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Information
and Quality
Authority**

An tÚdarás Um Fhaisnéis
agus Cáilíocht Sláinte

Health Technology Assessment of Scheduled Procedures

Vertebroplasty and kyphoplasty for osteoporotic vertebral compression fractures

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Safer Better Care

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1 Vertebroplasty and kyphoplasty for osteoporotic vertebral compression fractures

1.1 Scope of this health technology assessment

This health technology assessment (HTA) evaluates the appropriateness and potential impact of introducing clinical referral and treatment thresholds for vertebroplasty and kyphoplasty, two routine scheduled procedures within the publicly-funded healthcare system in Ireland. The effectiveness of these procedures may be limited unless undertaken within strict clinical criteria. This report is one of a series of HTAs of scheduled procedures. Details of the background to the request for the assessments from the Director General of the Health Service Executive (HSE), Mr Tony O'Brien, and the general methodology are included in the separate 'Background and Methods' document.⁽¹⁾

The scope of this HTA is to recommend clinical referral and treatment thresholds to be used in the assessment, referral and management of patients for whom vertebroplasty or kyphoplasty is being considered. Input from an expert advisory group in addition to a review of international guidelines, international policy documents and thresholds, and economic evaluations were used to inform the referral criteria. Additionally the resource and budget impact were assessed where appropriate.

1.2 Procedure indications

Vertebral compression fracture (VCF)* refers to a break in any of the bones (vertebrae) of the spinal column. It usually occurs when the front of the vertebral body collapses, and may be caused by osteoporosis, cancer or trauma.⁽²⁾ Most VCFs are caused by bone fragility associated with osteoporosis.⁽³⁾ It is estimated that approximately 300,000 people in Ireland have osteoporosis.^(4;5) It is also estimated that approximately four million osteoporotic fractures occur each year in Europe and that the numbers are increasing.⁽⁵⁾ In Ireland, it is reported that the absolute numbers of all osteoporotic-type fractures increased by 12% in females and by 15% in males between 2000 and 2009.⁽⁶⁾ Osteoporotic VCFs can cause the spine to curve and lose height, and can result in pain, difficulties in breathing, gastrointestinal problems, sleep disturbances and difficulties in performing activities of daily living.⁽²⁾ VCF secondary to osteoporosis is a cause of substantial morbidity in older adults⁽⁷⁾ with approximately one in four adults over the age of 50 years affected.⁽⁸⁾ It can

*A VCF is a type of stress fracture which results from normal stresses on abnormal bone, also known as an 'insufficiency fracture'.

affect both genders, but is more common among elderly females. Fractures can occur as a result of a fall or a minor trauma or during a simple activity such as picking up an object.⁽⁷⁾ Risk factors include age, low body mass index, smoking, alcohol misuse, family history, prolonged use of corticosteroids, and chronic illness.⁽⁸⁾ Although common, most osteoporotic VCFs are asymptomatic or result in minimal pain, with only approximately a third resulting in medical attention and being clinically diagnosed. Acute painful osteoporotic VCFs generally heal quickly⁽⁹⁾ with spontaneous resolution of pain; however, they may result in persistent severe, disabling back pain, marked reduction in mobility and, rarely, neurological deficit.⁽¹⁰⁾

1.3 Procedures, potential complications and alternative treatments

Treating VCF aims to restore mobility, reduce pain and minimise the incidence of new fractures.⁽²⁾ Non-invasive treatments (such as pain medication, bed rest, and back braces) focus on alleviating symptoms and supporting the spine.⁽²⁾ Lifestyle changes, hormone replacement therapy, and bisphosphonates have also been used.⁽⁸⁾ Open surgical decompression and fusion may be considered in a minority of patients (<2%) who present with VCF-associated neurological deficit.⁽¹⁰⁾ Percutaneous vertebroplasty (hereafter referred to as vertebroplasty or PVP) and percutaneous balloon kyphoplasty without stenting (hereafter referred to as kyphoplasty) are minimally invasive surgical procedures that involve injection of a cement-like material (polymethylmethacrylate, PMMA), under fluoroscopic guidance, into the vertebral body to stabilise and strengthen collapsed or crushed bone.⁽⁸⁾ In kyphoplasty, a cavity is created by first inflating a balloon in the vertebral body until its normal height is restored or the balloon reaches its maximum volume. Once inflated, the space is filled with cement. As a more recent innovation, a metal stent may be inserted into the vertebral cavity to prevent the vertebra from losing height after the balloon is deflated. Evidence to support stenting is as yet limited, therefore this HTA relates to balloon kyphoplasty without stenting.⁽²⁾

Vertebroplasty and kyphoplasty aim to alleviate pain caused by VCF and to stabilise the bone, preventing future fractures. In addition, kyphoplasty aims to reduce the curvature of the spine, preventing spinal deformity.⁽²⁾ Vertebroplasty may be undertaken in a day case setting under conscious sedation,⁽¹¹⁾ though general anaesthesia may be required in lengthy cases where there are multiple levels of vertebral fracture and where patients are unable to tolerate lying prone for several hours; kyphoplasty typically requires general anaesthesia and hospital admission.^(12;13) It is recommended that the procedure is undertaken by trained spine surgeons, interventional radiologists or anaesthetists in a sterile environment where there is access to general anaesthesia or surgical decompression if required.^(2;14) Vertebroplasty and kyphoplasty are typically considered as treatment options in

patients with recent vertebral fractures (duration of six weeks or longer) who have persistent, severe disabling back pain, marked reduction in mobility and quality of life. Access to vertebroplasty/kyphoplasty should be within an appropriate timeframe, prior to fracture healing when there is still an opportunity to restore vertebral height.^(2;10;15)

Adverse reactions can occur due to needle insertion and include local or systemic infection, bleeding and damage to neural or other structures.^(2;16) While several bone cements are approved for use in vertebroplasty and kyphoplasty, complications can occur with their use and alerts have been issued by a number of national agencies, including the US Food and Drug Administration (FDA), UK Medicines and Healthcare products Regulatory Agency (MHRA) and Health Canada in response to reports of cement leakage during vertebroplasty and kyphoplasty.^(2;13;17-19) These alerts have included cautions regarding the 'off-label'[†] use of bone cements,^(2;13;17-19) as well as specific safety recommendations regarding the importance of patient monitoring during procedures, the increased risk of adverse reaction to bone cement if more than three vertebral levels are treated in one procedure, and the risk of cement leakage in patients undergoing vertebroplasty or kyphoplasty for traumatic burst fractures with disruption of the posterior vertebral body.⁽¹⁷⁾

In 2013, the National Institute for Health and Care Excellence (NICE) reported on nine randomised controlled trials (RCTs) supplemented by observational studies and case reports for adverse events associated with vertebroplasty and kyphoplasty (see Section 2 for further details).⁽¹⁶⁾ It noted that seven RCTs reported cement leaks, and while these did not cause patients immediate complications, leaks into the inferior intervertebral disc increased the risk of incident vertebral fracture (odds ratio [OR] 7.2, 95% CI 1.7 to 69.3). Vertebroplasty is reported to be associated with an increased rate of procedure-related complications and cement leakage compared to kyphoplasty.^(20;21) Although rare, complications secondary to cement leakage include compression of neural elements and venous embolism.⁽²¹⁾

It should be noted though that there is also potential for serious complications associated with conservative management of VCFs. The NICE report highlighted that bed rest can result in muscle wasting, deconditioning, deep vein thrombosis and pulmonary emboli. It also noted that opioid analgesics can cause undesirable adverse reactions including cognitive impairment, constipation and nausea, and stated that non-steroidal anti-inflammatory drugs are associated with gastrointestinal and renal problems.⁽¹⁶⁾ High doses of analgesics used to treat the pain associated with VCF can have significant adverse effects.⁽²⁾

[†] 'Off-label' use refers to any use that is not included in the approved indications for use.

1.4 Current practice in Ireland

Patients with VCFs who are possible candidates for spinal intervention are generally referred for an outpatient consultant appointment by their general practitioner (GP) or by another hospital specialist. Referral or treatment thresholds (similar to those discussed in Section 2 below) may be used by GPs and surgeons in Ireland to identify eligible candidates for referral or treatment. However, it is unclear what thresholds are currently being used and how consistently they are being applied.

Vertebroplasty is a routine scheduled procedure in the publicly-funded healthcare system in Ireland. The Hospital In-Patient Enquiry (HIPE) system reports that there were approximately 66 vertebroplasties undertaken in 2011. Currently, there is no HIPE code for kyphoplasty, so it is coded using the vertebroplasty code.⁽²²⁾ As such, the data presented may include some kyphoplasty procedures. Vertebroplasty may be coded as the principal procedure or as a secondary procedure. For consistency and completeness, data are reported to include the principal and secondary procedures (i.e. 'all procedures') with all data presented on this basis. The International Classification of Diseases (ICD) intervention codes used to retrieve this data are listed in Table 1.1.

