NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

QUALITY AND OUTCOMES FRAMEWORK (QOF) INDICATOR DEVELOPMENT PROGRAMME

Review of QOF indicators

Potential output: Recommendations for indicator development

Date of Primary Care QOF Indicator Advisory Committee meeting: 3 June 2010

Introduction

In December 2009 the Advisory Committee reviewed the topic of osteoporosis in relation to a recommendation in NICE technology appraisal 161: Osteoporosis – secondary prevention including strontium ranelate. The Committee agreed that this was an important clinical condition and that the topic area met the Department of Health's prioritisation criteria. However, the Committee did not recommend this topic for indicator development on the basis that: a) the evidence base presented was for a single drug; b) there were concerns around availability of investigations (provision of DXA scanning); and c) the potential overlap with an existing directed enhanced service (DES).

This briefing note brings together the wider evidence base to support indicator development for osteoporosis along the following lines:

1. A [prospective] register of people with a history of fragility fracture (A fragility fracture is defined as a fracture occurring after a fall from standing height or less) who have had a diagnosis of osteoporosis confirmed by a DXA scan **or** A [prospective] register of people with a history of fragility fracture.

2. An indicator on the percentage of people with history of fragility fracture in whom osteoporosis is confirmed on DXA scan, who are treated with an appropriate bone sparing agent.

3. An indicator on the percentage of women aged 75 years and older with a history of fragility fracture who are treated with an appropriate bone sparing agent.

4. An indicator on the percentage with a confirmed diagnosis of osteoporosis who are treated with bone sparing agents who have had a medication review in the previous X months to support adherence with treatment.

Background

It is estimated that 1.2 million women in the UK have osteoporosis. Osteoporosis occurs when there is a loss of some of the materials that make up bones. As a result, the bones become fragile and can fracture easily. The bones most likely to break are the hips, wrists and spine. Hip fracture is the major adverse consequence of osteoporosis. One in five people with osteoporotic hip fracture die within the first year of fracture while 50% are no longer able to live independently, and one in five require long-term nursing care.

In older women, fear of hip fracture is profound. Age is one of the major risk factors for primary osteoporosis. It can affect both sexes, but women who have gone through the menopause are at particular risk because their ovaries no longer produce oestrogen, which helps to protect against bone loss.

Prospective register of patients who have sustained a fragility fracture

The ability to identify men and women with a fragility fracture is required in order to implement NICE and SIGN recommendations on the treatment of osteoporosis. NICE technology appraisal 167 covers postmenopausal women, while the SIGN guideline covers both men and women (see Appendix A). The SIGN guideline recommends:

Patients who have suffered one or more fragility fractures should be priority targets for investigation and treatment of osteoporosis

Bone sparing agents for those with a confirmed osteoporotic fracture

NICE technology appraisal 167 relates only to treatments for the secondary prevention of fragility fractures in postmenopausal women who have osteoporosis (confirmed by energy X-ray absorptiometry (DXA) scanning), and who have sustained a clinically apparent osteoporotic fragility fracture. For those women aged 75 years or older, the diagnosis of osteoporosis may be assumed if the responsible clinician considers a DXA scan to be clinically inappropriate or unfeasible.

NICE technology appraisal 167 assumes that women who receive treatment have an adequate calcium intake and are vitamin D replete. Unless clinicians are confident that women who receive treatment meet these criteria, calcium and/or vitamin D supplementation should be considered.

Following a decision by the high court, NICE has been asked by the court to reach a fresh decision on the efficacy, and therefore cost effectiveness, of strontium ranelate (one of the drugs assessed in the technology appraisal). In these circumstances, NHS commissioning bodies make their own local arrangements as to the circumstances in which strontium ranelate can be prescribed in addition to the positive recommendation in the current technology appraisal. The guidance on the use of strontium ranelate is being reconsidered and will be reissued in due course. However, since the suggestion for indicator development is on the treatment of osteoporosis with a class of drugs, the decision of the high court does not preclude this topic from being progressed for indicator development.

The first-line drug for the treatment of osteoporosis is alendronate, the evidence base for which was outlined in the briefing paper presented at the last Advisory Committee meeting (see appendix C). The evidence base for the class of drugs that NICE recommends for the treatment of osteoporosis (that is, bone sparing agents) is presented in appendix B. It has been suggested by stakeholders that indicator development should be on incentivising the treatment of osteoporosis with the class of drugs, in the same way QOF does for other disease areas, rather than naming a particular drug in the indicator wording.

A referral for DXA scanning is a pre-requisite for the treatment of osteoporosis with bone sparing agents. This was explicitly modelled in the cost-effectiveness analysis carried out as part of NICE technology appraisal 167, and was considered to be a

cost-effective use of NHS resources in the diagnosis and subsequent treatment of osteoporosis.

The stakeholders suggest the development of an indicator to support treatment adherence/compliance. Potential non-compliance with prescribed medication was considered in the cost-effectiveness analysis for the technology appraisal. The expected non-compliance did not alter the overall cost effectiveness of the treatment regime. Neither the NICE technology appraisal nor the SIGN clinical guideline recommended specific regular follow-up to ensure medication compliance. It should also be noted that there is currently an indicator in QOF that requires a medication review on a 15-month basis (Medicines 12).

The current SIGN guideline on osteoporosis makes a specific recommendation for the treatment of osteoporosis in men (see appendix B). The stakeholders suggest that recommendations for men should be considered in indicator development.

The SIGN clinical guideline also makes other recommendations for treatment of osteoporosis, such as high-intensity strength training and low-impact weight-bearing exercise. These have not been submitted to NICE for indicator development but could be considered at a later date.

