thebmj

BMJ 2019;367:l5928 doi: 10.1136/bmj.l5928 (Published 11 October 2019)

EDITORIALS

HRT and breast cancer risk

We must prevent another setback in women's health

Janice Rymer *vice president*, Kate Brian *women's voices lead*, Lesley Regan *president*

Royal College of Obstetricians and Gynaecologists, London, UK

In the UK, most women go through the menopause between the ages of 45 and 55, with the average age being 51 years. Around half of women experience some physical or emotional symptoms from the decrease in ovarian function, including hot flushes, night sweats, low mood, anxiety, joint and muscle pain, vaginal dryness, decreased sex drive, and hip fractures in later life.

Every woman experiences the menopause differently. Although for many women this natural transition may be relatively straightforward, in around 25% the symptoms have a substantial or debilitating effect on their personal and professional lives.[1] Unfortunately, only a minority of women seek help to manage symptoms, often because they do not know who best to approach or because misinformation has led to fear of treatment.

About one million women in the UK currently use hormone replacement therapy (HRT),[2] the most commonly prescribed treatment for the symptoms of ovarian failure. HRT can bring many benefits, improving quality of life and offering protection against bone loss and fragility fractures.[2]

Not all women can take, or choose to take, HRT. Some have hormone dependent cancers, such as breast cancer; others may be put off by the focus on side effects, even though the benefits may outweigh the risks.

New data

The findings published in the *Lancet* in September provide data for both women and clinicians that could help in discussions around the use of HRT.[3] However, this new meta-analysis should be considered alongside the National Institute for Health and Care Excellence's (NICE) 2015 guidance *Menopause: Diagnosis and Management*,[2] which considered all the available evidence on benefits and risks of the different treatment options.

The *Lancet* meta-analysis is complex and includes data from a large number of studies, published and unpublished, totalling 108 647 women.[3] It showed that in the UK about 1 in 16 women who have never taken HRT will be diagnosed with breast cancer between the ages of 50 and 69. For women with a normal body mass index who start HRT in their 40s or 50s, the analysis found their additional risk of breast cancer was 1 in 200 for oestrogen-only HRT, 1 in 70 for sequential HRT (oestrogen daily and progestogen for part of each month), and 1 in 50 for continuous combined HRT (oestrogen and progestogen daily).

What this study adds is that taking oestrogen alone for longer than five years increases the risk of breast cancer, but by less than combined HRT. In addition, the risk associated with both oestrogen and combined oestrogen and progestogen may continue for longer than was previously thought after HRT is stopped. However, women should be counselled that other factors, including body weight and alcohol consumption, have a greater effect on breast cancer risk than HRT. For example, the extra risk of breast cancer associated with being overweight or obese is six times higher than the extra risk associated with combined HRT, according to NICE.[2]

The new findings are consistent with NICE recommendations[2] and should be viewed alongside the benefits of HRT,[4] which for many women considerably outweigh the risks. Risk means different things to different women, and each woman must be given information in context and be supported to make an informed choice about her best treatment options.

The *Lancet* study did not address mortality, only incidence of breast cancer, so findings must be weighed against a recent systematic review that showed that starting HRT close to the menopause may also reduce all-cause mortality and cardiac death, with no evidence of an increase in breast cancer mortality.[5] Also, the most recent paper from the Women's Health Initiative randomised trials showed that women who started treatment with oestrogen alone between the ages of 50 and 59 had a lower mortality than placebo controls when followed for 18 years.[6]

Public anxiety

After the *Lancet* study was published, the Medicines and Healthcare Products Regulatory Agency (MHRA) issued a drug safety alert to all doctors to communicate the breast cancer risk to women considering or taking HRT. It included only the data from this publication and did not mention benefit in terms of bone loss and providing protection from cardiovascular disease. Nor did it mention that there was no increased risk of death from breast cancer or all causes.

The alert has caused considerable anxiety, particularly in women who go through the menopause before the age of 40 and have a higher risk of early death and heart disease if left untreated.[7]

Correspondence to: J Rymer janice.rymer@kcl.ac.uk

The *Lancet* study did not compare the risk of breast cancer for women taking HRT with that of women of the same age with normal ovarian function and gives a misleading presentation of the risk. Young women who stop HRT are likely to adversely affect their long term health and raise their risk of death.[8-10]

We all have a role in empowering women to make the best choices for their health by providing high quality, unbiased evidence and supporting them to make decisions. Women now live longer in the postmenopausal period than in their reproductive phase, and our focus must be on not merely extending women's lives but improving their quality of life. After decades of misinformation and scaremongering headlines focusing on side effects of hormone treatment, we must all work together to avoid another damaging setback in women's health. We need to treat individual women, not statistics.

Competing interests: We have read and understood BMJ policy on declaration of interests and have no relevant interests to declare.

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

1 Royal College of Obstetricians and Gynaecologists. *Treatment for symptoms of the menopause.* RCOG, 2018.
2 National Institute for Health and Care Excellence. *Menopause: diagnosis and management.* NICE, 2015.
3 Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. *Lancet* 2019;394:1159-68. 10.1016/S0140-6736(19)31709-X 31474332
4 Rossouw JE, Anderson GL, Prentice RL, etal. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33. 10.1001/jama.288.3.321 12117397
5 Nudy M, Chinchilli VM, Foy AJ. A systematic review and meta-regression analysis to examine the 'timing hypothesis' of hormone replacement therapy on mortality, coronary heart disease, and stroke. *Int J Cardiol Heart Vasc* 2019;22:123-31. 10.1016/j.ijcha.2019.01.001 30705938
6 Manson JE, Aragaki AK, Rossouw JE, etal. WHI Investigators. Menopausal hormone therapy and long-term all-cause and cause-specific mortality. *JAMA* 2017;318:927-38. 10.1001/jama.2017.11217 28898378
7 Tao XY, Zuo AZ, Wang JQ, Tao FB. Effect of primary ovarian insufficiency and early natural menopause on mortality: a meta-analysis. *Climacteric* 2016;19:27-36. 10.3109/13697137.2015.1094784 26576012
8 Rocca WA, Grossardt BR, Miller VM, Shuster LT, Brown RDJr. Premature menopause or early menopause and risk of ischemic stroke. *Menopause* 2012;19:272-7. 10.1097/gme.0b013e31822a9937 21993082
9 Muka T, Oliver-Williams C, Kunutsor S, etal . Association of age at onset of menopause and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis. *JAMA Cardiol* 2016;1:767-76. 10.1001/jamacardio.2016.2415 27627190
10 Rocca WA, Grossardt BR, de Andrade M, Malkasian GD, Melton LJ3rd. Survival patterns after oophorectomy in premenopausal women: a population-based cohort study. *Lancet Oncol* 2006;7:821-8. 10.1016/S1470-2045(06)70869-5 17012044