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Agenda

- GI OnDEMAND and Ambry Genetics partnership
- Benefits to GI practices to utilize genetic testing services
- Case Studies
- Review of Hereditary Cancer Syndromes Encountered in GI Practices
- Special Guest: Dr. Mark Molos, and his practice’s experience of implementing this program
- Q&A

GI OnDEMAND Partnership with Ambry

- What it is?
  - GI OnDEMAND has partnered with Ambry Genetics, one of the leading genetic testing companies to provide genetic testing and counseling services to GI practices throughout the United States.
- Why?
  - Break down barriers to allow GI patients and providers access to genetic testing and counseling to improve outcomes.
Why should my practice use GI OnDEMAND for genetic services?

- Genetic testing is guideline recommended and can assist in preventing cancer in patients
- If genetic testing identifies a hereditary cancer syndrome in a patient, we can offer genetic counseling and testing to their at-risk family members
- Practices that embrace technology and the most up to date guidelines will be attractive to patients
- This service is available at no cost to your practice

Why should my practice use GI OnDEMAND for genetic services?

- Many patients in your GI practice have hereditary cancer syndromes, but you just have not identified them yet
- These cancer syndromes are associated with very high lifetime cancer risks (increased morbidity and mortality)
- Over time, these patients can develop cancer while you are taking care of them in your practice
- By identifying these patients, you can save lives through earlier and more frequent endoscopic surveillance protocols
- Screening for other GI cancers may also be required, including pancreatic cancer and others
- You can also recruit new at-risk family members to your practice
Case Study #1

► A 32 year-old male was seen by you in 2019 for EoE. Doing well with plan for follow up in 1-2 years to reassess symptoms.
► Hospitalist service consults you today for an obstructing colon mass. Colonoscopy reveals a 5 cm sigmoid mass--microsatellite unstable on tumor testing. Germline testing confirms Lynch syndrome.
► You review your old notes from 2019; there is documentation that there is no FH of CRC in first degree relatives.
► However, you obtain further FH in the hospital now and realize that the patient’s paternal grandfather had CRC at age 55 and a paternal aunt had uterine cancer at age 52. Based on this FH the patient would have met criteria for genetic testing back in 2019; PREMM score 3.7% (PREMM= PREdiction Model for Gene Mutations)
► How could I have prevented this from happening?

Case Study #2

► A 54 year-old female presents w/ rectal bleeding for 3 months. Colonoscopy reveals a transverse colon mass.
► Review of old records reveals the patient underwent screening colonoscopy by you 4 years prior (normal, good prep). Plan was for a 10 year repeat.
► There is no documentation of FH in the prior colonoscopy records. As the endo unit can be very busy it is not uncommon for FH info to sometimes be overlooked. However you did make note at that time that the patient had uterine cancer at age 47.
► After finding the mass this time, you ask more questions in recovery and uncover that the patient’s father also had CRC at age 67.
► The biopsies end up showing microsatellite unstable CRC and germline testing ultimately reveals Lynch syndrome.
So how many patients in my practice are carrying a GI related hereditary cancer syndrome?

- Based on Lynch syndrome carrier frequency of 1:279 (1.2 million people in the U.S. alone) and a potential concentration of patients in GI practices with stronger cancer family histories and numerous polyps (due to referral bias), we can estimate ~1:200 people in a GI practice are carrying a LS or polyposis (FAP, MUTYH) mutation

- **Working example based on 1:200:** GI provider working 4 days as week, 46 weeks out of the year
  - 10 clinic patients per half day, 4 sessions per week (40 patients)
  - 15 patients undergo procedures per full day, 2 days per week (30 patients)
  - Single provider encountering 1-2 hereditary patients per month, or **12-24 per year**
  - In a practice with 10 GI providers, that amounts to up to **120-240 patients per year**

Who are these patients in our practices with hereditary CRC syndromes?

- Some we may have already identified due to clearly obvious phenotypes
  - Very strong family history of CRC, CRC at a young age, multiple polyps
- Many others are hiding in plain sight and have not been identified yet
  - Seemingly low risk patients with GERD, IBS, gastroparesis, chronic pancreatitis etc. who have not had an adequate family history taken
  - However, over the years, as you take care of these patients, they can and will develop cancer if they have a missed underlying mutation
Tip of the iceberg (obvious phenotypes)
- Early-onset CRC
- Multiple polyps
- Multiple family members w/ CRC

Under the water and out of view
- Cancers other than colorectal (uterine, etc)
- Patients with less striking FH

Hereditary Cancer “Iceberg”

Patients you may be missing who, based on guidelines, should be offered genetic counseling/testing
(exceed PREMM score threshold of 2.5% or greater)

- **33 year-old male** with chronic GERD and no personal history of cancer whose father had CRC at age 56.
- **56 year-old female** who just had a negative screening colonoscopy and has no family history of cancer, but has a personal history of uterine cancer at age 49.
- **26 year-old male** with EoE and no personal history of cancer with a single aunt with CRC diagnosed at age 49
- **42 year-old female** with personal history of bladder cancer and a grandmother with uterine cancer diagnosed at age 51. No CRC in the family.

