



Medical Services Advisory Committee

Public Summary Document

Reference No. 27.1 – Review of Interim Funded Service: Vertebroplasty and new Review of Kyphoplasty

Sponsors/Applicants: Department of Health and Ageing
Johnson & Johnson Medical Pty Ltd
(Vertebroplasty)
Medtronic Australasia Pty Ltd (Kyphoplasty)

Date of MSAC consideration: 52nd MSAC meeting, 27 April 2011

Part 1: Vertebroplasty

1. Purpose of application

In August 2009 the Department of Health and Ageing commenced the review of the interim funded service vertebroplasty. On 30 April 2010 the original applicant for kyphoplasty (Medtronic Australasia Pty Ltd) again applied for consideration of public funding so the Department sought input from the applicants for the previous assessment of vertebroplasty and kyphoplasty (Reference 27): Johnson & Johnson Medical Pty Ltd and Medtronic Australasia Pty Ltd, as well as from the Spine Society to inform a joint review of vertebroplasty and kyphoplasty.

Vertebroplasty is a minimally invasive procedure used to stabilise fractured vertebrae with the aim of relieving the associated pain. The procedure involves the percutaneous injection, under radiographic guidance, of synthetic opacified bone cement into the inter-trabecular marrow space of the fractured vertebral body.

Vertebroplasty is most commonly performed to treat incident, painful vertebral fractures caused by osteoporosis, which are unresponsive to conservative management; however, there is considerable variation both in Australia and internationally with regards to the definition of “unresponsive” and thus the duration of conservative management often varies before vertebroplasty is performed.

Vertebral fracture occurs in a broad demographic of patients with clinical presentation that is highly varied, ranging from asymptomatic to life-threatening or disabling. Vertebral fractures are associated with both a short-term and potentially long-term reduction in quality of life (Lips et al. 1999) and a modest increase in mortality which is most pronounced in the first year after a fracture (Johnell et al. 2004) but equates to about a 5 per cent increase in 5-year mortality (Woolf & Pflieger 2003). As well as acute pain, vertebral fractures can lead to chronic pain, immobility and depression (Lips et al. 1999). When kyphotic deformity is present it may impair biomechanical or respiratory function (Lombardi Jr. et al. 2005; Pakzaban 2010).

With osteoporotic vertebrae the goal is to fill the spaces in porous bone with artificial bone cement and thus strengthen the bone so that it is unlikely to fracture, or fracture further; and to reduce pain from bone rubbing on bone. The procedure is conducted *in addition* to conservative therapies. For patients with these fractures, conservative management may include: back bracing, simple analgesics ± narcotic agents, muscle relaxants or heat treatments, anti-resorptive agents, falls prevention strategies and/or bed rest followed by early mobilisation.

Vertebroplasty is undertaken less commonly in patients with vertebral fracture caused by malignant tumours. In such cases, the procedure is considered palliative and is performed over a background of conservative treatment which, in addition to the above therapies used for osteoporotic vertebral fracture, also includes: radiation therapy, chemotherapy and/or surgical removal of the tumour ± stabilisation of the vertebrae.

2. Background

In 2004-05, an MSAC assessment of vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture was conducted. On the strength of the evidence pertaining to safety, effectiveness and cost-effectiveness of vertebroplasty, MSAC supported interim public funding for:

- vertebroplasty in patients with painful osteoporotic 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

The procedure should be performed by appropriately qualified medical practitioners and this recommendation was to have been reviewed within five years.

On 27 September 2005 the Minister for Health and Ageing accepted MSAC's advice for vertebroplasty to be granted funding on an interim basis, with a planned review of funding within five years, and that there was insufficient evidence to support public funding of kyphoplasty at that time.

Following the Minister for Health and Ageing's approval of MSAC's advice supporting interim public funding for vertebroplasty for the treatment of vertebral compression fractures, MBS Item Numbers 35400 and 35402 were created and were due to cease in May 2011.

After receiving an application to review kyphoplasty, the Department agreed to review it in conjunction with the review of the interim funded service for vertebroplasty, which it had already commenced, as both had initially been conducted under Reference 27 in 2004-05. Whilst the one Assessment Report was prepared, MSAC considered vertebroplasty and kyphoplasty separately and therefore a Public Summary Document for each procedure has been produced by MSAC.

3. Prerequisites to implementation of any funding advice

Table 5 of the Assessment Report details the vertebroplasty (and kyphoplasty) equipment listed on the Australian Register of Therapeutic Goods (ARTG).

4. Proposal for public funding

The current listing of vertebroplasty items on the MBS provide publicly funded access to the procedure, on an interim basis, to patients with painful osteoporotic vertebral compression fractures, who have not had the pain adequately controlled through conservative measures, and have radiographic evidence to support the benefit of vertebroplasty (MBS item 35400). Patients with painful metastatic deposits or multiple myeloma in a vertebral body are also eligible (MBS item 35402). The listings cover only the operator fee and specifically do not include the cost of the bone cement (see Table 1).

