Menopause management NICE Implementation

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Why a NICE guideline (NG 23)

- Media reports about HRT have not always been accurate
- No consensus about the long-term benefits and risks of HRT
- A knowledge gap has caused an overestimation of risks and underestimation of the impact of menopausal symptoms on a woman's quality of life (QoL)

Why a NICE guideline (NG23)

- To help GPs and other HCPs to be more confident in prescribing HRT
- To help women to be more confident in taking HRT
- Ultimate goal – Help HCPs to support women to make an informed decision about individual benefits and risks of HRT

Learning Objectives

'Adopt an individualised approach at all stages of diagnosis, investigation and management of menopause' (NG 23)

- Symptoms and long term consequences
- Diagnosis
- Treatment
- HRT: benefits and risks
- Reviewing, starting and stopping HRT
- Premature ovarian insufficiency (POI)

Learning Objectives

Short-term symptoms & long-term consequences

Symptoms

- Vasomotor symptoms
  - Hot flushes
  - Night sweats
- Neuromuscular, skin, nail and hair changes
- Psychological (depression, anxiety, sleep disturbance)
- Urogenital tract
  - Vaginal dryness
  - Bladder symptoms

Potential long term consequences of the menopause

- Osteoporosis
- Cardiovascular disease
- Cognitive decline

Learning Objectives

Definitions & Diagnosis

Definitions

- Post-menopause – 12 months after last menstrual period (LMP)
- Peri-menopause (menopause transition)
  - ~ 5-10 year period
  - Characterised by hormone imbalance
    - Irregular ovulation
    - Low levels of progesterone
    - Variable oestrogen levels
- Premature ovarian insufficiency POI (< 40 years) https://poiregistry.net

Diagnosis (NG 23)

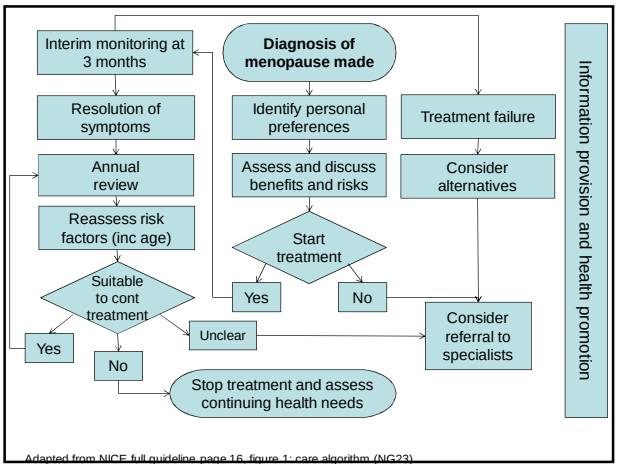
- Diagnosis should be based on clinical symptoms and menstrual history
- Only consider using a FSH test to diagnose menopause:
  - In women aged 40-45 years with menopausal symptoms
  - In women aged under 40 years in whom menopause is suspected

Learning Objectives

Treatment

Symptom control
Vasomotor symptoms

- Adopt an individualised approach (NG 23)
- HRT remains the most effective therapy for vasomotor and oestrogen-deficient urogenital symptoms
- Other menopause-related complaints, such as joint and muscle pains, skin problems, mood swings, sleep disturbances and sexual dysfunction (including reduced libido) generally improve with HRT
- Do not routinely offer SSRIs, SNRIs or Clonidine as first line treatment for vasomotor symptoms alone (NG 23)



Adapted from NICE full guideline page 16, figure 1: care algorithm (NG23)

Which regime? (NG 23)

- Post-hysterectomy
  - Oestrogen only
- Intact uterus
  - Need progestogen in addition to oestrogen (endometrial protection)

