10 minutes, joint motion and stretching should be done at the beginning of every session, with a 5 - 10 minute cool-down and stretch period at the end of the session. Attention must be paid to exercise form to help to prevent any injuries.

References available on request.

THE MILLION WOMEN STUDY AND THE CONSEQUENCES OF POOR TRIAL DESIGN

CLAIRE JAMIESON, *BSc, MB ChB*
Private Practitioner, *Constantia, Cape Town*

The Million Women Study (MWS), undertaken in the UK, was published in *The Lancet* in August 2003.[1] The media reported this study in a sensational way. It seems that the wave of unfavourable reporting was a major factor in inhibiting clear and critical analysis of this observational study. Of more concern is that the health regulators in Britain used this study to advise against the use of long-term HRT and against its use in women over 50 with an increased risk of osteoporosis. This has changed the prescribing habits of doctors treating post-menopausal women.
Understandably, many doctors have lost confidence in HRT, largely because of the conflicting and often inappropriate information available. This has had a negative impact on the lives of many symptomatic menopausal women.

The MWS, set up to investigate the relationship between patterns of HRT use and breast cancer, was a poorly designed trial, which did not adequately exclude observational bias and therefore resulted in misinterpretation of the results. Women, recruited from a cohort of 2 million women invited to attend selected breast cancer screening clinics, answered a questionnaire. A total of 828 923 women were selected. These large numbers cannot correct the faults in design; in fact, the opposite can occur as the mistake may be compounded. Personal data and data on current HRT use were gathered, and the incidence of breast cancer and mortality was obtained from the British national cancer and death records.

The most obvious question is whether the women recruited were representative of the whole population. They had accepted the opportunity to be screened by the National Health Service (NHS), which may indicate that they could have been at higher risk initially. Further, no details were given about any previous HRT product used, other than the one currently used. This results in actual exposure categories being in question at recruitment. The absence of information about total exposure means that the main determinant of risk was the reported current exposure. Follow-up was continued to 31 December 2000, and women who were recruited to the trial in the final 3 months of that year were included in the study, although they could not have been followed up. Furthermore, the design made it possible that the exposure category could have been determined years before the diagnosis of breast cancer.

An alarm should have rung with the emergence of biologically implausible results. It is accepted that a breast cancer will take on average 6.8 years from initiation to detection. If HRT accelerates tumour growth, it would still take years. Therefore the MWS conclusion that the incidence of breast cancer increases in the first year of use, and decreases again in the first year off HRT, does not inspire confidence. A further confounding factor is that mammography may detect tumours earlier, leading to an apparent increase in incidence.

The conclusion of the MWS investigators that HRT was responsible for 20 000 cases of breast cancer in the previous 10 years is a gross overestimation of the actual breast cancer risk. Although the estimates of 50 000 extra breast cancers due to obesity and 16 000 due to alcohol use are equally speculative, it is worth noting these risk factors. According to Professor Richard Farmer, an epidemiologist from Surrey, 'It is a very sad thing that the regulatory authority took such a poorly designed study at face value and without discussion imposed regulatory changes, with little regard for the health and well-being of women.'

There is a need for clear, critical analysis of all published trial data. Major therapeutic decisions should not be made on the basis of a single trial. There should be caution where the media are concerned, and advice dispensed by respected regulatory bodies should have the full weight of the academic community behind it and not be influenced by non-scientific factors.

The impact of this British study has been felt in South Africa. The Board of Healthcare Funders has removed HRT from chronic medication lists, and medications approved for treating osteoporosis in postmenopausal women (despite all the irrefutable evidence that HRT prevents fracture), citing the MWS and the advice given by the Committee on Safety of Medicines (CSM) in the UK. South Africa has such a scarcity of health resources and the cost-effective option of HRT for osteoporosis is under siege. We simply cannot afford to prescribe expensive bisphosphonates or other expensive drugs widely. There are no data to suggest that, for a 50-year-old woman, these products will be effective in 20 years' time.

The MWS has confused the issues around treating and managing the menopause. This, together with the collusion of regulatory bodies who should be more circumspect, has resulted in confusion and distress in all aspects of women's health. It is regrettable.

Problems with the MWS

- Not representative of all women
- No consistent follow-up
- No completeness of follow-up
- All HRT was given the same effect
- Inaccurate classification of HRT use
- Biologically implausible results