

HRT

Hormone replacement therapy (HRT) was once one of the widely used and heavily promoted treatments. Then two major studies in the early 2000s warned of the dangers of HRT and many stopped using it. More recently we have been told it is safe after all. What is the truth?

HRT was originally approved in 1942 (this was an oestrogen only preparation) and started to be used extensively in the 1990s (in a combined form with progestogens). It was used for the treatment of menopausal symptoms and the prevention of osteoporosis and heart disease.

It took two major studies to sound alarm bells. The 15 year Women's Health Initiative which followed 161,000 women was stopped early after 10 years in 2002. It had found **HRT increased breast cancer by 26%** (with a slight decrease with the oestrogen-only form). The study found it also increased heart attacks and strokes. One year later, the Million Women Study, which followed one million women over 50, found that **HRT doubled the risk of breast cancer** (with a 26% increase in the oestrogen-only form of HRT). It also increased the risk of ovarian cancer by 20%. They estimated it had caused an excess of 1300 deaths from ovarian cancer in the UK alone.

Sales of HRT plummeted. The incidence of breast cancer, which had been steadily rising, fell by 23% in the USA in 2003 with 14,000 fewer diagnoses of breast cancer.

However I had become worried about HRT long before this. There had already been warning signs. A paper in 1989 suggested it quadrupled the rate of breast cancer. In 1997 another study found an increase in breast cancer (by 2.3% for every year it was taken). The Nurse's Health Study which followed 121,700 women for 18 years from 1976 found that, over 10 years, the combined forms of **HRT increased breast cancer 100%** and oestrogen-only form increased it by a third.

The American Cancer Society followed 240,000 women and found a 40% increased risk of ovarian cancer for those taking it at least 6 years.

Note that combined oestrogen and progesterone forms of HRT increase the risk of breast cancer more than oestrogen-only forms but oestrogen-only forms are linked with endometrial cancers. These are mainly used in patients who have had hysterectomies.

In the UK, NICE unexpectedly came out in favour of HRT saying that the risk of breast cancer was small. Why the change?

Their conclusions were based on small study by an American gynaecologist who tracked just 80 women for 14 years and found no increase in cancer. They ignored both the two previous huge studies (larger studies are usually more reliable) and other smaller ones and, of particular concern, the fall in breast cancer deaths which followed the drop in sales of HRT. More worryingly the gynaecologist who wrote the paper had previously been recruited by the makers of HRT. In addition a number of members of the NICE panel reputedly had financial ties to the makers of HRT. This made me very wary of the recommendations.

A further large study in 2019, based on 58 global studies, also found an increase in breast cancer. What was different was the study found the risk persisted for 10 to 15 years after stopping HRT. They found taking **HRT for 5 years increased the risk of breast cancer from 6.3% to 8.3% (32% increase)**. Although this is small it means that HRT is responsible for 1 in 20 cases of breast cancer (3000 women a year in the UK).

And at a time when the media were castigating doctors for not prescribing enough HRT another major study came out. The study was from Oxford University and the University of Nottingham led by Dr Yana Yinogradova. It reviewed 24 studies in 12 countries with a total of 98,611 women. The results were worrying and lead author Professor Beral stated "previous estimates of risk were approximately doubled". **They found a combined oestrogen and progesterone increased the risk of breast cancer by 79%** (15% for oestrogen only). The risk was higher the longer HRT was taken with a **doubling of risk of breast cancer after 10 years use**. The risk could persist for up to 10 years after stopping. (BMJ, 2020 DOI.10.1136/bmj.m3873.)

No other single factor increases the risk of breast cancer as much as HRT and two studies have shown a doubling of breast cancer (compare this with smoking which increases cancer overall by 25%).

I would add that **there is another major difficulty with HRT which rarely gets publicity**. It is a highly addictive drug and symptoms often rebound on stopping treatment.

So in conclusion, HRT certainly has a place in treatment of menopausal symptoms but the risk of breast cancer should never be ignored or played down.

