

# Establishing Universal Lynch Syndrome Screening in the Community

November 12, 2016

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# Universal Tumor Screening for Lynch Syndrome: *The Ohio State Experience*

Lynch Syndrome Common  
and Preventable

Success of Citywide and  
Statewide Initiatives

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# Lynch Syndrome

Over 1.2 million individuals in the U.S. have Lynch Syndrome

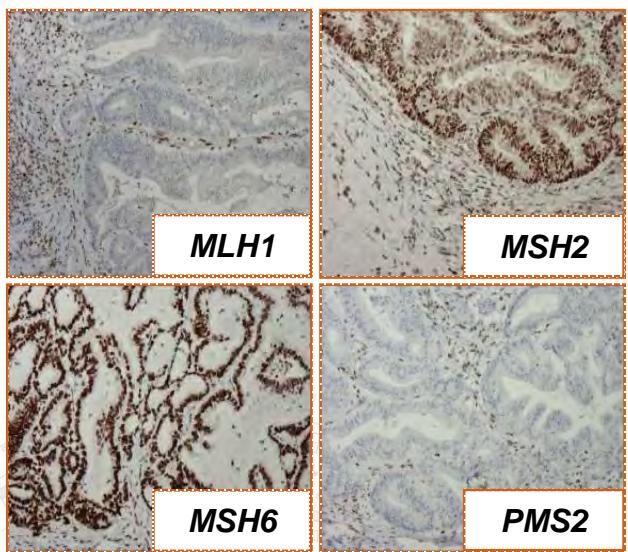
Inherited condition that causes high risks for colorectal cancer, endometrial cancer and other cancers

Preventable cancers with early and more frequent screening

95% of affected individuals do not know they have Lynch Syndrome

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# Genetic Features of Lynch Syndrome



- Genes belong to DNA mismatch repair (MMR) family
  - Mutations in MMR genes lead to microsatellite instability (MSI)
    - Test is positive in 15% of colorectal and 24% of endometrial tumors
    - Sensitivity is 77-89% for Lynch Syndrome
  - MMR proteins missing in tumor tissue making Immunohistochemical (IHC) staining useful
    - 1-2 proteins absent in 20% of colorectal and 25% of endometrial tumors
    - Sensitivity is 83% for Lynch Syndrome
  - Immune therapy recently shown very effective in treating patients whose tumors have defective MMR

Le DT et al. N Engl J Med. 2015;372(26):2509-20.

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# **Universal Tumor Screening for Lynch Syndrome:**

