



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 2: Kyphoplasty

1. Purpose of application

On 30 April 2010 the original applicant for kyphoplasty, which MSAC assessed in 2004-05 (Medtronic Australasia Pty Ltd), again applied for consideration of public funding. As the Department had already commenced the review of the interim funded service vertebroplasty in August 2009, 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.

Kyphoplasty is used to stabilise fractured vertebrae with the aim of relieving the associated pain as well as to correct any associated functional kyphotic deformity (abnormal wedging). Kyphoplasty is performed under radiographic guidance but involves the additional insertion of a small high pressure balloon catheter into the vertebral body which is then inflated with a liquid, under pressure, to raise the fractured compressed bone and create a cavity. The balloon catheter is then deflated and removed prior to the injection of the synthetic bone cement so as to correct the vertebral deformity (Eckel & Olan 2009, Anselmetti et al 2010). Generally kyphoplasty requires a general anaesthesia.

Kyphoplasty is a modification of the vertebroplasty technique.

In otherwise healthy patients, vertebral fractures will usually heal with time and conservative management. In patients with osteoporotic or malignant vertebral fractures, healing may be impaired and patients' response to conservative therapy may be slow; it is in these patients that vertebroplasty and kyphoplasty are potentially considered in addition to continued conservative therapies. Figures 8 and 9 in the Assessment Report set out the clinical decision trees for the treatment of painful vertebral fractures and for structural correction of functional kyphotic deformity.

Kyphoplasty is also indicated for patients with functional kyphotic deformity resulting in pulmonary dysfunction, although it is possible that there will be limited demand for kyphoplasty for this particular indication.

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.

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. One Assessment Report was prepared, MSAC considered vertebroplasty and kyphoplasty separately and therefore a separate MSAC Public Summary Document has been produced.

3. Prerequisites to implementation of any funding advice

Table 5 in the Assessment Report details the vertebroplasty and kyphoplasty equipment listed on the Australian Register of Therapeutic Goods (ARTG), including the balloon kyphoplasty procedure kit manufactured by Medtronic Australasia Pty Ltd (ARTG Number 151354), which is used in addition to the insertion of the synthetic bone cement.

4. Proposal for public funding

Kyphoplasty is not currently listed on the Medicare Benefits Schedule (MBS). The majority of patients that would be eligible to undergo kyphoplasty procedures receive vertebroplasty instead.

The applicant's submission suggested the following MBS item descriptor and fee:

Table 1 Proposed MBS item descriptors and fees for kyphoplasty

Category 3 – THERAPEUTIC PROCEDURES	
MBS Item Number	Descriptor
—	BALLOON KYPHOPLASTY, for the treatment of a painful osteoporotic vertebral fracture, where: (a) the patient to whom the service is provided has not had the pain arising from the vertebral fracture controlled by conservative medical therapy; and (b) diagnostic imaging has confirmed that kyphoplasty will be of benefit; in association with item 61109, 57341 or 57345. Multiple Services Rule (Anaes.) Fee: \$794.45 Benefit: 75% = \$562.10 85% = \$637.05 (See explanatory note)
—	BALLOON KYPHOPLASTY, for the treatment of a painful metastatic deposit or multiple myeloma in a vertebral body, in association with item 61109, 57341 or 57345. Multiple Services Rule (Anaes.) Fee: \$794.45 Benefit: 75% = \$562.10 85% = \$637.05 (See explanatory note)

(Table continued over)

—	<p>BALLOON KYPHOPLASTY, for the treatment of functional kyphotic deformity arising from osteoporotic vertebral fracture, where:</p> <p>(a) the patient is presenting with symptoms uncontrolled by conservative medical therapy; and</p> <p>(b) diagnostic imaging has confirmed that kyphoplasty will be of benefit;</p> <p>in association with item 61109, 57341 or 57345.</p> <p>Multiple Services Rule (Anaes.) Fee: \$794.45 Benefit: 75% = \$562.10 85% = \$637.05 (See explanatory note)</p>
—	<p>BALLOON KYPHOPLASTY, for the treatment of functional kyphotic deformity arising from vertebral fracture that is associated with metastatic deposit or multiple myeloma in a vertebral body, where:</p> <p>(a) the patient is presenting with symptoms uncontrolled by conservative medical therapy; and</p> <p>(b) diagnostic imaging has confirmed that kyphoplasty will be of benefit;</p> <p>in association with item 61109, 57341 or 57345.</p> <p>Multiple Services Rule (Anaes.) Fee: \$794.45 Benefit: 75% = \$562.10 85% = \$637.05 (See explanatory note)</p>
<p>Explanatory Notes:</p> <p>The items do not cover the cost of the cement injected, or operative equipment used during the procedure. Where a charge is made for the cement or operative equipment, it must be separately listed on the account and not billed to Medicare.</p>	

