NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women

Comments received from non- consultees and commentators on the Appraisal Consultation Document (ACD) issued in Sept 2006

Consultee or Commentator	Section of ACD (if specified) - Comment		Institute Response
Metabolic Bone Centre Sheffield Teaching Hospital		As the Clinical Lead in one of the leading UK Centres for the management of osteoporosis I am writing on behalf of my colleagues to give some feedback we have in relation to these consultation documents. I apologise for sending a letter but unfortunately it was not possible to incorporate our feedback within the constraints of the website. Whilst we were encouraged to see that the secondary care guidance now recognises the need for anabolic therapy in a wider group of women with very severe osteoporosis we feel that in general, the proposed guidance is extremely restrictive, and nihilistic in its approach to osteoporosis as a clinical entity. There are serious illogicalities within the consultation documents and we are concerned that implementation of the proposed guidance would have a major adverse impact on osteoporosis management in the UK. We outline some of our specific concerns below: **1. Anti-fracture efficacy** A great deal of confusion has arisen as the appraisal process has progressed. In TA 87, the relative risk reductions were derived from studies of patients with osteoporosis (low BMD and/or a prior fracture). Subsequently, in the first ACD for primary prevention and the revised ACD for secondary prevention, the relative risk reductions were derived from the whole study populations, i.e. included patients with BMD above the osteoporosis threshold with or without a prior fracture. Generally, these led to small but important decreases in the apparent efficacies of most interventions. Importantly, these populations also included patients with a variety of other risk factors, including low BMI, smoking, moderate alcohol intakes and family history of fracture to name but a few. The relative risk reductions are an average derived from these diverse populations. If the Committee declares that the therapies are unable to reverse the risk due	

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		to these other risk factors, then the corollary is that the benefit must be even greater in groups who lack these risk factors. This inevitable result has been ignored by the present analysis that uses the average risk reduction from the whole study populations and yet excludes an effect on the risk associated with these risk factors. The focus appears to be on limiting drug use in osteoporosis. **2. Didronel PMO/Etidronate** In contrast to alendronate, risedronate and strontium ranelate, the use of etidronate to prevent hip fracture remains unproven. It is unclear from the data presented about the assumptions made for the efficacy of etidronate on hip fracture. If the relative risk is correctly assumed to be 1, then it is difficult to see how etidronate would be more cost effective than risedronate, given the latter's effect to reduce hip fracture incidence. If the relative risk for hip fracture with etidronate is taken as the "single-point RR of fracture calculated from the log-normal efficacy distributions" then clearly this ignores the very wide, non-significant confidence intervals derived from 2 small RCTs. It would appear that the Committee has little regard for the quality of evidence, a stance that would inevitably lead the whole field of clinical research into disarray, with a progressive weakening of the evidence base. The recommendation of etidronate for widespread use totally discredits this technology appraisal and is very unlikely to be implemented in practice by clinicians educated in the principles of evidence-based medicine. If the Committee persists with a low evidence threshold for etidronate, a similar approach should be taken to other therapies but we strongly argue that this would also discredit the whole process. **3. Incremental cost-effectiveness ratios (ICERs)** In the setting of secondary osteoporosis, an ICER threshold of £30000 has been chosen for first line therapies but for any subsequent use of another agent (second-line treatment strategy) the threshold is set at £20000. While we recognise that the second-line strategy will not incur identification costs or BMD scanning, there appears to be little or no justification for moving to such a stringent threshold when the second line therapies are equally efficacious to generic alendronate and yet incur a	

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		higher cost. The latter would already limit their use to some extent without the artificial and unjustifiable move to a lower ICER. **4. Generic Price of Alendronate** The price of generic alendronate used in the modelling is now out of date. The NHS drug tariff price is currently £7.51 for 4 tablets, implying a yearly cost of £95.03. However, in the near term, the tariff price will fall further and should stabilise at around £3.50 per month, or £45.50 per year. **5. Practical implications** From a practical, clinical viewpoint, we do not believe the guidance is workable and think it will disadvantage and disenfranchise many patients. We are concerned that the sole use of BMD measurement at the femoral neck ignores the significant proportion of patients who have large discrepancies between BMD at the spine and hip. We have previously examined data from 1586 clinical referrals to our centre aged between 40 and 95. Femoral neck BMD could not be measured in 73 individuals. Osteoporosis was diagnosed in 17.3% at both LS and FN, in 14% at FN alone, and 8.3% at LS alone. LS T score was lower than FN T score in 38% of individuals. Our data suggested that it is only beyond the age of 80 that LS measurement ceases to provide additional information. Most UK clinical services have used the Royal College of Physicians guidance (2002) to develop referral criteria and inform management decisions. We fully acknowledge the need to take resources into account, and to incorporate our increasing knowledge base around absolute fracture risk into our treatment decisions. Nonetheless, the current guidance is so far removed from the RCP guidance we have worked with for several years, we cannot see how we can alter the perceptions around management in a single dramatic step. We would argue that patients already on therapy for osteoporosis should be reassured that treatment will not be withdrawn. On the other hand, this would be perceived as unfair by patients who are not assessed until after the guidance is implemented.	

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		Similiarly, we are astonished by the proposal that a patient has severe enough osteoporosis to warrant treatment but that if they cannot tolerate alendronate we may have to explain to them that they no longer have severe enough disease to warrant treatment with a clinically equivalent treatment. Ethically, we could not put this into practice. Finally, whilst we agree that osteoporosis treatment should be targeted towards those at greatest clinical risk we do not believe that the primary prevention guidance will give clinicians the autonomy to identify those younger women with very low BMD who have not currently sustained a fracture. We feel it offers a very cynical approach to osteoporosis by implying that it does not exist if it has not yet resulted in a clinical outcome. The guidance also conflicts with recommendations issued about groups of patients such as those with liver or coeliac disease and women using the contraceptive agent, depo provera. We hope that these comments are felt to be constructive within the consultation process and look forward to seeing that they have been addressed in the revised draft of this guidance.	
Roche		Please find attached feedback from Roche and GSK on the above Appraisal Consultation Document. Roche and GSK have launched ibandronate (Bonviva®) which is the first once monthly bisphosphonate treatment and first intravenous bisphosphonate treatment for osteoporosis and hence our interest in this particular appraisal. Both of these products have been assessed and approved for use in NHS Scotland by the Scottish Medicines Consortium (SMC). We have a number of points of feedback to make which are organised within the three sections below. ***1. "Whether you consider that all of the relevant evidence has been taken into account"***	

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		We are unsure whether all the available evidence relating to section 4.1.11 (Persistence and Compliance) has been taken into account, since this section does not reference the studies it reviewed. A fuller commentary on this issue is detailed in our response under section 3 below. ***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 reiterate the question (from our response to the previous ACD) as to 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, 2005). Therefore, we suggest that a 'lifetime' horizon for the cost-effectiveness model is aligned with NICE's standard methodology and would provide for a more accurate assessment of bisphosphonate treatments. When adopting a lifetime horizon, the results of the cost-effectiveness analysis of bisphosphonates could be significantly different – in particular, the current recommendations for women aged under 70 years might also change. Additionally, the resource impact forecasting would be impacted by this change. It is unclear as to what assumptions were made about the relationship between treatment time and the long-term effect or "offset" time of treatment, within the Assessment Group's model. We acknowledge that evidence in this area is sparse and so suggest that this could also be very usefully addressed in section 6 (Proposed recommendations for further research) alongside recommendations 6.2 and 6.3.	

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		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 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 reiterate the suggestion (from our response to the previous ACD) that the Committee revisit the inclusion of this group in the recommendations on the basis of a further consideration of the point related to cost effectiveness described in section 2 above (ie; lifetime model horizon), since it is not evident from the ACD that this scenario has been examined by the Assessment group's sensitivity analyses. We suggest that the Appraisal Committee give consideration to stressing the issues around compliance with bisphosphonate treatments even further in the wording of the guidance, in light of the following points: • The guidance already recognises that: o bisphosphonates have complex instructions for administration (section 3.6) o persistence and compliance with bisphosphonates is sub-optimal, particularly outside the controlled setting of clinical trials (section 4.1.11) • The guidance incorporates inability to comply within its recommendations on choosing appropriate therapies (sections 1.3 and 1.4) • We suggest that the terms 'persistence', 'discontinuation' and 'compliance' could usefully be defined within section 4.1.11, in order to provide clarity and aid understanding	

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		• We suggest that 'unable to comply' should also be defined within section 1, in the same way that 'intolerance of bisphosphonates' is (section 1.7) • A significant amount of work studying persistence and compliance has been conducted and published since the ACD was last circulated. As indicated above, it is unclear whether this evidence has been considered. Of particular note is: o Evidence on factors influencing persistence and compliance to bisphosphonates. We referenced an abstract (Thompson et al, 2005) in our previous response to this ACD, reporting that the frequency of administration of bisphosphonates is a significant factor for compliance. This research has now been published in full (Carr et al, 2006) o This link between dosing frequency and persistence had already been reported within additional publications available to the Assessment Group (Ettinger et al, 2004; Cramer et al, 2004) o A further study has recently reported on both the absolute levels of compliance and persistence observed for different bisphosphonate therapeutic options in the UK and the impact of dosing frequency (Brankin et al, 2006) o 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) o The previous ACD recognised the importance of compliance in economic modelling (previous section 4.3.13), noting that "compliance with antiresorptive therapy is generally low, and there is evidence that cost effectiveness is sensitive to compliance". Although this statement has been removed, it is clear that 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	

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		o The impact of compliance on health outcomes and thereby cost effectiveness has been reported in the literature. In particular, the impact of compliance with therapies for PMO on fracture outcomes has been studied, showing that fracture risk is increased in non-compliant patients (Caro, 2004; Huybrechts, 2005; McCombs, 2004; Siris, 2006; Van den Boogaard, 2006; Sebaldt, 2004; Goettsch, 2005; Penning-van Beest, 2006; Ethel, 2005) o It is unclear in the provisional guidance as to what the Committee's views are on bisphosphonate frequency of dosing. The available evidence highlighted above has established that compliance and persistence with current bisphosphonate therapies is poor and that there is a clear causal relationship between frequency of dosing, side effects and compliance. We therefore suggest that a recommendation on the frequency of dosing would also be appropriate within the guidance. o We would like to suggest that although ibandronate was not assessed as part of this appraisal, the guidance nevertheless acknowledges that the first monthly oral bisphosphonate and the first intravenous (IV) bisphosphonate are now therapeutic options within the NHS. This is appropriate, since: • The availability of these therapies is a matter of fact and as such, their mention within the guidance would ensure 'completeness' from the practical clinical perspective of the audience • Evidence clearly indicates that monthly oral and IV bisphosphonate administration options may provide part of the solution to the current sub-optimal compliance levels, as already discussed within the guidance • These therapies are likely to be mentioned within the forthcoming NICE Clinical Guideline in this area, which should complement this Technology Appraisal.	

