## EXPERIENCE IN THE COMMUNITY ONCOLOGY PRACTICE WITH A 25-GENE HEREDITARY CANCER PANEL

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### INTRODUCTION

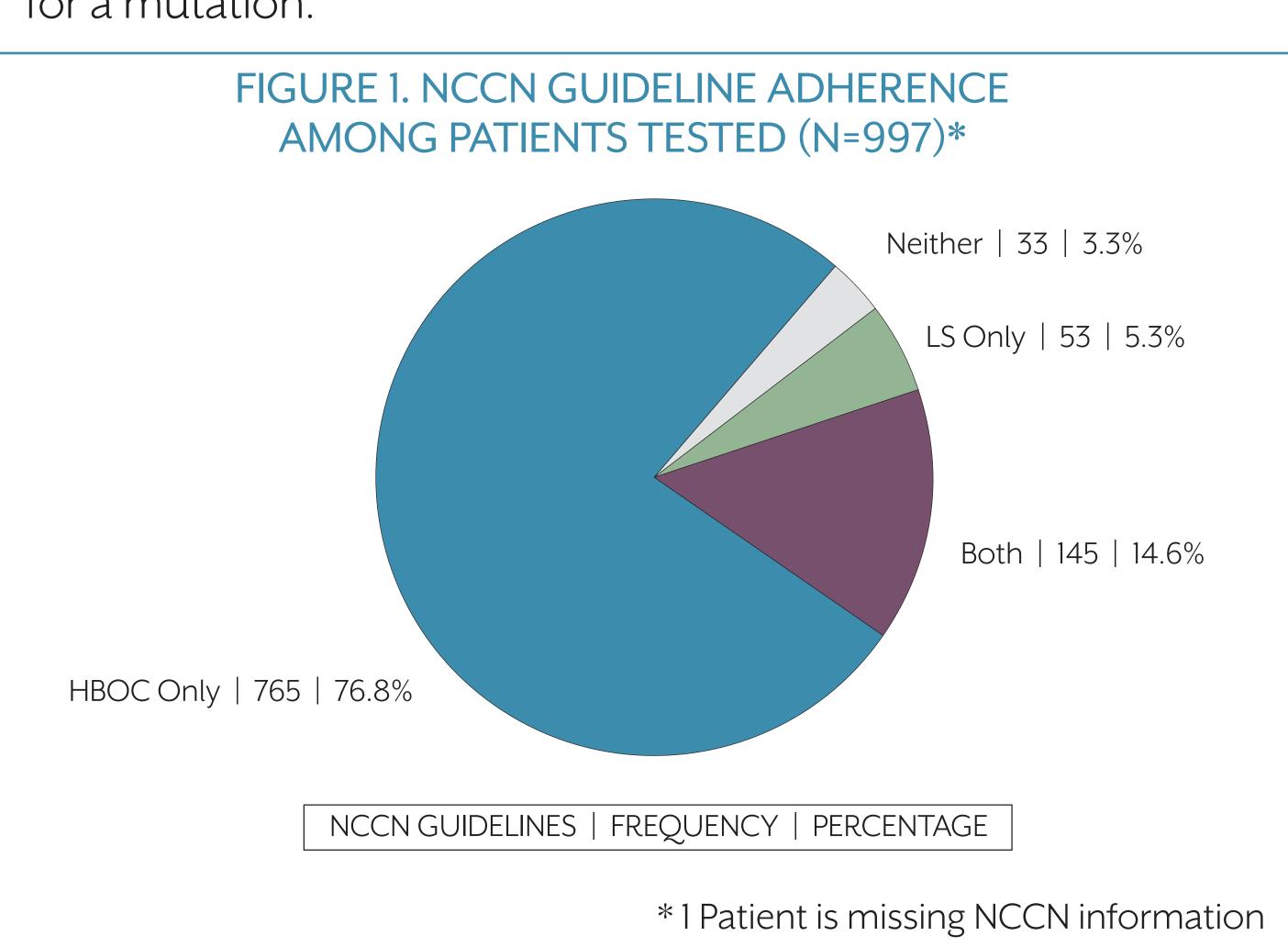
- The identification of patients with an inherited cancer syndrome is becoming increasingly relevant in the treatment and prevention of cancer.
- Testing with a panel of genes provides the opportunity to rapidly identify or rule out deleterious mutations in several genes simultaneously and, thus, has the potential to streamline the testing process and more efficiently and accurately provide results.
- US Oncology practices began offering a 25-gene panel based on Next Generation Sequencing (NGS) to patients through a commercial early access clinical program in September 2013.
- We report on the experience of panel-based testing in the community oncology setting.
- The aim of this study is to evaluate the performance of a 25-gene hereditary cancer test in the community oncology setting and describe the patient characteristics and test findings.