Source: developed on the basis of the MSAC application and adapted from Table 1; fee for kyphoplasty = 120% of fee for vertebroplasty.

Kyphoplasty 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 commonly done under general anaesthesia in an operating theatre, although it can be done under local anaesthesia by a specially trained interventional radiologist under fluoroscopic guidance (with or without computed tomography).

5. Consumer Impact Statement

While vertebroplasty and kyphoplasty are available in both public and private hospitals, the majority are performed in private hospitals.

It is likely that vertebroplasty and kyphoplasty 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.

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, are vertebroplasty or kyphoplasty considered. 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, both vertebroplasty and kyphoplasty are used *in addition* to conservative management, as required by the individual patient.

Kyphoplasty involves inserting a high pressure small balloon catheter into a vertebra at the point where it has collapsed. The balloon is inflated with a liquid under pressure to raise the bone and correct abnormal wedging of the fractured vertebra. Once the balloon has been maximally inflated, it is then deflated and removed, and the space that has been created is filled with artificial bone cement. Generally kyphoplasty requires a general anaesthesia, while most vertebroplasty procedures are performed using local anaesthesia, with or without conscious sedation.

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 to each other for the same patient indications. For treatment of patients with functional kyphotic deformity, surgery is an additional comparator.

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).

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. 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.

For kyphoplasty, there were three clinical studies and one modelled economic evaluation meeting the inclusion criteria that compared the procedure to conservative management, one study that compared the procedure with surgery, and 49 case series and studies with other comparators. The highest level of evidence was provided by one level II study, which compared kyphoplasty to conservative management in an open-label setting, followed by two level III-2 studies. As with vertebroplasty, all of the comparative studies were conducted in patients with osteoporosis; there were no studies meeting the inclusion criteria for evaluation of the effectiveness of kyphoplasty in patients with 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.

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

Cement leakage is commonly associated with kyphoplasty, but adverse clinical consequences are rare. The frequency of cement leakage at any site varied from seven to 47% of procedures. No cases of spinal cord injury or pulmonary cement embolism (PCE) were observed in the studies for which data were extracted, but one case of permanent partial paralysis of one leg was observed in one of the smaller studies that were reviewed. Radicular pain associated with cement leakage was reported in up to 1.5% of patients.

There is one good quality level II study that provides evidence that kyphoplasty may increase the risk of subsequent vertebral fracture, but this is contrasted by one moderate quality level III-2 study that kyphoplasty reduces the risk of subsequent vertebral fracture. Most other adverse events were only reported in one or two studies. The most frequent other adverse event to be associated with kyphoplasty was urinary tract infection which occurred in six per cent of patients in one series. Also observed in a small number of cases were haematoma and rib fracture. In the studies meeting the inclusion criteria, no deaths were found to be directly associated with kyphoplasty.

As in the previous MSAC assessment, no studies were identified that investigated the amount, or clinical consequences of radiation exposure received because of kyphoplasty.

Kyphoplasty 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 were concerned solely with patients with vertebral malignancies, however some 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). There were two small case series and studies with comparators other than conservative management, surgery, or vertebroplasty, in which patients all had malignant vertebral fractures, the largest of which included 65 patients, that were included in the assessment but for which data were not extracted. In these studies, the types and frequencies of adverse events did not differ notably from those observed in the studies of osteoporotic or mixed populations.

In the absence of comparative studies, the best available evidence for the safety of kyphoplasty in this population is provided by a small number of level IV studies, and from studies of kyphoplasty in osteoporotic patients, accepting the limitations of generalising this evidence.

