

Introduction

Physical activity reduces the risk of many diseases: for example, diabetes, cardiovascular disease, osteoporosis and cancer. The World Health Organisation (WHO) estimates 2 million deaths are attributable to physical inactivity (1).

Breast cancer is the most common cancer in women globally (2). Many factors, known as "risk factors", are associated with its development and spread (3). Some of these are inherited and beyond the control of an individual, such as being born with a faulty **BRCA** gene. Others associated with diet, lifestyle or environmental factors, individuals can choose to change. An example is physical activity, defined as any bodily movement produced by skeletal muscles that requires energy expenditure (4). Exercise refers to physical activity that is planned, structured, repetitive, and which aims to improve or maintain one or more components of physical fitness (4). Although the health benefits of exercise are well known, not everyone is able to do regular exercise. But almost anyone can be physically active. In this context, physical activity refers to activity above and beyond normal/routine activities of daily living.

This brief provides an overview of the role of physical activity in reducing breast cancer risk and mortality and discusses the biology behind its protective effect.

How much physical activity is needed to lower breast cancer risk?

Most health bodies, including Public Health England (PHE), recommend doing at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity physical activity each week. PHE also recommends muscle strengthening activities at least twice a week (5). "Moderate" means sufficient to increase the heart rate: for example, brisk walking, dancing, gardening and cleaning. "Vigorous" intensity activity, such as running, cycling or heavy lifting during household and

SUMMARY

Physical activity reduces the risk of breast cancer, breast cancer recurrence, and mortality following a breast cancer diagnosis. There is an inverse relationship between physical activity and risk. Inactivity often leads to increased body fat: - a breast cancer risk factor for post-menopausal women as well as for men. The protective effects of physical activity may be associated with changes in levels of circulating growth factors and hormones, reduced chronic inflammation & improved immune function.

gardening tasks involves more effort and causes a substantial increase in heart rate (6).

All types of physical activity, whether recreational or occupational, help reduce breast cancer risk (7). The more individuals do, the more they will be protected against breast cancer. One international study compared sample groups with different levels of recreational physical activity. Those that spent 150 min a week in moderate activity [e.g. 5×30 min cycling] lowered their risk by 6%; spending 300 min a week [e.g. 3×100 min gardening] reduced their risk by 10% and 600 min per week [e.g. 3×120 min gardening and 4×60 min brisk walking] lowered risk by 14%, compared to the inactive sample (8).

Sedentary behaviour (activities characterised by low energy expenditure that are undertaken with sitting or reclining posture, e.g. computer use) for extended periods, over many years, increases breast cancer risk for post-menopausal women (7). Consistent with WHO guidance (4), Breast Cancer UK recommends for additional health benefits and protection against breast cancer that individuals do at least 300 min of moderate physical activity, or 150 min of vigorous physical activity each week if this is possible (9). If not, do as much as you can. Any level of activity reduces your breast cancer risk.

Physical activity reduces breast cancer risk by around 20%

Numerous studies have examined the role of physical activity on breast cancer occurrence.



Although percentages vary (8, 10, 11, 12, 13), overall, physical activity reduces risk by around 20% (14). The greatest reduction is seen in pre-menopausal women who do vigorous activity (10). One large UK study found women who were in the top quarter of self-reported physical activity had a 23% lower risk of pre-menopausal breast cancer and a 17% lower risk of post-menopausal breast cancer (10).

Physical activity also reduces breast cancer risk in men (15) and individuals with a family history or known genetic susceptibility to breast cancer, such as BRCA mutation carriers (12). A recent study of women with a family history of breast cancer found they had a 20% lower risk if they were physically active, compared to genetically susceptible women who were inactive (12).

Worldwide, it is estimated that 1 in 8 postmenopausal breast cancers can be prevented by being active at least 30 minutes per day (16).

Physical activity reduces breast cancer recurrence and increases survival

Following a breast cancer diagnosis, there is an inverse relationship between increased physical activity and reduced risk of breast cancer recurrence and mortality (17, 18, 19). Physical activity reduces breast cancer recurrence by 20-30% (17, 19) and risk of mortality in those with a diagnosis by over 40% (18, 19). One review that compared women diagnosed with breast cancer doing the least physical activity to those doing the most found that physically active women had a 40% lower risk of breast cancer mortality and a 42% lower risk of mortality from any cause (19).

What is the biological basis linking physical activity to breast cancer risk?

Physical activity affects numerous metabolic, hormonal and immunological pathways (see Fig. 1). Several biological mechanisms are proposed to explain its role in reducing breast cancer. These include changes in levels of circulating sex

hormones; changes in metabolic hormones and growth factors which improve metabolic function; reduced low-grade chronic inflammation, improved immune function and loss of fat tissue. Sedentary behaviour may increase risk due to increased fat tissue, and possibly reduced metabolic function (13).