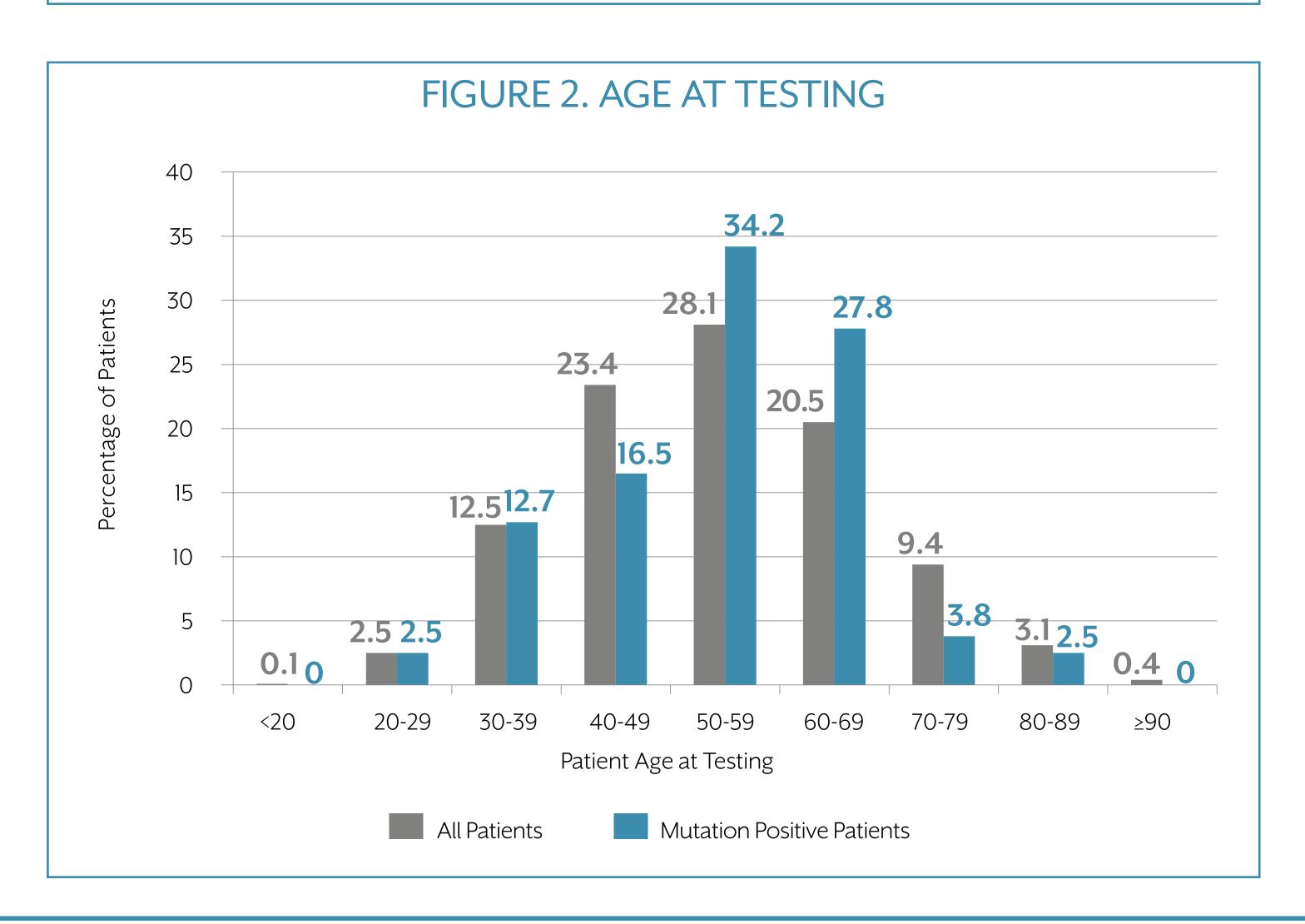
### METHODS

- We retrospectively evaluated patients tested with a 25-gene panel between September 2013 and October 2014 in 6 large community oncology practices.
- The gene panel included BRCA1, BRCA2, MLH1, MSH2, MSH6, PMS2, EPCAM, APC, MUTYH, CDKN2A, CDK4, PALB2, CHEK2, SMAD4, BMPR1A, STK11, TP53, CDH1, PTEN, ATM, NBN, BARD1, BRIP1, RAD51C, and RAD51D.
- The gene panel targets the following 8 cancers: breast, ovarian, colorectal, endometrium, pancreas, melanoma, prostate, and/or stomach.
- Personal and family history was obtained by health care provider report on test requisition forms.

#### TABLE 1. PATIENT DEMOGRAPHICS DISTINCT PATIENT COUNT (%) ANCESTRY 497 (49.8%) Western/Northern Europe 117 (11.7%) Multiple Ancestries Indicated 76 (7.6%) Latin American/Caribbean 31 (3.1%) African 19 (1.9%) Asian 27 (2.7%) Central/Eastern Europe 15 (1.5%) Ashkenazi 5 (0.5%) Neareast/Mideast 2 (0.2%) Native American 208 (20.9%) None Specified 997 TOTAL

- The panel test was performed on 997 individuals during the study time period. 773 (77.5%) of these patients had a personal history of at least one of the eight panel cancers.
- 96.7% of the patients tested met the NCCN guidelines for Hereditary Breast and Ovarian Cancer Syndrome (HBOC), Lynch Syndrome (LS), or both (Figure 1).
- 1 patient is missing NCCN information
- 965 women (96.8%), 32 men (3.2%)
- Figure 2 shows that 48.6% of all patients were tested between the ages of 50 and 69 compared to 60.2% of patients positive for a mutation.





- 83 mutations were found in 79 distinct patients (Table 2).
- Of the patients with a personal history of cancer, 72 (9.3%) were found to have a pathogenic mutation (Figure 3).
- 7 patients that were found to have a pathogenic mutation did not have a personal history of cancer (Figure 3).
- 4 patients were identified with 2 mutations.