HRT + Intact uterus

- Current practice - add progestogen to reduce risk of endometrial hyperplasia/cancer
- Peri or postmenopausal?
  - <12 months amenorrhoea
    - Cyclical progestogen
  - >12 months amenorrhoea (or >54 on cyclical preparation)
    - Continuous combined HRT/ Tibolone
- At any age
  - Levonorgestrel-releasing intrauterine system and continuous oestrogen

Continuous-Combined HRT

- Continuous progestogen maintains an atrophic endometrium
- Suitable for postmenopausal women
  - 'No period' HRT
- Provides better endometrial protection than cyclical progestogen
  - Consider changing from cyclical to continuous combined therapy after approximately 5 years

Symptom control
Urogenital atrophy (NG 23)

- Offer vaginal oestrogen to women with urogential atrophy (including those on systemic HRT) and continue treatment for as long as needed
- Consider vaginal oestrogen for women with urogenital atrophy in whom HRT is contraindicated, after seeking advice from a HCP with menopause expertise
- Advise women with vaginal dryness that moisturisers and lubricants can be used alone or in addition to vaginal oestrogen

Learning Objectives

HRT: Benefits & Risks

Treatment- HRT
Benefits

- The objective of replacing oestrogen is to
  - Alleviate short term menopausal symptoms
  - Minimise/prevent long term risks of oestrogen deficiency

NICE on osteoporosis (NG 23)

- The risk of fragility fracture decreases while taking HRT
- This benefit is maintained during treatment but decreases once treatment stops
- Benefit may continue for longer in women who take HRT for longer.

Difference in any **fragility fracture** incidence per 1,000 menopausal women over 3.43 years	
Baseline population risk in the UK over 3.43 years	69 per 1,000
Women on any HRT	46 per 1,000 (23 fewer)

RCTs estimate of absolute rates of any fragility fracture for current HRT users compared with no HRT (or placebo)

Treatment- HRT
Putting the risks into perspective

- Venous Thromboembolism (VTE)
- Coronary Heart Disease
- Stroke
- Breast cancer

NICE on VTE (NG 23)

- Risk of VTE is increased by oral HRT compared with baseline population
- Consider transdermal for menopausal women who are at increased risk of VTE
- The progestogen component of HRT may also influence the risk of a DVT, which may be greater with androgenic synthetic progestogens than natural progesterone (findings from observational studies)

NICE on CVD (NG23)

- HRT does not increase CVD risk when started in women aged under 60 years
- Baseline risk of CHD and stroke varies between individuals
- The presence of cardiovascular risk factors is not a contraindication to HRT if optimally managed

NICE on CHD (NG23)

- HRT with oestrogen alone is associated with no, or reduced, risk of CHD
- HRT with oestrogen and progestogen is associated with little or no increase in risk

Difference in **coronary heart disease** incidence per 1,000 menopausal women over 7.5 years	
Baseline population risk in the UK over 7.5 years	26 per 1,000
Women on oestrogen alone	20 per 1,000 (6 fewer)
Women on oestrogen + progestogen	31 per 1,000 (5 more)

RCTs estimate of absolute rates of coronary heart disease for different types of current HRT users compared with no HRT (or placebo)

NICE on stroke (NG23)

- Baseline population risk of stroke in women aged under 60 years is very low

Difference in **stroke** incidence per 1,000 menopausal women over 7.5 years	
Baseline population risk in the UK over 7.5 years	11 per 1,000
Women on oestrogen alone	11 per 1,000 (0 more)
Women on oestrogen + progestogen	17 per 1,000 (6 more)

RCTs estimate of absolute rates of stroke for different types of current HRT users compared with no HRT (or placebo)

Breast Cancer

- Overall HRT seems to confer a similar degree of risk associated with late natural menopause (2.3%per yr/2.8%per yr)
- Risk returns to same as never users within 5 years of stopping
- Mortality from breast cancer is not increased
- Drinking 2 to 3 units of alcohol per day may be more harmful to the breasts than HRT!

