

Latest evidence on using hormone replacement therapy in the menopause

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Key content

- Hormone replacement therapy (HRT) is the most effective treatment for symptoms of estrogen deficiency. When HRT is individually tailored women gain maximum advantages and the risks are minimised.
- Several types and regimens of HRT and different routes of delivery exist. Results from studies using only one type and route may not therefore apply to all users.
- The use of HRT is an individual decision, which a woman can only make once she has been given correct information and advice from healthcare professionals.
- HRT should be recommended in women with premature ovarian insufficiency with advice to continue until the average age of the menopause at 51.4 years.

Learning objectives

- To review the current research and the evidence on the use of HRT in women.

- Application of the evidence in relation to the management of the symptomatic menopausal woman.
- To promote confidence in prescribing HRT in most symptomatic women.
- To have a general overview of prescribing in women with relative contraindications.

Ethical issues

- The use of HRT is a patient informed choice.
- Where evidence is limited and quality of life a priority, then a multidisciplinary approach may be necessary and informed written consent documented.

Keywords: breast cancer / cardiovascular disease / hormone replacement therapy / menopause / quality of life / thromboembolism

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Introduction

Menopause is the term given to the cessation of the menstrual cycle and naturally occurs at a median age of 51.4 years.¹ Vasomotor symptoms are common, and respond effectively to replacement doses of estrogen. Hormone replacement therapy (HRT) in which the estrogen is similar to natural ovarian production should not be confused with the potent ethinyl estradiol used in combined oral contraceptive regimens. The addition of a progestogen or micronised progesterone is essential if a woman still has a uterus to prevent endometrial hyperplasia and cancer. Estradiol can be delivered orally (micronised estradiol, estradiol valerate, estrone, estriol or conjugated equine estrogens), or transdermally (17 β -estradiol). Topical vaginal administration of estrogen is used for localised symptoms. Various progestogens are used in combination with estradiol, either in a sequential cyclical regimen or as continuous combined therapy

(CCT). Progestogens are mostly administered orally, with only two formulations being available transdermally. The levonorgestrel-releasing intrauterine system Mirena[®] (Bayer Plc., Newbury, UK) is licensed for 4 years in the UK along with estrogen replacement. Tibolone is an oral synthetic steroid with estrogenic, androgenic and progestogenic actions that can be used as HRT in postmenopausal women. The role of supplemental testosterone will not be covered in this article.

Vasomotor symptoms (hot flushes and night sweats) are common, affecting about 70% of women (severely in about 20%), for a median duration of 5.2 years, but may continue for many more years in about 10% of women.² Menopausal symptoms adversely affect quality of life. HRT is the most effective treatment. In spite of this, the risk–benefit ratio has always been debated. An 80% reduction in its use³ followed the report of the Women's Health Initiative.⁴ Independent research informs us that the continued negative attitude to the use of HRT for symptom relief is not justified.^{5–8}

What we know so far: the main large studies

The Heart and Estrogen/progestin Replacement Study (HERS) I & II^{8,10}

In the 1970s epidemiological studies identified that the most common cause of death in both men and women is cardiovascular disease (CVD). For men the onset occurred several years earlier than in women and women with an early onset of the menopause were more at risk. The possibility that estrogens may be protective to the female cardiovascular system led to much research into looking at the effect of estrogens on the cardiovascular system (Box 1).

Since epidemiological studies identified a lower incidence of heart disease in users of HRT, many clinicians promoted and prescribed HRT as preventative for this reason. Critics pointed out that the epidemiological observations were biased as, at that time, predominantly healthy women took HRT. Hence randomised controlled trial evidence was sought. The first study was the Heart and Estrogen/progestin Replacement Study (HERS)⁹ designed to identify if HRT prevented recurrence of coronary heart disease (CHD) in women with established CHD. Postmenopausal women (with an average age of 66.7 years) randomised to conjugated equine estrogens (CEE)/medroxy progesterone acetate did not benefit. The treatment did increase the risk of venous thromboembolism (VTE) (more pronounced in the first year) and gall bladder disease. The oral route of delivery, the dose given and the type of HRT could together have promoted the thrombotic effect seen in these older women. For those patients who survived the first years and continued with HRT, then there appeared to be a reduction in recurrence of CVD events. A follow-up study of this cohort, the HERS II¹⁰ in 2002 concluded that this benefit did not persist and stated that HRT should not be used for secondary prevention in women with established heart disease.

