



MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement.

THESE ANSWERS WILL BE REVIEWED.

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NSGC CEU Credit



The National Society of Genetic Counselors (NSGC) has authorized CGA-IGC to offer up to

0.6 CEUs or 6 Category 1 contact hours for the activity CGA-IGC 2023 Webinar Series about Inherited GI Cancers.

The American Board of Genetic Counseling (ABGC) will accept CEUs earned at this program for the purposes of genetic counselor certification and recertification.

HOW TO CLAIM NSGC CEUS



- If you are attending the live event:
 - Sign into the webinar with your first and last name
 - Check your email after the webinar for a link to complete an evaluation form
 - If you do not receive the email, please contact info@cgaigc.com
- If you are watching a previously recorded event:
 - Complete an evaluation form
 - Take a quiz
 - You must score 80%
 - The link to the evaluation form and the quiz are available on the CGA website, below the link you used to access the webinar

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FUTURE CGA-IGC WEBINARS



STAY TUNED FOR OUR 2023 WEBINAR SERIES

May 3: Joint webinar with NASPGHAN: Constitutional mismatch repair deficiency syndrome Speakers: Carol Durno, MD; Melyssa Aronson, MS, CGC

Summer - date TBD: Living with FAP: Life after prophylactic surgery and other quality of life considerations

Speakers: Paul Wise, MD; Karen Hurley, PhD

Sep 28: Joint webinar with ACG: Surveillance for hereditary pancreatic cancer **Speakers:** Bryson Katona, MD, PhD; Beth Dudley Yurkovich, MS, MPH, CGC

Nov - date TBD: Emerging topics in the field of hereditary gastrointestinal cancer













Historical and current approaches to identifying individuals with Lynch syndrome





Peter Stanich, M.D. 2023 CGA-IGC President Gastroenterologist & Associate Professor Ohio State University Wexner Medical Center, OH



Heather Hampel, M.S., CGC Clinical Professor & Associate Director City of Hope, CA

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Outline

Lynch Syndrome

- Common & Treatable
- Cancer Risks Management

Family History-Based Identification Methods

Tumor-Based Identification Methods

- Columbus-area HNPCC Study
- Ohio Colorectal Cancer Prevention Initiative

Putting it all into Practice

- Universal MGPT for all Colorectal Cancer Patients
- What is the role of the GI practitioner in this process?

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 $\label{thm:continuous} \textbf{Lynch Syndrome Awareness: Historical and Current Approaches to Identifying Individuals With Lynch Syndrome}$

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Lynch Syndrome

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- Over 1.2 million individuals in the U.S. have Lynch Syndrome
- Inherited condition that causes high risks for colorectal, endometrial, ovarian, gastric, and other cancers
- Preventable cancers with early and more frequent screening
- 95% of affected individuals do not know they have Lynch Syndrome

Lynch Syndrome Awareness: Historical and Current Approaches to Identifying Individuals With Lynch Syndrome

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Lynch Syndrome Cancer Risks (to 70)

Cancer Type	MLH1	MSH2	MSH6	PMS2	General Public
Colon cancer	46-61%	33-52%	10-44%	8.7-20%	4.2%
Endometrial cancer	34-54%	21-57%	16-49%	13-26%	2.7%
Ovarian	4-20%	8-38%	≤1-13%	1.3-3%	1.3 %
Renal pelvis or Ureter	0.2-5%	2.2-28%	0.7-5.5%	≤1-3.7%	Not in SEER
Prostate	4.4-13.8%	3.9-23.8%	2.5-11.6%	4.6-11.6%	11.6%
Stomach	5-7%	0.2-9%	<u><</u> 1-7.9%	Not known	0.9%
Pancreatic	6.2%	0.5-1.6%	1.4-1.6%	≤1-1.6%	1.6%

NCCN Guidelines for Colorectal Cancer Screening and Prevention v1.2022

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GI cancer risks in Lynch syndrome

NCCN Clinical Practice Guidelines. Genetic/Familial High-Risk Assessment: Colorectal. 2.2022.

	MLH1	MSH2	MSH6	PMS2
CRC	46 - 60%	33 - 52%	10 - 44%	8 - 20%
Gastric	5 - 7%	0.2 - 9%	0 - 8%	NI?
Small bowel	0.5 - 11%	1 - 10%	0 - 4%	NI
Pancreas	6.2%	NI	NI	NI
Biliary	2 - 4%	0 - 2%	NI	NI



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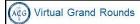
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GI cancer screening in Lynch syndrome

NCCN Clinical Practice Guidelines. Genetic/Familial High-Risk Assessment: Colorectal. 2.2022.

