



**PROPOSED REVIEW OF SIGN GUIDELINE
CONSULTATION FORM**

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| Title of guideline | SIGN 71: Management of osteoporosis |
| Date of publication | June 2003 |
| SIGN scoping search – sources | <p>MeSH headings for the condition specified and any common variations as free text, plus terms for the interventions and care processes discussed in the guideline</p> <p>Sources: Guidelines: NICE; National Library for Health guidelines finder; National Guidelines Clearinghouse; GIN Web site. Technology appraisals: NICE; UK HTA database (Southampton); INAHTA database. Cochrane reviews: Cochrane Library. Other good quality systematic reviews: UK HTA database (Southampton); DARE.</p> |
| SIGN scoping search - summary | <p>Guidelines – 3 HTAs – 3 Cochrane reviews – 2 Other good quality systematic reviews – 5</p> |
| Other guidelines/HTAs | <p>International Society for Clinical Densitometry. <i>Diagnosis of osteoporosis in men, premenopausal women, and children. J Clin Densitom</i> 2004 Spring;7(1):17-26. There is no clear indication of what evidence this guideline is based on.</p> <p>National Institute for Health and Clinical Excellence. <i>Osteoporosis: assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk. London;NICE</i></p> <p>Prodigy. <i>Osteoporosis: treatment and prevention of fragility fractures. May 2006. [cited 1 August 2006] Available from url: http://www.prodigy.nhs.uk/osteoporosis_treatment_and_prevention_of_fragility_fractures</i> This guidance is based on the NICE technology assessment of bisphosphonates, NICE guideline on falls, the SIGN osteoporosis guideline, and the RCPL guideline on glucocorticoid induced osteoporosis.</p> <p>Agency for Healthcare Research and Quality. <i>Percutaneous kyphoplasty for vertebral fractures caused by osteoporosis and malignancy and percutaneous vertebroplasty for vertebral fractures caused by osteoporosis and malignancy. Rockville: Agency for Healthcare Research and Quality (AHRQ), 2005.</i></p> <p>National Institute for Health and Clinical Excellence. <i>The clinical effectiveness and cost effectiveness of technologies for the primary prevention of osteoporotic fragility fractures in postmenopausal women. London;NICE: n.d.</i> Covers bisphosphonates (alendronate, etidronate, risedronate), raloxifene, strontium ranelate, and teriparatide.</p> <p>National Institute for Health and Clinical Excellence. <i>The clinical effectiveness and cost effectiveness of technologies for the secondary prevention of osteoporotic fractures in postmenopausal women. London;NICE:2005. (Technology Assessment 87).</i> Covers bisphosphonates (alendronate, etidronate, risedronate), raloxifene, and teriparatide. Excludes women who have been taking corticosteroids. Recommends all these drugs for use in specific classes of patient depending on a range of factors including age, bone density, and fracture history</p> |
| Main conclusions from new evidence | <ul style="list-style-type: none"> ▪ A Cochrane review found evidence to support the efficacy of strontium ranelate for the reduction of vertebral fractures (and to a lesser extent non-vertebral fractures) in postmenopausal osteoporotic women and an increase in BMD (all sites) in postmenopausal women with and without osteoporosis. Adverse events leading to study withdrawal were not significantly increased in the strontium ranelate group. Potential risks to |