Table 1 MBS items for vertebroplasty

MBS Item Number	Descriptor
35400	<p>VERTEBROPLASTY, for the treatment of a painful osteoporotic vertebral compression fracture, where:</p> <p>(a) the patient to whom the service is provided has not had the pain arising from the vertebral compression fracture controlled by conservative medical therapy; and</p> <p>(b) diagnostic imaging has confirmed that vertebroplasty will be of benefit;</p> <p>in association with item 61109, 57341 or 57345.</p> <p>Multiple Services Rule (Anaes.)</p> <p>Fee: \$624.55 Benefit: 75 per cent = \$468.45 85 per cent = \$555.45</p> <p>(See para T8.41 of explanatory notes to this Category)</p>
35402	<p>VERTEBROPLASTY, for the treatment of a painful metastatic deposit or multiple myeloma in a vertebral body, in association with item 61109, 57341 or 57345.</p> <p>Multiple Services Rule (Anaes.)</p> <p>Fee: \$624.55 Benefit: 75 per cent = \$468.45 85 per cent = \$555.45</p> <p>(See para T8.41 of explanatory notes to this Category)</p>
<p>Explanatory Notes:</p> <p>T8.41 Vertebroplasty - (Items 35400 and 35402)</p> <p>Items 35400 and 35402 have been introduced on an interim basis for five years following a recommendation of the Medical Services Advisory Committee (MSAC). The MSAC assessment of vertebroplasty showed that finding either bone oedema or gas cleft on a magnetic resonance image was the most effective way of confirming that vertebroplasty would be effective in relieving pain due to osteoporotic vertebral compression fractures: the absence of either of these findings on a magnetic resonance image is considered a contra-indication to vertebroplasty. The items do not cover the cost of the cement injected during the procedure. Where a charge is made for the cement, it must be separately listed on the account and not billed to Medicare.</p>	

Source: www.mbs.gov.au [accessed 18/10/2010]

Vertebroplasty requires specialist referral (physician, geriatrician, rheumatologist, spinal surgeon), prior to magnetic resonance imaging MRI (or bone scan) to confirm the recency of the fracture. The procedure is performed as day surgery or inpatient by a specially trained interventional radiologist under fluoroscopic guidance (with or without computed tomography). Patients receive a local anaesthetic at the injection site and the procedure is performed under conscious sedation.

5. Consumer Impact Statement

While vertebroplasty (and kyphoplasty) procedures are available in both public and private hospitals, the majority (85 per cent 2007-08) are performed in private hospitals.

It is likely that vertebroplasty would not be available in rural and remote areas as the procedure needs to be undertaken by an interventional radiologist and their availability in such locations is limited. This is in contrast to second line conservative medical management which may be administered in rural and remote areas, although preferably in a local hospital or medical clinic.

Furthermore, the likelihood of accessing vertebroplasty depends on where a patient resides in Australia. Usage (and thus availability) is higher in New South Wales than in the other States and Territories, equivalent to 5.26 vertebroplasties per 100,000 (based on population statistics from March 2010). Whereas, Western Australia and Queensland performed 4.20 and 3.31 vertebroplasties per 100,000 population in the 2009-10 financial year, and Victoria performed only 0.38 vertebroplasties per 100,000 population over the same period.

6. Proposed intervention's place in clinical management

First line therapy for patients with symptomatic vertebral fractures is conservative management. Only in cases of osteoporosis or vertebral tumours, when bone healing may be impaired, and if the patient's response to conservative management is inadequate, is vertebroplasty or kyphoplasty considered.

In general, patients are selected for vertebroplasty on the basis of pain that is incapacitating and unresponsive to conservative treatment, as well as on specific physical indications found through imaging and clinical assessment. Figure 14 in the Assessment Report identifies the patient journey for a person diagnosed with osteoporotic or malignant vertebral fracture.

The alternative to these procedures is continued or intensified conservative management, or in cases of severe functional kyphotic deformity, open surgical stabilisation and realignment may be considered. If provided, vertebroplasty and kyphoplasty are used *in addition* to conservative management, as required by the individual patient.

7. Comparator to the proposed intervention

The comparator for vertebroplasty or kyphoplasty in the management of painful vertebral fractures caused by osteoporosis or vertebral tumours is conservative management. This is the primary comparator of interest for both procedures. Vertebroplasty and kyphoplasty were also compared with each other for the same patient indications.

Conservative management of osteoporotic fractures does not itself require patients to be hospitalised, but in cases of severe pain, when the patient is unable to cope at home, the patient may be hospitalised. The case is similar with respect to palliative care provided to patients with vertebral tumours, although radiation therapy, chemotherapy, and surgical excision of tumours require a higher level of medical care.

