Editorial

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Hormone replacement therapy and the risk of breast cancer: How much should women worry about it?

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A recent *Lancet* paper,[1] updating the evidence on the association between hormone replacement therapy (HRT) and the risk of breast cancer made prominent headlines. These ranged from '*Breast cancer risk from using HRT is "twice what was thought"*' (*Guardian*), to the more dramatic '*PAUSE IT: HRT treatment for menopause increases risk of breast cancer by a THIRD, experts warn*' (*The Sun*), to the simply wrong '*Breast cancer: HRT found to double risk of developing disease in worrying new study*' (*Daily Express*). These are potentially very worrying headlines, and women's concern was expressed on social media and countered by explanation and reassurance from organisations such as the British Menopause Society, International Menopause Society and Menopause Matters.

One issue is that the *Lancet* paper reviews the evidence from epidemiological rather than experimental studies the randomised Women's Health Initiative trials have, for example, recently reported that women receiving estrogen post hysterectomy had a *lower* long term risk of breast cancer.[2]

But, assuming that the conclusions of the *Lancet* paper are correct, how could these risks be communicated in a more helpful way than did the media?

Communicating risks transparently

The use of capitals in saying a risk is increased '*by a THIRD*' provides emphasis but not much clarity, since the importance of such a 'relative risk' cannot be assessed without knowing the answer to the simple question: a third of what? The *Lancet* paper does provide this essential detail, saying that 'for women of average weight in developed countries, 5 years of HRT starting at age 50 years, would increase breast cancer incidence at ages 50–69 by about 1 in every 50 users of estrogen plus daily progestogen'. The number of patients that need to be treated to harm one person is 50 which is known as the number needed to harm (NNH), so in this context the NNH is 50: the NNH was estimated to be 70 for women taking estrogen plus intermittent progestogen, and 200 for those having estrogen only.

This number may reflect the research findings, but is still insufficient to be able to understand the risks of getting breast cancer due to HRT. There are established strategies and tools to communicate such risks in transparent and comprehensible ways[3,4]:

- Presenting absolute risks with and without the treatment, expressed as how many cases of breast cancer between the ages of 50 and 69 would be expected in a group of women of average weight in developed countries who do not take HRT. The Lancet paper clearly reported a 6.3% baseline risk, which means that out of 50 women without HRT, 3 would be expected to develop breast cancer anyway. This would go up to four (the one-third increase) for women taking estrogen plus daily progestogen for five years starting at age 50.
- Providing a clear graphical display of the risk, for example the icon arrays shown in Figure 1.

This clarifies what 'risk increased by a THIRD' in the headlines actually means: the baseline risk is 3 out of 50, 'a third' of three is 1, and that is the extra case expected in women with HRT. The *Lancet* results also mean: (a) of 70 women taking estrogen plus intermittent progestogen, we would expect 5 rather than 4 cases of breast cancer; (b) of 200 women taking estrogen only, we would expect 14 rather than 13 cases.

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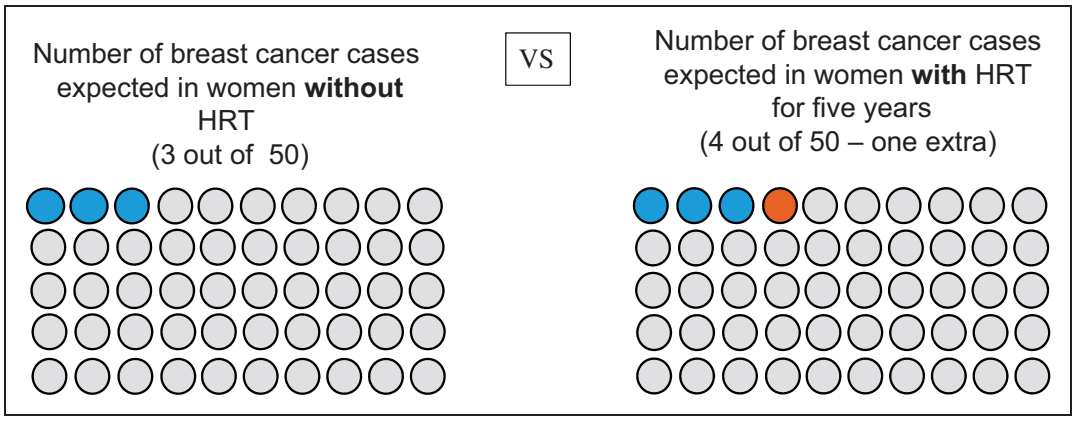

Figure 1. Icon arrays showing that for women not taking HRT, we expect 3 out of 50 to develop breast cancer between 50 and 69 years, compared to 4 women taking estrogen plus daily progestogen for five years. In other words, for one extra woman to develop breast cancer between 50 and 69 years, 50 women would need to take HRT. Of these, three would develop breast cancer anyway.

Risks for populations or individuals?

One of the strongest statements in the *Lancet* paper was '*If the associations are largely causal, MHT use in western countries has already caused about 1 million breast cancers, out of a total of about 20 million since 1990*'. However, these apparently dramatic effects on populations, while important when it comes to policy recommendations, are strictly speaking irrelevant when it comes to an individual making a decision about her treatment.

