Clinical utility of hereditary cancer panel testing: impact of *PALB2*, *ATM*, *CHEK2*, *NBN*, *BRIP1*, *RAD51C*, and *RAD51D* results on patient management and adherence to provider recommendations

Valentina Vysotskaia, PhD; K. Eerik Kaseniit, MEng; Leslie Bucheit, MS, CGC; Kaylene Ready, MS, CGC;
Kristin Price, MS, CGC; Katherine Johansen Taber, PhD

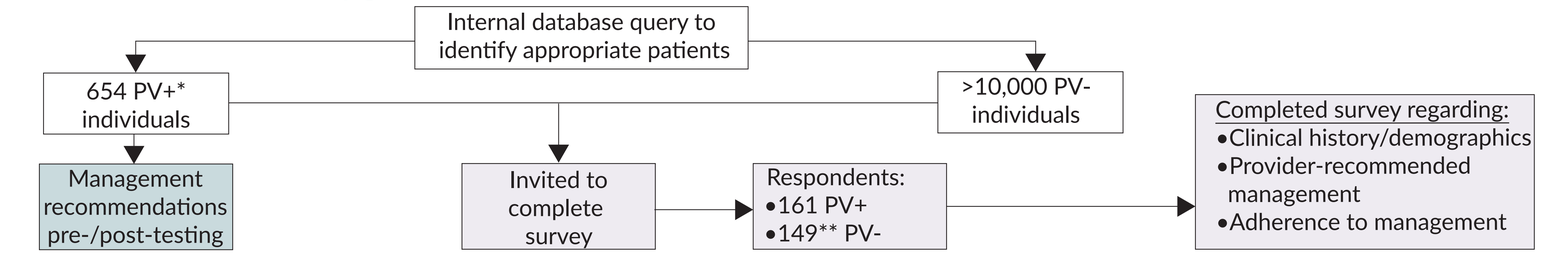
Myriad Women's Health, South San Francisco, CA

BACKGROUND

- Hereditary cancer panel testing that includes genes associated with a 2-5 fold increase in relative risk for certain cancers is increasingly used in clinical practice.
- Although management guidelines exist for these genes, their clinical value remains controversial.
- We sought to demonstrate that testing for these genes directs management, that health care providers recommend management according to guidelines, and that patients adhere to recommendations.

METHODS

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



*Internal commercial testing lab database.
**Survey access was disabled after 150 had completed it. One PV-negative individual's response was not used after it was found he/she did not meet the qualification criteria.

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.

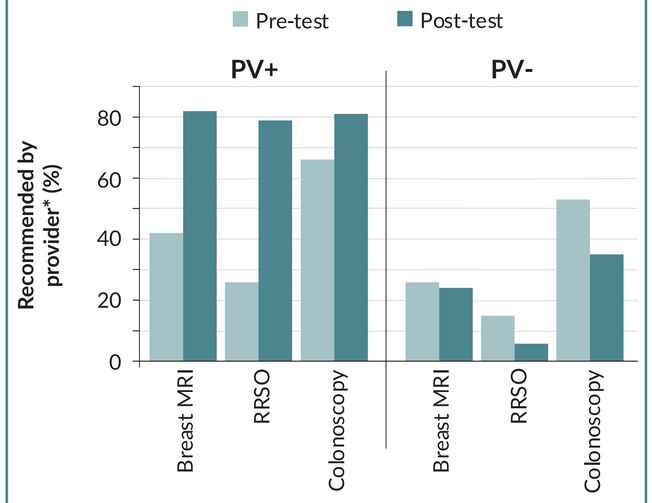
Table 2. Impact of genetic testing on eligibilty for enhanced screening and prevention.

Enhanced Breast Cancer Screening[a]		
Women <75 years with PVs in *ATM*, *CHEK2*, *PALB2* and/or *NBN*[h]	Eligible ***without*** genetic testing[b]	Eligible ***only with*** genetic testing[c]
386	91 (24%)	295 (76%)*
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	Eligible ***without***	Eligible ***only with***
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; *$p<0.05$; [h]No personal history of breast cancer.

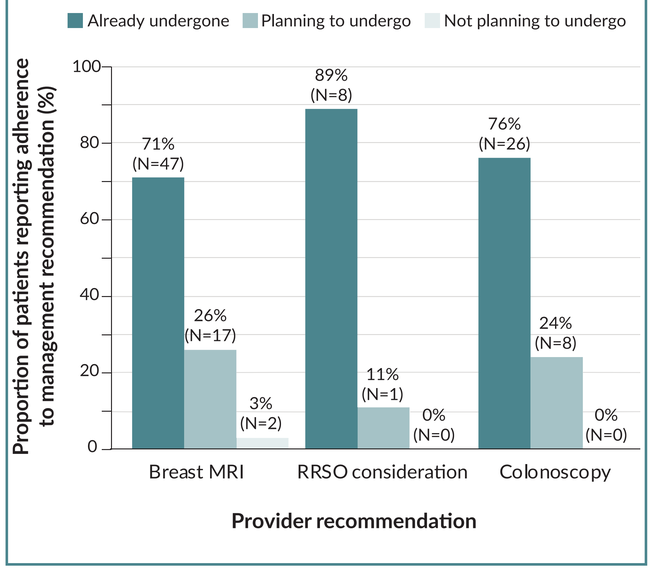
Figure 2. Patient-reported impact of test results on management and adherence.

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*, *BRIP1*, *RAD51C*, or *RAD51D*. 92% of patients had a family history of any cancer, and 40% had a personal history (Table 1). A similar proportion of survey respondents had family and personal histories of any cancer (Table 1).
- 386 individuals had PVs in the breast cancer risk genes *CHEK2*, *ATM*, *PALB2*, or *NBN* and were appropriate candidates for annual breast MRI screening; only 24% of these individuals were candidates before genetic testing (Table 2).
- 86 individuals had PVs in the ovarian cancer risk genes *BRIP1*, *RAD51C*, or *RAD51D*, and were appropriate candidates for risk-reducing salpingo-oophorectomy (RRSO); none were candidates before genetic testing (Table 2).
- 301 individuals had PVs in the colorectal cancer risk gene *CHEK2* and were appropriate candidates for earlier and more frequent colonoscopy; only 17% of these individuals were candidates before genetic testing (Table 2).
- 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 (Figure 2A). In PV- individuals, providers recommended RRSO and colonoscopy less often after genetic testing (15% vs. 6% and 53% vs. 35%, respectively) (Figure 2A).
- Nearly all PV carriers reported already undertaking or planning to undertake recommended management (97% for annual breast MRI, 100% for RRSO, and 100% for colonoscopy) (Figure 2B).

CONCLUSIONS

- Testing for *PALB2*, *ATM*, *CHEK2*, *NBN*, *BRIP1*, *RAD51C*, and *RAD51D* changed management strategies for those carrying PVs.
- Further, provider recommendations were aligned with guidelines, and patients adhered to such recommendations, both critical in reducing cancer morbidity and mortality over the long term.

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