Table 1.1 HIPE ICD-10AM/ACHI list of intervention codes for vertebroplasty

Intervention code	Description
35400-00	Vertebroplasty, one vertebral body <i>Injection of polymethylmethacrylate [PMMA] into one vertebral body</i>
35400-01	Vertebroplasty, ≥ two vertebral bodies <i>Injection of PMMA into two or more vertebral bodies.</i>

Note: There is no HIPE code currently for kyphoplasty; it is usually coded using this vertebroplasty code.⁽²²⁾

Current data do not permit identification of the precise indication for which procedures are performed as the intervention and diagnosis codes are not linked. HIPE data capture the principal and up to 29 secondary diagnoses recorded in the patient medical notes for each episode of care. In 2011, 'Osteoporosis with pathological fracture' was listed as the primary diagnosis in 21% of cases, fractures of the thoracic and lumbar spine in 15% of cases, and dorsalgia in 14%, the latter clearly not being an indication on its own. It is possible that a number of the procedures are undertaken for VCF secondary to other causes including malignant involvement of the spinal column; for example, 32% of procedures were undertaken in patients with a principal diagnosis of a malignancy.⁽²³⁾ However, as noted it is not

possible to identify the precise indication for which procedures are undertaken with the current data.

The number of vertebroplasties undertaken in the publicly-funded healthcare system has ranged from 82 (2009), 91 (2010) to 66 (2011). There are no reports of the National Treatment Purchase Fund (NTPF) procuring vertebroplasty in private hospitals for the public healthcare system.⁽²⁴⁾ The majority of vertebroplasties (83%) in Ireland are undertaken in adults over 60 years of age.⁽²³⁾ Table 1.2 provides a breakdown of activity by the proposed Health Service Executive (HSE) hospital groups that were recently announced by the Department of Health.⁽²⁵⁾

Table 1.2 HIPE data per HSE proposed hospital group (2011)⁽²⁵⁾

Hospital group	Number (%)	ALOS (days)	Inpatient bed days	% day case	Avg. age (years)
Dublin North East	10 (15)	32.4	199	30.0	74.8
Dublin Midlands	27 (40)	22.4	698	7.4	57.0
Dublin East	8 (12)	3.2	34	0	63.7
South/South West	19 (28)	7.6	111	42.1	71.6
West/North West*	N/R	N/R	N/R	N/R	N/R
Midwest	-	-	-	-	-
Acute paediatric services, Dublin	-	-	-	-	-

**Note: Not reported (N/R) as contains five or fewer cases. HIPE data include all activity in publicly-funded hospitals, including procedures in patients that used private health insurance.*

The procedures were undertaken in 13 different individual hospitals, with nine hospitals reporting completing fewer than five procedures. Although vertebroplasty is described as an outpatient procedure,⁽¹¹⁾ HIPE indicate that only 20% of procedures were undertaken in the day case setting. Hospital admission is typically required for kyphoplasty, but as there is no specific code for kyphoplasty it is possible that it accounts for some of the inpatient activity. The patients undergoing vertebroplasty are typically older (>60 years) with osteoporosis, painful VCFs and potentially other co-morbidities where a prolonged hospital stay may be required. The ALOS varies from three to sixty-three days. However, the number of vertebroplasties is low, so this data is likely skewed by a small number of outliers; as such, it is difficult to draw any conclusions from the HIPE data.

Data from the NTPF reflecting surgical and medical inpatient and day case waiting lists for all public hospitals, indicate that vertebroplasty does not currently feature on these waiting lists.⁽²⁶⁾ It is unclear what proportion of patients who are referred for outpatient review with VCFs are subsequently listed for this intervention. The use of clear referral criteria and treatment thresholds may help clarify the criteria under which referral should take place, potentially limiting inappropriate referrals and ensuring timely access for those that would benefit from the procedure. Before being

referred for surgery, patients must first be reviewed at an outpatient consultant appointment. The length of time a patient must wait to be reviewed varies according to the referral pathway and the individual hospital and consultant to which a patient is referred. At the end of March 2013, it was reported that there were 384,632 patients on the Outpatient Waiting List database collated by the NTPF, 52% of whom were waiting less than six months, with 73% waiting less than 12 months.⁽²⁷⁾ Within orthopaedics, it was reported that as of August 2013 there were 52,455 patients on the waiting list, 45% of whom were waiting less than six months and 67% waiting less than 12 months.⁽²⁸⁾

Initiatives are underway by the HSE to standardise the management of outpatient services and to ensure that there are consistent management processes across all publicly-funded healthcare facilities that provide outpatient services. This includes the publication of a protocol for the management of these services by the NTPF in January 2013 which provides the core guidance for the Outpatient Services Performance Improvement Programme.⁽²⁹⁾ This specifies that patients should be treated based on clinical urgency, with urgent referrals seen and treated first. It is intended that the definition of clinical urgency and associated maximum wait times is to be developed at specialty or condition level and agreed by the National Clinical Programmes. Initiatives are also underway by the Orthopaedic and Rheumatology Clinical Programmes in the HSE to develop interface clinics and consultations between primary and secondary care services in Ireland and to implement agreed national referral guidelines for all patients with musculoskeletal disease. In January 2013, the NTPF published a national waiting list management policy⁽³⁰⁾ that outlines the standardised approach to managing scheduled care treatment for inpatient, day case and planned procedures in all publicly-funded hospitals. It outlines a consistent structured approach that must be adopted to the management of the waiting list; monitoring of the implementation of the policy will be routinely undertaken by the NTPF in the form of annual quality assurance reviews.

2 Clinical referral/treatment threshold

2.1 Review of the literature

A comprehensive review of the literature was conducted during May 2013 to identify international clinical guidelines, health policy documents describing treatment thresholds that are in place in other health systems, and economic evaluations for vertebroplasty and kyphoplasty. The approach and general search terms are described in Appendix 1 in the 'Background and Methods' document; a summary of the results is included in Table 2.1.

Table 2.1 Included evidence sources to inform clinical referral thresholds

Publication Type	Number	References
Clinical guidelines/HTA*	13	(2;3;7;13;14;31-38)
Systematic reviews	13	(39-51)
Clinical studies**	3	(52-54)
Cost-effectiveness studies	6	(2;35;55-58)

**Note: Clinical guidelines for osteoporosis and chronic pain management only included here, other indications are included in Appendix 2. **Note: RCTs after 2009 included.*

2.2 Clinical evidence

A comprehensive review of the literature retrieved several international guidelines for the use of vertebroplasty and kyphoplasty and are summarised in Appendix 1. The most comprehensive and recent technology appraisal guidance for vertebroplasty and kyphoplasty for VCFs is from the National Institute for Health and Care Excellence (NICE) in 2013.^(2;59) The NICE technology appraisal includes a systematic review of the literature in which nine relevant RCTs for vertebroplasty were identified. For vertebroplasty, it references two sham-controlled randomised controlled trials, which provide evidence that vertebroplasty may not improve health outcomes for osteoporotic vertebral fractures when compared to a sham procedure.^(52;53) These two trials have been criticised because of the limitations in their size, patient selection criteria, and methodology; however this potential for bias is acknowledged in the relevant clinical guidelines and considered in the recommendations provided.

Vertebroplasty was compared to operative placebo in two RCTs (n=79 and n=131),^(52;53) to optimal pain management (five trials with trial size ranging from 46-202)⁽⁵²⁾ and to kyphoplasty (n=100).⁽⁶⁰⁾ Only the two trials comparing vertebroplasty to operative placebo were double blinded.^(52;53) When compared to operative placebo, no difference in pain improvement was reported for vertebroplasty at one month (adjusted mean difference -0.6 (95% CI -1.4 to 0.2)). When compared to optimal pain management, NICE reported that three earlier RCTs⁽⁶¹⁻⁶³⁾ showed statistically significant improvements between groups in short- and medium-term changes from baseline, and two of these studies (the third did not report long-term results)⁽⁶³⁾ showed benefits in longer term pain outcomes after vertebroplasty. NICE reported that mortality data is available from a large study based on US Medicare registry data which followed patients for four years and reports a statistically significant mortality benefit for vertebroplasty or kyphoplasty compared to optimal pain management.⁽⁶⁴⁾ The appraisal acknowledged the debilitating impact osteoporotic VCFs have on patients' physical and emotional well being and concluded

that the potential for adverse events due to cement leakage was manageable if the procedures are undertaken by skilled clinicians with specialist training. Clinician discretion was recommended in terms of the late referral of patients: it was noted that while the procedure was recommended in patients with recent (>six weeks) fracture, that there are also patients with unhealed fractures who could benefit from treatment months after the onset of pain. The conclusion of the NICE appraisal was that vertebroplasty and kyphoplasty are recommended as an option for treating osteoporotic VCFs only in people who have severe ongoing pain after recent, unhealed vertebral fracture 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.

