



Breast Cancer: A Comprehensive Review of Epidemiology, Diagnosis and Treatment

1ABHISHEK NINORE, 2SRUSHTI GAWANDE, 3TANVI SHINDE, 4SHRUTIKA GAIKWAD, 5ANSHUL DOSE

1Student, 2Student, 3Student, 4Student, 5Student

1Shri Sant Gajanan Maharaj College of pharmacy,

2Shri Sant Gajanan Maharaj College of pharmacy,

3Shri Sant Gajanan Maharaj College of pharmacy,

4Shri Sant Gajanan Maharaj College of pharmacy,

5Shri Sant Gajanan Maharaj College of pharmacy

Abstract:

Breast cancer is causing and alarming increasing in the quantity of loss of life approximately 685,000 annually. Breast most cancers is come to be most normally arise in particular in girl. This review provides an outline of the present day states of expertise on breast cancer inclusive of its prognosis, remedy option and similarly instructions. We talk the genetic and hormonal factors. That contribute to breast most cancers development, in addition to the function of environmental and lifestyle issue, we also observe the diverse analysis method together with mammography, biopsy, ultrasound, and magnetic resonance imaging (MRI) and the significance of early detection treatment alternative which include surgical operation, radiation remedy, chemotherapy and focused remedy are talk in addition to the trendy increase in immune remedy and precision medicine. And also have a look at about the epidemiological facts and responses of cosmetics to motive breast cancer in ladies' because of disturbing body hormones. It offers ratio of loss of life peoples of each 12 months due to the breast most cancers.

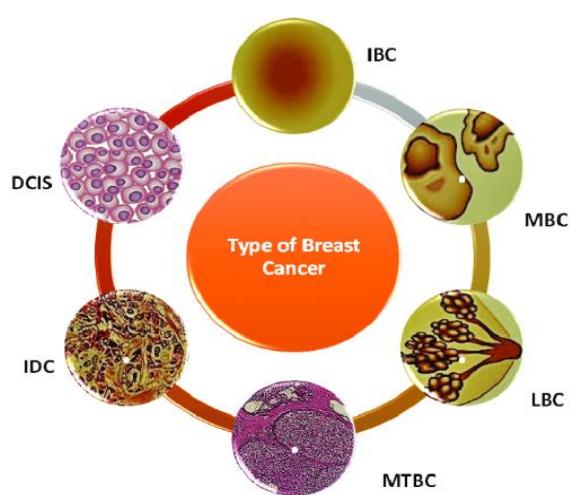
Keywords:

Breast cancer, therapy, diagnosis, treatment, epidemiology, factors, and lifestyle.

Introduction:

Better health recognition and availability of breast cancer screening programmes and remedy facilities could motive a favourable and high-quality clinical image inside the USA. The cancer cells unfold all through the tumor that due to the fact specific degrees of cancer there are different forms of breast most cancers which occur while affected cell and tissue unfold at some stage in the body consisting of **Ductal carcinoma in Situ** (DCIS) is sort of non-invasive breast cancer that money owed for approximately 20-30% of all breast most cancers diagnoses^[1].

Characterized with the aid of the presence of malignant cells within the milk duct of breast, DCIS is considered a precursor to invasive breast cancer. Despite its non-invasive nature, DCIS is an enormous scientific entity, as it may development to invasive most cancers if left untreated. With the massive use of mammography screening,



the incidence of DCIS has growth, and it's far now understand as a primary public fitness difficulty.

The 2nd kind is **Invasive Carcinoma** (IDC) and it is also called infiltrative ductal carcinoma and it also includes located in men^[2]. It is the maximum common sort of breast most cancers accounting for about 70-80% of all breast most cancers diagnoses this aggressive form of breast cancer takes place whilst cancer cells wreck through the basement membrane of the breast ducts or lobules and invade surrounding tissues, such as fat, muscle mass and lymph nodes. Invasive carcinoma can unfold to remote organs, together with lungs, liver, bones and brain making it potentially life threatening ailment^[3]. **Mixed Tumor Breast Cancer** (MTBC) is a 3rd type of breast most cancers Mixed tumor breast most cancers, additionally referred to as metaplastic carcinoma, is a rare and heterogeneous group of breast cancers that account for approximately 1-5% of all breast cancer diagnoses^[4]. These tumors are characterized by the presence of or greater distinct histological additives, consisting of epithelial and mesenchymal factors, in the same tumor. Mixed tumor breast cancers can exhibit an extensive variety of morphological and immunohistochemical functions, making prognosis and category hard. Due to their rarity and complexity, mixed tumor breast cancers pose widespread medical and healing demanding situations, and knowledge their biology and conduct is vital for growing powerful treatment strategies and improving patient results.

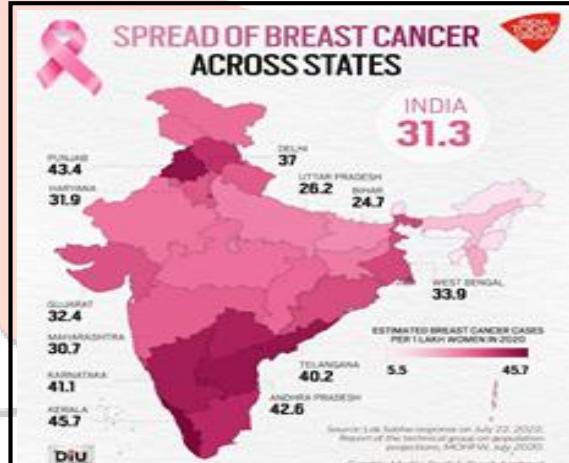
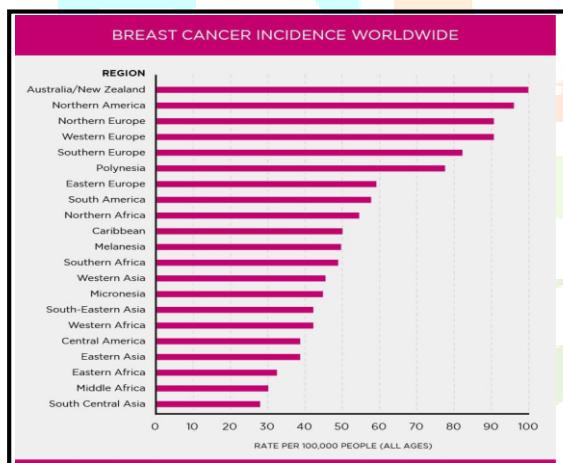
Forth sort of breast most cancers is **Lobular Breast Cancer** (LBC) Lobular breast cancer, a malignancy originating in the lobules of the breast, money owed for about 10-15% of all invasive breast cancer diagnoses^[5]. **Invasive lobular carcinoma** (ILC), the maximum common subtype, is characterized by using the infiltration of most cancers cells into the encompassing breast tissue, doubtlessly main to lymph node involvement and remote metastasis^[6]. The distinct biology and medical behavior of lobular breast cancer present precise demanding situations in analysis, remedy, and control. Unlike ductal breast most cancers, lobular carcinoma frequently manifests as a diffused, diffuse thickening of the breast tissue, making mammographic detection greater tough. Furthermore, lobular breast cancer is often associated with estrogen receptor (ER) and progesterone receptor (PR) positivity that may effect remedy techniques. **Mucinous Breast Cancer** (MBC) is the fifth kind that occurs due to invasive ductal cells, it is also called colloid breast cancer^[7]. It is an unprecedented and distinct subtype of invasive breast most cancers, accounting for approximately 2-3% of all breast most cancers diagnoses. Characterized via the presence of plentiful extracellular mucin, a thick, jelly-like substance, mucinous breast cancer tends to have an extra favorable prognosis as compared to different varieties of breast cancer. The specific histological capabilities of mucinous breast cancer, along with the presence of mucin pools and a loss of lymphatic invasion, distinguish it from different breast cancer subtypes. **Inflammatory Breast Cancer** (IBC) is a final kind characterized by means of the speedy onset of infection and growth of the breast, regularly followed by pain, redness, and swelling^[8]. IBC is clinically prominent with the aid of its diffuse erythema, which could cover up to 1-third of the breast, and its peau d'orange appearance, equivalent to the skin of an orange. The most cancers cells in IBC regularly block the lymph vessels, leading to the accumulation of fluid and the function irritation. This sort of most cancers has a tendency to expand quickly and may unfold swiftly to different parts of the frame, making its diagnosis generally poorer than other varieties of breast most cancers.

