Cancer Association of South Africa (CANSA)

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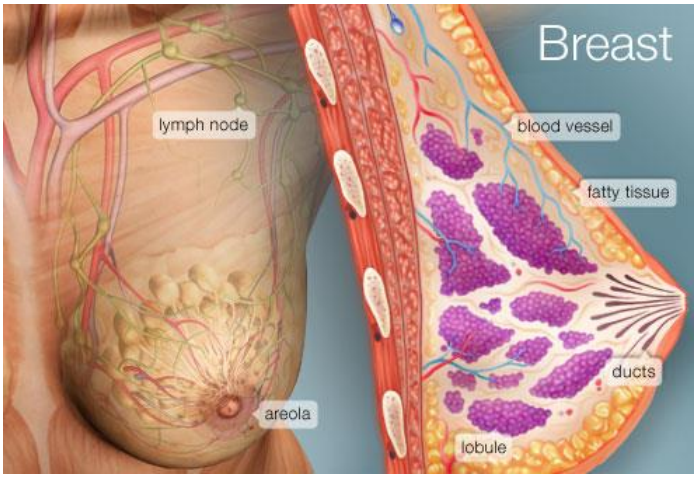
Fact Sheet
on
Breast Cancer in Women

Introduction

The female breast is the tissue overlying the chest (pectoral) muscles. Women's breasts are made of specialised tissue that produces milk (glandular tissue) as well as fatty tissue. The amount of fat determines the size of the breast.



[Picture Credit: Female Breast]

Although both men and women have breasts, it is in the female that the breast becomes prominent and a vital component of her persona. In the male, the breast is rudimentary.

Structure of the Female Breast - **t**he anatomy of the breast is quite simple. It is made up of about eighteen lobules of glandular tissue. These lobules resemble bunches of grapes and each grape represents the secreting unit, called alveolus (pleural: alveoli). The alveolus consists of cells, which line the unit and produce the milk.

Walsh, S.M., Zabor, E.C., Flynn, J., Stempel, M., Morrow, M. & Gemignani, M.L. 2020.
Background: Young age at breast cancer diagnosis is associated with negative prognostic outcomes, and breast cancer in black women often manifests at a young age. This study evaluated the effect of age on breast cancer management and outcomes in black women.
Methods: This was a retrospective cohort study of all black women treated for invasive breast cancer between 2005 and 2010 at a specialized tertiary-care cancer centre. Clinical and treatment characteristics were compared by age. Kaplan-Meier methodology was used to estimate overall survival (OS) and disease-free survival (DFS).
Results: A total of 666 black women were identified. Median BMI was 30 (range 17-56) kg/m^2 and median tumour size was 16 (1-155) mm. Most tumours were oestrogen receptor-positive (66·4 per cent). Women were stratified by age: less than 40 years (74, 11·1 per cent) versus 40 years or more (592, 88·9 per cent). Younger women were significantly more likely to have a mastectomy, axillary lymph node dissection and to receive chemotherapy, and were more likely to have lymphovascular

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invasion and positive lymph nodes, than older women. The 5-year OS rate was 88·0 (95 per cent c.i. 86·0 to 91·0) per cent and the 5-year DFS rate was 82·0 (79·0 to 85·0) per cent. There was no statistically significant difference in OS by age (P = 0·236). Although DFS was inferior in younger women on univariable analysis (71 versus 88 per cent; P < 0·001), no association was found with age on multivariable analysis.
Conclusion: Young black women with breast cancer had more adverse pathological factors, received more aggressive treatment, and had worse DFS on univariable analysis. Young age at diagnosis was, however, not an independent predictor of outcome.

Zouzoulas, D., Tsolakidis, D., Gitas, G., Zafrakas, M., Goulis, D.G., Douganiotis, G., Sympilidis, G. & Grimbizis, G. 2020.
Purpose: Women ≤ 35 years old with breast cancer constitute a special group. Considering the impact of the disease and its prognosis, these patients face some specific problems that are not present in older women. What are the prognostic features of the survival rate in very young women with breast cancer?
Methods: Retrospective analysis of very young women with breast cancer from the Surgical-Oncologic Breast Cancer Department at "Theagenio" Anticancer Hospital, 2003-2016. Patient and tumor characteristics, treatment options and follow-up information were collected. Univariate-multivariate analyses were conducted and survival rates were calculated.
Results: The median age was 34 years old. 53 patients (41%) had T1, 36 (28%) had T2, 7 (5.4%) had T3 and 33 (25.6%) had T4 stage tumors. Most women, 114 (88.4%), had ductal carcinoma in their histology. Furthermore, positive axillary lymph nodes were present in 62 women (48%). In the immunochemistry report, 91 patients (70.5%) were hormone receptor positive, HER2 was overexpressed in 32 patients (24.8%) and 27 patients presented with triple-negative subtype. Out of 65 patients tested for Ki-67, 51 (78.5%), had a high expression (cut-off value of 20%). After adjusting for all possible factors, the risk of recurrence and death was six times higher in the positive lymph node group, (p < 0.001). The median disease-free and overall survival was 133 and > 173 months, respectively.
Conclusion: Breast cancer in very young women appears with large size and high-grade tumors, high incidence of infiltrated axillary lymph nodes, high Ki-67 expression and intrinsic subtypes with poor prognosis. As a result, these women need to be treated by a multidisciplinary team.

García-Albéniz, X., Hernán, M.A., Logan, R.W., Price, M., Armstrong, K. & Hsu, J. 2029.
Background: Randomized trials have shown that initiating breast cancer screening between ages 50 and 69 years and continuing it for 10 years decreases breast cancer mortality. However, no trials have studied whether or when women can safely stop screening mammography. An estimated 52% of women aged 75 years or older undergo screening mammography in the United States.
Objective: To estimate the effect of breast cancer screening on breast cancer mortality in Medicare beneficiaries aged 70 to 84 years.
Design: Large-scale, population-based, observational study of 2 screening strategies: continuing annual mammography, and stopping screening.
Setting: U.S. Medicare program, 2000 to 2008.
Participants: 1 058 013 beneficiaries aged 70 to 84 years who had a life expectancy of at least 10 years, had no previous breast cancer diagnosis, and underwent screening mammography.
Measurements: Eight-year breast cancer mortality, incidence, and treatments, plus the positive predictive value of screening mammography by age group.
Results: In women aged 70 to 74 years, the estimated difference in 8-year risk for breast cancer death between continuing and stopping screening was -1.0 (95% CI, -2.3 to 0.1) death per 1000 women (hazard ratio, 0.78 [CI, 0.63 to 0.95]) (a negative risk difference favors continuing). In those

aged 75 to 84 years, the corresponding risk difference was 0.07 (CI, -0.93 to 1.3) death per 1000 women (hazard ratio, 1.00 [CI, 0.83 to 1.19]).
Limitations: The available Medicare data permit only 8 years of follow-up after screening. As with any study using observational data, the estimates could be affected by residual confounding.
Conclusion: Continuing annual breast cancer screening past age 75 years did not result in substantial reductions in 8-year breast cancer mortality compared with stopping screening.

