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## Test Ordering Practices in Cancer Genetic Counseling

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TEST ORDERING PRACTICES IN CANCER GENETIC COUNSELING

Lauren Costantin & Tiana Grgas

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Sarah Lawrence College

## **Abstract**

The widespread use of Next Generation Sequencing (NGS) has allowed multi-gene panel testing to become common practice in clinical cancer genetic testing over the past six years. Over this time, guidelines have been established and modified, but there is no consensus on how panel testing should be utilized in cancer genetic counseling. There is also limited research into how cancer genetic testing is ordered among different providers. In our study, 1,402 cancer genetic tests were ordered by a variety of provider types from a large academic institution consisting of 16 private and public hospitals as well as a laboratory serving the Long Island and New York City metropolitan area. Data was collected between 01/01/2018 and 09/30/2019 and analyzed to identify discrepancies in the ordering practices among different provider types. Out of the 1,402 cancer genetic tests ordered, 505 were general multi-gene panels, 330 of which were ordered by genetic counselors and geneticists, and the other 175 were ordered by a variety of non-genetics providers. Based on our analysis, there is a statistically significant difference ( $P\text{-value} < 0.0001$ ) in test ordering practices among genetics and non-genetics providers. Our study serves as a foundation for future research into these discrepancies, as well as for research into how to rectify these differences in test ordering practice.

## **Key Words**

Cancer genetic counseling, genetic testing, multi-gene panel testing, hereditary cancer genetics, genetic test ordering practices

## **Introduction**

Hereditary cancer genetic testing began before the discovery of the *BRCA1* and *BRCA2* genes; however, once these genes were uncovered, they became the primary target of breast

cancer genetic testing for their role in contributing to Hereditary Breast and Ovarian Cancer (HBOC) (Shah & Nathanson, 2017). The *BRCA1* and *BRCA2* genes were identified and patented by Myriad Genetics in 1994 and 1996, respectively. Myriad offered sequencing on the *BRCA1* and *BRCA2* genes for a limited number of patients with a greater than 30% predicted risk of having a mutation in either gene. In 2006, Myriad integrated deletion and duplication testing for patients who were negative for Sanger sequencing but still at a high risk for having a *BRCA1/2* mutation (King & Mahon, 2017). In 2013, the Supreme Court of the United States ruled that genes cannot be patented, ending Myriad's monopoly on *BRCA1/2* testing (*Association for Molecular Pathology et al. v. Myriad Genetics, Inc., et al.*, 2013). Multiple genetic testing laboratories began offering testing for *BRCA1/2* along with several other genes implicated in hereditary cancer syndromes (King & Mahon, 2017), which greatly increased the number and diversity of tests offered. The rise of Next Generation Sequencing (NGS) dramatically reduced the cost of analyzing genes, and its use skyrocketed for clinical purposes in multi-gene panel testing (Willoughby, Andreassen, & Toland, 2019). NGS technologies allow for massively parallel sequencing (MPS) alongside deletion/duplication analysis of multiple genes simultaneously. This has allowed the scope of cancer genetic testing to rapidly expand with clinical cancer research to include analysis of several other genes associated with hereditary breast and ovarian cancers (King & Mahon, 2017; Willoughby, Andreassen, & Toland, 2019).

Together *BRCA1* and *BRCA2* are responsible for up to half of heritable breast cancers (Tung et al., 2015); however, variants in *BRCA1/2* do not explain all cases of HBOC. A significant proportion of cases may be due to a pathogenic or likely pathogenic variant in a breast cancer-associated gene that is not *BRCA1* or *BRCA2* (Beitsch et al., 2018; Tung et al., 2015).

Multi-gene panel testing is defined, for the purposes of this study, as genetic testing which analyzes genes for multiple hereditary cancer predisposition syndromes at once, in contrast to syndrome-specific testing which may look at only one or a few genes distinct to a particular hereditary cancer syndrome. Panel testing comes with its own challenges which can arise in test interpretation: the discovery (and classification) of a variant of uncertain significance (VUS), testing low-risk populations, and understanding and conveying the impact of rarer variants on risk assessment (Hiraki et al., 2014; Shah & Nathanson, 2017; Stanislaw et al., 2016; and Tung et al., 2015).

Guidelines have been created by several different professional organizations to help providers identify appropriate candidates for cancer genetic testing. The National Society of Genetic Counselors (NSGC), the National Comprehensive Cancer Network (NCCN), the American College of Obstetricians and Gynecologists (ACOG), and the United States Preventive Services Task Force (USPSTF) have all published such position statements and guidelines. When it comes to recommendations regarding multi-gene panel testing, however, these organizations do not provide consistency in how they describe the utility of multi-gene panels and for which candidates they may be the most useful. This lack of consistency may provide a potential source of discrepancy in how different providers select tests to order for their patients. Additional sources of discrepancies that can affect test ordering practices include differences in provider educational experiences in regard to genetics knowledge, ambiguous test results like variants of uncertain significance (VUS), and mutations identified in genes without clear management guidelines (Baars, Henneman, & ten Kate, 2005; Cragun et al., 2014b; Cox et al., 2012; Klitzman et al., 2012; King & Mahon, 2017; Miller et al., 2014; Richter et al., 2019).

Some recent recommendations are encouraging population-based cancer genetic testing for all patients with breast cancer (ASBrS, 2019; Beitsch et al., 2018; Helwick, 2015), yet significant barriers regarding population-based testing remain. These barriers include the varying educational and practice backgrounds of ordering providers, issues such as interpreting and disclosing VUS results, not having enough genetic counselors to support such a testing demand, and figuring out how to parse out cancer risks between families with different cancer histories (Willoughby, Andreassen, & Toland, 2019).

After the Myriad patents ended in 2013, cancer genetic testing diversified along with the evolving technology, and guidelines were established to identify candidates for genetic testing. While more recent recommendations call for a shift towards population-based genetic testing, barriers remain to its implementation. Of these barriers, discrepancies in test ordering practices between different providers serves as an important consideration as little research has been done to investigate how ordering practices have changed over the past six years. The purpose of this study is to help bridge that gap by quantifying current trends in ordering practices of cancer genetic tests among different types of providers.

## **Materials & Methods**

The data analyzed in this study consisted of cancer genetic tests ordered by several provider types. Data was sampled from an internal database shared by a large academic institution consisting of 16 private and public hospitals as well as a laboratory serving the Long Island and New York City metropolitan area. Collected data spanned from 01/01/2018 to 09/30/2019. The parameters for sampling data included the type of cancer genetic tests ordered, the dates the tests were accessioned and verified, and the ordering clinician. Patient identifiers

and demographics were not collected. Duplicate entries and cancelled tests were excluded from analysis.

The types of genetic tests ordered were grouped into four categories. The breast-specific category included *BRCA1/2* gene sequencing and deletion/duplication analysis, site-specific analysis of the three Ashkenazi Jewish founder mutations (c.68\_69delAG, c.5266dupC, c.5946delT), and small multi-gene panels containing 9-17 genes related to increased risk of hereditary breast cancer. The breast/GYN category included multi-gene panels containing 19-25 genes related to increased risk of breast and gynecological cancers, which shares genes in common with panels for increased risk of gastrointestinal cancers. The Lynch/CRC category included multi-gene panels containing 5-20 genes associated with increased risk of colorectal cancers. The general multi-gene panel category included the largest multi-gene panels containing 37-83 genes associated with increased risk of common hereditary cancers. The number of genes and the specific genes tested varied based on the genetic testing laboratory's individual panel and were not included in the analysis.