Epidemiology:

Breast most cancers is the most commonplace malignant tumour in ladies inside the world. Breast most cancers sufferers account for as a good deal as 36% of oncological sufferers. A predicted 2.089 million women have been diagnosed with breast cancer in 2018^[9, 10]. The prevalence of this malignant tumour is growing in all areas of the world, but the highest incidence happens in industrialized international locations. Almost half of the instances on a worldwide scale are in advanced international locations^[10, 11]. This fashion is particularly because of the so-referred to as Western life-style, associated with a bad weight loss plan, nicotinism, immoderate pressure and little bodily interest^[11]. In the case of breast most cancers, mammography has become recognized as screening. The greatest price of mammography is observed within the institution of ladies aged 50–sixty nine years^[9, 11]. Classical mammography is characterized by using 75–95% sensitivity and specificity at the extent of 80–95%^[12]. For ladies with suspected hereditary breast cancer, magnetic resonance mammography is used as a screening test. If a suspicious lesion is determined in mammography, an ultrasound exam is done and, if important, a thick needle biopsy in conjunction with a histopathological examination of the tumour. In 2018, there had been 234,087 instances of breast most cancers within the United States (crude price: 85/105), 55,439 within the United Kingdom (crude price: ninety four/a hundred and five), 56,162 in France (crude charge: 99/one zero five), seventy one, 888 in Germany (crude rate: 85.4/one hundred and five) and sixty six, 101 in Japan (crude fee: 58/one hundred and five)^[10]. The maximum incidence price inside the international is located in Belgium (crude rate: 113/105), and most of the continents in Australia

(crude charge: 94/one zero five)^[10]. In Poland, breast cancer is likewise the most-normally identified malignant tumour in women. There is a regular increase in cases (1990, 8000 new cases; 2018, 20,203 new instances)^[10]. The average occurrence charge in Europe is eighty four/one zero five^[10]. The lowest occurrence takes place within the international locations of Southeast Asia and Africa, where the standardized occurrence charge does now not exceed 25/one hundred and five^[10]. The lowest occurrence rates in 2018 had been recorded in Bhutan (crude price: five/a hundred and five) and the Republic of The Gambia (crude charge: 6.5/one zero five)^[10]. Despite the greater effectiveness of initial diagnostics or the speedy development of pharmacotherapy in latest years, breast most cancers is the first cause of dying from in 2018, 626,679 humans died from breast maximum cancers. Unlike morbidity, the nice mortality from this malignant tumour is recorded in developing nations^[10]. (Fiji, crude price 36/a hundred and five, highest charge; Somalia, crude charge 29/one hundred and 5; Ethiopia, crude rate 23/one hundred and five; Egypt, crude rate 21/one 0 five; Indonesia, crude fee 17/one hundred and 5; Papua New Guinea, crude price 25/100 and 5^[10], in which as plenty as 60% of all deaths. From breast cancer occur. This trend is particularly related to the dearth of screening, that's much less than in evolved international locations, the supply of diagnostics and cutting-edge strategies of remedy^[13]. In contrast, the standardized loss of life crude price in Belgium 16.3/105, in the United States thirteen/105, and in Japan 9.3/a hundred and five^[10]. The number of breast cancer cases in Poland is much lower than

In EU international locations (in 2013, the standardized incidence charge for Polish fifty one.8, for the EU 106.6)^[14]. The prevalence of person premenopausal women (20–49 years) has almost doubled during the last 30 years. Unfortunately, Polish women are nevertheless not very sensitive to prevention. They forget their breasts and underestimate the importance of normal test-ups. Compared to other European international locations, Polish women have a low prevalence of preventative care within the Netherlands, eighty% of women report free mammogram prevention packages, in England 71%, and in Poland handiest forty four%^[14].



The percent of five-yr. survival because of breast cancer in Poland is 78.5%, differing drastically from, for example, the end result of 90% done in the United States^[15]. Breast cancer is the maximum commonplace most cancers in India, accounting for 28.2% of all lady cancers, with an Estimated 216,108 cases by 2022. The age-standardized prevalence fee of female breast cancer has improved by 39.1% from 1990 to 2016, and this fashion has been visible in every kingdom of India over the past 26 years. Breast cancer has ranked number one cancer amongst Indian women with age adjusted rate as high as 25.8 according to 100,000 girls and mortality 12.7 consistent with one hundred,000 girls. Data reviews from various latest country wide cancer registries were as compared for prevalence, mortality quotes. The age adjusted prevalence fee of carcinoma of the breast turned into found as excessive as forty one in keeping with one hundred, 000 women for Delhi, accompanied through Chennai (37.9), Bangalore (34.4) and Thiruvananthapuram District (33.7). A statistically considerable growth in age adjusted rate over the years (1982-2014) in all the PBCRs namely Bangalore (annual percent alternate: 2.84%), Barshi (1.87%), Bhopal (2.00%), Chennai (2.44%), Delhi (1.44%) and Mumbai (1.42%) become located. Mortality-to-incidence ratio turned into located to be as high as sixty six in rural registries whereas as little as 8 in city registries. Besides this young age has been found as a primary risk thing for breast most cancers in Indian girls. Breast cancer projection for India for the duration of time intervals 2020 suggests the number to go as high as 1797900.

Risk factors

Risk elements play essential function in the onset and progression of tumors and can be labelled into modifiable and non-modifiable elements. Addressing modifiable threat elements can notably lessen the worldwide cancer burden^[16]. For breast cancer, there are threat factors commonplace to different cancer kinds as well as those particular to it^[17]. Genetic chance elements hereditary breast cancer money owed for about five% to 10% of all breast most cancers cases. Individuals with a high-quality circle of relatives history, specifically people with a first-diploma relative affected, are at a significantly expanded danger for breast cancer^[18]. BRCA1 and BRCA2 are two commonplace genetic mutations which can be involved in DNA restore via homologous recombination^[19]. BRCA1 and BRCA2 Mutations are responsible for 35% and 25% of hereditary breast cancer, respectively^[20, 21]. The incidence of BRCA1 and BRCA2 mutations is notably excessive in sure populations like Ashkenazi Jewish^[22]. Apart from BRCA1 and BRCA2, different high-penetrance genes related to breast cancer encompass PTEN, TP53, CDH1, and STK11, even as mild-penetrance genes encompass CHEK2, BRIP1, ATM, and PALB2 which can be concerned within the DNA repair and cellular cycle manipulate^[19]. Different genetic mutations found in patients are associated with positive molecular subtypes of breast cancer^[23]. Breast cancer is the type of cancer that develops in the breast tissue, typically in the duct or lobules. It occurs when abnormal cell in the breast grow and multiply uncontrollably, forming a tumour. This kind of breast cancer depends on which cells in the breast turn into cancer. Breast cancer is the second cause of death among women. After skin cancer, breast cancer is the most common cancer diagnosed in women. Breast cancer remains one of the most prevalent and devastating cancer worldwide, accounting for approximately 15% of all cancer related to death among women. According to the world health organization (WHO), over 2.3 million new cases of breast cancer are diagnosed annually, with mortality rate exceeding 700000 death per year.

Hormonal risk factors

Oestrogen, a steroid hormone, is chargeable for growing Women sexual characteristics and plays an important role within the metabolism. However, oestrogen and oestrogen metabolites also have capacity carcinogenic results, either through performing on ER, affecting cellular proliferation and cell cycle progression, or by way of inflicting oxidative damage to DNA^[24]. Thus, abnormally excessive oestrogen stages resulting from both endogenous and exogenous resources of oestrogen may growth the hazard of developing breast most cancers^[25].

Reproductive patterns

The ages at menarche and menopause are both extensive danger elements, as they may be associated with the period of oestrogen exposure. Several preceding case-control research and pooled analyses have shown that an age at menarche older than 15 years extensively will increase the hazard in comparison to an age at menarche of 12–thirteen years or more youthful^[26, 28]. Inversely, early menopause lowers the hazard of breast most cancers, in particular when comparing ladies who enjoy menopause at age 55 years or older with those at an age more youthful than 45 years^[17]. In addition, menstrual cycle capabilities additionally affect the breast most cancers risk. Short and normal menstrual cycles, which lead to expanded lifetime publicity to oestrogen and progesterone, are determined greater frequently in women with breast most cancers than in healthful ladies^[29]. Other characteristics, consisting of the range of menstrual cycles earlier than the first complete-term being pregnant and early menstrual regularity, also are related to breast cancer chance^[29, 30]. Several factors related to pregnancy play an enormous function in modulating the chance of breast most cancers. Regarding the age at the start childbirth, increasing age seems to raise the threat of HR-tremendous breast most cancers. Women having their first baby at age 30 years or older have a better chance for breast cancer as compared to those aged 25–29 years, but a lower risk compared to nulliparous ladies^[27]. A recent look at determined that this affiliation presentations and ethnicity-particular profile^[31]. The courting among the age at the start start and the prognosis of breast cancer patients has shown conflicting consequences^[31]. The quantity of pregnancies, together with parity and abortions, have been also studied. Some findings indicate that parity is associated with a decrease risk of HR-effective ailment, but no longer HR-negative disorder^[28, 32]. Though pregnancy might also boom the risk in the quick-term because of transient exposure to excessive degrees of sexual hormones, it exerts shielding effects inside the long term^[33, 34]. Early studies mentioned an association among abortion and next breast most cancers threat^[35]. However, the causal dating between both brought on or spontaneous abortion and breast most cancers chance become no longer confirmed in later, greater rigorous research^[36]. Breastfeeding is every other well-mounted element in decreasing breast cancer danger. A large-

scale observe reported that every three hundred and sixty five days of breastfeeding reduced the breast cancer hazard by way of 4.3% [37]. A meta-evaluation concluded that breastfeeding may want to exert shielding consequences against HR poor ailment. It additionally determined a discount of danger in BRCA1 vendors, but now not in BRCA2 vendors [38]. The association among breastfeeding and the risk of HR high-quality breast most cancers is still uncertain [39]. The defensive outcomes can be attributed to the biological mechanisms regarding the immunological components in breast milk [40], and the regeneration and differentiation of breast cells [41].