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		We would be more than happy to share data recently collected on compliance and persistence with bisphosphonates if this would be helpful to the Appraisal Committee.	
Carer 1	1	It is of great concern that women below the age of 75, who have osteoporosis confirmed by having a T-score of -2.5 SD, but have not suffered a fragility fracture, are to receive no preventative treatment to help them to avoid having a fracture. Why is osteoporosis being treated differently from other diseases like heart disease and strokes where great stress is placed on prevention at a very great cost? Why are is the NICE defination of clinical risk factors so much more stringent than the WHO"s? Is it just to reduce the number of women who may receive treatment i.e a money saving exercise.	
	4	I can find no definition of "quality-adjusted life year". What price can be put on premature death,loss of independence, severe pain and loss of self-esteem through height loss, curvature of the spine and bulging stomachs that sometmes accompanies spinal fractures and creates difficulty in finding suitable fashionable clothing?	
Carer 2	1	I do not know of or understand all the technical data and references from this passage. I can only speak as the daughter of an osteoporosis sufferer and I am sure that all drugs should be made available to anyone who needs them. The prevention of bone breakages is surely better than trauma of coping with fractures.	
	2	Surely the recognition that osteoporosis is not always detected until there is a fracture, when it is too late and considerable discomfort is already being experienced confirms the need to prescribe drugs to women of any age who may be at risk.	
	3	Some of the above costs seem to be relatively reasonable/low. Surely compared with loss or earnings, hospital and other medically related costs plus the costs to personal and family life, these drugs should not be denied on financial grounds.	
NHS Professional 1	1	Dear All this document represent a set back in the care of patients with osteoporosis. non of the first line treatemnt (alendronate nor etidronate) have a clear hip fracture data which is the main burden of osteoporosis. your criteria for using the most effective treatemnt (risedronate and strontium) however are very strict which means that no one with the real problem of osteoporosis will recieve the appropriate treatemnt to reduce hip fracture risk. this document need careful rethinking taking into account the big problem imposed by hip fracture. residronate and strontium should	

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		be made easy to access not with such a rigid indication. dear all hip fracture is the most devastating complication of osteoporosis. non of the first line drugs you are proposing (alendronate nor etidronate) have any clear hip data while drugs which have clear effect on reducing hip fracture like residronate and strontium are made difficult to prescribe. even if the argument depend on cost saving then it will be more logic to access treatment which reduces the risk of the most expensive complication (hip fracture) which means having lower threshold to use the most effective treatment residronate and strontium and not having the outdated etidronate back as treatment. this is a real st back for the care of patients with osteoporosis	
NHS Professional 2	1	how long should the drugs be given for?	
	1.1	makes sense, don''t change	
	1.2	given that the evidence base for etidronate is less robust than that for risedronate, why is etidronate second choice? The order should be alendronate, risedronate, then etidronate.	
	1.3	having different criteria for access to the 3 bisphosphonates is confusing. Better to have the same criteria and the order of preference as above.	
	1.4	makes sense, don''t change.	
	1.5	makes sense, don''t change.	
	4.3.28	""The Committee suggested that the forthcoming clinical guideline could specify how such assessment should be made and what supplementation should be prescribed."" This cannot wait - advice is needed in this document. Make it simple - when these drugs are used co-prescription of calcium 1-1.2g and vit D 800iu per day (preferably in the same preparation) is required.	
	5	You need to add that people not meeting the criteria for bisphosphonates should have them stopped (consider calcium and vit D) as it wastes scarce resources.	
NHS Professional 3	2	If the majority of vertebral fracture are clinically silent (50-75), it follows that many individuals who are being considered for primary prevention have, in reality, already fractured. Many of these individuals will be under 75 years old. This guidance is clearly a high risk strategy, tacitly acknowledging that preventable fractures in the young elderly will occur. As a minimum, you could offset this risk by recommending strategies aimed at the better detection of vertebral fracture	

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	4	As I understand it, the cost effectiveness of generic alendronate is based on the efficacy data for branded Alendronate. Anecdotally the latter appears to have different (lower) tolerability and possibly different efficacy. Does not this call the validity of your conclusion into serious question? The entire RCT hip fracture evidence for Etidronate is 180 patients (compared to 11 770 on Risedronate and on this basis, you can judge it a more suitable alternative to Alendronate? A recommendation has to be plausible before it can be given credibility and this one isn"t!	
	4.3.17	You acknowledge that DXA screening at age 75 is not supported by evidence, nor indeed expert opinion, but if you are to deny treatment (and by implication measurement) on such exclusively age related grounds, a recommendation to screen becomes the logical conclusion. You hint at this but stop short of saying so on purely pragmatic grounds. The healthy 75 year old who drinks (or at least says they drink) alcohol gets treatment but the underweight 70 year old rheumatoid does not. If policy becomes purely age related it will lead to absurdies of this nature (and it isn"t hard to think of others)	
	6.1	Who do you anticipate will fund a head to head study with hip fracture as an end point?	
NHS Professional 4	1	Advice should be based on absolute risk, and using trial based evidence. It would be wrong to make it easier to prescribe alendronate (in preference to risedronate)as the potential adverse effects of alednronate have not been considered (see below)	
	2	Low BMI is conventionally defined as less than or equal to 19 kg/m2	
	3	1) Evidence for efficacy of etidronate is poor compared to second generation bisphosphonates. 2) There is virtually no evidence that drugs prevent hip fractures, if the patient is a habitual faller	
	4	1) There are significant differences in operational definitions of non-vertebral fractures. Primary prevention studies with alendronate suggested virtually no impact on all fractures recorded during the study. 2) There are a variety of absolute fracture risk tools available, one of which has been developed and at least partially validated by myself, with Prof David Reid in Aberdeen. There is no doubt that treatment decisions should be based on absolute fracture risk estimates. I am using a 20% 10 year risk for hip, spine or forearm. 3) The potential adverse effects of long lasting bisphosphonates are ignored in all the models. These include the (as yet) rare jaw osteonecrosis, but also impaired fracture healing and increased bone fragility after prolonged bisphosphonate therapy. 4) The evidence that the cited risk factors (especially parental history of hip fracture) has	

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		any effect on fracture risk independent of BMD is very poor, and it is surprising that NICE has included this. 5) BMD measurement at the hip may well be optimal for population studies, but not always so for individual case finding - spine may be best using qCT if reqd	
NHS Professional 5	1	alendronate is first choice because of lowest acquisition costs and recommended for use with T score <-2.5, risedronate should be recommended at the same T score as it is not good clincical care to deny therapy to a patient who has been advised to have treatment at a tscore of -2.5 just because they cannot take alendronate. Other products should be included as second or third line for patient choice	
	2	many fractures occur in women under 75 and with the proposed strategy this will increase. The WHO algorithm should be awaited and an individuals fracture risk determined. Then intervention can be achieved at a predetermined level of risk which is much better medicine and in line with the model used in other specialities such as cardiology.	
	4	Why have you undervalued osteoporosis by reducing the cost/qaly to 20,000 from 30,000? As a clinician in the real world I consider that these recommendations will be very difficult indeed to apply and they suggest that the intention is to privatise care of patients at risk of osteoporosis. These go against care provded for such patients in both the EU and North America and our patients will feel very short changed. The idea that because it is difficult to detect younger people at risk should not equate with them being denied treatment, especially if the who algorithm suggest that they are at significant risk of fracture in the next 5 years.	
NHS Professional 6	1	There are practical difficulties in persuading patients that there are similar drugs of similar effectiveness but one can be given if you have a T score of -2.7 but if you do not tolerate that you cannot have a similar drug which you may tolerate because your t score is >-3.0. Is smoking a risk factor? There are educational problems if there is no indication for DXA scanning if age <75 until you fracture	
	2	If WHO algorithm published will appraisal be reviewed?	
	4	Acquisition costs need not include risk stratification. Patients will be identified by the professional assessing or managing them for their risk factor. Is it likely that studies in patients with specific risk factors other than low BMD will ever be performed with sufficient patients to demonstrate an effect on fracture effect? If a drug given to patients with a risk factor and the BMD rises, can this be taken as a surrogate for fracture risk. It is demonstrated that improvement in fracture risk is greater than would be expected from the demonstrated change in BMD.	

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	8	?Pending publication of WHO algorithm	
NHS Professional 7	1	By definition, post menopausal women are usually aged 50 years +. What are the recommendations for those aged 50-75 years? Presumably following NICE guidance a woman, in this age range who may present with at least 3 relevant clinical risk factors would be denied a DXA scan as even the presence of osteoporosis would not warrant any therapeutic intervention. It is worth highlighting that if a woman is unable to comply with dosing regime of alendronate she will also have problems in complying with risedronate as it is given in the same manner, therefore this is a meaningless reason for changing to risedronate. Clinical practice would suggest that the dosing regime of etidronate is the most complicated and least acceptable to the patient, this needs to be considered in the recommendation on the use of etidronate.	
	2	Although DXA measurements at the spine may clearly be affected by degenerative changes, it would be inadequate to recommend that only femoral neck measurements should be used to diagnose osteoporosis. It is well known that osteoporosis may be site specific and previous studies on the use of all treatments have used spine and hip BMD measurements.	
	4	The inclusion of etidronate on a cost effective basis alone is contrary to good clinical practice. It is established tht it is less effective than other bisphphosphonates in reducing hip and vertebral fracture risk, there are no data on long term persistance or impact on quality of life. G-i symptoms are reported in approx third of patients using bisphosphonates, whereas strontium is not associated with such problems. It would therefore seem inappropriate that a woman msut have a T score >-4.0 before this can be considered when previous intolerance of bisphosphonates has already been demonstrated or when g-i disease is already established.In recommending DXA scanning on all women >75 years, in the absence of any clinical risk factors has consideration been given to other co-morbidities in the advanced age group, the cost of transport to the venue and declining cognitive function that increases with advancing age. Is it the intention to have an upper age limit?	
NHS Professional 8	1	This advice does not consider prevention of osteoporosis in post menopausal women below 75yrs of age. It reflects previous RCP guidance. Primary fracture prevention appears to be very cost related rather than what is best for the individual. It is my experience that etidronate is often taken incorrectly and has limited effictiveness. It is well recognised that fracture risk doubles with each SD decrease in BMD- so why wait until individuals have a SD of -3 or -4 before initiating treatment.	

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		Alendronate and Risedronate have simmilar mode of action on bone resorption -yet Risedronate is recommended at a lower level T -score, surely they should both be used at a T score of - 2.5 which after all is a diagnosis of Osteoporosis. Has DXA use been taken into the cost effectiveness algorithym?? Also Strontium Ranelate should be available for individuals unable to tollerate Bisphosphonates at a diagnostic level of Osteoporosis at a T score of -2.5 SD. In previous guidance we are advised to treat without DXA scanning in patients over 75yrs with fractures. Artifacts alter the reliability of DXA results in the elderly,so will we be performing unnecessary,unhelpful investigations	
	2	The NSF for Older people states osteoporosis prevention should be considered with falls; how do we prevent osteoporosis when treatments are restricted to individuals who have already fractured or the very elderly (who are less likely to comply with treatment options)? Surely risk of falling should be included in preventative advice.	
	3	Generic alendronic acid now 7.31 therefore increasing the cost efficetiveness ratio.	
	4	Would it be posible to have an algorithym to summaries the treatment options available?	
	5	Please consider how data is to be collected when reviewing implementation of these guidelines?	
	7	What happens to the RCP guidance now??	
	8	While it is appreciated that guidance and research take time to develop, it is in the patients best interest if development of guidelines is prompt and delivered on the predicted date.	
NHS Professional 9	1	I cannot understand the logic of the guidance re: etidronate - your document says etidronate is not effective but because it is cheaper than risedronate (which is effective) it is recommended above risedronate. Effectiveness should rank above cost and etridronate shoudl not be recommended at all. There is no mention in these primary prevention guidelines of osteoporosis prevention in patients taking long-term corticosteroids. A recent audit in my Care Trust revealed that this was the commonest reason for prescribing bisphosphonates in primary prevention and, therefore, a major ommission from your guidance. The RCP corticosteroid guidelines are still being used and, on my understanding, do not appear to be evidence based so, in my opinion, it is really important to get some evidence based guidelines for the NHS.	
NHS Professional 10	1	I am unsure if the BMD values cited are because of lack of efficacy outwith these parameters or lack of cost effectiveness and would welcome	

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		clarification	
	2	The move to use clinical risk plus BMD is desirable but not yet agreed - WHO algorith still pending. NICE seem to have reduced the no of medical conditions which are normally included. Relating value of treatment to age is important but the age of 75 seems an arbitary cut-off since bone density decline is a continuous variable.	
	4	The decision seems heavily weighted towards QALY data - the assumptions there in are not widely accepted as valid and robust. The costs of lifetime care for those younger than 75 requiring supported care following hip fracture are not adequately evaluated	
NHS Professional 11	1	Etidronate is inappropriate-no good hip fracture prevention data exists: it is a difficult regime for patients to comply with: I do not believe it would cause satisfactory reductions in Hip fracture. Generic alendronate is not the medication studied in the numerous trials. Anecdotal evidence from patients suggests more sideeffects and poorer efficacy. At the very least its efficacy is unproven. Risedronate is a well proven drug, and should be immediately available to women who fail to tolerate alendronate. Women under 75 at comparable risk are not being considered here. I.E. the woman with RA and a t score of -4 aged 65 years who has never been treated with corticosteroids. Her risk of fracture is high but we are not allowed to prevent her fracture?	
	2	Total Hip is the preferred site for DXA estimation of osteoporotic risk, particularly in the elderly.	
	4	generic alendronate is not neccessarily the same as Fosamax. Etidronate was superseeded in effect by alendronate and risedronate, to use this would be out of step with the rest of the worldwide osteoporotic community. Risedronate is a good, well tolerated medication, to insist of more severe osteoporosis prior to its use is incorrect.	
NHS Professional 12	1	It does not make sense to only allow prescription of Risderonate and strontioum ranelate if the T-scores have to be even lower than for the prescription of alnedronate in case of intolerance of alendronate. Why use different measures here? This is confusing and hence not helpful. Also, since risedronate is better tolerated and has a shorter half life I prefer to use it as a drug of first choice; I consider it safer longterm and more effective (as patients are more likely to take it than alendronate).	
	2	I agree that osteoporotic fractures, especially of the hip, often have devastating consequences for the affected individual (loss of independence, high risk of death) and their relatives and carers.	

