



Million Women Study and Endometrial Cancer

The findings from the Million Women Study with respect to post menopausal hormone therapy and cancer of the uterus (endometrial cancer) have been published in the medical journal, Lancet.¹

The aim of this study was to explore the risks of endometrial cancer with different postmenopausal hormone therapies.

This report provides important information about the overall risks of hormone therapies with respect to both endometrial cancer and breast cancer combined, and the significant impact of obesity on endometrial cancer risk.

MAIN CLINICAL RELEVANCE OF THESE FINDINGS:

1. **No therapy is without risk, even if the risk is small**
2. **Each individual woman's risk profile, including body weight, needs to be carefully considered when deciding upon whether or not to use HT and which HT formulation to use.**

SIGNIFICANT FINDINGS:

- A woman's body weight has a significant impact on the risk of endometrial cancer, and influences the effects of HT use on endometrial cancer
- Being moderately overweight to obese was associated with a strong increase in risk of endometrial cancer - incidence rates were seen to be 4 fold higher for women who were obese (body mass index ≥ 30 kg weight/height m^2) versus women who were not (BMI < 25 kg / m^2).
- The risk of endometrial cancer was lower in women who reported last using continuous combined HT compared with never users of HT,
- **Tibolone (Livial®)** was associated with an overall increase in relative risk of endometrial cancer versus non users of HT
- For obese women (BMI ≥ 30) users of both continuous and cyclic HT had a lower incidence of endometrial cancer than never users, and tibolone users had similar rates to never users.

The authors considered the overall effects of 5 years use of various types of HT therapies on endometrial and breast cancer combined

- Combined rates of breast cancer and endometrial cancer were higher for current users of continuous and cyclic oestrogen progestin therapy than for current users of tibolone or oestrogen-only therapy.



What does this all mean?

- Excess body weight (BMI >30) is a major risk factor for endometrial cancer
30 % of Australian women over the age of 50 have a BMI >30kg/m²

This was not a randomised controlled trial and thus reasons for women choosing a particular therapy will influence the outcomes. Results need to be put in the context of what is known from randomised controlled trials.

- Estrogen + progestin HT use in this study was associated with a reduction in uterine cancer risk, particularly in obese women.
In the WHI study² oestrogen plus progestin overall was not associated with a reduction in endometrial cancer risk versus placebo. Thus in this study the apparent “protective effect” of HT may be an over estimation.
- Tibolone in this study appears to increase the risk of endometrial cancer in non obese women and has a similar effect to never use of HT in obese women

These findings need to be confirmed in a randomised controlled clinical trial: the Thebes Study involving 3200 women being treated with either oral oestrogen (Premarin®) +progestin (medroxy progesterone acetate) or tibolone (Livial®) is being undertaken to provide safety regarding the uterus and results should be available by the end of this year.

- If balancing OVERALL risk of breast and endometrial cancer, estrogen + progestin therapy is associated with a greater risk for both cancers combined than tibolone or non use of HT.

Study details:

This study involved over one million women recruited between May, 1996, and March, 2001. Each woman completed a questionnaire including questions about HT use and 2-3 years after recruitment a follow-up questionnaire was sent to each participant to update their use of HT.

The participants were flagged on the NHS cancer registers so cancer registrations and deaths were notified to the investigators.

The Lancet report¹ provides information regarding endometrial cancer risk for

- the traditional use of oestrogen plus progestin as continuous combined therapy (both taken daily) or cyclical therapy (estrogen taken daily and progestin taken for part of the month),
- estrogen alone in women with a uterus and
- tibolone (28,028 women).

Compared with never use of HT the relative risk observed for use of various HT therapies are shown in the table below.

	Relative risk compared with never use of HT	Number of women included
Never	1.0	395,785
Continuous combined	0.71 (0.56–0.90)	69,577
Cyclic combined	1.05 (0.91–1.22)	145,486
Tibolone	1.79 (1.43–2.25)	28,028
Oestrogen only	1.45 (1.02–2.06)	14,204
Other	1.17 (0.96–1.41)	63,658

Reference List

1. **Million Women Study Collaborators. Endometrial cancer and hormone-replacement therapy in the Million Women Study. *Lancet* 2005;365:1543-51.**
2. **Anderson GL, Judd HL, Kaunitz AM, Barad DH, Beresford SA, Pettinger M, Liu J, McNeeley SG, Lopez AM. Effects of estrogen plus progestin on gynecologic cancers and associated diagnostic procedures: the Women's Health Initiative randomized trial. *JAMA* 2003;290:1739-48.**