GENE

# TABLE 2. MUTATIONS FOUND IN PATIENTS WHO RECEIVED PANEL TESTING (n=83)\*

% OF TOTAL

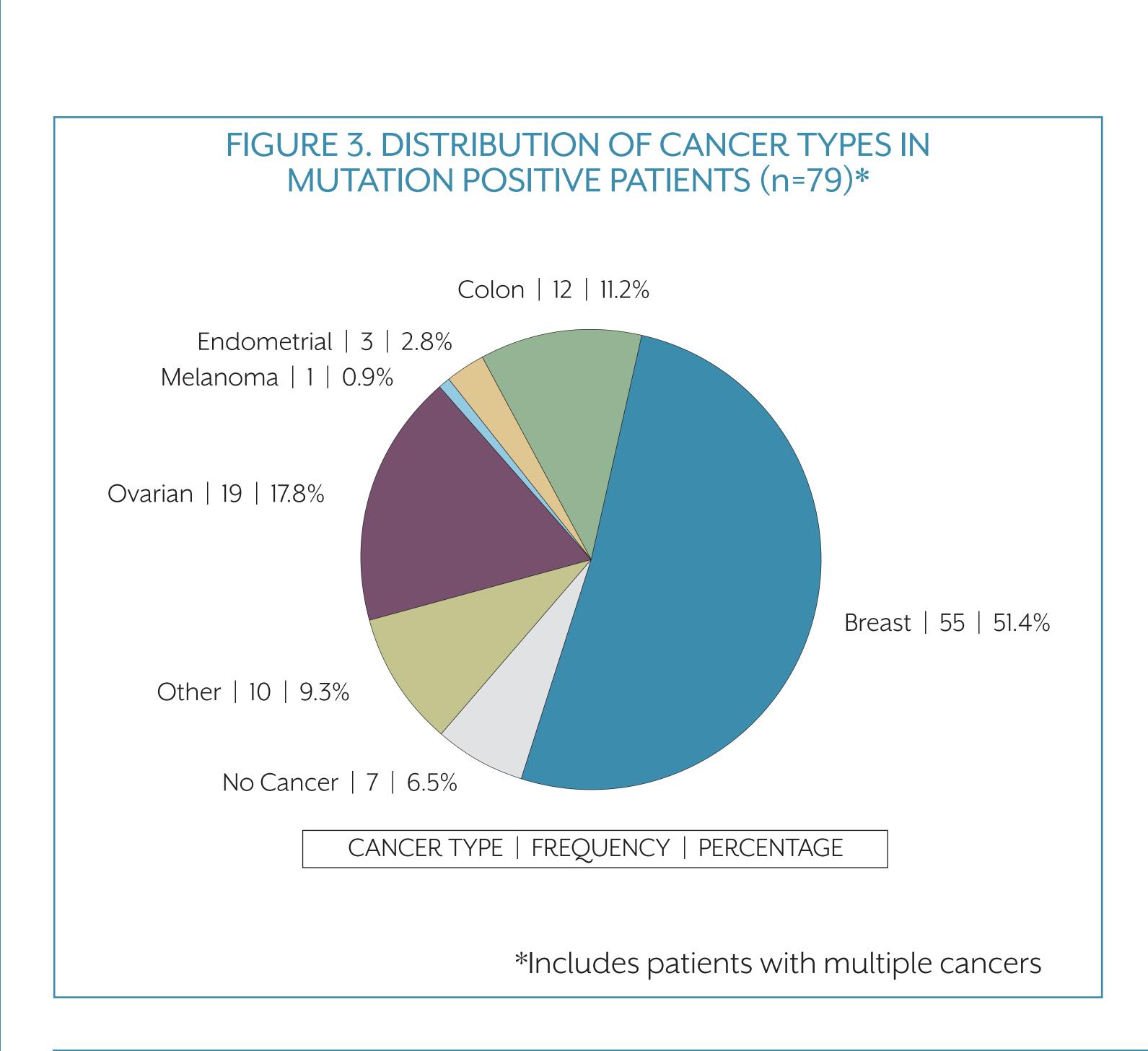
Genes included in Single-Syndrome HBOC and LS Testing		
BRCA2	23	27.7%
BRCA1	16	19.3%
MSH6	4	4.8%
MLH1	3	3.6%
PMS2	2	2.4%
MSH2	1	1.2%
Genes not included in Single-Syndrome HBOC and LS Testing		
ATM	9	10.8%
CHEK2	7	8.4%
PALB2	7	8.4%
BRIP1	3	3.6%
RAD51D	3	3.6%
Biallelic MUTYH	2	2.4%
BARD1	1	1.2%
NBN	1	1.2%
TP53	1	1.2%

