



Hormone Replacement Therapy & Breast Cancer

One of the ongoing issues with breast cancer treatment is management of menopausal symptoms, such as hot flashes, mood changes, vaginal dryness, etc. These symptoms can be attributed to premature menopause after chemotherapy treatment or side effects related to endocrine therapies for hormone-positive breast cancers. Hormone replacement therapy (HRT) can help lessen menopausal symptoms, but there is a concern in patients with a prior history of breast cancer. This apprehension arises from studies done in women with no breast cancer history as well as in breast cancer survivors. Most oncologists recommend no replacement therapy due to the theoretical increased possibility of breast cancer recurrence. In actuality, the data has been conflicting.

The **Women's Health Initiative** was a large study that looked at multiple factors related to HRT use, including breast cancer risk. The study was stopped early for several issues including an increased breast cancer risk seen in the HRT arm. Women who utilized combination estrogen-progestin therapy specifically demonstrated an increased risk of breast cancer compared to placebo. While this risk seemed to decrease after discontinuation, the overall risk at long-term follow-up remained higher than for women who did not take combination HRT. On the other hand, women who took estrogen alone did not seem to have an increased risk of breast cancer. However, uterine cancer became a significant issue in these patients. There were many confusing variables in

this study including length of treatment, timing of treatment (i.e. immediately upon menopause vs. years later), type of medications, etc. However, the overall consensus was that HRT increased the risk of breast cancer.

The safety of HRT is even more difficult to interpret in people with a prior history of breast cancer. Observational studies have indicated no increased risk, but this data is likely confounded by selection biases for healthier patient participants. Two large randomized studies tried to answer the question more definitively. The **HABITS trial** randomized breast cancer survivors (Stage 0 to II with no evidence of recurrence) who required treatment for menopausal symptoms to either HRT or non-hormonal symptom management. The trial was stopped early due to increased risk seen in the HRT arm. In contrast, the **Stockholm trial** with similar trial set up did not show an increased risk of breast cancer in treatment or control arms. However, it too closed early partly because of the findings in the HABITS trial. Given the early closure of both studies and the conflicting results, the answer is still not clear. **However, oncology guidelines continue to not recommend HRT in breast cancer survivors.**

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