National Institute for Health and Clinical Excellence

Multiple Technology Appraisal (MTA)

Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for the treatment of osteoporotic vertebral fractures

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	ArthroCare UK	As an organisation we believe this review is appropriate.	Comment noted.
	British Society of Skeletal Radiologists (BSSR)	This is an appropriate topic. There have been several recent randomised trials addressing this area.	Comment noted.
	Cook Medical	Yes.	Comment noted.
	DePuy Spine / Johnson & Johnson	This MTA attempts to reconcile some complicated questions which surround the optimal use of vertebroplasty and kyphoplasty for the treatment of patients suffering from painful osteoporotic vertebral compression fractures (VCFs). Current evidence may not be conclusive on a number of important considerations. According to the HES data reported by NICE in the draft scope there are a relatively few vertebroplasty procedures performed in England. Using a crude calculation based on the approximate figure of 800 vertebroplasty procedures quoted by NICE in the draft scope multiplied by the basic tariff for these procedures of £2,813 (HRG HC05C) this gives an estimate of the approximate budget impact for	Comments noted.

Section	Consultees	Comments	Action
		England in the region of £2,2 million (2008/2009). This modest budget impact relative to most technology appraisals undertaken by NICE should inform the priority and scope of the proposed appraisal.	
	National Osteoporosis Society	The National Osteoporosis Society feels it is appropriate to refer this topic for appraisal by NICE.	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	It is relevant and timely to review NICE's guidance at this stage as there has been significant new evidence since the previous review.	Comment noted.
	NHS Quality Improvement Scotland (comment from NHS professional 2)	Highly appropriate for appraisal at this time	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 3)	Yes	Comment noted.
	Orthovita	Yes. Especially since the publication of 2 studies in the New England Journal of Medicine in August 2009 there is much confusion regarding the effectiveness of vertebral augmentation, the criteria for patient selection, and the optimal treatment regimen for those who are treated conservatively. The recent publication of guidelines by the American Association of Orthopedic Surgeons has increased	Comments noted.

Section	Consultees	Comments	Action
		the confusion rather than help resolve it.	
	Pain Relief Foundation	Yes	Comment noted.
	Royal College of Physicians	Yes, this topic is appropriate.	Comment noted.
	The Society and College of Radiographers	This is an appropriate area for NICE appraisal.	Comment noted.
Wording	ArthroCare UK	Yes	Comment noted.
	British Society of Skeletal Radiologists (BSSR)	Yes	Comment noted.
	Cook Medical	We agree with the current wording for the remit.	Comment noted.
	DePuy Spine / Johnson & Johnson	The remit should include all pathologic VCFs, including those resulting from benign lesions (e.g.,haemangioma), metastatic lesions, multiple myeloma, and osteoporosis.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	Medtronic	As suggested in the remit the scope should consistently refer to this technology as "balloon kyphoplasty"	Comment noted. The remit and scope have been amended to refer consistently to *percutaneous balloon kyphoplasty*.

Section	Consultees	Comments	Action
		"Nonoperative treatment" or "conventional medical treatment" would be more consistent with terminology more frequently used in medical literature. We recommend to consistently use "nonoperative treatment" throughout the document	
	National Osteoporosis Society	Yes, the wording of the remit reflects the issues of clinical and cost effectiveness related to theses technologies.	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	No. In the UK vertebroplasty is regularly used to treat patients with insufficiency fractures due to metastatic disease, myeloma and vertebral haemangioma. NICE appraisal would be of more value if specific advice could be given about the use of these techniques for all indications.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was considered appropriate to limit the remit to the use of these technologies for osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	NHS Quality Improvement Scotland (comment from NHS professional 2)	Yes	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS	Yes	Comment noted.

Section	Consultees	Comments	Action
	professional 3)		
	Orthovita	By and large it does. The estimated number of fractures in the UK seems low; open surgery is usually only performed on patients that have neurological complications as a result of their fracture(s); vertebroplasty is capable of restoring vertebral height, mainly through positioning of the patient on the operating table; for kyphoplasty it has not been proven that the overall curvature of the spine improves, nor that it is better than vertebroplasty at preventing the sequelae of immobility and deformity. There is no provable difference in safety or efficacy between a Vertebroplasty and Kyphoplasty using bone cement (PMMA) so an appraisal of this would be useful given the large pricing variance between the two procedures. The cost implication within this question should be defined across not just QALYs but also for the immediate cost to the trust of the procedure itself, impact upon waiting lists for other patients (length of time of procedure etc), reduction in GP care giving and conservative care costs. Associated co-morbidities from non-treatment and their reduction post-successful treatment should also be reflected in this question.	The scope has been amended to reflect that the number of fractures may be higher. The differences between percutaneous vertebroplasty and percutaneous balloon kyphoplasty – in terms of efficacy, safety and cost effectiveness – will be addressed in the appraisal. If there is evidence of economic impact beyond immediate costs, this should be detailed in consultee submissions. Any such evidence will be considered by the Assessment Group and Appraisal Committee. If there is evidence of the effect of the technologies and their comparators on the incidence and impact of comorbidities, this should be detailed in consultee submissions. Any such evidence will be considered by the Assessment Group and Appraisal Committee.
	Pain Relief Foundation	Yes	Comment noted.
	Royal College of Physicians	Yes	Comment noted.
	The Society and College of	The wording appears appropriate for the inclusion of osteoporotic fractures, but should other reasons for	It was agreed at the scoping workshop that relatively few people with non-osteoporotic

Section	Consultees	Comments	Action
	Radiographers	vertebral fracture where patients may benefit be included, for example traumatic fractures and those fractures resulting from metastatic disease.	vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
Timing Issues	ArthroCare UK Ltd	Yes	Comment noted.
	British Society of Skeletal Radiologists (BSSR)	The topic is currently undergoing clinical re-evaluation following recent publications and hence the appraisal is timely rather than urgent.	Comment noted.
	DePuy Spine / Johnson & Johnson	These procedures are low volume and have a modest impact on the NHS budget. Moreover, access to these procedures is already governed by IPG #12, IPG #166, and NICE Clinical Guidance 75, the availability of which decreases the urgency for additional appraisal.	Comment noted.
	National Osteoporosis Society	No timing for the submission of evidence has been given.	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	Relatively low urgency.	Comment noted.
	NHS Quality Improvement	Urgent. Timing appropriate.	Comment noted.

Section	Consultees	Comments	Action
	Scotland (comment provided by NHS professional 2)		
	NHS Quality Improvement Scotland (comment provided NHS professional 3)	The use of spinal augmentation techniques such as vertebroplasty & kyphoplasty is increasing in the UK. At present there are 5 centres in Scotland providing a regular vertebroplasty service. Results of recent randomised trials show sustained benefit for patients with recent vertebral fractures using both techniques but, for vertebroplasty, no benefit has been demonstrated over sham procedures in patients with older fractures. There are substantial cost implications for the wider implementation of both procedures. I would regard the degree of urgency of this proposed appraisal to be moderately high.	Comment noted.
	NICE CHTE - Interventional Procedures	Both these procedures have received 'normal arrangements' guidance from NICE Interventional procedures programme so suitable for inclusion in the TA programme. Potentially little in the way of RCT data available. None available in 2003 and 2006 when we assessed these topics, although we were aware of some in progress	Comment noted.
	Orthovita	I do think that the discussion of this pathology and its potential treatments is timely. As well as the weight of recent published data and the contracting opinions following this - there is also a great deal of 'marketing material' in circulation along with oft-hyped claims. Many of these claims are unfounded and unprovable. It is time for many of these myths to be de-bunked.	Comment noted.

