics

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