

BCUK Background Briefing | Male breast cancer

Introduction

It's not only women who get breast cancer. In 2014, 389 men in the UK were diagnosed with the disease, and 30 with **carcinoma** *in situ*, a type of **non-malignant** breast **tumour**. Seventy-five men died as a result of their breast cancer. Most (55%) were over 75 years old (1).

The age standardised incidence rate for male breast cancer in the UK is 1.5 cases per 100,000 men (2). Rates are similar in most developed countries, and generally lower in those that are less developed (where female breast cancer rates are also lower) (3). By comparison, breast cancer is the most common female cancer in most countries around the world, including the UK, where the age standardised rate is 172 cases per 100,000 women (4). Since the late 1970s, male breast cancer incidence rates in Great Britain have remained stable for most age groups, although there have been some increases. The most significant changes were observed at age 50 -59, with incidence rates rising by 53% between [1979-1981] and [2011-2013], and at age 70-79, with incidence rates rising during the same period by 27% (5).

Breast cancer develops in the small amount of breast tissue men have behind their nipples (6). The most common symptom is a hard, painless lump in the breast. Other symptoms may include an inverted nipple, nipple discharge, pain or sores



Scanning electron micrograph of dividing breast cancer cell

or enlarged lymph nodes under the arm (7).

Why don't more men get breast cancer?

Men are far less likely to get breast cancer than women due to their lack of breast tissue, and their lower levels of circulating **oestrogen** (female sex hormones), compared to pre-menstrual women. Oestrogen encourages a high rate of cell division which increases the risk of **mutations**, including those that lead to breast cancer (8). The more breast tissue mass the more likelihood there is for a cell to undergo mutations which may lead to breast cancer.

Does the type of breast cancer and age of onset differ between the sexes?

Over 90% of male breast cancers are **oestrogen receptor positive** (9). This means breast tumour

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cells produce **oestrogen receptor proteins**, which bind to oestrogen and stimulate tumour growth. Tumours of this type can be treated using hormone therapies, such as **tamoxifen**. In women, only around 70% of breast cancers are oestrogen receptor positive (10). Men tend to be diagnosed with breast cancer at an older age than women, with most cases diagnosed in men over 60. Studies in the US suggest the average age of onset for men is 5-10 years later than for women (11). This could be partly due to later diagnosis because of reduced awareness and absence of screening programmes, but is also likely to represent a genuine difference due to gender.

Are risk factors for breast cancer the same for both sexes?

Several risk factors for female breast cancer are associated with reproduction and will not apply to men. Other risk factors associated with age, genetics, hormones and the environment are shared, but there is some variation.

Perhaps surprisingly, men and post-menopausal women have similar levels of circulating oestrogen (12). Men who have higher levels of circulating oestrogen are at a higher risk of breast cancer (13). This is also true for women.

High oestrogen levels are commonly a result of inheritance, excessive body fat (fat tissue being a



Increased physical activity reduces breast cancer risk

source of oestrogen), or liver disease (which often leads to lower levels of male hormones and higher levels of oestrogen). Very heavy drinking is another risk factor for male breast cancer (14). Alcohol reduces the body's ability to regulate oestrogen levels (15), and alcohol metabolism produces acetaldehyde and other carcinogens.

Men who have low levels of testosterone may also be at greater risk because testosterone limits the effects of oestrogen. Patients with prostate cancer also have a greater chance of developing breast cancer; it is unclear why although it may be associated with hormone-related treatments (16).

Increased physical activity is thought to reduce breast cancer risk in both men and women (17).

Genetics plays a significant role in both male and female breast cancer, but variations exist here also. Around 20% of men with breast cancer have a first degree relative with the disease (18). First



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sisters, daughters or sons. Men who develop breast cancer are more likely (than women) to carry an inherited BRCA2 mutation, which affects DNA repair. Such men have a 7% (approximately 1 in 14) lifetime chance of inheriting breast cancer (19). By contrast, the average British male has a lifetime risk of 1 in 870 (20). Approximately 10% of male breast cancer cases are associated with inheriting a single mutated (high penetrance) breast cancer susceptibility gene such as BRCA2 (21); for women this figure is around 5-10% (22). Men with Klinefelter's syndrome (who inherit an extra X chromosome) are at increased risk, due to hormonal imbalance leading to increased levels of oestrogen. These individuals account for up to 7% of all male breast cancers (23).

Occupational and environmental exposures associated with male breast cancer

Radiation exposure is a known risk factor for many cancers, including breast cancer. Repeated or lengthy exposure to diagnostic radiographs or radiation therapy increases the risk of male breast cancer (24). A recent paper (25) which examined male incidence and mortality of breast cancer in atomic bomb survivors found a much higher radiation-associated relative risk for male than for female breast cancer.

There is increasing evidence that male breast cancer is associated with exposure to environmental pollutants, including **carcinogens** and **endocrine disrupting chemicals** (EDCs), especially **oestrogen mimicking chemicals** (26), which induce similar actions to those of oestrogen and have been linked to increased breast cancer risk and other health problems, including prostate cancer. For further details about EDCs and breast cancer risk read our <u>Background Briefing on EDCs</u>.