Section	Consultees	Comments	Action
	Pain Relief Foundation	This is not an urgent appraisal issue for NICE. There have 2 recent conflicting trials (Lancet study/ NEJM Aug 2009)	Comment noted.
	Royal College of Physicians	Yes	Comment noted.
	The Society and College of Radiographers	This is an important area for a timely appraisal since national practice is variable.	Comment noted.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	British Society of Skeletal Radiologists (BSSR)	Background information does not specify "best" non-invasive management for vertebral fractures with resistant symptoms.	It is the purpose of the background information to provide an overview of relevant issues – in particular, current routine practice in the NHS – not to make judgements about recommended treatments.
	Cook Medical	We agree that the background information is accurate and complete.	Comment noted.
	DePuy Spine / Johnson & Johnson	We are broadly in agreement with the background information as presented.	Comment noted.
	Medtronic Ltd	Between 35-50% of all women over 50 years of age had at least one vertebral fracture which account for 15-20% of all osteoporosis related fractures. It is estimated that more than 2 million women - in England and Wales - have osteoporosis and that there are 180'000 osteoporosis-related symptomatic fractures in England and Wales per year. Vertebral fractures are associated with significant morbidity and increased mortality. UK-specific data indicate a 4.4–fold increase in mortality related to vertebral fracture. (NICE TAG 161)	Comments noted. The large number of people who could benefit from effective treatment of osteoporotic vertebral compression fractures is one reason why NICE believes that an appraisal of percutaneous vertebroplasty and percutaneous balloon kyphoplasty is appropriate.
		Using the annual fracture incidence stratified by age (Kanis et al Osteoporosis Int 2000;11: 669-74) which is consistent with data from Western countries, there are 43'200 clinical osteoporotic vertebral fractures per annum in England and Wales. (Kanis et al. HTA Assessment 2002; Vol.6, No.26)	The scope has been amended to reflect that the number of fractures may be higher.
		While only up 30% of patients may come to clinical attention, only up to 10% require hospitalisation	Comments noted.

Section	Consultees	Comments	Action
		[Cooper C, J Bone Miner Res 1992;7:221-7; van Staa TP et al, Bone 2001 29:517-22. Gehlbach et al Osteo Int 2000;11: 577-82], i.e. approximately 4'300 patients per annum in England and Wales. In 2008 / 2009 (combined) there were approximately 2'000 balloon kyphoplasties in England and Wales, of these 47%, were due to OVCF, 40% high-energy trauma, 12% tumour and 1% other reasons. [MDT data, on file].	
		Acute back pain is the initial symptom of vertebral fractures often followed by deformity, loss of height, and chronic pain with resultant reduction in mobility. Even if the initial pain subsides many patients with vertebral fractures will have developed irreversible spinal deformity (increased kyphosis) associated with significant health consequences : increased mortality, decreased physical functioning, increased future fracture risk, reduced lung functioning, impaired balance and increased incidence of falls.	Comments noted.
		Management of pain and prevention of spinal deformity are two key treatment objectives in patients with vertebral fractures. Whilst the majority of patients will become symptom-free upon nonoperative treatment, up to 75% have persistent chronic pain at 12 months (Suzuki, 2008), revealing limitations of nonoperative treatment	Comments noted.
		Balloon kyphoplasty should be considered when clinical practice suggests no amelioration upon a trial of nonoperative management. There are several recommendations (Brunton J Fam Prac 2005; DVO Guideline Germany 2009) to limit the trial period of conservative management in patients with high level	Comments noted.

Section	Consultees	Comments	Action
		of pain, deformity or disability in line with findings on symptom relief from the RCT of balloon kyphoplasty vs nonoperative treatment (Wardlow et al. Lancet 2009).	
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	Happy with the accuracy and completeness.	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 2)	Para 1. Compression fractures do not always affect only the front portion - insert "usually" Para 2: interference with sleep and side-effects from high doses of analgesics are also significant - "asymptomatic" better replaced with "not recognised as such at the time of their occurrence"	The scope has been amended to reflect this information.
	NHS Quality Improvement Scotland (comment provided by NHS professional 3)	I would suggest the insertion of the following statement into para 2, line 3. "Population studies show a substantial increase in age-related mortality in women who sustain a clinically evident osteoporotic vertebral compression fracture. This additional mortality is of a similar magnitude to that of an osteoporotic fracture of the femoral neck.	The scope has been amended to reflect this information.
	Orthovita	Succinct but fairly complete	Comment noted.
	Pain Relief Foundation	Agree	Comment noted.
	Royal College of Physicians	Our experts disagree with some of the background. We believe that it should be made much clearer that it refers to osteoporotic vertebral fractures, not any other causes of vertebral fracture for this remit.	The scope has been amended to clarify that people with osteoporotic vertebral compression fractures are the sole population of interest.

Section	Consultees	Comments	Action
		Then, a clear distinction needs to be made between new, incident vertebral fractures presenting with new onset back pain, and longer standing back pain associated with prevalent vertebral fractures. This is extremely important, as the natural history of new incident vertebral fractures is that the majority become pain free within 6-8 weeks, and so should not have either vertebroplasty or kyphoplasty during this time. These interventions should be reserved for people in whom the back pain does not resolve.	Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by time between fracture and treatment should be considered in the appraisal if evidence allows.
		In addition, the non-invasive treatments discussed are incorrect. Bed-rest and back braces are not recommended for osteoporotic vertebral fractures - they will make spinal osteoporosis worse.	Conflicting evidence was received on this point. The definition of routine standards of non-invasive management will be important in the appraisal.
	The Society and College of Radiographers	I'm concerned where the data suggesting 50-70% of vertebral fractures are asymptomatic is from. It's certainly true that there are some asymptomatic fractures, but it's also true that many fractures while causing acute back pain are not brought to clinical attention or are not adequately investigated, resulting in missed fractures.	The scope has been amended to clarify that fractures that do not come to attention are not necessarily asymptomatic.
The technology/ intervention	ArthroCare UK Ltd	ArthroCare would like to see the inclusion of the term "Enhanced Percutaneous Vertebroplasty" In which the Cavity Spine wand is used, in appropriate patients prior to augmentation.(Spincal Metasteses and Myeloma)	Since the appraisal is limited to osteoporotic vertebral compression fractures, this technology is not relevant to this appraisal.
	British Society of Skeletal Radiologists (BSSR)	Yes. Kyphoplasty has potential to restore height but frequently does not achieve this.	Comment noted.

Section	Consultees	Comments	Action
	Cook Medical	Based on the evidence on vertebroplasty and kyphoplasty, we do not agree with the full description of the technologies and have the following comments and suggestions: On vertebroplasty: - First paragraph: the wording "The procedure may relieve pain and stabilize a fracture", should be replaced with "The latest evidence suggests that the procedure relieves pain significantly and stabilizes fractures". This is based on the evidence reported in the recently published results from the Vertos II trial, which show significant reduction in pain after vertebroplasty versus conservative therapy. - First paragraph: the wording "…but it does not directly restore vertebral body height", should be replaced with a sentence "Although vertebroplasty is not intended to directly restore vertebral body height, it avoids further deformation of the vertebal body after the procedure.". Also, some studies have reported that vertebroplasty can, in selected patients, restore vertebral body height, suggesting that factors not directly related to the device play an important role in height restoration (Hiwatashi et al, AJNR Am J Neuroradiol 2003;24:185–189 and McKiernan et al, J Bone Miner Res 2003;18:24–29). On kyphoplasty: - Third paragraph: a majority of studies on kyphoplasty showing height restoration were performed on vertebrae with characteristics, which presence increases the probability that the fracture is mobile, therefore strongly suggesting that kyphoplasty may only be successful in restoring	Comments noted. It is not the purpose of the scope to pass judgement on the strength of evidence that will be assessed in the appraisal; rather, it seeks to summarise current routine practice. The draft scope suggested that percutaneous balloon kyphoplasty may be used to prevent the sequelae of immobility and deformity; this sentence has been removed from the final scope, to reflect uncertainty about the relative benefits of percutaneous vertebroplasty and percutaneous balloon kyphoplasty, in this area. This will now be an issue to be addressed in the appraisal.

Section	Consultees	Comments	Action
		height if the fracture is mobile; the wording used in this paragraph should reflect that the potential of the procedure to restore body height is limited. - Fourth paragraph (describing the indications for kyphoplasty) states: "In addition, kyphoplasty may be used to prevent the sequelae of immobility and deformity due to vertebral compression fractures…". Note that several studies suggest that the sequelae because of kyphotic deformity can also be prevented by vertebroplasty! AJNR Am J Neuroradiol 25:840–845, May 2004: "patients who are pain free following vertebroplasty or kyphoplasty usually experience less muscle spasm and tend to stand straighter with the elimination of spine pain. Mathis demonstrated this effect in a vertebroplasty case with 50% kyphosis reduction after vertebroplasty alone. Teng et al reported kyphosis improvement following vertebroplasty in 45 of 53 patients, with 49% having a kyphotic angle reduction of 5° or more."	
	DePuy Spine / Johnson & Johnson	Percutaneous vertebroplasty and kyphoplasty can be performed using a wide variety of technologies, incorporating both different types of cement and different delivery systems. First-generation systems have been available for many years, and more recent innovations in technology platforms and cements have been developed to reduce the risk of cement extravasation.	Comments noted.
	Medtronic Ltd	Balloon kyphoplasty is a minimally invasive procedure designed to restore vertebral body height, correct angular deformity, and stabilize the spine after vertebral compression fractures due to osteoporosis, cancer or benign tumors. It is the first	Comments noted.

