NICE National Institute for Health and Care Excellence

NICE Pathways

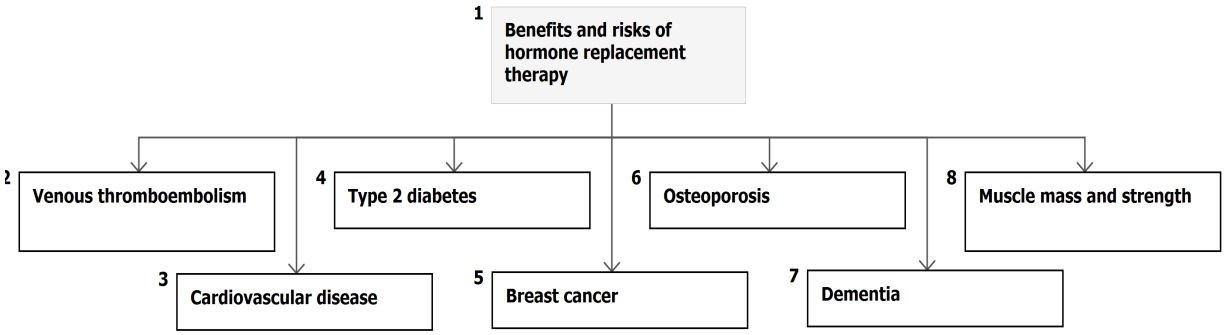
Benefits and risks of hormone replacement therapy

NICE Pathways bring together everything NICE says on a topic in an interactive flowchart. NICE Pathways are interactive and designed to be used online.

They are updated regularly as new NICE guidance is published. To view the latest version of this NICE Pathway see:

http://pathways.nice.org.uk/pathways/menopause
NICE Pathway last updated: 19 June 2018

This document contains a single flowchart and uses numbering to link the boxes to the associated recommendations.



1 Benefits and risks of hormone replacement therapy

No additional information

2 Venous thromboembolism

Explain to women that:

- the risk of venous thromboembolism is increased by oral HRT compared with baseline population risk
- the risk of venous thromboembolism associated with HRT is greater for oral than transdermal preparations
- the risk associated with transdermal HRT given at standard therapeutic doses is no greater than baseline population risk.

Consider transdermal rather than oral HRT for menopausal women who are at increased risk of venous thromboembolism, including those with a BMI over 30 kg/m^2.

Consider referring menopausal women at high risk of venous thromboembolism (for example, those with a strong family history of venous thromboembolism or a hereditary thrombophilia) to a haematologist for assessment before considering HRT.

See what NICE says on venous thromboembolism.

3 Cardiovascular disease

Ensure that menopausal women and healthcare professionals involved in their care understand that HRT:

- does not increase cardiovascular disease risk when started in women aged under 60 years
- does not affect the risk of dying from cardiovascular disease.

Be aware that the presence of cardiovascular risk factors is not a contraindication to HRT as long as they are optimally managed.

Using the tables difference in coronary heart disease incidence [See page 6] and difference in stroke incidence [See page 6], explain to women that:

- the baseline risk of coronary heart disease and stroke for women around menopausal age

- varies from one woman to another according to the presence of cardiovascular risk factors
- HRT with oestrogen alone is associated with no, or reduced, risk of coronary heart disease
- HRT with oestrogen and progestogen is associated with little or no increase in the risk of coronary heart disease.

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 the table difference in stroke incidence [See page 6]).

See what NICE says on cardiovascular disease prevention.

4 Type 2 diabetes

Explain to women that taking HRT (either orally or transdermally) is not associated with an increased risk of developing type 2 diabetes.

5 Breast cancer

Using the table difference in breast cancer incidence [See page 8], 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
- 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.

6 Osteoporosis

Give women advice on bone health and discuss these issues at review appointments (see what NICE says on osteoporosis).

Using the table difference in any fragility fracture incidence [See page 10], explain to women that the baseline population risk of fragility fracture for women around menopausal age in the UK is low and varies from one woman to another.

