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North Carolina (NC) Division of Medical Assistance (DMA), Clinical Policy Section
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North Carolina Department of Health and Human Services

Re: NC Medicaid and NC Health Choice Program coverage of genetic testing for susceptibility to breast and ovarian cancer

Dear esteemed members of the North Carolina Division of Medical Assistance (DMA) and Physician Advisory Group,

We are pleased to submit the following comments in support of coverage of genetic testing for susceptibility to breast and ovarian cancer.

What is important to your constituents/colleagues in regard to this proposed policy?

Our 30+ organizations represent millions of Americans, including North Carolina residents, affected by hereditary breast, ovarian, and related cancers. Screening for germline mutations that place an individual at increased risk of cancer has become standard of care. As you likely know, North Carolina is one of only four state Medicaid programs in the U.S. that does not provide genetic counseling and testing for cancer susceptibility.

North Carolina Medicaid recipients are being denied access to a potentially life-saving intervention. Genetic counseling and testing is a useful tool in identifying individuals who are at increased risk of breast, ovarian, and other cancers. Knowledge of an inherited genetic mutation in genes such as BRCA1, BRCA2 and others allows an unaffected, high-risk individual and their health care providers to make informed decisions in an effort to prevent or detect cancer at an early stage when it is easier to treat. For those who already have or had a cancer diagnosis, genetic testing is useful in guiding surgical and treatment decisions, and may improve the ability to prevent recurrences and additional primary cancers.

Would you recommend any unit or other limitations to the service?

Clinical assessment of an individual's risk of hereditary cancer should be based on the evaluation of family history, age of onset, and type of cancer. Patients who appear to meet criteria for further risk assessment and testing should be referred to a genetics expert for pre- and post-test counseling. A genetics expert can determine the appropriateness of genetic testing, discuss medical implications of a positive or a negative test result, the possibility that a test result might not be informative, the psychological implications of genetic test results, and the risk of passing a mutation to children. Upon receipt of the test

results, a genetic counselor can explain the result implications for the individual and their family members, provide guidance on recommended follow-up care, and refer to appropriate health care professionals. With this in mind, a minimum of two appointments with a genetic counselor should be covered.

The most recognized hereditary causes of breast, ovarian and related cancers are pathogenic mutations in the BRCA1 and BRCA2 genes. Screening for these mutations should be the minimum “unit” provided (full sequencing, duplication/deletion, and large rearrangements testing).

It is important to acknowledge that many familial breast and ovarian cancers do not have mutations in a BRCA gene. Mutations in over 20 other genes have also been shown to significantly increase risk of hereditary breast, ovarian and related cancers. The National Comprehensive Cancer Network (NCCN) has developed clinical management guidelines and recommendations for a number of these mutations.¹ As such, results of multigene panel testing can directly impact prevention, screening, treatment plans, and clinical decision-making. Many consider multigene panel testing a more practical and cost-effective approach versus separate gene tests or targeted panels. NCCN notes, “When more than one gene can explain an inherited cancer syndrome, then multi-gene testing may be more efficient and/or cost-effective.” Additionally, it states, “There may be a role for multi-gene testing in individuals who have tested negative (indeterminate) for a single syndrome, but whose personal or family history remains suggestive of an inherited susceptibility.”

The clinical value of identifying people with an inherited mutation associated with increased susceptibility to cancer lies in an individual’s ability to access appropriate, evidence-based screening and preventive services that significantly lowers their risk for cancer or facilitates better surgical and treatment decisions. As such, it is crucial that individuals identified as high-risk are able to receive recommended screenings and risk-reducing interventions. NCCN has well-defined management guidelines for these patients. For women who carry a germline BRCA mutation, this may include clinical breast exams, breast screening MRIs, mammograms, transvaginal ultrasound with serum CA-125, chemoprevention, and/or risk-reducing surgery.² For men who carry a BRCA mutation this may include clinical breast exams and prostate cancer screening at an early age. We strongly recommend that NC Medicaid and Health Choice follow the NCCN BRCA-Mutation Positive Management guidelines for patients identified as BRCA mutation carriers.

If these services should be limited to certain diagnoses please include your recommendations with evidence to support the diagnoses that you have recommended.