Section	Consultees	Comments	Action
		procedure that addresses all AO Principles of Surgical Fracture Management 1) Anatomical Reduction - Inflatable bone tamps to reduce the fracture; 2) Stable internal fixation - Bone cement to create a cast inside the vertebral compression fracture and stabilize the fracture; 3) Preservation of blood supply - Procedure performed minimally invasively; 4) Safe and early mobilisation - there is no muscle stripping or bone removal, and because the bone cement hardens rapidly, the patients are immediately load-bearing. [Helfet, JBJS 2003; Müller ME et al. (1995) Manual of Internal Fixation. 3rd edition; Springer. Aebi M et al. (2007) AOSPINE Manual (2 vols), Stuttgart, New York: Thieme] It involves the bilateral insertion of two balloons into the vertebral body. The two balloons are then slowly inflated until the normal height of the vertebral body is restored or the balloons reach their maximum volume. When the balloon is deflated and removed, the cavity is filled with bone cement. The creation of a cavity within the vertebral body allows for the insertion of a pre-known volume of a more viscous cement at lower pressure [Weißkopf, Spine 2003], reducing the risk of cement extravasations. The procedure is performed under general or local anaesthesia. Balloon kyphoplasty and percutaneous vertebroplasty are both minimally invasive surgical	

Section	Consultees	Comments	Action
		approaches – but have different treatment outcomes: percutaneous vertebroplasty aims to achieve spinal stabilization and pain relief. Balloon kyphoplasty additionally aims to correct and prevent spinal deformity.	
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	I would not agree with the statement about indications for kyphoplasty. It is rarely possible to obtain significant kyphosis reduction using this technique and there is no evidence for making this statement about additional indications for use.	The draft scope suggested that percutaneous balloon kyphoplasty may be used to prevent the sequelae of immobility and deformity; this sentence has been removed from the final scope, to reflect uncertainty about the relative benefits of percutaneous vertebroplasty and percutaneous balloon kyphoplasty, in this area. This will now be an issue to be addressed in the appraisal.
	NHS Quality Improvement Scotland (comment provided by NHS professional 2)	Para 4: the additional sequelae potentially prevented by kyphoplasty may also be prevented by vertebroplasy. True height restoration by kyphoplasty is usually marginal at best and likely only in very recent fractures (which are not usually treated in the UK). The main difference between the 2 procedures is that in kyphoplast the balloon creates a large cavity within the bone which is then filled with cement, whereas in vertebroplasty cement fills the interstices in the cancellous bone	The draft scope suggested that percutaneous balloon kyphoplasty may be used to prevent the sequelae of immobility and deformity; this sentence has been removed from the final scope, to reflect uncertainty about the relative benefits of percutaneous vertebroplasty and percutaneous balloon kyphoplasty, in this area. This will now be an issue to be addressed in the appraisal.
	NHS Quality Improvement Scotland (comment provided by NHS professional 3)	Suggested alterations to the text include; Para 2, line 2& 3. Change "severe, painful osteoporosis with loss of height and/or compression fractures of the vertebral body.." to painful osteoporotic vertebral compression fractures".	Amendment accepted.

Section	Consultees	Comments	Action
		Para 3, line 4. The kyphoplasty balloon(s) may not reach " maximum" volume due to inflation pressure constraints. Suggest change of word to "maximal" or "highest achievable".	Amendment accepted.
		Para 3, line 5/6. Change to "but usually requires a general anaesthetic".	During consultation, consultees stated that balloon kyphoplasty can be performed under either local or general anaesthetic.
		Para 4, line 3. Typo error. "osteolytic" is correct.	Amendment accepted.
		Para 4, lines 3-6 (sentence 2). Suggest deletion of this sentence for the following reasons; The superiority of kyphoplasty over vertebroplasty for painful vertebral compression fractures has not been proven with respect to pain relief or reduction of immobility-related complications, including decubitus ulcers, urinary tract infections or deep venous thrombosis. Restoration in vertebral height after kyphoplasty appears to be modest and the effect of this technique on lung function is unknown.	The draft scope suggested that percutaneous balloon kyphoplasty may be used to prevent the sequelae of immobility and deformity; this sentence has been removed from the final scope, to reflect uncertainty about the relative benefits of percutaneous vertebroplasty and percutaneous balloon kyphoplasty, in this area. This will now be an issue to be addressed in the appraisal.
		Para 4, line 6-7. The main indication for kyphoplasty is for painful vertebral compression fractures: kyphosis or curvature of the spine is not. Suggest deletion.	
	Orthovita	With the exception that vertebroplasty can also restore the height of the vertebral body and the fact that for neither verterboplasty nor kyphoplasty has it been proven that the change in height leads to an improvement in overall curvature or reduced complication caused by the deformity.	The draft scope suggested that percutaneous balloon kyphoplasty may be used to prevent the sequelae of immobility and deformity; this sentence has been removed from the final scope, to reflect uncertainty about the relative benefits of percutaneous vertebroplasty and

Section	Consultees	Comments	Action
			percutaneous balloon kyphoplasty, in this area. This will now be an issue to be addressed in the appraisal.
	Pain Relief Foundation	In the technology section of the draft remit- reference is made to 'height restoration' and ' reduction of curvature'- this is now thought to be outdated concept and this is not usually the outcome in most cases.	The draft scope suggested that percutaneous balloon kyphoplasty may be used to prevent the sequelae of immobility and deformity; this sentence has been removed from the final scope, to reflect uncertainty about the relative benefits of percutaneous vertebroplasty and percutaneous balloon kyphoplasty, in this area. This will now be an issue to be addressed in the appraisal.
	Royal College of Physicians	Paragraph 2: Percutaneous vertebroplasty is not used for severe painful "osteoporosis" - as there is no such thing. It may be used for severe back pain in people with osteoporotic compression fractures of the vertberal body. It should not be used for people with severe back pain and height loss without osteoporotic vertebral fractures. We wonder why other causes of vertebral fracture are discussed here when the title of this remit is osteoporotic vertebral fractures.	Wording of indication for percutaneous vertebroplasty has been clarified. Reference to other causes of vertebral compression fractures have been removed.
	The Society and College of Radiographers	This seems appropriate	Comment noted.
Population	ArthroCare UK Ltd	Patients with Spinal Metastases and Myeloma should be considered as a separate group.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite

Section	Consultees	Comments	Action
			different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	British Society of Skeletal Radiologists (BSSR)	There is some evidence that certain configurations of vertebral fracture are at risk of rapid progression/collapse and that cement augmentation offered to this group early could prevent such collapse.	Comment noted.
	Cook Medical	Yes. Osteoporotic patients make up the vast majority of cases (statistics available from the International Spinal Plasty Registry, Dendrite Clinical Systems). Please note that within this population (osteoporotic fracture patients) not every case is a suitable candidate for treatment. In the Vertos II trial the three most important criteria that need to be met are defined: o Fracture needs to be visible on X-ray o Bone oedema needs to be present on MRI o Physical investigation by a clinician needs to confirm that the pain comes from the level seen on X-ray and MRI. If the patient population were to include people who have non-osteoporotic/traumatic vertebral fractures, vertebroplasty should not be considered for that patient population as a comparator to kyphoplasty, since kyphoplasty might be a better option for (young) traumatic non-osteoporotic patients.	Comments noted.

Section	Consultees	Comments	Action
	DePuy Spine / Johnson & Johnson	The population should include fractures occuring as a result of benign lesions (haemangioma) and resulting from neoplastic pathology which constitutes malignant lesions as a result of bone metastases and multiple myeloma.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	Medtronic Ltd	Balloon kyphoplasty should be considered in patients where clinical practice suggests no benefit from nonoperative treatment trial. These include: - patients with osteoporotic vertebral fractures upon failure of nonoperative treatment trial. - patients who could benefit from earlier surgery due to fracture morphology and other clinical practice considerations. These may include patients intolerant to analgesics or in whom narcotic analgesics are contraindicated (e.g., respiratory depression, asthma, drug interactions with CNS depressants). It may also include patients experiencing severe vertebral collapse and deformity due to osteoporotic fractures, patients with osteoporosis in whom additional bone loss is deemed hazardous.	Comments noted. Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by time between fracture and treatment should be considered in the appraisal if evidence allows.
	National Osteoporosis Society	We would suggest that the population is 'People with osteoporotic vertebral fractures'. As it is currently stated the population could vary	In line with these comments, the scope population has been amended to 'People with painful osteoporotic vertebral fractures'.