Ranganathan, K., Singh, P., Raghavendran, K., Wilkins, E.G., Hamill, J.B., Aliu, O., Newman, L.A., Hutton, D. & Momoh, A.O. 2020
OBJECTIVE: In this study, we quantified the global macroeconomic burden of breast cancer to underscore the critical importance of improving access to oncologic surgical care internationally.
SUMMARY BACKGROUND DATA: Breast cancer mortality in many low and middle-income countries (LMICs) is dramatically higher than in high-income countries. Prior to identifying solutions, however, it is important to first define the burden of disease.
METHODS: Data from the Institute of Health Metrics and Evaluation (2005-2015) were used to assess epidemiologic trends for 194, middle, and low-income countries. Economic burden defined by Welfare Loss (WL) was calculated by measuring disability-adjusted-life-years lost to breast cancer alongside the dollar equivalent of a value of statistical life year and as a function of each country's gross domestic product (GDP).

RESULTS: Annual mortality rates among breast cancer patients were significantly greater in LMICs in South Asia (3.06 per 100 women) and Sub-Saharan Africa (2.76 per 100 women), compared with high-income countries like the United States (1.69 per 100 women). From 2005-2015, mortality in South Asia increased by 8.20% and decreased by 6.45% in Sub-Saharan Africa; mortality rates in 2015 were observed as 27.9 per 100,000 in South Asia and 18.61 per 100,000 in Sub-Saharan Africa. Countries in South Asia demonstrated the greatest rise in WL due to breast cancer, from 0.05% to 0.08% of GDP.
CONCLUSIONS: The burden of disease and economic impact of breast cancer is intensifying in LMICs. Global efforts to improve access to surgical care for women with breast cancer could reduce mortality and mitigate the social and financial impact of this disease in LMICs.

Incidence of Breast Cancer in South Africa
According to the outdated National Cancer Registry (2017), known for under reporting, the following number of breast cancer cases in women was histologically diagnosed during 2017:

Group 2017	Actual Number of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	9 642	1 : 25	23,11%
Asian females	515	1 : 17	39,52%
Black females	4 077	1 : 45	25,53%
Coloured females	1 365	1 : 19	29,81%
White females	3 667	1 : 10	21,48%

Frequency of Histologically Diagnosed Cases of Breast Cancer

According to the National Cancer Registry (2017), the frequency of histologically diagnosed cases of breast cancer in women in South Africa is as follow:

Group 2017	0 to 19 Years	20 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 to 69 Years	70 to 79 Years	80 + Years
All females	5	144	942	2 109	2 229	2 142	1 339	624
Asian females	0	4	43	112	129	124	81	22
Black females	5	95	595	1 091	1 088	737	419	187
Coloured females	0	17	102	311	323	348	175	89
White females	0	28	202	598	826	933	814	325

According to **Bruni, *et al*.,** (2019), the burden of Breast cancer for South Africa for 2018 is estimated as (based on Globocan estimates):

- Annual number of breast cancer cases 14 097
- Annual number of breast cancer deaths 4 690

Sancho-Garnier, H. & Colonna, M. 2019.

"The breast is the leading cancer site in women throughout the world. That said, breast cancer incidence varies widely, ranging from 27/100,000[2] (Central-East Asia and Africa) to 85-94/100,000[2] (Australia, North America and Western Europe). Its frequency in France is among the highest in Europe. While in most countries, its incidence has been increasing for more than 40 years, in a few other countries (USA, Canada, Australia, France…), it has been decreasing since 2000-2005. Possibly due to a substantial reduction of hormone-based treatments at menopause, the decrease may be transient. It is also the leading cause of female cancer deaths in almost all countries, with the exception of the most economically developed, in which it is currently second to lung cancer. That much said, for thirty years in highly industrialized countries such as France, breast cancer mortality has been declining. Taken together, early diagnosis and improved treatment explain this success. In France, 5-year survival and 10-year survival approximate 88 % and 78 % respectively; these rates are among the most elevated in Western Europe. Excess mortality due to breast cancer is consequently low (<5 %) but variable according to age, and maximal during the first two years of follow-up. Several thousand epidemiological studies on risk factors for breast cancer have been carried out worldwide; it is difficult to draw up an overall assessment, especially insofar as the identified factors interact and vary according to whether the cancers occur before or after menopause and depending on their histological, biological (receptors) or molecular characteristics. Moreover, their prevalence varies in time and from one region to another. For the majority of these factors, the level of relative risk is≤2. Genetic particularities: presence of proliferative mastopathy, a first child after 35 years of age and thoracic irradiation are the sole factors entailing relative risk from 2 to 5 (comparatively speaking, the risk levels associated with tobacco consumption reach values from 10 to 20, and in some cases even higher). However, exposure to risk factors≤2 may be relatively frequent and consequently favorable to development of a substantial number of breast cancers. Estimation (based on degree of risk and frequency of exposure) of the proportion of risk attributable to a given factor facilitates decision-making aimed at determining the most effective primary prevention actions. Taking into consideration the identified factors pertaining to post-menopausal cancers, only 35 % [23 to 45 %] of the attributable proportions could be reduced by primary prevention. In view of achieving this level of reduction, it is possible to put forward the following recommendations: for the women themselves: have a first child before the age of 30, breastfeed for several months, engage in sufficiently intense and regular physical activity, avoid or reduce excess weight after turning thirty, avoid exposure to active or passive smoking, limit alcohol consumption; for their physicians: do not

prescribe pointless thoracic irradiations (unnecessary mammography in particular) or unjustified hormonal treatments. *persons/years."

Risk Factors for Breast Cancer in Women

The following are known risk factors for breast cancer in women:

Sex - just being a woman is the biggest risk factor for developing breast cancer.

Age - as with many other diseases, one's risk of breast cancer goes up as one gets older.

Family history - women with close relatives who have been diagnosed with breast cancer have a higher risk of developing the disease. If one has had one first-degree female relative (sister, mother, daughter) diagnosed with breast cancer, one's risk is doubled.

Also, if one has had one first-degree male relative (brother, father, son) diagnosed with prostate cancer, the risk of breast cancer is increased, especially if the prostate cancer was found at a young age.

Genetics - about 5% to 10% of breast cancers are thought to be hereditary, caused by abnormal genes passed from parent to child. Certain gene mutations that increase the risk of breast cancer can be passed from parents to children. The most common gene mutations are referred to as BRCA1 and BRCA2. These genes can greatly increase one's risk of breast cancer and other cancers, but they do not make cancer inevitable.

Personal history of breast cancer - if one has been diagnosed with breast cancer, one has a 3 to 4 times increased risk to develop a new cancer in the other breast or a different part of the same breast.

Radiation to chest before age 30 - if one has had radiation to the chest to treat another cancer (not breast cancer), such as Hodgkin's lymphoma or non-Hodgkin's lymphoma, one has a higher-than-average risk of breast cancer.

Race or ethnicity – It is said that white women are slightly more likely to develop breast cancer than African American, Hispanic, and Asian women. But African American women are more likely to develop more aggressive, more advanced-stage breast cancer that is diagnosed at a young age. There is still insufficient evidence to categorically make this statement for South African Black women.

Being overweight - overweight and obese women have a higher risk of being diagnosed with breast cancer compared to women who maintain a healthy weight, especially after menopause.

Pregnancy history - women who haven't had a full-term pregnancy or had their first child after age 30 have a higher risk of breast cancer compared to women who gave birth before age 30.

Breastfeeding history - breastfeeding can lower breast cancer risk, especially if a woman breastfeeds for longer than 1 year.

Menstrual history - women who started menstruating (having periods) younger than age 12 have a higher risk of breast cancer later in life. The same is true for women who go through menopause when they are older than 55.

