BMJ 2015;351:h5746 doi: 10.1136/bmj.h5746 (Published 12 November 2015)

PRACTICE

GUIDELINES

Diagnosis and management of menopause: summary of NICE guidance

Grammati Sarri *senior research fellow and guideline lead*[1], Melanie Davies *clinical director, consultant gynaecologist*[2], Mary Ann Lumsden *professor of medical education and gynaecology, honorary consultant gynaecologist*[3], on behalf of the Guideline Development Group

[1]National Collaborating Centre for Women's and Children's Health, Royal College of Gynaecologists and Obstetricians, London NW1 4RG, UK; [2]National Collaborating Centre for Women's and Children's Health, Royal College of Gynaecologists and Obstetricians; University College London Hospitals, London, UK; [3]Reproductive and Maternal Medicine, University of Glasgow; Glasgow Royal Infirmary, Glasgow, UK

This is one of a series of *BMJ* summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

The average age of menopause in the United Kingdom is 51 years, although 1% of women experience premature ovarian insufficiency (menopause before the age of 40 years). Eight out of 10 women experience perimenopausal symptoms, most commonly hot flushes and night sweats (figure⇓), which typically last about four years.[1] Quality of life may be severely affected.[2]

Services and information available for menopausal women in the UK are variable.[3] The use of hormone replacement therapy has been highly controversial.[4 5]

This article summarises the most recent recommendations on the diagnosis and management of menopause from the National Institute for Health and Care Excellence (NICE).[6]

Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

Individualised care

- Adopt an individualised approach at all stages of diagnosis, investigation, and management of menopause. [*Based on the experience and opinion of the Guideline Development Group (GDG).*]

Diagnosis of menopause

- Diagnose menopause in otherwise healthy women aged over 45 years when:
  -They have not had a period for at least 12 months and are not using hormonal contraception, or
  -They do not have a uterus and do have menopausal symptoms (such as vasomotor, musculoskeletal, and urogenital symptoms; effects on mood; or sexual difficulties).

[*Based on very low to moderate quality evidence from observational studies and the experience and opinion of the GDG.*]

- Consider using a follicle stimulating hormone (FSH) test to diagnose menopause only in:
  -Women aged 40-45 years with menopausal symptoms (including a change in their menstrual cycle) or in women under 40 years in whom menopause is suspected, and
  -Only if they are not taking combined oestrogen and progestogen contraception or high dose progestogens.

[*Based on low to moderate quality evidence from observational studies and the experience and opinion of the GDG.*]

Information and advice

- Give information that includes:
  -An explanation of the stages of menopause (perimenopausal or postmenopausal)
  -Common symptoms and diagnosis

Correspondence to: G Sarri gsarri@rcog.org.uk

What you need to know

- Menopause is a clinical diagnosis in healthy women over 45 years who have not had a period for at least 12 months and are not using hormonal contraception, or who do not have a uterus and have menopausal symptoms
- For vasomotor symptoms, offer hormone replacement therapy (HRT) after discussing the short term and longer term benefits and risks (box); prescribe oestrogen and progestogen to women with a uterus, and oestrogen alone to women without a uterus
- Advise women to report unscheduled vaginal bleeding in the first three months of HRT use (a common side effect) at routine review, but to report such bleeding promptly if it occurs after three months

What's new in this guidance

- Twenty five percent of women have severe menopausal symptoms, which can seriously affect a woman's quality of life. Millions of women worldwide now live 30-40% of their lives after the menopause.
- HRT is the most effective treatment for the relief of vasomotor symptoms although other options, including non-pharmacological ones, are available.
- For most symptomatic, menopausal women, the benefits of HRT outweight the risks
- Any increase in risk of breast cancer, experienced with some HRT preparations, disappears once HRT is stopped

-Lifestyle changes and interventions that could help general health and wellbeing, such as smoking cessation, exercise and dietary advice, screening for breast and cervical cancer

-Benefits and risks of hormonal, non-hormonal, and non-pharmacological treatments for menopausal symptoms

-Contraception

-Long term health implications of menopause, such as osteoporosis.