- MLH1 and MSH2
 - Colonoscopy every 1-2 years starting at age 20-25
 - EGD every 2-4 years at age 30-40
 - Consider enteroscopy
 - Stomach biopsies at initial procedure
 - Consider pancreatic screening at age 50 years if ≥1 close relatives from the side of pathogenic variant with MRI/MRCP and/or EUS

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GI cancer screening in Lynch syndrome

NCCN Clinical Practice Guidelines. Genetic/Familial High-Risk Assessment: Colorectal. 2.2022.

- MSH6 and PMS2
 - Colonoscopy every 1-2 years starting at age 30-35
 - EGD every 2-4 years at age 30-40
 - Consider enteroscopy
 - Stomach biopsies at initial procedure
 - Consider pancreatic screening at age 50 years if ≥1 close relatives from the side of pathogenic variant with MRI/MRCP and/or EUS
 - *Clinical judgement in PMS2



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Lynch syndrome and colonoscopy interval

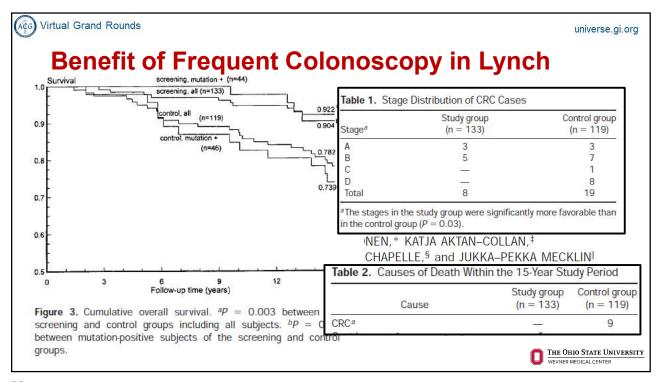
There is **rapid progression** from adenoma to CRC in comparison to accepted 10-20 year interval for sporadic polyps

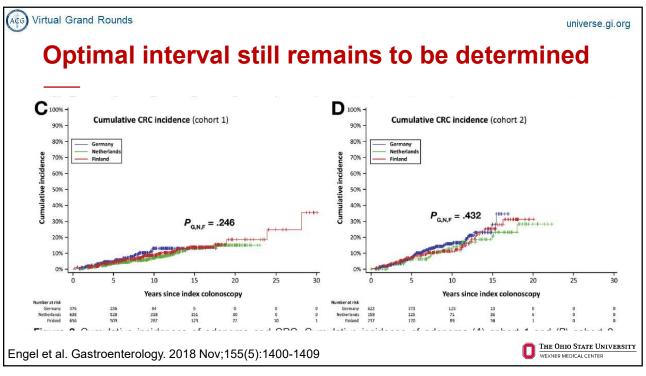
Table 5. Dwell Time of Advanced Adenoma and Colorectal Cancer

	Advanced adenoma (mo)	Colorectal cancer (mo)	
Mean ± standard deviation (range)	33.0 ± 16.2 (12–56)	35.2 ± 22.3 (7–96)	

Edelstein et al. Rapid development of colorectal neoplasia in patients with Lynch syndrome. Clin Gastroenterol Hepatol 2011 Apr;9(4):340-3.

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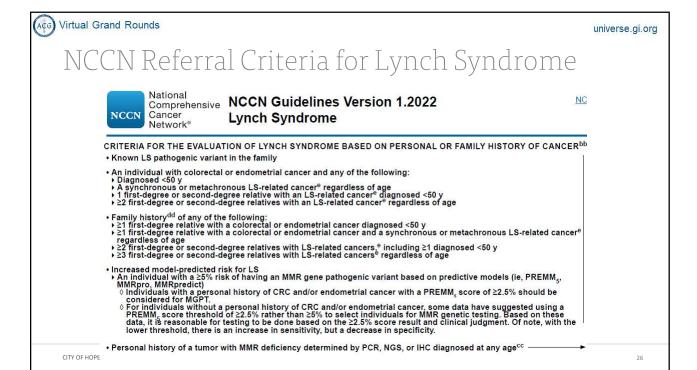
How was Lynch Syndrome Diagnosed in the Past?

