Australian Government

Department of Health

Application 1466:

Vertebroplasty for severely painful osteoporotic vertebral fractures of less than 6 weeks duration

PICO Confirmation

(to guide a new application to MSAC)

(Version 1.0)

This PICO Confirmation Template is to be completed to guide a new request for public funding for new or amended medical service(s) (including, but not limited to the Medicare Benefits Schedule (MBS)). It is relevant to proposals for both therapeutic and investigative medical services.

Please complete all questions that are applicable to the proposed service, providing relevant information only.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment (HTA Team) on the contact number and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

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Version Control

Document History

Version Number	Date Changed	Author	Reason for Change
0.1	10 March 2016	MSAC Reforms	Final template for publication
0.2	19 May 2016	MSAC WEB	Accessibility compliance

Document Approval

Version Number	Date Changed	Author	Reason for Change
1.0	19 May 2016	MSAC Web	Template released for online publication

Summary of PICO criteria to define the question to be addressed in an Assessment Report to the Medical Services Advisory Committee (MSAC)

Component	Description
Patients	Patients with severely painful osteoporotic vertebral fractures of less than 6 weeks duration not responding to conservative medical therapy (opioids)
Intervention	Vertebroplasty performed in a non-mobile fluoroscopy suite using local anaesthesia
Comparator	Intensified and extended conservative medical therapy
Outcomes	**Safety Outcomes** ▪ Mortality ▪ New fracture incidence ▪ Adverse events associated with vertebroplasty ▪ Adverse events associated with opioid use (eg falls, confusion, nausea, constipation drug dependency) ▪ Adverse events associated with progressive fracture compression and retropulsion **Clinical Effectiveness Outcomes** ▪ Reduction in pain, short- and long- term ▪ Reduced disability, short- and long- term ▪ Quality of life scores, short- and long- term ▪ Reduced fracture deformity ▪ Reduced duration of hospital stay ▪ Reduced analgesic, namely opiate, use ▪ Improved mobility

PICO rationale for therapeutic and investigative medical services only

Population

The population for this application is patients with acute severe back pain (numerical rating scale [NRS[1]] ≥ 7/10) due to osteoporotic vertebral fracture with duration of less than six weeks where pain is not adequately controlled by medical therapy. The initial proposed population was patients aged 60 years and over, based on the trial population. In light of the incidence of osteoporotic vertebral fracture being so small for patients aged less than 60 years, the proposed age restriction has been removed, but should be considered during the assessment.

Vertebroplasty has been the focus of two previous MSAC reviews. The service was previously listed on the Medicare Benefits Schedule (MBS) to receive funding on an interim basis after MSAC Assessment 27 in 2005 (Medical Services Advisory Committee 2006). This listing was for:

- patients with painful osteoporotic vertebral compression fractures confirmed by diagnostic imaging and not controlled by conservative medical therapy and/or;
- patients with pain from metastatic deposits or multiple myelomas in a vertebral body.

In November 2011 the procedure was removed from the MBS following MSAC Assessment 27.1 (Medical Services Advisory Committee 2011). This present application is for a proposal for public funding citing new evidence and includes a more specific population than the previous assessments.

In Australians over 50 years 144,000 fractures occurred due to osteoporosis or osteopenia in 2013. It is estimated that over the next 10 years, the total number of osteoporotic fractures will be over 1.6 million, including new and re-fractures (Osteoporosis Australia 2014). Ascertaining the spinal fracture rate in particular is more difficult as there is no universally accepted definition and a substantial proportion of these escape clinical diagnosis. It is reported that women around 60 years of age in the USA and Europe have approximately a two- to three-fold greater incidence of osteoporotic vertebral fractures than do men. The percentage prevalence of osteoporotic vertebral fractures for women by age group in Europe and Minnesota (USA) has been reported below (Cummings and Melton 2002).

Vertebral fracture prevalence data in women by age in Europe and Minnesota (USA) from population-based studies

Age (years)	Europe (%)	Minnesota, USA (%)
60-64	16.8	6.3
65-69	23.5	13.2
70-74	27.2	15.0
75-79	34.8	22.2

Most vertebral fractures are sub-clinical and do not present for medical therapy. A minority of fractures result in severe back pain that is exacerbated by standing or walking. A proportion of those

[1] The NRS is used to assess pain, which involves assigning an ordinal score, usually from 0 = 'no pain' to 10 = 'worst pain imaginable', to describe the intensity of pain perceived by the patient.

have acute pain that cannot be managed with oral analgesics (Clark et al. 2016). It has been reported that one third of all vertebral compression fractures become chronically painful (Riggs and Melton 1995).