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	4	I have grave concerns about the above. Many patients I see in my daily practice as a consultant rheumatologist are well below the age of 75, have several risk factors for osteoporosis and many have an increased falls risk due to the disabilities sustained from their arthritis. Primary prevention is bound to be cost effective here although there is no data yet to prove this. The above guidance would exclude this high risk group of patients. My advice on the need for primary prevention of fragility fractures in my patietns is likely to be overruled in primary care when they follow your propposed guidance! This would have disastrous consequences for a significant part of my patients. I also provide a regional osteoporosis service and report all DXA perforemd withtin our trust. More often than not are DXA scans requested because patients have several risk factors for osteoporosis but are below the age of 75. I feel a siginificant number of patietns will loose out on fracture prevention if your guidance is approved.	
	5	I feel a siginificant number of patietns will loose out on fracture prevention if your guidance is approved. Approval of this guidance would be another example of how ""evidence based medicine"" does not work in the best interest of the patient as the evidence is based on data which was not aquired with the question in mind it is now used for to base this guidance on. Since particularly hip fracturs have such devastating effects on the individual (and has significant longterm costs such as provision of 24 hour care) I seriously hope your guidance will be reviwed bearing this in mind.	
NHS Professional 13	1	The different T-score thresholds for Alendronate and Risedronate and Strontium are confusing. It does not seem right that (for example) women who are age 75+ with T-score below -2.5 that merits treatment with alendronate would not merit treatment with Risedronate until the t-score had fallen below -3.0 and Strontium till the T-score is below -4.0. This will be denying treatment for many older patients with severe osteoporosis who are at high risk of fracture.	
NHS Professional 14	1	Diagnostic threshold based on T score @ fem. neck not evidenced -WHO was for epidemiological reasons only - see ISCD position statement (Hans et al. JCD 2006;9(1):15-21) Changes to economic model to neutralise risk gradient for risk factors means indefensible clinical scenarios e.g 70yrs T -3.0, multiple risk factors could have 10 year AR 30% and denied treatment. No normative DXA data beyond 80 so only 5 years to Rx Etidronate no RCT evidence for hip as yr analysis indicates u r advocating ineffective Rx first line over 75 = high risk hip #? Medico-legal + ethical	

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		risk if pt gets hip # on Rx know to be ineffective Sr has evidence for efficacy in + 80 (Seeman E et al JBMR 2006;21(7):1113-20) also RIS (Boonen S et al JAGS 2004;52(11):1832-9). Reasonable second line but unethical as discriminates against those unlucky to have GI s/a - endorses hazardous practice encouraging persistence with harmful meds because no other allowed unless higher risk. ? Breach of professional code of conduct. Circular argument - RIS if the pt unable to comply with instr. for ALN but 3.6 states ALN & RIS instr. are the same. Why no smoking? (Kanis JA et al Ost Int 2005;16(7):737-42)	
	2.12	2.12 WHO risk predictor In view of the imminent arrival of an absolute risk predictor tool that is based on very large observational studies, would it not be best to await this to ensure we do not recreate the confusion that surrounded conflicting NICE and JBS guidelines on hypertension management. The guidance is based upon stepped assessments of absolute risk. This approach could be considered cumbersome. This has the advantage of simplicity and agility to cope with the changing costs of therapeutic interventions such as alendronate which puts at risk the relevance of this guidance within months.	
	4	Why pooled RIS and ALN data they are not alternatives in this appraisal. Efficacy = RR of 0.71. Is this used to alter the economic model? Why? Why ICER 20,000 and 30,000 in TA 87? The HRG tariffs underestimate NHS cost of hip # by about 50% (Lawrence TM et al Injury. 2005;36(1):88-91. Have you counted social care properly? (Kanis JA et al Health Technology Assessment. 2002;6 ((29)) T-score thresholds would be more permissive is too imprecise Why assumed that the bone remodelling agents act only on BMD related # risk? Unlikely theory (Heaney, Bone. 2003;33(4):457-65) No justification for refusal to accept Sr data on hip in + 74 year olds with low BMD. This appraisal is directed at this age group. Treat all drugs same if trying to apply to a subset of the RCT population Raloxifene has same efficacy as etidronate and breast data better than tamoxifen (Vogel et al JAMA. 2006 June 5, 2006:295.23) so dont believe yr model is sound	
	5	We don"t feel your consultation process is likely to be effective, fair or reasonable as it is very difficult to construct a sound referenced scientific argument on a wide ranging set of paragraphs in 1200 characters (including spaces). Try it sometime! Apologies for the txt speech but we think that is a problem that you have caused!	
NHS Professional 15	1	These guidelines seem excessively strict and the age cut off too high. It seems wrong that a woman who is 70 with a T score -2.6 and a 10 year risk of hip fracture of approx 18.3% (Kanis et al 2001) would be denied	

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		treatment. Moreover if she were intolerant of alendronate and etidronate, even if she were 75 years old (with a hip fracture risk of 24.6%)she would be denied further therapy that would reduce her fracture risk. This seems wrong. Despite the other risk factors mentioned in 2.11, there is no algorithm by which additional risk factors can be integrated into the treatment decision particularly the factors that confer risk in addition to that assessed by BMD.	
NHS Professional 16	1	I note that you have not mentioned the use of calcium and vitamin D supplementation in the elderly, infirm who are immobile and in institutional care. Was this deliberate?	
NHS Professional 17	4	Comment on how Clinicians should determine adequacy of calcium and vitamin D intake: The dietary calcium and vitamin D intake of the patient would be best determined by a dietary assessment carried out by a State Registered Dietitian. Whilst this impacts on the cost per case, the cost of a Dietetic assessment could be offset by the potential savings generated through avoiding unnecessary calcium and vit D supplements being prescribed when dietary intake is adequate. Prescribing calcium and vitamin D supplements when dietary intake is adequate could result in calcium intakes of >2000mg daily which can increase the risk of kidney stone formation. Alternatively (in the absence of a Dietetic assessment) a tool to assess ""dietary calcium and vitamin D intake"" could be developed by Dietitians for Clinicians or patients to use.	
NHS Professional 18	1	I must oppose the recommendation for these treatment sto only be offered to patients aged 75 or over.We cannot ignore patients in the younger age group who have been diagnosed with osteoporosis but not yet fractured we will be denying them effective treatment.We have strived since the publication of the NSF for Older People stnadard 6 to reduce falls and fractures.This is an uphill struggle but it is crucial that we identify risk and intervene early. We have to reduce this epidemic of osteoporotic fractures. These have a major impact on quantity and quality of life and are huge expense in terms of health and social care costs. Hip fracture is associated with a significant mortality (25% at 1 year).To deny primary prevention treatments to this group would be amjor retrograde step in our quest . Did you consider the quality of life impact of sustaining a fracture and the social care costs?	
NHS Professional 19	1	1. Treatment thresholds are such that a minority of the population is eligible for therapy. In practice this guidance is likely to be ignored: you may beleive it is cost-ineffective to treat an 85 year old who has one risk factor and a T score of -3.7, but I doubt a single clinician in the country will agree with you. 2. Etidronate should not be promoted over risedronate or	

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		strontium - compliance with this agent is poor, supportive data in hip fracture is poor (mostly from GPPRD study, not RCT). 3. Fortunately the GDG seems to be developing a far more rational guideline with a wider remit (not ignoring men, steroid users etc) and I hope their recommendations will be adopted over yours.	
	2	If there are only 1.1 million women with T <-2.5 in the UK, and 180000 of them sustain a fracture each year, then the annual fracture risk is 16% (7% for hip fracture alone) ... I"d be interested in what % of the at risk population you feel it is warranted to treat. Your treatment thresholds seem unduly restrictive and only the worst of the worst will be treated. Have you considered the medicolegal costs of cases brought by women who fall close to the treatment threshold but are not treated? Inevitably a substantial number of these will eventually fracture a bone and might consider taking legal action, particularly as it is unlikely your guidance will have international credibility except as a rationing exercise.	
	3	None, other than to point out once more that to seriously recommend we go back to using etidronate at this stage in our understanding of the disease seems rather bizarre.	
	4	1. Easier by far to explain to a patient that based on her age and DEXA scan result, her risk of fracture is X% and therefore we will or will not be treating them. Also avoids medicolegal issue raised above as risk will have been discussed. 2. Identification costs of some groups will be nil - 4.2.14 is wrong: patients who smoke present to chest physicians, patients with RA to rheumatologists, patients with IBD and coeliac disease to gastroenterologists. Opportunistic identification of patients with clinical risk factors is done every day. Offsetting identification costs against net benefit of treatment also ignores the fact that many patients present with concerns about osteoporosis, which may well be reasonable and require DEXA and an offer of treatment to address. Your guidance suggests that it is cost-ineffective even to assess risk factors in those <70 years (but is based on a model that assumes they won"t present in our surgeries and ask!). We could try telling them that as a population they are cost-ineffective to screen or treat no matter how bad their BMD or risk factors but I don"t beleive that is true.	
	5	See my comments on 2ry prevention guidance. Basically, if your guidance doesn"t match best clinical practice and is refuted by everyone who has any involvement in clinical care of patients with OP I don"t expect it to be followed. Essentially, your guidance is based on your model. If your model gives these treatment thresholds, I"m sorry, it must be flawed. Because it doesn"t reflect the real world of patient care. From Experts, RCP, RCGP,	

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		GDG (and even SCHARR!) comments there would appear to be numerous debatable assumptions on which your model is based and then last-minute adjustment in treatment thresholds without consultation to reflect spurious concerns over compliance and toxicity, which in fact do not alter cost-effectiveness.	
	7	1200 chars is inadequate for section 4 of the guidance - consider revising in future ACDs?	
	8	May need to be brought forward to cover Zoledronate when released. Or to redress mismatch with the GDG guideline.	
NHS Professional 20	1	The guidance above is at odds with the current Scottish Inter-collegiate Guidelines Network (SIGN) recommendations, namely by denying younger post-menopausal women the option of therapy. Current practice in Glasgow is to offer bisphosphonates to any person over 60year old with a T-score < -2.5. One could argue that in older persons (>65years) even greater benefit is derived and as such we offer bisphosphonates if their T-scores are < -2.0. I find it curious that this guidance states that a person over 75years with a t-score of -2.5 who is intolerant of bisphosphonates, has to wait until their T-score falls to below -4.0 before they are to be offered strontium as an alternative intervention. This seems unfair.	
NHS Professional 21	1	one fails to understand the lower t score for other bisphosphonates when good rct dataa shows that vert. fracture is the same as with alendronate. Why 3 units of alcohol when the evidence from the epidemiological studies suggests 2 or more units.	
	3	the use of etidronate is based on poor data as seen in the first 2 rct. Patients had major problems adhering to the dosing requirements and many abandoned therapy all together. Others had marked GI symptoms due to the calcium. Separate prescription of etidronate alone led to excessive use of the drug leading to a risk of mineralisation defect.I know as i started to use the drug when it became available and this is my patients" experience.	
	4.1.5.2	these studies were not powered to see fracture reduction	
	4.1.6.2	it is difficult to see how you have arrived at a RR for hip fractures as the 2 major studied did not show this but there is data showing a slight increase in hip BMD.Are you giving a gloss to lower quality studies and arriving at these conclusions simply because you know before the modelling is done that this drug is cheapest?	
	4.1.6.5	My clinical experience that gi side effects were considerable often due to the calcium in didronel pmo and certainly greater than with the other bisphosphonates. This is from the real world experience where patients	

