

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

Guideline

Menopause (update)

Draft for consultation, November 2023

This guideline covers the identification and management of menopause, including in people who have premature ovarian insufficiency. It aims to improve the consistency of support and information provided to people experiencing menopause. **It includes updated recommendations on the management of genitourinary symptoms and on the effects of hormone replacement therapy (HRT) on cardiovascular disease and stroke, breast cancer and dementia. It also includes new information on endometrial cancer, ovarian cancer and all-cause mortality (life expectancy) and the effects of either taking or not taking hormone replacement therapy (HRT) on health outcomes for people experiencing early menopause (age 40 to 44).**

This guideline will update NICE guideline NG23: Menopause: diagnosis and management (published November 2015).

Who is it for?

- Healthcare professionals who care for women, trans men and non-binary people registered female at birth experiencing menopause symptoms
- Women, trans men, and non-binary people registered female at birth experiencing menopause symptoms, their families or carers, and the public.

What does it include?

- the recommendations
- recommendations for research

- rationale and impact sections that explain why the committee made the 2023 recommendations and how they might affect practice
- the guideline context.

Information about how the guideline update was developed is on the [guideline's webpage](#). This includes the evidence reviews (and supplements), the scope, details of the committee and any declarations of interest.

New and updated recommendations

We have reviewed the evidence on:

- cognitive behavioural therapy to manage symptoms associated with the menopause
- interventions to manage genitourinary symptoms associated with the menopause
- the effects of HRT on overall health outcomes (including breast, endometrial and ovarian cancer, cardiovascular disease dementia and life expectancy) for women, trans men and non-binary people registered female at birth who are experiencing menopause or early menopause.

The recommendations in these sections do not apply to people taking cross-sex hormones as gender-affirming hormone therapy. You are invited to comment on the new and updated recommendations. These are marked **[2023]** and **[2015, amended 2023]**.

You are also invited to comment on recommendations that we propose to delete from the 2015 guideline.

We have not reviewed the evidence for the recommendations shaded in grey, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See [update information](#) for a full explanation of what is being updated.

Full details of the evidence and the committee's discussion on the 2023 recommendations are in the [evidence reviews](#). Evidence for the 2015 recommendations is in the [full version](#) of the 2015 guideline.

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1 Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [NICE's information on making decisions about your care](#).

NICE guidelines set out the care and services suitable for people with a specific condition or need, and people in particular circumstances or settings. We aim to improve quality by ensuring that people receive the best care and advice. Using inclusive language in healthcare is important for safety, and to promote equity, respect and effective communication with everyone.

Some recommendations in this guideline do not use inclusive language because:

- the evidence has not been reviewed, and expert opinion is that groups covered by these recommendations cannot be extended **or**
- the evidence has been reviewed, but the information available for some groups was too limited to make specific recommendations.

Healthcare professionals should use their clinical judgement when implementing the recommendations, taking into account each person's circumstances, needs and preferences, and ensuring all people are treated with dignity and respect throughout their care.

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

2

This guideline covers women, trans men and non-binary people registered female at birth currently going through the menopause transition or who will be going through it in future. The guideline does not cover people who are having cross-sex hormones as gender-affirming therapy. For trans men and non-binary people who have taken such therapy in the past and are no longer taking it, only

[recommendations 1.4.8 and 1.4.9](#) and [research recommendation 6](#) apply. All other recommendations apply to women, trans men and non-binary people registered female at birth who have **never** taken cross-sex hormones as gender-affirming therapy.

1.1 Individualised care

1.1.1 Tailor your approach to the person at all times when identifying, investigating and managing menopause (based on their changing symptoms). Follow recommendations in [NICE's guideline on patient experience in adult NHS services](#). [2015]

1.1.2 For general principles on how to discuss treatment plans with people, including how to communicate risks, benefits and consequences, see [NICE's guideline on shared decision making](#). [2023]

1.2 Information and advice

1.2.1 Share information about menopause with people with menopause symptoms or approaching the age of menopause, and their family members or carers (as appropriate). Information shared should include:

- what menopause is, including that it is a normal life transition
- commonly associated symptoms (see recommendation 1.2.2) and
- lifestyle changes and interventions that can support health and wellbeing. [2015]

1.2.2 Explain that the menopause may be associated with symptoms which may vary in severity from minor to more troublesome and be experienced over long or short time periods. As well as changes in menstrual cycle, symptoms may include:

- vasomotor symptoms (hot flushes and sweats)
- genitourinary symptoms (for example, vaginal dryness)
- effects on mood (for example, depressive symptoms)

- 1 • musculoskeletal symptoms (for example, joint and muscle pain)
- 2 • sexual difficulties (for example, low sexual desire). **[2015]**

3 1.2.3 Share information on and discuss the following types of treatment with
4 people with troublesome menopause symptoms, and their family
5 members or carers (as appropriate):

- 6 • non-hormonal, for example, non-hormonal vaginal lubricants and
7 moisturisers
- 8 • hormonal, for example, hormone replacement therapy (HRT)
- 9 • non-pharmaceutical, for example, cognitive behavioural therapy (CBT).

10 Ensure the potential benefits and risks associated with these treatments
11 are covered in the discussion (see sections 1.6 and 1.7) **[2015]**

12 1.2.4 Share information on menopause and its management using appropriate
13 written or other formats, and discuss it, taking the needs and wishes of the
14 individual person into account. **[2015]**

15 1.2.5 Share information about contraception with women, trans men and non-
16 binary people registered female at birth who have menopause symptoms.
17 See the [Faculty of Sexual & Reproductive Healthcare guidance on](#)
18 [contraception for women aged over 40 years](#). **[2015]**

19 1.2.6 Offer support and provide information to people who are likely to
20 experience menopause as a result of medical or surgical treatment and,
21 before they have that treatment:

- 22 • discuss fertility and menopause with them
- 23 • offer them referral to a [healthcare professional with expertise in](#)
24 [menopause](#). **[2015]**

25 1.2.7 Give people experiencing menopause advice on bone health and discuss
26 these issues at review appointments (see [NICE's guideline on assessing](#)
27 [the risk of fragility fracture in people with osteoporosis](#)). **[2015]**

1.2.8 Explain to people experiencing menopause that muscle mass and strength is maintained through, and is important for, activities of daily living. **[2015]**

Women, trans men and non-binary people registered female at birth with a personal history or high risk of breast cancer

1.2.9 Offer people with troublesome menopause symptoms who have a personal history or high risk of breast cancer:

- information on all available treatment options
- referral to a [healthcare professional with expertise in menopause](#).

[2015, amended 2023]

1.3 Identifying perimenopause and menopause

1.3.1 Identify the following without laboratory tests in otherwise healthy women, trans men, and non-binary people registered female at birth who are over 45 and have menopause symptoms:

- perimenopause, if they have new onset vasomotor symptoms and any changes in their menstrual cycle
- menopause, if they have not had a period for at least 12 months and are not using hormonal contraception
- menopause, based on the symptoms they have, in those without a uterus. **[2015]**

1.3.2 Take into account that it can be difficult to identify menopause in people who are taking hormonal treatments, for example, for the treatment of heavy menstrual bleeding. **[2015]**

1.3.3 Be aware that people from ethnic minority backgrounds may experience menopause at a younger age compared with people from White backgrounds. **[2023]**

1.3.4 Do not use the following laboratory and imaging tests to identify perimenopause or menopause in people over 45:

- anti-Müllerian hormone
- inhibin A
- inhibin B
- oestradiol
- antral follicle count
- ovarian volume. **[2015]**

1.3.5 Consider using a serum follicle-stimulating hormone (FSH) test to confirm menopause only:

- in people aged 40 to 45 with menopause symptoms, including a change in their menstrual cycle
- in people under 40 in whom menopause is suspected (see also section 1.8). **[2015]**

See also the recommendations on offering psychological support to:

- [people experiencing early menopause \(aged 40 to 44\)](#) and
- [people with premature ovarian insufficiency](#). **[2023]**

1.3.6 Do not use an FSH test to identify menopause in people using combined oestrogen and progestogen contraception or high-dose progestogen. **[2015]**

For a short explanation of why the committee made the 2023 recommendation on the age of menopause in ethnic minority groups and how it might affect practice, see the [rationale and impact section on identifying menopause and perimenopause](#).

Full details of the evidence and the committee's discussion are in [evidence review I: early menopause](#).

1.4 Managing troublesome menopause symptoms in people aged 40 or over

This section covers people aged 40 or over.

For younger (under 40) women, trans men, and non-binary people registered female at birth, see [recommendations on diagnosing and managing premature ovarian insufficiency](#).

Discussing treatment options

1.4.1 When discussing treatment options with people who have troublesome menopause symptoms, explain the risks and benefits associated with those treatments. **[2023]**

HRT

1.4.2 When discussing hormone replacement therapy (HRT) as a possible treatment for troublesome menopause symptoms, talk about the benefits and risks associated with:

- combined versus oestrogen-only HRT (see [recommendation 1.5.1 on indications for combined and oestrogen only HRT](#))
- transdermal versus oral HRT
- types of oestrogen and progestogen
- sequential versus continuous HRT
- dosage and duration. **[2023]**

Tailor the information about benefits and risks to the person's age, individual circumstances and potential risk factors. Use the information in the [section on the effect of HRT on health outcomes](#) to support this discussion.

1.4.3 If a person chooses to take HRT:

- Discuss the duration of treatment at the outset, taking account of the benefits and risks.

- Discuss the likelihood of symptoms returning when HRT is stopped, the possibility of restarting treatment if necessary, and the risks associated with prolonged use (see, for example, breast cancer in [table 1: effects of combined HRT on health outcomes](#) and [table 2: effects of oestrogen-only HRT on health outcomes](#)). [2023]

CBT

1.4.4 When discussing CBT as a possible treatment for troublesome menopause symptoms, discuss available options, for example:

- individual face-to-face
- individual virtual
- group sessions
- self-help
- online. [2023]

For a short explanation of why the committee made the 2023 recommendations on discussing treatment options and how they might affect practice, see the [rationale and impact section on discussing treatment options](#).

Full details of the evidence and the committee's discussion are in

- [evidence review A: cognitive behavioural therapy](#)
- [evidence review B1: managing genitourinary symptoms \(network meta-analysis\)](#)
- [evidence review D: breast cancer](#)
- [Evidence review I: early menopause](#).

Complementary therapies and unregulated preparations

1.4.5 Explain to people with menopause symptoms that the efficacy and safety of **unregulated** hormone **preparations** are unknown. [2015]

1.4.6 Explain to people who wish to try complementary therapies **for menopause symptoms**, that the safety, quality and purity of constituents in **unregulated preparation** may be unknown. [2015]

1.4.7 Advise people with a history of, or at high risk of, breast cancer that, although there is some evidence that St John's wort may help relieve vasomotor symptoms associated with menopause, there is uncertainty about:

- appropriate dosage
- persistence of effect
- variation in the nature and potency of preparations
- potential serious interactions with other drugs (including tamoxifen, anticoagulants and anticonvulsants). [2015]

People who have taken gender-affirming therapy in the past

1.4.8 Ensure that trans men or non-binary people registered female at birth who have taken gender-affirming hormone therapy in the past and have troublesome menopause symptoms can discuss these with a [healthcare professional with expertise in menopause](#). [2023]

1.4.9 Consider CBT for troublesome vasomotor symptoms, difficulties with sleep or depressive symptoms associated with the menopause in trans men and non-binary people registered female at birth who have taken cross-sex hormones as gender-affirming therapy in the past. [2023]

For a short explanation of why the committee made this recommendation and how it might affect practice, see the [rationale and impact section on people who have taken gender-affirming therapy in the past](#).

Full details of the evidence and the committee's discussion are in [evidence review C: cardiovascular disease](#).

Taking comorbidities into account

People with type 2 diabetes

1.4.10 Consider HRT for menopause symptoms in people with type 2 diabetes after taking comorbidities into account and seeking specialist advice if needed. [2015].

People at increased risk of venous thromboembolism [2015]

1.4.11 Consider transdermal rather than oral HRT for people with menopause symptoms who are at increased risk of venous thromboembolism (VTE), including those with a body mass index (BMI) over 30 kg/m². [2015]

1.4.12 Consider referring people with menopause symptoms who are at high risk of VTE (for example, those with a strong family history of VTE or a hereditary thrombophilia) to a haematologist for assessment before considering HRT. [2015]

People with a history of coronary heart disease or stroke [2023]

1.4.13 For people with a history of coronary heart disease or stroke, ensure that combined or oestrogen-only HRT is discussed with and, if appropriate, initiated by a [healthcare professional with expertise in menopause](#). [2023]

In November 2023, this was an off-label use of combined or oestrogen-only HRT. See [NICE's information on prescribing medicines](#).

People with, or at high risk of, breast cancer

1.4.14 For advice on the treatment of menopause symptoms in people with breast cancer or at high risk of breast cancer, see the [section on menopause symptoms in NICE's guideline on early and locally advanced breast cancer](#) and the [section on risk reduction and treatment strategies in NICE's guideline on familial breast cancer](#). [2015]

Also see:

- [information and advice for women, trans-men and non-binary people registered female at birth with, or at high risk of, breast cancer](#) (recommendation 1.2.9) and
- [complementary therapy and unregulated preparations](#) (recommendations 1.4.5 to 1.4.7).

People at high familial risk of ovarian cancer

[NICE is developing a guideline on identifying and managing familial and genetic risk of ovarian cancer](#), which will cover HRT after risk-reducing surgery for people at increased risk of ovarian cancer.

For a short explanation of why the committee made the 2023 recommendation on taking comorbidities into account how it might affect practice, see the [rationale and impact section on taking comorbidities into account when choosing treatment options](#).

Full details of the evidence and the committee's discussion are in

- [evidence review C: cardiovascular disease](#)
- [evidence review F: ovarian cancer](#).

Vasomotor symptoms

1.4.15 Offer HRT to people with troublesome vasomotor symptoms associated with the menopause after discussing with them the short-term (up to 5 years) and longer-term benefits and risks. **[2015]**

1.4.16 Consider CBT for troublesome vasomotor symptoms associated with the menopause. **[2023]**

1.4.17 Do not routinely offer selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) or clonidine as first-line treatment for vasomotor symptoms alone. **[2015]**

1.4.18 Explain to people with menopause symptoms that there is some evidence that isoflavones or black cohosh may relieve vasomotor symptoms associated with the menopause. However, explain that:

- multiple preparations are available and their safety is uncertain
- different preparations may vary
- interactions with other medicines have been reported. **[2015]**

For a short explanation of why the committee made the recommendation on CBT and how it might affect practice, see the [rationale and impact section on cognitive behavioural therapy](#).

Full details of the evidence and the committee's discussion are in [evidence review A: cognitive behavioural therapy](#).