Ordering clinicians were identified based on their area of specialty as classified by their national provider identification (NPI) number. Clinicians were grouped into six categories: genetic counselors (GC) and geneticists (GC/Genetics), obstetricians and gynecologists (OBGYN), hematologists and oncologists (HemOnc), gastroenterologists (GI), surgeons (Surgery), and all other provider types sampled (Other). Other providers included internists, pathologists, nurse practitioners, physician assistants, midwives, and specialties otherwise unspecified.

The data were initially separated by year (2018 vs. 2019) and grouped based on test category. Three paired samples t-tests were run using Microsoft Excel for non-genetics, genetics, and all providers to identify potential biases in ordering practices between 2018 and 2019. One genetics provider's data was excluded from these analyses because dates were not included to distinguish in which year the tests were ordered. This data was included in the remaining analysis, and the 2018 and 2019 data were aggregated together. A chi-square analysis was run using Microsoft Excel to identify if a relationship was present between provider type and the type of genetic test ordered in the aggregated data set.

## **Results**

A total of 1,402 cancer genetic tests were ordered by all provider types between 01/01/2018 and 09/30/2019. 640 tests (45.6%) fell into the breast-specific category, 164 tests (11.7%) were breast/GYN, 93 tests (6.6%) were Lynch/CRC, and 505 (36%) were general multi-gene panels (Appendix A: Figures (Figure 1)).

When separating the tests by the year in which they were ordered, 52 tests were excluded from analysis due to missing accession dates. The total number of each test type ordered by year is presented in Figure 2 (Appendix A: Figures). The tests were grouped by test type and a paired samples t-test was run for non-genetics, genetics, and all providers to determine if test ordering practices differed between 2018 and 2019. For non-genetics, genetics, and all providers combined, the P-values were 0.34, 0.54, and 0.45, respectively, suggesting differences between test types ordered in 2018 and 2019 were not statistically significant (Appendix B: Tables (Table 1)). Based on these results, the 52 excluded tests were reincorporated into the data set for further analysis.



The test types ordered were separated into their constituent categories (breast-specific, breast/GYN, Lynch/CRC, general multi-gene panels) and stratified based on provider type (GC/Genetics, OBGYN, HemOnc, GI, Surgery, Other, All). Of the 640 breast-specific tests ordered, 110 were ordered by genetic counselors and geneticists, 78 were ordered by obstetricians and gynecologists, 70 were ordered by hematologists and oncologists, 2 were ordered by gastroenterologists, 60 were ordered by surgeons, and 320 were ordered by other provider types, predominantly internists (Appendix A: Figures (Figure 3)). Of the 164 breast/GYN tests ordered, 118 were ordered by genetic counselors and geneticists, 9 were ordered by obstetricians and gynecologists, 4 were ordered by hematologists and oncologists, 1 was ordered by gastroenterologists, 18 were ordered by surgeons, and 14 were ordered by other providers (Appendix A: Figures (Figure 4)). Of the 93 Lynch/CRC tests ordered, 42 were ordered by genetic counselors and geneticists, 5 were ordered by obstetricians and gynecologists, 1 was ordered by hematologists and oncologists, 24 were ordered by gastroenterologists, none were ordered by surgeons, and 21 were ordered by other providers (Appendix A: Figures (Figure 5)). Of the 505 general multi-gene panels ordered, 330 were ordered by genetic counselors and geneticists, 92 were ordered by obstetricians and gynecologists, 14 were ordered by hematologists and oncologists, 6 were ordered by gastroenterologists, 5 were ordered by surgeons, and 58 were ordered by other providers (Appendix A: Figures (Figure 6)).

A chi-square analysis was run to determine if there was a relationship between the types of tests ordered and the type of provider ordering them. The chi-square value from this analysis was 704.977, which exceeded the critical value of 24.996. The resulting P-value from the analysis was  $<0.0001$ , which is a statistically significant result (Appendix B: Tables (Table 2)).

The observed types of tests ordered differed from expected based on which provider was ordering the test. When visualizing the data, it appears that genetics providers, including genetic counselors, tend to order larger or broader panels, such as the breast/GYN panel and the general multi-gene panels, more frequently than other providers considered in this analysis.

## **Discussion**

Our null hypothesis postulates that there is no statistically significant difference in cancer genetic test ordering practices between genetics providers and non-genetics providers. Based on the results of our chi-square analysis we reject the null hypothesis. Our P-value ( $<0.0001$ ) indicates that there is a statistically significant relationship between the type of cancer genetic test selected and the type of provider ordering the test. The overall trend, as demonstrated in the figures, is that genetics providers order larger multi-gene panels more frequently compared to other types of providers.

This point is particularly salient when looking at breast-specific testing in comparison to other categories of cancer genetic tests. Roughly 83% (530/640) of breast-specific tests were ordered by OBGYNs, HemOncs, surgeons, and other providers (largely internists), whereas 17% (110/640) were ordered by genetics providers. Breast specific tests are comparatively narrower in the scope of analysis because they look at fewer genes that predispose individuals to developing breast cancer compared to multigene panels which include genes associated with other types of hereditary cancer.

The breast/GYN tests, which include a larger number of genes and identify a broader spectrum of cancer risks (compared to the breast specific tests), were ordered predominantly by genetics providers. Approximately 72% (118/164) of these tests were ordered by genetics

providers, whereas 28% (46/164) of breast/GYN panels were ordered by non-genetics providers. Similarly, around 65% (330/505) of general multi-gene panels were ordered by genetics providers, and 35% (175/505) were ordered by non-genetics providers, more than half of which were OBGYNs.

Approximately 45% (42/93) of the Lynch/CRC panels were ordered by genetics providers, 26% (24/93) were ordered by GIs, and 29% (27/93) were ordered by other providers. While the majority of genetic testing was ordered by non-genetics providers, GIs are more likely to encounter individuals with colorectal and other types of gastrointestinal cancers compared to other provider types. The delineation as to whether or not a colorectal or gastrointestinal cancer is due to a hereditary predisposition may also fall into the scope of practice more frequently for genetics providers and GIs than for other provider types.