Technology assessments, reviews and guidelines from five other organisations^(3;13;34;35;38) have considered the two RCTs^(52;53) comparing vertebroplasty to a placebo (sham operation) as part of their evidence base (Appendix 1); however, they differ in their recommendations depending on their interpretation of the potential for bias with the sham trials and the extent to which the trial data is consistent with lower level observational data. A 2010 guideline from the American Academy of Anesthesiologists⁽³¹⁾ agreed that these two RCTs show equivocal pain relief for patients with osteoporotic vertebral compression fractures, but also considered lower quality observational studies and concluded that minimally invasive spinal procedures may be used for the treatment of pain related to vertebral compression fractures. Also, a 2010 HTA by the Danish Centre for Health Technology Assessment (DACEHTA) recommends that vertebroplasty is offered to patients with persistent pain after two to three months of conservative treatment.⁽¹⁴⁾ From an organisational perspective it specifies a number of preconditions: for example, that a minimum of 50 to 60 vertebroplasties or percutaneous transpedicular approaches are completed per year with a minimum of two clinicians performing the procedure regularly; that the aseptics during the vertebroplasty procedure must be at the level of an operating theatre; that some patients may need hospitalisation following vertebroplasty; that a few patients will need acute surgical decompression of the neural structures following vertebroplasty and that some fragile patients need general anaesthesia and post-operative intensive care. It also recommends that vertebroplasty is performed by spine surgeons and interventional radiologists. A 2010 guideline⁽³⁸⁾ from the American Academy of Orthopaedic Surgeons (AAOS) recommended against vertebroplasty for osteoporotic VCFs on the basis of the findings of the two RCTs comparing vertebroplasty to placebo. Similarly, a HTA for Bluecross/Blueshield in 2011 concludes that the evidence is insufficient to determine if vertebroplasty or kyphoplasty improves the net health outcome or is as beneficial as any established alternatives.⁽¹³⁾ While acknowledging the potential for bias in the sham trials, it was noted that the findings were not inconsistent with three Level II

trials which also documented inconclusive results for clinically significant pain relief with vertebroplasty.⁽³⁸⁾

For kyphoplasty, two national organisations base their recommendations on one RCT of 'medium quality' which compared kyphoplasty to non-surgical treatment of vertebral compression due to osteoporosis.^(3;34) The RCT indicated that in the short term (up to one year) kyphoplasty offers somewhat better pain relief, increased quality of life and functional capacity.⁽⁵⁴⁾ In 2011, the Swedish Council on Health Technology Assessment reported that the scientific evidence is insufficient to determine if kyphoplasty provides better pain relief, functional capacity, or quality of life than non-surgical options in treating vertebral compression, and that the evidence is insufficient to appraise the long-term effects, risks, and side effects of the method.⁽³⁾ Also in 2011, the Australian Medical Services Advisory Committee (MSAC) reported that all studies had a moderate or high risk of confounding and conclusions were difficult to draw when comparing kyphoplasty to vertebroplasty.^(35;54) In contrast, 2010 clinical guidelines from the AAOS provided a limited recommendation for kyphoplasty on the basis that clinical trial evidence suggested it provided improved pain relief at up to 12 months compared to conservative treatment in one RCT, and that there was RCT evidence from Level II trials of improved pain relief at durations up to two years compared to vertebroplasty.⁽³⁸⁾ A meta-analysis in 2012 comparing kyphoplasty to vertebroplasty in treating osteoporotic vertebral compression fractures reported that kyphoplasty may be superior to vertebroplasty in patients with large kyphosis angles, vertebral fissures, fractures in the posterior edge of the vertebral body or significant height loss in the fractured vertebrae. However, it noted that the evidence was of poor quality and high quality RCTs are required.⁽⁴⁰⁾ Systematic reviews have revealed continuing uncertainties about treatment effects for kyphoplasty.^(65;66)

The remaining systematic reviews and health technology assessment findings are summarised in Appendix 1.

2.3 Cost-effectiveness evidence

In 2013, NICE reported on three economic models which assessed the cost-effectiveness of vertebroplasty.⁽²⁾ A Medtronic model (Markov tunnel model) compared the cost-effectiveness of kyphoplasty, vertebroplasty and optimal pain management in patients hospitalised with VCFs, while a Johnson and Johnson (J&J) model (one year treatment site model) and NICE's own model (scenario analysis) compared the cost-effectiveness of vertebroplasty, kyphoplasty, optimal pain management and an operative placebo comprising local anaesthesia (sham procedure).

The Medtronic model reported that kyphoplasty was cost-effective when compared to vertebroplasty (an incremental cost-effectiveness ratio [ICER] of £15,000 per quality-adjusted life year [QALY] gained). It noted that the assumption that vertebroplasty and kyphoplasty cause patients to live longer (greater for kyphoplasty) was a key driver of the cost-effectiveness results. The J&J model predicted that vertebroplasty was both more effective and less costly than kyphoplasty, and that it was cost-effective (ICER of £4,392 per QALY gained) compared to optimal pain management. On review of the data, the NICE appraisal committee acknowledged that the ICERs established for vertebroplasty were generally at the lower end of what is usually considered cost-effective but that the results were extremely sensitive to the mortality benefit assumptions.

In 2011, the Swedish Council on Health Technology Assessment (SBU) reported that the scientific evidence is insufficient to determine the cost-effectiveness of vertebroplasty and balloon kyphoplasty.⁽³⁾ It reported on three studies that addressed the costs and cost-effectiveness of vertebroplasty or kyphoplasty, stating that vertebroplasty and associated treatment (up to one year) is estimated to cost less than kyphoplasty (between SEK 64,000 and 87,000 versus SEK 70,000), with the cost of non-surgical treatment estimated to be in the same range (SEK 60,000 to SEK 82,000).

Other studies report that kyphoplasty may be more cost-effective than vertebroplasty for the treatment of vertebral compression fractures. For example, in 2011, the Belgian Bone Club reported that kyphoplasty may be a cost-effective treatment in osteoporotic patients hospitalised with painful vertebral compression fractures based on two studies.^(67;68) In 2013, Svedbom et al. concluded that kyphoplasty may be a cost-effective strategy compared to non-surgical management and vertebroplasty, respectively (ICER £2,706, £15,982 per QALY), in osteoporotic vertebral compression fractures.⁽⁵⁶⁾ Also, in 2013 Ong et al. reported that kyphoplasty patients had significantly lower adjusted treatment costs (6.8-7.9%) two years post-surgery compared to those undergoing vertebroplasty.⁽⁶⁹⁾ In 2012, Edidin et al. reported that among patients for whom surgical treatment was indicated, kyphoplasty was cost-effective, and perhaps even cost saving, compared to vertebroplasty.⁽⁷⁰⁾

In 2011, the MSAC reported on a cost-minimisation analysis that vertebroplasty has an additional cost (AUS\$1,593 more over one year) compared to conservative treatment, with no improvement in outcomes.⁽³⁵⁾

2.4 Budget impact and resource implications

In the EU approximately four million osteoporotic fractures occur each year costing €32 billion; it is estimated that these costs will double over the next 30 years if current trends continue.⁽⁵⁾

The estimated average cost of a vertebroplasty in Ireland in 2011 is included in Table 2.2. The HSE National Casemix Programme does not include a diagnosis-related group (DRG) specific to vertebroplasty. Therefore, more general DRG codes for musculoskeletal procedures are included to give an estimate of the cost. HIPE discharge data suggests that 60% (128A 30%, 128B 30%) of vertebroplasty procedures in 2011 used these codes. This code equates to an approximate total cost of €420,000 based on 66 procedures, or a weighted average cost of €6,636 per procedure.⁽²³⁾ These estimated procedure costs likely underestimate the actual cost of vertebroplasty given the acquisition cost of the cement kit alone in the UK was estimated to range from £800 (lower viscosity cement) to £1,403 (high viscosity cement, average of three prices: £1,546, £1,472 and £1,193 used by the assessment group for NICE, Johnson and Johnson and Medtronic cost-effectiveness models, respectively) in 2009.^(2;59) The average acquisition cost of the kyphoplasty kit was estimated as £2,492 (£2,639, £2,842 and £1,996: NICE, Johnson and Johnson and Medtronic respectively).^(2;59)

Table 2.2 Cost of HSE inpatient and day case surgery summarised by diagnosis-related group (based on 2011 costs and activity)

DRG code	Description	Cost/case (€)
I28A	Other musculoskeletal procedures with catastrophic complications	14,134
I28B	Other musculoskeletal procedures without catastrophic complications	4,669
I28	Other musculoskeletal procedures	1,799
-	Outpatient appointment	130

Data summary from the HSE National Casemix Programme based on activity and costs reported by 39 participating hospitals.

**Note: there is no specific code for vertebroplasty, the nearest codes are included and as such provide an estimate of the cost.*

2.5 Advice on clinical treatment threshold

There is a lack of consensus in recent clinical guidelines, HTAs and systematic reviews in relation to the role of vertebroplasty and kyphoplasty in the management of osteoporotic VCFs. While there is limited RCT evidence that vertebroplasty may not improve health outcomes for patients with painful osteoporotic vertebral compression fractures when compared to a sham procedure, these two trials have been criticised because of the limitations in their size, patient selection criteria, and

methodology.^(52;53) Data from prospective randomised trials provide evidence in favour of the use of vertebroplasty and kyphoplasty over conservative medical management and there is limited RCT data that suggest kyphoplasty may be associated with improved outcomes compared to vertebroplasty in some patients. The potential for bias with the various trials was considered in recent guidelines, resulting in a limited recommendation supporting the use of vertebroplasty and/or kyphoplasty for those with recent (proposed as six weeks) unhealed VCFs, with severe, ongoing pain despite optimal pain management.^(2;14;31;38) This was accepted as reasonable; therefore, the following treatment criteria are advised in line with this:

Percutaneous vertebroplasty and balloon kyphoplasty without stenting are recommended as an option for treating osteoporotic vertebral compression fractures only in people:

- who have severe ongoing pain after a recent, unhealed vertebral fracture 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.