PREMM: https://premm.dfci.harvard.edu/
GI doctors and how they manage hereditary syndromes: The Data

- National Survey of GI doctors in 2018 asking questions about barriers to genetic analysis of colorectal cancer patients
- 509 respondents (private practice, academic center, urban, rural)
- Barriers preventing test ordering (percentage of providers stating the following are barriers)….
  - Perceived cost - 33.3%
  - Unfamiliarity interpreting results - 29.2%
  - Unavailable genetic counseling - 24.9%


So how can we identify these patients?

- We are so busy seeing so many patients per week, it is hard to take a comprehensive family history on all our patients
- A tool to risk stratify every patient in our practices by personal and FH would be the best way to identify those at risk for hereditary cancer syndromes, but who has the time and personnel to do this?
- Even if we identify these patients, it can be very challenging to get patients to genetic counselors, so how are we going to manage these patients?
Basic principles of the genetic counseling and testing process through GI OnDEMAND and Ambry’s CARE Program

► Utilize electronic, easy to use FH questionnaire that is sent to a patient’s smartphone prior to their clinic appointment; assess all patients in a given GI practice (regardless of their diagnosis)
  ► Prevents workflow disruptions at the time of the office visit
  ► Allows patients to have more time to collect accurate FH information
  ► GI provider does not need to worry about getting the FH themselves
► If thresholds are met for genetic analysis, and the patient is agreeable, genetic testing can be arranged automatically
► A custom GI cancer related gene panel has been developed
  ► GI providers do not have to make decisions regarding which gene tests to order
► Expedited genetic counseling is available for patients with abnormal results (no need to wait months for referral)
Unique End-to-End Solution

- **Identification**: Using Ambry’s Virtual Assistant (AVA) High Risk Screening Tool
- **Genetic Testing**: Ordered through Ambry for High Risk Individuals
- **Results Delivery**: Testing results are delivered to the ordering provider and then made available through the CARE Program
- **Post-test Counseling**: Made available to all patients who have testing

**Pre-test Education**
How genetic testing can guide early detection & prevention

**Documentation**
Increase quality, decrease liability

- **Frequent**: Over 1.2 million individuals in the United States have Lynch syndrome
- **Cancer Risks**: Inherited condition that causes high risks for colorectal, endometrial, ovarian, gastric, pancreatic, hepatobiliary, and other cancers
- **Actionable**: Preventable cancers with early and more frequent screening
- **Underdiagnosed**: 95% of affected individuals do not know they have Lynch syndrome

Cancer Epidemiol Biomarkers Prev; 26(3) March 2017: https://cebp.aacrjournals.org/content/cebp/26/3/404.full.pdf
Lynch Syndrome Significantly Increases Lifetime Cancer Risks

- **COLORECTAL CANCER**
  - General Population: Up to 5.5%
  - Lynch Syndrome: Up to 61%

- **UTERINE CANCER**
  - General Population: Up to 2.7%
  - Lynch Syndrome: 13-57%

- **STOMACH CANCER**
  - General Population: <1%
  - Lynch Syndrome: 1-9%

- **OVARIAN CANCER**
  - General Population: <1%
  - Lynch Syndrome: <1-38%

- **SMALL BOWEL CANCER**
  - General Population: <1%
  - Lynch Syndrome: <1-11%

- **BRAIN CANCER**
  - General Population: <1%
  - Lynch Syndrome: <1-8%

*Risks vary depending on specific Lynch gene

Impact on Clinical Management

- **ENDOMETRIAL**
  - Option of risk-reducing surgery

- **OVARIAN**
  - Option of risk-reducing surgery

- **UROTHELIAL/BLADDER**
  - Optional depending on family history; increased risk in males
  - Urinalysis
  - Annually beginning at age 30-35

- **BRAIN**
  - Annual neurologic exam

- **STOMACH AND SMALL BOWEL**
  - Optional depending on family history; increased risk in males, older age, specific ethnicity
  - Upper endoscopy/EGD
  - Baseline at age 40; every 3-5 years in high risk

- **COLORECTAL**
  - Colonoscopy
  - Every 1-2 years beginning at age 20-25

American College of Gastroenterology
Familial Adenomatous Polyposis

► **Less Frequent**: Accounts for 1% of all CRC
► **Cancer Risks**: 100% risk of colorectal cancer if untreated; Increased risks for duodenal, thyroid, hepatoblastoma, and medulloblastoma cancers
► **Actionable**: Colectomy recommended to prevent CRC
► **Overdiagnosed and undertested**: There are now ~9 adenomatous polyposis genes each with different risks and management

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3281354/#:~:text=Familial%20adenomatous%20polyposis%20(FAP)%20is%20an%20effective%20method%20for%20CRC%20prevention.