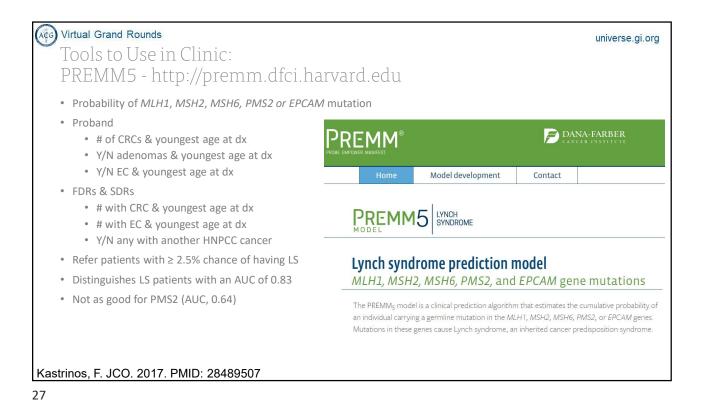
- Had to rely on family history
- Amsterdam II criteria
 - 3 cases of LS-associated cancers
 - o 2 generations affected at least
 - o 1 affected individual is a first-degree relative of the other 2
 - o 1 diagnosed <50
- Bethesda criteria
 - o CRC dx <50
 - o 3 cases of LS-associated cancers at any age
 - o CRC + 1 relative with a LS-associated cancer dx <50
- None of these models worked very well even if someone was taking a good family history and trying to apply them

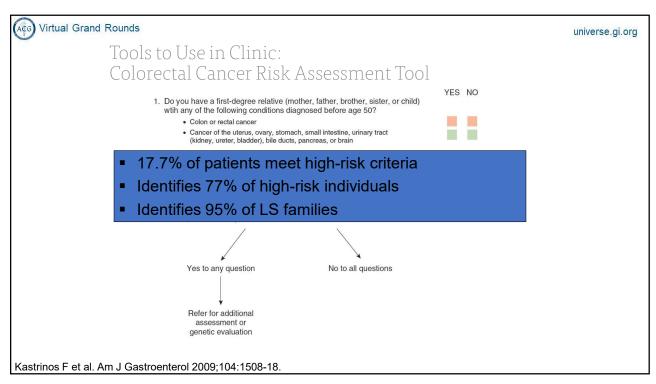
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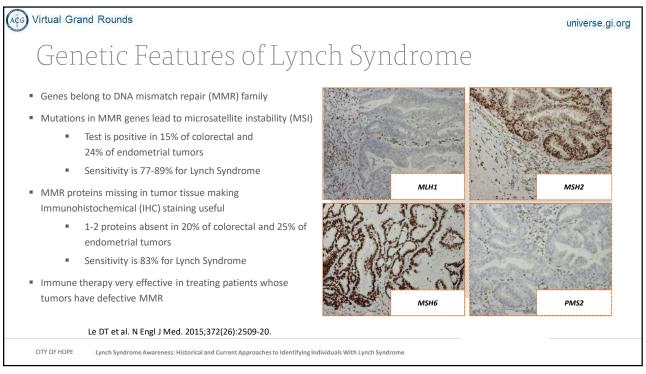
ynch Syndrome Awareness: Historical and Current Approaches to Identifying Individuals With Lynch Syndrom

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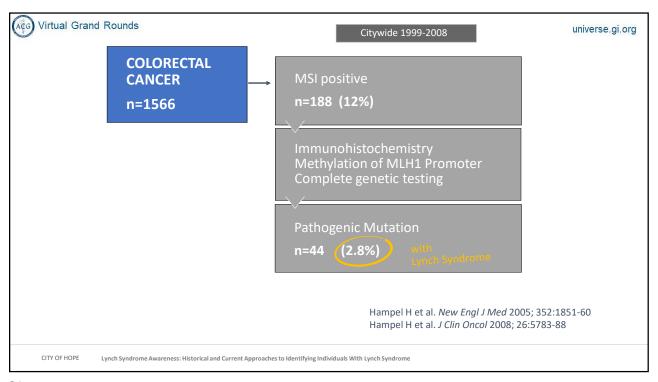