8. Comparative safety

A structured assessment of vertebroplasty and kyphoplasty for the treatment of vertebral fractures based on clinical need, clinical effectiveness, safety, and economic considerations was conducted, the basis of which was a systematic literature review.

For evaluation of the effectiveness of either intervention, only comparative studies were included (studies comparing vertebroplasty with conservative management or kyphoplasty, and studies comparing kyphoplasty with conservative management or surgery). For evaluation of safety, case series containing at least 20 patients and with an average follow-up of at least six months were also considered in order to capture infrequent and rare adverse events. For evaluation of vertebroplasty compared with conservative management, it was only necessary to include studies published since completion of searches conducted in the original MSAC evaluation. Because of the additional indication being considered for kyphoplasty, some of the searches needed to be extended further back in time to encompass all of the available literature.

One hundred and nine studies were identified that met the inclusion criteria for selecting studies to assess the safety of vertebroplasty for the treatment of incident, painful vertebral fractures (Assessment Report Box 1). Good comparative evidence was provided by two double-blind (sham-controlled) randomised controlled trials (RCTs; (Buchbinder et al. 2009; Kallmes et al. 2009) and this was supplemented by three open label RCTs (Klazen et al. 2010c; Rousing et al. 2010; Voormolen et al. 2007; Klazen et al. 2010a), five nonrandomised trials or observational studies, and 99 case series or studies with other comparators. Due to the large number of case series and studies with other comparators, data were only extracted for studies with at least 200 patients (26 of 99 studies) while the rest were reviewed and any additional relevant information that they provided was discussed. In total, the studies for which safety data were extracted included approximately 10,000 patients with an estimated 16,000 vertebral fractures treated with vertebroplasty. The exact numbers cannot be determined due to the overlap among studies.

For vertebroplasty, there were 10 studies meeting the inclusion criteria that compared the procedure with conservative management, along with 106 case series and studies with comparators other than conservative management or kyphoplasty. The highest level of evidence was provided by five randomised controlled trials (RCTs; level II evidence), two of which incorporated a control arm that received placebo treatment (sham vertebroplasty) and provided evidence of the best methodological quality. One of the three other level II studies was considered to be of good quality despite being conducted in an open-label setting, and there were five level III-2 studies of poor to moderate quality. All of the comparative studies were conducted in patients with osteoporosis; there were no studies meeting the inclusion criteria for evaluation of the comparative effectiveness of vertebroplasty in patients with fractures caused by vertebral tumours.

Fifteen studies meeting the inclusion criteria directly compared vertebroplasty to kyphoplasty, including one level II study, one level III-1 study, 10 level III-2 studies and three level III-3 studies. No studies directly comparing the procedures were considered to be of good quality; all had a moderate or high risk of confounding. One of these studies compared the procedures in patients with multiple myeloma while the rest treated patients with osteoporotic fractures.

Vertebroplasty versus conservative management for treatment of patients with painful vertebral osteoporotic fracture(s)

Cement leakage is commonly associated with vertebroplasty, but adverse clinical consequences are rare. The frequency of cement leakage at any site varied between 8 and 72 per cent in the evidence base. In the only Australian study reporting cement leakage, 37 per cent of procedures were associated with cement leakage although no clinical sequelae were observed. One study provided good evidence that pulmonary cement embolism (PCE: leakage of cement into veins which then is transported to the lungs) occurs much more frequently than was previously thought – 26 per cent of patients receiving vertebroplasty as opposed to 0-2 per cent that was reported in other studies – but that it is nearly always asymptomatic and of no known clinical relevance at mid-term follow-up. Serious adverse events were uncommon; the most common adverse events were rib fracture and radicular pain.

The best evidence for the effect of vertebroplasty upon the risk of subsequent or adjacent vertebral fracture was provided by one moderate quality open-label randomised controlled trial (level II evidence) which found that subsequent fracture rates were higher in the conservatively treated arm, but that the difference was not statistically significant. This evidence was contrasted by the findings of three level III-2 studies which found that vertebroplasty patients had statistically significantly higher risks of subsequent fracture.

In all of the studies included in this assessment, only one death was directly associated with vertebroplasty. This death occurred in a patient with multiple, severe, pre-existing comorbidities that would also appear to have contributed to his death.

As in the previous MSAC assessment, no studies were identified that investigated the amount, or clinical consequences of radiation exposure received by the health professional or patient throughout the vertebroplasty procedure.

Vertebroplasty versus conservative management for treatment of patients with painful vertebral fracture(s) caused by vertebral malignant tumours (without neural compression)

No comparative studies or large case series meeting the inclusion criteria reported solely on patients with vertebral malignancies, although several of the larger case series included mixed populations of patients with both osteoporotic and malignant fractures (although patients with malignant fractures were always the minority). Results were not stratified by patients' clinical indication. In those studies that consisted of cancer patients only, the type and frequency of adverse events did not differ from those observed in the studies of osteoporotic or mixed populations.

