NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for treating osteoporotic vertebral compression fractures

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD)

Definitions:

Consultees – Organisations that accept an invitation to participate in the appraisal including the manufacturer or sponsor of the technology, national professional organisations, national patient organisations, the Department of Health and the Welsh Assembly Government and relevant NHS organisations in England. Consultee organisations are invited to submit evidence and/or statements and respond to consultations. They are also have right to appeal against the Final Appraisal Determination (FAD). Consultee organisations representing patients/carers and professionals can nominate clinical specialists and patient experts to present their personal views to the Appraisal Committee.

Clinical specialists and patient experts – Nominated specialists/experts have the opportunity to make comments on the ACD separately from the organisations that nominated them. They do not have the right of appeal against the FAD other than through the nominating organisation.

Commentators – Organisations that engage in the appraisal process but that are not asked to prepare an evidence submission or statement. They are invited to respond to consultations but, unlike consultees, they do not have the right of appeal against the FAD. These organisations include manufacturers of comparator technologies, NHS Quality Improvement Scotland, the relevant National Collaborating Centre (a group commissioned by the Institute to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups (for example, the NHS Confederation, NHS Information Authority and NHS Purchasing and Supplies Agency, and the *British National Formulary*).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but may be summarised by the Institute secretariat – for example when many letters, emails and web site comments are received and recurring themes can be identified.

Comments received from consultees

Consultee	Comment	Response
British Association of Spine Surgeons	• Overall we are in agreement with conclusions but it is important to state that whilst Operative Placebo Local Anaesthesia (OPLA) –may alleviate pain, as part of the optimal pain management described in point 1.1 of the appraisal committee's preliminary recommendations, in the short term, but will not treat any progressive vertebral collapse. There are quite a few critique papers published on the RCTs analysed. Their analysis highlights the two issues below as well as controversy about optimal timing. The major problem is that the dose of cement is not stated in one study, and is inconsistent in the other. No drug trial (eg hypertension, chemootherapy, antibiotics etc) would be accepted for publication with this fairly major flaw. It is also compounded by the fact that the placebo OPLA was not standardised for exact anatomical location. This was highlighted by one of your health economists in a personal communication with one of the senior authors. Higher quality studies with these problems addressed are needed. We still have a lot to learn about this technique. Also the technology is evolving in terms of cement viscosity and delivery systems. For NICE there is a moving target!	Comment noted. The Committee agreed that operative placebo could not be considered established clinical practice for the majority of the patients, and that although operative placebo which included local anaesthesia may itself reduce pain, it is not intended to treat any progressive vertebral collapse (for further details see FAD section 4.3.4). Although the Committee was aware that results from the double-blind Buchbinder and INVEST trials did not show statistically significant improvements in clinically relevant outcomes, it noted that the open-label studies comparing vertebroplasty or kyphoplasty with optimal pain management showed improvement in pain following intervention. The Committee considered that the open-label trials better reflected 'real life' and included the comparator that would be used in clinical practice. The Committee concluded that it could not disregard the results from the open-label trials, and was persuaded that there was sufficient evidence to conclude that vertebroplasty and kyphoplasty are more effective in reducing pain and restoring vertebral body height than optimal pain management in people with recent, painful osteoporotic vertebral compression fractures (for further details see FAD sections 4.3.4 and 4.3.5).
	• I think it is not appropriate to mention specific manufacturers in NICE guidance - 3.2 and 3.4 and 3.5. There are also many other techniques evolving which vary in nuances - e.g. osseofix, Dfine etc..	The manufacturers listed in section 3 of the FAD are those that have participated in the appraisal process, as is standard in NICE Guidance. The FAD has been amended to indicate that alternative cements for use in kyphoplasty are