## *The Ohio State Experience*

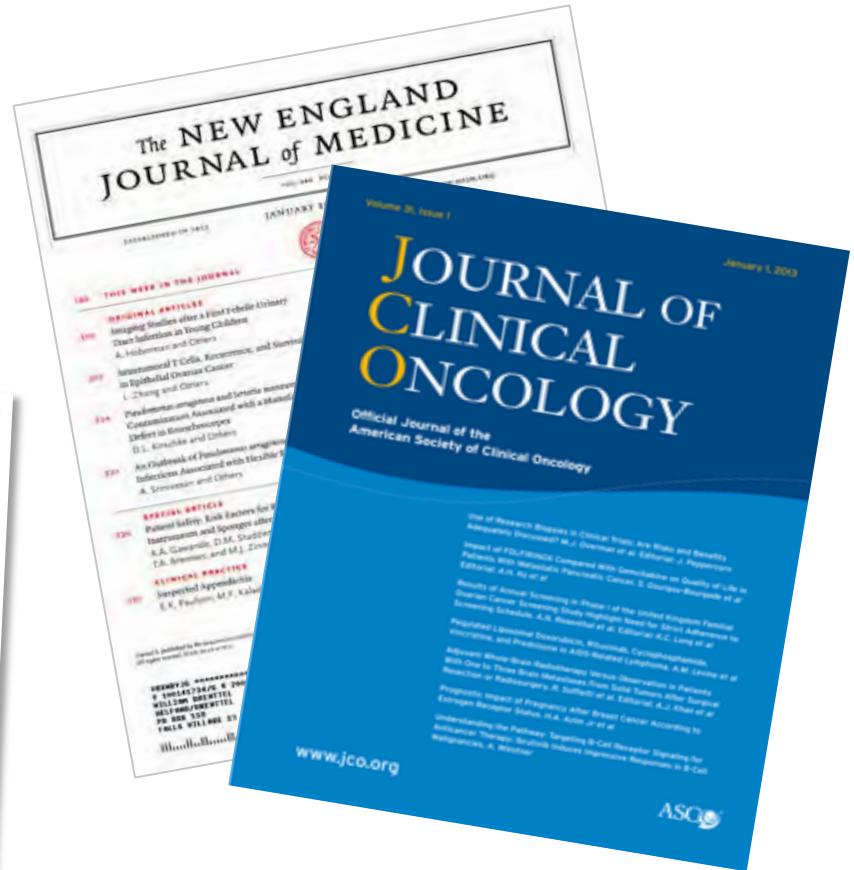
# Lynch Syndrome Common and Preventable

# Success of Citywide and Statewide Initiatives

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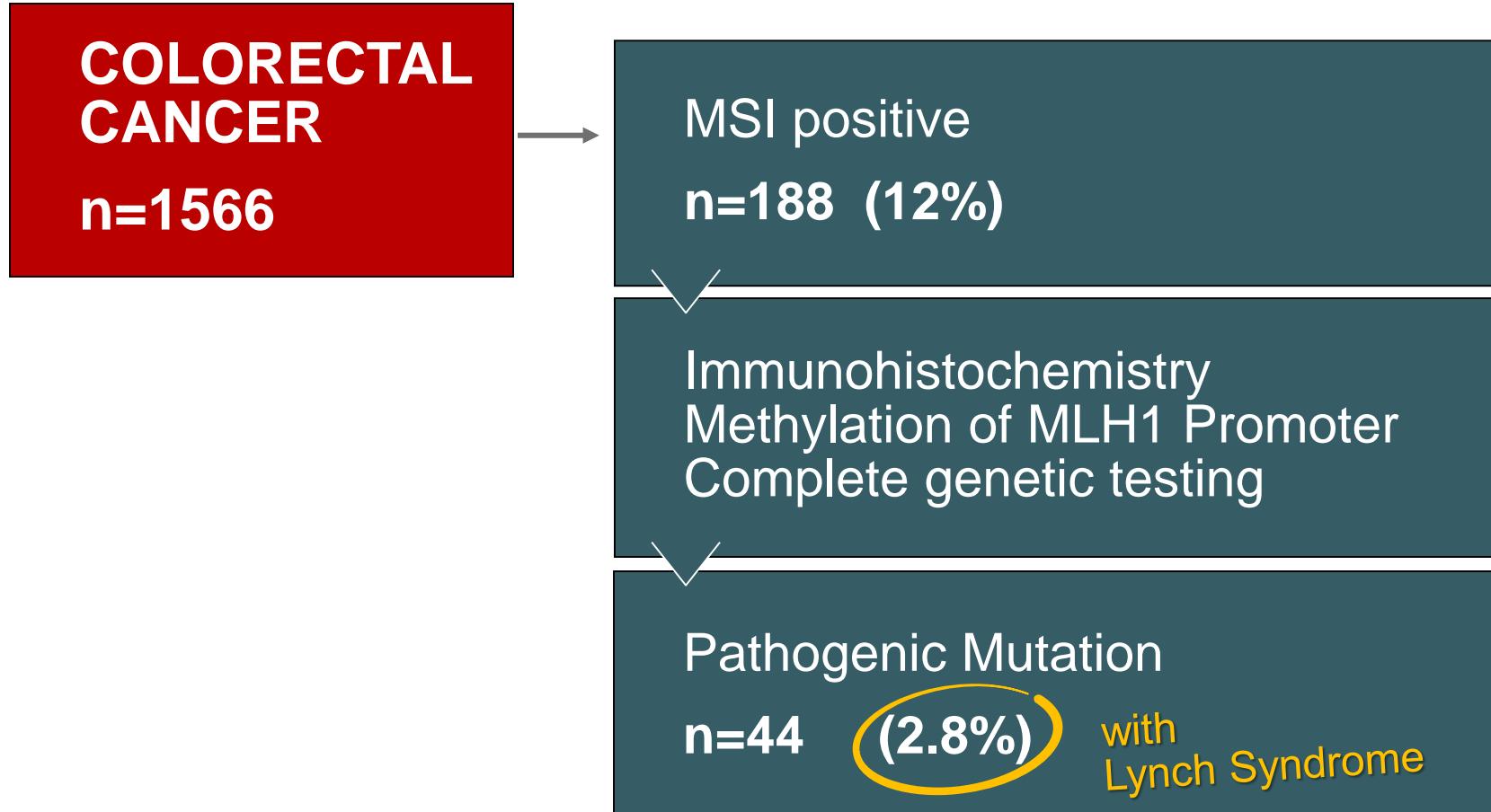