The applicant advises that the number of patients who would be eligible for vertebroplasty under the proposed items is a small proportion of the number of patients with osteoporotic fractures. Approximately half of eligible patients are expected to have been hospitalised due to the fracture while half are expected to have been treated as outpatients or be under the care of a GP.

The use of vertebroplasty in Australia has fluctuated over time. The most recent listing of vertebroplasty on the MBS (with broader population criteria than the proposed item) showed 645 claims in the 2010/11 financial year (Australian Government). Australian Institute of Health and Welfare (AIHW) data was first recorded for the procedure in 2004/05 when 571 patients underwent vertebroplasty (AIHW). The peak usage of the service was in 2008/09 when 995 patients underwent the procedure (AIHW). However, as the current application targets a smaller population than was eligible under previous MBS items, the annual use of the proposed MBS service is estimated to be less than that of previously listed items.

Rationale

The proposed population is based on the patient inclusion criteria used by the randomised controlled trial (RCT) conducted in response to MSAC assessment 27.1. The Vertebroplasty for Acute Painful Osteoporotic fractURes (VAPOUR) trial was a multicentre trial conducted in four centres in Sydney between 2011 and 2015 (Clark et al. 2016). It randomly assigned 120 patients to either vertebroplasty or a placebo method, in which patients underwent a sham procedure. The trial was funded by an unrestricted educational grant CareFusion Corporation (San Diego, CA, USA).

Current approach

Currently vertebroplasty is not reimbursed on the MBS and patients who need the procedure are paying for it out of pocket. There is still some use in the public system, with the most recent available AIHW data showing that 353 patients underwent vertebroplasty in 2013/14 (AIHW).

Prior test (investigative services only)

Not applicable.

Intervention

The proposed intervention is vertebroplasty performed in a non-mobile fluoroscopy suite. Vertebroplasty is the injection of acrylic cement into fractured vertebrae of the spine (Kallmes et al. 2009).

Most patients with severely painful fractures are seen by their general practitioner or alternatively present by ambulance to the emergency room of hospitals and are hospitalised. Medical specialists particularly aged care physicians, rheumatologists, endocrinologists, and spine surgeons may also consult the patient in this acute, early fracture phase. The patient has a spinal radiograph to confirm a fracture. The first line of management of vertebral fractures is conservative medical therapy

(Diamond et al. 2006). In osteoporosis bone healing may be impaired, so if the patient experiences severe pain that does not respond to conservative management then vertebroplasty is considered. Suitable patients will then be referred to an Interventional Radiologist for assessment for vertebroplasty.

PASC recommended that this procedure should be restricted to Interventional Radiologists (due to the additional training required by the Royal Australian and New Zealand College of Radiologists and the Interventional Radiology Society of Australasia). PASC suggested "broadening the category of who can deliver this intervention, to include other specialists, may be considered if competency is adequately demonstrated, to help address rural/remote accessibility issues"(PASC Minutes 2017).The work-up for vertebroplasty includes an MRI, or if MRI is contra-indicated for a patient or MRI unavailable in the facility, SPECT-CT nuclear medicine imaging. If the MRI confirms a suitable fracture and the patient's symptoms are severe and of less than 6 weeks duration, then vertebroplasty would be offered to the patient.

Once the decision to vertebroplasty has been made, patients are brought to the non-mobile fluoroscopy suite and put under conscious sedation. They lie in a prone position with their arms raised. An Interventional Radiologist inserts an 11-gauge or 13-gauge needle—depending on the vertebral pedicle and the size of the bone being injected—into the central aspect of the target vertebra or vertebrae transpendicularly. Frequently both needle sizes will be utilized based upon technical factors and factors relating to the patient.

