GENETIC SCREENING BEYOND NEWBORNS: A STATE PERSPECTIVE

Michigan Department of Health and Human Services (MDHHS) Genomics Program

Debra Duquette, MS, CGC
duquetted@michigan.gov
517.335.8286

January 30, 2017
WHAT IS ROLE OF STATE PUBLIC HEALTH IN POPULATION-BASED GENETIC SCREENING BEYOND NEWBORNS?

- Reduce Morbidity and Mortality
- Work to achieve Healthy People 2020 (HP2020) genomics objectives
- Utilize Ten Essential Services and Core Public Health Functions
- Promote Evidence-Based Recommendations and National Guidelines
- Address Health Disparities & Reduce Health Inequities
- Build and Sustain Partnerships
Possible populations and hereditary conditions to consider for universal screening beyond newborns:

- Population with significant risk of hereditary condition
- Genetic screening/testing available with proven validity
- Autosomal dominant condition with cascade screening for unaffected relatives
- Health disparities likely exist
- Detection of hereditary condition will change clinical management of individual and/or relatives
- Interventions exist to reduce mortality and morbidity for individual and/or relatives

Lynch syndrome screening on all newly diagnosed colorectal cancers
- Multi-gene panel testing for all patients with colorectal cancers under 50 years

BRCA and Lynch syndrome genetic testing for all women with ovarian, fallopian tube and primary peritoneal cancers

BRCA testing on all women with breast cancer diagnosed at a young age (50 or under)

BRCA testing for all men with breast cancer

Dyslipidemia (Familial Hypercholesterolemia) screening for all 9-11 year olds and earlier if known family history

Multi-gene panel postmortem genetic testing on all sudden unexplained/cardiac deaths especially if young age with normal autopsy

Examples of populations beyond newborns to consider for universal genetic screening/testing with cascade screening to relatives
Improved health outcomes and an enhanced quality of life for the people of Michigan through appropriate use of genetic information, technology, and services

www.michigan.gov/genomics
MDHHS Genomics Program, 2003-2017

CDC Cooperative Agreement: Genomics Applications in Practice and Prevention, 2008-2011

CDC Cooperative Agreement: Genomics Integration in Public Health Programs, 2003-2008

Cancer Program participates in genetics needs assessment and state plan process

MDHHS Genomics Program, 2003-2017

Cancer objectives in State Genetics Plan, 2003-2008

MDHHS Genomics Program, 2003-2017

CDC DCPC supplemental funding for young breast cancer survivors activities, 2010

CDC DCPC supplemental funding for young breast cancer survivors activities, 2010

CME online module launched

MI Informed Consent Law for Genetic Testing Begins in 2000

LSSN formed

CDC Prevention Research Center-Special Interest Project: Potential for Cancer Screening Interventions for Cancer Survivors Delivered Through Central Cancer Registries, 2011-2014

Healthy plan policy Work begins


Cancer Program participates in genetics needs assessment and state plan process


Genomics objective in State Cancer Plan, 2016-2020

CME online module launched

Genomics goal and objectives in State Cancer Plan, 2009-2015


HEALTHY PEOPLE 2020
(HP 2020) CANCER GENOMICS OBJECTIVES

- **HP 2020 marks first time for genomics objectives**
  - Drafted by multiple federal agencies and one state health department (MDHHS) in 2009 and approved by HP2020 in 2010

- **Increase the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling**

- **Increase the proportion of persons with newly diagnosed colorectal cancer who receive genetic testing to identify Lynch syndrome (or familial colorectal cancer syndromes)**

**http://www.healthypeople.gov/2020/topics-objectives/topic/genomics/objectives**
Sufficient evidence to offer counseling & genetic testing for Lynch syndrome to patients newly diagnosed with colorectal cancer to reduce morbidity & mortality in relatives

Relatives of patients who test positive for Lynch could be offered counseling, testing &, if positive, increased colonoscopy

Evidence of benefit to the patient’s relatives

2009 EGAPP RECOMMENDATION ON GENETIC TESTING FOR LYNCH SYNDROME

Autosomal dominant hereditary cancer syndrome

- Most common hereditary colorectal (CRC) and endometrial cancer syndrome
  - ~1/33 individuals with CRC
  - ~1/400 individuals in general population
- Increased risk of CRC, endometrial, ovarian, urinary tract, gastric tract, small bowel, pancreas, sebaceous cancers
  - 20-80% lifetime risk for CRC cancer
- Due to mutations in MLH1, MSH2, MSH6, PMS2 or EPCAM genes
Screening is complex!
- Bethesda and Amsterdam criteria
- Multiple approaches including IHC, MSI and/or other testing on tumor with DNA testing

Cancer surveillance & prophylactic surgery options
- Colonoscopy every 1-2 years beginning at ~20-25 years old or 2-5 years prior to earliest CRC if before age 25
- Aspirin may decrease risk of CRC; optimal dose and duration unknown
- Annual endometrial sampling is option
- Transvaginal ultrasound & serum CA-125 consideration by clinician
- Annual urinalysis starting at 30-35 years
- Annual physical/neurologic exam starting at 25-30 years
- Prophylactic surgery including subtotal colectomy, hysterectomy and bilateral salpingo-oophorectomy
- Routine EGDs with extended duodenoscopy for select patients or those of Asian descent consider; H. pylori testing consider