# Feasibility of Screening for Lynch Syndrome Among Patients with Colorectal and Endometrial Cancer



R01 CA 67941

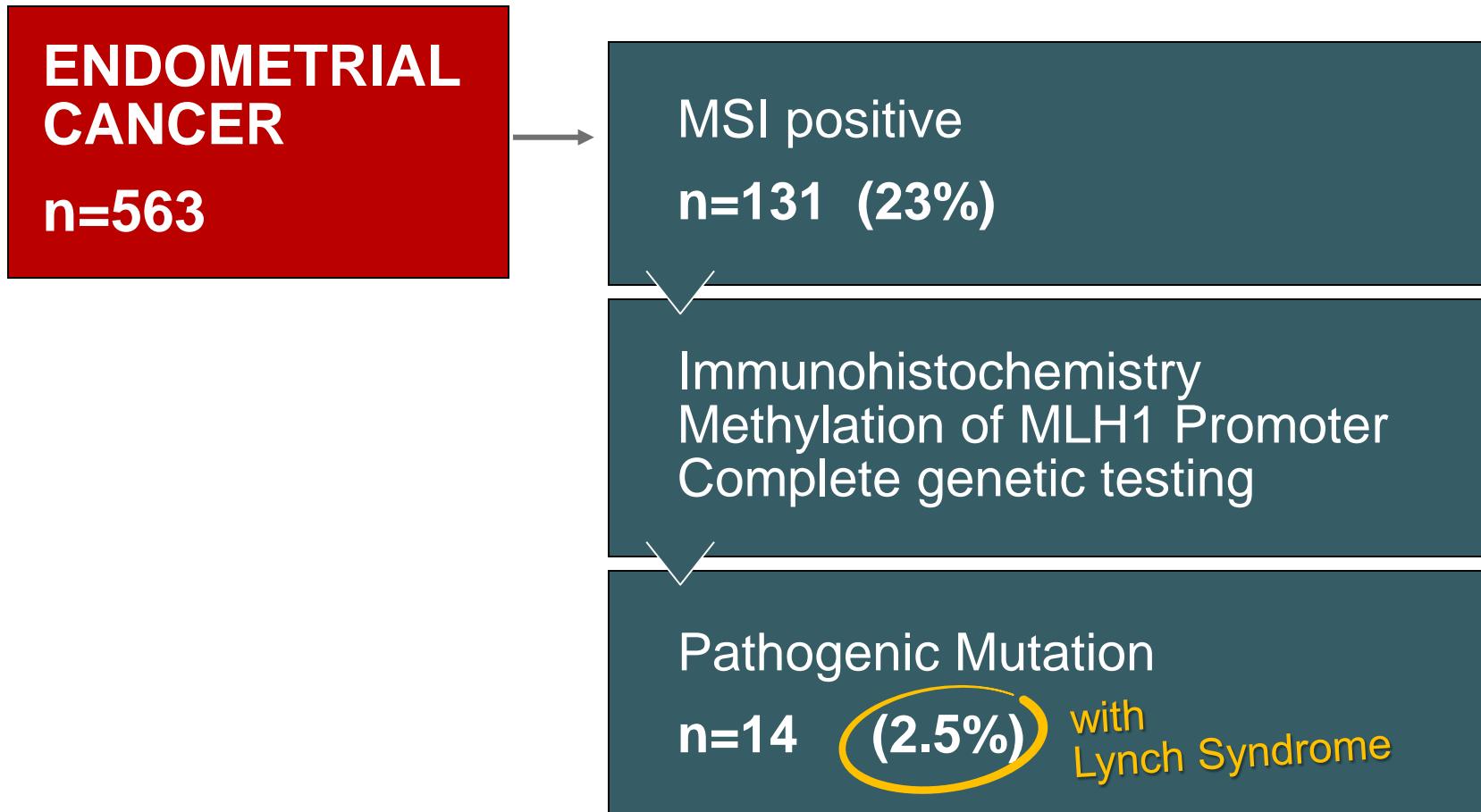
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Hampel H et al. *New Engl J Med* 2005; 352:1851-60  
Hampel H et al. *J Clin Oncol* 2008; 26:5783-88

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Hampel H et al. Cancer Res. 2006;66:7810-7817  
Hampel H et al. Cancer Res. 2007;67:9603

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## 44 Colorectal Cancer Patients with Lynch Syndrome

- 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 13.6% MSH6
  - 52.3% MSH2 13.6% PMS2



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Hampel et al. NEJM 2005;352:1851-60

