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## Physical activity and prevention of breast cancer

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### Abstract

Breast cancer is the most commonly diagnosed invasive malignancy and the second leading cause of cancer death in women. As per the literature available there is a low risk of cancer among physically active women as compared to the least active women. The associations were strongest for recreational activity, for activity sustained over the lifetime or done after menopause, and for activity that is of moderate to vigorous intensity and performed regularly. There is also some evidence for a stronger effect of physical activity amongst postmenopausal women, women who are normal weight, have no family history of breast cancer, and are parous. It is likely that physical activity is associated with decreased breast cancer risk via multiple interrelated biologic pathways that may involve adiposity, sex hormones, insulin resistance, adipokines, and chronic inflammation.

**Keywords:** breast cancer, physical activity, menopause

### Introduction

Most of the established risk factors for breast cancer such as family history of the disease, early age at menarche, late age at menopause, late age at first childbirth, and nulliparity are not easily amenable to intervention. In contrast, physical inactivity is a modifiable risk factor that has been associated with increased risk of breast cancer [1-3]. Physical activity may protect against breast cancer through reduced lifetime exposure to sex steroid hormones, reduced exposure to insulin and insulin-like growth factors, and prevention of overweight and obesity. Increase of physical activity is, therefore, a potentially promising preventive measure against breast cancer.

Breast cancer is the second most common cancer in the world and, by far, the most frequent cancer among women with an estimated 1.67 million new cancer cases diagnosed in 2012 (25% of all cancers). It is the most common cancer in women both in more and less developed regions with slightly more cases in less developed (883,000 cases) than in more developed (794,000) regions. Incidence rates vary nearly four-fold across the world regions, with rates ranging from 27 per 100,000 in Middle Africa and Eastern Asia to 92 in Northern America.

Breast cancer ranks as the fifth cause of death from cancer overall (522,000 deaths) and while it is the most frequent cause of cancer death in women in less developed regions (324,000 deaths, 14.3% of total), it is now the second cause of cancer death in more developed regions (198,000 deaths, 15.4%) after lung cancer. The range in mortality rates between world regions is less than that for incidence because of the more favorable survival of breast cancer in (high-incidence) developed regions, with rates ranging from 6 per 100,000 in Eastern Asia to 20 per 100,000 in Western Africa. The number of cases worldwide has significantly increased in low and middle-income countries since the 1970s, a phenomenon partly attributed to increased life expectancy, changing reproductive patterns (such as later age at first childbirth and less breastfeeding), and the adoption of western lifestyles. The breast cancer fact sheet is shown in Table 1.

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**Table 1:** Breast Cancer Estimated Incidence, Mortality and Prevalence Worldwide in 2012

Estimated numbers (thousands)	Cases	Deaths	5-year prev.
World	1671	522	6232
More developed regions	788	198	3201
Less developed regions	883	324	3032
WHO Africa region (AFRO)	100	49	318
WHO Americas region (PAHO)	408	92	1618
WHO East Mediterranean region (EMRO)	99	42	348
WHO Europe region (EURO)	494	143	1936
WHO South-East Asia region (SEARO)	240	110	735
WHO Western Pacific region (WPRO)	330	86	1276
IARC membership (24 countries)	935	257	3591
United States of America	233	44	971
China	187	48	697
India	145	70	397
European Union (EU-28)	362	92	1444

Source: [http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx)

### Known and probable risk factors for getting breast cancer:

- Being a woman
- Getting older
- Genetics (having a mutation in the BRCA1 or BRCA2 breast cancer genes)
- Having a previous biopsy showing hyperplasia (abnormal cell growth) or carcinoma in situ (usually not a tumor, but a flat growth that can be a precursor of cancer)
- Having a family history of breast cancer or ovarian cancer
- Having high breast density on a mammogram (a mammogram is a painless test that uses X rays to diagnose breast disease in women)
- Starting menopause after age 55
- Never having children
- Having the first child after age 35
- Being overweight after menopause or gaining weight as an adult
- Having more than one drink of alcohol per day
- Currently or recently using combined estrogen and progestin hormone replacement therapy
- Having first menstruation before age 12
- A new lump or lumpiness, especially if it's only in one breast
- A change in the size or shape of the breast
- A change to the nipple, such as crusting, ulcer, redness or inversion
- A nipple discharge that occurs without squeezing
- A change in the skin of the breast such as redness or dimpling
- An unusual pain that doesn't go away.

People with any of these signs should go to the doctor right away. The sooner the cancer is diagnosed, the better the chances of survival.

The available statistics sum up survival rates by breast cancer stage. The stages shown below are based on studies of a 5-year survival rate (CDC 2008a).

- Stage 0—No cancer. *Survival rate:* 100%.
- Stage I—Tumor is smaller than 2 cm and no lymph nodes are involved. *Survival rate:* 100%.
- Stage IIA—Tumor is smaller than 5 cm and there may be cancer cells in the lymph nodes under the arm that are not stuck together. *Survival rate:* 92%.
- Stage IIB—Tumor is bigger than 5cm and the cancer has

not spread. *Survival rate:* 81%.

- Stage IIIA—Tumor is bigger than 5cm and the lymph nodes in the armpit contain cancer cells that may be stuck together, but there is no further spread. *Survival rate:* 67%.
- Stage IIIB—Tumor is fixed to the skin or chest wall and the lymph nodes may or may not contain cancer cells, but there is no further spread. *Survival rate:* 54%.
- Stage IV—Tumor can be any size, the lymph nodes may or may not contain cancer cells, and the cancer has spread to other parts of the body such as the lungs, liver, or bones. *Survival rate:* 20%.

