## Can a healthy diet and lifestyle prevent breast cancer?



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#### Breast cancer incidence, prevalence and mortality

Breast cancer affects 49,936 women and 349 men in the UK (2011 figures). Female rates have doubled in the UK in the last 30 years. Similar increases have been seen globally, particularly within Asian and developing countries which traditionally had low rates<sup>1</sup> due to adverse trends in lifestyle as well as hormonal risk factors, e.g. early menarche, late pregnancy, nulliparity and use of hormone replacement therapy.

Earlier detection and improved treatment has reduced breast cancer mortality by 37 per cent in the past 20 years. The most recent and undoubtedly conservative estimates indicate there were approximately 570,000 women in 2010 living in the UK with a history of breast cancer, which equates to two per cent of the total female population and nearly 10 per cent of women aged 65 years and older.<sup>2</sup> Prevention of breast cancer and long-term management of breast cancer patients are priorities for research and healthcare professionals.

#### Current cancer prevention guidelines

The World Cancer Research Fund/American Institute for Cancer Research (2007) and the American Cancer Society (2012) have guidelines for preventing a range of cancers which focus on weight control, regular exercise, reduced alcohol and a plant-based diet (see **Table One**).

#### Table One: WCRF Cancer Prevention Guidelines, Breast Cancer and Cardiovascular Disease

	Breast cancer risk reduction	CVD risk reduction
1. Be as lean as possible without becoming underweight	$\checkmark\checkmark$	$\checkmark\checkmark$
2. Be physically active for at least 30 minutes every day	$\checkmark\checkmark$	$\checkmark\checkmark$
3. Avoid sugary drinks. Limit consumption of energy-dense foods	$\checkmark\checkmark$	$\checkmark\checkmark$
4. Eat more vegetables, fruits	No effect	$\checkmark\checkmark$
5. Eat more whole grains and legumes such as beans	$\checkmark\checkmark$	$\checkmark\checkmark$
6. Limit red meats (i.e. beef, pork and lamb) and avoid processed meats	Modest effect	$\checkmark\checkmark$
7. Limit alcoholic drinks to 2 for men and 1 for women a day	$\sqrt{}$	Lowest risk of CHD 1-2 drinks/day Stroke< 1 drink/day (40)
8. Limit consumption of salty foods and foods processed with salt	No effect	$\checkmark\checkmark$
9. Don't use nutritional or vitamin supplements to reduce risk of disease	$\sqrt{\sqrt{\sqrt{1-1}}}$	$\sqrt{\sqrt{4}}$

Key: CHD = coronary heart disease; 🗸 🗸 Supported by reviews, meta analyses and clinical trials; 🗸 Association in numerous (3+) observational studies

### So what is the evidence that these guidelines can prevent breast cancer?

Several large observational studies have reported lower rates of breast cancer amongst women who adhere to these guidelines. Two studies amongst postmenopausal women reported 22-60 per cent risk reductions, mainly linked to reduced body fatness and alcohol rather than specific differences in dietary patterns.<sup>3, 4</sup> In contrast, a population of both pre and postmenopausal women had 31 per cent less breast cancer if they adhered to the specific dietary recommendations, i.e. increased wholegrain, reduced meat and alcohol, rather than the other lifestyle factors.<sup>5</sup>

#### What is the strength of the evidence?

Cancer prevention guidelines are mainly based on cohort studies, i.e. prospective studies of large populations of unaffected individuals (typically 20,000-40,000). Few randomised data (the highest level of evidence) have been used to inform these recommendations. Cohort studies include less recall and selection bias than case control studies, which compare cancer cases to unaffected individuals. However cohort studies can only highlight associations between lifestyle behaviours and cancer risk, and cannot provide definitive proof of their role in cancer aetiology. Healthy lifestyle behaviours tend to cluster, so someone who eats a healthy diet is often a healthy weight, takes regular exercise, has a moderate alcohol intake and does not smoke. Researchers attempt to adjust for the other confounding risk factors in analyses but residual confounding cannot be ruled out.

Defining the true anti-cancer effects of lifestyle choices without confounding factors can only be achieved with randomised controlled trials. Such trials would need to be large (~26,000–36,000 subjects) thus potentially prohibitively expensive.<sup>6</sup> Testing whether lifestyle interventions can prevent breast cancer is a bigger challenge than their effects on cardiovascular disease, where well defined surrogate end points (e.g. cholesterol and blood pressure) are markers of disease. The absence of good markers for breast cancer risk makes it unlikely that we will have much randomised data to support or refute the cancer prevention recommendations in the near future.