Patients who do not meet these criteria should remain under the care of their primary care practitioner who will manage conservative treatment of the patient.

3 Discussion

A treatment threshold has been recommended based on a comprehensive review of the literature with the aim to treat the right patients at the right time and to avoid unnecessary interventions, particularly in those who are unlikely to benefit substantially from surgery. It is possible that this treatment threshold is currently being applied by clinicians in Ireland, but not necessarily consistently.⁽²²⁾

It is not possible to determine the precise indications for which vertebroplasty and kyphoplasty are being undertaken in Ireland from the current data. It is possible that a proportion of these procedures are for VCF secondary to other causes, including malignant involvement of the spinal column. Guidelines for vertebroplasty in cancer patients were retrieved as part of this analysis; however, they are mainly dated prior to the 2009 placebo-controlled RCTs which cast doubt over the efficacy of vertebroplasty.

As noted in section 1.4, current HIPE data do not include a unique procedure code for kyphoplasty; these procedures are usually coded as vertebroplasty, therefore it is not possible to determine activity levels for the individual procedures. Although vertebroplasty/kyphoplasty are routine procedures, they are used relatively

infrequently in the Irish healthcare system (n=66 in 2011), perhaps reflecting the concerns about efficacy and the potential for adverse reactions or alternatively issues with timely access to this treatment. The stated threshold specifies recent (>6 weeks) fractures; acute (<6 weeks) osteoporotic VCFs generally heal quickly, implying that most patients do not benefit from early invasive intervention. However, the fracture must be unhealed for the intervention to be indicated, meaning that there is a limited timeframe within which referral and treatment should occur. Significant waiting lists for outpatient review and subsequent treatment may therefore exclude certain patients from access to potentially beneficial treatment.

It is difficult to estimate what impact, if any, the introduction of formal thresholds would have on outpatient referrals and surgical activity for osteoporotic VCFs in Ireland. The fact that the recommended threshold is consistent with well established clinical guidelines and the findings of literature reviews means it is unlikely to represent a major change from current practice, but rather a standardisation of referral and treatment criteria across all areas of the publicly-funded healthcare system. However, as noted, it is possible that there is a current under-utilisation of the procedure in otherwise eligible patients due to delays in accessing surgical review. As noted, initiatives are underway: for example, by the Orthopaedic and Rheumatology Clinical Programmes in the HSE to develop interface clinics and consultations between primary and secondary care services in Ireland and to implement agreed national referral guidelines for all patients with musculoskeletal disease. Implementation of guidelines for the management of osteoporotic VCFs that incorporate the stated threshold would clarify when and which patients should be referred and help to ensure timely access to review so that patients are not excluded from potentially beneficial treatment. Finally, as outlined in the ethical analysis report, if clinical referral or treatment thresholds are implemented, it is imperative that there are opportunities for appeal mechanisms to ensure good governance.⁽⁷¹⁾

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Appendix 1 – Summary of evidence and examples of international clinical referral thresholds

Guideline	Scope	Vertebroplasty thresholds – Osteoporotic vertebral compression fractures/chronic pain management	Evidence
NICE TA 279 (2013) ⁽²⁾ UK	Indications: Osteoporotic vertebral compression fractures Population: Not specified	<i>PVP and percutaneous balloon KP for treating OP vertebral compression fractures:</i> PVP, and percutaneous balloon KP without stenting, are recommended as options for treating osteoporotic vertebral compression fractures only in people: <ul style="list-style-type: none"> ▪ who have severe ongoing pain after a recent, unhealed vertebral fracture 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. 	Literature review: Systematic review Grading system: NICE Key references: Buchbinder, Kallmes RCTs, IPG12, IPG166
Belgian Bone Club (2011) ⁽³⁴⁾ Belgium	Indications: Chronic pain management Population: Not specified	<i>Non-pharmacological management of osteoporosis: a consensus of the Belgian Bone Club:</i> Limitations of both vertebroplasty and kyphoplasty are the lack of long-term data and the absence of conclusive comparative trials.	Literature review: Systematic review Grading system: Not specified Key references: Buchbinder, Kallmes RCTs
MSAC (2011) ⁽³⁵⁾ Australia	Indications: Vertebral compression fractures, malignant tumours Population: Not specified	<i>Reference No. 27.1 – Review of interim funded service: Vertebroplasty and new review of kyphoplasty:</i> In 2004-05, an MSAC assessment of vertebroplasty and kyphoplasty for treatment of vertebral compression fracture was conducted and updated in 2010. On the strength of the evidence pertaining to safety, effectiveness and cost-effectiveness of vertebroplasty, MSAC supported interim public funding for: <ul style="list-style-type: none"> ▪ vertebroplasty in patients with painful OP vertebral compression fractures confirmed by diagnostic imaging and not controlled by conservative medical therapy ▪ vertebroplasty in patients with pain from metastatic deposits or multiple myeloma in a vertebral body. <p>The procedure should be performed by appropriately-qualified medical practitioners and this recommendation was to have been reviewed within five years.</p> <p>Found no studies that met inclusion criteria for assessment of effectiveness of vertebroplasty for treating vertebral malignancies.</p> <p>MSAC noted that two RCTs of good methodological quality (sham-controlled, Buchbinder, Kallmes) found no clinically or statistically significant additional beneficial effect of vertebroplasty over a sham procedure with respect to overall outcomes.</p> <p>MSAC concluded that on the best available evidence, vertebroplasty has not been proven to be more effective than conservative treatment (in terms of pain, analgesic use, quality of life, functional status), and entails additional (albeit small) risk and additional costs.</p>	Literature review: Systematic review Grading system: – Key references: Buchbinder, Kallmes RCTs

		Comparing kyphoplasty and vertebroplasty, all studies had a moderate or high risk of confounding and conclusions were difficult to draw.	
SBU Alert (2011) ⁽³⁾ Sweden	Indications: Osteoporotic vertebral compression fractures Population: Not specified	<i>PVP and balloon KP in treating painful OP VCFs:</i> The scientific evidence is insufficient to determine if PVP or balloon KP yield better outcomes than nonsurgical strategies or placebo (sham operations) in treating symptomatic VCFs due to OP. The scientific evidence is insufficient to determine the cost-effectiveness of PVP and balloon KP. Randomised and blinded trials should be conducted, but such trials are associated with substantial methodological problems. Long-term evaluation of the methods' effects and risks would require systematic follow-up, e.g. via a national quality registry.	Literature review: Systematic review Grading system: SBU grading Key references: Buchbinder, Kallmes RCTs
TEC/BCBS (2011) ⁽¹³⁾ US	Indications: Osteoporosis Population: Not specified	<i>PVP or KP for Vertebral Fractures Caused by Osteoporosis:</i> <i>Vertebroplasty.</i> Two placebo-controlled, randomised trials, three open-label, randomized trials, one comparative study, and six case series studies met selection criteria. The key limitation to both placebo-controlled randomised trials is that they were underpowered. Without adequate power, it is not possible to determine if vertebroplasty was effective or not. Thus, the results should be interpreted as uncertainty, rather than a lack of effect. It concluded that the evidence is insufficient to determine if vertebroplasty improves the net health outcome or is as beneficial as any established alternatives. <i>Kyphoplasty.</i> One randomised trial, two non-randomised studies comparing kyphoplasty to medical management, one study comparing kyphoplasty to vertebroplasty, and four case series studies met selection criteria. Historically, there has been a lack of rigorous comparative trials of kyphoplasty. A 2009 randomised, controlled trial of kyphoplasty versus medical management was both unblinded and lacked a sham control. It concluded that the evidence is insufficient to determine if kyphoplasty improves the net health outcome or is as beneficial as any established alternatives.	Literature review: Systematic review Grading system: Set specific criteria Key references: Buchbinder, Kallmes RCTs
Pichon-Riviere et al (2011) ⁽³⁶⁾ Argentina (In Spanish)	Indications: Osteoporotic vertebral fractures Population: Not specified	<i>Percutaneous acrylic vertebroplasty for the treatment of vertebral fractures:</i> Is an effective therapy and has a low rate of adverse effects. As regards the usefulness of PVP in osteoporotic vertebral fractures, the evidence recently found in two randomised, blind, controlled clinical trials with few patients that percutaneous vertebroplasty is not better than standard treatment. For these studies, it is worth mentioning that, in order to keep the double-blind status, a vertebral infiltration with local anaesthetics was performed; this intervention might have resulted in a beneficial effect in the control group. Two other randomised, controlled but open-label clinical trials did not show benefits with PVP over the conventional treatment either. Therefore, considering what is herein stated, conventional treatment is still the first choice for osteoporotic vertebral fractures. As regards the usefulness of PVP in the treatment of fractures secondary to metastasis or multiple myeloma, no randomised, controlled clinical trials have been found. The evidence from case series suggests that PVP might be useful in these patients. It is necessary to conduct clinical trials with an adequate number of patients, with a representative control group and adequate methodological quality to assess PVP usefulness for these indications.	Literature review: Systematic review Grading system: – Key references: Buchbinder, Kallmes RCTs