Consultee	Comment	Response
British Association of Spine Surgeons (cont.)	I assume this is for this document only and not for the final guidance. CPC - CPC is by no means to be considered a standard alternative. Biomechanics are sketchy as are clinical results. Probably only suitable when MRI verifies no endplate lesion. Adverse reactions: when balloons rupture contrast is set free - this can theoretically be of concern in patients with hyperthyroidism. The Buchbinder and Kallmes trials are simply invalid - allthough this seems a ridiculous claim to make, it is based in fact as the cement volume was not recored in the Kallmes trial and is documented to be insufficient in the Buchbinder trial - see Boszczyk Volume matters ESJ 2010 – attached Simple vertebroplasty can be done for under £500 per level using standard Jamshidi needles and a pack of confidence. This may not be the technically most advanced way of doing this but it places the dedicated systems into perspective. What does make sense is the radiation reducing systems such as DFine which reduce patients and operator radiation. • We agree with many of the points in the guidance. I have one major issue. In Ipswich we see a lot of elderly patients who are treated for back pain in the community by the GP. They reach us many months down the line with pain that is not improving. An MRI scan is then performed 6-9 months after the original injury. This scan often shows oedema on the scan at the level of the fracture. In our experience these patients then benefit from a procedure at this later stage. These patients do not appear to be covered in any way by the above. Please consider this in your formal review	available, without specifying these cements – see FAD section 3.4. In section 4.3.7 of the FAD, the Committee noted that adverse reactions from vertebroplasty and kyphoplasty relate primarily to cement leakage, particularly for vertebroplasty, and that these were manageable. No evidence was available to the Committee on the risk of balloon rupture in people with hyperthyroidism. Comment noted. NICE is bound by the remit of the appraisal. For this appraisal, the remit is to appraise the clinical and cost effectiveness of percutaneous vertebroplasty and percutaneous balloon kyphoplasty (with or without vertebral body stenting) for the treatment of osteoporotic vertebral fractures. Following consultation, the Committee discussed the impact of stipulating a specific time period in which to undergo the procedures. The Committee considered that a key factor in determining the timing of vertebroplasty and kyphoplasty was whether the fracture remained unhealed and whether it caused the ongoing pain. While the Committee appreciated the complexities in offering vertebroplasty and kyphoplasty too early (before

Consultee	Comment	Response
		natural healing has resulted in pain relief) or too late (when there is little chance of restoring vertebral height), it concluded that the appropriate timing in relation to the age of the fracture could be left for clinicians to judge. Please see section 4.3.3 of the FAD for further detail.
British Pain Society	• Yes. I feel that they have taken into account all of the most important evidence. • I do no feel qualified to question the cost-effectiveness data, although my understanding from reading the paper is that they have come to a reasonable conclusion. With regard to the clinical data, I feel that although generally they have come to a reasonable conclusion, I question why they have set a limit of acute fracture less than 6 weeks old. Many of the papers do not put such a time limit, and, in fact, the 2 double blind placebo studies (Buckbinder & INVEST) allowed patients with fractures up to 12 months old. I would agree with their view that kyphoplasty is most useful in relatively recent fractures, but feel that the time that vertebroplasty should be considered needs to be extended, particularly if there is MRI evidence of non-healing of the fracture. • Apart from my comments above, I feel that the recommendations are sound • I do not feel that there are any aspects of the recommendations that need particular consideration.	Following consultation, the Committee discussed the impact of stipulating a specific time period in which to undergo the procedures. The Committee considered that a key factor in determining the timing of vertebroplasty and kyphoplasty was whether the fracture remained unhealed and whether it caused the ongoing pain. While the Committee appreciated the complexities in offering vertebroplasty and kyphoplasty too early (before natural healing has resulted in pain relief) or too late (when there is little chance of restoring vertebral height), it concluded that the appropriate timing in relation to the age of the fracture could be left for clinicians to judge. Please see section 4.3.3 of the FAD for further detail.
Department of Health	No substantive comments to make, regarding this consultation.	Comment noted, no changes required.