Kyphoplasty versus conservative management or surgery for patients with vertebral osteoporotic fracture(s) causing functional kyphotic deformity and associated symptoms

Only one low quality level III-2 study compared kyphoplasty to surgery and this study did not report safety outcomes comprehensively. The study did note that surgery resulted in substantially more blood loss, and reported on the complications that were related to the fixation devices used in the surgery.

In summary, there is limited poor quality evidence that kyphoplasty may be safer than surgery, but it is not possible with the available evidence to draw any firm conclusions.

Kyphoplasty versus conservative management or surgery for patients with vertebral fracture(s) caused by malignant tumours and producing functional kyphotic deformity and associated symptoms

No studies were identified that investigated the safety of kyphoplasty in the treatment of functional kyphotic deformity resulting from malignant vertebral fractures.

As with vertebroplasty, the relationship between kyphoplasty and risk of subsequent vertebral fracture is poorly understood, and assessment was hampered by limitations of the data in the available evidence base. There is one good quality level II study that provides evidence that kyphoplasty may increase the risk of subsequent vertebral fracture, but this is contrasted by one moderate quality level III-2 study that kyphoplasty reduces the risk of subsequent vertebral fracture.

Owing to the procedure specific complications, such as cement leakage, kyphoplasty is not considered to be as safe as conservative management.

MSAC concluded that kyphoplasty is likely to be as safe as vertebroplasty in osteoporotic patients.

9. Comparative effectiveness

The best quality evidence on the effectiveness of kyphoplasty was provided by one good quality level II study that compared kyphoplasty to conservative management. Moderate quality evidence was also provided by two level III-2 studies comparing kyphoplasty to conservative management. Kyphoplasty was found to have statistical and clinically important benefits in pain reduction at one week in the level II study and one of the level III-2 studies.

Only one study was identified which compared kyphoplasty with spinal surgery and this provided only a limited amount of poor quality level III-2 evidence. The study did find that open surgery resulted in substantially more blood loss, and found a benefit of kyphoplasty over surgery in improving patient-assessed pain at one day follow-up and no difference in the degree of vertebral height restoration.

No studies were identified that assessed the use of kyphoplasty to alleviate breathing difficulties associated with kyphotic deformity, relative to intensified or extended conservative management or spinal surgery.

Based upon this limited evidence, no conclusions can be drawn with respect to the comparative safety or effectiveness of kyphoplasty and spinal surgery.

Kyphoplasty versus conservative management for patients with painful vertebral osteoporotic fracture(s), compared to rehabilitation (conservative management)

Compared to conservative management, kyphoplasty was found to have statistical and clinically important benefits in pain reduction at one week in one good quality level II study. Statistically significant reductions in pain were also seen in the one moderate quality level III-2 study, although the differences were not clinically important.

One good quality level II study provided evidence of statistically significant and clinically important benefits of kyphoplasty over conservative management in improving patient-assessed quality of life; however, it is likely that effects that are not clinically meaningful could occur.

No studies meeting the inclusion criteria and comparing kyphoplasty to conservative management, surgery, or vertebroplasty, reported outcomes of observer-assessed functional status or patient psychological wellbeing.

One good quality level II study found kyphoplasty to be superior to conservative management in three patient-assessed measures of functional status, two of which are well validated, however the differences were only clinically important with two of the three tools (one validated and one unvalidated tool). Using another unvalidated tool, one level III-2 study found kyphoplasty to be statistically superior to conservative management at six months, but not at three months, one year or three years.

The level II study found kyphoplasty to result in statistically significantly fewer patients requiring opioid analgesia at one month, three months, and six months follow-up, but not at one week or one year.

No studies meeting the inclusion criteria were identified which investigated the effectiveness of kyphoplasty with respect to observer-assessed measures of either patient symptoms or quality of life.

One moderate quality level III-2 study provided evidence that kyphoplasty increased hospital length-of-stay by an average of just less than one day.

One moderate quality level III-2 study provided evidence that kyphoplasty increased vertebral height, while conservative management resulted in progressive loss of height.