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| | <p>the vascular and neurological system associated with taking 2 g of strontium ranelate daily need to be further explored and quantified. <i>The guideline does not discuss strontium ranelate and to reduce vertebral fracture risk in postmenopausal women who have suffered at least one vertebral fracture and who have had osteoporosis confirmed by DXA scanning currently recommends either oral raloxifene (60 mg daily + calcium ± vitamin D) (A) or intranasal calcitonin (200 IU daily + calcium ± vitamin D) (B).</i></p> <ul style="list-style-type: none"> ▪ A Cochrane review concludes that the limited evidence currently available does not support the use of calcitonin to control pain from bone metastases. <i>The guideline notes that calcitonin has been shown to be of value in control and treatment of chronic back pain, but makes no recommendations about any aspect of pain management.</i> ▪ A systematic review concludes that compared with placebo, raloxifene's primary clinical benefit is a reduction in vertebral fracture in older postmenopausal women, particularly if some vertebral fractures are present at baseline. This benefit is offset by a similar increase in serious adverse events due to venous thromboembolic disease. Raloxifene causes significantly more mild to moderate adverse effects such as hot flashes and leg cramps compared with placebo, but significantly less vaginal bleeding than estrogen-progestin combination therapy <i>In postmenopausal women who have suffered at least one vertebral fracture and who have had osteoporosis confirmed by DXA scanning, the guideline recommends oral raloxifene (60 mg daily + calcium ± vitamin D) (A). In frail, elderly (aged 80+ years) women with or without previous osteoporotic fractures, the guideline recommends either oral risedronate (5mg daily or 35 mg once weekly + calcium ± vitamin D) or oral alendronate (10 mg daily or 70 mg once weekly + calcium ± vitamin D) to reduce fracture risk at all sites (A).</i> <p>Additional comments</p> <p>Comments</p> <p>This guideline specifically does not cover fall prevention.</p> <p>Many American osteoporosis guidelines have been updated in the past few years, but most either predate or were published around the time of the SIGN guideline.</p> <p>Assessment of risk was a major issue in the original SIGN guideline that was not completely resolved. A “quick and dirty” Medline search over the last three years suggests that a fair amount of work has gone on in this area and some risk scores have been developed, though there is no clear indication of consensus on which is the best.</p> <p>A protocol for a new Cochrane review has been published on Interventions for improving the appropriate use of imaging in people with musculoskeletal conditions. No expected date of publication is given, but it is likely to be 1-2 years away.</p> <p>The Cochrane Review on calcitonin is included as this was the only drug referred to as possibly controlling pain in the previous guideline. Pain control was identified as a major patient concern at the time of the last guideline.</p> |
| New areas that could be added to the guideline | <ul style="list-style-type: none"> ▪ Pain control ▪ Role of strontium ranelate |
| Summary of the recommendations that could be updated | <ul style="list-style-type: none"> ▪ Recommendations on use of raloxifene |

Please answer the following questions as fully as possible:

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| Name, designation, organisation: | GP: 3 Biochemist: 1 Other: 7 Academics: 2 Consultant Physician: 1 Rheumatologist: 1 |
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1(a) Is there still a requirement for an evidence-based guideline on this topic?

- Yes = 14
- Osteoporotic fractures are a major cause of morbidity and mortality and have a major impact on individual patients, their families and carers, as well as more generally on society. In addition, osteoporosis is a major burden on the NHS, both in financial terms and also with respect to overall resource consumption.
For example:
 - Osteoporosis is the most common human metabolic bone disorder ¹
 - One in two women and one in five men will suffer a fracture after the age of 50 ²
 - Half of people suffering an osteoporotic hip fracture can no longer live independently as a result of the injury ³
 - About 20% of hip fracture patients die within a year as a result of the fracture ⁴
 - Hip fracture patients occupy one in five orthopaedic beds ⁵
 - 40% of patients sustaining a clinical vertebral fracture will have constant pain and the majority will have difficulties with activities of daily living ⁶
 - The combined cost of social and hospital care for patients with a hip fracture amounts to more than £1.8 billion per year in the UK and is likely to increase to 2.1 billion by 2020 ⁷
 - Each year fractures in patients aged 60 years and over account for more than 2 million hospital bed days in England, which is more than cardiac ischemia, diabetes, heart failure or obstructive airway disease ⁷
 - It is estimated that only 23% of patients with osteoporosis are currently treated ⁸, yet it is one of the few areas in which early intervention can make a real impact on the burden of the disease ⁹

All of the above facts build a strong case for the ongoing requirement for up-to-date evidence-based guidelines on this topic. Furthermore since SIGN 71 on the management of osteoporosis was produced in 2003 there have been significant advances in the management of this condition, including the arrival of new treatments such as strontium ranelate, as well as the bisphosphonates ibandronate and zoledronate (licensed in the treatment of post-menopausal osteoporosis from middle of October 2007). The availability of new and efficacious treatments since the development of the initial guideline would support a complete revision of the existing national clinical guideline.