Section	Consultees	Comments	Action
		depending on different timeframes used for determining refractory pain and interpretation of conservative management. These areas need to be defined within the appraisal to reduce potential variation in access to these technologies.	
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	As above, I would suggest extending the remit to include all indications for these procedures.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	NHS Quality Improvement Scotland (comment from NHS professional 2)	The time interval between fracture and treatment is crucial. The optimal time for treatment is when pain has not improved after 6 weeks. At present many patients in this country are not treated until 6 or even 12 months after injury, when successful treatment is less likely. Time from injury to treatment should be clearly identified in the appraisal.	Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by time between fracture and treatment should be considered in the appraisal if evidence allows.
	NHS Quality Improvement Scotland (comment provided by NHS professional 3)	Patients with primary or secondary osteoporosis should be considered eligible for a clinical trial. Inclusion / exclusion criteria may need to be modified in the light of recent clinical trials. QALY assessment would be enhanced by a minimum of 1y follow up. Patients who have primary osteoporosis but also	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit

Section	Consultees	Comments	Action
		have malignant disease without skeletal metastases should be excluded because of their potentially limited life span and the possibility of subsequent development of spinal metastases. In my experience this is a substantial group of patients that would justify separate clinical trial. Patients with (non-osteporotic) traumatic fractures should be excluded from this proposal because of the need for major adjuvant spinal surgical interventions, the younger age of the patients, the relatively high neurological complication rate, the lack of published data and the relatively small numbers of patients suffering from traumatic spinal fractures compared to osteoporotic lesions.	the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	NICE CHTE - Interventional Procedures	Yes it should be patients refractory to conservative treatments. Consider including this in the title?	Since discussion at the scoping workshop indicated that timing of intervention is an important issue in the efficacy of the technologies, it was agreed that the population should not be limited to people with a particular history. Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by time between fracture and treatment should be considered in the appraisal if evidence allows.
	Orthovita	Yes. Within the osteoporotic population patients with recent fractures may require a different treatment algorithm than patients with old(er) fractures, The definition of recent and old(er) should be debated.	Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by time between fracture and treatment should be considered in the appraisal if evidence allows.
	Pain Relief	Yes	Comment noted.

Section	Consultees	Comments	Action
	Foundation		
	Royal College of Physicians	Yes	Comment noted.
	The Society and College of Radiographers	Traumatic vertebral fractures should be considered.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
Comparators	British Society of Skeletal Radiologists (BSSR)	Best non-invasive management must be defined.	It will be for consultees and the Assessment Group to address this issue in the appraisal, to enable the Committee to reach conclusions on routine and best NHS practice.
	Cook Medical	Non invasive management is a relevant comparator and includes (but may not be limited to) the following: pain medication, bisphosphonates, Vitamin D and bed rest. We agree that comparing kyphoplasty and vertebroplasty against each other is very relevant, especially from a cost-effectiveness perspective.	Comments noted.
	DePuy Spine / Johnson & Johnson	A precise definition of what constitutes gold standard conservative (non-invasive) medical management is difficult to establish, given an absence of expert clinical consensus and guidelines Moreover, there is	It will be for consultees and the Assessment Group to address this issue in the appraisal. The Appraisal Committee will also be informed by clinical specialists about routine and best

Section	Consultees	Comments	Action
		significant variation in clinical practices for management of VCFs across the UK. Hence we anticipate that estimation of resource utilisation and allocation of costs to conservative medical management for VCFs will be challenging.	NHS practice.
	Medtronic Ltd	Considering that the current standard of care within the NHS for treatment of vertebral compression fractures is conservative, i.e. nonoperative treatment and in view of the lack of robust evidence comparing surgical options, the appropriate primary comparator for balloon kyphoplasty would be nonoperative treatment. Given the unmet clinical need and the socioeconomic burden of osteoporotic vertebral compression fractures and the difficulties in designing and executing randomised clinical trials for these interventions (ongoing studies NCT00323609, NCT00749086, NCT00749060), priority should be given to a STA comparing balloon kyphoplasty vs nonoperative treatment.	Comments noted. It was agreed at the scoping workshop that an MTA comparing percutaneous vertebroplasty and percutaneous balloon kyphoplasty with each other and non-invasive management was feasible and has the potential to add value to the NHS.
	National Osteoporosis Society	Non-invasive management needs to be more clearly defined.	It will be for consultees and the Assessment Group to address this issue in the appraisal. The Appraisal Committee will also be informed by clinical specialists about routine and best NHS practice.
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	Yes	Comment noted.

Section	Consultees	Comments	Action
	NHS Quality Improvement Scotland (comment provided by NHS professional 2)	Scope of non-invasive management should perhaps be defined Some patients may also benefit from less invasive procedures such as nerve block or facet joint injection	It will be for consultees and the Assessment Group to address this issue in the appraisal, to enable the Committee to reach conclusions on routine and best NHS practice. Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 3)	Non-invasive management of painful vertebral compression fractures is probably non-uniform in Scotland A pragmatic approach would be to accept regional variations in referral / availability of specialist back pain physiotherapy services, patient tolerance of opiate or derivative drugs and availability or tolerance of back bracing.	It will be for consultees and the Assessment Group to address this issue in the appraisal, to enable the Committee to reach conclusions on routine and best NHS practice.
	NICE CHTE - Interventional Procedures	Standard management is pain medication and immobilisation. However, if the population to be considered is as above then this is not a meaningful comparator. Other comparators might include radiaition therapy - for compression fractures resulting from metastases.	It will be for consultees and the Assessment Group to address this issue in the appraisal, to enable the Committee to reach conclusions on routine and best NHS practice. It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.

Section	Consultees	Comments	Action
	Orthovita	The best alternative is the prescription of optimised analgesic medication and where possible physical therapy. Bracing has not been shown to lead to a real effective immobilisation of the fracture(s) and therefore is less important. Bed rest should be avoided at all cost, as especially in the elderly population this very quickly leads to loss of capabilities regarding the Activities of Daily Life.	Comments noted.
	Pain Relief Foundation	Yes	Comment noted.
	Royal College of Physicians	Yes	Comment noted.
	The Society and College of Radiographers	Conservative treatment is probably the best comparator at present	Comment noted.
Outcomes	British Society of Skeletal Radiologists (BSSR)	Yes	Comment noted.
	Cook Medical	Yes.	Comment noted.
	DePuy Spine / Johnson & Johnson	It is important that cement leakage rates are used as an indicator of the safety profile of individual cement types, as this is dependent on the viscosity and delivery system of individual technologies. There are significant "system benefits" which can be gained by treating patients using percutaneous vertebroplasty in a day-case setting versus a lengthy ward stay for conservative (non-invasive) management of the symptoms associated with	We expect that this issue will form an important part of the review of adverse events from treatment in the appraisal. If there is evidence of these benefits, NICE expects them to be captured in the economic analyses that will be available to the Committee.

Section	Consultees	Comments	Action
		symptomatic vertebral fractures.	
	Medtronic Ltd	Considering the role of the physical dimension in decreased quality of life in patients with vertebral fractures over time, the recognised impact of spine deformity on morbidity [Borgstrom 2005, Hallberg 2009] and mortality [Lau, 2008; Kado 1999; Johnell 2004; Kado 2004], the existence of recommendations from medical societies to measure physical function when evaluating vertebral augmentation interventions [Radvany 2009] and the known limitations of Visual Analogue Scale (VAS) pain, "Mortality" and "Disability", in addition to the already indicated outcomes measures, should be considered in health policy recommendations.	It was agreed at the scoping workshop that *mortality* is an important outcome that should be added to the scope. Consultees also discussed whether *disability* should be included as an outcome measure, however there was broad agreement that functional status/mobility, which is already proposed as an outcome measure, would capture this treatment effect.
	National Osteoporosis Society	Yes, these outcome measures capture the most important health related benefits (and harms) of the technology.	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	Yes	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 2)	vertebral body height and angular deformity is not affected by vertebroplasty and cannot be compared rate of new fractures is not affected by either treatment	As specified outcomes of interest, these issues should be addressed by consultees and the Assessment Group in the appraisal.
	NHS Quality Improvement Scotland (comment	Yes	Comment noted.