Consultee	Comment	Response
Johnson & Johnson	**1. Has all of the relevant evidence been taken into account?** We agree the committee considered all the relevant evidence and this is clearly reflected in the provisional recommendations. **2. Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?** We consider the summaries of clinical and cost effectiveness to be reasonable interpretations of the evidence. **3. Are the provisional recommendations sound and a suitable basis for guidance to the NHS?** We are in agreement with the provisional recommendations; however we seek clarification of one point in section 1.1: *"Percutaneous vertebroplasty and percutaneous balloon kyphoplasty are recommended as options for treating osteoporotic vertebral compression fractures only in people who have severe ongoing pain after a recent vertebral fracture (within 6 weeks) despite optimal pain management"* To add clarity to the NHS we recommend section 1.1 is slightly amended regarding the 6 week statement. It is assumed this 6 weeks period stated in section 1.1 refers to the period of time that the specified patient population has had ongoing and severe pain following a recent vertebral fracture. We would be concerned if this referred to the time window in which treatment should occur as it would be a significant challenge for treatment to be carried within six weeks given the current infrastructure in the NHS. The result could be guidance which is not applicable or implementable within the NHS context.	Following consultation, the Committee discussed the impact of stipulating a specific time period in which to undergo the procedures. The Committee considered that a key factor in determining the timing of vertebroplasty and kyphoplasty was whether the fracture remained unhealed and whether it caused the ongoing pain. While the Committee appreciated the complexities in offering vertebroplasty and kyphoplasty too early (before natural healing has resulted in pain relief) or too late (when there is little chance of restoring vertebral height), it concluded that the appropriate timing in relation to the age of the fracture could be left for clinicians to judge. Please see section 4.3.3 of the FAD for further detail.
Medtronic	**Key conclusions** • *Page 3: Percutaneous balloon kyphoplasty (without stenting) and Percutanteous vertebroplasty recommended only for OVCF people who:* – *have severe ongoing pain after a recent vertebral fracture (within 6 weeks) despite optimal pain management and* – *in whom the pain has been confirmed to be at the level of the fracture (by physical examination and imaging).* Medtronic suggests to further clarify AC's recommendation by substituting "percutaneous balloon kyphoplasty" with "Percutaneous balloon kyphoplasty	Comment noted. Section 2.3 of the FAD indicates that 'percutaneous balloon kyphoplasty without stenting' will be referred to as 'kyphoplasty'

Consultee	Comment	Response
Medtronic (cont.)	(without stenting)". This aims to ensure consistency with AC's recommendation in section 3.3 of the ACD, where the technology is featured as above and confirms which technology the body of evidence refers to. Therefore, Medtronic will refer to kyphoplasty as percutaneous balloon kyphoplasty (without stenting). **The technology** • *Page 44: "no specific claim of innovation was made"* • *3.3. Page 5: Kyphoplasty (without stenting) is a variation of vertebroplasty* Percutaneous balloon kyphoplasty (without stenting) should not be considered as a variation of percutaneous vertebroplasty. It is best referred to as a relevant incremental innovation. The innovative step of using the balloon to induce spinal realignment with angular correction, coupled with pain relief is specific to Percutaneous Balloon Kyphoplasty (without stenting). Furthermore, balloon cavity creation and crushed trabecular bone border coupled with low pressure cement injection minimises the risk of the cement leakage. This step is related to the "improvement in biomechanical factors after treatment" referred by the AG as a possibility for the mortality benefit. In fact, according to the *academic-in-confidence* evidence submitted along with comments to the AG report (Supplementary references, Edidin 2012 morbidity), a credible biological plausibility for the mortality benefit is emerging, consistent with hypothesis from clinical specialists heard by the committee. While Medtronic agrees there may still be unobserved, uncontrolled confounding, these relative differences in morbidity risks contribute to understanding the mortality risk differences, which are best explained by the surgical approach. In summary, Medtronic requests the technology description is corrected for the final appraisal document, to percutaneous balloon kyphoplasty (without stenting) and without stating this technology is a variation of vertebroplasty. • *3.4 Page 5: Kyphon Percutaneous Balloon Kyphoplasty (without stenting) kit (Medtronic) is available in the UK for kyphoplasty (…)* Medtronic would like to clarify that Kyphon ActivOs cement is not part of the Kyphopak (single use sterile pack), but rather supplied as a separate component.	throughout the document. In addition, the Guidance in section 1.1 of the FAD specifically refers to 'percutaneous balloon kyphoplasty without stenting'. The FAD has been amended to reflect this – see FAD section 3.3. The FAD has been amended to reflect this – see FAD section 3.4.

