

HRT, menopause and breast cancer

Tiphaine Boulin, Isla Whitcroft, Hannah Moody

Peer reviewed by two members of Breast Cancer UK independent [Science Panel](#)

1. Summary

Hormone replacement therapy (HRT) is used to manage the symptoms of menopause. It has been associated with an increased risk of developing breast cancer; however, this risk varies according to the type of HRT and duration of use. Evidence suggests that oestrogen-only HRT has little to no increased risk of breast cancer; however, it is generally only prescribed to people who have had a hysterectomy as it carries an increased risk of uterine cancer. Combined HRT is associated with a duration-dependent increase in breast cancer risk when used over five years. This increase in risk then reduces after combined HRT treatment is stopped, but some risk remains if used for over 10 years. To date, HRT is considered the most effective approach for managing menopausal symptoms. The decision on whether to take HRT should be an individual choice, made in consultation with a specialist healthcare practitioner based on personal symptoms, risks, benefits, treatment suitability and duration.

2. Introduction

Breast cancer is the most common form of cancer for women. Around 55,500 women and 370 men in the United Kingdom receive a breast cancer diagnosis each year, representing 15% of all new cancer cases. Although breast cancer incidence rates are rising with an ageing population and increased detection rates, mortality rates from breast cancer have decreased. Nevertheless, breast cancer remains the second most common cause of cancer death for women in the UK [1].

Many factors can influence the risk of developing breast cancer, including non-modifiable factors such as age, genetics,

starting menstruation before the age of 12, reaching menopause after the age of 55, first-person family history of breast cancer and dense breasts. However, Breast Cancer UK (BCUK) estimates that at least 30% of all breast cancers, around 17,000 breast cancer cases each year, are attributable to preventable causes or modifiable risk factors. These include behavioural risk factors such as being overweight and post-menopausal weight gain, lack of physical activity, pregnancy after the age of 30 or having no children, not breastfeeding, and alcohol consumption [1], as well as environmental risk factors such as exposure to certain environmental chemicals [2].

Footnote: BCUK aims to use inclusive language where possible, however when the data is derived from a gender-specific subset (e.g. women), we respect the gender-specific categorisation used in the data set.

How to cite: Boulin T., Whitcroft I., Moody H. HRT, menopause and breast cancer Breast Cancer UK. 2024. <https://www.breastcanceruk.org.uk/resources/hrt-menopause-and-breast-cancer/>

The use of prescription hormones is also a modifiable risk factor, including those used in hormone replacement therapy (HRT), sometimes called menopausal hormone therapy (MHT), to manage some of the symptoms of menopause. A link between HRT and the risk of breast cancer was first highlighted in the publication of the Women’s Health Initiative (WHI) study in 2002 [3] and the Million Women Study (MWS) in 2004 [4]. In the UK, this led to a dramatic drop in HRT use [5], a trend that has only recently been reversed [6]. In recent years, several studies have provided further evidence considering the potential risks associated with HRT, including breast cancer, stroke, and dementia, compared to the potential benefits of HRT for conditions such as cardiovascular disease and osteoporosis

This review aims to provide information to enable the reader to make an informed choice on whether HRT is a suitable therapy for them in discussion with their healthcare provider. We will discuss menopause and the use of HRT to relieve menopausal symptoms, explain the mechanism of HRT on breast cancer, evaluate and contextualise the latest research on the risk of HRT in breast cancer, and summarise the risks versus benefits of this therapy.

3. Menopause

3.1 What is menopause?

Menopause occurs when a person with a uterus stops menstruating without other causes, such as medication or pregnancy. It is a natural part of ageing and usually affects individuals aged 45 to 55. Transgender men and non-binary individuals, born female, may also experience menopause [7].

During the reproductive years, the ovaries release an egg each month, which can be fertilised by sperm or eliminated through menstruation when the egg is not fertilised. This monthly cycle is controlled by the follicle-stimulating hormone (FSH) and luteinising hormone (LH), which stimulate the ovaries to produce the hormones oestrogen and progesterone. Oestrogen is the primary female sex hormone and regulates the menstrual cycle, egg development, and ovulation. Progesterone prepares the endometrium, which lines the uterus for egg implantation. With age, the number of stored eggs in the ovaries decreases, and fewer hormones, including oestrogen, are produced [8].

The menopausal phase naturally occurs when ovaries produce less oestrogen

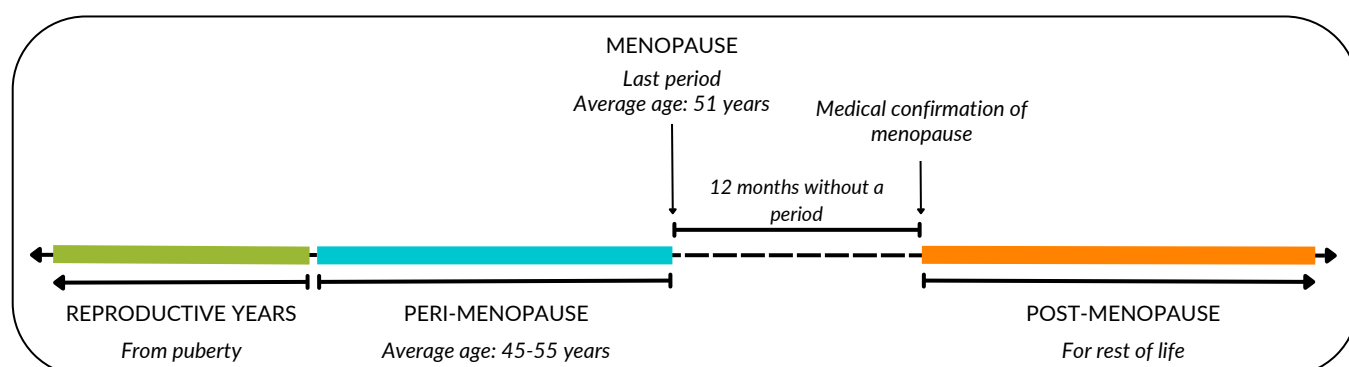


Figure 1. Diagram of the peri-menopause, menopause, and post-menopause.

and stop releasing eggs, ending the reproductive cycle. From the start of menopausal symptoms (for example, less frequent or irregular periods) until the last period, an individual is pre- or perimenopausal. Menopause is a singular event defined by the last period; however, it is only medically confirmed after an individual has been without a period for 12 months, after which they are technically post-menopausal [7] (See Figure 1). In addition to ageing, menopause can also happen after certain surgeries, such as a bilateral oophorectomy where ovaries are surgically removed or due to cancer treatments like chemotherapy or radiation [7,9].

