25-GENE PANEL TESTING AND INTEGRATED RISK MANAGEMENT TOOL IMPACTS MEDICAL MANAGEMENT IN HEREDITARY CANCER SYNDROME EVALUATION

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BACKGROUND

- The identification of patients with hereditary cancer syndromes such as Hereditary Breast and Ovarian Cancer (HBOC) or Lynch syndrome (LS) leads to clinical management changes. Using next generation sequencing, more comprehensive gene panels with greater sensitivity have been developed.
- Integrating personal and family cancer history identified during the screening process with genetic test results can offer refined management recommendations.
- The aim of this study was to determine the clinical utility of hereditary cancer panel testing.
  - This presentation is focused on the breast, colon, endometrial and ovarian cancer medical management decisions made by health care providers based on gene panel results.

METHODS

SCREENING

- Patients were identified using criteria for HBOC or LS and tested using a 25-gene hereditary cancer panel.

TESTING

- Panel genetic testing included next generation sequencing and rearrangement analysis of 25 genes with cancer risk data:
  - *BRCA1, BRCA2*
  - *MLH1, MSH2, MSH6, PMS2, EPCAM*
  - *APC, MUTYH*
  - *CDKN2A, CDK4*
  - *PALB2, CHEK2, SMAD4, BMPR1A, STK11, TP53, CDH1, PTEN,* and *ATM*
  - *NBN, BARD1, BRIP1, RAD51C,* and *RAD51D*
- Affected patients evaluated in this study included those with a personal history of breast, ovarian, colon, endometrial, gastric, pancreatic, melanoma, and prostate cancers.

EVALUATION: PRE- AND POST-TEST SURVEYS

- Recommendations from testing incorporated the genetic test result and a personalized cancer risk and management tool (myRisk management tool (MMT)) based on a patient's personal and family history and professional guidelines.
- Health care providers were surveyed for their management advice to the patient for breast (BC), ovarian (OC), endometrial (EC) and colorectal (CRC) cancer before and after testing.
- Data based on matched pre- and post-test surveys for 1111 patients.
- Interventions were ranked from least aggressive (surveillance) to most aggressive (surgery).

Least Aggressive	Surveillance	Chemoprevention	Surgery	Most Aggressive

RESULTS

Table 1. *Clinical Characteristics*

Characteristic	N=1111
Age at Testing (Yrs)	
Mean	50.0
Range	16 - 88
Gender	
Female	1077 (96.9%)
Male	34 (3.1%)
Ancestry	
Western/Northern Europe	631 (56.8%)
Central/Eastern Europe	79 (7.1%)
African	59 (5.3%)
Latin American/Caribbean	48 (4.3%)
Ashkenazi	25 (2.3%)
Asian	19 (1.7%)
Native American	9 (0.8%)
Neareast/Mideast	3 (0.3%)
Multiple Ancestries Indicated	88 (7.9%)
None Specified	150 (13.5%)
Personal History of Cancer	
Affected	516 (46.4%)
Unaffected	595 (53.6%)
NCCN Guideline Adherence	
2013 HBOC Only	734 (66.1%)
2012 Lynch syndrome Only	82 (7.4%)
Both HBOC and LS	214 (19.3%)
Neither	81 (7.3%)