[*Based on very low to low quality evidence from qualitative studies and the experience and opinion of the GDG.*]

- Offer women who are likely to go through menopause as a result of medical or surgical treatment support and information about menopause and fertility. [*Based on very low to low quality evidence from qualitative studies and the experience and opinion of the GDG.*]

Managing short term menopausal symptoms

Vasomotor symptoms

- Offer hormone replacement therapy (HRT) after discussing the short term (up to five years) and longer term benefits and risks (box). Offer a choice of preparations as follows:

  -Oestrogen and progestogen to women with a uterus

  -Oestrogen alone to women without a uterus.

[*Based on low to moderate quality evidence from randomised studies in the network and health economic analysis and the experience and opinion of the GDG.*]

- Do not routinely offer selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine (noradrenaline) reuptake inhibitors (SNRIs), or clonidine as first line treatment for vasomotor symptoms alone. [*Based on low to moderate quality evidence from randomised studies in the network and health economic analysis and the experience and opinion of the GDG.*]
- Explain that there is some evidence that isoflavones and black cohosh may relieve vasomotor symptoms. However, explain that:

  -Preparations vary

  -The safety of different preparations is uncertain and interactions with other drugs have been reported.

[*Based on low to moderate quality evidence from randomised studies in the network and health economic analysis and the experience and opinion of the GDG.*]

Psychological symptoms

- Consider HRT to alleviate low mood due to menopause. [*Based on very low to moderate quality evidence from randomised studies and the experience and opinion of the GDG.*]
- Consider cognitive behavioural therapy (CBT) to alleviate low mood or anxiety due to menopause. [*Based on moderate quality evidence from randomised studies and the experience and opinion of the GDG.*]
- Ensure that women and healthcare professionals understand that there is no clear evidence that SSRIs or SNRIs ease low mood in menopausal women who have not been diagnosed with depression.[7] [*Based on low to moderate quality evidence from randomised studies and the experience and opinion of the GDG.*]

Urogenital atrophy

- Offer vaginal oestrogen to women with urogenital atrophy (including those on systemic HRT) and continue treatment for as long as needed to relieve symptoms. [*Based on very low to moderate quality evidence from randomised studies and the experience and opinion of the GDG.*]
- Advise women with vaginal dryness that moisturisers and lubricants can be used alone or in addition to vaginal oestrogen. [*Based on the experience and opinion of the GDG.*]
- Do not offer routine monitoring of endometrial thickness during treatment for urogenital atrophy. [*Based on low quality evidence from a randomised study and the experience and opinion of the GDG.*]

Unregulated preparations

- Explain to women that the efficacy and safety of unregulated compounded bioidentical hormones are unknown. [*Based on the experience and opinion of the GDG.*]

Review of treatment

- Explain to women with a uterus that unscheduled vaginal bleeding is a common side effect of HRT during the first three months of treatment but should be reported at the three month review appointment. It should be reported

Summary of benefits and risks of hormone replacement therapy (HRT) started before 65 years to treat menopausal symptoms

Benefits

- Relief of vasomotor symptoms, musculoskeletal symptoms, low mood, and sexual difficulties (systemic HRT)
- Relief of urogenital symptoms (topical or systemic HRT)
- Osteoporosis prevention (systemic HRT). The absolute risk of any fragility fracture is 69/1000 women over 3.5 years in women not using HRT; in those using systemic HRT, 23 fewer women per 1000 (95% confidence interval –10 to –33) would be at risk. This benefit is maintained during treatment but reduces once treatment stops