### TABLE 4: HIGH-RISK CRC GENES ON MULTI-GENE PANELS

<table>
<thead>
<tr>
<th>GENETIC TESTING</th>
<th>ASSOCIATION</th>
<th>RISK LEVEL</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>APC</td>
<td>Familial adenomatous polyposis (FAP) &amp; Attenuated FAP</td>
<td>High</td>
<td>See APC and MUTYH Genetic Testing Criteria (APC/MUTYH-1)</td>
</tr>
<tr>
<td>BMPR1A</td>
<td>Juvenile polyposis syndrome</td>
<td>High</td>
<td>See Juvenile Polyposis Syndrome Guidelines (JP8-1)</td>
</tr>
<tr>
<td>EPCAM</td>
<td>Lynch syndrome</td>
<td>High</td>
<td>See Lynch Syndrome Guidelines (LS-1)</td>
</tr>
<tr>
<td>GREM1</td>
<td>Hereditary mixed polyposis syndrome due to a 40kb duplication upstream of GREM1 in Ashkenazi Jewish ancestry only</td>
<td>Not known – presumed high risk from reported families with duplication</td>
<td>Jaeger E, et al. Nat Genet 2012; 44:699-703</td>
</tr>
<tr>
<td>MLH1</td>
<td>Lynch syndrome</td>
<td>High</td>
<td>See Lynch Syndrome Guidelines (LS-1)</td>
</tr>
<tr>
<td>MSH2</td>
<td>Lynch syndrome</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>MSH6</td>
<td>Lynch syndrome</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>MUTYH</td>
<td>MUTYH-associated polyposis</td>
<td>High</td>
<td>See APC and MUTYH Genetic Testing Criteria (APC/MUTYH-1)</td>
</tr>
<tr>
<td>PM82</td>
<td>Lynch syndrome</td>
<td>High</td>
<td>See Lynch Syndrome Guidelines (LS-1)</td>
</tr>
<tr>
<td>PTEN</td>
<td>Cowden syndrome</td>
<td>Moderate-High</td>
<td>See NCCN Guideline Genetic Familial High-Risk Assessment: Breast and Ovarian</td>
</tr>
<tr>
<td>SMAD4</td>
<td>Juvenile polyposis syndrome</td>
<td>High</td>
<td>See Juvenile Polyposis Syndrome Guidelines (JP8-1)</td>
</tr>
<tr>
<td>STK11</td>
<td>Peutz-Jeghers syndrome</td>
<td>High</td>
<td>See Peutz-Jeghers syndrome Syndrome Guidelines (PJS-1)</td>
</tr>
<tr>
<td>TP53</td>
<td>Li Fraumeni syndrome</td>
<td>High</td>
<td>See NCCN Guideline Genetic Familial High-Risk Assessment: Breast and Ovarian</td>
</tr>
</tbody>
</table>

*AXIN2, NTHL1, and RPS20 are emerging as genes that are potentially linked to CRC, and there are not enough data at present to include these genes on this list.

**Note:** All recommendations are category 2A unless otherwise indicated. Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

**Continued on next page**

*See nccn.org for with moderate- and low-risk CRC genes*
PROMOTING SYSTEM CHANGE THROUGH EDUCATION, SURVEILLANCE & POLICY TO ADVANCE CANCER GENOMICS BEST PRACTICES IN MICHIGAN, 2014-2019

- **CDC Cooperative Agreement, 2014-2019**
  - Awarded to Michigan, Oregon, Connecticut, Utah, Colorado

- **Purpose**: Enhance state health department’s capacities to promote and apply evidence-based breast and ovarian cancer genomics guidelines in public health practice
  - Develop, enhance and evaluate education, surveillance and policy/systems change
  - Emphasis on partnerships
    - Required collaborations with relevant funded CDC programs (i.e., BCCCP, cancer registries, comprehensive cancer control programs)
    - Required collaborations with external partners (i.e., academic medical institutions, non-profits, clinical cancer genetics clinics)
  - Focus on *BRCA* but may also include Lynch syndrome
  - May identify target populations disproportionately affected and lacking genetic services
**Purpose:**
Reduce breast, ovarian, colorectal and endometrial cancer incidence and mortality rates by overcoming barriers and advancing health system changes to promote cancer genomics best practices.
Michigan residents at risk for or with HBOC/LS

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

State Health Partners:
- MDCH Cancer Genomics;
- MDCH Cancer Prevention & Control
- MCSP
- Michigan Medicaid
- MiBRFS
- MCC
- MAHP
- MCGA

Local Health Partners:
- BCBSM
- Priority Health
- WSU Genetic Counseling Program
- GVSU
- Local cancer registrars

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

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

Family members at risk for HBOC/LS

CANCER PLAN FOR MICHIGAN, 2016-2020

OBJECTIVE 11
Increase the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling from 8.8% to 9.7%.

STRATEGIES

11.1 Primary care providers should screen women who have family members with breast, ovarian, tubal, or peritoneal cancer with one of several screening tools designed to identify a family history that may be associated with an increased risk for potentially harmful mutations in breast cancer susceptibility genes (BRCA1 or BRCA2).

11.2 Women with positive screening results should receive genetic counseling and, if indicated after counseling, BRCA testing.

11.3 Clinicians should engage in shared, informed decision making with women who are at increased risk for breast cancer about medications to reduce their risk. Clinicians should offer to prescribe approved risk-reducing medications for women who are at low risk for adverse medication effects.

OBJECTIVE 22
Increase the percentage of Michigan residents with a personal history of breast or ovarian cancer that are offered appropriate genetic counseling from 3.6% (ovarian) and 3.3% (breast) to 4.0% and 3.6%.

STRATEGIES

22.1 Promote patient education on underlying genetic/heritable causes of common cancers and the importance of genetic counseling and testing when recommended.

22.2 Promote and support the efforts of Michigan providers to meet national standards on genetic counseling and testing as recommended (i.e. NCCN, ACOG).