References:

1. *Osteoporosis in Focus*. Niall Ferguson. Pharmaceutical Press. 2004.
2. National Osteoporosis Society website. *What is Osteoporosis*. www.nos.org.uk/osteo
3. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *The Lancet* 2002;359(9319):1761-7
4. Cooper C, Atkinson EJ, Jacobsen SJ et al. *Am J Epidemiology* 1993; 137: 1001-1005
5. Lindsay R. The Burden of Osteoporosis: Cost. *Am J Medicine* 1995; 98 (2a): 9S – 11S
6. Scane AC, Sutcliffe AM and Francis RM, The sequelae of vertebral crush fractures in men. *Osteoporos Int* 1994; 4:89-92
7. National Osteoporosis Society. *A proposal to improve health outcomes for people at risk of osteoporotic fractures through the Quality and Outcomes Framework*. NOS Working Party on the GMS Contract. May 2005
8. NHS R&D HTA Programme. The clinical effectiveness and cost effectiveness of technologies for the primary prevention of osteoporotic fragility fractures in postmenopausal women. Dr Matt Stevenson, Dr Lloyd Jones, Ms Sarah Davis, Ms Catherine Beverly
9. National Osteoporosis Society. *Primary Care strategy for osteoporosis and falls: A framework for health improvement programmes implementing the national service framework for older people*. 2002. Message from the Chief Medical Officer, Sir Liam Donaldson.
10. National Service Framework (NSF) for Older People 2001. Accessed from www.dh.gov.uk

- Yes, although the treatment options for patients with osteoporosis remained static for many years, new chemical entities have entered mainline treatment with robust evidence since the last review. This includes both monthly and intravenous preparations.¹ Bonviva (ibandronic Acid) 150mg & 3mg Summary of Product Characteristics, October 2006.
- yes, there is a need for an evidence-based guideline on the management of osteoporosis.
- There is still a requirement for an evidence-based guideline on this topic undoubtedly. The existing recommendations still hold true but the original guideline, as you have identified, did not include assessment of Strontium Ranelate, Synthetic PTH of which there are now two variants, Ibandronate and Zoledronic Acid (that is “hot off the press” and soon to get its licence for osteoporosis and for which SMC approval is about to be sought following the publication of the HORIZON Study recently in the *New England Journal of Medicine*).

1(b) If no, should the guideline be withdrawn?

2(a) Do you agree with the assessment of the impact of the new evidence and its likely effect on recommendations?

- Yes = 14

- Yes – there is a possibility for a chronic pain guideline rather than adding pain control here
- The new evidence listed omits to mention that both a once monthly oral bisphosphonate and intravenous bisphosphonate are now licenced by the regulatory authorities¹ and approved by the SMC for the treatment of osteoporosis.²

Similarly recently published evidence on compliance to current therapy has been omitted.^{3,4,5,6,7} Both these areas must alter recommendations as they will both influence current and future clinical practice.

1. Bonviva (ibandronic Acid) 150mg & 3mg Summary of Product Characteristics, October 2006.

2. <http://www.scottishmedicines.org.uk> SMC ID 228/05 & 301/06

3. Brankin E, Walker M, Lynch N, Aspray T, Lis Y, Cowell W. The impact of dosing frequency on compliance and persistence with bisphosphonates among postmenopausal women in the UK: evidence from three databases. *Curr Med Res Opin.* 2006;22(7):1249-56

4. Cooper A, et al. *Int J Clin Practice* 2006;60:896-905

5. Cramer JA, Amonkar MM, Hebborn A, Altman R. Compliance and persistence with bisphosphonate dosing regimens among women with postmenopausal osteoporosis. *Curr Med Res Opin.* 2005;21(9):1453-60.