Hampel H et al. J Clin Oncol 2008; 26:5783-88



## 14 Endometrial Cancer Patients with Lynch Syndrome

- Age at diagnosis 51.4 (range 39-69)
- 65% diagnosed over age 50
- 65% did not meet either Amsterdam or Bethesda criteria
- Mutations
  - 14.3% MLH1 64.3% MSH6
  - 21.4% MSH2 0% PMS2



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Hampel et al. NEJM 2005;352:1851-60

Hampel H et al. J Clin Oncol 2008; 26:5783-88

# Cascade Testing: Follow mutation through Lynch Syndrome families

297

# 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

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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:
    - Evaluation of Genetic Applications in Practice & Prevention (CDC)
    - National Comprehensive Cancer Network
    - US Multi-society Task Force on colorectal cancer
    - Society for Gynecologic Oncology & American College of Obstetrics and Gynecology
    - Healthy People 2020 goal: Increase # of newly diagnosed colorectal patients screened for Lynch Syndrome at diagnosis

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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# Slow Adoption of Universal Tumor Screening for Lynch Syndrome

## Cancer Center Adoption Rates:

**71%** NCI-Comprehensive Cancer Centers

**36%** COS-accredited Community Hospital Comprehensive Cancer Programs

**15%** Community Hospital Cancer Programs

***80% of cancer patients  
are treated in community  
hospitals with lowest  
adoption rates***

Beamer et al, JCO 2012;30(10):1058-63

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# Supported by Pelotonia \$ 4.5 Million



# Research Project

1

## Universal Screening for Lynch Syndrome



# Albert de la Chapelle



# Heather Hampel



Richard  
Goldberg



Wendy  
Frankel

2

## Adherence to Colorectal Cancer Screening



Electra  
Paskett

3

## Molecular Epidemiology of Colorectal Cancer



Peter  
Shields

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# Building the Network

- Met with stakeholders in person
- Track record of success with citywide project
  - Testimonials from collaborators ensuring that we had not stolen patients
- Neutral branding – OCCPI has its own logo that is not related to Ohio State
- Patients stay local
  - Samples come to Ohio State for testing but patients stay local
  - For those with a mutation, genetic counseling provided by a local genetic counselor, telephone genetic counselor or we provided it at their location
- Reimbursement for expenses
  - Sites reimbursed for the costs of accrual on a per patient basis (including pathology costs)