Many Colorectal Cancer & Polyposis Genes Have Been Identified

Alvarez MD, et al. The Inherited and Familial Component of Early-Onset Colorectal CancerCells 2021, 10, 710.
Why worry about non-colorectal cancer genes?

In addition to risks for breast, ovarian, prostate, and other cancers, many of these genes have an increased risk for GI cancers.

NCCN recommends that individuals with BRCA1/2, ATM, PALB2, TP53, or Lynch genes (except PMS2) with a FDR or SDR with pancreatic cancer:

► Consider pancreatic cancer screening beginning at age 50 or 10 years younger than the earliest dx in family.

► Annual contrast-enhanced MRI/MRCP and/or EUS with consideration of shorter screening intervals for individuals found to have worrisome abnormalities on screening.

► Most small cystic lesions found on screening will not warrant biopsy, surgical resection, or any intervention.

https://www.nccn.org/guidelines/guidelines-detail?category=2&id=1503
Multiple Professional Organizations Recommend Genetic Testing

Mark Molos, MD
MANAGING PARTNER
WESTGLEN GI CONSULTANTS
Why Did WestGlen GI Decide to Take Advantage of This Program?

IDENTIFY PATIENTS
Help us identify those at risk who qualify for genetic testing, as well as their family members

SIMPLIFIED PROCESS
It's based upon a streamlined, best-practice based process

SAVE TIME
Integrates seamlessly into our existing workflow, we didn't have to change what we do

IMPACTFUL RESULTS
May lead to enhanced surveillance/personalized screening, therapeutics and/or preventative procedures

Our Initial Results – WestGlen GI

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Positive  | %  | Carrier  | %  | Inconclusive  | %  | Negative  | % |
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The Results of Our Decision

► Helps us to risk stratify our patients and their families for potential hereditary cancers
► Seamless integration into our existing workflows
► No cost to our practice to implement the program (all costs paid for by GI OnDEMAND)
► Thorough training for our providers and staff – ensuring efficiency and confidence with the platform
► Simple ordering process
► No cost counseling & results delivery
► Personalized medical management
► Improved patient services
FAQs

Q: What does it cost to take advantage of setting up CARE for my practice?
A: Covered by GI OnDEMAND, no cost to the practice.

Q: What is the cost of testing?
A: Covered by most insurance. 4 out of 5 patients pay $0.

Q: Have you/your partners been able to identify patients at risk as a result of this program that may have otherwise gone undetected?
A: Yes, the most important outcome.

Q: Where do I go to learn more or set up an initial discussion for my practice?
A: Visit GI OnDEMAND website at: giondemand.com or email us at genetics@giondemand.com.

Other questions? Please type them into the Chat Box.

Thank you for participating!
## Appendix

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Provides clinicians with accurate results to inform patient care.

Comprehensive 38-gene panel that identifies inherited risks.
AVA Chat: HIPAA Compliant + SOCII Secure

► Results disclosure customized per site
► All patients have access to genetic counseling
► Telehealth appointments available within 24 hours
► Patient scheduling can be accessed on a mobile device via the virtual assistant
► Detailed medical management reports for patients with positive results
Pre-Test Education

Dive Deeper
We have two ways for you to dive deeper into the world of genes and genetics. You can watch a short animated video, or read and look at pictures about the topic. Which do you prefer?

Genetics 101 00:46
Watch Now
OR
View a Slideshow
Read and look at pictures about the topic. Which do you prefer?
Start Now

Basic elements of informed consent

Local GCs can be involved in the process

Implementing a Program, Based Upon Best Practices

Phase 1: Planning Stage

1. Execute Contracts
2. IT Security Clearance
3. Create Shared Co and Clinical Committees
4. Define and align around program goals, mission and vision
5. Identify Key Departments that are part of HBA, and create a Project Plan
6. IT Integration
7. Schedule Kick Off Meeting & Project Cadence Meetings

Phase 2: Project Management, On Boarding & Implementation

1. Kick Off Meetings
2. Workflow Analysis, Operational, Clinical & Technical
3. On Board Software
4. Program Communication, Outreach and Marketing (Internally & Externally)
5. Confirm & Finalize Program Plan
Implementing a Program, Based Upon Best Practices

Phase 3: Pre Launch & Launch

- Operational, Clinical & Technical Training
- Launch Program
- Schedule Post Launch Cadence Meetings

Phase 4: Account Management

- Monitor & Review Program Performance Metrics
- VOC
- Expand the Program
- Facilitate Marketing Resources, Collaboration and Execution
- Day to Day Account Management
- Contract Renewal

Medical Benefits of the CARE Program

**EARLY DETECTION**
Empowers our patients to undergo individualized cancer screening—recommended based on their specific cancer risk

**PREVENTION**
Gives our patients the choice to make informed decisions about preventive surgical options to reduce cancer risk

**TREATMENT**
Ability to tailor surveillance and treatment recommendations based on genetic test results

**FAMILY**
Empowers our patients’ family members to access appropriate cancer screening by finding those at increased risk for cancer