Referral to a genetics expert for further evaluation should be available to individuals who meet the hereditary cancer risk threshold as determined by an evidence-based familial risk-stratification tool. This evaluation instrument should include health/cancer history for three generations of family members (parents, grandparents, aunt/uncles, cousins, siblings) for all biological relatives.

Historically, women have been the focus of screening for a genetic mutation associated with increased risk of breast and ovarian cancer. However, men also carry these mutations and may benefit from genetic counseling and testing. Men with mutations are at increased risk of prostate (often aggressive), pancreatic, melanoma and breast cancers. We urge you to consider offering genetic services to men who meet the criteria for risk assessment.

Testing for BRCA1, BRCA2 and/or other germline mutations should be limited to individuals age 18 and above. The only possible exception is Li-Fraumeni syndrome (LFS), which can onset before 18 years of age. Cancer.Net explains that, "Testing a child in a family with LFS is a complex situation since the decision to do testing must be made by the child's parents, with the help of medical experts. However, since cancers occur often among children in families with LFS, testing at-risk children, rather than delaying testing until young adulthood, must also be strongly considered when the goal is to find LFS-related cancers early and treat them more effectively."³ Two recent studies explored the implications of testing children in families with a known TP53 mutation, however, guidelines for testing children for this condition do not currently exist.^{4, 5}

Is there any additional evidence in medical literature on the procedure that you would like to present?

There is broad consensus on the medical benefits of genetic counseling and testing to identify individuals at high risk of breast, ovarian, and related cancers. The U.S. Preventive Services Task Force (USPSTF),⁶ National Comprehensive Cancer Network (NCCN), American Congress of Obstetricians and Gynecologists (ACOG),⁷ American Society of Clinical Oncology (ASCO),⁸ Society of Gynecologic Oncology (SGO),⁹ and others recommend screening and identification of individuals at increased risk of cancer.

A recent study published in the *American Journal of Managed Care* showed that genetic counselors save costs across the genetic testing spectrum.¹⁰ In addition to ensuring that hereditary cancer testing is appropriate for the patient, genetic counselors help physicians choose the right test, which ultimately improves clinical outcomes and saves money.

While the clinical utility of identifying people who have susceptibility to breast, ovarian, and related cancers is well-recognized, there is increasing evidence that genetic testing for BRCA and other mutations is a cost-effective approach to patient care.^{11, 12, 13} "Testing allows targeted high-level surveillance for gene mutation carriers, which ensures the cost-effective use of resources and reduces cancer-related morbidity if clinical recommendations for intervention are adopted."¹⁴ Additional research indicates that risk-reducing surgeries result in further cost savings.^{15, 16} "Surgical prophylactic interventions for known BRCA mutation carriers are very effective and cost-effective, although more so in younger women... These interventions are life-saving even when delayed."¹⁷

What criteria would you include in the proposed policy to define the service and identify community standards of practice?

Although the U.S. Preventive Services Task Force endorses genetic screening for “women who have family members with breast, ovarian, tubal, or peritoneal cancer” it does not specify criteria for risk assessment, a preferred screening tool, or standards of practice. USPSTF initially maintained that its guidelines are aimed at prevention—and that once a woman has cancer, genetic testing is no longer preventive. However, these women are at risk of other cancers that can be prevented. Appropriately, a clarification was issued jointly by the U.S. Departments of Labor and Health and Human Services indicating that the guidelines also apply to women who have “previously been diagnosed with cancer.”¹⁸ The National Comprehensive Cancer Network is commonly recognized as the expert in defining appropriate services and interventions related to cancer. Therefore, we recommend that NC Medicaid and NC Health Choice refer to NCCN when developing its policies and standards of practice. cursory research indicates that other state Medicaid programs refer to NCCN for guidance.^{19, 20, 21, 22}

Are you aware of any procedure codes that are currently being used for this service?