Indicator development for osteoporosis has been considered under the previous process for QOF indicator development. It was recommended at that time that proposed indicators should be piloted because of potential educational issues (for example, defining a fragility fracture, or knowledge of bone sparing agents).

Key considerations

SIGN recommends that patients who have suffered one or more fragility fractures should be priority targets for investigation and treatment of osteoporosis.

The SIGN guideline covers men and women, and the NICE technology appraisal covers postmenopausal women only.

The NICE technology appraisal carries with it a three month funding mandate post publication of the guidance (applies only to England and Wales).

The suggestion is for indicator development on the treatment of osteoporosis with recommendation to use a class of drugs not a single specific agent.

A referral for DXA scanning is a pre-requisite for the treatment of osteoporosis with bone sparing agents. This was explicitly modelled in the cost-effectiveness analysis carried out as part of the NICE technology appraisal, and was considered to be a cost-effective use of NHS resources. The position statement on service provision (previously circulated to the NICE QOF Advisory Committee) outlines that the availability of services should not be the basis on whether topics are recommended for indicator development or recommended for consideration for inclusion on the NICE menu of indicators. Where indicators from the NICE menu are not included in the national QOF, they are available for PCTs to adopt for local quality schemes using local contracts, informed by NICE's advice on clinical- and cost-effectiveness evidence.

Indicator development would need to consider whether the proposed register should be a prospective register of incident cases or include prevalent cases of fragility fractures.

Indicator development would need to consider the age range and gender to which the indicators should apply.

There is a current Directed Enhanced Service (DES) on osteoporosis which is similar to the proposed indicators in which a large number of practices are participating. However all DESs (except for topics outside NICE's remit on QOF) are time limited and are due to expire at the end of March 2011. The position statement on DESs outlines that an overlap with a DES should not preclude a topic being recommended for indicator development.

Committee actions

The Advisory Committee is asked to consider the issues raised in this briefing note and advise on whether or not the recommendations identified should be progressed for indicator development.

Appendix A: List of guidance recommendations in NICE technology appraisal 161

NICE recommendation 1.1

Alendronate is recommended as a treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (that is, a T-score of −2.5 SD or below). In women aged 75 years or older, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.

When the decision has been made to initiate treatment with alendronate, the preparation prescribed should be chosen on the basis of the lowest acquisition cost available.

NICE recommendation 1.2

Risedronate and etidronate are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women:

- who are unable to comply with the special instructions for the administration of alendronate, or have a contraindication to or are intolerant of alendronate (as defined in section 1.6) **and**

who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table.

T-scores (SD) at (or below) which risedronate or etidronate is recommended when alendronate cannot be taken

	Number of independent clinical risk factors for fracture (section 1.5)		
Age (years)	**0**	**1**	**2**
50–54	–[a]	−3.0	−2.5
55–59	−3.0	−3.0	−2.5
60–64	−3.0	−3.0	−2.5
65–69	−3.0	−2.5	−2.5
70 or older	−2.5	−2.5	−2.5

[a] Treatment with risedronate or etidronate is not recommended

If a woman aged 75 years or older has not previously had her BMD measured, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.

In deciding between risedronate and etidronate, clinicians and patients need to balance the overall proven effectiveness profile of the drugs against their tolerability and adverse effects in individual patients.

NICE recommendation 1.3

Strontium ranelate and raloxifene are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women:

- who are unable to comply with the special instructions for the administration of alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate (as defined in section 1.6) **and**
- who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table.

T-scores (SD) at (or below) which strontium ranelate or raloxifene is recommended when alendronate and either risedronate or etidronate cannot be taken

	Number of independent clinical risk factors for fracture (section 1.5)		
Age (years)	**0**	**1**	**2**
50–54	– [a]	−3.5	−3.5
55–59	−4.0	−3.5	−3.5
60–64	−4.0	−3.5	−3.5
65–69	−4.0	−3.5	−3.0
70–74	−3.0	−3.0	−2.5
75 or older	−3.0	−2.5	−2.5

[a] Treatment with raloxifene or strontium ranelate is not recommended

If a woman aged 75 years or older who has one or more independent clinical risk factors for fracture or indicators of low BMD has not previously had her BMD

measured, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.

For the purposes of this guidance, indicators of low BMD are low body mass index (defined as less than 22 kg/m^2), medical conditions such as ankylosing spondylitis, Crohn's disease, conditions that result in prolonged immobility, and untreated premature menopause[1].

In deciding between strontium ranelate and raloxifene, clinicians and patients need to balance the overall proven effectiveness profile of these drugs against their tolerability and other effects in individual patients.

NICE recommendation 1.4

Teriparatide is recommended as an alternative treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women:

- who are unable to take alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate (as defined in section 1.6), **or** who have a contraindication to, or are intolerant of strontium ranelate (as defined in section 1.7), **or** who have had an unsatisfactory response (as defined in section 1.8) to treatment with alendronate, risedronate or etidronate **and**
- who are 65 years or older and have a T-score of –4.0 SD or below, or a T-score of –3.5 SD or below plus more than two fractures, **or** who are aged 55–64 years and have a T-score of –4 SD or below plus more than two fractures.

SIGN recommendation 2.3

Patients who have suffered one or more fragility fractures should be priority targets for investigation and treatment of osteoporosis.

[1] Rheumatoid arthritis is also a medical condition indicative of low BMD.

SIGN recommendation 6.6.1

To reduce fracture risks at all sites, men with low BMD and/or history of one or more vertebral fractures or one non-vertebral osteoporotic fracture should be treated with oral alendronate (10 mg + 500 mg +/- 400 IU vitamin D daily).