Vertebroplasty versus kyphoplasty for treatment of patients with painful vertebral osteoporotic fracture(s)

The best evidence available for the comparison of vertebroplasty with kyphoplasty is provided by a single poor quality level II study, and several poor-to-moderate quality level III studies. Supporting these direct comparison studies is the evidence provided by studies that compared each procedure to conservative management, as well as case series.

There is moderate quality level III-2 evidence that vertebroplasty results in more cement leakage than kyphoplasty, and this evidence is supported by three poor quality level III-2 or III-3 studies and by comparing the findings of the previous sections of this assessment (comparing each procedure to conservative management). Whether this difference translates into a difference in clinically significant adverse events related to cement leakage could not be assessed with the available evidence.

There is poor quality evidence from one level III-3 study that kyphoplasty results in an increased risk of subsequent adjacent-level vertebral fracture compared with vertebroplasty. While the effects of each procedure upon fracture risk compared with conservative management are unclear, this finding is supported by the highest evidence level in each comparison (i.e. the findings of one level II study that vertebroplasty tended to decrease subsequent fracture risk and the finding of one level II study that found that kyphoplasty may increase fracture risk—there is, however, also contrasting evidence in both cases).

No studies have assessed the comparative safety of vertebroplasty and kyphoplasty with respect to radiation exposure. Being a longer procedure, with more stages in the procedure, kyphoplasty is likely to result in more radiation exposure from intra-operative imaging, but this difference is likely to have negligible clinical consequences.

Vertebroplasty versus kyphoplasty for treatment of patients with painful vertebral fracture(s) caused by vertebral malignant tumours (without neural compression)

One moderate quality level III-2 study compared vertebroplasty to kyphoplasty in patients with vertebral compression fractures caused by multiple myeloma. No significant differences in safety outcomes were observed in this study. This evidence is supported by comparisons of the procedures in patients with osteoporotic fractures, owing to the limitations of generalising the evidence in this population.

Owing to the procedure-specific complications, such as cement leakage, rib fractures, radicular pain and potential for increase in subsequent vertebral fracture, MSAC concluded that vertebroplasty is not considered to be as safe as conservative management.

9. Comparative effectiveness

The evidence base for assessment of the comparative effectiveness of vertebroplasty and kyphoplasty was the same as for their comparative safety, as described in the Assessment Report, except that the vertebroplasty and kyphoplasty case series which contributed to evaluation of their comparative safety were not considered in evaluation of their comparative effectiveness.

Two double-blind (sham-controlled) randomised controlled trials (RCTs) (Buchbinder et al. 2009; Kallmes et al. 2009), three open-label RCTs (Klazen et al. 2010c; Rousing et al. 2010; Voormolen et al. 2007; Klazen et al. 2010a) and three nonrandomised comparative studies (Alvarez et al. 2006; Diamond et al. 2006; Masala et al. 2008b) were eligible for assessing the effectiveness of vertebroplasty compared with conservative management.

Both of the double-blind (sham-controlled) RCTs were considered to be of good quality. Buchbinder et al. (2009) was of the highest methodological quality (and was conducted in Australia), followed by Kallmes et al. (2009).

Both good quality RCTs had relatively low recruitment rates (30–42 per cent of eligible patients who were screened). Selection criteria differed somewhat between the blinded and open-label studies.

Quality assessment primarily related to the likelihood of bias and confounding – bias and confounding were considered unlikely in the Buchbinder et al. trial, whereas biased outcome assessment was considered possible in the Kallmes et al. (2009) trial – despite attempts being made to minimise this occurrence.

Vertebroplasty versus conservative management for patients with painful vertebral osteoporotic fracture(s)

The best methodological quality evidence on the effectiveness of vertebroplasty was provided by two good quality level II studies that compared vertebroplasty to placebo (sham procedure). One of these studies was conducted entirely in Australia, and one of 11 treatment centres used in the other study was also located in Australia.

Both of the sham-controlled trials of good methodological quality found vertebroplasty to be no better than conservative management with respect to the outcomes of interest that were defined *a priori* (including patient-assessed pain, patient-assessed quality of life, patient-assessed functional capacity, psychological wellbeing and analgesia usage). Some of the open-label studies of low to good quality and/or evidence level found vertebroplasty to be superior to conservative management, most often in the short to medium-term (with respect to patient-assessed pain, patient-assessed quality of life, observer-assessed functional status, patient-assessed functional status and analgesia usage). With respect to hospital length-of-stay, an economic analysis accompanying one level II study provided indirect evidence that vertebroplasty increases hospital length-of-stay in outpatients treated with vertebroplasty, beyond the one day required for the procedure itself, while one moderate quality level II study and one moderate quality level III-2 study provided evidence that hospital length-of-stay is reduced in inpatients treated with vertebroplasty. Further, one poor quality level III-2 study provided evidence that hospital length-of-stay was reduced in a combined inpatient/outpatient population treated with vertebroplasty. It is possible, however, that the results of all four studies were confounded. One open-label level II study provided evidence that vertebroplasty significantly reduces the risk of progressive fracture of the treated vertebral body.

