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**TITLE**

**HRT: OPTIMAL TREATMENT FOR OSTEOPOROSIS PREVENTION**

**AUTHOR/S**

Stevenson J (GB) [1]

**ABSTRACT**

Hormone replacement therapy (HRT) is effective for skeletal conservation in postmenopausal women. It has been shown to reduce fracture risk in both osteoporotic and non-osteoporotic women. It is now increasingly realised that low doses of oestrogen may be effective for bone conservation in most women. HRT is a mainly safe therapy providing it is used appropriately. There are no cardiovascular risks, and likely coronary benefits, when HRT is initiated early in the menopause. Venous thrombo-embolic events can be avoided with non-oral HRT, and any increased risk of breast cancer remains controversial and unproven. Bisphosphonates are a widely used treatment for postmenopausal osteoporosis. However, long term safety issues have become apparent. An increased incidence of atrial fibrillation has been found in some clinical trials; osteonecrosis of the jaw and inflammatory eye disease has also been reported. There are increasing numbers of reports of fragility fractures of the femur, transverse sub-trochanteric fractures occurring spontaneously, with long-term bisphosphonate use. Thus bisphosphonates certainly appear no safer than HRT in terms of unwanted effects, and other unexpected adverse effects could yet arise in the future. Bisphosphonates have an extremely prolonged skeletal retention time, and because of the known and unknown risks of these drugs they should be avoided where possible in women aged below 60 years. Denosumab, a RANK-L antibody, does not have skeletal retention, but osteonecrosis of the jaw and femoral fragility fractures are seen with long term use. Newer agents which affect the Wnt-LRP signal to osteoblasts may be promising but safety needs to be established, and a cathepsin K inhibitor has been withdrawn because of safety issues. HRT should remain the first-line therapy for primary prevention of osteoporosis.

**INSTITUTE**

[1] Imperial College London