Certain occupations may also carry a higher risk of breast cancer. For example, motor vehicle mechanics have a higher breast cancer incidence. This may be associated with occupational exposures to petrol and petroleum solvents, polyaromatic hydrocarbons (known carcinogens), and alkylphenolic compounds (known EDCs) (27).

Men who work in high temperature environments such as blast furnaces and steel works have an elevated risk of breast cancer (28). The reasons for this are unclear but may be associated with temperature effects on reproductive organs (affecting oestrogen levels) or increased exposure to environmental pollutants.



Exposure to radiation increases the risk of male breast cancer



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One study which examined occupational exposures in those employed in the 1960s and 1970s found that men who worked in factories that manufactured perfumes and soaps were more than seven times more likely to develop breast cancer than the male population at large (29). The authors suggest that this may be as a result of exposure to oestrogen mimicking chemicals, commonly used in these products. The same study found men involved in the print and newspaper industry had elevated breast cancer rates. At the time, newspapers were not produced digitally; the increased risk may have been a consequence of exposure to EDCs in ink. Long-term consumption of contaminated drinking water by men living at a marine corps base in North Carolina was shown to result in higher incidence of breast cancer (30). Contaminants included the volatile organic compound 1,2, dichloroethylene, tetrachloroethylene - an EDC (31) and suspected carcinogen (32) - and vinyl chloride, a known carcinogen (33).

The results of these studies support strongly the concerns of Breast Cancer UK that environmental exposures may be increasing the risk of breast cancer in both men and women.

How likely is it that a man will get breast cancer?

In the UK it's estimated that men have a 1 in 870 lifetime chance of getting breast cancer (34). Although this figure is much lower than the

corresponding figure for women (who have a 1 in 8 chance over their lifetime), it doesn't mean we should neglect male breast cancer or not try and do whatever is possible to reduce its incidence. There is evidence that environmental exposures increase risk for men as well as for women. Breast Cancer UK will continue to campaign to reduce environmental exposures and so reduce breast cancer risk for everyone, regardless of gender. For more details about breast cancer risk factors see our Biology of Breast Cancer Background Briefing.

Glossary

Carcinoma *in situ*: non-invasive tumour that hasn't spread **Malignant**: tumour that has become invasive and spread to other sites in the body

Mutation: change in hereditary material (DNA) in a cell

Lymph node: rounded mass of tissue containing immune cells; lymph passes through, is filtered and cleaned

Oestrogen: principal female sex hormones associated with breast development and reproduction; also present in men

Oestrogen receptor: protein that binds oestrogen; binding triggers pathways that lead to increased cell multiplication

Oestrogen receptor positive: breast cancer cells that have oestrogen receptors and grow in response to oestrogen

Tumour: a mass of cells formed by uncontrolled cell division

Tamoxifen: drug used to treat oestrogen receptor positive breast cancer

BRCA2: breast cancer susceptibility gene; a *BRCA2* mutation affects ability to repair DNA; increases breast cancer risk

Klinefelter's syndrome: rare genetic condition; males have an extra X chromosome (XXY); affects sexual development

Carcinogen: substance or agent that can cause cancer

Endocrine disrupting chemical: any chemical that can interfere with hormone functions in humans and/or animals and have adverse effects

Oestrogen mimicking chemical: a type of EDC, often a synthetic compound, that imitates natural oestrogen and triggers the same biological actions

