

NOFSA EDITORIAL

NOFSA statement on the appropriate management of osteoporosis in the elderly – myth and reality

The National Osteoporosis Foundation of South Africa (NOFSA) would like to comment on 2 areas of contention namely calcium and vitamin D supplementation and the use of pharmacotherapy to prevent fractures. These controversies are fundamentally based on 2 papers by Järvinin¹ and Greg & Bollard². There have been several published responses to these articles by respected sources such as the International Osteoporosis Foundation (IOF) available on the NOFSA website (www.osteoporosis.org), which allow the reader to formulate a balanced opinion. For the sake of scientific balance, we will address several key points raised in these papers.

1. NOFSA agrees that better management of patients who have suffered a hip fracture is essential and a joint publication by NOFSA and the South African Geriatrics Society (SAGS) offers local recommendations for patients who have suffered a fracture of the proximal femur³.
2. NOFSA agrees that “most hip fractures occur in people older than 75 years, many of whom are frail or have co-morbidities”. Focussing only on hip fractures however, as done in the Järvinin¹ paper greatly undervalues the total benefit of therapy for osteoporosis. Hip fractures constitute only a small percentage of total fractures due to osteoporosis and many of these fractures occur after extremely minor trauma. Spine fractures and non-vertebral non-hip fractures constitute the vast majority of insufficiency fractures in the elderly and are associated with considerable morbidity and even increased mortality⁴. Falls prevention strategies should indeed form part of the clinical assessment of all older patients. This is however only a small part of total fracture prevention.
3. The Järvinin¹ paper claims that “it is the trauma of the fall that causes the fracture of their fragile bones” and “it is the propensity to fall, not bone fragility that predicts fractures”. This begs the question of why babies who fall more than the elderly do not sustain fractures consequent to these falls. We differ from this opinion on the following basic principles:
 - a. There is a clear association between low bone mass and fracture risk in post-menopausal women and older men.
 - b. Other risk factors for fracture are important and should be included when assessing individual fracture risk. These risk factors (age, previous fractures, low BMI, smoking, excess alcohol, secondary osteoporosis, glucocorticoids, etc) have been included in various fracture risk algorithms including those advocated by NOFSA and FRAX[®]
 - c. Randomised clinical trials (RCT’s) have consistently demonstrated efficacy at reducing fractures at spine, hip and non-vertebral sites. RCT’s serve as the gold standard for evidence based medicine.
 - d. Compston⁵ addresses the claim that osteoporosis medications have not been proven to work in the elderly.

She offers several explanations for this. A number of studies have suggested lack of efficacy of treatment in the elderly. In one study subjects were randomised based only on risk factors and not BMD⁶. A second study was not adequately powered to demonstrate fracture efficacy in the older woman⁷. In a third study hip fracture was not a primary endpoint⁸. A fourth study was grossly underpowered to demonstrate hip fracture efficacy⁹. As stated by Compston “absence of evidence does not constitute evidence for absence of effect”.

- e. The aim of treatment is the prevention of all fragility fractures as stated above. Analyses from some of the pivotal studies have in fact shown efficacy in this regard in the older patient. Boonen et al¹⁰ analysed pooled data from RCT’s in women 80 years and older and showed an 81% reduction in new vertebral fractures in women treated with risedronate compared to placebo after only 1 year. Analysis of data from 3658 women treated with alendronate showed a consistent relative risk reduction for hip, spine and wrist fractures across all age groups¹¹. Boonen et al¹² also showed significant relative risk reduction in all new clinical fractures (35%), clinical vertebral fractures (66%) and non-vertebral fractures (27%) in women >75 years on zoledronic acid compared to placebo enrolled on the Horizon trial.
4. We agree with IOF regarding:
 - a. Osteoporosis is still alarmingly under-diagnosed and undertreated, even after a fragility fracture.
 - b. The elderly are particularly vulnerable where levels of diagnosis and treatment are lowest.
5. Like the IOF, NOFSA in its guidelines advocates a systemic approach to fracture prevention which includes lifestyle modification (stop smoking and reduce alcohol), good diet, exercise and fall prevention strategies.
6. The harsh reality however is that the vast majority of falls prevention programs have failed to reduce fracture risk¹³. The meta-analysis which suggests that preventing falls can reduce fracture risk¹⁴ is inherently flawed in that most women on the study were under 75 years of age and many did not have risk factors for falling. Extrapolating this data to the frail elderly at high risk of falls and fracture is ill advised, as a simple exercise program including advice to exercise or walk is extremely hazardous, and if not done under controlled conditions with expert guidance (biokinetics), will serve to increase the risk of falls and fractures.
7. Measures to prevent falls should be an integral part of a fracture prevention program. However assertions that such measure are as effective or more effective in preventing fractures as pharmacotherapy is a misrepresentation of current evidence.