Risks

- Unscheduled vaginal bleeding: common during first 3 months; report to a healthcare professional if it occurs after the first 3 months [*Based on the experience and expert opinion of the Guideline Development Group.*]
- Venous thromboembolism (VTE): absolute risk is 12.5/1000 over 5 years in women not using HRT. In those using oral HRT, 10 (6 to 14) more women per 1000 would be at risk. Transdermal HRT is not associated with increased risk of VTE
- Stroke: small increased risk in women taking oral but not transdermal oestrogen
- Breast cancer: absolute risk is 22.5/1000 over 7.5 years in women not using HRT. In those using oestrogen and progestogen, 5 more women (–4 to 36) per 1000 are at risk; in those using oestrogen alone, 4 (–11 to 8) fewer women per 1000 are at risk. The increased risk of breast cancer while taking oestrogen plus progestogen disappears once HRT is stopped

No change in risk

- Coronary heart disease (CHD): the risk of CHD is not increased in women who use HRT compared with non-users

*The impact of HRT that is started after 65 years was outside the scope of the guideline (see tables 1-4 of full guideline[6]).

promptly if it occurs after the first three months.[8] [*Based on the experience and opinion of the GDG.*]

- Explain to women that gradually reducing or immediately stopping HRT makes no difference to their symptoms in the longer term, although gradually reducing HRT may limit recurrence of symptoms in the short term. [*Based on very low to low quality evidence from randomised studies and the experience and opinion of the GDG.*]

Women with or at high risk (such as *BRCA* gene carriers) of breast cancer[9 10]

- HRT is contraindicated for women with a history of a hormone sensitive cancer, such as breast cancer. [*The GDG did not review the evidence on the effect of HRT for this group because HRT was considered a contraindication.*]
- For advice on the treatment of menopausal symptoms in women with breast cancer or at high risk of breast cancer, see section 1.13 of the NICE guideline on early and locally advanced breast cancer[9] and section 1.7 of the NICE guideline on familial breast cancer[10].
- Offer women with or at high risk of breast cancer:
  -Information on all available treatment options (and any interactions with drugs such as tamoxifen with St John's wort)

  -Information that those with breast cancer who are taking tamoxifen should not be given the SSRIs paroxetine and fluoxetine

  -Referral to a healthcare professional with expertise in menopause.

[*Based on the experience and opinion of the GDG.*]

Long term benefits and risks of HRT (see box)

Venous thromboembolism (VTE)

- Explain that:
  -Oral HRT increases this risk of VTE

  -Transdermal HRT at standard therapeutic doses does not increase the risk.

[*Based on very low to moderate quality evidence from randomised and observational studies and the experience and opinion of the GDG.*]

- Consider transdermal rather than oral HRT for menopausal women at increased risk of VTE, including those with a body mass index over 30. [*Based on very low to moderate quality evidence from randomised and observational studies and the experience and opinion of the GDG.*]

Cardiovascular disease (CVD)

- Explain that:
  -HRT does not increase the risk of CVD when started before age 60 (the impact of starting HRT after 65 years was outside the guideline's scope)

  -HRT does not affect the risk of dying from CVD

  -HRT is an option for women with cardiovascular risk factors as long as these are optimally managed.

  Taking oral (but not transdermal) oestrogen is associated with a small increase in stroke.

Type 2 diabetes

- Explain that taking HRT (orally or transdermally) is not associated with an increased risk of developing type 2 diabetes and does not have an adverse effect on blood glucose control. [*Based on very low to low quality evidence from one randomised study, observational studies, and the experience and opinion of the GDG.*]

Breast cancer

- Explain that:
  -Oestrogen alone is associated with very little or no increase in the incidence of breast cancer

  -Oestrogen and progestogen can be associated with an increase in the incidence of breast cancer

  -Any increase in risk of breast cancer occurs during treatment and returns to baseline after stopping HRT.

[*Based on very low to moderate quality evidence from randomised and observational studies and the experience and opinion of the GDG.*]

Osteoporosis

- Explain that:

  -The risk of fragility fracture is reduced while taking HRT

  -This benefit is maintained during treatment but decreases once treatment stops

  -The beefit may continue for longer (after treatment stops) in women who have taken HRT for longer (more than 10 years).