Using HRT (Hormone Replacement Therapy) - current or recent past users of HRT have a higher risk of being diagnosed with breast cancer.

Drinking alcohol - research consistently shows that drinking alcoholic beverages - beer, wine, and spirits - increases the risk of hormone-receptor-positive breast cancer.

Having dense breasts - research has shown that dense breasts can be 6 times more likely to develop cancer and can make it harder for mammograms to detect breast cancer.

Thorat, M.A. & Balasubramanian, R. 2020.
"Women at high risk of developing breast cancer are a heterogeneous group of women including those with and without high-risk germline mutation/s. Prevention in these women requires a personalised and multidisciplinary approach. Preventive therapy with selective oestrogen receptor modulators (SERMs) like tamoxifen and aromatase inhibitors (AIs) substantially reduces breast cancer risk well beyond the active treatment period. The importance of benign breast disease as a marker of increased breast cancer risk remains underappreciated, and although the benefit of preventive therapy may be greater in such women, preventive therapy remains underutilised in these and other high-risk women. Bilateral Risk-Reducing Mastectomy (BRRM) reduces the risk of developing breast cancer by 90% in high-risk women such as carriers of BRCA mutations. It also improves breast cancer-specific survival in BRCA1 carriers. Bilateral risk-reducing salpingo-oophorectomy may also reduce risk in premenopausal BRCA2 carriers. Further research to improve risk models, to identify surrogate biomarkers of preventive therapy benefit and to develop newer preventive agents is needed."

Comstock, C.E., Gatsonis, C., Newstead, G.M., Snyder, B.S., Gareen, I.F., Bergin, J.T., Rahbar, H., Sung, J.S., Jacobs, C., Harvey, J.A., Nicholson, M.H., Ward, R.C., Holt, J., Prather, A., Miller, K.D., Schnall, M.D. & Kuhl, C.K. 2020.
IMPORTANCE: Improved screening methods for women with dense breasts are needed because of their increased risk of breast cancer and of failed early diagnosis by screening mammography.
OBJECTIVE: To compare the screening performance of abbreviated breast magnetic resonance imaging (MRI) and digital breast tomosynthesis (DBT) in women with dense breasts.
DESIGN, SETTING, AND PARTICIPANTS: Cross-sectional study with longitudinal follow-up at 48 academic, community hospital, and private practice sites in the United States and Germany, conducted between December 2016 and November 2017 among average-risk women aged 40 to 75 years with heterogeneously dense or extremely dense breasts undergoing routine screening. Follow-up ascertainment of cancer diagnoses was complete through September 12, 2019.
EXPOSURES: All women underwent screening by both DBT and abbreviated breast MRI, performed in randomized order and read independently to avoid interpretation bias.
MAIN OUTCOMES AND MEASURES: The primary end point was the invasive cancer detection rate. Secondary outcomes included sensitivity, specificity, additional imaging recommendation rate, and positive predictive value (PPV) of biopsy, using invasive cancer and ductal carcinoma in situ (DCIS) to define a positive reference standard. All outcomes are reported at the participant level. Pathology of core or surgical biopsy was the reference standard for cancer detection rate and PPV; interval cancers reported until the next annual screen were included in the reference standard for sensitivity and specificity.

RESULTS: Among 1516 enrolled women, 1444 (median age, 54 [range, 40-75] years) completed both examinations and were included in the analysis. The reference standard was positive for invasive cancer with or without DCIS in 17 women and for DCIS alone in another 6. No interval cancers were observed during follow-up. Abbreviated breast MRI detected all 17 women with invasive cancer and 5 of 6 women with DCIS. Digital breast tomosynthesis detected 7 of 17 women with invasive cancer and 2 of 6 women with DCIS. The invasive cancer detection rate was 11.8 (95% CI, 7.4-18.8) per 1000 women for abbreviated breast MRI vs 4.8 (95% CI, 2.4-10.0) per 1000 women for DBT, a difference of 7 (95% CI, 2.2-11.6) per 1000 women (exact McNemar P = .002). For detection of invasive cancer and DCIS, sensitivity was 95.7% (95% CI, 79.0%-99.2%) with abbreviated breast MRI vs 39.1% (95% CI, 22.2%-59.2%) with DBT (P = .001) and specificity was 86.7% (95% CI, 84.8%-88.4%) vs 97.4% (95% CI, 96.5%-98.1%), respectively (P < .001). The additional imaging recommendation rate was 7.5% (95% CI, 6.2%-9.0%) with abbreviated breast MRI vs 10.1% (95% CI, 8.7%-11.8%) with DBT (P = .02) and the PPV was 19.6% (95% CI, 13.2%-28.2%) vs 31.0% (95% CI, 17.0%-49.7%), respectively (P = .15).
CONCLUSIONS AND RELEVANCE: Among women with dense breasts undergoing screening, abbreviated breast MRI, compared with DBT, was associated with a significantly higher rate of invasive breast cancer detection. Further research is needed to better understand the relationship between screening methods and clinical outcome.
TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT02933489.

Lack of exercise - research shows a link between exercising regularly at a moderate or intense level for 4 to 7 hours per week and a lower risk of breast cancer.

Smoking - smoking causes a number of diseases and is linked to a higher risk of breast cancer in younger, premenopausal women.

Low Vitamin D levels - research suggests that women with low levels of vitamin D have a higher risk of breast cancer. Vitamin D may play a role in controlling normal breast cell growth and may be able to stop breast cancer cells from growing.

Diet – diet seems to be playing a more important role in Breast Cancer than previously thought.

Petersen, L.L., Park, S., Park, Y., Coldtiz, A., Anbardar, N. & Turner, D.P. 2020.
BACKGROUND: Advanced glycation end products (AGEs) are reactive metabolites produced as a by-product of sugar metabolism and are consumed through the diet in high-fat and highly processed foods. They are associated with chronic inflammatory diseases, and evidence suggests that they play a role in carcinogenesis. The authors evaluated the association of dietary AGE intake and the risk of postmenopausal invasive breast cancer.
METHODS: This was a prospective cohort study of 183,548 postmenopausal women in the National Institutes of Health-AARP Diet and Health Study. The main outcome was incident invasive breast cancer. AGE intake was estimated from food-frequency questionnaires. Incident breast cancer cases were identified through state cancer registries. Cox proportional hazards regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals for developing breast cancer according to AGE intake quintiles. Multivariable regression models were adjusted for breast cancer risk factors.
RESULTS: The mean follow-up was 12.8 years, and 9851 breast cancers (1978 advanced stage) were identified. The median AGE daily intake was 5932 kilo units per 100 kilocalories (KU/1000 kcal). Women with higher intake tended to have lower education levels, higher body mass index, less

physical activity, were current smokers, and had higher fat and meat intake. The highest quintile of AGE intake (compared with the lowest) was associated with an increased risk of breast cancer (HR, 1.09; 95% CI, 1.02-1.16; P = .03) after adjusting for breast cancer risk factors and particularly was associated with 37% of advanced-stage tumors (HR, 1.37; 95% CI, 1.09-1.74; P < .02) after adjusting for risk factors and fat and meat intake.
CONCLUSIONS: Dietary AGEs may play a role in the development of postmenopausal breast cancer.