8. The potential of therapeutic harm with osteoporosis medication is overstated. Patients with active upper gastrointestinal problems should not be prescribed an oral bisphosphonate. In other patients upper GI adverse events are extremely rare provided the drug is taken in the correct manner. Atypical fractures and osteonecrosis of the jaw (ONJ) are extremely rare complications in patients with osteoporosis treated for <5 years or when the recommended doses for fracture protection are used as opposed to the far higher doses used in oncology.
9. The perception that there is harm in being treated with drugs of no proven benefit in the elderly that are not proven to be cost effective and have known side effects is inaccurate and misleading. An approach to fracture prevention which includes drug therapy has in fact been shown to be cost effective⁵. Intervention thresholds based on clinical assessment and rational use of guidelines will allow appropriate and cost effective treatment of those at greatest risk of fracture.
10. Juliet Compston⁵ succinctly states “Editors of academic journals have a responsibility to ensure that published papers are balanced and reflect the available evidence”. This is true of a journal such as the British Medical Journal (in which the 2 papers were published) which is widely read by primary care practitioners and healthcare commissioners who cannot be expected to have in-depth knowledge of specialist topics. We agree with Compston that unbalanced opinions, such as those in these 2 publications do a disservice to the elderly who suffer fragility fractures and to the scientists and patient organizations that have worked tirelessly over many years to improve their management.
11. Regarding calcium & vitamin D – Updated guidelines regarding adequate calcium and vitamin D are available from IOF and NOFSA (www.iofbonehealth.org, www.osteoporosis.org). NOFSA does not advocate routine calcium or vitamin D supplementation. Calcium needs should be met via dietary sources if possible. Our updated guidelines recommend only supplementing calcium (maximum 500mg per day) in those who have osteoporosis or are at risk of fracture and who cannot or will not take adequate calcium in the diet. For vitamin D our guidelines recommend 800IU daily only for those who have osteoporosis or who are at high risk of fracture. Any suggestion that doctors are prescribing

calcium and vitamin D because of perverse incentives is firmly rejected by NOFSA. Doctors do after all prescribe anti-hypertensives, statins, diabetes medication, anti-depressants and menopausal hormone therapy; all of which are marketed and sold by the pharmaceutical industry. All pharmaceutical products should be prescribed in an appropriate manner in patients deserving of treatment. There is no perverse incentive in prescribing the best available and most cost effective treatment for the appropriate patient.

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On behalf of the National Osteoporosis Foundation of South Africa

References

1. Jarvinen TL, Michaëlsson K et al (2015) Overdiagnosis of bone fragility in the quest to prevent hip fracture. *BMJ* 350:h2088
2. Grey A, Bolland M. Web of industry, advocacy, and academia in the management of osteoporosis. *BMJ*, July 2015 DOI: 10.1136/bmj.h3170.
3. Cassim B, Lipschitz S, Paruk F, Tipping B (2013) Recommendations for the acute and long-term medical management of low-trauma hip fractures. *JEMDSA* 18:21-32
4. Roux C, Wyman A,GLOW investigators et al (2012) Burden of non-hip, non-vertebral fractures on quality of life in post-menopausal women: the Global Longitudinal study of Osteoporosis in Women (GLOW). *Osteopor Int* 23:2863-2871
5. Compston J (2015) Editorial Overdiagnosis of Osteoporosis: fact or fallacy? *Osteopor Int* 26:2051-2054
6. McClung MR, Geusens P et al Effect of risedronate on the risk of hip fracture in elderly women. *HIP Intervention Program Study Group. NEJM* 344:333-340
7. Eastell R, Black DM, et al. HORIZON Pivotal Fracture Trial et al (2009) Effect of once-yearly zoledronic acid five milligrams on fracture risk and change in femoral neck bone mineral density, *J Clin Endocrinol Metab* 94:3215-3225
8. Lyles KW, Colon-Emeric CS.....for the HORIZON Recurrent Fracture Trial et al (2007). Zoledronic acid in reducing clinical fracture and mortality after hip fracture. *NEJM* 357:nihp40967
9. Greenspan SL, Perera S (2015) Efficacy and safety of single-dose zoledronic acid for osteoporosis in frail elderly women: a randomised clinical trial. *JAMA Intern Med* 175:913-921
10. Boonen S, McClung et al (2004) Safety and efficacy of risedronate in reducing fracture risk osteoporotic women aged 80 and older: implications for the use of antiresorptive agents in the old and oldest old. *J Am Geriatr Soc* 52:1832-1839
11. Hochberg MC, Thompson DE, FIT Research Group et al (2005) Effect of alendronate on the age-specific incidence of symptomatic osteoporotic fractures. *J Bone Miner Res* 20:971-976
12. Boonen S, Black DM et al (2010) Efficacy and safety of a once-yearly intravenous zoledronic acid 5mg for fracture prevention in elderly post-menopausal women with osteoporosis aged 75 and older. *J Am Geriatr Soc* 58:292-299
13. Silva RB, Eslick GD et al (2013) Exercise for falls and fracture prevention in long-term care facilities: a systemic review and meta-analysis. *L Am MedDir Assoc* 14:685-689
14. Gillespie LD, Robertson MC et al (2012) Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 9:CD007146
15. El-Khoury F, Cassau B et al (2013) The effect of fall prevention exercise programmes on fall induced injuries in community dwelling older adults: systemic review and meta-analysis of randomised controlled trials. *BMJ* 347:f6234