The Lynch Syndrome Screening Network: Promoting Universal Screening for Newly Diagnosed Colorectal Cancers in Michigan and the Nation

Karmanos Cancer Institute
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Learning Objectives

- State the Healthy People 2020 objective regarding Lynch syndrome and the importance of the EGAPP evidence-based recommendation
- Name three ways that Michigan is working to increase awareness of the EGAPP recommendation for Lynch syndrome
- Describe the Lynch Syndrome Screening Network (LSSN) as a resource for health systems to implement universal screening for Lynch syndrome on newly diagnosed colorectal cancers
Governor Snyder Proclaims Lynch Syndrome Hereditary Cancer Awareness Week as March 22nd-March 28th

Michigan Cancer Genetics Alliance Membership Meeting
March 20, 2015
Examples of MDCH Promotion of Governor’s Proclamation

- Michigan Cancer Genetics Alliance (MCGA) celebrated on March 20th; photo taken and posted to Lynch Syndrome International (LSI); LSI promotional materials disseminated to MCGA members
  - Anyone can become member of MCGA
  - Contact duquetted@michigan.gov to join
  - Banner to promote universal screening for Lynch syndrome
- Michigan Department of Community Health (MDCH) to release news of Lynch Syndrome Hereditary Cancer Awareness Week through press release
- Post a variety of Lynch syndrome informational messages to MDCH Facebook and MDCH Twitter
- Partner with LSI, MCGA, CDC, and others to increase awareness
“Genomics will be to the 21st century what infectious disease was to the 20th century...Genomics should be considered in every facet of public health: infectious disease, chronic disease, occupational health, environmental health, in addition to maternal and child health”

Gerard et al. Journal Law, Medicine, Ethics 2002; vol 30(suppl):173-176
What is “Public Health Genomics”? (Bellagio Statement, 2006)

“A multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technologies to improve population health.”
Healthy People 2020 (HP 2020)

- Started in 1979
- 10-year national objectives for promoting health and preventing disease
- HP 2020 marks first time for genomics objectives
- Encourage collaborations across sectors, guide individuals toward making informed health decisions, and measure the impact of prevention activities
- Works to achieve increased quality and years of healthy life and the elimination of health disparities.
Healthy People 2020
Approved Genomics Objective
(Developmental)

“Increase the proportion of persons with newly diagnosed colorectal cancer who receive genetic testing to identify Lynch syndrome”
What is Lynch Syndrome (LS)?

- Autosomal dominant hereditary cancer syndrome
  - Most common hereditary colorectal (CRC) and uterine cancer syndrome
    - 20-80% lifetime risk for CRC cancer
  - Increased risk of endometrial, ovarian, urinary tract, gastric tract, small bowel, pancreas, sebaceous cancers
- Due to mutations in MLH1, MSH2, MSH6, PMS2 or EPCAM genes
  - Risk varies based on specific mutation
# NCCN Guidelines Version 2.2014
## Lynch Syndrome

### Cancer Risk Up to Age 70 Years in Individuals with Lynch Syndrome Compared to the General Population

<table>
<thead>
<tr>
<th>Cancer</th>
<th>General Population Risk</th>
<th>MLH1 and MSH2</th>
<th>MSH6</th>
<th>PMS2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk</td>
<td>Mean Age of Onset</td>
<td>Risk</td>
</tr>
<tr>
<td>Colon</td>
<td>5.5%</td>
<td>40%-80%</td>
<td>44-61 years</td>
<td>10%-22%</td>
</tr>
<tr>
<td>Endometrium</td>
<td>2.7%</td>
<td>25%-60%</td>
<td>48-62 years</td>
<td>16%-26%</td>
</tr>
<tr>
<td>Stomach</td>
<td>&lt;1%</td>
<td>1%-13%</td>
<td>56 years</td>
<td>3%</td>
</tr>
<tr>
<td>Ovary</td>
<td>1.6%</td>
<td>4%-24%</td>
<td>42.5 years</td>
<td>1%-11%</td>
</tr>
<tr>
<td>Hepatobiliary tract</td>
<td>&lt;1%</td>
<td>1.4%-4%</td>
<td>50-57 years</td>
<td>Not reported</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>&lt;1%</td>
<td>1%-4%</td>
<td>54-60 years</td>
<td>&lt;1%</td>
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<td>Small bowel</td>
<td>&lt;1%</td>
<td>3%-6%</td>
<td>47-49 years</td>
<td>Not reported</td>
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<tr>
<td>Brain/CNS</td>
<td>&lt;1%</td>
<td>1%-3%</td>
<td>~50 years</td>
<td>Not reported</td>
</tr>
<tr>
<td>Sebaceous neoplasms</td>
<td>&lt;1%</td>
<td>1%-9%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Pancreas</td>
<td>&lt;1%</td>
<td>1%-6%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>