Genitourinary symptoms

Women, trans men, and non-binary people registered female at birth with no history of breast cancer

1.4.19 Offer a choice of vaginal oestrogen preparations (oestrogen cream, gel, tablet, pessary or ring) to people with troublesome genitourinary menopause symptoms (including those on systemic HRT) and continue treatment for as long as needed to relieve symptoms. **[2023]**

1.4.20 When discussing the option of vaginal oestrogen with a person with troublesome genitourinary menopause symptoms, explain that:

- serious adverse effects are very rare (see advice from the [2019 Medicines and Healthcare products Regulatory Agency \[MHRA\] drug safety update on hormone replacement therapy](#))
- symptoms often return when treatment is stopped
- some oestrogen is absorbed but, compared with systemic HRT, the amount is small
- if they choose this option, they should report vaginal bleeding to their GP. **[2023]**

1.4.21 If vaginal oestrogen does not relieve genitourinary symptoms, consider increasing the dosage, within the standard therapeutic range, after seeking advice from a [healthcare professional with expertise in menopause](#). **[2023]**

1.4.22 For the use of vaginal oestrogen in people with troublesome genitourinary menopause symptoms and an overactive bladder, see [medicines for overactive bladder: choosing medicines, in NICE's guideline on managing urinary incontinence and pelvic organ prolapse in women](#). **[2023]**

1.4.23 Consider non-hormonal vaginal moisturisers and lubricants for people with troublesome genitourinary menopause symptoms in whom vaginal oestrogen preparations are contraindicated or who would prefer not to take vaginal oestrogen. **[2023]**

1 1.4.24 Consider vaginal prasterone as a treatment option for troublesome
2 genitourinary menopause symptoms if vaginal oestrogen, moisturisers or
3 lubricants have been ineffective or are not tolerated. **[2023]**

4 1.4.25 Consider ospemifene as an oral treatment option for troublesome
5 genitourinary menopause symptoms, if locally applied treatments are
6 impractical, for example, because of disability. **[2023]**

7 See also recommendations for [all women, trans men, and non-binary people](#)
8 [registered female at birth with genitourinary menopause symptoms](#).

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on genitourinary symptoms in women, trans men, and non-binary people registered female at birth with no history of breast cancer with no history of breast cancer](#).

Full details of the evidence and the committee's discussion are in [evidence review B1: managing genitourinary symptoms \(network meta-analysis\)](#).

9 **Women, trans men, and non-binary people registered female at birth with a**
10 **history of breast cancer [2023]**

11 1.4.26 For people with a personal history of breast cancer and troublesome
12 genitourinary menopause symptoms, offer non-hormonal moisturisers,
13 lubricants, or both. **[2023]**

14 1.4.27 Only consider vaginal oestrogens for people with a personal history of
15 breast cancer and troublesome genitourinary menopause symptoms that
16 have continued despite trying non-hormonal treatments.

17 In November 2023, this was an off-label use of vaginal oestrogen. See
18 [NICE's information on prescribing medicines](#). **[2023]**

19 1.4.28 When vaginal oestrogen is considered for people with a personal history
20 of breast cancer, discuss with them the uncertainty about its efficacy for
21 treating troublesome genitourinary menopause symptoms, particularly if

other cancer therapies (such as aromatase inhibitors) are also being used. **[2023]**

1.4.29 When assessing the safety of vaginal oestrogens for someone in relation to breast cancer recurrence, take into account:

- the uncertainty about risks of breast cancer recurrence
- their general risk factors for breast cancer recurrence (see [recommendations 1.7.6 and 1.7.7 in NICE's guideline on early and locally advanced breast cancer](#) for factors related to low, medium and high risk of recurrence)
- the hormone receptor status of their breast cancer
- the fact that vaginal oestrogen is absorbed but the amount is small compared with systemic HRT **and**
- the type of adjuvant treatment they are taking, if any. **[2023]**

1.4.30 When considering local vaginal oestrogen for someone with a history of breast cancer who is having adjuvant aromatase inhibitor treatment, discuss appropriate options with an oncology specialist, including whether to change their adjuvant treatment to tamoxifen. **[2023]**

See also recommendations for [all women, trans men, and non-binary people registered female at birth with genitourinary menopause symptoms](#).

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on genitourinary symptoms in women, trans men and non-binary people with a history of breast cancer](#).

Full details of the evidence and the committee's discussion are in [evidence review B2: managing genitourinary symptoms – breast cancer recurrence](#).

All women, trans men, and non-binary people registered female at birth

1.4.31 For people having been given any treatment for troublesome genitourinary menopause symptoms, see the [recommendation on when to review](#)

[symptoms in the section on starting, stopping and reviewing treatment: review and referral.](#) [2023]

1.4.32 Advise people with vaginal dryness associated with the menopause that moisturisers and lubricants can be used alone or in addition to vaginal oestrogen. [2023]

1.4.33 Do not offer vaginal laser treatment for troublesome genitourinary menopause symptoms unless as part of a randomised controlled trial. [2023]

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on all women, trans men and non-binary people with genitourinary menopause symptoms.](#)

Full details of the evidence and the committee's discussion are in [evidence review B2: managing genitourinary symptoms – breast cancer recurrence.](#)

Depressive symptoms

1.4.34 Consider HRT to alleviate mild depressive symptoms with onset in association with other menopause symptoms. [2015, amended 2023]

1.4.35 Consider CBT for depressive symptoms associated with the menopause. [2023]

1.4.36 For people experiencing menopause who are suspected to have, or are diagnosed, with depression, take into account recommendations on both together to achieve an optimal treatment plan. For the treatment of depression, see [NICE's guideline on treating and managing depression in adults.](#) [2023]

For a short explanation of why the committee made the recommendations on CBT and how they might affect practice, see the [rationale and impact section on cognitive behavioural therapy.](#)

Full details of the evidence and the committee's discussion are in [evidence review A: cognitive behavioural therapy](#).

Sleep

1.4.37 Consider CBT for difficulties with sleep associated with the menopause (such as nighttime awakening). **[2023]**

For a short explanation of why the committee made the recommendation on CBT and how they might affect practice, see the [rationale and impact section on cognitive behavioural therapy](#).

Full details of the evidence and the committee's discussion are in [evidence review A: cognitive behavioural therapy](#).

Altered sexual function

1.4.38 Consider testosterone supplementation for people with low sexual desire associated with the menopause if HRT alone is not effective. **[2015]**

1.5 Starting, stopping and reviewing treatment for anyone

Starting and stopping HRT

Starting HRT

1.5.1 For people who wish to take hormone replacement therapy (HRT) for troublesome menopause symptoms, offer:

- oestrogen and progestogen (that is, combined HRT) to people with a uterus
- oestrogen alone to people who have had a hysterectomy. **[2023]**

1.5.2 If a person chooses to take HRT, use the lowest effective dosage. **[2023]**

1.5.3 Explain to women with a uterus, and trans men and non-binary people with a uterus, that vaginal bleeding is a common side effect of HRT within the first 3 months of treatment and should be reported at the 3-month

review appointment, or promptly if it occurs after the first 3 months (see the [section on endometrial cancer in the NICE guideline on suspected cancer](#)). [2015]

Stopping HRT

1.5.4 Offer people who are stopping HRT a choice of gradually reducing or immediately stopping treatment.

1.5.5 Explain to people that:

- gradually reducing HRT may limit recurrence of symptoms in the short term
- gradually reducing or immediately stopping HRT makes no difference to their symptoms in the longer term. [2015]

1.5.6 See the [section on menopause symptoms in the NICE guideline on early and locally advanced breast cancer](#) for recommendations on stopping systemic HRT in people who are diagnosed with breast cancer. [2023]

For a short explanation of why the committee made the 2023 recommendations related to starting and stopping HRT and how they might affect practice, see the [rationale and impact section on starting, stopping and reviewing treatment](#).

Full details of the evidence and the committee's discussion are in:

- [evidence review D: breast cancer risk](#)
- [evidence review E: endometrial cancer risk](#).

Review and referral for any treatment for menopause symptoms

1.5.7 Discuss with people the importance of keeping up to date with nationally recommended health screening. [2015]

1.5.8 Review each treatment for menopause symptoms:

- at 3 months to assess efficacy and tolerability

- annually thereafter, unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events). **[2015]**

1.5.9 Refer people to a [healthcare professional with expertise in menopause](#) if treatments do not improve their menopause symptoms or they have ongoing troublesome side effects. **[2015]**

1.5.10 Consider referring people to a healthcare professional with expertise in menopause if:

- they have troublesome menopause symptoms and contraindications to HRT **or**
- there is uncertainty about the most suitable treatment options for their troublesome menopause symptoms. **[2015]**

1.5.11 Offer psychological support to people with early menopause (aged 40 to 44) who are distressed by their diagnosis or its consequences. If needed, refer them to specialist psychology services. **[2023]**

For a short explanation of why the committee made the 2023 recommendation and how it might affect practice, see the [rationale and impact section on starting, stopping and reviewing treatment](#).

Full details of the evidence and the committee's discussion are in [evidence review I: early menopause](#).

1.6 Effects of hormone replacement therapy on health outcomes

People aged 45 or over

1.6.1 When talking about hormone replacement therapy (HRT) as a treatment option for troublesome menopause symptoms with someone:

- explain that, overall, taking either oestrogen-only or combined HRT is unlikely to increase or decrease life expectancy

- discuss factors that best balance benefits and risks for this person
- share information from [table 1: effect of combined HRT on health outcomes](#) and [table 2: effect of oestrogen-only HRT on health outcomes](#), as appropriate, on how HRT affects health outcomes
- refer to [appendix A: incidence of health outcomes with and without the use of HRT](#) to provide estimates of the size of benefits and risks associated with HRT (expressed as natural frequencies per 1,000 people). **[2023]**

See also:

- [the recommendation on discussing risks and benefits of HRT](#), including the need to tailor the treatment to the person's age, personal circumstances and potential risk factors and
- the [section on communicating risks, benefits and consequences \(including how to discuss numerical information\) in NICE's guideline on shared decision making](#).

1.6.2 Do not offer combined or oestrogen-only HRT for primary or secondary prevention of cardiovascular disease. For ways to prevent cardiovascular disease (for example, lifestyle changes), refer to [NICE's guideline on cardiovascular disease: risk assessment and reduction, including lipid modification](#). **[2023]**

1.6.3 Do not offer HRT for the purpose of dementia prevention. For dementia prevention, see [NICE's guideline on dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset](#). **[2023]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on effect of HRT on health outcomes in people aged 45 or over](#).

Full details of the evidence and the committee's discussion are in:

- [evidence review C: cardiovascular disease](#)
- [evidence review D: breast cancer](#)

- [evidence review E: endometrial cancer](#)
- [evidence review F: ovarian cancer](#)
- [evidence review G: dementia](#)
- [evidence review H: all-cause mortality](#).

1

2 **Combined HRT**3 **Table 1 Combined HRT: effect on health outcomes**

–	Baseline risk	How does taking hormone replacement therapy (HRT) impact the risks related to this outcome?	Does the way HRT is taken affect these risks?	Does the type of hormone taken affect these risks?
Cancer: breast (Information in this table applies to people with no history of breast cancer)	The risk of breast cancer varies depending on a person's modifiable and non-modifiable risk factors (see lifestyle-related risk factors in NICE's guideline on early and locally advanced breast cancer and recommendation 1.7.1 in NICE's guideline on familial breast cancer). [2023]	Combined HRT increases the risk of breast cancer compared with not taking HRT and <ul style="list-style-type: none"> • the increase rises with duration of use • the increase is higher in current users than in past users • the increase declines after stopping but persists at least 10 years after stopping use 	Combined HRT preparations containing transdermal oestrogen increase the risk of breast cancer less than combined HRT preparations containing oral oestradiol. [2023] Sequential combined HRT preparations increase the risk of breast cancer less than continuous combined HRT preparations. [2023]	It is not known whether preparations containing micronised progesterone or dydrogesterone have a different increased risk for breast cancer compared with preparations containing other progestogens. [2023]

		<ul style="list-style-type: none"> there is a very small increase in risk of death from breast cancer. <p>Use Appendix A, tables 1 and 2, for the number of breast cancer cases per 1,000 people taking combined HRT over a 5- or 10-year period. [2023]</p>		
Cancer: endometrial (Information in this table applies to people with no history of endometrial cancer)	—	—	<p>Continuous combined HRT does not increase the risk of endometrial cancer (use Appendix A, table 5, for the number of endometrial cancer cases per 1,000 people taking combined HRT over a 5-year period. [2023]</p> <p>Sequential combined HRT may slightly increase the risk of endometrial cancer, and that risk may be greater with:</p> <ul style="list-style-type: none"> longer duration of use and fewer days of progestogen per cycle 	—

			<ul style="list-style-type: none"> increased dosage of oestrogen. [2023] 	
Cancer: ovarian (Information in this table applies to people with no history of ovarian cancer)	The baseline population risk of ovarian cancer in people under 60 is very low (use Appendix A, tables 7 and 8 , for the number of ovarian cancer cases per 1,000 people over a 5-year and a 10-year period). [2023]	In people with ovaries, combined HRT very slightly increases the risk of ovarian cancer after 5 years of use, and this risk increases with duration of use (use Appendix A, tables 7 and 8 , for the number of ovarian cancer cases per 1,000 people over a 5-year and a 10-year period). [2023]	–	–
Coronary heart disease (Information in this table applies to people with no history of coronary heart disease)	–	Combined HRT does not increase the risk of coronary heart disease (use Appendix A, tables 10 and 11 , for the number of coronary heart disease cases per 1,000 people over a 5-year period). [2023] Combined HRT does not increase mortality from cardiovascular disease. [2023]	–	–

Dementia	–	Combined HRT might increase the risk of dementia if started over the age of 65 (use Appendix A, table 12 for the number of dementia cases per 1,000 people over a 4-year period). [2023]	–	–
Muscle mass and strength	–	There is limited evidence suggesting that HRT may improve muscle mass and strength. [2015]	–	–
Osteoporosis	<p>The baseline population risk of fragility fracture:</p> <ul style="list-style-type: none"> • is low in the UK for women, trans men and non-binary people registered female at birth who are around the age of menopause, and • varies from one person to another <p>(Use table 14 from appendix A for the incidence of fragility fractures in people in menopause.) [2015]</p>	<p>The risk of fragility fracture is decreased while taking HRT and this benefit:</p> <ul style="list-style-type: none"> • is maintained during treatment but decreases once treatment stops • may continue for longer in people who take HRT for longer. <p>(Use table 14 from appendix A for the incidence of fragility fractures in people in menopause.) [2015]</p>	–	–

Stroke (Information in this table applies to people without a history of stroke)	The baseline population risk of stroke in women under 60 is very low. [2023]		Combined HRT containing oral oestrogen increases the risk of stroke and the increase: <ul style="list-style-type: none"> • rises with higher oestrogen dosage and longer duration of treatment, for example, if used for more than 5 years • is greater with increasing age at first starting HRT • differs between ethnic groups and may be greater in Black people (see Appendix A, table 15, for the number of stroke cases per 1,000 people over a 5-year period). [2023]	–

			Combined HRT with transdermal oestrogen is unlikely to increase the risk of stroke when the oestrogen is given at a standard therapeutic dosage (see Appendix A, table 15, for the number of stroke cases per 1,000 people over a 5-year period). [2023]	
Type 2 diabetes	–	<p>Taking HRT (either transdermally or orally) is not associated with an increased risk of developing type 2 diabetes. [2015]</p> <p>HRT is not generally associated with an adverse effect on blood glucose control. [2015]</p>	See 'how does taking HRT affect the risks of or from this condition'	–
Venous thromboembolism	–	The risk of venous thromboembolism (VTE) is increased by oral HRT compared with baseline population risk. [2015]	The risk of VTE associated with HRT is greater for oral than transdermal preparations. [2015]	–

		The risk associated with transdermal HRT given at standard therapeutic dosage is no greater than baseline population risk. [2015]		
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1 A [downloadable version](#) of this table is also available.