22.3 Promote provider education to increase compliance with national standards on genetic counseling and testing, understanding of underlying genetic/heritable causes of common cancers, and the importance of genetic counseling and testing when recommended.

22.4 Increase the number of health plans that have cancer genomic best practices for hereditary breast and ovarian cancer and Lynch syndrome as recommended by USPSTF, NCCN, EGAPP, and Michigan Law.

OBJECTIVE 23
Increase the percentage of newly diagnosed colorectal cancer patients who are screened for Lynch Syndrome from 2% to 2.2%.

STRATEGIES

23.1 Promote patient education to increase understanding underlying genetic/heritable causes of common cancers and the importance of genetic counseling and testing when recommended.

23.2 Promote and support the efforts of Michigan providers to meet national standards on genetic counseling and testing as recommended (i.e. NCCN, ACOG).

23.3 Promote provider education to increase compliance with national standards on genetic counseling and testing, understanding of underlying genetic/heritable causes of common cancers, and the importance of genetic counseling and testing when recommended.

23.4 Increase the number of health plans that have cancer genomic best practices for hereditary breast and ovarian cancer and Lynch syndrome as recommended by USPSTF, NCCN, EGAPP, and Michigan Law.

No source of national data
   - HP2020 objective is developmental
   - MSI only included in cancer registry reporting since 2010

Michigan surveillance efforts for Lynch Syndrome
   - 2010 MiBRFS indicates nearly 80% of individuals at risk for familial CRC syndrome report no knowledge of genetic test
     - Only 3% at risk for familial CRC syndrome had genetic test
   - Of 610 CRC charts reviewed from 2006-2010 diagnoses, less than 2% had Lynch syndrome screening
     - 6 had MSI testing; 11 had IHC; 0 had BRAF; 5 had MMR; 6 had genetic counseling (all among 119 cases aligned with NCCN guidelines)
Meeting held at CDC in September 2010 with multidisciplinary group

Purpose to develop framework and partnerships to:
- Implement clinical/public health approach to reduce morbidity and mortality associated with Lynch syndrome in the United States

Recommendations:
- Consider public health approach strongly integrated with all aspects of clinical care
- Need to address multiple barriers before implementation on large scale
- Need for education of providers, patients, families, payers, and public health professionals
- Convene national conferences to further dialogue
- Seriously consider newborn screening as a model for implementing universal Lynch Syndrome screening on a national level
- Need pilot studies
LYNCH SYNDROME SCREENING NETWORK (LSSN)

LSSN Vision:
- To reduce the cancer burden associated with Lynch Syndrome.

LSSN Mission:
- To promote universal Lynch Syndrome screening on all newly diagnosed colorectal and endometrial cancers; to facilitate the ability of institutions to implement appropriate screening by sharing resources, protocols and data through network collaboration; and to investigate universal screening for other Lynch Syndrome related malignancies.

- Created in 2011 with one-time funding from CDC; small amount of funding from NCI
- LSSN Board of Directors
  - MDHHS (Chair); The Ohio State University; Emory; Geisinger; University of South Florida/Moffitt
- Membership is by institution
  - 95 leading cancer institutions and others
  - No cost to join
  - Website with multiple resources to assist institutions to implement Lynch syndrome screening
  - Active listserv
  - Database developed but not yet launched
  - Research and networking opportunities

http://www.lynchscreening.net/
LSSN MEMBERS ACHIEVING HP2020 LYNCH SYNDROME OBJECTIVE

- 95 current and active LSSN members/partners from 30 states and three countries
  - Michigan with largest number (n=11)
- LSSN Membership data assisting to measure HP2020 Lynch syndrome objective
  - Almost 44,000 cancers screened since 2008
  - Annual increases shown
  - 31,695 CRCs screened; over 1/3rd screened since 2014
  - Most LSSN members initially screen by IHC alone
  - 12,013 endometrial cancers screened; over one-half screened since 2014

<table>
<thead>
<tr>
<th>Type</th>
<th>2014</th>
<th>2015</th>
<th>All years combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>7221</td>
<td>7958</td>
<td>31695</td>
</tr>
<tr>
<td>Endometrial</td>
<td>3031</td>
<td>3428</td>
<td>12013</td>
</tr>
<tr>
<td>Small bowel</td>
<td>23</td>
<td>17</td>
<td>112</td>
</tr>
<tr>
<td>Sebaceous adenoma/carcinoma</td>
<td>26</td>
<td>28</td>
<td>89</td>
</tr>
<tr>
<td>Other</td>
<td>22</td>
<td>31</td>
<td>87</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>10323</td>
<td>11462</td>
<td>43996</td>
</tr>
</tbody>
</table>
The Blue Ribbon Panel recommendations call for a nationwide demonstration project to systematically screen all people diagnosed with colorectal and endometrial cancer for Lynch syndrome.

THE OHIO COLORECTAL CANCER PREVENTION INITIATIVE

• Ohio Colorectal Cancer Prevention Initiative
  • The Ohio State University coordinated with 51 Ohio hospitals
  • Statewide universal tumor screening for newly diagnosed CRC
  • 2,785 patients with newly diagnosed invasive colorectal adenocarcinoma prospectively enrolled
    • 450 unrelated patients diagnosed under 50
    • All tumors screened for MMR deficiency by MSI and/or IHC and MLH1 methylation if needed
      • 48 (10.7%) with MMR-deficient tumors
    • All patients had germline testing for 25 cancer susceptibility genes
      • 1/6 patients with CRC under 50 had at least one pathogenic cancer susceptibility gene mutation
      • 75 pathogenic or likely pathogenic mutations found in 72 patients (16%)
        • 38 with Lynch Syndrome
        • 2 with second hereditary cancer syndrome
        • 34 with different hereditary cancer syndrome

http://jamanetwork.com/journals/jamaoncology/article-abstract/2593042
UTILIZING STATEWIDE CANCER REGISTRY DATA TO IDENTIFY POTENTIAL HEALTH DISPARITIES