Consultee	Comment	Response
Medtronic (cont.)	**Adverse Reactions** • *3.7 Page 6; 4.3.7 page 39:* *Adverse reactions from vertebroplasty and kyphoplasty relate primarily to cement leakage, particularly for vertebroplasty. The Committee concluded that cement leakage associated with vertebroplasty and kyphoplasty was manageable if a skilled clinician with specialised training in these procedures performs the operation.* *In addition, the balloon can rupture in kyphoplasty which can result in the retention of balloon fragments within the vertebral body.* Medtronic would further reinforce that cement leakages of clinical relevance can be minimised by choosing higher viscous cements, creating a cavity and crushed trabecular bone border. With respect to the reference made to risk of balloon rupture (4.3.7), Medtronic would like to report a complaint ratio of .54% and an adverse event ratio of .011%, specific to their Kyphon Balloon (from our internal report system - March 2007 to November 2012). **Evidence for clinical effectiveness – Availability, nature and quality of evidence** • *4.1.2 Page 7:* *The FREE study included less than 80% of randomised patients in its final analysis, had an imbalance in drop-outs by treatment arm, and reported outcomes selectively.* *The Blasco, FREE and VERTOS II trials had substantial numbers of patients crossing over (changing treatment arms).* Concerning the largest RCT submitted as evidence of percutaneous balloon kyphoplasty (without stenting) compared to optimal pain management (FREE study), further explanation seems warranted as well as highlighting inaccuracies in the ACD:	The Committee was aware that, to reduce cement leakage and its complications, high-viscosity cements have been developed as an alternative to low-viscosity cements. The FAD has been amended to reflect this – see FAD section 3.7. The FAD has been amended to reflect the comment about cross-over in the FREE study – see FAD section 4.1.2.

Consultee	Comment	Response
Medtronic (cont.)	78% follow-up at 12-months and 77% at 24-months is anticipated for this elderly patient population. Contrary to statement that outcomes were reported selectively, all primary and secondary outcomes per study protocol were reported in the following papers for publication: – "FREE 1 year results" (Wardlaw, Lancet 2009), – "FREE 2 year results" (Boonen, JBMR 2011) and – "FREE surgical" (van Meirhaeghe 2012, in peer-review process, submitted to AC by Medtronic along with comments to AG report, under "supplementary refs" as academic in confidence) Cross-over in FREE study was less than 10% and an intent to treat analysis was conducted leaving them in the control arm. **Mortality benefit** • *4.3.5 page 37: Mortality data available from a large study based on US Medicare registry data that followed patients for up to 4 years indicated a statistically significant mortality benefit with narrow confidence intervals, with both vertebroplasty and kyphoplasty compared with optimal pain management. The Committee noted these results, which were substantiated by 5 year mortality data from the Medicare registry as well as mortality data from a smaller German study.* • *4.1.21 Page 17; 4.3.2 Page 35: The Assessment Group stated that, apart from the possibility of uncontrolled confounding, these studies raise the possibility that improvement in biomechanical factors after treatment improves survival* Further to the AG comment on the possibility that improvement in biomechanical factors after treatment improves survival, please refer to Medtronic's comment above, relating to section 3.3. of the ACD.	Comment noted, no changes required.
National Osteoporosis Society	**1. Has all of the relevant evidence been taken into account?** • We are not aware of any relevant evidence that has not been taken into account. **2. Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?** • We feel that the interpretation of clinical and cost effectiveness are	