# Weight, weight gain, physical activity, alcohol and breast cancer risk

Cohort studies consistently link overweight, obesity and adult weight gain to risk of postmenopausal breast cancer. Women who gain 20 kg or more during adulthood double their breast cancer risk.<sup>4</sup> These gains also bring about large increases in risk of diabetes (12-fold),<sup>7</sup> cardiovascular disease (3-fold)<sup>8</sup> and colorectal cancer (1.5-fold).<sup>9</sup>

Cohort studies suggest modest weight loss (5-10%) can reduce risk. Our analysis in the lowa Women's Health Study (34,000 women) showed that a weight loss of  $\geq$ 5 per cent either before or after the menopause reduced risk of breast cancer by 25-40 per cent compared to women who continued to gain weight; whereas Eliassen *et al.* reported a 50 per cent reduction in risk with a 10-12 per cent weight loss (37,000 women in the Nurse's Health Study).<sup>10</sup>

Modest weight loss of five to 10 per cent will also reduce risk of diabetes by up to 60 per cent, reduce LDL cholesterol by 15 per cent, triglycerides by 20-30 per cent, increase HDL cholesterol by 8-10 per cent, and reduce blood pressure by around five per cent. These changes in CVD risk markers suggest a 30 per cent or greater reduction in risk of CVD disease. There is an increasing interest in whether intermittent energy restriction may be as good, or perhaps better than, conventional daily dieting for weight control and reducing risk of breast cancer (reviewed in reference<sup>11</sup>). This approach has good adherence and appears to have beneficial effects on insulin sensitivity compared to standard daily energy restricted diets.<sup>12</sup>

Alcohol and sedentary behaviour both increase risk. An additional 10 g of alcohol (1 unit) on a daily basis increases risk by 10 per cent.<sup>13</sup> Risk of breast cancer decreased by three per cent (relative risk [RR] = 0.97, 95 % Cl = 0.95–0.98, P < 0.00) for every 10 MET-hour per week increment in recreational activity (roughly equivalent to 4 hrs/wk of walking in 2 mph).<sup>14</sup> Whilst being 'fit but fat' protects against heart disease,<sup>15</sup> this is not the case for breast cancer where the anti-cancer effects of exercise are mainly seen in women who are a healthy weight and not amongst the overweight and obese.<sup>14</sup>

## Dietary factors and breast cancer risk

If a women is a healthy weight, takes regular exercise and moderates her alcohol does the actual composition of the diet matter?

#### Fruit and vegetables and fibre

The 5-A-DAY campaign was launched in the USA in 1991 by The National Cancer Institute and the Produce for Better Health Foundation to prevent cancer. In 2003, 5-A-DAY was adopted by the Department of Health in the UK to help prevent cancer and other diseases. Emerging evidence since these initial campaigns has consistently linked fruit and vegetable intake, particularly vegetable intake, to reduced overall and cardiovascular mortality, but not specifically to cancer mortality.<sup>16</sup> The WCRF Continuous Update Project recently stated there is no convincing evidence that fruits and vegetables play a role in the aetiology of colorectal, breast and pancreatic cancer.<sup>17</sup>

Recent systematic reviews have linked higher fibre intakes with a lower risk of breast cancer, with a five per cent risk reduction for every additional 10 g of fibre per day. Fibre may reduce risk by reducing reabsorption of oestrogen and androgens in the bowel and hence circulating levels. Soluble fibre appears to be the most protective, possibly via its beneficial effects on insulin sensitivity.<sup>18</sup> Fibre may reduce risk by reducing reabsorption of oestrogen and androgens in the bowel and hence circulating levels.

#### Meat, fish and dairy foods

Vegetarian or vegan diets do not specifically reduce risk. Higher meat consumers are at slightly increased risk; each additional 100 g of red meat per day increases risk by four per cent (RR 1.04 [1.00 - 1.07]) and each additional 30 g of processed meat per day increases risk by three per cent (RR 1.03 [1.00 - 1.06]).<sup>19, 20</sup> It is not clear why meat might be having an effect. Risk does not appear to relate to its saturated fat or carcinogenic heterocyclic amine content. Heterocyclic amines are also found in poultry and fish which respectively have neutral and protective effects on breast cancer risk. It is possible that meat may be an innocent bystander in these studies, and a marker of an overall unhealthy lifestyle.<sup>19, 20</sup> Marine n-3 fats – the polyunsaturated fatty acids (PUFAs) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) - reduce breast cancer risk; each additional 0.1 g marine n-3 PUFA per day reduces risk by five per cent. Two portions of oily fish per week provides approximately 0.45 g/day n-3 and a potential 25 per cent risk reduction, however the vegetarian n-3 fat alpha linolenic acid did not reduce risk.<sup>21</sup>