In one moderate quality level III-2 study, vertebral alignment was not improved immediately by kyphoplasty, but improved in the treatment arm during follow-up, while it deteriorated in the conservatively treated arm during the same period. The reason for the delayed improvement in the kyphoplasty arm is not clear.

Kyphoplasty versus conservative management 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, which were excluded from this assessment update, and from studies of vertebroplasty in osteoporotic patients, accepting the limitations of generalising this evidence.

Kyphoplasty versus conservative management or surgery for patients with functional kyphotic deformity caused by vertebral osteoporotic fracture(s)

One level III-2 study compared kyphoplasty to surgery (pedicle screw fixation system) for the treatment of symptoms associated with kyphotic deformity, but it was of poor quality so it is difficult to draw any conclusions from the evidence. The study did find a benefit of kyphoplasty over surgery in improving patient-assessed pain at one day follow-up, no difference in the degree of vertebral height restoration, and that open surgery resulted in substantially more blood loss.

Kyphoplasty versus conservative management or surgery for patients with vertebral fracture(s) caused by malignant tumours and producing functional kyphotic deformity

No studies were identified that assessed the effectiveness of kyphoplasty at alleviating symptoms associated with kyphotic deformity resulting from malignant vertebral fractures.

There is some good quality evidence that kyphoplasty in addition to conservative management is more effective than conservative management alone in the treatment of vertebral fractures. Kyphoplasty may have a role in the management of vertebral fractures but, in light of the contrasting results between blinded and unblinded studies assessing the similar vertebroplasty procedure, further information is required from placebo-controlled studies to confirm a biological treatment effect from kyphoplasty.

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 in the Assessment Report (comparing each procedure to conservative management). 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 make any firm conclusions.

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

The best evidence available for the comparison of vertebroplasty with kyphoplasty in the treatment of patients with osteoporotic fractures is provided by a single poor quality randomised controlled trial (RCT; level II evidence) and a moderate quality pseudo-randomised controlled trial (level III-1 evidence). Supporting these are several other poor-to-moderate quality level III-2 or III-3 studies, and the evidence provided by studies that compare each procedure to conservative management. All studies that directly compared vertebroplasty with kyphoplasty had a moderate to high risk of confounding, limiting the strength of conclusions that can be drawn. The RCT was small in size and did not adjust for observed differences in baseline measurements. The pseudo-randomised trial had a broken method of allocation that introduced confounding, and also observed a mid-term deterioration of outcomes in the arm treated with vertebroplasty, which is not reflected in the rest of the evidence base comparing vertebroplasty to either kyphoplasty or conservative management. The reason for this is unclear.

Patient-assessed functional status was assessed 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 improvements in Oswestry disability index (ODI), but the differences were not clinically important. Only one study observed 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 the one level II study found that vertebroplasty resulted in some improvement in vertebral height and alignment, but that kyphoplasty resulted in greater improvements. As these are surrogate outcomes, the clinical importance of the observed differences is unknown.

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

One moderate quality retrospective cohort study (level III-2 evidence) compared vertebroplasty to kyphoplasty in the treatment of patients with vertebral fractures associated with multiple myeloma. Apart from this one study, with no studies comparing either treatment to conservative management in this population, the only supporting evidence is that which can be generalised from studies of patients with osteoporotic fractures.

The effectiveness outcomes that Kose et al. (2006) reported in their study were patient-assessed pain as measured on a numerical rating scale (NRS) and analgesia usage; however, only overall analgesia usage was reported without any between-group comparisons. No statistically significant or clinically important differences were found in NRS pain score between patients treated with vertebroplasty and those who were treated with kyphoplasty.

MSAC noted that, on the basis of currently available limited evidence of moderate-to-poor quality (Level II and III data), kyphoplasty is possibly more effective than conservative treatment in patients with a painful osteoporotic vertebral fracture, but entails additional (albeit small) risk and additional costs.

Published evidence (particularly a randomised open-label trial by Wardlaw *et al* 2009) suggests that kyphoplasty has an effect in the short-term when compared with conservative treatment, but not in the long-term. In this trial, kyphoplasty patients achieved statistically significant additional improvements in pain relief at all time points up to one year. MSAC noted that these data do not provide an opportunity to assess placebo response, and that the weakness in the evidence base at best provides limited evidence of additional benefit for kyphoplasty over its comparators.