Appendix B: evidence summary

Evidence summary of selected NICE and SIGN recommendations

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
NICE TA161 1.1	Alendronate is recommended as a treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (that is, a T-score of −2.5 SD or below). In women aged 75 years or older, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.When the decision has been made to initiate treatment with alendronate, the preparation prescribed should be chosen on the basis of the lowest acquisition cost available.	Sixteen RCTs of alendronate in postmenopausal women were included in the assessment report	Clinically apparent fractures	In the studies reviewed, there was sufficiently robust evidence to suggest a reduction in hip-fracture risk in women with osteoporosis. All the studies were conducted in women who had adequate blood levels of calcium, from either dietary intake or calcium supplementation. The Committee noted that approximately one-third of alendronate users experience gastrointestinal adverse events	Health economic evidence presented showed that alendronate would be an appropriate use of NHS resources for secondary preventative treatment in postmenopausal women with fragility fractures and confirmed osteoporosis (that is, a T-score of −2.5 SD or below). The Committee noted that the prices of different brands of alendronate vary greatly and concluded that alendronate should be prescribed on the basis of the lowest acquisition cost available. The Committee noted that the drugs other than alendronate are cost effective only for patients at higher risk of fracture than the risk levels at which alendronate is cost effective.

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
1.2	Risedronate and etidronate are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women: • who are unable to comply with the special instructions for the administration of alendronate, or have a contraindication to or are intolerant of alendronate (as defined in section 1.6) **and** • who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table. If a women aged 75 years or older has not previously had her BMD measured, a DXA scan may not be required if the responsible clinician considers it to be	Twelve RCTs of etidronate and one observational study Seven RCTs of risedronate	Clinically apparent fractures	The Committee accepted that there was sufficiently robust evidence to suggest a reduction in hip-fracture risk. The Committee noted that the available RCTs for etidronate were of insufficient size to show statistically significant reductions in hip-fracture risk, but that observational data lent support to a reduction in hip-fracture risk. In deciding between risedronate and etidronate, clinicians and patients need to balance the overall effectiveness profile of the drugs against their tolerability and adverse effects in individual patients.	The Committee noted that risedronate, etidronate, raloxifene and strontium ranelate were dominated by alendronate (based on the price of £53.56 per year for alendronate); that is, these drugs have a higher acquisition cost than alendronate, but are not more efficacious. The Committee considered the cost effectiveness of etidronate and noted that in previous modelling etidronate had a better cost-effectiveness profile than risedronate; since then there has been no change in the evidence base that would affect the relative position of these two drugs. In view of its concerns surrounding evidence base for etidronate, and taking into account the views of clinical specialists and consultees, the Committee decided that etidronate should not be recommended in preference to risedronate.

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
	clinically inappropriate or unfeasible. In deciding between risedronate and etidronate, clinicians and patients need to balance the overall proven effectiveness profile of the drugs against their tolerability and adverse effects in individual patients.				

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
1.3	Strontium ranelate and raloxifene are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women: • who are unable to comply with the special instructions for the administration of alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate (as defined in section 1.6) **and** • who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table. If a woman aged 75 years or older who has one or more independent clinical risk factors for fracture or	Three RCTs of raloxifene	Vertebral and non-vertebral fracture	The Committee noted that the evidence for raloxifene showed an effect on risk of vertebral fractures, but did not show any effect on risk of hip fractures. In addition, there was evidence for a beneficial side effect of raloxifene on the incidence of breast cancer. The Committee noted that a higher proportion of the overall benefit associated with raloxifene was attributable to its effect on the prevention of breast cancer than to its effect on the prevention of osteoporotic fragility fractures.	The Committee concluded that the possible benefits in addition to fracture prevention meant that, in cases where women are unable to comply with the special instructions for the administration of alendronate and either risedronate or etidronate, or have contraindications to or are intolerant of alendronate and either risedronate or etidronate, raloxifene could be recommended

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
	indicators of low BMD has not previously had her BMD measured, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.				
SIGN 6.6.1	To reduce fracture risks at all sites, men with low BMD and /or history of one or more vertebral fractures or one non-vertebral osteoporotic fracture should be treated with oral alendronate (10mg + 500mg +/- 400 IU vitamin D Daily	One RCT	Lumbar spine and femoral neck BMD and morphometric vertebral fracture risk	While there is a clear link between BMD and fracture risk in women, it is uncertain whether this is true in men. The evidence base relating to calcium and vitamin D is inconsistent. The efficacy of calcium and vitamin D in the absence of concurrent anti-resorptive therapy is unknown	None provided

Appendix C: Briefing paper on osteoporosis presented at the December 2009 committee

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

QUALITY AND OUTCOMES FRAMEWORK (QOF) INDICATOR DEVELOPMENT PROGRAMME

Briefing paper

QOF indicator area: Osteoporosis

Potential output: Pilot QOF indicators, 2012/13

Date of Primary Care QOF Indicator Advisory Committee meeting: 10 December 2009

Introduction

This briefing paper presents an assessment of the suitability of NICE clinical guideline recommendations relevant to primary care and proposed by stakeholders to progress for QOF indicator development.

The QOF indicator area is osteoporosis and the recommendation(s) and underlying evidence review are taken from the following guidance:

> 'Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women' (NICE technology appraisal 161).