One of the sham-controlled high quality level II studies found a nonsignificant trend towards vertebroplasty patients being *more* likely to require opioid analgesia than patients treated with placebo at one month follow-up, and the other (the Australian study) did not observe any differences in analgesia usage between the treatment groups. Contrasting these findings, one open-label level II study and two level III-2 studies found that vertebroplasty patients required significantly less analgesia during follow-up.

There is evidence from one open-label level II study that patients treated conservatively experience more frequent and more severe progressive loss of height in vertebrae showing bone oedema on magnetic resonance imaging at baseline, than is seen in vertebrae treated with vertebroplasty. The clinical relevance of the benefits in terms of maintenance of vertebral height is yet to be determined.

Vertebroplasty versus conservative management (palliative care) for patients with painful vertebral fracture(s) caused by vertebral malignant tumours (without neural compression)

No studies were identified that met the inclusion criteria for assessment of the effectiveness of vertebroplasty in the treatment of vertebral malignancies. The best available evidence is provided by level IV studies only, which were excluded from this assessment update, and from studies of vertebroplasty in osteoporotic patients, owing to the limitations of generalising this evidence.

Vertebroplasty versus kyphoplasty for treatment of patients with painful vertebral osteoporotic fracture(s)

One level II study found no statistically significant or clinically important differences between the treatment groups with respect to patient-assessed pain. In the level III-1 study, statistically greater improvements were observed in the kyphoplasty group, but the difference was not clinically important according to the predefined criteria, even after a worsening in pain scores in the vertebroplasty group between short and mid-term follow-up. In the only study to observe a clinically important difference in patient-assessed pain it was not possible to determine the statistical significance. Two moderate quality level III-1 and III-2 studies compared vertebroplasty to kyphoplasty with respect to patient-assessed quality of life. In the level III-1 study, kyphoplasty was observed to result in greater improvements in patient-assessed quality of life; however, analytical errors in the study prevented interpretation of the statistical significance of the results. The other study did not observe any significant differences in patient-assessed quality of life, either between the two procedures or between each procedure and an age- and sex-matched reference sample.

Patient-assessed functional status was reported in one moderate quality level III-1 study and five poor quality level III-2 or III-3 studies that compared vertebroplasty to kyphoplasty in the treatment of patients with osteoporotic fractures. The level III-1 study found that kyphoplasty resulted in statistically significantly greater functional improvement as measured using the Oswestry disability index (ODI), but the differences were not clinically important. Only one study found clinically important differences, which favoured kyphoplasty, but the statistical significance of the difference could not be determined. No studies meeting the inclusion criteria compared vertebroplasty to kyphoplasty with respect to analgesia usage, observer-assessed patient symptoms, observer-assessed quality of life, or hospital length-of-stay. However, most of the studies comparing vertebroplasty to kyphoplasty did report the radiographic outcomes of changes in vertebral height and alignment. Most studies, including one level II study, found that vertebroplasty resulted in some improvement in vertebral height and alignment, but that kyphoplasty resulted in greater improvements.

MSAC noted that as a consequence of the different enrolment criteria, there were differences in the likely average fracture duration at baseline between the two sham-controlled RCTs. The median pain duration (proxy for vertebral fracture age) was 9 weeks (IQR 4, 13) in the vertebroplasty arm and 10 weeks (IQR 3, 17) in the sham control arm at baseline in the Buchbinder et al. trial. In the RCT by Kallmes et al., mean pain duration at baseline was 16 weeks (IQR 10, 36) and 20 weeks (IQR 8, 38) in the vertebroplasty and sham control arms, respectively.

MSAC noted that overall, in the best available studies, vertebroplasty was found to have no significant or clinically important benefits over placebo in the short-term or in the long-term with respect to pain control as measured by numerical pain ratings (NRS). This was contrasted by the findings of three open-label studies that found vertebroplasty to be of additional benefit, especially in the short-term post-operative period.

MSAC also noted that the best available evidence does not support a benefit of vertebroplasty over placebo in quality of life as measured by European Quality of Life–5 Dimensions (EQ-5D). In an open-label setting, the evidence is conflicting; there is evidence of an enhanced effect but also some evidence supporting conservative management over vertebroplasty.