Table 2. *Case Studies*

	Mutations Detected	Affected	Survey Category	Pre-Test Recommendation	Post-Test Recommendation	Change in Management	MMT Recommendations
Positive Patients							
Patient #1	*BRCA2*	Yes	OC	BSO	CA-125	Less	Transvaginal US, CA-125, BSO, Ovarian chemoprevention, Mammography, Breast MRI, Breast chemoprevention, Clinical breast exam, Mastectomy, Pancreas cancer screening
			BC	Lumpectomy and Radiation	Bilateral mastectomy	More	
Patient #2	*CHEK2*	No	OC	Transvaginal ultrasound	Pelvic exam	Less	Mammography, Breast MRI, Breast cancer reduction strategies, CRC screening
			EC	None	Pelvic exam	More	
			BC	Clinical breast exam	Breast MRI	More	
Patient #3	*PMS2*	No	OC	Chemoprevention	Transvaginal ultrasound	Less	Colonoscopy, Endometrial sampling, Hysterectomy, BSO, Transvaginal US, CA-125, Upper endoscopy, Capsule endoscopy, Urinalysis, Pancreatic screening, Physical exam
			CRC	None	Colonoscopy	More	
			EC	Pelvic exam	Transvaginal ultrasound	More	
			BC	None	Clinical breast exam	More	
Patient #4	*PMS2*	Yes	BC	Bilateral mastectomy	Mammography	Less	Colonoscopy, Endometrial sampling, Hysterectomy, Mammography, BSO, Transvaginal US, CA-125, Upper endoscopy, Capsule endoscopy, Urinalysis, Pancreatic screening, Physical exam
			CRC	None	Colonoscopy	More	
			OC	BSO	BSO	None	
Negative Patients							
Patient #5	---	No	BC	Mammography	Breast MRI	More	Colonoscopy, Mammography, Breast MRI, Clinical breast exam
			OC	Pelvic exam	Pelvic exam	None	
			EC	None	Pelvic exam	More	
			CRC	None	Colonoscopy	More	
Patient #6	---	No	BC	Mammography	Breast MRI	More	Mammography, Breast MRI, Clinical breast exam
			CRC	None	Colonoscopy	More	
			OC	Chemoprevention	Transvaginal ultrasound	Less	
Patient #7	---	No	OC	BSO	Chemoprevention	Less	Skin cancer screening
			BC	Bilateral mastectomy	Mammography	Less	
Patient #8	---	No	CRC	None	Colonoscopy	More	Colonoscopy, Mammography, Breast MRI, Clinical breast exam, Breast cancer risk reduction strategies
			BC	Bilateral mastectomy	Breast MRI	Less	

Figure 1. *Mutations Detected in Positive Patients*

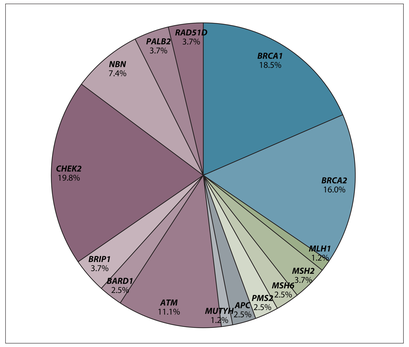

Figure 2. *Information Used to Make Medical Management Decisions*

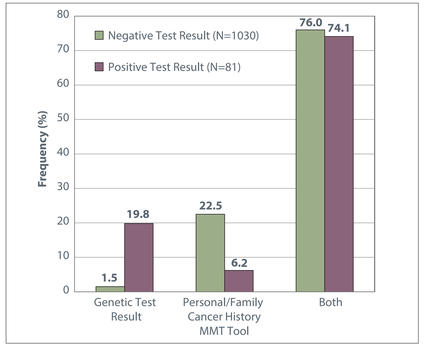

Table 3. *Changes in Management Recommendations*

	Positive Test Result (n=81)	Negative Test Result (n=1030)
More Aggressive	27 (33.3%)	78 (7.6%)
Mixed	13 (16.0%)	89 (8.6%)
Less Aggressive	5 (6.2%)	38 (3.7%)
Minor Change	9 (11.1%)	32 (3.1%)
No Change	18 (22.2%)	769 (74.7%)

*Surveys for an additional nine (11.1%) positive test result patients and 24 (2.3%) negative test result patients indicated a change in medical management on the post-test survey but not the type of change.

CONCLUSIONS

- Over 74% of physicians used both the genetic test result and the personal and family cancer history from the MMT to make management decisions.
- Patients with positive genetic test results had management changes 77.8% of the time after testing.
- Patients with negative test results had management changes after testing in 25.3% of cases based on information gained from the MMT.

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