MSAC considered the place for kyphoplasty in treating or preventing medical conditions that may be associated with kyphosis, including functional disturbances associated with kyphotic deformity, but concluded that there is no published evidence to support its use for these indications.

10. Economic evaluation

A cost-effectiveness analysis is only undertaken 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.

The cost of treating one patient with painful vertebral fracture is largely driven by the costs of hospitalisation, analgesia usage, community care and procedural costs (e.g., operator fees and equipment costs for vertebroplasty and kyphoplasty).

The average cost of treating one patient with painful vertebral fracture with conservative management alone, including all non-trivial expenses over a period of one year, is estimated to be \$6,074. The average additional cost of treating one patient with vertebroplasty, assuming no change to analgesia usage or duration of hospitalisation, is \$1,593. The same additional cost of treating one patient with kyphoplasty is estimated to be [REDACTED]. The disparity in costs between vertebroplasty and kyphoplasty is largely driven by the higher cost of the kyphoplasty equipment – it is possible that this cost may reduce when generic kyphoplasty kits become TGA-approved.

MSAC noted the Wardlaw trial and estimated an incremental cost-effectiveness ratio (ICER) of [REDACTED] per extra quality-adjusted life-year (QALY) gained for kyphoplasty over conservative treatment, on the basis of accepting the clinically significant utility differences reported despite the inability in an unblinded trial to assess the extent of placebo response. This range of ICER results is beyond the range that is normally found to be acceptable, and the estimate is uncertain due to limitations in the clinical data and study design and because the assessment report did not disaggregate the data to allow more detailed scrutiny.

MSAC also found it difficult to support public funding for kyphoplasty for vertebral pain relief in osteoporotic patients in the face of two RCTs showing no additional benefit over conservative treatment for a comparator procedure (vertebroplasty), and with a much higher cost profile for kyphoplasty compared to vertebroplasty. MSAC concluded that kyphoplasty is likely to be as safe as vertebroplasty in these patients, but appears to be no more effective and is more costly.

The Applicant's submission suggested that the procedural time for kyphoplasty would be 20% longer than for vertebroplasty (Australian expert opinion), so they proposed this be reflected in the proposed fee (where fee of kyphoplasty = 120% of cost of vertebroplasty) (Table 2 Assessment Report refers). The MBS fee for percutaneous vertebroplasty for the treatment of painful osteoporotic vertebral compression fracture (MBS item number 35400) and painful metastatic deposit or multiple myeloma in a vertebral body (MBS item number 35402) is \$610.05. When this is increased by 20%, the proposed fee for the service of performing balloon kyphoplasty was calculated to be \$732.06.

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

The potential utilisation of vertebral augmentation procedures is based upon a predicted current utilisation. However, the recent trend of Medicare reimbursed vertebroplasty procedures has been slightly downward. This trend may represent either a decline in the use of vertebroplasty across Australia, or a shift in utilisation from the private healthcare sector to the public healthcare sector. Changes to the public / private share of vertebroplasty procedures will have implications for the distribution of costs.

The potential utilisation of kyphoplasty in Australia is largely unknown. If kyphoplasty was publicly funded it is likely that it would partly replace a proportion of patients who would otherwise undergo vertebroplasty (which has been listed on the MBS for the past five years on an interim basis pending review) because the two procedures have similar clinical indications.

Kyphoplasty is also indicated for patients with functional kyphotic deformity resulting in pulmonary dysfunction. It is unknown what the potential utilisation rate would be of kyphoplasty for this indication. However, given that patient quality of life was not found to be overly affected by kyphosis – despite diminished pulmonary function - in one study of osteoporotic women (Lombardi Jr et al 2005), it is possible that there will be limited demand for kyphoplasty for this particular indication.

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 1999). 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% or 800) are potential candidates for vertebroplasty or kyphoplasty.

MSAC costed the use of kyphoplasty in addition to conservative treatment at [REDACTED] per annum (with 50% substitution) and [REDACTED] (with 100% substitution). MSAC noted the incremental cost of kyphoplasty only would be [REDACTED] (at 50% substitution, current usage figures) or [REDACTED] with 100% substitution, high use).