6. Poole KE, Compston JE. *BMJ* 2006;333:1251-1256

7. Siris ES, et al. *Mayo Clin Proc* 2006;81:1013-1022

2(b) Based on the information given above, and your own clinical judgement, does the guideline require revision in the light of new evidence? *Please give details.*

- yes = 11
- no = 1
- Not full revision, but maybe updated information on risk assessment and strontium is needed
- There is also a need for ibandronate (oral + i.v) zoledranate (i.v) and PTH (1-84sc) to be included in the guideline
- Recommendations on the use of existing drugs should be updated and new ones, such as strontium ranelate and long-acting bisphosphonates included. The question of compliance should be addressed. Advice on monitoring and frequency of repeat scans should be expanded. Given an extension of the remit, other factors than bone mineral measurement, such as falls assessment, pain control and clinical factors should be considered.
- Yes, in addition consider review of comments on HRT in 2003, teriparatide, iandronate/role of intravenous bisphosphonates
- Yes. Strontium ranelate is a first class treatment licensed to reduce the risk of both vertebral and hip fracture in the management of post-menopausal osteoporosis. There is emerging evidence that PPI is associated with increased fracture risk and therefore strontium ranelate is a first line treatment option in patients at risk of PPI use. Consequently, this new evidence will impact on clinical practice and the 2003 guideline requires revision to reflect these changes.
- Yes. In order to improve the outcome for patients with osteoporosis we must ensure that patients have the best chance of remaining with their preventive intervention. This must include the increased options available to clinicians in 2007/8.^{1,2,3,4}
 1. Eastell R, et al. *Calcif Tissue Int* 2003;72:408 (Abstract P297).
 2. Sebaldt RJ, et al. *Osteoporos Int* 2004;15(Suppl. 1):S107 (Abstract P391SA).
 3. Siris ES, et al. *Mayo Clin Proc* 2006;81:1013-1022.
 4. Huybrechts KF, et al. *Bone* 2006;38:922-928.
- Yes, the current guideline requires a revision to be in line with the current evidence. Evidences are as follows:
 - Persistence is poor among patients who are on bisphosphonates. It is known that only 22% of patients persist with a daily bisphosphonate and only 39% of patients persist with a weekly bisphosphonate within the first year.
 - Most patients fail to adhere to bisphosphonate therapy as a result of side effects, taking the treatment incorrectly or failure to renew prescriptions.
 - Less frequent dosing and alternative routes of delivery of bisphosphonates while retaining efficacy, may provide greater convenience, thereby promoting long-term adherence and helping to improve therapeutic outcomes.
 - Newer formulations such as ibandronic acid 150mg monthly and 3mg intravenous are available.
 - One year of persistence with bisphosphonate medication can reduce the risk of osteoporotic fracture by 30%.
 - A recent study shows that additional healthcare professional support of people with osteoporosis increases adherence to antiresorptive therapy by 57% compared to standard care

- Ibandronic acid 2.5mg has been shown to reduce vertebral fractures by 62% and non-vertebral fractures in a high risk sub-group by 69% over three years
- Ibandronic acid 150mg monthly has been shown to be non-inferior to alendronic acid 70mg weekly in terms of bone mineral density gain at the lumbar spine and total hip.
Ibandronic acid plus a patient support programme has been showed to improve persistence by 57% over weekly alendronic acid
- While I am confident that the current recommendations that are in SIGN 71 will remain, particularly in light of the availability of generic Alendronate, there certainly would be value in updating to reflect the current range of pharmaceutical preparations that are available, specifically with regard Strontium Ranelate, Ibandronate (oral and intravenous), Zoledronic Acid (intravenous) and the two forms of parathyroid hormone.