This guidance was issued by NICE in October 2008[2] and consultation on the Final Appraisal Determination document was held in July 2008. This paper is based on the evidence presented in NICE technology appraisal 161. It should be noted that no update searches on the evidence presented in the guidance have been performed. Recent literature searches and analysis of practice

[2] This guidance replaces NICE technology appraisal guidance 87 issued in January 2005. The review and re-appraisal of alendronate, etidronate, risedronate, raloxifene and teriparatide for secondary prevention of osteoporotic fragility fractures has resulted in changes in the criteria for offering these drugs. In addition, strontium ranelate has also been appraised.

data have been performed to provide information for the Advisory Committee on the current management of practice, impact on primary care and the timeliness of potential incentivisation. The briefing paper is split into the following three sections:

- An overview of osteoporosis, including an epidemiological summary and its current management in primary care.
- Specific recommendation(s) relevant to primary care from NICE technology appraisal 161 identified for indicator development, a summary of the evidence that informs the recommendation(s), and an initial assessment of their feasibility.
- A summary of the key considerations against NICE's prioritisation criteria.

Related existing QOF indicators from 2009/10 indicator set

Osteoporosis does not relate to an existing QOF clinical domain as defined in the 2009/10 GMS Contract guidance.

Related indicators from the NICE menu of indicators

There are no osteoporosis related indicators on the NICE menu of indicators.

1 Overview: osteoporosis - secondary prevention

Epidemiological summary

Definition

Osteoporosis is a progressive, systemic skeletal disorder characterised by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.

Osteoporosis is defined by a T-score[3] of –2.5 standard deviations (SD) or lower on dual-energy X-ray absorptiometry (DXA) scanning. However, the

[3] The World Health Organization (WHO) has established diagnostic criteria for osteoporosis based on the measurement of BMD, expressed as the T-score. A T-

diagnosis may be assumed in women aged 75 years or older if the responsible clinician considers a DXA scan to be clinically inappropriate or unfeasible.

Incidence and prevalence and evidence of variation by age, sex and ethnicity

Bone formation exceeds bone resorption in youth, but by the third decade of life there is a gradual loss of bone mass. Osteoporosis is therefore usually an age-related disease. It can affect both sexes, but women are at greater risk because the decrease in oestrogen production after the menopause accelerates bone loss to a variable degree. Family history is also a (non-modifiable) predictor of osteoporosis risk.

It is estimated that more than 2 million women have osteoporosis (that is have a T-score of –2.5 SD or below) in England and Wales. Osteoporosis is most common in older white women. After the menopause, the prevalence of osteoporosis increases markedly with age, from approximately 2% at 50 years, rising to more than 25% at 80 years. The NICE cost impact report for TA161 uses a prevalence of 11% of post-menopausal women aged 50 years or over with osteoporosis and a clinically apparent osteoporotic fragility fracture, rising to 19% for ages 65 and over. There are an estimated 180,000 new fragility fractures in postmenopausal women in the UK each year, of which three quarters would expected to be in ages 65 and over.

Morbidity and mortality

Fractures are most common in the vertebrae, hip and wrist. Osteoporotic fragility fractures are associated with substantial disability, pain and reduced quality of life. Hip fractures impair a person's ability to live independently: a high proportion of women are permanently unable to walk unaided or to perform other activities of daily living. Vertebral fractures are also associated with pain, deformity and disability.

---

score is the number of standard deviations by which a patient's BMD differs from the mean peak BMD for young normal subjects of the same gender.

Postmenopausal women with an initial fracture are at substantially greater risk of subsequent fractures. Half of patients with a hip fracture have previously had a fragility fracture of another bone.

Hip fractures are associated with increased mortality; estimates of the relative mortality risk vary from 2 to greater than 10 in the 12 months following hip fracture. However, it is unclear to what extent this can be attributed to fracture alone, as opposed to pre-existing comorbidity.

Impact on health services

Primary care

Patients with osteoporosis, including osteoporotic fractures, form a significant part of general practice workload. It is reported that osteoporotic fractures can result in up to 13 extra consultations in the year following injury (Dolan and Torgerson 1998). The majority of prescriptions (93%) for bone sparing agents are written and issued in primary care (HSCIC 2009).

Secondary care

In England and Wales, it is estimated that 180,000 osteoporosis-related fractures occur annually.

Current management in primary care

Primary care plays a significant role in confirming diagnosis and in the long term management of osteoporosis. In the absence of fracture, osteoporosis is asymptomatic and often remains undiagnosed.

Interventions in individual people with osteoporotic fragility fracture include prescribing appropriate pharmacological secondary prevention and persistence with therapy.

Management of osteoporosis should include all patients being offered lifestyle advice to reduce the risks of osteoporosis, including advice on adequate nutrition, especially with calcium and vitamin D, regular weight bearing exercise, stopping smoking and avoiding alcohol.

Current baseline

The guidance for NICE technology appraisal 161 assumes that women who receive treatment have an adequate calcium intake and are vitamin D replete. In a large study of general practice patient records conducted to assess standards of care for osteoporosis and falls in primary care (Hippisley Cox et al. 2007), 54% of patients on specific osteoporosis treatments had evidence of a co-prescribed combined calcium and vitamin D3 preparation. One third (37%) of older patients recorded on the computer as living in residential or nursing care homes were identified as receiving combined calcium and vitamin D.

A clinical audit of postmenopausal women presenting with a low trauma fracture to a specialist fracture clinic reported that calcium and vitamin D supplements were received by a minority (36%) of cases (Premaor et al 2009).

Additional information on baseline practice derived from primary care data will be provided at the QOF Advisory Committee on 10 December 2009 if available.