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		are warned about side effects . The discontinuatioin rates were high due to above and complex dosing requirements.	
	4.1.11.2	The rate of adherence is lower in primary care than indiccated here. The guidance is aimed at reducing the use of drugs to treat osteporosis, we will be out of line with the rest of the world. It will lead the well-off seeking advise and tratment privately sinc the NHS will treat them only if their fracture risk exceed that of othe women in other parts of world. Pluckin T score is a mockery of well conducted RCT.	
	5	We are going to ask our patients to accept a higher risk of fracture befoe they are treated. I f such a patient was denied therapy as their T score was not NICE low enough and she sibsequently fractured, could she sue NICE? My adice to such a patient will still be that she needs treatment and she should seek legal advise.	
	6	Head to head studies wil not be done unless the goverments funds them. The y will be very expensive. There is evidence of a falling effect already but indivual variations must be great.The long terms effects are now well known How lonf should one wait? Similar ruled dont apply to statins or other biological therapies in inflammatory diseases.	
NHS Professional 22	4	Dear NICE, re ACD Osteoporosis in Primary Care I write with my concerns on your draft ACD for consultation as NEOxon PCT lead for osteoporosis. 1] Your change of the economic model assumptions without justification is most worrying, and basically negates any possible evidence based conclusions you attempt to draw. If I were a cynic, one could conclude the only reason you have changed the underlying model is to reduce the effect of the recent dramatic decrease [>50%] in cost price of generic alendronate, which would have otherwise been highly cost effective for a very large number of patients. I think the media may be most interested to know this. In particular, a] the assignment of zero efficacy of interventions for the contributions of clinical risk factors other than age, BMD and fracture, to fracture risk goes against my understanding of the literature. b] hip fracture has been given a lower disutility than is correct c] Your new model assumes a lower cost-effectiveness of hip-fracture reduction with alendronate without any new evidence through the iterations of your ACD, which cannot be justified. 2] If you assume there should be an evidence base for your recommendations then there can be no place for etidronate, as the hip fracture data is non-existent. Just because it is cheap does not mean it works. I have not prescribed etidronate for 20 years, and will advise all future patients with hip fractures whilst taking etidronate to recover their home care costs or residential home costs from you for recommending	

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		such a treatment as alternative first line. 3] By recommending that all women at risk should be screened with a DXA in primary prevention before treatment there is no clinical lee way for the patient who would benefit from bisphosphonates but could not physically or psychologically get to a DXA machine. For example, a frail demented 93 yr old who starts to fall in an old peoples home would be at highest risk of fracture, and under these present recommendations my PCT would not allow me to prescribe for her, until after she has broken her hip. There is no funding for ambulance transportation costs. If NICE really want all my patients housebound/residential home elderly patients to have a DXA before I am allowed to prescribe this will be a huge overlooked cost. It seems the money could be better spent just treating them. 4] There is no mention how often to re- DXA the population of >75 yr olds with risk factors who do not have a T score of -2.5 when first done on their 75th birthday. Have you thought about this? Should it be every 5 years [75, 80,85,90,95,100,and 105] ? Have you costed for this? [+ transport as they get older] ? 5] Strontium Ranelate: women with more than one clinical risk factor the T score threshold would be more permissive Where are these thresholds? Should be in the text to be a level playing field i.e. 2 CRF T score X, 3 CRF T score Y etc. I actually think it is a non-workable clinical guideline to say that if the woman cannot tolerate a bisphosphonate that she then may have to wait many years and have many more DXAs before her T score drops sufficiently below what we already know to be Osteoporotic to then allow her to have strontium treatment.	
NHS Professional 23	1	This does not seem to be primary prevention. By the time a woman reaches the age of 75 and has a T score of -2.5 she is already osteoporotic. Many women will have had their first fracture before the age of 75. Thus we have missed the chance of prevention. Bisphosphnates have ben shown to be effective in women aged 55-80 years (J Clin Endocrin and Metabolism 85,no 11 2000) so why not give the chance of treating earlier.	
	2	Diagnosis of osteoporosis can be made by BMD measurements but this is not the only way. eg diagnosis can be by having low trauma fractures or by bone histology. Previously we have taken the expectation that 38% of women aged 70-79 would be osteoporotic (Kanis J, Pitt AA epidemiology of osteoporosisBone S7-S15) This is a large change - is it more reliable ?	
	4	The model is flawed it only uses a time horizon of ten years and this will have a major impact on cost effectiveness of treating women at a younger age. Studies with bisphosphonates have shown that the effects on BMD persist for longer than ten years (FITII), and though the studies have not	

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		had time to be done it may be expected that the effect of treating a women at 65 may affect her lifetime fracture risk and certainly her fracture risk up to 75. This is especially important when considering the effectiveness of treating younger osteopenic women who if not treated will become osteoporotic and fracture in later age.	
	4.3.5	Treatment has been found to be efficacious in osteopenic women with T-scores less than -2 and more than -2.5(FOSIT trial). It is also not clear if the number of fractures prevented in the studies you look at are primary fractures or secondary fractures. The model also takes no cognizance of the fact that a patient may be treated in earlier life with one drug (HRT even) and then go on to another drug and then a third. The cost effectiveness of this process has not been looked at but is what perhaps happens in clinical practice	
	5	The committee are looking at cost effectiveness, but if effectiveness alone were considered and the woman was willing to pay the 300 a year (6 a week the cost of a few drinks) for the drug does she have the right to do that, or will the clinician not be allowed to consider that for ethical reasons under the implementation	
	6	If head to head studies are done the time horizons need to be over at least 20 or better still 30 years	
	8	Suggest that a review date be set earlier in order to look at how the advice is received and implemented	
NHS Professional 24	1	This suggests there is no circumstance beneath age 75 where bone protection is appropriate unless prior fracture (omitting corticosteroid use). I have particular concerns for those with ongoing medical causes of bone loss (such as rheumatoid arthritis) and very early untreated menopause. I believe denying treatment to an individual with known very low, and continuing to deteriorate bone density constitutes to negligence. The different t-score levels required for the different treatments will cause confusion with both patients and clinicians. I am both shocked and baffled.	
NHS Professional 25	1	Not sure why different T scores for different drugs are recommended.Is it price only? You have to have a bigger risk of fracture to be allowed a more expensive drug?	
	4	An ostoporotic woman of 75 (Tscore-2.5)who is intolerant of alendronate is denied treatment unless her Tscore drops further to -3 for risedronate or - 4 for strontium? I may have missed the point here but it seems unfair on the woman.Intolerance of alendronate does not prevent fracture!	
	6	agree that 6.1, 6.2 and 6.4 are very reasonable. If only women over 75 are treated it is going to be difficult to get long term results on quality,and	

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		longterm quality may not matter as much in that age group as it would if 50 year olds were allowed treatment.(shorter duration of exposure in elderly- don"t we have sufficient data already for thatage group?)I hope 6.5 will give much better guidance than these proposals and it would seem sensible to delay these proposals to incorporate the results of the WHOstudy.	
	7	The present guidelines on secondary prevention are very complex. I report bone density scans and still have to have a copy laid out beside me as I do so. GPs are not aware of them and haven"t read or don"t remember them. I have done several meetings to talk about them and simply they seem impossible to remember for the GPs. The primary prevention ones also seem complex but unless I"ve got it wrong no one under the age of 75 can get treated no matter what their T score unless they have fractured so no one of under 75 not having fractured should have a DEXA!Ideally we should prevent that first very painful vertebral fracture and not wait until bone loss is irreversible.I"m worried about missing younger women with very low Tscores who will then present in their 60"s with multiple vertebral fractures.I saw a 66 year old today who presented with 6 vertebral fractures and multiple risk factors who should have had a DEXA before fracture if the Royal College Guidelines had been implemented.The NICE guidelines will not help patients like that.	
	8	This should be reviewed as soon as the WHO study comes out.	
NHS Professional 26	1	To suggest that the only women elligible for primary prevention are those over 75 is quite outrageous. The DoH along with many other organisations has highlighted the public health problem of osteoporosis over the last 20 years. Having raised public awareness it seems rather perverse to now say that, even if you are at high risk, there is nothing you can do about it until you either 75 or break a bone. This turns the whole philosophy of preventative medicine on its head: maybe that is your intention but it seems a dangerous precedent. I would urge you to include premature menopause in the list of risk factors. It is a well established risk factor and sadly I"m now seeing a lot of women who have been taken off HRT in the 30"s because of erroneous fears about HRT in this age group.	
	2	I agree. Surely this just highlights the need to do something not just wait till a woman reaches 75.	
	4	Whilst accepting that there are limited RCT data to suggest reduction in fracture risk in women with low BMD only there is abundant evidence of conservation of bone with these preparations. Surely some consideration should be given to other evidence beyond fracture RCTs. There cannot	

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		always be RCTs to answer every question. Would it not be posssible to target BMD at those with established risk factors and then recommend treatment at those with T score < -2.5. At present a 60 year old woman with a T score of -3 is going to be offered nothing until she fractures!	
NHS Professional 27	1	The diagnostic threshold for osteoporosis should apply to spine or femoral neck or total hip. The current suggestion of total hip only, does not take in to account those with severe spinal osteoporosis alone which do form a significant proportion of the osteoporotic population. You seem to be placing less "value" on spinal fractures where the QOL impact is similar to hip fracture. Including alcohol as a clinical risk factor and not smoking seems odd and requires explanation.	
	2	By making the age threshold 75 years the guidance is almost ignoring its stated aim of primary prevention in the way that most doctors and patients understand it. You are effectively only treating severe established disease. This may be primary prevention of fractures but not of "osteoporosis". This will be very difficult to sell to patients (with low bone density) who have relatives with severe osteoporosis and fear suffering the same fate.	
	3	Treating osteoporosis first or second line with etidronate is turning back the clock and flying in the face of evidence based medicine. It is setting flawed data from observational studies above that obtained from double blinded randomised trials. In my view the idea of producing different treatment thresholds for commonly used drugs is neither wise or ethical. It would be difficult for GP"s to implement in practice and impossible for us to explain and justify to patients. It effectively discriminates against people who have upper GI problems with bisphosphonate intolerance.	
	4	What is the justification for using 20,000 per QUALY rather than 30,000 as usual?	
NHS Professional 28	1	The document states that treatment will only be offered for primary prevention after the age of 75 and with a BMD value of - 2.5 However age and BMD are important predictors of future fracture and it is too late once a fracture has occurred The guideline also includes etidronate which is the least evidence based treatment we have for established osteoporosis Also if a patient is intolerant of alendronate then they can only be offered additionally treatment if their BMD value is lower.This will be unworkable in day to day practice and appears to be based on cost and not evidence.It will be impossible to mange a patient who has a T score of -2.6 who can not tolerate or comply with a bisphosphonate As a clinician I will have to tell them I can not offer them an alternative therapy as their osteoporosis is not severe enough This guideline is ageist.also the clinical risk factors have failed to include smoking and steroid use which were	

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		used in the WHO guideline	
	2	As indicated the subsequent morbidity and mortality associated with a hip fracture and a vertebral fracture is immense and yet we are goinf to have to wait until the age of 75 yto institute primary prevention	
	4	Cost is being used as a guideline for treatment	
	5	This guideliune will be impossible to implement in clinical practice	
NHS Professional 29	1	1) ""prevention"" seems to start at 75; how do I approach younger women? One of my patient had an opportunistic DXA at 49 (her cousin was having one and she was curious about her BMD; hip T-score was normal and spine T-score was - 4.9; nothing was done. I saw her 3 years later and, unconvinced by the result I asked for another scan: Hip normal again but spine: -5.2. Should I have waited until her spine crumbles before offering treatment? 2) the definition of intolerance to bisphosphonate is not helpful; if patient have to suffer persistent severe upper GI problems, they are going to stop taking the medication before it reaches that point and they may not ask for another type of product.As you know very well adherence to treatment is a major problem at the best of time and it is not helped by this kind of directive.	
	2	Why not wait for Kanis"s advice on the WHO algorithm and why was he not consulted?	
	3	None of the above are recommended for severe renal impairment	
	4	How can etidronate be put on the same level as the other bisphosphonate; you are not talking about evidence here but cost cutting. It is only licenced for vertebral OP and if it is given to older women there is a big risk that there is also OP involvment at the hip, therefore, it is a waste of money and it does not protect these women. Despite your anecdotal evidence, all my patients (except 1) asked to change to a weekly bisphosphonate as soon as it became available. It is interesting that you are happy to use anecdotal evidence for 1 product but are not considering hip fracture data for protelos. I would suggest that the reason is the cheapness of the product and not its efficacy.	
	5	It is a shame and a disgrace that prevention should start at such a late time. This put practitionners in an impossible situation, especially when a number of private providers offer heel scanners to a specific population of younger women; They come to my clinic with their result, showing a ""substantial loss""; If I send them away saying that there is no point for a scan to confirm/disprove as, even if they have OP they will not be treated.	