In the UK, the average age for menopause is 51; however, 1% experience premature menopause - before age 40. An estimated 13 million women in the UK are currently perimenopausal or menopausal, representing around a third of the UK female population [10].

3.2 Symptoms of menopause

During the menopause phase (perimenopause, menopause, and occasionally post-menopause), individuals may experience symptoms related to decreased oestrogen levels. These symptoms can be broadly separated into five areas [9]:

- Physical symptoms - e.g. breast tenderness, changes in body shape and weight gain, fatigue, dry skin, hair loss or thinning, headaches or migraines, heart palpitations, joint aches, sleep disturbances (insomnia and sleep apnoea), and vasomotor symptoms (constriction or dilation of

blood vessels) like hot flushes and night sweats;

- Cognitive symptoms - e.g. brain fog, forgetfulness, and impaired memory and concentration;
- Psychological symptoms - e.g., anxiety, depression, and mood disturbances;
- Urogenital symptoms - e.g., urinary incontinence, leaks and frequency and urinary tract infections;
- Sexual or vaginal symptoms - e.g., decreased libido, dyspareunia (pain during intercourse), and vaginal atrophy (the thinning, drying and inflammation of the vaginal walls), which can cause discomfort and potential trauma during intercourse or pelvic examinations [9,11].

4. Hormone replacement therapy

4.1 What is HRT?

HRT is a pharmaceutical treatment used to help relieve symptoms of menopause. It replaces either oestrogen and progesterone or just oestrogen, which are at decreased levels when an individual approaches or has experienced menopause [13]. In 2021/2022, an estimated 1.93 million people were prescribed HRT in England, a 30.5% increase from an estimated 1.48 million in 2020/2021 [6].

4.2 Types of HRT

There are two main types of HRT: combined HRT, which includes oestrogen and progestogen (a synthetic form of progesterone), and oestrogen-only HRT [12].

Most often, combined HRT is prescribed, as taking oestrogen alone without progestogen (known as unopposed oestrogen) can cause thickening of the uterine lining, which increases the risk of uterine cancer. Therefore, oestrogen-only HRT is usually only recommended when the uterus has been removed (hysterectomy) [13–15].

4.3 HRT treatment routines

HRT treatment routines vary depending on what stage of the menopausal phase an individual is at, whether they are still menstruating regularly or irregularly, or if they have had a hysterectomy [14].

Continuous combined HRT is often recommended for post-menopausal individuals and consists of taking both oestrogen and progestogen daily without a break. It can be taken as one formulation (oestrogen and progestogen combined in one formulation) or separately (oestrogen and progestogen in separate formulations).

Cyclical (sequential) combined HRT is usually prescribed to people who are peri-menopausal and still have periods but experience menopausal symptoms. There are two types of cyclical combined HRT that involve taking oestrogen every day but taking progestogen less often:

- For individuals with regular periods - monthly HRT with oestrogen daily and progestogen for the last 10-14 days of the menstrual cycle every month.
- For individuals with irregular periods - 3-monthly HRT with oestrogen daily and progestogen for around 10-14 days every three months.

Oestrogen-only HRT is for individuals who have had a hysterectomy and consists of taking only oestrogen daily [14].

HRT can be taken in different ways, including tablets, skin patches, spray, gel, implant, intrauterine system or vaginal cream, gel, tablet, pessary or ring [9,14].

5. HRT and breast cancer

5.1 Hormones and breast cancer

Hormones are natural chemical messengers in the body that travel via the bloodstream to initiate or control specific physiological activities [16]. Most breast cancers are hormone-sensitive, meaning hormones like oestrogen or progesterone can influence their growth. Hormone-sensitive breast cancers contain proteins called hormone receptors (either oestrogen receptors (ER) or progesterone receptors (PR)) that oestrogen and progesterone can bind to and activate, which can change the expression of genes causing breast cancer cell growth and replication [16]. Greater exposure to oestrogen is associated with a higher risk of breast cancer [17,18], and around 67%-80% of all diagnosed breast cancer tumours are oestrogen receptor positive[16].

5.2 HRT and breast cancer

HRT contains oestrogen, exposure to which is a known breast cancer risk factor, making HRT a potential risk factor for breast cancer [17]. The publication of the Women's Health Initiative (WHI) study in 2002 [3] and

the Million Women Study (MWS) in 2004 [4] highlighted an increased risk of breast cancer for HRT users. These results indicated that the risks of HRT outweighed the benefits [3,4], and the UK regulatory authorities issued new guidelines with safety restrictions recommending doctors prescribe the lowest effective dose, causing many doctors to stop prescribing HRT and many people to choose not to take HRT [19]. However, the methodology and limitations of these studies have been critiqued, including the lack of distinction in the safety of different formulations, delivery methods and participants' ages, which ranged from the onset of menopause to over 10 years on from menopause [19].

Recent studies have focused on determining the extent of HRT risk, considering variables such as treatment type and routine, age when HRT is started, length of time on HRT and amount of time after stopping HRT. Between 2017-2023, a consensus emerged that combined oestrogen-progestogen HRT carries an increased risk of breast cancer compared to never using HRT, while oestrogen-only HRT has little to no increase in risk [20–25]. The evidence also indicates that duration of use is an important variable.

If combined HRT is used for less than a year, there is little or no increase in breast cancer risk in current or previous users. Breast cancer risk increases further with more prolonged use and gradually decreases once HRT is stopped. However, some increased risk remains when used for over 10 years [21–25]. Therefore, the extent of breast cancer risk associated with HRT use varies based on the type of HRT, the duration of treatment, and the amount of time since discontinuation [20–25]. This is reflected in the current National Institute for Health and Care Excellence (NICE) guidelines on menopause diagnosis and management, which state that oestrogen-only HRT has little to no change in the risk of breast cancer, while combined oestrogen-progestogen HRT can be associated with an increase in breast cancer risk, although any increase in breast cancer risk is related to treatment duration and reduces after HRT is stopped [15].