Bahri, N., Eathi Najafi, T., Homael Shandiz, F., Toshodinik, H.R. & Khajavi, A. 2019.
PURPOSE: Breast cancer is the most common cancer among women with high rate of mortality. This systematic review and meta-analysis was conducted to investigate the relation between stressful life events and breast cancer.
METHODS: We searched PubMed, Scopus, ScienceDirect, and Google scholar databases from their inception until June 2018. The keywords and phrases we used in the search were (life events AND stress AND breast cancer OR neoplasm) to identify potentially relevant cohort studies that reported relative risk estimates and confidence intervals of this association. Pooled Risk ratio and 95% confidence intervals (CIs) were calculated using random effects model.
RESULTS: Out of 168 potentially relevant publications, 11 documents met the inclusion criteria. The results showed that history of stressful life events slightly increases the risk of breast cancer [pooled Risk Ratio: 1.11 (95% CI 1.03 to 1.19)].
CONCLUSIONS: History of stressful life events could be associated with a moderate increase in the risk of breast cancer. We advise that receiving psychological and counseling services after occurrence of stressful life events of women should be taken seriously.

Caution Expressed Around Consumption of Foods High in Phytoestrogens by Individuals Diagnosed with a Hormone-Sensitive Cancer
The Cancer Association of South Africa (CANSA) has noted:

- A statement by Memorial Sloan Kettering Cancer Center saying that "… because compounds isolated from rooibos leaves demonstrated estrogenic activity, patients with hormone-sensitive cancers should use caution before taking rooibos." (Memorial Sloan Kettering Cancer Center).

- That phytoestrogens were successfully isolated from rooibos leaves by scientists from the School of Pharmaceutical Sciences, University of Shizuoka, Japan (Shimamura, *et al.*, 2006).

- That according to Deng, et al., (2010), "… there are important safety concerns associated with dietary supplements and foods rich in phytoestrogens, especially for breast cancer patients with hormone-sensitive disease. Based on current evidence, we propose recommendations for advising breast cancer patients, …"

- That, according to Nelles, Hu & Prins (2011), "Early work on the hormonal basis of prostate cancer focused on the role of androgens, but more recently estrogens have been implicated as potential agents in the development and progression of prostate cancer."

- That, according to Reger, *et al*., (2016), "Experimental studies suggest that phytoestrogen intake alters cancer and cardiovascular risk. Some urinary phytoestrogens were associated

with cardiovascular and all-cause mortality in a representative sample of 5 179 participants. This is one of the first studies that used urinary phytoestrogens as biomarkers of their dietary intake to evaluate the effect of these bioactive compounds on the risk of death from cancer and cardiovascular disease."

CANSA, therefore, wishes to advise individuals diagnosed with the following hormone-sensitive cancers, namely: Breast Cancer, Ovarian Cancer, Endometrial Cancer, and Prostate Cancer, to:

- use caution before taking Rooibos tea and to discuss the issue around Rooibos tea consumption with their treating Oncologist prior to consuming Rooibos tea
- also use caution before taking the following high phytoestrogen-containing foods: all soy foods (including soybeans, tofu, miso, and tempeh); legumes (especially lentils, peanuts and chickpeas) and flaxseed-containing foods. Patients are advised to discuss consumption of the listed high phytoestrogen-containing foods with their treating Oncologist prior to consuming them.

Fraser, G.E., Jaceldo-Siegl, K., Orlich, M., Mashchak, A., Sirirat, R. & Knutsen, S. 2020.
BACKGROUND: Associations between soy, dairy intakes and breast cancer risk are inconsistent. No studies exist with large numbers of dairy consumers and soy consumers to assess mutual confounding.
METHODS: The study cohort contains 52 795 North American women, initially free of cancer, followed for 7.9 years (29.7% were Black). Dietary intakes were estimated from food frequency questionnaires and, for 1011 calibration study subjects, from six structured 24-h dietary recalls. Incident invasive breast cancers were detected mainly by matching with cancer registries. Analyses used multivariable proportional hazards regression.
RESULTS: The participants (mean age of 57.1 years) experienced 1057 new breast cancer cases during follow-up. No clear associations were found between soy products and breast cancer, independently of dairy. However, higher intakes of dairy calories and dairy milk were associated with hazard ratios (HRs) of 1.22 [95% confidence interval (CI): 1.05-1.40] and 1.50 (95% CI 1.22-1.84), respectively, comparing 90th to 10th percentiles of intakes. Full fat and reduced fat milks produced similar results. No important associations were noted with cheese and yogurt. Substituting median intakes of dairy milk users by those of soy milk consumers was associated with HR of 0.68 (95% CI: 0.55-0.85). Similar-sized associations were found among pre- and post-menopausal cases, with CIs also excluding the null in estrogen receptor (ER+, ER-), and progesterone receptor (PR+) cancers. Less biased calibrated measurement-error adjusted regressions demonstrated yet stronger, but less precise, HRs and CIs that still excluded the null.
CONCLUSIONS: Higher intakes of dairy milk were associated with greater risk of breast cancer, when adjusted for soy intake. Current guidelines for dairy milk consumption could be viewed with some caution.

Research on Foods High in Phytoestrogens and Breast Cancer

Deng, G., Davatgarzadeh, A., Yeung, S. & Cassileth, B. 2010. Phytoestrogens: science, evidence, and advice for breast cancer patients. *Soc Integr Oncol*. 2010 Winter;8(1):20-30.
"There are important safety concerns associated with dietary supplements and foods rich in phytoestrogens, especially for breast cancerpatients with hormone-sensitive disease. However, no

consensus has been reached concerning specific dietary items that should be avoided, and safe levels of potentially problematic foods have yet to be determined. Excellent qualitative reviews of phytoestrogens and breast cancerhave been published. These list agents that contain phytoestrogens and offer general cautions. Quantitative reviews, however, are needed but not yet available. Here we review quantitative data on phytoestrogens, their interaction with estrogen receptors, their bioavailability and pharmacokinetics, and their effects on breast cancer cells and animal models. We also note foods and botanicals with substances that interact with estrogen receptors and discuss the phytoestrogens they contain. Based on current evidence, we propose recommendations for advising breast cancer patients, which may also serve as a basis for the development of clinical practice guidelines."

Shimamura, N., Miyase, T., Umehara, K., Warashina, T. & Fuji, S. 2006. Phytoestrogens from aspalathus linearis. *Biol Pharm Bull.* 2006 Jun;29(6):1271-4.
"From the leaves of Aspalathus linearis, 24 known compounds and a new one, aspalalinin (25), were isolated. The structures of the compounds were determined mainly based on spectral evidence. The absolute configuration of aspalalinin was presented on the basis of X-ray analysis. Each isolate was assessed for its estrogenic activity by an estrogen ELISA assay. Compounds 12, 15, and 24 showed the estrogenic activity."

Patisaul, H. & Jefferson, W. 2010. The pros and cons of phytoestrogens. *Front Neuroendocrinol*.. Author manuscript; available in PMC 2011 Apr 12.
Phytoestrogens are plant derived compounds found in a wide variety of foods, most notably soy. A litany of health benefits including a lowered risk of osteoporosis, heart disease, breast cancer, and menopausal symptoms, are frequently attributed to phytoestrogens but many are also considered endocrine disruptors, indicating that they have the potential to cause adverse health effects as well. Consequently, the question of whether or not phytoestrogens are beneficial or harmful to human health remains unresolved. The answer is likely complex and may depend on age, health status, and even the presence or absence of specific gut microflora. Clarity on this issue is needed because global consumption is rapidly increasing. Phytoestrogens are present in numerous dietary supplements and widely marketed as a natural alternative to estrogen replacement therapy. Soy infant formula now constitutes up to a third of the US market, and soy protein is now added to many processed foods. As weak estrogen agonists/antagonists with molecular and cellular properties similar to synthetic endocrine disruptors such as Bisphenol A (BPA), the phytoestrogens provide a useful model to comprehensively investigate the biological impact of endocrine disruptors in general. This review weighs the evidence for and against the purported health benefits and adverse effects of phytoestrogens.