CRC incidence decreasing for 50 and over; increasing for less than 50

Rural population with lack of cancer genetic services; MDHHS partner with Thumb Rural Health Network to increase access and awareness
Higher age-adjusted incidence and mortality for CRC higher for blacks; decreasing for all ages and over 50, but not under 50
Genomics and Population Health Action Collaborative

Goal:
- To explore opportunities for genetics and genomics-based research to improve public health, reduce health disparities, and promote genomic literacy
- Formed following diverse stakeholders meeting in November 2015
- Significant increases in membership and activities in first year
- Focus of first year on state public health; evidence-based approaches to improve early detection and clinical care of individuals with pathogenic variants for HBOC and Lynch syndrome

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

Evidence Working Group
Chair: Ned Calonge

- Work Stream 1:
  - Using case studies (BRCA1/2 and Lynch syndrome) consider how genomic applications can reach ‘Tier 1’ level

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

Implementation Working Group
Chair: Deb Duquette

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

- Work Stream 2:
  - Using principles of implementation science, designing a set of common outcome metrics for public health genomics programs that are implementing genomic applications

Work Stream 3:
- Addressing health disparities related to hereditary cancer syndromes
- Outlining possible approaches for public health genomics programs to alleviate health disparities
HEREDITARY CARDIOVASCULAR CONDITIONS AND POPULATIONS TO CONSIDER?
Aim: Prevention of SCDY (1-39 years of age) in Michigan through early detection of individuals at risk, treatment of those with predisposing conditions, & intervention for victims experiencing sudden cardiac arrest
SUDDEN CARDIAC DEATH IN THE YOUNG (SCDY)

- **General SCD Definition:**
  - Deaths occurring out-of-hospital or in the emergency room or as “dead on arrival” with an underlying cause of death reported as a cardiac disease

- **Age group of SCDY variably defined**

- **Often unexpected and especially tragic**
  - Nearly 50% of SCD victims under 35 years have no warning signs or family history of SCD
  - 30% of cases have no abnormality found in the heart on autopsy

- **A potentially preventable condition, due to the heritable nature of certain cardiac disorders**
  - More likely to have genetic determinants than similar conditions in older persons
  - Genetic testing helps to identify inherited cardiac disease in up to 35% of cases of SCDY
  - Immediate family members of SCDY victims may be at increased risk of sudden death
    - ~8.9 surviving relatives per family
    - Cascade genetic screening!

---

Tester et al. Curr Opin Cardiol. 2006 May;21(3):166-72
EXAMPLES OF SCDY ETIOLOGIES

- Coronary artery disease
- Coronary artery abnormalities
- Myocardial disorders
  - Hypertrophic cardiomyopathy*
  - Arrhythmogenic right ventricular dysplasia (ARVD)*
  - Dilated cardiomyopathy
- Other structural/functional abnormalities
  - Primary pulmonary hypertension
  - Restrictive cardiomyopathy
  - Marfan syndrome with aortic dissection
  - Aortic valve stenosis
- Primary electrical abnormalities/ion channelopathies
  - Long QT syndromes*
    - Romano Ward*
    - Jervell Lange Nielsen
    - Acquired
  - Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)*
  - Brugada syndrome*
  - Short QT Syndrome
  - Wolf-Parkinson White syndrome
  - Heart block: congenital or acquired
- Environmental causes
  - commotio cordis, cocaine, stimulants, inhalants, others

*ACMG Recommendations, Genetics in Medicine, 2013
MDHHS SCDY CASE DEFINITION

- Age 1-39
- Death occurred out of the hospital or in the emergency room
- Michigan resident
- Death occurred in Michigan
- Underlying cause of death cardiac-related, congenital cardiac malformations, or ill-defined/unexplained

Cases selected from 220 ICD-10 Codes

Cardiac Related Codes
ICD 10: I00-I51
Examples:
- Cardiomyopathy
- Cardiac arrhythmia
- Atherosclerotic CVD

Congenital Cardiac Malformations
ICD 10: Q20-Q24
Examples:
- Atrial septal defect
- Dextrocardia

Ill-defined/ Unexplained
ICD 10: R96-R99
Examples:
- Instantaneous death
- Death occurring less than 24 hours from onset of symptoms, not otherwise explained
## MICHIGAN DEATH CERTIFICATES REVIEW, 1999-2009

### Table 1

| Sudden cardiac deaths (SCDs)* of Michigan residents aged 1-39 years, 1999-2009 |
|---------------------------------|-----------------|-------------------|
| **Total**                       | 3,134           |                   |
| **Sex**                         |                 |                   |
| Male                            | 2,179           | 69.5              |
| Female                          | 955             | 30.5              |
| **Race**                        |                 |                   |
| White                           | 1,961           | 62.6              |
| Black                           | 1,089           | 34.7              |
| Other                           | 84              | 2.7               |
| **Age**                         |                 |                   |
| 1-4 years                       | 91              | 2.9               |
| 5-9 years                       | 45              | 1.4               |
| 10-14 years                     | 64              | 2.0               |
| 15-19 years                     | 137             | 4.4               |
| 20-24 years                     | 213             | 6.8               |
| 25-29 years                     | 380             | 12.1              |
| 30-34 years                     | 716             | 22.8              |
| 35-39 years                     | 1,488           | 47.5              |
| **Place of death**              |                 |                   |
| Home                            | 1,339           | 42.7              |
| Nursing home, extended care     | 28              | 0.9               |
| Hospital: emergency room / outpatient | 1,462      | 46.6              |
| Ambulance                       | 34              | 1.1               |
| Other / unknown                 | 271             | 8.6               |

