Kaiser Permanente Research Brief

Breast Cancer

This brief summarizes the contributions of Kaiser Permanente Research since 2007 on the topic of breast cancer.

Breast cancer is a common disease. Approximately 1 in 8 American women and 1 in 1,000 American men will develop invasive breast disease during their lifetimes. Although the incidence of breast cancer has decreased since 2000, nearly 350,000 new cases of breast cancer are expected to be diagnosed in 2018. Improvements in detection and treatment have led to higher survival rates, but breast cancer still accounts for about 41,000 deaths every year in the United States.[1] Non-invasive "in situ" tumors – that is, those still confined to the breast ducts or lobules – are less dangerous than those that progress into other parts of the breast tissue, and some types of invasive breast cancer are more aggressive than others.

Kaiser Permanente Publications Related to Breast Cancer since 2007

Source: Kaiser Permanente Publications Library and PLUM metrics, as of 23 March 2018.
a Number of citing journal articles, according to Scopus.
b Number of references in PubMed guidelines.
c Citations in DynaMed Plus, a point-of-care clinical reference tool.

Breast cancer is an active area of study for Kaiser Permanente Research. Scientists across the program have used our rich, comprehensive, longitudinal data to advance knowledge in the areas of understanding risk, improving patient outcomes, and translating research findings into policy and practice. We have published nearly 500 articles related to breast cancer since 2007. Together, these articles have been cited more than 15,000 times. These articles are the product of observational studies, randomized controlled trials, meta-analyses, and other studies led by Kaiser Permanente scientists. Our unique environment – a fully integrated care and coverage model in which our research scientists, clinicians, medical group, and health plan leaders collaborate – lets us contribute important knowledge about breast cancer, and many other topics of research.

This brief summarizes a selection of the publications contained within the Kaiser Permanente Publications Library, which indexes journal articles and other publications authored by individuals affiliated with Kaiser Permanente. The work described in this brief originated from across Kaiser Permanente's 8 regions and was supported by a wide range of funding sources including internal research support as well as both governmental and non-governmental extramural funding.

Understanding Risk

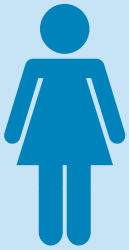
Who is at risk for developing breast cancer?

Most women diagnosed with breast cancer have no clear hereditary or genetic risk for the disease.[2-6] However, our scientists have helped to further the understanding of factors associated with elevated risk, including a personal history of benign breast disease,[4,7] histories of breast or ovarian cancer among first- or second-degree relatives,[4,5,8] and dense breasts,[3,4,6,9] as well as clinically significant alterations in genes associated with elevated risk.[10]

Numerous factors are associated with a higher risk of breast cancer, and not all of them can be altered through lifestyle choices

Non-Modifiable Risk Factors:

- History of Breast Cancer
- Breast Cancer in a 1st-Degree Relative
- Breast Cancer in a 1st or 2nd-Degree
- Relative Before Age 50
- Ovarian Cancer in a 1st or 2nd-Degree
- Relative
- Dense Breasts
- Older Age
- Caucasian Race
- Ashkenazi Jewish Ethnicity
- Prior Chest Radiation Therapy
- Menarche at Younger Age
- First Pregnancy at Younger Age
- Menopause at Later Age



Modifiable Risk Factors:

- Smoking
- Alcohol Use
- Obesity
- Diet
- Hormone Therapy
- Not Breastfeeding
- Fewer Children

Our researchers have studied links between breast cancer risk and race and ethnicity. Caucasian women[11] and those of Ashkenazi Jewish heritage[10,12] are more likely to be diagnosed with breast cancer, while African-American women are more likely to be diagnosed with aggressive subtypes of breast cancer.[13-15] Our research has also connected numerous reproductive factors with the risk for breast cancer. Women who experience menarche at earlier ages are at elevated risk,[16,17] as well as those who enter menopause at later ages.[16,18] Higher risks have also been found in women whose first term pregnancy occurs at a later age.[19] Conversely, women who breastfeed[13] and have a greater number of children[19,20] are at lower risk.

In addition, Kaiser Permanente has conducted studies of numerous modifiable risk factors. Smoking has been associated with elevated breast cancer risk,[21,22] along with alcohol use,[21,23,24] obesity,[21,25] and diets higher in fat.[21,26,27] In addition, use of menopausal hormone therapy has been associated with greater risk.[3,28-30] For example, in the Women's Health Initiative, the use of estrogen with progestin (relative to placebo) was associated with significantly greater risks of breast cancer and mortality.[29]

What other health risks do people with breast cancer face?

In patients treated for breast cancer, chemotherapies and other treatments can have significant side effects, including cardiotoxicity,[31-34] peripheral neuropathy,[35-37] and poor bone health.[38,39] For example, a population-based study using data from the Cancer Research Network found that, relative to women treated without chemotherapy, heart failure was 4 times more likely in those treated

with trastuzumab and 7 times more likely in those treated with trastuzumab and anthracycline.[31] Even in those treated successfully, disease recurrence is a continued risk, especially in older women,[40-42] who may also be more likely to experience cardiotoxicity or peripheral neuropathy from chemotherapy.[43]

Improving Patient Outcomes

Kaiser Permanente Programs Increase Rates of Screening Mammography

What strategies are effective in preventing breast cancer?

