

Breast cancer: Risk factors

Breast cancer is the most commonly occurring female cancer in developed countries but earlier diagnosis and improvements in treatment are resulting in the majority of women surviving their diagnosis. In the UK breast cancer survival has improved significantly (by about 40%) over the last 40 years. Eight in ten women diagnosed and treated for breast cancer today in the UK are predicted to survive their cancer for at least ten years.

At present, knowledge of all the factors resulting in the development and growth of breast cancer is incomplete. Gene mutations in breast cells are necessary for all breast cancers to be initiated but progression and further development also depends on complex interactions with lifestyle and reproductive risk factors. Most women diagnosed with breast cancer (about 90%) are considered to be at population risk. The gene mutations resulting in their diagnosis develop during their lifetime. This contrasts with the small proportion of women at an elevated risk due to a family history, where the gene mutations are inherited (up to 10% of all breast cancers diagnosed annually in the UK).

In women at population risk, by far the greatest risk factors for being diagnosed with breast cancer during their lifetime are being female and growing older, which cannot be avoided. In addition, there are some lifestyle and reproductive factors associated with an increased risk of breast cancer diagnosis. These are summarised below. It has been estimated approximately 23% of all the breast cancers diagnosed in the UK could be prevented by avoiding or reducing exposure to lifestyle risk factors. However, it is important to understand most women exposed to any of these risk factors will never be diagnosed with breast cancer in their lifetime and it is currently not possible to predict on an individual basis, who might be at risk with exposure.

Factors associated with an increased breast cancer risk include:

1. Gender (breast cancer diagnosis is overall 200 times more common in women than in men)
2. Increasing age (most breast cancers are diagnosed in women over 50)
3. Family history
4. 'High risk' benign breast conditions
5. Risk factors associated with lifestyle and female reproduction
 - I. Endogenous sex hormone exposure (i.e. prolonged exposure to sex hormone [oestrogen] produced within the body)
 - a. Early age at starting menstrual periods and late age at menopause
 - b. Being overweight / obese and post-menopausal
 - II. Exogenous hormone exposure (i.e. exposure to sex hormones [oestrogen and progestogen] taken in the form of medication)
 - a. Use of hormonal contraceptives
 - b. Use of hormone replacement therapy (HRT)
 - III. Changes to metabolism of female sex hormones
 - a. Smoking
 - b. Alcohol
 - IV. Factors increasing the risk of normal breast cells becoming malignant
 - a. Not having children or a first full-term pregnancy at a later age
 - b. Not breast-feeding
 - V. Lack of physical activity

Increasing Age

In the UK, the lifetime risk of being diagnosed with breast cancer for women is 1 in 8. However, this means that 7 in 8 women will never be diagnosed in their lifetime. Risk of diagnosis increases with advancing age. Most breast cancers (over 80%) are diagnosed in women aged over 50. In women aged less than 30, breast cancer is diagnosed in about 1 in 1900 women, where this increased to 1 in 15 for women by the age of 70 years. The highest incidence of diagnosis in the UK occurs in women aged 85 to 89 years.

Family History

This refers to the risk of *inheriting* a gene mutation that can result in the development of breast cancer. However, only a minority of gene mutations resulting in the development of breast cancer are inherited (i.e. familial breast cancer). Currently it is estimated that inherited breast cancers account for up to about 10% of those diagnosed annually in the UK. Inherited breast cancers are more likely to be diagnosed at a younger age (i.e. less than 50 years), affect both breasts and affect more than one relative within a family. In some families, there is clustering of breast with ovarian, endometrial and bowel cancers. If a woman has a single first degree relative (i.e. mother or sister) or second degree relative (e.g. aunt) diagnosed with breast cancer over the age of 50 it is very unlikely that this places her at an increased risk of breast cancer and she will be considered to be at population risk. There is no need to refer for further risk assessment.

For any woman who has a family history of cancer, discussion with her GP should determine whether this is likely to be significant. The GP should take a family history (national guidance from NICE provides advice to GPs about this). If the family history suggests a woman may be at increased risk (i.e. greater than the general population for her age), the GP will refer to either the local breast unit or local family history risk assessment clinic as appropriate, where more detailed assessment will take place including whether there is any indication for gene testing and advice about surveillance and possible prevention strategies. Most women with a family history will not be diagnosed with breast cancer in their lifetime.

