Implementation of hereditary cancer genetic testing in the primary care setting

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Introduction

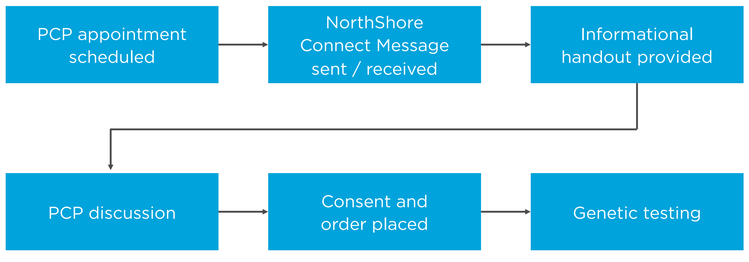
Historically, genetic testing for hereditary cancer has been restricted to high risk individuals and delivered by specialized genetics providers. However, recent studies have revealed that many individuals who harbor inherited pathogenic variants associated with increased cancer risk do not meet classic testing criteria, questioning the predictive value of a family history.[1-4] To overcome access barriers to important genetic information, individuals are seeking this information through non-traditional channels that do not involve a patient's healthcare team.

To address the continued debate in the field regarding population screening, we initiated a pilot to increase access to hereditary cancer testing. This study explores the experience of providing patients the opportunity to access genetic testing through their primary care physician (PCP), with the oversight of the Center for Personalized Medicine, irrespective of personal or family history.

Methods

The study design and flow is summarized in Figure 1 and describe in detail below. Four primary care sites representing Internal Medicine, OB/GYN, and Family Medicine were selected as enrollment sites for the pilot. Participants were identified as non-Medicare patients 18 years and older who had an appointment with their PCP. Three days before their PCP appointment, patients (as potential participants) received a secure message ('NorthShore Connect Message') via NorthShore's Electronic Medical Record Patient Portal informing them of an opportunity to receive genetic testing for hereditary cancer through their PCP. Three days later, when checking-in to their appointment, these patients were provided an informational handout about the pilot. Other patients who were walk-ins, had scheduled an appointment less than three days in advance, or had not accessed the Patient Portal were also given the informational handout to increase uptake. All patients who were interested in participating were then given the opportunity to review the consent and discuss any questions or concerns they may have with their PCP. Patients who agreed to participate gave informed consent for their de-identified sample and information to be used in anonymized studies, and their PCP ordered the Color test.

Figure 1. Study design and flow



The Color test analyzes 30 genes associated with elevated risk for hereditary breast, ovarian, uterine/endometrial, colorectal, melanoma, pancreatic, prostate, and stomach cancer. These genes are *APC, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A* (p14ARF and p16INK4a)*, CHEK2, EPCAM, GREM1, MITF, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, SMAD4, STK11,* and *TP53*. Laboratory procedures were performed at the Color laboratory under CLIA and CAP compliance. Variants were classified according to the American College of Medical Genetics and Genomics 2015 guidelines for sequence variant interpretation,[5] and all variant classifications were signed out by a board certified medical geneticist or pathologist. Results were counted as positive if one or more pathogenic or likely pathogenic (hereafter referred to as pathogenic) variant was detected and negative if no variant/and only benign, likely benign, or variant of uncertain significance was detected at the time of data collection.

Health history was assessed to determine whether patients met or did not meet National Comprehensive Cancer Network (NCCN) consideration for genetic testing as provided by Genetic/Familial High-Risk Assessment: Breast and Ovarian Version 2.2017 (*BRCA1, BRCA2, TP53,* and *PTEN*),[6] Genetic/Familial High-Risk Assessment: Colorectal Version 2.2016 (*MLH1, MSH2, MSH6, PMS2, EPCAM, APC* [excluding APC p.I1307K], biallelic *MUTYH, SMAD4,* and *BMPR1A*),[7] and Gastric Cancer Version 1.2017 (*CDH1*).[8] All information was reported by the patient. Patients who did not provide sufficient health history information were excluded from analyses or noted as such.

Results

Table 1. Cohort demographics details

Of the 2577 patients who received the NorthShore Connect Message and/or the informational handout about the pilot, 1005 (39%) patients elected to undergo genetic testing.

Of the 311 patients in the cohort who reported their health history, only 10 (3.2%) patients reported a personal history of a cancer associated with the genes on the panel. This is consistent with a low risk population recruited in the primary care setting. *Unknown includes information not provided. PV, pathogenic variant.

