


MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)	
Effective Date: 01/01/2021  <div style="text-align: right;">1/1/2021</div>	Section: GT	Policy No: 388
	Medical Policy Committee Approved Date: 1/18; 1/19; 5/19; 11/19; 03/2020; 12/2020	
Medical Officer	Date	

See Policy CPT CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All lines of business except Medicare

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

Notes:

- Genetic tests addressed in this policy only include the following well-defined inherited cancer syndromes:
 - Hereditary Non-Polyposis Colorectal Cancer (HNPCC, also known as Lynch Syndrome);
 - Familial Adenomatous Polyposis (FAP) and Attenuated FAP (AFAP);
 - MYH-associated Polyposis (MAP).
- Testing for additional, lower penetrant syndromes or genes are not addressed by this policy.
- This policy does not address immunohistochemistry (IHC) or microsatellite instability (MSI) tests, which may be considered medically necessary and standard of care in patients with colon or endometrial cancer.

MEDICAL POLICY

**Genetic Testing: Inherited
Susceptibility to Colorectal Cancer
(All Lines of Business Except
Medicare)**

- Both maternal and paternal family histories must be considered separately when identifying families with an increased risk of colorectal cancer.
- When possible, family members with cancer associated with inherited colorectal cancer should be tested first, prior to testing unaffected members. Testing an unaffected member has significant limitations on interpreting test results. Pre-test counseling notes should document the reason why an affected family member cannot be tested prior to testing an unaffected member.

Genetic Counseling

- I. The following genetic counseling criteria must be met prior to testing of *APC*, *MUTYH*, mismatch repair (MMR) genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*) and/or *EPCAM* gene:
 - A. Provider meets NCCN guidelines as a certified genetic counselor or board-certified physician trained in cancer genetics*; (see Policy Criteria Guidelines section below) **and**
 - B. A full personal and family history, which includes first-, second-, and third-degree pedigree**, has been conducted and is documented; **and**
 - C. Genetic testing information and pre-test counseling has been provided and is documented; **and**
 - D. Patient has undergone and signed informed consent for genetic testing; **and**
 - E. Post-test counseling to review the test results and determine future medical management and treatment plans has been discussed and will be scheduled.

Genetic Testing: Covered Testing

- II. Genetic testing for a single gene or any combination of the following genes (*APC*, *MUTYH*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, and/or *EPCAM*) may be considered **medically necessary and covered** for the evaluation of high-risk colorectal cancer syndromes when criterion I. above is met **and any one** of the following criteria (A.-D.) are met:
 - A. Documentation indicates a first-degree relative** has a known pathogenic mutation in one of the genes listed above and testing is based on the identified mutation; **or**
 - B. Patient has a personal history of **any one** of the following (1.-6.):
 1. Greater than 10 adenomas; **or**
 2. Colorectal or endometrial cancer diagnosed <50 years; **or**
 3. Colorectal or endometrial cancer and another Lynch Syndrome (LS)-related cancer*** (can be synchronous or metachronous); **or**
 4. Colorectal or endometrial cancer and one or more first- or second-degree relative(s) with an LS-related cancer diagnosed <50 years; **or**
 5. Colorectal or endometrial cancer and two or more first- or second-degree relatives with an LS-related cancer, regardless of age; **or**

MEDICAL POLICY

**Genetic Testing: Inherited
Susceptibility to Colorectal Cancer
(All Lines of Business Except
Medicare)**

6. Colorectal or endometrial cancer at any age with tumor showing evidence of mismatch repair deficiency, either by microsatellite instability (MSI) or loss of MMR protein expression; **or**
- C. Patient has a family history of **any one** of the following (1.-5.):
 1. One or more relative(s) with polyposis (greater than 10 adenomas); **or**
 2. One or more first-degree relative(s)** with colorectal or endometrial cancer diagnosed <50 years; **or**
 3. One or more first-degree relative(s)** with colorectal or endometrial cancer and another LS-related cancer***; **or**
 4. Two or more first- or second-degree relative(s)** with LS-related cancers, including one or more diagnosed <50 years; **or**
 5. Three or more first- or second-degree relative(s)** with LS-related cancers, regardless of age; **or**
- D. An individual with a LS-related cancer or an unaffected individual with a ≥5% risk for having an MMR gene mutation based on one of the following prediction models: MMRpro, PREMM5, or MMRpredict. **** (See Policy Guidelines for links to tools.)

