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Letter to the editor

# Treatment adherence and risk of vertebral fracture

Osteoporosis is a prevalent disease worldwide. Our recent projection showed that the number of hip fractures would substantially increase by 2050 [1]; thus, timely management of osteoporosis is required to reduce the burden of the coming "fracture tsunami". Pharmacological intervention is an effective way to improve bone mineral density (BMD) and reduce fracture risk. However, treatment adherence to anti-osteoporosis agents is known to be low. Treatment adherence is commonly defined as the extent to which a person's behavior taking medication corresponds with the agreed medication regime. It was previously reported that approximately 50–75% of women discontinue anti-osteoporosis treatment within the first year [2,3]. However, the association of treatment adherence on vertebral fracture prevention is largely unstudied.

To study the effect of treatment adherence on fracture prevention, randomized controlled trial (RCT) is considered the gold standard. However, participants in RCT are often highly selected, thus leading to an issue in generalizability. Conversely, the real-world cohort is considered having high generalizability, as it contains participants from a real-world clinical setting. When the data in a real-world cohort is analyzed using an appropriate statistical technique (such as propensity score matching), the findings could emulate an RCT, which is known as an emulating RCT [4].

In a recent real-world cohort study conducted by Kim et al [5], the association of treatment adherence of bisphosphonates with the risk of clinical vertebral fracture was evaluated using an emulating RCT design. In this study, those with high adherence, as defined as medication possession rate (MPR) $\geq$ 90%, had a significantly lower risk of clinical vertebral fracture (HR of 0.822) when compared to those with MPR < 90%. Similarly, significant difference in the risk of clinical vertebral fracture was observed for the comparison in MPR $\geq$70% vs < 70% and MPR $\geq$50% vs < 50%, despite the HRs were closer to 1. Notably, such a relationship was observed in various subgroups, such as patients aged $\geq$75 years and patients with type 2 diabetes. Oldest old usually have a different pharmacokinetic and pharmacodynamic profile due to presence of comorbidities [6]. Among comorbidities, type 2 diabetes is now recognized a robust risk factor of fracture, despite it is also associated with higher BMD [6]. This population-based study indeed emphasized the importance of medication adherence in vertebral fracture prevention, even in patients aged $\geq$75 years and patients with type 2 diabetes.

Although this study reassured the importance of treatment adherence to bisphosphonates [7,8] in fracture reduction in a real-world cohort, careful interpretation is required. MPR is commonly used as a measure of treatment adherence. However, medication possession is different from actual treatment adherence. The patient can get the prescribed medication without taking it. Moreover, the cutoff point of treatment adherence used to define optimal therapeutic efficacy was unstudied. The generalizability of that real-world study to other populations is unknown. Nevertheless, future studies should define the cutoff point of treatment adherence for optimal therapeutic efficacy. Lastly, education and patient empowerment are always crucial for improving treatment outcomes.

## Conflicts of interest

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