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Minimally Invasive Approaches to Vertebral Fractures and Osteolytic Lesions of the Spine

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Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

Percutaneous Vertebroplasty and Sacroplasty

Percutaneous vertebroplasty **may be considered medically necessary** for:

- The treatment of symptomatic osteoporotic vertebral fractures that have failed to respond to conservative treatment (e.g., analgesics, physical therapy, rest) for at least 6 weeks; OR
- The treatment of symptomatic osteoporotic vertebral fractures that are less than 6 weeks in duration that have led to hospitalization or persist at a level that prevents ambulation; OR
- The treatment of severe pain due to osteolytic lesions of the spine related to multiple myeloma or metastatic malignancies.

Percutaneous vertebroplasty **is considered experimental, investigational and/or unproven** for all other indications, including but not limited to use in acute vertebral fractures due to osteoporosis or trauma.

Percutaneous sacroplasty **is considered experimental, investigational and/or unproven** for all indications, including but not limited to use in sacral insufficiency fractures due to osteoporosis and sacral lesions due to multiple myeloma or metastatic malignancies.

Percutaneous Balloon Kyphoplasty or Mechanical Vertebral Augmentation
Percutaneous balloon kyphoplasty or mechanical vertebral augmentation with a United States (U.S.) Food and Drug Administration (FDA) cleared device **may be considered medically necessary** for the treatment of:

- Osteolytic vertebral metastasis, myeloma, or plasmacytoma with severe back pain related to destruction of the vertebral body **NOT** involving a major part of the cortical bone, when chemotherapy or radiation therapy has failed to relieve symptoms; OR
- Vertebral hemangiomas with severe pain or nerve compression, or aggressive radiologic signs, when radiation therapy has failed to relieve symptoms; OR
- Eosinophilic granuloma with pain and spinal instability; OR
- Vertebral compression fracture due to osteoporosis or osteopenia when **ALL** the following requirements are met:
    - Recent onset of back pain localized to the fracture site which has not responded to at least 6 weeks of conservative medical management (e.g., analgesics, physical therapy, rest); and
    - Tenderness to palpation directly over the fracture site; and
    - Advanced imaging studies confirming a non-traumatic, acute compression fracture; and
    - Recent imaging studies (MRI or CT) which eliminate disc herniation or other causes of spine pain; and
    - Absence of imaging findings which would confer unacceptable risk to the spinal cord or related structures, such as:
        1. Spinal stenosis of greater than 20% due to retropulsed fragments; or
        2. Vertebral body collapse to less than one third (33%) original height; or
        3. Vertebral plana (collapse greater than 90%); or
        4. Anatomical damage of the vertebra that prevents safe access of the needle to the vertebral body; or
        5. Burst fracture with retropulsed fragments demonstrated by imaging.

Percutaneous balloon kyphoplasty or mechanical vertebral augmentation with an FDA cleared device **is considered experimental, investigational and/or unproven** for all other indications, including use in acute vertebral fractures due to osteoporosis or trauma.

Radiofrequency kyphoplasty **is considered experimental, investigational and/or unproven.**

Mechanical vertebral augmentation using any other device, including but not limited to vertebral body stenting **is considered experimental, investigational and/or unproven.**

Policy Guidelines

None.

Description

Percutaneous vertebroplasty, percutaneous balloon kyphoplasty, radiofrequency kyphoplasty, and mechanical vertebral augmentation are interventional techniques involving the fluoroscopically guided injection of polymethylmethacrylate (PMMA) into a weakened vertebral body or a cavity created in the vertebral body with a balloon or mechanical device. The techniques have been investigated to provide mechanical support and symptomatic relief in patients with osteoporotic vertebral compression fractures or those with osteolytic lesions of the spine (e.g., multiple myeloma, metastatic malignancies); as a treatment for sacral insufficiency fractures; and as a technique to limit blood loss related to surgery.

Treatment of Vertebral Compression Fracture
Chronic symptoms do not tend to respond to the management strategies for acute pain such as bed rest, immobilization or bracing device, and analgesic medication, sometimes including narcotic analgesics. The source of chronic pain after vertebral compression fracture may not be from the vertebra itself but may be predominantly related to strain on muscles and ligaments secondary to kyphosis. This type of pain frequently does not improve with analgesics and may be better addressed through exercise or physical therapy. Improvements in pain and ability to function are the principal outcomes of interest for the treatment of osteoporotic fractures.

Treatment of Sacral Insufficiency Fractures
Similar interventions are used for sacral fractures and include bed rest, bracing, and analgesics. Initial clinical improvements may occur quickly; however, resolution of all symptoms may not occur for 9 to 12 months. (1, 2)

Vertebral and Sacral Body Metastasis
Metastatic malignant disease of the spine generally involves the vertebrae/sacrum, with pain being the most frequent complaint.

Treatment of Vertebral and Sacral Body Metastasis
While radiotherapy and chemotherapy are frequently effective in reducing tumor burden and associated symptoms, pain relief may be delayed days to weeks, depending on tumor response. Further, these approaches rely on bone remodeling to regain strength in the vertebrae/sacrum, which may necessitate supportive bracing to minimize the risk of vertebral/sacral collapse during healing. Improvements in pain and function are the primary outcomes of interest for treatment of bone malignancy with percutaneous vertebroplasty or sacroplasty.

Surgical Treatment Options
Percutaneous Vertebroplasty and Kyphoplasty
Vertebroplasty is a surgical procedure that involves the injection of synthetic cement (e.g.,

polymethylmethacrylate, bis-glycidal dimethacrylate [Cortoss]) (3) into a fractured vertebra. It has been suggested that vertebroplasty may provide an analgesic effect through mechanical stabilization of a fractured or otherwise weakened vertebral body. However, other mechanisms of effect have been postulated, including thermal damage to intraosseous nerve fibers.

Balloon kyphoplasty is a variant of vertebroplasty and uses a specialized bone tamp with an inflatable balloon to expand a collapsed vertebral body as close as possible to its natural height before injection of polymethylmethacrylate. Radiofrequency kyphoplasty (also known as radiofrequency targeted vertebral augmentation) is a modification of balloon kyphoplasty. In this procedure, a small diameter articulating osteotome creates paths across the vertebra. An ultra-high viscosity cement is injected into the fractured vertebral body, and radiofrequency is used to achieve the desired consistency of the cement. The ultra-high viscosity cement is designed to restore height and alignment to the fractured vertebra, along with stabilizing the fracture.

Percutaneous Sacroplasty

Sacroplasty evolved from the treatment of insufficiency fractures in the thoracic and lumbar vertebrae with vertebroplasty. The procedure, essentially identical to vertebroplasty, entails guided injection of polymethylmethacrylate through a needle inserted into the fracture zone. Although first described in 2000 as a treatment for symptomatic sacral metastatic lesions, (4, 5) it is most often described as a minimally invasive alternative to conservative management (6-8) for sacral insufficiency fractures.

Mechanical Vertebral Augmentation

Kiva is a mechanical vertebral augmentation technique that uses an implant for structural support of the vertebral body to provide a reservoir for bone cement. The Kiva vertebral compression fractures treatment system consists of a shaped memory coil and an implant, which is filled with bone cement. The coil is inserted into the vertebral body over a removable guide wire. The coil reconfigures itself into a stack of loops within the vertebral body and can be customized by changing the number of loops of the coil. The implant, made from PEEK-OPTIMA™, a biocompatible polymer, is deployed over the coil. The coil is then retracted, and polymethyl methacrylate is injected through the lumen of the implant. The polymethyl methacrylate cement flows through small slots in the center of the implant, which fixes the implant to the vertebral body and contains the polymethyl methacrylate in a cylindrical column. The proposed advantage of the Kiva system is a reduction in cement leakage.

SpineJack is a mechanical vertebral augmentation technique that utilizes bipedicular 4.2 mm to 5.0 mm self-expanding jacks to restore vertebral height. Placement of the titanium devices are verified in anteroposterior and lateral view prior to expansion. Once the devices are expanded, a proprietary bone cement is injected. The proposed benefit is greater control over expansion and greater restoration of vertebral height compared to balloon kyphoplasty. The procedure requires good bone quality.

Pain and function are subjective outcomes and, thus, may be susceptible to placebo effects. Furthermore, the natural history of pain and disability associated with these conditions may vary. Therefore, controlled comparison studies would be valuable to demonstrate the clinical effectiveness of vertebroplasty and sacroplasty over any associated nonspecific or placebo effects and to demonstrate the effect of treatment compared with alternatives such as continued medical management.

In all clinical situations, adverse events related to complications from vertebroplasty, kyphoplasty, sacroplasty, and mechanical vertebral augmentation are the primary harms to be considered. Principal safety concerns relate to the incidence and consequences of leakage of the injected polymethyl methacrylate or another injectate.

Regulatory Status

Vertebroplasty is a surgical procedure and, as such, is not subject to U.S. Food and Drug Administration (FDA) approval.

Polymethylmethacrylate bone cement was available as a drug product before enactment of the FDA's device regulation and was at first considered what the FDA terms a "transitional device." It was transitioned to a class III device requiring premarketing applications. Several orthopedic companies have received approval of their bone cement products since 1976. In 1999, polymethylmethacrylate was reclassified from class III to class II, which requires future 510(k) submissions to meet "special controls" instead of "general controls" to assure safety and effectiveness. Thus, use of polymethylmethacrylate in vertebroplasty represented an off-label use of an FDA-regulated product before 2005. In 2005, polymethylmethacrylate bone cements such as Spine-Fix® Biomimetic Bone Cement and Osteopal® V were cleared for marketing by the FDA through the 510(k) process for the fixation of pathologic fractures of the vertebral body using vertebroplasty procedures.

The use of polymethylmethacrylate in sacroplasty is an off-label use of an FDA-regulated product (bone cements such as Spine-Fix® Biomimetic Bone Cement [Teknimed] and Osteopal® V [Heraeus]) because the 510(k) approval was for the fixation of pathologic fractures of the vertebral body using vertebroplasty procedures. Sacroplasty was not included. FDA product code: NDN.

In 2009, Cortoss® (Stryker) Bone Augmentation Material was cleared for marketing by the FDA through the 510(k) process. Cortoss® is a nonresorbable synthetic material that is a composite resin-based, bis-glycidyl dimethacrylate. The FDA classifies this product as a polymethylmethacrylate bone cement.

In 2010, the Parallax® Contour® Vertebral Augmentation Device (ArthroCare) was cleared for marketing by FDA through the 510(k) process. There have been several other augmentation and bone expander devices (e.g., Balex® Bone Expander System, Arcadia® Ballon Catheter, Kyphon Element® Inflatable Bone Tamp) that were also cleared for marketing by FDA through

the 510(k) process. These devices create a void in cancellous bone that can then be filled with bone cement. FDA product code: HXG.

Kyphoplasty is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration (FDA).

In July 2004, KyphX® HV-RTM bone cement was cleared for marketing by the FDA through the 510(k) process for the treatment of pathologic fractures of the vertebral body due to osteoporosis, cancer, or benign lesions using a balloon kyphoplasty procedure. Subsequently, other products such as Spine-Fix® Biomimetic Bone Cement, KYPHON® HV-R® Bone Cement, KYPHONTM VuETM Bone Cement, and Osteopal® V (Heraeus) have received 510(k) marketing clearance for the fixation of pathologic fractures of the vertebral body using vertebroplasty or kyphoplasty procedures.

Balloon kyphoplasty requires the use of an inflatable bone tamp. In July 1998, one such tamp, the KyphX® inflatable bone tamp (Medtronic), was cleared for marketing by the FDA through the 510(k) process. Additional devices for balloon kyphoplasty are listed in Table 1.

There are several mechanical vertebral augmentation devices that have received marketing clearance by the FDA through the 510(k) process; these are listed in Table 1.

StabiliT® Vertebral Augmentation System (Merit Medical) for radiofrequency vertebral augmentation was cleared for marketing in 2009. FDA product code: NDN.

Table 1. Kyphoplasty and Mechanical Vertebral Augmentation Devices Cleared by the U.S. Food and Drug Administration

Device	Manufacturer	Date Cleared	510(k) Number	Indication
Balloon Kyphoplasty				
Balloon Inflation System	Ningbo Biotechnology Co., Ltd	2/29/2024	K23842	Reduction of fractures and/or creation of a void
Renova Spine Balloon Catheter	Biopsybell S.R.L.	10/30/2023	K231340	Reduction of fractures and/or creation of a void
TRACKER Plus Kyphoplasty System	GS Medical Co., Ltd	10/28/2021	K211797	Reduction of fractures and/or creation of a void

Joline Kyphoplasty System Allevo	Joline GmbH & Co.	5/27/2020	K192449	To repair vertebral compression fractures
TRACKER Kyphoplasty System	GS Medical Co., Ltd	12/4/2019	K192335	Reduction of fractures or creation of a void
Stryker iVAS Elite Inflatable Vertebral Augmentation System (Stryker iVAS Elite Balloon Catheter)	Stryker Corporation	12/21/2018	K181752	To repair vertebral compression fractures
SpineKure Kyphoplasty System	Hanchang Co. Ltd.	05/29/2018	K172871	To repair vertebral compression fractures
Modified Winch Kyphoplasty (15 and 20 mm) 11 Gauge Balloon Catheters	G-21 s.r.l.	08/23/2017	K172214	To repair vertebral compression fractures
13G InterV Kyphoplasty Catheter (Micro) and 11G InterV Kyphoplasty Catheter (Mini-Flex)	Pan Medical Ltd.	11/1/2016	K162453	To repair vertebral compression fractures
MEDINAUT Kyphoplasty System	Imedicom Co. Ltd.	07/29/2016	K153296	To repair vertebral compression fractures
AVAflex Vertebral Balloon System	Carefusion	11/24/2015	K151125	To repair vertebral compression fractures
Osseoflex SB Straight Balloon 10g/4ml Osseoflex SB Straight Balloon 10g/2ml	Osseon LLC	4/9/2015	K150607	To repair vertebral compression fractures
InterV Kyphoplasty Catheter (Balloon Length: 1015 and 20mm) InterV Kyphoplasty Catheter (Mini) (Balloon Length: 10 15 and 20mm)	Pan Medical Ltd.	3/6/2015	K150322	To repair vertebral compression fractures
GUARDIAN-SG Inflatable Bone Expander System	BM Korea Co. Ltd.	1/16/2015	K143006	To repair vertebral

				compression fractures
ZVPLASTY	Zavation LLC	09/12/2014	K141419	To repair vertebral compression fractures
Mechanical Vertebral Augmentation				
KIVA VCF Treatment System	Benvenue Medical Inc.	8/14/2014	K141141	To repair vertebral compression fractures
SpineJack Expansion Kit	Vexim SA	08/30/2018	K181262	To repair vertebral compression fractures
V-Strut Vertebral Implant	Hyprevention SAS	3/5/2020	K191709	Treatment of vertebral fractures in the thoracic and lumbar spine

Rationale

Medical policies assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events

and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

The natural history of pain and disability associated with these conditions vary. Also, pain and functional ability are subjective outcomes, susceptible to placebo effects. Nonspecific or placebo effects can be quite large for an invasive procedure such as kyphoplasty for which there is no blinding. (9, 10) The placebo effect may be on the order of 6 to 7 mm on a 100-mm scale, for invasive procedures, (9-12) and even larger effects (10%) have been observed in the sham-controlled vertebroplasty trials. (13, 14) Therefore, sham-controlled comparison studies are important to demonstrate the clinical effectiveness of kyphoplasty over and above any associated nonspecific or placebo effects. Adverse effects related to kyphoplasty are the primary harms to be considered. Principal safety concerns relate to the incidence and consequences of leakage of the injected polymethylmethacrylate (PMMA).