Rodriquez-Garcia, C., Sánchez-Quesada, C., Toledo, E., Delgado-Rodriquez, M. & Gaforio, J.J. 2019.
"Dietary guidelines universally advise adherence to plant-based diets. Plant-based foods confer considerable health benefits, partly attributable to their abundant micronutrient (e.g., polyphenol) content. Interest in polyphenols is largely focused on the contribution of their antioxidant activity to the prevention of various disorders, including cardiovascular disease and cancer. Polyphenols are classified into groups, such as stilbenes, flavonoids, phenolic acids, lignans and others. Lignans, which possess a steroid-like chemical structure and are defined as phytoestrogens, are of particular interest to researchers. Traditionally, health benefits attributed to lignans have included a lowered risk of heart disease, menopausal symptoms, osteoporosis and breast cancer. However, the intake of naturally lignan-rich foods varies with the type of diet. Consequently, based on the latest humans' findings and gathered information on lignan-rich foods collected from Phenol Explorer database this review focuses on the potential health benefits attributable to the consumption of different diets

containing naturally lignan-rich foods. Current evidence highlight the bioactive properties of lignans as human health-promoting molecules. Thus, dietary intake of lignan-rich foods could be a useful way to bolster the prevention of chronic illness, such as certain types of cancers and cardiovascular disease."

The World Health Organization about Breast Health and Cancer

The World Health Organization (WHO) states the following about breast health and cancer:

Early diagnosis - early diagnosis remains an important early detection strategy, particularly in low- and middle-income countries where the diseases is diagnosed in late stages and resources are very limited.

Mammography screening - mammography screening is the only screening method that has proven to be effective. Although there is evidence that organised population-based mammography screening programmes can reduce breast cancer mortality by around 20% in the screened group versus the unscreened group across all age groups, in general there appears to be a narrow balance of benefits compared with harms, particularly in younger and older women.

Breast Self-examination (BSE) - there is no evidence on the effect of screening through breast self-examination (BSE). However, the practice of BSE has been seen to empower women, taking responsibility for their own health. Therefore, BSE is recommended for raising awareness among women at risk rather than as a screening method.

Clinical Breast Examination (CBE) - research is underway to evaluate CBE as a low-cost approach to breast cancer screening that can work in less affluent countries. Promising preliminary results show that the age-standardised incidence rate for advanced-stage breast cancer is lower in the screened group compared to the unscreened group.

Doing a Breast Self-Examination (BSE)

Breast self-examination (BSE) is to be performed each month in addition to any mammograms or a clinical breast examination. Knowing the cyclical changes, what is normal and what regular monthly changes in the breast feel like is the best way to keep an eye on breast health.

Breast tissue extends from under the nipple and areola up towards the armpit.

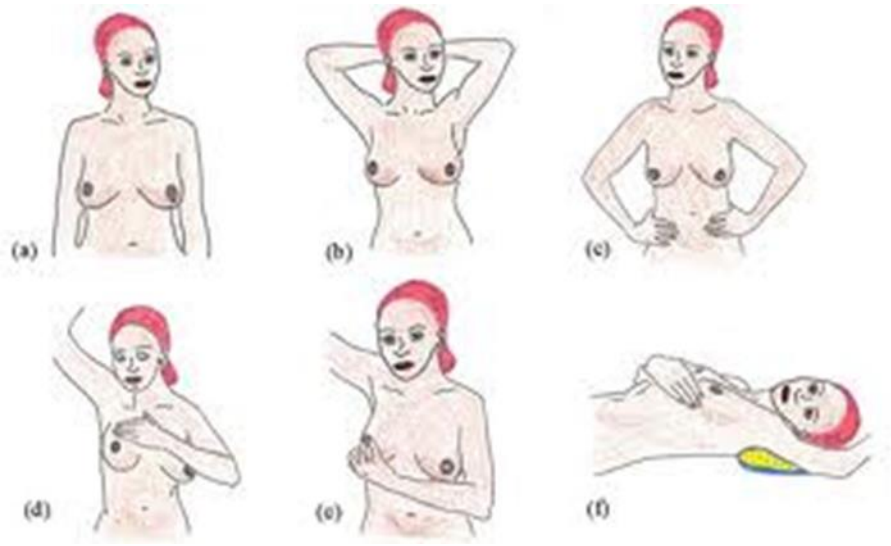
Make a Regular Date for Doing a BSE - If pre-menopausal**:** Set a regular time to do the BSE a few days after the menstruation when hormone levels are relatively stable and the breasts are less tender.

If already menopausal (have not had a period for a year or more), pick a particular day of the month to do the BSE and then repeat the BSE on that day every month

Visual Examination of Breasts - Hands on Hips - In the privacy of the bathroom or bedroom, strip to the waist and stand in front of a mirror. Both breasts must be visible at the same time. Stand with the hands on hips and check the appearance of both breasts. Look at size, shape, colour, whether both nipples are at the same level and contour. Note any changes in the skin colour or texture. Look at the nipples and areolas, to see how healthy they look

Visual Examination - Arms Over the Head - Still standing in front of the mirror, raise both arms over the head and see if both breasts move in the same way, and make a note of any differences.

Look at the size, shape, and drape - checking for symmetry. Pay attention to both nipples and areolas, to see if there are any dimples, bumps, or retraction (indentation). Look up toward the armpits and note if there is any swelling in the lower armpit area.



[Picture Credit: Breast Examination]

Manual Examination - Stand and Stroke - Raise the left arm overhead, and use the right-hand fingers to apply gentle pressure to the left breast. Stroke from the top to the bottom of the breast, moving across from the inside of the breast all the way into the armpit area. Make use of a circular motion, being sure to cover the entire breast area. Take note of any changes in texture, colour, or size. Switch sides and repeat the examination. This may be best done in the shower, as wet skin will have the least resistance to the friction of the fingers.

Manual Examination - Check Both Nipples - Still facing the mirror, lower both arms. With the index and middle fingers of the right hand, gently squeeze the left nipple and pull it forward. Does the nipple spring back into place? Does it pull back into the breast? Note whether or not any fluid leaks out. Reverse the hands and check the right nipple in the same manner.

Manual Examination - Recline and Stroke - This is best done in the bedroom, where one can lie down. Place a pillow on the bed so as to lie with both head and shoulders on the pillow. Lie down and put the left hand behind the head. Use the right hand to stroke the breast and underarm. Take note of any changes in texture, colour, or size. Switch sides and repeat the examination.

Guidelines For Doing a BSE:

- Mark the calendar as a reminder to do a BSE regularly.
- Stay relaxed and breathe normally while doing the BSE. Becoming tense may produce some knots that may be mistaken for something worrisome
- Report any changes or unusual pain to a doctor or nurse practitioner
- Keep a log of changes
- Remember to have an annual clinical breast examination and mammogram as described above

CANSA's Position on BSE

CANSA advocates that every woman should do regular (monthly) breast self-examinations (BSE) at the same time every month following her menstrual cycle from age 20 and to report any changes or concerns to a doctor or professional nurse practitioner without delay.