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

- Screening is complex!
  - Bethesda and Amsterdam criteria
  - Multiple approaches including IHC and/or MSI testing on tumor with DNA testing
  - Different genes involved in LS
    - MSH2, MSH6, MLH1, PMS2, EPCAM
- Cancer surveillance & prophylactic survey options
  - Colonoscopy every 1-2 years beginning at ~20-25 years old or 10 years earlier that youngest case in family
  - Annual endometrial sampling and transvaginal ultrasound beginning at 30 years old
  - History and exam annually begin at 21 years
  - Annual urinalysis
  - Prophylactic surgery including subtotal colectomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy
Evaluation of Genomic Applications in Practice and Prevention (EGAPP)

- Launched by CDC in 2004
- Aims:
  - Establish systematic evidence-based process for assessing genetic tests and genetic technology in transition from research to clinical and public health practice
- Process:
  - Develop process for evaluation
  - Independent multidisciplinary workgroup of non-federal experts to develop methods, make recommendations
  - Steering Committee of federal agencies
  - Stakeholder Group for consultation, evaluation

http://egappreviews.org
EGAPP Lynch Recommendation

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

Evidence Report/Technology Assessment

Number 150

Hereditary Nonpolyposis Colorectal Cancer: Diagnostic Strategies and Their Implications

GIM, 2009;1:35

EGAPP supplementary evidence review: DNA testing strategies aimed at reducing morbidity and mortality from Lynch syndrome

GIM, 2009;1:42

May, 2007

EGAPP Recommendation on Genetic Testing for Lynch Syndrome

- 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

“...efforts are needed not only to implement what is known in genomics to improve health but also to reduce potential harm and create the infrastructure needed to derive health benefits in the future.”

Three-Tier Classification of Recommendations on Genomic Applications

- **Tier 1: Ready for implementation**
  - Demonstrated analytic validity, clinical validity, clinical utility and evidence-based recommendations
  - Health professionals: encourage use; can save lives!
    - Examples: *BRCA (Grade B)*, Lynch syndrome, familial hypercholesterolemia, newborn screening

- **Tier 2: Informed decision making**
  - Adequate information on analytic and clinical validity, promising but not definitive information on clinical utility; no evidence-based guidelines recommending clinical use
  - Health professionals: provide information for shared decision making
    - Examples: Gene expression profiles in breast cancer, family history assessment in primary care

- **Tier 3: Discourage use**
  - No or little information on analytic, clinical validity or clinical utility; or evidence of harm
  - Health professionals: discourage use; may be considered for research in select instances; reduce potential harms and save unnecessary healthcare costs
    - Examples: *BRCA (Grade D)*, Population screening for hereditary hemochromatosis, personal genomic tests sold directly to consumers

Three-Tier Classification

Green
- FDA label requires use of test to inform choice or dose of a drug
- CMS covers testing
- Clinical practice guidelines based on systematic review supports testing

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

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

*Can be reassigned to Green or Red of one or more conditions in these categories apply

http://www.cdc.gov/genomics/gtesting/tier.htm
**MDCH-CDC Cancer Genomics Cooperative Agreements**

**Promoting Cancer Genomics Best Practices through Surveillance, Education, and Policy Change in the State of Michigan, CDC-RFA-GD08-801**

- **Purpose:** move human genome applications into health practice to maximize health benefits and minimize harm through non-research activities
- **Awarded from CDC Office of Public Health Genomics, 2008-2012**
  - 3 year cooperative agreement (2008-2012) awarded to three grantees
  - Any organization eligible (except federal agency)
  - Translation of evidence-based recommendations for genetic tests into practice
    - 2005 USPSTF *BRCA* recommendations
    - EGAPP recommendations on Lynch syndrome
    - EGAPP recommendation on breast cancer gene expression profiling