Percutaneous Vertebroplasty for Vertebral Compression Fractures of Between 6 Weeks and 1 Year Old

Clinical Context and Therapy Purpose

Osteoporotic compression fractures are common. It is estimated that up to one-half of women and approximately one-quarter of men will have a vertebral fracture at some point in their lives. However, only about one-third of vertebral fractures reach clinical diagnosis, and most symptomatic fractures will heal within a few weeks or 1 month with medical management. Nonetheless, some individuals with acute fractures will have severe pain and decreased function that interferes with the ability to ambulate and is not responsive to usual medical management. Also, a minority of patients will exhibit chronic pain following osteoporotic compression fracture that presents challenges for medical management.

The purpose of vertebroplasty is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with symptomatic osteoporotic or osteolytic vertebral fractures between 6 weeks and 1 year old.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with symptomatic osteoporotic or osteolytic vertebral fractures between 6 weeks and 1 year old. With acute fractures, these individuals experience severe pain, decreased ambulatory function, and a lessened response to conservative medical management. Risk factors for osteoporotic or osteolytic vertebral fractures can include osteopenia, osteoporosis, advanced age, inactivity, corticosteroid use, female sex, and depression.

Interventions

The therapy being considered is vertebroplasty, a procedure for stabilizing compression fractures in the spine, during which bone cement is injected into the fractured vertebra through a small hole in the skin in order to relieve back pain.

Comparators
Comparators of interest include conservative management. Conservative management includes measures to reduce pain and improve mobility. Physical therapy, analgesics, narcotics, and hormone treatments can be prescribed to achieve this. Bed rest and braces may also be utilized as conservative management; however, these modalities are associated with prolonged immobilization which can further exacerbate bone loss and fail to relieve systems.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, quality of life, hospitalizations, medication use, and treatment-related morbidity. Negative outcomes can include complications with sedation, further injury during transfer to the radiology table, and the possibility of abuse after the prescription of narcotics. The outcomes of interest for vertebroplasty as a treatment for symptomatic vertebral fractures have varying follow-up times to fully examine the impact on the patient, ranging from shorter term outcomes like medication use to outcomes that require extended follow-up, such as functional outcomes. Given that the existing literature evaluating vertebroplasty as a treatment for symptomatic vertebral fractures between 6 weeks and 1 year old has varying lengths of follow-up, ranging from 6 months to 2 years, follow-up timing of 1 year is appropriate to demonstrate efficacy.

Disability, a major factor on quality of life, is measured using various tools throughout the literature. Three such tools include the Roland-Morris Disability Questionnaire (RMDQ), (15) the visual analogue scale (VAS), (16) and QUALEFFO (a quality-of-life questionnaire in patients with vertebral fractures). The RMDQ is a self-administered disability measure in which greater levels of disability are reflected by higher numbers on a 24-point scale and on VAS. The RMDQ has been shown to yield reliable measurements, which are valid for inferring the level of disability, and to be sensitive to change over time for groups of patients with low back pain. Visual analogue scale is commonly used as the outcome measure for such studies. It is usually presented as a 100-mm horizontal line on which the patient's pain intensity is represented by a point between the extremes of "no pain at all" and "worst pain imaginable." With QUALEFFO (a quality-of-life questionnaire in patients with vertebral fractures), quality of life is measured by the scale 0 to 100, higher scores indicating worse quality of life.

<u>Study Selection Criteria</u>
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Buchbinder et al. (2018) published a Cochrane review of the literature up to November 2014. (17) Studies compared vertebroplasty versus placebo (2 studies with 209 randomized participants), usual care (6 studies with 566 randomized participants), and kyphoplasty (4 studies with 545 randomized participants). The majority of participants were female, between 63.3 and 80 years of age, with symptom duration ranging from 1 week to more than 6 months. At 1 month, disease-specific quality of life measured by the QUALEFFO (a quality-of-life questionnaire in patients with vertebral fractures; scale 0 to 100, higher scores indicating worse quality of life) was 0.40 points worse in the vertebroplasty group. Based upon moderate quality evidence from 3 trials (1 placebo, 2 usual care, 281 participants) with up to 12 months follow-up, it is unclear if vertebroplasty increases the risk of new symptomatic vertebral fractures. Similarly, based upon moderate quality evidence from 2 placebo-controlled trials, it is unclear to what extent risk of other adverse events exists. There were 3/106 adverse events observed in the vertebroplasty group compared with 3/103 in the placebo group (risk ratio [RR], 1.01; 95% confidence interval [Cl]: 0.21 to 4.85). Serious adverse events that have been reported with vertebroplasty included osteomyelitis, cord compression, thecal sac injury, and respiratory failure.

Staples et al. (2011) conducted a patient-level meta-analysis of the 2 sham-controlled trials to determine whether vertebroplasty is more effective than sham in specific subsets of patients. (18) This subset analysis focused on duration of pain (≤6 weeks vs. >6 weeks) and severity of pain (score <8 or ≥8 on an 11-point numeric rating scale). The analysis included 209 participants (78 from the Australian trial, 131 from the U.S. trial); 27% had pain of recent onset and 47% had severe pain at baseline. The primary outcome measures (pain scores and function on the RMDQ at 1 month) did not differ significantly between groups. Responder analyses were also conducted based on a 3-unit improvement in pain scores, a 3-unit improvement in RMDQ scores, and a 30% improvement in each of the pain and disability outcomes. The only difference observed between groups was a trend in the vertebroplasty group to achieve at least 30% improvement in pain scores (RR, 1.32; 95% Cl, 0.98 to 1.76; p=0.07), a result that may have been confounded by the greater use of opioid medications in that group.

Xie et al. (2017), in a meta-analysis of RCTs, evaluated the efficacy and safety in percutaneous vertebroplasty and conservative treatment for patients with osteoporotic vertebral compression fractures. (19) Thirteen studies were selected (N=1231 patients; 623 to vertebroplasty, 608 to conservative treatment). Outcomes included pain relief (from 1 week to 6 months), quality of life assessments, and the rate of adjacent-level vertebral fracture. Vertebroplasty was superior for pain relief at 1 week and at 1 month. It was inferior to conservative treatment for pain relief at 6 months. Vertebroplasty showed improvement over conservative treatment for quality of life, as measured using QUALEFFO. No statistically significant differences were found between treatments for the rate of adjacent-level vertebral fractures. Limitations included the inclusion of several studies with inadequate blinding and heterogenous reporting of patient characteristics outcomes.

Hinde et al. (2020), in a meta-analysis of retrospective and prospective cohort studies, assessed the mortality outcomes of vertebral augmentation versus nonsurgical management in patients with osteoporotic vertebral compression fractures. (20) The meta-analysis included 7 studies (N=2,089,944; 382,070 treated with vertebral augmentation and 1,707,874 treated with nonsurgical management). Vertebral augmentation improved mortality compared with nonsurgical management at both 2- and 5-year follow-up. Limitations included heterogeneity in the number of enrolled patients in included studies as well as differences in health status.

Zhang et al. (2020), in a meta-analysis of RCTs, assessed the efficacy of percutaneous vertebroplasty versus conservative treatment for patients with osteoporotic vertebral compression fractures. (21) Ten studies were included, and outcomes consisted of pain relief at 1 week, 1 month, and 6 months; quality of life assessments; and the rate of new vertebral fractures. Compared with conservative treatment, percutaneous vertebroplasty was superior for pain relief at 1 week and 1 month, but not at 3 months. Results varied for quality-of-life assessments with similar outcomes between percutaneous vertebroplasty and conservative treatments on the RMDQ. Limitations included an imbalance in baseline demographics and the clinical characteristics of patients in included studies.

Chang et al. (2021), in a meta-analysis of RCTs and cohort studies, evaluated the effectiveness and safety of various interventions, including vertebroplasty versus kyphoplasty or conservative treatment, for treating osteoporotic vertebral compression fractures. (22) Thirty-nine studies included vertebroplasty as a comparative arm. Outcomes included scores based on the VAS and Oswestry Disability Index (ODI). Vertebroplasty decreased scores on the VAS and ODI compared with conservative treatment, but had similar outcomes compared with kyphoplasty. The rate of new fractures was similar for vertebroplasty versus conservative treatment and vertebroplasty versus kyphoplasty. Limitations consisted of the differences in indications, data types, follow-up times, and variables in included studies.

A network meta-analysis of RCTs conducted by Liu et al. (2023) assessed the safety and efficacy of 12 interventions, including vertebroplasty, compared to conventional and sham treatments for osteoporotic vertebral compression fractures. (23) The analysis included 34 RCTs, encompassing a total of 4383 participants with an average age of 73.4 years. Each study required a control group and an intervention group and reported on outcomes measured by the VAS pain scale or the ODI. The authors included several subgroups of vertebroplasty (vertebroplasty with facet joint injection, unilateral vertebroplasty, and curved vertebroplasty), which are not discussed here. Improvements compared to conservative treatment were observed in both short-term and long-term VAS and ODI scores. Compared to sham treatment, no significant difference was noted in short-term VAS scores; however, a notable improvement favoring the vertebroplasty group was observed in long-term VAS outcomes, as well as in both short-term and long-term ODI outcomes. No significant differences were observed in the relative risk of new fractures between vertebroplasty and the sham or conservative control groups. Limitations consisted of differences in indications and follow-up times, significant heterogeneity across study findings, and more than 50% of included studies having been assessed with a moderate or high risk of bias.

Table 2. Characteristics of Systematic Reviews and Meta-Analyses on Percutaneous Vertebroplasty For Vertebral Compression Fractures Between 6 Weeks and 1 Year Old

Study	Dates	Trials	Participants	Intervention	N (Range)	Design
Buchbinder et al. (2018) (17)	2007-2016	21	Patients with osteoporotic vertebral fractures (mean age ranged from 63.3 to 80 years); symptom duration ranged from 1 week to ≥ 6 months	Vertebroplasty	2862 (46-404)	RCT
Staples et al. (2011) (18)	NR	2	Participants with 1-2 painful osteoporotic vertebral fractures >12 months duration and unhealed, as confirmed by MRI, were randomly assigned to vertebroplasty or to a sham procedure	Vertebroplasty vs. placebo (5 studies); kyphoplasty (7 studies); facet joint steroid injection (1)	209 (78-131)	RCT
Xie et al. (2017) (19)	NR-2017	13	Patients with OVCFs	PVP vs. conservative treatment	2561 (NR)	RCT
Hinde et al. (2020) (20)	NR-2018	7	Patients with OVCFs	Vertebral augmentation (vertebroplasty or balloon kyphoplasty) vs. nonsurgical management	2,089,944 (NR)	Retro-spective and prospective cohort studies
Zhang et al. (2020) (21)	NR-2018	10	Patients with OVCFs	PVP vs. conservative treatment	NR	RCT
Chang et al. (2021) (22)	NR-2020	56	Patients with OVCFs	Vertebroplasty vs. conservative treatment (15 studies); kyphoplasty (24 studies)	6974 (14-191)	RCT, cohort studies

Liu et al. (2023) (23)	NR-2023	34	Patients with OVCFs	Network meta-analysis Of kyphoplasty, curved kyphoplasty, conservative treatment, sham procedure, pedicle screw fixation/fusion with or without vertebral augmentation, vertebroplasty with facet joint injection, vertebroplasty, unilateral vertebroplasty, curved vertebroplasty, kyphoplasty with facet joint injection, vertebral augmentation devices, unipedicular kyphoplasty	4384 (39-661)	RCT

NR: not reported; OVCF: osteoporotic vertebral compression fracture; PVP: percutaneous vertebroplasty; RCT: randomized controlled trial; vs: versus.