Hormone-containing medications

Besides the carcinogenic outcomes of endogenous hormones, medications containing artificial variations of oestrogen and/or progesterone like oral contraceptives (OC) and HRT that introduce exogenous hormones into the frame also are associated with breast cancer. The use of OC is popular amongst ladies of reproductive age, especially in western nations. The common dosage shape is the blended OC (COC), known for its great efficacy and protection, which contains synthetic oestrogen and progestin [42]. Previous evidence regarding the connection between COC use and breast cancer danger has been inconsistent. A meta-analysis involving greater than 150,000 women from Fifty four research confirmed that girls who're presently the usage of COC or have used it inside the past 10 years had a barely extended threat of breast most cancers as compared to never-users [43]. Similarly, a more recent big-scale observe performed among Danish women yielded comparable findings, although absolutely the boom in threat is small [44]. However, a case-control examine based totally on US ladies elderly 35–64 years did not aid the association [45]. HRT is prescribed to patients experiencing climacteric symptoms during menopause by using mimicking the outcomes of natural hormones. Additionally, lengthy-time period HRT has shown numerous advantages including decreasing the risks of coronary heart disease (CHD) and mortality [46]. Based on system and management routes, HRT may be classified into different types [47]. It may be composed of oestrogen best or blended with progestin, and may be administered orally, transdermally, or topically to relieve systemic or genitourinary signs [48]. The relationship among HRT and breast most cancers has been a subject of discussion for many years. The risk evaluation concerning breast cancer varies across unique research, varieties of HRT, and other contributing factors. Previous facts from the Women's Health Initiative (WHI) [49] and the Million Women Study [50] hooked up that the hazard of breast most cancers escalates with using HRT. An extra latest nested case-manage study in addition substantiated this association, revealing that blended HRT and longer duration gift a higher hazard [51]. A meta-evaluation suggested that an increased danger was displayed throughout all types of molecular subtypes, with the strongest affiliation found in luminal a breast most cancers [39].

Behavioural and environmental risk factors

Physical activity

Several observational research have found that more physical pastime have been associated with decrease breast cancer risks [52, 53]. Dose-reaction analyses indicated that the better the level of activity, the lower the risk [45, 55]. To decipher the causality, Mendelian randomization research have been performed. The doubtlessly inverse causal relationship between bodily hobby and risks of breast cancer was supported by means of the paintings of Papadimitriou [56]. Another take a look at via Dixon-Suen, employing a comparable methodology in addition confirmed the conclusions, with steady effects generated across extraordinary molecular subtypes [57]. In addition, sedentary behaviour is likewise an unbiased chance aspect for breast cancer, with a linear courting present between them [58]. Besides analysing the general population of breast most cancers sufferers, researches have additionally been stratified primarily based on specific subgroups. Some research have found menopause-dependent subgroup effects regarding the protective effect of physical pastime, with more potent evidence of risk discount in postmenopausal women in comparison to premenopausal women [59]. In addition to menopausal status, different factors consisting of BMI, race, HR repute, own family history, and parity also warrant consideration when discussing the results of physical pastime [60]. The potential biologic intent underlying the useful consequences of physical interest encompasses the discount of body fat, main to reduced exposure to endogenous sex hormones. Other viable mechanisms may include the discount of insulin and other increase factors, in addition to changes in immune gadget responses [61].

Body weight

BMI is broadly used to quantify body weight and classify somatotype. Overweight is described as a BMI of 25.0–29.9 kg/m², and obesity as a BMI of 30.0 kg/m² or better (ninety eight)^[62]. Accumulating statistics recommend that obesity is associated with an improved threat breast most cancers in postmenopausal girls, particularly for ER-advantageous subtypes. A preceding meta-analysis of 10 research showed that every 5-unit boom in BMI was related to a 33% extra chance of developing ER-fine and progesterone receptor (PR)-tremendous tumors^[63]. Results from WHI medical trials, which enrolled 67,142 postmenopausal women, revealed that a BMI of 35.0 kg/m² or higher turned into strongly associated with ER /PR tumors and advanced ailment, characterized by tumour size, lymph node involvement, level, and prognosis^[64]. Contrarily, weight reduction has been shown to exert protective outcomes in postmenopausal girls, suggesting that weight management might be protected as an approach for preventing breast cancer^[65]. The courting between BMI and breast cancer danger in premenopausal women is much less clean. Several meta-analyses have shown a sizeable lower inside the hazard of developing HR-tremendous breast most cancers^[63, 66, and 67]. However, an elevated threat of growing TNBC has been located^[67]. The timing and pattern of weight gain or loss also play important roles in figuring out their effect on breast cancer danger^[68]. Differences in show among ladies with varying menopausal statuses endorse underlying oestrogen-pushed mechanisms. In postmenopausal ladies, excess adiposity elevates oestrogen stages, which are broadly speaking derived from the conversion of androgens to oestrogen via aromatase^[69]. Chronic hyperinsulinemia, low-grade inflammation, and oxidative stress associated with obesity are oestrogen independent mechanisms that increase the risk of breast cancer^[70].

Diet

Dietary patterns were diagnosed as important hazard Dietary patterns have been identified as vital risk factors. The exists complex interaction between diet, metabolism and most cancers development. The Western and Mediterranean diets, as consultant dietary styles, have distinct characteristics and institutions with breast cancer chance^[71]. The Western weight-reduction plan is usually high in energy and low in vitamins. While there may be a longstanding debate over the affiliation among saturated fats consumption and breast cancer, a few research have discovered a fine association^[72,73], especially with HR-positive tumors^[72], whereas others have no longer determined a great link^[74,75]. Similarly, the position of dietary sugar as a danger thing for breast most cancers has yielded inconsistent results^[76, 77]. However, no matter those blended findings, excessive intake of fat and sugars may make contributions to weight advantage, main to obese or obesity, that's without delay associated with an increased risk of breast most cancers thru the pathway referred to above. The Mediterranean weight loss program, characterized by using a high consumption of fruits, greens, legumes, unrefined cereals, and olive oil, is famed for its several capacity fitness benefits^[71]. Studies have indicated that adherence to the Mediterranean food regimen reduces the hazard of growing breast cancer in each pre- and postmenopausal girls^[78], which is regular across all molecular subtypes^[79]. The antioxidants in the food regimen's major components may be chargeable for discount of oxidative stress and inflammation, consequently potentially main to a lower cancer occurrence^[80]. Alcohol intake has been recognized as a hazard enhancer in breast cancer, with studies demonstrating a dose-response dating^[81]. A meta-evaluation of fifty three research located that for every each day growth of 10 grams in alcohol intake, the threat accelerated by 7%^[82]. Even mild drinkers, ingesting 12.5 g/d or much less, face a five% increased chance as compared to non-drinkers^[83]. Regarding the molecular subtype, an elevated danger of luminal A and HER2-kind breast most cancers became found in a large-scale have a look at^[84]. The mechanisms in the back of this encompass hormonal imbalances, especially in oestrogen tiers, and the era of cancer causing agents for the duration of ethanol metabolism^[85]. A latest have a look at through Zhou et al. Discovered that epigenetic modifications at several CpG web sites also play a function in the pathogenic impact of alcohol on breast most cancers^[86].

Smoking

Accumulating records shows a modest but real association between both smoking and 2d-hand smoke with breast cancer^[87]. A wonderful pooled evaluation of 14 cohort studies, involving 934,681 participants, determined that the chance of breast cancer, in particular ER-superb breast most cancers, increases with the length of smoking before the first start. This association changed into located to be impartial of grownup alcohol intake^[88]. Supporting this, any other have a look at and meta-analysis drew comparable conclusions^[89]. A linear dose-reaction relationship among the hazard of breast cancer and each the depth and period of

smoking has been discovered^[90]. The carcinogenic compounds in tobacco smoke, which includes polycyclic fragrant hydrocarbons (PAH) and aromatic amines, are absorbed and metabolized with the aid of mammary tissues, contributing to the improvement of breast most cancers^[91].

Environmental exposures

The environmental risk elements underlying the etiology of breast cancer involves exposure to radiation, chemical substances, synthetic mild, and contamination in air, water, and soil in the course of distinctive home windows of susceptibility like prenatal, pubertal, pregnancy, and menopausal intervals^[92,93]. Radiation publicity is a nicely-set up hazard thing for breast most cancers. In the Life Span Study of Japanese atomic bomb survivors, each the occurrence of woman breast cancer and MBC appreciably extended^[94]. The threat for female breast most cancers increases linearly with the dose of ionizing radiation, and this risk is changed with the aid of the age at publicity and attained age^[94]. Numerous research also recommend a hyperlink among radiation used for scientific functions, which includes diagnostic radiation and radiotherapy, and an accelerated threat of breast most cancers^[95]. Women survivors of Hodgkin lymphoma (HL) dealt with chest radiotherapy at a young age face a breast most cancers occurrence of 16.6% as much as 30 years later^[96]. In male survivors, the occurrence will increase dramatically, as much as 23-fold in comparison with the general population over a forty-year length^[97]. Chronic exposures to numerous chemical substances at more youthful a long time might also increase the danger of developing breast most cancers, as indicated via each laboratory and human evidence. Known chemical substances of subject encompass dichlorodiphenyltrichloroethane (DDT), dioxins, perfluorooctane-sulfonamide (PFOSA), and certain air Pollutants. These materials are concept to contribute to cancer development either thru genotoxic or hormone-changing pathways^[98]. Additionally, exposure to outdoor mild at night time (LAN) is being studied as every other hazard thing for breast most cancers. High degrees of LAN disrupt nocturnal melatonin secretion and circadian rhythms, doubtlessly selling mammary carcinogenesis^[99]. However, the affiliation between LAN and breast cancer danger remains unclear. Some recommend an advantageous correlation^[100], at the same time as others do not^[101]. A recent look at by means of Sweeney highlights the want to don't forget additional environmental elements like NO₂ and noise pollutants while speak the results of outdoor LAN on breast cancer chance^[102].