**Enhancing Breast Cancer Genomics Best Practices and Policies in the State of Michigan, CDC-RFA-DP11-1114**

- **Purpose:** develop or enhance activities related to breast cancer genomics
- **Authorized from Affordable Care Act**
- **Awarded from CDC Division of Cancer Prevention & Control, 2011-2014**
  - 3 year cooperative agreement (2011-2014) awarded to three grantees
  - State health departments and Tribal governments eligible
  - Promote use of *BRCA1/2* clinical practices as recommended by USPSTF and NCCN
    - Must conduct programs in policy plus surveillance and/or health education
    - Cannot use funds for research, clinical practice or lobbying
CDC Funding Announcement


- **5 year** cooperative agreement awarded to four projects
  - Authorized from Affordable Care Act
  - State health departments and Tribal governments eligible

**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
- Focus on HBOC but may also include Lynch syndrome
- May identify target populations disproportionately affected by HBOC and lack genetic services
Ultimate long term outcome
- Reduce incidence and mortality related to hereditary cancers, including breast, ovarian and colorectal cancer

Short- and intermediate term outcomes (by 2019):
- Increase knowledge among key clinical and policy stakeholders about cancer genetic best practices; improved access to and coverage of cancer genomics best practices [Policy/system change]
- Improve ability to assess the burden of hereditary cancers and use of cancer genomics best practices; increased production and dissemination of periodic cancer surveillance reports. [Surveillance]
- Increase knowledge of hereditary cancers and appropriate use of cancer genomics best practices among the public and health care providers. [Education]
- Improve partnerships and coordination among key stakeholder groups regarding cancer genomics services and care. [Partnerships]
High incidences are in geographic regions and counties that lack genetic services.
Example of increasing knowledge of hereditary cancers among public and providers

- Cascade screening!
- Individuals of a relative with a known deleterious mutation
  - 50% risk to inherit known deleterious mutation for first degree relatives
- Single site testing is extremely informative and much less expensive

http://kintalk.org/

Michigan Cancer Genetics Alliance Corner
Cascade Genetic Screening: Improving Hereditary Cancer Risk Identification
By Angela Trepianer, MS, CGC, Michigan Cancer Genetics Alliance

One of the goals in Michigan’s current Comprehensive Cancer Control Plan is to “increase the availability of cancer-related genetic information to the Michigan public and decrease barriers to risk-appropriate services.” This goal is in line with the more targeted Healthy People 2020 objective to increase the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling. Through a cooperative agreement with the Centers for Disease Control, the Michigan Department of Community Health has been working to increase the number of Michigan residents receiving appropriate genetic counseling, genetic testing, and follow up for hereditary breast ovarian cancer syndrome (HBOC). According to data from 2011 and 2012 Michigan Behavioral Risk Factor Surveillance System (MI BRFSS), just 7% of women in Michigan have been counseled on HBOC.

Three Core Public Health Functions and Ten Essential Services

- **Assessment**: The regular systematic collection, assembly, analysis, and dissemination of information, including genetic epidemiologic information, on the health of the community.
Assurance: That genomic information is used appropriately and that genetic tests and services meet agreed upon goals for effectiveness, accessibility, and quality.
Three Core Public Health Functions and Ten Essential Services

- **Policy Development**: The formulation of standards and guidelines, in collaboration with stakeholders, which promote the appropriate use of genomic information and the effectiveness, accessibility, and quality of genetic tests and services.
Utilized statewide cancer registry and mortality data to conduct cancer genomics surveillance since 2003

Existing data analyzed through ‘genomics lens’

Identify cases at high risk by age, gender, cancer type and with disparities based on race and county

- Young women with breast cancer
- Men with breast cancer
- Women with ovarian cancer
- **Multiple primary cancers** (i.e. breast-ovarian; colorectal-endometrial)
- **Individuals with colorectal cancer**

Able to then utilize data for:

- Health system and provider education
- Patient education
- Survey cancer patients and at-risk relatives
- Monitor trends over time
Bidirectional Cancer Genomics Reporting using MCSP Data

