Table 1. Proposed pathophysiologic links between depression and bone deterioration

**Poor lifestyle, tobacco and alcohol abuse, physical inactivity, dietary imbalances**

**Hormones**
- Gonadal hormones. Suppression due to chronic stress
- GH. Suppression due to chronic stress
- Cortisol. Excessive secretion due to hyperactivity of the hypothalamic-pituitary-adrenocortical axis
- Leptin. Not adequate data to support definite involvement.
- Vitamin D and PTH. Depression linked with hyperparathyroidism, and low vitamin D levels. No association of depression and PTH in majority of studies.

**Sympathetic Nervous System.** Inhibitor of bone mass accrual. Excessive activity in depression.

**Serotonin**
- a. gut-derived: direct effect on bone, promoting reduction in osteoblast proliferation
- b. brain-derived: indirect effect on bone, through decrease of the activity of the sympathetic nervous system. In depression, brain 5HT levels fall. SSRIs may increase the direct effect on osteoblasts.

**Cytokines.** Stimulated, by CRH, production of IL-6

GH: Growth hormone, PTH: Parathyroid hormone, 5HT: Serotonin, SSRI: Selective Serotonin reuptake inhibitor, CRH: Corticotropin releasing hormone, IL: interleukin

not in men. Thus different methodology, inclusion criteria and treatment options may have made the use of depression in this tool impractical.

In the authors’ opinion, since the use of the FRAX score for clinical assessment of osteoporosis is gaining ground, further research work should be performed evaluating the role of depression on the FRAX® score and its overall significance as independent predictive marker.

**F. AVAILABLE GUIDELINES**

According to recent recommendations of the Canadian Network for Mood and Anxiety Treatments (CANMAT) task force for the management of patients with mood disorders and select co-morbid medical conditions: 18

1. The massively growing body of research on mood disorders and their effect on bone health suggests that this relationship is complex, and interpreting these findings has proved to be challenging. Patients age >40 with long-term SSRI exposure (>2 years) should be routinely screened for bone density via dual-energy X-ray absorptiometry (level 2).

2. The data related to long-term use of some mood stabilizers are more definitive, however, and we know that exposure is directly related to decreased BMD. Patients receiving long-term exposure to these medications should be routinely screened for bone density (level 1).

3. For adults age >50 who are at moderate risk of vitamin D deficiency, supplementation with 800 to 1000 IU (20 to 25 mcg) of vitamin D3 daily is recommended (level 2).

**CONCLUSIONS**

The majority of studies and meta-analyses provide evidence of an unfavorable effect of depression on bone health, which is likely to come about via more than one mechanism, suggesting that depression is a risk factor for osteoporosis and fractures. Additionally, patients with osteoporosis suffer the mental consequences of this chronic disease. The relationship is not only limited to postmenopausal women, who tend to be the focus of our interest when we discuss osteoporosis and fractures, but also involves men and young populations. However, because studies and meta-analyses use different diagnostic criteria, populations and methods of analysis, they may provide data that tend to be controversial and conflicting. It is therefore evident that the need for clinical trials to evaluate the effect of different types of depressive disorders as well as the impact on specific populations still exists.

Until then, we strongly believe that psychiatrists should be encouraged to provide patients with depression lifestyle modification instructions in order to improve bone health and avoid falls, while selected patients with depression should be evaluated for osteoporosis. We also agree with Haney et al. that at least SSRI s should be considered medications that contribute to osteoporosis and consequently SSRI users should be screened accordingly. 109