NHS priorities and timeliness for guidance

The NICE QOF Indicator Programme team examined national clinical guidelines, policy documents and national strategies across the UK to assess timeliness of indicators in this topic area. The following were found to be of relevance to osteoporosis:

- Clinical directed enhanced services (DES) exist for osteoporosis in England, Northern Ireland and Scotland (see Appendix C)
- The Prevention Package for Older People, DH 2009
- National Service Framework for Older People (Chapter 6 – Falls)
- NICE technology appraisal 160 ‘Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women’ (October 2008)

- NICE technology appraisal 161 ‘Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women' (October 2008)
- SIGN clinical guideline 71 ‘The Management of Osteoporosis’ (June 2003)
- SIGN clinical guideline 111‘Management of hip fractures in older people’ (June 2009)

2 Review of NICE guideline recommendations for 'Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women' (NICE technology appraisal 161)

Summary of NICE guidance recommendations

The recommendations presented in this briefing paper were identified as being potentially suitable for QOF indicator development and relate to a topic suggestion received through NICE’s online suggestion facility in September 2009. The topic presented in this briefing paper was submitted by a patient organisation.

One recommendation (recommendation 1.1) from NICE technology appraisal 161 has been identified as being potentially suitable for QOF indicator development.

NICE technology appraisal 161 relates only to treatments for the secondary prevention of fragility fractures in postmenopausal women who have osteoporosis and have sustained a clinically apparent osteoporotic fragility fracture. Osteoporosis is defined by a T-score of –2.5 standard deviations (SD) or lower on dual-energy X-ray absorptiometry (DXA) scanning. However, the diagnosis may be assumed in women aged 75 years or older, if the

responsible clinician considers a DXA scan to be clinically inappropriate or unfeasible.

This guidance assumes that women who receive treatment have an adequate calcium intake and are vitamin D replete. Unless clinicians are confident that women who receive treatment meet these criteria, calcium and/or vitamin D supplementation should be considered.

NICE recommendation 1.1

> Alendronate is recommended as a treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (that is, a T-score of −2.5 SD or below). In women aged 75 years or older, a DXA scan may not be required, if the responsible clinician considers it to be clinically inappropriate or unfeasible.
>
> When the decision has been made to initiate treatment with alendronate, the preparation prescribed should be chosen on the basis of the lowest acquisition cost available.

Evidence summary

This is a summary of the evidence supporting the proposed NICE recommendation (recommendation 1.1) presented above in ‘Summary of NICE guideline recommendations’. This section relates to the evidence summary table in appendix A of this briefing paper.

For the purposes of information, a list of all recommendations for NICE technology appraisal 161 is provided in appendix B of this briefing paper.

Clinical effectiveness

There is evidence from meta-analyses and/or randomised controlled trials (level 1 evidence) for relevant health outcomes to support the use of alendronate as first line treatment for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (recommendation 1.1).

The Appraisal Committee considered the clinical effectiveness data for the bisphosphonates alendronate, etidronate and risedronate, strontium ranelate, raloxifene and teriparatide. The Committee noted that all these drugs have proven efficacy in reducing the incidence of vertebral fragility fractures in women with osteoporosis. However, the Appraisal Committee also noted that there were differences between the drugs as to the degree of certainty that treatment results in a reduction in hip fracture (considered a crucial goal in osteoporosis management). In the case of alendronate and risedronate, the Appraisal Committee accepted that there was sufficiently robust evidence to suggest a reduction in hip-fracture risk.

Cost effectiveness

There is health economic evidence to suggest that alendronate is the most cost-effective first-line treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (recommendation 1.1).

Assessment of recommendations against current practice

Reduction of health inequalities

There is no evidence presented in the NICE guidance that directly shows that the recommendations outlined in this briefing paper can reduce health inequalities. Our conclusion is that QOF incentivisation of this topic is unlikely to have an adverse or negative impact on any group or community. Rather, it has the potential to have a positive impact by reducing barriers that are known to exist in the care of the elderly. Relevance to inequalities: medium

Will implementation of these recommendations lead to improvements in the delivery of primary care?

The NICE costing report produced for technology appraisal 161 estimates that implementation of the guidance would require a 60% increase in the numbers of post-menopausal women aged 50 years or over with osteoporosis and a clinically apparent osteoporotic receiving treatment. This represents an increase in the treatment population from the current baseline of 206,000 (at November 2008) to 329,000. This estimate is based on a phased

implementation over 5 years and assumes that the proportion of those receiving alendronate will remain the same as current levels (around 70% of the proportion receiving drugs receiving alendronate). Therefore, based on the above, recommendation 1.1 presented in this paper is likely to lead to a moderate-major change in practice.

Feasibility assessment

A summary of the initial feasibility assessment incorporating advice and expert opinion is provided below. This includes comments from the National Primary Care Research and Development Centre (NPCRDC), the NHS information Centre for Health and Social Care (NHSIC) and NICE.

Two key questions are asked to make the initial assessment.

Q1 *Would the proposed primary care recommendations allow the development of indicators that can be used in primary care information systems?*

Q2 *Are the proposed primary care recommendations likely to lead to indicators that can be measured in a clear, reproducible and precise manner?*

Osteoporosis does not relate to an existing QOF clinical domain. This feasibility assessment identifies recommendation 1.1 as potentially suitable for indicator development. The creation of a prospective register should be considered that focuses on incident population. This would need to take into account the following:

- The definition of postmenopausal and previous osteoporotic fragility fracture requires clarification.

The following exceptions should be considered:

- Women who began treatment with alendronate before this guidance (TA161) was issued, but for whom treatment would now not be recommended;
- Women who are on long-term systemic corticosteroid treatment;

- Women aged 75 years or older who have not had a dual-energy X-ray absorptiometry (DXA) scan because their clinician considers it to be clinically inappropriate or unfeasible;
- Women for who treatment with alendronate would be unsuitable because of contraindication, intolerance or being unable to comply with special administration instructions;
- Exclusions due to traumatic fracture (these would be small as majority of fractures would be low trauma).