A complex vertebroplasty delivery system is used to progressively fill the trabecular space of the vertebral body with polymethyl methacrylate (PMMA) cement under constant lateral fluoroscopy. Infusion is halted when the cement reaches the posterior aspect of the vertebral body or enters the extra-osseous space (Buchbinder et al. 2015). Sometimes a bipedicular approach is taken where two needles are used to provide more even cement distribution. The procedure, from entering the procedure room to departing to the recovery suite, takes approximately one hour for the first fracture requiring treatment. Each additional fracture adds approximately 15 minutes to the procedure time. Once in recovery, patients are monitored lying in a supine position for one hour as the cement hardens, then discharged on the same day (Wong and McGirt 2013).

Vertebroplasty can be performed as an inpatient procedure for those already hospitalised prior to referral for the procedure, or in a day surgery setting for outpatients. The day surgery centre would need to be equipped with a non-mobile fluoroscopy suite. Advice from the applicant is that these are usually only found in tertiary hospitals.

Advice from the applicant is that for each clinical presentation, there should be no more than three acute fractures treated. PASC recommended that repeat procedures for the same fracture should be precluded in the proposed item descriptor.

The applicant has advised that an estimate of up to 10 to 15 per cent of patients may develop another, metachronous acute vertebral fracture causing severe, uncontrolled pain and benefit from another vertebroplasty within the same 12 month period.

As vertebroplasty has been funded previously by the MBS and is also available in public hospitals, there is no concern about adequate operators to perform the intervention. All tertiary hospitals will

have at least one Interventional Radiologist experienced in vertebroplasty, as advised by the applicant.

The required prostheses for the procedure are on the Prostheses List[2]. The devices listed below all include PMMA and a complex delivery system. Consumables required for the intervention are skin antiseptic, sterile drapes, sterile gown and gloves for the operator.

Vertebroplasty devices listed on the Prostheses List

Name	Code	Description	Minimum benefit
G-21 Kit	OH503	Radiopaque Bone Cement for Vertebroplasty	$500.00
Vertebroplasty System	JJ609	Vertebroplasty System	$174.00
Traumacem	SY429	Cement with mixing and delivery system	$500.00
AVAmax	HW577	Radiopaque bone cement system	$500.00

Advice from the applicant is that the longest learning curve associated with the procedure is gaining dexterity with high grade interventional fluoroscopy and needle placement and that Interventional Radiologists develop these skills during their formative training.

Although vertebroplasty is safe for most patients there are adverse events associated with the procedure. A rare safety issue in vertebroplasty patients is cement extravasation into the spinal canal or neuroforamen. It is generally asymptomatic or transient, but on rare occasions can be responsible for severe complications, painful radiculopathy and weakness (Wong and McGirt 2013). Cement extravasation can result in neurological deficits or a cement embolism to the lungs and other organ systems. Surgical management may include decompression which can further destabilise the spine, especially in severe osteoporosis (Sidhu et al. 2013). Advice from the applicant is that the incidence of extravasation can be reduced by use of fluoroscopy in a dedicated non-mobile suite.

Other adverse events, occurring at a rate of one to three per cent after vertebroplasty, are haemorrhage, blood loss, fracture of ribs, fever, nerve root irritation and infection (Wong and McGirt 2013). There is a suspected risk of subsequent fractures in the long-term; however, this has not been reported widely in the literature.

The clinical claim is that vertebroplasty will reduce pain in patients with severely painful osteoporotic vertebral fractures of less than 6 weeks duration not responding to conservative medical therapy and is superior to the comparator, intensified and extended conservative medical therapy. No follow-up treatment is routinely given after vertebroplasty.

Rationale

There has been disagreement in past studies over the most appropriate volume of cement used in vertebroplasty. The volume of cement used has ranged from 2.8 cm^2 in an earlier trial by Buchbinder

[2] http://www.health.gov.au/internet/main/publishing.nsf/Content/health-privatehealth-prostheseslist.htm

(2009) to 7.5 cm^2 in the VAPOUR trial (Clark et al. 2016). The "adequate vertebral fill technique" as used in the VAPOUR trial is now standard clinical practice according to the applicant.

Comparator

Change in practice

It is expected vertebroplasty will be provided in addition to conservative medical therapy (opiates, early mobilisation and fall prevention).