There are several factors that may contribute to discrepancies in test ordering practices between different provider types, including provider educational background and understanding of genetics as well as inconsistencies between cancer genetic testing guidelines. Baars, Henneman, and ten Kate (2005) sampled general practitioners, gynecologists, and pediatricians to examine the differences in providers' knowledge of genetic concepts and genetic testing. When providers have exposure to genetics in their training or provide genetic counseling to patients, they demonstrate having more knowledge about genetics and testing principles than providers with limited exposure (Baars, Henneman, & ten Kate, 2005). In a small sample of internists in the US, Klitzman et al. (2012) demonstrated that 73.7% of the providers surveyed rated their knowledge of genetics as very/somewhat poor, and 87.1% rated their knowledge of the guidelines for genetic testing as very/somewhat poor. 79% of respondents felt they needed

more training on when to order testing, 82% felt they needed more training on how to counsel patients, and 77.3% felt they needed more training on how to interpret the results of genetic tests, addressing the need for increased training in these areas (Klitzman et al., 2012). Within the same study, 44% of providers reported ordering genetic testing for their patients (Klitzman et al., 2012), which may include providers who are knowledgeable as well as those who may not feel as well-equipped to counsel patients. Cox et al. (2012) report that several providers, including primary care physicians, OBGYNs, surgeons, and oncologists, feel insecure about their knowledge of genetics. Of note, the most common reason a provider of any classification did not recommend or order genetic testing was a lack of familiarity (Cox, 2012). While these studies were able to comment on providers' perception of their knowledge of cancer genetics and genetic testing, it is important to note that both studies were published prior to the availability of large multigene cancer panels.

Our research did not address the demographics of the patients or the indications for genetic testing to determine adherence to published guidelines for genetic testing. In 2013, the NSGC released a practice guideline for risk assessment and genetic counseling for hereditary breast and ovarian cancer. NSGC recommends that providers who are considering ordering genetic testing should consult professional guidelines from organizations such as the National Comprehensive Cancer Network (NCCN) and the American College of Obstetricians and Gynecologists (ACOG). The NSGC 2017 position statement also supported the use of multi-gene panel testing with the caveat that it be done thoughtfully in context of the patient as well as the parameters of the test's clinical validity and utility, the limitations of the technology, and the ways in which variants are interpreted and reported. NSGC advises that knowledgeable

experts should order these tests because multi-gene panel testing may present with complications (NSGC, 2017).

Recommendations from NCCN are regularly updated, and while we acknowledge there are newer guidelines available in 2020, our research analysis primarily relies on guidelines released in 2018 and 2019. At the time of data collection, the NCCN guidelines for *Genetic/Familial High Risk Assessment: Breast and Ovarian* were updated in 2019 (v.3.2019) while the *Genetic/Familial High Risk Assessment: Colorectal* guidelines were updated in 2018 (v.1.2018). According to the NCCN (2019) genetic/familial high risk assessment for breast and ovarian cancer guidelines, it remains inappropriate to utilize multi-gene testing when a patient has a personal or family history indicative of a single hereditary cancer predisposition syndrome. Syndrome-specific testing is suggested as it tests for more than one gene that may be responsible for the suspected inherited cancer syndrome, albeit with a more limited scope of analysis. In the context of breast and ovarian cancers, NCCN (2019) suggests that multi-gene panel testing may be utilized when a patient tests negative for a suspected hereditary cancer predisposition syndrome and when the personal and/or family history remains suspicious of an inherited syndrome (NCCN, 2019). In following the NCCN (2019) breast and ovarian cancer guidelines, one or two tests may be ordered depending on the patient's initial result and personal/family history of cancer. The NCCN guidelines for genetic/familial high risk assessment of colorectal cancer highlight scenarios where multi-gene panel testing should be considered: when personal and/or family history meets criteria for more than one hereditary cancer syndrome, when the patient has colon polyposis with uncertain histology, when the family history of cancer does not meet guidelines for testing but there is an appropriate panel based on risk, in patients with

limited or unknown family history and a concern for cancer, in cases of adenomatous polyposis, and as second-line testing when the results of prior testing is inconclusive (NCCN, 2018). The breast and ovarian cancer guidelines from NCCN (2019) do not provide similar examples for when multi-gene panel testing may be most useful, which can potentially contribute to discrepancies in test ordering practices due to inconsistency of information.

Another point of consideration in ordering cancer genetic tests is that different commercial laboratories analyze different genes, so it is important for the ordering provider (regardless of specialty) to choose the laboratory and specific panel with care. Providers should be aware that clinical features of hereditary breast and ovarian cancer syndrome overlap with features of other hereditary cancer syndromes that are due to different underlying genes (Berliner, Fay, Cummings, & Burnett, 2013). Based on the results of our analysis, non-genetics providers may be either ordering syndrome-specific testing only or ordering up to two cancer genetic tests for their patients, whereas genetics providers may be more likely to order multi-gene panels from the outset as they cover multiple cancer predisposition syndromes simultaneously, which is a point indicated in the NCCN colorectal guidelines and not the breast and ovarian cancer guidelines.

The guidelines suggested by NCCN differ from those suggested by ACOG. ACOG's committee opinions recommend that OBGYNs should perform hereditary cancer risk assessments for their patients (ACOG, 2015). They also suggest that providers offering genetic testing, including OBGYNs, should provide pre- and post-test counseling for patients that includes a discussion about the benefits and limitations of testing, the ability to opt-out of testing (which is not directly stated in the NCCN guidelines), and potential effects testing has on

insurance. While ACOG does not disclose or recommend which genetic tests to offer patients, they do suggest that OBGYNs should establish consistent testing strategies within their practice so patients receive consistent care (ACOG, 2017). Additionally, if OBGYNs feel unable to counsel patients effectively about genetics and genetic testing, they should refer patients to a genetics specialist (ACOG, 2017). ACOG practice guidelines for multi-gene panel testing in hereditary breast cancer closely mirror those discussed in NCCN guidelines for the same hereditary cancer syndromes, and NCCN guidelines are primarily referenced to review the utility of multi-gene panel testing (*Hereditary breast and ovarian cancer syndrome*, 2017). The ACOG practice bulletin on Lynch syndrome from 2015 was reaffirmed in 2019 recommending that testing begin with tumor testing and immunohistochemistry (IHC) or microsatellite instability testing (MSI). This practice bulletin, however, does not address panel testing of multiple genes involved in the mismatch repair pathway and instead focuses on tumor testing being the first method of testing (*Lynch Syndrome*, 2014).

The conclusions made by Beitsch et al. (2018) regarding the yield of multi-gene panel testing to capture mutations in genes other than *BRCA1/2* influenced The American Society of Breast Surgeons (ASBrS) to publish guidelines in 2019 that recommended genetic testing for all patients with breast cancer. In contrast, the USPSTF's 2019 draft recommendations upheld that genetic testing should only be offered when a woman screens positive on a brief familial risk assessment tool that is validated to predict the risk of carrying a mutation in *BRCA1/2* (USPSTF, 2019).

The continual updates and modifications to guidelines and testing recommendations creates a lag time between the publication of updates and implementation in clinical practice.

Over the timeframe of data collection, modifications were made to testing practices established by NCCN, ACOG, USPSTF, and ASBrS. While other recommendations, such as the 2014 recommendation by Dr. Mary-Claire King proposing that all women at age 30 (regardless of family history) should be tested for *BRCA1/2* germline mutations to decrease incidences of hereditary breast and ovarian cancers (Helwick, 2015) have remained unchanged. When comparing the genetic tests ordered in 2018 and 2019 in our dataset, the differences between the types of testing ordered were not statistically significant for genetics, non-genetics, and all providers combined. This indicates that any changes in test ordering practice due to updated testing guidelines likely did not impact the number or type of testing ordered.