[*Based on very low quality to moderate evidence from randomised observational studies and the experience and opinion of the GDG.*]

Dementia

- Explain that the likelihood of HRT affecting their risk of dementia is unknown. [*Based on very low to low quality evidence from one randomised study, observational studies, and the experience and opinion of the GDG.*]

Premature ovarian insufficiency

- Taking into account the woman's clinical history (for example, previous medical or surgical treatment) and family history, diagnose premature ovarian insufficiency in women aged under 40 years on the basis of:

  -Menopausal symptoms, including no or infrequent periods, and

  -Raised FSH levels on two blood samples taken four to six weeks apart.

[*Based on very low to low quality evidence from observational studies and the experience and opinion of the GDG.*]

- Do not routinely use anti-Müllerian hormone testing to diagnose this. [*Based on very low to low quality evidence from observational studies and the experience and opinion of the GDG.*]
- Offer a choice of HRT or a combined hormonal contraceptive unless contraindicated (for example, in women with hormone sensitive cancer) up to the age of natural menopause. [*Based on low quality evidence from a randomised study and the experience and opinion of the GDG.*]
- Consider referral to healthcare professionals with the relevant experience to help women manage all aspects of physical and psychosocial health related to their condition. [*Based on the experience and opinion of the GDG.*]

The members of the Guideline Development Group were: Terry Aspray, Claire Bowring, Melanie Davies (until November 2014), Deborah Holloway, Sally Hope, Deborah Keatley, Mary Ann Lumsden, Sara Moger, Prunella Neale, Nicholas Panay, Anthony Parsons, Imogen Shaw, and Christine West (from January 2015). The members of the National Collaborating Centre for Women's and Children's Health technical team were: Grammati Sarri, Melanie Davies (from December 2014), Annabel Flint, Yelan Guo, Sadia Janjua, Hugo Pedder, Paul Jacklin, and Zosia Beckles.

Contributors: All authors contributed to the initial draft, helped revise the manuscript, and approved the final version for publication. GS is guarantor.

Funding: The National Collaborating Centre for Women's and Children's Health was commissioned and funded by the National Institute for Health and Care Excellence to develop this guideline and write this *BMJ* summary.

Competing interests: We declare the following interests based on NICE's policy on conflicts of interests (available at: www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/code-of-practice-for-declaring-and-managing-conflicts-of-interest.pdf). MAL has been remunerated for chairing NICE guideline development committees and is vice chair of the the Women's Health Expert Advisory Group to the Medicines and Healthcare products Regulatory Agency (MHRA). MD receives no direct funding for her advisory or educational roles. The authors' full statements can be viewed at www.bmj.com/content/bmj/351/bmj.h5746/related#datasupp.

Provenance and peer review: Commissioned; not externally peer reviewed.

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Cite this as: *BMJ* 2015;351:h5746

How patients were involved in the creation of this article

Committee members involved in this guideline included three lay members who contributed to the formulation of the recommendations summarised here.

Further information on the guidance

This guideline aims to standardise the care of women in menopause and fill in the knowledge gap regarding the risks and benefits of treatments for menopausal symptoms.

Overcoming barriers

Around a million women in the UK use treatment for their menopausal symptoms.[11] The advice on different treatments and support available is variable and is based on studies that have now been reanalysed and the conclusions amended.

Methods

This guidance was developed by the National Collaborating Centre for Women's and Children's Health in accordance with National Institute for Health and Care Excellence (NICE) guideline development methods (www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf). A Guideline Development Group was established by the National Collaborating Centre for Women's and Children's Health, which incorporated healthcare professionals (including gynaecologists, nurses, physicians, and two GPs) and lay members. The GDG identified relevant clinical questions, collected and appraised clinical evidence, and evaluated the cost effectiveness of proposed interventions where possible. A network meta-analysis was undertaken to identify the clinical effectiveness of different types of treatments (pharmacological and non-pharmacological) for the treatment of menopausal symptoms and used to inform a cost effectiveness analysis.