		Individuals (n)	Population	Individuals w/ PV (n)	Pathogenic Frequency
Total		1005	100%	88	8.8%
Gender	Female	682	67.9%	56	8.2%
	Male	323	32.1%	32	9.9%
Age (Years)	18-30	111	11.0%	12	10.8%
	31-40	186	18.5%	18	9.7%
	41-50	244	24.3%	21	8.6%
	51-64	425	42.3%	34	8.0%
	65+	39	3.9%	3	7.7%
Ethnicity	Caucasian	201	20.0%	17	8.5%
	Ashkenazi Jewish	36	3.6%	1	2.8%
	Asian	25	2.5%	4	16.0%
	Multiple Ethnicities	21	2.1%	0	0.0%
	Hispanic	18	1.8%	0	0.0%
	African	10	1.0%	0	0.0%
	Unknown*	694	69.1%	65	9.4%
Personal Cancer History	Breast	5	0.5%	0	0.0%
	Ovarian/ Fallopian	2	0.2%	0	0.0%
	Melanoma	3	0.3%	0	0.0%

Figure 3. NCCN guideline qualification by result type

A total of 303 patients in the cohort provided enough information to determine whether or not they would have met NCCN considerations for genetic testing criteria for breast and ovarian, colorectal, or gastric cancer.[6-8]

Of those 303 patients, 30.7% (93/303) of patients would have met criteria for testing: 28.9% (81/280) of those with a negative result and 52.2% (12/23) of those with a positive result. The pathogenic frequency was higher amongst those who met criteria (12.9%, 12/93) than amongst those who did not meet criteria (5.2%, 11/210) (p = 0.03, Fisher's exact test).

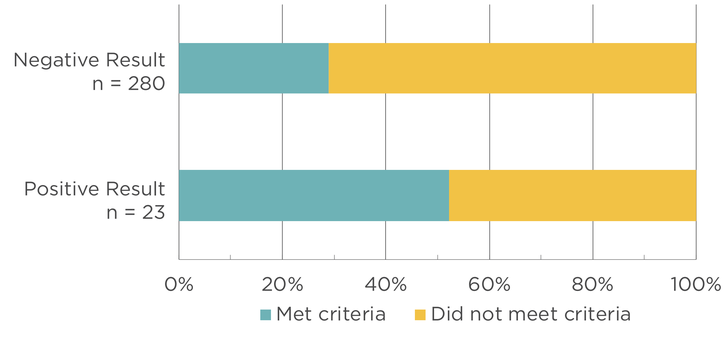
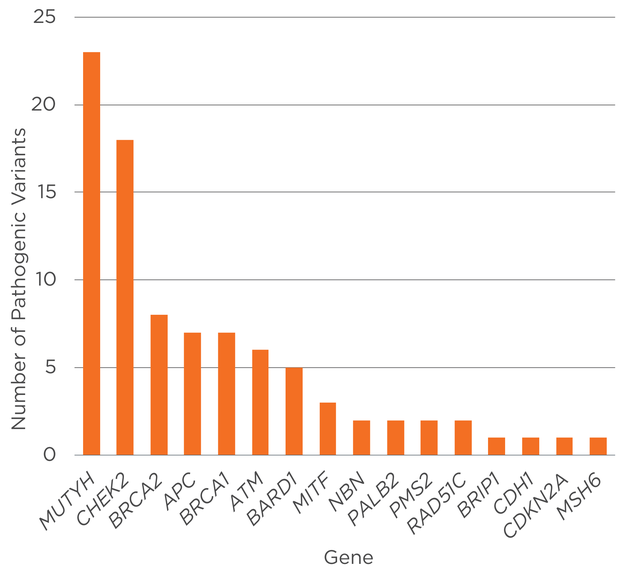


Figure 2. Genes with pathogenic variants identified

A total of 89 pathogenic variants were identified in the 1005 patients. One patient carried two pathogenic variants (one each in *CHEK2* and *MUTYH*), for an overall pathogenic frequency of 8.8% (88/1005).



Conclusions

- Here we present the results of a pilot initiative to offer hereditary cancer genetic testing in the primary care setting.
- 39% of patients who received the NorthShore Connect Message about the pilot elected to undergo genetic testing.
- Of the 1005 patients who received genetic testing, 88 had a positive result, for an overall pathogenic frequency of 8.8%.
- Most patients did not report a personal history of cancer, and only 30.7% of patients would have met testing criteria based on their personal and family history of cancer.
- Pathogenic variants were identified in patients who would have met criteria and would not have met criteria, reinforcing the concern that screening guidelines may fail to identify all patients who could benefit from genetic testing for well-established inherited cancer genes.
- The data presented here, coupled with the demonstrated public interest in obtaining genetic information regarding health risks, suggest that health systems need to engage patients interested in proactively identifying risk through genetic testing screening, rather than have patients bypass their healthcare providers.

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