- Michigan identified over 15,000 cases of cancer relevant to HP 2020 cancer genomics objectives (2007-2008 MCSP data)
  - Numbers of breast (female at young age; male), ovarian, colorectal, endometrial and multiple primaries
- Informed key administrators at over 150 reporting institutions of their specific numbers of above cancer cases
- Included informational materials about hereditary breast and ovarian cancer and Lynch syndrome
  - Copies of evidence-based guidelines, Michigan cancer genetics directory, Michigan informed consent brochure, etc
  - Generate interests in Grand Rounds to learn more from cancer genetic professionals
- Connecticut reported back over 5,000 cases of cancer through a Healthy People 2020 Action Award (2008-2009 data)
Public Health Genomics Implementation to Save Lives: From National Vision to State Success

https://www.youtube.com/watch?v=OfjkY1ILxbE&feature=youtu.be

- 2014 video created by CDC and Genetic Alliance
- Highlights Michigan as model for other states
- Importance of Partnerships!
State and National Data on Lynch Syndrome Screening and Diagnosis

- No current source of national data
  - HP2020 objective is developmental
  - MSI only included in cancer registry reporting since 2010
    - Current pilot in select states regarding use of data element

- Michigan surveillance efforts for Lynch syndrome
  - Only 4 current health plans in Michigan have written policy aligned with EGAPP Lynch syndrome recommendations
  - Not feasible to utilize Medicaid claims data to determine CRC patients receiving Lynch syndrome testing
  - 2010 MiBRFS indicates nearly 80% of individual 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)
Underutilization of Lynch syndrome screening in a multisite study of patients with colorectal cancer.


- National study utilized medical records from 7 HMO/health systems in Cancer Research Network to determine the availability of Lynch syndrome screening criteria and actual Lynch syndrome screening
- Supports case for universal screening
- Examined medical records of 1,188 patients diagnosed with metastatic colorectal cancer between 2004 and 2009
- Found infrequent use (less than 5%) of Lynch syndrome screening (41/1,188)
- Family history was available for 937 of the 1,188 patients (79%)
  - Sufficient to assess Lynch syndrome risk using family history-based criteria in 719 patients
  - 107 could not be evaluated due to missing information such as age of cancer onset
  - Only 11% percent of patients who met the Bethesda criteria and 25% of individuals who met the Amsterdam II criteria were screened for Lynch syndrome.
2.8% of CRC probands with deleterious mutations (n=44)

- Age at diagnosis – 51.4 (range 23-87)
- 50% diagnosed over age 50
- 25% did not meet either Amsterdam or Bethesda criteria
- Mutations
  - 20.5% MLH1
  - 52.3% MSH2
  - 13.6% MSH6
  - 13.6% PMS2

Rationale for Lynch Syndrome Screening of Newly Diagnosed CRC

- Common: ~3% of all CRC
- Age/screening criteria miss 25% or more
- Accurate methods (MSI/IHC) using easily accessible tumor tissue
- Benefits of medical intervention
  - Cascade testing of family members
  - Surveillance/prevention
  - CRC treatment decisions
- Evidence of cost-effectiveness
Universal LS Screening Implementation in US?

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
Meeting Conclusions & Recommendations

1. Genetic screening of all newly diagnosed CRC cases for LS (universal LS screening) can theoretically result in population health benefits, and feasibility has been demonstrated in research and clinical settings.

2. Utilizing a public health approach strongly integrated with all aspects of clinical care may provide the greatest opportunity for successful implementation on a regional or national scale.

3. There are several challenges and barriers to implementation of universal LS screening which need to be evaluated and addressed prior to consideration of large scale efforts at the state, regional or national level.

4. Education of clinicians, patients, families, healthcare system administrators, payers, and state and national public health entities and policy makers will be critical to any national effort.

Bellcross, Genet Med. 2012;14:152
5. National level conferences should be convened to allow further dialogue among key organizations, groups, and individuals regarding development of protocols, policies and guidelines addressing universal LS screening on a state and/or national level.

6. Serious consideration should be given to the paradigm of newborn screening as a model for implementing universal LS screening on a national level.

