Evidence to Practice | HEALTH CARE REFORM

Diagnosis and Management of Menopause
The National Institute of Health and Care Excellence (NICE) Guideline

Mary Ann Lumsden, MD, MB, BS, BSc, FRCOG; Melanie Davies, MB, BS, MA, MRCP, FRCOG; Grammati Sarri, PhD;
for the Guideline Development Group for Menopause: Diagnosis and Management (NICE Clinical Guideline No. 23)

The Issue

Menopause is a natural process that occurs in all women who live long enough. Many women experience no menopausal symptoms or only mild ones that do not require active medical management. However, a substantial proportion of women (about 20%) experience bothersome symptoms, such as hot flushes, night sweats, and trouble sleeping.[1] The National Institute of Health and Care Excellence (NICE), based in the United Kingdom, has recently published guidelines for diagnosis and management of menopause. These guidelines provide clear and evidence-based advice to support both primary care physicians and those specializing in the care of women in midlife.

Objective

This Guideline was published by NICE in November 2015[2] to inform health care professionals and their patients and to standardize care. It includes recommendations on diagnosis of menopause and on individualized care of symptomatic women. Several versions of the guidelines are available: a "patient-friendly" version for women; a "short" summary of the recommendations with tables of the benefits and risks of hormone therapy (HT); and the "full" version, which contains details of the literature searches, quality assessment of the evidence, results of meta-analysis, and how the recommendations were derived from the evidence (https://www.nice.org.uk).

The Evidence

All review questions posed (17 in all) were subject to systematic reviewing of the current evidence base, and meta-analysis when appropriate. The evidence was assessed using the GRADE system (Grading of Recommendations, Assessment, Development and Evaluations Working Group).[3] Recommendations were written by a guideline development group comprising gynecologists, other physicians, nurses, lay members, and a technical team including reviewers, statisticians, and health economists.

We discuss selection of the recommendations from the NICE Guideline[2] to illustrate the breadth of topics covered. The numbers included are those used in the Guideline itself for easy cross-referencing. Some are included in the **Box**, but all should be reviewed in the context of the complete Guideline document.

Diagnosis

Moderate- to very-low-quality evidence from studies of the diagnostic accuracy of biochemical tests for women older than 45 years concluded that measurement of follicle-stimulating hormone (FSH) added no useful information to the clinical diagnosis of the menopause and therefore should not be used. In symptomatic women, the diagnosis of menopause should be based on age and menstrual cyclicity only (recommendation 4). However, measurement of FSH

Box. Selected Recommendations From The National Institute of Health and Care Excellence for the Diagnosis and Treatment of Menopause[a]

Recommendation 7: Give information to menopausal women that includes:
- Common symptoms and diagnosis
- Benefits and risks of treatments for menopausal symptoms
- Long-term health implications of menopause

Recommendation 14: Offer women hormone therapy (HT) for vasomotor symptoms after discussing with them the short-term (up to 5 years) and longer-term benefits and risks. Offer a choice of preparations as follows:
- Estrogen and progestogen to women with a uterus
- Estrogen alone to women without a uterus

Recommendation 25: Offer menopausal women with, or a high risk of, breast cancer:
- Information that the selective serotonin reuptake inhibitors paroxetine and fluoxetine should not be offered to women with breast cancer who are taking tamoxifen
- Referral to a health care professional with expertise in menopause

Recommendation 42: Ensure that menopausal women and health care professionals involved in their care understand that HT:
- Does not increase cardiovascular disease risk when started in women younger than 60 years
- Does not affect the risk of dying from cardiovascular disease

Recommendation 49: Explain to women around the age of natural menopause that:
- 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
- HT with estrogen alone is associated with little or no change in the risk of breast cancer
- HT with estrogen 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 HT.

Recommendation 56: Diagnose premature ovarian insufficiency in women younger than 40 years based on:
- Elevated follicle-stimulating hormone levels in 2 blood samples taken 4 to 6 weeks apart

Recommendation 61: Explain to women with premature ovarian insufficiency:
- The importance of starting treatment either with HT or a combined hormonal contraceptive and continuing treatment until at least the age of natural menopause (unless contraindicated)

[a] The Guideline[2] contains 63 recommendations relating to clinical care and 7 research recommendations; some subsections of recommendations are included here, numbered as in the Guideline.

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is of value in younger women with symptoms where diagnosis is uncertain (recommendation 56).