Main alternative

The comparator for this intervention is intensified and extended conservative medical therapy, which usually consists of treatment with analgesics (including simple analgesics, with or without opiates) and rest, followed by aided mobilisation with or without physiotherapy. Conservative medical therapy can include a number of approaches, such as heat therapy, spinal injections, muscle relaxants and anti-resorptive agents. Once the patient can start mobilising, rehabilitation may commence to facilitate confidence with mobilisation and independence, which may involve transfer of the patient to a specialist rehabilitation hospital, before discharge home.

Rationale

There are no direct comparators to vertebroplasty. Intensified and extended conservative medical therapy is what this patient population receives in clinical practice when vertebroplasty is not available.

PASC considered a potential comparator could be spinal fusion surgery; however the applicant advised that spinal fusion is not appropriate for patients with osteoporosis. PASC also considered that a potential comparator was kyphoplasty; however the applicant suggested this is not used in Australia and therefore not relevant to this application.

Limitations on the provider or the setting

Intensified and extended conservative medical therapy, namely analgesics with or without opiates followed by rest and mobilisation, is a standard practice and can be provided in all settings in Australia.

Outcomes

Patient relevant

It is proposed that vertebroplasty will result in clinically significant improvements in pain reduction, disability reduction, anatomic deformity of the fracture, and the duration of hospital stay. Further, opioids are often poorly tolerated, particularly in the elderly with the adverse effects of opiate medication and immobilisation leading to additional health issues including poor cognition, increased risk of falls, constipation and nausea (Goldstein et al. 2015). The applicant claims vertebroplasty will reduce the adverse events associated with opioid use in the target population.

Clinical effectiveness:

- Reduction in pain, short- and long-term
- Reduced disability, short- and long-term
- Quality of life scores, short- and long-term
- Reduced fracture deformity
- Reduced duration of hospital stay
- Reduced analgesic, namely opiate, use
- Improved mobility

Safety outcomes:

- Mortality
- New fracture incidence
- Adverse events associated with vertebroplasty
- Adverse events associated with opioid use (e.g. falls, confusion, nausea, and constipation drug dependency)
- Adverse events associated with progressive fracture compression and retropulsion, including neural compression

Healthcare system

Vertebroplasty is expected to be associated with the following outcomes to the healthcare system:

- Cost of the procedure (and any adverse events)
- Increase in the number of MRIs required
- The number of radiographs performed is not expected to change
- A change in costs associated with ongoing management in patients where vertebroplasty is successful (hospital, medication, patient costs)
- A change in costs associated with adverse events due to opioid use
- Reduction in use of radio-isotope bone scans – being replaced by MRI

The uptake of the proposed service is estimated to reach 400–500 cases per year. This number is slightly lower compared with data from the previous listing of vertebroplasty on the MBS, due to a more restricted eligible population. The applicant advised that these cases are already occurring in both public and private hospitals, with all necessary infrastructure in place. The treatment is therefore in current clinical practice, but not funded through the MBS. No difficulties are expected in meeting patient demand.

The applicant has advised that the chance of leakage to non-targeted populations is expected to be small, given there was modest usage of vertebroplasty when MBS funding was previously available.

