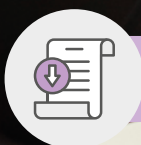


## Breast cancer & HRT: Putting risks into perspective

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New data analysed exclusively for the Primary Care Women's Health Forum explores whether HRT impacts a woman's risk of being diagnosed with breast cancer.

**T**here is much publicity regarding breast cancer which women understandably see as very frightening. In

2000, a study<sup>1</sup> designed to assess the awareness and perception of risk factors in women's health revealed that 34% of those surveyed thought that they were going to die from breast cancer and, interestingly, more women aged 25 to 44 years identified breast cancer as the leading cause of death than women 65 years or older.

Research published in 1997 told us that HRT does influence breast cancer diagnosis, with estimates that would stand critical review today. However, the initial publications of the Women's Health Initiative (WHI) in 2002 and the Million Women Study (MWS) in 2003, distorted the fear. Women perceived that the WHI suggested a 26% increase in risk of breast cancer and the MWS a doubling in risk, if they used HRT. HRT was seen as unacceptably dangerous. Messaging based on relative and percentage risk was disseminated by the medical press and, consequently, both clinicians and research bodies shied away from prescribing HRT. A distorted breast cancer risk perception since has significantly affected the behaviour of both menopausal women and their healthcare professionals and has undoubtedly denied some women relief from symptoms and precluded various other benefits.

In more recent years in the UK, we have seen a systematic dismantling of this disproportionate response. The analysis of existing data by the National Institute of Health and Care Excellence (NICE)

in 2015 was generally reassuring that, for women around the time of their last period and indeed for up to 10 years after, HRT generally offered more benefits than risks. Peer and workplace support, celebrity documentaries and social media have continued this trend, and, in the UK, we are seeing a surge in demand rather than the previous reticence. Many women are coming forward and you are seeing these women in primary care.

This means that when counselling women, it is important that the information you give them is accurate and delivered in a way that they can understand to allow them to make a decision that is appropriate for them.

We have heard the call for clear information about the real risks regarding breast cancer for women at menopause. Therefore, starting with a statistical analysis of available data, looking at women in their 40s 50s and 60s, we have studied some of the factors that can influence breast cancer diagnosis. We have considered which of these are modifiable. Specifically, we have looked at the potential impact that HRT would have on her risk of breast cancer diagnosis in each of these decades.

### Holistic assessment

The symptoms due to the loss of reproductive hormones at menopause are multiple and can have a profound impact on quality of life, relationships, and work. The clinical challenge is working out what can be offered and what it might help. Replacing hormones is exactly that and can result in unwanted symptoms. Risks

### THE DATA

The PCWHF worked with Jo Marsden, retired Consultant Breast Surgeon at King's College Hospital, and Hugo Pedder, Statistician, Population Health Sciences, University of Bristol, on these statistics. They provided the most robust data available reflecting the effect of lifestyle choices on the health of women in the decades of their 40s 50s and 60s. The PCWHF also requested data regarding the effects of HRT in each of these decades. As the last complete year before the Covid-19 pandemic hit, 2018 was used as the reference year for mortality statistics. Together, we have analysed the evidence that has been identified.

and benefit in the longer term for breast health, cardiovascular health, bone health, the pelvic organs and others needs to be evaluated, applied, and explained to the patient so that she can make an informed decision. Between you, a negotiated and agreed plan is needed.

### Don't dismiss the facts

Of course, breast tissue is sensitive to the effects of both oestrogen and progesterone. HRT is replacing or supplementing these natural hormones and the effect on breast tissue will be similar.

However, when you dig into the data of causes of death amongst women and then consider the overall effect of HRT on breast cancer rates, things become interesting.

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### THE CHALLENGE YOU HAVE, IS TO WORK OUT AND EXPLAIN WHAT YOUR PATIENT'S STARTING RISK IS AND WHAT MIGHT HRT ADD TO THAT

Overall, 1 in 7<sup>2</sup> women will be diagnosed with breast cancer during their lifetime, which means 1 in 6 will not.