7. Carefully constructed pilot implementation projects and “real-world” studies are needed to demonstrate effectiveness and provide additional evidence of the feasibility and utility of population-level universal LS screening.
Cost effectiveness Data

- Lowest cost testing strategy
- IHC as a preliminary test for all newly diagnosed CRCs
- Detects twice as many cases as using age-targeted testing
- Cost $\leq$ $25,000 per life-year saved relative to no testing
- Increasing number of relatives tested would improve cost-effectiveness

Table 2 Cost-effectiveness ratios associated with Lynch syndrome testing strategies among new diagnosed patients colorectal cancer (CRC) and testing and surveillance for CRC among their first degree relatives

<table>
<thead>
<tr>
<th>Strategies</th>
<th>Description of testing strategy</th>
<th>Incremental cost-effectiveness ratio of universal testing relative to no testing and relative to previous strategy, dollars per life-year saved</th>
<th>Incremental cost-effectiveness ratio of age-targeted testing relative to no testing and relative to previous strategy, dollars per life-year saved</th>
<th>Incremental cost-effectiveness ratio of universal testing relative to age-targeted testing and relative to previous strategy, dollars per life-year saved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>IHC, \textit{BRAF} testing and sequencing</td>
<td>$22,552$ and $22,552$</td>
<td>$7,832$ and $7,832$</td>
<td>$37,010$ and $37,010$</td>
</tr>
<tr>
<td>2</td>
<td>IHC testing and sequencing</td>
<td>$23,321$ and $273,915$</td>
<td>$7,944$ and $60,509$</td>
<td>$38,411$ and $429,973$</td>
</tr>
<tr>
<td>3</td>
<td>MSI testing and sequencing</td>
<td>$41,511$ and $764,917$</td>
<td>$11,680$ and $168,905$</td>
<td>$70,792$ and $1,355,910$</td>
</tr>
<tr>
<td>4</td>
<td>Genetic sequencing for 4 genes</td>
<td>$142,289$ and $737,025$</td>
<td>$44,902$ and $252,643$</td>
<td>$237,278$ and $1,192,575$</td>
</tr>
</tbody>
</table>

*Sequencing includes detection of large deletions and rearrangements.

Creation of a Network to Promote Universal Screening for Lynch Syndrome: The Lynch Syndrome Screening Network

Sarah Mange, Cecelia Bellcross, Deborah Cragun, Deb Duquette, Lisa Gorman, Heather Hampel, Kory Jasperson

- Created in September 2011 with one-time funding from CDC Office of Public Health Genomics:
  - Support for in-person meeting
  - Seed funding for database

- Founding Board of Directors from MDCH, Emory University, Huntsman Cancer Institute, The Ohio State University
LSSN Vision and Mission

- **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.
Members & Partners

**Full Membership**
- Institutions (hospitals, clinics, and academic medical centers) currently performing routine* tumor testing on colorectal cancers and/or endometrial cancers; AND
- Commitment to enter data (outlined by the research guidelines) regularly into the LSSN database for surveillance and/or research purposes; AND
- Institutional review board (IRB) approval (either obtained or in process) to enter data (outlined by the research guidelines) into the LSSN database; AND
- A genetic counselor or other qualified healthcare provider† trained in providing cancer genetic services is required to be at the institution; AND
- A genetic counselor or other qualified healthcare provider† must have access (either through clinical responsibilities and/or IRB approval) to both normal and abnormal routine* tumor testing results

**Affiliate Membership**
- Institutions (hospitals, clinics, and academic medical centers) performing routine testing*, but not meeting all criteria for full membership; OR
- Institutions interested in starting routine testing*

**Official Partners**
- Organizations interested in promoting routine testing* on all newly diagnosed colorectal and/or endometrial cancers that fall into the following categories:
  - Federal/state agencies
  - Professional societies
  - Patient support/advocacy groups
  - Laboratories (non-profit only) or companies

*Automatic tumor testing to evaluate for Lynch syndrome at the time of cancer diagnosis/surgery
Recruitment

- Institutions were invited to participate in the LSSN via select professional organizations involved in cancer genetics.
- Interested institutions completed an application that included information on:
  - existing screening protocols
  - plans for future implementation
  - screening for endometrial/other LS cancers
  - changes in number of cancers screened over time
  - willingness to contribute to a shared online database
**Application Data**