With regards to vertebroplasty versus kyphoplasty, all of the studies in the evidence base had moderate or high risks of confounding or bias, which makes it difficult to draw conclusions regarding any of the effectiveness outcomes. In the moderate quality level III-1 study which, together with the poor quality II study provided the best evidence available, there was a mid-term decline in many outcome measures in the group treated with vertebroplasty. The reason for this deterioration is unclear, and the pattern is not represented in the rest of the literature on vertebroplasty.

10. Economic evaluation

A cost-effectiveness analysis is undertaken only if there is evidence that the new procedure is more effective and/or less harmful than the designated comparator; otherwise a financial impact analysis is all that is required by MSAC. The balance of benefit and harm in the evidence-base does not favour vertebroplasty relative to conservative management in the treatment of osteoporotic patients with painful vertebral fracture. The effectiveness of kyphoplasty relative to conservative management in osteoporotic patients with painful vertebral fracture could not be established without a placebo control and there was also a likelihood of increased harm over conservative management. Similarly, there were insufficient data comparing kyphoplasty and surgery to determine the relative safety and effectiveness in osteoporotic patients with kyphotic deformity. No comparative evidence was available in the population with painful fractures caused by vertebral tumours. As a consequence, no modelled cost-effectiveness analyses or cost-consequences analyses have been presented.

MSAC noted that a cost-minimisation analysis was undertaken against the comparator (conservative management) due to insufficient evidence to demonstrate that vertebroplasty results in improved health outcomes compared with conservative treatment for either 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).

The total cost to the Australian healthcare system including MBS for vertebroplasty is estimated to be 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 therefore concluded that vertebroplasty comes at an additional cost to conservative treatment but, based on the best available evidence, provides no improved health outcomes.

The current MBS fee (interim listing) for vertebroplasty is \$624.55 per fracture treated.

There were no data on the average fee charged.

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, the cost of vertebroplasty will involve the same consumption of analgesia, the same need for hospitalisation and the same requirement for home care due to pain as conservative care. Consequently, the cost of providing vertebroplasty will be precisely the same as the cost of conservative care, with the addition of the cost of providing the vertebroplasty procedure.

The best estimate of the cost of performing one vertebroplasty procedure including all non-trivial costs accrued over the period of one year is \$7,667. This is \$1,593 more than conservative care.

MSAC noted that 85 per cent of procedures are performed in private hospitals and that the patient/private health insurer bear approximately 40 per cent of the cost of conservative treatment and vertebroplasty.

Any Extended Medicare Safety Net implications would depend upon the average fee charged. Only Medicare services rendered out of hospital count towards the Medicare Safety Net or Extended Medicare Safety Net. MSAC had no data on these potential costs.

11. Financial/budgetary impacts

Approximately 16,000 radiographically diagnosed vertebral fractures are estimated to occur in Australia each year, and the incidence is predicted to increase as the population ages (Sanders et al. 1999a). However, because the symptoms associated with many vertebral fractures are not severe, and the majority of patients respond to conservative therapy, only a small number of these (about 5 per cent or 800) are potential candidates for vertebroplasty or kyphoplasty.

Current utilisation of vertebroplasty in Australia is influenced by access to a provider of the service, as evidenced by large geographical variations in utilisation. Since its interim listing on the MBS for over five years, utilisation rates have been constant, at approximately 800 services per annum. MSAC noted a large variation across States – 55.4 per cent of all procedures are performed in New South Wales and 3.1 per cent in Victoria (2009-10).

Disparity in the utilisation of vertebroplasty across Australian states raises uncertainty when estimating future utilisation. As the precise incentives or barriers to service provision across States are largely unknown, predicting whether they will continue or alter is impossible. Therefore, it is uncertain whether States providing low levels of vertebroplasty will increase their capacity into the future toward New South Wales levels, or indeed, whether New South Wales will further increase its service provision.

MSAC agreed that the academic argument surrounding vertebroplasty is not settled, and the dynamic nature of the underlying pathology makes it difficult to specify the patient group that may benefit from vertebroplasty.

The expected uptake of vertebroplasty for the treatment of painful vertebral fractures is estimated at between 1012 to 1730 procedures per year within 10 years.

The total cost to the MBS for performing vertebroplasty with all relevant costs over a period of one year is estimated to be between \$2.191 million and \$3.745 million annually. Compared with conservative care, the incremental cost to the MBS of providing vertebroplasty is between \$0.694 million and \$1.187 million with a similar increase in cost borne by the patient or private insurer.

Whilst vertebroplasty remains a procedure performed most frequently in the private healthcare sector, the added burden to State or Territory Governments over conservative care will be relatively minor (between \$0.201 million and \$0.344 million).