2

1 Oestrogen-only HRT

2 Table 2 Oestrogen-only HRT: effect on health outcomes

–	Baseline risk	How does taking hormone replacement therapy (HRT) impact the risks related to this outcome?	Does the way HRT is taken affect these risks?	Does the type of hormone taken affect these risks?
Cancer: breast (Information in this table applies to people with no history of breast cancer)	The risk of breast cancer varies depending on a person's modifiable and non-modifiable risk factors (see lifestyle-related risk factors in NICE's guideline on early and locally advanced breast cancer and recommendation 1.7.1 in NICE's guideline on familial breast cancer). [2023]	Oestrogen-only HRT slightly increases the risk of breast cancer compared to not taking HRT and the increase: <ul style="list-style-type: none"> • rises with longer duration of use • is greater in current users than in past users • declines after stopping but persists for at least 10 years after stopping use. Use Appendix A table 3 and 4, for the number of breast cancer cases per 1,000 people taking oestrogen-only HRT over a 5- or 10-year period . [2023]	There is no difference in the increase of breast cancer risk between transdermal and oral oestrogen. [2023]	There is no difference in the increase in breast cancer risk between oestradiol and conjugated equine oestrogen when given at standard therapeutic dosage. [2023]

Cancer: endometrial (Information in this table applies to people with no history of endometrial cancer)	–	Oestrogen-only HRT increases the risk of endometrial cancer for people with a uterus (use Appendix A, table 6 , for the number of endometrial cancer cases per 1,000 people taking oestrogen-only HRT over a 5-year period). [2023] See also recommendation 1.5.1 on which type of HRT to offer depending on whether people have a uterus or not . [2023]	The increased risk is present in both oral and transdermal routes of oestrogen administration. [2023]	–
Cancer: ovarian (Information in this table applies to people with no history of ovarian cancer)	The baseline population risk of ovarian cancer in women under 60 is very low. [2023]	In women with ovaries, oestrogen-only HRT very slightly increases the risk of ovarian cancer after 5 years of use and this risk increases with duration of use (use Appendix A, tables 7 and 9 , for the number of ovarian cancer cases per 1,000 people over a 5-year and a 10-year period). [2023]	–	–
Coronary heart disease	–	Oestrogen-only HRT does not	–	–

(Information in this table applies to people with no history of coronary heart disease)		<p>increase the risk of coronary heart disease. (use Appendix A, tables 10 and 11, for the number of coronary heart disease cases per 1,000 people over a 5-year period). [2023]</p> <p>Oestrogen-only HRT does not increase mortality from cardiovascular disease. [2023]</p>		
Dementia	–	<p>Oestrogen-only HRT is unlikely to increase the risk of dementia Appendix A, table 13 for the number of dementia cases per 1,000 people over a 5-year period). [2023]</p>	–	–
Muscle mass and strength	–	<p>There is limited evidence suggesting that HRT may improve muscle mass and strength. [2015]</p>	–	–
Osteoporosis	<p>The baseline population risk of fragility fracture:</p> <ul style="list-style-type: none"> is low in the UK for women, trans men and non-binary people registered female at birth who 	<p>The risk of fragility fracture is decreased while taking HRT and this benefit:</p> <ul style="list-style-type: none"> is maintained during treatment but decreases once 	–	–

	<p>are around the age of menopause , and</p> <ul style="list-style-type: none"> varies from one person to another. <p>(Use table 12 from appendix A for the incidence of fragility fractures in people in menopause.) [2015]</p>	<p>treatment stops</p> <ul style="list-style-type: none"> may continue for longer in people who take HRT for longer. <p>(Use table 12 from appendix A for the incidence of fragility fractures in people in menopause.) [2015]</p>		
<p>Stroke</p> <p>(Information in this table applies to people with no history of stroke)</p>	<p>The baseline population risk of stroke in women under 60 is very low. [2023]</p>	—	<p>Taking oral oestrogen-only HRT increases the risk of stroke and the increase:</p> <ul style="list-style-type: none"> rises with the dosage of oestrogen is greater if HRT is started after the age of 60 <p>(see Appendix A, table 13, for the number of stroke cases per 1,000 people over a 5-year period.) [2023]</p> <p>Transdermal oestrogen-only HRT is unlikely to increase the risk of stroke when given at standard therapeutic dosage (see Appendix A,</p>	—

			table 13, for the number of stroke cases per 1,000 people over a 5-year period). [2023]	
Type-2 diabetes	–	<p>Taking HRT (either transdermally or orally) is not associated with an increased risk of developing type 2 diabetes. [2015]</p> <p>HRT is not generally associated with an adverse effect on blood glucose control. [2015]</p>	See ‘how does taking HRT affect the risks of or from this condition’	–
Venous thromboembolism	–	<p>The risk associated with transdermal HRT given at standard therapeutic dosage is no greater than baseline population risk. [2015]</p>	<p>The risk of VTE is increased by oral HRT compared with baseline population risk. [2015]</p> <p>The risk of VTE associated with HRT is greater for oral than transdermal preparations. [2015]</p>	–

1 A [downloadable version](#) of this table is also available.

2

1 People in early menopause (ages 40 to 44)

2 1.6.4 When discussing HRT as a treatment option, explain to people
3 experiencing early menopause, that, for them:

- 4 • Evidence is lacking about possible benefits or risks of using HRT in
5 relation to most health outcomes considered in this guideline. Breast
6 cancer is the only outcome for which evidence is available.
- 7 • The benefits and risks of either taking or not taking HRT are likely to lie
8 between those for people with premature ovarian insufficiency and
9 those for people aged 45 or over.
- 10 • Taking HRT increases the risk of breast cancer. When discussing this,
11 refer to the section on people experiencing early menopause, [in](#)
12 [Appendix A](#), to provide estimates of the size of this risk (expressed as
13 natural frequencies per 1,000 people). **[2023]**

14 See also [the recommendation on discussing risks and benefits of HRT](#), including the
15 need to tailor the treatment to the person's age, personal circumstances and
16 potential risk factors.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on effects of HRT on health outcomes in early menopause](#).

Full details of the evidence and the committee's discussion are in [evidence review I: early menopause](#).

17 1.7 Diagnosing and managing premature ovarian insufficiency

18 Diagnosing premature ovarian insufficiency

19 1.7.1 Take into account the person's clinical history (for example, previous
20 medical or surgical treatment) and family history when diagnosing
21 premature ovarian insufficiency. **[2015]**

22 1.7.2 Diagnose premature ovarian insufficiency in women, trans men and non-
23 binary people registered female at birth who are under 40 based on:
24

- menopause symptoms, including no or infrequent periods (taking into account whether the person has had a hysterectomy) **and**
- elevated follicle stimulating hormone (FSH) levels on 2 blood samples taken 4 to 6 weeks apart. **[2015]**

1.7.3 Do not diagnose premature ovarian insufficiency on the basis of a single blood test. **[2015]**

1.7.4 Do not routinely use anti-Müllerian hormone testing to diagnose premature ovarian insufficiency. **[2015]**

1.7.5 If there is doubt about the diagnosis of premature ovarian insufficiency, refer the person to a specialist with expertise in menopause or reproductive medicine. **[2015]**

Managing premature ovarian insufficiency

1.7.6 Offer sex steroid replacement with a choice of hormone replacement therapy (HRT) or a combined hormonal contraceptive to people with premature ovarian insufficiency, unless contraindicated (for example, in people with hormone-sensitive cancer). **[2015]**

1.7.7 Explain to people with premature ovarian insufficiency:

- the importance of starting hormonal treatment either with HRT or a combined hormonal contraceptive and continuing treatment until at least the age of natural menopause (unless contraindicated)
- that the baseline population risk of diseases such as breast cancer and cardiovascular disease increases with age and is very low in people under 40
- that HRT may have a beneficial effect on blood pressure when compared with a combined oral contraceptive
- that both HRT and combined oral contraceptives offer bone protection
- that HRT is not a contraceptive. **[2015]**

1.7.8 Give people with premature ovarian insufficiency and contraindications to hormonal treatments advice, including on bone and cardiovascular health, and symptom management. [2015]

1.7.9 Consider referring people with premature ovarian insufficiency to healthcare professionals with the relevant experience to help them manage all aspects of physical and psychosocial health related to their condition. [2015]

Terms used in this guideline

This section defines terms that have been used in a particular way for this guideline. For other definitions, see the [NICE glossary](#) and the [Think Local, Act Personal Care and Support Jargon Buster](#).

Combined HRT

HRT with oestrogen and progestogen.

Continuous combined HRT

HRT in which oestrogen and progestogen are taken together, daily.

Healthcare professional with expertise in menopause

A menopause specialist, as [defined by the British Menopause Society](#). These healthcare professionals have specialist knowledge, skills and training in assessing and treating:

- troublesome menopause symptoms
- premature ovarian insufficiency
- complex medical problems that potentially affect use of treatments for menopause symptoms
- menopause symptoms for those at elevated risk of breast or ovarian cancer or with a personal history of hormone dependent cancer, in collaboration with oncologists.

They can advise and support colleagues in managing complex menopause-related needs and risk factors affecting decision making.

Sequential combined HRT

Sometimes also referred to as combined cyclical HRT. A form of HRT in which oestrogen is taken every day, and the progestogen is taken for (usually) half of the month.

Systemic HRT

HRT in which the hormones are absorbed into the bloodstream and have an effect throughout the body. Oestrogen within systemic HRT can be taken orally, in the form of a pill, or transdermally, as a patch, gel or spray that delivers the hormones through the skin, whereas progestogens within HRT can be taken orally, transdermally as a patch, or delivered through an intrauterine system.

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

1 Impact of HRT on health outcomes in early menopause

What is the effect of either taking or not taking hormone replacement therapy (HRT) on health outcomes for people with early menopause (aged 40 to 44)? **[2023]**

For a short explanation of why the committee made this recommendation for research, see the [rationale section on effects of HRT on health outcomes in early menopause](#).

Full details of the evidence and the committee's discussion are in [evidence review 1: early menopause](#).

2 Type of progestogen in HRT and breast, endometrial cancer or cardiovascular disease

Do different types of progestogens (for example, micronised progesterone) alter the risk of breast cancer, endometrial cancer and cardiovascular disease? **[2023]**

For a short explanation of why the committee made this recommendation for research, see the [rationale section on breast or endometrial cancer](#).

Full details of the evidence and the committee's discussion are in:

- [evidence review C: cardiovascular disease](#)
- [evidence review D: breast cancer](#)
- [evidence review E: endometrial cancer](#).

1 **3 Long-term safety of vaginal oestrogen**

2 What is the long-term (beyond 12 months) safety of vaginal oestrogen? **[2023]**

For a short explanation of why the committee made this recommendation for research, see the [rationale section on treatments for genitourinary symptoms associated with the menopause for women, trans-men and non-binary people registered female at birth with no history of breast cancer](#).

Full details of the evidence and the committee's discussion are in [evidence review B1: managing genitourinary symptoms \(network meta-analysis\)](#).

3 **4 Safety of vaginal oestrogen in terms of breast cancer recurrence**

4 After breast cancer, or for people at high familial or genetic risk of breast cancer, 5 does vaginal oestrogen increase the risk of recurrence of or new breast cancer?

6 **[2023]**

For a short explanation of why the committee made this recommendation for research, see the [rationale section on treatments for genitourinary symptoms associated with the menopause for women, trans men and non-binary people registered female at birth with a history of breast cancer](#).

Full details of the evidence and the committee's discussion are in [evidence review B2: managing genitourinary symptoms – breast cancer recurrence](#).

1 **5 Vaginal laser for genitourinary symptoms**

2 What is the safety and efficacy of vaginal laser for genitourinary menopause
3 symptoms? **[2023]**

For a short explanation of why the committee made this recommendation for research, see the [rationale section on treatments for genitourinary symptoms associated with the menopause for all women, trans-men and non-binary people registered female at birth](#).

Full details of the evidence and the committee's discussion are in [evidence review B1: managing genitourinary symptoms \(network meta-analysis\)](#).

4 **6 Health outcomes of HRT for trans men and non-binary people**
5 **registered female at birth (who are not taking cross-sex hormones as**
6 **gender-affirming therapy at the time of taking HRT or in the follow-up**
7 **period)**

8 What is the impact of HRT on health outcomes for trans men and non-binary people
9 registered female at birth (who are not taking gender-affirming hormone therapy at
10 the time of taking HRT or in the follow-up period) in relation to:

- 11 • cardiovascular disease
- 12 • stroke
- 13 • breast, endometrial and ovarian cancer
- 14 • dementia
- 15 • all-cause mortality? **[2023]**

For a short explanation of why the committee made this recommendation for research, see the [rationale section on people who have taken gender-affirming therapy in the past](#).

Full details of the evidence and the committee's discussion are in [evidence review C: cardiovascular disease](#).

7 Health outcomes of HRT for people from ethnic minority family backgrounds

What is the impact of HRT on health outcomes for people from ethnic minority family backgrounds in relation to:

- cardiovascular disease
- stroke
- breast, endometrial and ovarian cancer
- dementia
- all-cause mortality? **[2023]**

For a short explanation of why the committee made this recommendation for research, see the [rationale section on cardiovascular disease](#).

Full details of the evidence and the committee's discussion are in [evidence review C: cardiovascular disease](#).

Other recommendations for research

8 People with a history of breast cancer

What is the safety and effectiveness of alternatives to systemic HRT as treatments for menopause symptoms in people who have had breast cancer? **[2015]**

9 Effects of HRT on dementia risk

What are the effects of HRT use on the risk of dementia? **[2015, amended 2023]**

10 Premature ovarian insufficiency

What are the main clinical manifestations of premature ovarian insufficiency and the short- and long-term impact of the most common therapeutic interventions? **[2015]**

11 Breast cancer and venous thromboembolism

What is the impact of oestradiol in combination with the levonorgestrel-releasing intra-uterine system (LNG-IUS) on the risk of breast cancer and venous thromboembolism (VTE)? **[2015]**

12 Breast cancer recurrence

What is the impact of systemic HRT usage in people with a previous diagnosis of breast cancer for the risk of breast cancer recurrence, mortality or tumour aggression? [2015]

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice.

Identifying menopause and perimenopause

[Recommendations 1.3.3](#)

Why the committee made the recommendation

The committee noted that research on early menopause in people from ethnic minority backgrounds was lacking. However, the committee was aware, from experience, that some ethnic minority groups experience menopause at a younger age than people from White backgrounds. The committee agreed that healthcare professionals should be aware of this to correctly identify symptoms of the menopause in ethnic minority populations. The committee discussed that raising awareness of this could lead to earlier identification and therefore would provide an opportunity for offering interventions for troublesome menopause symptoms where appropriate

How the recommendations might affect practice

The recommendation will raise awareness of healthcare professionals about the possibility that people from some ethnic minority groups experience menopause at a younger age. It is unclear whether this will change clinical practice but it might lead to earlier identification of menopause and could lead to earlier treatment of troublesome menopause symptoms.

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Discussing treatment options

[Recommendations 1.4.1 to 1.4.4](#)

1 **Why the committee made the recommendations**

2 Based on experience, the committee emphasised that, to allow people to make an
3 informed choice about treatment options, applying basic principles of care is
4 particularly important especially:

- 5 • using an individualised approach with discussions about benefits and risks of
6 treatment options and
- 7 • tailoring information to individual circumstances and potential risk factors.