MSAC noted that further trials (including four RCTs) of kyphoplasty are underway, and the cost of kyphoplasty kits may fall, but this is unlikely to alter the economic analyses in favour of kyphoplasty. MSAC noted that there is limited demand for kyphoplasty in Australia, and that the kyphoplasty kit price [REDACTED] would be borne by the patient or private health insurance provider.

Table 3 in the Assessment Report shows the disaggregated costs of providing vertebroplasty, kyphoplasty and conservative management (current and predicted for 2020):

Patients receive vertebroplasty	MBS	Other Govt	Patient or Insurer	Total Costs
Per-patient costs	\$2,165	\$2,357	\$3,145	\$7,667
Current use	\$1,747,007	\$1,902,227	\$2,537,646	\$6,186,880
Predicted 2020 ^a	\$3,745,132	\$4,077,885	\$5,440,059	\$13,263,076
Patients receive vertebroplasty or kyphoplasty (50:50)	MBS	Other Govt	Patient or Insurer	Total Costs
Per-patient costs	\$2,252	[REDACTED]	[REDACTED]	[REDACTED]
Current use	\$1,816,975	[REDACTED]	[REDACTED]	[REDACTED]
Predicted 2020 ^a	\$3,895,126	[REDACTED]	[REDACTED]	[REDACTED]
Patients receive kyphoplasty	MBS	Other Govt	Patient or Insurer	Total Costs
Per-patient costs	\$2,338	[REDACTED]	[REDACTED]	[REDACTED]
Current use	\$1,886,943	[REDACTED]	[REDACTED]	[REDACTED]
Predicted 2020 ^a	\$4,045,119	[REDACTED]	[REDACTED]	[REDACTED]
Patients receive conservative management alone	MBS	Other Govt	Patient or Insurer	Total Costs
Per-patient costs	\$1,479	\$2,159	\$2,437	\$6,074
Current use	\$1,193,192	\$1,741,913	\$1,966,554	\$4,901,659
Predicted 2020 ^a	\$2,557,896	\$3,734,213	\$4,215,785	\$10,507,894

^a current utilisation adjusted for population ageing and increases in investment of other states to match current NSW investment.

The cost of treating one patient with painful vertebral fracture is largely driven by the costs of hospitalisation, analgesia usage, community care and procedural costs (e.g., operator fees and equipment costs for vertebroplasty and kyphoplasty).

The average cost of treating one patient with painful vertebral fracture with conservative management alone, including all non-trivial expenses over a period of one year, is estimated to be \$6,074. The average additional cost of treating one patient with vertebroplasty, assuming no change to analgesia usage or duration of hospitalisation, is \$1,593. The same additional cost of treating one patient with kyphoplasty is estimated to be [REDACTED]. The disparity in costs between vertebroplasty and kyphoplasty is largely driven by the higher cost of the kyphoplasty equipment – it is possible that this cost may reduce when generic kyphoplasty kits become TGA-approved.

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.

12. MSAC key issues

Only one study was identified which compared kyphoplasty with spinal surgery and this provided on a limited amount of poor quality level III-2 evidence. Based upon this limited evidence, no conclusions can be drawn with respect to the comparative safety or effectiveness of kyphoplasty and spinal surgery.

The contrasting results between blinded and unblinded studies assessing the similar vertebroplasty procedure provide some evidence for the existence of a placebo-effect in the minimally invasive treatment of osteoporotic vertebral fracture. This finding creates uncertainty about the degree to which a placebo effect is implicated in the treatment effects reported in the kyphoplasty evidence base, considering that the primary outcomes reported in the literature are (appropriately) subjective in nature (eg pain) - and thus susceptible to placebo effect - and because patient selection in the key kyphoplasty randomised controlled trial was similar to that in the vertebroplasty randomised controlled trials. There were no studies in the evidence base comparing kyphoplasty to conservative management, surgery or vertebroplasty that also reported objective outcomes such as observer-assessed functional status, patient psychological wellbeing, observer-assessed patient symptoms or observer-assessed quality of life.