Stakeholder comments

The stakeholder organisation for this topic suggestion suggests that GP IT systems cannot include T-scores in a retrievable form, so it is not possible to validate qualifiers for treatment options beyond alendronate. Accepting licensed preparations with prescribing monitored by PCT inspection of generic rates is suggested.

3 Topic and recommendation status

This section provides the overall topic and recommendation status that has been produced by the QOF programme team. This takes into account information presented in this briefing paper against the revised prioritisation checklist as agreed at the July 2009 Advisory Committee.

Topic Status

Overall the topic has been given a status of **GREEN**. This overall topic status is based on an assessment the prevalence, primary care management and disease severity as outlined in 1A, 1B and 1C below.

1 A Population	
The condition is considered to have population prevalence that is high	GREEN
1 B Management	
The condition is commonly diagnosed in primary care*	AMBER
The condition is commonly treated in primary care*	GREEN
The condition is commonly monitored in primary care*	GREEN
** by general practitioners or directly employed practice staff*	

1C	Disease Severity	
	Criteria	
1	Minor quality-of-life impact, no disability, limited morbidity impact	☐
2	Definite quality-of-life impact, no disability, limited morbidity impact	☐
3	Definite quality-of-life impact, some disability and/or intermediate morbidity impact	☐
4	**Definite quality-of-life impact, significant disability and/or significant morbidity impact**	☒

Recommendation Status

The status of each recommendation is given in the below table.

Overall recommendation status	
Recommendation 1.1	**GREEN**
Comments: This feasibility assessment identifies recommendation 1.1 as potentially suitable for indicator development. The creation of a prospective register could be considered that focuses on incident population. There are a number of exceptions to the denominator that would need to be considered, e.g. contraindications.	

The individual recommendation status provided in the table above is based on an assessment of feasibility, strength of clinical and cost effectiveness evidence and expected change in practice.

Feasibility of each recommendation			
Recommendation 1.1			AMBER
Scores for each recommendation			
	Evidence of clinical effectiveness	**Evidence of cost effectiveness**	**Expected change in practice**
Recommendation 1.1	High	Likely to be cost effective	Moderate-Major

4 Key considerations

The following key considerations summarise the key points made in the briefing paper and should be used by the Committee in their deliberations.

- Osteoporosis and osteoporotic fragility factures represent a significant cost to the NHS and social care. There is strong clinical and health economic evidence to support the use of alendronate as first line treatment for the secondary prevention of osteoporotic fragility fractures in postmenopausal women.
- The Committee should note that the NICE technology appraisal 161guidance and underlying the evidence relates only to treatments for the secondary prevention of fragility fractures in postmenopausal women. The submitting stakeholder organisation for this topic suggestion has urged consideration of men and women in QOF development.
- The information and analysis presented in this briefing paper suggests that there are currently relatively low rates of prescribing of calcium and vitamin D3 preparations when co prescribed with osteoporosis treatments.
- There is potential overlap with current specifications for Directed Enhanced Services for osteoporosis (see Appendix C)
- Inclusion of this recommendation in the QOF could incentivise improved care to the elderly and increase the numbers of elderly women able to live independently.
- Initial consideration of feasibility suggests that this recommendation is feasible for inclusion in the QOF, with some specified exceptions and that the creation of a register needs to be considered.

References

Dolan P, Torgerson DJ (1998) The cost of treating osteoporotic fractures in the United Kingdom female population. Osteoporosis Int 8: 611−7.

The Health and Social Care Information Centre (2009) Use of NICE appraised medicines in the NHS in England – Experimental Statistics [online] Available from www.ic.nhs.uk/statistics-and-data-collections/primary-

care/prescriptions/use-of-nice-appraised-medicines-in-the-nhs-in-england--experimental-statistics [Accessed 18 November 2009]

Hippisley-Cox J, Bayley J, Potter J et al. (2007) Evaluation of standards of care for osteoporosis and falls in primary care: final report to the Information Centre for health and social care [online]. Available from www.ic.nhs.uk/statistics-and-data-collections/primary-care/general-practice/evaluation-of-standards-of-care-for-osteoporosis-and-falls-in-primary-care [Accessed 18 November 2009]

Premaor MO, Pilbrow L, Tonkin C et al. (2009) Low rates of treatment in postmenopausal women with a history of low trauma fractures: results of audit in a fracture liaison service. QJM. 2009 Oct 28. [Epub ahead of print]

Appendix A: evidence summary

Evidence summary of NICE technology appraisal 161 selected recommendations

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
1.1	Alendronate is recommended as a treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (that is, a T-score of −2.5 SD or below). In women aged 75 years or older, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible. When the decision has been made to initiate treatment with alendronate, the preparation prescribed should be chosen on the basis of the lowest acquisition cost available.	Sixteen RCTs of alendronate in postmenopausal women were included in the assessment report	Clinically apparent fractures	In the studies reviewed, there was sufficiently robust evidence to suggest a reduction in hip-fracture risk in women with osteoporosis. All the studies were conducted in women who had adequate levels of calcium, from either dietary intake or calcium supplementation. The Committee noted that approximately one third of alendronate users experience gastrointestinal adverse events.	Health economic evidence presented showed that alendronate would be an appropriate use of NHS resources for secondary preventative treatment in postmenopausal women with fragility fractures and confirmed osteoporosis (that is, a T-score of –2.5 SD or below). The Committee noted that the prices of different brands of alendronate vary greatly and concluded that alendronate should be prescribed on the basis of the lowest acquisition cost available. The Committee noted that the drugs other than alendronate are cost effective only for patients at higher risk of fracture than the risk levels at which alendronate is cost effective.