It is possible that this adverse outcome would not have been the same with lower doses of micronised estrogen given to younger postmenopausal women. The Women's Hormone Intervention Secondary Prevention Study¹¹ used 1 mg oral estrogen and 0.5 mg norethisterone in women taking statins within 28 days of a cardiac infarction. There were no significant differences in lipid levels between the treatment

and placebo groups, probably due to concomitant statin use. Antithrombin and factor VII levels were significantly lower in women in the HRT group, whereas fibrinogen was slightly decreased in those in the placebo group. This suggests a more favourable outcome with micronised estrogen.

The Women's Health Initiative Study⁴

This randomised controlled trial was planned to evaluate the effect of HRT on healthy postmenopausal women with a particular interest in cardiovascular outcomes. The subject age range was 50–79 years. Women who had had a hysterectomy were randomised to CEE only or placebo, while those with an intact uterus were randomised to CEE and medroxy progesterone acetate or placebo. The same dose was given throughout all age groups and vasomotor symptom relief was not a primary end point. In fact, severe vasomotor symptoms were an exclusion criterion. In 2003 the combined arm of the study was closed, with a press release of the detrimental effects seen. Increase in breast cancer, heart disease, stroke and VTE events were reported, while a reduction in fracture rate, bowel cancer and diabetes were the advantages gained. These adverse events were not seen in the CEE-only arm, which remained open. In routine clinical practice, lower doses are initiated in older women. The reanalysis of the Women's Health Initiative study in 2007 demonstrated that giving HRT to women within 10 years of the menopause was associated with fewer risks and a reduction in cardiovascular events (–6/10 000 women years). Giving HRT to women many years past the menopause was associated with harm (more than 20 years from menopause +17/10 000 women years).¹² Administering HRT for symptom relief during the early phase of the menopausal transition is now described as 'the window of opportunity' for treatment benefit. Of particular interest was the fact that the breast cancer risk was not seen in the women in the CEE-only arm and now much attention is being paid to possible differences between the progestogens and the effect they have on the breast.¹³

The Million Women Study^{14,15}

Women aged 50–64 years in the UK attending the NHS breast screening programme were invited and subsequently followed by completion of a questionnaire. A significant increased risk of breast cancer was seen in the women on combined HRT (estrogen and progestogens) and less so with estrogen only and tibolone. These findings were challenged by Shapiro and colleagues arguing that:⁸ the breast cancers already present at the time of entry into the study were not excluded; patients on HRT concerned for their wellbeing were more likely to attend; the rapid onset of the breast cancer development did not fit the biological course of the disease; and significant amounts of data, such as menopausal status, time since menopause, age at menopause and body mass index changes were missing during the follow-up questionnaires. They concluded that this study did not

Box 1. Key cardiovascular benefits of estrogens

- Reduces atherosclerosis
- Increases HDL-cholesterol
- Lowers LDL-cholesterol
- Promotes coronary artery vasodilatation
- Prevents platelet aggregation
- Decreases lipoprotein-a and inhibits LDL-cholesterol oxidation

HDL=high-density lipoprotein. LDL=low-density lipoprotein.

‘establish causality and that the size (of one million women) alone does not guarantee that the findings are reliable’.

2012 Cochrane Collaboration systematic review¹⁶

The 2012 Cochrane Collaboration systematic review assessed the clinical effects of using HRT for 1 year or more. Twenty-three randomised double-blind studies were included involving 42 830 women aged 26–91 years. Since 70% of the data were derived from the Women’s Health Initiative and HERS, most participants were postmenopausal American women, with a mean age of over 60 years. The randomised studies included all estrogens, with or without progestogens (administered by oral, transdermal, subcutaneous or intranasal routes), with placebo for at least 1 year. None of the studies focused on younger, recently diagnosed postmenopausal women. Therefore it is not surprising that the findings agreed with the large publications, with an increased risk of VTE, CVD, stroke, breast cancer, gall bladder disease and dementia in women over 65 years old. So the review concluded that there was no indication to use HRT for primary or secondary prevention of CVD or dementia or for protection of cognitive function. There was a significant benefit and reduction in the risk of bone fracture after 5 years of use. It was deemed to be effective in prevention of postmenopausal osteoporosis as an option only for those women at significant risk where other treatments are unsuitable. The study had insufficient data to assess the risk of long-term HRT use in perimenopausal women or postmenopausal women younger than 50 years of age.