In conclusion, 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. If the effectiveness of kyphoplasty compared with placebo can be established with methodologically sound research, it may have a role in displacing vertebroplasty in the treatment of vertebral fracture.

MSAC noted that new evidence had become available after the assessment report had been generated, but because it had not been formally evaluated, MSAC could not adequately consider this evidence. Therefore, MSAC only considered the use of kyphoplasty in osteoporotic patients for the purpose of relieving pain, as the cancer-related and other indications requested in the application to MSAC were not able to be adequately appraised due to lack of evidence or because relevant evidence was not available in time to be considered in the assessment report. MSAC noted that applicants may wish to consider the appropriate timing of any re-submission in light of the timing of the publication of relevant evidence.

Future utilisation 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 reveals that a single vertebra is treated 74% of the time, two vertebrae are treated 19% of the time and three or more are treated 7% 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% of vertebroplasty procedures resulted in an admission lasting longer than one day. Only Medicare services rendered out of hospital count towards the Medicare Safety Net or Extended Medicare Safety Net.

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

MSAC noted that, on the basis of currently available limited evidence of moderate-to-poor quality (Level II and III data), kyphoplasty is possibly more effective than conservative treatment in patients with a painful osteoporotic vertebral fracture, but entails additional (albeit small) risk and additional costs.

Published evidence (particularly a randomised open-label trial by Wardlaw *et al* 2009) suggests that kyphoplasty has an effect in the short-term when compared with conservative treatment, but not in the long-term. In this trial, kyphoplasty patients achieved statistically significant additional improvements in pain relief at all time points up to one year. MSAC noted that these data do not provide an opportunity to assess placebo response, and that the weakness in the evidence base at best provides limited evidence of additional benefit for kyphoplasty over its comparators.

MSAC noted the Wardlaw trial and estimated an incremental cost-effectiveness ratio (ICER) of [REDACTED] per extra quality-adjusted life-year (QALY) gained for kyphoplasty over conservative treatment, on the basis of accepting the clinically significant utility differences reported despite the inability in an unblinded trial to assess the extent of placebo response. This range of ICER results is beyond the range that is normally found to be acceptable, and the estimate is uncertain due to limitations in the clinical data and study design and because the assessment report did not disaggregate the data to allow more detailed scrutiny.

MSAC also found it difficult to support public funding for kyphoplasty for vertebral pain relief in osteoporotic patients in the face of two RCTs showing no additional benefit over conservative treatment for a comparator procedure (vertebroplasty), and with a much higher cost profile for kyphoplasty compared to vertebroplasty. MSAC concluded that kyphoplasty is likely to be as safe as vertebroplasty in these patients, but appears to be no more effective and is more costly.

MSAC noted that new evidence had become available after the assessment report had been generated, but because it had not been formally evaluated, MSAC could not adequately consider this evidence. Therefore, MSAC only considered the use of kyphoplasty in osteoporotic patients for the purpose of relieving pain, as the cancer-related and other indications requested in the application to MSAC were not able to be adequately appraised due to lack of evidence or because relevant evidence was not available in time to be considered in the assessment report. MSAC noted that applicants may wish to consider the appropriate timing of any re-submission in light of the timing of the publication of relevant evidence.

MSAC noted that further trials (including four RCTs) of kyphoplasty are underway, and the cost of kyphoplasty kits may fall, but this is unlikely to alter the economic analyses in favour of kyphoplasty. MSAC noted that there is limited demand for kyphoplasty in Australia, and that the kyphoplasty kit price [REDACTED] would be borne by the patient or private health insurance provider.

MSAC considered the place for kyphoplasty in treating or preventing medical conditions that may be associated with kyphosis, including functional disturbances associated with kyphotic deformity, but concluded that there is no published evidence to support its use for these indications.

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 kyphoplasty for painful vertebral compression fractures, and noting the applicant's submissions, MSAC does not support public funding for this procedure due to unacceptable cost-effectiveness and uncertainty regarding the extent of additional clinical benefit and consequently the incremental cost-effectiveness ratio over its comparators of conservative treatment or vertebroplasty. MSAC also does not support public funding of kyphoplasty to relieve symptoms associated with functional kyphotic deformity due to a lack of evidence to support its use for this indication.

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