Figures from the Medicine Healthcare Regulatory Agency (MHRA) use the latest research providing a summary risk of breast cancer cases per 1,000 women who use/have used HRT in various treatment routines, compared to non-HRT users, comparing risk after five and ten years of use (see Table 1) [26].

Table 1. Breast Cancer Risks and HRT [26].

Summary of risks for HRT and breast cancer	Risk after 5 years of HRT use (extra cases per 1,000 compared to non-users)	Risk after 10 years of HRT use (extra cases per 1,000 compared to non-users)
All combined HRT	+8	+20
Sequential combined HRT	+7	+17
Continuous combined HRT	+10	+25
Oestrogen only HRT	+3	+7

The breast cancer risk associated with combined HRT use also varies according to the type of progestogen used. A systematic review and meta-analysis (large studies that combine and analyse results from several similar past studies) found an increased risk when oestrogen is combined with medroxyprogesterone (MPA), norethisterone or levonorgestrel (types of synthetic progesterone). There was no increase in risk when combined with dydrogesterone (another synthetic form of progesterone) or micronised progesterone (a bioidentical hormone), and the risk rises with prolonged use [27]. In addition, another systematic review found that oestrogens combined with micronized progesterone did not increase the risk of breast cancer for up to five years of treatment duration and found limited evidence that use for more than five years was associated with an increased breast cancer risk [28].

Being overweight and adult weight gain, particularly after menopause, is a risk factor for breast cancer [17]. Interestingly, recent studies have found

that Body Mass index (BMI), a categorising measure using height and weight to determine if a person's weight category may lead to health problems, is a modifier for the breast cancer risk associated with HRT. In HRT users with a higher BMI, there was a lower risk association compared to HRT users with a lower BMI for both types of HRT treatments. Therefore, a higher BMI seems to attenuates the breast cancer risk associated with current HRT use [21-23,25].

Context is essential when considering risk factors. In the UK, a woman born after 1960 has a 15% estimated lifetime risk of having breast cancer, equating to 150 cases per 1,000 women [17]. When compared to other lifestyle factors, there is little difference in the risk incurred with HRT use (see Table 2) [29]. Table 2 shows the added risk over five years in cases per 1,000 women for known breast cancer risk factors – i.e. obesity and alcohol intake – compared to the added risk of using HRT for over 5 years in cases per 1,000 women.

Table 2. Contextualising HRT compared to other known breast cancer health risks [17,29]

Risk Factors	Absolute excess risk per 1,000 women over 5 years aged 50-59
Post-menopausal BMI > 25 (overweight) vs BMI <25 (healthy)	+4
Post-menopausal BMI > 30 (obesity) vs BMI <25 (healthy)	+7
Alcohol intake of 4-6 units per day	+8
Alcohol intake of ≥6 units per day	+11
Combined HRT use for 5 years	+8 to +10
Oestrogen-only HRT use for 5 years	-6 to +3

5.3 HRT and breast cancer risk in BRCA1 and BRCA2 carriers

BRCA1 and BRCA2 (Breast Cancer gene 1 and Breast Cancer gene 2) produce proteins that help repair DNA damage and help prevent cancer from developing. Mutations in DNA repair pathways of BRCA1 and BRCA2 predispose carriers to an elevated lifetime risk for breast cancer and ovarian cancer [30]. Studies looking at breast cancer risk in BRCA mutation carriers found that postmenopausal HRT use did not increase the risk of breast cancer [31,32]. Similarly, studies looking at breast cancer risk in BRCA mutation carriers after risk-reducing salpingo-oophorectomy (removal of the ovaries and fallopian tubes to manage the elevated risk of ovarian cancer) showed that HRT does not negate the reduction in breast cancer risk associated with the surgery and that breast cancer risk associated with oestrogen-only use was lower in comparison to combined oestrogen-progestogen use [33–35]. A recent retrospective study reported that receiving HRT after undergoing salpingo-oophorectomy beyond the age of 45 years was associated with an increased risk of breast cancer, while there was no increased risk for individuals who underwent salpingo-oophorectomy before the age of 45 years; however, this needs to be assessed in larger cohorts [36]. For individuals with a germline BRCA1 or BRCA2 mutation but with no personal history of breast cancer, NICE guidance recommends they be offered HRT if they have had a bilateral salpingo-

oophorectomy before their natural menopause and continued up until the time they would have expected natural menopause [37].

5.4 HRT and breast cancer recurrence

The current NICE guidelines recommend that individuals with current, past, or suspected breast cancer should not be prescribed HRT [38] due to concerns of increased risk of breast cancer recurrence. Breast cancer treatment may include oestrogen-depleting or blocking therapies and chemotherapy, leading to premature menopause and frequent menopause symptoms [39].

The evidence on the impact of HRT use on breast cancer recurrence in breast cancer survivors is inconsistent. A recent systematic review and meta-analysis found that HRT increases the risk of breast cancer recurrence; this risk was significant in patients with hormone receptor-positive cancers and not in hormone receptor-negative cancers [40]. Another retrospective cohort study showed no increase in breast cancer recurrence when taking adjuvant Tamoxifen and using vaginal oestrogens, suggesting this may be a safe method to manage vulvovaginal symptoms [41]. Analysis from a study in 2021 concluded that there is not enough evidence to demonstrate an increased risk of breast cancer recurrence with HRT, and each patient should be assessed and treated based on their specific symptoms and cancer risk [42]. NICE guidance recommends that women with breast cancer be referred to a healthcare professional with expertise in menopause [15].

6. Other health risks and benefits of HRT

6.1 Other HRT risks

Besides breast cancer, HRT is a risk factor for other diseases, including stroke and venous thromboembolism (blood clots). With HRT tablets, the risk of blood clots is very low, while there is a slight increase in the risk of stroke; however, there is no increased risk for either stroke or blood clots with HRT patches, sprays and gels as the oestrogen is absorbed through the skin [15,43]. According to the MHRA figures, current oestrogen-only HRT use or combined HRT use for 5 years increases the risk of stroke by 1 case per 1,000 women aged 50-59 and 3 cases per 1,000 women aged 60-69 [26]. This means that a patient is more likely to have an increased risk of stroke if they are taking HRT at an older age. In the case of venous thromboembolism, the risk increases by 2 cases per 1,000 women regardless of age for oestrogen-only use, while for combined HRT, the risk increases by 7 cases per 1,000 women aged 50-59 and 10 cases per 1,000 women aged 60-69 [26,44]. Therefore, the risk of venous thromboembolism increases if you are using combined HRT compared to oestrogen-only HRT.