8 The committee noted that there are different ways of prescribing hormone
9 replacement therapy (modes of administration, types of hormones, schedule, and
10 dosage and duration) and that clinicians should provide information about the
11 benefits and risks associated with these options. Baseline risks of specific health
12 outcomes and the benefits and risks of hormone replacement therapy (HRT) all
13 change with a person's age at the start of the menopause transition, as well as with
14 their individual circumstances and risk factors. It is particularly important to take age
15 into account, for example when considering:

- 16 • the risks of dementia or stroke with HRT and
- 17 • the use of HRT in people experiencing early menopause.

18 The way HRT is prescribed influences these benefits and risks, so it also influences
19 the balance between them. As a result, the best parameters of HRT prescription are
20 different from one person to another and should be carefully chosen with, and for,
21 each person.

22 The committee agreed that, when a person chooses to take HRT, discussing
23 duration of use with them is essential. They also agreed that it is impossible to
24 recommend one specific duration of use because this would depend on several
25 factors, including the reason for starting HRT and a person's health history, age and
26 symptoms. The committee acknowledged that, in many people, menopause
27 symptoms may return when HRT is stopped. They agreed this should also be
28 discussed with the person in the context of duration of use. The person should also
29 be aware that, if this happens, HRT may be restarted, but this would depend on the
30 factors that best balance benefits and risks for the person.

The committee also agreed that evidence showed that CBT could be an option for some people (see [sections on vasomotor symptoms](#), [depressive symptoms](#) and [sleep](#)). However, they noted that the evidence showed that several types of CBT (for example online or group sessions) were effective but did not show that one option was better than another. They therefore recommended that the options that are available should be discussed with the person.

How the recommendations might affect practice

The recommendations reflect current shared decision-making practice between the person and the healthcare professional to enable people to make informed choices. The recommendations will make healthcare professionals aware of what to discuss and will standardise it.

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People who have taken gender-affirming therapy in the past

[Recommendation 1.4.8 and 1.4.9](#)

Why the committee made the recommendations

The committee noted a lack of evidence on hormone replacement therapy (HRT) use in trans-men and non-binary people registered female at birth who have taken gender-affirming hormone therapy in the past. Given this uncertainty (which, for example, means that it is not known whether past hormone treatment could influence the choice of HRT, and whether giving HRT to someone who previously had hormone therapy would alter their health risks) the committee agreed that trans-men and non-binary people registered female at birth who have taken gender-affirming hormone therapy in the past should be able to discuss their troublesome menopause symptoms with a healthcare professional with expertise in menopause. They can then make a shared decision about any potential treatment they may wish to have. Because of the lack of evidence, the committee also made a [recommendation for research](#) on this.

The committee discussed the evidence related to cognitive behavioural therapy (for the details see, the rationale on cognitive behavioural therapy [CBT]). This did not

1 include evidence related to trans-men or non-binary people registered female at
2 birth.

3 The committee agreed that their decisions about use of CBT for troublesome
4 menopause symptoms applies equally to women and to trans-men and non-binary
5 people registered female at birth, regardless of whether they have taken gender-
6 affirming hormone therapy in the past because:

- 7 • CBT is not a risky intervention, and
- 8 • there is no possibility of interaction with gender-affirming hormone therapy or risks
9 from it.

10 The committee decided to make a specific recommendation for trans-men and non-
11 binary people registered female at birth who have taken gender-affirming hormone
12 therapy in the past. They agreed that this would promote equality in access to CBT
13 services for managing menopausal symptoms within this group, acknowledging its
14 unique experiences and needs. Because, without further evidence, other
15 recommendations in this guideline cannot be extended to this group, the committee
16 thought that a separate recommendation would also improve clarity.

17 **How the recommendations might affect practice**

18 It is currently not known whether having taken gender-affirming hormone therapy in
19 the past may affect the benefits and risks associated with someone's options of
20 menopause treatment. Evidence was looked for but not found. In the committee's
21 experience, there is no clear current practice related to this. A recommendation to
22 refer people who have taken gender-affirming hormone therapy in the past to a
23 healthcare professional with expertise in menopause may lead to an increase in
24 such referrals but should lead to more appropriate care and improved outcomes.

25 They noted that there is pressure on services providing CBT and that the
26 recommendation in favour of CBT for people who have taken gender-affirming
27 hormone therapy in the past may increase referrals although will ensure equity of
28 access.

29 The committee agreed that access to a healthcare professional with expertise in
30 menopause and access to CBT is a matter of equality and inclusivity.

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Taking comorbidities into account

[Recommendation 1.4.13](#)

Why the committee made the recommendation

People with a history of coronary heart disease or stroke

For people with a history of coronary heart disease or stroke, the committee agreed that different risk factors mean that people have different baseline levels of risk. They concluded that decisions on hormone replacement therapy (HRT) use for menopause symptoms would need to be tailored to the person and their particular risk factors and risk levels and that, therefore, these decisions should be made with a [healthcare professional with expertise in menopause](#).

How the recommendations might affect practice

It is current practice that people with pre-existing conditions get expert advice on HRT as a treatment option for menopause symptoms. However, there is variation in which expert would be consulted on this. This recommendation to discuss this with a healthcare professional with expertise in menopause will standardise practice.

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Cognitive behavioural therapy

[Recommendations 1.4.4, 1.4.9, 1.4.16, and 1.4.35 to 1.4.37](#)

Why the committee made the recommendations

The committee based its recommendations on both the evidence and its expert knowledge. It looked at evidence on cognitive behaviour therapy (CBT) compared to no treatment and CBT compared to treatment as usual.

There was no evidence available for trans men and non-binary people registered female at birth.

Vasomotor symptoms

[Recommendation 1.4.16](#)

Overall, the evidence showed CBT was beneficial for women with vasomotor symptoms associated with the menopause. The benefits related to frequency of symptoms, severity of symptoms and how much the symptoms bothered the person.

The committee noted that not all the evidence on vasomotor symptoms showed that CBT was beneficial. Most of the benefits were seen in reducing how much women were bothered by the symptoms. The committee also discussed some limitations that affected the quality of the evidence (see uncertainties section below). So they decided that CBT should be an option rather than a routine treatment for all.

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Depressive symptoms

[Recommendations 1.4.35 and 1.4.36](#)

There were many different scales and measurements for psychological symptoms, and most of the evidence on depressive symptoms, in the context of menopause, showed no difference between CBT and the comparison groups. There was evidence showing CBT improved mood in people with depressive symptoms as measured on 1 specific scale, but measuring the emotional wellbeing and mental health components of the [Quality of Life scale \(SF-36\)](#) showed CBT made no difference.

Given that effectiveness of CBT on depressive symptoms overall is established (see [NICE's guideline on depression in adults](#)), the committee decided that CBT should also be an option to treat depressive symptoms in the context of menopause.

The committee agreed to refer to depressive symptoms in their recommendations, rather than to low or depressed mood because:

- it would be difficult to define low or depressed mood outside of a diagnosis of depression
- without a definition, low or depressed mood associated with the menopause would be difficult to measure.

However, if depression is suspected, the committee noted that the optimal treatment plan can only be achieved by following both the menopause guideline and [NICE's guideline on depression in adults](#).

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Sleep

[Recommendation 1.4.37](#)

Evidence showed CBT improved sleep quality, but this varied depending on the scale used to measure sleep disturbances. The committee agreed it was difficult to define difficulties with sleep, but the evidence showed that CBT was beneficial for various aspects of sleep, as defined by each scale (measures contributing to scales included a number of hours of sleep per night, how long it takes someone to fall asleep, number and duration of nighttime awakenings as well as some scales specifically related to insomnia). The committee acknowledged that there may be other options to manage difficulties with sleep associated with the menopause. NICE will monitor evidence on these for a future update.

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Trans men and non-binary people registered female at birth

[Recommendation 1.4.9](#)

The committee thought that their conclusion from the available evidence could be extended to trans men and non-binary people registered female at birth regardless of whether they have taken cross-sex hormones as gender-affirming therapy in the past. For the reasons why a separate CBT recommendation was made for some of these groups, see the [rationale on people who have taken gender-affirming therapy in the past](#).

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Uncertainties

There were:

- some concerns related to study design and biases in how studies were carried out

- uncertainties around outcomes for vasomotor, sleep disturbance and depressive symptoms, with results depending on different outcome measurement scales and subgroups
- uncertainties around how large the effect was, even where effectiveness was shown.

As a result, the committee recommended CBT as an option rather than as a routine treatment for troublesome menopause symptoms.

How the recommendations might affect practice

The committee acknowledged that this would be a change to clinical practice. They noted that people would potentially be able to manage their own symptoms after the standard amount of CBT sessions. This would benefit the NHS because people may not need other treatments which would require regular reviews and ongoing prescriptions, such as hormone replacement therapy (HRT).

Currently, the usual treatment for vasomotor symptoms associated with the menopause is HRT. Having CBT as an option will give people a wider choice. Access to CBT may also address some health inequalities, bringing other effective options for those who do not wish to use pharmacological treatments for menopause symptoms. The committee noted that this would lead to higher demand on limited resources and staff although might reduce downstream costs through lower use of pharmacological interventions and reducing contact with health services and professionals. However, the evidence was not restricted to face-to-face contact. It also included online and group CBT, which may be easier and less costly to implement.

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Genitourinary menopause symptoms

Women, trans men and non-binary people registered female at birth with no history of breast cancer

[Recommendations 1.4.19 to 1.4.25](#)

Why the committee made the recommendations

The committee discussed evidence from network meta-analyses (NMA) of a number of treatment options for specific subtypes of genitourinary symptoms such as vaginal dryness, pain with sex, and vulvovaginal discomfort or irritation. They also took into consideration evidence from the associated bespoke health economic model.

There was no evidence available for trans men and non-binary people registered female at birth. The committee thought that their conclusion from the available evidence could be extended to those who have never taken cross-sex hormones as gender-affirming therapy. But they did not think they could be extended to those who have taken cross-sex hormones as gender-affirming therapy in the past, because it is not known whether having taken such therapy would alter the benefits and risks of any treatment (especially hormonal treatments), or which treatment option might be best for the person.

Evidence showed that vaginal oestrogen (particularly estriol but also oestradiol) was effective in reducing vaginal dryness and pain with sex. Estriol also showed effectiveness in reducing vulvovaginal discomfort or irritation. The bespoke economic model conducted for this review showed that vaginal oestrogen was cost-effective.

There were some differences between preparations in their effectiveness, but there were also uncertainties around these differences. So the committee agreed that, overall, it was unlikely that one type of vaginal oestrogen preparation would be more effective than another. They concluded that different vaginal oestrogen preparations should be offered for genitourinary symptoms so that people could choose the option they prefer.

There was limited evidence on long-term use of vaginal oestrogens. However, the committee agreed that systemic absorption of oestrogen is relatively low with vaginal oestrogen so it would likely be safe to continue treatment for as long as needed to relieve symptoms. To gain a better understanding on this and inform future updates the committee also prioritised this topic for a [research recommendation](#).

Based on their expertise, the committee discussed key points to take into account before offering vaginal oestrogen:

- 1 • Current Medicines and Healthcare products Regulatory Agency (MHRA) safety
2 advice states that serious adverse effects from vaginal oestrogen are rare. This
3 was consistent with the findings from network meta-analysis showing that
4 discontinuation due to adverse events was relatively low. The committee therefore
5 recommended that this should be explained.
- 6 • In the committee's experience, people are not always aware that, when vaginal
7 oestrogen is stopped, it is common that symptoms return. They agreed this should
8 be highlighted in discussions with the person.
- 9 • The committee also decided that it was important to discuss with the person that,
10 with vaginal oestrogen, some oestrogen is absorbed into the bloodstream, but
11 generally much less than with systemic HRT. They agreed to highlight this
12 because it means that there is no need to combine low-dose vaginal oestrogens
13 with systemic progestogen treatment to protect the person against endometrial
14 hyperplasia and cancer. (Conversely, with systemic HRT, progestogen treatment
15 protection is needed for people with a uterus – see the [rationale section on](#)
16 [starting and stopping HRT](#)).
- 17 • The committee also highlighted, based on experience, that vaginal bleeding can
18 occur when vaginal oestrogen is started. They agreed that people should be
19 aware of this to ensure they see their GP so that other causes for the bleeding
20 can be ruled out.

21 The committee agreed that lower dosages may not always relieve all symptoms and
22 that, if symptoms persist, increasing the dosage is an option. They noted that, more
23 and more frequently, people vary the dosage themselves. This can even go beyond
24 the standard therapeutic range, which may impact on safety. To address this, the
25 committee highlighted that the dosage should remain within standard ranges.
26 However, varying the dosage may not always be the best option, so the committee
27 recommended that this should only be done with input from a [healthcare](#)
28 [professional with expertise in menopause](#).

29 The committee was aware that overactive bladder can co-occur with genitourinary
30 menopause symptoms and that vaginal oestrogen can be given in these
31 circumstances. They acknowledged that this was recommended in [NICE's guideline](#)
32 [on urinary incontinence and pelvic organ prolapse in women](#). The committee decided
33 not to include people with a history of breast cancer in this recommendation because

1 vaginal oestrogen is not the first-line treatment for them for genitourinary menopause
2 symptoms.

3 The NMA suggested that non-hormonal vaginal moisturisers and lubricants were
4 less effective than vaginal oestrogens but that they were less often discontinued by
5 people using them than other options. This suggests that, when non-hormonal
6 vaginal moisturisers and lubricants worked for a person, the person felt comfortable
7 to keep using them. While the evidence highlighted uncertainty about the
8 effectiveness of these treatments, based on their experience, the committee decided
9 that moisturisers and lubricants could be tried when local vaginal oestrogen is
10 contraindicated or not preferred.

11 The committee discussed the role of prasterone and ospemifene in the management
12 of troublesome genitourinary menopause symptoms. They noted that both of these
13 medicines are more expensive than vaginal oestrogen or moisturisers and lubricants.
14 However, the NMA showed them to be effective in reducing vaginal dryness and
15 pain with sex but not vulvovaginal discomfort or irritation. They were also not
16 significantly discontinued due to adverse events.

17 The economic model showed prasterone was not a cost-effective strategy as a first-
18 line option. However, given its clinical effectiveness, the committee agreed that
19 prasterone could be offered as a second line treatment when other treatments
20 (vaginal oestrogen, moisturisers or lubricants) are ineffective or not tolerated and
21 troublesome genitourinary symptoms persist.

22 Ospemifene was effective for vaginal dryness and pain with sex but not vulvovaginal
23 discomfort or irritation. However, the committee noted that it was not cost-effective
24 and could therefore not be recommended as a first-line treatment option for all
25 people with genitourinary symptoms. They also noted that it is recommended for
26 people in special circumstances in Scotland, such as for people with a history of
27 breast cancer. The committee was not confident about this because evidence on the
28 safety of ospemifene is insufficient for this group. However, the committee noted
29 that, for some people, local application of vaginal oestrogen may be impractical. For
30 example, people with physical or intellectual disabilities may find it difficult to use

1 local vaginal oestrogen. Ospemifene is a tablet and should therefore be considered
2 as an option in such specific circumstances.

3 **How the recommendations might affect practice**

4 The evidence indicated that the most cost effective option for the treatment of
5 genitourinary symptoms was vaginal oestrogen, which is current practice. The
6 recommendations will standardise practice rather than change it.