12. MSAC key issues

The effect of vertebroplasty upon subsequent vertebral fracture risk is poorly understood and this review of the literature was unable to produce any strong conclusions regarding it. Analysis of fracture risk is hampered by the relationship between vertebral fracture and subsequent fracture risk, by the availability of multiple methods for measuring risk (i.e. per patient, per unfractured vertebra, or per unfractured adjacent vertebra), and by the presence of a large range of potential confounding variables (e.g. number of pre-existing fractures, age of most recent fracture, bone mineral density, body mass index). All of the level II studies were underpowered for this analysis, and meta-analysis was deemed inappropriate because of differences in patient selection and length of follow-up. However, one of these studies found a non-significant trend towards conservatively treated patients being more likely to experience subsequent vertebral fracture. This was contrasted by the findings of three level III-2 studies that found that patients treated with vertebroplasty experienced significantly *more* fractures during follow-up.

There is also uncertainty regarding the impact of vertebroplasty upon iatrogenic adverse events in a particular subgroup of patients. If vertebroplasty were found to be effective at reducing hospital length-of-stay or analgesia usage in this subgroup, then this would be associated with a theoretical reduction in risk of adverse events, such as hospital-acquired illness or side effects of medication; however, no data on this were provided in the available evidence base.

There is moderate quality evidence that rates of cement leakage, and rates of clinical complications associated with cement leakage, are lower in kyphoplasty than in vertebroplasty, however much of this evidence is provided through indirect comparison. Because clinically important adverse events associated with cement leakage are rare, a reduction in their frequency in kyphoplasty could be outweighed by a small increase in the risk of subsequent or adjacent vertebral fracture, but there is insufficient evidence at this time to arrive at any firm conclusions.

Although there are concerns regarding patient selection and technique in the sham-controlled trials, these trials are still considered to provide evidence of the best methodological quality to determine the effectiveness of vertebroplasty with respect to conservative management, in the majority of patients with osteoporotic vertebral fractures; they provide good quality evidence that the addition of vertebroplasty to the conservative management of painful vertebral fractures is no more effective than placebo. Vertebroplasty may have a role in the management of a subgroup of patients with acute, unstable vertebral fractures and intractable pain but further information is required from good quality research before any such treatment effect modification can be confirmed.

There is limited poor to moderate quality evidence that indicates that kyphoplasty may be more effective than vertebroplasty, although none of the effects observed in the literature were demonstrated to be both clinically important and statistically significant.

MSAC also noted differences in patient recruitment into RCTs as well as different views about optimal age of fractures to be treated and cement volumes used.

MSAC noted the dissenting opinions of clinical experts including some members of the Advisory Panel who disagreed with the methodology of the sham-controlled RCTs due to issues with selection of patient population with recent fractures and techniques used to perform the vertebroplasty operations.

It has been suggested that the procedural technique used in the sham-controlled studies was inappropriate; specifically, that the volume of cement that was injected was insufficient to achieve a benefit from the procedure. Only nine of the 25 comparative studies meeting the inclusion criteria reported on cement volumes, and only 18 of the 51 total vertebroplasty studies for which data were extracted. One of the placebo-controlled randomised trials did not report cement volume, and the other (which was conducted in Australia) reported an average that was lower than most other studies that reported average cement volume; however, the differences between the studies were not large, varying from an average of 2.5 mL to 5.2 mL. Given the similarities between the cement volumes used in the studies, it is unclear whether the average reported in the Australian study would be responsible for the near-zero incremental treatment effects observed in that study. While it is possible that many patients may have received *suboptimal* volumes, enough patients may have received a *subthreshold* cement volume to account for a treatment effect, should a treatment effect exist. However, it is equally possible that a low volume of cement injected partially contributed to the differences in treatment effect observed between the Australian placebo-controlled trial and the Dutch open-label trial.

Experts have suggested that there is a subgroup of patients with acute, unstable vertebral fractures, intractable pain and severely limited functional capacity who currently derive the most benefit from vertebroplasty. From analysis of patient selection criteria and the baseline characteristics of patients included in all of the comparative studies, there is some evidence that this subgroup of patients may have been underrepresented in the placebo-controlled trials compared with some of the open-label studies, although most of the clinical characteristics were comparable. This may also have contributed to the differences in treatment effects observed between the placebo-controlled and open-label studies.

Given the conflicting results between the open-label and blinded randomised controlled trials that have been conducted in two *predominantly* different patient groups, MSAC noted that a multi-centre, sham-controlled trial of vertebroplasty in patients with acute painful osteoporotic vertebral fracture (VERTOS IV) commenced in January 2011 but has yet to begin patient recruitment.

MSAC noted that a cost-minimisation analysis was undertaken against the comparator (conservative management) due to insufficient evidence to demonstrate that vertebroplasty results in improved health outcomes. MSAC also noted a lack of high quality data demonstrating changed hospital length of stay and this added to uncertainty regarding economic benefit, although it was acknowledged that many vertebroplasties in Australia are performed as day procedures.