Kaiser Permanente researchers have evaluated numerous interventions for preventing breast cancer. In addition to its diligent efforts to screen women at average risk for breast cancer, Kaiser Permanente has programs aimed at identifying women at high genetic risk,[44-46] and has studied the use of patient navigators and electronic alerts to physicians to increase the rate at which these patients are referred for genetic counseling.[44,47,48] In women at high risk for developing breast cancer, medications that block the effects of estrogen in breast cells, such as tamoxifen or raloxifene, are options. However, concerns remain regarding the risks of cardiovascular disease or endometrial cancer in patients taking tamoxifen,[49] and raloxifene may not be as effective as tamoxifen.[49] In other women facing a high risk of breast cancer, prophylactic mastectomy may also be considered. However, poor psychosocial outcomes are not uncommon following this procedure,[50-52] and it should only be undertaken as a shared decision that accounts for the patient's wishes and needs.

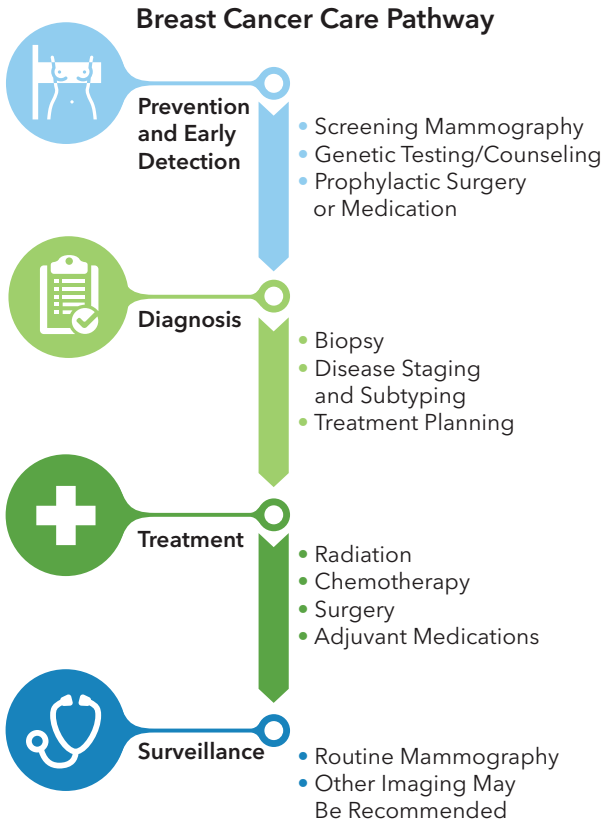
How does early identification of breast cancer affect outcomes?

Years of research on screening have demonstrated that early detection of breast cancer is associated with lower mortality, superior treatment outcomes, and lower rates of disease recurrence.[30,53] Screening mammography is a well-established early detection strategy,[30] and our scientists have explored several approaches for improving screening rates and outcomes. These have included a screening strategy centered on risk-based screening in women ages 40–49 years,[6] mammography reminder programs including both written reminders and phone calls,[54,55] eliminating cost-sharing for mammograms,[56] using prior mammogram results to interpret new scans more accurately,[57] mammography self-referral,[58] and outreach efforts tailored to racial or ethnic minorities.[59,60] In addition, our researchers have been involved in the development of the Breast Cancer Research Consortium's (BCSC's) Risk Calculator, an online tool that allows women to estimate their risk based on their clinical and demographic characteristics.[61]

Kaiser Permanente researchers have contributed to the development of risk prediction tools designed to identify patients who may derive greater benefits from ongoing surveillance,[62-65] and to the validation of multi-gene tests that predict prognosis or response to therapy,[66] thus improving the matching of treatment intensity with underlying risk. These multi-gene tests have allowed clinicians to identify patients who are more likely to experience overtreatment,[67] as well as those at greater risk of treatment failure.[68] Overdiagnosis is an acknowledged harm associated with breast cancer screening. False-positive screening results, and the identification of non-malignant lesions via screening, can lead to psychological distress, financial burden, and even unnecessary treatment.[69-71]

What are the key factors in effective treatment of people with breast cancer?

At Kaiser Permanente, patients with breast cancer benefit from receiving care in a system with ongoing research, and are frequently able to receive cutting-edge medicine through participation in clinical trials,[72-76] often through our involvement in the National Cancer Institute's (NCI's) Community Oncology Research Program[77] and National Research Group[78,79] initiatives. In addition, as part of an integrated health care organization, Kaiser Permanente's researchers have a long-standing interest in improving care pathways for patients with breast cancer. Several studies have explored the impact of care team factors in the care of these patients, particularly the role of clinicians in helping patients to navigate the healthcare system.[80,81] Of particular interest are factors that influence the time between an abnormal mammogram result and evaluation through biopsy.[82-85] Our scientists have also demonstrated the importance of maintaining care for other conditions,[86,87] as there is some evidence that patients with breast cancer may lose contact with primary care providers following their diagnosis.[87]



Researchers at Kaiser Permanente have conducted several studies of the effectiveness of chemotherapy in patients with breast cancer.[76,78,88,89] We have studied factors associated with initiation of and adherence to adjuvant endocrine therapies such as tamoxifen and aromatase inhibitors – these include social support[81] and other psychosocial factors,[90] age,[91,92] receipt of other breast cancer treatment,[91] tumor size[92] and lymph node status.[93]

Our scientists have also studied numerous aspects of surgery for breast cancer.[94,95] Research conducted in Kaiser Permanente has linked improvements in care planning for disease survivors with superior treatment outcomes and longer survival.[96] Our researchers have also studied surgical approaches associated with improved cosmetic outcomes, including judicious use of breast-conserving surgery and appropriate avoidance of axillary lymph node dissection.[97,98]

Even after successful treatment, breast cancer is best thought of as a chronic illness, in which the risks of recurrence, disease progression, and development of comorbid illnesses must be carefully monitored.[87,99,100] Studies in Kaiser Permanente have explored why some patients may struggle to follow recommendations for post-treatment surveillance,[87,99-103] and are actively testing interventions that foster greater engagement with surveillance.