While our primary scope of analysis centered on test ordering practices, we also evaluated the types of results generated from these tests and compared the percentages between genetics and non-genetics providers. Testing ordered by a genetics provider ended in a positive result in 15.71% of tests, compared to 7.25% in tests ordered by a non-genetics provider. Negative results occurred in 55% of tests ordered by genetics providers and 77.38% of tests ordered by non-genetics providers. VUS results occurred in 29.29% of tests ordered by genetics providers and 15.38% of tests ordered by non-genetics providers. Overall, the testing ordered by genetics providers produced a higher percentage of positive and VUS results (Appendix B: Tables (Table 3)). These differences could be reflective of genetics providers ordering larger panels compared to non-genetics providers. Zirkelbach et al. (2018) found that genetic counselors tend to order multi-gene panels more frequently than syndrome-specific or other limited-gene tests. The study produced no difference in the number of variant discrepancies (VUS classifications) discovered by providers ordering panel testing versus providers ordering



syndrome-specific testing, indicating that providers ordering syndrome-specific panels were not doing so to avoid results with discrepancies. Overall, the surveyed genetic counselors agreed that there was a lack of data sharing, lack of a central database, lack of educational resources, and lack of communication between the laboratories. The genetic counselors also indicated that when discrepancies occur they tailor recommendations to include personal and family history for a personalized risk, making it clear that the care of patients goes beyond the results of a genetic counseling panel (Zirkelbach et al., 2018).

### ***Limitations and Future Research Directions***

There were several limitations to this study. Notably, the data is inclusive of a single academic institution and may not be representative of all providers or provider types. It would be valuable to replicate this study using data from multiple institutions, including ones that may be more targeted in their approach to cancer genetic testing. In this particular study population, non-genetics providers ordered testing solely through two laboratories for the types of cancer-specific panels mentioned above whereas the genetics providers utilized additional genetic testing laboratories, and testing included syndrome-specific testing in addition to the cancer-specific panels. Syndrome-specific testing, which tests a single gene or a few genes related to a specific hereditary cancer predisposition syndrome, is the most straightforward form of genetic testing that carries a lower potential for a VUS result as well as a quicker turnaround time that may have importance in the medical management of cancer (Hall et al. 2014).

Lynch syndrome testing, while commonly tested for in the field of genetics, can be considered a syndrome-specific test since it looks at a limited set of genes specifically distinct to this syndrome. Although not included as part of our analysis, we recorded that 53

syndrome-specific tests were ordered by genetic counselors for hereditary cancer predisposition syndromes other than Lynch syndrome. Appropriate test codes were not available to investigate syndrome-specific testing patterns in other providers, so this may be an area for future investigation that can further delineate trends in cancer genetic testing practices among different providers.

Clinical indications for genetic testing were not available and not included in this analysis. As a result, it is unclear which proportions of the patients tested were personally affected with cancer and potentially looking to make treatment decisions and which proportions were unaffected and looking to understand and manage future cancer risks. Patient demographics including age, gender, personal history of cancer, ethnicity, insurance coverage, and education level were not considered in our analysis. Review of the current literature shows patient demographics such as age, sex, education, and socioeconomic status all play a role in how patients perceive and are able to access healthcare as well as the type of genetic testing a patient chooses to undergo (or to decline) (Olaya et al., 2009; Richter et al., 2013; Trivedi et al., 2019). Patients can seek coverage for genetic testing through their health insurance company or pay for it out-of-pocket. Some insurance companies require a patient to have pre- and post-test counseling by a board certified genetic counselor to have their testing covered (King & Mahon, 2017), but there is no guarantee that a patient's insurance company will cover a genetic test. Some patients do not have insurance and may be unable to afford genetic testing out-of-pocket, but insurance status does not seem to significantly affect patients' decisions to undergo testing (Olaya et al., 2009; Trivedi et al., 2019). On the other hand, those with a personal history of breast cancer and a higher level of education were more likely to have genetic testing.

Individuals with VUS results and lower levels of education (i.e. high school) also tended to incorrectly recall their result as well as the associated risk (Richter et al., 2013).

The specific genetic testing results were also not included in our analysis as our data only indicated positive, negative, or VUS results. Understanding the specific gene that was positive can give insight into the clinically actionable decisions inherent in that result. Testing can uncover a mutation in a lower penetrant gene that lacks specific management guidelines at this time. It can be argued that in the absence of available treatment or preventive measures, risk can still be provided to that patient and that "personal utility" can be beneficial to the patient (Hiraki et al., 2014). Alternatively, Shah and Nathanson (2017) argue the use of genetic testing and its importance is based solely on the follow-up interventions or screenings that will benefit the patients.

Future research involves understanding more about these lower penetrance genes and how to incorporate them into an actionable composite risk score for the patient (Hiraki et al., 2014). Tung et al. (2016) acknowledge the controversy in the field due to lack of clinical utility and uncertainty regarding the association of a mutation with the development of cancer (clinical validity). When mutations are found in genes with no current clinical guidelines for medical management, this can lead to inappropriate or unnecessary management for the patient. In an attempt to reduce this controversy, Tung et al. (2016) created a framework for clinicians to counsel and make clinical decisions, recognizing the importance of developing a framework as individuals will continue to be tested for moderate penetrance genes that do not have established guidelines for management while noting that the delineation of moderate and high penetrance

genes is arbitrary. There is complexity involved in understanding these moderate relative risks and how to apply these risks to medical management.

## **Conclusion**

Our study aimed to identify discrepancies in cancer genetic test ordering practices among genetics providers, including genetic counselors and geneticists as well as non-genetics providers. Analysis of 1,402 cancer genetic tests ordered over the span of 01/01/2018 to 09/30/2019 revealed that when the ordering provider was classified by provider type and ordered genetic tests were sorted by types of genes tested, there were discrepancies in test ordering practices. The 1,402 ordered tests were categorized into breast-specific panels, breast/GYN panels, Lynch/CRC panels, and general multi-gene panels including genes globally associated with common hereditary cancers. 505 of the 1,402 tests ordered (36%) were general multi-gene panels of which 330 were ordered by genetic counselors and geneticists. These discrepancies may be influenced by provider education and understanding of genetics, as well as patient demographics as suggested in the literature. While guidelines for test ordering have been proposed by different organizations, there are currently no guidelines to establish consistency among providers or across specialties. While our study was limited to a single institution, it was able to address that differences in test ordering practice are occurring among providers of that institution. Additional research will be necessary to see if ordering practice differs among providers across other institutions as well as how to address and avoid these discrepancies in the future.

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**Conflicts of Interest**

The authors have no conflicts of interest to disclose.