7 [Return to recommendations](#)

8 **Women, trans men and non-binary people registered female at birth with** 9 **a history of breast cancer**

10 [Recommendations 1.4.26 to 1.4.30](#)

11 **Why the committee made the recommendations**

12 The committee acknowledged that evidence was sparse, with only 4 studies
13 providing information on breast cancer recurrence in people with a history of breast
14 cancer taking vaginal hormone treatment for genitourinary menopause symptoms.

15 The committee also had methodological concerns about some of the studies,
16 particularly about:

- 17 • how they accounted for confounding factors (methodologically, and in what and
18 how many factors they accounted for) and
- 19 • duration of follow-up, which was insufficiently long to capture breast cancer
20 recurrence.

21 There was no evidence available for trans men and non-binary people registered
22 female at birth. The committee thought that their conclusion from the available
23 evidence could be extended to those who have never taken cross-sex hormones as
24 gender-affirming therapy. But they did not think they could be extended to those who
25 have taken cross-sex hormones as gender-affirming therapy in the past, because it
26 is not known whether having taken such therapy would alter the benefits and risks of
27 any treatment (especially hormonal treatments), or which treatment option might be
28 best for the person.

1 Evidence from one study included both women who had used adjuvant treatment for
2 breast cancer and women who had not. It considered all women together and did not
3 provide separate results for any specific subgroups.

4 Based on the evidence from this study, it is not possible to say with certainty whether
5 vaginal oestrogen leads to a small increase or a small decrease in breast cancer
6 recurrence, when taken for genitourinary menopause symptoms. This is because the
7 confidence interval for the data is wide and goes in both directions. The committee
8 highlighted that these uncertainties should be included in discussions with people
9 about treatment options, particularly if they are also using other cancer therapies,
10 because these therapies in themselves can be associated with an increase or
11 decrease in genitourinary symptoms. This will support people to make an informed
12 choice.

13 The uncertainties around the evidence also lead the committee to agree that:

- 14 • the first choice for people with a history of breast cancer and troublesome
15 genitourinary symptoms should be non-hormonal moisturisers and lubricants
- 16 • local vaginal oestrogens should only be considered as a second option, when
17 non-hormonal treatment has not been effective and symptoms continue to impact
18 negatively on the person's quality of life.

19 This is because:

- 20 • non-hormonal treatment may be less effective than local hormonal treatment and
- 21 • increasing the risk of breast cancer recurrence would be worse than treating
22 menopausal symptoms slightly less effectively.

23 The committee noted that treatment decisions would need to be tailored to each
24 person:

- 25 • Some people have lower recurrence risks than others. For example, those with
26 lymph node-negative breast cancer and smaller or lower-grade tumours would
27 have lower risk of recurrence than those who have lymph node-positive breast
28 cancer, with tumours that are T2 or greater and higher grade (see

[recommendations 1.7.6 and 1.7.7 in NICE's guideline on early and locally advanced breast cancer](#)).

- Genitourinary symptoms vary depending on hormone receptor status and type of adjuvant treatment.

These factors should therefore be taken into account when discussing treatment plans for genitourinary symptoms with people with a history of breast cancer.

The committee agreed it could not be confident in the evidence on the safety of local vaginal oestrogens in those taking either tamoxifen or aromatase inhibitors. This was due to:

- concerns about the quality of the evidence and
- lack of data on aromatase inhibitor use only.

However, using its expertise, the committee advised that, for people taking adjuvant treatments and considering using local vaginal oestrogens, decisions about appropriate options should be made in discussion with an oncology specialist, because such decisions are complex and depend on a variety of different factors.

They also advised that the mechanism of action of aromatase inhibitors makes genitourinary symptoms likely whereas the mechanism of action of tamoxifen is less likely to cause genitourinary symptoms, and may even alleviate some of them. Vaginal oestrogen may also lessen the efficacy of aromatase inhibitors. So discussions could include the option of switching adjuvant treatment from aromatase inhibitors to tamoxifen.

People who carry genetic variants that increase the risk of breast cancer

No evidence was identified for people who carry genetic variants that increase the risk of breast cancer. The committee therefore decided that it was unable to make a recommendation relating to the use of local vaginal oestrogens for this group.

Research recommendation

There was relatively little evidence for vaginal oestrogen in the management of genitourinary menopause symptoms after breast cancer, particularly related to long-term use and use in conjunction with adjuvant therapy. Therefore, the committee made a [recommendation for research](#).

How the recommendations might affect practice

The recommendation about the use of non-hormonal treatment options as first line treatment for people with a history of breast cancer and troublesome genitourinary symptoms is in line with current practice. There is variation in:

- the clinical factors taken into account when considering local vaginal oestrogens after an ineffective first-line treatment
- when to seek specialist oncology advice
- the content of discussions with people, particularly about the uncertainty of the evidence.

The recommendations will standardise this.

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All women, trans men and non-binary people registered female at birth

[Recommendations 1.4.31 to 1.4.33](#)

Why the committee made the recommendations

The committee made some recommendations that apply to people with genitourinary symptoms associated with the menopause, regardless of whether they have a history of breast cancer.

The committee was aware that many people seem to adjust vaginal oestrogen dosages by themselves and that this is not always safe. While they thought it is relatively uncommon that people do not tolerate vaginal oestrogen, they noted it can happen. To address this, the committee referred to the relevant recommendation on reviewing treatments in another section of the guideline.

Moisturiser and lubricants

The committee thought that people were not always aware that moisturisers or lubricants can be used alone or in addition to vaginal oestrogen and therefore thought that this information should be shared with the person.

Laser treatment

The evidence showed that laser treatment was effective for all outcomes. However, the committee agreed that, despite some promising results, the evidence base was

1 too small, there is a potential for harm (for example scarring) and evidence showed it
2 was not cost-effective. As a result, laser treatment should only be offered in the
3 context of research. They also made a [research recommendation](#) to address this.

4 **Population covered by the recommendations**

5 There was no evidence available for trans men and non-binary people registered
6 female at birth. The committee thought that their conclusion from the available
7 evidence could be extended to those who have never taken cross-sex hormones as
8 gender-affirming therapy. But they did not think they could be extended to those who
9 have taken cross-sex hormones as gender-affirming therapy in the past, because it
10 is not known whether having taken such therapy would alter the benefits and risks of
11 any treatment (especially hormonal treatments), or which treatment option might be
12 best for the person.

13 **How the recommendations might affect practice**

14 Laser treatment was not considered in the previous guideline, but the
15 recommendation to only consider it in the context of research does not affect
16 practice.

17 Other recommendations will standardise practice rather than change it.

18 [Return to recommendations](#)

19 **Starting, stopping and reviewing treatment**

20 [Recommendations 1.5.1, 1.5.2 and 1.5.6](#)

21 **Why the committee made the recommendations**

22 **Starting HRT**

23 When a person decides that they want to take hormone replacement therapy (HRT)
24 for troublesome menopause symptoms, the committee recommended, based on
25 expertise, that, if the person has a uterus, they should be offered combined
26 oestrogen and progestogen, whereas, if the person has had a hysterectomy, they
27 should be offered oestrogen alone.

1 The main reason for this is established biological knowledge that oestrogen alone, if
2 given to people with an intact uterus, can stimulate the growth of the uterine lining
3 (endometrium). In turn, this oestrogen stimulation can lead to an increased risk of
4 endometrial hyperplasia (overgrowth of the endometrium) and potentially,
5 endometrial cancer.

6 This is consistent with the evidence showing that oestrogen-only HRT increases the
7 incidence of endometrial cancer in people with a uterus (see section related to the
8 effect of HRT on endometrial cancer). However, because it is now considered unsafe
9 to give oestrogen-only HRT to people with a uterus, no further research is being
10 carried out, and the recommendation is based on knowledge more than on the
11 identified evidence. Adding progesterone to the HRT regimen helps protect the
12 endometrium by counteracting the stimulating effects of oestrogen, reducing the risk
13 of endometrial issues.

14 Since progesterone is given to protect the uterine lining, it is not needed for people
15 who have had a hysterectomy.

16 The committee noted that it is common clinical practice to prescribe the smallest
17 effective dosage to balance the benefits and risks of a treatment and recommended
18 this for HRT, too. Effectiveness can vary between people, so starting with the lowest
19 effective dosage can help find the right balance between effectively treating
20 symptoms and risks from the treatment, taking into account each person's specific
21 needs.

22 **Stopping HRT**

23 The committee agreed, based on their expertise, that HRT could potentially lead to
24 cancer progression or risk of recurrence. They agreed that HRT should be stopped
25 in people who are diagnosed with breast cancer because of other safety concerns.
26 However, they agreed that this is already covered in the [section on menopause](#)
27 [symptoms in the NICE guideline on early and locally advanced breast cancer](#) and
28 therefore cross-referred to it.

Referral

In the committee's experience, some people can be distressed by going through the menopause at an earlier age than expected and earlier than their peers. If someone is experiencing emotional distress to a level that raises concerns, the committee agreed that they may need to be referred to specialist psychology services.

How the recommendations might affect practice

The recommendations reflect current practice in choice of HRT prescribing for people with a uterus or for people who have had a hysterectomy.

Stopping HRT if a person is diagnosed with breast cancer is current practice.

The committee agreed that it is also common practice that healthcare professionals provide psychological support to people. Whilst a recommendation related to potential referral will have a resource impact, withholding such referral when it is needed would be unethical. Specialist psychological services will also lead to improvements in quality of life and reduce future contacts with health services.

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Effect of HRT on health outcomes in people aged 45 or older

[Recommendations 1.6.1 to 1.6.3](#)

What this rationale covers

The committee agreed that, as part of shared decision making, presenting a complete picture of benefits and risks was important, so people can make an informed decision about the treatment they wish to have. The rationale briefly describes the available evidence on hormone replacement therapy (HRT) and how it affects overall life-expectancy as well as the risks related to:

- cancer: [breast](#)
- cancer: [endometrial](#)
- cancer: [ovarian](#)
- [cardiovascular disease \(coronary heart disease and stroke\)](#)
- [dementia](#).

1 There was no evidence available for trans men and non-binary people registered
2 female at birth. The committee thought that their conclusion from the available
3 evidence could be extended to those who have never taken cross-sex hormones as
4 gender-affirming therapy. But they didn't think they could be extended to those who
5 have taken cross-sex hormones as gender-affirming therapy in the past, because it
6 is not known whether having taken such therapy would alter the benefits and risks of
7 any treatment (especially hormonal treatments), or which treatment option might be
8 best for the person. So they made a [research recommendation for this group](#).

9 **Discussing benefits and risks**

10 [Recommendations 1.6.1](#)

11 **Why the committee made the recommendations**

12 The committee discussed the evidence on the impact of HRT on all-cause mortality.
13 Due to the multitude of confounding factors, they restricted the evidence to
14 randomised controlled trials. Evidence showed that there was no difference in
15 mortality, with either oestrogen-only or combined HRT, compared to not taking HRT.

16 Though HRT treatment does not affect overall life-expectancy, the committee agreed
17 that the discussion should aim to establish the best balance between effectively
18 treating symptoms and alleviating risks from the treatment, taking into account the
19 person's age, symptoms, medical history, preferences and personal circumstances.
20 See also the [section on discussing treatment options](#).

21 **How the recommendations might affect practice**

22 It is current practice that risks are discussed with people when treatment options are
23 considered. The recommendations will standardise the information that will be given.
24 But it is unclear how this affects treatment choices.

25 [Return to recommendations](#)

26 **Cancer: breast**

27 [Recommendations 1.6.1](#) and breast cancer rows in [table 1: effect of combined HRT](#)
28 [on health outcomes](#), and [table 2: effect of oestrogen-only HRT on health outcomes](#)

Why the committee made the recommendations

The committee discussed the evidence on the effect of using HRT on breast cancer incidence and breast cancer related mortality. Most of the evidence was from a meta-analysis of individual patient data from observational studies, but there was also evidence from randomised controlled trials (RCTs).

Based on their experience, the committee agreed that advice needs to be tailored to the person according to their individual risk factors, such as being overweight, drinking alcohol or family history of breast cancer. The committee acknowledged that people need to be aware of these factors because the absolute risks associated with HRT use will be greater in those who have a greater risk of breast cancer to start with. The committee was aware that such factors were listed in other NICE guidelines and cross referred to them.

They noted that overall, the evidence showed the risk of breast cancer associated with combined HRT was consistently greater than that associated with oestrogen-only HRT. Only women and trans and non-binary people who have had a hysterectomy are eligible to take oestrogen-only HRT, and so most people taking HRT will take combined HRT. The committee therefore decided to consider risks with oestrogen-only and combined HRT separately.

Combined HRT

The committee looked at the evidence on [combined HRT](#) and breast cancer incidence, which came from RCTs, more specifically long-term follow up studies from the Women's Health Initiative (WHI), and from observational studies.

Evidence from observational studies showed the following.

For current users of combined HRT:

- the risk of breast cancer incidence was higher than in people not using HRT
- there was an increase in risk for people who had been using HRT for less than 1 year
- the risk increased with duration of use.

For past users of combined HRT, the risk:

- remained higher than for people not using HRT
- was greater the longer people had used combined HRT
- reduced after stopping HRT but was still increased as long as at least 10 years after stopping use.

The committee noted that the RCT evidence was consistent with the evidence from observational studies in showing an increased risk of breast cancer with combined HRT compared to people not taking HRT.

The observational evidence showed the rate of mortality from breast cancer was slightly higher in women taking combined HRT than in those not taking HRT. The committee agreed that the difference was consistent with an increase in breast cancer incidence. They decided that people should be aware of these risks so that they can make an informed choice.

The committee noted that the evidence showed that there was a smaller increase associated with taking transdermal oestrogen rather than oral oestradiol. The evidence also showed a smaller increase associated sequential rather than continuous combined preparations. They therefore decided that both mode of administration and type of preparations and their associated breast cancer risk should be discussed so that people can make an informed choice.

All types of progestogen were associated with an increased risk of breast cancer, although there was limited evidence assessing the risk of breast cancer with micronised progesterone. Overall, there was insufficient evidence to say whether one type (for example micronised progesterone) may be safer than others and therefore the committee made a [research recommendation](#) to address this.

Oestrogen-only HRT

The committee discussed the evidence from the analysis of different durations of use of oestrogen-only HRT versus no HRT or versus placebo.

Evidence from observational studies showed the following.

For current users of oestrogen-only HRT,

- the risk of breast cancer was higher in those who had been taking HRT for at least 1 year, and

- 1 • that risk increased with duration of use.

2 For past users of oestrogen-only HRT,

- 3 • the risk was not quite as high as in current users
4 • the risk of breast cancer was greater the longer they had used HRT
5 • the risk remained higher than for people who had never used HRT, up to at least
6 10 years after stopping use.

7 The committee agreed that it is important that people are aware of these facts so
8 that they can make an informed decision.

9 The committee also discussed the findings from the RCT evidence on oestrogen-
10 only HRT versus placebo. This evidence was not consistent with the observational
11 studies. It showed a reduced risk in the incidence of breast cancer for oestrogen-only
12 HRT users compared with people taking placebo. The committee noted that the
13 population of the RCT studies differed from that of the observational studies in that
14 the average age at starting HRT use was higher in the RCT (63 years, with an age
15 range of 50 to 79 years old) than in the observational studies (50 years), and a
16 greater proportion of women were overweight or obese in the RCT than in the
17 observational studies. The observational evidence found that the increased risk of
18 breast cancer in users of oestrogen-only HRT was relatively lower in those with
19 higher body mass index (not analysed for this guideline but based on committee
20 knowledge), and who started HRT at older ages. As a result, the differences in the
21 characteristics of the observational and RCT study populations could have
22 contributed to the difference in findings about oestrogen-only HRT between the two
23 study types.