Section	Consultees	Comments	Action
	provided by NHS professional 3)		
	NICE CHTE - Interventional Procedures	should rate of new fractures be a subsection of adverse events of treatment? Other adverse events include infection, periprocedural balloon rupture (kyphoplasty), and cement leaks / extravasion which if leading to canal intrusion can result in paralysis	This is now included as a separate outcome. Comments noted.
	Orthovita	Yes. What could be added is future hospitalisations and treatments for the same pathology, i.e. the new fractures caused by osteoporosis.	Progression of the treated fracture and rate of new vertebral fractures are included as outcome measures in the final scope.
	Pain Relief Foundation	Yes,. As a part of the 'pain' outcome it would be worth looking at number and amount of analgesics used pre and post procedure - this would be a surrogate marker of pain.	Comment noted.
	Royal College of Physicians	Our experts do not believe that vertebral body height and angular deformity are important measures (although they are easy to do) - pain and function are the most important. Please also clarify that it is the rate of new vertebral fractures, not any fracture	Comment noted. The scope has been amended to specify that the outcome of interest is new vertebral fractures.
	The Society and College of Radiographers	Yes	Comment noted.
Economic analysis	ArthroCare UK Ltd	If Metastatic patients are included within the group QOL indicators will need to be different this should be looked at within the parameters of end of life care.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous

Section	Consultees	Comments	Action
			balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	Cook Medical	We believe that a 1 year time horizon is appropriate to capture costs and effects for the interventional procedures under consideration. This patient population is normally elderly and frail, making long term follow up challenging.	The NICE Guide to the methods of technology appraisal stipulates that a lifetime time horizon is preferred unless there is no evidence of mortality impact associated with the technologies and any differences in costs and health-related quality of life relate to a relatively short period (see sections 5.2.13–5.2.15). As mortality is an outcome of interest, in this appraisal, and there is evidence of long-term effects (including new fractures), it would not be appropriate to limit the time horizon in this instance.
	DePuy Spine / Johnson & Johnson	The time horizon should be sufficiently long to reflect any differences in costs or outcomes between comparator groups. This should be informed by the most recent clinical evidence published on the subject.	The NICE Guide to the methods of technology appraisal stipulates that a lifetime time horizon is preferred unless there is no evidence of mortality impact associated with the technologies and any differences in costs and health-related quality of life relate to a relatively short period (see sections 5.2.13–5.2.15).
	Medtronic Ltd	The economic analysis to be submitted will use a Markov model with a cost-utility approach with projections over appropriate time horizons including	Comments noted.

Section	Consultees	Comments	Action
		life-time as base case. A budget impact analysis will be submitted with a shorter time horizon.	
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	At least one year of follow up would be necessary.	Comment noted.
	NHS Quality Improvement Scotland (comment from NHS professional 2)	Adverse effects of pain and immobility from untreated vertebral fractures may continue for the lifetime of the patient	Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 3)	In a recent randomised trial QALYs were estimated with EuroQoL-5 dimensions at 1 month and at 1 year. (Vertebroplasty vs conservative treatment in acute vertebral compression fractures (Vertos II): an open-label randomised trial. Klazen CAH et al; Lancet 2010; 376:1085-1092. I do not have specialist statistical knowledge but this would seem a reasonable time horizon.	The NICE Guide to the methods of technology appraisal stipulates that a lifetime time horizon is preferred unless there is no evidence of mortality impact associated with the technologies and any differences in costs and health-related quality of life relate to a relatively short period (see sections 5.2.13–5.2.15). As mortality is an outcome of interest, in this appraisal, and there is evidence of long-term effects (including new fractures), it would not be appropriate to limit the time horizon in this instance.
	NICE CHTE - Interventional Procedures	Long term analysis important with potential fracture at adjacent levels	The NICE Guide to the methods of technology appraisal stipulates that a lifetime time horizon is preferred unless there is no evidence of mortality impact associated with the technologies and any differences in costs and health-related quality of life relate to a relatively short period (see sections 5.2.13–

Section	Consultees	Comments	Action
			5.2.15).
	Orthovita	Most of the clinical sequelae and subsequent fractures tend to occur within the first 3 to 6 months after the initial treatment. However, new fractures continue to occur after that as well, and in a prospective study comparing Cortoss and PMMA we could measure the effects of treatment over a period of 24 months. This is remarkable given the fact that the study population on average was ~78 years old and had many co-morbid conditions.	Comments noted.
	Pain Relief Foundation	QUALY may be a misleading measure in this group of patient as the population on the whole are elderly (>60 Yr) , and often develop other morbidities (spinal or extra spinal) which may skew the effectiveness of a single procedural event.	Comment noted. It should be noted that the basis of the analysis will be the incremental costs and benefits associated with the technologies; hence, the key point of interest is relative, rather than absolute, patient benefits.
Equality	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	There is potential for inequality of care provision on the grounds of patient age. The population involved is elderly.	NICE has noted this concern and will bring it to the attention of the Appraisal Committee when it meets to consider this appraisal. NICE has been established to address variation in clinical practice.
	NICE CHTE - Interventional Procedures	Osteoporosis likely to me more common in women.	This is not expected to lead to unfair access to treatment, so no changes to the scope are necessary. NICE have however noted this concern and will bring it to the attention of the Appraisal Committee when it meets to consider this appraisal.
Other considerations	NHS Quality Improvement Scotland (comment	Use of these procedures is limited not only by lack of funding, but by absence of appropriate multidisciplinary teams to care for these patients and	Comment noted.

Section	Consultees	Comments	Action
	provided by NHS professional 2)	ensure they are directed to treatment timeously	
	NHS Quality Improvement Scotland (comment provided by NHS professional 3)	Cost assessment may be affected because of the differing cost reimbursement arrangements for interventional procedures and materials between the NHS England & Wales and Scotland. A proposed randomised trial of vertebroplasty vs. kyphoplasty vs. conservative therapy would be a considerable undertaking and is not possible at Scottish level or possibly at national level. There is 1 pending NIH funded trial of vertebroplasty vs kyphoplasty but I do not know if recruitment has commenced. A major problem of randomised, patient blinded interventional trials is patient recruitment. Regarding the most recent trial of vertebroplasty vs. conservative treatment (Vertos II) performed in Belgium and Holland (ref below), 934 patients were screened and 202 were randomised during a 3 year period. The INVEST trial involved a placebo teatment and although this was designed and managed by the investigators at the Mayo Clinic the majority of patients were recruited from European and Australian centres. An RCT involving 3 patient groups would require international collaboration and would probably take 3-5 years to complete.	Comments noted.
	NICE CHTE - Interventional Procedures	Anecdotal reports that complications are more common in patients with metastases	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite

Section	Consultees	Comments	Action
			different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	Orthovita	1. An algorithm to prescribe the optimal analgesic regimen. This should address the type of medications while taking side effects into account (especially for narcotics), how long a drug should be given if the pain does not respond, how many 'tries' should be made before invasive therapy is justified. 2. A description of radiological parameters that demonstrate continued vertebral collapse and that would warrant the immediate administration of a vertebroplasty or kyphoplasty to prevent further collapse.	These issues are beyond the scope of this appraisal. However, it will be necessary for the Assessment Group and consultees to take a view on current standards in these areas in order to analyse the costs and effects of the technologies and their comparators.
	The Society and College of Radiographers	The optimum timing for intervention post fracture should be considered. It's possible that patients treated earlier have a better outcome, though the literature is sparse. Also, types of fracture most likely to benefit.	Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by time between fracture and treatment should be considered in the appraisal if evidence allows.
Innovation	ArthroCare UK Ltd	Use of the cavity spinewand in combination with a vertebroplasty procedure, allows surgeons to perform surgery for relief for palliative care offering a better standard of living in patients coming to the end of their life. Use of the Cavity Spinewand increases safety of procedure, and allows surgeons to perform more complex surgery.	Since the appraisal is limited to osteoporotic vertebral compression fractures, this technology is not relevant.