Procedure codes often used in relation to this service include, but are not limited to:

CPT Codes	Description
81162	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis
81211	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (e.g., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)
81212	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
81213	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants
81214	BRCA1 (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants (i.e., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)
81215	BRCA1 (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant

NC Medicaid & Health Choice Program

Genetic testing for susceptibility to breast and ovarian cancer

CPT Codes	Description
81432	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53
81433	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11
81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
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
81297	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal 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; full sequence analysis
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
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81321	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
81323	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant
96040	Medical genetics and genetic counseling services, each 30 minutes, face-to-face with patient/family
HCPCS Coding	Description
S0265	Genetic counseling, under physician supervision, each 15 minutes

*NC Medicaid & Health Choice Program
Genetic testing for susceptibility to breast and ovarian cancer*

Thank you for your consideration. We trust that you will see the value of genetic testing for high-risk individuals and look forward to working with you to improve care for North Carolina Medicaid and Health Choice Program beneficiaries.

Sincerely,

Lisa Schlager
Vice President, Public Policy
FORCE: Facing Our Risk of Cancer Empowered

Kelly Kashmer
Founder & President
NothingPink

American Women Unite for Breast Cancer Screening
Association for Molecular Pathology
Breast Cancer Comfort Site
CancerCare
Cancer Support Community
CCARE Lynch Syndrome
Colorectal Cancer Alliance
Critical Mass: The Young Adult Cancer Alliance
Don't be a Chump! Check for a Lump!
Foundation for Women's Cancer
HIS Breast Cancer Awareness
Living Beyond Breast Cancer
Male Breast Cancer Coalition
Men Against Breast Cancer
National Association of Nurse Practitioners in Women's Health
National Patient Advocate Foundation
National Ovarian Cancer Coalition
National Society of Genetic Counselors
Nothing Pink
Oncology Nursing Society
Ovarian Cancer Research Fund Alliance
Pretty In Pink Foundation
SHARE
Sharsheret
Society of Gynecologic Oncology
Teal Diva
The Jewish Federations of North America
Tigerlily Foundation
Triage Cancer
ZERO - The End of Prostate Cancer

NC Medicaid & Health Choice Program
Genetic testing for susceptibility to breast and ovarian cancer

¹ NCCN Clinical Practice Guidelines in Oncology, Genetic/Familial High-Risk Assessment: Breast and Ovarian Cancer, Version 1.12018, GENE-1-5
(https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf)

² NCCN Clinical Practice Guidelines in Oncology, Genetic/Familial High-Risk Assessment: Breast and Ovarian Cancer, Version 1.12018, BRCA-A, 1 of 2
(https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf)

³ Cancer.Net, Li-Fraumeni Syndrome, Approved by the Cancer.Net Editorial Board, 10/2017
(<https://www.cancer.net/cancer-types/li-fraumeni-syndrome>)

⁴ Should Genetic Testing be Offered for Children? The Perspectives of Adolescents and Emerging Adults in Families with Li-Fraumeni Syndrome, Alderfer, M.A., Lindell, R.B., Viadro, C.I. et al. *J Genet Counsel* (2017) 26: 1106-1115. <https://doi.org/10.1007/s10897-017-0091-x>

⁵ Parent decision-making around the genetic testing of children for germline *TP53* mutations, Alderfer, M. A., Zelly, K., Lindell, R.B., Novokmet, A., Mai, P.L., Garber, J.E., Nathan, D., Scollon, S., Chun, N.M., Patenaude, A.F., Ford, J.M., Plon, S.E., Schiffman, J.D., Diller, L.R., Savage, S.A., Malkin, D., Ford, C.A. and Nichols, K.E. (2015), Parent decision-making around the genetic testing of children for germline *TP53* mutations. *Cancer*, 121: 286-293. doi:10.1002/cncr.29027

⁶ USPSTF: Final Recommendation Statement: BRCA-Related Cancer: Risk Assessment, Genetic Counseling, and Genetic Testing
(<https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/brca-related-cancer-risk-assessment-genetic-counseling-and-genetic-testing>)

⁷ Hereditary Cancer Syndromes and Risk Assessment (<http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Genetics/Hereditary-Cancer-Syndromes-and-Risk-Assessment>)

⁸ American Society of Clinical Oncology Policy Statement Update: Genetic and Genomic Testing for Cancer Susceptibility (<http://jco.ascopubs.org/content/early/2015/08/31/JCO.2015.63.0996.full>)

⁹ SGO Clinical Practice Statement: Genetic Testing for Ovarian Cancer (<https://www.sgo.org/clinical-practice/guidelines/genetic-testing-for-ovarian-cancer/>)

