

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 the disease. In the United Kingdom, whilst 50,000 women are diagnosed every year, 11,500 die from their breast cancer and this number is likely to fall even further.

At present, knowledge of all the factors that result in the development and growth of breast cancer is incomplete.

Factors that have been associated with an increased breast cancer risk include:

1. Increasing age (most breast cancers are diagnosed in women over 50)
2. Family history (~2% of cancer diagnosed annually are attributed to an inherited gene mutation)
3. 'High risk' benign breast conditions (i.e. atypia of breast cells on a breast biopsy)
4. 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
5. 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 hormones replacement therapy (HRT)
6. Changes to metabolism of female sex hormones
 - a. Smoking
 - b. Alcohol
7. 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
8. Lack of physical activity

It is important to realise that although these factors have been identified, knowledge of why breast cancers develop is complex and not fully understood. Many women diagnosed with breast cancer have no known risk factors other than growing older and even with exposure to any of these factors are never diagnosed with this condition.

Increasing Age

In the UK the lifetime risk of being diagnosed with breast cancer for women is 1 in 9. However, this means that 8 in 9 women will never be diagnosed in their lifetime. The risk of diagnosis increases with increasing age and most breast cancers (~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.

Family History

This refers to the risk of inheriting a gene mutation that can result in the development of breast cancer. Gene mutations are necessary for all breast cancers to develop. However, only a minority of gene mutations resulting in the development of breast cancer are inherited (i.e. familial breast cancer). Inherited breast cancers account for about 2% of breast cancers diagnosed annually in the UK. Most breast cancers arise as a result of gene mutations that develop during a women's lifetime. Inherited breast cancers are more likely to be diagnosed at a younger age (i.e. less than 40 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 (i.e. aunt) diagnosed with breast cancer over the age of 40 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 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 breast cancer in their lifetime.

Benign Breast Conditions and Lobular Carcinoma in Situ

Benign breast conditions refer to a wide range of conditions of the breast. They are categorised 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, fibroadenomas).

'High risk' benign condition refers to the finding of atypical (i.e. abnormal appearing) breast cells when a breast biopsy is undertaken. Atypia is currently considered to be a marker of future risk (this is equal in both breasts) rather than a precursor lesion and therefore managed by annual surveillance mammograms for 5 years. Lobular carcinoma in situ (LCIS) refers to the finding of abnormal cells in a breast biopsy that is also considered to be a marker of future increased risk of breast cancer diagnosis. It is managed in the same way as atypia.

Most women with a diagnosis of atypia or LCIS 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 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. Breast cancer is a condition that predominantly affects women, being 200 times more common than in men. The evidence implicating female sex hormones has largely been drawn from population studies that have revealed an increased risk of breast cancer diagnosis in women who commence their menstrual periods at a younger age or who develop the menopause at an older age (either can result in a longer time of ovarian activity).

- An earlier age at menarche (onset of periods) is associated with an increased risk of breast cancer diagnosis later in life
- An earlier age at menopause is associated with a reduced risk of diagnosis of breast cancer.
- Breast-feeding may reduce the risk of breast cancer as the ovaries do not produce eggs when women breast-feed

In women who have undergone the menopause, oestrogen and progesterone hormones are no longer produced by the ovary. Instead small amounts of oestrogen are produced in fat cells 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.

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).



Hormonal contraception

Overall there does appear to be a very small increase in the risk of being diagnosed with breast cancer in women who have used hormonal contraception. Review of clinical studies suggests that this risk might be restricted to younger women (i.e. aged less than 35 years) who have used hormonal contraception for more than 5 years. Most of the clinical studies that have looked at this question are restricted to women who have used the combined (oestrogen with progestogen) oral contraceptive pill (COCP) and were conducted many years ago using COCPs that are no longer in clinical use. These tended to contain higher dosages of sex hormones. On the basis of these studies, it has been estimated that for every 10,000 women aged between 25 to 29 years who take the COCP for 5 years an extra 5 cases of breast cancer are diagnosed.

For all other types of hormonal contraception (e.g. progesterone only pill, progestogen implants, injectable progestin and the Mirena Device) there is too little information from clinical studies to draw any significant conclusions. 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.