Translating Research Findings into Policy & Practice

How has Kaiser Permanente research on breast cancer contributed to changes in policy and practice?

As part of a learning health care organization that uses research to inform and improve practice, Kaiser Permanente's research, clinical, and operational partners have tested a range of interventions to reduce the risk of breast cancer and improve outcomes for patients with this disease. Our work in risk prediction has enabled our clinicians to tailor more effective care pathways for individual patients with breast cancer. This has included the use of genetic profiling to optimize the use of chemotherapy,[45,66,67,104] personalized risk counseling for women with mammographically dense breasts,[105] and the proper coordination of breast cancer surgery and the surgical removal of the ovaries and fallopian tubes.[106]

Our researchers also continue to explore ways to improve the timing of care pathway elements, including increasing appropriate use of surveillance mammography,[64,65,101] addressing delays in treatment,[107-109] and evaluating concurrent (versus sequential) use of multiple treatments.[88] Extensive interviews with Kaiser Permanente physicians have suggested new care pathways leading to enhanced care, including improving the quality of shared decision-making with patients,[110] increasing appropriate referrals for treatment of breast cancer-related lymphedema,[111] and using diagnostic and surveillance testing more effectively.[112,113] Our research on long-term surveillance practices has significantly improved the integration and coordination of care after our patients complete breast cancer treatment.[114,115] Studies of more advanced care practices include interventions

Our research has identified ways to improve the timing of the breast cancer care pathway

Compliance with surveillance care
More active PCP participation and survivorship programs[101]

Delayed radiotherapy
Patient and provider education, and navigation and notification programs[107]

Non-initiation of adjuvant treatments
Patient education regarding efficacy and side effects[108,109]

Timing of multiple chemotherapies
Sequential treatment may be superior to concurrent administration[88]

aimed at maintaining the patient's contact with their primary-care provider,[87] and the use of specialized care teams (including nurse navigators)[47] to help patients effectively navigate through a system of multidisciplinary care.[87,99,101]

Kaiser Permanente hospitals in Northern California,[116] Hawaii,[117] and Oregon[118] have received Commission on Cancer accreditation through the American College of Surgeons. In addition to providing organizational models and performance measurement tools that can lead to improved patient outcomes, accredited programs are also provided with extensive data on their patients, and may participate in special studies of important clinical questions facing patients with cancer.[119]

Collectively, research from Kaiser Permanente authors on the topic of breast cancer has been cited 75 times within recent consensus statements and clinical practice guidelines published by a wide range of entities, including the American Cancer Society[120] and the American Society of Clinical Oncology.[121] Our researchers and clinician scientists have also directly contributed as authors of breast-cancer-related systematic reviews conducted for the U.S. Preventive Services Task Force.[122]

Kaiser Permanente has shown considerable leadership in the field of breast cancer research. Our scientists have led a number of prominent studies, including the Northern California region's Pathways Study, a study of lifestyle factors, quality of care, prognosis and survival in women diagnosed with breast cancer,[123] the Breast Cancer Treatment Effectiveness in Older Women study,[43] a randomized study of genetic counseling for women at high risk,[47] and a randomized trial assessing whether pre-screening cessation of hormone replacement therapy increases mammogram accuracy.[124] Ongoing work of interest to the broader research community includes a BCSC study exploring ways of incorporating breast density information into decisions around screening and pre-operative diagnosis.[125] Kaiser Permanente oncologists in Northern and Southern California, Hawaii, Colorado, and the Northwest participate in the NCI Community Oncology Research Program, which funds numerous trials of breast cancer treatment, prevention, imaging, and symptom control.[77] Our researchers are also involved in the development of novel breast cancer treatments, including next-generation genetic sequencing of tumor subtypes, and the evaluation of off-label treatments for advanced disease.[126,127]

Kaiser Permanente's nearly 170 research scientists and more than 1,600 support staff are based at 8 regional research centers and 1 national center. There are currently more than 2,500 studies underway, including clinical trials. Since 2007, our research scientists and clinicians have published more than 12,000 articles. Kaiser Permanente currently serves more than 12 million members in 8 states and the District of Columbia.

This brief was written by Nicholas P. Emptage, Anna C. Davis, and Elizabeth A. McGlynn. It is available online from share.kp.org/research/briefs. The authors wish to thank the following researchers for their contributions to the development of this brief: Diana S. Buist, Laurel A. Habel, and Debra P. Ritzwoller.

