BMS Consensus Statement
The Risks and Benefits of HRT before and after a Breast Cancer Diagnosis

Jo Marsden, Hugo Pedder on behalf of The British Menopause Society with acknowledgement to Professor Richard Santen

(2020). Risks and benefits of hormone replacement therapy before and after a breast cancer diagnosis. *Post-Reproductive Health*. https://doi.org/10.1177/2053369120934026

University of BRISTOL

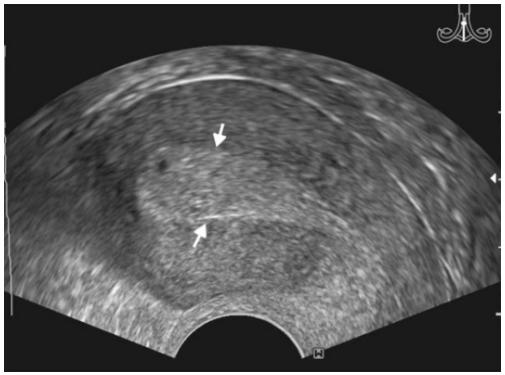
Summary

The British Menopause Society is of the view that the 2019 CGHFBC re-analysis provides important additional information on the risk of breast cancer diagnosis with HRT. The only findings which should influence clinical advice is that risk does not appear to be elevated with low-dose vaginal oestrogen and that risk may persist after systemic HRT is stopped but this can still be explained by a growth-promoting effect. No arbitrary limits should be placed on the dose or duration of usage of HRT as decisions should be made on an individualised basis after discussing the benefits and risks with each patient. In addition to the potential increased risks of breast cancer and VTED, they should also be considered in the context of the overall benefits obtained from using HRT including symptom management and improved quality of life as well as the cardiovascular and bone protective effects

Endometrial cancer and hormone-replacement therapy in the Million Women Study

Lancet, April 2005

*Million Women Study Collaborators**



716.738 postmenopausal women in the UK 1996-2001

provided informations about HRT use (45% of them had used HRT)

	Average years of use of HRT†	Average years since last use of HRT†	Cases/ population (1000s)	Relative risk (95% CI)
Never	-	-	763/395·8	1·00
Continuous combined	5·0	0·2	73/69·6	0·71 (0·56–0·90)
Cyclic combined	5·1	1·0	242/145·5	1·05 (0·91–1·22)
Tibolone	5·2	0·7	86/28·0	1·79 (1·43–2·25)
Oestrogen only	4·6	1·3	33/14·2	1·45 (1·02–2·06)
Other/unknown	2·1	4·5	123/63·7	1·17 (0·96–1·41)

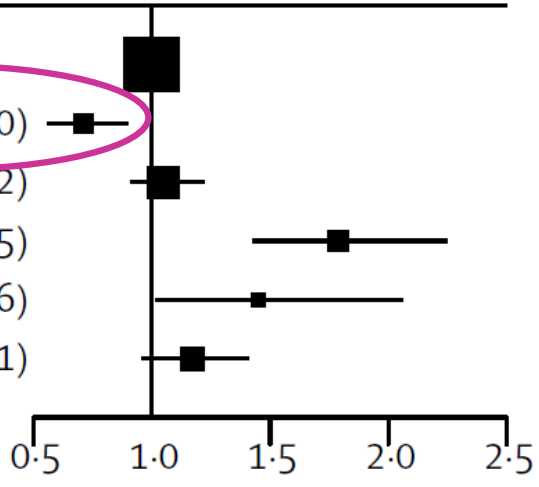


Figure 1: **Relative risk* of endometrial cancer according to type of HRT last used, reported at recruitment**

Compared with never users of HRT, the **overall incidence of endometrial cancer decreased in users of continuous combined HRT**

QOL and in PATIENTS WITH PREVIOUS CANCER

Advances in the early detection and treatment of cancer have provided gains in patients survival time. However, these gains are often accompanied by a variety of treatment associated toxicities that influence QOL

Women treated for cancer have to face the consequences of estrogen deficiency due to:

- **the surgical resection of the ovaries,**
- **the adjuvant postoperative irradiation,**
- **the concomitant chemotherapy**
- **or simply because of natural aging after menopause.**

Menopausal symptoms are typically **more severe in young patients**

Knobf 2006

HRT AFTER BREAST CANCER

Some observational studies suggested that *HRT use may not increase the risk of recurrent breast cancer*. These reports have been questioned because of the potential bias from the selection of women at lower risk of recurrence for HRT use.