### Age-Adjusted Mortality Rates:

- **Statewide:** 5.5 per 100,000
- **White Males:** 6.1 per 100,000
- **Black Males:** 16.5 per 100,000
- **White Females:** 2.4 per 100,000
- **Black Females:** 8.3 per 100,000

- **1-9 years:** 1.0 per 100,000
- **10-19 years:** 1.2 per 100,000
- **20-29 years:** 4.1 per 100,000
- **30-39 years:** 14.5 per 100,000

*Includes decedents who died out of the hospital, or in an emergency department, or were dead on arrival to an emergency department, and had one or more identified ICD-10 codes reported as the underlying cause of death on the death certificate.
TOP TEN CAUSES OF SCDY IN MICHIGAN

Table 2
Ten most frequent underlying causes of death of Michigan SCD victims, 1-39 years, 1999-2009 (n=3,134)

<table>
<thead>
<tr>
<th>ICD 10 Code</th>
<th>Cause of death</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>I25.0</td>
<td>Atherosclerotic cardiovascular disease</td>
<td>464</td>
<td>14.8</td>
</tr>
<tr>
<td>I42.0</td>
<td>Dilated cardiomyopathy</td>
<td>444</td>
<td>14.2</td>
</tr>
<tr>
<td>I21.9</td>
<td>Acute myocardial infarction</td>
<td>331</td>
<td>10.6</td>
</tr>
<tr>
<td>I25.1</td>
<td>Atherosclerotic heart disease</td>
<td>303</td>
<td>9.7</td>
</tr>
<tr>
<td>I11.9</td>
<td>Hypertensive heart disease without heart failure</td>
<td>221</td>
<td>7.1</td>
</tr>
<tr>
<td>I42.2</td>
<td>Other hypertrophic cardiomyopathy</td>
<td>180</td>
<td>5.7</td>
</tr>
<tr>
<td>R99</td>
<td>Other ill-defined and unspecified causes of mortality</td>
<td>124</td>
<td>4.0</td>
</tr>
<tr>
<td>I42.9</td>
<td>Cardiomyopathy</td>
<td>121</td>
<td>3.9</td>
</tr>
<tr>
<td>I49.9</td>
<td>Cardiac arrhythmia</td>
<td>109</td>
<td>3.5</td>
</tr>
<tr>
<td>I26.9</td>
<td>Instantaneous death</td>
<td>86</td>
<td>2.7</td>
</tr>
</tbody>
</table>

- Blacks most common cause was dilated cardiomyopathy (n=255)
- Blacks disproportionately represented among top 10 causes of deaths (except acute myocardial infarction)
- Males also represented more than 60% for the top 10 causes of death (except instantaneous death)
Family History of Sudden Cardiac Death of the Young

### Michigan 2007 Behavioral Risk Factor Survey (MiBRFS)

- **2,856 Michigan adults** were asked about SCDY
- **6.3%** have a family history of SCDY
  - **26.2%** with multiple relatives
  - **35.5%** with first degree relative
- Significantly more **blacks (11.2%)** than **whites (5.4%)** reported SCDY

---

#### Table 3
Family History of Sudden Cardiac Death of the Young*
2007 Michigan Behavioral Risk Factor Survey

<table>
<thead>
<tr>
<th>Age</th>
<th>%</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>6.3</td>
<td>(5.2 - 7.7)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 – 24</td>
<td>3.8</td>
<td>(1.6 - 8.7)</td>
</tr>
<tr>
<td>25 – 34</td>
<td>8.6</td>
<td>(4.9 - 14.6)</td>
</tr>
<tr>
<td>35 – 44</td>
<td>4.2</td>
<td>(2.4 - 7.1)</td>
</tr>
<tr>
<td>45 – 54</td>
<td>7.7</td>
<td>(5.4 - 10.9)</td>
</tr>
<tr>
<td>55 – 64</td>
<td>5.9</td>
<td>(4.1 - 8.5)</td>
</tr>
<tr>
<td>65 – 74</td>
<td>8.5</td>
<td>(5.4 - 13.3)</td>
</tr>
<tr>
<td>75 +</td>
<td>5.4</td>
<td>(3.5 - 8.2)</td>
</tr>
</tbody>
</table>

#### Gender

<table>
<thead>
<tr>
<th></th>
<th>%</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>5.4</td>
<td>(3.9 - 7.4)</td>
</tr>
<tr>
<td>Female</td>
<td>7.7</td>
<td>(6.1 - 9.6)</td>
</tr>
</tbody>
</table>

#### Race/Ethnicity

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>%</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>White non-Hispanic</td>
<td>5.4</td>
<td>(4.3 - 6.8)</td>
</tr>
<tr>
<td>Black non-Hispanic</td>
<td>11.2</td>
<td>(7.7 - 16.0)</td>
</tr>
<tr>
<td>Other non-Hispanic</td>
<td>9.4</td>
<td>(3.8 - 21.3)</td>
</tr>
<tr>
<td>Hispanic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Education

<table>
<thead>
<tr>
<th>Education</th>
<th>%</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than high school</td>
<td>10.8</td>
<td>(5.8 - 19.3)</td>
</tr>
<tr>
<td>High school graduate</td>
<td>8.8</td>
<td>(6.6 - 11.7)</td>
</tr>
<tr>
<td>Some college</td>
<td>4.7</td>
<td>(3.3 - 6.8)</td>
</tr>
<tr>
<td>College graduate</td>
<td>4.4</td>
<td>(2.8 - 6.9)</td>
</tr>
</tbody>
</table>