Summary of these studies

The above studies, while large, were for the most part focused on cardiovascular risk and failed to address or accurately assess the effect of HRT in the symptomatic younger postmenopausal woman. They have not therefore addressed the benefits of HRT given at ‘the window of opportunity’, before aging has advanced and collagen has been lost.

Effect of HRT on cardiovascular events in recently postmenopausal women

A randomised study by Schierbeck et al.¹⁷ that was carried out in Denmark in 1990–1993, has been the first one to address the correct timing and the long-term effect of HRT on CVD in recently postmenopausal women. The number of patients was relatively small, with 502 patients randomly selected to receive HRT and 504 to receive no treatment. The publication of adverse reports from other trials led to the discontinuation of the intervention at 11 years but follow-up was continued for a total of 16 years. After 10 years, women on HRT were found to have had a significant reduction in mortality and CVD-related

events, with no apparent increased risk of VTE, stroke or cancer. The health benefits were seen for up to 6 years after stopping.

Since this was a small study, the advice given by the MHRA remains: “No single recommendation for optimum duration of treatment or safe upper-age limit for use of HRT is therefore possible because they will be specific to every woman’s circumstances. For most women, short-term treatment will be sufficient to relieve vasomotor symptoms; for others, HRT may need to be continued for longer. For all women, the lowest effective dose should be used for the shortest possible time, and the need to continue HRT should be reviewed at least yearly, taking into consideration the change in balance of risks and benefits.”¹⁸

A new guideline from NICE is expected in 2015.

Premature ovarian insufficiency

In the developed world, menopause under 45 years is classified as premature.¹⁹ Women with premature ovarian insufficiency have an earlier onset of both CVD episodes and osteoporosis. They are also noted to have a reduced breast cancer risk compared with their menstruating peers. The risk of breast cancer with HRT use in these women is deemed to be no greater than the population risk for their age, while the benefits are greater by prevention of long-term morbidity. Hence it is strongly advised that these women should consider taking HRT, at least until the age of 50.^{20,21} Bisphosphonates are not considered first-line treatment²² for prevention of osteoporosis in younger women, as HRT has been shown to be effective in women of this age group. The WHO Fracture Risk Assessment Tool should be consulted.

Practical guidance on HRT prescribing (Figure 1²³)

The British Menopause Society published guidelines in 2013²⁰ based on a review of the evidence to offer both doctors and patients advice on the use of HRT for climacteric symptoms.

HRT in low-risk women (Table 1 and Box 2)

There are few women in whom HRT is an absolute contraindication. The fear of increased breast cancer risk is foremost for most women and physicians. The risk as a result of taking HRT is much lower than the risk associated with obesity, moderate alcohol intake or delaying first pregnancy until after 35 years.²⁴ The absolute increase in breast cancer risk is 6 extra cases per 1000 women for 5 years of estrogen and progestogens, and reverts back to the population risk 5 years after stopping.¹⁸ Once the risks have been explained