Breast-related risk factors

Breast density

Breasts are composed of fibrous tissue, glandular tissue, and fat. Breast density is quantified the use of mammogram and is characterised by using the share of fibrous and glandular tissue relative to fatty tissue within the breasts. Nearly 1/2 of ladies aged forty years and older have dense breasts, which is associated with hereditary factors, productive factors and BMI^[103]. Women with dense breasts are at a greater risk of breast most cancers compared to people with fatty breasts^[104,105]. This fashion remains regular throughout different age corporations and menopausal statuses^[105,106]. Dense breast approach it tough to hit upon early breast cancer from mammograms, leading to the put off inside the diagnosis and remedy. Furthermore, breast most cancers normally originates from epithelial cells, and the dense breast, with its higher amount of epithelial additives, certainly will increase the chance of developing breast most cancers^[107]. However, despite the aggressive organic characteristics of breast cancer associated with dense breasts, no great distinction changed into detected in mortality among patients with dense breasts and fatty breasts^[108].

History of breast

Individuals with a records of breast cancer are at a better danger of developing a 2d number one breast most cancers. According to a SEER-based totally analysis of 812,851 girls with unilateral breast most cancers, there's an annual hazard of zero.37% for contralateral invasive breast cancer, which accumulates to nine. Nine% over 25 years. The danger is higher in Black girls and those with ER-terrible ailment as compared to their opposite numbers^[109]. Breast cancer patients wearing BRCA1/2 mutations experience a cumulative danger of 18.4% of a second primary contralateral breast most cancers in comparison to 4.9% for non-companies^[110]. Furthermore, pre-invasive breast lesions, along with both lobular carcinoma in situ (LCIS) and ductal carcinoma in situ (DCIS), are related to increased dangers of growing invasive breast cancer even after surgical excision^[111,112]. Beyond malignant breast lesions, there are numerous benign breast diseases (BBD) with excessive prevalence^[113], which could be divided into diverse classes. Overall, as proliferative

interest and atypia increase, so does the danger of growing breast cancer. A take a look at regarding nine,087 ladies over a fifteen-12 months observe-up length anticipated the relative dangers (RR) related to extraordinary sorts of BBD [114]. The RRs for non-proliferative (NP) modifications, proliferative ailment without atypia (PDWA), and extraordinary hyperplasia (AH) are 1.27, 1.88, and 4.24, respectively. Additionally, clinical elements which includes the time due to the fact biopsy, menopausal popularity, and family records of breast most cancers can also affect the connection between those lesions and the chance of breast cancer [115].

Lifestyle

Modern lifestyles including excessive alcohol intake and too much dietary fat consumption can boom the hazard of breast cancer. Alcohol consumption can increase the level of oestrogen-related hormones within the blood and cause the oestrogen receptor pathways. A meta-evaluation primarily based on fifty three epidemiological research indicated that a consumption of 35-44 grams of alcohol in keeping with day can boom the chance of breast most cancers by 32%, with a 7.1% increase within the RR for every additional 10 grams of alcohol in step with day. Modern western eating regimen includes an excessive amount of fats and extra intake of fats, especially the saturated fat, is related to mortality (RR=1.3) and bad analysis in breast cancer sufferers. Although the relationship among smoking and breast most cancers risk stays controversial, mutagens from cigarette smoke had been detected inside the breast fluid from non-lactating ladies. The threat of breast cancer is also elevated in girls who both smoke and drink (RR=1.54). Up to now, accumulating evidences show that smoking, particularly at an early age, has a higher hazard on breast most cancers occurrence.

Diagnosis

MACHINE LEARNING ALGORITHMS FOR BREAST CANCER PREDICTION

Machine mastering is an automated studying method the algorithms are designed to study from beyond dataset, we input a big range of records, gadget mastering model analyse that data and on the basis of that educate model we can make a prediction approximately destiny for breast cancer predictions, important machine mastering algorithms are as observe:

- A. ARTIFICIAL NEURAL NETWORK (ANN) Artificial Neural Network is a not unusual set of rules for data mining manner. Neural community includes enter layer, hidden layer and output layer. This technique is used to extract the sample this is too complex. Algorithm is based totally on parallel processing, disbursed memory, collective solution and network structure [116].
- B. LOGISTICS REGRESSION (LR) it's miles a supervised getting to know set of rules that consists of greater structured variables. The response of this algorithm is inside the binary form. Logistics regression can provide the continuous outcome of a particular information. This set of rules includes statistical version with binary variables [117].
- C. K-NEAREST NEIGHBOR (KNN) This set of rules is utilized in pattern recognition. It is a great approach for breast cancer prediction. In order to apprehend the pattern, each class has given an identical significance. K Nearest Neighbour extract the similar featured statistics from a huge dataset. On the idea of capabilities similarity we classify a massive dataset [118].
- D. DECISION TREE (DT) Decision tree is primarily based on type and regression version. Dataset is split into smaller number of subsets. These smaller set of information could make prediction with the best stage of precision. Decision tree method includes CART and conditional tree [119].
- E. NAIVE BAYES ALGORITHM (NB) This version is used to make an assumption of large schooling dataset. The algorithm is used to calculate the probability via Bayesian approach. It provides the very best accuracy at the same time as calculating the possibilities of noisy statistics that is used as an enter. It is an analogy classifier that is used for evaluating training dataset with training tuple [120].
- F. SUPPORT VECTOR MACHINE (SVM) it's miles a supervised mastering algorithm that is used for both classification and regression problems. It consists of theoretical and numeric capabilities to remedy the regression problem. It gives the best accuracy price at the same time as doing prediction of big dataset. It is a sturdy machine learning approach this is primarily based on 3-d and 2D modelling [121].
- G. RANDOM FOREST (RF) Random Forest set of rules is primarily based on supervised mastering this is used to solve each classification and regression troubles. It is a building block of system studying that is used for prediction of recent facts on the basis of preceding dataset [122].

H. K MEAN ALGORITHM K suggest is clustering algorithm that offers the partition of facts within the form of small clusters. Algorithm is used to discover the similarity among special facts factors. Data factors precisely include at least one cluster this is maximum suitable for the assessment of large dataset^[123].

I. MEAN ALGORITHM Clusters are identified on the similarity basis. Cluster that include similar statistics point belongs to 1 single family. In C suggest set of rules each records point belongs to one single cluster. It is on the whole utilized in medical pix segmentation and disorder prediction.

J. HIERARCHICAL ALGORITHM Hierarchical algorithm commonly affords the evaluation of uncooked records in the shape of matrix. Each cluster is separated from other clusters inside the shape of hierarchy. Every single cluster consists of similar data points. Probabilistic version is used to degree the space among every cluster^[124].

K. GAUSSIAN MIXTURE ALGORITHM it is most popular approach of unsupervised mastering. It is known as tender clustering technique that's used to compute the opportunity of various varieties of clustered data. The implementation of this set of rules is primarily based on expectation maximization^[125].

ENSEMBLE TECHNIQUES FOR BREAST CANCER PREDICTION

Ensemble techniques are considered as homogeneous and heterogeneous; homogenous ensemble techniques are the combination of 1 base method and two or more configuration strategies which includes bagging and boosting method while the heterogeneous is used to combine two or extra base methods, and ensemble method is based on supervised getting to know that offers the coolest prediction on the premise of a few speculation^[126].

- BAGGING the opposite name of the bagging technique is bootstrap aggregation which is used for the prediction of any disorder. It is based on multiple fashions, each version is skilled one by one after which blended collectively for prediction.
- BOOSTING Boosting is homogenous week learner that creates one strong classifier from a few susceptible classifiers. It is primarily based on step by step strategies for building up the model from a few education records^[127].
- STACKING Stacking is heterogeneous weak learner that mixes the one of a kind machine getting to know algorithms for prediction on equal dataset. It consists of or extra base models and merges the prediction of base version^[127],

DEEP LEARNING TECHNIQUES FOR BREAST CANCER PREDICTION

Deep gaining knowledge of is broader form of ANN (Artificial Neural Network). Deep getting to know algorithms consist of more than one layers structure. These algorithms are used to system the big variety of natural facts and feature ability to apprehend all of the information from one-of-a-kind classes. We basically apply the unsupervised deep getting to know techniques whilst we've large quantity of unlabelled records^[128].

A. AUTO ENCODER Auto encoder essentially consists of encoder that followed the decoder, encoder generally switch the input inside the form of variables like x, y and decoder takes that input and try to get returned all of the original input. The main motive of vehicle encoder is to research from a massive dataset, through education its network that forget about the inappropriate signals together with noisefr^[128].

B. SPARSE AUTO ENCODERS Sparse Auto Encoders automatically learn from unlabelled information. The Sparse Auto Encoder is largely a feed forward and returned propagation algorithm with an ordinary car encoder. A sparse automobile encoder can manage the sparsity regularizer. Sparsity regularizer presents the sparsity of output from the hidden layer of neural network^[128].

C. STACKED SPARSE AUTO ENCODER (SSAE) When the simple layer of Stacked Sparse Auto Encoder (SSAE) are combined collectively it will assemble the stretched sparse, the output of the primary layer is merged with the output of the second one layer, each stacked spare includes hidden layers which might be based on classifier and offer the output.^[128]

D. CONVOLUTIONAL NEURAL NETWORK CNN can examine the most cancers dataset within the form of photographs, in the course of the pre-processing phase it makes use of CovNet to examine the exceptional set of facts and using a few filters the CovNet can capture the special dimensions of images. Layers are divided in to pooling layer, convolutional layer, category layer and completely contacted layer^[129].

