

## **Appendix 11. Early Onset Breast Cancer Research Gaps and Opportunities (by Topic)**

### **Genetic Risk Factors for Early Onset Breast Cancer**

- Strategies such as three-site testing have been developed to identify risk in Ashkenazi Jews, but the implementation and effectiveness of the approach have not been widely studied. There is little evidence to determine whether screening Ashkenazi Jews is routinely conducted, effective in reducing morbidity or mortality, or cost-effective.
- Because of the lack of evidence, no national guidelines exist for testing other racial or ethnic groups, and population-based screening is not recommended.
- Standardized risk assessment tools have not been identified.
- It is unclear how frequently risk assessment for genetic risk of early onset breast cancer is performed during primary care or annual visits. In addition, if risk assessment is performed, there are not reliable data available to determine whether recommended counseling, testing, or interventions are performed for women who may be at risk for genetic predisposition to early onset breast cancer.

### **Dense Breasts on Mammography as a Risk Factor for Early Onset Breast Cancer**

- Because fewer women are dying from breast cancer, it may be appropriate to consider other outcomes, such as cancer detection rates, to determine the benefit of screening modalities in women with dense breasts.

### **Family History as a Risk Factor for Early Onset Breast Cancer**

- Recommendations for U.S. populations are mostly based on findings in European populations.

### **Prior History Risk Factors for Early Onset Breast Cancer**

- Few data address the benefits of screening women with prior history risk factors for breast cancer, and none specifically address early onset breast cancer.
- There are minimal data evaluating the ideal screening strategy for women with common benign proliferative breast diseases.
- Education about the safety of oral contraception should be improved, and data are needed about other forms of hormonal contraception.
- There is no literature discussing testosterone use by the transgender community.
- The impact of fertility treatment on early onset breast cancer should be assessed.

#### **Role of Health Disparities in Early Onset Breast Cancer**

- More research is needed on how to understand and address implicit bias among providers and within medical systems that leads to differences in outcomes for certain groups (eg, differences in rates of genetic screening and lymph node dissection).
- Although there are robust data on health disparities for black women, limited data are available for some populations (eg, American Indian, Asian, and Latina/Hispanic women; sexual and gender minority individuals; those who are undocumented; and incarcerated individuals). There is almost no research regarding breast cancer outcomes for sexual and gender minority individuals, those who are undocumented, and incarcerated individuals.
- Modeling or prospective studies are needed to understand how different screening regimens might benefit certain groups. For example, should black women, who are more likely to be diagnosed with early onset breast cancer, be advised to begin routine mammography in their 40s instead of starting at age 50?

- Health care access and lack of insurance or underinsurance contributes to the mortality differences between white and nonwhite patients with breast cancer, according to some studies.

### **Tools for Assessing Risk of Early Onset Breast Cancer**

- More research is needed to develop tools to assess the risk of early onset breast cancer. Many of the risk factors identified by current models are not relevant to young women. Risk factors for premenopausal breast cancer might be different from postmenopausal breast cancer. Existing models have been validated for older populations.

### **Ways to Communicate Risk to Patients and Improve Patient Understanding of Risk**

- There are no guidelines or recommendations about risk communication for those at risk for early onset breast cancer or the general population (with the exception of hereditary breast and ovarian cancer), although National Institute of Health and Care Excellence guidelines refer to shared decision making for women with a family history of breast cancer. No guidelines offer specific recommendations about effective tools, decision aids, or strategies.
- Development and validation of tools for decision making and communication of risk are needed.
- Further exploration is needed of the validity of narrative risk communication tools for the uptake and acceptance of earlier screening in women at risk for early onset breast cancer.
- More patient-oriented evidence is needed so that clinicians will elevate the importance of early onset breast cancer screening, given the many competing demands of practice. Partner tools such as the National Cancer Institute's breast cancer screening and prevention PDQ should be tested.

### **Understanding Genetic Counseling and Testing**

- Most of the studies come from academic medical centers, and it is not clear whether the findings apply to underrepresented populations, such as those in rural areas.
- Findings usually focus on short-term outcomes, such as early detection of breast cancer, and not long-term mortality rates, which represents an important knowledge gap.
- Virtually no data compare the various tools used to facilitate risk assessment, referral, and counseling or assess whether they are effective in improving access to genetic testing and counseling.
- The training needed to ensure the tools are used effectively and that patients receive appropriate genetic counseling has not been determined.
- The American Society of Breast Surgeons recommended all women with a history of breast cancer be screened for BRCA genes, despite the lack of strong evidence to support the recommendation.
- Current guidelines result in missing a lot of pathogenic variants, but there are insufficient studies to estimate the unintended consequences of casting a wider net.
- Resource barriers must be addressed, such as insurance coverage for genetic testing and counseling and the lack of professionals with adequate training in genetic counseling and testing.

#### **Risk Reduction for Early Onset Breast Cancer**

- Additional studies are needed to assess the effects of modifying risk factors, particularly for early onset breast cancer, and specifically the long-term effect on mortality.

#### **Special Considerations for Early Onset Breast Cancer**

- Gaps related to contraceptive counseling in women with early onset breast cancer should be explored.
- Further study is needed on contraception options for women who have had triple-negative breast cancers.
- The Society of Family Planning's recommendation to withhold use of combined oral contraception in women with prior chest wall radiation should be evaluated.
- Knowledge gaps remain regarding the optimal timing of pregnancy after a diagnosis of early onset breast cancer, chemotherapy, and endocrine therapy.
- Further study is warranted regarding barriers to fertility preservation related to cost and insurance coverage. (Some states have legislated coverage for this population.)