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
1.2	Risedronate and etidronate are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women: • who are unable to comply with the special instructions for the administration of alendronate, or have a contraindication to or are intolerant of alendronate (as defined in section 1.6) **and** • who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table. If a women aged 75 years or older has not previously had her BMD	Twelve RCTs of etidronate and one observational study Seven RCTs of risedronate	Clinically apparent fractures	The Committee accepted that there was sufficiently robust evidence to suggest a reduction in hip-fracture risk. The Committee noted that the available RCTs for etidronate were of insufficient size to show statistically significant reductions in hip-fracture risk, but that observational data lent support to a reduction in hip-fracture risk. In deciding between risedronate and etidronate, clinicians and patients need to balance the overall effectiveness profile of the drugs against their tolerability and adverse effects in individual patients.	The Committee noted that risedronate, etidronate, raloxifene and strontium ranelate were dominated by alendronate (based on the price of £53.56 per year for alendronate); that is, these drugs have a higher acquisition cost than alendronate, but are not more efficacious. The Committee considered the cost effectiveness of etidronate and noted that in previous modelling etidronate had a better cost-effectiveness profile than risedronate; since then there has been no change in the evidence base that would affect the relative position of these two drugs. In view of its concerns surrounding evidence base for etidronate, and taking into account the views of clinical specialists and consultees, the Committee decided that etidronate should not be recommended in preference to risedronate.

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
	measured, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible. In deciding between risedronate and etidronate, clinicians and patients need to balance the overall proven effectiveness profile of the drugs against their tolerability and adverse effects in individual patients.				

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
1.3	Strontium ranelate and raloxifene are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women: • who are unable to comply with the special instructions for the administration of alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate (as defined in section 1.6) and • who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table. If a woman aged 75	Three RCTs of raloxifene	Vertebral and nom Vertrebal fracture	The Committee noted that the evidence for raloxifene showed an effect on risk of vertebral fractures, but did not show any effect on risk of hip fractures. In addition, there was evidence for a beneficial side effect of raloxifene on the incidence of breast cancer. The Committee noted that a higher proportion of the overall benefit associated with raloxifene was attributable to its effect on the prevention of breast cancer than to its effect on the prevention of osteoporotic fragility fractures	The Committee concluded that, the possible benefits in addition to fracture prevention meant that, in cases where women are unable to comply with the special instructions for the administration of alendronate and either risedronate or etidronate, or have contraindications to or are intolerant of alendronate and either risedronate or etidronate, raloxifene could be recommended

	Recommendation	Level of evidence	Key outcomes considered (for interventions)	Specific considerations highlighted by Appraisal Committee	Cost-effectiveness evidence
	years or older who has one or more independent clinical risk factors for fracture or indicators of low BMD has not previously had her BMD measured, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.				

Appendix B: full list of guidance recommendations for NICE technology appraisal 161

For the purposes of additional information and context, this appendix provides the full list of recommendations (1.1–1.9) for NICE technology appraisal 161.

This guidance does **not** cover the following:

- The use of alendronate, etidronate, risedronate, raloxifene, strontium ranelate or teriparatide for the secondary prevention of osteoporotic fragility fractures in women with normal bone mineral density (BMD) or osteopenia (that is, women with a T-score between −1 and −2.5 SD below peak BMD).
- The use of these drugs for the secondary prevention of osteoporotic fragility fractures in women who are on long-term systemic corticosteroid treatment.

The following recommendation (1.1) has been prioritised for consideration by the December 2009 QOF Advisory Committee:

NICE recommendation 1.1

Alendronate is recommended as a treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (that is, a T-score of −2.5 SD or below). In women aged 75 years or older, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.

When the decision has been made to initiate treatment with alendronate, the preparation prescribed should be chosen on the basis of the lowest acquisition cost available.

The following recommendations (1.2–1.9) are not included for consideration by the December 2009 QOF Advisory Committee and are provided here for the purposes of additional information only.

NICE recommendation 1.2

Risedronate and etidronate are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women:

- who are unable to comply with the special instructions for the administration of alendronate, or have a contraindication to or are intolerant of alendronate (as defined in section 1.6) **and**
- who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table.

T-scores (SD) at (or below) which risedronate or etidronate is recommended when alendronate cannot be taken

	Number of independent clinical risk factors for fracture (section 1.5)		
Age (years)	**0**	**1**	**2**
50–54	–[a]	−3.0	−2.5
55–59	−3.0	−3.0	−2.5
60–64	−3.0	−3.0	−2.5
65–69	−3.0	−2.5	−2.5
70 or older	−2.5	−2.5	−2.5

[a] Treatment with risedronate or etidronate is not recommended

If a women aged 75 years or older has not previously had her BMD measured, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.

In deciding between risedronate and etidronate, clinicians and patients need to balance the overall proven effectiveness profile of the drugs against their tolerability and adverse effects in individual patients.

NICE recommendation 1.3

Strontium ranelate and raloxifene are recommended as alternative treatment options for the secondary prevention of osteoporotic fragility fractures in postmenopausal women:

- who are unable to comply with the special instructions for the administration of alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate (as defined in section 1.6) **and**
- who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table.