#### Household Income

<table>
<thead>
<tr>
<th>Household Income</th>
<th>%</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; $20,000</td>
<td>7.8</td>
<td>(5.1 - 11.7)</td>
</tr>
<tr>
<td>$20,000 - $34,999</td>
<td>8.4</td>
<td>(5.9 - 11.8)</td>
</tr>
<tr>
<td>$35,000 - $49,999</td>
<td>8.8</td>
<td>(5.5 - 13.8)</td>
</tr>
<tr>
<td>$50,000 - $74,999</td>
<td>4.1</td>
<td>(2.1 - 7.9)</td>
</tr>
<tr>
<td>$75,000 +</td>
<td>3.2</td>
<td>(1.9 - 5.2)</td>
</tr>
</tbody>
</table>

* Among all respondents (n = 2,856), the proportion who reported having at least one biological family member that had a sudden cardiac death, or sudden unexplained death, between the ages of 1 and 39.

**Note:** Interviewers were instructed not to include spouses of the respondent, infants less than one year of age, as well as drug-related deaths, traumatic deaths (such as car crashes), suicides, homicides, or individuals who had a long illness.

The denominator in this subgroup is less than 50.

http://www.mdpi.com/journal/healthcare/special_issues/genomics
Confirm the cause of death or suggest an alternative cause

Describe the factors that may have contributed to the death

Identify possible risk to family members

Suggest recommendations for prevention of future deaths
### Clinical and Family History
- African American teenage male
- Student, basketball player
- Symptoms 4 months – “skipped beats and fluttering” especially while playing basketball; dizzy when rising from chair; tired all the time; legs hurt all the time; he thought these symptoms meant he was out of shape so he would practice harder
- Private health insurance coverage
- Family History - mother had “stroke“ as teen; maternal uncle had heart attack at 40 years old
- Sports physical 4.5 months prior
- Never referred to cardiologist or specialist
- Weight 82nd percentile

### Day of Death
- Playing basketball, collapsed
- No CPR prior to EMS, police were needed to allow EMS access
- Locked AED at site, coach had no training on AED
- No pulse/not breathing

### Autopsy
- Hypertrophic cardiomyopathy
- Toxicology – negative for alcohol, illicit drugs
- Family members not made aware of genetic implications
EXPERT PANEL FINDINGS

**Patient-related factors**
- Education when to seek medical care
- Family history and screening

**Physician-related factors**
- Quality of pre-participation sports physical
- Awareness of need to screen family members, and when genetics or cardiology referral indicated
- Education on content of family history screening form

**System-related factors**
- CPR training for coaches, or CPR training for community and schools
- If AED present on-site, require training and availability
- Update Michigan High School Athletic Association pre-participation sports screening template to include 2007 AHA 12 point screen and 2004/2010 national consensus recommendations
- Mechanism for family contact, including assuring autopsy report reaches primary care provider
- Storage of biologic specimen/DNA banking
Based on SCDY expert mortality review, 21 action steps identified to prevent SCDY

Grouped into 5 major themes:

✓ Pre-participation sports physicals and screenings
✓ Provider education and public awareness of SCDY risk factors
✓ Emergency response protocols
✓ Public awareness of cardiac symptoms and CPR/AED training
✓ Medical examiner protocols

DATA TO ACTION, 2008-2017
Table 1. The 14-Element AHA Recommendations for Preparticipation Cardiovascular Screening of Competitive Athletes

Medical history*

1. Chest pain/discomfort/tightness/pressure related to exertion
2. Unexplained syncope/near-syncope†
3. Excessive and unexplained dyspnea/symptoms or palpitations, associated with exercise
4. Prior recognition of a heart murmur
5. Elevated systemic blood pressure
6. Prior restriction from participation in sports
7. Prior testing for the heart, ordered by a physician

Family history

8. Premature death (sudden and unexpected, or otherwise) before 50 y of age attributable to heart disease in ≥1 relative
9. Disability from heart disease in close relative ≤50 y of age

10. Hypertrophic or dilated cardiomyopathy, long QT syndrome, or other channelopathies, Marfan syndrome, or clinically significant arrhythmias, specific knowledge of genetic cardiac conditions in family members

Physical examination

11. Heart murmur‡
12. Femoral pulses to exclude aortic coarctation
13. Physical stigmata of Marfan syndrome
14. Brachial artery blood pressure (sitting position)§

AHA indicates American Heart Association.
*Parental verification is recommended for high school and middle school athletes.
†Judged not to be of neurocardiogenic (vasovagal) origin; of particular concern when occurring during or after physical exertion.
‡Refers to heart murmurs judged likely to be organic and unlikely to be innocent, auscultation should be performed with the patient in both the supine and standing positions (or with Valsalva maneuver), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.
§Preferably taken in both arms.

Modified with permission from Maron et al. Copyright © 2007, American Heart Association, Inc.

http://circ.ahajournals.org/content/130/15/1303.long
http://www.mhsaa.com/schools/health-safety-resources
Vision: The MAP-SCDY strives to prevent sudden cardiac death of the young

Mission: The MAP-SCDY is a statewide collaborative network that provides leadership, education, and resources to help communities prevent sudden cardiac death of the young

Created in 2012
Facilitated by MDHHS Genomics
Very active listserv
Membership meetings twice per year
Over 100+ members representing multiple sectors

Current activities:

- Increase public and professional awareness of SCDY
- Promote AHA ‘Chain of Survival’
- Create and maintain website
- Assist members in their SCDY prevention activities
- Promote MI HEARTSafe Schools
  - 268 schools awarded in 2014-2016

https://migrc.org/Library/HeartSafe.html
• Suggest consideration of DNA banking/postmortem genetic testing for SCDY cases; explore expense and insurance reimbursement
• Increase awareness of familial risks among medical examiners
• Develop mechanism to ensure autopsy results and recommended follow-up are conveyed to families and primary providers
• Develop suggested protocols for autopsy of SCDY cases
2013 HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes

Publication Date: May 10, 2013
Barriers to Post Mortem Genetic Testing

- Death
  - Was an autopsy conducted?
  - Were the circumstances witnessed?