Section	Consultees	Comments	Action
		Please see references attached.	
	British Society of Skeletal Radiologists (BSSR)	1. Cement augmentation is well established in many hospitals across the UK and hence many patients suitable for this treatment will already be receiving it. 2. Reduction in subsequent GP consultations and/or hospital admissions	Comments noted.
	Cook Medical	Yes, this is a step-change innovation. Given the patient population being elderly we believe that the major benefits are the quality of life improvements resulting from the alleviation of symptoms (pain and disability in particular). There are disease specific questionnaires to measure quality of life in patients with vertebral fractures (e.g. Quality of Life Questionnaire of the European Foundation for Osteoporosis - QUALEFFO).	Comments noted.
	DePuy Spine / Johnson & Johnson	As with utility assessment for other disease states, , the benefits of having a single generic instrument must be weighed against the potential consequences in terms of reduced relevance and sensitivity for many patients (Barton GR, 2004) (Espallargues M, 2005). This tradeoff was made evident in a study to evaluate the discriminative performance over time of specific, generic and preference-based instruments in patients with low back pain (LBP (M. E. Suarez-Almazor, 2000). We therefore suggest that the quality-of-life impact of interventions for VCF be measured not only by the EQ5D, but also by validated, condition- specific instruments that are adequately sensitive to the quality-of-life impacts of treatments for patients with VCFs. that We also encourage thoughtful	Comments noted. The NICE Guide to the methods of technology appraisal states that 'The EQ-5D may not be an appropriate measure of health-related utility in all circumstances. If the EQ-5D is considered inappropriate, empirical evidence should be provided on why the properties of the EQ-5D are not suitable for the particular patient population. These properties may include the content validity, construct validity, responsiveness and reliability of EQ-5D. When an alternative measure is preferred, those submitting analysis should provide reasons, supported by empirical data on the properties of the instrument used. They should also indicate any evidence that will help the

Section	Consultees	Comments	Action
		interpretation of the EQ-5D, given that differences in key domains for the VCF population may not be adequately reflected in the composite score [Patient Reported Outcome Measures (PROMs): Report to the Department of Health. Health Services Research Unit, Health Services Research Unit, London School of Hygiene & Tropical Medicine. 12/12 2007]	Committee understand to what extent their choice of instrument has impacted on the valuation of the QALYs gained' (section 5.4.9).
	Medtronic Ltd	Balloon kyphoplasty is innovative: Balloon kyphoplasty is the first surgical approach to vertebral compression fractures bringing to spine the established AO Principles of Surgical Fracture Management. This concept has been clinically demonstrated by the available body of evidence which consistently shows significant sustained pain relief; correction of vertebral body height and kyphosis, quality of life and physical function improvement. Only balloon kyphoplasty has shown to be cost effective compared to standard of care in the UK [Strom et al. Osteoporosis Int 2010) QALY covers both morbidity and mortality The QALY considers health gains both in terms of morbidity and mortality. If both improvements of morbidity (such as quality of life, pain) and mortality (increased survival) will be included in the scope of this appraisal then the QALY will adequately capture the health-related benefits of balloon kyphoplasty. Available data for submission The data to be used for the submission include best available clinical evidence (RCTs, large observational studies, meta-analysis) also used to	Comments noted.

Section	Consultees	Comments	Action
		populate the Markov model. "How should non-invasive management (without the use of either intervention) be defined?" To best of our knowledge, there is no evidence or clinical consensus on standardised 'non-invasive management' for Vertebral Compression Fractures. This explains why in the balloon kyphoplasty randomised clinical trial (Wardlaw, Lancet, 2009) non-invasive treatment was according to the standards of the study centres. In addition, investigators were encouraged to ensure biphosphonates or equivalents were prescribed to all patients. In this study, Non Surgical Management was thus according to the normal practice of the recruiting centers to ensure treatment and results were more naturalistic.	
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	The technologies can lead to significant improvement in patient health, particularly in carefully selected patients. In this group this could be seen as a step change in management. The benefits of appropriate vertebroplasty treatment should be evident in a QALY calculation.	Comments noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 2)	This is very much a step-change - there are no other active interventions available to these patients I cannot comment on the 2nd question until I see the tools which are proposed for the QALY calculations Extensive research literature exists. The UK Vertebroplasty Group is operating a database of procedures performed which may provide useful information.	Comments noted. It was confirmed at the scoping workshop that data from the UK Vertebroplasty Group database could be made available to inform this appraisal.

Section	Consultees	Comments	Action
	NHS Quality Improvement Scotland (comment provided by NHS professional 3)	I believe that spinal augmentation procedures (vertebroplasty & kyphoplasty) are innovative technologies which can have a major impact on the management of painful vertebral compression fractures due to osteoporosis and malignant disease. The current evidence (Level 2) suggests that early intervention in the treatment of osteporotic fractures can produce sustained benefit in pain relief and QOL and may represent a "step-change" in management of this condition. The benefit of later intervention in the natural history condition is less clear and a number of criticisms have been made of the "sham treatment" trials which remain a matter of debate (see ref 2 & 3 below). I could provide a more extensive criticism of the these trials but this probably outwith the scope of this exercise. The main published randomised trials include: 1. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. Wardlaw D et al; Lancet 2009; 373: 1016- 24 2..A randomized trial of vertebroplasty for osteoporotic spinal fractures. Kallmes DF et al. N Engl J Med 2009; 361: 569-79 3. A randomized trial of vertebroplasty for painful osteoporotic veterbral fractures. Buchbinder R et al. N Eng J Med 2009; 361: 557-68. 4. Vertebroplasty vs conservative treatment in acute vertebral compression fractures (Vertos II): an open-label randomized trial. Klazen CAH et al;	Comments noted.

Section	Consultees	Comments	Action
		Lancet 2010; 376:1085-92	
	Orthovita	Yes. The technology has the potential to reduce the number of patients that as a result of their vertebral fracture will have to rely on assisted living facilities, or at least postpone the moment that such need arises for an individual. In addition, vertebral augmentation provides a much needed simple, quick and relatively safe treatment option in the continuum between conservative measures and open surgical fixation, or corpectomy and fixation. Open fixation procedures are major surgeries in which these elderly patients have a high rate of complications.	Comments noted.
	Pain Relief Foundation	Yes	Comment noted.
	Royal College of Physicians	No. They represent an innovative technology originally developed for metastatic disease but have less potential to be used in the much larger patient group of osteoporotic vertebral fractures. There is currently little evidence of benefit over and above placebo except in very specific clinical situations such as isolated osteoporotic vertebral fractures with back pain clearly related anatomically to the site of the osteoporotic vertebral fracture, with the back pain present for at least 8-10 weeks unresponsive to standard management.	Comments noted.
	The Society and College of Radiographers	Yes There are some RCT's against sham procedures, but these are flawed to a degree and should be treated with caution.	Comments noted.

Section	Consultees	Comments	Action
		Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. Wardlaw D, Cummings SR, Van Meirhaeghe J, Bastian L, Tillman JB, Ranstam J, Eastell R, Shabe P, Talmadge K, Boonen S. Lancet. 2009 Mar 21;373(9668):1016-24. Epub 2009 Feb 24 Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. Wardlaw D, Cummings SR, Van Meirhaeghe J, Bastian L, Tillman JB, Ranstam J, Eastell R, Shabe P, Talmadge K, Boonen S. Lancet. 2009 Mar 21;373(9668):1016-24. Epub 2009 Feb 24.	
Questions for consultation	British Society of Skeletal Radiologists (BSSR)	Should people who have traumatic vertebral fractures also be included in the population for this scope? This is a different population and would benefit from a separate exercise comparing augmentation to (different) best non-invasive management	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		How should non-invasive management (without the use of either intervention) be defined? Most patients	Comments noted. It will be for consultees and the Assessment Group to address this issue in

Section	Consultees	Comments	Action
		undergoing augmentation have osteoporosis. The national osteoporosis society, british geriatrics society and royal college of physicians have guidelines on management of osteoporosis including treatment of fracture pain. Fractures due to other causes are typically malignant and treatment should be compared with radiotherapy although this could not be considered "non-invasive".	the appraisal, to enable the Committee to reach conclusions on routine and best NHS practice.
		Should different types of bone cement be considered? If so, which bone cements are routinely used in the UK for percutaneous vertebroplasty or balloon kyphoplasty procedures? I am not aware of any evidence linking type of bone cement with efficacy.	At the scoping workshop, it was agreed that treating each type of cement as a separate technology would needlessly complicate the appraisal.
		Among fractures that would be considered suitable for vertebroplasty and/or kyphoplasty, what proportion are caused by osteoporosis, and what proportion are associated with other causes? I would estimate at least 80% are osteoporotic.	Comment noted.
		Is the population in the scope defined appropriately? Do the populations considered for percutaneous vertebroplasty and balloon kyphoplasty differ? Essentially they are the same group.	Comment noted.
		Are there any other subgroups of people in whom these technologies are expected to be more clinically effective and cost effective or other groups that should be examined separately? Patients with MRI evidence of bone marrow oedema or intervertebral clefts appear to benefit more reliably and could be assessed as an independent subgroup. It would be helpful to assess those	Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by time between fracture and treatment should be considered in the appraisal if evidence allows. Following discussion at the scoping workshop, it was agreed that the scope should specify