E. RECURRENT NEURAL NETWORK Recurrent Neural Network (RNN) is a category of neural network that includes a few hidden states, which uses the output of preceding kingdom as an input of next kingdom. It can technique a sequence of inputs that uses the identical parameters at every layer which reduces the complexity of that parameters more as it should be than the other neural networks however it can't manner a big quantity of series of inputs thru ReLU and Tanh activation capabilities^[128]

Treatment

Breast most cancers remedy regularly begins with surgery to dispose of the cancer. Most humans with breast cancer will have other remedies after surgery, together with radiation, chemotherapy and hormone remedy. Some humans can also have chemotherapy or hormone remedy earlier than surgery. These drugs can help decrease the most cancers and make it simpler to cast off. Your treatment plan will depend on your precise breast cancer. Your healthcare crew considers the degree of the cancer, how fast it is developing and whether or not the most cancers cells are touchy to hormones^[129]. Your care group also considers your general health and what you choose. There are many alternatives for breast cancer treatment. It can feel overwhelming to don't forget all the options and make complex decisions about your care. Consider seeking a 2d opinion from a breast professional in a breast center or health center. Talk to breast cancer survivors who've confronted the identical selection^[130].

Breast cancer surgery

Breast cancer surgical operation normally includes a method to dispose of the breast most cancers and a system to do away with some close by lymph nodes. Operations used to treat breast most cancers encompass:

- Removing the breast cancer.

A lumpectomy is surgery to get rid of the breast most cancers and some of the wholesome tissue around it. The relaxation of the breast tissue isn't eliminated. Other names for this surgical operation are breast-conserving surgical treatment and huge neighbourhood excision. Most human beings who have a lumpectomy also have radiation remedy. Lumpectomy might be used to get rid of a small most cancers. Sometimes you may have chemotherapy earlier than surgical procedure to decrease the cancer so that lumpectomy is viable^[131].

- Removing all the breast tissue.

A mastectomy is surgical operation to remove all breast tissue from a breast. The most common mastectomy procedure is overall mastectomy, also called easy mastectomy. This technique eliminates all of the breast, consisting of the lobules, ducts, fatty tissue and some skin, which includes the nipple and areola. Mastectomy is probably used to dispose of a huge cancer. It additionally is probably wished when there are more than one regions of most cancers inside one breast. You would possibly have a mastectomy in case you cannot have or don't need radiation therapy after surgical treatment. Some newer forms of mastectomy tactics may not take away the skin or nipple. For example, a pores and skin-sparing mastectomy leaves a few skin. A nipple-sparing mastectomy leaves the nipple and the skin round it, called the areola. These more recent operations can enhance the look of the breast after surgical procedure, but they are not options for everybody^[132].

- Removing numerous lymph nodes.

Axillary lymph node dissection is an operation to eliminate many lymph nodes from the armpit. Your breast most cancers surgical operation may encompass this operation if imaging exams display the most cancers has spread to the lymph nodes. It also might be used if most cancers is observed in a sentinel node biopsy.

- Removing a few lymph nodes.

A sentinel node biopsy is an operation to take out some lymph nodes for testing. When breast most cancers spreads, it often goes to the nearby lymph nodes first. To see if the most cancers has unfold, a surgeon removes some of the lymph nodes near the cancer. If not most cancers is discovered in those lymph nodes, the hazard of finding most cancers in any of the other lymph nodes is small. No different lymph nodes need to be removed

- Removing both breasts.

Some humans who've cancer in a single breast might also choose to have their other breast eliminated, even though it would not have cancer. This method is referred to as a contralateral prophylactic mastectomy. It is

probably a choice when you have a high danger of getting cancer within the different breast. The risk might be excessive if you have a strong own family records of most cancers or have DNA adjustments that boom the chance of cancer. Most human beings with breast cancer in one breast will never get cancer within the other breast. Complications of breast most cancers surgical treatment rely on the methods you choose. All operations have a hazard of ache, bleeding and contamination. Removing lymph nodes in the armpit contains a danger of arm swelling, called lymphedema ^[133].

You may additionally select to have breast reconstruction after mastectomy surgery. Breast reconstruction is surgical procedure to repair shape to the breast. Options would possibly encompass reconstruction with a breast implant or reconstruction using your own tissue. Consider asking your healthcare group for a referral to a plastic general practitioner earlier than your breast most cancers surgical operation.

Chemotherapy

Chemotherapy treats cancer with sturdy drugs. Many chemotherapy drugs exist. Treatment frequently entails an aggregate of chemotherapy drugs. Most are given through a vein. Some are to be had in pill shape. Chemotherapy for breast most cancers is often used after surgery. It can kill any cancer cells that might continue to be and lower the threat of the most cancers coming again. Sometimes chemotherapy is given before surgical procedure. The chemotherapy might decrease the breast cancer so that it's less difficult to dispose of. Chemotherapy before surgical procedure also might control most cancers that spreads to the lymph nodes. If the lymph nodes now not show symptoms of cancer after chemotherapy, surgical operation to do away with many lymph nodes might not be needed. How the most cancers responds to chemotherapy before surgery facilitates the healthcare group make decisions about what treatments is probably needed after surgical procedure. When the cancer spreads to different components of the body, chemotherapy can assist control it. Chemotherapy may also relieve signs and symptoms of a sophisticated cancer, such as pain. Chemotherapy facet results rely upon which drugs you receive. Common facet results encompass hair loss, nausea, vomiting, feeling very tired and having an expanded threat of having a contamination. Rare facet effects can include premature menopause and nerve damage. Very rarely, certain chemotherapy drug treatments can reason blood mobile most cancers ^[134].

Radiation therapy

Radiation remedy treats cancer with effective energy beams. The power can come from X-rays, protons or other source for breast most cancers remedy, the radiation is frequently outside beam radiation. During this type of radiation therapy, you lie on a table even as a system movements round you. The system directs radiation to unique factors on your body. Less frequently, the radiation can be placed inside the frame. This form of radiation is known as brachytherapy. Radiation therapy is frequently used after surgery. It can kill any cancer cells that might be left after surgery. The radiation lowers the hazard of the most cancers coming again. Side results of radiation remedy consist of feeling very worn-out and having a sunburn-like rash where the radiation is aimed. Breast tissue additionally might also look swollen or experience extra firm. Rarely, more-serious issues can happen. These consist of damage to the heart or lungs. Very rarely, a new cancer can grow inside the treated vicinity ^[135].

Hormone Therapy

- Hormone remedy uses medicines to dam certain hormones in the body. It's a remedy for breast cancers which might be touchy to the hormones oestrogen and progesterone. Healthcare specialists call those cancers oestrogen receptor effective and progesterone receptor fantastic. Cancers which can be touchy to hormones use the hormones as gas for their boom. Blocking the hormones can reason the cancer cells to cut back or die. Hormone remedy is often used after surgery and other remedies. It can lower the threat that the cancer will come returned. If the cancer spreads to other parts of the body, hormone remedy can assist manage it. Treatments that may be utilized in hormone therapy include:
- Medicines that block hormones from attaching to cancer cells. These medicines are called selective oestrogen receptor modulators.
- Medicines that prevent the frame from making oestrogen after menopause. These medicines are called aromatase inhibitors.

- Surgery or medicines to prevent the ovaries from making hormones. Hormone remedy side consequences depend on the remedy you receive. The side results can consist of warm flashes, night time sweats and vaginal dryness. More-critical facet consequences include a threat of bone thinning and blood clots ^[136].

Targeted therapy

Targeted therapy uses drugs that attack unique chemical substances in the most cancers cells. By blocking off these chemical substances, focused remedies can cause most cancers cells to die. The most commonplace centered therapy medicines for breast most cancers target the protein HER2. Some breast most cancers cells make extra HER2. This protein enables the most cancers cells grow and survive. Targeted therapy medicinal drug assaults the cells which might be making greater HER2 and doesn't hurt healthful cells. Many different targeted therapy drugs exist for treating breast cancer. You're most cancers cells may be tested to peer whether or not those drug treatments would possibly help you. Targeted therapy drug treatments can be used before surgical treatment to decrease a breast most cancers and make it less complicated to eliminate. Some are used after surgical procedure to decrease the danger that the most cancers will come returned. Others are used simplest when the most cancers has spread to different parts of the frame ^[137].

Immunotherapy

Immunotherapy is a treatment with medicine that helps the body's immune machine to kill cancer cells. The immune device fights off illnesses by attacking germs and different cells that shouldn't be within the frame. Cancer cells continue to exist by way of hiding from the immune device. Immunotherapy helps the immune machine cells locate and kill the most cancers cells. Immunotherapy is probably a choice for treating triple-poor breast cancer. Triple-negative breast cancer way that the most cancers cells don't have receptors for oestrogen, progesterone or HER2 ^[138].

Palliative care

Palliative care is a unique sort of healthcare that helps you feel higher when you have an extreme infection. If you have most cancers, palliative care can assist relieve pain and other signs and symptoms. A crew of healthcare professionals affords palliative care. The team can include medical doctors, nurses and different in particular trained specialists. Their purpose is to enhance pleasant of life for you and your circle of relatives. Palliative care specialists paintings with you, your circle of relatives and your care crew that will help you feel better. They provide an additional layer of aid even as you have got cancer remedy. You may have palliative care on the same time as robust most cancers remedies, such as surgical operation, chemotherapy or radiation remedy. When palliative care is used together with all of the different appropriate treatments, humans with most cancers can also feel higher and live longer ^[139].