This is because it is possible for the same risk to be concerning from a public health perspective, but from an individual's point of view, it may be considered small enough to be traded off against the potential benefits of treatment. People therefore should know what the risks mean for an individual, as this may ultimately guide their health decisions. This is an essential part of the aims of personalised medicine.

Communicating both potential benefits and harms

Epidemiological research focuses on the causes of disease, in this case breast cancer, and so it is inevitable that the media reports centre their attention on potential harms. But a health decision cannot be made by only considering a single outcome measure such as risk of cancer; people need balanced information on all potential harms and benefits of treatments so they can properly make an informed choice that reflects their preferences and values. This was reflected in responses to the article on social media, for example @HormoneEquilibrium tweeted

> Women are more likely to die from cardiovascular disease, Osteoporosis or dementia than from breast cancer. The *Lancet* study completely ignores these health outcomes, as well as the quality of life benefits which HRT provides. Safer types of HRT were ignored.

The *Lancet* paper and its subsequent coverage focussed only on the *incidence* of breast cancer, and not *mortality* from breast cancer. This is a crucial outcome, not only because it is so important, but because it may be influenced by the treatment through mechanisms that are not fully understood. Overall mortality should also, in principle, be reported, as HRT may well benefit women's overall health in a variety of ways.

Having examined the potential harms and benefits, for some groups of people there may be a clear recommendation to either take HRT or not. But many people will be in what is known as a 'preference zone', where the decision can quite reasonably depend on a trade-off based on the values and preferences of the individual patient.

What can be done to improve communication of risk and evidence?

Sources of information on HRT do report both potential benefits and harms. For example, the NHS website leads with the relief of menopausal symptoms and

prevention of osteoporosis (weak bones) before mentioning risks, and concludes that '*The benefits of HRT are generally believed to outweigh the risks*'. The National Institute for Health and Care Excellence (NICE) guidelines provide detailed information on a variety of outcomes (except menopausal symptoms) based on expected frequencies in 1000 women, but refer to the Medicines and Healthcare products Regulatory Agency (MHRA), which supervises quality and safety of medicines in the UK, for breast cancer risks.

The MHRA use a 'fact box', which is a visual display showing the benefits and harms of medical treatments based on absolute risks (in this case 1000 women), and which have been shown to improve people's understanding of health-related risk information.[5] But the MHRA neither quote breast cancer nor all-cause mortality or report any benefits, except to add as a footnote *Menopausal symptom relief is not included in this table, but is a key benefit of HRT and will play a major part in the decision to prescribe HRT*. They also do not give any indication of the quality of the underlying evidence, in contrast to the MAGIC approach used in the British Medical Journal's Rapid Recommendations, that uses a fact box with associated GRADE ratings.

Cancer Research UK provides a 'balance sheet' listing the risks and benefits of HRT, but without numbers. They also point out that '*the increase in cancer risk is small compared to many lifestyle risk factors*', illustrating this claim by saying

- Minimising HRT could prevent 1400 cancer cases a year
- Keeping a healthy weight could prevent 13,200 cancer cases a year
- Being smoke free could prevent 22,000 cancer cases a year.

While these statistics are dramatic, as we pointed out earlier, they are only really relevant from a public-health and not an individual perspective, and it would be better to compare HRT with the individual risks associated with specific behaviours.

We conclude that researchers, health-related organisations, health practitioners, and journalists could all improve their communication skills. And in such a complex area, more personalised presentations that adapt to individual circumstances seem appropriate: the Winton Centre for Risk and Evidence Communication has developed online platforms such as Predict Breast Cancer and Predict Prostate where we apply these principles to communicate the future survival following alternative adjuvant therapies.

What can women do when confronted with claims about the risks of HRT?

There are things that we can all do when we come across a claim about any risk, the first being to be aware that the way that risks or benefits are 'framed' can influence our perception on their magnitude, and that we may end up with exaggerated fears or reassurances. It is then important to ask some critical questions such as:

- What does that risk mean for 100 or 1000 people like me?
- Does the information provide both benefits and risks?
- Why am I hearing this? What interests do the communicators have, and are they trying to properly inform and empower me, or manipulate and persuade me?

In the end, there is no a straightforward answer to whether HRT is a good option for a particular woman, and we can only recommend seeking reliable sources of information, talking to a trusted health care professional, and together consider the benefits and risks and make a personalised choice.

Research on potential harms and benefits is essential to keep us updated about the best available options for our health, but the way that research is reported can needlessly increase anxiety. Better communication and understanding of risk might move us towards less confusion and better personalised decisions.

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References

1. 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: 1159–1168.
2. Norton A. US News https://www.usnews.com/news/health-news/articles/2019-12-13/new-study-shakes-up-thinking-on-hormone-replacement-therapy

3. Trevena LJ, Zikmund-Fisher BJ, et al. Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers. *BMC Med Inform Decis Mak* 2013; 13 (Suppl 2): S7.
4. Freeman ALJ and Spiegelhalter DJ. Communicating health risks in science publications: time for everyone to take responsibility. *BMC Med* 2018; 16: 207.
5. Schwartz LM and Woloshin S. The Drug Facts Box: improving the communication of prescription drug information. *Proc Natl Acad Sci* 2013; 110: 14069–14074.