MAS (2010) ⁽⁷⁾ Canada	Indications: Osteoporotic vertebral compression fractures Population: Not specified	<i>Percutaneous vertebroplasty for treatment of painful OP vertebral compression fractures: an evidence-based analysis:</i> Five RCTs on vertebroplasty identified through literature search. Two compared vertebroplasty with sham procedure, two compared vertebroplasty with conservative treatment, and one compared vertebroplasty with balloon KP. All studies included patients with painful VCFs and mean age of patients ranged from 72 to 80 years. Two blinded RCTs on vertebroplasty in which vertebroplasty was compared with sham procedure provided highest level of evidence available to date. Results of two trials supported by findings of one open randomised trial with 12 months follow-up. OHTAC weighed in favour of conservative treatment and made the following recommendations: <ul style="list-style-type: none"> ▪ Vertebroplasty should not be considered as standard treatment for patients with OP VCFs ▪ Conservative treatment which allows fracture to heal naturally and is safer than vertebroplasty is preferred as first line of treatment in these patients. 	Literature review: Systematic review Grading system: GRADE Working Group Key references: Buchbinder, Kallmes RCTs
DACEHTA (2010) ⁽¹⁴⁾ Denmark	Indications: Osteoporotic vertebral fractures Population: Not specified	<i>Percutaneous vertebroplasty as a treatment for osteoporotic vertebral fractures:</i> It recommends that PVP is offered to patients with persistent pain after a period of conservative treatment. Patients with persistent pain after two to three months of conservative treatment may be offered PVP preceded by MRI-scanning or SPECT. Though some acute patients may benefit from early PVP, for instance patients with intense pain, who still need hospitalisation after a few days of conservative treatment, patients with chronic obstructive lung disease, who cannot be treated with opioids, and other weak patients who might not recover after several weeks of immobilisation. From an organisational perspective it recommends that: <ul style="list-style-type: none"> ▪ A minimum of 50-60 PVP or percutaneous transpedicular approaches per year with a minimum of two clinicians performing the procedure regularly ▪ The aseptics during the PVP procedure must be at the level of an operating theatre ▪ Some patients need hospitalisation following PVP ▪ A few patients will need acute surgical decompression of the neural structures following PVP ▪ Some fragile patients need general anaesthesia and post-operative intensive care. It also recommends that PVP is performed by spine surgeons and interventional radiologists.	Literature review: Systematic review Grading system: – Key references: Buchbinder, Kallmes RCTs
INAHTA (2010) ⁽³⁷⁾ Austria (In German)	Indications: Osteoporotic vertebral compression fractures Population: Not specified	<i>Kyphoplasty and vertebroplasty for osteoporotic vertebral compression fractures:</i> In addition to studies included in a previous MEL report (2008), identified nine recent studies assessing benefits and harms of both interventions for this update. Results of two recent placebo-controlled RCTs showed no advantage of vertebroplasty over a placebo intervention. For the direct comparison of both interventions there are still no RCTs available.	Literature review: Systematic review Grading system: – Key references: Buchbinder, Kallmes RCTs
American Academy of Orthopaedic Surgeons (2010) ⁽³⁸⁾	Indications: Osteoporotic spinal compression fractures Population: Not specified	<i>Vertebroplasty</i> 'We recommend against vertebroplasty for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.' Strength of recommendation: 'Strong'. Implications: practitioners should follow a 'Strong' recommendation unless a clear and compelling rationale for an alternative approach is present.	Literature review: Systematic Grading system: GRADE Key references: Buchbinder, Kallmes RCTs (level I evidence);

		<p><i>Kyphoplasty</i></p> <p>'Kyphoplasty is an option for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.' Strength of recommendation: 'Limited'. A Limited recommendation means that the quality of the supporting evidence is unconvincing or that well-conducted studies show little clear advantage to one approach over another. Implications: practitioners should exercise clinical judgment when following a recommendation classified as limited, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a strong influencing role.</p>	<p>3 Level II studies (vertebroplasty); 5 Level II studies (kyphoplasty)</p>
<p>American Society of Anesthesiologists (2010)⁽³¹⁾ US</p>	<p>Indications: Chronic pain management Population: Not specified</p>	<p><i>Practice guidelines for chronic pain management:</i></p> <p>Minimally-invasive spinal procedures: including vertebroplasty, kyphoplasty, and percutaneous disc decompression. Randomised sham-controlled trials of VP are equivocal regarding pain relief for patients with OP vertebral compression fractures (Category C2 evidence). Studies with observational findings indicate that vertebroplasty and kyphoplasty provide effective relief for OP compression fracture pain for assessment periods ranging from six to twelve months (Category B2 evidence). Recommendations: Minimally-invasive spinal procedures may be used for the treatment of pain related to vertebral compression fractures.</p>	<p>Literature review: Systematic Grading system: Task Force Key references: Buchbinder, Kallmes RCTs</p>
<p>American Society of Interventional Pain Physicians (2007)⁽³²⁾ US</p>	<p>Indications: Chronic spinal pain Population: Not specified</p>	<p><i>Interventional techniques: Evidence-based practice guidelines in the management of chronic spinal pain:</i></p> <p>Conclude that for vertebral augmentation procedures, the evidence is moderate for both vertebroplasty and kyphoplasty.</p>	<p>Literature review: Systematic Grading system: Developed own system based on various publications Key references: 2007 guideline, later RCTs not included.</p>
<p>Institute for Clinical Systems Improvement (2004)⁽³³⁾ US</p>	<p>Indications: Osteoporotic compression fractures Population: Not specified</p>	<p><i>Vertebroplasty and balloon-assisted vertebroplasty for the treatment of OP compression fractures:</i></p> <p>Should be offered only to carefully selected patients whose pain is not controlled by conservative management (typically when severe pain has persisted for > 10 to 12 weeks). In eight of ten studies cited, significant decreases in mean visual analogue scale (VAS) pain scores were reported after treatment. In six studies that reported individual responses, 84% to 100% of patients reported partial or complete pain relief. Of five studies that assessed medication use, four reported decreased use. Three of five studies that assessed mobility found improved mobility. However, three of ten studies cited relied on a retrospective assessment of pain and in all studies it was unclear if an adequate trial of conservative management was attempted. (Conclusion Grade III) It should be performed in the context of controlled clinical trials. Evidence, to date, is from uncontrolled series with small sample sizes, subjective outcome measures, and limited follow-up.</p>	<p>Literature review: – Grading system: – Key references: –</p>

Guideline	Scope	Vertebroplasty thresholds – other indications	Evidence
NCC-C (2008) ⁽⁷²⁾ UK	Indications: Metastatic spinal cord compression Population: Not specified	<i>Metastatic spinal cord compression: Diagnosis and management of patients at risk of or with metastatic spinal cord compression:</i> The use of vertebroplasty and kyphoplasty in preventing MSCC in patients with vertebral metastases should be investigated in prospective comparative studies. These procedures have been investigated in observational studies without comparators and largely in patients with osteoporotic vertebral collapse. There is limited evidence about their use in patients with MSCC. Recommend vertebroplasty and kyphoplasty for patients who have vertebral metastases and no evidence of MSCC or spinal instability if they have: – mechanical pain resistant to conventional analgesia, or – vertebral body collapse. Vertebroplasty and kyphoplasty for spinal metastases should only be performed after agreement between appropriate specialists (including an oncologist, interventional radiologist, and spinal surgeon), with full involvement of the patient and in facilities where there is good access to spinal surgery.	NICE IPG12
SIGN 106 (2008) ⁽¹¹⁾ UK	Indications: Cancer patients Population: Adults	<i>Control of pain in adults with cancer. A national clinical guideline:</i> Patients with bone pain from malignant vertebral collapse proving difficult to control by pharmacological means should be referred for consideration of vertebroplasty where this technique is available.	–
NCC-C CG 121 (2011) ⁽⁷³⁾ UK	Indications: Lung cancer patients Population: Adults	<i>The diagnosis and treatment of lung cancer (update):</i> Methods of treating bone metastases include radiotherapy, bisphosphonates and nerve blocks. Increasingly, orthopaedic interventions can be considered, e.g. vertebroplasty.	–
BOA (2007) ⁽⁷⁴⁾ UK	Indications: Fragility fractures Population: Aged	<i>The care of patients with fragility fracture:</i> Vertebral augmentation procedures relieve pain, at least in the short term. No difference in pain relief and deformity correction between vertebroplasty and kyphoplasty procedures has yet been demonstrated with certainty. Evidence supports the use of vertebral augmentation procedures with appropriate backup (NICE).	–