References

1. American Cancer Society. *Breast Cancer Facts & Figures, 2017-2018.* Atlanta, GA: American Cancer Society, Inc.; 2017.
2. Wacholder S, Hartge P, Prentice R, et al. Performance of common genetic variants in breast-cancer risk models. *N Engl J Med.* 2010;362(11):986-993.
3. Lowery JT, Byers T, Hokanson JE, et al. Complementary approaches to assessing risk factors for interval breast cancer. *Cancer Causes Control.* 2011;22(1):23-31.
4. Engmann NJ, Golmakani MK, Miglioretti DL, et al. Population-Attributable Risk Proportion of Clinical Risk Factors for Breast Cancer. *JAMA Oncol.* 2017;3(9):1228-1236.
5. Ahern TP, Sprague BL, Bissell MCS, et al. Family History of Breast Cancer, Breast Density, and Breast Cancer Risk in a U.S. Breast Cancer Screening Population. *Cancer Epidemiol Biomarkers Prev.* 2017;26(6):938-944.
6. Price ER, Keedy AW, Gidwaney R, et al. The Potential Impact of Risk-Based Screening Mammography in Women 40-49 Years Old. *AJR Am J Roentgenol.* 2015;205(6):1360-1364.
7. Kabat GC, Jones JG, Olson N, et al. A multi-center prospective cohort study of benign breast disease and risk of subsequent breast cancer. *Cancer Causes Control.* 2010;21(6):821-828.
8. Shiyanbola OO, Arao RF, Miglioretti DL, et al. Emerging Trends in Family History of Breast Cancer and Associated Risk. *Cancer Epidemiol Biomarkers Prev.* 2017;26(12):1753-1760.
9. Habel LA, Capra AM, Achacoso NS, et al. Mammographic density and risk of second breast cancer after ductal carcinoma in situ. *Cancer Epidemiol Biomarkers Prev.* 2010;19(10):2488-2495.
10. Fu R, Harris EL, Helfand M, Nelson HD. Estimating risk of breast cancer in carriers of BRCA1 and BRCA2 mutations: a meta-analytic approach. *Stat Med.* 2007;26(8):1775-1787.
11. Brentnall AR, Cuzick J, Buist DSM, Bowles EJA. Long-term Accuracy of Breast Cancer Risk Assessment Combining Classic Risk Factors and Breast Density. *JAMA Oncol.* 2018;4(9):e180174.
12. Lea CS, Gordon NP, Prebil LA, et al. Differences in reproductive risk factors for breast cancer in middle-aged women in Marin County, California and a sociodemographically similar area of Northern California. *BMC Womens Health.* 2009;9:6.
13. Kwan ML, Kushi LH, Weltzien E, et al. Epidemiology of breast cancer subtypes in two prospective cohort studies of breast cancer survivors. *Breast Cancer Res.* 2009;11(3):R31.
14. Sweeney C, Bernard PS, Factor RE, et al. Intrinsic subtypes from PAM50 gene expression assay in a population-based breast cancer cohort: Differences by age, race, and tumor characteristics. *Cancer Epidemiol Biomarkers Prev.* 2014;23(5):714-724.
15. Dehal A, Abbas A, Johna S. Racial disparities in clinical presentation, surgical treatment and in-hospital outcomes of women with breast cancer: analysis of nationwide inpatient sample database. *Breast Cancer Res Treat.* 2013;139(2):561-569.
16. Hiatt RA, Porco TC, Liu F, et al. A multi-level model of postmenopausal breast cancer incidence. *Cancer Epidemiol Biomarkers Prev.* 2014;23(10):2078-2092.
17. Alexeeff SE, Odo NU, Lipson JA, et al. Age at menarche and late adolescent adiposity associated with mammographic density on processed digital mammograms in 24,840 women. *Cancer Epidemiol Biomarkers Prev.* 2017;26(9):1450-1458.
18. Kabat GC, Kim MY, Woods NF, et al. Reproductive and menstrual factors and risk of ductal carcinoma in situ of the breast in a cohort of postmenopausal women. *Cancer Causes Control.* 2011;22(10):1415-1424.
19. Kabat GC, Jones JG, Olson N, et al. Risk factors for breast cancer in women biopsied for benign breast disease: a nested case-control study. *Cancer Epidemiol.* 2010;34(1):34-39.
20. Butler LM, Gold EB, Greendale GA, et al. Menstrual and reproductive factors in relation to mammographic density: the Study of Women's Health Across the Nation (SWAN). *Breast Cancer Res Treat.* 2008;112(1):165-174.
21. Arthur R, Wassertheil-Smoller S, Manson JE, et al. The combined association of modifiable risk factors with breast cancer risk in the Women's Health Initiative. *Cancer Prev Res (Phila).* 2018;11(6):317-326.
22. Nyante SJ, Gierach GL, Dallal CM, et al. Cigarette smoking and postmenopausal breast cancer risk in a prospective cohort. *Br J Cancer.* 2014;110(9):2339-2347.
23. Li Y, Baer D, Friedman GD, et al. Wine, liquor, beer and risk of breast cancer in a large population. *Eur J Cancer.* 2009;45(5):843-850.
24. Coronado GD, Beasley J, Livaudais J. Alcohol consumption and the risk of breast cancer. *Salud Publica Mex.* 2011;53(5):440-447.
25. Neuhouser ML, Aragaki AK, Prentice RL, et al. Overweight, Obesity, and Postmenopausal Invasive Breast Cancer Risk: A Secondary Analysis of the Women's Health Initiative Randomized Clinical Trials. *JAMA Oncol.* 2015;1(5):611-621.
26. Caan BJ, Aragaki A, Thomson CA, et al. Vasomotor symptoms, adoption of a low-fat dietary pattern, and risk of invasive breast cancer: a secondary analysis of the Women's Health Initiative randomized controlled dietary modification trial. *J Clin Oncol.* 2009;27(27):4500-4507.

