Public Health Genomics and Cancer: Family History and Burden

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Director
Division of Cancer Prevention and Control
National Center for Chronic Disease Prevention and Health Promotion

Accessible Version: https://youtu.be/nw0almfi-ew

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Incidence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>105.3</td>
</tr>
<tr>
<td>Lung &amp; Bronchus</td>
<td>71.6</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
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</tr>
<tr>
<td>Urinary Bladder</td>
<td>35.4</td>
</tr>
<tr>
<td>Melanomas of the Skin</td>
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<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>22.3</td>
</tr>
<tr>
<td>Kidney &amp; Renal Pelvis</td>
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<tr>
<td>Leukemias</td>
<td>16.9</td>
</tr>
<tr>
<td>Oral Cavity &amp; Pharynx</td>
<td>16.8</td>
</tr>
<tr>
<td>Pancreas</td>
<td>14.1</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
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<tr>
<td>Colon &amp; Rectum</td>
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<tr>
<td>Uterine Corpus</td>
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<tr>
<td>Thyroid</td>
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<tr>
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<tr>
<td>Ovary</td>
<td>11.3</td>
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<tr>
<td>Kidney &amp; Renal Pelvis</td>
<td>11.2</td>
</tr>
<tr>
<td>Pancreas</td>
<td>10.9</td>
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</table>

Incidence Rate per 100,000 population
Matt Brooks, Community Manager and Designer at The Noun Project. License available at creativecommons.org/licenses/by/3.0/us/legalcode
### Leading Causes of Cancer Mortality in the United States, 2012

#### Males

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Mortality Rate</th>
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<tbody>
<tr>
<td>Lung &amp; Bronchus</td>
<td>56.2</td>
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<tr>
<td>Prostate</td>
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<tr>
<td>Colon &amp; Rectum</td>
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<tr>
<td>Pancreas</td>
<td>12.7</td>
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<tr>
<td>Liver &amp; Intrahepatic Bile Duct</td>
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<tr>
<td>Leukemias</td>
<td>9.2</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>7.6</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>7.6</td>
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<tr>
<td>Esophagus</td>
<td>7.3</td>
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<tr>
<td>Kidney &amp; Renal Pelvis</td>
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#### Females

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; Bronchus</td>
<td>36.4</td>
</tr>
<tr>
<td>Breast</td>
<td>21.3</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>12.4</td>
</tr>
<tr>
<td>Pancreas</td>
<td>9.6</td>
</tr>
<tr>
<td>Ovary</td>
<td>7.4</td>
</tr>
<tr>
<td>Leukemias</td>
<td>5.1</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>4.6</td>
</tr>
<tr>
<td>Uterine Corpus</td>
<td>4.5</td>
</tr>
<tr>
<td>Liver &amp; Intrahepatic Bile Duct</td>
<td>3.8</td>
</tr>
<tr>
<td>Brain &amp; other Nervous System</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Mortality Rate per 100,000 population
Matt Brooks, Community Manager and Designer at The Noun Project. License available at creativecommons.org/licenses/by/3.0/us/legalcode
Risk Factors for Different Types of Cancers

- **Common risk factors for cancer**
  - Age
  - Alcohol
  - Cancer-causing substances
  - Diet
  - Family history
  - Genetic mutations
  - Hormones
  - Infectious agents
  - Obesity
  - Radiation
  - Tobacco use

- **Inherited genetic mutations play a major role in about 5%–10% of all cancers**

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**Genomics**

Genomics refers to the functions and interactions of all the genes in the genome. It is a more comprehensive field than genetics, which refers to the study of heredity as well as the function and composition of individual genes.
Hereditary Breast and Ovarian Cancer (HBOC) Syndrome

- Involves mainly mutations to tumor suppressor genes
  - BRCA1 or BRCA2
- Associated with increased risks for breast, ovarian, prostate, and pancreatic cancers
- About 1 in every 500 women in the U.S. has a mutation in either the BRCA1 or BRCA2 genes

Tumor suppressor genes
The BRCA1 and BRCA2 genes produce a protein that repairs damaged DNA. Mutations in these genes lead to the accumulation of genetic defects that can allow cells to grow and divide too fast or in an uncontrollable way.
Lynch Syndrome

- Involves mutations in mismatch repair genes, which lead to tumors with microsatellite instability
- Associated with increased risks for colorectal, endometrial, ovarian, stomach cancers and other types of cancer

Mismatch repair genes
When DNA is replicated during cell division, errors or mismatches may occur. Mutations in the MLH1, MLH2, MSH6, and PMS2 genes prevent repairs from being properly made.