Rationale

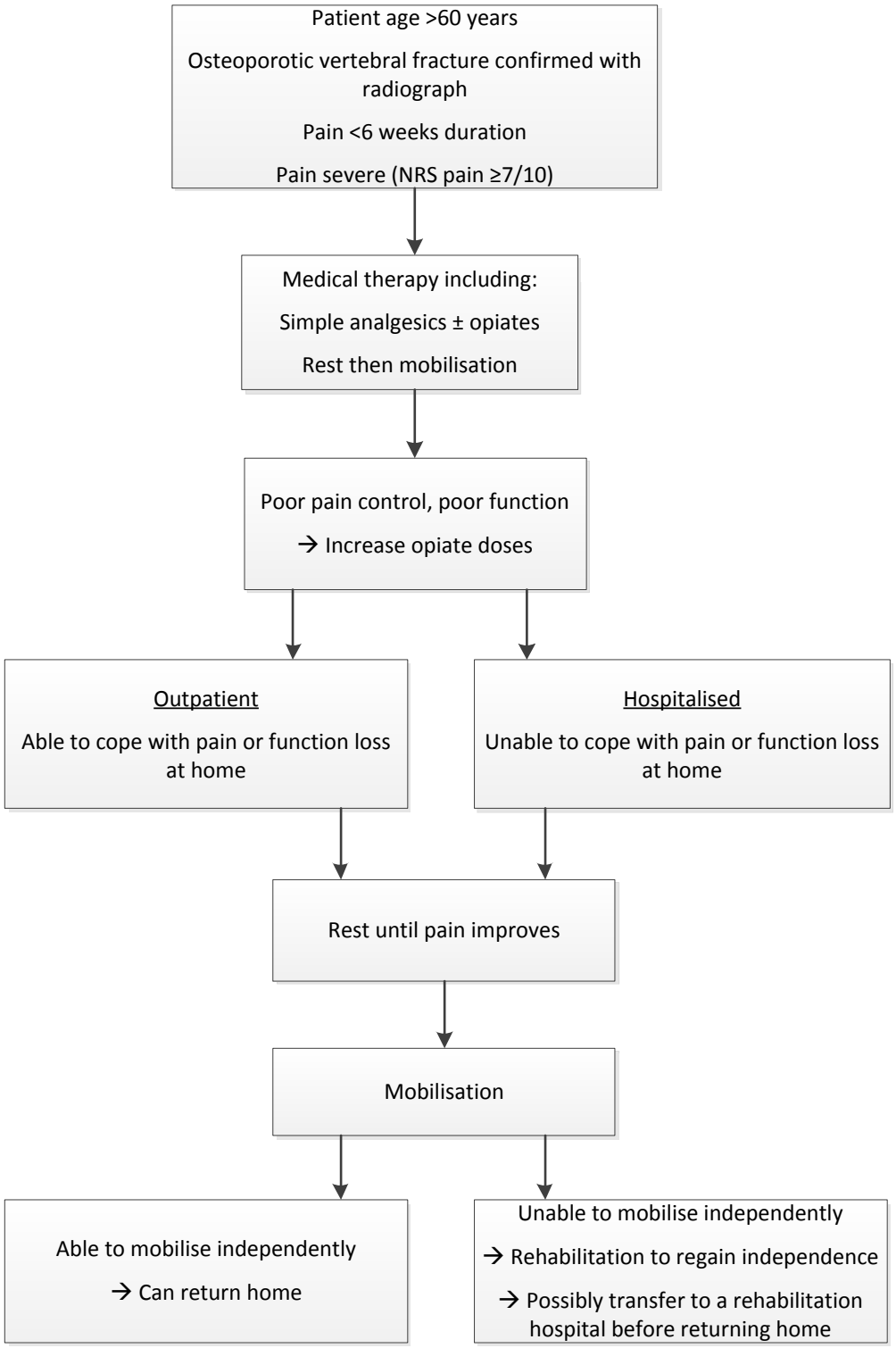
These outcomes are based on those reported in the pivotal study by Clark et al. (2016), cited in the application documents, as well as informed by feedback from the applicant and consultation documents.

Conflicting responses were provided on whether a spinal or neurosurgeon must be present for the procedure. Consultation feedback suggested this should be the case, given risks associated with cement extravasation. Advice from an independent neurosurgeon indicated it is not necessary for a spinal or neurosurgeon to be present at the procedure. PASC agreed that a surgeon would not add value in the event of extravasation of cement.

Current clinical management algorithm for identified population

Figure 1 provides a clinical management algorithm explaining the current approach, conservative medical therapy, in the absence of public funding for the proposed medical service, with reference to existing clinical practice in Australia.