6.2 Other benefits of HRT

The main benefit of HRT is to help relieve symptoms of peri-menopause and menopause. Research has also demonstrated that HRT provides a protective benefit for other diseases and conditions, including preventing

osteoporosis and the maintenance of muscle strength [15,43].

NICE Guidelines note that HRT has a positive effect on the risk of osteoporosis, a thinning of the bones due to reduced oestrogen levels, which can lead to bone fractures [15,43]. Summarising the current research (randomised controlled trials and observational studies), the guidelines estimate that in comparison with menopausal non-HRT users, current HRT users have 16-23 fewer cases of fragility fractures per 1,000 women, whilst HRT use for more than five years showed 15-25 fewer cases per 1,000 women. This reduction in risk decreases once HRT treatment is stopped but may continue for longer for those who take HRT for longer [15,45].

HRT can also improve muscle strength, which is often lost when menopause is reached [15]. Nonetheless, the evidence is limited, and exercise and daily physical activity should be prioritised to maintain muscle mass and strength [15].

6.3 Other conditions and HRT

A condition that has been investigated in relation to HRT is coronary heart disease. Current evidence suggests that HRT has little to no effect on the risk of coronary heart disease [43]. The NICE Guidelines currently state that there is no or reduced risk of coronary heart disease with six fewer cases per 1,000 women taking oestrogen-only HRT and little or no increased risk of coronary heart disease with five extra cases per 1,000 women taking combined HRT [15].

There are also ongoing investigations into the effects of HRT on other conditions, such as dementia and diabetes. Regarding dementia, a 2023 Danish observational study found an association between short- and long-term use of combined HRT and an increased risk of dementia [46]. However, a large-scale American study reported in 2021 that women who took transdermal (delivered via skin patch, sprays, or gel) or oral (tablets) combined HRT had a reduced risk of all forms of neurodegenerative diseases, including dementia [47]. To date, both NICE and the NHS state that it is unknown whether HRT affects the risk of dementia [15,43]. In the case of type 2 diabetes, the current NICE guidelines state that HRT does not increase the risk of developing type 2 diabetes [15]. However, the latest evidence suggests that HRT may positively affect glucose homeostasis (maintaining stable blood glucose levels), which may slightly reduce the risk of developing type 2 diabetes [43,48].

7. Alternatives to HRT

There are cases in which HRT is not considered suitable, such as individuals with a history of breast cancer, blood clots, untreated high blood pressure, liver disease or who are pregnant or considering pregnancy [13]. Some individuals may find that there are barriers to accessing HRT, such as the reluctance of healthcare practitioners to prescribe HRT or lack of knowledge of healthcare practitioners around HRT and peri-menopause [10]. Additionally, many people may not wish to take HRT due to historical controversy around HRT,

preferring to pursue natural alternatives or choosing not to treat their symptoms and accepting them as a natural life phase [10]. Alternative treatments or replacement therapies to manage menopause symptoms include non-hormonal treatments, herbal remedies, and behavioural changes.

7.1 Non-hormonal treatments

There are several non-hormonal alternatives to HRT; they are not as effective as HRT in managing menopause symptoms and can only be prescribed or referred to by a doctor [49]. Non-hormonal alternatives include:

- Antidepressants which can help with mood symptoms, depression, and vasomotor symptoms (e.g. selective serotonin reuptake inhibitors (SSRIs) and serotonin-noradrenaline reuptake inhibitors (SNRIs)). NICE does not recommend these as a first-line treatment for vasomotor symptoms [15]. Side effects include feeling agitated, shaky, dizzy, nauseous, or anxious, and a reduced sex drive [49,50].
- Gabapentin is an anticonvulsant approved for the treatment of epilepsy. It can be effective in relieving the frequency and severity of hot flashes. Side effects include drowsiness, dizziness, and fatigue [50]. A low dose of pregabalin may also be a well-tolerated alternative.
- Oxybutynin is an anticholinergic medicine used to treat symptoms of an overactive bladder. A placebo-controlled trial showed low doses of oxybutynin (2.5 mg or 5 mg twice a day) improved hot flashes and

quality of life in patients with and without breast cancer and can be helpful for urogenital symptoms. Side effects include dry mouth, difficulty urinating, and abdominal pain [51].

- Cognitive Behavioural Therapy (CBT) is a type of talking therapy that can help with mood changes, anxiety, sleep problems, hot flushes and joint pain arising from menopause [15,52].
- Fezolinetant is a neurokinin 3 receptor antagonist that blocks the thermoregulatory centre in the hypothalamus and can significantly reduce vasomotor symptoms compared with placebo. Side effects include headache [53].
- Clonidine is an antihypertensive agent that reduces blood pressure and heart rate, which may help with migraines and menopausal vasomotor symptoms, such as hot flushes and night sweats [52,54]. It is the most popular non-hormonal alternative to HRT; however, research suggests it is not the most effective approach [50,52,54], and NICE does not recommend it as a first-line treatment for vasomotor symptoms [15]. Side effects include dry mouth, drowsiness, depression, and constipation [49].

7.2 Herbal remedies

Regarding alternative therapies and menopause, it is important to note the guidance from the Royal College of Obstetrics and Gynaecology, which states:

“The evidence from clinical trials of benefit on menopausal symptoms is limited and conflicting. There are no recognised international criteria for the

design of clinical trials of alternative therapies as there are for standard medicines and medical devices for endpoints of treatment and safety evaluations. A major concern is that herbal medicines have pharmacological actions and thus can cause unwanted effects and have potentially dangerous interactions with other medicines (both herbal and conventional)” [50].

BCUK recommends that you speak to your doctor before taking any alternative therapies, as they may interact with other medications.

