We, at the University of Minnesota, are writing this letter to respectfully propose a change to the above mentioned guideline. This change would echo the recent consensus guidelines from the American Society of Breast Surgeons (ASBS). This professional society guideline recommends that genetic testing be offered to all patients with a personal history of breast cancer and that such testing include at a minimum 3 genes: BRCA1, BRCA2, and PALB2; while testing of an additional 17 genes may be considered (TP53, PTEN, CDH1, STK11, ATM, CHEK2, NBN, NF1, BARD1, MLH1, MSH2, MSH6, PMS2, EPCAM, BRIP1, RAD51C, and RAD51D). Of these 20 potentially testable genes, mutations in 11 of them could alter the breast screening or management of a patient (ATM, BRCA1, BRCA2, CDH1, CHEK2, NBN, NF1, PALB2, PTEN, STK11, TP53) according to the National Comprehensive Cancer Network (NCCN) Genetic/Familial High-Risk Assessment: Breast and Ovarian guideline version 3.2019. Management guidelines for cancer screening and/or medical management are also available for all 20 genes, with the exception of BARD1.

The ASBS guideline is based on studies that show a significant number of patients with a hereditary cancer predisposition are missed using clinical criteria for testing. These studies will be discussed below.

Yang, et al. (PMID 29998407) showed that Medicare patients had statistically similar rates of pathogenic/likely pathogenic results for BRCA1/2 alone, breast cancer management genes, breast or GYN cancer management genes, or all genes whether they met clinical criteria for testing or not. A study by Beitsch, et al. (PMID 30526229) tested patients with a personal diagnosis of breast cancer who were enrolled in two cohorts: those who met 2017 NCCN genetic testing guidelines and those who did not. This study revealed a substantial number of mutations in both cohorts and found that 76% of the patients who did not meet clinical criteria were eligible for specific clinical management recommendations based on the test results. Furthermore, some studies show that the current process requiring identification and referral to a genetic counselor may miss patients. Exome sequencing of 50,000 patients revealed 267 patients with pathogenic/likely pathogenic BRCA1 or BRCA2 mutations, of these 48% had been identified previously through clinical testing, but the remaining cases were not detected via routine clinical care. (PMID 30646163)
Finally, patients with breast cancer who have mutations in many of these genes may have changes in their breast cancer management (details are in the NCCN Guidelines Version 1.2019, 03/14/19, Invasive Breast Cancer).

We are recommending changing the bullet point on page 12 from “Personal history of breast cancer + one or more of the following:” to “Personal history of breast cancer” and to delete the subpoints under the bullet point. We believe this change will improve identification of patients with BRCA1/2 mutations leading to improved patient care.

Sincerely,

Douglas Yee, MD, Medical Oncology
Director, Masonic Cancer Center
Professor Department of Medicine, Professor Department of Pharmacology
University of Minnesota, Minneapolis, MN

Anne Blaes, MD, Medical Oncology
Director, Long-Term Follow-Up Clinic for Cancer Survivors
Department of Medicine, Division of Hematology, Oncology, and Transplantation
University of Minnesota, Minneapolis, MN

Todd Tuttle, MD, MS, Surgical Oncology
Medical Director, University of Minnesota Breast Center
Professor, Department of Surgery
University of Minnesota, Minneapolis, MN

Boris Winterhoff, MD, MS, Gynecologic Oncology
Assistant professor, Department of OB/GYN & Women’s Health
University of Minnesota, Minneapolis, MN
Sophia Yohe, MD
Medical Director, Molecular Diagnostics Laboratory
Department of Laboratory Medicine and Pathology
University of Minnesota, Minneapolis, MN

Andrew Nelson, MD, PhD
Department of Laboratory Medicine and Pathology
University of Minnesota, Minneapolis, MN

Sarah Bray
Department of Genetic Counselling
Faiview Health Services, Minneapolis, MN

Whiwon Lee
Department of Genetic Counselling
Faiview Health Services, Minneapolis, MN