Reduced levels of circulating sex hormones

High levels of circulating sex hormones, especially oestrogen, and lower levels of sex hormone binding globulin (SHBG), a protein which binds to oestrogen preventing its biological function, are associated with increased female breast cancer development and progression (20). Compared to those of average weight, overweight post-menopausal women have higher levels of oestrogen and lower levels of SHBG. Following menopause, the main source of oestrogen is adipose (fat) cells, where it is synthesised from androgens (male sex hormones) (20). In postmenopausal women, excessive fat tissue increases circulating oestrogen, increasing breast cancer risk. In pre-menopausal women oestrogen is made mainly in the ovaries. Overweight pre-menopausal women have lower circulating oestrogen compared to those of average weight (21). In consequence they have a lower risk of developing premenopausal breast cancer (20).

Independently, physical activity and loss of fat tissue (post-menopause) *increase* levels of SHBG and *reduce* levels of circulating oestrogen and free <u>testosterone</u> (22). This lowers breast cancer risk in women, regardless of menopausal status.

Altered levels of metabolic hormones & growth factors and improved metabolic function

Physical activity and less body fat lower levels of metabolic hormones in males and females, including <u>insulin</u>, and the growth factor <u>IGF-1</u>. Both of these hormones help regulate blood glucose levels.

High levels of insulin and IGF-1 promote cell proliferation in breast tissue and inhibit <u>apoptosis</u> (programmed cell death), actions that increase breast cancer risk (23).



Physical activity improves the body's response to insulin and reduces <u>insulin resistance</u>, a <u>metabolic disorder</u> that results in high blood sugar levels and high levels of insulin (24). The condition is associated with increased risk of breast and other cancers, as well as other diseases such as type 2 diabetes.

Reduced chronic inflammation and improved immune function

In both men and women, obesity, weight gain and physical inactivity lead to a persistent state of low-grade chronic inflammation that involves chronic activation of the immune system.

During weight gain, adipose tissue cells accumulate fat. When these cells die, they release their contents into their surroundings (25). This triggers an immune response and pro-inflammatory state characterised by increased levels of pro-inflammatory factors. Loss of body fat and physical activity alters levels of adipokines - proteins released by fat tissue. For example there is a reduction in the level of Leptin. Lower levels of circulating leptin are associated with a reduced breast cancer risk (13).

Physical activity *lowers* levels of pro-inflammatory factors and *increases* levels of anti-inflammatory factors. Thus, chronic inflammation is reduced, and immune function strengthened. One function of the immune system is the removal of cancer cells. A stronger immune system reduces cancer risk (13).

Other biological effects

Physical activity increases <u>antioxidant activity</u>, reducing <u>oxidative stress</u> which occurs when there is an excess of <u>free radicals</u> in cells. These highly reactive molecules play a role in initiation and progression of breast cancer (13).

Active individuals often have higher sunlight exposure and higher <u>vitamin D</u> levels, which may modify cell proliferation and reduce tumour formation (16). Women diagnosed with breast cancer generally have lower vitamin D levels, but it is unclear whether the cancer is a cause or consequence of low vitamin D.

Poor gut health may be associated with increased breast cancer risk (26). Physical activity may improve gut health by increasing the diversity of gut microorganisms and encouraging growth of those that influence oestrogen levels (26).

Physical activity can help lower levels of persistent organic pollutants which accumulate inside fat tissue. A recent study found lower concentrations of circulating organochloride pesticides in those physically active (27). Some of these are oestrogenic and may increase breast cancer risk (28).

Conclusion

"If exercise were a pill it would be one of the most cost-effective drugs ever invented." (29)

Physical activity is one of several lifestyle factors that help to prevent breast cancer. It not only helps to lower risk, but also helps prevent recurrence and mortality following a breast cancer diagnosis. Any type of additional physical activity is beneficial; the more the better. For greater protection, other lifestyle behaviours, such as maintaining a healthy diet and weight, should be adopted.

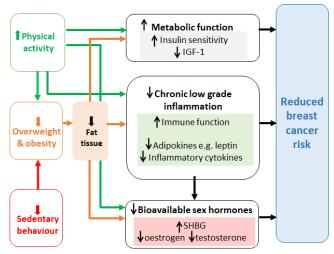


Figure 1. Hypothesised biological mechanisms linking physical activity, excess body fat and sedentary behaviour to cancer risk. IGF-1: insulin like growth factor-1; SHBG: sex hormone binding globulin. Only links with strong evidence are shown. Adapted and simplified from reference (13).



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About Breast Cancer UK

Who are we?

Breast Cancer UK aims to prevent breast cancer through scientific research, collaboration, education and policy change. We educate and raise awareness of the risk factors for breast cancer and provide practical information to help people reduce these risks. We campaign to ensure government policies support the prevention of breast cancer. And we fund scientific research that helps to better understand what risk factors contribute to breast cancer, and how to address them

For further information on breast cancer risk factors please visit our website www.breastcanceruk.org.uk To view this information in a more accessible format or to provide feedback, please contact us.

Disclaimer

This brief is for information purposes only and does not cover all breast cancer risks. Nor does it constitute medical advice and should not be used as an alternative to professional care. If you detect a lump or have any concerns, seek advice from your GP. Breast Cancer UK has made every effort to ensure the content of this leaflet is correct at the time of publishing but no warranty is given to that effect nor any liability accepted for any loss or damage arising from its use.

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