Dairy foods are perceived to be a cause of breast cancer by many populist web sites and patient advocacy groups as they contain potentially cancer promoting hormones, i.e. oestrogen and insulin like growth factor.<sup>22</sup> These concerns are not supported by evidence. A recent meta analyses including 24,187 cases and 1,063,471 participants found 16 per cent less breast cancer amongst high (>3 servings/day) *vs.* low dairy consumers (<1 serving/day). Risk is reduced with low but not high fat versions possibly related to their content of calcium, conjugated linoleic acids (CLA) and vitamin D; the latter is found in fortified milk products.<sup>23</sup>

#### Soy foods and isoflavones

Eight out of 10 breast cancers are oestrogen dependent. Soy foods contain isoflavones which have weak oestrogenic and anti-oestrogenic effects as well as non-hormonal effects which inhibit cancer cell growth in the laboratory. Not surprisingly many studies have examined whether soy can protect or even increase risk of breast cancer. A recent meta-analysis summarised 14 studies involving 369,934 participants and 5,828 cases of breast cancer. This showed that women consuming moderate amounts of soy throughout their life have lower breast cancer risk; intakes of 5 g of soy protein per day (10 mg isoflavone, equivalent to 170 ml of soy milk or 120 g soy voghurt) reduced risk by four per cent.24 The effect was mainly seen within Asian but not Western populations. Risk reduction may largely relate to biological effects of sov on the developing breast, hence soy intake as a child or adolescent may be more important than its introduction to the adult diet. These data are based on intakes of soy food rather than over the counter isoflavone supplements, the effects of supplements for breast cancer or indeed for cholesterol lowering have not been demonstrated.<sup>25</sup>

#### Vitamin supplements

One in three adults in the UK take vitamin supplements in the hope of protecting themselves against ill health and cancer. Large-scale, randomised supplement trials have mainly been negative, with some notable adverse and beneficial effects. For example, beta-carotene increases the risk of lung and stomach cancer, vitamin E increases prostate cancer and colorectal adenoma, and selenium reduces gastric and lung cancer in populations with low selenium levels but increase rates in those with higher levels. Both beta-carotene and vitamin E supplementation increase overall mortality.<sup>26</sup> Supplementation with vitamin D,<sup>27</sup> calcium,<sup>28</sup> folic acid<sup>29</sup> or a multivitamin<sup>30</sup> neither decrease or increase risk of breast cancer. Therefore, advice is to avoid supplements unless indicated for a specific reason.

## Lifestyle prevention of breast cancer across the life course

Seventy-five per cent of breast cancer cases occur after the menopause; however, successful prevention of these, and the 25 per cent of cases which are premenopausal, needs to start earlier in life. Breast cancer risk can accumulate during childhood, adolescence and particularly in the period between the menarche and first pregnancy before breast cells become differentiated and less susceptible to carcinogenesis (see Table Two). Rates of growth in childhood and excess alcohol and smoking in early adulthood increase risk. Weight gain during pre and postmenopausal years mainly increases risk of postmenopausal (but not premenopausal) breast cancer.<sup>31, 32</sup> Breast cancer prevention interventions should focus on preventing weight gain during the premenopausal years; approximately 10 kg of the total 12 kg average adult weight gain reported in UK women occurs before the age of 50 years according to Department of Health statistics.<sup>33</sup> Greater adiposity in childhood or early adulthood does not increase breast cancer risk and can, sometimes, put women at lower risk. The reason for this weight paradox in breast cancer is not clear but most likely reflects the fact that heavier young women do not experience as much weight gain during adulthood, and it is adult weight gain which appears to put women at particularly high risk.

Timing of exposure	Before n	nenarche	After menarche an	d before first birth	Premenop	ausal years	Postmenopausal years
Linked to pre or post menopausal breast cancer	Pre	Post	Pre	Post	Pre	Post	Post
Greater adiposity	$=$ or $\downarrow$	= or ↓	= or <b>↓</b>	= or ↓	=	Ť	Ť
Height growth velocity	Ť	Ť	NA	NA	NA	NA	NA
High physical activity	?	?	ţ	Ļ	Ļ	t	ţ
High alcohol	NA	NA	Ť	1	Ť	t	ſ
Smoking	?	?	Ť	1	=	=	=
High soy intake	Ļ	Ļ	Ļ	Ļ	=	=	=

Table Two: Breast Cancer Prevention across the Life Course<sup>36, 37</sup>

Key: NA = not applicable; Pre = premenopausal breast cancer; Post = postmenopausal breast cancer

