Clinical Utility of Testing for *PALB2*, *ATM*, *CHEK2*, *NBN*, *BRIP1*, *RAD51C*, and *RAD51D*: Management Changes and Patient Adherence to Provider Recommendations

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Disclosure: All authors are current or former employees of Myriad Genetics, Inc. and/or Myriad Women's Health

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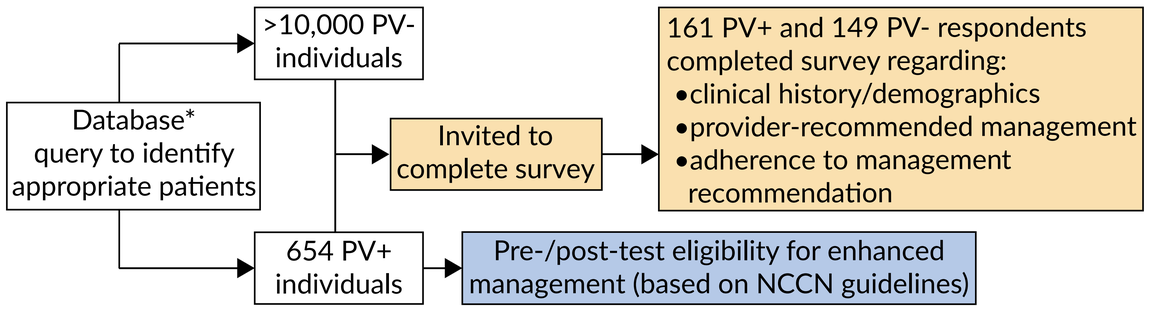
BACKGROUND

- The NCCN provides cancer risk management guidelines for patients with pathogenic variants (PVs) in *PALB2*, *ATM*, *CHEK2*, *NBN*, *BRIP1*, *RAD51C*, and *RAD51D*, but the clinical utility of testing for these genes has been questioned.
- This study assessed: whether testing changed management; provider alignment with guidelines; and patient adherence to management recommendations.

METHODS

Figure 1. Design of study to assess management in patients with PVs in PALB2, ATM, CHEK2, NBN, BRIP1, RAD51C and RAD51D (PV+), and in those without PVs in any gene tested (PV-).

*Internal commerical testing lab database



RESULTS

Table 1. Cancer history of study cohort.

	Personal History			Family History		
	Database	Survey		Database	Survey	
Cancer[a]	PV+	PV+	PV-	PV+	PV+	PV-
Any	256 (40%)	58 (36%)	54 (36%)	599 (92%)	153 (95%)	135 (91%)
Breast	171 (67%)	45 (28%)	34 (23%)	474 (79%)	128 (84%)	110 (81%)
Colorectal	5 (2%)	0	2 (1%)	143 (24%)	35 (23%)	32 (24%)
Ovarian[b]	22 (9%)	6 (4%)	4 (3%)	132 (22%)	29* (19%)	46 (34%)
Other	93 (14%)	18 (11%)	15 (10%)	367 (56%)	108* (67%)	81 (54%)

*Significantly different than PV- group ($p<0.05$); [a]Patients could indicate >1 cancer on the survey; [b]Includes fallopian and peritoneal cancer

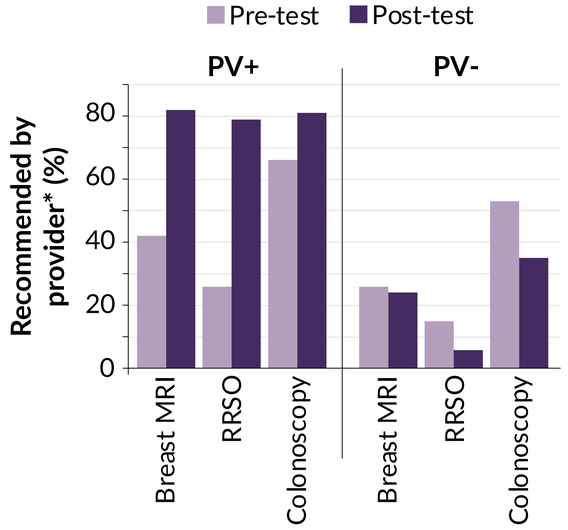
Table 2. Impact of genetic testing on eligibilty for enhanced screening and prevention.