### Background

There is a small amount of data on the role of exercise in cancer patients undergoing chemotherapy, but many of the studies are limited by small size, imperfect design or patient selection. More information about exercise in outpatient chemotherapy patients is needed, as are more comprehensive studies of the effects of chemotherapy on functional status and psychological states. In the mid 1980s, MacVicar and Winningham, two oncology nurses, began studying exercise in breast cancer patients [1-3]. They noticed that patients who exercised during treatment experienced positive mood enhancing effects, and, incidentally, reported less nausea [4]. This led to a second study in 42 breast cancer patients, which confirmed that those who exercised experienced less nausea than the non-exercisers or those who stretched only [5]. A third, similar study found that patients who exercised had significant improvements in functional capacity, as measured by Vo2Lmax [6]. In 1991, Young-McCaughan and Sexton investigated the relationship between exercise and quality of life (QOL) [4]. This retrospective study of 42 previously treated breast cancer patients found that those who had exercised during treatment had a significantly improved quality of life (based on an 18 question QOL Index) than the non-exercisers. This study was limited by size, as well as retrospective design and the select group of predominately white, upper class women with early stage breast cancer. Similarly, a study by Mock *et al* enrolled 14 predominately white, married; college educated women with breast cancer, with nine of them participating in a comprehensive rehabilitation program of walking and support groups. They noticed increased physical performance, and less fatigue, difficulty sleeping, and depression among the rehabilitation patients [5]. There has also been research in the area of fatigue in chemotherapy patients. In a retrospective study, Schwartz

reported patients felt physically renewed and more alert after exercise [6], though in this study the patients were recalling events that occurred several years prior to the questionnaire. Dimeo, *et al* have performed a number of studies on patients receiving high dose chemotherapy with stem cell transplant, and have reported benefits of exercise ranging from increased physical performance and decrease in fatigue [7-10], decreased duration of pancytopenia [11,12], and other toxicities, such as severity of diarrhea and pain, and length of hospitalization [13]. Furthermore, psychological parameters, such as somatization, anxiety, and obsessive compulsive traits were significantly decreased in exercise groups [11]. It may be difficult, however, to apply these data to other cancer patients, who are outpatients and receiving lower doses of chemotherapy.

### Role of exercise in prevention of breast cancer

#### Sex hormones and adiposity

It is well-established that women with increased exposure to sex hormones, namely estrogen and progesterone, are at an increased risk for breast cancer [12, 13]. Elevated levels of sex hormones and cumulative exposure to sex hormones stimulates tumor development and growth through mammary cell proliferation [14]. Consequently, women with an early onset of menarche, regular lifetime ovulatory cycles, and late menopause are at an elevated risk for breast cancer [15] with an increased risk ranging from 20% to over 400% [16-20]

Participation in regular physical activity might reduce circulating levels of sex hormones, and thus reduce breast cancer risk, by delaying the onset of menarche in childhood, and in adulthood, inducing menstrual cycle irregularities, such as anovulation, oligomenorrhoea and amenorrhoea. Adipose cells act as a secondary hormonal gland by secreting estrone and estradiol; thus, reduced circulating levels of sex hormones might require both prolonged exercise and caloric restriction to minimize adipose cell hypertrophy and proliferation.

#### Immune function

Chronic inflammation has been recognized as a risk factor for cancer [21] particularly through cellular changes and oxidative stress associated with inflammation [22]. At moderate levels and intensities, regular participation in physical activity might help reduce inflammation by decreasing proliferation of immunological products, such as C-reactive protein, interleukin-6, macrophages, natural killer cells, lymphokine-activated killer cells, and lymphocytes [23]

#### Insulin-related factors

Long-term exposure to elevated levels of insulin has also been associated with breast cancer risk [24]. Specifically, high insulin levels stimulate the production of insulin-like growth factors (IGFs), which are associated with increased breast cancer risk through their stimulatory effect on cell turnover [25]. Regular participation in physical activity is positively associated with insulin sensitivity [26] and inversely associated with fasting insulin levels [27] and IGFs [28]. The physical activity-lowering effect on IGFs might not only inhibit mammary cell turnover, but decreased IGFs might also reduce the availability of sex hormones through hepatic synthesis of sex hormone binding globulin [29]

Apart from above regular physical activity can help maintain or improve health during and after treatment, and can:

- Help avoid or reduce some side effects of cancer treatment – such as fatigue, weight gain, osteoporosis and lymphoedema
- Improve your long-term health, reducing the risk of heart

attacks and strokes, and may reduce the risk of the cancer coming back

- Help your mental wellbeing by reducing anxiety, stress, depression and improving your overall mood
- Prevent or reduce the loss of muscle tone and aerobic fitness that can happen during treatment.

### Conclusion

Exercise during adjuvant treatment for breast cancer can be regarded as a supportive self-care intervention which results in improved physical fitness and thus the capacity for performing activities of daily life, which may otherwise be impaired due to inactivity during treatment. Women may reduce their risk of breast cancer by maintaining a healthy weight, being physically active and breastfeeding their children. The benefits with moderate exercise such as brisk walking, jogging, slow running etc. are seen at all age groups including postmenopausal women. Strategies that encourage regular physical activity and reduce obesity could also have other benefits, such as reduced risks of cardiovascular disease and diabetes.

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