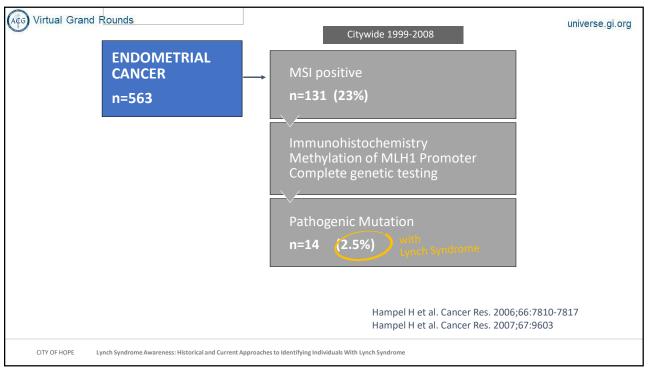


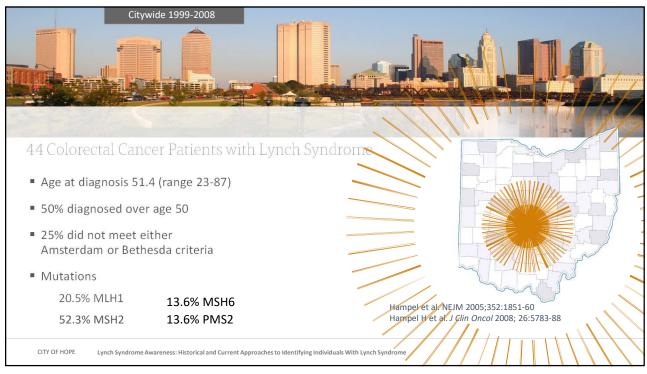
















Cascade Testing: Follow Mutation through Lynch Syndrome Families

Relatives Tested

130 Positive

Average 6 relatives tested per family revealing 3 with Lynch Syndrome

Differentiators of Citywide Initiative

- 1. Free genetic counseling
- 2. Free genetic testing
- 3. Counseling provided locally

Citywide 1999-2008

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Lynch Syndrome Awareness: Historical and Current Approaches to Identifying Individuals With Lynch Syndrome

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Universal Tumor Screening for Lynch Syndrome Cost Effective and Recommended

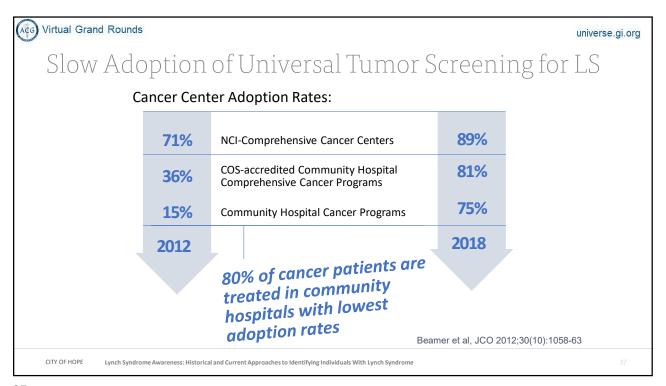
- Incremental Cost Effectiveness Ratio = \$31,391 per year of life saved
 - Experts agree that interventions with an Incremental Cost Effectiveness Ratio <\$50,000 per year of life saved are cost
 effective
- Universal tumor screening for Lynch Syndrome is recommended by:
 - o Evaluation of Genetic Applications in Practice & Prevention (CDC)
 - National Comprehensive Cancer Network
 - o American College of Gastroenterology
 - o US Multi-Society Task Force on Colorectal Cancer
 - o Society for Gynecologic Oncology & American College of Obstetrics and Gynecology
 - o Healthy People 2030 goal: Increase # of newly diagnosed colorectal patients screened for Lynch Syndrome at diagnosis