T-scores (SD) at (or below) which strontium ranelate or raloxifene is recommended when alendronate and either risedronate or etidronate cannot be taken

	Number of independent clinical risk factors for fracture (section 1.5)		
Age (years)	**0**	**1**	**2**
50–54	–[a]	−3.5	−3.5
55–59	−4.0	−3.5	−3.5
60–64	−4.0	−3.5	−3.5
65–69	−4.0	−3.5	−3.0
70–74	−3.0	−3.0	−2.5
75 or older	−3.0	−2.5	−2.5

[a] Treatment with raloxifene or strontium ranelate is not recommended

If a woman aged 75 years or older who has one or more independent clinical risk factors for fracture or indicators of low BMD has not previously had her BMD measured, a DXA scan may not be required if the responsible clinician considers it to be clinically inappropriate or unfeasible.

For the purposes of this guidance, indicators of low BMD are low body mass index (defined as less than 22 kg/m^2), medical conditions such as ankylosing spondylitis, Crohn's disease, conditions that result in prolonged immobility, and untreated premature menopause[4].

[4] Rheumatoid arthritis is also a medical condition indicative of low BMD.

In deciding between strontium ranelate and raloxifene, clinicians and patients need to balance the overall proven effectiveness profile of these drugs against their tolerability and other effects in individual patients.

NICE recommendation 1.4

Teriparatide is recommended as an alternative treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women:

- who are unable to take alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate (as defined in section 1.6), **or** who have a contraindication to, or are intolerant of strontium ranelate (as defined in section 1.7), **or** who have had an unsatisfactory response (as defined in section 1.8) to treatment with alendronate, risedronate or etidronate **and**
- who are 65 years or older and have a T-score of –4.0 SD or below, or a T-score of –3.5 SD or below plus more than two fractures, **or** who are aged 55–64 years and have a T-score of –4 SD or below plus more than two fractures.

NICE recommendation 1.5

For the purposes of this guidance, independent clinical risk factors for fracture are parental history of hip fracture, alcohol intake of 4 or more units per day, and rheumatoid arthritis.

NICE recommendation 1.6

For the purposes of this guidance, intolerance of alendronate, risedronate or etidronate is defined as persistent upper gastrointestinal disturbance that is sufficiently severe to warrant discontinuation of treatment, and that occurs even though the instructions for administration have been followed correctly.

NICE recommendation 1.7

For the purposes of this guidance, intolerance of strontium ranelate is defined as persistent nausea or diarrhoea, either of which warrants discontinuation of treatment.

NICE recommendation 1.8

For the purposes of this guidance, an unsatisfactory response is defined as occurring when a woman has another fragility fracture despite adhering fully to treatment for 1 year and there is evidence of a decline in BMD below her pre-treatment baseline.

NICE recommendation 1.9

Women who are currently receiving treatment with one of the drugs covered by this guidance, but for whom treatment would not have been recommended according to sections 1.1 to 1.4, should have the option to continue treatment until they and their clinicians consider it appropriate to stop.

Appendix C: additional information – directed enhanced service (DES) specifications for osteoporosis

England: Clinical directed enhanced service (DES) for osteoporosis (2008/09 – 2010/11)

A pre-requisite for taking part in this two-year DES (to run for 2 years from April 2008) is that the practice holds and maintains a register of women aged 65 years and older with fragility fractures sustained after 1 April 2008.

Specification criteria

Practices will be expected to compile an audit of:

- Criterion 1: the proportion of women aged between 65 and 74 years with a history of fragility fracture in the previous 12 months who have had a diagnosis of osteoporosis confirmed by a DEXA scan
- Criterion 2: the proportion of women aged between 65 and 74 with a positive diagnosis of osteoporosis confirmed by a DEXA scan (i.e. criterion 1) who are receiving treatment with a bone-sparing agent
- Criterion 3: the proportion of women aged 75 and over with a history of fragility fracture in the previous 12 months who are receiving treatment with a bone-sparing agent.

Northern Ireland: Clinical directed enhanced service (DES) for osteoporosis secondary prevention scheme (2008/09 – 2010/11)

Specification criteria

a. The contractor should develop a register of female patients aged 50 and over who have suffered at least one hip or non-hip fragility fracture to be known as the Osteoporosis/Secondary Prevention of Fractures.

b. Conduct a review for each patient to ensure all key elements of care pathway are completed. These are:

- Assessment of the cause of the relevant fragility fracture;
- Provision of written advice on bone health and falls;
- Advice on the consultation of an optician e.g. for assessment of visual acuity, etc.;
- Assessment and treatment of signs of orthostatic hypotension;
- Ensure patients are on appropriate pharmacological treatment, e.g. bisphosphonates or other bone sparing therapy;
- Referral of patients, as appropriate, for DEXA scans. However patients over the age of 75 should not be referred for a DEXA scan.

Scotland: Clinical directed enhanced service (DES) for osteoporosis secondary prevention scheme (to be reviewed at the end of 2009/10)

This DES was introduced in November 2008 and requires practices to identify women aged 60 and over who have osteoporosis (through their fracture history) and to offer them bone sparing treatment. For women aged 60-74, this also entails confirming a diagnosis of osteoporosis by DEXA scan. The full specification and guidance for this DES is attached.

Specification criteria

- A.1. Register of women recorded as having a fragility fracture on or after 1 November 2008 **when aged 60 and over**.
  [Define age 60 including and after date of 60th birthday]
- A.2. For women on the register at A.1 aged 60-74 on the date of fracture, record of having had or having been referred for DEXA scan **on any date**.
  [Define age 74 as up to and including day before 75th birthday]
- A.3. For women on the register age 75 and over on the date of fracture, record of those offered bone sparing treatment **on any date**.
  [Define age 75 as including and after date of 75th birthday]
- A.4. For women on the register at A.1 aged 60-74, who have a recorded diagnosis of osteoporosis on any date, record of those offered bone sparing treatment **on any date**.
  [Define recorded diagnosis of osteoporosis using code N330. as in Annex A.]