Study	Description	Sample size (n)	Finding
Robinson and Olerud (2012) ⁽³⁹⁾ Sweden	Systematic review	Eight studies	<i>Vertebroplasty and kyphoplasty – a systematic review of cement augmentation techniques for OP VCF compared to standard medical therapy:</i> After > two decades the treatment effect of cement augmentation of OP VCF is questioned by two blinded randomised placebo-controlled trials (Buchbinder, Kallmes). This systematic review analyses RCTs on VP and KP to provide an overview on current evidence. Only two studies were properly blinded using a sham-operation as control. Other studies were using a non-surgical treatment control group. Further possible bias may be caused by manufacturer involvement in financing of three published RCTs. There is level Ib evidence that VP is no better than placebo, which is conflicting with the available level IIb evidence that there is a positive short-term effect of cement augmentation compared to standard medical therapy with regard to QoL, function and pain. KP is not superior to VP with regard to pain, but with regard to VCF reduction (evidence level IIb). KP is probably not cost-effective (evidence level IIb), and VP has not more than short-term cost-effectiveness (evidence level IV). VP and KP cannot be recommended as standard treatment for osteoporotic VCF. Ongoing sham-controlled trials may provide further evidence in this regard.
Ma et al (2012) ⁽⁴⁰⁾ China	Meta-analysis	Twelve studies, n=1,081 patients	<i>Balloon KP versus PVP in treating osteoporotic vertebral compression fracture: grading the evidence through a systematic review and meta-analysis:</i> Overall GRADE system evidence quality was very low. KP and VP are both safe and effective surgical procedures for treating OVCF. KP may be superior to VP in patients with large kyphosis angles, vertebral fissures, fractures in the posterior edge of the vertebral body or significant height loss in the fractured vertebrae. Due to the poor quality of the evidence currently available, high-quality RCTs are required.
Shi et al (2012) ⁽⁴¹⁾ PRChina	Meta-analysis	Nine articles, n=886 patients	<i>Is there really no benefit of VP for osteoporotic vertebral fractures? A meta-analysis:</i> Pain scoring similar between PVP group and sham injection group at one to twenty-nine days and 90 days. However, compared with non-operative therapy, PVP reduced pain at all times studied. QOL in PVP group was improved or tended to be improved compared with QOL for both control groups. Risk of new fractures similar between PVP groups and both control groups. Different control groups may have accounted for different conclusions in literature regarding ability of PVP to relieve pain and restore function recovery. Compared with non-operative treatment PVP relieved pain better and improved QOL. PVP did not increase the risk of new fractures.
Chew et al (2011) ⁽⁴²⁾ UK	Systematic review	Thirty studies, one RCT, seven prospective studies. N=978 patients	<i>Safety and efficacy of PVP in malignancy: a systematic review:</i> Five deaths attributable to VP, further 19 patients suffering a serious complication related to procedure. Some evidence to suggest that complication rate may be related to higher cement volume used, although the data are not robust enough for meta-analysis. Pain reduction ranged between 47-87%, similar to the results for osteoporosis. There was no correlation between pain reduction and cement volume. Concludes that systematic review reveals paucity of good-quality, robust data available on PVP in malignancy. Also highlights apparent high risk of serious complication (2%).

<p>Schroeder et al (2011)⁽⁴³⁾ Israel</p>	<p>Systematic review</p>	<p>Two studies</p>	<p><i>Cement augmentation in spinal tumours: a systematic review comparing VP and KP:</i> Limited evidence from comparative studies (two small retrospective cohort studies) regarding benefits of VP versus KP in patients with spinal fractures caused by tumours. Both appear to be effective in reducing pain with relatively few complications. Whether one method provides superior results over the other cannot be determined from the available evidence. Study limitations preclude making definitive conclusions. The overall strength of evidence is very low.</p>
<p>Han et al (2011)⁽⁴⁴⁾ China</p>	<p>Meta-analysis</p>	<p>Eight studies, n=848 patients</p>	<p><i>PVP versus balloon KP for treatment of osteoporotic vertebral compression fracture: a meta-analysis of randomised and non-randomised controlled trials:</i> Outcome showed VP more effective in short-term (no more than seven days) pain relief. Kyphoplasty had superior capability for intermediate-term (around three months) functional improvement. As for long-term pain relief and functional improvement, no significant difference between two interventions. Consistently, both interventions have similar risk for subsequent fracture and cement leakage. Thus considering the higher cost of the KP procedure, we recommend VP over KP for treatment of osteoporotic VCFs.</p>
<p>INAHTA (2010) Austria (In German)</p>	<p>HTA (observational study)</p>		<p><i>Kyphoplasty and vertebroplasty for the treatment of osteoporotic vertebral compression fractures-observational study:</i> The groups (KP, VP) differed in baseline characteristics (e.g. spontaneous vs. traumatic fracture, osteoporosis, Oswestry Disability Index). Observed cement leakages in both groups, none required further intervention. Oswestry Disability Index improved by an average of 50 points after KP and by 37 points after VP. Pain was reduced by 67 VAS-points in the KP-group and 61 VAS-points in the VP-group. The pain reduction and the improvement in the ODI-Score was sustained with minimal losses until the end of the observation period after two years. Observational study shows that KP and VP were able to improve functionality and to reduce pain under routine care conditions. Because of between group differences in baseline characteristics direct comparison of outcomes was not feasible. Because of study limitations not all research questions could be fully answered.</p>
<p>McGirt et al (2009)⁽⁴⁶⁾ US</p>	<p>Systematic review (1980-2008)</p>	<p>74 VP studies, 35 KP studies</p>	<p><i>VP and KP for the treatment of vertebral compression fractures: an evidence-based review of the literature:</i> Patients with osteoporotic or tumor-associated VCFs included. 74 VP studies for OP VCF (one level I, three level II, 70 level IV), 35 KP studies for OP VCF (two level II, 33 level IV), and 18 VP/KP for tumor VCFs (all level IV) reviewed. Good evidence (level I) that VP results in superior pain control within first two weeks of intervention compared with optimal medical management for OP VCFs. Fair evidence (level II-III) that VP results in less analgesia use, less disability, and greater improvement in general health compared with optimal medical management within first three months after intervention. Fair evidence (level II-III) that by two years after intervention, VP provides a similar degree of pain control and physical function as optimal medical management. Poor quality evidence that VP or KP results in greater pain relief for tumor-associated VCFs. Although evidence suggests that physical disability, general health, and pain relief are better with VP and KP than those with medical management within first three months after intervention, high quality randomised trials with two-year follow-up are needed to confirm this. Furthermore, reported incidence of symptomatic procedure-related morbidity for both VP and KP is very low.</p>

Mendel et al (2009) ⁽⁴⁷⁾ US	Systematic review	28 articles for VP, n=877 patients	<p><i>Percutaneous techniques in the treatment of spine tumors: what are the diagnostic and therapeutic indications and outcomes?</i></p> <p>Medical and neurologic complications varied from 0% to 7.1% and 0% to 8.1%, respectively. Pain and functional outcomes were successful using either VP or KP. Ten studies on embolisation reported on 330 patients. Four permanent complications (1.4%). Complete or partial embolisation possible in 97.5% with an estimated reduction of intra-operative blood loss of 2.3 L.</p> <p>Strong recommendation and moderate evidence for vertebral augmentation as safe and effective in providing pain relief and improving functional outcome in patients with vertebral body fractures and axial pain due to metastatic disease. There is a strong recommendation and very low evidence for embolisation techniques as safe and effective in decreasing intra-operative blood loss in hypervascular tumors.</p>
Eck et al (2008) ⁽⁴⁸⁾ US	Meta-analysis	N=168 studies.	<p><i>Comparison of VP and balloon KP for treatment of vertebral compression fractures: a meta-analysis of the literature:</i></p> <p>Effectiveness of pain control and risk of complications after VP versus balloon KP. Outcomes measures include visual analog scale and complications. 168 studies. Mean pre- and post-operative VAS scores for VP were 8.36 and 2.68, respectively, with mean change of 5.68 (p<.001). Statistically greater improvement found with VP versus KP (p<.001). Risk of new fracture was 17.9% with VP versus 14.1% with KP (p<.01). Risk of cement leak was 19.7% with VP versus 7.0% with KP (p<.001).</p> <p>Both VP and KP provided significant improvement in VAS pain scores. VP had significantly greater improvement in pain scores but also had statistically greater risk of cement leakage and new fracture.</p>
Ploeg et al (2008) ⁽⁴⁹⁾ Netherlands	Systematic review	15 studies (11 prospective, 3 retrospective and 1 RCT). N=1,136 interventions on 793 patients.	<p><i>PVP as a treatment for OP vertebral compression fractures: a systematic review:</i></p> <p>Studies of any design were eligible for inclusion, provided they included at least 10 participants and followed them up for at least six months. The included studies comprised controlled studies and case series. Mean follow-up varied from six to sixty-five months.</p> <p>Review concluded that insufficient evidence to determine efficacy and safety of PVP for painful OP VCF. Despite methodological weaknesses in review process, lack of good quality evidence means conclusion likely to be reliable.</p>
Gill et al (2007) ⁽⁵⁰⁾ US	Systematic review, meta-analysis	Twenty-one studies, 14 VP / 7 KP, n=1,046 VP, n=263 KP patients	<p><i>Comparing pain reduction following KP and VP for osteoporotic vertebral compression fractures:</i></p> <p>KP and VP resulted in more than five-point drop in VAS in immediate post-operative period (p<0.00001). Between the two, difference in early pain relief was not significant. At final follow-up, long-term VAS was improved for both procedures, but final follow-up VAS for VP and KP was not significant when compared to initial postoperative VAS (p=0.25, p=0.38, respectively).</p> <p>Analysis demonstrates that both procedures reduce amount of pain in immediate post-operative period by approximately 50%. Both procedures reduce pain in symptomatic osteoporotic vertebral compression fractures that have failed conservative treatment. Randomised controlled trials are needed to provide definitive data on which procedure is the most effective for vertebral compression fractures.</p>

