

GYNAECOLOGY & OBSTETRICS UPDATE

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Author

Mark Malak

MB, BCh., M.Sc.,
Ph.D., DFFP,
MRCOG, FRCOG

Lead Urogynaecologist
East Sussex NHS
Hospitals Trust

Tel: 01323 413735

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M Malak, A Grimston,
J Andrews, N Lawton,
A Spirou, W Fletcher

Integrated management of pelvic floor disorders: Prolapse, urinary incontinence (1ry & recurrent), frequency, urgency and recurrent cystitis

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HRT 2010

Since the publication of the **Women's Health Initiative (WHI) study** in 2002; many re-analyses of the data suggested a "timing hypothesis," which proposes that the effects of HRT might vary depending on when in their menstrual history women begin treatment. According to this hypothesis, HRT may reduce the risk of CHD (coronary heart disease) among younger women who do not yet have advanced atherosclerotic plaque but conversely trigger CHD in older women (ie, those with advanced lesions). A new analysis of WHI study has found that, among recently menopausal women, estrogen-plus-progestin hormone-replacement therapy (HRT) slightly increased the risk of coronary heart disease, of around 29%, during the first two years of use. The risk disappeared after six years of use. In fact, after that, the researchers identified a possible cardioprotective effect of HRT in this group of women. But because women generally use HRT for less than six years, recently menopausal women should not expect HRT to protect them from heart attacks.

Overall, in the 16 608 postmenopausal women in the WHI study, who were randomized to either conjugated equine estrogens 0.625 mg plus medroxyprogesterone acetate 2.5 mg (n=8506) or matching placebo (n=8102). Compared with no use of HRT, the hazard ratio for CHD for continuous use of HRT was 2.36 for the first two years and 1.69 for the first eight years. But among recently menopausal women (within 10 years of the menopause) only, the hazard ratios for CHD were 1.29 for the first two years and 0.64 for the first eight years for continuous use of HRT (n=2782) vs matching placebo (n=2712). The CHD-free survival curves for continuous use of HRT and no use crossed over at about six years. These numbers were combined with data from the **Nurses' Health Study**, to further strengthen the analysis, and the conclusions did not substantially change (See Table).

There appear to be different effects for estrogen and progestin and for estrogen only, and it is very likely that different hormone and treatment regimens and different doses have different effects on women at different stages of the menopause. Furthermore the number of younger women in the WHI trial was not large and therefore there was not quite enough statistical power to be entirely certain of these findings of the above new analysis. The findings, however, support the recommendations suggested by the Author in the "Update Issue 54" and the current recommendations by the **FDA** for women to take HRT, if required, to relieve menopausal symptoms, but to use it at the lowest dose and for the shortest time possible.

“
An expected reduction of **CHD risk** should not be a consideration for initiation or continuation of HRT in most newly menopausal women.
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**For the full recommendations on HRT
please see "Update Issue 54"**

References:

- Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33.
- Toh S, Hernandez-Diaz S, Logan R, et al. CHD in postmenopausal recipients of estrogen plus progestin therapy: Does the increased risk ever disappear? A randomized trial. *Ann Intern Med* 2010; 152:211-217.

Variable	Overall	<2 y after baseline	>2 y after baseline
All women	1.48	2.06	1.28
Time since menopause			
<10 y	0.66	1.29	0.53
>10 y	1.86	2.42	1.58
p for heterogeneity*	0.021	0.12	0.018
Age at baseline, y			
50-59	1.05	2.15	0.92
>60	1.82	2.07	1.45
p for heterogeneity*	0.12	0.92	0.22

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