Treatment

Although a majority of menopausal women require little or no medical intervention for symptoms, some will require treatment, and all must be given information (recommendation 7) about menopause and what to expect. In the absence of randomized clinical trials involving a direct comparison of all treatments of interest, a network meta-analysis was undertaken to estimate the relative effectiveness of treatments for vasomotor symptoms, which informed the cost-effectiveness analysis. The network meta-analysis concluded that HT was the most effective treatment for common menopausal symptoms such as hot flushes (recommendation 14). Comparison was made between prescribed medications such as HT and selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors (SSRIs/SNRIs), nonprescribed preparations such as phytoestrogens or herbal preparations, and some nonpharmacological therapies such as cognitive behavior therapy, acupuncture, and hypnosis. Both the benefits and the risks of treatments were reviewed. For HT, longer-term outcomes such as cardiovascular disease (recommendation 42), breast cancer (recommendation 49), and osteoporosis prevention were considered and tables of risk estimates, including any change in risk that could be attributed to HT, compiled. The balance of benefits and harms varies among women according to their personal risk factors for cardiovascular disease and breast cancer. But overall, moderate to low-quality evidence suggests that there is no increase in cardiovascular disease risk with HT (recommendation 42) when such treatment is started in women younger than 60 years. However, evaluation of general health and the delivery of appropriate advice is important. In a given patient, risk factors for disorders such as cardiovascular disease (eg, diabetes and high blood pressure or lipid levels) might be present, and these could affect the treatment offered (recommendation 43). Such risk factors must be adequately controlled before commencing hormone therapy. The guidelines suggest that all women should have access to a sympathetic, knowledgeable practitioner to discuss their needs.

For those for whom HT is not appropriate (eg, women with breast cancer), the Guideline group reviewed moderate-quality evidence relating to alternative treatments (recommendation 25), particularly SSRIs/SNRIs. However, warnings are included regarding use of SSRIs in those being treated with tamoxifen and also the use of St John's Wort, which showed limited benefit.

Although the number of women experiencing menopause before age 40 years is small (1%), the occurrence has significant implications for long-term health, both physical and psychological, so diagnosis and management is extremely important.[4] Evidence in this area was low to very-low quality, since the studies were often small and at serious risk of bias. However, implementing recommendations to diagnose based on menopausal symptoms and elevated FSH levels, as opposed to anti-Mullerian hormone testing, should cut the time to diagnosis (recommendations 56 and 58) and ensure that women receive relief of any symptoms and long-term health advice to protect particularly the cardiovascular and skeletal systems (recommendation 61). The evidence comparing HT and the combined oral contraceptive in the management of premature ovarian insufficiency was low to very-low quality, and the final choice of treatment will follow discussion between the woman and her health care professional.

Implementation

Further resources are available from NICE that may help to support Guideline implementation, including the development of auditable quality standards and working with professional organizations to maximize educational opportunities for trainees and continuous professional development of more senior staff.

ARTICLE INFORMATION

Author Affiliations: University of Glasgow, Glasgow, Scotland (Lumsden); Chair, Guidelines Development Group, National Collaborating Centre for Women's And Children's Health, London, England (Lumsden); The National Collaborating Centre for Women and Children's Health, London, England (Davies, Sarri).

Corresponding Author: Mary Ann Lumsden, MD, MB, BS, BSc, FRCOG, Department of Reproductive and Maternal Medicine, School of Medicine, University of Glasgow, New Lister Bldg, Glasgow Royal Infirmary, Glasgow G31 2ER, Scotland (Maryann.lumsden@glasgow.ac.uk).

Published Online: June 20, 2016. doi:10.1001/jamainternmed.2016.2761.

Conflict of Interest Disclosures: None reported.

Group Information: The members of the Guideline Development Group for Menopause: Diagnosis and Management (NICE Clinical Guideline No. 23) are as follows: *Medical professional members:* Terry Aspray, Musculoskeletal Unit, Freeman Hospital; Melanie Davies, University College London Hospitals (until November 2014); Deborah Holloway, Guys and St Thomas's NHS Foundation Trust; Sally Hope, GP, Oxford, Oxfordshire; Mary Ann Lumsden, University of Glasgow and Glasgow Royal Infirmary; Prunella Neale, Herschel Medical Centre, Slough; Nicholas Panay, Queen Charlotte's and Chelsea & Chelsea and Westminster Hospitals, London; Anthony Parsons, Coventry and Warwickshire Partnership Trust; Imogen Shaw, GP, Finchingfield, Essex; and Christine West, Simpson Centre for Reproductive Health, Royal Infirmary of Edinburgh (from Jan 2015). *Lay members:* Claire Bowring, Deborah Keatley, and Sara Moger. *Expert advisors:* Charlotte Coles (until October 2014), Addenbrooke's Hospital, Cambridge; Peter Collins, Imperial College London; Rebecca Hardy, MRC Unit for Lifelong Health and Aging, University College London; Adrian Harnett, Norfolk and Norwich University Hospital; and Myra Hunter, King's College London.

REFERENCES

1. Avis NE, Crawford SL, Greendale G, et al; Study of Women's Health Across the Nation. Duration of menopausal vasomotor symptoms over the menopause transition. *JAMA Intern Med*. 2015;175(4):531-539.

2. The National Institute of Health and Care Excellence (NICE) Guideline. Menopause: Diagnosis and Management. https://www.nice.org.uk/guidance/ng23. Accessed May 24, 2016.

3. Jaeschke R, Guyatt GH, Dellinger P, et al; GRADE Working Group. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive. *BMJ*. 2008;337:a744.

4. Shuster LT, Rhodes DJ, Gostout BS, Grossardt BR, Rocca WA. Premature menopause or early menopause: long-term health consequences. *Maturitas*. 2010;65(2):161-166.

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