<p>Taylor et al (2006)⁽⁵¹⁾ US</p>	<p>Systematic review (through 2004) and meta-regression</p>	<p>VP: one nonrandomised comparative study against conventional medical care and 57 cases series. KP versus VP (one nonrandomised comparative study).</p>	<p><i>Balloon kyphoplasty and vertebroplasty for vertebral compression fractures: a comparative systematic review of efficacy and safety:</i> Majority of studies undertaken in older women with OP vertebral compression fractures with long-term pain refractory to medical treatment. At this time, no good quality direct comparative evidence of balloon KP versus VP. From indirect comparison of case series evidence, the procedures appear to provide similar gains in pain relief while for balloon KP there is better documentation of gains in patient functionality and quality of life. The level of cement leakage and number of reported adverse events (pulmonary emboli and neurologic injury) in balloon KP significantly lower than for VP. These findings were confirmed by meta-regression analysis. Level III evidence to support balloon KP and VP as effective therapies in management of patients with symptomatic OP vertebral compression fractures refractory to conventional medical therapy. Although there was a good ratio of benefit to harm for both procedures, balloon KP appears to offer better adverse event profile. Conclusions need to be updated on basis of findings of ongoing RCTs.</p>
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RCTs	Scope	Finding
<p>Kallmes et al (2009)⁽⁵²⁾ US</p>	<p>RCT N=131 patients</p>	<p><i>A randomized trial of VP for osteoporotic spinal fractures:</i> Primary outcomes were scores on modified Roland-Morris Disability Questionnaire (RDQ) (scale 0–23, higher scores indicating greater disability) and patients' ratings of average pain intensity during preceding 24 hours at one month (scale 0–10, higher scores indicating more severe pain). Patients allowed to cross over to other study group after one month. All patients underwent assigned intervention (68 VP and 63 simulated procedures). Baseline characteristics were similar in two groups. At one month, no significant difference between VP group and control group in either RDQ score (difference, 0.7; 95% CI, -1.3 to 2.8; P=0.49) or pain rating (difference, 0.7; 95% CI, -0.3 to 1.7; P=0.19). Both groups had immediate improvement in disability and pain scores after intervention. Although two groups did not differ significantly on any secondary outcome measure at one month, there was a trend toward a higher rate of clinically meaningful improvement in pain (a 30% decrease from baseline) in the VP group (64% vs. 48%, P=0.06). At three months, there was a higher crossover rate in the control group than in VP group (51% vs. 13%, P<0.001). One serious adverse event in each group. <u>Improvements in pain and pain-related disability associated with osteoporotic compression fractures in patients treated with VP were similar to improvements in a control group.</u> (ClinicalTrials.gov number, NCT00068822.)</p>
<p>Buchbinder et al (2009)⁽⁵³⁾ Australia</p>	<p>RCT Multicenter, randomised, double-blind, placebo-controlled trial. N=71 (VP =25, placebo=36)</p>	<p><i>A randomized trial of VP for painful osteoporotic vertebral fractures:</i> At six-month follow-up, VP did not result in significant advantage in any measured outcome at any time point. Significant reductions in overall pain in both study groups at each follow-up assessment. At three months, mean (+/-SD) reductions in score for pain in VP and control groups were 2.6+/-2.9 and 1.9+/-3.3, respectively (adjusted between-group difference, 0.6; 95% confidence interval, -0.7 to 1.8). Similar improvements seen in both groups with respect to pain at night and at rest, physical functioning, quality of life, and perceived improvement. Seven incident vertebral fractures (three in VP group, four in placebo group) occurred during six-month follow-up period. <u>No beneficial effect of VP compared with sham procedure in patients with painful osteoporotic vertebral fractures, at one week or at one, three or six months after treatment.</u> (Australian New Zealand Clinical Trials Registry number, ACTRN012605000079640.)</p>

UK PCT* /US examples of thresholds	Scope	Threshold	Evidence
Oxfordshire PCT ⁽⁷⁵⁾	<p>Indications: Symptomatic osteoporotic vertebral fractures</p> <p>Population: Not specified</p>	<p>Surgery should be an option for patients who have severe pain that is adversely affecting their quality of life and has not responded to conservative measures (i.e. at least four weeks' trial of maximal analgesic treatments with no improvement, and including (for appropriate patients) a local anaesthetic/steroid injection into the affected region).</p> <p>In all other circumstances, percutaneous vertebroplasty is considered a low priority treatment for osteoporotic vertebral fractures due to limited evidence of clinical effectiveness. Exceptional cases may be considered by Oxfordshire PCT on an individual basis.</p>	NICE IPG12
Hampshire, Isle of Wight, Portsmouth and Southampton PCT ⁽⁷⁶⁾	<p>Indications: Vertebral body fracture</p> <p>Population: Not specified</p>	<p>Vertebroplasty for the treatment of pain due to vertebral body fracture which is refractory to conservative, medical treatment can be a treatment option for selected patients. The procedure must be performed in line with NICE IPG.</p> <p>The clinician performing the procedure is an accredited interventional spinal radiologist, who is suitably trained and experienced and that data is collected and submitted to the UK Vertebroplasty registry supported by Liverpool University.</p> <p>Indications for Percutaneous Vertebroplasty: Osteoporotic vertebral compression fractures more than four weeks old in the cervical, thoracic, and lumbar spine causing moderate to severe pain and unresponsive to conservative therapy Painful metastasis and multiple myelomas with or without adjuvant radiation or surgical therapy Painful fractures due to vertebral hemangiomas Painful fractures due to vertebral osteonecrosis Reinforcement of a pathologically weak vertebral body before a surgical stabilisation procedure.</p>	NICE IPG12
Brighton and Hove PCT ⁽⁷⁷⁾	<p>Indications: Osteoporotic vertebral compression fractures, metastatic deposits or multiple myeloma in the vertebral body</p> <p>Population: Not specified</p>	<p>These criteria are evidence based. If you cannot say 'Yes' to one of the questions for this patient, then they do not meet the evidence-based threshold criteria. If the patient does not meet all the criteria but you think they may have exceptional circumstances, please follow the procedure for an Exceptional Cases Panel decision. On the strength of evidence relating to the safety and effectiveness of vertebroplasty, does the patient have EITHER:</p> <ol style="list-style-type: none"> 1. Painful osteoporotic vertebral compression fractures confirmed by diagnostic imaging and not controlled by conservative medical therapy? Yes/No OR 2. Pain from metastatic deposits or multiple myeloma in the vertebral body? Yes/No <p>Exceptionality: If the patient does not meet these criteria but you think they have exceptional circumstances, this procedure may be referred to the exceptional cases panel in the PCT. See the link on the website for information on this process.</p>	-
Thames Valley Priorities Committees Berkshire PCT	<p>Indications: Vertebral body fracture</p> <p>Population: Not specified</p>	<p>Vertebroplasty for the treatment of pain due to vertebral body fracture which is refractory to conservative, medical treatment and recommends that it is a treatment option for selected patients. The procedure must be performed in line with NICE IPG.</p> <p>Due to the low number of procedures performed and the nature of the procedure, it is recommended that the clinician performing the procedure is an accredited interventional spinal radiologist, who is suitably trained and experienced and that data is collected and submitted to the UK Vertebroplasty registry</p>	NICE IPG12

		<p>supported by Liverpool University.</p> <p>Indications for Percutaneous Vertebroplasty:</p> <ul style="list-style-type: none"> ▪ Osteoporotic vertebral compression fractures more than four weeks old in the cervical, thoracic, and lumbar spine causing moderate to severe pain and unresponsive to conservative therapy ▪ Painful metastasis and multiple myelomas with or without adjuvant radiation or surgical therapy ▪ Painful fractures due to vertebral hemangiomas ▪ Painful fractures due to vertebral osteonecrosis ▪ Reinforcement of a pathologically weak vertebral body before a surgical stabilization procedure. 	
<p>Bluecross Blueshield US medical insurance, 2012⁽⁷⁸⁾</p>	<p>Indications: Osteoporotic fractures, osteolytic vertebral metastasis or myeloma, vertebral hemangiomas</p> <p>Population: Not specified</p>	<p>Percutaneous vertebroplasty or kyphoplasty is considered medically appropriate if ANY ONE of the following criteria are met:</p> <p>Osteoporotic fractures with ALL of the following:</p> <ul style="list-style-type: none"> ▪ Persistent debilitating pain not responding to standard medical therapy (e.g. initial bed rest with progressive activity, bisphosphonates, physical therapy, bracing, analgesics) ▪ A period of more than six weeks that is documented in the medical records. <p>Osteolytic vertebral metastasis or myeloma with ALL of the following:</p> <ul style="list-style-type: none"> ▪ Severe back pain related to destruction of the vertebral body not involving the major part of the cortical bone ▪ Chemotherapy and radiation therapy have failed to relieve symptoms. <p>Vertebral hemangiomas with ALL of the following:</p> <ul style="list-style-type: none"> ▪ Aggressive clinical signs (e.g. severe pain or nerve compression) and/or aggressive radiological signs ▪ Radiation therapy failed to relieve symptoms. 	<p>Bouza 2009, Buchbinder 2009, Kallmes 2009</p>

*Note: In April 2013, it was announced that the UK PCTs are being abolished; however, they are being replaced by other new organisations including clinical commissioning groups. The PCT thresholds will still apply.

