



## HRT: Risks

### **Risks of HRT**

Risks associated with HRT include association with increased risks of breast cancer (with long duration HRT), blood clot and, if HRT is started many years after the menopause, possibly cardiovascular disease. For the majority of women who use HRT under the age of 60, and for many beyond that age, the benefits of HRT outweigh any risks but for some, alternative treatments for either symptom control or osteoporosis prevention/treatment may be recommended or preferred.

### **Breast Cancer**

Current opinion is that HRT taken for less than 5 years does not significantly increase the risk of breast cancer but studies have shown that after 5 years of use, there is an association with a small increased risk. Once HRT has been stopped, the risk returns back to baseline. This suggests that the use of HRT may promote the growth of breast cancer cells which are already present if HRT is taken for more than 5 years after the age of 50, in some women; there is no evidence that HRT causes breast cancer.

It seems very likely that different types of HRT are associated with different risk, estrogen appears to increase the risk very little while there appears to be a small increased risk of cancer promotion with long term use of estrogen combined with progestogen (combined HRT).

The NICE guideline on Diagnosis and Management of Menopause concluded that for every 1000 women aged 50 to 59, combined HRT may be associated with an extra 5 cases of breast cancer over 7.5

years, with no extra cases for women taking estrogen only. (NICE guideline)

More recent analysis of risk with different types of HRT is shown at ([publishing.service.gov.uk](http://publishing.service.gov.uk) - Table1.pdf) and ([publishing.service.gov.uk](http://publishing.service.gov.uk) - Table2.pdf )

Comparing other known risk factors for breast cancer with HRT risk can be helpful in putting risk into perspective. Excess risk per 1000 women aged 50-59 over 5 years:

- more than 4-6 units of alcohol per day: +8
- more than 6 units of alcohol per day: +11
- postmenopausal obesity: + 10
- more than 5 years of estrogen only HRT: +3 to +6
- more than 5 years of combined HRT: +8 to +10
- a [downloadable diagram](#) showing the relative risks of breast cancer with HRT, alcohol and obesity (PDF 186Kb) updated 23 May 2016
- See our [blog](#) about hormones and breast cancer.

If HRT is commenced at a young age because of premature menopause, then the use of HRT up to the age of 50 does not increase breast cancer risk any more than in women who continue to have periods up to the age of 50. Additional risk from HRT only applies if it is then taken for more than 5 years after 50.

### **Clotting Problems - Venous thromboembolism (VTE)**

Tablet (oral) form of HRT has been shown to cause a small increase in risk of blood clot [Ref 2] (e.g. deep vein thrombosis) The greatest risk is within the 1st year of use and is most relevant to women who have other risk factors. If there is a past or family history of blood clot, appropriate investigations may be carried out and fully discussed. For some who are particularly at risk of blood clot, including women who have a Body Mass index greater than 30, the pros and cons of use of HRT should be discussed and if using HRT, a non-oral preparation should be considered, since there is strong evidence that transdermal estrogen does

not confer the same increased risk [ref 22]. [ref 100].

### **Cardio-vascular disease**

For many years, it was thought, from the results of observational studies, that HRT significantly reduced the risk of heart disease and stroke. However, recent (1998) studies such as HERS [Ref 8] and the WHI study suggested that certain types of HRT may lead to a small increased risk of heart attack and stroke. However, final analysis of the WHI trial showed that there was no increased risk with estrogen only and in fact there was a reduction in heart disease compared to placebo (inactive tablet). For women taking combined HRT, there was an increased risk only in women who were 20 or more years post menopausal, and the increase was in the 1st year of use with no overall increase by the end of the trial. The dose, type and route of HRT used are important in cardiovascular effect, as is the timing of commencement of therapy; more studies recently demonstrating a reduced risk of heart disease in women commencing HRT near the time of the menopause. HRT should not currently be taken for presumed cardiovascular benefit [Ref 4] but HRT used in the early menopausal years for control of menopausal symptoms is very unlikely to be harmful to the heart and may yet prove to be beneficial. It is very likely that there is a "window of opportunity" whereby, if HRT is commenced early, it may be beneficial not only for control of symptoms and prevention of osteoporosis, but also prevention of heart disease but if commenced later when disease of the blood vessels has developed, further damage may occur. HRT should therefore only be taken by women who have, or are at risk of cardiovascular disease, if there are very good indications and after full discussion.

### **Endometrial Cancer**

Estrogen only therapy given to women with an intact uterus increases the risk of endometrial hyperplasia (thickening of the lining of the uterus) and eventually endometrial cancer. Daily estrogen combined with progestogen given for 10 to 14 days

per month (sequential HRT) reduces this risk but does not eliminate it. Sequential HRT given for more than 5 years does increase the risk of endometrial cancer by a small amount but no increased risk appears to apply to estrogen combined with daily progestogen (continuous combined or period-free HRT).  
bibliography reference [Ref 3]

## **Ovarian Cancer**

There continues to be uncertainty about the possibility of increased risk of ovarian cancer with use of HRT. Many studies have given inconclusive results, the Women's Health Initiative trial showed no increase in users of HRT, yet the million Women study suggested an increased risk. This increase was of the order of 1 extra case for every 2,500 women taking HRT for 5 years and so if there is an association, this risk is very small.

- News item: Lancet study examines use of HRT and ovarian cancer risk. 13 Feb 2015.
- News item: HRT and ovarian cancer-is there a link? 18 Apr 2007.

## **Contraindications for HRT.**

- Pregnancy
- Undiagnosed abnormal vaginal bleeding
- Active or recent blood clot or myocardial infarction (heart attack)
- Suspected or active breast or endometrial (womb) cancer
- Active liver disease with abnormal liver function tests
- Porphyria cutanea tarda

**See also:** Balancing the risks and benefits.