Enhanced Breast Cancer Screening[a]		
Women <75 years with PVs in *ATM*, *CHEK2*, *PALB2* and/or *NBN*	Eligible ***without*** genetic testing[b]	Eligible ***only with*** genetic testing[c]
525	110 (21%)	415 (79%)*
Ovarian Cancer Prevention[d]		
Women[e] with PVs in *BRIP1*, *RAD51C*, and/or *RAD51D*	Eligible ***without*** genetic testing[c]	Eligible ***only with*** genetic testing[c]
86	0	86 (100%)*
Enhanced Colorectal Cancer Screening[f]		
Women/men <75 years with PVs in *CHEK2*	Eligible ***without*** genetic testing[g]	Eligible ***only with*** genetic testing[c,g]
301	50 (17%)	251 (83%)*

[a]Annual MRI plus mammogram, starting age ≤40 (based on family history); [b]Using Claus model (lifetime risk >20%); [c]Using NCCN criteria; [d]Consider Risk-Reducing Salphingo-Oophorectomy (RRSO), age 45-50; [e]Assumed women w/ personal history of ovarian cancer had undergone bilateral oophorectomy; [f]Colonoscopy every 5 years, starting age ≤40 (based on family history); [g]Based on Tung, et al., *Nat Rev Clin Oncol*, 2016;13(9):581-8; *$p<0.05$.

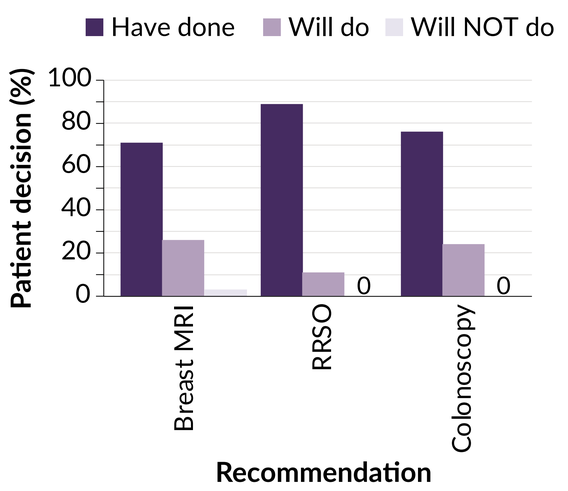
Figure 2. Patient-reported impact of test results on management and adherence.

A) Management recommended by provider



*Now or in the future

B) Adherence to provider recommendations among PV+ individuals



- 654 PV+ individuals were identified with PVs in *ATM*, *CHEK2*, *NBN*, *PALB2*, *RAD51C*, or *RAD51D*.
  - 92% of patients had a family history of any cancer, and 39% had a personal history (Table 1).
  - 46%, 20%, and 15% of patients (database) had a single PV in *CHEK2*, *ATM*, and *PALB2*, respectively.
  - 1.7% of patients had a PV in more than one gene.
- Genetic testing significantly increased the number of patients eligible for enhanced breast cancer and colorectal screening, as well as risk-reducing salpingo-oophorectomy (RRSO; Table 2).
- Genetic testing increased provider recommendation of enhanced screening and RRSO for PV+ individuals (Figure 2A).
  - Breast MRI, colonoscopy, and RRSO were recommended for 82%, 79%, and 79% of eligible patients, respectively, after testing, compared to 42%, 66%, and 26%, respectively, prior to testing.
  - In PV- individuals, providers recommended RRSO and colonoscopy less often after genetic testing (15% vs. 6% and 53% vs. 35%, respectively).
- Of PV+ patients recommended to undergo screening or RRSO immediately, only 2 (1.83%) patients had no plans to follow recommendations (Figure 2B).

CONCLUSIONS

- This study demonstrates the clinical utility of testing for *PALB2*, *ATM*, *CHEK2*, *NBN*, *BRIP1*, *RAD51C*, and *RAD51D*.
- Genetic testing provided information beyond personal and family history that impacted patient management.
- Providers recommended management according to NCCN guidelines for >75% of PV+ patients, and the overwhelming majority of patients adhered to their provider's management recommendation.

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