Table 3. Results of Systematic Reviews and Meta-Analyses on Percutaneous Vertebroplasty for Vertebral Compression Fractures Between 6 Weeks and 1 Year Old

Study	**Quality of Life**	**New Fractures**
	QUALEFFO	
Buchbinder et al. (2018) (17)		
Placebo group at 1-month, score (N)	4.58 (71)	NR
Vertebroplasty group at 1-month, score (N)	5.38 (71)	NR
Absolute change between groups	0.4% worse (5% worse-5% better [n=71])	NR

Relative change between groups	0.7% worse (9% worse-8% [n=71])	NR
Intervention group, n (%)	NR	28 (19.58)
Placebo group, n (%)	NR	19 (50.00)
RR (CI)	NR	1.47 (0.39-5.50)
	Duration of Pain	
Staples et al. (2011) (18)		
Mean change score (SD) of pain, at 2 weeks, PVP vs. placebo	2.2 (2.8) vs. 2.5 (3.0)	NR
Adjusted between group difference (CI) at 2 weeks	-0.2 (-0.9 to -0.6)	
Mean change score (SD) of pain, at 1 month, PVP vs. placebo	2.08 (3.0) vs. 2.2 (3.2)	NR
Adjusted between group difference (CI) at 2 weeks	0.6 (-0.2 to 1.4)	
	Pain Relief	
Xie et al. (2017) (19)	N=1231	NR
At 1-week (vertebroplasty superior), MD (CI)	1.36 (0.55 to 2.17)	NR
At 1-month (vertebroplasty superior), MD (CI)	1.56 (0.43 to 2.70)	NR
At 6-months (vertebroplasty inferior), MD (CI)	-1.59 (-2.9 to -0.27) p<0.05	NR
Total (vertebroplasty superior), MD (CI)	-5.03 (7.94 to -2.12)	NR
	Mortality	
Hinde et al. (2020) (20)		
Mortality, 2-year follow up, HR (CI), vertebral augmentation vs nonsurgical management	0.70 (0.69 to 0.71)	NR
Mortality, 5-year follow up, HR (CI), vertebral augmentation vs nonsurgical management	0.79 (0.62 to 0.9999)	NR
	Pain relief and QOL	
Zhang et al. (2020) (21)		
Pain relief at 1 week (PVP superior), MD (CI)	1.67 (0.84 to 2.51) p<0.0001	
Pain relief at 1 month (PVP superior), MD (CI)	1.98 (0.61 to 3.36) p=0.005	
Pain relief at 3 months, MD (CI)	−0.44 (−2.03 to 1.15)	OR, 1.09 (0.72 to 1.64)
EuroQol questionnaire (PVP superior), MD (CI)	0.11 (0.01 to 0.20) p=0.03	
Quality of Life Questionnaire of the European Foundation for Osteoporosis, MD (CI)	−7.29 (−12.60 to −1.99)	

Roland-Morris Disability Questionnaire, MD (CI)	0.66 (−2.00 to 3.33)	
	Pain and disability relief	
Chang at al. (2021) (22)		
Treatment effect for visual analog scale, mean (CI), vertebroplasty vs conservative treatment	-0.66 (-1.10 to -0.21)	OR, 1.09 (0.79 to 1.50)
Treatment effect for visual analog scale, mean (CI), vertebroplasty vs kyphoplasty	0.28 (-0.06 to 0.61)	OR, 0.99 (0.74 to 1.33)
Treatment effect for ODI, mean (CI), vertebroplasty vs conservative treatment	-5.27 (-9.19 to -1.35)	
Treatment effect for ODI, mean (CI), vertebroplasty vs kyphoplasty	1.23 (-1.59 to 4.04)	
Liu et al. (2023) (23)		
Short-term follow-up VAS, mean (Cl), vertebroplasty vs. conservative treatment	3.14 (2.31 to 3.98)	
Short-term follow-up VAS, mean (Cl), vertebroplasty vs. sham treatment	0.17 (-1 .19 to 0.86)	
Long-term follow-up VAS, mean (Cl), vertebroplasty vs. conservative treatment	1.08 (0.62 to 1.55)	
Long-term follow-up VAS, mean (Cl), vertebroplasty vs. sham treatment	0. 76 (0.07 to 1.45)	
Short-term follow-up OD1, mean (Cl), vertebroplasty vs. conservative treatment	14.13 (11 .5 to 16.8)	
Long-term follow-up ODI, mean (Cl), vertebroplasty vs. conservative treatment	8.69 (3.16 to 14.21)	
New fracture, relative risk (Cl), vertebroplasty vs. conservative treatment	1.28 (0.8 to 2.03)	
New fracture, relative risk (Cl), vertebroplasty vs. sham treatment	1.18 (0.53 to 2.62)	

CI: 95% confidence interval; HR: hazard ratio; MD: mean difference; N: number; NR: not reported; ODI: Oswestry Disability Index; OR: odds ratio; PVP: percutaneous vertebroplasty; QOL: quality of life; QUALEFFO: Questionnaire: a quality-of-life questionnaire in patients with vertebral fractures; RR: relative risk; SD: standard deviation; VAS: visual analogue scale.

Randomized Controlled Trials

Vertebroplasty Versus Medical Management with Sham Controls

Three sham-controlled trials compared vertebroplasty with medical management using a sham control (that included local anesthetic), which mimicked the vertebroplasty procedure up to the point of cement injection. (13, 14) Buchbinder et al. (2009) reported on results for a 4-center, randomized, double-blind, sham-controlled trial with 78 patients with 1 or 2 painful osteoporotic vertebral fractures with a duration of less than 1 year. (13) Patients were assigned

to vertebroplasty or sham procedure (i.e., injection of local anesthetic into the facet capsule and/or periosteum). Ninety-one percent of participants completed 6 months of follow-up. The participants, investigators (other than the radiologists performing the procedure), and outcome assessors were blinded to the treatment assignment. Kroon et al. (2014) reported results of the same trial at 12 and 24 months, maintaining blinding throughout the follow-up period. (24) The primary outcome was overall pain measured on a VAS from 0 to 10, with 1.5 points representing the minimal clinically important difference. For the primary outcome, reviewers reported no significant differences in VAS pain score at 3, 12, or 24 months. With reductions in pain and improvements in quality of life observed in both groups, the authors concluded routine use of vertebroplasty provided no benefit.

Kallmes et al. (2009) conducted a multicenter, randomized, double-blind, sham-controlled, investigational vertebroplasty safety and efficacy trial in which 131 participants with 1 to 3 painful osteoporotic vertebral fractures were assigned to vertebroplasty or sham procedure (injection of local anesthetic into the facet capsule and/or periosteum). (14) Participants had back pain for no more than 12 months and had a current pain rating of at least 3 on VAS at baseline. Participants were evaluated at various time points to 1-year post-procedure. Ninety-seven percent completed a 1-month follow-up; 95% completed 3 months. The primary outcomes were RMDQ scores and average back pain intensity during the preceding 24 hours at 1 month, with a reduction of 30% in RMDQ and VAS pain scores considered a clinically meaningful difference. (25)

For the primary endpoints at 1 month, there were no significant between-group differences. There was a trend toward a higher clinically meaningful improvement in pain at 1 month (30% reduction from baseline) in the vertebroplasty group (64% vs. 48%, respectively; p=.06). At 3 months, 51% from the control group and 13% in the vertebroplasty group crossed over ($p<0.001$). Comstock et al. (2013) reported on patient outcomes at 1 year, at which point 16% of patients who underwent vertebroplasty and 60% of control subjects had crossed over to the alternative procedure ($p<0.001$). (26) The as-treated analysis found no significant difference in RMDQ or pain scores between the 2 groups. Intention-to-treat analysis found a modest 1-point difference in pain rating and no significant difference in RMDQ score. There was a significant difference in the percentage of patients showing a 30% or greater improvement in pain (70% of patients randomized to vertebroplasty vs. 45% of patients randomized to the control group). One limitation of this study is that at 14 days, 63% of patients in the control group correctly guessed they had the control intervention, and 51% of patients in the vertebroplasty group correctly guessed they had the vertebroplasty.

Firanescu et al. (2018) published the results of a randomized, double-blind, sham-controlled clinical trial performed in 4 community hospitals in the Netherlands from 2011 to 2015. (27) The main outcome measured was mean reduction in VAS scores at 1 day, 1 week, and 1, 3, 6, and 12 months. The mean reduction in VAS score was statistically significant in the vertebroplasty and sham procedure groups at all follow-up points after the procedure compared with baseline. These changes in VAS scores were not statistically significant between the groups during 12 months of follow-up.

Table 4. Summary of Characteristics of Key RCT Comparing Vertebroplasty Versus Medical Management with Sham Controls

Study	Countries	Sites	Dates	Participants (N)	Interventions	
					Active (n)	Comparator (n)
Buchbinder et al. (2009) (13)	U.S.	4	2003-2008	Patients with 1-2 painful OVCF, duration <1 year	Vertebroplasty (38)	Sham procedure[1] (40)
Kallmes et al. (2009) (14)	U.S., UK., Aus	10	2004-2008	Participants with 1-3 painful OVCF, pain ≤ 12 mo, current pain VAS ≥ 3	Vertebroplasty (68)	Sham procedure[1] (63)
Firanescu et al. (2018) (27)	Netherlands	4	2011-2015	Participants with acute OVCF	Vertebroplasty (91)	Sham procedure[1] (89)

Aus: Australia; Mo: months; OVCF: osteoporotic vertebral compression fracture; RCT: randomized controlled trial; U.K.: United Kingdom; U.S.: United States; VAS: visual analogue scale.
[1] injection of local anesthetic into the facet capsule and/or periosteum

Table 5. Summary of Results of Key RCT Comparing Vertebroplasty Versus Medical Management with Sham Controls

Study	VAS	RMDQ
Buchbinder et al. (2009) (13)	N=73, at 3-months	
Intervention (mean±SD)	Reduction: 2.6±2.9	
Control (mean±SD)	Reduction: 1.9±3.3	
Adjusted between-group difference (CI)	0.6 (-0.7-1.8)	
Kallmes et al. (2009) (14)		
Day 14 Mean difference between groups (CI)	0.1 (-0.8-1.1)	-0.6 (-2.4-1.2)
P-value	0.77	0.35
Month 1 Mean difference between groups (CI)	0.7 (-0.3-1.70)	0.7 (-1.3-2.8)
P-value	0.19	0.49
Firanescu et al. (2018) (27)	N=180	
Day 1 Mean difference between groups (CI)	-0.43 (-1.17 - 0.31)	
Week 1 Mean difference between groups (CI)	-0.11 (-0.85 - 0.63)	

Month 1 Mean difference between groups (CI)	0.41 (-0.33 - 1.15)	
Month 3 Mean difference between groups (CI)	0.21 (-0.54 - 0.96)	
Month 6 Mean difference between groups (CI)	0.39 (-0.33 - 1.15)	
Month 12 Mean difference between groups (CI)	0.45 (-0.37-1.24)	

CI: 95% confidence interval; NR: not reported; RCT: randomized controlled trial; RMDQ: Roland-Morris Disability Questionnaire; SD: standard deviation; VAS: visual analogue score.

Table 6. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-up[e]
Buchbinder et al. (2009) (13)					
Kallmes et al. (2009) (14)				3. No reporting of harms. 5. Investigator modified pain window from 6 to 9 weeks.	
Firanescu et al. (2018) (27)	2. Lack of screening for co-occurring pain conditions. 2. MRI was not conducted.			5. Investigator modified pain window from 6 to 9 weeks.	

MRI: magnetic resonance imaging.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5. Other.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not established and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 7. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-up[d]	Power[e]	Statistical[f]
Buchbinder et al. (2009) (13)			2. 30% of eligible participants declined to participate, selection bias cannot be ruled out.			
Kallmes et al. (2009) (14)		1. At 14 days, > 50% of participants in either arm correctly identified their intervention assignment.		4. Due to high crossover the group differences in outcomes were complicated.		
Firanescu et al. (2018) (27)	4. Screening logs not retained.					

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated

Vertebroplasty Versus Medical Management Without Sham Controls

Chen et al. (2014) reported on a nonblinded RCT comparing vertebroplasty with conservative management. (28) The trial included 89 patients with chronic compression fractures confirmed by magnetic resonance imaging (MRI) and persistent severe pain for 3 months or longer. The evaluation was performed at 1 week and 1, 3, 6, and 12 months. Over the course of 1 year, pain scores decreased from 6.5 to 2.5 in the vertebroplasty group and from 6.4 to 4.1 in the control group ($p<0.001$). Complete pain relief was reported by 84.8% of patients in the vertebroplasty group and 34.9% of controls. The final ODI score was 15.0 in the vertebroplasty group and 32.1 in the conservative management group ($p<0.001$), and the final RMDQ score was 8.1 for vertebroplasty and 10.7 for controls ($p<0.001$).

Farrokhi et al. (2011) reported on a blinded RCT that compared vertebroplasty with optimal medical management in 82 patients. (29) Patients had painful osteoporotic vertebral compression fractures that were refractory to analgesic therapy for at least 4 weeks and less than 1 year. Control of pain and improvement in QOL were measured by independent raters before treatment and at 1 week and 2, 6, 12, 24, and 36 months after treatment began. Radiologic evaluation to measure vertebral body height and correction of deformity was performed before and after treatment and after 36 months of follow-up. Adverse events include new symptomatic adjacent fractures in 1 patient in the treatment group and 6 in the control group. Additionally, 1 patient experienced epidural cement leakage, which caused severe lower extremity pain and weakness, and had to be treated with bilateral laminectomy and evacuation of the bone cement.

Table 8. Summary of Key RCT Characteristics -Vertebroplasty Versus Medical Management Without Sham Controls

Study	Countries	Sites	Dates	Participants (N)	Interventions	
					Active	**Comparator**
Chen et al. (2014) (28)	China	1	2007-2012	Patients with chronic compression fractures confirmed by MRI and persistent severe pain for ≤3 months (89)	Vertebroplasty	Conservative Management
Farrokhi et al. (2011) (29)	Iran	1	2004-2005	Patients with painful osteoporotic vertebral compression fractures refractory to analgesic therapy for ≥4, but <1 year (82)	Vertebroplasty	Optimal Medical Management

MRI: magnetic resonance imaging; RCT: randomized controlled trial.

Table 9. Summary of Key RCT Results

Study	Pain Score	ODI Score	RMDQ
	Overall pain (scale 0-10)		
Chen et al. (2014) (N=89) (28)			
Intervention Group, Pooled at 1-year	2.5	15.0	8.1
Control Group, Pooled at 1-year	4.1	32.1	10.7
P-value	<0.001	<0.001	<0.001
Farrokhi et al. (2011) (29)	**VAS Score**		
Week 1 Mean difference between groups (CI); p-value	-3.1 (-3.72 to -2.28); <0.001	-14.0 (-15.00 to -12.82); <0.028	
Month 2 Mean difference between groups (CI); p-value	-2.9 (-4.9 to -0.82); <0.011	-15.0 (-16.76 to -13.24); <0.019	
Month 6 Mean difference between groups (CI); p-value	-1.9 (-3.25 to -0.55); <0.021	-11.0 (-12.17 to -7.83); <0.011	
Month 12 Mean difference between groups (CI); p-value	-1.9 (-2.9 to 0.9); <0.11	-12.0 (-13.5 to -11.5); <0.021	

CI: confidence interval; N: number; ODI: Oswestry Disability Index, RCT: randomized controlled trial; RMDQ: Roland-Morris Disability Questionnaire; VAS: visual analogue scale.