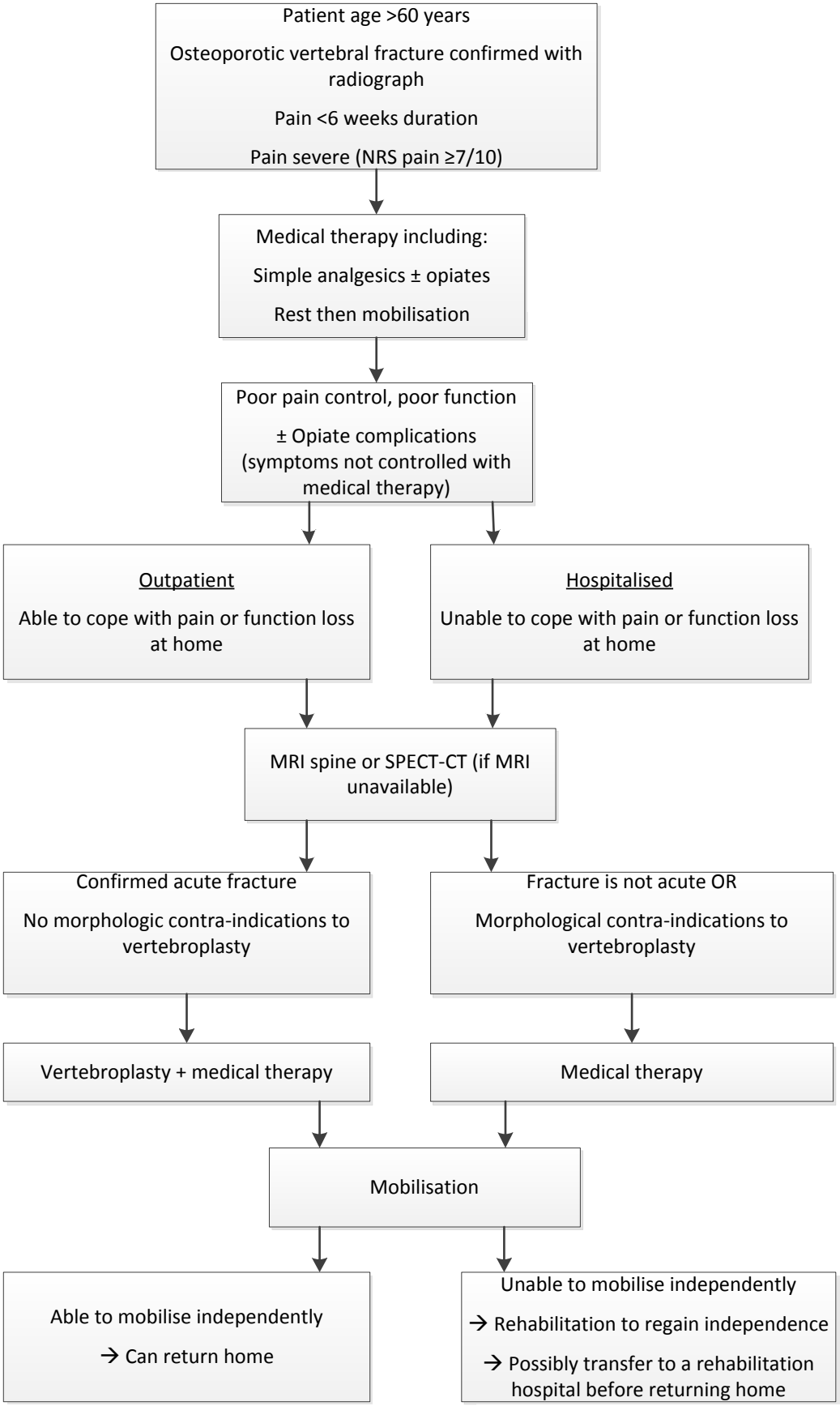
Figure 1 Clinical management pathway of current clinical practice—conservative medical therapy



Proposed clinical management algorithm for identified population

Figure 2 provides a clinical management algorithm explaining the expected management of the eligible population if the proposed medical service, vertebroplasty, were to be publicly funded.

Figure 2 Clinical management pathway of proposed clinical practice—vertebroplasty



Proposed economic evaluation

If the applicant's claim of superiority is founded then a complex economic model (incorporating cost effectiveness evaluation and cost utility evaluation) plus utilisation and financial analysis should be undertaken.

Proposed item descriptor

The proposed MBS item descriptor defining the population and medical service usage characteristics that are expected to define eligibility for MBS funding is outlined below.

Category 3—therapeutic procedures
Proposed item descriptor VERTEBROPLASTY, *performed by an interventional radiologist,* for the treatment of a painful osteoporotic vertebral compression fracture, where ~~*the patient is aged >60*~~ (a) pain is severe (numeric rated pain score ≥7 out of 10); (b) symptoms are poorly controlled by analgesic therapy, namely opiates; (c) severe pain duration is <6 weeks; and (d) there is MRI (or SPECT-CT if MRI unavailable) evidence of acute vertebral fracture *Not to be performed more than once on the same fracture* (Anaes.) MBS Fee: $700

Note: The item descriptor has been amended (as marked in *red italics*) to reflect PASC's advice that the age restriction be removed; the procedure be restricted to interventional radiologists; and repeat procedures be precluded on the same fracture.