- 80 Institutions submitted applications to LSSN by 2014
  - 64 (80%) institutions currently providing routine tumor screening for Lynch syndrome on all or subset of colorectal cancers
  - 16 (20%) in the process of or planning to develop protocols for routine screening
  - 92% reported EGAPP justified, altered or supported LS screening protocols
EGAPP Recommendation
Released in January 2009
Number of cancers screened for Lynch syndrome at time of pathological diagnosis, per year

- **Colorectal**
- **Endometrial**

<table>
<thead>
<tr>
<th>Year</th>
<th># of Cancers Screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>1,000</td>
</tr>
<tr>
<td>2009</td>
<td>2,000</td>
</tr>
<tr>
<td>2010</td>
<td>3,000</td>
</tr>
<tr>
<td>2011</td>
<td>4,000</td>
</tr>
<tr>
<td>2012</td>
<td>6,000</td>
</tr>
</tbody>
</table>
CRC Screening Protocols
Screening Protocols

*hypermethylation
LSSN Website

www.lynchscreening.net
Implementation

There are multiple Lynch syndrome screening algorithms to choose from. These are briefly described below and detailed in their respective sections.

**MSI:** Microsatellite instability (MSI) testing can be performed on tumor tissue to gain more information about the likelihood of Lynch syndrome. Approximately 90% of colon tumors from individuals with Lynch syndrome demonstrate microsatellite instability (MSI), whereas only approximately 15% of sporadic colon tumors do.

**IHC:** Immunohistochemical (IHC) testing can be performed on tumor tissue to analyze mismatch repair protein function. Tumors from individuals with Lynch syndrome are likely to demonstrate loss of mismatch repair protein expression. The pattern of loss observed can provide information about which gene is not functioning properly. As a result, IHC can be helpful both in providing information about the likelihood of Lynch syndrome and in directing testing for a germline mutation to a specific gene.
LSSN Listserv

- Anyone from LSSN member or partner institution can be added to the listserv
  - Includes Karmanos!
- Very active listserv
- Excellent way for health professionals to receive variety of input quickly regarding:
  - Difficult dilemmas
  - Protocols
  - Ethical questions
  - Informed consent
  - Billing issues

- Example of recent inquiry from health professional at member institution
  - Method of informed consent (if any) used prior to universal screening?
  - 45 LSSN institutions replied within 3 days of inquiry
    - 73.33% no informed consent
    - 24.44% informed consent via information sheet provided in advance
    - 0% verbal consent
    - 2.22% written consent
Database

Who can use the database?

Institutions that have full membership will have access to aggregate database information. Institutions who participate in the database will have open access to their own data for internal purposes.

Link to Password Protected Database
Example of LSSN Implementation Study

- Multiple-case study of 15 LSSN institutions
- Categorized as Low-PF (≤25% underwent germ-line testing), Medium-PF (26-55%), or High-PF (>56%)
- Five High-PF institutions:
  - disclosure of screen-positive results to patients by genetic counselors
  - genetic counselors either facilitate physician referrals to genetics professionals or eliminate the need for referrals
  - automatic reflex testing
  - ability to contact screen-positive patients was not a barrier
Figure 1. Patient Reach Scores and Factors associated with Patient Reach

<table>
<thead>
<tr>
<th>Institution</th>
<th>Patient reach score</th>
<th>Implementation challenges&gt; facilitators</th>
<th>Automatic reflex testing (i.e., BRAF)</th>
<th>Genetics receives copy of positive screens</th>
<th>Genetics discloses result to patient</th>
<th>Difficulty contacting patients</th>
<th>Physician refers follow-up testing</th>
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<tr>
<td>H1</td>
<td>6</td>
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<td>x</td>
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- **H-R**: 7 =>85%, 6 = 71-85%, 5 = 56-70%
- **M-R**: 4 = 41-55%, 3 = 26-40%
- **L-R**: 2 = 11-25%, 1 = <10%
Today’s Reality: Many Unanswered Questions

- Of the ~400 people in US who will be diagnosed with CRC today, ~12 of these people will have Lynch syndrome
  - How many of these 400 people are being screened for Lynch syndrome?
  - How many of the 12 are being diagnosed with Lynch syndrome?
  - How many of their relatives are being screened?
  - How many lives saved by Lynch syndrome diagnosis?
Thank you!

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