Table 10. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-up[e]
Chen et al. (2014) (28)			3. Investigator modified duration of the conservative therapy from 6 to 4 weeks		
Farrokhi et al. (2011) (29)				4. Language translation of Oswestry scale not validated	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 11. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-up[d]	Power[e]	Statistical[f]
Chen et al. (2014) (28)		1, 2. This study was not blinded.				
Farrokhi et al. (2011) (29)						

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Nonrandomized Comparative Studies

Edidin et al. (2011, 2015) reported mortality risk rates in Medicare patients who had vertebral compression fractures and had been treated with vertebroplasty, kyphoplasty or nonoperatively. (30, 31) These studies were industry funded. In the 2015 report, they identified 1,038,956 patients who had vertebral compression fractures between 2005 and 2009. The data set included 141,343 kyphoplasty patients and 75,364 vertebroplasty patients. The matched cohort included 100,649 non-operated patients, 36,657 kyphoplasty patients, and 24,313 vertebroplasty patients. Survival was calculated from the index diagnosis date until death or the end of follow-up (up to 4 years). Analysis of the whole data set before matching indicated that patients in the non-operated cohort had a 55% (95% CI, 53% to 56%, $p<0.001$) higher risk of mortality than the kyphoplasty cohort and a 25% (95% CI, 23% to 26%, $p<0.001$) higher mortality risk than the vertebroplasty cohort. After propensity matching, the risk of mortality at 4 years was 47.2% in the non-operated group compared to 42.3% in the kyphoplasty group ($p<0.001$) and 46.2% in the vertebroplasty group ($p<0.001$).

Lin et al. (2017) reported on mortality risk in elderly patients (>70 years old) who had vertebral compression fractures and were treated with early vertebroplasty (within 3 months) or conservative therapy. (32) The data set consisted of 10,785 Taiwanese patients who were selected through the National Health Insurance Research Database, of whom 1,773 patients received vertebroplasty, and 5,324 did not; a minority of these patients had osteoarthritis. The authors found that a "significant difference in survival curves of mortality and respiratory failure" existed between both groups of patients ($p<0.05$). The incidence of death at 1 year in the vertebroplasty group was 0.46 per 100 person-months (95% CI, 0.38 to 0.56). The incidence of death at 1 year in the nonvertebroplasty group was 0.63 per 100 person-months (95% CI, 0.57 to 0.70). With regard to respiratory failure, hazard ratio between groups was 1.46 (95% CI, 1.04 to 2.05; $p=0.028$). Limitations of this study included the broad selection of the population, which was not restricted only to patients with osteoporotic lesions. Also, authors were limited by the database, which did not report on pain or functional outcomes.

Section Summary: Percutaneous Vertebroplasty for Vertebral Compression Fractures of Between 6 Weeks and 1 Year Old

Despite evidence from numerous RCTs, including several with sham controls, the efficacy of vertebroplasty for painful osteoporotic compression fractures of less than 1 year remains uncertain. Seven meta-analysis studies have been published, but all of them have numerous limitations due to heterogeneity of included studies. Another major limitation to several meta-analyses is that they do not specify the timeframe for osteoporotic vertebral compression fractures. There remains some uncertainty related to the interpretation of these conclusions. While the use of a sham procedure is a major methodologic strength to control for nonspecific (placebo) effects, the sham used is controversial, given that the effect of injecting local anesthetic in the facet capsule and/or periosteum is unknown. Also, the appropriateness of outcome measures used to detect clinically meaningful differences in pain might not have been optimal, because the studies were underpowered to detect differences in clinical response rates. Questions have also been raised about the low percentage of patients screened who participated in the trial, the volume of PMMA injected, and the inclusion of patients with chronic pain.

Percutaneous Vertebroplasty for Vertebral Compression Fractures of Less Than 6 Weeks Old

Clinical Context and Therapy Purpose

The purpose of vertebroplasty is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as conservative management, in individuals with symptomatic osteoporotic vertebral fractures less than 6 weeks old.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest are individuals with symptomatic osteoporotic vertebral fractures less than 6 weeks old. With acute fractures, these individuals experience severe pain, decreased ambulatory function, and a lessened response to conservative medical management.

Interventions
The therapy being considered is vertebroplasty.

Comparators
Comparators of interest include conservative management. A detailed review of the comparators is listed in the above indication.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, QOL, hospitalizations, medication use, and treatment-related morbidity. Symptoms can include backpain and demonstrated fracture on radiography. The most current research available tracks follow-up to 12 months or more. A number of studies have longer term follow-up at more than 5 years, which is ideal for understanding all of the outcomes, particularly the occurrence of new vertebral compression fractures after vertebroplasty.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Randomized Controlled Trials
Vertebroplasty Versus Medical Management with Sham Controls
Clark et al. (2016) reported on results from the Safety and Efficacy of Vertebroplasty of Acute Painful Osteoporotic Fractures (VAPOUR) trial (see Table 12). (33) VAPOUR was a multicenter, double-blind trial of vertebroplasty in 120 patients with vertebral fractures of less than 6 weeks in duration and back pain of at least 7 out of 10 on a numeric rating scale. This trial followed a similar protocol as that used in the Kallmes et al. (2009) trial (discussed above). The primary outcome (the percentage of patients with a numeric rating scale score <4 out of 10 at 14 days post procedure) was met in a greater percentage of patients in the vertebroplasty group (44%) than in the sham control group (21%). This between group difference was maintained through 6 months.

Other outcome measures were significantly improved in the vertebroplasty group at 1 or both of the time points (see Table 13). The benefit of vertebroplasty was found predominantly in the thoracolumbar subgroup, with 48% (95% CI, 27% to 68%) more patients meeting the primary endpoint (61% in the vertebroplasty group vs. 13% in the control group). The investigators commented that the thoracolumbar junction is subject to increased dynamic load, and fractures at this junction have the highest incidence of mobility. No benefit from vertebroplasty was found in the non-thoracolumbar subgroup. Postprocedural hospital stay was reduced from

a mean of 14 days in the control group to 8.5 days after vertebroplasty, even though physicians who determined the discharge date remained blinded to treatment. In the vertebroplasty group, there were 2 serious adverse events due to sedation and transfer to the radiology table. In the control group, 2 patients developed spinal cord compression; 1 underwent decompressive surgery and the other, not a surgical candidate, became paraplegic.

Vertebroplasty Versus Medical Management Without Sham Controls
Klazen et al. (2010) reported on the vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures, an open-label randomized trial of 202 patients at 6 hospitals in the Netherlands and Belgium. (34) Of 431 patients eligible for randomization, 229 (53%) had spontaneous pain relief during assessment. Participants with at least 1 painful osteoporotic vertebral fracture of 6 weeks or less in duration were assigned to vertebroplasty or conservative management. The primary outcome was pain relief of 3 points measured on a 10-point VAS at 1 month and 1 year.

A total of 101 subjects were enrolled in the treatment group and the control arm; 81% completed 12-month follow-up. There were no significant differences in the primary outcome (pain relief of 3 points) measured at 1 month and 1 year. Vertebroplasty resulted in greater pain relief than did medical management through 12 months (<0.001); there were significant between-group differences in mean VAS scores at 1 month or at 1 year. Survival analysis showed significant pain relief was quicker (29.7 days vs. 115.6 days) and was achieved by more patients after vertebroplasty than after conservative management.

Yi et al. (2014) assessed the occurrence of new vertebral compression fractures after treatment with cement augmenting procedures (vertebroplasty or kyphoplasty) versus conservative treatment in an RCT with 290 patients (363 affected vertebrae). (35) Patients treated conservatively had a mean length of stay of 13.7 days. Return to usual activity occurred at 1 week for 87.6% of operatively treated patients and 2 months for 59.2% of conservatively treated patients. All patients were evaluated with radiographs and MRI at 6 months and then at yearly intervals until the last follow-up session. At a mean follow-up of 49.4 months (range, 36-80 months), 10.7% of patients had experienced 42 new symptomatic vertebral compression fractures. There was no significant difference in the incidence of new vertebral fractures between the operative (18 total; 9 adjacent, 9 nonadjacent) and conservative (24 total; 5 adjacent, 16 nonadjacent, 3 same level) groups but the mean time to a new fracture was significantly shorter in the operative group (9.7 months) than in the nonoperative group (22.4 months).

Leali et al. (2016) published a brief report on a multicenter RCT enrolling 400 patients with osteoporotic thoracic or lumbar vertebral compression fractures who were treated with vertebroplasty or conservative therapy. (36) Fractures were treated within 2 weeks of pain onset. Details of randomization and rates of follow-up were not reported. At 1 day after treatment, the vertebroplasty group had a reduction in pain scores and improvement in physical function, with VAS pain scores decreasing from 4.8 (maximum, 5.0) to 2.3 (p=0.023) and ODI scores improving from 53.6% to 31.7% (p=0.012). Sixty-five percent of patients treated

with vertebroplasty had stopped all analgesic use within 48 hours. The conservatively managed group showed no benefit in the first 48 hours, but by 6 weeks VAS and ODI scores were described as similar in both groups (specific data not reported). Evaluation of this trial was limited by incomplete reporting.

Yang et al. (2016) compared vertebroplasty with conservative therapy in 135 patients over 70 years of age with severe back pain due to an osteoporotic vertebral fracture after minor or mild trauma. (37) Vertebroplasty was performed at a mean of 8.4 days after pain onset. Patients in the conservative therapy group were placed on bed rest and analgesics for at least 2 weeks after diagnosis, followed by bracing and assistive devices. All patients receiving vertebroplasty could stand and walk with a brace at 1-day post treatment, while only 12 (23.5%) patients in the control group could stand up and walk after 2 weeks of bed rest. The average duration of bed rest from pain onset was 7.8 days (range, 2-15 days) in the vertebroplasty group compared with 32.5 days (range, 14-60 days) in the conservative therapy group. At 1-year follow-up, there was a similar percentage of additional compression fractures but a significantly higher complication rate in the conservative therapy group (35.3%) than in the vertebroplasty group (16.1%; $p<0.001$). Complications included pneumonia, urinary tract infection, deep vein thrombosis, depression, and sleep disorders.

Table 12. Summary of Key RCT Characteristics Involving Vertebroplasty Versus Medical Management without Sham Controls

Study; Trial	Countries	Sites	Dates	Participants (N)	Interventions	
					Active (n)	**Comparator (n)**
Klazen et al. (2010) (34)	EU	6	2005-2008	Patients ≥50 years with radiographically confirmed VCF, backpain for <6 weeks, VAS ≥5	Vertebroplasty (101)	Medical Management without Sham Controls (101)
Yi et al. (2014) (35)	China	1	2005-2009	Patients with OVCF	PVP or PKP (169)	Conservative treatment (121)
Leali et al. (2010) (36)	International	4	NR	Post-menopausal women with 1 thoracic or lumbar symptomatic OVCF caused by primary or secondary osteoporosis	PVP including analgesic and osteoporosis medication (200)	Conservative care including analgesic and osteoporosis medication (200)

Yang et al. (2015) (37	China	1	2009-2011	Patients ≥ 70 years with acute OVCF, severe pain from minor or mild trauma	PVP (56 at one year)	Conservative treatment (51 at one year)

N: number; NR: not reported; OVCF: osteoporotic vertebral compression fractures; PKP; percutaneous kyphoplasty; PVP: percutaneous vertebroplasty; RCT: randomized controlled trial; VCF: vertebral compression fracture; VAS: visual analog scale.

Table 13. Summary of Key RCT Results Involving Vertebroplasty Versus Medical Management without Sham Controls

Study	VAS	Quality of Life	Refracture Rate
Klazen et al. (2010) (34)			
Mean difference between groups in reduction of mean VAS score from baseline		RMDQ[1]	Median follow-up of 12.0 months (range: 1-24)
Month 1 (CI)	2.0 (1.13-2.80)	PVP: 12.5	PVP: 18 (16.48%)
p-value	<0.0001	Control: 13.5	Control: 30 (24.71%)
Month 12 (CI)	2.0 (1.13-2.80)	PVP: 9	
p-value	<0.0001	Control: 12	
Yi et al. (2014) (35)			
Month 12 (%)			PVP/PKP: 18 (8.28%)
			Control: 24 (19.83%)
			Time interval of recompression
Intervention			9.7 ± 17.8 months
Control			22.4 ± 7.99 months
p-value			0.017
Leali et al. (2016) (36)		ODI, %	
Intervention 24 hours after surgery, mean	2.3	31.7	
p-value	≤0.023	≤0.012	
Yang et al. (2015)[2] (37)			
Analysis of variance models, Month 1 (SD)	PVP: 2.4±1 Control: 4.8±1	PVP: 48±10 Control: 71±7	

Analysis of variance models, Month 12 (SD) p-value	PVP: 1.8±0.3 Control: 3±0.5	PVP: 30±5	PVP: 5 (8.9%) Control: 4 (7.8) <0.0001

CI: 95% confidence interval; ODI: Oswestry Disability Index; PKP: percutaneous kyphoplasty; PVP: percutaneous vertebroplasty; RCT: randomized controlled trials; RMDQ: Roland-Morris Disability Questionnaire; VAS: visual analogue scale; SD: standard deviation.

[1]The RMDQ results from the Klazen paper are based on estimates due to the graphical presentation of the results, rather than the reporting of the numerical values.

[2] The results from the Yang paper are based on estimates due to the graphical presentation of the results; numerical results not reported.

Table 14. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-up[e]
Klazen et al. (2010) (34)				3. None reported	
Yi et al. (2014) (35)	4. Selection criteria for PVP or PKP unclear, some patients had > fracture				
Leali et al. (2010) (36)	1.Limited to post-menopausal women				1,2 Follow-up period limited to < 6 months
Yang et al. (2015) (37)	4. Study population limited to >70 years of age at single spine center				

PVP: percutaneous vertebroplasty; PKP: percutaneous kyphoplasty.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 15. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-up[d]	Power[e]	Statistical[f]
Klazen et al. (2010) (34)		1,2. No masking				
Yi et al. (2014) (35)						
Leali et al. (2010) (36)		1,2,3. unclear if masking occurred	2. Outcomes beyond 48 hours post-surgery not reported			
Yang et al. (2015) (37)		1,2,3. No masking				3.Results reported only in graphic form

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Percutaneous Vertebroplasty for Vertebral Compression Fractures of Less Than 6 Weeks Old

In a sham-controlled randomized trial, where no anesthetic was injected into the periosteum, there was a significant benefit of vertebroplasty in patients who had severe pain of less than 6 weeks in duration following vertebral fracture at the thoracolumbar junction. Other RCTs without sham controls have reported that vertebroplasty is associated with significant

improvements in pain, earlier improvements in function, and reductions in the duration of bedrest compared to conservatively managed patients.