Microsatellite instability
Microsatellites are stretches of DNA with a repetitive sequence, which are susceptible to replication errors. Compared to normal tissue, cells with defective mismatch repair genes show a different number of microsatellite repeats.

Cancers Associated with Hereditary Cancer Syndromes

HBOC Syndrome
- Up to 10% or approximately 22,000 cases of breast cancer each year
- 15% or approximately 3,000 cases of ovarian cancer each year

Lynch Syndrome
- Up to 3% or approximately 4,000 cases of colorectal cancer each year

Women with HBOC Syndrome Have Increased Risk for Breast Cancer

Out of 100 women in the U.S. general population:

- About 12 will get breast cancer by age 70

Out of 100 women with HBOC Syndrome:

- About 65 will get breast cancer by age 70


Women with HBOC Syndrome Have Increased Risk for Ovarian Cancer

Out of 100 women in the U.S. general population:

About 1 will get ovarian cancer by age 70

Out of 100 women with HBOC Syndrome:

About 39 will get ovarian cancer by age 70

Individuals with Lynch Syndrome Have Increased Risk for Colorectal Cancer

Out of 100 individuals in the U.S. general population:
- About 4 will get colorectal cancer by age 70

Out of 100 individuals with Lynch Syndrome:
- About 40 will get colorectal cancer by age 70

Family History Associated with HBOC Syndrome

- Younger age at diagnosis
- Cancer in both breasts or in conjunction with ovarian cancer
- Breast cancer at any age in men
- Known BRCA mutations in relatives
- Ashkenazi Jewish ancestry
Family History Associated with Lynch Syndrome

- Younger age at diagnosis
- Colorectal cancer in conjunction with, or separately from, another Lynch syndrome-related cancer
- Relatives with Lynch syndrome-related cancers
- Known Lynch syndrome-related mutations in relatives
Genomic Recommendations for Cancer Screening

- **U.S. Preventive Services Task Force recommendation on BRCA-related cancer:** Risk assessment, genetic counseling and genetic testing
  - Screening to identify family history associated with BRCA1 or BRCA2
  - If positive, receive genetic counseling and if indicated after counseling, then BRCA testing

- **Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group recommendation for people with newly diagnosed colorectal cancer**
  - Access to genetic testing to identify Lynch syndrome to prevent cancer in their close relatives

Mitigating Risk among Individuals with Hereditary Cancer Syndromes

- **Provider and patient determine best course of action to reduce risk**

- **Possible interventions for HBOC Syndrome**
  - Risk-reducing medications for breast cancer (e.g., tamoxifen or raloxifene)
  - Mammography (when to start, frequency, and when to combine with breast MRI)
  - Bilateral mastectomy and bilateral salpingo-oophorectomy

- **Possible interventions for Lynch Syndrome**
  - Colonoscopy starting at age 25 or earlier
  - Screen based only on colonoscopy and not other colorectal cancer screening tests (e.g., sigmoidoscopy, fecal occult blood test)
Genomic Activities in Public Health

- Surveillance
- Epidemiology and Research
- Communication and Partnerships
- Public Health Practice
Know:BRCA

An interactive web resource with unique areas for consumers and healthcare providers

Launched on May 8, 2014

www.knowbrca.org
Bring Your Brave

"#BraveBecause life is an amazing gift and I want to make sure I can enjoy it as long as possible!"
Cara, 30, Cancer-free since 2011

Share your story on Facebook and Twitter using #BraveBecause to inspire other young women to understand their breast cancer risk.
● Provides leadership and builds capacity for cancer genomics activities in state public health departments

- Implement education, surveillance, and policy or systems change activities that will translate and implement national recommendations for cancer genomics

● Funded programs currently in five U.S. states

- Colorado
- Connecticut
- Michigan
- Oregon
- Utah


CDC Awards Funding to Support Cancer Genomics. cdc.gov/cancer/breast/what_cdc_is_doing/genomics_foa.htm
Due to current state of the science, current efforts focused on the hereditary cancer syndromes for which screening and intervention are recommended.

