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HRT for prevention of osteoporosis

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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. Importantly, it prevents osteoporotic fractures at all the classical sites, such as spine, wrist and hip, which is not seen with all the alternative treatment options. It is now increasingly realised that low doses of oestrogen may be effective for bone conservation in most women. Older women may conserve bone and prevent fractures with very low doses whereas younger women, and especially those with premature ovarian insufficiency, require higher doses. Thus the starting dose of HRT is very age dependent. HRT is a 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 and even stroke risk can be avoided with non-oral HRT, and probably even with very low dose oral HRT. Any increased risk of breast cancer remains controversial. The overall safety of HRT is really established by the fact that there is no increase, and indeed a decrease, in all cause mortality. Of the alternative therapies to HRT for prevention of osteoporosis, bisphosphonates are most widely used. 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 have also been reported. There are increasing numbers of reports of sub-trochanteric fragility fractures of the femur 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. HRT should remain the first-line therapy for primary prevention of osteoporosis.

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