Percutaneous Sacroplasty

Clinical Context and Therapy Purpose

Sacral insufficiency fractures (SIFs) are the consequence of stress on weakened bone and often cause low back pain in the elderly population. (1) Osteoporosis is the most common risk factor for SIFs. Lourie (1982) described spontaneous fracture of the sacrum in patients with osteoporosis as presenting as lower back and buttock pain with or without referred pain in the legs. (38) Although common, SIFs can escape detection due to low provider suspicion and poor sensitivity on plain radiographs, slowing the application of appropriate intervention.

The purpose of sacroplasty is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as conservative management, in individuals with SIFs.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest are individuals with SIFs. SIFs are a stress fracture, resulting from a regular stress applied to a bone with reduced elasticity. Often, these fractures are associated with underlying metabolic bone disease condition like osteoporosis. Examples of risk factors include corticosteroid therapy use, female sex, pelvic radiation, rheumatoid arthritis, and hyperparathyroidism.

Interventions

The therapy being considered is sacroplasty, a minimally invasive procedure for treating pathological fractures of the sacral vertebral body or sacral ala. The procedure involves percutaneous insertion of 1 or more bone needles into the sacrum and injection of bone cement under fluoroscopy and/or computed tomography visual guidance.

Comparators

Comparators of interest include conservative management. Conservative management includes physical therapy, analgesics, narcotics, and hormone treatments. Examples of conservative management for SIFs are varied and can include bed rest and pain medication to early physical therapy.

*Outcome**s***

The general outcomes of interest are symptoms, functional outcomes, QOL, hospitalizations, medication use, and treatment-related morbidity. Possible negative outcomes include complications with sedation, cement leakage into the presacral space, spinal canal, sacral foramen, or sacroiliac joint, and possible spinal compression due to extravasation of cement. At least 1 year of follow-up is desirable to adequately evaluate outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Observational Studies

Sacroplasty is an evolving technique achieved using numerous methods (short axis, long axis, balloon-assisted short axis, iliosacral screws). No randomized trials of sacroplasty were identified. Frey et al. (2008) conducted the largest prospective observational cohort study, assessing 52 consecutive patients undergoing sacroplasty for SIFs using the short-axis technique. (39) Patients had a mean age of 75.9 years, a mean duration of symptoms of 34.5 days (range, 4-89 days), and a mean VAS score of 8.1 at baseline. Improvements in VAS scores were measured at 30 minutes and 2, 4-, 12-, 24-, and 52-weeks post procedure. At each interval, statistically significant improvements over baseline were observed and maintained through 52 weeks.

Kortman et al. (2013) reported on the largest series, a retrospective multicenter analysis. (40) They evaluated 204 patients with painful SIFs and 39 patients with symptomatic sacral lesions treated with the short-axis or long-axis technique. One hundred sixty-nine patients had bilateral SIFs, and 65 patients had additional fractures of the axial skeleton. VAS scores improved from 9.2 before treatment to 1.9 after treatment in patients with SIFs and from 9.0 to 2.6 in patients with sacral lesions. There was 1 case of radicular pain due to extravasation of cement requiring surgical decompression.

Frey et al. (2017) reported on patients treated with percutaneous sacroplasty, particularly the long-term efficacy of sacroplasty versus nonsurgical management. (41) This prospective, observational cohort study spanned 10 years and comprised 240 patients with SIFs. Thirty-four patients were treated with nonsurgical methods, and 210 patients were treated with sacroplasty. Pain, as measured by VAS, was recorded before treatment and at several follow-ups. Mean pretreatment VAS for the sacroplasty group was 8.29; for the nonsurgical treatment group, it was 7.47. Both forms of treatment resulted in significant VAS improvement from pretreatment to the 2-year follow-up ($p<0.001$). However, the sacroplasty treatment group experienced significant VAS score improvement consistently at many of the follow-up points (pretreatment to post [$p<0.001$]; post treatment through 2 weeks [$p>0.001$]; 12 weeks through 24 weeks [$p=0.014$]; 24 weeks through 1 year [$p=0.002$]). Meanwhile, the group with nonsurgical treatment only experienced 1 significant pain improvement score, which was at the 2-week follow-up posttreatment ($p=0.002$). One major limitation of this study was that the nonsurgical treatment group was not followed up at the 10-year mark whereas the sacroplasty group did receive follow-up.

Beall and colleagues (2023) published interim findings on patients who underwent percutaneous sacroplasty. (42) These patients were part of a prospective registry study conducted across multiple centers, which aimed to assess the effectiveness of sacroplasty in treating SIFs. Pain improvement according to the numeric rating scale (NRS) showed a significant reduction from a mean of 7.8 (standard deviation [SD], 2.4) at baseline to 0.9 (SD, 2.2; p<.001) with 92% showing a clinically meaningful reduction in pain at 6 months follow-up. Rolland-Morris Disability Questionnaire (RMDQ) scores also significantly decreased from baseline levels from a mean of 17.7 (SD 6.4) to 5.2 (SD, 5.2; p<.001) at 6 months follow-up, with 84% achieving a clinically meaningful reduction. One patient had a new neurologic deficit due to cement extravasation, but no other adverse events were reported. A major limitation of this study is an imbalance in baseline characteristic and at the time of publication only 48% of patients have 6-month follow-up data.

Sarigul et al. (2023) retrospectively described a single-center's experience with treating SIFs with sacroplasty (n=83) or conservative treatment (n=102). (43) Participants had a mean age of 69.2 years and required 5 years of follow-up to be included in the study (mean follow-up time was 7.2 years). At baseline, both VAS (8.82 vs. 4.18) and ODI (68.6 vs. 51.8) were significantly higher in the sacroplasty group than those conservatively treated. By 1 year follow-up, mean VAS scores had significantly decreased in the sacroplasty group to 1.5 and was favored over conservative treatment, which had a reduction to 2.82 (p<.001); a similar trend was observed for ODI, which showed a decrease to 8.4 in the sacroplasty group compared to 21 .2 in the conservative treatment group (p<.001). Cement leaks were identified in 2 patients, but no postoperative radiculopathy or pulmonary embolism were reported. Despite requiring 5-year data for all participants, only 1-year outcomes were reported by the authors.

There are several retrospective reviews with roughly 50 patients per publication. One reported by Dougherty et al. (2014) described a series of 57 patients treated with sacroplasty for SIFs. (44) The short- or the long-axis approach was dictated by the length and type of the fracture and patient anatomy. Follow-up data at 2.5 weeks were available for 45 (79%) patients, and the outcome measures were inconsistent. For example, activity pain scores were collected from 13 patients, and rest pain scores were collected from 29 patients. Of the 45 patients with outcomes data, 37 (82%) had experienced a numeric or descriptive decrease from initial pain of at least 30%.

Adverse Events

There are complications related to cement leakage with sacroplasty that are not observed with vertebroplasty. Leakage of PMMA into the presacral space, spinal canal, sacral foramen, or sacroiliac joint may result in pelvic injection of PMMA, sacral nerve root or sacral spinal canal compromise, or sacroiliac joint dysfunction. (45) Performing sacroplasty only on zone 1 fractures can minimize these risks. (46)

Section Summary: Percutaneous Sacroplasty

No RCTs on percutaneous sacroplasty for sacral insufficiency were identified. The available evidence includes 3 prospective cohort studies and several retrospective series. These studies

have reported rapid and sustained decreases in pain following percutaneous sacroplasty. Additional reports are mostly consistent in reporting immediate improvement following the procedure. Due to the limited number of patients and the retrospective nature of the evidence base, harms associated with sacroplasty have not been adequately studied. The small numbers of treated patients leave uncertainty regarding the impact of sacroplasty on health outcomes.

Kyphoplasty or Mechanical Vertebral Augmentation for Osteoporotic Vertebral Compression Fractures

Clinical Context and Therapy Purpose

The purpose of balloon kyphoplasty or mechanical vertebral augmentation is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with osteoporotic vertebral compression fractures (OVCF).

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with OVCF.

Interventions

The therapy being considered is balloon kyphoplasty or mechanical vertebral augmentation. The intervention involves the fluoroscopically guided injection of PMMA into a cavity created in the vertebral body with a balloon or mechanical device to provide support and symptomatic relief in patients.

Balloon kyphoplasty is a variant of vertebroplasty and uses a specialized bone tamp with an inflatable balloon to expand a collapsed vertebral body as close as possible to its natural height before injection of PMMA. Radiofrequency kyphoplasty (RFK; also known as radiofrequency targeted vertebral augmentation) is a modification of balloon kyphoplasty. In this procedure, a small diameter articulating osteotome creates paths across the vertebra. An ultra-high viscosity cement is injected into the fractured vertebral body, and radiofrequency is used to achieve the desired consistency of the cement. The ultra-high viscosity cement is designed to restore height and alignment to the fractured vertebra, along with stabilizing the fracture.

Kiva is another mechanical vertebral augmentation technique that uses an implant for structural support of the vertebral body to provide a reservoir for bone cement. The Kiva VCF Treatment System consists of a shaped memory coil and an implant, which is filled with bone cement. The coil is inserted into the vertebral body over a removable guidewire. The coil reconfigures itself into a stack of loops within the vertebral body and can be customized by changing the number of loops of the coil. The implant, made from PEEK-OPTIMA, a biocompatible polymer, is deployed over the coil. The coil is then retracted, and PMMA is injected through the lumen of the implant. The PMMA cement flows through small slots in the center of the implant, which fixes the implant to the vertebral body and contains the PMMA in a cylindrical column. The proposed advantage of the Kiva system is a reduction in cement leakage.

SpineJack is a mechanical vertebral augmentation technique that utilizes bipedicular 4.2 mm to 5.0 mm self-expanding jacks to restore vertebral height. Placement of the titanium devices are verified in anteroposterior and lateral view prior to expansion. Once the devices are expanded, a proprietary bone cement is injected. The proposed benefit is greater control over expansion and greater restoration of vertebral height compared to balloon kyphoplasty. The procedure requires good bone quality.

Comparators
Comparators of interest include conservative care. Treatment includes bed rest, local and systemic analgesia, and bracing. Conventional vertebroplasty procedures may also be used to treat this condition.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. Kyphoplasty may also restore lost vertebral body height and reduce kyphotic deformity. Potential health outcomes related to kyphotic deformity include pulmonary or gastrointestinal compression and associated symptoms, and vertebral compression fractures may be associated with lower health-related QOL (e.g., European Quality of Life-5 Dimensions).

The existing literature evaluating balloon kyphoplasty or mechanical vertebral augmentation as a treatment for osteoporotic vertebral compression fractures has varying lengths of follow-up, ranging from one month to four years.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
The Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review on selected interventional treatments for acute and chronic pain in September 2021. (47) The review included 37 RCTs for 10 interventional procedures and conditions that evaluated pain, function, health status, QOL, medication use, and harm. Results of the review concluded that vertebroplasty (13 trials) was probably more effective at reducing pain and improving function in patients >65 years of age, but benefits were small (<1 point on a 10-point pain scale). Benefits of vertebroplasty appeared smaller in sham-controlled trials compared with trials involving usual care as a control and larger in trials involving patients with more

acute symptoms. Vertebroplasty was also found to be probably not associated with an increased risk of incident vertebral fracture. Kyphoplasty (2 trials) was concluded to probably be more effective than usual care for pain and function in older patients with vertebral compression fracture at up to 1 month and may be more effective at >1 month to ≥1 year but has not been compared against sham therapy. The evidence regarding the risk of incident fracture with kyphoplasty was conflicting. The overall evidence base for vertebroplasty had several limitations including variations in patient selection criteria, technical factors such as volume of PMMA, and sham interventions. Usual care interventions were also not well standardized or defined and the majority of results were based on mean differences in outcomes. Few trials reported the likelihood of achieving a clinically relevant response and data on long-term outcomes were limited. For kyphoplasty, a major limitation is the absence of sham-controlled trials.

Kyphoplasty or Vertebroplasty versus Conservative Treatment

Meta-analyses

In a Bayesian network meta-analysis, Zhao et al. (2017) examined the efficacy and safety of vertebroplasty, kyphoplasty, and conservative treatment for the treatment of OVCF. (48) Sixteen RCTs were identified (N=2046 participants; vertebroplasty, n=816; kyphoplasty, n=478; conservative treatment, n=752). Eleven of the RCTs compared vertebroplasty with conservative treatment; two RCTs compared kyphoplasty with conservative treatment, and three RCTs compared kyphoplasty with vertebroplasty. Each trial assessed at least one of the following: visual analog score (VAS), the Roland-Morris Disability Questionnaire (RMDQ), the European Quality of Life-5 Dimensions, and the observance of any new fractures. Network meta-analysis demonstrated that kyphoplasty was superior to conservative therapy as assessed by VAS (mean difference, 0.94; 95% CI, -0.40 to 2.39), European Quality of Life-5 Dimensions (mean difference -0.10; 95% CI, -0.17 to -0.01), and RMDQ (mean difference, 5.72; 95% CI, 1.05 to 10.60). Insufficient data were present to complete pairwise comparison of kyphoplasty with conservative treatment for some metrics. No significant differences were found between vertebroplasty and kyphoplasty for pain relief, daily function, and QOL. Kyphoplasty was associated with the lowest risk of new fractures, while vertebroplasty was the most effective treatment for pain relief. This policy was limited by significant heterogeneity across measured outcomes and length of follow-up in studies; the presence of performing and reporting bias in studies was also a concern.

Hinde et al. (2020) performed a meta-analysis of 7 studies on the effect of vertebral augmentation (either vertebroplasty and/or balloon kyphoplasty) compared with nonsurgical management in over 1.5 million patients with osteoporotic vertebral compression fractures. (20) Compared with nonsurgical management, vertebral augmentation reduced risk of mortality (hazard ratio [HR], 0.78; 95% CI, 0.66 to 0.92). These benefits remained significant in stratified analyses of mortality over a period of 2 years (HR, 0.70; 95% CI, 0.69 to 0.71) and 5 years (HR, 0.79; 95% CI, 0.62 to 1.00). Most studies were rated with scores of 7 to 9 on the Newcastle-Ottawa rating scale.

