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**Effects of Estrogen Therapy for Osteoporosis**

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**The aim of this report is to fulfill the content of the BMS.**

**Abstract:**

Osteoporosis is a disease that weakens bones, increasing the risk of sudden and unexpected fractures. It results in an increased loss of bone mass and strength. The disease often progresses without any symptoms or pain. Generally, osteoporosis is not discovered until weakened bones cause painful fractures (bone breakage), often in the back (causing chronic back pain) or hips. There is a direct relationship between the lack of estrogen after menopause and the development of osteoporosis. After menopause, bone resorption (breakdown) overtakes the building of new bone. Early menopause (before age 45) and any long phases in which the woman has low hormone levels and no or infrequent menstrual periods can cause loss of bone mass. Hormone therapy (HT) is believed to be useful in preventing or decreasing the increased rate of bone loss that leads to osteoporosis. Hormone therapy is generally recommended for postmenopausal women who have an early menopause, a low bone mass, as measured by a bone density test and menopausal symptoms, and several other risk factors for osteoporosis, such as: a petite, thin frame; family history of osteoporosis, or a medical problem associated with osteoporosis.<sup>(1)</sup>

**Introduction:**

Osteoporosis is a common problem that causes bones to become abnormally thin, weakened, and easily broken (fractured). Women are at a higher risk for osteoporosis after menopause due to lower levels of estrogen, a female hormone that helps to maintain bone mass. The major physiological effect of estrogen is to inhibit bone resorption. Bone cells have two kinds of intracellular steroid receptors for estrogen. Osteoclast apoptosis is regulated by estrogens. With estrogen deficiency, the osteoclasts live longer and are therefore able to resorb more bone.<sup>(1,2)</sup>

**Discussion:**

Menopause predisposes women to osteoporosis due to declining estrogen levels. This results in a decrease in bone mineral density (BMD) and an increase in fractures. The Women's Health Initiative (WHI) randomized controlled trial first proved hormonal therapy (HT) reduces the incidence of all osteoporosis-related fractures in postmenopausal women. However, the study concluded that the adverse effects outweighed the potential benefits on bone, leading to a significant decrease in HT use for menopausal symptoms. Additionally, HT was not used as first-line therapy for osteoporosis and fractures. These studies support that HT improves BMD and reduces fracture risk in women with and without osteoporosis. Furthermore, the studies suggest that low-dose and transdermal HT are less likely associated with the adverse effects of breast cancer, endometrial hyperplasia, coronary artery disease (CAD), and venous thromboembolism (VTE) previously observed in standard-dose oral HT regimens. HT should be individualized and the once "lowest dose for shortest period of time" concept should no longer be used. HT formulations used for the prevention and treatment of osteoporosis, exploring the safety profile of low-dose and transdermal HT that have been shown to be safer than oral standard-dose HT.<sup>(2)</sup>

Hormone replacement therapy (HRT) may consist of oestrogens alone or in combination with progestin. HRT slows bone turnover and increases bone mineral density (BMD) at all skeletal sites in early and late postmenopausal women. The analyses show that HRT decreases fragility fracture risk by 20-35%. Discontinuation

of HRT results in acceleration of bone turnover, decrease in BMD and eventual loss of anti-fracture efficacy. However, despite this anti-fracture efficacy and a decrease in the risk for colon cancer, overall health risks generally outweigh benefits from HRT in older postmenopausal women with a higher incidence of cardiovascular events (unstable angina, thromboembolic stroke, venous thromboembolism including pulmonary embolism) and increased incidence of the endometrial and breast cancer [3-6]. HRT can also induce vaginal bleeding and breast tenderness. Finally, HRT may increase the risk of myocardial infarction, ovarian cancer as well as deterioration of the global cognitive function; however, the evidence is weaker. More recent studies show that even low doses of HRT may protect bone by decreasing bone turnover markers (BTM) levels and preventing bone loss. HRT is regarded as the acceptable treatment for osteoporosis only after all other treatments have been considered and when all the risks and benefits are carefully explained to the patient. Women who decide to take HRT to relieve menopausal symptoms should use the lowest effective dose and for the shortest possible time.(3)

Hormone Replacement Therapy (HRT) has been used successfully for many years to relieve the symptoms of menopause, such as hot flushes, vaginal dryness and loss of libido. Osteoporosis and fractures are more common after the menopause, when estrogen levels drop significantly. HRT is particularly useful for women who have undergone early menopause (before 45 years of age); these women are at greater risk of osteoporosis. In the largely older population of women studied, the researchers reported that whilst HRT significantly reduces the rate of fracture, it increased the risk of heart disease and stroke. Breast cancer risk was found to increase slightly in combined (oestrogen plus progestogen) HRT after several years of use, but decreased in women taking oestrogen – only HRT. Whilst the general protective effects of HRT on bone are not controversial, the role of HRT as a specific treatment for osteoporosis is still the subject of research and discussion. The risks of using HRT increase with increasing age. In women below the age of 60 who do not have risk factors for breast cancer, cardiovascular disease, stroke or venous thrombosis, the risks associated with short-term HRT are very low. Osteoporosis Australia advises that HRT should be considered as a short-term treatment (up to 5 years) for osteoporosis for women below the age of 60 if other osteoporosis treatments cannot be used, or if there are additional reasons for using HRT (ie., relief of menopausal symptoms). Women over 60, who are more likely more likely to develop osteoporosis and experience fracture, are also at higher risk of cardiovascular disease, stroke and venous thrombosis. Treatments for osteoporosis such as bisphosphonates, SERMs, denosumab or strontium ranelate are more suitable for women over 60. It is still not known how long, if at all, the protective effects of HRT on bone continue after HRT treatment ceases. (4)

### **Conclusion:**

Osteoporosis is a condition of fragile bone with an increased susceptibility to fracture. It weakens bone and increases risk of bones breaking. Bone mass (bone density) decreases after 35 years of age, and bone loss occurs more rapidly in women after menopause. Patients with osteoporosis have no symptoms until bone fractures occur. HRT has been shown to prevent bone loss, increase bone density, and reduce and prevent bone fractures.

## References:

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