Various products and herbal remedies are available; however, their safety and efficacy are unknown. These include:

- Soy and red clover contain phytoestrogens (particularly isoflavones), which are plant substances with similar effects to oestrogen, making them the subject of much interest for managing menopausal symptoms [50]. However, evidence is mixed and unclear if they reduce menopausal symptoms, with, at best, a modest effect on vasomotor symptoms [55,56].
- Evening Primrose Oil is a widely used oil that contains phytoestrogen and omega-6 fatty acids, including gamma-linolenic acid (GLA). There is no evidence of its efficacy in treating menopause symptoms, even though it has long been cited as a treatment for hot flushes and night sweats [50,55].
- Black Cohosh is a herb that is commonly used as a treatment for symptoms of menopause, including hot flushes, night sweats, vaginal

dryness, and sleep disturbances [57]. It is believed to balance oestrogen and progesterone levels [58], which may help with menopause symptoms; however, it is not understood how this is achieved and is not supported by scientific evidence [55]. Further research is needed, particularly in terms of dosage, duration, and safety, as it has been associated with severe liver damage [59].

- St John's Wort is a plant shown to help treat mild to moderate depression. Its efficacy in treating vasomotor menopausal symptoms, including hot flushes and night sweats, is not proven, and the varying products contained in St John's Wort means their effect is uncertain, and they can interfere with other medications [15,50].
- Acupuncture is an ancient Chinese treatment where fine needles are inserted at specific sites in the body to stimulate healing responses. The evidence around acupuncture and menopause symptoms is conflicting due to difficulties in trial design [50]. One Danish trial in 2019 showed clinically relevant results that acupuncture effectively reduced mild to moderate menopause symptoms [60]. Further research is needed within the area of acupuncture and menopause to establish the effectiveness of this therapy.

7.3 Behavioural changes

Weight

Weight gain is one of the most common side effects of peri-menopause and menopause, with body fat redistribution and changes in body composition, such

as increased fat mass and reduced lean mass [55]. Body weight and composition changes have been associated with common menopause symptoms like vasomotor and urogenital symptoms [55]. Studies have noted that a higher BMI (overweight or obese) is associated with more severe menopausal symptoms and that clinically significant weight loss results in marked improvement of these symptoms, especially hot flushes, mood disorders and sleep disturbances [61–63]. Maintaining a healthy weight can help reduce the severity of menopausal symptoms and the risk of breast cancer [64].

Diet

Eating a healthy and varied diet can help manage menopausal symptoms and reduce the risk of breast cancer [64]. Evidence suggests that following a Mediterranean-style diet (rich in fruits, vegetables, wholegrains and oily fish, and limiting saturated fat, added sugar and salt) can protect against the risk of osteoporosis and heart disease, help with cognitive symptoms, and provide better sleep quality, which are all associated with menopause [55,65,66]. This diet can also support maintaining a healthy weight [65]. There is limited evidence that diet can help improve vasomotor symptoms [65]; however, foods like caffeine, alcohol or spicy foods can trigger or worsen hot flushes, night sweats, and migraines [66].

Physical activity

Evidence suggests that various types of exercise can effectively help manage menopause-related symptoms. There are many benefits to regular exercise during menopause, such as improvement of

chronic disorders such as mood disorders, dementia, diabetes, strokes, and cardiovascular disease, enhancing overall quality of life, and reducing the risk of breast cancer [67].

Aerobic exercise, a type of exercise that uses large muscle groups, is rhythmic and requires oxygen to produce energy (e.g., swimming, running, walking, or cycling), has been shown to improve psychological health, mood, vasomotor symptoms, sleeping problems, and health-related quality of life [50,67–70]. Resistance training exercise, which includes any form of exercise involving lifting or pulling against resistance, helps maintain bones and muscle mass, both of which are important during menopause, where osteoporosis and muscle loss are common [67,68].

Exercises like practising yoga have been found to help with psychological well-being and quality of sleep and may also help reduce vasomotor symptoms in menopausal individuals [50,67,68,71].

Not all types of exercise are beneficial for menopause symptoms; infrequent high-impact exercises (i.e. exercises which have a greater impact on joints and bones, such as running or jumping) can potentially make symptoms worse [50].

8. Conclusion

The findings from this review demonstrate that all types of HRT are associated with an increase in the risk of

developing breast cancer; the extent of risk depends on the type of HRT and the duration of use.

With oestrogen-only HRT, there appears to be a minimal increase in the risk of breast cancer. However, this type of HRT can only be taken by individuals who have had a hysterectomy.

There is a duration-dependent increase in breast cancer with combined HRT, which was noticeably higher when used for over 5 years. This risk reduces after HRT treatment is stopped, but some increased risk remains when HRT is used for over 10 years. Additionally, using micronised progesterone or dydrogesterone in combined HRT appears to have a lower risk than other synthetic progesterone.

There is currently not enough evidence regarding the risk of HRT and breast cancer in BRCA1 and BRCA2 carriers or breast cancer recurrence.

In context with other risk factors for breast cancer and HRT, there is little difference in the risk incurred with HRT use compared to obesity (BMI > 30) and alcohol intake (> 4 units per day).

There are alternative remedies to HRT; however, HRT remains the most effective solution for the management of menopause symptoms.

The decision on whether to take HRT must be an individual choice in consultation with a healthcare practitioner, weighing the individual breast cancer risk versus other benefits, treatment suitability and duration.