Sun et al. (2020) performed a meta-analysis of 32 studies (N=945) in patients with osteoporotic vertebral compression fracture treated with vertebral augmentation or conservative treatment. (49) No significant differences were observed in the risk of clinical fracture (risk ratio [RR], 1.22; 95% CI, 0.70 to 2.12) or radiological fracture (RR, 0.91; 95% CI, 0.71 to 2.12). Overall, 10 studies were rated as high quality, and the remainder were rated as low quality. Results remained consistent when stratified by RCTs and non-RCTs.

Halvachizadeh et al. (2021) conducted a systematic review and meta-analysis comparing vertebroplasty, kyphoplasty, and nonoperative management in patients with osteoporotic vertebral compression fractures. (50) A total of 16 RCTs (N=2731 patients) were included with 11 trials comparing vertebroplasty to nonoperative management, 1 trial comparing kyphoplasty to nonoperative management, and 4 comparing kyphoplasty and vertebroplasty. Surgical intervention was associated with greater improvement of pain as compared to nonoperative management and was unrelated to the development of adjacent level fractures or quality of life. Of the trials comparing kyphoplasty and vertebroplasty, no significant differences in outcome measures were observed. Fourteen of the 16 trials provided some concern for bias, and the remaining 2 trials provided a high concern for bias. The authors noted the heterogeneity of the included studies as a limitation. Nonoperative management was not standardized, and the majority of studies failed to provide evidence of osteoporosis despite indicating that the treated fractures were osteoporotic vertebral fractures. Tables 16, 17, and 18 present a comparison of studies included in the systematic reviews, review characteristics, and results, respectively.

A network meta-analysis of RCTs conducted by Liu et al. (2023) assessed the safety and efficacy of 12 interventions, including kyphoplasty, compared to conventional and sham treatments for osteoporotic vertebral compression fractures. (23) The analysis included 34 RCTs, encompassing 4383 participants with an average age of 73.4 years. Each study required a control group and reported on outcomes measured by the VAS pain scale or the ODI. The authors included several subgroups of kyphoplasty (kyphoplasty with facet joint injection and curved kyphoplasty), which are not discussed further here. Improvements compared to conservative treatment were observed in both short-term and long-term VAS and ODI scores. Compared to sham treatment, no significant difference was noted in short-term VAS scores. However, a notable improvement favoring the kyphoplasty group was observed in long-term VAS outcomes, as well as in both short-term and long-term ODI outcomes. No significant differences were observed in the relative risk of new fractures between kyphoplasty and the sham or conservative control groups. Limitations consisted of differences in indications and follow-up times, significant heterogeneity across study findings, and more than 50% of included studies having been assessed with a moderate or high risk of bias.

Table 16. Comparison of Studies Included in Systematic Reviews & Meta-analyses on Percutaneous Kyphoplasty for Vertebral Compression Fractures

Study	Zhao (2017) (48)	Hinde (2020) (20)	Sun (2020) (49)	Halvachizadeh (2021) (50)	Liu (2023) (23)
Chen (2013)	●	●	●		●

Blasco (2012)	●		●	●	
Boonen (2011)	●				
Farrokhi (2011)	●		●	●	●
Klazen (2010a)	●		●	●	●
Klazen (2010b)			●		
Rousing (2009)	●		●	●	●
Kallmes (2009)	●			●	
Buchbinder (2009)	●		●	●	●
Voormolen (2006)	●			●	
Liu (2009)	●				
Endres (2012)	●				●
Dohm (2014)	●			●	●
Clark (2016)	●		●	●	●
Staples (2015)	●		●		
Yang (2015)	●				
Berenson (2011)	●				
Ong (2018)		●			
Edidin (2015)		●			
Edidin (2011)		●			
McCullough (2013)		●			
Lin (2017)		●			
Zampini (2010)		●			
Lange (2014)		●			
McDonald (2011)		●			
Lavelle (2008)		●			
Gerling (2011)		●			
Becker (2011)		●			
Levy (2012)		●			
Diamond (2016)		●			
Klezl (2012)		●			
Liu (2015)		●			
Bornemann (2012)			●		

Kroon (2013)			●		●
Diamond (2003)			●		
Firanescu (2018)			●	●	●
Giannotti (2012)			●		
Grafe (2005)			●		
Kasperk (2010)			●		
Klazen (2010)			●		
Lee (2012)			●		
Rousing (2010)			●		
Voormolen (2007)			●		
Wang (2016)			●	●	●
Wang (2010)			●		
Wardlaw (2009)			●	●	
Boonen (2011)			●		●
Van Meirhaeghe (2013)			●		
Yang (2016)			●		●
Yi (2014)			●		
Martinez-Ferrer (2013)			●		
Kroon (2013)			●		
Diamond (2006)			●		
Kasperk (2005)			●		
Lee (2012)			●		
Chen (2014)			●	●	●
Du (2018)			●		
Firanescu (2019)			●		
Kroon (2014)			●		
Movrin (2012)			●		
Voormolen (2007)			●		
Evans (2016)				●	●

Korovessis (2013)				●	●
Liu (2010)				●	●
Carli (2023)					●
Lv (2023)					●
Shi (2023)					●
Dang (2022)					●
Xu (2021)					●
Wang (2021)					●
Geng (2021)					●
Noriega (2019)					●
Li (2017)					●
Zhang (2015)					●
Gu (2015)					●
Tutton (2015)					●
Wang (2015)					●
Yan (2014)					●
Comstock (2013)					●
Bae (2010)					●
Chen (2010)					●

Table 17. Systematic Reviews & Meta-analyses Characteristics

Study	Dates	Trials	Participants	N (Range)	Design
Zhao (2017) (48)	2006-2016	16	Patients with osteoporotic vertebral compression fracture	2046 (34 to 381)	RCTs
Hinde (2020) (20)	2010-2018	7	Patients with osteoporotic vertebral compression fracture	1,649,247 (40 to 378,988)	Retrospective and prospective
Sun (2020) (49)	2005-2019	32	Patients with osteoporotic vertebral compression fracture	945 (34 to 300)	Prospective and RCTs
Halvachizadeh (2021) (50)	2006-2019	16	Patients with osteoporotic	2731 (34 to 381)	RCTs

			vertebral compression fracture		
Liu (2023) (23)	NR-2023	34	Patients with osteoporotic vertebral compression fracture	4384 (39-661)	RCT

RCT: randomized controlled trial.

Table 18. Systematic Reviews & Meta-Analyses Results

Study	VAS	EQ-5D	RMDQ	New Fractures	Mortality
Zhao (2017) (48)					
MD (95% CI) CT vs KP	0.94 (-0.40 to 2.39)	-0.10 (-0.17 to -0.01)	5.72 (1.05 to 10.60)	1.11 (0.46 to 2.86)	
MD (95% CI) KP vs Vertebroplasty	0.05 (-0.18 to 0.27)	-0.02 (-0.06 to 0.02)	-2.50 (-3.40 to -1.60)	1.29 (0.84 to 1.99)	
Hinde (2020) (20)					
HR (95% CI) VA vs. CT					0.78 (0.66 to 0.92)
HR (95% CI) Balloon KP vs. Vertebroplasty					0.77 (0.77 to 0.78)
Sun (2020) (49)					
RR (95% CI) VA vs. CT				Clinical fracture: 1.22 (0.70 to 2.12) Radiological fracture: 0.91 (0.71 to 2.12)	
Halvachizadeh (2021) (50)		**Adjacent level fractures**			
VAS change: short-term; long-term (95% CI) Vertebroplasty or KP vs. CT	1.31 (0.41 to 2.21); 0.89 (0.16 to 1.62)				
p value	<.0001; <.0001				
I^2	99.8%; 99.2%				

VAS change: short-term; long-term (95% CI) KP vs. Vertebroplasty	-0.20 (-0.34 to -0.05); -0.30 (-0.98 to 0.37)				
p value	.90; .02				
I^2	0%; 81.9%				
Log OR (95% CI) Vertebroplasty or KP vs. CT		-0.16 (-0.83 to 0.50)			
MD (95% CI) Vertebroplasty or KP vs. CT			1.7 (0.01 to 3.47)		
Liu (2023) (23)	**VAS**	**ODI**	**New Fractures**		
Short-term follow-up, mean (CI), KP vs conservative treatment	3.32 (2.32 to 4.31)	15.93 (1.32 to 19.54)			
Short-term follow-up, mean (CI), KP vs sham treatment	-0.34 (-1.66 to 0.98)				
Long-term follow-up, mean (CI, KP vs conservative treatment	1.17 (0.63 to 1.72)	10.46 (3.52 to 17.40)	RR: 1.16 (0.73 to 1.82)		
Long-term follow-up, mean (CI), KP vs sham treatment	0.86 (0.04 to 1.67)		RR: 0.93 (0.37 to 2.38)		

CI: confidence interval; CT: conservative therapy; EQ-5D: European Quality of Life-5 Dimensions; HR: hazard ratio; KP: kyphoplasty; MD: mean difference; ODI: Oswestry Disability Index; OR: odds ratio; RMDQ: Roland-Morris Disability Questionnaire; RR: relative risk; VA: vertebral augmentation; VAS: visual analogue score.

Observational Studies

Edidin et al. (2011) reported on mortality risk in Medicare patients who had OVCFs and had been treated with vertebroplasty, kyphoplasty, or nonoperatively. (30) Using the U.S. Medicare dataset, the authors identified 858,978 patients who had VCFs between 2005 and 2008. The data set included 119,253 kyphoplasty patients and 63,693 vertebroplasty patients. Survival was calculated from the index diagnosis date until death or the end of follow-up (up to 4 years).

Cox regression analysis was used to evaluate the joint effect of multiple covariates, which included sex, age, race/ethnicity, patient health status, type of diagnosed fracture, site of service, physician specialty, socioeconomic status, year of diagnosis, and census region. After adjusting for covariates, patients in the surgical cohorts (vertebroplasty or kyphoplasty) had a higher adjusted survival rate (60.8%) than patients in the nonsurgical cohort (50.0%) and were 37% less likely to die. The adjusted survival rates for vertebroplasty or kyphoplasty were 57.3% and 62.8%, respectively, a 23% lower relative risk for kyphoplasty. As noted by the authors, a causal relation could not be determined from this study.

An industry-sponsored analysis by Ong et al. (2018) evaluated the effect of the sham-controlled vertebroplasty trials on utilization of kyphoplasty/vertebroplasty, morbidity, and mortality in the Medicare population. (51, 13, 14) Using the complete inpatient/outpatient U.S. Medicare data set from 2005 to 2014, the investigators evaluated utilization of vertebral augmentation procedures in patients with osteoporotic vertebral compression fractures who were treated in the 5-year period before 2009 and those who were treated in the 5 years after the sham-controlled trials were published. Use of the 2 procedures peaked at 24% of the osteoporotic vertebral compression fracture population in 2007 - 2008, then declined to 14% of osteoporotic vertebral compression fracture patients in 2014. Compared to patients with osteoporotic vertebral compression fractures treated non-surgically, the kyphoplasty cohort (n=261,756) had a 19% (95% CI, 19 to 19%) lower propensity-adjusted 10-year mortality risk. Compared to patients with osteoporotic vertebral compression fracture treated with vertebroplasty (n=117,232), the kyphoplasty cohort had a 13% (95% CI, 12-13%) lower propensity-adjusted 10-year mortality risk. The study also found that patients treated with non-surgical management were more likely to be discharged to nursing facilities. Although the analysis did adjust for possible confounding factors, the observational nature of the study precludes any inference of causality.

Balloon Kyphoplasty vs Conservative Care

The largest trial of kyphoplasty vs conservative care is by Wardlaw et al. (2009), who reported on the Fracture Reduction Evaluation (FREE) trial, a nonblinded industry-sponsored, multisite RCT in which 300 adults with 1 to 3 painful OVCFs of less than 3 months in duration. (52) Twenty-four-month results were reported by Boonen et al. (2011) and by Van Meirhaeghe et al. (2013). (53, 54) Scores for the primary outcome, 1-month change in 36-Item Short-Form Health Survey (SF-36) Physical Component Summary (PCS) score, were significantly higher for those in the kyphoplasty group. The difference between groups was 5.2 points (95% CI, 2.9 to 7.4 points; $p<0.001$). Kyphoplasty was associated with greater improvements in SF-36 PCS scores at 6-month follow-up (3.39 points), but not at 12- or 24-month follow-ups. Greater improvement in back pain was observed over 24 months for kyphoplasty (-1.49 points) and remained statistically significant at 24 months. Participants in the kyphoplasty group also reported greater improvements in quality of life and Roland-Morris Disability Questionnaire (RMDQ) scores at short-term follow-up. At 12 months, fewer kyphoplasty patients (26.4% vs 42.1%) had received physical therapy or walking aids, back braces, wheelchairs, miscellaneous aids, or other therapy. Fewer kyphoplasty patients used opioid medications through 6 months (29.8% vs 42.9%) and fewer pain medications through 12 months (51.7% vs. 68.3%). Other differences

between groups were no longer apparent at 12 months, possibly due to natural healing of fractures. Tables 19 and 20 summarize the key characteristics and results of the FREE trial. Tables 21 and 22 detail the relevance and design/conduct limitations of the study.

Table 19. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Wardlaw (2009), Boonen (2011), Van Meirheghe (2013) (52-54)	EU	21	2003-2005	Patients with 1-3 vertebral fractures	Balloon kyphoplasty (n=149)	Non-surgical care (n=151)

EU: European Union; RCT: randomized controlled trial; n: number.

Table 20. Summary of Key RCT Results

Study	Mean SF-36 PCS Score Improvement at 1 mo (95% CI)	Difference in SF-36 Scores between Groups at 24 mo (95% CI)	Serious Adverse Events within 30 days	Serious Adverse Events within 12 mo	Serious Adverse Events within 24 mo
Wardlaw (2009), Boonen (2011), Van Meirheghe (2013) (52-54)					
Kyphoplasty	7.2 (5.7 to 8.8)		24 (16.1%)	58 (38.9%)	74 (49.7%)
Control	2 (0.4 to 3.6)		17 (11.3%)	54 (35.8%)	73 (48.3%)
MD (95% CI)		3.24 (1.47 to 5.01)			
p-value	<0.0001	0.0004			

CI: confidence interval; MD: meann difference; mo: month; RCT: randomized controlled trial; SF-36 PCS: 36-Item Short-Form Physical Component Score.