Future use of vertebroplasty and kyphoplasty is uncertain and contingent upon several factors: the increase in demand due to the increase in vertebral fractures in an ageing community; the increase of provision in Australian States currently offering low levels of service; and the extent to which kyphoplasty will replace vertebroplasty as a treatment for painful vertebral fractures.

Data derived from the Department of Health and Ageing reveal that a single vertebra is treated 74 per cent of the time, two vertebrae are treated 19 per cent of the time and three or more vertebrae are treated 7 per cent of the time. Treatment of multiple vertebrae will have implications for the cost of each procedure, requiring more materials and will allow multiple billing by the physician.

The National Hospital Morbidity Database published by the Australian Institute of Health and Welfare shows that in 29 per cent of cases, a same day (or overnight) flag was present and therefore 71 per cent of vertebroplasty procedures resulted in an admission lasting longer than one day.

MSAC had no data on the average fee charged and any implications for the Extended Medicare Safety Net.

Vertebroplasty is performed in addition to conservative management, but MSAC was uncertain as to cost offsets arising from differences in age of fractures treated, possible reduction in hospital length of stay and reduced analgesia usage.

13. Summary of consideration and rationale for MSAC's advice

MSAC noted that two randomised controlled trials (RCTs) of good methodological quality (sham-controlled) found no clinically or statistically significant additional beneficial effect of vertebroplasty over a sham procedure with respect to overall outcomes.

MSAC focussed its discussion on the relative merits of the results from these two sham-controlled randomised trials (Buchbinder *et al.* and Kallmes *et al.*) versus unblinded randomised trials such as VERTOS II which compared vertebroplasty with conservative therapy. MSAC considered dissenting submissions from clinical experts that questioned the methodology and relevance of the sham trials in the Australian context. In particular, MSAC discussed uncertainties around operator skill, placebo effect, and optimal cement volume, optimal fracture age and pain severity for treatment. It also discussed trial recruitment issues, which may have affected the power of the studies. MSAC noted that data from the sham-controlled trials did not fully resolve the uncertainty as to whether cement volume correlates with symptomatic outcomes. MSAC also accepted that there was level II evidence suggesting that a placebo effect cannot be excluded.

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.

MSAC noted that a cost-minimisation analysis was undertaken against the comparator (conservative management) due to insufficient evidence to demonstrate that vertebroplasty results in improved health outcomes compared with conservative treatment for either 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). MSAC also noted a lack of high quality data demonstrating changed hospital length of stay and this added to uncertainty regarding economic benefit, although it was acknowledged that many vertebroplasties in Australia are performed as day procedures.

MSAC noted utilisation data that showed an uneven geographic distribution of uptake of vertebroplasty across Australian States and Territories during the period of its interim funding under the Medicare Benefits Schedule (MBS), with more than half of all vertebroplasties performed in one state (New South Wales). Since its interim listing on the MBS for over five years, utilisation rates have been constant, at approximately 800 services per annum. MSAC questioned whether this distribution arose from the need for a highly skilled workforce to perform the procedure and, if so, whether any publicly-funded access would be better served by a Nationally Funded Centre. However, MSAC was not able to draw firm conclusions from the data in this respect.

MSAC agreed that the academic argument surrounding vertebroplasty is not settled, and the dynamic nature of the underlying pathology makes it difficult to specify the patient group that may benefit from vertebroplasty. MSAC noted that a new randomised sham-controlled trial (VERTOS IV) is currently recruiting, but is not expected to report provisional results for several years. MSAC believed that this trial may address some residual uncertainties about the use of vertebroplasty for acute osteoporotic fractures. MSAC also noted that the assessment report referred to a meta-analysis of pooled individual patient data (IPD) from the Buchbinder and Kallmes trials, the results of which were also not available at the time of MSAC's consideration.

MSAC weighed up the uncertainties regarding the currently available evidence, noting that two sham-controlled RCTs showed no evidence of significant benefit for vertebroplasty, and that dissenting views were submitted by clinical experts, including some members of the Advisory Panel convened to assist with the evaluation. MSAC also noted uncertainties relating to patient recruitment into the RCTs, access and equity issues for patients, and whether the success of the procedure is highly dependent on fracture age, operator skill or volume of cement used. MSAC noted that studies addressing these uncertainties were in progress.

14. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to the safety, effectiveness and cost-effectiveness of percutaneous vertebroplasty for painful vertebral compression fractures, and having noted the dissenting expert opinion, MSAC does not support continued public funding for this procedure.

15. Context for decision

This advice was made under the MSAC Terms of Reference.

MSAC is to:

- Advise the Minister for Health and Ageing on medical services that involve new or emerging technologies and procedures and, where relevant, amendment to existing MBS items, in relation to:
 - the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;
 - whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
 - the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;
 - the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
 - other matters related to the public funding of health services referred by the Minister.
- Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.
- MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

16. Linkages to other documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au.

The MSAC Assessment Report is available at <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/Completed-References1-40>