24 The committee decided that they would put more weight on the observational
25 evidence to support their recommendations, as this was more reflective of the target
26 population.

27 Evidence also showed there was no difference between:

- 28 • oestradiol or conjugated equine oestrogen
29 • transdermal or oral routes of administration.

1 The committee therefore decided that people should be aware of this.

2 **How the recommendations might affect practice**

3 It is usual practice to inform people of the risks associated with a treatment option.

4 While the content of this information has changed compared to the previous
5 guideline, it is unclear how this will change the treatment choices made and how this
6 will impact on practice.

7 [Return to recommendation](#)

8 **Cancer: endometrial**

9 [Recommendations 1.6.1](#) and endometrial cancer rows in [table 1: effect of combined](#)
10 [HRT on health outcomes](#), and [table 2: effect of oestrogen-only HRT on health](#)
11 [outcomes](#)

12 **Why the committee made the recommendations**

13 The committee discussed the evidence from randomised controlled trials (RCTs) and
14 observational studies. They noted that the evidence from RCTs was uncertain
15 because, often, no or few cases of endometrial cancer were observed in any of the
16 study groups and some studies:

- 17 • used very low doses of progestogens (which may not be effective to prevent
18 endometrial cancer) or
- 19 • did not divide by continuous combined and sequential combined HRT, even
20 though this is an important consideration in the context of endometrial cancer, or
- 21 • included women without a uterus, and therefore no endometrium, meaning that
22 these participants could not develop endometrial cancer.

23 The committee therefore focused mainly on the evidence from observational studies.

24 **Combined HRT**

25 The evidence showed a reduced risk of endometrial cancer in:

- 26 • current users of continuous combined HRT, with any duration of use and
- 27 • in current users of all combined HRT with less than 5 years of use.

1 The committee agreed that progestogens counteract the adverse effect of
2 oestrogens on the endometrium, and this occurs in a dose-dependent manner. As a
3 result, they concluded that [continuous combined HRT](#), where a progestogen is taken
4 every day with oestrogen, decreases the risk of developing endometrial cancer.

5 The committee discussed the evidence, which showed that [sequential combined](#)
6 [HRT](#), when used for over 10 years, increases the risk of endometrial cancer. Based
7 on their own knowledge and experience, they were also aware that, in a sequential
8 combined preparation, the protective effect of progestogen increases with the
9 number of days on which progestogen is added to oestrogen every month. They
10 decided to highlight the different elements of sequential preparation that affect the
11 risk of endometrial cancer (duration of use, days of progestogen per cycle, and
12 higher oestrogen dose). They noted that, overall, this corresponded to an absolute
13 risk that they considered to be small, hence the wording 'may slightly increase'.

14 There was insufficient evidence about whether the impact of combined HRT on
15 endometrial cancer varied by type of progestogen so the committee made a
16 [research recommendation](#) to address this.

17 **Oestrogen-only HRT**

18 The committee discussed the evidence on oestrogen-only HRT versus no HRT in
19 people with a uterus. It shows that the risk of endometrial cancer is increased in:

- 20 • current oestrogen-only HRT users and
- 21 • for all (past and current) oestrogen-only HRT users who have used HRT for over
22 10 years.

23 This increase in risk was present regardless of the route of administration (oral or
24 transdermal).

25 The committee discussed the well-established association of oestrogen-only HRT
26 and risk of endometrial cancer. They recommended explaining to people that this is
27 why they would be offered combined HRT (see [recommendation 1.5.5 in the section](#)
28 [on starting HRT](#)).

How the recommendations might affect practice

It is current practice that combined preparations are prescribed to people with a uterus who wish to take HRT for menopause symptoms. The recommendations will standardise the information that will be given so that risks are discussed with people when treatment options are considered. But it is unclear how this might affect overall treatment choices related to taking HRT for menopause symptoms.

[Return to recommendation](#)

Cancer: ovarian

[Recommendations 1.6.1](#) and ovarian cancer rows in [table 1: effect of combined HRT on health outcomes](#), and [table 2: effect of oestrogen-only HRT on health outcomes](#)

Why the committee made the recommendation

The committee discussed the evidence from randomised control trials (RCTs) as well as from observational studies. Overall, the evidence showed that the risk of ovarian cancer:

- was higher in those who had been taking HRT for at least 5 years
- increased with duration of HRT use.

They agreed that, although the risk was increased overall, the risk was small in absolute terms, especially with the low baseline risk of ovarian cancer. The increase was 1 in 1,000 people for combined HRT and 3 in 1,000 for oestrogen-only HRT, when used over 10 years. The committee therefore agreed that all of this should be explained when HRT is being considered.

How the recommendations might affect practice

It is current practice that risks are discussed with people when treatment options are considered. The recommendations will standardise the information that will be given. But it is unclear how this affects treatment choices.

[Return to recommendation](#)

Cardiovascular disease

[Recommendations 1.6.1 and 1.6.2](#) and coronary heart disease and stroke rows in [table 1: effect of combined HRT on health outcomes](#), and [table 2: effect of oestrogen-only HRT on health outcomes](#)

Why the committee made the recommendations

The committee based their recommendations on the evidence as well as on their expertise. The evidence included randomised controlled trials (RCTs) and observational studies. Some evidence came from studies that aimed to find out whether HRT alters the risk of cardiovascular disease events after menopausal women with a history of cardiovascular disease. Other evidence looked at cardiovascular events as one overall health outcome in women who use HRT for troublesome symptoms associated with the menopause.

Coronary heart disease

People with no history of coronary heart disease

Findings from the RCT evidence varied. In one RCT, the pattern of evidence was inconsistent: there was a reduced risk of coronary heart disease for women starting HRT aged 50 to 59 but not for those starting HRT in other age groups. Some other RCT evidence showed an increased risk of coronary heart disease in current users who had been taking continuous combined HRT for less than 1 year, and an increased risk for combined cardiac events in current users taking continuous combined HRT for 1 to 4 years.

In contrast to this, the committee noted that observational evidence consistently showed an overall decrease in coronary heart disease risk in current users of either oestrogen-only or combined HRT.

The committee agreed that it is unclear how much the observational findings may have been influenced by residual confounding factors such as sociodemographic, smoking, prior morbidities or other factors which may be related to HRT use and cardiovascular risk.

While confounding is a potential source of bias in all observational studies, the likely impact of confounding on any given association will vary depending on:

- the strength of the association of potential confounders with both HRT and the outcome of interest, and
- how reliably such confounders are measured.

Based on the committee's knowledge, previous studies have found that HRT users differ from people not using HRT in terms of sociodemographic factors, BMI, and other behavioural factors such as smoking and physical activity. Some of these factors (such as BMI) are, at most, moderately associated with most health outcomes considered in this guideline (such as breast cancer risk), but many have more substantial effects on cardiovascular disease (such as social factors, education, smoking and BMI). For this reason, the scope for residual confounding of associations of HRT with cardiovascular disease is likely to be much greater than it is for associations of HRT with other health outcomes (for example, breast cancer). On this basis, the committee decided that assessment of the evidence for the association of HRT with cardiovascular diseases should give relatively more weight to RCT evidence, particularly where the findings from observational studies and RCTs are qualitatively different.

Given that the majority of the RCT and observational evidence both showed that the risk of coronary heart disease was not increased, the committee agreed that this conclusion should be shared with people to allow them to make an informed decision.

Mortality related to coronary heart disease

The evidence showed that, for people with no history of coronary heart disease, there was no increase in mortality from cardiovascular disease from taking HRT and the committee agreed that it was important for people to know this to make an informed choice.

Stroke

People experiencing menopause who do not have a history of stroke

Evidence from RCTs showed that, overall, there is an increased risk of stroke in people currently taking either combined HRT with oral oestrogen or oral oestrogen-only HRT. Observational evidence concurs. The committee noted that national statistics show that the baseline risk for stroke in women under 60 is very low. They

1 agreed that this should be explained to anyone considering HRT because the risk
2 may remain small despite any change in risk.

3 Combined HRT

4 Evidence showed a significant difference in risk depending on the mode of
5 administration. Combined HRT does not increase the risk of stroke when the
6 oestrogen component is taken transdermally, but it does increase the risk if taken
7 orally. The committee decided that it was important to note this so that it could be
8 taken into consideration.

9 Evidence on oral oestrogen doses , when compared with not taking HRT , showed:

- 10 • an increased risk of stroke in people taking continuous combined HRT when the
11 oestrogen dose was high, and
- 12 • no important difference in risk when the oestrogen dose was lower.

13 RCT evidence on duration of use showed that:

- 14 • the risk did not increase when HRT was used for up to 4 years but
- 15 • an increased risk of stroke when combined HRT was taken for 5 to 9 years.

16 Evidence related to age at starting combined HRT containing oral oestrogen also
17 showed greater risk of stroke in people currently taking HRT that increased with age,
18 with the risks not being significant in those aged 50 to 59 (with considerable
19 uncertainty around the size of the effect), significantly increased in those between 60
20 and 69, and a higher risk in people 70 to 79. This was when HRT was taken for 5 to
21 9 years.

22 RCT evidence showed significant differences in risk of stroke depending on ethnicity.
23 Among combined HRT users, the risk of stroke was greater in people from a black
24 family background compared to others, though numbers of cases in all ethnic
25 minority groups were small. Because of the small size of the population, the test was
26 not very robust, so the committee expressed uncertainty about the conclusion by
27 saying that the risk 'may be greater' (rather than 'is greater') for Black people. The
28 committee agreed that all of this should be explained to help the person reach a
29 decision.

Oestrogen-only HRT

Evidence showed that transdermal oestradiol did not increase the risk of stroke whereas oral oestradiol did. The committee noted that this was consistent with the pattern in combined HRT. They agreed that this should be explained so that people can factor this into their decision-making process.

The evidence showed an increased risk of stroke when oestrogen-only HRT was given at a high dose while, at low and middle doses, there was no increase in risk for oestrogen-only HRT compared to no HRT. Risk was also increased in people currently taking oestrogen-only HRT who had been taking it for 5 to 9 years when they had been aged 60 years or more at first HRT use. The committee decided that both of these points should feature in the shared decision-making discussion.

Preventing coronary heart disease and stroke

Given the findings about the effect of HRT on coronary heart disease and stroke, the committee agreed that the evidence did not support taking combined or oestrogen-only HRT for primary or secondary prevention of cardiovascular disease.

Research recommendation

There was insufficient evidence to conclude whether one type of progestogen in combined HRT differed to another in its impact on cardiovascular disease. The committee therefore prioritised this for a [research recommendation](#).

The committee noted that there was little evidence for people from ethnic minority family background for cardiovascular health and stroke (as well as all other health outcomes), so they made an overarching [recommendation for research](#) to address this.

How the recommendations might affect practice

It is usual practice to inform people of the risks associated with a treatment option. While the content of this information has changed compared to the previous guideline, it is unclear how this will change the treatment choices made and how this will impact on practice. It is possible that the recommendations may increase transdermal administration of HRT since this was not associated with an increased risk of stroke.

It is unclear whether it is current practice to use HRT for the specific purpose of primary or secondary coronary heart disease prevention in current practice. So, the related recommendation will standardise practice.

[Return to recommendations](#)

Dementia

[Recommendations 1.6.1 and 1.6.3](#) and dementia rows in [table 1: effect of combined HRT on health outcomes](#), and [table 2: effect of oestrogen-only HRT on health outcomes](#)

Why the committee made the recommendations

The committee noted that there was relatively little evidence compared to other health outcomes, with only 7 studies identified. They acknowledged that most of the evidence was from observational studies and therefore adjustments for various confounders needed to be carefully considered.

The committee agreed that some of the evidence did not make the necessary adjustments for confounding factors, such as socioeconomic status, or did not reliably ascertain incidence of dementia.

To guide their discussions and support their recommendations, the committee agreed to focus on an observational study from the UK and one from Denmark (which both made the most appropriate adjustments for confounders), as well as on the Women's Health Initiative Memory Study (WHIMS) of women starting HRT over the age of 65, which is based on data from a randomised controlled trial (RCT) from the Women's Health Initiative (WHI).

Combined HRT

The committee agreed that the evidence from the two observational studies was inconsistent:

- One study showed no difference in risk of dementia between combined HRT use and no HRT, with different durations of use.
- The other study showed an increase in incidence of dementia with combined HRT use when compared to no HRT, and the risk increased with duration of use.

1 The committee agreed that although both studies adjusted for many relevant
2 confounders, neither adjusted for all. They concluded that the evidence might be at
3 risk of bias from confounding.

4 They noted that the evidence was for all types of dementia. The risk for some types
5 of dementia may be different to others, and the proportion of each type identified at
6 follow-up may differ for each study. The committee thought this may explain some of
7 the differences in risk.

8 Evidence from the WHIMS on combined HRT compared to placebo was inconsistent
9 with the observational evidence from the UK, but in line with that from Denmark
10 (showing an increased risk in dementia in the HRT group). In the WHIMS study ,
11 participants were aged 65 or over when they started HRT, which is older than typical
12 users of HRT. The committee was not unanimous in its interpretation of the evidence
13 and how to formulate a recommendation best reflecting the evidence base. Part of it
14 had concerns about highlighting a risk of dementia when evidence from a UK setting
15 showed no difference in risk.

16 However, the committee reached a majority decision. Taking all evidence into
17 account, they decided the evidence pointed towards a possible increased risk in
18 dementia incidence, particularly with results showing increased risk when started at
19 a later age. They agreed it was important that people considering HRT for
20 troublesome menopause symptoms should be made aware of the potential risk, so
21 that they could make an informed decision.

22 As part of this, the committee:

- 23 • chose to use the word 'might' to express uncertainty, given the differences
24 between study results
- 25 • agreed that it was important to highlight, based on WHIMS evidence, that one of
26 the situations in which studies showed an increase in risk was when the start age
27 of HRT was over 65.

Oestrogen-only HRT

The observational evidence showed no significant differences in dementia risk when comparing oestrogen-only HRT with no HRT use. The evidence from WHIMS also showed no significant differences for incidence of dementia, between oestrogen-only HRT users and placebo users.

The committee discussed some of the limitations in the WHIMS study, such as the low incidence rate of dementia in the placebo arm, which was lower than the incidence of dementia in the UK. They also noted that the population was slightly different from typical users of HRT, in that they first started using HRT at a age of 65 or over. The committee agreed that, for this age group, indications for HRT were less likely to be menopause symptoms, and more likely to be the prevention of other diseases.

Dementia prevention

The committee noted the scope of this guideline and agreed that the indication for HRT prescriptions in the UK was menopause symptoms and therefore the aim of the included studies was not dementia prevention. However, they also agreed that there may be a misconception that HRT protects against dementia. They agreed it was important to highlight that the evidence did not support this and recommended not to offer HRT to prevent dementia.

Research recommendations

The committee noted that there are still uncertainties and further research is needed to add to the current evidence base. They noted that the previous guideline included a [research recommendation](#) related to dementia and decided to keep this.