Consultee	Comment	Response
National Osteoporosis Society (cont.)	reasonable. **3. Are the provisional recommendations sound and a suitable basis for guidance to the NHS?** • The National Osteoporosis Society supports the recommendations on the use of percutaneous vertebroplasty and percutaneous balloon kyphoplasty in patients with osteoporosis. • However the proposed time frame gives us cause for concern. – Given inherent delays in referral we feel it is unlikely that patients will make it from presentation in primary care, through a trial of optimum analgesia, subsequent referral to secondary care for assessment, imaging and re-referral for intervention within 6 weeks. – Throughout this 6 week window patients must be given time to consider the options available to them and make a considered decision about treatment. – Of additional concern is that patients may be fast-tracked, because of the time pressures, without proper trial of optimal analgesia. – In practice the proposed guidance means percutaneous vertebroplasty and percutaneous balloon kyphoplasty will be a realistic option only for those minority of patients admitted to hospital with acute vertebral fracture. • We would like further consideration to be given to a 12 week window, based on – The practical considerations outlined above. – The evidence from the open label trials where many of these studies had inclusion criteria greater than 6 weeks. – Current practice which considers the procedures as treatment options in patients with fractures at least up to 12 weeks (also see comment p515 "…given by the AG's clinical advisor that vertebral augmentation is typically performed around 3 months after the VCF…"). • There is a lack of clarity within the document on what constitutes optimal pain management and how it should be achieved. From p6 of the ACD 'The Assessment Group adopted the term 'optimal pain management' to encompass comparator treatments in the trials that consisted of optimising pain medication, treating conservatively, or management without surgery.' – It is important for patients to have a clear understanding of what they	Following consultation, the Committee discussed the impact of stipulating a specific time period in which to undergo the procedures. The Committee considered that a key factor in determining the timing of vertebroplasty and kyphoplasty was whether the fracture remained unhealed and whether it caused the ongoing pain. While the Committee appreciated the complexities in offering vertebroplasty and kyphoplasty too early (before natural healing has resulted in pain relief) or too late (when there is little chance of restoring vertebral height), it concluded that the appropriate timing in relation to the age of the fracture could be left for clinicians to judge. Please see section 4.3.3 of the FAD for further detail. Following consultation, the Committee discussed whether 'optimal pain management' should be more specifically defined. The Committee considered that, because optimal pain management encompasses a broad array of treatments, and it means clinicians individualise therapies, it would be beyond the Committee's remit to define optimal

Consultee	Comment	Response
National Osteoporosis Society (cont.)	can expect to receive as part of optimal pain management. – There are implications for services as achieving optimal pain management will result in greater referral rates into pain management services. – Potentially relevant guidance on management of back pain (CG88 Low back pain: Early management of persistent non-specific low back pain) specifically excludes back pain from fractures. **4. Are there any aspects of the recommendations that need particular consideration to ensure that we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?** • We are not aware of any such issues. We would like to see the following NICE guidance included in the section on related NICE guidance. • Osteoporosis: assessing the risk of fragility fracture CG146 • Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women TA160 • Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women TA161 • Denosumab for the prevention of osteoporotic fractures in postmenopausal women TA204	pain management. Please see section 4.3.3 of the FAD for further detail. Comment noted. The suggested guidance documents relate to the prevention and risk assessment of fragility fractures rather than the treatment of painful osteoporotic vertebral compression fractures. They have therefore not been included under related NICE guidance.
Royal College of Nursing	There are no further comments to submit at this stage.	Comment noted, no changes required.

Comments received from commentators

Commentator	Comment	Response
Healthcare Improvement Scotland	**1. Do you consider that all the relevant evidence has been taken into account? *If not, what evidence do you consider has been omitted, and what are the implications of this omission on the results?*** This comprehensive review appears to have taken account of all available	Comment noted, no changes required.