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# Statewide Coverage

50 participating  
hospitals

Patients enrolled  
in all 88 counties

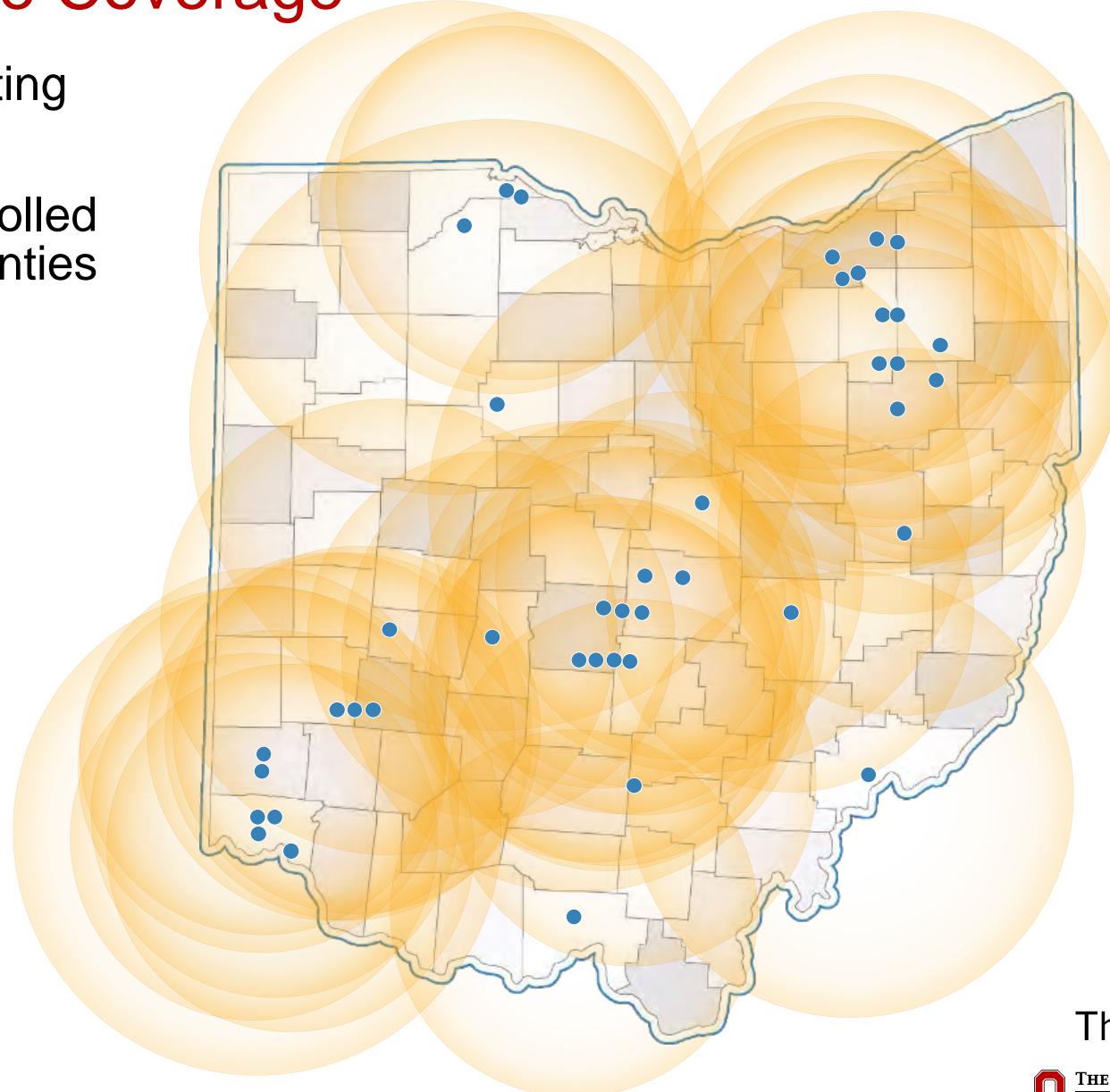