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		What happens if one of them has an OP fracture within the following month and she takes me to court? The whole process is cost driven (to the Chancellor"s benefit and not to the families involved/looking/paying N/H fees for their relatives, not to mention the ersonal cost to the patients. The evidence is flawed, the T-score set much too low; as you well know many OP fractures occur in the osteopenic range. All in all a very disapointing and unhelpful document; The criteria are so complex how do you expect the ordinary GPs to apply them? As mentioned earlier, compliance/adherence is very low and to improve it it is essential to give patients a choice of medicines that are equally effective and most appropriate to their lifestyle.	
	7	It would be useful to have something done on OP in men.	
NHS Professional 30	1	1. We are surprised by the high prominence of etidronate in this guidance. It is generally accepted that it is not as good as other bisphosphonates. The research evidence behind it is less good. However, it is cheap. PCT"s may well use this as first line treatment. I do not think this is what your GDG will have wanted. If you really thought it was good, you would have it as second line if alendronate is not tolerated, however, you have risedronate second line. Please reconsider this. 2. We feel there are some difficult inconsistances in this document. Imagine you are a patient with a risk factors and a high falls risk and t score -2.8. You are put on alendronate and get terrible indigestion. We tell you there are other treatment options but you don"t need them? I cannot see how we can work with this anomaly in a pragmatic clinical practice. Please try and review this.	
	2	1. Why has falls risk not been included as a risk factor for fractures? All the patients we see with hip fractures have fallen! Please consider adding this to your list of fracture risk. 2. We feel it is not sensible to use only the T score at the femoral neck. The reason for this is not made clear in the document. 3. Many people with osteoporosis will not get medical treatment. This document does not mention non medical treatments such as stopping smoking, reduce alcohol intake, regular exercise and increasing fruit and vegetables. This should be made clear and highlighted in the document. 3. Do you mean current alcohol intake of greater than 3 units per day? If the patients cut down on alcohol, should we stop any treatments prescribed. This should be made clear. Also, conditions associated with prolonged immobility is not clear- confined to bed as a teenager for a year for TB or curently bed bound or somewhere in between. Please clarify.	

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	3	The cost of generic alendronate is still coming down- does this change your calculations?	
	4	What is an acceptable QALY? 20,000 or 30,000. You seem to have changed the goal posts- why is this?	
	6	I would suggest that you should be encouraging research into the effectiveness of etidronate. If this guidance is published as it stands, this will be the first line treatment for primary prevention in all patients who fit the criteria. It is generally accepted that this is less good than other bisphosphonates. Prove that it isn''t and fast.	
NHS Professional 31	1	evidence for etidronate weak and difficult to take. why risedronate different to alendronate? strontium seems alternative if unable etc with bisphisphonates- why different t score? why wait till age 75/ what of prevention?	
	2	dexa scanning noit available at all localities, travel and delay with long waiting lists. lists will increase ith greater reliance on t score	
	3	my experience was v poor compliance with etidronate, a lot of GI upset with the calcium between course	
	4	cost seems to play a large role rather than choice.	
	6	who would fund head to head studies which would need to be large to detect what will be small differences, require much effort and produce little benefit. cannot see the drug companies doing so as the recommended alendronate is of patent. would the mrc or nhs?	
NHS Professional 32	1	It would be appropriate and non-ageist to assess patients,as we do in clinical practice, on likelyhood of fracture risk rather than age >75. The evidence for Hip density for assessment is not given and Spine density measurements are more appropriate and useful. It is not appropriate to equate alendronate with etidronate as the latter is now hardly used and not considered adequately effective nor practical. Will the guidelines change when Risedronate comes off patent? Why is Ibandronate not mentioned? Why is smoking not considered a risk factor as there is hard evidence for that as an independent risk factor whilst only soft and conflicting evidence for alcohol at the levels given?	
	2	The WHO risk of fracture algorithm will be most useful and the guidelines should await the publication and use these rather than age cut-offs which are close to being unethical.	
	4	Please see earlier comments about smoking as a risk factor. I am confused that WHO and other data on this is ignored.	
	8	I think this will need earlier review in the light of impending WHO fracture risk algorithm and the need to include new drugs such as ibandronate.	

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NHS Professional 33	1	These recommendations appear to be a selective interpretation of the evidence base, stratified to fulfil the requirements of a preselected economic goal. It does not really consider the results of the relevent clinical trials in their entirerity for effectiveness.For example, I know of no trial evidence where patients were specifically entered for treatment on risedronate with a T- score of -3, or -4 for strontium.I am not clear that there is an evidence base only for treating patients from age 75 i.e. that there is no evidence of clinical effectiveness under this age. Restrictive mention of femoral neck only diagnosis of osteoporosis condems spinal osteoporosis patients to no treatment and anyway clinical practice uses total hip and not femoral neck for hip assessment. This is a flawed, bizarre, economically biased document which would result in unnecessary suffering and reduced life expectancy in many individual people who will be deprived of clinically proven treatments.	
NHS Professional 34	4	Cost effectiveness appears to have taken precedence over clinical effectiveness	
NHS Professional 35	1	Etidronate is a less effective and often poorly tolerated treatment and should not be recommended purely on economic grounds. The administration requirements for risedronate are very similar to those for alendronate and still need to be adhered to if the medication is to be effective. There are no recommendations for primary prevention for patients with low bone density and multiple risk factors before the age of 75. This means that there will be no attempt to reduce fracture risk below this age, unless the patient has already fractured, usually indicating a loss of bone mass of 30% or more. This is very retrogressive medicine.	
	2	Would it not be more sensible to await the WHO algorithm and suggest 10 year fracture risk treatment thresholds on the basis of this? There will be a tremendous amount of confusion between the two documents, especially if PCTs are taking over the management of most osteoporosis.	
	3	The calcium carbonate component of Didronel PMO is often poorly tolerated, and thus coprescription of a different calcium compound is given, increasing cost.	
	6	This guidance should be provisional, and when the WHO algorithm is published, the advice on primary prevention should be reevaluated.	
Other 1	1	I am completely opposed to the proposals that women under the age of 75 should no longer be entitled to these important drugs. If implemented, they would deny women vital drugs which could prevent the agony of broken bones. These proposed rules make no sense to anyone who believes that prevention is better than cure not only in terms of cost, but in terms of	

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		what is best for the patient. If these recommendations are accepted, who knows how many women could be forced to endure the pain and suffering of broken bones. Osteoporosis should be treated in precisely the same way as other diseases and medical conditions where those at risk should be entitled to preventative treatment. I would also like to echo the words of the National Osteoporosis Society in condemning these proposed changes. I am grateful to you for taking the time to read my comments. I sincerely hope you will take my views and those of my constituents on board.	
Other 2	1	I feel that 75, as recommended, is too late to intervene. Most of the members of my support group are younger than that and would all have suffered severely if they had not received treatment.	
	2	ALL GPs should be made aware of the risk factors and should be routinely checking patients. They should be able to act on this information WHATEVER the age of the patient.	
	3	I am interested to see the relative costs of the various medications. Taken in context with the cost of a hip fracture, for instance, prevention is ccertainly the cheaper option.	
	4	I have read all of the above with interest.But I am still puzzled by the emphasis on age, 75,which is a very great age to be making interventions. Imagine if cholestorol was never tested until 75 the impact would be enormous.It seems that except in extreme cases osteoporosis is to be swept under the table when the reality is that it has a devastating effect on the every day life of millions of people.It seems that you are keeping the treatment period as short as possible for cost reasons.I see money being spent,for instance, on same sex couples being allowed IVF,which is not a matter of life and death, when other conditions such as osteoporosis appear to be rationed.	
	5	Whatever the implemetation of this report nothing has been said about education. We have, growing up, a generation of fat, badly fed,food ignorant children.Some of their parents have no idea what is in their food and what it can, or can"t do for you.Nutrition appears to be appearing on the national curriculum it should be mandatory that heart and bone health be included.	
	6	Research is essential. I have often wondered, after more than 10 years of treatment what sort of bone I actually have.It would also be good if research could be carried out on PRE menopausal women with osteoporosis.	
	7	Can the ""Related Guidance"" please be in PLAIN English. This document	

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		has been very difficult to read. If you are inviting Joe Public to comment it must be written in Joe Public English.	
Other 3	1	Thank you for giving me an opportunity to comment on this HTA as an invited clinical expert for NICE. Of all the guidance documents by NICE this one is the most complex and difficult one to implement. There are inconsistencies in the guidance, some not robustly evidence based, making implementation for both practitioner and patient almost impossible leaving a huge unmet need, if because of confusion in interpretation or mis-interpretation, patients do not get appropriate prevention and treatment. One can see that the dilemmas faced when compounding cost and clinical effectiveness. Choosing a cut-off at 20,000 per QALY seriously undervalues osteoporosis which has a great impact on morbidity and mortality but also healthcare costs of the nation. I would urge the committee to reformat its recommendations and I would suggest taking into account the following: Bisphosphonates are recommended for the primary prevention of osteoporotic fragility fractures in women aged 75 years or older, who are identified as having one or more clinical risk factors (see section 1.6) and confirmed as having a T-score of -2.5 SD or below. When the decision has been made to initiate treatment, drug choice should be prescribed on the basis of the lowest acquisition cost. This is an important point to clarify since some formulations (weekly vs daily) of the same drug, have different costs. Having a differential T-score for choice of bisphosphonate is unnecessarily complex and dangerous for a patient intolerant of alendronate who will not be eligible for risedronate until attaining a lower T-score. This differential rating for bisphosphonates should be removed. The same applies for strontium, if it is an alternative for patients intolerant to bisphosphonates. However, the recommendation could stand, based on cost-effectiveness, if there is a need to use this drug first line for other reasons. Raloxifene may be only drug left for patients with severe osteoporosis intolerant to bisphosphonates and strontium or who cannot cope with the prescribed fast before and after taking the drugs recommended in 1.1, 1.3 and 1.4. Without this alternative, such patients would go untreated, yet there is data that using raloxifene is effective in this age group even without taking into account its benefits on breast cancer prevention. Of high importance made even more evident by its absence is any recommendation for women less than 75 years. The committee will have to make a statement or give guidance for this age group who despite clinical needs, will go untreated.	
	4	Evidence for etidronate is weak for prevention of hip fractures compared to the other bisphosphonates considered in the HTA. Therefore inclusion	