## References

- American College of Obstetricians and Gynecologists. (2015). Committee Opinion No. 634. Washington, DC: American College of Obstetricians and Gynecologists.
- American College of Obstetricians and Gynecologists. (2017). Committee Opinion No. 693. Washington, DC: American College of Obstetricians and Gynecologists.
- The American Society of Breast Surgeons. (2019). Consensus Guideline on Hereditary Genetic Testing for Hereditary Breast Cancer. Columbia, MD: The American Society of Breast Surgeons.
- Association for Molecular Pathology et al. v. Myriad Genetics, Inc., et al.* 133 S. Ct. 2107 (June 13, 2013).
- Baars, M. J. H., Henneman, L., & ten Kate, L. P. (2005). Deficiency of knowledge of genetics and genetic tests among general practitioners, gynecologists, and pediatricians: A global problem. *Genetics in Medicine*, 7(9), 605–610. <https://doi.org/10.1097/01.gim.0000182895.28432.c7>
- Beitsch, P. D., Whitworth, P. W., Hughes, K., Patel, R., Rosen, B., Compagnoni, G., ... Nussbaum, R. L. (2018). Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle
- Berliner, J. L., Fay, A. M., Cummings, S. A., & Burnett, B. (2013). NSGC Practice Guideline : Risk Assessment and Genetic Counseling for Hereditary Breast and Ovarian Cancer. *J Genet Counsel*, 155–163. <https://doi.org/10.1007/s10897-012-9547-1>
- Cragun, D., Camperlengo, L., Robinson, E., Caldwell, M., Kim, J., Phelan, C., ... Pal, T. (2014b). Differences in BRCA counseling and testing practices based on ordering provider type. *Genetics in Medicine*, 17(1), 51–57. <https://doi.org/10.1038/gim.2014.75>
- Cox, S. L., Zlot, A. I., Silvey, K., Elliott, D., Horn, T., Johnson, A., & Leman, R. F. (2012). Patterns of Cancer Genetic Testing: A Randomized Survey of Oregon Clinicians. *Journal of Cancer Epidemiology*, 2012, 1–11. <https://doi.org/10.1155/2012/294730>
- Hall, M. J., Forman, A. D., Pilarski, R., Wiesner, G., & Giri, N. (2014). Gene Panel Testing for Inherited Cancer Risk. *Journal of the National Comprehensive Cancer Network*, 12, 1339–1346.
- Helwick, C. (2015, February 10). Dr. Mary-Claire King Proposes Population Screening in All Young Women for BRCA Mutations. *The ASCO Post*. Retrieved from <http://www.3post.com/issues/february-10-2015/dr-mary-claire-king-proposes-population-screening-in-all-young-women-for-brca-mutations/>.

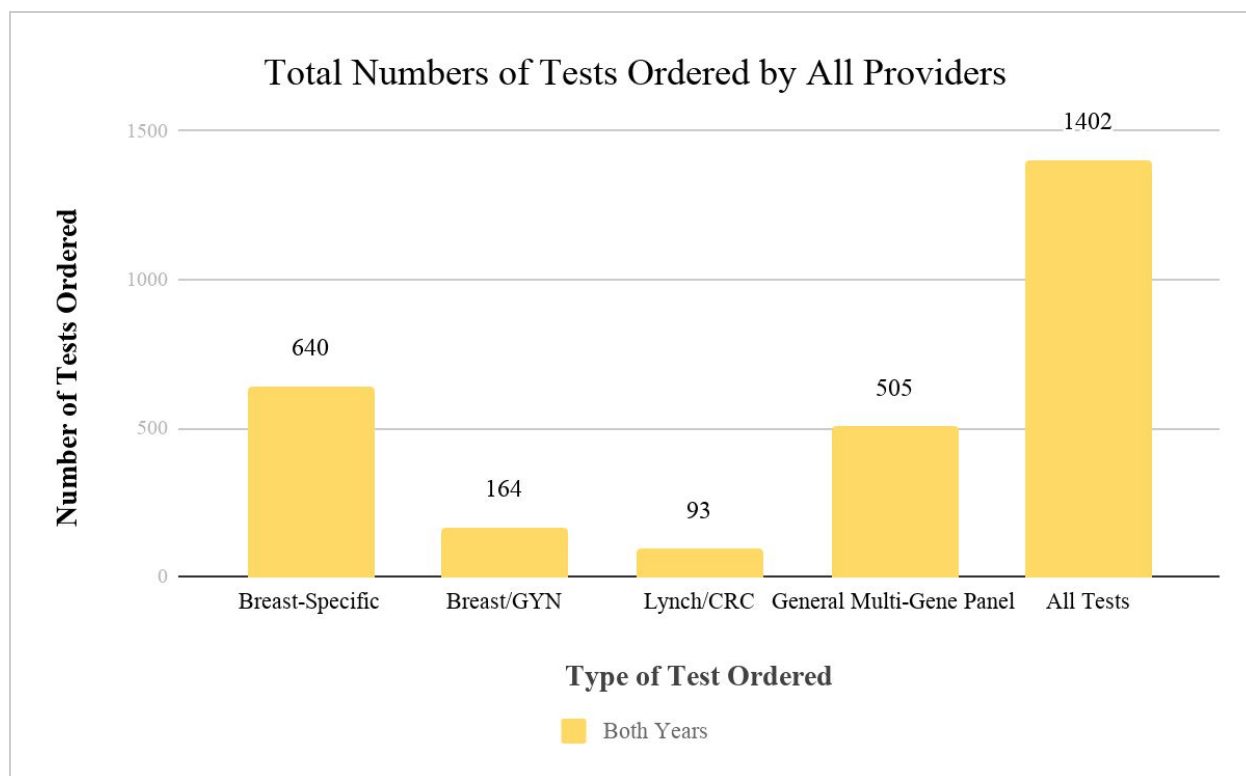
- Hereditary breast and ovarian cancer syndrome*. Practice Bulletin No. 182. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2017;130:e110–26.
- Hiraki, S., Rinella, E. S., Schnabel, F., Oratz, R., & Ostrer, H. (2014). Cancer Risk Assessment Using Genetic Panel Testing: Considerations for Clinical Application. *Journal of Genetic Counseling*, 23(4), 604–617. <https://doi.org/10.1007/s10897-014-9695-6>
- King, E., & Mahon, S. M. (2017). Genetic testing challenges and changes in testing for hereditary cancer syndromes. *Clinical Journal of Oncology Nursing*, 21(5), 589–599.
- Klitzman, R., Chung, W., Marder, K., Shanmugham, A., Chin, L. J., Stark, M., ... Appelbaum, P. S. (2012). Attitudes and Practices Among Internists Concerning Genetic Testing. *Journal of Genetic Counseling*, 22(1), 90–100. <https://doi.org/10.1007/s10897-012-9504-z>
- Lynch syndrome*. Practice Bulletin No. 147. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2014;124:1042–54.
- Miller, C. E., Krautscheid, P., Baldwin, E. E., Tvrdik, T., Openshaw, A. S., Hart, K., & LaGrave, D. (2014). Genetic counselor review of genetic test orders in a reference laboratory reduces unnecessary testing. *American Journal of Medical Genetics Part A*, 164(5), 1094–1101. <https://doi.org/10.1002/ajmg.a.36453>
- National Comprehensive Cancer Network (NCCN) Guidelines, Inc. (2018). Genetic/Familial High Risk Assessment: Colorectal (v.1.2018). Plymouth Meeting, PA: National Comprehensive Cancer Network.
- National Comprehensive Cancer Network (NCCN) Guidelines, Inc. (2019). Genetic/Familial High Risk Assessment: Breast and Ovarian (v.3.2019). Plymouth Meeting, PA: National Comprehensive Cancer Network.
- National Society of Genetic Counselors (2017). *Use of Multi-Gene Panel Tests* [Position statement]. Retrieved from <https://www.nsgc.org/p/bl/et/blogaid=870>.
- Nelson, HD, Pappas, M, Cantor, A, Haney, E, Holmes, R. Risk Assessment, Genetic Counseling, and Genetic Testing for *BRCA*-Related Cancer in Women: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*. 2019;322(7):666–685. <https://doi.org/10.1001/jama.2019.8430>
- Olaya, W., Esquivel, P., Wong, J. H., Morgan, J. W., Freeberg, A., Roy-Chowdhury, S., & Lum, S. S. (2009). Disparities in *BRCA* testing: when insurance coverage is not a barrier. *The American Journal of Surgery*, 198(4), 562–565. <https://doi.org/10.1016/j.amjsurg.2009.07.003>