¹⁰ AJMC, Evidence-Based Oncology, August 10, 2017, Genetic Counselors Save Costs Across the Genetic Testing Spectrum (<http://www.ajmc.com/journals/evidence-based-oncology/2017/august-2017/genetic-counselors-save-costs-across-the-genetic-testing-spectrum?p=2>)

¹¹ The cost effectiveness of testing for the BRCA1 and BRCA2 breast-ovarian cancer susceptibility genes. Tengs and Berry, 2000.
(https://www.researchgate.net/publication/292301371_The_cost_effectiveness_of_testing_for_the_BRCA1_and_BRCA2_breast-ovarian_cancer_susceptibility_genes)

¹² Cost Effectiveness Analysis of Genetic Testing for Breast and Ovarian Cancer Susceptibility Genes (BRCA1/BRCA2) (https://s3.amazonaws.com/myriad-web/myriadpro.com/publications/Li_SABC+2011_Poster.pdf)

¹³ Cost-effectiveness analysis of germ-line *BRCA* testing in women with breast cancer and cascade testing in family members of mutation carriers. *GENETICS in MEDICINE*, doi:10.1038/gim.2017.231

¹⁴ Cost-effectiveness of predictive genetic tests for familial breast and ovarian cancer. *Genomics, Society and Policy* 2005, Vol.1, No.2, pp.67-79.
(<https://pdfs.semanticscholar.org/72a5/04b2c7c1f9abf703abd5fda6c6e5dfc690ef.pdf>)

¹⁵ Cost-effectiveness of risk-reducing surgeries in preventing hereditary breast and ovarian cancer. Schrauder, Michael G. et al. *The Breast*, Volume 32, 186 - 191
(<https://doi.org/10.1016/j.breast.2017.02.008>)

¹⁶ Genetic testing and economic evaluations: a systematic review of the literature. *Epidemiol Prev* 2015; 39(4) Suppl 1: 45-50 (http://www.epiprev.it/materiali/suppl/2015/EP2015_V4S1_045.pdf)

¹⁷ Cost-effectiveness of surgical interventions for BRCA gene mutation carriers: impact of delaying decision-making. EM Ozanne, L Cipriano, M Cameron, T Newman and LJ Esserman. *Cancer Res* January 15 2009 (69) (2 Supplement) 503; DOI:10.1158/0008-5472.SABCS-503 (http://cancerres.aacrjournals.org/content/69/2_Supplement/503)

¹⁸ FAQs About Affordable Care Act Implementation (Part XXVI) (https://www.cms.gov/ccio/resources/factsheets-and-faqs/downloads/aca_implementation_faqs26.pdf)

¹⁹ Wisconsin BadgerCare Plus and Medicaid, Covered Services and Requirements, Topic #16957 (<https://www.forwardhealth.wi.gov/WIPortal/Subsystem/KW/Print.aspx?ia=1&p=1&sa=50&s=2&c=61&nt=Emerging+Molecular+Pathology+and+Diagnostic+Genetic+Testing>)

²⁰ CLINICAL MEDICAL POLICY, BRCA1 and BRCA2 Genetic Mutation Testing and Related Genetic Counseling Gateway Health, PA Medicaid, Effective: 4/15/18 (https://www.gatewayhealthplan.com/Portals/0/med_drug_policies/PA%20BRCA_318.pdf)

²¹ CLINICAL MEDICAL POLICY, BRCA1 and BRCA2 Genetic Mutation Testing and Related Genetic Counseling, West Virginia Family Health, Annual Approval Date: 06/26/2017 (<http://www.wvfh.com/sites/default/files/BRCA1AndBRCA2.pdf>)

²² PRIORITIZED LIST OF HEALTH SERVICES, JANUARY 1, 2018 (Revised), DIAGNOSTIC GUIDELINE D1, NON-PRENATAL GENETIC TESTING GUIDELINE (<http://www.oregon.gov/oha/HPA/CSI-HERC/PrioritizedList/1-1-2018%20Prioritized%20List%20of%20Health%20Services.pdf>) and (<http://www.oregon.gov/oha/HPA/CSI-HERC/SearchablePLdocuments/Prioritized-List-GN-D001.docx>)