Using the table difference in any fragility fracture incidence [See page 10], explain to women that their risk of fragility fracture is decreased while taking HRT and that this benefit:

- is maintained during treatment but decreases once treatment stops
- may continue for longer in women who take HRT for longer.

7 Dementia

Explain to menopausal women that that the likelihood of HRT affecting their risk of dementia is unknown.

8 Muscle mass and strength

Explain to women that:

- there is limited evidence suggesting that HRT may improve muscle mass and strength
- muscle mass and strength is maintained through, and is important for, activities of daily living.

Absolute rates of coronary heart disease for different types of hormone replacement therapy (HRT) compared with no HRT (or placebo), different durations of HRT use and time since stopping HRT for menopausal women

		Difference in coronary heart disease incidence per 1000 menopausal women over 7.5 years (95% confidence interval) (baseline population risk in the UK over 7.5 years: 26.3 per 1000[1])			
		Current HRT users	**Treatment duration <5 years**	**Treatment duration 5–10 years**	**>5 years since stopping treatment**
Women on oestrogen alone	RCT estimate[2]	6 fewer (–10 to 1)	No available data	No available data	6 fewer (–9 to –2)
	Observational estimate[3]	6 fewer (–9 to –3)	No available data	No available data	No available data
Women on oestrogen + progestogen	RCT estimate	5 more (–3 to 18)	No available data	No available data	4 more (–1 to 11)
	Observational estimate	No available data	No available data	No available data	No available data

HRT, hormone replacement therapy; RCT, randomised controlled trial

For full source references, see Appendix M in the full guideline.

Absolute rates of stroke for different types of hormone replacement therapy (HRT)

[1] Results from Weiner 2008 were used for the baseline population risk estimation.

[2] For women aged 50–59 years at entry to the RCT.

[3] Observational estimates are based on cohort studies with several thousand women.

compared with no HRT (or placebo), different durations of HRT use and time since stopping HRT for menopausal women

		Difference in stroke incidence per 1000 menopausal women over 7.5 years (95% confidence interval) (baseline population risk in the UK over 7.5 years: 11.3 per 1000[1])			
		Current HRT users	**Treatment duration <5 years**	**Treatment duration 5–10 years**	**>5 years since stopping treatment**
Women on oestrogen alone	RCT estimate[2]	0 (–5 to 10)	No available data	No available data	1 more (–4 to 9)
	Observational estimate[3]	3 more (–1 to 8)	No available data	No available data	No available data
Women on oestrogen + progestogen	RCT estimate	6 more (–2 to 21)	No available data	No available data	4 more (–1 to 13)
	Observational estimate	4 more (1 to 7)	No available data	No available data	No available data

HRT, hormone replacement therapy; RCT, randomised controlled trial

For full source references, see Appendix M in the full guideline.

Absolute rates of breast cancer for different types of hormone replacement therapy (HRT) compared with no HRT (or placebo), different durations of HRT use and time since stopping HRT for menopausal women

[1] Results from Weiner 2008 were used for the baseline population risk estimation.

[2] For women aged 50–59 years at entry to the RCT.

[3] Observational estimates are based on cohort studies with several thousand women.

		Difference in breast cancer incidence per 1000 menopausal women over 7.5 years (95% confidence interval) (baseline population risk in the UK over 7.5 years: 22.48 per 1000[1])			
		Current HRT users	**Treatment duration <5 years**	**Treatment duration 5–10 years**	**>5 years since stopping treatment**
Women on oestrogen alone	RCT estimate[2]	4 fewer (–11 to 8)	No available data	No available data	5 fewer (–11 to 2)
	Observational estimate[3]	6 more (1 to 12)[4]	4 more (1 to 9)	5 more (–1 to 14)	5 fewer (–9 to –1)
Women on oestrogen + progestogen	RCT estimate	5 more (–4 to 36)	No available data	No available data	8 more (1 to 17)
	Observational estimate	17 more (14 to 20)	12 more (6 to 19)	21 more (9 to 37)	9 fewer (–16 to 13)[5]

HRT, hormone replacement therapy; RCT, randomised controlled trial

For full source references, see Appendix M in the full guideline.