Benign Breast Conditions

Benign breast conditions refer to a wide range of conditions of the breast. They are categorized according to whether they are associated with an increased risk of being diagnosed with a breast cancer later in life or not. Most benign breast conditions are not associated with an increased risk of diagnosis (this includes for example breast cysts and fibroadenomas).

'High risk' benign conditions do not usually cause any breast symptoms and are usually an incidental finding on a breast biopsy. The two high risk conditions are (1) breast atypical hyperplasia or (2) Lobular Carcinoma in Situ (LCIS). These result in ordinary breast cells having a characteristically abnormal appearance when viewed down a microscope. Both are currently considered to be a marker of future breast cancer risk (which is equal in both breasts) rather than precursor lesions and therefore managed by annual surveillance mammograms for 5 years. Most women with a diagnosis of atypia or LCIS, however, will never be diagnosed with breast cancer in their lifetime.

Endogenous sex hormone exposure

Endogenous sex hormones are produced naturally within the body and here, refers to the female sex hormones, oestrogen and progesterone. In pre-menopausal women, these hormones are produced by eggs released monthly from the ovaries. In post-menopausal women, the main source of oestrogen production is in fat cells. Female sex hormones have an important but incompletely understood role in the development of most breast cancers. The evidence implicating them has largely been drawn from population studies, which revealed an association between an increased risk of breast cancer diagnosis in women who have a greater number of ovarian menstrual cycles in their lifetime. This accounts for the following observations:

The risk of breast cancer diagnosis is increased:

1. With an earlier age at menarche (onset of menstrual periods)
2. With an older at menopause (cessation of menstrual periods)
3. In women who do not breast feed (in those who do, ovarian activity is inhibited)

In post-menopausal women, ovarian production of oestrogen and progesterone ceases. Small amounts of oestrogen are produced in fat cells, however, by the action of an enzyme called aromatase. Postmenopausal women who are overweight are at an increased risk of breast cancer and this has been attributed to the fact that there is more fat tissue in which this synthesis of oestrogen can take place. It is estimated 8% of breast cancer cases in the UK are attributable to overweight and obesity.

Exogenous hormone exposure

This refers to sex hormones, which originate outside the body and includes all hormonal contraception (birth control) and hormone replacement therapy (HRT).

1. Hormonal contraception

There is a very small increased risk of breast cancer diagnosis associated with hormonal contraceptives but for most women at population risk, the benefit in reducing un-intended pregnancy and the risk of diagnosis of other cancers (i.e. ovary, endometrium) outweighs this potential concern. Overwhelmingly, clinical studies that have looked at the question of breast cancer risk are restricted to women who have used the combined oral contraceptive pill (i.e. containing oestrogen with a progesterone) and were conducted many years ago on preparations that are no longer in clinical use, which tended to contain higher dosages of sex hormones. There is a lack of information about the progestogen-only pill, progestogen implants, injectable progestin, intra-uterine progesterone [the Mirena Device]) and no clinical studies have yet reported on risk with combined vaginal or transdermal preparations. If with any of these the risk of diagnosis of breast cancer is increased it is likely to be small and similar in degree to that with COCP. Less than 1% of breast cancer cases in the UK are thought to be attributable to the use of oral contraceptives.

2. Hormone replacement therapy (HRT)

Unopposed HRT (i.e. preparations containing oestrogen alone) is associated with little or no change in risk of breast cancer but combined HRT (i.e. oestrogen with a progestogen) can be associated with a small increased risk when used for more than 5 years. After HRT is stopped, the risk of breast cancer diagnosis initially falls but it may increase again a few years after cessation. This can be explained by the action of HRT on the growth of undetectable, microscopic cancers already present in the breast. When HRT is started, it may speed the growth of some of these cancers, resulting in them being diagnosed sooner. When HRT is stopped, the growth of any remaining undetectable cancers slows down. However, they will still continue to grow but at a slower rate, which would lead to them being diagnosed many years after HRT cessation. Despite this, the risk of breast cancer with combined HRT is less than that associated with being overweight over the age of 50 or that associated with drinking 2 or more units of alcohol per day. For women experiencing hot flushes and night sweats, with a low underlying risk of breast cancer (i.e. most of the population) the benefits of HRT in the short-term (up to 5 years' use) will exceed any potential harm. Approximately 2% of breast cancer cases in the UK are thought to be attributable to the use of HRT.