Exploring the risk of breast cancer, the biggest risk is due to cis-female gender, followed by increasing age and inherited genetic susceptibility. These are classed as unmodifiable risk factors and influence a woman's individual, or baseline risk of breast cancer. Older women are more likely to be diagnosed with breast cancer due to an increased lifelong accumulation of acquired genetic mutations that result in abnormal cell division and clearance by the body. Over 80% of breast cancers are being diagnosed in those over 50. Inherited genetic susceptibility can increase diagnosis in women of all ages but accounts for a larger proportion of diagnoses in younger women. The influence of genes is much smaller than many imagine and is associated with only 1 in 20 of all breast cancers<sup>4</sup>. Most women you see will not have a significant family history of breast cancer and be at an average (population) baseline risk of breast cancer, determined by their gender and age. Breast cancer is much less common in men although it can occur, and in those cases is even more likely to be linked with an inherited genetic anomaly<sup>5</sup>. This is explained in NICE CG 164 guidance<sup>6</sup>.

#### Lifestyle choices

Beyond age, sex at birth and genetics, there are lifestyle risk factors associated with breast cancer that can be changed or modified. The risk associated with these is smaller than factors that cannot be changed.

Both obesity and increased alcohol consumption influence the risk of breast cancer diagnosis and a reduction in both will also lower cardiovascular risk. Breast cancer risk is not increased in women with a BMI > 30.

The use of combined HRT with oestrogen and a progestogen will apply to most women as they require the latter to protect endometrial tissue from the stimulating effects of oestrogen. It may be associated with a small, time-dependent increase in risk of breast cancer.

Women who have had a hysterectomy and have no remaining endometrium (endometriosis or a residual cervix will make a difference here) can have unopposed oestrogen and an impact on breast cancer risk is small but still likely to exist.

#### Putting it into context

**Risk estimates are imprecise as every woman will have a different starting point (i.e. baseline risk).**

When discussing risk with your patient, use absolute rather than relative risk estimates to put the figures into context and use expressions that women will appreciate. Wembley Stadium seats 90,000 so 1 in 10,000 means that there would be nine affected people in that crowd. You may have a local theatre or other venue which seats about 1,000. Talk about that.

**As we have said, breast cancer becomes more likely with age:**

- Between age 40–49, 17 in 1000 women will be newly diagnosed with breast cancer (and 983 in 1000 will not).
- In their 50's, for women of recommended weight (BMI 19–24.9), the rate is 25 in 1000 (975 will not) and in the 60's, 29 in 1000 (971 will not). If they have a BMI > 30 add an extra 7 in 1000 for women in their 50's and 15 in 1000 if they are aged 60–69.

Recent epidemiological data would appear to confirm the findings published in 1997 – that use of HRT by women in their 40's is not associated with a greater risk of breast cancer than for their peers who are still

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having periods. Exogenous hormones at physiological levels have the same effect as those produced by the body. This is logical.

Ten years use of HRT throughout the 50's would add an extra 10 cases per 1000 average women. Ten years use through the 60's would add eight per thousand. Remember, however, that they start at higher risk because of their age.

### Conclusion

All women are different. Their risk estimates are not perfect and are derived from a variety of studies. Furthermore, there may be interactions between multiple unmodifiable and modifiable risk factors that either reduce or magnify their combined impacts on breast cancer risk – these are difficult to explore and understand in detail. The challenge you have, is to work out and explain what your patient's starting risk is and what might HRT add to that. Is this addition of risk acceptable to reduce the symptoms that are afflicting her?

- You should appreciate that there may be factors that you can do nothing about, that raise her risk at the beginning. Women with clear genetic factors, premalignant breast changes or even a previous cancer should be referred to a specialist.
- Following your discussion, your patient may come to appreciate the impact of her lifestyle choices and be open to change. That would be a result.
- You may decide that, for her, adding HRT is reasonable. The benefits provided for most women within ten years of their last period outweigh the risks. They may do for women in their 60's and even for some in their 70's. There is no arbitrary limit.
- In this complex mix, which we all agree is almost impossible with a single 10-minute consultation, the breast discussion is vitally important. ♀



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