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		in this HTA is inconsistent unless it is only because of its lowest acquisition costs. This drug is well known for poor compliance and its method of administration with long per and post prandial precautions make it a cruel choice to prescribe to patients.	
	6	A software package for desk-top computers working out 5-10 fracture risk scores, would be a welcome development in the management of this disease	
	7	Intravenous bisphosphonates and novel new agents such as the biologics for osteoporosis treatments will need to be assessed in a HTA by NICE	
Patient 1	1.1	on what basis has the age 75 been chosen? There seems to be no mention made of choosing the best treatment for a person, regardless of age or effectiveness, merely the cheapest - ""it should be prescribed on the basis of the lowest acquisition cost""	
	4	Whilst much of this is too technical for a lay person like myself the overall emphasis seems to be on the cost of treatment - was there anywhere that the cost of treating a single fracture was put into the equation, let alone a hip fracture with its resulting high costs of hospital stay, physiotherapy etc. Quality of life doesn"t seem to come into it anywhere. Having had treatment for the past 18 months (I was found because I am high risk, I have never had a fracture) my bone density has increased. Under your new proposals I wouldn"t receive treatment for another 18 years by which time it would be so advanced that you would be condemning me to a life of pain.	
Patient 2		With a strong family history of osteoporosis, and having gone through a relatively early menopause, I had a bone density scan in April 2005 and was diagnosed with oesteopenia in my spine at the age of 50. Since diagnosis I have been taking alendronic acid in the firm belief that this will help to prevent the symptoms of osteoporosis that my 77 year old mother is now experiencing. She was only diagnosed three years ago when the osteoporosis in her spine was already apparent: she is at least 3 - 4 inches shorter in height and already has a very curved back. My maternal grandmother, who died in her 80s, could no longer lift her head from where it rested on her chest, so I am in no doubt as to how my currently treated osteopenia will develop if I am denied access to alendronic acid. I urge you to reconsider your recommendation and give women under 75 who face the consequences of osteoporosis the best possible opportunity for a more positive outcome to this crippling disease.	
Patient 3	1	I am concerned because I want to prevent a hip fracture, not have to wait until I get a fracture before I can get effective treatment. Waiting until age	

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		75 seems a long way off when so many women get fractures in their 50s. The risk factors in 1.6 seem to have omitted things such as hypogonadism, which I have.	
	2	I agree that the prediction of actual fracture does not depend on bone density alone. But nevertheless it is a factor.	
	3	I have taken two forms of bisphosphonate and find the weekly alendronic acid a lot easier to deal with than the quarterly cycle of etidronate. Taking the alendronic acid ealry on Saturday morning with plenty of water, fasting for an hour whilst I read or catch up on eamils is not complicated or onerous. And if I forget Saturday, then there is Sunday... These drugs seem very cheap compared with the costs of painkillers and after care of hip fractures.	
	4	I am always astonished at the number of people who discontinue treatment early. I"ve been on continuous treatment now for over 10 years and intend to continue as long as possible becasue I"m doing everything I possibly can to avoid disabling fractures. i eat well, I stay active, and I take my medicines. I"m also aware that I"m a lab rat. There is little evidence of the long term effect of bisphosphonates of the quality of bone. I know that fracture depends on brittleness, not just density. I"m doing what I can to maintain density, but I suspect that there is little more that I can do to avoid brittleness - that seems to be a factor of age. But it makes sense to me that maintaining density, even with poor quality bone gives one a fighting chance of fending off fractures as long as possible. I wish to continue treatment, not lose it for another 15 years.	
	6	I agree that far mor research is necessary. I"ve already highlighted my concerns about quality of bone and long term effects. But I"m a willing lab rat. I"ve weighed up the personal pros and cons and wish to continue treatment until it is proved that my long term treatment would acutally increase the risk of disabling fractures and not reduce the risk.	
	7	I look forward to reading these. Especially 7.2 which seems to include people (men and women) like myself with pre-disposing medical conditions	
Patient 4	1	The proposal to restrict strontium ranelate to women aged 75 years or older will leave patients like myself,aged 55 & intolerant to other treatments, with NO treatment options at all. What is the point of the medical profession advising us to have tests & identify low bone density before it causes a fracture, if you then want us to wait until the damage is done before making treatment available? The choice of age 75 seems quite arbitrary if only applied to strontium ranelate or it is just a question of	

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		cost? Surely the NHS should be aiming first for preventation of problems, rather than letting us break bones to prove that we need treatment.	
Patient 5	1	I am a ""youngish"" 58 year old woman with Osteoporosis. I do not feel that NICE has come to the best decision, regarding the prescription of drugs to women under 75 years of age. The sole cause of my Osteoporosis is a genetic disposition. I have always had a good diet and taken plenty of load bearing exercise. I have had 3 fractures and since taking Alendronate I have had no fractures for at least 2 years. There are a lot of women who also have a genetic disposition who have not had the ""good fortune"" to break a bone and have the disease diagnosed. The cost to the NHS and the country in dealing with fractures, loss of work time and care of the elderly, who have become disabled due to fractures, would be vastly reduced, if preventative drug treatment was allowed in both primary and secondary cases.	
Patient 6	1	I have a T score of -2.5 and I am only 59	
	3	I take strontium ranelate and my spine is still bending	
Patient 7		I was diagnosed with osteoporosis three years ago when I was 61, despite having a healthy lifestyle including daily walks, teaching Yoga and taking calcium/magnesium supplements (not then paid for by the NHS, but funded by myself.) Since then I have been on weekly Alendronic Acid 70mg tablets. I have continued to teach Yoga without problems. If I was denied treatment I would become more vulnerable to fracture and pain and would not risk teaching. That would deny the Chancellor about 4,000 a year of tax - much more than the 300 you would save on my treatment. How much sense does that make? And what if I fracture my hip? How much is a stay in hospsital going to cost? Economically this is short sighted and stupid - and does not take into account the pain and resulting lowered waulity of life a fracture would cause. Is prevention not better than waiting for problems to happen? Apart from time out when my children were young I have worked from 17 until 60 - and am still working. The only other regular medication I take is an inhaler for mild asthma. I have not been a burden on the NHS but a contributor financially for nearly 40 years. I think my health and peace of mind are worth 300 a year.	
	1	You ignore women under 75 who have some of the risk factors above. I have osteoporosis in the lower spine and hips although I am only 64. I was diagnosed at 61. I also have a low body mass index - 20 - despite eating very well. I am also on inhaled steroids for asthma. Where does than leave me - floating in painful limbo?	

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	2	You list a huge number of potential problems (see 2.11) but appear not to acknowledge that these can exist before the age of 75?	
	3	I am on Alendronate once weekly, have followed the guidelines safely and have had no side effects. You talk a great deal about cost, but do not compare those for medication with the cost of a stay in hospital and an operation if a fracture occurs. Pain and quality of life are also completely disregarded.	
	4	I have asked for Calcium/D tablets from my doctor as I know a combination is mor effective but I continue to receive Calcium only. I supplement myself with Vitamin D and also take magnesium. Magnesium"s role in helping the absorption of calcium seems to have been ignored. You talk about a ""non significant 15% reduction in hip fracture,"" 4.3.3. Considering the numners of women involved this is hardly insignificant.	
	5	If women with already established osteoporosis were denied medical assistance until they were 75 it would be a national scandal.	
	6	I would take this for granted.	
	7	Fine but until this has been done and until an improved drug has been developed continue to provide what to date is available to all women at risk.	
	8	Difficult to comment	
Patient 8	4	I am an osteopenic woman of 49 whose BMD has been assessed as part of my treatment at the Royal Brompton Hospital for difficult asthma. I and other female (and male) patients at this hospital have received BMD preventive screening since it became available. This is because of our long-term steroid use. Thus 4.3.8 above is not the case in women like me - we ARE screened before fracture.	
	7	I am concerned that as a pre-menopausal osteopenic woman the guidance for use in pre-and post-menopausal women with proven low BMD should be consistent and should recommend the use of preventive proven treatments for this group, including those who have had long-term steroid use.	
Patient 9		This is a copy of my recent email to the National Osteoporosis Society. ********** I have just quickly read the latest recommendations made by NICE (such an inappropriate name) regarding women under 75 being denied drug treatment until they break a bone,with a sinking heart. At the grand age of 50, I am in the strange position of being a woman who had an early	

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		menopause when I was 14. My risks regarding osteoporosis were not mentioned or investigated until 1992, when I was 36 , & then the only treatment I was offered when a DEXA scan showed up bone problems, was the dreaded HRT. For many & varied reasons I resisted this drug, but really had no choice & so reluctantly took it in various forms, & just about survived the experience, for 8 years. Then, when I was almost at an emotional breaking point, my wonderful GP prescribed Didronell, followed a few years later by Alendronate. Two years ago I was referred back to my Consultant & had another Dexa scan, & was told I had osteopaenia, not osteoporosis. I am still not sure what the original diagnosis was with regard to my T-score, though I was told I had osteoporosis, but all the years of various treatments did have a beneficial effect on my bones. I was advised to stop Allendronate in 2005 to see what would happen without drugs, I had another bone scan in early 2006, & will have a further scan in December 2007 when, according to my Consultant, he will discuss if further drug treatment would be appropriate, obviously depending on the scan results. The results of the last scan did not show much deterioration. This latest missive from NICE seems to leave patients like me in a strange position, & whilst I admit I am very fortunate that my bones are stronger than you would think, given my medical history, I am obviously concerned that another year without drug treatment could show up a severe deterioration in bone density. If this was the case, from what I understand of the NICE report, I would have to break something to get drug treatment, if needed. Perhaps I had better hope for a bad winter & a fall on an icy pavement? It is all very confusing & worrying. Whilst I agree that taking drugs for my bones over along period is probably not wise, as no one really knows if there would be long term effects considering my age, surely prevention is better than breaking a bone? Sometimes the medical world, or rather that part of it dictated to by NICE, is crazy.	
Patient 10	1	There is no mention of the bisphosphonate, Ibandronic acid (Bonviva). Is this also to be included in the appraisal?	
	2	There are post menopausal women under the age of 75 currently receiving preventative treatment. Clarification is needed as to whether this will continue if the recommendations are implemented.	
	3	There is no mention of Ibandronic acid.	
	6.5	Does this study include post-menopausal women who have had a TAH & BSO, have a strong family history of Osteoporosis and in whom Dexa scans show progession of bone loss despite HRT and adequate levels of calcium and Vitamin D?	

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	7.3	Will the use of Ibandronic acid be included in this guidance?	
Patient 11	1	I do not understand the relevance of the 75 year age limit. This denies treatment to younger people who have the chance of living a better life if drug treatment is prescribed earlier rather than later. Could this be regarded as ageist?	
	2	The 1.1 million sufferers does not tie up with the NOS figure of 1 in3 women who will become osteoporotic. Prevention at osteopenic stage is better to prevent future more drastci and costly treatment.	
	3	Difficult to comment on the technology as a lay person.As long as the treatment works it should be prescribed.	
	4	A long complex section. The NOS is best placed to comment but as a sufferer I have to say that primary prevention is paramount, natinal screening should be the norm and just giving treatment to women over 75 can never be justified.	
	6	Further research is always to be recommended	
	7	Secondary prevention should be exactly that - secondary. Primary prevention should be where everything is focused so that future secondary prevention necomes unncecssary.	
	8	Let"s hope that by March 2009, prescribing of drugs for all treateble illnesses and diseases is no longer governed by cost but by necessity to maintain good quality of life for all.	
Patient 12	1	I write to express my concern at the recent announcement recommending that women under 75 years should not receive any drug treatment to prevent broken bones due to Osteoporosis. I am 59 and was diagnosed with Osteoporosis in both hips. This diagnosis was the result of a DEXA scan recommended by my GP because I had broken my wrist after a minor fall. The T. Score of my scan was -2.6, which means that my bone density is just below the deciding figure of -2.5. Having survived the shock of being told I had Osteoporosis, I felt I could see a light at the end of the tunnel because with treatment I would be able to prevent my bone density from decreasing further and could look forward to many years of active life. Since reading the article produced by NICE, I have had time to absorb the consequences of their proposal. I am angry and horrified at the short-sighted and pompous attitude of a group of people who are able to decide whether or not I, and thousands of men and women like me, are entitled to receive treatment to prevent broken bones and the resulting pain and incapacity that results from these fractures, but also that	
Patient 13	5	I am dismayed to read this report which seems blinkered in its approach.	