Three randomised trials on HRT after breast cancer diagnosis

"Menopausal Hormone Therapy After Breast Cancer: The Stockholm Randomized Trial"
Stockholm Breast Cancer Study Group, 2005

"Increased risk of recurrence after HRT in breast cancer survivors"
HABITS Study Group J Natl Cancer Inst, 2008

Effects of tibolone on climacteric symptoms and quality of life in breast cancer patients: LIBERATE trial
Oncol Lancet, 2009

All closed prematurely due to concern about the safety of treatment

In **1997 two independent randomised trials** were started in Sweden
In **2002** interim safety analysis → **significant risk of recurrence from HRT for the two trials combined (HR=1.8) → both studies were prematurely stopped in December 2003**.

Significant heterogeneity between the studies

HR for **HABITS** at a median follow-up of 2.1 years was **3.5**
HR for **Stockholm** at a median follow-up of 4.1 years was **0.82**

Breast cancer recurrence

HR	95% CI	
Global	**1.8**	**1.03-3.1**
HABITS study	**3.5**	**1.5-7.4**
Stockolm trial	**0.82**	0.35-1.94

L Holmberg et al, Lancet, 2004

LIBERATE Trial

Contents lists available at SciVerse ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Effects of tibolone on climacteric symptoms and quality of life in breast cancer patients—Data from LIBERATE trial

Piero Sismondi[a,*], Rainer Kimmig[b], Ernst Kubista[c], Nicoletta Biglia[a], Jan Egberts[d], Roel Mulder[d], Juan Planellas[d], Giulia Moggio[a], Mirjam Mol-Arts[d], Peter Kenemans[e]

TIBOLONE

Synthetic steroid, with a mixture of oestrogenic, progestogenic and androgenic properties.

- Multinational, multicentre, randomised, **placebo controlled trial** to investigate the **safety and efficacy of tibolone** in women with climacteric symptoms and a history of breast cancer.
- 3148 women enrolled at 245 clinical centres in 31 countries worldwide between June 2002 and Dec 2004
- **Tibolone 2.5 mg daily** (n=1575) vs **placebo** (n= 558)
- Median duration of treatment 2.75 years
- Primary objective: to demonstrate that tibolone was **non inferior to placebo regarding breast cancer recurrence**
- Secondary endpoints: **mortality, climacteric symptoms and bone mineral density.**

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Tibolone, given for three years on average to women with vasomotor symptoms and a history of breast cancer, showed:

Efficacy in relief of **vasomotor symptoms**

A beneficial effect on **bone mineral density**

No difference in other relevant safety parameters: mortality, cardiovascular events, gynecological malignancies

- **Overall increased risk of breast cancer recurrence vs placebo [HR=1.40 (95%CI: 1.14-1.70)]**

↓

Contraindication in women with known, past or suspected breast cancer must remain in the labeling of tibolone

Menopause: The Journal of The North American Menopause Society
Vol. 29, No. 7, pp. 767-794
DOI: 10.1097/GME.0000000000002028

NAMS Position Statement

The 2022 hormone therapy position statement of The North American Menopause Society

Systemic hormone therapy is generally not advised for survivors of breast cancer, although hormone therapy use may be considered in women with severe VMS unresponsive to nonhormone options, with shared decision-making in conjunction with their oncologists. (Level III)

HRT after endometrial cancer

Journal of Clinical Medicine

MDPI

Review

Hormone Replacement Therapy in Endometrial Cancer Survivors: A Meta-Analysis

J. Clin. Med. **2021**, 10, 3165

N=7944

Ambrogio P. Londero [1,2,*], Nadia Parisi [1], Alice Tassi [1], Serena Bertozzi [2,3] and Angelo Cagnacci [4,*]

HT use does not increase the incidence of EC recurrences in women treated for early stages EC (FIGO I or II), except for Black American women where a significantly increased recurrence risk is evident.

Therefore, the positive effects of HT outweigh eventual risks, with the exception of Black American women.

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ENDOMETRIAL
CANCER

- Use of hormone therapy is an option for the treatment of bothersome menopause symptoms in women with surgically treated, early stage, low-grade endometrial cancer in consultation with a woman's oncologist if nonhormone therapies are ineffective. (Level II)
- Systemic hormone therapy is not advised with high-grade, advanced-stage endometrial cancers or with endometrial stromal sarcomas or leiomyosarcomas. (Level II)