What CDC is doing:
- Educating public and providers
- Developing or expanding surveillance systems
- Assessing system- or policy-level barriers
A State Health Department Approach to Cancer Genomics Surveillance, Education and Policy

Debra Duquette, MS, CGC
Genomics Coordinator
Michigan Department of Health and Human Services (MDHHS)
Improved health outcomes and an enhanced quality of life for the people of Michigan through appropriate use of genetic information, technology, and services

michigan.gov/genomics
Michigan Cancer Genomics Goals and Objectives

- Increasing genetic literacy related to cancer
- Assessing the public health impact of hereditary cancer and the utilization of clinical genetics services
- Enhancing communications with cancer genetic service providers and promoting partnerships
- Reducing morbidity and mortality related to hereditary cancer
Comprehensive Cancer Control Plan for Michigan, 2009–2015

Genomics Goal
➢ Increase availability of cancer-related genetic information to the Michigan public and decrease barriers to risk-appropriate services

Ovarian Cancer Goal
➢ Improve understanding of, and access to, genetic counseling services for women who may be at high risk for developing ovarian cancer

michigancancer.org/

- **Purpose**
  - Move human genome applications into health practice to maximize health benefits and minimize harm through non-research activities

- **Awarded from CDC to four grantees**

- **Goals**
  - Develop and implement surveillance model of inherited cancer and use of relevant tests
  - Identify model provider education programs to increase use of appropriate screening, counseling and evidence-based genetic tests
  - Identify model health insurance policy for BRCA1/2 genetic counseling and testing
Goals

- Promote adoption of health plan policies to increase coverage of \textit{BRCA} clinical services
- Increase healthcare provider knowledge and use of \textit{BRCA} clinical practices
- Expand surveillance of \textit{BRCA} clinical practices

\textit{BRCA} counseling, testing, and clinical services

1. Record family and personal history of cancer
2. Perform cancer genetic risk evaluation referral and counseling
3. Perform \textit{BRCA} testing and interpret results
4. Provide recommended \textit{BRCA} related clinical service
Utilizing State Cancer Registry Data for Cancer Genomics Surveillance

MDHHS Cancer Genomics and Michigan Cancer Surveillance Program (MCSP)

- Examined potential cases at risk for HBOC or Lynch syndrome
  - Multiple primary sites of cancer
  - Early onset breast cancer (age 50 or younger)
  - Triple negative breast cancer
    - Does not express the genes for estrogen receptor, progesterone receptor, or HER2/neu
  - Male breast cancer
  - Ovarian cancer
  - Early onset endometrial cancer (before age 50)
  - Colorectal cancer

- Disseminated data to healthcare systems and providers to reinforce educational messages
Use of Cancer Genetic Services among Young Breast Cancer Survivors

- Black women were less likely than white/other women to use cancer genetic services

<table>
<thead>
<tr>
<th>Use of cancer genetic services</th>
<th>Total (n=828)</th>
<th>Black (n=317)</th>
<th>Other (n=511)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Had genetic counseling*</td>
<td>32.9%</td>
<td>26.6%</td>
<td>37.1%</td>
</tr>
<tr>
<td>Had genetic testing*</td>
<td>28.5%</td>
<td>19.9%</td>
<td>33.7%</td>
</tr>
<tr>
<td>Had genetic counseling and testing*</td>
<td>27.5%</td>
<td>18.3%</td>
<td>32.9%</td>
</tr>
</tbody>
</table>

* Significant at the 0.001 level for black vs. other

MDHHS provided in-person interactive case-based cancer genetics presentations since 2009