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		Having set out in detail the costs of the various drugs there is no mention of the counterbalancing costs of treating extra fractures if these drugs are not available. As a statistician I would have expected at least a stab at this with the appropriate caveats. Presumably most of this just comes down to funding.	
	6	More research is vital. It appears that the NHS is weighed down by its success in the identification of osteoporosis. No-one likes being on medication so reserch into the post cessation benefits would contribute towards keeping costs to an acceptable level.	
	8	There should be a caveat to bring forward reviews if relevant and vital research reports become available.	
Patient 14		I am genetically "at risk" of osteoporosis. Now aged 63. Low bone density diagnosed in 1993. Father - diagnosed at age 66, died other causes 67; mother - diagnosed similar age, spine collapsed by age 70, broke hip 3 times, died in distress and pain aged 75; father"s sister - diagnosed age 65, subsequently broke hip and died shortly after, aged 67. I have been receiving DXA scans once every three years until this year, when I have been refused a scan "under the Health Authority guidance for NHS scans". Is it really cheaper to replace broken joints than take preventive action? Of course not. Prevention is better (and cheaper) than cure.	
	1	75 is too late. Early diagnosis and early preventive treatment saves costly (in terms of both human suffering and cost to the NHS0 joint replacement later.	
	2	I am in the high risk category, but have just been refused a DXA scan for the first time in 10 years. (Now aged 63). I was diagnosed with genetically low bone density at age 50, father & mother both osteoporotic by mid-60s, father died (other causes) at 67, mother - spine collapsed, broke hip three times, ended days in pain and distress at 75, father"s sister, diagnosed at 65, broke hip and died shortly after aged 67.	
	3	These costs need to be set against the cost of joint replacement and hospitalisation.	
	4	If high risk patients are refused monitoring, levels of vit D/calcium cannot be monitored either. Do we need a new approach to monitoring, rather than a complete withdrawal of all monitoring for under 75s?	
Patient 15	1	I am currently taking actonel (risedronate) 35mcg once a week. I am 58 and have not had a fracture but I have been diagnosed with osteopaenia of the hip and osteoporosis of the spine. my spine tscore i s-3.3. I would like to know your reasons for suggesting this be stopped. Do you believe	

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		the drug to be harmful in some way?	
	4	This is extremely difficult for a patient to understand but as far as I can see there is"robust evidence" to support the use of risedronate in my case. I have a spine t score of -3.3.	
Patient 16	1	I think treatment of osteoporosis should start at a much younger age than 75 years to prevent fractures.	
	2	Since osteoporosis is a progressive disease, it is important to start therapy as soon as it is diagnosed to halt its progression.	
	3	The prices for these medications seem very reasonable, especially when compared to the cost of treatment for possible fractures.	
	4	As someone who first showed evidence of low bone density at age 46, I was prescribed HRT to prevent osteoporosis. Eight years later I broke my wrist. At age 62, after mentioning to my gynaecologist that my sister had severe osteoporosis, I was sent for my first bone density scan, diagnosed with osteoporosis, and have been on medication ever since. I took alendronate for seven years and then risedronate for one year. My doctor prescribed strontium ranelate as soon as it became available and I took it for nearly a year; my T score improved, but I had to give it up because it caused acute eczema. I have now been taking ibandronic acid (Bonviva) for nearly one year and am scheduled to see my doctor in December with a new bone density scan. I feel that at 71 years of age, my good health and excellent quality of life are due to continued treatment for my osteoporosis. My older sister, at age 74, now has five vertebral fractures, a broken femur, has lost 5 inches in height, and has surgery scheduled for a rod to be put in her other fractured femur this week. She has a much reduced quality of life and no longer is able to travel for a vacation.	
Patient 17		I am 68 and have taken alendronate for 4 years and risedronate for 2 since being diagnosed with severe osteoporosis. I have not had a fracture. These bisphosphonates have enabled me to maintain my bone density and I hope will continue to do so. Fractures cost the NHS far more than these drugs, and will be more frequent of those with low bone density are deprived of the appropriate drugs. The effect will not only be on hospitals but on community care for those with broken bones who cannot manage simple tasks at home.It will be a false economy to limit them to those over 75.	
	1	I am 68 and have taken alendronate for 4 years and now risedronate. My T-score is below -3. I have not had a fracture. €Restricting use of these drugs to those over 75 will result in more fractures, which are said to be very expensive both for hospitals and for the community care needed. To	

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		say nothing of the socail impact on people"s lives.I feel it would be very much a false economy, indeed no economy at all, to limit these drugs to the over 75s,	
Patient 18	1	This preliminary recommendation can be restated "If you are a postmenopausal woman under 75 you cannot have a DXA scan or osteoporosis treatment until you sustain a fragility fracture, whatever your pain or risk factors (other than prolonged corticosteroid treatment.) Does this really justify the term "primary prevention"? How can it be acceptable to postmenopausal women under 75 who know they have multiple risk factors, who already have a poor quality of life because of these, are struggling to maintain some independence and know that a fracture will have a devastating effect of their quality of life and ability to cope?	
	2	Why produce these guidelines in advance of the WHO algorithm? Either the risk factors used in the NICE models are suppositional and unreliable, or there is no need for the algorithm that is being produced under WHO auspices.	
	4	Do the models take into account that women who know themselves to have multiple risk factors in addition to osteoporosis as defined by T-score are much more highly motivated to persist with medication? Do the models provide a realistic assessment of QoL effects when fracture interacts strongly and negatively with other risk factors which themselves reduce QoL - the straw that breaks the camels back? The same question applies to NHS costs (eg increases in GP consultations compared to the norm for fracture cases in that age range, treatment for depression etc)and also need for social services support.	
Patient 19	1	I can find no reference to women under 75. I was born in 1935 and had a bone density scan in October 2002, following a compound fracture of the wrist resulting from a low-impact fall. My T-score was -3.1. Would I under the proposed rules have received no treatment had I had a scan showing a T-score of -3.1 before breaking my wrist? I take alendronic acid. My latest T-score (Aug 2006) was -2.9.	
	2	Interesting. It seems to confirm that treatment should be provided as soon as there is evidence of osteoporosis.	
	4	Patients under 70 don"t even get a mention. And those between 70 and 75 are apparently to be denied treatment, even though it is shown to be effective.	
	6	There certainly needs to be research into possible side effects as against continued benefits from continued treatment. Para 6.5 (need to identify women at high risk) seems to fly in the face of earlier recommendations to	

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		do nothing for women aged under 75.	
	8	I hope that the review of the decision not to treat patients under 75 who have not suffered a fracture will be reviewed before March 2009.	
Patient 20	1	My Mother has had 4 vertebral fractures, 2 broken wrists and a broken humerus. She was not diagnosed with Osteoporosis until it was too late to treat her. The suffering my Mother has endured has been severe and could so easily have been prevented by drug intervention at an early stage. I have now been diagnosed with Osteoporosis and will not be included in preventative treatment as I am only 58 years old despite suffering a fractured humerus in the past 4 years. Not a happy future to look forward to!	
Patient 21	1	I suffer from osteoporosis experiancing the trauma and indignity of a hip fracture at 52 I had an early menopause As a result of the hip fracture: 1) I could not follow my previous employment - working with young children 2) I had to have a private full hip operation the pin from the NHS emergency operation was wearing into my pelvis due to the osteoporosis 3) I have had to employ a home help 4) My whole life has been adversely affected there are many limitations now and constant fear that I may fracture again As a result of the above I have studied information from: The WHO The NOA The IOF The NOS AND all agree that until there is an accurate method of detecting those at risk prevention is the best course of action If the ACD becomes guidelines then hundreds of thousands of women will suffer the trauma and indignity that I did, and even an early death Not only is the personal cost high, but the financial cost to the country of a no preventative treatment policy, will in the near future cripple the NHS and our children	
Patient 22	1	Patients should be able to have medication even if they are under 75 years old.FOR PREVENTION OF further bone density loss, improvement of quality of life & to avoid a possible fracture, which is more costly than the cost of drugs. Hosp admission & after care.	
	2	With any op there is a risk of mortality. With a hip replacement there is also a risk that the patient will be not as fit or active as previously. So the quality of life is an issue as well as the expence of physios, social workers,home helps & adjustments & aids in the home.	
	3	The correct medication needs to be prescribed for each individual, taking into account their other medical problems & medications.	
	4	My interpretation is that it is economically viable to provide medication to all patients with osteoporosis to prevent fractures, to maintain or improve	

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		quality of life & in the long run to save money. Preventative medication.	
	6	NICE have a massive task in assessing various drugs & their costs & they are under pressure to be quick. The press also report about NICE.	
	8	Whatever NICE publish will be helpful.	
Patient 23	1	During 1995, at the age of 62, an aunt of mine suffered two collapsed vertebrae and a fractured hip. I asked my GP if at the age of 52 I could be at risk and, following a DXA scan, was diagnosed with severe osteopenia in 1996. I was prescribed daily Fosamax and my scan a year later showed improvement in bone density. However the Fosamax caused problems with my oesophagus and I stopped taking it, continuing only with HRT and calcium tablets. No longer able to take HRT I have recently been prescribed a monthly bisphosphonate. In the intervening years I have not suffered a fracture. However in the same period since 1995 another of my aunts, only one year older than I am, took no action to discover if she too had low bone density. Now, aged 64, she has just broken her hip and her wrist at the same time. Surely the foresight of my GP in sending me for a scan and prescribing a bisphosphonate has saved me the pain and discomfort of broken bones and the NHS the costs of repairing fractures and hospitalising yet another patient. Why should age come into it?	
Patient 24	4	I am 62. In 2000 I was identified as at rist of osteoporosis as I had a low body mass measurement. A DXA scan gave me a spine T-score of -3.31. I was prescribed Raloxifene and took it continually until my next scan in 2003. This gave me a spine T-score of -3.4. My GP changed my medication to a Bisphosphonate - Alendronate and I have been taking it regularly ever since. In 2005 a further scan gave me spine T-score of -3.1 and the hospital report stated ""a statistically significant increase can be seen in the spine BMD since the previous measurement"". If I were no longer able to have Alendronate prescribed for me I consider I would be adversely affected and my risk of fracture is likely to increase significantly.	
Patient 25	4.3.28	coeliacs need more calcium and Vitamin D than non-coeliacs (includes male coeliacs)	
Patient 26	1	I wish to object in the strongest terms at your recommendation to prohibit patients under 70 from receiving the medication Raloxifene. I was absolutely horrified to learn of your intentions as, at the age of just 46, I was diagnosed 2 years ago with osteoporosis and prescribed raloxifene to take, on an ongoing basis. I had suffered back pain since 2000 and had requested a bone density scan to rule out (as I then thought) any osteoporotic problems. I was subsequently shocked to learn of the	

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		diagnosis, with thinning of the bone in particular on one of my hips. My GP had intended to do a scan anyway when I reached the age of 50 as I had had a very early menopause at age 41 and this was a very high risk factor for developing osteoporosis, as my scan subsequently proved. I notice that all your documentation on primary prevention and raloxifene makes no provision whatsoever for younger people who have had an early menopause, and are therefore at high risk from developing osteoporosis - and at an early age. My GP prescribed raloxifene for me with great confidence saying that ""we know it works"", and I was therefore extremely relieved that there was something I could take.	
	3	It costs the NHS 5million a day to treat fractures, but just 83p a day to prescribe Raloxifene. Raloxifene also has the additional benefits of lowering LDL cholesterol and preventing breast cancer. The treatment of heart problems and breast cancer also cost the NHS millions every year.	
	4	You take no account of the fact that many younger women have an early menopause (such as myself at 46, which triggers a dramatic lowering of oestrogen causing bone thinning. My mother aged 84 had an early menopause as well, at age 40, and has now fractured her wrist and has been put on medication for osteoporosis, so now I am in an even higher risk category in that I have a family history of it.	
	5	Your intentions make no financial sense at all. It costs the NHS 5million a year to treat fractures, not to mention the cost of heart problems and breast cancer which raloxifene also helps to prevent. I will be writing to my MP about your scandalous proposals regarding raloxifene, and I urge you in the strongest terms possible to continue the prescribing of this medication to people under the age of 70, and particularly to younger people (like myself) who have had an early menopause and who have osteoporosis already in the family. (My mother also had an early menopause at age 40, and now has the pain and distress of a fractured wrist due to osteoporosis, and has only now been put on medication for it.	
Patient 27	1	Many postmenopausal women under 75 are Carers. As with annual influenza vaccination, GPs should be permitted to excercise their discretion in providing protection for people who have a key role as Carer.	
Patient 28	1	I think it will be a negative step in stopping women under 75 years old to have the present prophylaxis treatment. Women deserve to have a better quality of life before 75 and will soon be expected to work until 65.	
	3	This proposal is not cost effective as the cost of once weekly Alendroate is 279.21 and I know the cost of a fracture would be a lot more to the NHS.	
	4	I understand that there must be evidence against improvement of bone	