Regular monthly BSE should be seen as a method to raise awareness of breast cancer and taking responsibility for own breast health rather than as a screening method for breast cancer.

Symptoms and Signs of Breast Cancer in Women

Changes that could be due to a breast cancer include:

- A lump or thickening in an area of the breast
- A change in the shape of the nipple, particularly if it turns in, sinks into the breast, or has an irregular shape
- A blood stained discharge from the nipple
- A rash on a nipple or surrounding area
- A swelling or lump in the armpit
- Nipple tenderness or a lump or thickening in or near the breast or underarm area
- A change in the skin texture or an enlargement of pores in the skin of the breast (some describe this as similar to an orange peel's texture)
- Any unexplained change in the size or shape of the breast
- Dimpling anywhere on the breast
- Unexplained swelling of the breast (especially if on one side only)
- Unexplained shrinkage of the breast (especially if on one side only)
- Recent asymmetry of the breasts (Although it is common for women to have one breast that is slightly larger than the other, if the onset of asymmetry is recent, it should be checked.)
- Nipple that is turned slightly inward or inverted
- Skin of the breast, areola, or nipple that becomes scaly, red, or swollen or may have ridges or pitting resembling the skin of an orange

These signs do not necessarily mean cancer. Inverted nipples, blood stained nipple discharge or a rash can all be due to other medical conditions. In the event of any changes to what is normal, one should see a health professional. It is most likely to be a benign condition that can easily be treated. The health professional will refer to a breast health clinic or medical specialist where the staff can provide reassurance or provide any necessary treatment.

Diagnosis of Breast Cancer in Women

The doctor will check both breasts during a clinical breast examination, feeling for any lumps or other abnormalities.

Doctors use various tests to diagnose breast cancer and find out if the cancer has spread to other parts of the body. Some of the tests may also help the doctor decide which treatments may be the most effective.

For most types of breast cancer, a biopsy is the only way to make a definitive diagnosis of cancer. A biopsy is the removal of a small amount of tissue for examination under a microscope.

Tagliafico, A.S., Piana, M., Schenone, D., Lai, R., Massone, A.M. & Houssami, N. 2020.
"Diagnosis of early invasive breast cancer relies on radiology and clinical evaluation, supplemented by biopsy confirmation. At least three issues burden this approach: a) suboptimal sensitivity and suboptimal positive predictive power of radiology screening and diagnostic approaches, respectively; b) invasiveness of biopsy with discomfort for women undergoing diagnostic tests; c) long turnaround time for recall tests. In the screening setting, radiology sensitivity is suboptimal, and when a suspicious lesion is detected and a biopsy is recommended, the positive predictive value of radiology is modest. Recent technological advances in medical imaging, especially in the field of artificial intelligence applied to image analysis, hold promise in addressing clinical challenges in cancer detection, assessment of treatment response, and monitoring disease progression. Radiomics include feature extraction from clinical images; these features are related to tumor size, shape, intensity, and texture, collectively providing comprehensive tumor characterization, the so-called radiomics signature of the tumor. Radiomics is based on the hypothesis that extracted quantitative data derives from mechanisms occurring at genetic and molecular levels. In this article we focus on the role and potential of radiomics in breast cancer diagnosis and prognostication."

Gilbert, F.J. & Pinker-Domenig, K. 2020.
"Breast cancer is the most cause of female cancer deaths in the western world, with early detection of cancer being pivotal for an improved prognosis and survival. Imaging plays a pivotal role in breast cancer detection and staging and helps guiding treatment decisions. Imaging modalities for diagnosis and staging of breast cancer comprise mammography, digital breast tomosynthesis (DBT), ultrasound, contrast-enhanced mammography (CEM), and magnetic resonance imaging (MRI). Mammography is the mainstay of breast cancer screening and diagnosis. Mammography, together with ultrasound and MRI, is used to detect and characterize lesions found at screening and to evaluate symptomatic women. In patients with breast cancer, mammography, often in conjunction with specialized views, can determine lesion size and location and assess the surrounding tissue and lymph nodes. DBT is a three-dimensional (3D) imaging method with the potential to overcome the main limitation of standard two-dimensional mammography, a masking effect due to overlapping fibroglandular breast tissue, improving diagnostic accuracy in breast cancer, particularly in dense breasts. CEM allows both a morphologic evaluation comparable to routine digital mammography and through contrast agent application a simultaneous assessment of tumor neovascularity as an indicator of malignancy similar to MRI. Data indicate that CEM has an improved sensitivity and increases the specificity compared with mammography. Breast US is widely used to confirm a diagnosis of cancer, to look for additional disease in the breast, for image-guided breast biopsy and localization, assessment of the axilla, and as a second-look tool in patients with abnormalities found on MRI. MRI of the breast is the most sensitive modality for breast cancer detection. MRI of the breast is used for the assessment of disease extent and detection of additional lesion and seems to be more useful than mammography when staging multifocal and multicentric disease or when DCIS is present. This chapters will provide an overview of when and how to use mammography, DBT, ultrasound, CEM, and MRI for diagnosis and staging of breast cancer."

Candelaria, R.P., Adrada, B.E., Wei, W., Thompson, A.M., Santiago, L., Lane, D.L., Huang, M.L., Arribas, E.M., Rauch, G.M., Symmans, W.F., Gilcrease, M.Z., Huo, L., Lim, B., Ueno, N.T., Moulder, S.L. & Yang, W.T. 2019.
OBJECTIVE: Different molecular subtypes of triple-negative breast cancer (TNBC) have previously been identified through analysis of gene expression profiles. The luminal androgen receptor (LAR)

subtype has been shown to have a lower rate of pathologic complete response to neoadjuvant chemotherapy than other TNBC subtypes. The purpose of this study was to determine if the imaging features of TNBCs differ by AR (androgen receptor) status, which is a surrogate immunohistochemical (IHC) marker for the chemoresistant LAR subtype of TNBC.
MATERIALS AND METHODS: This sub-study was part of a clinical trial in patients with stage I-III TNBC who were prospectively monitored for response while receiving neoadjuvant systemic therapy (NAST) at a single comprehensive cancer center. This interim imaging analysis included 144 patients with known AR status measured by IHC. AR-positive (AR+) tumors were defined as those in which at least 10% of tumor cells had positive nuclear AR staining. Two experienced, fellowship-trained breast radiologists who were blinded to the IHC results retrospectively reviewed and reached consensus on all imaging studies for the index lesion (i.e., mammogram, ultrasound, and breast magnetic resonance imaging). The index lesion for each patient was reviewed and described according to the fifth edition of the Breast Imaging Reporting and Data System lexicon. Logistic regression modeling was used to identify imaging features predictive of AR status. $p \leq 0.05$ was considered statistically significant.
RESULTS: Univariate logistic regression models for AR status showed that AR+ TNBC was significantly associated with heterogeneously dense breast composition on mammography ($p = 0.02$), mass with calcifications ($p = 0.05$), irregular mass shape on mammography ($p = 0.03$), and irregular mass shape on sonography ($p = 0.003$). Multivariate logistic regression models for AR status showed that AR+ TNBC was significantly associated with heterogeneously dense breast composition on mammography ($p = 0.01$), high mass density on mammography ($p = 0.003$), and irregular mass shape on sonography ($p = 0.0004$).
CONCLUSION: The imaging features of TNBCs differ by AR status. Multimodality breast imaging may help identify the LAR subtype of TNBC, which has been shown to be a subtype that is relatively resistant to neoadjuvant chemotherapy.