References

- [1] Cancer Research UK (CRUK). Breast cancer statistics 2021. <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer> (accessed October 25, 2023).
- [2] Wan MLY, Co VA, El-Nezami H. Endocrine disrupting chemicals and breast cancer: a systematic review of epidemiological studies. *Crit Rev Food Sci Nutr* 2022;62:6549–76. <https://doi.org/10.1080/10408398.2021.1903382>.
- [3] Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative Randomized Controlled Trial. *JAMA* 2002;288:321–33. <https://doi.org/10.1001/jama.288.3.321>.
- [4] Million Women Study Collaborators, Banks E, Beral V, Bull D, Reeves G, Austoker J, et al. Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet* 2003;362:419–27. [https://doi.org/10.1016/S0140-6736\(03\)14065-2](https://doi.org/10.1016/S0140-6736(03)14065-2).
- [5] Watson J, Wise L, Green J. Prescribing of hormone therapy for menopause, tibolone, and bisphosphonates in women in the UK between 1991 and 2005. *Eur J Clin Pharmacol* 2007;63:843–9. <https://doi.org/10.1007/S00228-007-0320-6>.
- [6] NHS Business Services Authority. Hormone Replacement Therapy – England – April 2015 to June 2022 2022. <https://www.nhsbsa.nhs.uk/statistical-collections/hormone-replacement-therapy-england/hormone-replacement-therapy-england-april-2015-june-2022> (accessed September 28, 2023).
- [7] NHS Inform. Menopause 2022. <https://www.nhsinform.scot/healthy-living/womens-health/late-years-around-50-years-and-over/menopause-and-post-menopause-health/menopause/> (accessed October 25, 2023).
- [8] Briggs P. Fast Facts for Patients: Menopause 2021;2. <https://www.liverpoolwomens.nhs.uk/media/4252/fast-facts-for-patients-menopause-resource.pdf> (accessed October 4, 2023).
- [9] Grant MD, Marbella A, Wang AT, Pines E, Hoag J, Bonnell C, et al. Menopausal Symptoms: Comparative Effectiveness of Therapies 2015;147. <https://www.ncbi.nlm.nih.gov/books/NBK285463/> (accessed September 28, 2023).
- [10] Harper JC, Phillips S, Biswakarma R, Yasmin E, Saridogan E, Radhakrishnan S, et al. An online survey of perimenopausal women to determine their attitudes and knowledge of the menopause. *Women's Health* 2022;18. <https://doi.org/10.1177/17455057221106890>.
- [11] National Health Service (NHS). Menopause - Symptoms 2022. <https://www.nhs.uk/conditions/menopause/symptoms/> (accessed December 12, 2023).
- [12] Fawcett Society, Bazeley A, Marren C, Sheperd A. Menopause and the Workplace 2022. <https://www.fawcettsociety.org.uk/Handlers/Download.ashx?IDMF=9672cf45-5f13-4b69-8882-1e5e643ac8a6> (accessed October 25, 2023).
- [13] National Health Service (NHS). About hormone replacement therapy (HRT) 2023. <https://www.nhs.uk/medicines/hormone-replacement-therapy-hrt/about-hormone-replacement-therapy-hrt/> (accessed October 25, 2023).
- [14] National Health Service (NHS). Types of hormone replacement therapy (HRT) 2023. <https://www.nhs.uk/medicines/hormone-replacement-therapy-hrt/types-of-hormone-replacement-therapy-hrt/> (accessed September 28, 2023).
- [15] National Institute for Health and Care Excellence (NICE). Menopause: diagnosis and management 2019. <https://www.nice.org.uk/guidance/ng23> (accessed September 28, 2023).
- [16] National Cancer Institute. Hormone Therapy for Breast Cancer Fact Sheet 2022. <https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet> (accessed October 25, 2023).
- [17] Cancer Research UK. Breast cancer risk. Cancer Research UK 2015. <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/risk-factors> (accessed September 28, 2023).

- [18] National Health Service (NHS). Breast cancer in women - Causes 2019. <https://www.nhs.uk/conditions/breast-cancer/causes/> (accessed December 11, 2023).
- [19] Cagnacci A, Venier M. The Controversial History of Hormone Replacement Therapy. *Medicina* 2019, Vol 55, Page 602 2019;55:602. <https://doi.org/10.3390/MEDICINA55090602>.
- [20] Chlebowski RT, Anderson GL, Aragaki AK, Manson JE, Stefanick ML, Pan K, et al. Association of Menopausal Hormone Therapy With Breast Cancer Incidence and Mortality During Long-term Follow-up of the Women's Health Initiative Randomized Clinical Trials. *JAMA* 2020;324:369. <https://doi.org/10.1001/jama.2020.9482>.
- [21] Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. *The Lancet* 2019;394:1159–68. [https://doi.org/10.1016/S0140-6736\(19\)31709-X](https://doi.org/10.1016/S0140-6736(19)31709-X).
- [22] Wang K, Li F, Chen L, Lai YM, Zhang X, Li HY. Change in risk of breast cancer after receiving hormone replacement therapy by considering effect-modifiers: a systematic review and dose-response meta-analysis of prospective studies. *Oncotarget* 2017;8:81109. <https://doi.org/10.18632/ONCOTARGET.20154>.
- [23] Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: Nested case-control studies using the QResearch and CPRD databases. *The BMJ* 2020;371. <https://doi.org/10.1136/bmj.m3873>.
- [24] Zhang GQ, Chen JL, Luo Y, Mathur MB, Anagnostis P, Nurmatov U, et al. Menopausal hormone therapy and women's health: An umbrella review. *PLoS Med* 2021;18:e1003731. <https://doi.org/10.1371/JOURNAL.PMED.1003731>.
- [25] Jones ME, Schoemaker MJ, Wright L, Mcfadden E, Griffin J, Thomas D, et al. Menopausal hormone therapy and breast cancer: what is the true size of the increased risk? *British Journal of Cancer* 2016 115:5 2016;115:607–15. <https://doi.org/10.1038/bjc.2016.231>.
- [26] Medicines and Healthcare products Regulatory Agency (MHRA). Hormone replacement therapy (HRT): further information on the known increased risk of breast cancer with HRT and its persistence after stopping 2019. <https://www.gov.uk/drug-safety-update/hormone-replacement-therapy-hrt-further-information-on-the-known-increased-risk-of-breast-cancer-with-hrt-and-its-persistence-after-stopping> (accessed October 25, 2023).
- [27] Yang Z, Hu Y, Zhang J, Xu L, Zeng R, Kang D. Estradiol therapy and breast cancer risk in perimenopausal and postmenopausal women: a systematic review and meta-analysis. *Gynecological Endocrinology* 2017;33:87–92. <https://doi.org/10.1080/09513590.2016.1248932>.
- [28] Stute P, Wildt L, Neulen J. The impact of micronized progesterone on breast cancer risk: a systematic review. *Climacteric* 2018;21:111–22. <https://doi.org/10.1080/13697137.2017.1421925>.
- [29] British Menopause Society. Tool for clinicians - Fast Facts: HRT and breast cancer risk 2022. <https://thebms.org.uk/wp-content/uploads/2022/12/12-BMS-TfC-Fast-Facts-HRT-and-Breast-Cancer-Risk-NOV2022-A.pdf> (accessed October 25, 2023).
- [30] Daly MB, Pal T, Berry MP, Buys SS, Dickson P, Domchek SM, et al. Genetic/familial high-risk assessment: Breast, ovarian, and pancreatic, version 2.2021. *JNCCN Journal of the National Comprehensive Cancer Network* 2021;19:77–102. <https://doi.org/10.6004/JNCCN.2021.0001>.
- [31] Kotsopoulos J, Huzarski T, Gronwald J, Moller P, Lynch HT, Neuhausen SL, et al. Hormone replacement therapy after menopause and risk of breast cancer in BRCA1 mutation carriers: a case-control study. *Breast Cancer Res Treat* 2016;155:365–73. <https://doi.org/10.1007/s10549-016-3685-3>.
- [32] Huber D, Seitz S, Kast K, Emons G, Ortmann O. Hormone replacement therapy in BRCA mutation carriers and risk of ovarian, endometrial, and breast cancer: a systematic review. *J Cancer Res Clin Oncol* 2021;147:2035–45. <https://doi.org/10.1007/s00432-021-03629-z>.
- [33] Kotsopoulos J, Gronwald J, Karlan BY, Huzarski T, Tung N, Moller P, et al. Hormone Replacement Therapy After Oophorectomy and Breast Cancer Risk Among BRCA1 Mutation Carriers. *JAMA Oncol* 2018;4:1059–65. <https://doi.org/10.1001/JAMAONCOL.2018.0211>.