How the recommendations might affect practice

When making treatment choices, it is common practice to inform people of the benefits and risks associated with a treatment option. The recommendations standardise the information that will be provided but it is unclear what the resulting treatment choices may be. They are therefore not expected to change current clinical practice significantly.

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Effects of HRT on health outcomes in early menopause

[Recommendations 1.6.4](#)

Why the committee made the recommendations

Apart from evidence related to breast cancer, no other evidence on the benefits and risks of either taking or not taking hormone replacement therapy (HRT) on any health outcomes was identified for people experiencing early menopause. For people with premature ovarian insufficiency, HRT is offered for bone health and fracture prevention (because oestrogen helps maintain bone density) as well as cardiovascular health (because oestrogen is known to maintain vascular function). No evidence was identified relating to the benefits and risks of either taking or not taking HRT on these outcomes in people experiencing early menopause. The committee agreed that it was important to highlight the lack of evidence and also made a [recommendation for research](#) to address it. The committee did not look at evidence on the potential impact of early menopause on health outcomes and how to manage it.

The committee agreed that, to a certain extent, the role of HRT for early menopause mirrors the role of HRT for premature ovarian insufficiency. The committee considered the possibility that, like premature ovarian insufficiency, early menopause may either increase or decrease the baseline risk of some health outcomes. Although there is little evidence of the impact of HRT on health outcomes in people with premature ovarian insufficiency, it is current practice for this group to take HRT routinely. The committee acknowledged that the situation is similar for early menopause, with routine HRT being current practice. Hormone therapy might reverse some of the alterations to baseline risk of health outcomes in people with early menopause, but the committee did not review evidence on this. The committee agreed that a person's age at the onset of menopause symptoms is one important factor to take into account in HRT discussions (see [section on discussing treatment options](#)).

The committee agreed that the age cut-offs defining premature ovarian insufficiency, early menopause and typical menopause were somewhat arbitrary. They also agreed that, for people with early menopause, the benefits and risks of either taking

or not taking HRT lie somewhere between those for people with premature ovarian insufficiency and those for people aged 45 or over (for whom there is more evidence about these benefits and risks). Evidence showed an increased risk of breast cancer for people with early menopause who used HRT compared to those not using HRT.

The committee decided that it was important to explain this to people.

The committee thought that their conclusion from the available evidence could be extended to trans men and non-binary people registered female at birth who have never taken cross-sex hormones as gender-affirming therapy. But they did not think they could be extended to those who have taken cross-sex hormones as gender-affirming therapy in the past, because it is not known whether having taken such therapy would alter the benefits and risks of any treatment (especially hormonal treatments), or which treatment option might be best for the person.

How the recommendations might affect practice

While recommendations in this area will lead to people being better informed about treatment decisions they make, it is unclear how such information will change the treatment decisions made and how these will impact overall resource use. It would however be unethical to prevent such information being discussed with patients even if it did lead to an increase in resource use.

[Return to recommendations](#)

Context

Since the previous version of this guideline was published, new evidence that could affect recommendations was identified through NICE's surveillance process. Full details are set out in the [surveillance review decisions from 2019](#) and [2021](#).

Menopause is the point at which menstrual cycles stop. Menopause usually occurs naturally in women, and in some non-binary and trans people, when they are aged 45 to 55. The duration of the process varies, but typically lasts for a few years.

Based on evidence, 3% to 8% of people experiencing menopause are estimated to have early menopause (menopause transition starting between 40 and 44 years), and 1% to have premature ovarian insufficiency (menopause transition starting

before 40 years). Sometimes menopause is caused by surgical removal of the ovaries before natural menopause has occurred.

Menopause can affect people in a variety of ways. Most experience some symptoms, although not everyone seeks medical treatment. Some people have troublesome symptoms that may significantly impact their daily life, and they need treatment. Menopause symptoms may last for a long time, with a median duration of 7 years. Common symptoms associated with menopause are vasomotor symptoms (hot flushes and night sweats) and vaginal dryness.

In 2019 the Medicines and Healthcare products Regulatory Agency (MHRA) published a drug safety update on hormone replacement therapy based on the [Collaborative Group on Hormonal Factors in Breast Cancer's 2019 meta-analysis of type and timing of menopausal hormone therapy and breast cancer risk](#). Some of the conclusions on risk of breast cancer differ from the conclusions of the 2015 NICE guideline (NG23). Therefore, a review of new evidence is warranted. More information about this is provided in the [2019 surveillance of menopause: diagnosis and management \(NICE guideline NG23\)](#).

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the [NICE webpage on menopause](#).

For details of the guideline committee see the [committee member list](#).

Update information

This guideline is an update of NICE guideline NG23 (published November 2015).

We have reviewed the evidence on genitourinary symptoms, cardiovascular disease and stroke, breast cancer, endometrial cancer, ovarian cancer, dementia, all-cause mortality and early menopause (age 40 to 44).

Recommendations are marked **[2023]** if the evidence has been reviewed.

Recommendations that have been deleted, or changed without an evidence review

We propose to delete some recommendations from the 2015 guideline. Table 3 sets out these recommendations and includes details of replacement recommendations. If there is no replacement recommendation, an explanation for the proposed deletion is given.

For recommendations shaded in grey and ending **[2015, amended 2023]**, we have made changes that could affect the intent without reviewing the evidence. Yellow shading is used to highlight these changes, and reasons for the changes are given in table 4.

For recommendations shaded in grey and ending **[2015]**, we have not reviewed the evidence. In some cases, minor changes have been made – for example, to update links, or bring the language and style up to date – without changing the intent of the recommendation. Minor changes are listed in table 5.

See also the [previous NICE guideline and supporting documents](#).

Table 3 Recommendations that have been deleted

Recommendation in 2015 guideline	Comment
1.4.1 Adapt a woman's treatment as needed, based on her changing symptoms.	This has now been incorporated in recommendation 1.1.1
Cognitive behaviour therapy (CBT)	
1.4.6 Consider CBT to alleviate low mood or anxiety that arise as a result of the menopause.	Replaced by: 1.4.9 Consider CBT for troublesome vasomotor, difficulties with sleep or depressive symptoms associated with the menopause in trans men and non-binary people registered female at birth who have taken cross-sex hormones as gender-affirming therapy in the past. [2023] 1.4.16 Consider CBT for troublesome vasomotor symptoms associated with the menopause. [2023] 1.4.18 For people experiencing menopause and depression, take into

	<p>account recommendations on both to achieve an optimal treatment plan. See NICE's guideline on treating and managing depression in adults. [2023]</p> <p>1.4.37 Consider CBT for difficulties with sleep associated with the menopause (such as nighttime awakening). [2023]</p>
Urogenital atrophy	Genitourinary menopause symptoms
1.4.9 Offer vaginal oestrogen to women with urogenital atrophy (including those on systemic HRT) and continue treatment for as long as needed to relieve symptoms.	<p>Replaced by:</p> <p>1.4.19 Offer a choice of vaginal oestrogen preparations (oestrogen cream, gel, tablet, pessary or ring) to people with troublesome genitourinary menopause symptoms (including those on systemic HRT) and continue treatment for as long as needed to relieve symptoms. [2023]</p>
1.4.10 Consider vaginal oestrogen for women with urogenital atrophy in whom systemic HRT is contraindicated, after seeking advice from a healthcare professional with expertise in menopause.	<p>Replaced by:</p> <p>1.4.23 Consider non-hormonal vaginal moisturisers and lubricants for people with troublesome genitourinary menopause symptoms in whom vaginal oestrogen preparations are contraindicated or who would prefer not to take vaginal oestrogen. [2023]</p>
1.4.11 If vaginal oestrogen does not relieve symptoms of urogenital atrophy, consider increasing the dose after seeking advice from a healthcare professional with expertise in menopause.	<p>Replaced by:</p> <p>1.4.21 If vaginal oestrogen does not relieve troublesome genitourinary menopause symptoms, consider increasing the dosage, within the standard therapeutic range, after seeking advice from a healthcare professional with expertise in menopause. [2023]</p>
<p>1.4.12 Explain to women with urogenital atrophy that:</p> <ul style="list-style-type: none"> • symptoms often come back when treatment is stopped • adverse effects from vaginal oestrogen are very rare • they should report unscheduled vaginal bleeding to their GP. 	<p>Replaced by:</p> <p>1.4.20 When discussing the option of vaginal oestrogen with a person with troublesome genitourinary menopause symptoms, explain that:</p> <ul style="list-style-type: none"> • adverse effects are very rare (see advice from the 2019 Medicines and Healthcare products Regulatory

	<p>Agency [MHRA] drug safety update on hormone replacement therapy)</p> <ul style="list-style-type: none"> • symptoms often return when treatment is stopped • some oestrogen is absorbed but, compared with systemic HRT, the amount is small • if they choose this option, they should report vaginal bleeding to their GP. [2023]
1.4.13 Advise women with vaginal dryness that moisturisers and lubricants can be used alone or in addition to vaginal oestrogen.	Replaced by: 1.4.32 Advise people with vaginal dryness associated with the menopause that moisturisers and lubricants can be used alone or in addition to vaginal oestrogen. [2023]
1.4.14 Do not offer routine monitoring of endometrial thickness during treatment for urogenital atrophy.	Deleted – there was no evidence that was looked for in relation to this.
Cardiovascular disease	
1.5.4 Ensure that menopausal women and healthcare professionals involved in their care understand that HRT:	<p>Replaced by the following statements in table 1 and table 2, respectively:</p> <p>Combined HRT does not increase mortality from cardiovascular disease. [2023]</p> <p>Oestrogen-only HRT does not increase mortality from cardiovascular disease. [2023]</p>
1.5.5 Be aware that the presence of cardiovascular risk factors is not a contraindication to HRT as long as they are optimally managed.	Replaced by: 1.4.13 For people with a history of coronary heart disease or stroke, ensure that combined or oestrogen-only HRT is discussed with and, if appropriate, initiated by a healthcare professional with expertise in menopause. [2023]
1.5.6 Using tables 1 and 2, explain to women that:	<p>1.6.2 Do not offer combined or oestrogen-only HRT for primary or secondary prevention of cardiovascular disease. For ways to prevent cardiovascular disease (for example, lifestyle changes), refer to NICE's guideline on cardiovascular disease: risk assessment and reduction, including lipid modification. [2023]</p> <p>Replaced by the following statements in table 1 and table 2, respectively:</p>

	<p>Combined HRT does not increase the risk of coronary heart disease. [2023]</p> <p>Oestrogen-only HRT does not increase the risk of coronary heart disease. [2023]</p>
<p>1.5.7 Explain to women that taking oral (but not transdermal) oestrogen is associated with a small increase in the risk of stroke. Also explain that the baseline population risk of stroke in women aged under 60 years is very low (see table 2).</p>	<p>Replaced by the following statements in table 1:</p> <p>The baseline population risk of stroke in women under 60 is very low. [2023]</p> <p>Combined HRT containing oral oestrogen increases the risk of stroke and the increase:</p> <ul style="list-style-type: none"> • rises with higher oestrogen doses and longer duration of treatment, for example, if used for more than 5 years • is greater with increasing age at first starting HRT • differs between ethnic groups and may be greater in black people. <p>(see Appendix A, table 13, for the number of stroke cases per 1,000 people over a 5-year period). [2023]</p> <p>Combined HRT with transdermal oestrogen is unlikely to increase the risk of stroke when the oestrogen is given at a standard therapeutic dosage (see table 13 from appendix A for the number of stroke cases per 1,000 people over a 5-year period). [2023]</p> <p>Replaced by the following statements in table 2:</p> <p>The baseline population risk of stroke in women under 60 is very low. [2023]</p> <p>Taking oral oestrogen-only HRT increases the risk of stroke and the increase:</p>

	<ul style="list-style-type: none"> • rises with the dose of oestrogen • is greater if HRT is started after the age of 60 <p>(see Appendix A, table 13, for the number of stroke cases per 1,000 people over a 5-year period).. [2023]</p> <p>Transdermal oestrogen-only HRT is unlikely to increase the risk of stroke when given at standard therapeutic doses (see Appendix A, table 13, for the number of stroke cases per 1,000 people over a 5-year period). [2023]</p> <p>1.4.13 For people with a history of coronary heart disease or stroke, ensure that combined or oestrogen-only HRT is discussed with and, if appropriate, initiated by a healthcare professional with expertise in menopause. [2023]</p>
Breast cancer	
<p>1.5.11 Using the MHRA risk table, explain to women around the age of natural menopause that:</p> <ul style="list-style-type: none"> • the baseline risk of breast cancer for women around menopausal age varies from one woman to another according to the presence of underlying risk factors • HRT with oestrogen alone is associated with little or no change in the risk of breast cancer • HRT with oestrogen and progestogen can be associated with an increase in the risk of breast cancer • any increase in the risk of breast cancer is related to treatment duration and reduces after stopping HRT. 	<p>Replaced by the following statements in table 1:</p> <p>The risk of breast cancer varies depending on a person's modifiable and non-modifiable risk factors (see lifestyle-related risk factors in NICE's guideline on early and locally advanced breast cancer and recommendation 1.7.1 in NICE's guideline on familial breast cancer). [2023]</p> <p>Combined HRT increases the risk of breast cancer risk compared to not taking HRT and:</p> <ul style="list-style-type: none"> • the increase rises with duration of use • the increase is higher in current users than in past users • the increase declines after stopping but persists at least 10 years after stopping use <p>there is a very small increase in risk of death from breast cancer. [2023]</p> <p>Use Appendix A, tables 1 and 2, for the number of breast cancer cases per 1,000 people taking combined HRT over a 5- or 10- year period.[2023]</p>

	<p>It is not known whether preparations containing micronised progesterone or dydrogesterone have a different increased risk for breast cancer compared with preparations containing other progestogens. [2023]</p> <p>Combined HRT preparations containing transdermal oestrogen increase the risk of breast cancer less than combined HRT preparations containing oral oestradiol. [2023]</p> <p>Replaced by the following statements in table 2:</p> <p>The risk of breast cancer varies depending on a person's modifiable and non-modifiable risk factors (see lifestyle-related risk factors in NICE's guideline on early and locally advanced breast cancer and recommendation 1.7.1 in NICE's guideline on familial breast cancer). [2023]</p> <p>Oestrogen-only HRT slightly increases the risk of breast cancer compared to not taking HRT and the increase:</p> <ul style="list-style-type: none"> • rises with longer duration of use • is greater in current users than in past users <p>declines after stopping but persists for at least 10 years after stopping use. [2023]</p> <p>Use Appendix A table 3 and 4, for the number of breast cancer cases per 1,000 people taking oestrogen-only HRT over a 5- or 10-year period. [2023]</p> <p>There is no difference in the increase of breast cancer risk between oestradiol and conjugated equine oestrogen when given at standard therapeutic doses. [2023]</p> <p>There is no difference in the increase of breast cancer risk between transdermal and oral oestrogen. [2023]</p>
Dementia	

1.5.15 Explain to menopausal women that the likelihood of HRT affecting their risk of dementia is unknown.	<p>Replaced by the following statements in tables 1 and 2:</p> <p>Combined HRT may increase risk of dementia if started over the age of 60. [2023]</p> <p>Oestrogen-only HRT is unlikely to increase the risk of dementia. [2023]</p> <p>1.6.3 Do not offer HRT for the purpose of dementia prevention. For dementia prevention, see NICE's guideline on dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset. [2023]</p>
Research recommendations	
What is the difference in the risk of breast cancer in people in menopause on HRT with progesterone, progestogen or selective oestrogen receptor modulators?	This was deleted because it was essentially the same as another research recommendation.
How does the preparation of HRT affect the risk of venous thromboembolism (VTE)?	It is stated in the guideline that the risk with HRT is increased so it is unclear why further research would show a different pattern.
What are the effects of early HRT use on the risk of dementia?	This has been revised to: What are the effects of HRT use on the risk of dementia?

