



## Treating the Menopause – the Concept of Risk and Benefit

Women making decisions about treatment during menopause - or any other medical decisions - are going to be presented with information about risk, for instance the risk of taking hormone therapy (HT). How does a woman know if increased risk is relevant to her? It helps to have a good grasp of the way the terminology is used by doctors and researchers.

### How would this apply to taking HT/HRT?

- Medical studies, or trials, are conducted to look at a medication to see if it is effective, if it has side-effects, and whether the benefit of taking it outweighs the risk of complications. Trials assess the benefits of a treatment and also the risk, meaning the chance that a patient taking the drug is more likely to develop a complication over and above the background level of this complication in the community.
- In a "controlled" trial, patients taking placebo (dummy tablets) represent the community. At the end of the trial a statistical analysis of the data is conducted to ensure that any difference in benefits and complications between those taking a drug and those taking placebo has not just occurred by chance.

### Different kinds of risk

- Risk refers to the chance of an event occurring. Each time we drive a car we are "at risk" of being involved in a motor vehicle accident. Being "at risk" doesn't mean that the events will necessarily happen, just that we have the chance of them happening to us.
- It is useful to understand the difference between "relative risk" and "absolute risk". If you buy one entry in a lottery you have a certain chance (risk) of winning, say one in a million. If you buy two entries you will double your chances, or your "relative risk" of winning, i.e. your relative risk of winning is 2.

### Levels of evidence

- Not all medical trials are of equal value in informing us about risk. It is important to understand the strength of study results and whether they are likely to apply to you.
- Level 1 evidence produces the strongest evidence about a drug is called a "double-blind, randomised, placebo-controlled" trial (frequently called an RCT). It is "double-blind" because neither the researchers nor the patients were aware of the identity of the tablet being taken (placebo or a real drug). The patients are allocated to placebo or actual drug randomly to improve the likelihood that the two groups being compared are similar.
- Level 2 evidence comes from observational studies which compare users and non-users but without the benefits of random assignment or the use of placebo.
- Level 3 evidence comes from observational studies and does not compare users of the drug with non-users.
- Level 4 evidence includes opinions from experts, non-experts (e.g. relatives, friends) and vested interest parties.



### Some research on the risks of HT/HRT

The United States Women's Health Initiative (WHI) produced Level 1 evidence about the risks and benefits of a particular combination of hormone therapy/hormone replacement therapy. Results from the trial comparing women taking combined oestrogen and progestogen with those taking placebo were reported in 2002. The study reported that the risk of bowel cancer was reduced by HT/HRT use. They estimated that for every 10,000 women monitored for one year, 10 would develop bowel cancer if taking HT/HRT and 16 would develop it if on placebo. The absolute risk was 6 per 10,000 per year. In relative risk terms, women taking placebo were 1.6 times more likely to develop bowel cancer than women taking HT/HRT.

To get a clear idea of the real risk of unwanted side-effects from HT/HRT, it is useful to look at the absolute risks as set out in the following table.

For every 10,000 women followed up over 1 year	Number of events in the HT/HRT group	Number of events in the placebo group (not taking HT/HRT)	Change in number of events attributable to HT/HRT
Risks			
Heart attacks	37	30	7 extra
Strokes	29	21	8 extra
Breast cancer	38	30	8 extra
Clots in deep veins (DVT)	15	7	8 extra
Benefits			
Hip fracture	10	15	5 fewer
<i>Bowel cancer</i>	<i>10</i>	<i>16</i>	<i>6 fewer</i>

Important points to consider about the WHI trial include:

- We do not know if these same risks apply to other forms of HT/HRT, such as patches and sprays or to lower strength doses.
- The women in the WHI trial were older than most women going through menopause - the average age was 63 years. Many were smokers and had high blood pressure so it is hard to know if the risks and benefits of HT/HRT would be the same for healthier women.



**Making a decision: what is an acceptable level of risk?**

For some women any extra risk will be unacceptable but others may consider the benefits outweigh the risks.

Some questions women can ask themselves when considering HT/HRT:

- How much do my symptoms impact on my quality of daily life?
- What could happen if I did nothing at all?
- What are my treatment choices?
- What are their risks and benefits? How reliable is the evidence for these risks and benefits? Are the findings of these studies relevant to me and my treatment?
- Have I now got enough information to make a decision?

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