Smoking

Clinical studies have shown smoking does increase the risk of breast cancer diagnosis in current and former smokers. This risk appears to be increased particularly in teenagers who start to smoke prior to their first pregnancy. There is no clear evidence as to whether risk is affected by the duration or amount of smoking.

Alcohol

Alcohol consumption is associated with an increased risk of breast cancer diagnosis. Risk does not persist in past users of alcohol. Currently it is unclear whether there is a 'threshold' below which risk is not increased. It is estimated 8% of breast cancer cases in the UK are attributable to alcohol use.

Factors increasing the risk of normal breast cells becoming malignant

In women who have never had a pregnancy, or had a full-term pregnancy later in life, or never breast-fed, the cells in the breast are less resistant to the effects of carcinogens (substances initiating malignant change in cells). Part of the reason women in developed countries have a higher risk of breast cancer diagnosis than women in developing countries may be due to the former having fewer children and avoiding or limiting the duration of breast feeding.

The risk of breast cancer diagnosis is decreased:

1. In women who have their first full-term pregnancy at a younger age
2. In women who have more than one full-term pregnancy
3. In women who breast-feed (this protection may be restricted to the risk of diagnosis of breast cancer in pre-menopausal women only). About 5% of breast cancer cases in the UK are thought to be attributable to women not breast-feeding.

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This fact sheet has been prepared by Women's Health Concern and reviewed by the medical advisory council of the British Menopause Society. It is for your information and advice and should be used in consultation with your own medical practitioner.

Physical Activity

Lack of physical activity is also a risk factor for breast cancer diagnosis in post-menopausal women. Clinical studies show increasing physical activity to be protective but the optimal level of activity is yet to be determined. This protective effect may in part be related to weight reduction.

Breast Cancer Management

About one quarter of breast cancers diagnosed annually in women in the UK are done so via the NHS Breast Screening Programme. The remainder are diagnosed in those presenting to their GP with breast symptoms.

Currently, with optimal treatment 2 in 3 women will survive their disease beyond 20 years. For many women, it is a condition they live with, rather than die from. Female deaths from breast cancer per year in England and Wales (4%) are much lower than those due to Alzheimer's disease and dementia (16%), heart disease (8%) and stroke (7%). Once a diagnosis of breast cancer is confirmed, management generally involves varying combinations of the following treatments (e.g. surgery, radiotherapy, anti-oestrogen hormone therapy, chemotherapy and immunotherapy such as herceptin). Treatment recommendations are based on the individual features of a breast cancer (e.g. the size, grade and stage of the breast cancer) sometimes, menopausal status and an individual's general health.

Useful contacts

Breast Cancer Now

Telephone helpline: 0808 800 6000 Mon-Fri 9am to 4pm, or Sat 9am to 1pm

Website: www.breastcancer.org

Cancer Research UK

Telephone general enquiries: 0300 123 1022 Mon-Fri, 8am to 6pm (closed Wed 11am to 11:30am)

Website: www.cancerresearchuk.org

Macmillan Cancer Support

Telephone helpline: 0808 808 00 007 days a week, 8am-8pm

Website: www.macmillan.org.uk

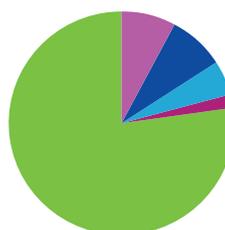
National Institute for Clinical Excellence (NICE)

Website: www.nice.org.uk

Familial Breast Cancer Guidance

Early and Locally Advanced Breast Cancer Guidance

Percentage of breast cancers diagnosed annually in the UK attributable to lifestyle factors



- Obesity and overweight 8%
- Alcohol 8%
- Lack of breast-feeding 5%
- Postmenopausal hormones 2%
- Remaining breast cancers 77%

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Women's Health Concern is the patient arm of the BMS.
We provide an independent service to advise, reassure and educate women of all ages about their health, wellbeing and lifestyle concerns.

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