- Autopsy
  - How can we make sure there are purple tops on hand when needed?
  - When to save a sample? → Guidelines!

- Communication
  - Between family and ME
  - Between family and medical providers
  - Between medical providers and ME
  - Between medical providers and community

- Sample Storage
  - 2-3 months before can be released for testing
  - Access to a -20 or -80 freezer

- Sample Shipping
  - Access to dry ice and shipping containers
  - Resources for who to send it to and how

- Test Ordered/DNA Banking
  - Who orders the test if ME won’t/can’t
  - Payment/Insurance coverage

- Results
  - Connect ME/coroner with a GC for result interpretation & additional test(s) if negative
  - If ME orders, need a contact for change in interpretation

http://www.nsgc.org/postmortem
The Legacy Of Wes Leonard

You may have heard about the Michigan high schooler who made a game-winning basket and then died. Here’s the rest of the story: a violent car crash, a bone-shaking tackle, a near-perfect season, a reluctant substitute and a search for the will to carry on.

After the autopsy, when the doctor found white blossoms of scar tissue on Wes Leonard’s heart, he guessed they had been secretly building there for several months. That would mean Wes’s heart was slowly breaking throughout the Fennville Blackhawks’ 2010–11 regular season, when he led them in scoring and the team won 20 games without a loss.

It would mean his heart was already moving toward electrical maltdown in December, when he scored 26 on Decatur with that big left shoulder clearing a path to the hoop. It would mean his heart swelled and weakened all through January (25 against Hopkins, 33 against Martin) even as it pumped enough blood to fill at least 10 swimming pools.

This heart pounded two million times in February, probably more, heaving under its own weight, propelling Wes’s 6’2”, 220-pound frame along the shimmering hardwood with such precision and force that finally a kid from Hartford gave up on the rules and tackled him in the lane. By March 3, the night of Wes’s last and most glorious game, his heart weighed 21½ ounces, double the weight of a normal heart, and it gave him all he needed from the opening tip to the final buzzer. Then the wiring failed, the current going as jegged as a thunderbolt, and Wes fell to the floor with his big heart quavering.

If all this seems implausible—that Wes could play so well for so long with such faulty equipment—consider a scientific phenomenon called functional reserve. The human heart has a reservoir of unused ability, like a powerful engine idling in the garage. Wes’s reserve was throttled, he was running on fumes when the wiring failed.

This site and our mission are dedicated to Wes (1994-2011)

Wes had a love for life and for the ‘game’ that was infectious. His enthusiasm was inspiring. He was truly happy playing any sport he could.He was often heard asking his mom for a little more time to play “Just One More Game”. Wes was taken from us far too early. While we don’t believe that this was his destiny, we will make sure his legacy will be carried on for many years to come. We are going to work with the same enthusiasm, drive and love he had every day to honor him and other children lost to SCA providing others a chance at ‘Just One More Game’.

Governor Snyder signs House Bill 4713

Governor Snyder has officially signed a bill that will require all Michigan schools to practice AED/CPR drills and have emergency Sudden Cardiac Arrest response plans. Being prepared saves lives. Never Forgotten.

http://www.wesleonardheartteam.org/

http://www.wesleonardheartteam.org/71/the-legacy-of-wes-leonard
NHLBI Report on Screening for SCDY (Kaltman et al. Circulation. 2011)

- NHLBI working group unanimously supports research that would determine the best approach to reduce SCDY
- NHLBI and CDC announced plans for SCDY registry in 2013
  - Count the number and types of sudden deaths in babies, children and young adults up to age 20
  - Try to understand the causes for the deaths
  - Find ways to prevent these deaths

- 10 SDY Case Registry Grantees, 2014-2018
- Key partners are CDC, NIH, Michigan Public Health Institute, National Center for the Review and Prevention of Child

Thank you to Heather MacLeod, MS, CGC
**Case Flow**

1. Sudden death in the young (SDY) occurs
2. Medical Examiner or Forensic Pathologist collects sample for DNA extraction
3. Child Death Review team reviews all cases
4. Advanced Review team categorizes cases
5. Researchers calculate incidence and identify high risk groups for prevention

**Phase I: SDY Case Registry**
- Build on existing Child Death Review programs to develop a surveillance system for SDY cases
- Conduct Advanced Review (clinical and forensic) to categorize SDY cases
- Collect and store DNA for future research, banking and diagnostic testing

**Phase II: Research**
- Make the SDY case information and DNA samples available to investigators
- Support studies using SDY case information to evaluate causes of and risk factors for SDY

---


Thank you to Heather MacLeod, MS, CGC for sharing this information
SDY Case Registry Updates: Researchers Funded

• Working together to explore the genetic causes of SDY and characterizing the medical evaluation of surviving family members.
  – Northwestern: Alfred George and Elizabeth McNally
  – Vanderbilt: Prince Kannankeril
  – University of Utah: Martin Tristani-Firouzi and Mark Yandell

• National Heart, Lung and Blood Institute (NHLBI)-funded researchers will collaborate with the National Institute of Neurological Disorders and Stroke (NINDS)-funded Center for SUDEP Research investigators


Thank you to Heather MacLeod, MS, CGC for sharing this information
“I thought we were forgotten….
I thought no one cared…”

- Mother of 18 year old Michigan SCDY victim, upon being asked for a next-of-kin interview
State health departments are promoting universal genetic screening for select populations beyond the newborn period.