27. Thomson CA, Van Horn L, Caan BJ, et al. Cancer incidence and mortality during the intervention and postintervention periods of the Women's Health Initiative dietary modification trial. *Cancer Epidemiol Biomarkers Prev.* 2014;23(12):2924-2935.
28. Arthur R, Wang Y, Ye K, et al. Association between lifestyle, menstrual/reproductive history, and histological factors and risk of breast cancer in women biopsied for benign breast disease. *Breast Cancer Res Treat.* 2017;165(3):623-631.
29. Chlebowski RT, Anderson GL, Gass M, et al. Estrogen plus progestin and breast cancer incidence and mortality in postmenopausal women. *JAMA.* 2010;304(15):1684-1692.
30. Glass AG, Lacey JV, Jr., Carreon JD, Hoover RN. Breast cancer incidence, 1980-2006: combined roles of menopausal hormone therapy, screening mammography, and estrogen receptor status. *J Natl Cancer Inst.* 2007;99(15):1152-1161.
31. Bowles EJ, Wellman R, Feigelson HS, et al. Risk of heart failure in breast cancer patients after anthracycline and trastuzumab treatment: a retrospective cohort study. *J Natl Cancer Inst.* 2012;104(17):1293-1305.
32. Ezaz G, Long JB, Gross CP, Chen J. Risk prediction model for heart failure and cardiomyopathy after adjuvant trastuzumab therapy for breast cancer. *J Am Heart Assoc.* 2014;3(1):e000472.
33. Wang SY, Long JB, Hurria A, et al. Cardiovascular events, early discontinuation of trastuzumab, and their impact on survival. *Breast Cancer Res Treat.* 2014;146(2):411-419.
34. Haque R, Shi J, Schottinger JE, et al. Cardiovascular Disease After Aromatase Inhibitor Use. *JAMA Oncol.* 2016;2(12):1590-1597.
35. Rashid N, Koh HA, Baca HC, et al. Clinical Impact of Chemotherapy-Related Adverse Events in Patients with Metastatic Breast Cancer in an Integrated Health Care System. *J Manag Care Spec Pharm.* 2015;21(10):863-871.
36. Greenlee H, Hershman DL, Shi Z, et al. BMI, Lifestyle Factors and Taxane-Induced Neuropathy in Breast Cancer Patients: The Pathways Study. *J Natl Cancer Inst.* 2017;109(2):1-8.
37. Bandos H, Melnikow J, Rivera DR, et al. Long-term Peripheral Neuropathy in Breast Cancer Patients Treated With Adjuvant Chemotherapy: NRG Oncology/NSABP B-30. *J Natl Cancer Inst.* 2018;110(2):djx162.
38. Pawloski PA, Geiger AM, Haque R, et al. Fracture Risk in Older, Long-Term Survivors of Early-Stage Breast Cancer. *J Am Geriatr Soc.* 2013;61(6):888-895.
39. Chau S, Chandra M, Grimsrud CD, et al. Femur fracture classification in women with a history of breast cancer. *J Bone Oncol.* 2014;3(2):49-53.
40. Geiger AM, Thwin SS, Lash TL, et al. Recurrences and second primary breast cancers in older women with initial early-stage disease. *Cancer.* 2007;109(5):966-974.
41. Bosco JL, Lash TL, Prout MN, et al. Breast cancer recurrence in older women five to ten years after diagnosis. *Cancer Epidemiol Biomarkers Prev.* 2009;18(11):2979-2983.
42. Buist DS, Chubak J, Prout M, et al. Referral, receipt, and completion of chemotherapy in patients with early-stage breast cancer older than 65 years and at high risk of breast cancer recurrence. *J Clin Oncol.* 2009;27(27):4508-4514.
43. Owusu C, Buist DS, Field TS, et al. Predictors of tamoxifen discontinuation among older women with estrogen receptor-positive breast cancer. *J Clin Oncol.* 2008;26(4):549-555.
44. Garcia C, Powell CB. A comprehensive approach to the identification and management of the BRCA patient. *Obstet Gynecol Surv.* 2015;70(2):131-143.
45. Goddard KA, Weinmann S, Richert-Boe K, et al. HER2 Evaluation and Its Impact on Breast Cancer Treatment Decisions. *Public Health Genomics.* 2012;15(1):1-10.
46. Pocobelli G, Chubak J, Hanson N, et al. Prophylactic oophorectomy rates in relation to a guideline update on referral to genetic counseling. *Gynecol Oncol.* 2012;126(2):229-235.
47. Rahm AK, Sukhanova A, Ellis J, Mouchawar J. Increasing utilization of cancer genetic counseling services using a patient navigator model. *J Genet Couns.* 2007;16(2):171-177.
48. Powell CB, Littell R, Hoodfar E, et al. Does the Diagnosis of Breast or Ovarian Cancer Trigger Referral to Genetic Counseling? *Int J Gynecol Cancer.* 2013;23(3):431-436.
49. Vogel VG, Costantino JP, Wickerham DL, et al. Update of the National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene (STAR) P-2 Trial: Preventing breast cancer. *Cancer Prev Res (Phila).* 2010;3(6):696-706.
50. Geiger AM, Nekhlyudov L, Herrinton LJ, et al. Quality of life after bilateral prophylactic mastectomy. *Ann Surg Oncol.* 2007;14(2):686-694.
51. Rolnick SJ, Altschuler A, Nekhlyudov L, et al. What women wish they knew before prophylactic mastectomy. *Cancer Nurs.* 2007;30(4):285-291.
52. Altschuler A, Nekhlyudov L, Rolnick SJ, et al. Positive, negative, and disparate--women's differing long-term psychosocial experiences of bilateral or contralateral prophylactic mastectomy. *Breast J.* 2008;14(1):25-32.
53. Hassett MJ, Uno H, Cronin AM, et al. Survival after recurrence of stage I-III breast, colorectal, or lung cancer. *Cancer Epidemiol.* 2017;49:186-194.
54. Feldstein AC, Perrin N, Rosales AG, et al. Effect of a multimodal reminder program on repeat mammogram screening. *Am J Prev Med.* 2009;37(2):94-101.