Section	Consultees	Comments	Action
		without such findings as a group as it is possible that the procedure would be shown to be unjustifiable in this cohort.	that subgroups defined by presence or absence of fracture-related deformity should be considered in the appraisal if evidence allows. Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by inpatient care should be considered in the appraisal if evidence allows.
	Cook Medical	No comments.	Response noted.
	DePuy Spine / Johnson & Johnson	Question 1) No, the literature base on the use of these modalities for traumatic fractures that occur in the absence of underlying osteoporotic or osteolytic bone is inadequate VCFs secondary to multiple myeloma & metastatic disease should be included in the scope as this is an important patient group who benefit from treatment with vertebroplasty.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		Question 2) It is very difficult to reach consensus on what constitutes conservative medical management (CMM) for VCFs, as there is no clear standard practice in the UK. Our observations are that approaches to CMM are highly variable, even at the individual-hospital level. Hospital Episode Statistics suggest a considerable length of stay of over 15 days for patients presenting with vertebral fracture. CMM is likely to consist of analgesia, bed rest and	Comments noted. It will be for consultees and the Assessment Group to address this issue in the appraisal, to enable the Committee to reach conclusions on routine and best NHS practice.

Section	Consultees	Comments	Action
		an orthopaedic back bracing. It is expected that this care will be delivered by geriatricians and not on orthopaedic wards. Question 3) Yes, distinctions between types of bone cement are important. Newer generation cements, including those that are highly viscous, have been designed to reduce the likelihood of cement leakage.	At the scoping workshop, it was agreed that treating each type of cement as a separate technology would needlessly complicate the appraisal.
	Medtronic Ltd	For reasons stated in the section on comparators, a single technology appraisal (STA) would be more appropriate than a multi-technology appraisal (MTA)	It was agreed at the scoping workshop that an MTA comparing percutaneous vertebroplasty and percutaneous balloon kyphoplasty with each other and non-invasive management was feasible and has the potential to add value to the NHS.
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	In answer to each of the specific questions: These techniques are rarely used to treat acute fractures in patients with normal bone density and it would not be necessary to include this patient group.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		There are many manufacturers of injectable cement for vertebroplasty. Most are based on PMMA and have relatively minor differences in formulation, but other classes of cement, notably 'Cortoss' have been used. I would suggest limiting consideration to PMMA cements as the use of Cortoss cement is	At the scoping workshop, it was agreed that treating each type of cement as a separate technology would needlessly complicate the appraisal.

Section	Consultees	Comments	Action
		relatively limited. This varies greatly with individual practice and referral base. UK wide I would estimate c. 70% osteoporosis cases. Kyphoplasty is promoted by the manufacturers to give better results in patients with relatively recent fractures with angular deformity. I suspect it is most beneficial in fractures at the thoracolumbar junction as these are prone to progressive collapse and significant morbidity due to spinal deformity. The role of vertebral augmentation in patients with multiple myeloma may merit dedicated analysis. This patient group has a significant predisposition to multiple level fractures and there are suggestions that multilevel prophylactic treatment may be beneficial when spinal fractures start to occur.	Comments noted. Comments noted. It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
	NHS Quality Improvement Scotland (comment provided by NHS professional 2)	Traumatic fractures can be included if the patient also has osteoporosis	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in

Section	Consultees	Comments	Action
			a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		There is no evidence that results are significantly different using other bone cements and this might needlessly complicate the appraisal	At the scoping workshop, it was agreed that treating each type of cement as a separate technology would needlessly complicate the appraisal.
	Orthovita	1. All osteoporotic fractures are traumatic, the difference is that only very little trauma is enough for causation. 'Regular' traumatic fractures could be included in individual cases following team discussions, but not routinely.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		2. Most bone cements used are PMMA based, and thus slight variations on a single theme. Cortoss is a methacrylate based bioactive composite formulated for this indication, and in an FDA-IDE study it was shown that its effect on pain and function is equal or better than that of PMMA, and there were fewer new fractures following the application of Cortoss than after PMMA. Calcium Phospate based cements have been tried but thus far no formulation has been proven to be as effective as PMMA or Cortoss.	At the scoping workshop, it was agreed that treating each type of cement as a separate technology would needlessly complicate the appraisal.
		3.It is estimated that approximately 90% of the fractures that could be treated are caused by	Comment noted.

Section	Consultees	Comments	Action
		osteoporosis. 4. The populations that can be treated with vertebroplasty and kyphoplasty are largely the same. Kyphoplasty could be preferred for patients with fresh fractures and significant collapse (~ > 70%), vertebroplasty for patients with fresh fractures with little or no collapse. Older fractures are not expected to benefit much from kyphoplasty. 5. I'm not too familiar with the components that go into the QALY calculations, however, I think that costs incurred with the need for assistance that results from the pain or disability caused by the vertebral fractures should be included in the calculations. 6. There are many clinical articles that will be helpful for the Appraisal Committee to understand the benefits and limitations of the procedures.	Comments noted. The NICE Guide to the methods of technology appraisal stipulates that the reference-case perspective on costs is that of the NHS and personal social services. Therefore, additional assistance that is funded within these resources should be captured in assessing the cost effectiveness of the technologies. Productivity costs and costs borne by patients and carers that are not reimbursed by the NHS or PSS are not included. Comment noted. We anticipate that the Assessment Group and consultees will identify all relevant literature using systematic techniques and provide the Appraisal Committee with a quantitative and/or narrative synthesis of available evidence.
	Royal College of Physicians	2. "How should non-invasive management (without the use of either intervention) be defined?" We would recommend appropriate management of secondary osteoporotic fracture prevention according to NICE TAG 161. We believe that the	Comments noted. It will be for consultees and the Assessment Group to address this issue in the appraisal, to enable the Committee to reach conclusions on routine and best NHS practice.

Section	Consultees	Comments	Action
		general consensus would suggest that for the back pain a combination approach of pain relieving medication, posture advice, physiotherapy, education and other pain management approaches would be appropriate.	
		3. "Among fractures that would be considered suitable for vertebroplasty and/or kyphoplasty, what proportion are caused by osteoporosis, and what proportion are associated with other causes?" We are unsure why this question is posed given that the title of the scope is osteoporotic vertebral fractures. Osteoporotic vertebral fractures are completely different to vertebral fractures due to other causes, and must be considered separately. In the elderly, the vast majority of vertebral fractures are osteoporotic in origin.	Comments noted. It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		4. "Is the population in the scope defined appropriately? Do the populations considered for percutaneous vertebroplasty and balloon kyphoplasty differ?" We believe that length of time of back pain needs to be included here as the majority of people with new onset vertebral fractures become pain free within 6-8 weeks. These interventions should not be offered within this time frame. In terms of burden of disease, the much larger group are those people with long standing back pain and prevalent osteoporotic vertebral fractures	Following discussion at the scoping workshop, it was agreed that the scope should specify that subgroups defined by time between fracture and treatment should be considered in the appraisal if evidence allows.
Additional comments on	DePuy Spine /	Question 4) Caution should be exercised when using the primary diagnosis of procedures undertaken as a	Comment noted.

Section	Consultees	Comments	Action
the draft scope	Johnson & Johnson	proxy to indicate aetiology of this condition as this will be skewed by referral patterns in addition to natural incidence of various fracture morphologies.	
		Question 5) To our knowledge there are no differences in the patient population indicated for either vertebroplasty or kyphoplasty. However, the scope of the appraisal should be consistent with the most recent evidence, which suggests that patients with acute osteoporotic compression fractures are the most appropriate candidates for these modalities.	Comment noted.
		Question 6) In addition to acute VCF of osteoporotic origin, the population should include VCFs occurring due to benign lesions (e.g., haemangioma), malignant lesions, and multiple myeloma.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		Question 7) None that we are aware of.	Comment noted.
		Question 8) The technology underpinning first generation delivery systems and cement technologies has been available for many years and as such is unlikely to be described as innovative. However second- generation technologies, including those that employ high- viscosity cement are important innovations for the provision of	Comment noted.