NICE on Breast Cancer (NG 23)

- Baseline risk of breast cancer varies between individuals
- 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 is related to treatment duration and reduces after stopping HRT

NICE on Breast Cancer cont (NG 23)

Difference in **breast cancer** incidence per 1,000 menopausal women over 7.5 years	
Baseline population risk in the UK over 7.5 years	22 per 1,000
Women on oestrogen alone	18 per 1,000 (4 fewer)
Women on oestrogen + progestogen	27 per 1,000 (5 more)

RCTs estimate of absolute rates of breast cancer for different types of current HRT users compared with no HRT (or placebo)

Benefits v Risks

Age	Benefit & risk balance	Advice
<50	Benefits >> Risks	All women should be offered HRT
50-60	Benefits > Risks	Offer to symptomatic women
60-70	Benefits = Risks	Individualise. Review dosage and route
>70	Risks > Benefits	???

Learning Objectives

Reviewing, starting & stopping HRT

Review (NG 23)

- Once HRT is initiated, review of treatment for short-term menopausal symptoms:
  - At **3 months** to assess efficacy and tolerability
  - **Annually** thereafter unless there are clinical indications for an earlier review. (Treatment ineffectiveness, side effects or adverse events)

Starting and stopping HRT (NG 23)

- Explain to women with a uterus that unscheduled vaginal bleeding is a common side effect of HRT within the first 3 month
- Offer women who are stopping HRT a choice of gradually reducing or immediately stopping treatment, and explain 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

HRT Conclusions- IMS View

- The safety of HRT largely depends on age
- Women younger than 60 years should not be concerned about the safety profile of HRT
- New data and re-analyses of older studies by women's age show that, for most women, the potential benefits exceed the risks, particularly when HRT is initiated within a few years of menopause

Updated 2013 IMS recommendations
De Villiers TJ et al. Climacteric 2013;16;316-37

HRT–Duration of treatment

- Symptoms may resolve in 2-5 years but the median duration is 7 years and sometimes longer (NG 23)

NHS menopause full guideline

- There are no reasons to place mandatory limitations on the length of treatment
- Whether or not to continue therapy should be decided at the discretion of the well-informed hormone user and her health professional

Updated 2013 IMS recommendations
De Villiers TJ et al. Climacteric 2013;16;316-37

Learning Objectives

Premature ovarian insufficiency (POI)

Premature ovarian insufficiency (POI) (NG 23)

- Diagnose POI in women aged under 40 based on:
  - Menopausal symptoms, including no or infrequent periods and
  - Elevated FSH level on 2 blood samples taken 4-6 weeks apart (Do not diagnose on the basis of a single blood test)
- Offer and start HRT or combined hormonal contraception and continue until at least the age of natural menopause
- Baseline risk of breast cancer and CVD is very low in women aged under 40.
- HRT may have a beneficial effect on blood pressure vs combined hormonal contraception

10 Top Tips for everyday practice

Courtesy of PCWHF

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1

The diagnosis of menopause in women aged > 45 is clinical. It does not require confirmation with an FSH level

2

Remember that contraception is needed until fertility is no longer a problem

3

Consider menopause as a possibility in women

< 40 who have amenorrhoea and are not using hormonal contraception

4

HRT should be recommended routinely to women who are menopausal aged <45, even if they are asymptomatic

5

Provide/signpost good patient information (e.g., www.menopausematters.co.uk) to allow informed and shared decision making between the woman and her HCP

6

Prescribing is not difficult and decision making guides are available

7

HRT is much safer than you think. NICE clinical Guidance (2015) will provide the evidence and reassurance

8

Support the woman to initiate and continue treatment and review at 3 months. If stable, annual review is recommended to reassess the risk/benefits of ongoing HRT use for her. There is no arbitrary limit to length of use

9

The benefits of HRT outweigh the risks for most women who start treatment aged < 60

10

Low dose vaginal oestrogens are safe to use for as long as required in all women who do not have breast cancer