Table 21. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Wardlaw (2009), Boonen (2011), Van Meirheghe (2013) (52-54)			3. Non-surgical treatment was not standardized		2. 24 mo. follow-up

The study limitations stated in this table are those notable in the current literature review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 22. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Wardlaw (2009), Boonen (2011), Van Meirheghe (2013) (52-54)	3. Allocation concealment unclear	1, 2. Not blinded				

The study limitations stated in this table are those notable in the current literature review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

<u>Mechanical Vertebral Augmentation (e.g., Kiva or SpineJack) vs Balloon Kyphoplasty</u>
Vertebral augmentation with the Kiva VCF system was compared with balloon kyphoplasty in a pivotal noninferiority RCT reported by Tutton et al. (2015). (55) This industry-sponsored, multicenter, open-label KIVA safety and effectiveness trial was conducted in 300 patients with 1 or 2 osteoporotic VCFs. Included were patients with VAS scores for back pain of at least 70 mm (/100 mm) after 2 to 6 weeks of conservative care or VAS scores of at least 50 mm after 6 weeks of conservative care, and Oswestry Disability Index (ODI) scores of at least 30%. The primary composite end point at 12 months was a reduction in fracture pain by at least 15 mm on the VAS, maintenance, or improvement in function on the ODI, and absence of device-related serious adverse events. The primary end point was met by 94.5% of patients treated with Kiva and 97.6% of patients treated with kyphoplasty (Bayesian posterior probability of

99.92% for noninferiority, using as-treated analysis). In the 285 treated patients, Kiva resulted in a mean improvement of 70.8 points in VAS scores, compared with a 71.8 point improvement for kyphoplasty. There was a 38.1 point improvement in ODI score for the Kiva group compared with a 42.2 point improvement for the kyphoplasty group. There were no device-related serious adverse events. The total volume of cement was 50% less with Kiva and there was less cement extravasation (16.9%) compared with kyphoplasty (25.8%).

Korovessis et al. (2013) reported on a randomized trial of 180 patients with osteoporotic vertebral compression fractures that compared mechanical vertebral augmentation with the Kiva device with balloon kyphoplasty in 180 patients with osteoporotic vertebral compression fractures. (56) The groups showed similar improvements in VAS scores for back pain, SF-36 scores, and ODI scores. For example, there was a more than 5.5-point improvement in VAS scores in 54% of patients in the Kiva group and in 43% of patients in the balloon kyphoplasty group. Radiologic measures of vertebral height were similar in both groups. Kiva reduced the Gardner kyphotic angle, while residual kyphosis of more than 5° was more frequently observed in the balloon kyphoplasty group. Patients and outcome assessors were reported to be unaware of group assignments, although it is not clear if the Kiva device was visible on radiographs. Cement leakage into the canal only occurred in 2 patients treated with balloon kyphoplasty, necessitating decompression, compared with none following the Kiva procedure.

Noriega et al. (2019) reported the pivotal multicenter non-inferiority trial of the SpineJack vertebral augmentation system. (57) Patients (n=152) with osteoporotic vertebral compression fractures less than 3 months old were randomized to treatment with SpineJack or balloon kyphoplasty. The primary outcome was a composite measure that included improvement in visual analog scale for pain of greater than 20 mm, maintenance or improvement in Oswestry Disability Index, and lack of adverse events. Vertebral height was prespecified to be included if the primary outcome was achieved. Non-inferiority was achieved with 89.8% of SpineJack patients achieving the composite of clinical success compared to 87.3% for balloon kyphoplasty. When including the restoration of vertebral body height, the SpineJack procedure was found to be superior to balloon kyphoplasty at 6 months (88.1% vs. 60.9%) and at 12 months (79.7% vs. 59.3%, $p<0.001$). There was also a reduction in adjacent vertebral fractures with the mechanical augmentation system (12.9% vs. 27.3%; $p=0.043$). Interpretation of this study is limited by the lack of a sham control group.

Table 23. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Tutton et al. (2015) (55)	US, EU	21	2010-2013	Patients with OVCF	Kiva (n=153)	BK (n=147)
Korovessis et al. (2013) (56)	Greece	1	2010-2011	Patients with OVCF	Kiva (n=82 patients, 133 fractures)	BK (n=86 patients, 122 fractures)

Noriega et al. (2019) (57)	EU	13	2015-2017	Patients with OVCF aged <3 mo and loss of height ≥15% but ≤40%, VAS ≥50 mm and ODI ≥30%	SpineJack (n=77, 68 in mITT)	BK (n=75, 73 in mITT)

BK: balloon kyphoplasty; EU: European Union; mITT; modified intention-to-treat; n: number; ODI: Oswestry Disability Index; US: United States; OVCF: osteoporotic vertebral compression fracture; RCT: randomized controlled trial; VAS: visual analog score.

Table 24. Summary of Key RCT Results

Study	**Improvement in VAS Score at 12 mo.**	**Improvement in ODI at 12 mo.**		**Restoration of VBH**	**Percent Success**
				Anterior	**VAS Improvement of 5.5 Points**
Tutton et al. (2015) (55)					
Kiva	70.8	38.1			
BK	71.8	42.2			
Korovessis et al. (2013) (56)					
Kiva				24%	44 (54%)
BK				23%	37 (43%)
P value				0.97	
	Improvement in VAS at 1 mo ± SD	**Improvement in ODI at 1 mo ± SD**	**Improvement in EQ-5D at 1 mo ± SD**	**Midline ± SD**	**Percent Achieving CCS (95% CI)**
Noriega et al. (2019) (57)					
Spine-Jack	56.4 ± 20.3	44.2 ± 21.2	0.45 ± 0.29	1.31 ± 2.58	89.8% (82.1%–97.5%)
BK	47.8 ± 25.7	39.9 ± 23.7	0.42 ± 0.29	0.10 ± 2.34	87.3% (78.5 to 96.1)
p-Value	0.029	0.321	0.598	0.0035	0.0016

BK: balloon kyphoplasty; CCS: composite clinical success; CI: confidence interval; EQ-5D: EuroQol 5-domain questionnaire; mo: month(s); ODI: Oswestry Disability Index; RCT: randomized controlled trial; SD: standard deviation; VAS: visual analog scale; VBH: vertebral body height.
Composite clinical success included greater than 20 mm improvement in visual analog score, maintenance or improvement in ODI, and absence of adverse events.

Table 25. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Tutton et al. (2015) (55)	2. Allocation not concealed throughout study	1, 2. Patients only blinded prior to procedure performance			2. Study not powered for primary or secondary endpoint	
Korovessis et al. (2013) (56)		1, 2. Not blinded				
Noriega et al. (2019) (57)		1. Not blinded for patient-reported outcomes. Radiographic assessments were blinded				

The study limitations stated in this table are those notable in the current literature review; this is not a comprehensive gaps assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Osteoporotic Vertebral Compression Fractures

An AHRQ review concluded that vertebroplasty was probably more effective at reducing pain and improving function in patients >65 years of age, but benefits were small (<1 point on a 10-point pain scale). Kyphoplasty was found to be probably more effective than usual care for pain and function in older patients with vertebral compression fracture at up to 1 month and may be more effective at >1 month to ≥1 year but has not been compared against sham therapy. The review found that the overall evidence base for vertebroplasty had several limitations while the absence of sham-controlled trials is a major limitation for kyphoplasty. A network meta-analysis

found that relative to conservative treatment kyphoplasty provided short-term and long-term improvements to pain and disability scores.

A moderately sized, unblinded RCT reported short-term benefits of kyphoplasty for pain and other outcomes in patients with painful osteoporotic fractures compared with conservative care. One systematic review of RCTs found no significant difference in subsequent fracture between vertebroplasty and conservative treatment, and another systematic review of prospective and retrospective studies reported improved mortality with either vertebroplasty or balloon kyphoplasty compared with conservative treatment. Other relevant studies, including additional RCTs and meta-analysis, found similar outcomes for kyphoplasty and vertebroplasty.

For mechanical vertebral augmentation with Kiva and SpineJack, the evidence includes industry-sponsored, multicenter investigational device exemption trials and a large independent randomized trial. These randomized comparative trials showed outcomes similar between Kiva and kyphoplasty. Mechanical vertebral augmentation with SpineJack was found to be non-inferior to balloon kyphoplasty for success on a composite outcome measure and superior to BK when vertebral height restoration was included in the composite. A major limitation of all these RCTs is the lack of a sham procedure. Due to the possible sham effect observed in the trials of vertebroplasty, the validity of the results from non-sham-controlled trials is unclear. Therefore, whether these improvements represent a true treatment effect is uncertain.

Osteolytic Vertebral Compression Fractures

Clinical Context and Therapy Purpose

The purpose of balloon kyphoplasty or mechanical vertebral augmentation is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as conservative care, in individuals with osteolytic vertebral compression fractures.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with osteolytic VCF.

Interventions

The therapy being considered is balloon kyphoplasty or mechanical vertebral augmentation. The intervention involves the fluoroscopically guided injection of PMMA into a cavity created in the vertebral body with a balloon or mechanical device to provide support and symptomatic relief in patients.

Comparators

Comparators of interest include conservative care. Treatment includes bed rest, local and systemic analgesia, and bracing.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity.

Table 26. Outcomes of Interest for Individuals with OVCFs

Outcomes	Details
Quality of Life	Reduced pain, disability, and analgesic use in patients

The existing literature evaluating balloon kyphoplasty or mechanical vertebral augmentation as a treatment for osteolytic OVCF has varying lengths of follow-up. At least one year of follow-up for the primary outcome is necessary to adequately assess outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
In a systematic review, Health Quality Ontario (2016) assessed vertebral augmentation for cancer related VCFs. (58) The assessment identified 33 reports with 1,690 patients who were treated with kyphoplasty for spinal metastatic cancers, multiple myeloma, or hemangiomas. For cancer-related VCFs there were 5 case series (110 patients) on multiple myeloma and 6 reports (2 RCTs, 4 case series; 308 patients) on mixed cancers with spinal metastases. Vertebral augmentation resulted in reductions in pain intensity scores, opioid or other analgesic use, and disability scores. One RCT (n=129) compared kyphoplasty with nonsurgical management for cancer-related VCFs, reporting that pain scores, pain related disability, and health-related quality of life were significantly improved in the kyphoplasty group than in the usual care group. The second RCT compared the Kiva device with kyphoplasty in 47 patients with cancer-related compression fractures, finding no significant differences between groups for improvements in VAS pain and ODI scores.

Mattie et al. (2021) conducted a systematic review and meta-analysis of 7 RCTs (N=476) that compared the magnitude and duration of pain relief with vertebral augmentation (i.e., balloon kyphoplasty or percutaneous vertebroplasty), with or without additional therapy, to any other intervention or placebo/sham for the treatment of cancer-related vertebral compression fractures. (59) In 5 of the 7 studies, vertebral augmentation alone comprised 1 group; comparative treatments included nonsurgical management, Kiva implantation, and

combinations of percutaneous vertebroplasty and radiofrequency therapy, chemotherapy, instrasomatic steroid injection, or ^{125}I seeds. Results revealed an overall positive and statistically significant effect of vertebral augmentation for the management of cancer-related vertebral compression fractures. This effect was particularly pronounced when comparing vertebral augmentation to nonsurgical management, radiofrequency ablation, or chemotherapy alone. The authors noted that there was much heterogeneity among the included studies regarding the treatment methods in the control groups and 1 study allowed patients to crossover to the intervention group, potentially leading to biased results.

Randomized Controlled Trials

The only RCT to compare kyphoplasty to non-surgical management was an international multicenter study reported by Berenson et al. (2011). (60) The trial enrolled 134 patients with cancer who were at least 21 years of age. Participants had at least 1 and not more than 3 painful VCFs. The primary outcome was change in functional status from baseline at 1 month as measured by the RMDQ. Treatment allocation was not blinded, and the primary outcome at 1 month was analyzed using all participants with data both at baseline and at 1 month. Participants needed to have a pain score of at least 4 on a 0-to-10 scale. Crossover to the balloon kyphoplasty arm was allowed after 1 month. Reviewers reported scores for the kyphoplasty and nonsurgical groups of 17.6 and 18.2 at baseline, respectively, and 9.10 and 18.0 at 1-month follow-ups (between-group difference in scores, $p<0.001$).

Korovessis et al. (2014) compared efficacy of Kiva and kyphoplasty in an RCT with 47 participants with osteolytic vertebral compression fractures. (61) Oswestry Disability Index scores improved by 42 and 43 points in the kyphoplasty and Kiva groups, respectively. Pain scores improved by 5.1 points in both groups, from baseline mean scores of 8.1 (kyphoplasty) and 8.3 (Kiva).

Section Summary: Osteolytic VCF

Results of RCTs and case series suggest vertebral augmentation reduces pain, disability, and analgesic use in patients with cancer-related compression fractures. However, because the results of the comparative studies of vertebroplasty have also suggested possible placebo or natural history effects, the evidence provided is insufficient to warrant conclusions about the effect of kyphoplasty on health outcomes.

Radiofrequency Kyphoplasty (RFK)

Clinical Context and Therapy Purpose

The purpose of RFK is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as conservative care, in individuals with osteoporotic or osteolytic vertebral compression fractures.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with osteoporotic or osteolytic VCF.

Interventions
The therapy being considered is RFK. The intervention uses radiofrequency energy to ablate metastatic malignant lesions in a vertebral body to provide symptomatic relief.

Comparators
Comparators of interest include conservative care. Treatment includes bed rest, local and systemic analgesia, and bracing.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity.

Table 27. Outcomes of Interest for Individuals with OVCFs

Outcomes	Details
Quality of Life	Reduced pain, disability, and analgesic use in patients

The existing literature evaluating RFK as a treatment for osteoporotic or osteolytic VCF has varying lengths of follow-up, ranging from 36-80 months. While studies described below all reported at least one outcome of interest, longer follow-up was necessary to fully observe outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Meta-Analysis
Feng et al. (2017) performed a meta-analysis comparing RFK with balloon kyphoplasty in patients with VCFs. (62) Six studies (n=833 patients) evaluating VCFs were identified. The main outcomes were pain relief (VAS), functionality improvement (ODI), operation time, reduction of deformity (i.e., the restoration of vertebral height and kyphosis angle), and incidence of cement leakage. VAS scores improved for both groups after the respective procedure; however, VAS score dropped 3.96 points more in the RFK group (95% CI, 1.67 to 6.24; p=0.001), with improvement persisting until the 12-month mark. While functionality improvement was initially improved more after RFK than balloon kyphoplasty (p=0.04), the difference between the two groups was not significant after a year (p=0.6). No significant difference in cement

leakage between groups was observed. This review was limited by the small number of studies included as well as the presence of significant bias within these studies.