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		density but must admit that my bone density has improved with biphosphonates	
	6	Since HRT has more or less been discontinued I think in the research consideration should be given for alternative therapies for osteoporosis	
Patient 29		I am saddened by the proposals to limit the use of risedronate to patients over the age of 75 or to those who have broken bones. My diagnosis was made ten years ago, when I was aged 55. The medication has prevented further deterioration in my bones and I wish to remain in good bone strength and not be debilitated by broken bones. It is beyond my understanding that for the cost of the drug it would be preferred by NICE that people should be put through the pain and EXPENSE of being treated in hospitals for broken bones. WHERE IS PREVENTATIVE MEDICINE IN ALL THIS.	
Private Sector 1	4	Primary prevention of osteoporosis and fracture in an at risk population, it is clear that only 1200mg of elemental calcium and 800 IU vitamin D have shown cost effective benefit. The only study to demonstrate hip fracture reduction was in the reporting of a 18/36 month reporting of the trial by Chapuy et al. N ENGL J MED. Vitamin D3 and Calcium to prevent hip fracture in elderly women. 1992; 327:1637-1642. Chapuy et al. Effect of calcium and cholecalciferol treatment for three years on hip fractures in elderly women. BMJ 1994; 308:1081-1082. The effects were reproduced in combination tablets -Chapuy et al. Osteoporo Int 2002 Mar;13(3):257-64. Combined calcium and vitamin D3 supplementation in elderly women: confirmation of reversal of secondary hyperparathyroidism and hip fracture risk: the Decalyos II study. Cost effectiveness is clear for this intervetion - Lilliu et al. Calcium-vitamin D3 supplementation is cost-effective in hip fractures prevention. Maturitas. 2003 Apr 25;44(4):299-305. When examining a strategy for primary prevention the most cost effective outcome is elemental calcium 1200mg/800 IU vitamin D. 1000mg does not shown this effect	
Private Sector 2	1	I agree that use of alendronate for prevention should be limited to age 75 or older. I personally was diagnosed at age 47 with PRE-menopausal osteoporosis by bone scan and took alendronate for 3 years. Now I have persistent chronic gastritis and moderately severe joint pain causally related to that treatment. I wish that my physician had been more conservative.	
	4	More information on the efficacy evidence for calcium & vitamin D and exercise should be included and this should be encouraged as the first treatment option for women less than 75 years of age.	

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Private Sector 3	1	We would like to see the data showing that the efficacy outweighs the gastrointestinal problems that can develop with the bisphosphonates. Parental history of hip fracture seems very general; much depends on lifestyle of children.	
	2	Will you be providing data sources for your statements for lifetime risks? Can you provide a number instead of saying ""a high proportion of women are permanently unable to walk""?	
	2.11	Can you add ""lack of weight-bearing excercise""?	
	3	Are you sure that GI side effects are limited to only those with abnormalities?	
	4	Please provide absolute risk as well as relative risk. Would you consider dividing fractures into cortical vs. trabecular which is more in line with the structure and provides a better idea of risk/benefit? The FDA Medical Officer reviewing bisphosphosphonate use urged this. You don"t mention the osteosarcoma risk with teriparatide	
	4.1.5.6	Industry data on adverse events can be very misleading; many AEs have been reported to FDA where women took the drug correctly and still had serious GI problems.	
	4.1.5.8	This has not been reproduced and should not be cited.	
	4.1.7.3/4	are contradictory statements	
	4.1.10.2	Should provide absolute risk. Cost Effectiveness: Why should you use the manufacturers" models when they are bound to be biased?	
	4.3.6	There should be more information as to the relatively small contribution of BMD to fracture risk; it is estimated as accounting for about 20% of fracture risk.	
	6.2	Add to the benefits ""and risks"" of the drug . . .	
Public 1		Many of my relatives have developed osteoporosis and I myself am pre-menopausal and at relatively strong risk of developing it, as are my children. My husband actually has osteoporosis and has been taking weekly Fosamax (alendronate) for several years.	
	4	How are these ICERs calculated? What factors have been taken into account - just fractures, or all aspects of the way osteoporosis degrades quality of life? My grandmother"s life from the age of 50 onwards was severely impacted by osteoporosis. She became totally immobile, was bent almost double with her ""dowager"s hump"", and suffered immense pain. But she didn"t get an actual fracture until she was 78, mostly because she couldn"t do anything! Your committee appears to be	

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		suggesting that someone in similar circumstances now would be denied treatment for 25 years. Thankfully I now live abroad, and can afford to pay privately for the relatively low costs of DXA scans (UKP300), and, if necessary, drugs (UKP800 per annum for my husband"s alendronate). But my children may return to the UK, and I am concerned that treatment that they may need will be witheld from them through a spurious economic argument. PS I have a degree in economics and am a chartered accountant with NHS experience - so I know just how dubious the figures are that support this sort of thing.	
Public 2	1	The ACD is an insult to all those who appreciate the importance of preventing the disease. NICE has taken almost 5yrs to present this ACD, and has completely ignored all international opinion on primary prevention. The remit should not have been given to NICE. NICE should have recognised that the remit is beyond its level of competency NICE must be abolished to prevent the continuous crises that it is generating in patients and clinicians. The advancement of medical treatment and policies suffers as the result of such ACDs. Politicians will be made to listen to the public, and realise that medical advancement comes, as it used to,by employing a free-market environment and not by imposition The concept of NICE has been tried. It has failed. Political strength must now be invoked to terminate NICE	
Public 3	2	I am responding to the recent NICE Appraisal Consultation Documents on the Primary and Seconday Prevention of Osteoporotic Fragility Fracture in Postmenopausal Women. I would like to draw attention to the situation in North Somerset concerning the lack of provision of a DXA scanner. The NOS recommend 1000 scans/100,000 population. Given the requirements in North Somerset there is a need for 1,900 DXA scans per year. The government recommendation is even higher at 2,527 DXA scans per year. At present the consultants at Weston General Hospital are funded for 100 scans per year. Patients have to travel to Bristol in order to have a scan. This is not an easy option for elderly people.	
	5	As a result of this very poor provision for DXA scanning in North Somerset and no formal provision of a protocol for general practice, there is a lot of unfocused prescribing of bisphosphanates, estimated at 354K per year. This is not only money very poorly spent but this particular medication is frequently intolerated and can result in serious digestive problems. My own experience has been intolerance of both Cyclical Editronate and Alendronate, resulting in long term dependence on Lansoprazole and I am now being investigated for abnormal liver enzymes, possibly caused by the Lansoprazole.. I am therefore stongly motivated to make this protest	

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		against unnecessary prescribing of bisphosphonates	
	7	Additionally in the absence of adequate DXA scanner provision, neither progress or deterioration of the disease can be monitored. This is certainly not the case with other diseases. The government has made provision for DXA scanners where at present none exist but so far the North Somerset Primary Care Trust has resolutely refused to provide adequate DXA scanner provision and the money allocated by the Department of Health to the SW Strategic Health Authority for this purpose, sits unused. I hope these comments will prove useful.	
	1	Drug therapy for the primary prevention of osteoporotic fragility fractures will be available to women aged 75 years or older: Whilst I can understand the cost implications for the NHS of no age limitations it is still unreasonable to allow younger patients no access to drug therapy. Practitioners will be both guided and constrained by these recommendations please reconsider.	
Voluntary Worker	2	I agree that all of the current research suggests age (older) is a determining factor in the risks associated with osteoporosis, but it should not be a constraining factor.	
	3	Greater considerion should be given to developing drug therapies which have greater calender duration, i.e 1, 3 or 6 monthly doses.	
	4	The evidence in essence supports the findings of the appraisal in its interpretation of the research. Greater effectiveness is evident in older age groups. This is an accepted fact but it does not support the premise that treatment should be restricted to these age groups.	
	5	An independent review of the findings of any performance review by for example the NOS would support the current NHS position on openess and transperency. Will Northern Ireland have the same reviews carried out, by wwhom and when?	

Summary of comments received from non- consultees and commentators by letter on the Appraisal Consultation Document (ACD) issued in Sept 2006

1 Introduction

This report summarises letters received by the NICE Communications team from individual patients and carers in response to the Appraisal Consultation Document (ACD) on primary prevention of osteoporotic fragility fractures. This document has been prepared for the Technology Appraisal Committee by staff from the Centre for Health Technology Evaluation (CHTE), National Institute for Health and Clinical Excellence (NICE or the Institute).

NICE wish to acknowledge the time and effort that was put into preparing and submitting these comments during the public consultation on the ACD. Much of the letters described personal experiences and reflected their strong feelings on osteoporosis (and osteopenia) and the prevention of fragility fractures. The main recurring themes in submitted letters were identified and are summarised below..

2 Correspondence received

In accordance with the Institute's published process, the ACD was placed on NICE's website for public consultation for a period of 15 working days (from 3 October 2006 up to 20 October 2006). In response to the consultation contributions in form of letters, emails or website comments were received by the Institute. Of these contributions, 17 letters where received and processed via the NICE Communications team.

3 How the Institute dealt with the correspondence

Ccorrespondence received during the consultation period was checked and logged by the NICE Communications team. All correspondents received a letter in return, thanking them for their contribution. Letters, were read and the most frequently occurring (or otherwise deemed important) themes were identified and categorised by a member of CHTE. This overview, describing the main themes, was prepared for consideration by the Technology Appraisal Committee at its meeting on 7 February 2007.

4 Main themes emerging from letters received

Main themes raised in the 17 letters are described below, with an indication of how many of those corresponding raised each issue category.

Theme	Correspondence reference
Concern over withdrawal of treatment for osteoporosis/prevention of fractures for those already receiving treatment.	1; 2; 7; 9; 10; 12
Concern over restricted access to treatment for osteoporosis/prevention of fractures.	3; 5; 6; 8; 16; 17
Concern over thresholds (age, BMD/T score, requirement for prior fracture)/requirement for scans for treatment for osteoporosis/prevention of fractures.	1; 5; 6; 7; 8; 11; 14; 15; 17
Descriptions of lack of efficacy/continued deterioration of BMD/fracture and consequent switching of treatment.	4;13;14;17
Description of intolerance/contraindications to treatment for osteoporosis/prevention of fractures.	3

Theme	Correspondence reference
Comments on impact of avoidable fractures on • mobility/quality of life/'human cost'; • carer(s)/family members; • NHS. – such as hospital stays avoided, by preventing fractures;	1; 3; 7; 9; 10; 12; 15; 16; 17
Prevention better than cure/prevention is cost saving ('false economy').	2; 4; 5; 7; 13; 15; 16; 17
'Reverse' age discrimination	1; 12; 15
Other issues:	
• Need for repeated scanning to evaluate appropriateness of therapy.	1
• Self funded therapy/scanning..	4; 11
• Other effects of osteoporosis are also important (Dowagers hump).	9
• "…generic form will not give the same protection…"	10
• Legal action against NICE in the event of fracture.	12; 15
• "…a less vulnerable group should be targeted."	15
• "… if I lived in Europe or the USA I would get the required medication."	17