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References

- 1. Cancer Research UK. Breast Cancer statistics. http:// www.cancerresearchuk.org/health-professional/cancer-12, 2017)
- 2. Cancer Research UK. Breast Cancer statistics. ibid.
- Kreiter, E. et al. (2014). Trends in National Incidence in men and 3. women. British Journal of Cancer 110 (7): 1891-1897. http:// 23. Ferzoco, R. M. and Ruddy, K. J. (2016). op. cit. www.nature.com/bjc/journal/v110/n7/full/bjc201466a.html
- Cancer Research UK. Breast Cancer statistics. op. cit. 4.
- Cancer Research LIK Breast Cancer statistics ibid 5
- NHS choices. Breast Cancer in Men. http://www.nhs.uk/ 25. 6. conditions/cancer-of-the-breast-male/pages/introduction.aspx (Accessed Mar 11, 2017)
- 7. BreastCancer.org. Symptoms and Diagnosis: Symptoms of Male Breast Cancer. Last reviewed June 23, 2016. http:// www.breastcancer.org/symptoms/types/male_bc/symptoms (Accessed Mar 12, 2017)
- Travis, R. C. and Key, T. J. (2003). Oestrogen exposure and breast 8. cancer risk. Breast Cancer Research 5: 239-247. http:// www.ncbi.nlm.nih.gov/pmc/articles/PMC314432/
- Severson, T. S. and Zwart, W. (2017). A Review of Estrogen 27. 9. Receptor/Androgen Receptor Genomics in Male Breast Cancer. 28. Fentiman, I. S. et al. (2016). op. cit. http://erc.endocrinology-journals.org/content/24/3/ R27.abstract
- 10. Cancer Research UK. Breast Cancer statistics. op. cit.
- 11. Ferzoco, R. M. and Ruddy, K. J. (2016). The Epidemiology of Male Breast Cancer. Current Oncological Reports 18: 1. https:// 30. www.ncbi.nlm.nih.gov/pubmed/26694922
- 12. Sofronescu, A. G. et al. (2015). Estradiol reference range. Medscape. http://emedicine.medscape.com/article/2089003overview (Accessed Mar 16, 2017)
- 13. Brinton, L. A. et al. (2015). Prediagnostic Sex Steroid Hormones 31. The Endocrine Disruptor Exchange (2017). Tetrachloroethylene in Relation to Male Breast Cancer Risk. Journal of Clinical Oncology 20: 33: 2041-2050. https://www.ncbi.nlm.nih.gov/ pubmed/25964249
- 14. Weiss J. R. et al. (2005). Epidemiology of male breast cancer. Cancer, Epidemiology, Biomarkers and Prevention 14 (1): 20-26. 32. http://cebp.aacrjournals.org/content/cebp/14/1/20.full.pdf
- 15. Shield, K. D. et al. (2016). Alcohol use and Breast Cancer: A critical review. Alcoholism. Clinical and Experimental Research 40(6): 1166-1181. https://www.ncbi.nlm.nih.gov/ pubmed/27130687
- 16. Weiss, J. R. et al. (2005). op. cit.
- 17. Kreiter, E. et al. (2014). op cit.
- 18. Ferzoco, R. M. and Ruddy, K. J. (2016). op. cit.
- 19. Fentiman, I. S. et al. (2016). Male breast Cancer is not congruent 34. Cancer Research UK. Breast Cancer statistics. op. cit. with the female disease. Critical Reviews in Oncology/ Hematology 101: 119-124. http://www.croh-online.com/article/ S1040-8428(16)30041-5/pdf
- 20. Cancer Research UK. Breast Cancer statistics. op. cit.
- 21. Rizzolo, P. et al. (2016). Male breast cancer: genetics,

epigenetics, and ethical aspects. Annals of Oncology 24(8): viii75 -viii82. https://www.ncbi.nlm.nih.gov/pubmed/24131976

- statistics/statistics-by-cancer-type/breast-cancer (Accessed Mar 22. Economopoulou, P. et al. (2015). Beyond BRCA: New hereditary breast cancer susceptibility genes. Cancer Treatment reviews 41: 1-8 http://www.sciencedirect.com/science/article/pii/ <u>S0305737214001741</u>

 - 24. Fentiman, I. S. (2009). Male Breast Cancer: a review. ecancermedicalscience 3: 140. https://www.ncbi.nlm.nih.gov/ pmc/articles/PMC3223984/pdf/can-3-140.pdf
 - Little, M. P and McElvenny, D. M. (2017). Male Breast Cancer Incidence and Mortality Risk in the Japanese Atomic Bomb Survivors - Differences in Excess Relative and Absolute Risk from Female Breast Cancer. Environmental Health Perspectives 125: 223-229. https://ehp.niehs.nih.gov/EHP151/
 - 26. Villeneuve, S. et al. (2010). Occupation and occupational exposure to endocrine disrupting chemicals in male breast cancer: a case-control study in Europe. Occupational and Environmental Medicine 67(12): 837-844. https:// www.ncbi.nlm.nih.gov/pubmed/20798010
 - Villeneuve, S. et al. (2010). ibid.

 - 29. McLaughlin, J. K. et al. (1988). Occupational risks for male breast cancer in Sweden. British Journal of Industrial Medicine 45(4): https://www.ncbi.nlm.nih.gov/pmc/articles/ 275-276. PMC1007989/
 - Ruckart, P. Z. et al. (2015). Evaluation of contaminated drinking water and male breast cancer at Marine Corps Base Camp Lejeune, North Carolina: a case control study. Environmental Health 14: 74. https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC4571057/
 - http://endocrinedisruption.org/endocrine-disruption/tedx-list-of -potential-endocrine-disruptors/chemicalsearch? snam<u>e=tetrachloroethylene&x=48&y=10&action=search&sall=1</u> <u>&searchfor=any&scas=&searchcats=all</u> (Accessed Feb 1, 2017)
 - International Agency for Research on Cancer (2014) Monographs on the evaluation of carcinogenic risks to humans. Trichloroethylene, Tetrachloroethylene and Some Other Chlorinated Agents 106. https://monographs.iarc.fr/ENG/ Monographs/vol106/mono106-002.pdf (Accessed Feb 1, 2017)
 - 33. International Agency for Research on Cancer (2012). Monographs on the evaluation of carcinogenic risks to humans. Vinyl chloride. Volume 100F. http://monographs.iarc.fr/ENG/ Monographs/vol100F/mono100F-31.pdf (Accessed Feb 1, 2017)

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This information has been written for members of the public to help them understand more about how and why certain chemicals may be linked to a potentially increased risk of breast cancer.

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