

Appendix 1 (posted as supplied by the authors)

Despite the widely-endorsed view that ‘vertebral fractures’ are ‘similar/equivalent’ to hip fractures in terms of disease burden, most of these are asymptomatic vertebral compressions visible in an x ray and represent a classic example of overdiagnosis.

- **Arbitrary diagnosis**
 - Depending on the criteria used for classifying a change in an x-ray as ‘a fracture’, their prevalence can vary by as much as 3 - 90% in a given elderly population [1].
- **Rarely “spontaneous” or purely osteoporotic**
 - At least 50% are trauma-induced [2-4].
- **Rarely symptomatic or disabling**
 - Only 1/3 of the x-ray changes termed ‘vertebral fractures’ are symptomatic [5].
 - Poorly predict either the existence of back pain or functional status of the spine [6].
- **Hardly cause death**
 - ‘Vertebral fractures’ have been alleged to be debilitating consequences and even increase the risk of death [7]. However, by the very virtue of the definition of the word “illness” as an indicator of frailty and weakness, almost every illness or degenerative change in older adults is related to increased morbidity and mortality, but few are a truly independent risk factor or direct cause of death.
- **Questionable evidence on the anti-fracture effect of bone-targeted pharmacotherapy**
 - A systematic review for postmenopausal women (Figure 3 of the main paper), estimates that bisphosphonates reduce vertebral compression rates as follows (combined estimates for asymptomatic and symptomatic patients):
 - Primary prevention: 41% relative reduction (95% CI: 39-51), translating to 2% absolute risk reduction (based on 6426 women, or 44% of potentially eligible patients, over an average of 3 years).
 - Secondary prevention: 57% relative reduction (95% CI: 48-63), translating to 8% absolute risk reduction (based on 5331 women; 57% of potentially eligible patients in trials).
 - However, little evidence is available on effects of bisphosphonates on *symptomatic* vertebral compression:
 - Primary prevention: 44% relative reduction (95% CI: 21-60); (based on only two trials comparing alendronate to placebo [8 9], n=4458 or 31% of potentially eligible patients).
 - Secondary prevention: 54% relative reduction (95% CI: 25-72); (based on only two trials comparing alendronate to placebo [10 11], n= 2047; 22% of potentially eligible patients).
 - These estimates are graded as being very low quality of evidence due to the large amount of missing data.
 - Most importantly, these *efficacy* trials and their carefully selected patient populations are poorly representative of the real-life clinical setting.

References:

1. Melton LJ, 3rd, Wenger DE, Atkinson EJ, et al. Influence of baseline deformity definition on subsequent vertebral fracture risk in postmenopausal women. *Osteoporos Int* 2006;**17**(7):978-85 doi: 10.1007/s00198-006-0106-1[published Online First: Epub Date]].
2. Cooper C, Atkinson EJ, Kotowicz M, et al. Secular trends in the incidence of postmenopausal vertebral fractures. *Calcif Tissue Int* 1992;**51**(2):100-4
3. Cooper C, Atkinson EJ, O'Fallon WM, et al. Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985-1989. *J Bone Miner Res* 1992;**7**(2):221-7 doi: 10.1002/jbmr.5650070214[published Online First: Epub Date]].
4. Myers ER, Wilson SE. Biomechanics of osteoporosis and vertebral fracture. *Spine (Phila Pa 1976)* 1997;**22**(24 Suppl):25S-31S
5. Cooper C, O'Neill T, Silman A. The epidemiology of vertebral fractures. European Vertebral Osteoporosis Study Group. *Bone* 1993;**14 Suppl 1**:S89-97
6. O'Neill TW, Cockerill W, Matthis C, et al. Back pain, disability, and radiographic vertebral fracture in European women: a prospective study. *Osteoporos Int* 2004;**15**(9):760-5 doi: 10.1007/s00198-004-1615-4[published Online First: Epub Date]].
7. Wahl DA, Cooper C, Boonen S. Clinicians need to treat underlying osteoporosis. *Bmj* 2011;**343**:d5040 doi: 10.1136/bmj.d5040[published Online First: Epub Date]].
8. Bone HG, Downs RW, Jr., Tucci JR, et al. Dose-response relationships for alendronate treatment in osteoporotic elderly women. Alendronate Elderly Osteoporosis Study Centers. *The Journal of clinical endocrinology and metabolism* 1997;**82**(1):265-74 doi: 10.1210/jcem.82.1.3682[published Online First: Epub Date]].
9. Cummings SR, Black DM, Thompson DE, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. *JAMA : the journal of the American Medical Association* 1998;**280**(24):2077-82
10. Black DM, Cummings SR, Karpf DB, et al. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. Fracture Intervention Trial Research Group. *Lancet* 1996;**348**(9041):1535-41
11. Qin L, Choy W, Au S, et al. Alendronate increases BMD at appendicular and axial skeletons in patients with established osteoporosis. *Journal of orthopaedic surgery and research* 2007;**2**:9 doi: 10.1186/1749-799X-2-9[published Online First: Epub Date]].