Types of Breast Cancer in Women
The following types of breast cancer have been identified in women:

Ductal Carcinoma *in Situ*
Ductal Carcinoma in Situ (DCIS) is a non-invasive breast cancer where abnormal cells have been contained in the lining of the breast milk duct.

Invasive Ductal Carcinoma
Invasive Ductal Carcinoma means that abnormal cells that originated in the lining of the breast milk duct have invaded surrounding tissue.

Triple Negative Breast Cancer
Triple negative breast cancer means that the cells in the tumour are negative for progesterone, oestrogen, and HER2/neu receptors.

Inflammatory Breast Cancer
Inflammatory breast cancer is a less common form of breast cancer that may not develop a tumour and often affects the skin of the breast.

Phyllodes Tumour of the Breast

Phyllodes tumours of the breast are rare, accounting for less than 1% of all breast tumours. Phyllodes tumours tend to grow quickly, but they rarely spread outside the breast.

Metastatic Breast Cancer

Metastatic breast cancer is cancer that has spread beyond the breast, sometimes into the lungs, bones, or brain. Metastatic breast cancer is also classified as Stage 4 breast cancer meaning that the cancer has spread to other parts of the body.

Cribriform Breast Cancer

Cribriform breast cancer is a rare form of breast cancer that is often combined with another form of breast cancer. It is typically a low-grade and slow-growing cancer with a better outlook than most other types of invasive breast cancer.

Other Types of Breast Cancer

Less common types of breast cancer include Medullary Carcinoma, Tubular Carcinoma, and Mucinous Carcinoma.

- Medullary carcinoma - medullary carcinoma accounts for 3-5% of all breast cancer types. The tumour usually shows up on a mammogram, but does not always feel like a lump.
- Tubular Carcinoma - making up about 2% of all breast cancer diagnosis, tubular carcinoma cells have a distinctive tubular structure when viewed under a microscope. It is usually found through a mammogram and is a collection of cells that can feel like a spongy area of breast tissue rather than a lump. Typically this type of breast cancer is found in women aged 50 and above and usually responds well to hormone therapy.
- Mucinous Carcinoma (Colloid) - mucinous carcinoma represents approximately 1% to 2% of all breast cancers. The main differentiating features are mucus production and cells that are poorly defined. It also has a favourable prognosis in most cases.
- Paget Disease of the Breast or Nipple - this condition (also known as mammary Paget disease) is a rare type of cancer affecting the skin of the nipple and often the areola, which is the darker circle of skin around the nipple. Most people with Paget disease evident on the nipple also have one or more tumours inside the same breast.

Special Tests

The following tests or examinations may be done:

Mammogram - A mammogram is a low-dose x-ray of the breast. You'll need to take off your top and bra for the mammogram. The radiographer will position you so that your breast is against the X-ray machine and is gently but firmly compressed with a flat, clear, plastic plate. You'll have two mammograms of each breast taken from different angles.

[Picture Credit: Mammogram]

The breast tissue needs to be compressed to keep the breast still and to get a clear picture. Most women find this uncomfortable, and

for some women it may be painful for a short time.

Mammograms are usually only used in women over the age of 35. In younger women, the breast tissue is more dense (has less fat), which makes it difficult to detect any changes on the mammogram.

García-Albéniz, X., Hernán, M.A., Logan, R.W., Price, M., Armstrong, K. & Hsu, J. 2029.
Background: Randomized trials have shown that initiating breast cancer screening between ages 50 and 69 years and continuing it for 10 years decreases breast cancer mortality. However, no trials have studied whether or when women can safely stop screening mammography. An estimated 52% of women aged 75 years or older undergo screening mammography in the United States.
Objective: To estimate the effect of breast cancer screening on breast cancer mortality in Medicare beneficiaries aged 70 to 84 years.
Design: Large-scale, population-based, observational study of 2 screening strategies: continuing annual mammography, and stopping screening.
Setting: U.S. Medicare program, 2000 to 2008.
Participants: 1 058 013 beneficiaries aged 70 to 84 years who had a life expectancy of at least 10 years, had no previous breast cancer diagnosis, and underwent screening mammography.
Measurements: Eight-year breast cancer mortality, incidence, and treatments, plus the positive predictive value of screening mammography by age group.
Results: In women aged 70 to 74 years, the estimated difference in 8-year risk for breast cancer death between continuing and stopping screening was -1.0 (95% CI, -2.3 to 0.1) death per 1000 women (hazard ratio, 0.78 [CI, 0.63 to 0.95]) (a negative risk difference favors continuing). In those aged 75 to 84 years, the corresponding risk difference was 0.07 (CI, -0.93 to 1.3) death per 1000 women (hazard ratio, 1.00 [CI, 0.83 to 1.19]).
Limitations: The available Medicare data permit only 8 years of follow-up after screening. As with any study using observational data, the estimates could be affected by residual confounding.
Conclusion: Continuing annual breast cancer screening past age 75 years did not result in substantial reductions in 8-year breast cancer mortality compared with stopping screening.

CANSA's Position on Mammography:
CANSA is aware that in the developed world the starting age for regular breast screening by means of a mammogram has been raised to 45 years. This applies to First World countries where access to health care is freely available to everyone.

The South African situation is, however, somewhat different:

- The majority of South African women do not enjoy access to health care
- During 2013 a total of 1 656+ women between the ages 20 and 44 were histologically diagnosed with breast cancer

  CANSA, therefore, advocates a mammogram every year for all women from age 40 for purposes of non-symptomatic breast screening.

  CANSA further advocates that:
  - Women who are at risk and those that have had breast health problems in the past should consult their respective health professional to determine a schedule applicable to them

- Every woman with a close female relative diagnosed with breast cancer, should go for a mammogram 10 years earlier than the age at which the close relative was diagnosed with breast cancer
- Women aged 40 to 54 should have an annual mammogram
- Women 55 years and older should change to having a mammogram every 2 years – or have the choice to continue with an annual mammogram
- Screening should continue as long as a woman is in good health and is expected to live 10 years or longer
- Every woman should be informed of the known benefits, limitations, and potential harms linked to breast cancer screening by means of a mammogram

Breast ultrasound - An ultrasound uses sound waves to build up a picture of the breast. It can show if a lump is solid (made of cells) or is a fluid-filled cyst.

Ultrasound of lymph glands – the patient may also have an ultrasound of the lymph nodes in the armpit. If any of the nodes feel swollen or look abnormal on the ultrasound, the doctor will do a fine needle aspiration on the node or nodes.

Biopsy - This is when the doctor removes a small piece of tissue or cells from the lump or abnormal area. A pathologist (doctor who specialises in analysing cells) examines the tissue or cells under a microscope to look for cancer cells.

Staging of Breast Cancer in Women

Every patient that has been diagnosed with breast cancer must have other tests performed to determine whether the cancer has spread. This process is known as breast cancer staging. An appropriate treatment plan can be developed once the stage of the cancer is known.