1 **Table 4 Amended recommendation wording (change to intent) without an**
2 **evidence review**

Recommendation in 2015 guideline	Recommendation in current guideline	Reason for change
<p>1.2.8 Offer people with troublesome menopause symptoms who have a personal history or high risk of breast cancer:</p> <ul style="list-style-type: none"> information on all available treatment options information that the SSRIs paroxetine and fluoxetine should not be offered to people with breast cancer who are taking tamoxifen referral to a healthcare professional with 	<p>1.2.9 Offer people with troublesome menopause symptoms who have a personal history or high risk of breast cancer:</p> <ul style="list-style-type: none"> information on all available treatment options referral to a healthcare professional with expertise in menopause. [2015] 	<p>SSRIs are not recommended in this guideline and the bullet could therefore cause confusion. The caution around tamoxifen is part of the Summary of Product Characteristic (SmPC) for these SSRIs. Therefore, it is assumed that healthcare professionals follow this guidance and this information does</p>

expertise in menopause. [2015]		not need to be repeated.
1.4.7 Consider HRT to alleviate low mood that arises as a result of the menopause.	1.4.34 Consider HRT to alleviate mild depressive symptoms with onset in association with other menopausal symptoms.	<p>The wording was revised to bring it in line with the NICE guideline on depression in adults: treatment and management.</p> <ul style="list-style-type: none"> • The category 'menopausal women with low mood' includes 'women with less severe depression that may not be caused by the menopause' • 'Women with less severe depression that may not be caused by the menopause' are covered by NG222 Depression in adults, not by NG23 Menopause • In NG222 the category 'less severe depression' includes people who feel themselves to be experiencing depression or depressive symptoms, even if they lack a clinical diagnosis of depression
1.4.7 Ensure that menopausal women and healthcare professionals involved in their care understand that there is no clear evidence for SSRIs or SNRIs to ease low mood in	It is proposed to stand this recommendation down.	This recommendation is inconsistent with the NICE guideline on depression in adults: treatment and

<p>menopausal women who have not been diagnosed with depression (see the NICE guideline on depression in adults: treatment and management)</p>		<p>management, because:</p> <ul style="list-style-type: none"> • The category 'menopausal women with low mood' includes 'women with less severe depression that may not be caused by the menopause' • 'Women with less severe depression that may not be caused by the menopause' are covered by NG222 Depression in adults, not by NG23 Menopause • In NG222 the category 'less severe depression' includes people who feel themselves to be experiencing depression or depressive symptoms, even if they lack a clinical diagnosis of depression • NG222 allows SSRIs as a second-line treatment for 'less severe depression'. • The link to the Depression guideline is now included in another recommendation.
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1 Table 5 Minor changes to recommendation wording (no change to intent)

New rec number	Comment
All	Language refreshed for patient-centredness, inclusivity and clarity, changed to show that menopause is a normal part of life (not a condition), and aligned with other NICE guidelines that have been updated. Hyperlink style updated for accessibility where needed.
1.4.13	Second half of recommendation deleted because it is superseded by a 2023 recommendation.

2

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Appendix A Incidence of health outcomes with and without use of hormone replacement therapy (HRT)

People over 45

Cancer: breast

Combined HRT

Appendix A, table 1 Number of breast cancer cases with no use, current use and past use of combined HRT in people who, if they used it, started HRT at 50 and used it for 5 years

–	50–54 years old	55–59 years old	60–64 years old	65–69 years old	50–69 years old
Number of breast cancer cases over a 5-year period per 1,000 people who never used HRT	12	13	15	19	–
Number of breast cancer cases over a 5-year period per 1,000 people who started HRT at 50 and used it for 5 years	21 (current user)	16 (past user)	19 (past user)	23 (past user)	–
Cumulative number of breast cancer cases over a 20-year period per 1,000 people who never used HRT	–	–	–	–	59
Cumulative number of breast cancer cases over a 20-year period per 1,000 people who	–	–	–	–	79

started HRT at 50 and used it for 5 years					
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1
2 In table 1, based on age at starting (50 years old) and duration of use (5 years),
3 people aged 50 to 54 were current users of HRT at the time the data was collected,
4 and had used HRT for under 5 years.

5 **Appendix A, table 2 Number of breast cancer cases with no use, current use**
6 **and past use of combined HRT in people who, if they used it, started HRT at 50**
7 **and used it for 10 years**

–	50–54 years old	55–59 years old	60–64 years old	65–69 years old	50–69 years old
Number of breast cancer cases over a 5-year period per 1,000 people who never used HRT	12	13	15	19	–
Number of breast cancer cases over a 5-year period per 1,000 people who started HRT at 50 years old and used it for 10 years	21 (current user)	26 (current user)	20 (past user)	25 (past user)	–
Cumulative number of breast cancer cases over a 20-year period per 1,000 people who never used HRT	–	–	–	–	59
Cumulative number of breast cancer cases over a 20-year period per 1,000 people who	–	–	–	–	92

started HRT at 50 years old and used it for 10 years					
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1
2 In table 2, based on age at starting (50 years old) and duration of use (10 years),
3 people aged 50 to 59 were current users of HRT at the time the data was collected,
4 and had used HRT for under 10 years.

5 **Oestrogen-only HRT**

6 Appendix A, table 3 Summary of breast cancer cases with no use, current use and
7 past use of oestrogen-only HRT in people who, if they used it, started HRT at 50 and
8 used it for 5 years

–	50–54 years old	55–59 years old	60–64 years old	65–69 years old	50–69 years old
Number of breast cancer cases over a 5-year period per 1,000 people who never used HRT	12	13	15	19	–
Number of breast cancer cases over a 5-year period per 1,000 people who started HRT at 50 and used it for 5 years	14 (current user)	17 (past user) NS	16 (past user) NS	22 (past user)	–
Cumulative number of breast cancer cases over a 20-year period per 1,000 people who never used HRT	–	–	–	–	59
Cumulative number of breast cancer cases over a 20-year period per 1,000	–	–	–	–	69

people who started HRT at 50 and used it for 5 years					
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2 In table 3:

- 3 • NS means that the difference between a figure for HRT users and the
- 4 corresponding figure for non-HRT users is non-significant.
- 5 • Based on age at starting (50 years old) and duration of use (5 years), people aged
- 6 50 to 54 were current users of HRT at the time the data was collected, and had
- 7 used HRT for under 5 years.

8 **Appendix A, table 4 Summary of breast cancer cases with no use, current use**

9 **and past use of oestrogen-only HRT in people who, if they used it, started HRT**

10 **at 50 and used it for 10 years**

–	50–54 years old	55–59 years old	60–64 years old	65–69 years old	50–69 years old
Number of breast cancer cases over a 5-year period per 1,000 people who never used HRT	12	13	15	19	–
Number of breast cancer cases over a 5-year period per 1,000 people who started HRT at 50 and used it for 10 years	14 (current user)	16 (current user)	18 (past user)	23 (past user)	–
Cumulative number of breast cancer cases over a 20-year period per 1,000 people who never used HRT	–	–	–	–	59

Cumulative number of breast cancer cases over a 20-year period per 1,000 people who started HRT at 50 and used it for 10 years	–	–	–	–	71
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In table 4, based on age at starting (50 years old) and duration of use (10 years) , people aged 50 to 59 were current users of HRT at the time the data was collected, and had used HRT for under 10 years.

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Cancer: endometrial

Combined HRT

Appendix A, table 5 Number of endometrial cancer cases over a 5-year period per 1,000 people with no use or current use of combined HRT in people who, if they used it, started HRT at 50, with an unknown duration of use

Non-HRT users	4
Combined HRT (sequential) users	8
Combined HRT (continuous) users	4 NS

In table 5:

- NS means that the difference between the figure for HRT users and the corresponding figure for non-HRT users is non-significant.
- All people included in the figures are aged 50 years or over.
- Figures shown are number of cases per 1,000 people.

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Oestrogen-only HRT

Appendix A, table 6 Number of endometrial cancer cases over a 5-year period per 1,000 people with no use or current use of oestrogen-only HRT in people who, if they used it, started HRT at 50, with an unknown duration of use

Non-HRT users	4
Oestrogen-only HRT users	11

In table 6:

- All people included in the figures are aged 50 years or over.
- Figures shown are number of cases per 1,000 people.

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Cancer: ovarian

Combined or oestrogen-only HRT: 5 years of use

Appendix A, table 7 Number of ovarian cancer cases over a 5-year period per 1,000 people with no use or current use of combined or oestrogen-only HRT in people who, if they used it, started HRT at 50 and used it for 5 years

Non-HRT users	1
HRT users	1 NS

In table 7:

- NS means that the difference between the figure for HRT users and the corresponding figure for non-HRT users is non-significant.
- All people included in the figures are aged 50 to 54.
- Figures shown are number of cases per 1,000 people.

Combined HRT: 10 years of use

Appendix A, table 8 Number of ovarian cancer cases over a 10-year period per 1,000 people with no use or current use of combined HRT in people who, if they used it, started HRT at 50 and used it for 10 years

Non-HRT users	6
HRT users	7

In table 8:

- All people included in the figures are aged 50 to 59.
- Figures shown are number of cases per 1,000 people.

Oestrogen-only HRT: 10 years of use

Appendix A, table 9 Number of ovarian cancer cases over a 10-year period per 1,000 people with no use or current use of oestrogen-only HRT in people who, if they used it, started HRT at 50 and used it for 10 years

Non-HRT users	6
HRT users	9

In table 9:

- All people included in the figures are aged 50 to 59.
- Figures shown are number of cases per 1,000 people.

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Coronary heart disease

Appendix A, table 10 Number of coronary heart disease cases per 1,000 people over a 5-year period with no use or current use of combined HRT in people who, if they used it, started HRT at 50, and used it for 5 years

Non-HRT users	9
HRT users	10 NS

In table 10:

- NS means that the difference between the figure for HRT users and the corresponding figure for non-HRT users is non-significant.
- All people included in the figures are aged 50 years or over.
- Figures shown are number of cases per 1,000 people.

Appendix A, table 11 Number of coronary heart disease cases per 1,000 people over a 5-year period with no use or current use of oestrogen-only HRT in people who, if they use it, started HRT at 50, and used it for 5 years

Non-HRT users	9
HRT users	9 NS

In table 11:

- NS means that the difference between the figure for HRT users and the corresponding figure for non-HRT users is non-significant.
- All people included in the figures are aged 50 years or over.
- Figures shown are number of cases per 1,000 people.

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Dementia

Combined HRT

Appendix A, table 12 Number of dementia cases over a 4-year period per 1,000 people with no use or current use of combined HRT in people who, if they used it, started HRT at 65 or over and used it for 4 years

Non-HRT users	9
Combined HRT users	18

In table 11:

- All people included in the figures are aged 65 or over
- Figures shown are number of cases per 1,000 people

Oestrogen-only HRT

Appendix A, table 13: Number of dementia cases over a 5-year period per 1,000 people with no use or current use of oestrogen-only HRT in people who, if they used it, started HRT at 65 or over and used it for 5 years

Non-HRT users	13
Oestrogen-only HRT users	19 NS

In table 12:

- NS means that the difference between a figure for HRT users and the corresponding figure for non-HRT users is non-significant.
- All people included in the figures are aged 65 or over
- Figures shown are number of cases per 1,000 people

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Osteoporosis

Appendix A, table 14 Osteoporosis: Absolute rates of any fragility fracture for HRT compared with no HRT (or placebo), different durations of HRT use and

- 1 **time since stopping HRT for people in menopause. Difference in fragility**
- 2 **fracture incidence are shown per 1,000 people**

		Current HRT users	Treatment duration <5 years	Treatment duration 5–10 years	>5 years since stopping treatment
HRT users	RCT estimate	23 fewer (-10 to -33) Baseline population risk: 69 per 1,000 women (follow-up: 3.43 years).	25 fewer (-9 to -37) Baseline population risk: 78 per 1,000 women (follow-up: 3.71 years).	No available data	No available data
	Observational estimate	16 fewer (-15 to -18) Baseline population risk: 15.4 per 1,000 women (follow-up: 2.8 years).	15 fewer (-11 to -17) Baseline population risk: 15.4 per 1,000 women (follow-up: 2.8 years).	18 fewer (-15 to -20) Baseline population risk: 15.4 per 1,000 women (follow-up: 2.8 years).	2 more (-19 to 27) Baseline population risk: 106 per 1,000 women (follow-up: 5 years).

- 3 Notes For full source references, [see appendix M in the full guideline](#).

- 4 [Return to recommendation](#)

5 **Stroke**

- 6 **Appendix A, table 15 Number of stroke cases per 1,000 people over a 5-year**
- 7 **period with no use or current use of combined or oestrogen-only HRT in**
- 8 **people who, if they used it, started HRT at 50, with an unknown duration of use**

Non-HRT users	3
Combined (oral) HRT users	3
Combined (transdermal) HRT users	3 NS
Oestrogen-only (oral) HRT users	4

Oestrogen-only (transdermal) HRT users	3 NS
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In table 15:

- NS means that the difference between the figure for HRT users and the corresponding figure for non-HRT users is non-significant.
- The difference between the figure for combined (oral) HRT users and the corresponding figure for non-HRT users is significant but this is too small to be apparent when expressed per 1000 people.
- All people included in the figures are aged 50 years or over.
- Figures shown are number of cases per 1,000 people.

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People experiencing early menopause (ages 40 to 44)

Appendix A, table 16 Number of breast cancer cases with no use, current use and past use of combined HRT in people with early menopause (age 40–44) who, if they used it, started HRT at 40 and used it for 10 years

–	40–44 years old	45–49 years old	50–54 years old	55–59 years old	40–59 years old
Number of breast cancer cases over a 5-year period per 1,000 people who never used HRT	5	8	10	10	–
Number of breast cancer cases over a 5-year period per 1,000 people who started HRT at 40 and used it for 10 years	8 (current user)	18 (current user)	12 (past user)	13 (past user)	–

Cumulative number of breast cancer cases over a 20-year period per 1,000 people who never used HRT	–	–	–	–	33
Cumulative number of breast cancer cases over a 20-year period per 1,000 people who started HRT at 40 and used it for 10 years	–	–	–	–	51

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- 2 **Appendix A, table 17 Number of breast cancer cases with no use, current use**
3 **and past use of oestrogen-only HRT in people with early menopause (age 40–**
4 **44) who, if they used it, started HRT at 40 and used it for 10 years**

–	40–44 years old	45–49 years old	50–54 years old	55–59 years old	40–59 years old
Number of breast cancer cases over a 5-year period per 1,000 people who never used HRT	5	8	10	10	–
Number of breast cancer cases over a 5-year period per 1,000 people who started HRT at 40 and used it for 10 years	5 (current user)	10 (current user)	13 (past user)	13 (past user)	–
Cumulative number of breast cancer cases over a 20-year	–	–	–	–	33

period per 1,000 people who never used HRT					
Cumulative number of breast cancer cases over a 20-year period per 1,000 people who started HRT at 40 and used it for 10 years	–	–	–	–	41

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