Based on the success of case-based approach, in 2012–2013 MDHHS collaborated with federal, state, and local partners to develop online hereditary breast and ovarian cancer genomics module

Michigan State University approved 2.0 CMEs until October 2016

- Available at no cost to participants
- Over 4,400 sessions since launch in February 2014

http://www.nchpeg.org/hboc/
Michigan Successes Related to BRCA Counseling Access and Referrals

Michigan Department of Health and Human Services, unpublished data.
Promoting Evidence-based Cancer Screening Polices Among Insurers
Members from specific health plan receiving BRCA counseling and testing, October 1, 2007–September 30, 2013
Lynch Syndrome Screening Network (LSSN)

- **LSSN Mission**
  - Promote Lynch syndrome screening on all newly diagnosed colorectal and endometrial cancers
  - Facilitate the ability of institutions to implement appropriate screening through network collaboration
  - Investigate universal screening for other Lynch syndrome-related malignancies

- **Institutional membership**
  - Over 120 leading cancer institutions are members
  - Over 20,000 newly diagnosed cancers screened
  - Membership data assisting to measure Healthy People 2020 Lynch syndrome objective

[http://www.lynchscreening.net/](http://www.lynchscreening.net/)
Summary

- State health department infrastructure can be used to integrate cancer genomics into public health programs
  - Comprehensive Cancer Control Program State Plans
  - State Cancer Registry Data

- In Michigan, cancer genetic counseling and testing is increasing, but appropriate use of these services remains low overall, and racial disparities are present

- Partnerships, dedicated staff, and use of core public health functions, e.g., assessment, policy, and assurance, are needed to advance cancer genomics activities
Raising Awareness About Understanding Family Risk for Cancer

Lindsay Avner
Founder and CEO
Bright Pink
Inspired By My Past To Take Action For My Future
We Are Bright Pink

- We save women’s lives from being cut short by breast and ovarian cancer
- Empowering them to live proactively at a young age
  - Our focus is health, not just cancer
- Actions to prevent and detect breast and ovarian cancer begin with knowledge
- Conversations can save lives
  - Within families, friends, healthcare providers
Awareness Doesn’t Save Lives, Action Does

We reach 18–45 Year Old Women and Health Providers Nationwide with Evidence-Based Breast and Ovarian Health Content Where they Work, Connect and Engage Inspiring Them to Put Awareness in Action

With Education Programs focused on Scale and Behavior Change
A New Approach to Breast and Ovarian Health

Empowered Women + Proactive Providers
OUR COMMUNITIES

150
Trained ambassadors in key communities nationwide

39
States with active Bright Pink programs

1000+
Volunteers nationwide
Education and Tools

Brighten Up® Educational Workshops

AssessYourRisk.org

2015

35,000 educated

120K completions

Growth in 2016

70,000 educated

335K completions
High Risk Support

PinkPal® One-on-One

Outreach Groups

Digital Connections

2015

1,000 matches*

16 communities

275 members

Growth in 2016

1,300 matches*

22 communities

700 members

*Coming later this year: Genetic Testing Info One-Stop Shop website
“After this talk I was approached by a sweet young woman, who shared with me her striking family history of breast and ovarian cancer. She cried as she told me she was so scared and didn't know where to start. She was terrified for her mother. The breast cancer in her family started at age 31. I encouraged her to reach out to Bright Pink ... she was relieved that there was genetic testing for her family.”

— Heather, Bright Pink Education Ambassador
“Thank you for providing accurate and evidence-based information on cancer risk. I am blown away by how effective Bright Pink has been in raising the visibility of genetic links to cancer. I already knew about my BRCA2 mutation ... but the information you provided helped me decide to undergo a prophylactic double mastectomy 6 weeks ago. I am now a success story. Bright Pink can provide you the information you need to determine whether you should seek genetic testing and ... manage your risk.”

— Katie, Takoma Park, Maryland
Women’s Health Provider Education Initiative

2015
- 4,000 providers educated at more than 80 institutions
- 14.4 million women primed for better care

Growth in 2016
- 6,000 providers educated at more than 100 institutions
- 21.6 million women primed for better care

Coming later this year: Digital Complement
“Thanks for an interesting and practical Grand Rounds this morning. Already starting to change the way I think about screening some of my patients.”