Conclusion:

Breast cancer is a major global health issue with varying patterns across populations. Its epidemiology highlights significant geographic and demographic disparities, influenced by genetics and life style. For accurate diagnosis our article reviews various machine learning, deep learning and data mining algorithms plays a crucial role in improving patient outcomes. Advances in treatment, including surgery, chemotherapy, hormone therapy, immunotherapy and targeted therapies, have improved survival rates. Public awareness, early intervention and a multidisciplinary approach are critical to reducing the burden of this disease future efforts must focus on prevention strategies, equitable health care access, and ongoing support for patient and survivors.

References

[1] Hou, M. A. Mazurowski, L. J. Grimm, J. R. Marks, L. M. King, C. C. Maley, E.-S.-S. Hwang, and J. Y. Lo, Prediction of upstaged ductal carcinoma in situ using forced labelling and domain adaptation, *IEEE Trans. Biomed. Eng.*, vol. 67, no. 6, pp. 1565-1572, Jun. 2020.

[2] A.R. Chaudhury, R. Iyer, K.K. Iyachettira, and A. Sreedevi, Diagnosis of invasive ductal carcinoma using image processing techniques, in *Proc. Int. Conf. Image Inf. Process.*, Nov. 2011, pp. 16.

[3] D. L. Page, W. D. Dupont, L. W. Rogers, and M. Landenberger, Intra ductal carcinoma of the breast: Follow-up after biopsy only, *Cancers*, vol. 49, no. 4, pp. 751-758, 1982.

[4] A. B. Tuck, F. P. O'Malley, H. Singhal, and K. S. Tonkin, Osteopontin and p53 expression are associated with tumor progression in a case of synchronous, bilateral, invasive mammary carcinomas, *Arch. Pathol. Lab. Med.*, vol. 121, no. 6, p. 578, 1997.

[5] S. Masciari, N. Larsson, J. Senz, N. Boyd, P. Kaurah, M. J. Kandel, L. N. Harris, H.C. Pinheiro, A. Troussard, P. Miron, N. Tung, C. Oliveira, L. Collins, S. Schnitt, J. E. Garber, and D. Huntsman, Germline E-cadherin mutations in familial lobular breast cancer, *J. Med. Genet.*, vol. 44, no. 11, pp. 726-731, Aug. 2007.

[6] A. Memis, N. Ozdemir, M. Parildar, E. E. Ustun, and Y. Erhan, Mucinous (colloid) breast cancer: Mammographic and US features with histologic correlation, *Eur. J. Radiol.*, vol. 35, no. 1, pp. 3943, Jul. 2000.

[7] A. Gradilone, G. Naso, C. Raimondi, E. Cortesi, O. Gandini, B. Vincenzi, R. Saltarelli, E. Chiapparino, F. Spremberg, M. Cristofanilli, L. Frati, A. M. Aglianò, and P. Gazzaniga, Circulating tumor cells (CTCs) in metastatic breast cancer (MBC): Prognosis, drug resistance and phenotypic characterization, *Ann. Oncol.*, vol. 22, no. 1, pp. 8692, Jan. 2011.

[8] F. M. Robertson, M. Bondy, W. Yang, H. Yamauchi, S. Wiggins, S. Kamrudin, S. Krishnamurthy, H. Le-Petross, L. Bidaut, A. N. Player, S. H. Barsky, W. A. Woodward, T. Buchholz, A. Lucci, N. Ueno, and M. Cristofanilli, Inflammatory breast cancer: The disease, the biology, the treatment, *CA, Cancer J. Clin.*, vol. 60, no. 6, pp. 351-375, 2010.

[9] Nardin, S.; Mora, E.; Varughese, F.M.; D'Avanzo, F.; Vachanaram, A.R.; Rossi, V.; Saggia, C.; Rubinelli, S.; Gennari, A. Breast Cancer Survivorship, Quality of Life, and Late Toxicities. *Front. Oncol.* 2020, 16, 864. [CrossRef] [PubMed]

[10] "Global Cancer Observatory" International Agency for Research on Cancer, Lyon, France. Available online: <https://gco.iarc.fr/> (accessed on 1 June 2020).

[11] Bellanger, M.; Zeinomar, N.; Tehranifar, P.; Terry, M.B. Are Global Breast Cancer Incidence and Mortality Patterns Related to Country-Specific Economic Development and Prevention Strategies? *J. Glob. Oncol.* 2018, 4, 1-16. [CrossRef] [PubMed]

[12] Elmore, J.G.; Armstrong, K.; Lehman, C.D.; Fletcher, S.W. Screening for breast cancer. *JAMA* 2005, 293, 1245-1256. [CrossRef]

[13] Frances, F.Z.; Hull, R.; Khanyile, R.; Dlamini, Z. Breast cancer in low-middle income countries: Abnormality in splicing and lack of targeted treatment options. *Am. J. Cancer Res.* 2020, 10, 1568-1591. [PubMed]

[14] Religioni, U. Cancer incidence and mortality in Poland. *Clin. Epidemiol. Glob. Health* 2020, 8, 329-334. [CrossRef]

[15] SEER. Available online: <http://seer.cancer.gov> (accessed on 1 June 2020).

[16] GBD 2019 Cancer Risk Factors Collaborators. The global burden of cancer attributable to risk factors, 2010-19: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2022;400:563-91.

[17] Singletary SE. Rating the risk factors for breast cancer. *Ann Surg* 2003;237:474-82.

[18] Ellisen LW, Haber DA. Hereditary breast cancer. *Annu Rev Med* 1998;49:425-36.

[19] Shiovitz S, Korde LA. Genetics of breast cancer: a topic in evolution. *Ann Oncol* 2015;26:1291-9.

[20] Antoniou A, Pharoah PDP, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: A combined analysis of 22 studies. *Am J Hum Genet* 2003;72:1117-30.

[21] Tai YC, Domchek S, Parmigiani G, et al. Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. *J Natl Cancer Inst* 2007;99: 1811-4. 57. Struewing JP, Hartge P, Wacholder S, et al. The risk 2003;72:1117-30. 56. Tai YC, Domchek S, Parmigiani G, et al. Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. *J Natl Cancer Inst* 2007;99: 1811-4.

[22] Struewing JP, Hartge P, Wacholder S, et al. The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews. *N Engl J Med* 1997;336:1401-8.

[23] Hu C, Hart SN, Gnanaolivu R, et al. A population based study of genes previously implicated in breast cancer. *N Engl J Med* 2021;384:440-51.

[24] Yager JD, Davidson NE. Estrogen carcinogenesis in breast cancer. *N Engl J Med* 2006;354:270-82.

[25] Al-Shami K, Awadi S, Khamees A, et al. Estrogens and the risk of breast cancer: A narrative review of literature. *Heliyon* 2023;9:e20224.

[26] Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. *Epidemiol Rev* 1993;15: 36-47

[27] Nelson HD, Zakhер B, Cantor A, et al. Risk factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. *Ann Intern Med* 2012;156:635-48.

[28] Anderson KN, Schwab RB, Martinez ME. Reproductive risk factors and breast cancer subtypes: a review of the literature. *Breast Cancer Res Treat* 2014;144:1-10.

[29] Olsson HL, Olsson ML. The menstrual cycle and risk of breast cancer: a review. *Front Oncol* 2020; 10:21.

[30] Butler LM, Potischman NA, Newman B, et al. Menstrual risk factors and early-onset breast cancer. *Cancer Causes Control* 2000;11:451-8.

[31] Aurin J, Thorlacius H, Butt ST. Age at first childbirth and breast cancer survival: a prospective cohort study. *BMC Res Notes* 2020;13:9.

[32] Li C, Fan Z, Lin X, et al. Parity and risk of developing breast cancer according to tumor subtype: A systematic review and meta-analysis. *Cancer Epidemiol* 2021;75:102050.

[33] Clavel-Chapelon F, Gerber M. Reproductive factors and breast cancer risk. Do they differ according to age at diagnosis? *Breast Cancer Res Treat* 2002;72: 107-15.

[34] Katuwal S, Tapanainen J, Pukkala E. Multivariate analysis of independent roles of socioeconomic status, occupational physical activity, reproductive factors, and postmenopausal hormonal therapy in risk of breast cancer. *Breast Cancer Res Treat* 2022; 193:495-505.

[35] Brind J, Chinchilli VM, Severs WB, et al. Induced abortion as an independent risk factor for breast cancer: a comprehensive review and meta-analysis. *J Epidemiol Community Health* 1996;50:481-96.

[36] Beral V, Bull D, Collaborative Group on Hormonal Factors in Breast Cancer, et al. Breast cancer and abortion: collaborative reanalysis of data from 53 epidemiological studies, including 83000 women with breast cancer from 16 countries. *Lancet* 2004;363:1007-16.

[37] Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. *Lancet* 2002;360:187-95.

[38] Islami F, Liu Y, Jemal A, et al. Breastfeeding and breast cancer risk by receptor status — a systematic review and meta-analysis. *Ann Oncol* 2015;26: 2398-407.

[39] Mao X, Omeogu C, Karanth S, et al. Association of reproductive risk factors and breast cancer molecular subtypes: a systematic review and meta-analysis. *BMC Cancer* 2023;23:644.