State health departments need to recognize that the testing is only one component of universal screening program.

Most state health department activities involve universal genetic testing on an affected individual with cascade testing to relatives.

Most (if not all) state health department efforts have potential to influence health disparities.

How can state public health departments best prepare for universal genetic screening beyond newborns for primary prevention on unaffected individuals?
THANK YOU TO OUR MAP-SCDY PARTNERS!

- **Academia**
  - Wayne State University, Michigan State University, University of Michigan, Oakland University, Ferris State University, Grand Valley State University, Central Michigan University, Saginaw Valley State University

- **Employers/industry**
  - AED distributors, Health plans

- **Health care delivery system**

- **Media**
  - Local television news, radio, newspapers
  - Detroit Free Press
  - APHA Newsletter
  - EMS Today

- **Communities**

- **Government**
  - Michigan Department of Health and Human Services (Cardiovascular Section; Vital Records; Genomics; EMS), Michigan Department of Education; Centers for Disease Control and Prevention, state legislatures, local health departments, local ISDs, NIH
**THANK YOU TO MDHHS CANCER GENOMICS STAFF & KEY PARTNERS!**

<table>
<thead>
<tr>
<th>MDHHS Cancer Genomics Team</th>
<th>Other National Partners</th>
<th>Clinical Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janice Bach, MS, CGC</td>
<td>Tuya Pal, MD</td>
<td>Beaumont Cancer Genetics Program</td>
</tr>
<tr>
<td>Robert Wahl, DVM, MS</td>
<td>Kate Reed, MPH, SCM, CGC</td>
<td>Beaumont Hospital-Dearborn Genetic Risk Assessment for Cancer</td>
</tr>
<tr>
<td>Jillian Schrager, MPH</td>
<td>Michael Dougherty, PhD</td>
<td>Henry Ford Health System Cancer Genetics Program</td>
</tr>
<tr>
<td>Maricar Macalincag</td>
<td>Megan Myers, MS, CGC</td>
<td>Karmanos Cancer Institute Genetic Counseling Service</td>
</tr>
<tr>
<td>Nancie Petrucelli, MS, CGC</td>
<td></td>
<td>InformedDNA</td>
</tr>
<tr>
<td>Angela Trepanier, MS, CGC</td>
<td></td>
<td>Michigan State University Hereditary Cancer Program</td>
</tr>
<tr>
<td>Carol Davis</td>
<td></td>
<td>Munson Cancer Genetics Clinic</td>
</tr>
<tr>
<td>Erin Van Haaren</td>
<td></td>
<td>Providence Hospital Medical Genetics</td>
</tr>
<tr>
<td>CDC</td>
<td></td>
<td>Sparrow Hospital Cancer Genetics</td>
</tr>
<tr>
<td>Juan Rodriguez, MPH</td>
<td>Sue Friedman</td>
<td>Spectrum Health Cancer Genetics Program</td>
</tr>
<tr>
<td>Sun Rim, MPH</td>
<td>Rebecca Sutphen, MD</td>
<td>St. Joseph Mercy Hospital Cancer Genetics Program</td>
</tr>
<tr>
<td>Marie Kumerow, MPH</td>
<td>Lisa Rezende, PhD</td>
<td>St. John Van Elslander Cancer Genetics Program</td>
</tr>
<tr>
<td>Dave Dotson, PhD</td>
<td>Lisa Schlager</td>
<td>St. Mary Health Care Lacks Cancer Center Genetics</td>
</tr>
<tr>
<td>LSSN Board of Directors</td>
<td></td>
<td>St. Mary Mercy Our Lady of Hope Cancer Center</td>
</tr>
<tr>
<td>Heather Hampel, MS, CGC</td>
<td>Glenn Copeland</td>
<td>University of Michigan Breast and Ovarian Cancer Risk and Evaluation Program</td>
</tr>
<tr>
<td>Cecelia Bellcross, PhD, MS, CGC</td>
<td>Georgetta Alverson</td>
<td>University of Michigan Cancer Genetics Clinic</td>
</tr>
<tr>
<td>Debi Cragun, PhD, MS, CGC</td>
<td>MDHHS Cancer Section</td>
<td>UP Health System-Marquette</td>
</tr>
<tr>
<td>Alanna Rahm, PhD, MS, CGC</td>
<td>Ann Garvin, MS, CNM, RN</td>
<td>West Michigan Cancer Center</td>
</tr>
<tr>
<td>Advocacy Partners</td>
<td>Sarah Mott, MPH, MS, RDN</td>
<td></td>
</tr>
<tr>
<td>Sherry Berry</td>
<td>Michigan Medicaid</td>
<td></td>
</tr>
<tr>
<td>Eileen Kastura</td>
<td>Catherine Reid, MD</td>
<td></td>
</tr>
<tr>
<td>Mollie Smith</td>
<td>MCGA</td>
<td></td>
</tr>
<tr>
<td>Alice Christensen</td>
<td>Julie Zenger Hain, PhD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kara Milliron, MS, CGC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Michigan Association of Health Plans</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rick Murdock</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lisa Farnum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BCBSM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sarah Mange, MPH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Besty Wasilevich, PhD</td>
<td></td>
</tr>
</tbody>
</table>

Some of this presented work was supported by the Cooperative Agreement Number 5U58DP003798 and NU58DP005357 from The Centers for Disease Control and Prevention (CDC). Its contents are solely the responsibility of the presenter and do not necessarily represent the official views of the CDC.