— Michael Rabovsky, M.D., Chairman, Family Medicine Vice Chair, Medicine Institute Cleveland Clinic
“This lecture gives the right perspective – it breaks it down, it gives us an option to say “I can do something more than say your mammogram is abnormal. I know how to have a conversation with the average person who comes to our office.” It’s more than studying for the boards … It’s the actual heart of practicing.”

— Dr. Aisha Redmond, Kaiser Permanente Town Park
Visit BrightPink.org and AssessYourRisk.org for more information
The Role of Genomics in Public Health

Muin J. Khoury, MD, PhD
Director
Office of Public Health Genomics
Division of Public Health Information Dissemination
Center for Surveillance, Epidemiology, and Laboratory Services
The CDC Office of Public Health Genomics

- Effective and responsible translation of genome-based discoveries into disease prevention and population health
  - Identify evidence-based genomic applications
  - Inform and communicate
  - Integrate into practice and programs
A Crucial Public Health Role is to Identify Population Health Impact of Genomics

- Identifying genomic tests and family health history applications that are supported by synthesized evidence for their use

- Estimating the potential population health impact of these applications
  - Lives saved
  - Disease prevented or detected earlier
  - Healthcare costs and savings

- Promoting appropriate and equitable use
Numerous Genetic Tests are Available
# 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>
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</tbody>
</table>

Tier 1 Genomic Tests can Save Lives and Many are Underused in Clinical Practice

➢ >40 tests supported by evidence for use in practice
  ● >30 cancer-related tests

➢ Many intended uses include
  ● Diagnosis
  ● Prognosis
  ● Risk prediction to inform prevention
  ● Treatment, including choice of medication and dosage
  ● Screening

Centers for Disease Control and Prevention. genomicsforum.org/editoruploads/ActionstoSaveLivesNowReport.pdf
Family Health History as a Tool for Public Health

- Family health history is a risk factor for many diseases
- Family health history offers opportunities for targeted screening and prevention
- The Surgeon General’s Family Health History Initiative
- Thanksgiving is National Family History Day

familyhistory.hhs.gov/
The Possibilities for Genomics to Improve Public Health are Growing Rapidly

- More than a decade after the Human Genome Project was completed
- Whole-genome sequencing as tool in clinical and public health practice
  - Human DNA sequencing (rare diseases, cancer, chronic diseases)
  - Pathogen DNA sequencing (CDC’s Advanced Molecular Detection initiative role in surveillance and outbreak response)
- Increased public awareness
  - Especially with celebrity announcements
- Proliferation of direct-to-consumer genetic tests
Public Health is 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
Public Health Genomics and Health Disparities: Ensuring Benefits for All

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

Probability of BRCA testing (Hazard Ratio)

Race/ethnicity

Genomics-Related Policies and Legislation

- **Affordable Care Act**
  - Covers *BRCA* genetic services in accordance with the USPSTF grade B recommendation

- **Genetic Information Nondiscrimination Act of 2008**
  - Prohibits discrimination in both health insurance and employment based on genetic information

- **Current Procedural Terminology (CPT) code revisions**
  - Implemented specific billing codes for many genetic tests

- **Healthy People 2020**
  - New cancer genomics topic area, including objectives on hereditary breast and ovarian cancer and Lynch syndrome

USPSTF: United States Preventive Services Task Force
Genomic Activities in Public Health

- Surveillance
- Epidemiology and Research
- Communication and Partnerships
- Public Health Practice
The U.S. Precision Medicine Initiative

-Launched in 2015, includes two components:

- A focus on molecularly targeted treatment for cancer

- A national cohort of at least 1 million people

What is precision medicine?

“An emerging approach for disease prevention and treatment that takes into account people’s individual variations in genes, environment, and lifestyle.”

Success of Precision Medicine Requires Public Health Partnerships

- Inclusion and generalizability
- Focus on prevention
- Implementing what we know
- A new era of precision public health