Web comments and other comments received by non consultees and commentators

10/10/2005-Oct-2005 17:17:12	
role:	NHS Professional
Section_1:	What about women below the age of 70 years?
10/11/2005-Oct-2005 14:34:43	
role:	other
Section_1:	Age threshold too high
Section_7:	It cannot be assumd that patients can tolerate medication. If a patient is intolerant of bisphosphonates and strontium, raloxifene may be considered
10/12/2005-Oct-2005 14:31:38	
role:	NHS Professional
Section_1:	Why is only the T-score for the femoral neck considered ? Much osteoporosis will be in the lumbar spine and this will affect the quality of life of patients, although not necessarily costs to the NHS. Cost effectiveness studies should include quality of life benefits not just cost benefits to the NHS Also can you makemuch more transparent the exact statistical model which arrives at the conclusion that it is only cost-effective to treat over 70 year olds. I believe that here may be a serious flaw in the statistical methods used and that this should be peer reviewed by statisticians and clinicians in the field and verified with actual data before such a momentous decision is made not to prevent osteoporosis in the under 70"s
Section_2:	In 2.4 why is only The T score at the femoral neck considered? The BMD at the lumbar spine is most closely correlated with the fracture risk at the lumbar spine and 2.10 states that vertebral fractures give an increased risk of morbitiy and mortality
Section_3:	None
Section_4:	In 4.2.1, and 4.2.4 the model used is for 10 year age bands. It has not been shown that the effectiveness of a drug ceases after the 10 year band. For example if a patient were treated for 5 years at age 50 it might well be that they have no loss of BMD during that time and that their lifetime risk of fracture is reduced. It has not been demonstrated that this is not the case. If lifetime risk of fracture is reduced than you cannot compare the number of fractures prevented in the younger group with the number of fractures prevented in the older group, since it is known that there are more fractures in the older group if no treatment is given. Further confirmation that the model used is suspect is the statement in 4.2.16 that the manufacturers used longer time horizons and got lower costs per CQG
Section_5:	In 5.4 The evidence that strontium ranelate interferes with DXA scanning is because strontium has a higher molecular weight than calcium and thus it appears that the patient is putting on around 8 times more bone than they are in reality - not because strontium has properties similar to calcium
Section_6:	None
Section_7:	None
Section_8:	None
Section_9:	None
10/18/2005-Oct-2005 16:13:50	
role:	NHS Professional
discuss:	If this goes ahead then the UK will be out of step with clinical practice in most other countries (and indeed with current practice in the UK) with constraints imposed simply on cost and to limit treatment rather than based on what is generally considered to be good clinical practice. There can be no prevention in an individual under 70, with fairly draconian requirements thereafter. The clinical risk factors are too restrictive and will apply to relatively few individuals. I would not argue against these proposals simply on cost but it is apparent that with generic alendronate, bisphoshonate treatment will become very inexpensive in the near future and that should have been considered. There is a concern relating to the discrepancy between the cost-effective fracture probability intervention thresholds in this document and those previously determined and reported by Kanis et al. These discrepancies will lead to confusion and undermine the credibility of the NICE appraisal particularly as the field is moving toward 10 year absolute fracure risk and in Canada this is now being used for clinical decision making. Expression in the NICE analysis of fracture risk as an annual risk rather than 10-year fracture probability (as in the WHO report) will add further to the confusion, since the two sets of figures cannot be directly compared but it is apparent that they are different!!!!
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10/20/2005-Oct-2005 13:51:44

role:	NHS Professional
Section_1:	1.I can see little rationale other than cost containment for not treating ages below 70 yrs. using a cut-off of 20K for primary prevention rather than 30K used for secondary prevention is inconsistent. The other anomaly is that your calculations make ot cost effective to treat all women with a T score of less that -4 but it is not clear how these are going to be detected. There is no guidance for women at risk age 60-70 and no justificaton for not doing this. This is a real concern. 3. the risk factors selected do not include early menopause and others recommended by the RCP guidelines 4.strontium has both hip and vertebral fracture reduction data and is only considered second line. The data for etidronate hip fracture reduction is less robust 5.Raloxifene is excluded despite its dual benefits with ca breast reduction and efficacy in vertebral fracture reduction. Clinicians treating patients with FH of breast cancer have found this a very helpful medication and much valued by patients With all these concerns I would strongly recommend that a statement to show consistency with secondary guidance ie ""guidance does not overrride the individual responsibility etc. is included
Section_2:	when the algorithm is available we should consider setting the level of absolute risk in line with other situations eg cardiology and this guidance will probabay need to be revised
Section_3:	given earlier