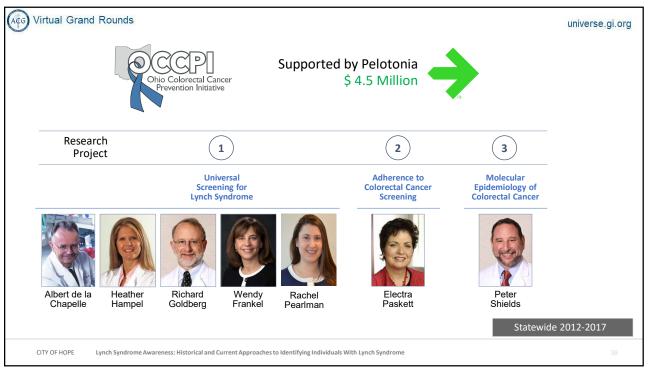
Citywide 1999-2008

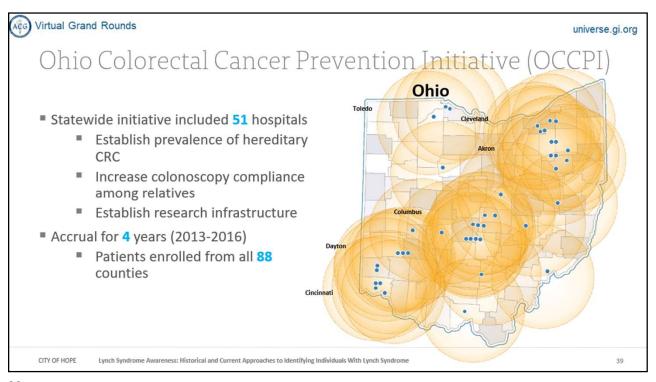
Mvundura et al, Genet Med 2010;12:93-104; Grosse et al, Genetic in Med 2015;17;510-11; EGAPP, Genet Med 2009;11:35-41; Giardiello et al, Am J Gastroenterol 2014;109:1159-79; ACOG & SGO Practice Bulletin Number 147, 2014

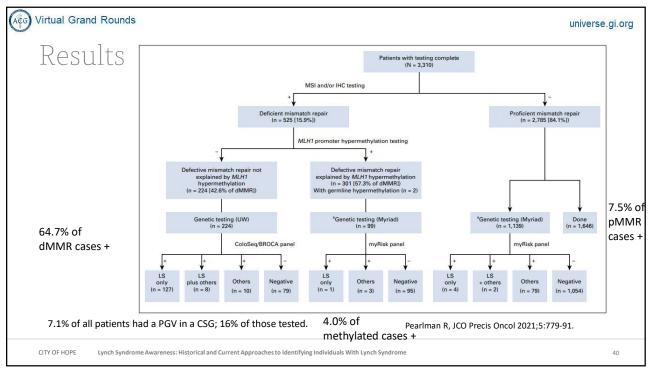
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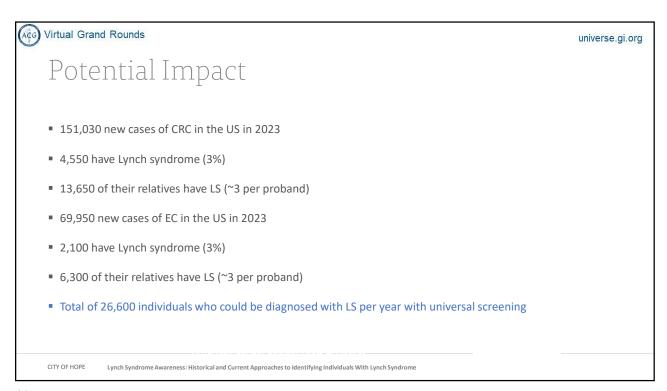
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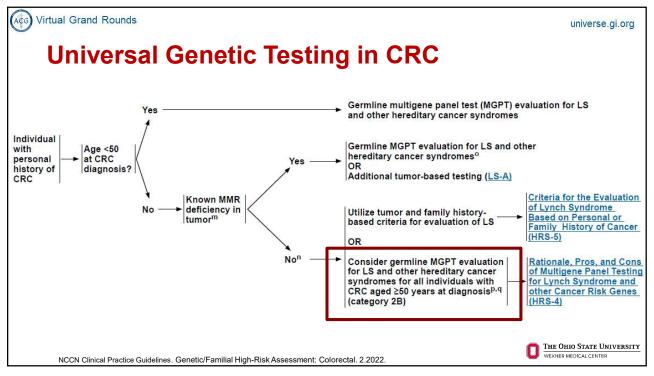