3 Please list any additions to the remit of the guideline that you think would be beneficial

- Possibly reference to horizon trial, now England Journal 2007, zoledronic acid
- Update on use of HRT
- The remit should be extended to embrace fracture risk assessment and advice, not just osteoporosis.
- The pain caused by osteoporotic fractures can be acute and breathtaking, or chronic and disabling. Living with pain can be very isolating. Being physically restricted by pain can have a massive impact on daily life and its activities. It also affects the person's own emotions and relationships with those around them. Good pain management should include all available therapies from medication to hydrotherapy and be tailored to the individual's needs.
Can there be some expansion of the 2003 section on the management of pain and better communication with the patient in order to aid compliance with medications and encourage better self management of the condition?
- Fall prevention
- An appendix on falls management and prevention would be helpful
- The authors might consider the implications of the new WHO risk algorithm soon to be published.
- Given the size of the problem with associated mortality, morbidity and financial cost to society, I feel that the guideline should remain as a straightforward management of osteoporosis. This does not undermine the needs for a robust NHS strategy around Falls, Fractures and Osteoporosis which pulls together clinical and social care.
- Other additions to the present guideline that might be beneficial:
 - Treatment of severe osteoporosis, for example, use of calcitonin, parathyroid hormone
 - Investigation plans for osteoporosis
 - Monitoring of patients when they have been prescribed with anti-osteoporotic medications to ensure that they are protected against fracture
 - Screening for new osteoporosis patients as only around 10-20% of female osteoporosis patients receive drug treatment for osteoporosis in the UK
 - Patient support programme through practice or hospital practice nurse to enhance persistence and understanding of the disease.
- Length of treatment. Treatment of the elderly. Treatment of men. Treatment of corticosteroid induced osteoporosis & prophylactic treatment with corticosteroids.
- I think we should be very careful about extending the guideline to include falls. The reality is that there is currently virtually no evidence that falls interventions can reduce fracture risk. Whilst, undoubtedly, falls services should be integrated with those striving to achieve fracture risk reduction through provision of osteoporosis assessments and treatment, to include this in a single guideline I think would be difficult to achieve. Falls-related issues are highly politically driven just now and the drive has largely preceded the availability of quality evidence of efficacy. There is efficacy that very specific interventions work in specific groups of people to reduce the risk of falls but not of fractures. My recommendation would be to avoid integrating falls interventions into the management of osteoporosis guideline but on might argue that this deserves to be looked at as a separate guideline exercise. This is a theme that many organisations and agencies internationally have, however, already dealt with – including publications of guidelines under the auspices of the British Geriatric Society amongst others.

4 Please tick your preferred option for reviewing this guideline

- a. there is no new evidence that will affect existing recommendations and the guideline should not be reviewed at this time

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| b. some recommendations will change in the light of the new evidence and selected elements of the guideline should be reviewed | 9 |
| c. the entire guideline should be reviewed | 5 |
| d. the guideline should be withdrawn | |

Thank you very much for taking part in this consultation.

Please return to: Safia Qureshi, SIGN Executive, 28 Thistle Street, Edinburgh EH2 1EN, safia.qureshi@nhs.net

Additional Comments:

The Scottish Exec is probably going to include Falls prevention in the new set of enhanced services for primary care this year. If this is not chosen then it certainly will be next year.

Osteoporosis has also been proposed for future QOF criteria.

There is a big drive on to try to prevent admissions to hospital and SPARRA data is being shared with general practices and various initiatives proposed to help prevent admission or at least re-admissions. I imagine that falls prevention would fit well under this too.

So as an evidence base to inform these NHS initiatives I could see the expansion of the guideline in this direction being useful.

What you may not be fully reflecting in your search for other guidelines is that NICE are on the point of competing their process for preparing ACDs on the secondary prevention of osteoporosis fractures and also on the primary prevention of osteoporosis fractures and these will inform publication of primary and secondary prevention guidelines