Commentator	Comment	Response
Healthcare Improvement Scotland (cont.)	evidence together with a sober assessment of its likely significance. **2. Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence? *If not, in which areas do you consider that the summaries are not reasonable interpretations*?** The summaries of clinical effectiveness are reasonable and rightly refer to the deficiencies in the evidence currently available. The summaries of cost effectiveness detail several models and the assumptions on which the analyses are based. These also appear reasonable **3. Are the provisional recommendations of the Appraisal Committee sound and do they constitute a suitable basis for the preparation of guidance to the NHS? *If not, why do you consider that the recommendations are not sound?*** The provisional recommendations are sound and provide a good basis for guidance. **4. Are the patient pathways and treatment options described in the assessment applicable to NHSScotland? *If not, how do they differ in Scotland?*** These are equally applicable to NHSScotland. **5. Would the provisional recommendations change the patient pathways and/or patient numbers in NHSScotland? *If so, please describe what these changes would be.*** Currently the few patients referred for vertebroplasty or kyphoplasty in Scotland have frequently been suffering pain for more than 6 months. Implementation of this guidance would mandate a patient pathway which would allow patients to be identified, assessed by suitable clinicians, imaged and treated within 6 weeks. This would require an education campaign aimed at GPs and hospital doctors, and the setting up of multidisciplinary teams involving some or all of bone metabolism physicians, pain anaesthetists, orthopaedic surgeons and interventional radiologists. Funding for imaging and for the procedures, and access to hospital beds will also be needed. **6. Do you think there is any reason why this provisional guidance would not be as valid in Scotland as it is in England and Wales? *If yes, please explain why this is the case.*** No. **7. Please add any other information which you think would be useful to NICE**	Following consultation, the Committee discussed the impact of stipulating a specific time period in which to undergo the procedures. The Committee considered that a key factor in determining the timing of vertebroplasty and kyphoplasty was whether the fracture remained unhealed and whether it caused the ongoing pain. While the Committee appreciated the complexities in offering vertebroplasty and kyphoplasty too early (before natural healing has resulted in pain relief) or too late (when there is little chance of restoring vertebral height), it concluded that the appropriate timing in relation to the age of the fracture could be left for clinicians to judge. Please see section 4.3.3 of the FAD for further detail.

Commentator	Comment	Response
Healthcare Improvement Scotland (cont.)	**or helpful in guiding the Scottish response to this assessment** Clinicians with experience of these techniques know that they can be very effective in reducing pain and improving quality of life. However NICE is correct in identifying that achieving good results is dependent on identifying and treating patients within a tight timescale, and their suggestion of 6 weeks is reasonable. There is a large number of these patients spread around all areas of the country. The minimum requirements for providing access to a satisfactory service are summarised at 5.above. This will need significant commitment and investment to realise. ***Additional Comments:*** **1. Do you consider that all the relevant evidence has been taken into account? *If not, what evidence do you consider has been omitted, and what are the implications of this omission on the results?*** YES **2. Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence? *If not, in which areas do you consider that the summaries are not reasonable interpretations*?** No. I do not think the summary of cost effectiveness is accurate since the blinded (sham procedure controlled) evaluations of vertebroplasty showed no benefit of the intervention and by the same token (through network meta-analysis) kyphoplasty can also not be considered to be superior to a sham procedure. To advise use of a procedure in the NHS where there is a clear risk of adverse effects with no evidence of benefit over a sham procedure cannot be supported in my view. If this was a drug treatment it would not and could not be approved. **3. Are the provisional recommendations of the Appraisal Committee sound and do they constitute a suitable basis for the preparation of guidance to the NHS? *If not, why do you consider that the recommendations are not sound?*** No. The recommendations are not evidence based for the reasons outlined above. Further research need to be done to clarify the role of these procedures. **4. Are the patient pathways and treatment options described in the assessment applicable to NHSScotland? *If not, how do they differ in Scotland?***	Ahough the Committee was aware that results from the double-blind Buchbinder and INVEST trials did not show statistically significant improvements in clinically relevant outcomes, it noted that the open-label studies comparing vertebroplasty or kyphoplasty with optimal pain management showed improvement in pain following intervention. The Committee considered that the open-label trials better reflected 'real life' and included the comparator that would be used in clinical practice. The Committee concluded that it could not disregard the results from the open-label trials, and was persuaded that there was sufficient evidence to conclude that vertebroplasty and kyphoplasty are more effective in reducing pain and restoring vertebral body height than optimal pain management in people with recent, painful osteoporotic vertebral compression fractures (for