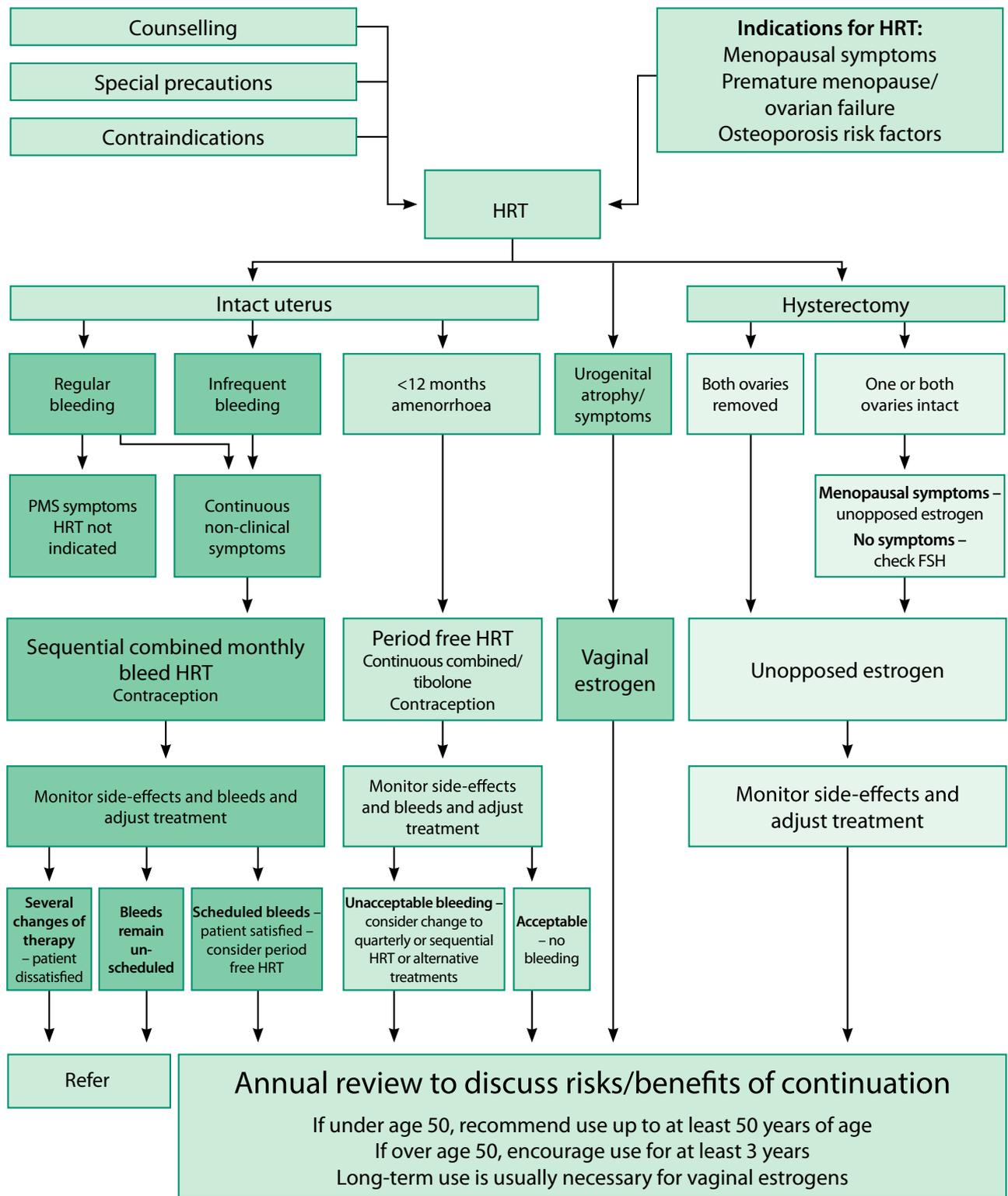


Figure 1. Guidance on HRT prescribing With permission from the West Midlands Menopause Society²³

Table 1. Simplifying decision selection of HRT in low-risk women

Condition	Type of HRT
Perimenopausal women Hysterectomised women Women with subtotal hysterectomy	Continuous estrogen/cyclical progestogen Estrogen only Estrogen only if no endometrium identified histologically at the lower resection margin CCT should be used if endometrium seen
Endometrial ablation Progestogen-sensitive	Either cyclical or CCT ?combined continuous Mirena plus systemic estrogen Micronised progesterone
Early menopause Older woman Potential malabsorption Postmenopausal, low libido Non-responders to standard treatment: young with surgical induced menopause	May require higher estrogen dose Start with lowest dose and adjust Non-oral route Try tibolone as first choice Subcutaneous implants of estrogen ^a

^aImplants only available in some clinics

and put into perspective, then a trial of three months of HRT will enable a woman to assess her quality of life, decide whether HRT has been of benefit, and then decide on duration, having been made aware that the breast cancer risk will be duration dependent. Should a woman develop breast cancer while on HRT, her mortality would not be adversely affected.²⁵

A full history will reveal any existing medical problems or family history of CVD or cancer. This information will point the clinician to the correct regimen, dose and route of administration. Baseline measurement of body mass index and blood pressure give guidance as to the need for further investigation. There is no indication for a pretreatment mammogram or breast examination, pelvic examination, cervical smear or endometrial thickness measurement by transvaginal scan. However, specific breast or abdominal

symptoms would need to be investigated before proceeding with treatment. Once established on HRT, a woman should not be made to discontinue abruptly but should wean off treatment gradually. After weaning there are a few in whom symptoms persist.²⁶ Continuing or restarting on HRT is a decision based on quality of life.