10/20/2005-Oct-2005 15:33:40

role:	other
Section_2:	2.3: Guidelines on the treatments and T-Scores is complex to follow and may be difficult to follow/ rememeber. 2.4: As DXA is now taken only from the femoral score will we stop spinal DXA? 2.11: Smoking and alcohol intake are not mentioned as risk factors have been removed and immobility is also not mentioned as a risk factor. There is also no mention of conditions that affect absorption of calcium such as chrohns disease and liver disease.

10/20/2005-Oct-2005 23:8:42

role:	NHS Professional
Section_1:	There is little rationale other than cost , for not treating under 70yrs. Using a cut-off of 20K for primary prevention rather than 30K used for secondary prevention is anomalous particularly since your calculations make it cost-effective to treat all ages when T-score is <-4. I"m concerned there is no guidance for women at risk aged 60-70 and appreciate this may be due to the level of QLAYs set. This should be revised. Risk factors selected are limited; in current practice the RCP guidelines have been widely used. Raloxifene has dual benefits for osteoporosis and breast cancer prevention. Clinicians treat the whole patient, and these benefits are important in the decision making process. In view of these concerns, Id like a statement in the guidelines similar to that in the HTA-87 on 2ry Prevention, to allow clinicians to "exercise their clinical judgement when assessing treatment options" for primary prevention of osteoporotic fragility fractures in postmenopausal women.
Section_2:	2.3 Osteoporosis is defined as having a T-score of 2.5 SD or below. No specific site is mentioned but in the document femoral neck T-score determines treatment choice. Current practice is to use a Total Hip measurement and a patient may be severely osteoporotic on a spine reading alone, and it is unclear if this should be ignored.
Section_3:	3.3 Etidronate has been grouped with Alendronate & Risedronate despite no hip fracture prevention data. This is a concern where Etidronate could be recommended as first line to prevent hip fractures when there is insufficient evidence and a difficult regime for patients to adhere to. 3.10 Why is Strontium ranelate recommended as a second line treatment to Bisphosphonates despite having both vertebral & hip fracture reduction data?
Section_6:	Good patient care is not just about cost efficiency.

10/21/2005-Oct-2005 12:45:46

role:	Public
discuss:	For past 20 years in contact with people with neurological and ideopathic illness. Some ill at a young age with restricted mobility and digestive problems. Therefore at risk of early osteopenia/osteoporosis. Essential that such patients not ruled out of diagnostic and treatment programmes as their lack of mobility may prevent fracture but mean they are neverthe less at risk. An early check may prevent serious damage. - An ounce of prevention is worth a pound () of cure. Could be the cheaper option, apart from being in the interest of good patient care.
Section_1:	1.3 Women under the age of 70 should be included since some with ideopathic, auto-immune or neurological illnesses may develop osteopenia at an early age.
Section_2:	2.10 This is important. Checks for vertebral fractures must be made in younger women and men and not be discounted due to young age.
Section_3:	Complicated medication administration needs to be eliminated or patients will not take their medicines appropriately - or at all. Consideration should be given to newer methods which need administration once a week, once a fortnight or at even longer intervals. These regimes may appear expensive but could be

