A PROSPECTIVE FEASIBILITY STUDY TO EVALUATE THE IMPLEMENTATION AND OUTCOMES OF A SYSTEMATIC GENETIC RISK ASSESSMENT AND COUNSELING PROCESS TO SCREEN FOR LYNCH SYNDROME

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BACKGROUND

- Lynch syndrome is the most common hereditary colorectal cancer syndrome, affecting 1 in 300 - 500 people.
- Many patients with Lynch syndrome are not identified, partly due to the complexity of existing diagnostic criteria and algorithms.
- The $PREMM_{1,2,6}$ model is a computerized personal and family history risk assessment tool that provides a quantitative risk estimate for Lynch syndrome mutations.[1,2]
- Systematic risk assessment, counseling, genetic testing and management for Lynch syndrome has not been assessed among individuals with and without cancer in a community medical practice.

AIMS

- To determine the feasibility of performing screening with the $PREMM_{1,2,6}$ model for unaffected and affected patients in a busy community gastroenterology practice and outcomes of offering Lynch syndrome genetic testing for individuals with ≥5% risk score.

METHODS

STUDY DESIGN

- Prospective, single arm, process-intervention study.

DESCRIPTION OF PARTICIPANTS

- Patients were recruited in the office and ambulatory endoscopy center.
  - Adults proficient in English were eligible to take the $PREMM_{1,2,6}$.
- $PREMM_{1,2,6}$ was offered on tablet computers as a self-administered questionnaire to eligible patients.
- Providers included 10 MDs, 1 NP, medical assistants, and scheduling and intake personnel.

PROCESS

- Patients advised to obtain family history of colon, uterine, and ovarian cancer at initial scheduling telephone call, in mailings of registration materials, and at a confirmation telephone call.
- Patients with a $PREMM_{1,2,6}$ score of ≥5% watched a 4 minute video on Lynch syndrome, received counseling by the provider, and were offered genetic testing.
- Endoscopy center patients with a $PREMM_{1,2,6}$ score of ≥5% were scheduled for a subsequent office visit for counseling and to have genetic testing.
- Patients that received genetic testing completed a survey about the process.
- Providers completed a survey at the end of the study period to evaluate the process.
  - Patients and providers reported on their experience using a five-point Likert scale (5=Definitely Yes; 0=Definitely No).

GENETIC TESTING

- Consenting patients submitted buccal mucosa and/or blood samples.
- Specimens analyzed by Myriad Genetic Laboratories, Inc., Salt Lake City, Utah.
- DNA sequencing and/or large rearrangement analysis was conducted using a panel which included *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM*.
- *MUTYH* was also analyzed as part of the panel.

RESULTS

INITIATION PHASE: β TESTING $PREMM_{1,2,6}$: 2 MONTHS

- 28 patients tested, 3 positive for mutations.

STUDY PERIOD: 6 MONTHS

- 5287/5393 (98%) of unique patients offered $PREMM_{1,2,6}$ screening.
- 3134/5287 (59.2%) patients were eligible and agreed to complete the $PREMM_{1,2,6}$.
- 177/3134 (5.6%) scored ≥ 5% with $PREMM_{1,2,6}$.
- 145/177 (81.9%) pursued genetic testing.
- 3 positive for mutations.

STUDY DURATION: 8 MONTHS

- 173 patients tested, 6 (3.5%) positive for Lynch mutations.

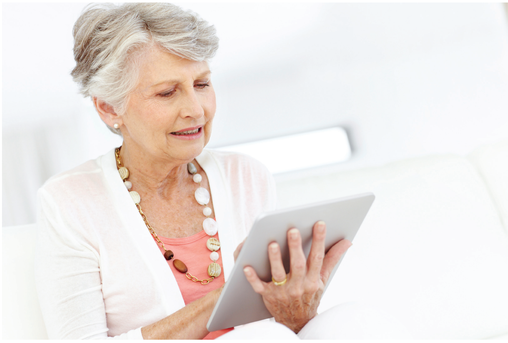

Table 1: Summary of Genetic Testing Results

RESULTS	INITIATION PERIOD (5/1/13 - 6/30/13) (N=28)	STUDY PERIOD (7/1/13 - 12/31/13) (N=145)	TOTAL DURATION (8 months) (N=173)
Negative	21 (75.0%)	120 (82.8%)	141 (81.5%)
Lynch Positive*	3 (10.7%)	3 (2.1%)	6 (3.5%)
MLH1	1	0	1
MSH2	1	0	1
MSH6	1	2	3
PMS2	0	1	1
Monoallelic *MYH* mutation	0 (0.0%)	3 (2.1%)	3 (1.7%)
Uncertain Variants	4 (14.3%)	19 (13.1%)	23 (13.3%)
MLH1	0	2	2
MSH2	0	2	2
MSH6	3	6	9
PMS2	1	3	4
MSH2 & PMS2	0	2	2
Monoallelic *MYH*	0	4	4

**Overall Lynch positive rate does not include 3 monoallelic MYH carriers*

PATIENT SURVEY RESULTS: N=145

- 83.5% of patients thought the survey prior to the appointment prepared them to answer questions regarding personal and family history.
- 84.1% believed that the information they provided was complete.
- 98.6% of patients understood information provided on genetic testing.
- 95.1% of patients had enough time to discuss their questions regarding hereditary cancer syndromes and genetic testing.

PROVIDER SURVEY RESULTS: N=11

- 100% of providers reported that patients provided enough family history information to complete the colon cancer risk assessment.
- 100% of providers thought that $PREMM_{1,2,6}$ was an adequate tool for identifying patients appropriate for genetic testing.
- 90.9% of providers had enough time to answer patient questions regarding hereditary cancer syndromes and genetic testing.
- 100% of providers will continue to use this process to screen and test patients at risk for hereditary cancer syndromes.
- For patients who tested negative, 81.9% of providers used patient personal and family history of cancer to improve patient care.
- For patients who tested positive, the clinical use of genetic testing information changed treatment decisions/medical management for 81.8% of providers.
- 100% of providers were satisfied with the implementation of cancer risk assessment and genetic testing into the practice.

CONCLUSIONS

- It is feasible to incorporate risk based screening for Lynch syndrome using the $PREMM_{1,2,6}$ model to direct genetic counseling and testing in a community gastroenterology practice.
- Systematic risk assessment of both affected and unaffected individuals can lead to identification of patients with inherited susceptibility to cancer, and provide the opportunity for appropriate screening, surveillance and prophylactic surgery for patients and their family members.

REFERENCES

1. Kastrinos F et al. Gastroenterology. 2011 Jan;140(1):73-81.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology for Genetic/Familial High-Risk Assessment: Colorectal, Version 1.2014; http://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf.

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