#### How can we engage women in breast cancer prevention?

Recent expert reports estimate successful lifestyle change could prevent 25-30 per cent of breast cancer cases in the UK.<sup>34</sup> There is a general public skepticism that their actions can influence whether they develop cancer. The most common perceived causes of breast cancer cited are mainly out of an individual's control, i.e. genetics, environmental pollutants, pesticides and god's will (see Table Three). Whilst many of the women who develop breast cancer have a genetic disposition, this is not the sole reason for them developing breast cancer which is often a complex interaction between genetic, reproductive and lifestyle factors. For example, changes in reproductive and lifestyle risk factors in the past century have increased breast cancer rates four-fold amongst BRCA2 carriers in Iceland.35

There is a need for consistent evidence-based cancer prevention messages, backed-up with effective programmes to support lifestyle across the life course. Our current research at the Genesis Breast Cancer Prevention Centre in Manchester is testing whether women attending the National Breast Screening can be engaged with healthy lifestyle to prevent breast cancer.

### Table Three: What causes breast cancer? – The mismatch between expert opinion and lay perception

Expert opinion (estimated attributable risk – UK <sup>34</sup> )		Common beliefs amongst healthy women (N = 1297 <sup>38</sup> )		
Non – modifiable	% of cases	Non – modifiable*	% citing this reasor	
Genetic factors <sup>39</sup>	47	Genetic factors	77.6	
Reproductive factors: nulliparity, ate parity, lack of breastfeeding <sup>40</sup>	11	Environmental pollutants	31.7	
Occupational – shift work	4.6	Stress	27.9	
Potentially modifiable factors	% of cases	Food additives	18.4	
Obesity	9.0	Pesticides	10.0	
Alcohol	6.4	Food additives	18.4	
Physical activity	3.4	Reproductive	7.2	
Use of HRT	3.2	Breast injury	6.6	
		Chance/fate/god's will	6.5	
		Potentially modifiable factors	% of cases	
		Diet	23.2	
		Alcohol	12.6	
		Physical activity	11.6	
		Smoking	11.6	
		Use of HRT	7.2	

\*Totals could exceed 100% as respondents could identify agents from multiple categories

#### Useful resources

- Cancer Research UK http://cancerhelp.cancerresearchuk.org/type/breast-cancer
- Breast Cancer Care www.breastcancercare.org.uk
- Genesis www.genesis.org.uk
- American Cancer Society www.cancer.org
- Michelle Harvie and Anthony Howell: The 2 Day Diet (Ebury 2013) ISBN-10: 0091948053 www.thetwodaydiet.co.uk
- Memorial Sloan-Kettering Cancer Center www.mskcc.org/mskcc/html/44.cfm
- National Institute for Health and Clinical Excellence Familial Breast Cancer: The classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (CG41) – www.nice.org.uk

#### About Genesis Breast Cancer Prevention

Genesis Breast Cancer Prevention is the only charity in the UK entirely dedicated to the PREDICTION and PREVENTION of breast cancer. We are a national charity based in Europe's first purpose built Breast Cancer Prevention Centre in Manchester and we exist to support vital medical research.

Currently one in 10 women in the UK will develop the disease; Genesis aims to make one in 10, none in 10, creating a breast cancer free future for the next generation.

With our much valued supporters and the fundraising that they undertake, Genesis' research simply could not happen.

If you are looking for a way to get involved, why not 'Get active, have fun and help prevent breast cancer' by undertaking some exercise based fundraising in our Million Miles Challenge. The Million Miles Challenge aims to raise  $\pounds 1$  million for pioneering breast cancer research, every  $\pounds 1$  raised in sponsorship = 1 mile and we would like you to help us get to  $\pounds 1$  million!

The Genesis Tea Party Challenge is another of our fundraising initiatives which incorporates all things cakes with all things fundraising – 'Bake, eat, have fun and help prevent breast cancer'. The challenge was created as a fun, simple way of raising vital funds and awareness and although this may test your diet disciple, The 2-Day Diet cookbook has plenty of healthy and delicious recipes you can incorporate!

For further fundraising ideas and to find out more about how you can get involved with Genesis then please visit: **www.genesisuk.org** or get in touch by emailing: **info@genesisuk.org** or by calling: **0161 291 4400**.

Performences 1. Bray F. McCarron P. Parkin DM. (2004). The changing global patterns of female breast cancer incidence and motality. Breast Cancer Res; 6(6): 229-39.2. Maddams. J. Uliey, M. Moller H. (2012). Projections of cancer prevalence in the United Kingdown, 2016): 2404 52.1 (2014). Additional cancer pacel and cancer-pacel interval time rest in the United Kingdown and Cancer pacel interval time rest. Prov. Prov.