	cost effective if the outcome is better.
Section_4:	In view of the serious effect on mobility and lifestyle generally of osteoporosis, and the cost to the NHS of treatments, it would seem best to institute a preventative campaign aimed at younger people (35+?) with information on the need for sunlight v the use of too much sunscreen, healthy eating and exercise. This may at least delay the onset of osteopenia. I am concerned at the number of younger people who seem to be heading for osteporosis which it ought to be possible to forestall if not entirely prevent and who seem entirely unaware of the preventive measures which they ought to be taking.
Section_5:	Recommendations agreed. DEXA scan results should perhaps be treated with caution
Section_6:	Prevention cheaper than cure. Though prevention not always possible, there do seem to be strategies that could be cost effective and improve outcomes for patients.
Section_7:	Solely concentrating on older women may be an expensive option.
Section_8:	Grateful for this vigorous agenda.
Section_9:	Is it not possible to bring this date forward? 2009 seems a long way away. Clinical practise may be ahead of NICE recommendations already.
10/21/2005-Oct-2005 12:47:9	
role:	NHS Professional
Section_1:	The internal validity of the arguments presented and the figures on which they are based is difficult to argue against without some detailed knowledge of health economics. Nevertheless the outcome of the appraisal seems to be counter intuitive and run up against ethics and common sense. It does not seem right to accept a definition of a disease (osteoporosis) and then say that it should not be treated until someone is elderly and at very high risk of fracture. This will put clinicians in an invidious position leading to unwanted conflict with patients. Cheaper generic drugs (if the savings eventually feed through to the NHS) should alter the balance in favour of greater availability of therapy. Raloxifene shoud be retained as a useful option.
Section_2:	The definition of osteoporosis presented overlaps with osteopenia. The original WHO definition was T less than -2.5
Section_3:	Are cheaper generic bisphosphonates going to have an impact on the appraisal?
Section_4:	It is difficult to argue against an "opaque" cost -effectiveness model but the answer forthcoming from the analysis has resulted in a highly restrictive treatment model whereby the vast majority of those who will fracture will be excluded from treatment.
10/21/2005-Oct-2005 15:48:39	
role:	NHS Professional
Section_1:	1. As Ibandronate has now been licensed for use in Post-menopausal Osteoporosis, it may be helpful if it is mentioned in this appraisal, other wise it will have to wait till next review.
10/21/2005-Oct-2005 15:53:6	
role:	Patient
dataprotection:	-1
Section_1:	I disagree entirely. I am now 59 year sold and have to date had 5 fractures,starting at the age of 42. There is no family history of this terrible illness and I do not smoke, drink heavily or eat a defficient diet. I am also fit and take a lot of regular exercise. I did have a complete hysterectomy attheage of 30, including the removal of one ovary , and I have been advised that it was thefact that my remaining ovary was diseased through endometriosis in my early twenties that caused osteoporosis. However, no one realized this until I started sustaining severe fractures that did not heal propelry. Treatment at firstwas HRT for 10years,which was ineffective until compemented by Fosomax,whcih I am still taking. I was part of the original trials for this drug and cannot praise it enough,It has caused a most radical improvement and my bone condition at my last scan 2 years ago was almost average for my age,although I do still have occasional farctures.However, I am fit and active. If I had been able to go onto a drug like Fosomax before suffering so many farctures my life would have been very much improved, and I think such treatment should be available for patients in need
Section_2:	A miracle drug wjhcih should be freely available to people who need it. See earlier comments
Section_3:	See earlier comments
Section_4:	I have never been offered Calcium,presumably because my diet already contains enough. Please see earlier comments
Other comments received by non consultees and commentators	
Pharmaceutical industry	1. “Whether you consider that all of the relevant evidence has been taken into account” We consider that all of relevant evidence has been taken into account. 2. “Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate”