Commentator	Comment	Response
Healthcare Improvement Scotland (cont.)	Yes **5. Would the provisional recommendations change the patient pathways and/or patient numbers in NHSScotland? *If so, please describe what these changes would be.*** Possibly – they might lead to an increase in demand for VP or KP which would have cost implications **6. Do you think there is any reason why this provisional guidance would not be as valid in Scotland as it is in England and Wales? *If yes, please explain why this is the case.*** No	further details see FAD sections 4.3.4 and 4.3.5). The Committee also considered the adverse reactions from vertebroplasty and kyphoplasty, and noted that they relate primarily to cement leakage, particularly for vertebroplasty. The Committee concluded that cement leakage associated with vertebroplasty and kyphoplasty was manageable if a skilled clinician with specialised training in these procedures performs the operation. Please see section 4.3.7 of the FAD for further detail.

Comments received from members of the public

Role*	Section	Comment	Response
Other – Policy Lead, British Society for Rheumatology	1	"The current appraisal is extremely thorough and inclusive of all relevant published literature on the techniques. The summary reflects published findings and consensus clinical opinion quite well. The BSR would be concerned that there is proposed limitation of access to the procedure, as advised by NICE, to within 6 weeks of the fracture'. Firstly, as indeed the document notes, there is weak evidence for such a stipulation on timing for intervention, and secondly the advice does not reflect the reality of clinical management where often patients present a late to clinicians, and may be delayed before 'optimal' pain management can be implemented, reviewed and changed accordingly (realistically a number of times ie to optimum). To accommodate the '6-week rule' the general approach to assessment of acute back pain will need to be addressed ' imaging early, changes in referral triage processes all with implications for established clinical management pathways. To accommodate fast-track referral and assessment there may be extra cost. More pragmatic (and in keeping with the uncertainty in terms of reported optimum time to intervention) would be to relax the time to intervention by rewording to 'up to 3 months' perhaps then indirectly ensuring specialist assessment, enough time to optimise pain control, triage of non-fracture cases and the input of an experienced assessor who would conclude pain is arising directly from the relevant vertebral fracture and not elsewhere. It is in NICE's interests to accommodate specialist assessment given that is the evidence base - ie patients in the studies reviewed, were all assessed by specialists! These comments would not apply if efficacy and/or cost-efficacy was robustly disproved for the time to intervention from fracture onset to procedure of >6 weeks to <3 months."	Following consultation, the Committee discussed the impact of stipulating a specific time period in which to undergo the procedures. The Committee considered that a key factor in determining the timing of vertebroplasty and kyphoplasty was whether the fracture remained unhealed and whether it caused the ongoing pain. While the Committee appreciated the complexities in offering vertebroplasty and kyphoplasty too early (before natural healing has resulted in pain relief) or too late (when there is little chance of restoring vertebral height), it concluded that the appropriate timing in relation to the age of the fracture could be left for clinicians to judge. Please see section 4.3.3 of the FAD for further detail.
NHS Professional	1	On balance I am happy/in support of the overall recommendations and content of the ACD	Comment noted, no changes required.

* When comments are submitted via the Institute's web site, individuals are asked to identify their role by choosing from a list as follows: 'patent', 'carer', 'general public', 'health professional (within NHS)', 'health professional (private sector)', 'healthcare industry (pharmaceutical)', 'healthcare industry'(other)', 'local government professional' or, if none of these categories apply, 'other' with a separate box to enter a description.