- [34] Marchetti C, De Felice F, Boccia S, Sassu C, Di Donato V, Pergnola G, et al. Hormone replacement therapy after prophylactic risk-reducing salpingo-oophorectomy and breast cancer risk in BRCA1 and BRCA2 mutation carriers: A meta-analysis. *Crit Rev Oncol Hematol* 2018;132:111–5. <https://doi.org/10.1016/J.CRITREVONC.2018.09.018>.
- [35] Gordhandas S, Norquist BM, Pennington KP, Yung RL, Laya MB, Swisher EM. Hormone replacement therapy after risk reducing salpingo-oophorectomy in patients with BRCA1 or BRCA2 mutations; a systematic review of risks and benefits. *Gynecol Oncol* 2019;153:192–200. <https://doi.org/10.1016/J.YGYNO.2018.12.014>.
- [36] Michaelson-Cohen R, Gabizon-Peretz S, Armon S, Srebnik-Moshe N, Mor P, Tomer A, et al. Breast cancer risk and hormone replacement therapy among BRCA carriers after risk-reducing salpingo-oophorectomy. *Eur J Cancer* 2021;148:95–102. <https://doi.org/10.1016/J.EJCA.2021.02.007>.
- [37] National Institute for Health and Care Excellence (NICE). Clinical Guideline Familial breast cancer: Classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer 2013. www.nice.org.uk/guidance/cg164 (accessed November 14, 2023).
- [38] National Institute for Health and Care Excellence (NICE). Menopause: Hormone replacement therapy (HRT) 2022. <https://cks.nice.org.uk/topics/menopause/prescribing-information/hormone-replacement-therapy-hrt/> (accessed October 26, 2023).
- [39] Cancer Research UK (CRUK). Breast cancer and menopausal symptoms 2023. <https://www.cancerresearchuk.org/about-cancer/breast-cancer/living-with/menopausal-symptoms> (accessed November 7, 2023).
- [40] Poggio F, Del Mastro L, Bruzzone M, Ceppi M, Razeti MG, Fregatti P, et al. Safety of systemic hormone replacement therapy in breast cancer survivors: a systematic review and meta-analysis. *Breast Cancer Res Treat* 2022;191:269–75. <https://doi.org/10.1007/S10549-021-06436-9>.
- [41] Cold S, Cold F, Jensen MB, Cronin-Fenton D, Christiansen P, Ejlersen B. Systemic or Vaginal Hormone Therapy After Early Breast Cancer: A Danish Observational Cohort Study. *J Natl Cancer Inst* 2022;114:1347–54. <https://doi.org/10.1093/JNCI/DJAC112>.
- [42] Ugras SK, Layeequr Rahman R. Hormone replacement therapy after breast cancer: Yes, No or maybe? *Mol Cell Endocrinol* 2021;525:111180. <https://doi.org/10.1016/J.MCE.2021.111180>.
- [43] National Health Service (NHS). Benefits and risks of hormone replacement therapy (HRT) 2023. <https://www.nhs.uk/medicines/hormone-replacement-therapy-hrt/benefits-and-risks-of-hormone-replacement-therapy-hrt/> (accessed October 26, 2023).
- [44] Vinogradova Y, Coupland C, Hippisley-Cox J. Use of hormone replacement therapy and risk of venous thromboembolism: Nested case-control studies using the QResearch and CPRD databases. *BMJ (Online)* 2019;364. <https://doi.org/10.1136/bmj.k4810>.
- [45] Vignozzi L, Malavolta N, Villa P, Mangili G, Migliaccio S, Lello S. Consensus statement on the use of HRT in postmenopausal women in the management of osteoporosis by SIE, SIOMMMS and SIGO. *J Endocrinol Invest* 2019;42:609–18. <https://doi.org/10.1007/S40618-018-0978-X>.
- [46] Pourhadi N, Mørch LS, Holm EA, Torp-Pedersen C, Meaidi A. Menopausal hormone therapy and dementia: nationwide, nested case-control study. *BMJ* 2023;381. <https://doi.org/10.1136/BMJ-2022-072770>.
- [47] Kim YJ, Soto M, Branigan GL, Rodgers K, Brinton RD. Association between menopausal hormone therapy and risk of neurodegenerative diseases: Implications for precision hormone therapy. *Alzheimer's and Dementia: Translational Research and Clinical Interventions* 2021;7. <https://doi.org/10.1002/trc2.12174>.
- [48] Paschou S, Papanas N. Type 2 Diabetes Mellitus and Menopausal Hormone Therapy: An Update. *Diabetes Therapy* 2019;10:2313. <https://doi.org/10.1007/S13300-019-00695-Y>.
- [49] National Health Service (NHS). Other medicines for menopause symptoms 2023. <https://www.nhs.uk/medicines/hormone-replacement-therapy-hrt/alternatives-to-hormone-replacement-therapy-hrt/other-medicines-for-menopause-symptoms/> (accessed October 26, 2023).
- [50] Royal College of Obstetricians and Gynaecologists (RCOG). Alternatives to HRT for the Management of Symptoms of the Menopause 2010. https://www.rcog.org.uk/media/gwbntgdu/sip_6.pdf (accessed October 26, 2023).