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# Statewide Coverage

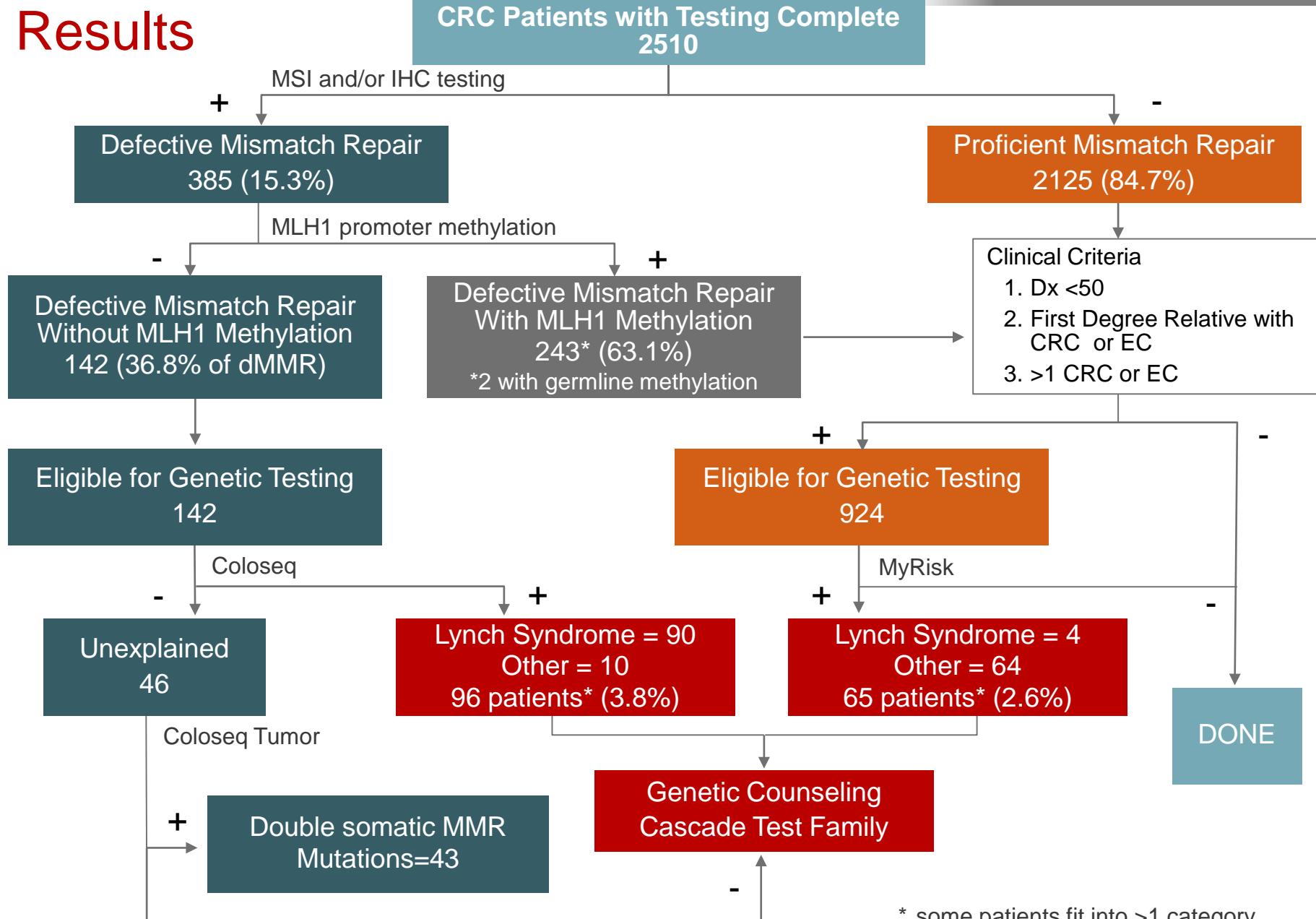
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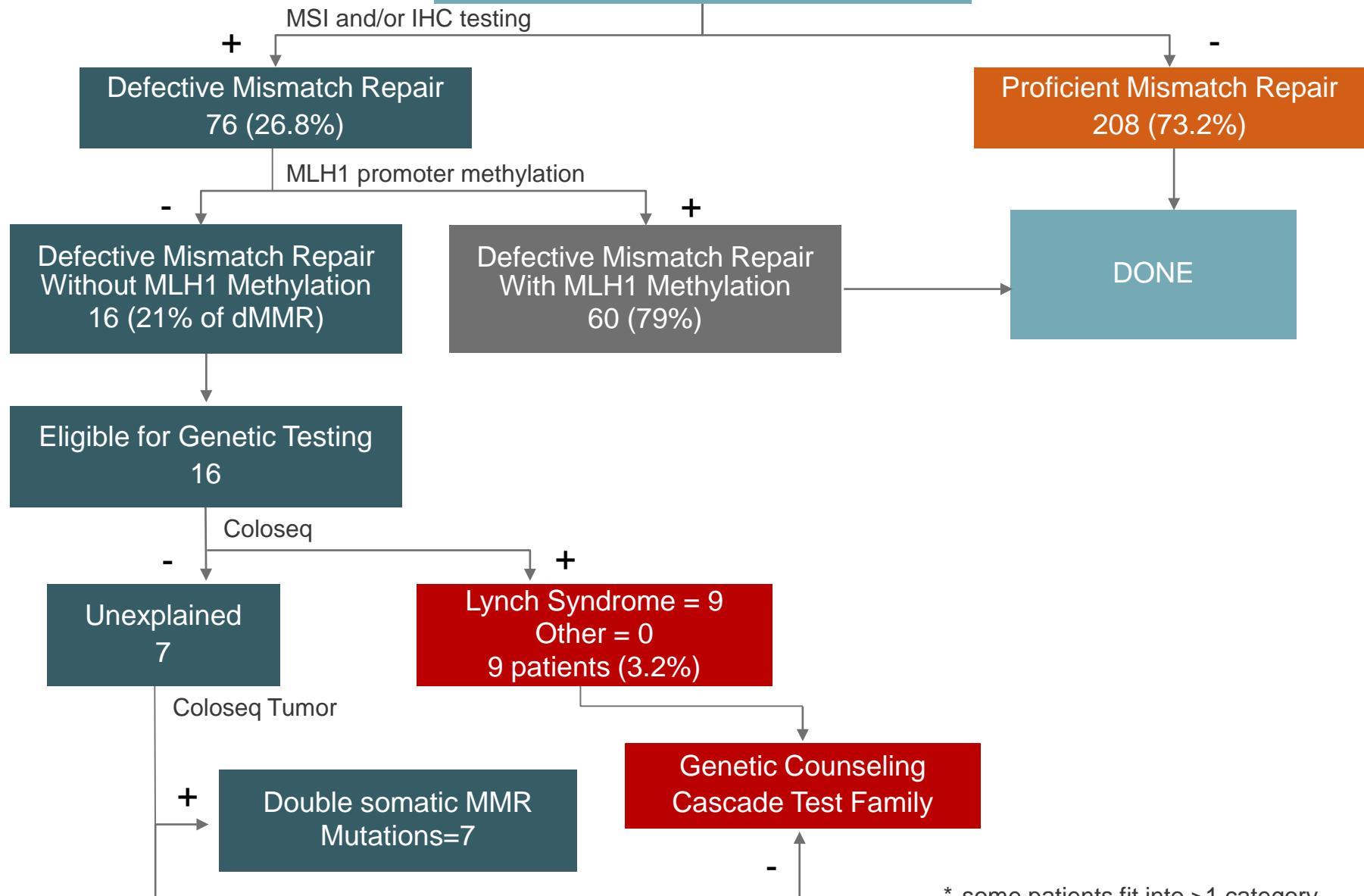
# Results