	We wanted to question whether the use of a 10 year time horizon in the Assessment Group's model is appropriate. This horizon is based on an assumption of 5 years treatment plus 5 years linear decline to no treatment effect. It is unclear what evidence base the assumption of 5 years maximum treatment time is based upon considering the lifelong nature of osteoporosis and its treatment. Indeed, a recent survey indicates that 70% of UK physicians believe that bisphosphonate treatment should last indefinitely and only 24% thought it should last for between 3 and 5 years (IOF, "The Adherence Gap" Survey). It is also unclear as to what assumptions were made about the relationship between treatment time and the long-term effect or "offset" time of treatment. We would like to suggest that an appropriate assumption would be that the offset time should be of equal proportion to the time on treatment rather than a fixed offset independent of treatment duration. In summary, we wondered whether a 'lifetime' horizon for the cost-effectiveness model would provide for a more accurate assessment of the treatments under consideration. When adopting a lifetime horizon, the results of the cost-effectiveness analysis of bisphosphonates could be significantly different and the current recommendations for women under 70 years might also change. 3. "Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS" We agree with the provisional recommendations for the use of bisphophonates for the primary prevention of osteoporosis. However, we do not consider that the recommendations entirely constitute a sound basis for guidance to the NHS as they presently exclude a substantial proportion of women who are at risk of osteoporosis, i.e those under 70 years of age. We would respectfully request that the Committee revisit the inclusion of this group in the recommendations on the basis of a further consideration of the points related to cost effectiveness described in section 2 above. We would however like to suggest that the Appraisal Committee give consideration to stressing the issues around compliance with bisphosphonate treatments even further in the wording of the guidance. The Committee already recognises the importance of compliance in their statement in paragraph 4.3.13, where it is noted that "compliance with antiresorptive therapy is generally low, and there is evidence that cost effectiveness is sensitive to compliance". The importance of ensuring that patients comply with their medication is therefore paramount in ensuring both the clinical and cost effectiveness of the recommended treatments. We respectfully suggest below how the issue of compliance might be further stressed in the final guidance should the Committee wish to do this: - In the recommendation outlined in 1.2, we would suggest that in addition to the considerations mentioned for proven effectiveness profile against tolerability and adverse effects, the likelihood of patients complying with the chosen bisphosphonate should be considered by clinicians. This statement would be supported by the comments made by the Committee in section 4.3.13 - In section 3.5, the Appraisal Committee recognises that gastrointestinal side- effects are common with bisphosphonates. We would like to suggest that this statement is qualified that these side effects are common with oral bisphosphonates - It is unclear in the provisional guidance as to what the Committee's views are on bisphosphonate frequency of dosing. There is evidence available establishing a clear causal relationship between frequency of dosing, side effects and compliance. The SIGN (Scottish Intercollegiate Guidance Network) guidelines for the Management of Osteoporosis state that the risk of gastrointestinal symptoms can be lessened by using the once weekly preparations. (SIGN Guideline 71, 2003). In Thompson et al, the frequency of administration of bisphosphonates is also well recognised as being an additional factor for compliance. We therefore wondered whether a recommendation on the frequency of dosing might also be appropriate. - In section 7.3.3, we wondered whether the likelihood of compliance might be added to the considerations made by the patient and their physician when choosing a bisphosphonate - In relation to the Proposed Recommendation for Further Research, we wanted to point out that there are already head-to-head trials on-going in this area such as the MOTION Study. We would be more than happy to share data recently collected on compliance and persistence with bisphosphonates if this would be helpful to the Committee. We also noticed that the titles of Appendices B and C are incorrect.
Patient Group	The guidelines only address primary and secondary prevention of fractures in postmenopausal women with osteoporosis and so do not address specific requirements for people with osteoporosis or reduced