55. Buist DSM, Gao H, Anderson ML, et al. Breast cancer screening outreach effectiveness: Mammogram-specific reminders vs. comprehensive preventive services birthday letters. *Prev Med.* 2017;102:49-58.
56. Jena AB, Huang J, Fireman B, et al. Screening Mammography for Free: Impact of Eliminating Cost Sharing on Cancer Screening Rates. *Health Serv Res.* 2017;52(1):191-206.
57. Hayward JH, Ray KM, Wisner DJ, et al. Improving Screening Mammography Outcomes Through Comparison With Multiple Prior Mammograms. *AJR Am J Roentgenol.* 2016;207(4):918-924.
58. Moiel D, Thompson J. Early detection of breast cancer using a self-referral mammography process: the kaiser permanente northwest 20-year history. *Perm J.* 2014;18(1):43-48.
59. Lee-Lin F, Menon U, Leo MC, Pedhiwala N. Feasibility of a targeted breast health education intervention for Chinese American immigrant women. *Oncol Nurs Forum.* 2013;40(4):361-372.
60. Coronado GD, Jimenez R, Martinez-Gutierrez J, et al. Multi-level Intervention to increase participation in mammography screening: A ¡Fortaleza Latina! study design. *Contemp Clin Trials.* 2014;38(2):350-354.
61. Tice JA, Miglioretti DL, Li CS, et al. Breast Density and Benign Breast Disease: Risk Assessment to Identify Women at High Risk of Breast Cancer. *J Clin Oncol.* 2015;33(28):3137-3143.
62. Collins LC, Achacoso N, Haque R, et al. Risk factors for non-invasive and invasive local recurrence in patients with ductal carcinoma in situ. *Breast Cancer Res Treat.* 2013;139(2):453-460.
63. Collins LC, Achacoso N, Haque R, et al. Risk Prediction for Local Breast Cancer Recurrence Among Women with DCIS Treated in a Community Practice: A Nested, Case-Control Study. *Ann Surg Oncol.* 2015;22(Suppl 3):S502-508.
64. Lee JM, Abraham L, Lam DL, et al. Cumulative Risk Distribution for Interval Invasive Second Breast Cancers After Negative Surveillance Mammography. *J Clin Oncol.* 2018;36(20):2070-2077.
65. Lee JM, Buist DS, Houssami N, et al. Five-year risk of interval-invasive second breast cancer. *J Natl Cancer Inst.* 2015;107(7):djv109.
66. Rayhanabad JA, Difronzo LA, Haigh PI, Romero L. Changing paradigms in breast cancer management: introducing molecular genetics into the treatment algorithm. *Am Surg.* 2008;74(10):887-890.
67. Ray GT, Mandelblatt J, Habel LA, et al. Breast cancer multigene testing trends and impact on chemotherapy use. *Am J Manag Care.*22(5):e153-160.
68. Natarajan L, Pu M, Parker BA, et al. Time-varying effects of prognostic factors associated with disease-free survival in breast cancer. *Am J Epidemiol.* 2009;169(12):1463-1470.
69. Mandelblatt JS, Stout NK, Schechter CB, et al. Collaborative Modeling of the Benefits and Harms Associated With Different U.S. Breast Cancer Screening Strategies. *Ann Intern Med.* 2016;164(4):215-225.
70. Mandelblatt JS, Cronin KA, Bailey S, et al. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. *Ann Intern Med.* 2009;151(10):738-747.
71. van Ravesteyn NT, Stout NK, Schechter CB, et al. Benefits and harms of mammography screening after age 74 years: model estimates of overdiagnosis. *J Natl Cancer Inst.* 2015;107(7):djv103.
72. Margolese RG, Cecchini RS, Julian TB, et al. Anastrozole versus tamoxifen in postmenopausal women with ductal carcinoma in situ undergoing lumpectomy plus radiotherapy (NSABP B-35): a randomised, double-blind, phase 3 clinical trial. *Lancet.* 2016;387(10021):849-856.
73. Ganz PA, Cecchini RS, Julian TB, et al. Patient-reported outcomes with anastrozole versus tamoxifen for postmenopausal patients with ductal carcinoma in situ treated with lumpectomy plus radiotherapy (NSABP B-35): a randomised, double-blind, phase 3 clinical trial. *Lancet.* 2016;387(10021):857-865.
74. Hertz DL, Barlow WE, Kidwell KM, et al. Fulvestrant decreases anastrozole drug concentrations when taken concurrently by patients with metastatic breast cancer treated on SWOG study S0226. *Br J Clin Pharmacol.* 2016;81(6):1134-1141.
75. Mamounas EP, Jeong JH, Wickerham DL, et al. Benefit from exemestane as extended adjuvant therapy after 5 years of adjuvant tamoxifen: intention-to-treat analysis of the National Surgical Adjuvant Breast And Bowel Project B-33 trial. *J Clin Oncol.* 2008;26(12):1965-1971.
76. Swain SM, Tang G, Geyer CE, et al. Definitive Results of a Phase III Adjuvant Trial Comparing Three Chemotherapy Regimens in Women With Operable, Node-Positive Breast Cancer: The NSABP B-38 Trial. *J Clin Oncol.* 2013;31(26):3197-3204.
77. National Cancer Institute. NCORP: About. https://ncorp.cancer.gov/about/. Accessed September 18, 2018.
78. Bear HD, Tang G, Rastogi P, et al. Neoadjuvant plus adjuvant bevacizumab in early breast cancer (NSABP B-40 [NRG Oncology]): secondary outcomes of a phase 3, randomised controlled trial. *Lancet Oncol.* 2015;16(9):1037-1048.
79. Bear HD, Tang G, Rastogi P, et al. The Effect on Surgical Complications of Bevacizumab Added to Neoadjuvant Chemotherapy for Breast Cancer: NRG Oncology/NSABP Protocol B-40. *Ann Surg Oncol.* 2017;24(7):1853-1860.
80. Scheel JR, Molina Y, Coronado G, et al. Healthcare Factors for Obtaining a Mammogram in Latinas With a Variable Mammography History. *Oncol Nurs Forum.* 2017;44(1):66-76.
81. Kroenke CH, Hershman DL, Gomez SL, et al. Personal and clinical social support and adherence to adjuvant endocrine therapy among hormone receptor-positive breast cancer patients in an integrated health care system. *Breast Cancer Res Treat.* 2018;170(3):623-631.