[40] do Carmo França-Botelho A, Ferreira MC, França JL, et al. Breastfeeding and its relationship with reduction of breast cancer: a review. *Asian Pac J Cancer Prev* 2012;13:5327-32.

[41] Yang L, Jacobsen KH. A systematic review of the association between breastfeeding and breast cancer. *J Womens Health (Larchmt)* 2008;17:1635-45.

[42] Altshuler AL, Gaffield ME, Kiarie JN. The WHO's medical eligibility criteria for contraceptive use: 20 years of global guidance. *Curr Opin Obstet Gynecol* 2015;27:451-9.

[43] Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53297 women with breast cancer and 100239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996;347:1713-27.

[44] Mørch LS, Skovlund CW, Hannaford PC, et al. Contemporary hormonal contraception and the risk of breast cancer. *N Engl J Med* 2017;377:2228-39.

[45] Marchbanks PA, McDonald JA, Wilson HG, et al. Oral contraceptives and the risk of breast cancer. *N Engl J Med* 2002;346:2025-32.

[46] Lobo RA. Hormone-replacement therapy: current thinking. *Nat Rev Endocrinol* 2017;13:220-31.

[47] Mehta J, Kling JM, Manson JE. Risks, benefits, and treatment modalities of menopausal hormone therapy: current concepts. *Front Endocrinol (Lausanne)* 2021;12:564781.

[48] Portman DJ, Gass ML, Vulvovaginal Atrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *J Sex Med* 2014;11:2865-72.

[49] Chlebowski RT, Kuller LH, Prentice RL, et al. Breast cancer after use of estrogen plus progestin in postmenopausal women. *N Engl J Med* 2009;360:

[50] Beral V, Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet* 2003;362:419-27.

[51] Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. *BMJ* 2020;371: m3873.

[52] Bianchini F, Kaaks R, Vainio H. Weight control and physical activity in cancer prevention. *Obes Rev* 2002;3:5-8.

[53] Moore SC, Lee IM, Weiderpass E, et al. Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. *JAMA Intern Med* 2016;176:816-25.

[54] Neilson HK, Farris MS, Stone CR, et al. Moderate/vigorous recreational physical activity and breast cancer risk, stratified by menopause status: a systematic review and meta-analysis. *Menopause* 2017;24:322-44.

[55] Diao X, Ling Y, Zeng Y, et al. Physical activity and cancer risk: a dose-response analysis for the Global Burden of Disease Study 2019. *Cancer Commun (Lond)* 2023;43:1229-43.

[56] Papadimitriou N, Dimou N, Tsilidis KK, et al. Physical activity and risks of breast and colorectal cancer: a Mendelian randomisation analysis. *Nat Commun* 2020;11:597.

[57] Dixon-Suen SC, Lewis SJ, Martin RM, et al. Physical activity, sedentary time and breast cancer risk: A Mendelian randomization study. *Br J Sports Med* 2022;56:1157-70.

[58] Chong F, Wang Y, Song M, et al. Sedentary behavior and risk of breast cancer: a dose-response meta-analysis from prospective studies. *Breast Cancer* 2021;28:48-59.

[59] Friedenreich CM. Physical activity and breast cancer risk: the effect of menopausal status. *Exerc Sport Sci Rev* 2004;32:180-4.

[60] Friedenreich CM, Cust AE. Physical activity and breast cancer risk: impact of timing, type and dose of activity and population subgroup effects. *Br J Sports Med* 2008;42:636-47.

[61] Xu Y, Rogers CJ. Physical activity and breast cancer prevention: possible role of immune mediators. *Front Nutr* 2020;7:557997.

[62] Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults — The evidence report. National Institutes of Health. *Obes Res* 1998;6 Suppl 2:51S-209S.

[63] Suzuki R, Orsini N, Saji S, et al. Body weight and incidence of breast cancer defined by estrogen and progesterone receptor status — a meta-analysis. *Int J Cancer* 2009;124:698-712.

[64] 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;1:611-21.

[65] Teras LR, Patel AV, Wang M, et al. Sustained weight loss and risk of breast cancer in women 50 years and older: a pooled analysis of prospective data. *J Natl Cancer Inst* 2020;112:929-37.

[66] Munsell MF, Sprague BL, Berry DA, et al. Body mass index and breast cancer risk according to postmenopausal estrogen-progestin use and hormone receptor status. *Epidemiol Rev* 2014;36: 114-36.

[67] Li X, Li J, Hu Q, et al. Association of physical weight statuses defined by body mass index (BMI) with molecular subtypes of premenopausal breast cancer: a systematic review and meta-analysis. *Breast Cancer Res Treat* 2023. [Online ahead of print]

[68] Playdon MC, Matthews SB, Thompson HJ. Weight change patterns and breast cancer risk: a brief review and analysis. *Crit Rev Eukaryot Gene Expr* 2013;23:159-69.

[69] Simpson ER. Sources of estrogen and their importance. *J Steroid Biochem Mol Biol* 2003;86: 225-30.

[70] Chen X, Wang M, Yu K, et al. Chronic stress-induced immune dysregulation in breast cancer: Implications of psychosocial factors. *J Transl Int Med* 2022;11:226-33.

[71] Tsai HH, Yu JC, Hsu HM, et al. The risk of breast cancer between Western and Mediterranean dietary patterns. *Nutrients* 2023;15:2057.

[72] Sieri S, Chiodini P, Agnoli C, et al. Dietary fat intake and development of specific breast cancer subtype. *J Natl Cancer Inst* 2014;106:dju068

[73] Sellem L, Srour B, Guéraud F, et al. Saturated, mono- and polyunsaturated fatty acid intake and cancer risk: results from the French prospective cohort NutriNet-Santé. *Eur J Nutr* 2019;58: 1515-27.

[74] Park SY, Kolonel LN, Henderson BE, et al. Dietary fat and breast cancer in postmenopausal women according to ethnicity and hormone receptor status: the Multiethnic Cohort Study. *Cancer Prev Res (Phila)* 2012;5:216-28.

[75] Farvid MS, Cho E, Chen WY, et al. Premenopausal dietary fat in relation to pre- and post-menopausal breast cancer. *Breast Cancer Res Treat* 2014;145: 255-65.

[76] Arthur RS, Kirsh VA, Mossavar-Rahmani Y, et al. Sugar-containing beverages and their association with risk of breast, endometrial, ovarian and colorectal cancers among Canadian women. *Cancer Epidemiol* 2021;70:101855.

[77] Chazelas E, Srour B, Desmetz E, et al. Sugary drink consumption and risk of cancer: results from NutriNet-Santé prospective cohort. *BMJ* 2019;366: l2408.

[78] Turati F, Carioli G, Bravi F, et al. Mediterranean diet and breast cancer risk. *Nutrients* 2018;10:326.

[79] Castelló A, Pollán M, Buijsse B, et al. Spanish Mediterranean diet and other dietary patterns and breast cancer risk: case-control EpiGEICAM study. *Br J Cancer* 2014;111:1454-62.

[80] Laudisio D, Castellucci B, Barrea L, et al. Mediterranean diet and breast cancer risk: a narrative review. *Minerva Endocrinol (Torino)* 2021;46: 441-52.

[81] McDonald JA, Goyal A, Terry MB. Alcohol intake and breast cancer risk: weighing the overall evidence. *Curr Breast Cancer Rep* 2013;5:10.1007/s12609- 013-0114-z.

[82] Hamajima N, Hirose K, Tajima K, et al. Alcohol, tobacco and breast cancer — collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *Br J Cancer* 2002;87:1234-45.

[83] Seitz HK, Pelucchi C, Bagnardi V, et al. Epidemiology and pathophysiology of alcohol and breast cancer: Update 2012. *Alcohol Alcohol* 2012; 47:204-12.

[84] Hirko KA, Chen WY, Willett WC, et al. Alcohol consumption and risk of breast cancer by molecular subtype: Prospective analysis of the nurses' health study after 26 years of follow-up. *Int J Cancer* 2016;138:1094-101.

[85] Rojas K, Stuckey A. Breast cancer epidemiology and risk factors. *Clin Obstet Gynecol* 2016;59:651-72.

[86] Zhou X, Yu L, Wang L, et al. Alcohol consumption, blood DNA methylation and breast cancer: a Mendelian randomisation study. *Eur J Epidemiol* 2022;37:701-12.

[87] Macacu A, Autier P, Boniol M, et al. Active and passive smoking and risk of breast cancer: a metaanalysis. *Breast Cancer Res Treat* 2015;154:213-24.

[88] Gaudet MM, Carter BD, Brinton LA, et al. Pooled analysis of active cigarette smoking and invasive breast cancer risk in 14 cohort studies. *Int J Epidemiol* 2017;46:881-93.

[89] Gaudet MM, Gapstur SM, Sun J, et al. Active smoking and breast cancer risk: original cohort data and meta-analysis. *J Natl Cancer Inst* 2013;105: 515-25.

[90] Scala M, Bosetti C, Bagnardi V, et al. Dose-response relationships between cigarette smoking and breast cancer risk: a systematic review and meta-analysis. *J Epidemiol* 2023;33:640-8

[91] Hecht SS. Tobacco smoke carcinogens and breast cancer. *Environ Mol Mutagen* 2002;39:119-26.

[92] Natarajan R, Aljaber D, Au D, et al. Environmental exposures during puberty: window of breast cancer risk and epigenetic damage. *Int J Environ Res Public Health* 2020;17:493.