Role*	Section	Comment	Response
NHS Professional (cont.)	5	"It is important that clarification is provided as to Operative Placebo Local Anaesthesia (OPLA). This procedure may alleviate pain, as part of the optimal pain management described in point 1.1 of the appraisal committee's preliminary recommendations, in the short term, but will not treat any progressive vertebral collapse/stablise vertebral body bone/micro movement. This procedure is more likely to be used downstream - for patients who have not had cement augmentation, and, as a result have persistent/chronic pain post fracture healing (sometimes in a deformed state). Based on my knowledge of the mortality database and NHS clinical experience, I am supportive of the assumption regarding incremental mortality gain cited in the ACD for patients treated with cement augmentation."	Comment noted. The Committee agreed that operative placebo could not be considered established clinical practice for the majority of the patients, and that although operative placebo which included local anaesthesia may itself reduce pain, it is not intended to treat any progressive vertebral collapse (for further details see FAD section 4.3.4).
Private Sector Professional	1	There should not be a limit to acute fractures. There is ample evidence that even chronic painful fractures benefit from treatment. 1. Syed MI, Shaikh A. Does Age of Fracture Affect the Outcome of Vertebroplasty? Results from Data from a Prospective Multicenter FDA IDE Study. J Vasc Interv Radiol 2012; 23.1416-1422. 2. Brown DB, et al. Treatment of Chronic Symptomatic Vertebral Compression Fractures with Percutaneous Vertebroplasty. AJR:182;319-322. There is also evidence that VCF's may continue to be painful despite conservative treatment 1. Suzuki N, et al. The course of the acute vertebral body fragility fracture: its affect on pain, disability and quality of life during 12 months. Eur Spine J. 2008;17(10):1380-90.	Following consultation, the Committee discussed the impact of stipulating a specific time period in which to undergo the procedures. The Committee considered that a key factor in determining the timing of vertebroplasty and kyphoplasty was whether the fracture remained unhealed and whether it caused the ongoing pain. While the Committee appreciated the complexities in offering vertebroplasty and kyphoplasty too early (before natural healing has resulted in pain relief) or too late (when there is little chance of restoring vertebral height), it concluded that the appropriate timing in relation to the age of the fracture could be left for clinicians to judge. Please see section 4.3.3 of the FAD for further detail.

Role*	Section	Comment	Response
Private Sector Professional (cont.)	2	Vertebroplasty should not be limited to patients who have failed conservative treatment. There is ample evidence that conservative therapy increases the risk of mortality in some patients. In the first longitudinal, population-based comparison of mortality risk between surgical and nonsurgical groups, a Medicare dataset from 2005 to 2008 containing 858,978 patients with vertebral compression fractures was analyzed (36). This included 119,253 patients treated with BKP, 63,693 patients treated with VP and the remainder treated with NSM. The findings at the 4 year follow-up showed that the VA treatment group was 37% less likely to die than the NSM group and that the adjusted life expectancy was 85% greater for the VA group. The adjusted life expectancy for the BKP was greater for that of VP and was increased 115% compared to the NSM group. Overall the median life expectancy was increased between 2.2 and 7.3 years across all treated groups as compared with nonsurgical management. 1. 36. Edidin A, et al. Mortality Risk for Operated and Non-Operated Vertbral Fracture Patients in the Medicare Population. JBMR, 2011: Feb 9. DOI: 10.1002/jbmr.353	The Committee heard that vertebroplasty and kyphoplasty are considered as treatment options in patients with recent vertebral fractures who have pain at the level of the fracture (confirmed by physical examination and magnetic resonance imaging) that is ongoing, severe, and does not respond to optimal pain management. The Committee heard that this was because, for many people, the severity of the pain will decline after 2 to 3 weeks and many people will be free of pain in 6 weeks, in line with the natural history of the condition (for further details see FAD section 4.3.3).