Troublesome menopausal symptoms can start in the perimenopausal state (last period within the past 12 months). To avoid unnecessary investigation of unscheduled bleeds, these women should be commenced on sequential (cyclical) HRT (that is, continuous estrogen with progestogen for 12–14 days per month). If periods are reasonably frequent, then HRT should start with the next bleed, but if infrequent (more than three months apart), then HRT can be commenced without awaiting a period. In such cases the woman should be informed that her first withdrawal bleed at the end of the first cycle may be heavy but subsequent periods would be as of her norm. The woman should also be informed that this regimen is not contraceptive. This article will not discuss contraception during the perimenopause.

Warning women of expected adverse effects will reduce fear and improve compliance. The most common adverse effects include headaches, breast tenderness, bloating and muscle cramps. Weight gain is not an adverse effect of HRT.²⁷ Adverse effects are transient and usually resolve by 3 months. They are more pronounced in women who have been estrogen-deficient for some time and are minimised by commencing with a low dose and increasing if necessary at a later date. Women sensitive to progestogens may notice that the adverse effects are pronounced at this phase of the cyclical regimen.

The woman can be asked to report back on her symptom control, any persistence of adverse effects and the timing of

Box 2. Conditions that are not contraindications to HRT

- Asthma
- Past history of benign breast disease
- Previous abnormal smears/cervical cancer
- Contact lens wearers
- Depression
- Diabetes
- Controlled blood pressure
- Hyperlipidaemia
- Melanoma
- Multiple sclerosis
- Obesity
- Renal failure
- Sickle cell anaemia
- Smoking
- Thyroid disease
- Osteoporosis prevention in young women with premature ovarian insufficiency

the withdrawal bleed (normally at the end of one cycle/ beginning of the next). Any unscheduled bleeding should be investigated. Persistent progestogenic adverse effects can be addressed by altering the progestogen or by using an intrauterine system. This will give the benefit of contraception, reduction to periods and endometrial protection with continuous estrogen use. A review should take place at 3 months. If no alteration to the regimen is needed a discussion about the duration of use could take place.

Once established on HRT an annual review is all that is necessary. HRT does not increase blood pressure and there is no indication to monitor more frequently. For the younger woman who still hopes for sporadic ovulation, sequential therapy is not contraceptive, so can be continued until this hope becomes unrealistic. Women who wish to stay on HRT for more than 5 years should be encouraged to switch to CC to avoid an increased risk of endometrial hyperplasia seen in women on long-term sequential therapy.²⁸

Lower doses may be evaluated prior to switching and, if tolerated, then the woman can switch to a lower dose of CCT by completing the month of sequential treatment so that the withdrawal bleed occurs before starting the CCT. If the woman had very few adverse effects with her previous cyclical combination, then it may be helpful to use a combination with the same estrogen and progestogen. As a rule, women aged 54 years would be advised to switch as 80% of women at this age will be postmenopausal.

CCT or tibolone are used in postmenopausal women (amenorrhoea for 12 months). Such women will have been estrogen-deficient for this time and starting with a low-dose combination will minimise adverse effects and breakthrough bleeding. The dose can be increased after 3 months if menopausal symptoms remain. Initial breakthrough bleeding is common but usually reduces and ceases with time. Persistent bleeding should be investigated after 6 months with an ultrasound scan and/ or endometrial biopsy. The risk of endometrial cancer is lower in those using CCT than in those not using HRT. If bleeding occurs after a time of amenorrhoea, then investigation is still required even if a causative factor is identified.²⁹

Causative factors include:

- forgotten pills, poor patch adhesion, poor compliance
- introduction of new medications or over-the-counter preparations
- all other causes of postmenopausal bleeding.

Patients with relative contraindications to HRT could be referred to a specialist service for advice (Box 3). Quality of life may be the deciding factor for women with contraindications, and in such circumstances a written

Box 3. Relative contraindications that should be referred for specialist advice

- Existing cardiac disease
- Active liver disease
- Systematic lupus erythematosus
- Previous breast cancer
- Previous ovarian/endometrial cancer
- Undiagnosed vaginal bleeding
- Previous personal/family history of venous thromboembolism

statement from the woman is helpful and may avoid any future medico-legal complications.