- Richter, S., Haroun, I., Graham, T. C., Eisen, A., Kiss, A., & Warner, E. (2013). Variants of unknown significance in BRCA testing: impact on risk perception, worry, prevention and counseling. *Annals of Oncology*, 24(suppl 8), viii69–viii74. <https://doi.org/10.1093/annonc/mdt312>
- Shah, P. D., & Nathanson, K. L. (2017). Application of Panel-Based Tests for Inherited Risk of Cancer. *Annual Review of Genomics and Human Genetics*, 18(1), 201–227. <https://doi.org/10.1146/annurev-genom-091416-035305>
- Stanislaw, C., Xue, Y., & Wilcox, W. R. (2016). Genetic evaluation and testing for hereditary forms of cancer in the era of next-generation sequencing. *Cancer Biol Med*, 13(1), 7–9. <https://doi.org/10.28092/j.issn.2095-3941.2016.0002>
- Trivedi, M. S., Jones, T., Jiang, X., Underhill, M. L., Bose, S., Silverman, T., ... Crew, K. D. (2019). Abstract P5-09-01: Racial/ethnic differences in BRCA1/2 and multigene panel testing among young breast cancer patients. *San Antonio Breast Cancer Symposium*, 79(4). <https://doi.org/10.1158/1538-7445.SABCS18-P5-09-01>
- Tung, N., Battelli, C., Allen, B., Kaldate, R., Bhatnagar, S., Bowles, K., ... Hartman, A. R. (2015). Frequency of mutations in individuals with breast cancer referred for BRCA1 and BRCA2 testing using next-generation sequencing with a 25-gene panel. *Cancer*, 121(1), 25–33. <https://doi.org/10.1002/cncr.29010>
- Tung, N., Domchek, S. M., Stadler, Z., Nathanson, K. L., Couch, F., Garber, J. E., ... Robson, M. E. (2016). Counselling framework for moderate-penetrance cancer-susceptibility mutations. *Nature Reviews Clinical Oncology*, 13(9), 581–588. <https://doi.org/10.1038/nrclinonc.2016.90>
- The U.S. Preventive Services Task Force. (2019). Draft Recommendation Statement: BRCA-Related Cancer: Risk Assessment, Genetic Counseling, and Genetic Testing - US Preventive Services Task Force. Retrieved June 6, 2019, from <https://www.uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/brca-related-cancer-risk-assessment-genetic-counseling-and-genetic-testing>
- Willoughby, A., Andreassen, P., & Toland, A. (2019). Genetic Testing to Guide Risk-Stratified Screens for Breast Cancer. *Journal of Personalized Medicine*, 9(1), 15. <https://doi.org/10.3390/jpm9010015>
- Zirkelbach, E., Hashmi, S., Ramdaney, A., Dunnington, L., Ashfaq, M., Nugent, E. K., & Wilson, K. (2018). Managing Variant Interpretation Discrepancies in Hereditary Cancer: Clinical Practice, Concerns, and Desired Resources. *Journal of Genetic Counseling*, 27(4), 761–769. <https://doi.org/10.1007/s10897-017-0184-6>