[93] Zeinomar N, Oskar S, Kehm RD, et al. Environmental exposures and breast cancer risk in the context of underlying susceptibility: A systematic review of the epidemiological literature. *Environ Res* 2020;187:109346

[94] Land CE, Tokunaga M, Koyama K, et al. Incidence of female breast cancer among atomic bomb survivors, Hiroshima and Nagasaki, 1950-1990. *Radiat Res* 2003;160:707-17.

[95] Ronckers CM, Erdmann CA, Land CE. Radiation and breast cancer: a review of current evidence. *Breast Cancer Res* 2004;7:21-32

[96] Schaapveld M, Aleman BMP, van Eggermond AM, et al. Second cancer risk up to 40 years after treatment for Hodgkin's lymphoma. *N Engl J Med* 2015;373:2499-511.

[97] de Vries S, Krul IM, Schaapveld M, et al. Risk of male breast cancer after Hodgkin lymphoma. *Blood* 2023;142:806-11.

[98] Rodgers KM, Udesky JO, Rudel RA, et al. Environmental chemicals and breast cancer: An updated review of epidemiological literature informed by biological mechanisms. *Environ Res* 2018;160:152-82.

[99] Stevens RG, Brainard GC, Blask DE, et al. Breast cancer and circadian disruption from electric lighting in the modern world. *CA Cancer J Clin* 2014;64: 207-18.

[100] Xiao Q, James P, Breheny P, et al. Outdoor light at night and postmenopausal breast cancer risk in the NIH-AARP diet and health study. *Int J Cancer* 2020;147:2363-72.

[101] Johns LE, Jones ME, Schoemaker MJ, et al. Domestic light at night and breast cancer risk: a prospective analysis of 105000 UK women in the Generations Study. *Br J Cancer* 2018;118:600-6.

[102] Sweeney MR, Nichols HB, Jones RR, et al. Light at night and the risk of breast cancer: Findings from the Sister Study. *Environ Int* 2022;169:107495.

[103] Checka CM, Chun JE, Schnabel FR, et al. The relationship of mammographic density and age: implications for breast cancer screening. *AJR Am J Roentgenol* 2012;198:W292-5.

[104] Lester SP, Kaur AS, Vegunta S. Association between lifestyle changes, mammographic breast density, and breast cancer. *Oncologist* 2022;27:548-54.

[105] Advani SM, Zhu W, Demb J, et al. Association of breast density with breast cancer risk among women aged 65 years or older by age group and body mass index. *JAMA Netw Open* 2021;4:e2122810

[106] Kim EY, Chang Y, Ahn J, et al. Mammographic breast density, its changes, and breast cancer risk in premenopausal and postmenopausal women. *Cancer* 2020;126:4687-96.

[107] Freer PE. Mammographic breast density: impact on breast cancer risk and implications for screening. *Radiographics* 2015;35:302-15.

[108] Gierach GL, Ichikawa L, Kerlikowske K, et al. Relationship between mammographic density and breast cancer death in the Breast Cancer Surveillance Consortium. *J Natl Cancer Inst* 2012;104:1218-27.

[109] Giannakeas V, Lim DW, Narod SA. The risk of contralateral breast cancer: a SEER-based analysis. *Br J Cancer* 2021;125:601-10.

[110] Malone KE, Begg CB, Haile RW, et al. Population based study of the risk of second primary contralateral breast cancer associated with carrying a mutation in BRCA1 or BRCA2. *J Clin Oncol* 2010;28:2404-10.

[111] King TA, Pilewskie M, Muhsen S, et al. Lobular carcinoma in situ: a 29-year longitudinal experience evaluating clinicopathologic features and breast cancer risk. *J Clin Oncol* 2015;33:3945-52.

[112] Estévez LG, Álvarez I, Seguí MÁ, et al. Current perspectives of treatment of ductal carcinoma in situ. *Cancer Treat Rev* 2010;36:507-17.

[113] Gutwein LG, Ang DN, Liu H, et al. Utilization of minimally invasive breast biopsy for the evaluation of suspicious breast lesions. *Am J Surg* 2011;202: 127-32.

[114] Hartmann LC, Sellers TA, Frost MH, et al. Benign breast disease and the risk of breast cancer. *N Engl J Med* 2005;353:229-37.

[115] Schnitt SJ. Benign breast disease and breast cancer risk: morphology and beyond. *Am J Surg Pathol* 2003;27:836-41.

[116] C. Prasetyo, A. Kardiana, and R. Yuliwulandari, "Breast cancer diagnosis using artificial neural networks with extreme learning techniques," *Int. J. Adv. Res. Artif. Intell.*, vol. 3, no. 7, pp. 10–14, 2014

[117] S. B. Imandoust and M. Bolandraftar, "Application of k-nearest neighbor (KNN) approach for predicting economic events: Theoretical background," *Int. J. Eng. Res. Appl.*, vol. 3, pp. 605–610, Sep. 2013.

[118] Y.-Y. Song and L. Ying, "Decision tree methods: Applications for classification and prediction," *Shanghai Arch. Psychiatry*, vol. 27, no. 2, p. 130, 2015.

[119] W. Wu, S. Nagarajan, and Z. Chen, "Bayesian machine learning: EEGMEG signal processing measurements," *IEEE Signal Process. Mag.*, vol. 33, no. 1, pp. 14–36, Jan. 2015.

[120] Y. Yang, J. Li, and Y. Yang, "The research of the fast SVM classifier method," in *Proc. 12th Int. Comput. Conf. Wavelet Act. Media Technol. Inf. Process. (ICCWAMTIP)*, Dec. 2015, pp. 121–124.

[121] H. Tran, "A survey of machine learning and data mining techniques used in multimedia system," *Dept. Comput. Sci., Univ. Texas Dallas Richardson, Richardson, TX, USA, Tech. Rep.*, Sep. 2019.

[122] Y. Li and H. Wu, "A clustering method based on K-means algorithm," *Phys. Procedia*, vol. 25, pp. 1104–1109, Jan. 2012

[123] J. C. Bezdek, R. Ehrlich, and W. Full, "FCM: The fuzzy c-means clustering algorithm," *Comput. Geosci.*, vol. 10, nos. 2–3, pp. 191–203, Jan. 1984.

[124] S. Patel, S. Sihmar, and A. Jatain, "A study of hierarchical clustering algorithms," in *Proc. 2nd Int. Conf. Comput. Sustain. Global Develop. (INDIACOM)*, Mar. 2015, pp. 537–541.

[125] J. Zhang, X. Hong, S.-U. Guan, X. Zhao, H. Xin, and N. Xue, "Maximum Gaussian mixture model for classification," in *Proc. 8th Int. Conf. Inf. Technol. Med. Educ. (ITME)*, Dec. 2016, pp. 587–591.

[126] M. S. Bala and G. R. Lakshmi, "Efficient ensemble classifiers for prediction of breast cancer," *Int. J. Adv. Res. Comput. Sci. Softw. Eng.*, vol. 6, no. 3, pp. 1–5, 2016.

[127] M. Togacar and B. Ergen, "Deep learning approach for classification of breast cancer," in *Proc. Int. Conf. Artif. Intell. Data Process. (IDAP)*, Sep. 2018, pp. 1–5.

[128] Y. LeCun, Y. Bengio, and G. Hinton, "Deep learning," *Nature*, vol. 521, no. 7553, pp. 436–444, 2015.

[129] D. Selvathi and A. A. Poornila, "Deep learning techniques for breast cancer detection using medical image analysis," in *Biologically Rationalized Computing Techniques For Image Processing Applications*. Cham, Switzerland: Springer, 2018, pp. 159–186.

[130] Breast cancer. *Cancer.Net*. <https://www.cancer.net/cancer-types/breast-cancer/view-all>. Accessed Aug. 2, 2023.

[131] Mukwende M, et al. Erythema. In: Mind the Gap: A Handbook of Clinical Signs in Black and Brown Skin. St. George's University of London; 2020. <https://www.blackandbrownskin.co.uk/mindthegap>. Accessed Aug. 10, 2023.

[132] Breast cancer risk reduction. National Comprehensive Cancer Network. <https://www.nccn.org/guidelines/guidelines-detail?category=2&id=1420>. Accessed Aug. 2, 2023.

[133] Breast cancer prevention (PDQ) – Patient version. National Cancer Institute. <https://www.cancer.gov/types/breast/patient/breast-prevention-pdq>. Accessed Aug. 2, 2023.

[134] Breast cancer. National Comprehensive Cancer Network. <https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1419>. Accessed Aug. 2, 2023.

[135] Palliative care. National Comprehensive Cancer Network. <https://www.nccn.org/guidelines/guidelines-detail?category=3&id=1454>. Accessed Aug. 2, 2023.

[136] Cancer-related fatigue. National Comprehensive Cancer Network. <https://www.nccn.org/guidelines/guidelines-detail?category=3&id=1424>. Accessed Aug. 2, 2023.

[137] Breast SPOREs. National Cancer Institute. <https://trp.cancer.gov/spores/breast.htm>. Accessed Aug. 9, 2023.

[138] Member institutions. Alliance for Clinical Trials in Oncology. <https://www.allianceforclinicaltrialsinoncology.org/main/public/standard.xhtml?path=%2FPublic%2FIstitutions>. Accessed Aug. 9, 2023.

[139] Giridhar KV (expert opinion). Mayo Clinic. Oct. 18, 2023.