Thrombosis risk

The risk of VTE associated with HRT use is mostly seen after initiation and falls over the ensuing 12 months. The choice of dose, type and route of delivery may contribute to the risk. The progestogen combination may also be influential. Transdermal HRT is associated with a lower risk of VTE than oral but lower doses of both routes at initiation may be less likely to promote this risk. Transdermal is the treatment of choice in certain medical conditions (Box 4).

Women who are sedentary, overweight and who smoke are already at increased risk of VTE. The background risk for women aged 50–59 years in Europe is 5/1000; this rises to 7/1000 for 5 years of estrogen only and 12/1000 for 5 years of estrogen and progestogen.^{18,30,31}

Other benefits of HRT²⁰

Other observed benefits of HRT other than those affecting vasomotor symptoms, include improvement of low mood and protection against loss of connective tissue. Several studies have identified a risk reduction of bowel cancer in women using HRT, but this is not deemed to be an indication to prescribe HRT as preventative for this disease. Some forms of Estrogen replacement therapy appear to be neuroprotective, preserving cognitive function and reducing the risk of Alzheimer's disease. Some protection against

Box 4. Indications for use of the transdermal route first line

- Personal preference
- Migraine
- Diabetes
- Controlled hypertension
- Existing gall bladder disease
- Hyperlipidaemia
- Obesity
- Smoking
- Previous venous thromboembolism
- Varicose veins

Parkinson's Disease has also been seen. The young healthy postmenopausal woman has the greater benefit.³² This benefit was not identified in the Cochrane review¹⁶ but the majority (70%) of the subjects studied in that review were older women. This again suggests that there may be a "window of opportunity" for preserving cognitive functions if HRT is used early in the menopause. Further studies are needed.

HRT is effective in preventing the bone loss normally associated with the menopause.³³ It is effective in both the vertebral spine and hips.²²

Topical vaginal estrogen

Atrophic vaginitis is treatable with topical estrogen, resulting in cornification and regeneration of the vaginal epithelium. This improves lubrication and sexual function. Systemic absorption is insignificant with low-dose topical estrogen. Additional systemic progestogen is not required. Vaginal estrogen may reduce symptoms of urgency of micturition and recurrent urinary tract infections. Vaginal symptoms can persist even when on adequate systemic HRT; in such cases both topical and systemic are required. The safety of topical vaginal estrogen has not been assessed in patients with breast cancer, where theoretically the risks are small. The benefits to the genitourinary tract along with improved sexual intimacy may outweigh the risk.

HRT after breast cancer^{34–37}

Breast cancer is a common condition that affects women of all ages. The vast majority of breast cancers are estrogen receptor positive (ER+) and require adjuvant tamoxifen or aromatase inhibitors, the adverse effects of which can be exacerbated and debilitating menopausal symptoms. Many breast cancers and precancerous change (ductal carcinoma in situ) are screen detected and caught at an early stage, with excellent prognosis. Adequate studies have not been done where such individuals have continued on adjuvant treatment with the addition of HRT.³⁸ Some case-control studies^{34–35} have shown no detriment to the mortality rate or recurrence rate with HRT. Randomised studies are, however, confusing.^{39–41}

Therefore, HRT use is a patient choice. There is inadequate information on the risks and benefits of herbal and alternative over-the-counter preparations.

The specialist needs to consider the following factors when discussing management in order to predict prognosis:

- Stage of the disease at diagnosis (size, ER status, grade of tumour and lymph node status). This gives a guide to the prognosis.
- Type of adjuvant therapy currently or previously used.
- Time since diagnosis.
- The woman's attitude to her symptoms.

Box 5. Self-help tips and coping strategies^a

- Avoid sudden temperature change (hot drinks)
- Reduce caffeine/alcohol intake
- Avoid spicy foods
- Increase exercise
- Wear layers of clothes to be able to take off and put on when necessary
- Practise relaxation techniques
- Use cooling devices e.g. facial spray, cold pillows/pads in bed
- Wear absorptive night attire

^aLong-term trials of alternative over-the-counter treatments have not been evaluated

- The woman's fear of recurrence/fear of using hormones.
- What she has tried already.