The draft guideline underwent a public consultation in which stakeholder organisations were invited to comment; the GDG took all comments into consideration when producing the final version of the guideline.

Four different versions of this guideline have been produced: a full version containing all the evidence, the process undertaken to develop the recommendations, and all the recommendations; a care pathway (http://pathways.nice.org.uk/pathways/menopause); a version containing a list of all the recommendations, known as the "short guideline;" and a version for patients (www.nice.org.uk/guidance/ng23/informationforpublic). All of these versions are available from the NICE website (www.nice.org.uk/guidance/ng23).

Updates of the guideline will be produced as part of NICE's guideline development programme.

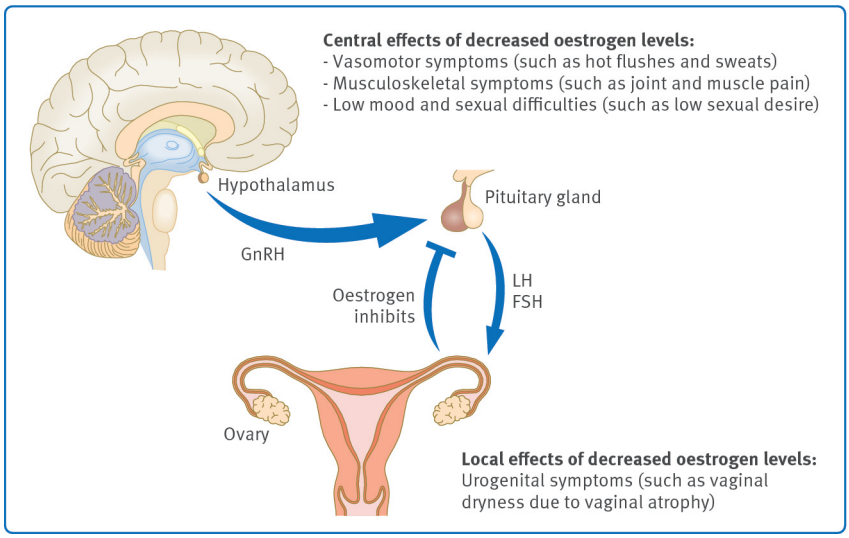
Guidelines into practice

- Audit hormone replacement therapy (HRT) prescriptions for women with body mass index over 30. Review those taking oral HRT preparations and offer transdermal HRT instead because the risk of venous thromboembolism (VTE) is associated with obesity and increased by oral HRT but not transdermal HRT.
- Audit requests for serum follicle stimulating hormone (FSH) tests—what proportion were in women over 45 years old? Do you need to change your practice by instead diagnosing menopause in this age group on the basis of clinical features alone (no periods for at least 12 months in women not using hormonal contraception or menopausal symptoms in women without a uterus)?

Future research

- In women who have been treated for breast cancer, what is the safety and effectiveness of alternatives to systemic HRT as treatments for menopausal symptoms?
- In women with a previous diagnosis of breast cancer, what is the impact of systemic HRT usage on the risk of breast cancer recurrence, mortality, or tumour aggression?
- What is the difference in the risk of breast cancer in menopausal women on HRT with progesterone, progestogen, or selective oestrogen receptor modulators?
- How does the HRT preparation affect the risk of VTE?
- What is the impact of estradiol combined with the levonorgestrel releasing intrauterine system on the risk of breast cancer and VTE?
- What are the effects of early HRT use on the risk of dementia?
- What are the main clinical manifestations of premature ovarian insufficiency and the short term and long term impact of the most common therapeutic interventions?

Figure



Perimenopausal symptoms. FSH=follicle stimulating hormone; GNRH=gonadotrophin releasing hormone; LH=luteinising hormone