



# INTERNATIONAL MENOPAUSE SOCIETY

THE SOCIETY FOR THE STUDY OF ALL ASPECTS OF THE CLIMACTERIC IN MEN AND WOMEN

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## Press Statement

ISSUED ON BEHALF OF THE INTERNATIONAL MENOPAUSE SOCIETY BY  
Amos Pines, *President*, David Sturdee, *President-Elect* and  
Martin Birkhäuser, *Treasurer*

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### **Health risks after cessation of postmenopausal hormone therapy**

The Women's Health Initiative (WHI) investigators have produced another article<sup>1</sup>, which probably marks the opening of another set of publications, in which the consequences of a further 2.4-year follow-up (after cessation of the study medication) on the estrogen + progestogen (E + P) cohort are reported. The WHI participants stopped their assigned medications prematurely in July 2002 after 5.6 years, but kept their scheduled visits until the end of March 2005. Only 4% of women who were receiving E + P during the initial WHI study restarted hormone therapy (HT) during the follow-up period, which reaffirms the fact that the WHI cohort mainly included asymptomatic, elderly women. Based on the follow-up data, the WHI investigators concluded that, by the end of the post-intervention period, the global index, a newly formed and unvalidated tool used in the WHI trial, was still higher in women randomly assigned to receive E + P compared with placebo, mainly because of the continuation of breast cancer and thromboembolism risk. Osteoprotection seemed to be lost once HT was stopped. However, the results for the post-intervention period were not statistically significant for many components of the WHI global index.

“After such long and painful debates over the results of the WHI study and the perception that age is a very important determinant of the benefit–risk evaluation, it is really a pity that once again the current information on the extended follow-up period is presented in an unsatisfactory way”, says Professor Amos Pines, the President of the International Menopause Society. It seems that the following mistakes were repeated:

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1. There is no mention of the results by age groups and yet, for the age group 50–59 years, the data recorded for the active phase of the WHI E + P arm showed no significant increase in risk of coronary events, strokes and breast cancer in the early postmenopause period. Also, there is no breakdown of the data by years of follow-up. It would be extremely important to know whether the results for the first year post cessation of therapy are similar to those for year 2 and year 3 of follow-up.
  2. The breast cancer results for first-time users of E + P were not presented, whereas breast cancer risk during the active phase of the WHI was similar to that of the placebo group in women with no prior use of E + P.
  3. There is little relevance in the presentation of the combined results for the active phase and the follow-up phase, since it has no real scientific importance. Combining the two periods and grouping the outcomes (all cancers, all cardiovascular events) ‘helped’ the authors to show significance in some of the variables. However, the overall differences in the annualized rates between the E + P arm and the placebo arm were in the order of 1.5 cardiovascular events per 1000 women/year and 1.2 cancers per 1000 women/year. Again, no data were shown for the younger age group.

There has been much speculation on the impact of cessation of hormone replacement therapy (HRT) on breast cancer incidence. Last year, Ravdin and colleagues<sup>2</sup> argued that the decline in HRT use in the USA immediately reduced breast cancer incidence. This has now proved to be unsupported, as breast cancer incidence in the 2.4-year follow-up showed no difference after cessation of HT from placebo. It appears that a gradual decrease in risk over several years, as shown by the Nurses’ Health Study, is more accurate.

“It seems that the WHI investigators have forgotten the turmoil and anxiety they caused in 2002 when they published the preliminary results of the E + P cohort”, concluded Professor Pines. By releasing the new data without performing all the necessary, important sub-analyses, women could face another unjustified turmoil related to hormone therapy.

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## References

1. Heiss G, Wallace R, Anderson GL, *et al.* *JAMA* 2008;299:1036
2. Ravdin PM, Cronin KA, Howlader N, *et al.* *N Engl J Med* 2007;356:1670

### THE INTERNATIONAL MENOPAUSE SOCIETY

The aims of the Society (IMS) are to promote knowledge, study and research on all aspects of aging in men and women; to organize, prepare, hold and participate in international meetings and congresses on menopause and climacteric; and to encourage the interchange of research plans and experience between individual members. The Society is a non-profit association, within the meaning of the Swiss Civil Code. It was created in 1978 during the first World Congress on the Menopause. In addition to organizing congresses, symposia, and workshops, the IMS owns its own journal: *Climacteric*. See website: [www.imsociety.org](http://www.imsociety.org)