Absolute rates of any fragility fracture for hormone replacement therapy (HRT) compared with no HRT (or placebo), different durations of HRT use and time since stopping HRT for menopausal women

		Difference in any fragility fracture incidence per 1000 menopausal women (95% confidence interval) (see footnotes

[1] Office for National Statistics (2010) breast cancer incidence statistics.

[2] For women aged 50–59 years at entry to the RCT.

[3] Observational estimates are based on cohort studies with several thousand women.

[4] Evidence on observational estimate demonstrated very serious heterogeneity without plausible explanation by subgroup analysis.

[5] Evidence on observational estimate demonstrated very serious imprecision in the estimate of effect.

		for information on baseline population risk and length of follow-up time over which absolute risk difference is calculated)			
		Current HRT users	**Treatment duration <5 years**	**Treatment duration 5–10 years**	**>5 years since stopping treatment**
Women on any HRT	RCT estimate[1]	23 fewer (–10 to –33)[2]	25 fewer (–9 to –37)[3]	No available data	No available data
	Observational estimate[4]	16 fewer (–15 to –18)[5]	15 fewer (–11 to –17)	18 fewer (–15 to –20)	2 more (–19 to 27)[6]

HRT, hormone replacement therapy; RCT, randomised controlled trial

For full source references, see Appendix M in the full guideline.

Absolute risks calculated by using the baseline population risk in the control arm for each analysis, following GRADE methodology.

Glossary

Compounded bioidentical hormones

unregulated plant-derived hormonal combinations similar or identical to human hormones that are compounded by pharmacies to the specification of the prescriber

Fragility fracture

fractures that result from mechanical forces that would not ordinarily result in fracture (such as a fall from a standing height or less). Reduced bone density is a major risk factor for fragility fractures, which occur most commonly in the spine, hip and wrist

[1] For women aged 50–59 years at entry to the RCT.

[2] Baseline population risk = 69 per 1000 women (follow-up: 3.43 years).

[3] Baseline population risk = 78 per 1000 women (follow-up: 3.71 years).

[4] Observational estimate is based on cohort studies with several thousand women.

[5] Baseline population risk = 15.4 per 1000 women (follow-up: 2.8 years).

[6] Baseline population risk = 106 per 1000 women (follow-up: 5 years).

HRT

hormone replacement therapy

Low mood

mild depression symptoms that impair quality of life but are usually intermittent and often associated with hormonal fluctuations in perimenopause

Menopause

a biological stage in a woman's life that occurs when she stops menstruating and reaches the end of her natural reproductive life. Usually it is defined as having occurred when a woman has not had a period for 12 consecutive months (for women reaching menopause naturally). The changes associated with menopause occur when the ovaries stop maturing eggs and secreting oestrogen and progesterone

Perimenopause

the time in which a woman has irregular cycles of ovulation and menstruation leading up to menopause and continuing until 12 months after her final period (also known as menopausal transition or climacteric)

Premature ovarian insufficiency

menopause occurring before the age of 40 years (also known as premature ovarian failure or premature menopause). It can occur naturally or as a result of medical or surgical treatment

Urogenital atrophy

thinning and shrinking of the tissues of the vulva, vagina, urethra and bladder caused by oestrogen deficiency. This results in multiple symptoms such as vaginal dryness, vaginal irritation, a frequent need to urinate and urinary tract infections

Vasomotor symptoms

menopausal symptoms such as hot flushes and night sweats caused by constriction and dilatation of blood vessels in the skin that can lead to a sudden increase in blood flow to allow heat loss. These symptoms can have a major impact on activities of daily living

Sources

Menopause: diagnosis and management (2015) NICE guideline NG23

Your responsibility

Guidelines

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Technology appraisals

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take these recommendations fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this interactive flowchart is at the discretion of health professionals and

their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Commissioners and/or providers have a responsibility to provide the funding required to enable the recommendations to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Medical technologies guidance, diagnostics guidance and interventional procedures guidance

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take these recommendations fully into account. However, the interactive flowchart does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the recommendations, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this interactive flowchart should be interpreted in a way that would be inconsistent with compliance with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.