	bone density due to coeliac disease. The guidelines should state that recommendations are not relevant for people with coeliac disease.
NHS Professional group	We are concerned that the application of this guidance will adversely affect osteoporosis management in the UK. 1. We are concerned by the decision to use £20,000 per QALY, rather than £30,000 as was used in the development of the secondary prevention guidelines. This lower amount is justified by saying 'the target population consists of women who are well and asymptomatic, and do not generally present seeking medical help for the condition.' We do not believe this to be the case. There is increasing public health awareness about osteoporosis and its risk factors. A considerable proportion of patients referred to this centre present with risk factors and wish to make informed decisions about the timing of treatment before they sustain fractures. In an era of patient partnership we believe this opportunity should be open to those at risk. 2. Although the proposed guidance purports to be based on the model developed by WHO, this does not appear to have been used consistently. Several of the risk factors defined by WHO have been dropped. In some cases this is logical, as other guidance is available for the management of secondary prevention and glucocorticoid-induced osteoporosis. However, we feel the reasons for other omissions are unsupportable. Current smoking and alcohol intake have been dropped because 'their effects on fracture risk were relatively small, and such behavioural risk factors are difficult to confirm reliably (section 4.3.7)'. It is very simple to assess 'current smoking' reliably, and this has been part of the NOF risk factor list for some time now. In the meta-analysis done for the WHO report, Kanis et al (Osteoporosis Int 2005; 16:155-62) report that current smoking was significantly associated with any fracture (RR=1.25) and the association was stronger for hip fracture (RR=1.84) and these risks were partially independent of BMD. We therefore feel that it is hard to dismiss current smoking as a risk factor based on either the risk being small or the difficulty in confirming current smoking. Similarly, the omission of BMI is justified within this document on the basis that it is accounted for by measurement of BMD. This is not, however, the case for all fractures. The exclusion of risk factors clearly reduces the potential target population. We feel this should be reconsidered, and would also suggest the inclusion of an estimate of the proportion of postmenopausal women falling within the categories identified. 3. We believe it may help physicians to have a listing of the medical conditions independently associated with bone loss, other than rheumatoid arthritis. 4. We are very concerned that there is no mention of teriparatide in primary prevention. It would seem to us reasonable to consider this treatment in patients who develop one or more incident fractures while taking a bisphosphonate. This guidance suggests that if a woman sustains a fracture within the first few months of starting bisphosphonate thereapy then it would be reasonable to continue bisphosphonates. We would however suggest that teriparatide treatment should be considered, providing the criteria from the secondary prevention report are met. 5. We believe that the wording of the section on bisphosphonate intolerance is restrictive and unrealistic. It is not current clinical practice to endoscope all patients with upper GI symptoms on a bisphosphonate. Furthermore, it would add substantially to the cost of managing osteoporosis patients if we were required to do so. 6. The guidelines state that their assumptions are based on a compliance of more than 25 to 50% and yet they make no recommendations on ensuring good compliance with medication. As in other chronic disease areas the question of compliance is crucial to the efficacy and cost-effectiveness of treatment. We believe the committee should reflect on the literature on compliance with long-term medication in general, and on the trials in the field of osteoporosis (which show that seeing a nurse 3-monthly after starting therapy enhances compliance, whether or not a bone turnover marker measurement is made). This may be felt to be another area where further research is needed. We hope that these comments are let to be constructive in the consultation process and look forward to seeing that they have been addressed in the revised draft of this guidance.
Pharmaceutical industry	Following our review we would like to raise the following concerns with respect to this proposed guidance: The guidance acknowledges the significant morbidity associated with osteoporotic fragility fractures. Primary prevention measures provide an opportunity to intervene prior to the onset of a clinically apparent osteoporotic fracture. As such, [we] believe that establishing such restrictive entry criteria runs counter to a public health remit whereby preventative strategies are seen to be of equal value to curative strategies. With regard to the economic modelling, we would like to query the rationale behind selecting £20 000/QALY as the maximum acceptable ICER. The guidance as it stands does not appear to provide provide any justification to support this assumption. The rationale put forward that the target population for this intervention consists of women who are well and asymptomatic does not seem rational given the morbidy associated with osteoporotic fragility fractures in previously asymptomatic osteopaenic or osteoporotic patients. The reference case as advocated by NICE takes into account that benefits and costs of a given health technology occur at various time points and this is taken into account by the application of

	discount rates. It therefore is fundamentally against NICE's recommended approach to assessing cost-effectiveness of technologies to bias against those whose benefit occurs in the future. Furthermore, It seems prejudicial at this stage to state a cost per QALY threshold. It is our understanding that these thresholds are not explicit and that the cost effectiveness of interventions is considered alongside other factors when formulating NICE guidance. By setting a lower threshold, the assessment group could be seen to imply that women in this age group have a lower level of need when compared to patients with other medical conditions. This would seem to place a lower value on this particular patient population. We are sure that this was not the intention of the writers however, it is understandable that patients with this condition, which can severely impair quality of life, could take issue with this. We would like to question the rationale behind excluding the protective effect that raloxifene demonstrates against breast cancer. It would seem appropriate to include all benefits delivered by a given health technology as this impacts the overall mortality and morbidity of the patient. The secondary prevention guideline indicates that experts acknowledge that the possibility of preventing vertebral fractures and breast cancer simultaneously could be attractive to many women. The Appraisal Committee also agreed that in principle the side effects of using a technology should be considered but concluded that the breast cancer benefit should not be the sole factor in deciding whether raloxifence is a cost effective option for the treatment of osteoporosis. The Appraisal Committee does not seem to have accounted for patient choice in an appropriate manner. We believe that the risk benefit should be explained to patients and they should be given this option as an informed choice.