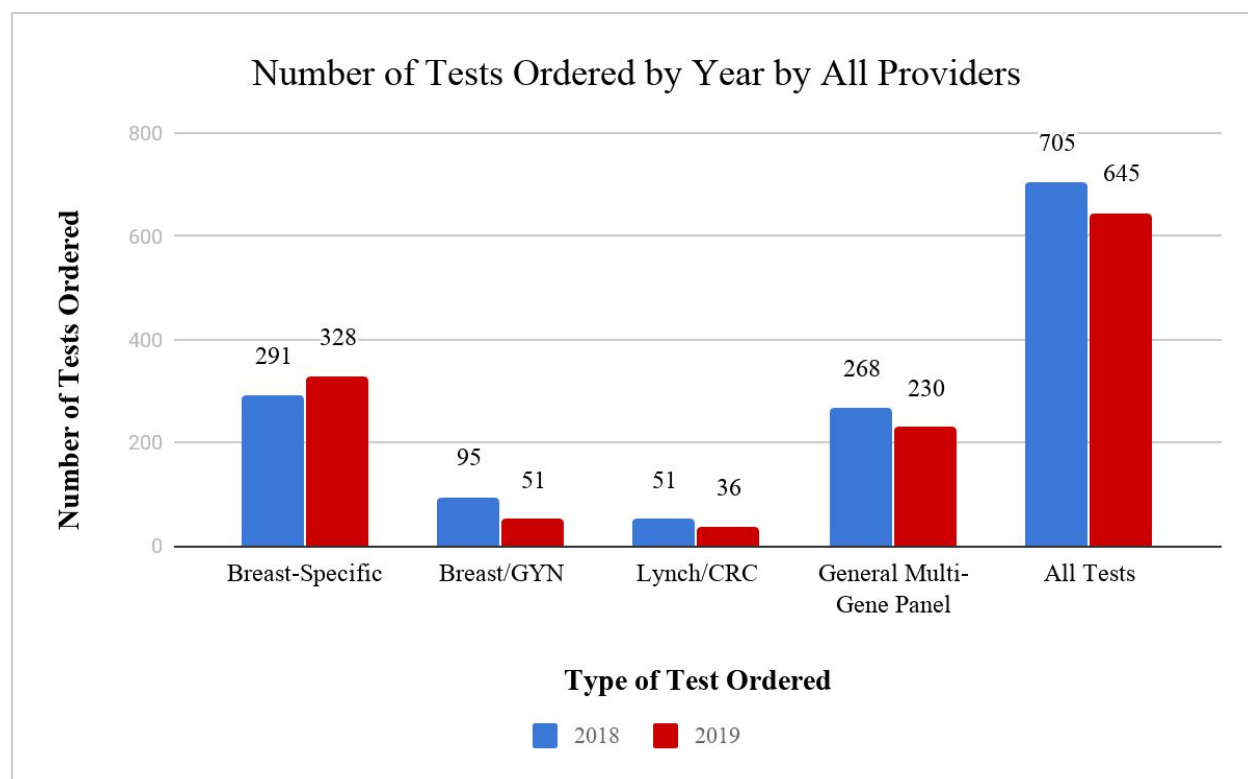


## Appendix A: Figures

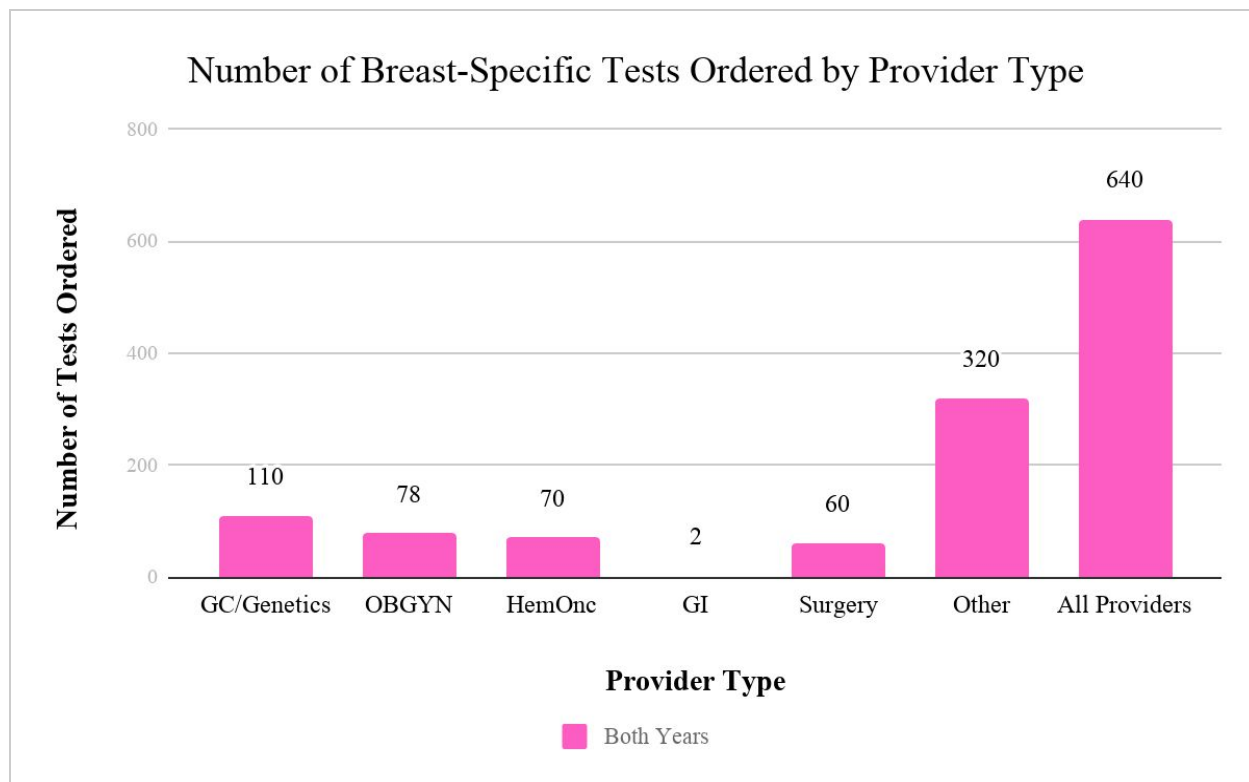
**Figure 1**



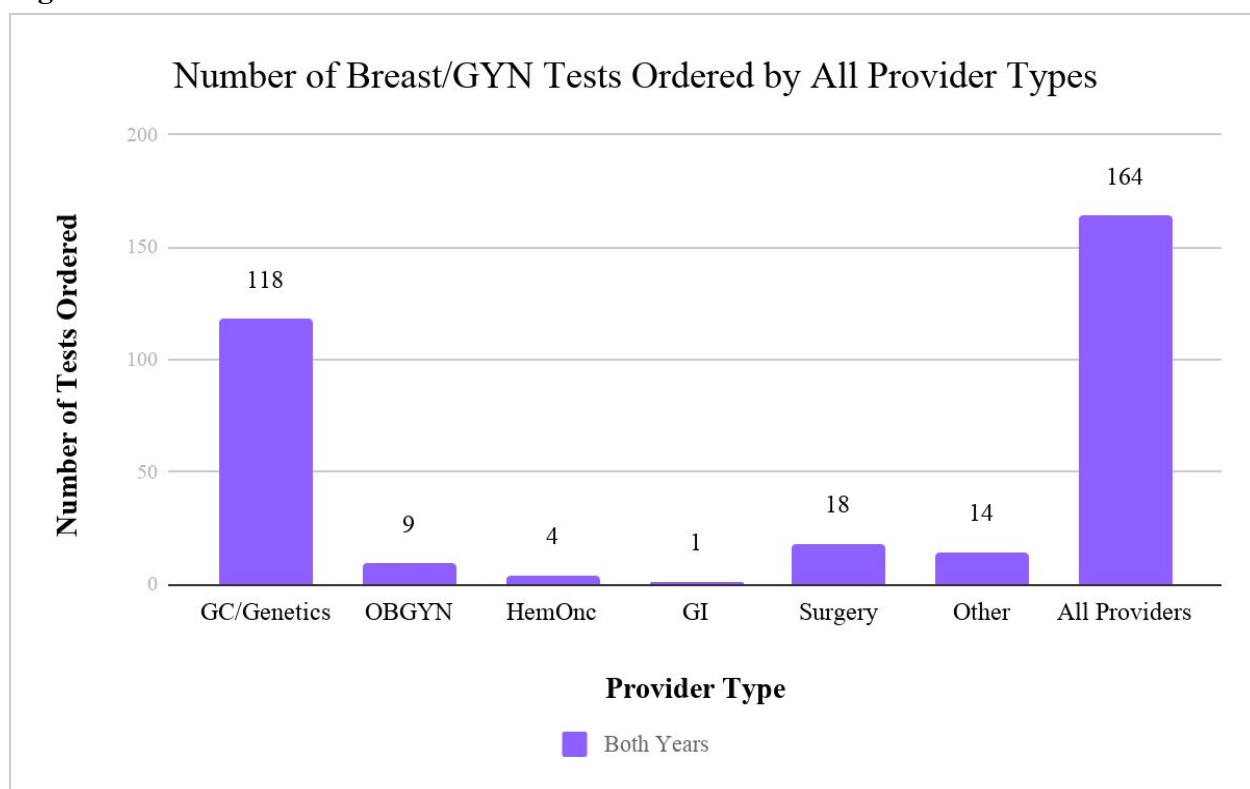
Total numbers of each cancer genetic test type ordered by all provider types