82. Perez-Stable EJ, Afable-Munsuz A, Kaplan CP, et al. Factors Influencing Time to Diagnosis After Abnormal Mammography Results in Diverse Women. *J Womens Health (Larchmt).* 2013;22(2):159-166.
83. McCarthy AM, Kim JJ, Beaber EF, et al. Follow-Up of Abnormal Breast and Colorectal Cancer Screening by Race/Ethnicity. *Am J Prev Med.* 2016;51(4):507-512.
84. Tosteson AN, Beaber EF, Tiro J, et al. Variation in Screening Abnormality Rates and Follow-Up of Breast, Cervical and Colorectal Cancer Screening within the PROSPR Consortium. *J Gen Intern Med.* 2016;31(4):372-379.
85. Rutter CM, Kim JJ, Meester RGS, et al. Effect of Time to Diagnostic Testing for Breast, Cervical, and Colorectal Cancer Screening Abnormalities on Screening Efficacy: A Modeling Study. *Cancer Epidemiol Biomarkers Prev.* 2018;27(2):158-164.
86. Caan BJ, Kwan ML, Shu XO, et al. Weight Change and Survival after Breast Cancer in the After Breast Cancer Pooling Project. *Cancer Epidemiol Biomarkers Prev.* 2012;21(8):1260-1271.
87. Lafata JE, Salloum RG, Fishman PA, et al. Preventive care receipt and office visit use among breast and colorectal cancer survivors relative to age- and gender-matched cancer-free controls. *J Cancer Surviv.* 2015;9(2):201-207.
88. Swain SM, Jeong JH, Geyer CE, Jr., et al. Longer therapy, iatrogenic amenorrhea, and survival in early breast cancer. *N Engl J Med.* 2010;362(22):2053-2065.
89. Robidoux A, Tang G, Rastogi P, et al. Lapatinib as a component of neoadjuvant therapy for HER2-positive operable breast cancer (NSABP protocol B-41): an open-label, randomised phase 3 trial. *Lancet Oncol.* 2013;14(12):1183-1192.
90. Hershman DL, Kushi LH, Hillyer GC, et al. Psychosocial factors related to non-persistence with adjuvant endocrine therapy among women with breast cancer: the Breast Cancer Quality of Care Study (BQUAL). *Breast Cancer Res Treat.* 2016;157(1):133-143.
91. Nichols HB, Bowles EJ, Islam J, et al. Tamoxifen Initiation After Ductal Carcinoma In Situ. *Oncologist.* 2016;21(2):134-140.
92. Bowles EJ, Buist DS, Chubak J, et al. Endocrine therapy initiation from 2001 to 2008 varies by age at breast cancer diagnosis and tumor size. *J Oncol Pract.* 2012;8(2):113-120.
93. Aiello Bowles EJ, Boudreau DM, Chubak J, et al. Patient-reported discontinuation of endocrine therapy and related adverse effects among women with early-stage breast cancer. *J Oncol Pract.* 2012;8(6):e149-157.
94. Aiello Bowles EJ, Feigelson HS, Barney T, et al. Improving quality of breast cancer surgery through development of a national breast cancer surgical outcomes (BRCASO) research database. *BMC Cancer.* 2012;12:136.
95. McCahill LE, Single RM, Aiello Bowles EJ, et al. Variability in reexcision following breast conservation surgery. *JAMA.* 2012;307(5):467-475.
96. Bodai BI, Tuso P. Breast cancer survivorship: a comprehensive review of long-term medical issues and lifestyle recommendations. *Perm J.* 2015;19(2):48-79.
97. Habel LA, Achacoso NS, Haque R, et al. Declining recurrence among ductal carcinoma in situ patients treated with breast-conserving surgery in the community setting. *Breast Cancer Res.* 2009;11(6):R85.
98. Yegiyants S, Romero LM, Haigh PI, Difronzo LA. Completion axillary lymph node dissection not required for regional control in patients with breast cancer who have micrometastases in a sentinel node. *Arch Surg.* 2010;145(6):564-569.
99. Lash TL, Fox MP, Buist DS, et al. Mammography surveillance and mortality in older breast cancer survivors. *J Clin Oncol.* 2007;25(21):3001-3006.
100. Buist DS, Bosco JL, Silliman RA, et al. Long-term surveillance mammography and mortality in older women with a history of early stage invasive breast cancer. *Breast Cancer Res Treat.* 2013;142(1):153-163.
101. Field TS, Doubeni C, Fox MP, et al. Under utilization of surveillance mammography among older breast cancer survivors. *J Gen Intern Med.* 2008;23(2):158-163.
102. Nekhlyudov L, Habel LA, Achacoso NS, et al. Adherence to long-term surveillance mammography among women with ductal carcinoma in situ treated with breast-conserving surgery. *J Clin Oncol.* 2009;27(19):3211-3216.
103. Salloum RG, Hornbrook MC, Fishman PA, et al. Adherence to surveillance care guidelines after breast and colorectal cancer treatment with curative intent. *Cancer.* 2012;118(22):5644-5651.
104. Pogue-Geile KL, Kim C, Jeong JH, et al. Predicting Degree of Benefit From Adjuvant Trastuzumab in NSABP Trial B-31. *J Natl Cancer Inst.*105(23):1782-1788.
105. Knerr S, Wernli KJ, Leppig K, et al. A web-based personalized risk communication and decision-making tool for women with dense breasts: Design and methods of a randomized controlled trial within an integrated health care system. *Contemp Clin Trials.* 2017;56:25-33.
106. Chapman JS, Roddy E, Panighetti A, et al. Comparing Coordinated Versus Sequential Salpingo-Oophorectomy for BRCA1 and BRCA2 Mutation Carriers With Breast Cancer. *Clin Breast Cancer.* 2016;16(6):494-499.
107. Gold HT, Thwin SS, Buist DS, et al. Delayed radiotherapy for breast cancer patients in integrated delivery systems. *Am J Manag Care.* 2009;15(11):785-789.
108. Neugut AI, Hillyer GC, Kushi LH, et al. Noninitiation of Adjuvant Chemotherapy in Women With Localized Breast Cancer: The Breast Cancer Quality of Care Study. *J Clin Oncol.* 2012;30(31):3800-3809.
109. Neugut AI, Hillyer GC, Kushi LH, et al. Non-initiation of adjuvant hormonal therapy in women with hormone receptor-positive breast cancer: The Breast Cancer Quality of Care Study (BQUAL). *Breast Cancer Res Treat.* 2012;134(1):419-428.