Appendix 2 – Cost-effectiveness studies

Study	Type	Approach/Findings
Ong et al (2013) ⁽⁶⁹⁾ US	Cost comparison	<i>Two-year cost comparison of vertebroplasty and kyphoplasty for the treatment of vertebral compression fractures: are initial surgical costs misleading?</i> The costs for treating kyphoplasty and vertebroplasty patients were evaluated at up to two years post-surgery. There were no significant differences in adjusted costs in the first nine months post-surgery, but kyphoplasty patients were associated with significantly lower adjusted treatment costs by 6.8-7.9% in the remaining periods through two years post-surgery. The average adjusted costs for vertebroplasty patients within the first quarter and the first two years post-surgery were \$14,585 [95% CI, \$14,109-15,078] and \$44,496 (95% CI, \$42,763-46,299), respectively. The corresponding average adjusted costs for kyphoplasty patients were \$15,117 (95% CI, \$14,752-15,491) and \$41,339 (95% CI, \$40,154-42,560). There were no significant differences in adjusted costs in the first nine months post-surgery, but kyphoplasty patients were associated with significantly lower adjusted treatment costs by 6.8-7.9% in the remaining periods through two years post-surgery.
NICE TA 279 (2013) ⁽²⁾ UK	Cost-effectiveness analysis	See section 2.3 for details.
Edidin et al, (2012) ⁽⁷⁰⁾ US	Cost-effectiveness analysis	<i>Cost-effectiveness analysis of treatments for vertebral compression fractures:</i> Cost per life-year gained for VCF patients in the US Medicare population compared between operated (kyphoplasty and vertebroplasty) and non-operated patients and between kyphoplasty and vertebroplasty patients, all as a function of patient age and gender. After accounting for the differences in median costs and using a discount rate of 3%, the cost per life-year gained for kyphoplasty and vertebroplasty patients ranged from \$US1,863 to \$US6,687 and from \$US2,452 to \$US13,543, respectively, compared with non-operated patients. The cost per life-year gained for kyphoplasty compared with vertebroplasty ranged from -\$US4,878 (cost saving) to \$US2,763. Among patients for whom surgical treatment was indicated, kyphoplasty was found to be cost-effective, and perhaps even cost saving, compared with vertebroplasty. Even for the oldest patients (85 years-of-age and older), both interventions would be considered cost-effective in terms of cost per life-year gained.
Masala (2010) ⁽⁵⁵⁾ Italy	Cost-effectiveness analysis	Objective was to examine the cost-effectiveness of percutaneous vertebroplasty in comparison with conservative medical therapy in patients with symptomatic acute amyelic osteoporotic vertebral fractures, without spinal cord involvement and with refractory pain after two weeks of analgesic therapy. The authors concluded that percutaneous vertebroplasty should be the first choice of treatment for these patients. The study was well presented, but some methodological limitations might have affected the validity of the authors' conclusions.
MSAC (2011) Australia ⁽³⁵⁾	CMA	A cost-minimisation analysis undertaken against the comparator (conservative management) due to insufficient evidence to demonstrate vertebroplasty results in improved health outcomes compared with conservative treatment for osteoporotic or malignant vertebral fractures; and safety issues with vertebroplasty compared with conservative treatment (rib fractures, radicular pain, potential for increase in subsequent vertebral fracture). Total cost to Australian healthcare system including MBS for vertebroplasty estimated as between \$7.759 million and \$13.263 million annually. This represents an additional cost to the Australian healthcare system of \$1.612 million and \$2.755 million annually over the cost of providing conservative care. MSAC concluded that vertebroplasty comes at an additional cost to conservative treatment but, based on the best available evidence, provides no improved health outcomes. MSAC noted that vertebroplasty has been costed under the assumption that the procedure is no more or less effective or safe than management with conservative care. Therefore, cost of vertebroplasty involves same consumption of analgesia, same need for hospitalisation and same requirement for home care due to pain as conservative care. Consequently, cost of providing vertebroplasty same as cost of conservative care, with addition of cost of providing vertebroplasty procedure. Best estimate of cost of performing one vertebroplasty including all non-trivial costs accrued over the period of one year is \$7,667. This is \$1,593 more than conservative care.

<p>Svedbom et al (2013)⁽⁵⁶⁾ UK</p>	<p>Cost-effectiveness analysis – Markov simulation model</p>	<p><i>Balloon KP compared to VP and nonsurgical management in patients hospitalised with acute osteoporotic vertebral compression fracture: a UK cost-effectiveness analysis:</i> Data on HRQoL with acute OVCF were derived from FREE and VERTOS II RCTs and normalised to NSM arm in FREE trial. Estimated differences in mortality among the treatments and costs for NSM were obtained from literature whereas procedure costs for BKP and PVP were obtained from three NHS hospitals. Assumed that BKP and PVP reduced hospital length of stay by six days compared to NSM. ICER estimated at £2,706 per QALY and £15,982 per QALY compared to NSM and PVP, respectively. Sensitivity analysis showed that cost-effectiveness of BKP vs. NSM was robust when mortality and health-related quality of life (HRQoL) benefits with BKP were varied. The cost-effectiveness of BKP compared to PVP was particularly sensitive to changes in the mortality benefit. BKP may be a cost-effective strategy for the treatment of patients hospitalised with acute OVCF in the UK compared to NSM and PVP. Additional RCT data on the benefits of BKP and PVP compared to simulated sham surgery and further data on the mortality benefits with BKP compared to NSM and PVP would reduce uncertainty.</p>
<p>Itagaki et al (2012)⁽⁵⁷⁾ US</p>	<p>Standard Medicare 5% anonymised inpatient files (1999-2009) retrospectively reviewed. N=451 patients</p>	<p><i>PVP and KP for pathologic vertebral fractures in the Medicare population: safer and less expensive than open surgery:</i> Patients with diagnosis of vertebral fracture without spinal cord injury and primary or metastatic bony malignancy divided into percutaneous or surgical groups based on whether they received VP/KP or surgical treatment. Patients who had no intervention or both interventions were excluded. Cost, length of stay, and type of discharge were examined while controlling for demographic and comorbidity variables. 52% received percutaneous treatment and 48% received surgery. Patients treated percutaneously were older ($P < .001$) and more likely to be female ($P = .04$). Percutaneous therapy predicted \$14,862 less Medicare cost and \$13,565 less overall cost ($P < .001$ for both), and 4.1 fewer inpatient days ($P < .001$). Patients who underwent surgery had higher odds of death (odds ratio = 3.38, $P = .016$), discharge to a rehabilitation facility (odds ratio = 3.3, $P = .003$), and transfer to another inpatient facility (odds ratio = 8.53, $P < .001$), and lower odds of discharge to home (odds ratio = 0.42, $P < .001$) and hospice (odds ratio = 0.08, $P = .002$). In a Medicare population with bony malignancy and vertebral fractures, percutaneous therapy predicted significantly reduced cost and length of stay versus surgery. Patients who underwent percutaneous therapy were significantly less likely to die, be transferred, or be discharged to rehabilitation facilities, and were more likely to be discharged to home or hospice.</p>
<p>Tang et al (2011)⁽⁵⁸⁾ China</p>	<p>Twelve month retrospective study</p>	<p><i>Osteoporotic vertebral compression fractures: surgery versus non-operative management:</i> Compared pain relief, QoL, treatment cost-effectiveness and complication rates in patients with acute osteoporotic vertebral compression fracture (OVCF) undergoing PVP (n = 58), PKP (n = 55), or conservative medical therapy (CMT; n = 55). After surgery, Cobb angle and vertebral height were significantly improved in PKP group. PVP and PKP patients had significantly less pain immediately after surgery than CMT patients, but this difference disappeared between weeks two to eight, only to return from months six to twelve. QoL significantly better among surgical groups after surgery and was lower in the CMT group than in the surgical groups. Treatment times shorter with PVP and PKP, but costs lower with CMT. The rate of secondary fractures during follow-up was greater with CMT. Overall, PVP was considered the first choice treatment for OVCF with refractory pain.</p>

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