**Figure 2**

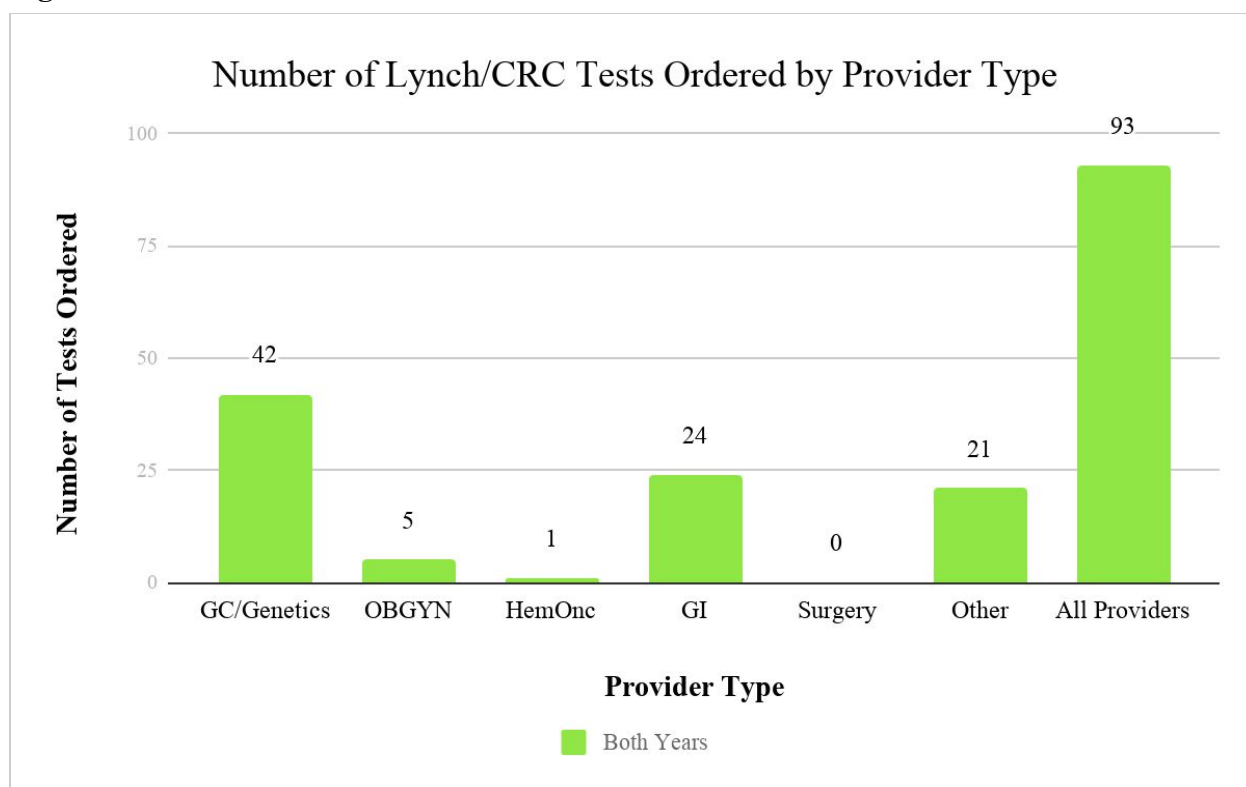
Numbers of each cancer genetic test type ordered by all provider types in 2018 and 2019

**Figure 3**

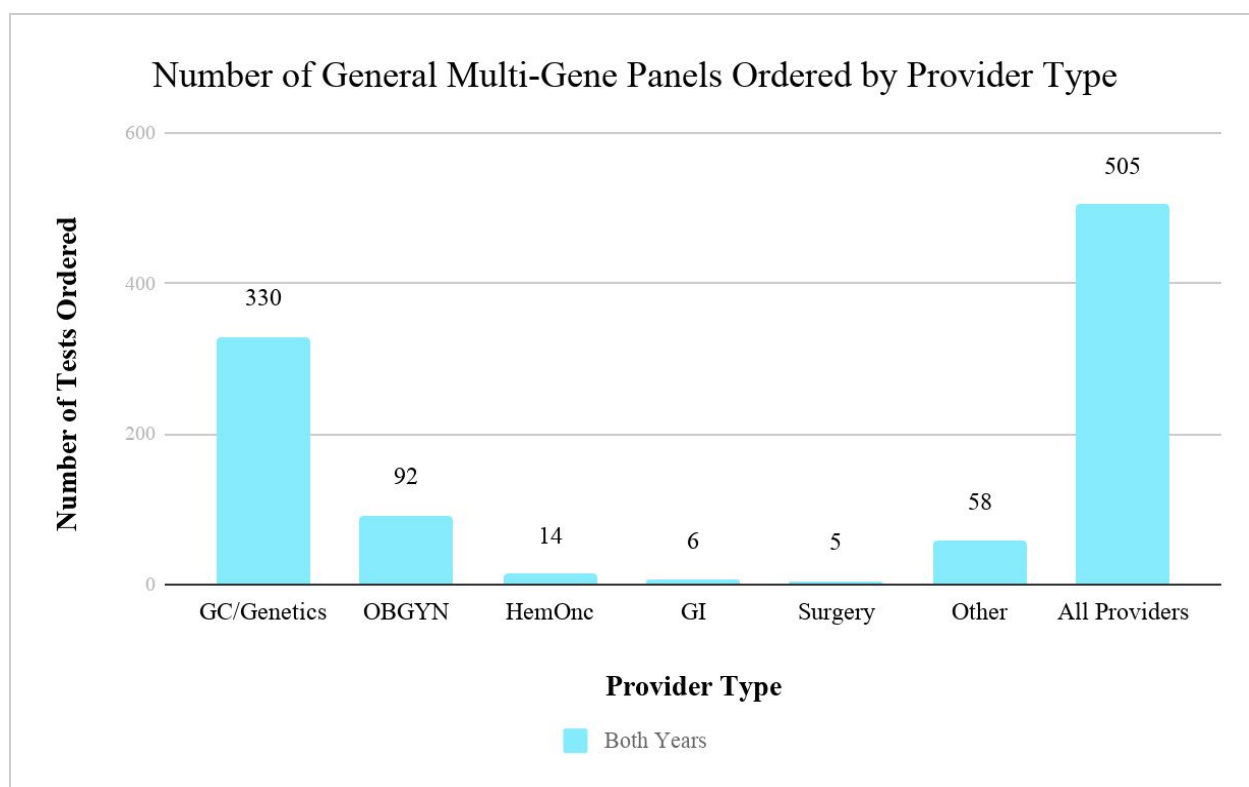
Numbers of breast-specific cancer genetic tests type ordered by each provider type

**Figure 4**

Numbers of breast/GYN cancer genetic tests type ordered by each provider type

**Figure 5**

Numbers of Lynch/CRC cancer genetic tests type ordered by each provider type

**Figure 6**

Numbers of general multi-gene panels ordered by each provider type

**Appendix B: Tables****Table 1**

<b>Provider Type</b>	<b>P-Value</b>
Non-Genetics Providers	0.34
Genetics Providers	0.53
All Providers	0.45

P-values for three paired samples t-tests comparing test types ordered by non-genetics, genetics, and all providers between 2018 and 2019

**Table 2**

Parameter	Results
Chi-Square Value	704.977
Critical Value	24.996
<b>P-Value</b>	<b>1.616E-140</b>

Chi-square, critical, and P-values generated from a chi-square analysis of test types ordered and provider type



**Table 3**

<b>Genetic Test Result</b>	<b>Genetics Providers</b>	<b>Non-Genetics Providers</b>	<b>All Providers</b>
VUS	41	123	164
Positive	20	50	70
Likely pathogenic variant	2	8*	10
Negative	77	619	696
Total with results	<b>140</b>	<b>800</b>	<b>940</b>
%VUS	29.29%	15.38%	17.45%
%Positive	15.71%	7.25%	8.51%
%Negative	55.00%	77.38%	74.04%

Genetic test results by provider type