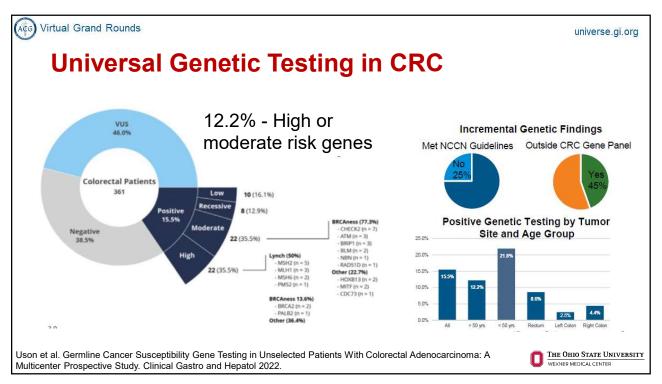
Results of genetic testing on patients with CRC

- Multigene panel testing performed in 34,244 at commercial lab
 - Pathogenic germline variant (PGV) found in 4,864 (14.2%)
 - 3,111 (9.1%) had a pathogenic variant associated with increased CRC or polyposis risk
 - Across all ages and races/ethnicities, the rate of clinically actionable PGVs on was 7.9% or greater.

Coughlin et al. Multigene Panel Testing Yields High Rates of Clinically Actionable Variants Among Patients With Colorectal Cancer. JCO PO 2022.

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The Very Near-Future

Genetic Testing of All Cancer Patients

- 2,984 cancer patients
- 1 in 8 patients (13.3%) with pathogenic variant
- 48% outside of guidelines

JAMA Oncology | Original Investigation

Comparison of Universal Genetic Testing vs Guideline-Directed Targeted Testing for Patients With Hereditary Cancer Syndrome

N. Jewel Samadder, MD, MSc; Douglas Riegert-Johnson, MD; Lisa Boardman, MD; Deborah Rhodes, MD; Myra Wick, MD; Scott Okuno, MD; Katie L. Kunze, PhD; Michael Golafshar, MS; Pedro L. S. Uson Jr, MD; Luke Mountjoy, MD; Natalie Ertz-Archambault, MD; Neej Patel, MD; Eduardo A. Rodriguez, MD; Blanca Lizaola-Mayo, MD; Michael Lehrer, MD; Cameron S. Thorpe, MD; Nathan Y. Yu, MD; Edward D. Esplin, MD; Robert L. Nussbaum, MD; Richard R. Sharp, PhD; Cindy Azevedo, MS; Margaret Klint, MS; Megan Hager, MS; Sarah Macklin-Mantia, MS; Alan H. Bryce, MD; Tanios S. Bekaii-Saab, MD; Aleksandar Sekulic, MD; Keith A. Stewart, MBBS

Samadder JAMA Oncol 2020

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Potential benefit of universal germline testing

- More equitable distribution of genetic referrals
- Traditionally underserved patients are also underrepresented in those receiving genetic evaluation
- 89% of underserved patients had their sample collected for genetic testing when offered
 - 86% rate in overall population

Muessig et al. Retrospective assessment of barriers and access to genetic services for hereditary cancer syndromes in an integrated health care delivery system. Hered Cancer Clin Pract 2022.

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Who should refer to Genetics in CRC?

- Possible options
 - GI doctor at time of endoscopic diagnosis or pathology
 - Colorectal surgeon at time of resection or pathology
 - Oncologist during treatment
 - Any clinician in the CRC diagnosis/treatment pathway
- Referral can be done at any time
 - Early referral can impact treatment options
 - Potentially easier to complete than during chemo/radiation?



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Timing of referral to Genetics for GI physicians

- Easy to arrange at time of pathology result discussion
 - Order CEA, CT chest/abdomen/pelvis
 - Colorectal Surgery referral
 - Genetic counseling referral





Genetic testing points for patients

There are many myths about genetic testing but this is now very common and very easy to obtain!

- Cost this is very commonly covered by insurance. If not, the out of pocket price is usually \$250 (if ordered through GC with lab knowledge)
 - Medicare/Medicaid free through many labs
 - Family testing free for several months after a positive result for many labs!
- GINA is an act of congress that prohibits genetic discrimination
 - Protects from employment and health insurance discrimination based on genetic testing
 - · Life insurance is not protected



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Identifying Lynch patients prior to CRC

- Community GI practice incorporated a tablet with PREMM into clinic and endoscopy
 - Genetic testing offered to those who qualified
- 5.6% of patients qualified as high risk and 86% of those eventually had genetic testing
- All providers were satisfied with the incorporation and patients had high rates of understanding information

Luba et al. Community Practice Implementation of a Self-administered Version of PREMM $_{1,2,6}$ to Assess Risk for Lynch Syndrome. CGH 2018.



