



Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit

A unit funded by the FFPRHC and supported by the University of Aberdeen to provide guidance on evidence-based practice

MEMBERS' ENQUIRY RESPONSE

Enquiry Reference: 1880

**Sent: 14 February 2007
Prepared: 14 February 2007**

A: Question

What is the current evidence concerning the use of hormone replacement therapy in a woman with breast cancer?

B: Response

The British Menopause Society does not give any recommendations specifically concerning the use of hormone replacement therapy (HRT) in women with current Breast Cancer.

A review of the available evidence was conducted by Gainford *et al* in 2005.³ Evidence suggested that the use of HRT in women with breast cancer is considered unwise due to its perceived association with breast cancer recurrence. The uncertainty regarding its benefits in healthy women raises further concern with respect to its use in breast cancer survivors.

An earlier publication (2002) discussed the role of hormone replacement therapy in women with a previous diagnosis of breast cancer. Following a systematic review of the literature in the English language the authors suggested that routine use of HRT (estrogen alone or estrogen plus progesterone) is not recommended for women who have breast cancer.

Advice from the Breast Cancer Care regarding hormone therapy in women with breast cancer states that HRT is not usually offered to women who have had breast cancer as there is still uncertainty whether HRT increases the risk of cancer recurring. However, a small number of women experience severe menopausal symptoms that significantly affect their quality of life and don't respond to other treatments or complementary therapies. In these cases HRT may be prescribed because the benefits are likely to outweigh any possible risk. This would be done only once a cancer specialist has discussed all the risks and benefits in order to decide whether it is appropriate.

The CEU could find no further evidence concerning the use of HRT in women with breast cancer.

C: Evidence-Based Medicine Question *(which guided our literature search strategy)*

Population: Women with breast cancer

Intervention: Hormone replacement therapy

Outcome: Safety/evidence

Keywords: Hormone replacement therapy; breast cancer; safety; evidence; 1880

D: Information Sources

The CEU searched the following sources in developing this Member's Enquiry Response

Source Searched	Information Identified
Existing FFPRHC and RCOG guidance	No relevant information
The National Guidelines Clearing House	No relevant information
The WHO <i>Improving Access To Quality Care In Family Planning. Medical Eligibility Criteria For Contraceptive Use 2004</i> and <i>Selected Practice Recommendations For Contraceptive Use, 2004</i>	No relevant information
The Cochrane Library	No relevant information
MEDLINE and EMBASE from 1996 to 2007	No relevant information

E: Evidence Reviewed

The CEU has already reviewed the referenced studies concerning breast cancer risk and HRT back when the evidence was first published. This is available from the CEU as required.

Advice from the British Menopause Society

The Women's Health Initiative (WHI) ¹ was a clinical trial was designed in 1991-1992 to, in part, study the possible long-term health benefits of HRT. Over 161, 000 women were recruited into a set of clinical trials. The British Menopause society released and updated paper ² on the outcomes of this study in April 2006. Concerning the risk of breast cancer they stated the following:

Although the WHI and MWS (Million Women Study) initially highlighted concerns about breast cancer risks with HRT resulting in regulatory authorities issuing urgent revisions of its recommended use, the more detailed WHI analyses demonstrate that these reactions were inappropriate. With combined HRT, there was a (just) significant increase in invasive breast cancer incidence when all women were grouped together, but no increase in *in situ* breast cancer. This increase in invasive cancer was seen only after 5 years use in women who had previously been exposed to HRT for more than 5 years; there was no increased risk in women who had not previously used HRT. With estrogen-alone HRT, there was a non-significant reduction in invasive breast cancer when all women were grouped together, but a significant reduction in those women with no previous HRT exposure. There was also a significant reduction in ductal cancer. Thus it appears that an increased breast cancer risk is in fact confined to those women who have been exposed to combined HRT for more than 10 years, and these clinical trial findings are completely contradictory to the reported findings from the observational MWS.

The British Menopause Society does not give any recommendations specifically concerning the use of HRT in women with current Breast Cancer.

Evidence concerning the use of HRT in women with breast cancer

A review of the available evidence was conducted by Gainford *et al* in 2005. ³Evidence suggested that the use of HRT in women with breast cancer is considered unwise due to its perceived association with breast cancer recurrence. The uncertainty regarding its benefits in healthy women raises further concern with respect to its use in breast cancer survivors. The paper refers to two trials which were designed to evaluate the risk of recurrence of breast cancer associated with HRT in breast cancer survivors. Data from this pooled analysis comparing HRT use with no HRT (placebo) showed a statistically significant relative hazard (RH 1.8; 95% CI 1.03-3.1). However, there was marked heterogeneity between the two studies, and the 1 trial was subsequently discontinued. Authors concluded that until the risk and benefits of HRT can be further evaluated, it would be wise to find an alternative treatment for the management of menopausal symptoms in breast cancer patients.

An earlier publication (2002) ⁴discussed the role of hormone replacement therapy in women with a previous diagnosis of breast cancer. Following a systematic review of the literature in the English language the following recommendations emerged.

- ◆ Routine use of HRT (estrogen alone or estrogen plus progesterone) is not recommended for women who have breast cancer. Randomised controlled trials are required to guide recommendations for this group of women. Women who have had breast cancer are at risk of recurrence and contralateral breast cancer.

The potential effect of HRT on these outcomes in women with breast cancer has not been determined in methodological sound studies. However, in animal and *in vitro* studies, the development and growth of breast cancer is known to be estrogen dependent. Given the demonstrated increases risk of breast cancer associated with HRT in women without a diagnosis of breast cancer, it is possible that the risk of recurrence and contralateral breast cancer associated with HRT in women with breast cancer could be of a similar magnitude.

- ◆ Postmenopausal women with a previous diagnosis of breast cancer who request HRT should be encouraged to consider alternatives to HRT. If menopausal symptoms are particularly troublesome and do not respond to alternative approaches, a well-informed woman may choose to use HRT to control these symptoms after discussing the risks with her physician. In these circumstances, both the dose and the duration of treatment should be minimized.

Advice from the Breast Cancer Care regarding hormone therapy in women with breast cancer states that HRT is not usually offered to women who have had breast cancer as there is still uncertainty if HRT increases the risk of cancer recurring.

Some studies report that HRT causes cancer to come back and others that it doesn't, so the safety of HRT is still unclear. A small number of women experience severe menopausal symptoms that significantly affect their quality of life and don't respond to other treatments or complementary therapies. In these cases HRT may be prescribed because the benefits are likely to outweigh any possible risk. This would be done only once a cancer specialist has discussed all the risks and benefits in order to decide whether it is appropriate. A full dose of HRT may not be necessary to reduce hot flushes, so it would be possible to try using smaller amounts.

This information is available at

http://www.breastcancercare.org.uk/docs/menopausal_symptoms_jun_2006_0.pdf

The CEU could find no further evidence concerning the use of HRT in women with breast cancer.

F: References

1. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;**288**:333.
2. Rees M and Stevenston J. Women's Health Initiative: the final outcome. <http://www.the-bms.org/BMS-WHCWHIarticle4-06revised24406.doc>. 2006.
3. Gainford M.C, Simmons C, Nguyen H, Verma S, Clemons M. A practical guide to the management of menopausal symptoms in breast cancer patients. *Support Care Cancer* 2005;**13**:573-8.
4. Pritchard, K I, Khan, H, and Levine, M. Clinical practice guidelines for the care and treatment of breast cancer: 14. The role of hormone replacement therapy in women with a previous diagnosis of breast cancer. *Canadian Medical Association Journal* 166(8), 1017-1022. 2002.

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Enquiry response by LA