Section	Consultees	Comments	Action
		vertebroplasty and kyphoplasty. Question 9) The debilitating pain arising from VCFs often limits tolerance for activities of daily living, and may impede the ability to live independently. Hence, this appraisal should seek to accurately reflect the cost and quality-of-life implications for caregivers of individuals with VCFs. We anticipate that the burden borne by caregivers for this population (e.g., working families, and community-based health professionals) is significant. Question 10) None.	The NICE Guide to the methods of technology appraisal stipulates that the reference-case perspective on outcomes should be all direct health effects, whether for patients or, when relevant, other people (principally carers). The NICE Guide to the methods of technology appraisal stipulates that the reference-case perspective on costs is that of the NHS and personal social services. Therefore, additional assistance that is funded within these resources should be captured in assessing the cost effectiveness of the technologies. Productivity costs and costs borne by patients and carers that are not reimbursed by the NHS or PSS are not included. Comment noted.
	NHS Quality Improvement Scotland (comment provided by NHS professional 1)	Regarding the questions for consultation 1. Inclusion of patients with traumatic vertebral fractures. See "Population" section. 2. Definition of non-invasive management. See "Comparators" section. 3. Consideration of different types of bone cements. There are approximately 10 commercially available bone cements used for vertebroplasty & kyphoplasty procedures in the UK. They are based on PMMA, calcium phosphate and ceramic formulations. Although competing manufacturers would claim superiority of their individual products it is unlikely that this can be proven apart from niche applications	Comments noted. At the scoping workshop, it was agreed that treating each cement as a separate technology would needlessly complicate the appraisal.

Section	Consultees	Comments	Action
		for the small minority of patients who may benefit from a resorbable cement e.g. calcium phosphate based cement for non-osteoporotic traumatic fractures. The UK Vertebroplasty Group Database has a relatively up-to-date list which I can provide if required. 4. Proportion of osteoporotic fractures vs others. I have no data regarding this on a national basis but in terms of referrals at my hospital I would estimate that 40% have primary or secondary osteoporosis, 40% have metastatic disease or myeloma and 20% have .osteoporosis but also have malignant disease without spinal metastases. 5. Population scope definition. No difference between vertebroplasty & kyphoplasty populations with the caveat mentioned in the "Population" section. 6. Subgroups who may benefit or should be examined separately. There are 2 main groups of patients who could benefit from vertebroplasty or kyphoplasty. a). Patients with metastatic spinal disease or myeloma with persistent pain after radiotherapy. or in whom radiotherapy is contraindicated b). Patients with impending malignant spinal cord compression without significant neurological complications.	Comments noted. Comments noted. It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		7. Discrimination & equality issues There are no specific discrimination issues on racial, ethnic or	Comments noted

Section	Consultees	Comments	Action
		other grounds. Equality issues do exist in Scotland in terms of "post code availability" of vertebroplasty & kyphoplasty The 3 remaining consultation questions have been addressed in previous sections.	
	Orthovita	Should people who have traumatic vertebral fractures also be included in the population for this scope? ABSOLUTELY YES. These are the people most affected by this procedure so they should have input. Patients who have BEEN treated should also have a voice here.	It was agreed at the scoping workshop that relatively few people with non-osteoporotic vertebral compression fractures receive percutaneous vertebroplasty or percutaneous balloon kyphoplasty, and the treatment pathways for these indications are quite different. Therefore, it was appropriate to limit the scope to osteoporotic vertebral compression fractures, as this would result in a focused appraisal that could be expected to provide guidance that will add value to the NHS.
		How should non-invasive management (without the use of either intervention) be defined? As conservative care with oral analgesics and bracing/rest.	Comment noted.
		Should different types of bone cement be considered? If so, which bone cements are routinely used in the UK for percutaneous vertebroplasty or balloon kyphoplasty procedures?	At the scoping workshop, it was agreed that treating each type of cement as a separate technology would needlessly complicate the appraisal.
		There are now many types of cement available for use in these procedures, but there are only two proven materials, Cortoss and PMMA. Theses are the two materials that should be appraised. Among fractures that would be considered suitable	Comments noted.

Section	Consultees	Comments	Action
		for vertebroplasty and/or kyphoplasty, what proportion are caused by osteoporosis, and what proportion are associated with other causes? 90% of fractures treated are caused by Osteoporosis. The remaining 10% can be attributable to other causes such as Metastatic disease. Is the population in the scope defined appropriately? Do the populations considered for percutaneous vertebroplasty and balloon kyphoplasty differ? Yes. For the majority of patients the treatments are the same, however as mentioned above, very fresh, severe fractures may gain greater benefit from a kyphoplasty procedure.	Comments noted. During consultation and at the scoping workshop, there was consensus that, for the purposes of an appraisal limited to osteoporotic vertebral compression fractures, it is appropriate to assume a single population with identical indications for percutaneous vertebroplasty and percutaneous balloon kyphoplasty.

Section	Consultees	Comments	Action
		Do you consider vertebroplasty and/or kyphoplasty to be innovative in their potential to make a significant and substantial impact on health-related benefits and how they might improve the way that current need is met (is this a 'step-change' in the management of the condition)?	Comments noted.
		Yes and the impact can be much greater if the patient selection is better defined to ensure that the correct patients are identified and treated quickly. Do you consider that the use of these technologies can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? Yes - the costs incurred with the need for assistance that results from the pain or disability caused by the vertebral fractures should be included in the calculations.	The NICE Guide to the methods of technology appraisal stipulates that the reference-case perspective on costs is that of the NHS and personal social services. Therefore, additional assistance that is funded within these resources should be captured in assessing the cost effectiveness of the technologies. Productivity costs and costs borne by patients and carers that are not reimbursed by the NHS or PSS are not included.
		Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits A brief selection of literature (more can be provided if desired): 1. A randomized trial of vertebroplasty for osteoporotic spinal fractures. NEJM 2009 vol. 361 (6) pp. 569-79 2. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. NEJM 2009 vol. 361 (6) pp. 557-68	Comment noted. We anticipate that the Assessment Group and consultees will identify all relevant literature using systematic techniques and provide the Appraisal Committee with a quantitative and/or narrative synthesis of available evidence.

Section	Consultees	Comments	Action
		3. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. Lancet on-line first August 2010 4. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. Lancet 2009 vol. 373 (9668) pp. 1016-24 5. The course of the acute vertebral body fragility fracture: its effect on pain, disability and quality of life during 12 months. Eur. Spine J. 2008 vol. 17 (10) pp. 1380-90 6. Percutaneous vertebroplasty for painful compression fractures in a small cohort of patients with a decreased expectation-related placebo effect due to dementia. AJNR 2008 vol. 29 (8) pp. 1461-4 7. Comparison of 5766 vertebral compression fractures treated with or without kyphoplasty CORR 2010 vol. 468 (7) pp. 1773-80 8. Long-term morbidity and mortality after a clinically diagnosed vertebral fracture in the elderly--a 12- and 22-year follow-up of 257 patients. Calcif Tissue Int.2005 vol. 76 (4) pp. 235-42 9. Local Anesthesia with Bupivacaine and Lidocaine for Vertebral Fracture Trial (LABEL): A Report of Outcomes and Comparison with the Investigational Vertebroplasty Efficacy and Safety Trial (INVEST). ANJR 2010 vol. 31 (9) pp. 1631-4 10. Age of fracture and clinical outcomes of percutaneous vertebroplasty. ANJR 2001 vol. 22	

Section	Consultees	Comments	Action
		(10) pp. 1860-3 11. Volume matters: a review of procedural details of two randomised controlled vertebroplasty trials of 2009. Eur Spine J. 2010 vol. 19 (11) pp. 1837-40 12. Percutaneous Vertebroplasty for Osteoporotic Vertebral Compression Fractures in the Nonagenarians: A Prospective Study Evaluating Pain Reduction and New Symptomatic Fracture Rate. Spine, ahead of print 2010	
	Pain Relief Foundation	We feel that a randomised multicentre trial looking at cement augmentation versus conservative treatment for osteoporotic fractures.	Comment noted.
	Royal College of Physicians	"Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits" There are recent RCTs which should be considered.	We anticipate that the Assessment Group and consultees will identify all relevant literature using systematic techniques and provide the Appraisal Committee with a quantitative and/or narrative synthesis of available evidence.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Department of Health
Public Health Wales NHS Trust
Royal College of Nursing
Stryker UK
Synthes GmbH
Welsh Government