Hormone replacement therapy (HRT)

Recent information from clinical trials has shown that combined HRT (i.e. oestrogen plus progestogen hormone) is associated with a very small increase in the risk of developing breast cancer but only if taken long-term (i.e. for more than 5 years after the age of 50). If 1000 women aged between 50 to 59 use combined HRT for 5 years, it is estimated an extra 3 breast cancers will be diagnosed. The small increase in risk associated with combined HRT falls after it is stopped and there is no evidence that the risk of dying from breast cancer is increased in women with a history of using it. 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. – See our related factsheet on HRT: What you should know about the risks and benefits.

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.

Factors increasing the risk of normal breast cells becoming malignant

In women who have never had a pregnancy, of 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:

- In women who have their first full-term pregnancy at a younger age
- In women who have more than one full-term pregnancy
- In women who breast-feed (this protection may be restricted to the risk of diagnosis of breast cancer in pre-menopausal women)

Physical Activity

About 3% of breast cancers diagnosed in the UK are attributed to lack of physical activity. Clinical studies suggest that increasing physical activity may only be protective and reduce the risk of breast cancer diagnosis in post-menopausal women. Evidence is unclear as to the level of physical activity that could be protective and how increasing physical activity confers this protection. It may in part be related to weight reduction.



Breast Cancer Management

Annually in the UK about one quarter of breast cancers are diagnosed via the NHS Breast Screening Programme (NHSBSP). The remainder are diagnosed in women (and some men) who present to their GP with troublesome breast symptoms (however most people with breast symptoms, once evaluated in their local breast unit are confirmed to have a benign breast condition that does not require any further treatment). Currently nearly 8 in 10 women diagnosed with breast cancer, with optimal treatment will survive their disease for at least ten years and 2 in 3 will survive their disease beyond 20 years. Female deaths from breast cancer per year in England and Wales (4%) are much lower than those due to Alzheimer's disease and dementia (12%), heart disease (11%) and stroke (8%).

Once a diagnosis of breast cancer is confirmed the management advised uses combinations of the following treatments (i.e. surgery, radiotherapy, anti-oestrogen hormone therapy, chemotherapy and immunotherapy such as herceptin). One or a combination of these therapies may be used. There are no set treatments for a specific type of breast cancer, all treatments are chosen on an individual basis and it is important to speak to your specialist about all treatments types and come to an agreement. Some of the factors that are considered when deciding on a treatment are:

- Whether you have had your menopause
- The type of breast cancer you have
- The size of your breast tumour
- The stage of your breast cancer
- The grade of your cancer cell
- The results of test on your cancer cells
- Your general health

If there is a specific treatment you are interested in and your doctor does not mention it, make sure to speak up. Similarly, if your doctor suggests a treatment that you are not comfortable with, make your concern known. Your specialist probably has good reasons for choosing the treatment s/he did and should be able to explain it to you.

For information on breast screening and self examination look at the factsheet 'Breast Care and Self-examination'.

Useful contacts

Breakthrough Breast Cancer

Weston House, 3rd Floor, 246 High Holborn,
London WC1V 7EX
Tel: 020 7025 2400
Fax: 020 7025 2401
Email: info@breakthrough.org.uk
Website: www.breakthrough.org.uk

Breast Cancer Care

Tel: 020 7384 2984
Helpline: 0808 800 6000 Mon-Fri 9am-5pm,
or Sat 9am-2pm
Email: info@breastcancercare.org.uk
Website: www.breastcancercare.org.uk

National Institute for Clinical Excellence (NICE)

<http://www.nice.org.uk>
Familial Breast Cancer Guidance
Early and Locally Advanced Breast Cancer
Guidance



	Absolute change in risk per 1000 women aged 50 to 59 at population risk		
	Number of cancers diagnosed	Number of cancers not diagnosed	Excess risk
No exposure	12	988	-
Postmenopausal obesity or overweight	29	971	+17
Nulliparity (vs first live birth aged < 20 years)	20	980	+8
Late age at first live birth (≥ 31 years)	16	984	+4
Alcohol (regular intake ≥ 6 g/day)	15	985	+3
Combined hormonal contraceptives	15	985	+3
Combined HRT	15	985	+3
Smoking (current smoker)	13	987	+1
Late age at menarche (≥ 15 years vs < 11years)	11	989	-1
Unopposed oestrogen replacement	9	981	-3
Parity (≥ 4 live births vs 1)	7	993	-5
Physical activity (> 9 MET-h/wk)	7	995	-5

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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.

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