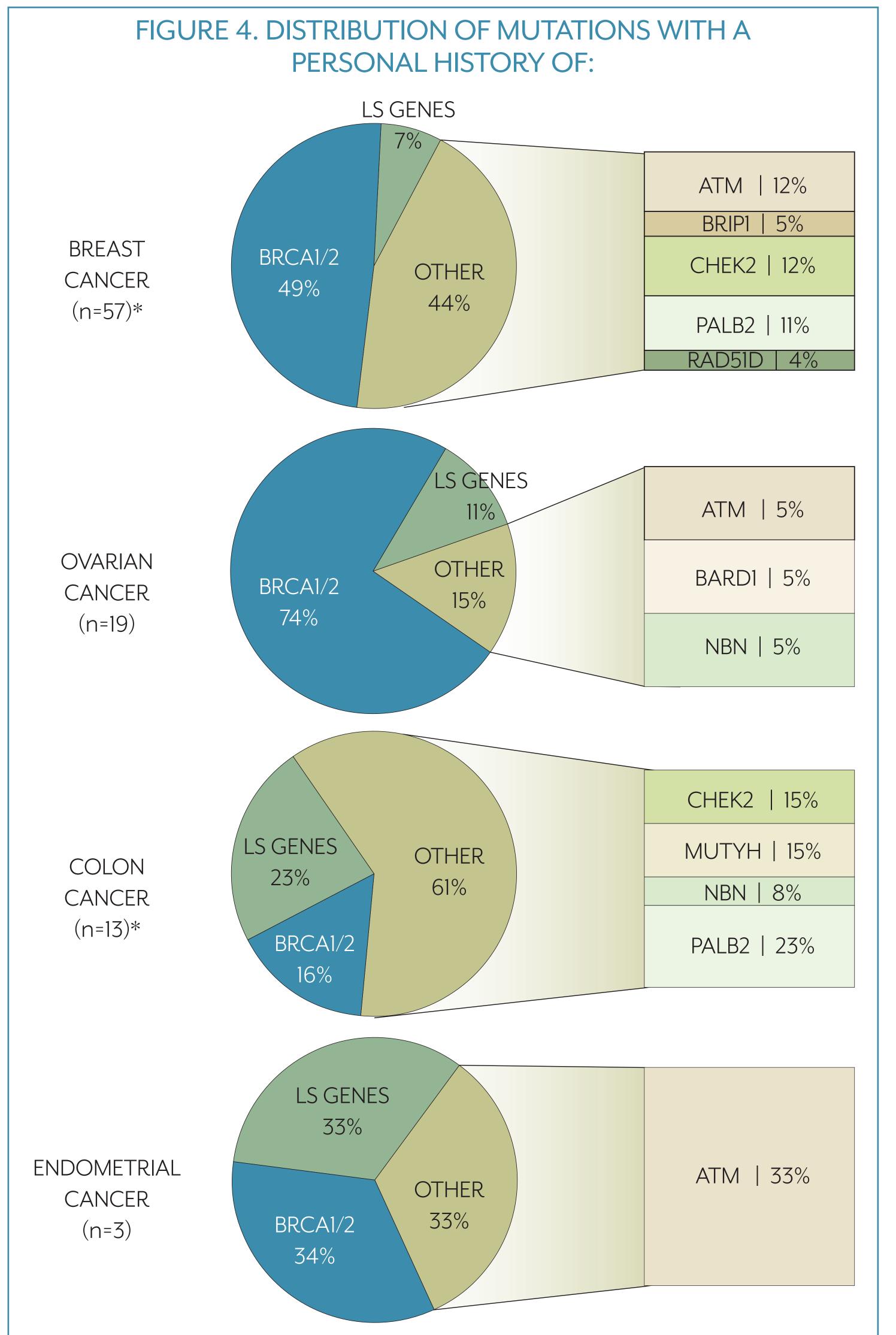
\*3 mutations in *APC I1307K* and 25 single *MUTYH* mutations were found, but are not included in this cohort

• One or more VUS was identified in 38.8% of patients, which is similar to the VUS rate in single-syndrome testing early in its development.

RESULTS

- Mutations were identified in 15 different genes (Table 2).
- Only 59.0% were found to be in the 6 genes included in single-syndrome HBOC (*BRCA1*, *BRCA2*) and LS (*MSH6*, *MLH1*, *MSH2*, *PMS2*) testing.
- Figure 4 shows the gene mutations according to cancer history for patients diagnosed with breast, ovarian, colon, or endometrial cancer. This shows that a significant portion of mutations were found in genes not traditionally associated with HBOC or LS.





\*Includes patients with multiple mutations

## CONCLUSIONS

- Personal and family history are sometimes not sufficient to determine the presence or absence of a cancer syndrome.
- The 25-gene hereditary cancer panel increased the identification of deleterious mutations by 69.4% over single-syndrome HBOC and LS testing alone.
- Use of a hereditary cancer panel in the community oncology practice may improve detection rates and provide an opportunity for enhanced cancer management.

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