III. Genetic testing for *BRAF* V600E or *MLH1* promoter methylation testing is considered **medically necessary and covered** to rule out a diagnosis of Lynch syndrome in patients with a loss of DNA protein expression of *MLH1* on IHC tumor testing or an MSI-H test result.

Genetic Testing: Non-covered Testing

- IV. Genetic testing for *APC*, *MUTYH*, *MLH1*, *MSH2*, *MSH6*, *PMS2* and/or *EPCAM* gene mutation(s) is considered **not medically necessary and is not covered** when criteria I., II., or III., are not met, including but not limited to the following:
 - A. Cancer risk assessment in the general population.
 - B. When the genetic variant reported in a family member is a variant of unknown significance (VUS) (also known as unclassified variant, variant of uncertain significance).
 - C. When testing in criteria III. above results in a positive test for the *BRAF* V600E mutation and/or *MLH1* promoter hypermethylation.
- V. Genetic panel testing which includes genes other than *APC*, *MUTYH*, *MLH1*, *MSH2*, *MSH6*, *PMS2* and/or *EPCAM* is considered **investigational and is not covered**. Examples of investigational panels include, but are not limited to, the following:
 - A. Myriad myRisk® panel test
 - B. Ambry ColoNext® panel test
 - C. GeneDx Colorectal Cancer Panel test

MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)
-----------------------	---

Link to [Policy Summary](#)

POLICY CRITERIA GUIDELINES

Genetic Panel Testing

The clinical utility of testing has been established for all six of the genes listed above in the policy criteria. Therefore, when medical necessity criteria are met, genetic panel testing for Lynch and well-defined polyposis syndromes may include one or more of **any combination** of the genes listed in this section above. For example, genetic panels, such as the Myriad’s COLARIS® panel test, which includes only the genes, or a subset of the genes, addressed in the medical necessity criteria (II.) above, may be considered medically necessary when criteria are met.

*Genetic Counseling Requirements¹⁻³

Genetic studies and counseling are approved subject to benefits when there is a medical condition that requires genetic counseling and potential subsequent testing to diagnose or to aide in planning a treatment course. Identification of a genetic disorder should result in medical and/or surgical management that is corrective and/or therapeutic in nature.

Prior to authorization of a genetic test, the member must have undergone pretest counseling by a certified genetic counselor or a provider trained in cancer genetics. A provider trained in cancer genetics is defined as providing cancer risk assessment on a regular basis and having received specialized ongoing training in cancer genetics. Education limited to learning how to order a test is not considered adequate training for cancer risk assessment and genetic counseling. The provider may be required to provide documentation of genetic training and ongoing continual medical education (CME). Examples of providers trained in genetic counseling are:

- Board-Eligible or Board-Certified Genetic Counselor (CGC)
- Advanced Genetics Nurse (AGN-BC), Genetic Clinical Nurse (GCN)
- Advanced Practice Nurse in Genetics (APNG)
- Board-Eligible or Board-Certified Clinical Geneticist
- Board-Certified Physician with training and ongoing experience in cancer genetics (e.g., Colorectal Surgeon, Surgeon Oncologist, Gastroenterologist, Oncology Nurse)

The genetic counseling visit is expected to encompass the following:

1. Pretest counseling documenting:
 - Comprehensive family history/pedigree which includes first-, second- and third-degree relatives on both maternal and paternal side of the family; **and**
 - Evaluation of a patients cancer risk; **and**

MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)
-----------------------	---

- Highlight the purpose of the genetic testing, potential outcomes and implications for the patient and his or her family members, and the cancer risks associated with the genes being tested; **and**
 - A differential diagnosis and documentation of having educated the member on inheritance patterns, penetrance, variable expressivity and the possibility of genetic heterogeneity; **and**
 - Documentation that the member has been prepared for possible outcomes of testing including positive, negative and uncertain findings; **and**
 - When possible, family members with cancer associated with inherited colorectal cancer should be tested first, prior to testing unaffected members.
 - Documentation that testing an unaffected member has significant limitations on interpreting test results. Pre-test counseling note should document the reason why none of these members can be tested prior to testing an unaffected member; **and**
 - Informed consent for genetic testing was obtained.
2. Posttest counseling will be scheduled and expected to provide the following:
- Results along with their significance and impact and recommended medical and/or surgical management options; **and**
 - Interpretation of results in context of personal and family history of cancer and other factors that inform risk assessment (e.g., medical/surgical history) ; **and**
 - Informing and recommending testing of at-risk family members; **and**
 - Providing available resources such as disease-specific support groups and research studies; **and**
 - Appropriate referral to medical specialties to assist with long term medical management and risk reduction strategies
 - If a mutation is found, post-test counseling will include not only the affected member but recommendations regarding inherited risk to relatives and options for risk assessment and management; **and**
 - If a mutation is found in a patient of reproductive age, post-test counseling will also include reproductive decision-making and/or risk assessment and management.
 - If a mutation is found in presymptomatic individuals, post-test counseling will also include screening, increased surveillance and the option of risk-reducing surgeries after risk assessment
 - If a mutation is not identified, post-test counseling is critical to avoid false-negative interpretations of test results.