Recurrent Breast Cancer

When breast cancer comes back, it may return in the same place. This is called a 'recurrence', because it is not a new cancer. But a recurrence can also appear in a place not directly related to the first breast cancer. This is called a 'metastasis', and if cancer is detected in several areas, these are called 'metastases'. When breast cancer comes back, it tends to show up in specific areas of the body:

- the breast or the area where the breast used to be
- the chest wall
- the lymph nodes
- the bones
- the lungs or around the lungs
- the liver
- the brain

Treatment Options for Breast Cancer in Women

People with cancer should be cared for by a multidisciplinary team (MDT), a team of specialists who work together to provide the best treatment and care. The team often consists of a specialist cancer surgeon, an oncologist (a radiotherapy and chemotherapy specialist), a radiologist, a pathologist, a radiographer, a reconstructive surgeon and a specialist nurse. Other members may include a physiotherapist, a dietician and an occupational therapist, and one may have access to clinical psychology support.

The main treatments for breast cancer may include:

Surgery - there are two types of surgery for breast cancer. These are surgery to remove just the cancerous lump (tumour), known as breast-conserving surgery, and surgery to remove the whole breast, which is called a mastectomy.

Breast-conserving surgery - breast-conserving surgery ranges from a lumpectomy or wide local excision, in which just the tumour and a little surrounding breast tissue is removed, to a partial mastectomy or quadrantectomy, in which up to a quarter of the breast is removed.

Mastectomy - a mastectomy is the removal of all the breast tissue, including the nipple. If there are no obvious signs that the cancer has spread to the lymph nodes, the patient may have a mastectomy, in which the breast is removed, along with a sentinel lymph node biopsy (SLNB). If the cancer has spread to the lymph nodes, the patient will probably need more extensive removal (clearance) of lymph nodes from the axilla (under the arm).

Robotic Surgery – A novel approach.

Donnely, E., Griffin, M.F. & Butler, P.E. 2020.

"Breast cancer is the most prevalent cancer and second leading cause of cancer-related deaths in both the US and UK female population, a prominent cause of morbidity and cost to both health services. All surgically fit patients are offered breast reconstruction following the initial surgery, and this is traditionally an open approach: either implant-based or an autologous tissue flap. Both lead to scarring that is difficult to conceal. This paper aims to evaluate the novel minimally invasive technique of robotic-assisted surgery."

METHODS: A systematic review was conducted using Medline (OvidSP) and Embase (OvidSP) to evaluate the current application of robotic-assisted surgery in breast surgery and reconstruction.

RESULTS: Twenty-one articles were identified and discussed, composing of level 4 and 5 evidence comparing different surgeons' experiences, techniques, and outcomes. To date, the robotic system has been utilized to harvest the latissimus dorsi muscle for use as a tissue flap (total harvest time of 92 minutes), to perform nipple-sparing mastectomy with immediate breast reconstruction (total operation time 85 minutes) and lately to harvest a deep inferior epigastric perforator flap via an intraabdominal approach.

CONCLUSIONS: Robotic-assisted surgery can successfully and reproducibly perform a nipple-sparing mastectomy with breast reconstruction. It can minimize the size of scarring and is superior to the laparoscopic technique, with improved 3-dimensional visualization, dexterity, and range of motion able to guide around the curvature of the breast. The main limiting factors are the lack of the US Food and Drug Administration approval, cost of the robot, and specialized skills required.

Radiotherapy - Radiation therapy is a form of cancer treatment that uses high levels of radiation to kill cancer cells or keep them from growing and dividing - while minimising damage to healthy cells.

Farrugia, C.E., Burke, E.S., Haley, M.E., Bedi, K.T. & Gandhi, M.A. 2019.
INTRODUCTION: Many cancer patients require radiation therapy and often experience adverse effects including erythema, itching, and pain. Aloe vera has been studied for its potential use in the prevention and treatment of radiation related adverse effects as it possesses a variety of properties and is considered an antioxidant and anti-inflammatory agent. Multiple controlled trials have been performed in order to evaluate the efficacy of aloe vera for the prevention and treatment of radiation side effects. Previous systematic reviews have examined the use of aloe vera for radiation-induced skin reactions, however updated literature now includes the use of aloe vera in proctitis.
OBJECTIVES: The aim of this comprehensive review is to summarize and evaluate the use of aloe vera in patients who have undergone radiation therapy for the treatment of cancer.
RESULTS: Aloe vera may not be effective for prophylaxis or treatment of radiation adverse effects in breast cancer patients. Moderate efficacy was seen when aloe vera was used in combination with mild soap versus soap as monotherapy for the treatment of radiation skin reactions. Aloe vera may be effective when cumulative radiation doses are greater than 2,700 cGy and for acute radiation proctitis.
CONCLUSIONS: There is contradictory evidence for the use of aloe vera in the setting of radiation in regards to its efficacy in the prevention and treatment of radiation-induced adverse effects.

Chemotherapy - chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

Hormone therapy - is often used to treat breast cancers that are sensitive to hormones. Doctors sometimes refer to these cancers as oestrogen receptor positive (ER positive) and progesterone receptor positive (PR positive) cancers.

Salvi, Ss., Bonafè, M. & Bravaccini, S. 2019.
"The possibility that a receptor for androgen is expressed in Breast Cancer (BC) is fascinating given that the tumor is predominantly estrogen-dependent. The androgen receptor (AR) is emerging as a new marker and a potential new therapeutic target in the treatment of BC patients. The recent availability of selective AR inhibitors (e.g. bicalutamide, enzalutamide, apalutamide) approved for the treatment of prostate cancer has opened up the possibility to use them in BC patients whose tumors express AR. However, AR appears to have various functions according to the BC subtype, e.g. ER-positive or triple negative BC and the patient prognosis is different on the basis of the presence or absence of estrogen and progesterone receptors. Moreover, a different AR expression was seen according to the various ethnicities. Of note, in population at low economical income, the availability of anti-AR compounds at low cost could open the possibility to treat AR-positive triple negative BC that are highly present in these populations. Up to now, AR detection is not routinely performed in BC. The standardization of AR detection methods could render AR an easily detectable marker in primary BC and metastatic samples. Nevertheless, the overall concordance of 60% of AR expression in primary tumor and metastasis implies that a clinician who need the AR value to give anti-AR therapy should have the data on both the tumor materials. Following the comprehensive studies on prostate cancer the possibility to test AR on liquid biopsies suggest the use of this biomarker for a real-time disease monitoring. Finally, considering the possibility to treat patients with immune

checkpoint inhibitors there is the need to know the relation between microenvironment and AR in BC."

Biological therapy (targeted therapy) - targeted therapies (sometimes called biological therapies) are new drugs that work differently from chemotherapy.

Follow-up Care and Treatment

Follow-up is recommended after treatment for breast cancer to check whether breast cancer has come back, to monitor side effects of treatment and to provide practical and emotional support.

Women who have been diagnosed and treated for early breast cancer have an increased risk of breast cancer coming back or developing in the other breast. Regular follow-up means that if breast cancer does come back or if a new breast cancer develops, it can be treated promptly. Follow-up also allows doctors to check for any side effects from treatment and to monitor any long-term treatments such as hormonal therapies. It also provides an opportunity for women to talk about how they're feeling.

Follow-up after treatment for breast cancer involves regular physical examinations and breast imaging tests (mammogram and/or ultrasound).

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/ heirs) relating to the use of any information contained in this Fact Sheet.

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