- [51] Leon-Ferre RA, Novotny PJ, Wolfe EG, Faubion SS, Ruddy KJ, Flora D, et al. Oxybutynin vs Placebo for Hot Flashes in Women With or Without Breast Cancer: A Randomized, Double-Blind Clinical Trial (ACCRU SC-1603). *JNCI Cancer Spectr* 2020;4. <https://doi.org/10.1093/JNCICS/PKZ088>.
- [52] National Health Service (NHS). Menopause: Treatment 2022. <https://www.nhs.uk/conditions/menopause/treatment/> (accessed October 26, 2023).
- [53] Lederman S, Ottery FD, Cano A, Santoro N, Shapiro M, Stute P, et al. Fezolinetant for treatment of moderate-to-severe vasomotor symptoms associated with menopause (SKYLIGHT 1): a phase 3 randomised controlled study. *The Lancet* 2023;401:1091–102. [https://doi.org/10.1016/S0140-6736\(23\)00085-5](https://doi.org/10.1016/S0140-6736(23)00085-5).
- [54] National Health Service (NHS). Common questions about clonidine 2023. <https://www.nhs.uk/medicines/clonidine/common-questions-about-clonidine/> (accessed October 26, 2023).
- [55] Yelland S, Steenson S, Creedon A, Stanner S. The role of diet in managing menopausal symptoms: A narrative review. *Nutr Bull* 2023;48:43–65. <https://doi.org/10.1111/NBU.12607>.
- [56] Geller S, Studee L. Soy and Red Clover for Midlife and Aging. *Climacteric* 2006;9:245. <https://doi.org/10.1080/13697130600736934>.
- [57] Medicines and Healthcare products Regulatory Agency (MHRA). Black Cohosh UK Public Assessment Report 2006. https://assets.publishing.service.gov.uk/media/5df7610ce5274a08f78bca34/Black_cohosh_and_live_r_injury.pdf (accessed October 26, 2023).
- [58] National Health Service (NHS). Herbal remedies and complementary medicines for menopause symptoms 2023. <https://www.nhs.uk/medicines/hormone-replacement-therapy-hrt/alternatives-to-hormone-replacement-therapy-hrt/herbal-remedies-and-complementary-medicines-for-menopause-symptoms/> (accessed October 26, 2023).
- [59] Cancer Research UK (CRUK). Complementary and alternative therapies | Black cohosh 2022. <https://www.cancerresearchuk.org/about-cancer/treatment/complementary-alternative-therapies/individual-therapies/black-cohosh> (accessed October 26, 2023).
- [60] Lund KS, Siersma V, Brodersen J, Waldorff FB. Efficacy of a standardised acupuncture approach for women with bothersome menopausal symptoms: a pragmatic randomised study in primary care (the ACOM study). *BMJ Open* 2019;9:e023637. <https://doi.org/10.1136/BMJOPEN-2018-023637>.
- [61] Koo S, Ahn Y, Lim JY, Cho J, Park HY. Obesity associates with vasomotor symptoms in postmenopause but with physical symptoms in perimenopause: a cross-sectional study. *BMC Womens Health* 2017;17:126. <https://doi.org/10.1186/S12905-017-0487-7>.
- [62] Huang AJ, Subak LL, Wing R, West DS, Hernandez AL, Macer J, et al. An intensive behavioral weight loss intervention and hot flushes in women. *Arch Intern Med* 2010;170:1161–7. <https://doi.org/10.1001/ARCHINTERNMED.2010.162>.
- [63] Thurston RC, Sowers MFR, Sutton-Tyrrell K, Everson-Rose SA, Lewis TT, Edmundowicz D, et al. Abdominal adiposity and hot flashes among midlife women. *Menopause* 2008;15:429–34. <https://doi.org/10.1097/GME.0B013E31815879CF>.
- [64] Buja A, Pierbon M, Lago L, Grotto G, Baldo V. Breast Cancer Primary Prevention and Diet: An Umbrella Review. *Int J Environ Res Public Health* 2020;17:1–54. <https://doi.org/10.3390/IJERPH17134731>.
- [65] British Nutrition Foundation (BNF). Managing menopause symptoms with nutrition and diet 2022. <https://www.nutrition.org.uk/life-stages/women/menopause/managing-menopause-symptoms-with-nutrition-and-diet/> (accessed October 26, 2023).
- [66] National Health Service (NHS). Lifestyle changes to make if you're unable to take HRT 2023. <https://www.nhs.uk/medicines/hormone-replacement-therapy-hrt/alternatives-to-hormone-replacement-therapy-hrt/lifestyle-changes-to-make-if-youre-unable-to-take-hrt/> (accessed October 26, 2023).
- [67] Chopra S, Sharma K, Ranjan P, Malhotra A, Vikram N, Kumari A. Weight Management Module for Perimenopausal Women: A Practical Guide for Gynecologists. *J Midlife Health* 2019;10:165. https://doi.org/10.4103/JMH.JMH_155_19.

- [68] Dąbrowska J, Dąbrowska-Galas M, Rutkowska M, Michalski BA. Twelve-week exercise training and the quality of life in menopausal women – clinical trial. *Prz Menopauzalny* 2016;15:20. <https://doi.org/10.5114/PM.2016.58769>.
- [69] Luoto R, Moilanen J, Heinonen R, Mikkola T, Raitanen J, Tomas E, et al. Effect of aerobic training on hot flushes and quality of life—a randomized controlled trial. *Ann Med* 2012;44:616. <https://doi.org/10.3109/07853890.2011.583674>.
- [70] Sternfeld B, Guthrie KA, Ensrud KE, Lacroix AZ, Larson JC, Dunn AL, et al. Efficacy of Exercise for Menopausal Symptoms: A Randomized Controlled Trial. *Menopause* 2014;21:330–8. <https://doi.org/10.1097/GME.0B013E31829E4089>.
- [71] Vaze N, Joshi S. Yoga and menopausal transition. *J Midlife Health* 2010;1:56–8. <https://doi.org/10.4103/0976-7800.76212>.

About Breast Cancer UK

Who we are?

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.





This review 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.

Date: 16/02/2024

Next update: 16/02/2027

We welcome your feedback, if you have any comments or suggestions about this review please contact us at info@breastcanceruk.org.uk or on 0208 1327088.

www.breastcanceruk.org.uk

 @BreastCancer_UK
 @breastcanceruk
 @breastcanceruk
 @Breast Cancer UK