# Results

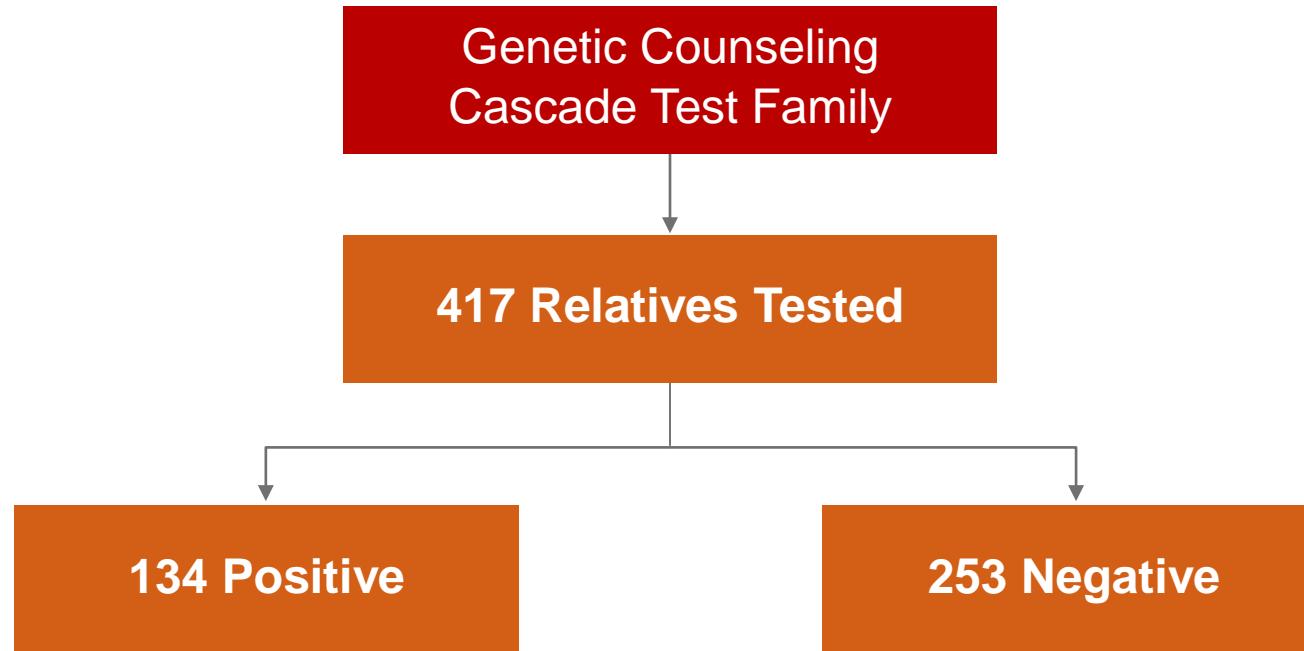
## EC Patients with Testing Complete 284

1



\* some patients fit into >1 category  
 some patients have > 1 gene mutation

# Results



- Receive intensive surveillance and prevention
- Children are at risk
- Receive general population screening
- Children are not at risk

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# Cancer Moonshot Blue Ribbon Panel



# Recommendation...

*A call for a “nationwide demonstration project to systematically screen all people diagnosed with colorectal and endometrial cancer for Lynch Syndrome.”*