****Close Blood Relatives**

The National Comprehensive Cancer Network (NCCN) defines close blood relative as first- (parents, siblings and children), second- (grandparents, aunts, uncles, nieces and nephews, grandchildren and half-siblings), and third degree-relatives (great-grandparents, great-aunts, great uncles, great grandchildren and first cousins) on same side of family.^{1,2}

MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)
-----------------------	---

***Lynch Syndrome-Related Cancers

Lynch syndrome-related cancers include: colorectal, endometrial, gastric, ovarian, pancreatic, ureter or renal pelvis, brain (usually glioblastoma), small intestinal cancers, sebaceous adenomas and carcinomas, and keratoacanthomas as seen in Muir–Torre syndrome.

****MMR Gene Mutation Risk Prediction Models

- MMRpro: <http://www4.utsouthwestern.edu/breasthealth/cagene/>
- PREMM5: <http://premm.dfc.harvard.edu/>
- MMRpredict: <http://hnpccpredict.hgu.mrc.ac.uk/>

CPT CODES

All Lines of Business Except Medicare	
Prior Authorization Required	
0157U	APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosis polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary procedure)
0158U	MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0161U	PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure)
0238U	Oncology (Lynch syndrome), genomic DNA sequence analysis of MLH1, MSH2, MSH6, PMS2, and EPCAM, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions
81201	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis[FAP] gene analysis, full gene sequence
81202	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis [FAP] gene analysis, known familial variants

MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)
-----------------------	---

81203	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis [FAP] gene analysis; duplication/deletion variants
81210	BRAF (v-raf murine sarcoma viral oncogene homolog B1) (e.g. Colon Cancer) gene analysis, V600E variant
81288	MLH1 (mutl. Homolog1, colon cancer, non-polyposis type 2 (e.g. hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
81292	MLH1 (mutl. Homolog1, colon cancer, non-polyposis type 2 (e.g. hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81293	MLH1 (homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non- polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-Polyposis colorectal cancer, Lynch Syndrome) gene analysis; duplication/deletion variants
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81297	MSH2 (mutS homolog 2, colon cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81298	MSH6 (mutS homolog 6 [E.coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81299	MSH6 (mutS homolog 6 [E.coli])(e.g. hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81300	MSH6 (mutS homolog 6 [E.coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) – when used for MUTYH (mutY homolog [E. coli]) (eg, MYH-associated polyposis), common variants (eg, Y165C, G382D)
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons) – when used for EPCAM (epithelial cell adhesion molecule) (eg, Lynch syndrome), duplication/deletion analysis

MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)
-----------------------	---

81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) – when used for MUTYH (mutY homolog [E. coli]) (eg, MYH-associated polyposis), full gene sequence
81435	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include sequencing of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11
81436	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); duplication/deletion analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
Not Covered	
0101U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with mRNA analytics to resolve variants of unknown significance when indicated (15 genes [sequencing and deletion/duplication], EPCAM and GREM1 [deletion/duplication only])
Unlisted Codes All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then prior-authorization is required.	
81479	Unlisted molecular pathology procedure

DESCRIPTION

Clinical Utility of Genetic Testing

Establishing the clinical utility of any test is a key component in determining its ultimate usefulness. Clinical utility may be established when published evidence demonstrates test results can be used to:

1. Guide treatment, management, or preventive decisions; **and**
2. Those decisions lead to improved primary health outcomes.

MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)
-----------------------	---

Genetic Panel Testing

Numerous genetic panels are available which test for various combinations of genes associated with hereditary colorectal cancers. Some well-designed genetic panel tests include only the genes that have demonstrated clinical utility and high penetrance for Lynch and well-defined polyposis syndromes. However, other panel tests include a broader range of genes for these and other related cancer syndromes for which penetrance levels are intermediate and low and the clinical utility of testing is not yet established. It is not recommended that patients undergo testing for gene mutations with unknown clinical significance as test results may lead to unnecessary interventions and additional testing which is not supported by current evidence or practice standards. Therefore, the clinical utility of each gene included in a panel must be demonstrated in order to establish the medical necessity of the panel test.

REVIEW OF EVIDENCE/CLINICAL PRACTICE GUIDELINES

The medical necessity criteria within this policy are primarily supported and guided by the National Comprehensive Cancer Network (NCCN) Genetic/Familial High-Risk Assessment: Colorectal clinical practice guidelines.

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines (v.3.2019) regarding genetic/familial high-risk assessment for colorectal cancer recommend a stepwise approach, with genetic testing performed in the following order:¹

1. Individual with personal history of cancer and a known genetic mutation in the family.
2. Individual with a personal or family history of polyps indicative of a polyposis syndrome.
3. Individual with a personal or family history of Lynch syndrome and LS-related cancers.

However, NCCN states that multi-gene testing has a number of advantages over sequential testing including that is more efficient, has a higher chance of providing an explanation for the cause of cancer, and the cost is similar to that of sequential testing.

In addition, NCCN states that there are many clinical scenarios in which multi-gene testing may be considered, with some examples including:

- When more than one gene can explain an inherited cancer syndrome (e.g., Lynch syndrome).
- When personal and/or family history meets criteria for more than one hereditary cancer syndrome (e.g., family meets both BRCA-related breast cancer and Lynch syndrome clinical criteria).
- When colonic polyposis has uncertain histology.

The NCCN guideline stated that multi-gene testing should be done in the context of pre- and post-test genetic counseling by certified genetic counselors or clinicians with extensive training in genetics.

MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)
-----------------------	---

POLICY SUMMARY

There is sufficient evidence that genetic testing for *APC*, *MUTYH*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, and/or *EPCAM* gene mutations associated with well-defined cancers syndromes including Lynch and polyposis syndromes (FAP and MAP) improves health outcomes for patients and their families where there is a history of colorectal cancer. In addition, current clinical practice guidelines recommend genetic testing for individuals at high risk for these colorectal cancer syndromes.

There is sufficient evidence that that tumor testing for a *BRAF* V600E mutation or for *MLH1* promoter methylation can help to exclude Lynch syndrome in patients with a personal history of cancer, since the presence of either is indicative of sporadic, rather than Lynch syndrome associated cancer. Testing prevents the need for additional genetic testing and directs medical management. In addition, current clinical practice guidelines recommend testing for *BRAF* V600E or *MLH1* promoter methylation as part of the evaluation of patients with a personal history of cancer and available tumor sample.

Genetic testing for Lynch and polyposis syndromes has not been shown to lead to improved health outcomes for individuals who do not have specific risk factors, as outlined in the policy criteria above. In addition, testing for a known familial variant that has been reported as a variant of uncertain significance (VUS) leads to uncertain clinical management and possible overtreatment and over-screening. Therefore, current clinical practice guidelines do not support testing in these situations.

There is insufficient evidence that multi-gene panel testing that includes genes other than *APC*, *MUTYH*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, and/or *EPCAM* for Lynch and polyposis syndromes leads to improved health outcomes. In addition, current clinical practice guidelines do not support testing in these situations.

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (All Lines of Business Except Medicare)
-----------------------	---

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

REFERENCES

1. National Comprehensive Cancer Network (NCCN) Guidelines. Genetic/Familial High-Risk Assessment: Colorectal. V.3.2019. December 13, 2019. https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf. Accessed 2/13/2020.
2. National Comprehensive Cancer Network (NCCN) Guidelines. Genetic/Familial High-Risk Assessment: Breast and Ovarian. V.1.2020. December 4, 2019. https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf. Accessed 2/13/2020.
3. Robson ME, Bradbury AR, Arun B, et al. American Society of Clinical Oncology Policy Statement Update: Genetic and Genomic Testing for Cancer Susceptibility. *Journal of Clinical Oncology*. 2015;33(31):3660-3667. <http://ascopubs.org/doi/abs/10.1200/JCO.2015.63.0996>