The applicant advised that the intention is that this item be co-claimed with item 61109 (FLUOROSCOPY – MBS fee**:** $258.90).

References

AIHW *Procedures data cubes 2004-05*, AIHW, viewed 8 February, 2017, <https://reporting.aihw.gov.au/Reports/openRVUrl.do>.

AIHW *Procedures data cubes 2008-09*, AIHW, viewed 8 February, 2017, <https://reporting.aihw.gov.au/Reports/openRVUrl.do?rsRID=SBIP%3A%2F%2FMETASERVER%2FAIHW%2FReleasedPublic%2FHospitals%2FReports%2FHDU_Procedures,%202008-09%20to%202009-10.srx%28Report%29>.

AIHW *Procedures data cubes 2013-14*, AIHW, viewed 8 February, 2017, <https://reporting.aihw.gov.au/Reports/openRVUrl.do>.

Australian Government Medicare Benefits Schedule (MBS), viewed 8 February, 2017,

Buchbinder, R, Golmohammadi, K, Johnston, RV, Owen, RJ, Homik, J, Jones, A, Dhillon, SS, Kallmes, DF & Lambert, RG 2015, 'Percutaneous vertebroplasty for osteoporotic vertebral compression fracture', *Cochrane Database Syst Rev*, vol.(4), pp. Cd006349.

Buchbinder, R, Osborne, RH, Ebeling, PR, Wark, JD, Mitchell, P, Wriedt, C, Graves, S, Staples, MP & Murphy, B 2009, 'A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures', *New England Journal of Medicine*, vol.361(6), pp. 557-568.

Clark, W, Bird, P, Gonski, P, Diamond, TH, Smerdely, P, McNeil, HP, Schlaphoff, G, Bryant, C, Barnes, E & Gebski, V 2016, 'Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): a multicentre, randomised, double-blind, placebo-controlled trial', *The Lancet*, vol.388(10052), pp. 1408-1416.

Cummings, SR & Melton, LJ 2002, 'Epidemiology and outcomes of osteoporotic fractures', *The Lancet*, vol.359(9319), pp. 1761-1767.

Diamond, TH, Bryant, C, Browne, L & Clark, WA 2006, 'Clinical outcomes after acute osteoporotic vertebral fractures: a 2-year non-randomised trial comparing percutaneous vertebroplasty with conservative therapy', *Medical Journal of Australia*, vol.184(3), pp. 113.

Goldstein, CL, Chutkan, NB, Choma, TJ & Orr, RD 2015, 'Management of the elderly with vertebral compression fractures', *Neurosurgery*, vol.77pp. S33-S45.

Kallmes, DF, Comstock, BA, Heagerty, PJ, Turner, JA, Wilson, DJ, Diamond, TH, Edwards, R, Gray, LA, Stout, L & Owen, S 2009, 'A randomized trial of vertebroplasty for osteoporotic spinal fractures', *New England Journal of Medicine*, vol.361(6), pp. 569-579.

Medical Services Advisory Committee 2006, *Vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture. Reference 27, MSAC Assessment Report.* , Canberra, viewed

Medical Services Advisory Committee 2011, *Vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture. Reference 27.1, MSAC Assessment Report.* , Canberra, viewed

Osteoporosis Australia 2014, *Statistics and Burden of Disease*, viewed 24 Jan 2017, <http://www.osteoporosis.org.au/statistics-burden-disease>.

PASC Minutes, *12 April 2017 PICO Advisory Sub-Committee Meeting*, 2017.

Riggs, BL & Melton, LJ, 3rd 1995, 'The worldwide problem of osteoporosis: insights afforded by epidemiology', *Bone*, vol.17(5 Suppl), pp. 505s-511s.

Sidhu, GS, Kepler, CK, Savage, KE, Eachus, B, Albert, TJ & Vaccaro, AR 2013, 'Neurological deficit due to cement extravasation following a vertebral augmentation procedure: Case report', *Journal of Neurosurgery: Spine*, vol.19(1), pp. 61-70.

Wong, CC & McGirt, MJ 2013, 'Vertebral compression fractures: a review of current management and multimodal therapy', *Journal of multidisciplinary healthcare*, vol.6pp. 205.