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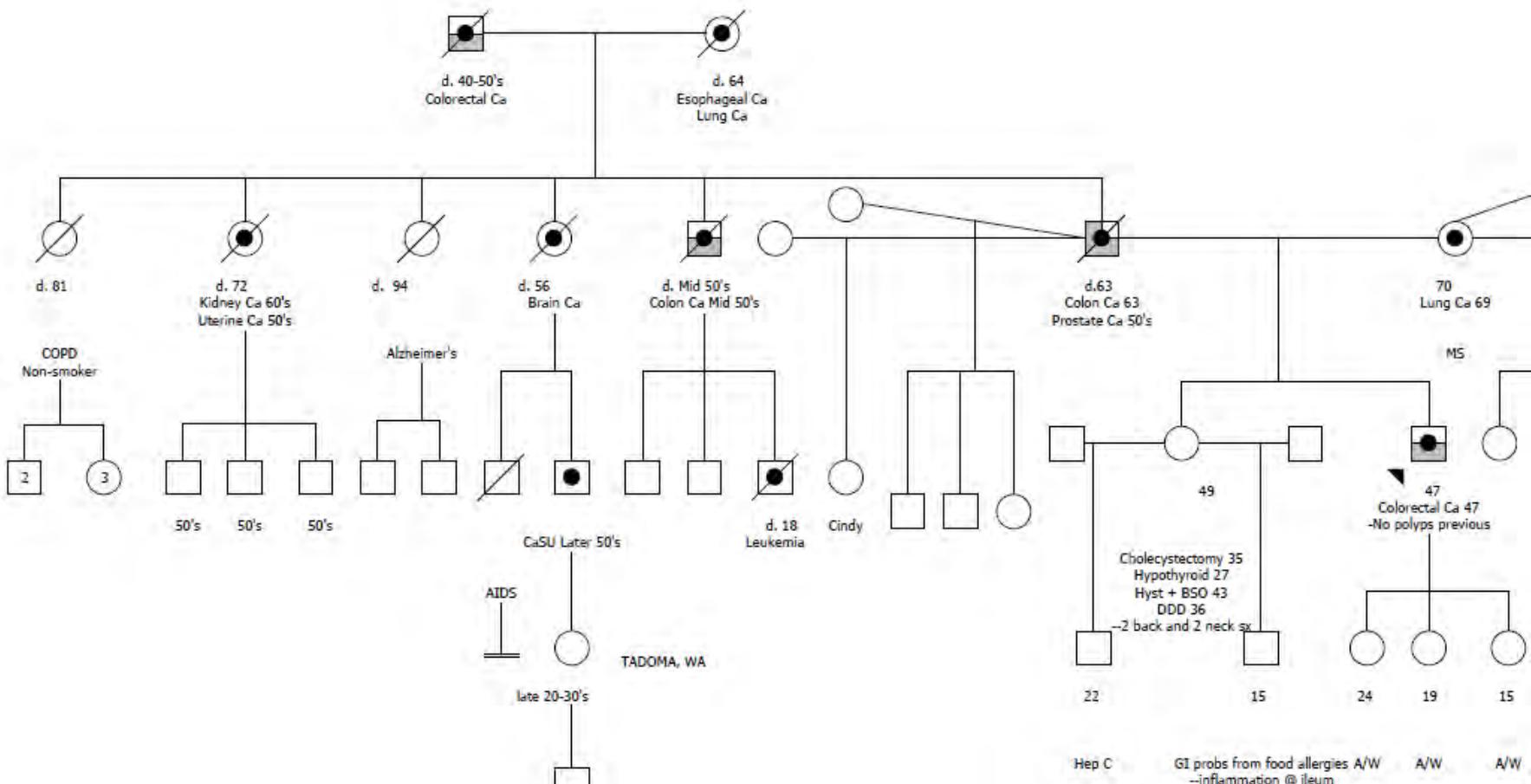
# Potential Impact

- 134,500 new cases of CRC in the US in 2016
  - 4,035 have Lynch syndrome (3%)
  - 12,105 of their relatives have LS (~3 per proband)
  - 60,050 new cases of EC in the US in 2015
  - 1,800 have Lynch syndrome (3%)
  - 3,600 of their relatives have LS (~2 per proband)
  - Total of 21,540 individuals who could be diagnosed with LS this year with universal screening

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# First patient diagnosed with Lynch syndrome in OCCPI



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# First patient diagnosed with Lynch syndrome in OCCPI



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# First patient diagnosed with Lynch syndrome in OCCPI



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# Conclusions

- 1 out of every 26 CRC patients has LS
  - 1 out of every 31 EC patients has LS
  - Family history criteria will miss 25% of CRC patients with LS and 65% of EC patients with LS
  - Lives can be saved by diagnosing LS early
  - Universal Screening for LS among all newly diagnosed CRC patients
    - Is feasible
    - Is recommended
    - Is cost-effective

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# A CANCER-FREE WORLD BEGINS HERE



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