Non-hormonal treatments

Women in need of treatment may be offered clonidine, selective serotonin reuptake (if not on tamoxifen) or selective noradrenaline reuptake inhibitors (unlicensed indication for vasomotor symptoms), or gabapentin, along with self-help tips (see Box 5) for a trial period of 3–4 months. If this is ineffective, then the next option may be evaluated. When all alternative prescribed medications have been tried, then a discussion about quality of life and survival is relevant. Should the patient wish to try HRT, it is recommended that this is discussed with her oncologist and care providers.

Each woman with breast cancer will have her own attitude to her diagnosis and prognosis. Some will oppose making any choices where there is no clinical evidence of safety, while others will be so desperate to get on with their lives, perceive that their remaining days should be ones of quality and not days to endure. The former category will want to avoid HRT while the latter will wish to evaluate it for quality of life reasons. Asking the patient how she would react and who she would blame if the cancer were to recur while she was on HRT, is useful to enable her to decide. The answer she gives may reveal how she perceives the dilemma.

Aromatase inhibitors will be rendered ineffective with HRT.⁴² Oncologists may want to consider and discuss the value in switching to tamoxifen while evaluating the effectiveness of HRT on quality of life. Should the patient benefit and wish to continue HRT after a trial period, then continued follow-up is advised. The concern will always be whether an occult ER+ cancer cell proliferates under estrogenic influence, causing recurrent disease. Medico-legal debate may be prevented, if there is good documentation or written consent in the notes.

Tibolone

Tibolone, a selective tissue estrogenic activity regulator, is effective in treating symptoms in postmenopausal women. The evidence of a reduced stimulatory effect on breast tissue compared with other HRT preparations meant that it was feasible to evaluate its safety in a randomised controlled trial in women with recently diagnosed breast cancer (LIBERATE study).⁴³ Quality of life was improved in the treatment group, but a higher rate of breast cancer recurrence was seen only in the women with ER+ disease. There are no data on whether it is safe to use in disease-free survivors who still experience menopausal symptoms many years after their initial treatment.

Family history of breast cancer

As seen in the Nurses' Health study,⁴⁴ HRT did not increase the risk of breast cancer in those women with a family history. Therefore a family history of breast cancer is not a contraindication to HRT, rather an opportunity for the clinician to identify whether the history is significant and warranting a referral to the clinical geneticist and additional screening under 50 years of age.

Carriers of BRCA mutations

BRCA1 and *BRCA2* mutation carriers are at increased risk of breast and ovarian cancer. Risk-reducing surgery with mastectomies and bilateral salpingo-oophorectomy (BSO) is usually carried out when the family is complete.⁴⁵ Surgical menopause in these premenopausal women causes acute and severe symptoms. Preoperative counselling will help the patient decide between BSO only, or hysterectomy plus BSO. The progestogen required when the uterus remains may influence the decision. HRT is indicated in these young women to avoid the early onset of osteoporosis and CVD associated with a premature menopause. The use of HRT following risk-reducing surgery appears to be safe with no additional increase of breast cancer, especially if estrogen-only therapy is used.^{46,47}

Written informed consent

HRT may be considered in cases where there is limited research (Box 3). With multidisciplinary input, all care providers being fully informed of the woman's wishes; it may still be prudent to obtain written patient consent. Such cases may be best advised in a specialist setting.

Conclusion

Symptomatic women benefit from the use of HRT. Strictly speaking, there are no absolute contraindications to HRT. No

doctor should be concerned about discussing the risks and benefits of HRT with women who have menopausal symptoms, or be hesitant to offer a trial of appropriate treatment. Women with relative contraindications should be granted the option of discussing this further with a menopause specialist. Doctors who are unfamiliar with the types and regimens of HRT can seek advice and education from the British Menopause Society, the Royal College of Obstetricians and Gynaecologists or the Faculty of Sexual and Reproductive Healthcare.

Disclosure of interests

SB is involved in the following activities in the Royal College of Obstetricians and Gynaecologists: Committee membership: Education Quality Assurance Committee as a member; Suitable Best Answer: MRCOG Membership Exam Part II Committee member; College publications: StratOG reviewer; BJOG reviewer.

JW is involved in the following activities: member of the British Menopause Society; Chair of the West Midlands Menopause Society; FSRH registered trainer for the certificate in Menopause; College publications: BJOG reviewer

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