110. Hillyer GC, Hershman DL, Kushi LH, et al. A survey of breast cancer physicians regarding patient involvement in breast cancer treatment decisions. *Breast.* 2013;22(4):548-554.

111. Tam EK, Shen L, Munneke JR, et al. Clinician awareness and knowledge of breast cancer-related lymphedema in a large, integrated health care delivery setting. *Breast Cancer Res Treat.* 2012;131(3):1029-1038.

112. Hahn EE, Munoz-Plaza C, Wang J, et al. Anxiety, Culture, and Expectations: Oncologist-Perceived Factors Associated With Use of Nonrecommended Serum Tumor Marker Tests for Surveillance of Early-Stage Breast Cancer. *J Oncol Pract.* 2017;13(1):e77-e90.

113. Buist DSM, Abraham L, Lee CI, et al. Breast Biopsy Intensity and Findings Following Breast Cancer Screening in Women With and Without a Personal History of Breast Cancer. *JAMA Intern Med.* 2018;178(4):458-468.

114. Hahn EE, Tang T, Lee JS, et al. Use of posttreatment imaging and biomarkers in survivors of early-stage breast cancer: Inappropriate surveillance or necessary care? *Cancer.* 2016;122(6):908-916.

115. Nekhlyudov L, Habel LA, Achacoso N, et al. Ten-Year Risk of Diagnostic Mammograms and Invasive Breast Procedures After Breast-Conserving Surgery for DCIS. *J Natl Cancer Inst.* 2012;104(8):614-621.

116. Permanente Excellence: Commission on Cancer Accreditation [press release]. June 21, 2018.

117. Kaiser Permanente Moanalua Medical Center Cancer Program Earns National Accreditation [press release]. April 10, 2017.

118. American College of Surgeons. Cancer Programs. 2018; https://www.facs.org/search/cancer-programs?name=kaiser&n=100. Accessed August 23, 2018.

119. American College of Surgeons. Value and Benefits of Accreditation. 2018; https://www.facs.org/quality-programs/cancer/coc/apply/benefitscoc. Accessed August 23, 2018.

120. Oeffinger KC, Fontham ET, Etzioni R, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. *JAMA.* 2015;314(15):1599-1614.

121. Runowicz CD, Leach CR, Henry NL, et al. American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline. *J Clin Oncol.* 2016;34(6):611-635.

122. Melnikow J, Fenton JJ, Whitlock EP, et al. Supplemental Screening for Breast Cancer in Women With Dense Breasts: A Systematic Review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2016;164(4):268-278.

123. Kwan ML, Ambrosone CB, Lee MM, et al. The Pathways Study: a prospective study of breast cancer survivorship within Kaiser Permanente Northern California. *Cancer Causes Control.* 2008;19(10):1065-1076.

124. U.S. National Library of Medicine. Radiologic Evaluation and Breast Density (READ). 2009; https://clinicaltrials.gov/ct2/show/NCT00117663. Accessed September 17, 2018.

125. U.S. National Library of Medicine. Assessing Breast Density's Value in Imaging - A Comparative Effectiveness Study (BCSC-ADVANCE). 2018; https://clinicaltrials.gov/ct2/show/NCT02980848. Accessed September 17, 2018.

126. Vujaskovic Z, Kim DW, Jones E, et al. A phase I/II study of neoadjuvant liposomal doxorubicin, paclitaxel, and hyperthermia in locally advanced breast cancer. *Int J Hyperthermia.* 2010;26(5):514-521.

127. Vuylsteke P, Huizing M, Petrakova K, et al. Pictilisib plus paclitaxel for the treatment of hormone receptor-positive, HER2-negative, locally recurrent, or metastatic breast cancer: interim analysis of the multicentre, placebo-controlled, phase II randomised PEGGY study. *Ann Oncol.* 2016;27(11):2059-2066.