Randomized Controlled Trials

Petersen et al. (2016) reported on an RCT with 80 patients that compared RFK with balloon kyphoplasty. (63) Patients had been admitted to the hospital for severe back pain and met criteria for surgery after failed conservative treatment. All had osteoporotic compression fractures. Prior to treatment, VAS pain scores on movement were similar in both groups (8.4 in the balloon kyphoplasty group vs 8.0 in the RFK group). Postoperatively, VAS scores improved by 4.6 after balloon kyphoplasty and 4.4 after RFK (p=NS). Pain at 12 months also did not differ significantly between both groups, with 58% of patients in the balloon kyphoplasty group and 66% of patients in the RFK group reporting no to mild pain on movement (p=NS). There was a trend for greater restoration of the kyphosis angle.

Section Summary: RFK

For RFK, the evidence includes a meta-analysis study and an RCT. While the RCT showed similar results compared with balloon kyphoplasty, an improvement in immediate pain relief after RCT was noted in the meta-analysis. Further high-quality studies are needed to determine with greater certainty whether RFK has outcomes similar to balloon kyphoplasty.

Adverse Events

Yi et al. (2014) assessed the occurrence of new VCFs after treatment with cement augmenting procedures (vertebroplasty or kyphoplasty) vs conservative treatment in an RCT with 290 patients (363 affected vertebrae). (35) Surgically treated patients were discharged the next day. Patients treated conservatively (pain medication, bedrest, a body brace, physical therapy) had a mean length of stay of 13.7 days. Return to usual activity occurred at 1 week for 87.6% of surgically treated patients and at 2 months for 59.2% of conservatively treated patients. All patients were evaluated with radiographs and magnetic resonance imaging at 6 months and then at yearly intervals until the last follow-up session. At a mean follow-up of 49.4 months (range, 36-80 months), 10.7% of patients had experienced 42 new symptomatic VCFs. There was no significant difference in the incidence of new vertebral fractures between the operative (n=18; 9 adjacent, 9 nonadjacent) and conservative (n=24; 5 adjacent, 16 nonadjacent, 3 same level) groups, but the mean time to a new fracture was significantly shorter in the surgical group (9.7 months) compared with the nonoperative group (22.4 months).

Summary of Evidence

For individuals who have symptomatic osteoporotic vertebral fractures of between 6 weeks and 1 year old who receive vertebroplasty, the evidence includes 2 randomized sham-controlled trials, nonblinded randomized controlled trials (RCTs) comparing vertebroplasty with conservative management, and several meta-analyses. Relevant outcomes are symptoms, functional outcomes, quality of life (QOL), hospitalizations, medication use, and treatment-related morbidity. Despite the completion of multiple RCTs, including 2 with sham controls, the efficacy of vertebroplasty for painful osteoporotic compression fractures remains uncertain. Two meta-analysis studies which included the 2 sham-controlled trials have demonstrated

mixed results. The 2 studies had methodologic issues, including the choice of sham procedure and the potential of the sham procedure to have a therapeutic effect by reducing pain. Questions have also been raised about the low percentage of patients screened who participated in the trial, the volume of polymethylmethacrylate (PMMA) injected, and the inclusion of patients with chronic pain. One network meta-analysis found that relative to conservative treatment, vertebroplasty provided short-term and long-term improvements to pain relief and disability scores. Other meta-analyses had numerous limitations due to the heterogeneity of included studies or not specifying the timeframe for osteoporotic vertebral compression fractures. Overall, conclusions about the effect of vertebroplasty remain unclear. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with symptomatic osteoporotic vertebral fractures less than 6 weeks old who receive vertebroplasty, the evidence includes a randomized sham-controlled trial and other nonblinded RCTs comparing vertebroplasty with conservative management. Relevant outcomes are symptoms, functional outcomes, QOL, hospitalizations, medication use, and treatment-related morbidity. For acute fractures, conservative therapy consisting of rest, analgesics, and physical therapy is an option, and symptoms will resolve in a large percentage of patients with conservative treatment only. However, a sham-controlled randomized trial in patients who had severe pain of less than 6 weeks in duration found a significant benefit of vertebroplasty for the treatment of osteoporotic vertebral fracture at the thoracolumbar junction. Other RCTs without sham controls have reported that vertebroplasty is associated with significant improvements in pain and reductions in the duration of bed rest. Given the high morbidity associated with extended bed rest in older adults, this procedure is considered to have a significant health benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with sacral insufficiency fractures (SIFs) who receive sacroplasty, the evidence includes 3 prospective cohort studies and a case series. Relevant outcomes are symptoms, functional outcomes, QOL, hospitalizations, medication use, and treatment-related morbidity. No RCTs have been reported. The available evidence includes a prospective cohort study and a retrospective series of 243 patients. These studies have reported rapid and sustained decreases in pain following percutaneous sacroplasty. Additional literature has mostly reported immediate improvements following the procedure. However, due to the small size of the evidence base, the harms associated with sacroplasty have not been adequately studied. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have osteoporotic vertebral compression fractures who receive balloon kyphoplasty or mechanical vertebral augmentation, the evidence includes an Agency for Healthcare Research and Quality (AHRQ) comparative effectiveness review, RCTs, and meta-analyses. Relevant outcomes include symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. The AHRQ review concluded that vertebroplasty was probably more effective at reducing pain and improving function in patients

>65 years of age, but benefits were small. Kyphoplasty was found to be probably more effective than usual care for pain and function in older patients with vertebral compression fracture at up to 1 month and may be more effective at >1 month to ≥1 year but has not been compared against sham therapy. A meta-analysis and moderately sized unblinded RCT have compared kyphoplasty with conservative care and found short-term benefits in pain and other outcomes. One systematic review of RCTs found no significant difference in subsequent fracture between vertebroplasty and conservative treatment, and another systematic review of prospective and retrospective studies reported improved mortality with either vertebroplasty or balloon kyphoplasty compared with conservative treatment. Other RCTs, summarized in a meta-analysis, have reported similar outcomes for kyphoplasty and vertebroplasty. Three randomized trials that compared mechanical vertebral augmentation (Kiva or SpineJack) with kyphoplasty have reported similar outcomes for both procedures. A major limitation of all these RCTs is the lack of a sham procedure. Due to the possible sham effect observed in the recent trials of vertebroplasty, the validity of the results from non-sham-controlled trials is unclear. Therefore, whether these improvements represent a true treatment effect is uncertain. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have osteolytic vertebral compression fractures who receive balloon kyphoplasty or mechanical vertebral augmentation, the evidence includes RCTs, case series, and a systematic review of these studies. Relevant outcomes include symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Two RCTs have compared balloon kyphoplasty with conservative management and another has compared Kiva with balloon kyphoplasty. Results of these trials, along with case series, would suggest a reduction in pain, disability, and analgesic use in patients with cancer-related compression fractures. However, because the results of the comparative studies of vertebroplasty have suggested possible placebo or natural history effects, the evidence these studies provide is insufficient to warrant conclusions about the effect of kyphoplasty on health outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have osteoporotic or osteolytic vertebral compression fractures who receive radiofrequency kyphoplasty, the evidence includes a systematic review and an RCT. Relevant outcomes include symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. The only RCT (N=80) identified showed similar results between radiofrequency kyphoplasty and balloon kyphoplasty. The systematic review suggested that radiofrequency kyphoplasty is superior to balloon kyphoplasty in pain relief, but the review itself was limited by the inclusion of a small number of studies as well as possible bias. Corroboration of these results in a larger number of patients is needed to determine with greater certainty whether radiofrequency kyphoplasty has outcomes similar to balloon kyphoplasty. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American College of Radiology (ACR)
The American College of Radiology (2014) and 7 other surgical and radiologic specialty associations published a joint position statement on percutaneous vertebral augmentation. (68) This document stated that percutaneous vertebral augmentation, using vertebroplasty or kyphoplasty and performed in a manner consistent with public standards, is a safe, efficacious, and durable procedure in appropriate patients with symptomatic osteoporotic and neoplastic fractures. The statement also indicated that these procedures be offered only when nonoperative medical therapy has not provided adequate pain relief, or pain is significantly altering the patient's quality of life.

A joint practice parameter for the performance of vertebral augmentation was updated in 2017. (65)

In 2022, the American College of Radiology revised its Appropriateness Criteria for the use of percutaneous vertebral augmentation in the management of vertebral compression fractures. (66) Table 28 shows the appropriateness categories for each variant.

Table 28. ACR Appropriateness Criteria for the Use of Percutaneous Vertebral Augmentation for the Management of Vertebral Compression Fractures

Variants	Appropriateness Category
"Asymptomatic, osteoporotic VCF. Initial treatment"	Usually Not Appropriate
"Symptomatic osteoporotic VCF with bone marrow edema or intravertebral cleft. Initial treatment"	Usually Appropriate
"New symptomatic VCF. History of prior vertebroplasty or surgery. Initial treatment."	Usually Appropriate
"Benign VCF with worsening pain, deformity, or pulmonary dysfunction. Initial treatment"	Usually Appropriate
"Pathological VCF with ongoing or increasing mechanical pain. Initial treatment"	Usually Appropriate

ACR: American College of Radiology; CT: computed tomography; MRI: magnetic resonance imaging; VCF: vertebral compression fracture.

Society of Interventional Radiology (SIR)
In a 2014 quality improvement guideline for percutaneous vertebroplasty from the SIR, failure of medical therapy was defined as follows (64):

1. "For a patient rendered nonambulatory as a result of pain from a weakened or fractured vertebral body, pain persisting at a level that prevents ambulation despite 24 hours of analgesic therapy;
2. For a patient with sufficient pain from a weakened or fractured vertebral body that physical therapy is intolerable, pain persisting at that level despite 24 hours of analgesic therapy; or
3. For any patient with a weakened or fractured vertebral body, unacceptable side effects such as excessive sedation, confusion, or constipation as a result of the analgesic therapy

necessary to reduce pain to a tolerable level."

American Academy of Orthopaedic Surgeons (AAOS)

In 2011, the AAOS published practice guidelines on the treatment of osteoporotic spinal compression fractures. (67) The AAOS approved "a strong recommendation against the use of vertebroplasty for patients who present with an acute osteoporotic spinal compression fracture and are neurologically intact."

National Institute for Health and Care Excellence

In 2003, NICE concluded in its guidance on percutaneous vertebroplasty that the current evidence on the safety and efficacy of vertebroplasty for vertebral compression fractures appeared "adequate to support the use of this procedure" to "provide pain relief for people with severe painful osteoporosis with loss of height and/or compression fractures of the vertebral body .... " The guidance also recommended that the procedure be limited to patients whose pain is refractory to more conservative treatment. A 2013 NICE guidance, which was reaffirmed in 2016, indicated that percutaneous vertebroplasty and percutaneous balloon kyphoplasty "are recommended as options for treating osteoporotic vertebral compression fractures" in persons having "severe, ongoing pain after a recent, unhealed vertebral fracture despite optimal pain management" and whose "pain has been confirmed to be at the level of the fracture by physical examination and imaging." In 2008, NICE issued guidance on the diagnosis and management of adults with metastatic spinal cord compression. (69) This guidance indicated that vertebroplasty or kyphoplasty should be considered for "patients who have vertebral metastases and no evidence of metastatic spinal cord compression or spinal instability if they have: mechanical pain resistant to conventional pain management, or vertebral body collapse." It was last reviewed in 2019, and a decision was made that the guideline required updating as "since its publication, there have been advances in the diagnosis and management of metastatic spinal cord compression." (70) The guidance currently still states that vertebroplasty or kyphoplasty should be considered for patients who have vertebral metastases, and no evidence of spinal cord compression or spinal instability, if they have mechanical pain resistant to conventional pain management and vertebral body collapse. Surgery should only be performed when all appropriate specialists agree. Despite a relatively small sample base, the Institute concluded the evidence suggests, in a select subset of patients, that early surgery may be more effective at maintaining mobility than radiotherapy.

The NICE (2013) issued a guidance that recommended percutaneous vertebroplasty and percutaneous balloon kyphoplasty as treatment options for osteoporotic vertebral compression fractures in persons having severe, ongoing pain after a recent unhealed vertebral fracture, despite optimal pain management, and whose pain has been confirmed through physical exam and imaging at the level of the fracture. (70) This guidance did not address balloon kyphoplasty with stenting, because the manufacturer of the stenting system (Synthes) stated there is limited evidence for vertebral body stenting given that the system had only recently become available.

American Society of Pain and Neuroscience

In 2021, the American Society of Pain and Neuroscience (ASPN) published practice guidelines for the interventional management of cancer-associated pain. (71) The guideline included a best practice statement that stated "vertebral augmentation should be strongly considered for patients with symptomatic vertebral compression fractures from spinal metastases (evidence level 1-A)." However, ASPN noted that there is little data to suggest the superiority of either vertebroplasty or kyphoplasty when treating malignant vertebral compression fractures.

Ongoing and Unpublished Clinical Trials

Some currently ongoing unpublished trials that might influence this policy are listed in Table 29.

Table 29. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04795765	Prospective SpineJack System Registry	400	Dec 2024
NCT06141187	Percutaneous Vertebroplasty vs. Sham for Osteoporotic Vertebral Compression Fractures Focusing on Pain and Economy: A Single-center, Double-blind Randomized Controlled Clinical Trial	240	Dec 2030
Unpublished			
NCT02489825	Pilot Study: Does Preventive Adjacent Level Cement Augmentation Positively Affect Reoperation Rates After Osteoporotic Vertebral Compression Fractures?	100	June 2019
NCT02902250	The Comparative Study About the Effect of Vertebral Body Decompression Procedure and Conservative Treatment for Benign Vertebral Compression Fracture - Prospective Randomized Control Study	80	Feb 2022
NCT03617094	Early Percutaneous Vertebroplasty Versus Standard Conservative Treatment in Thoracolumbar Vertebral Fractures. Monocentric, Prospective, Randomised and Compared Clinical Study	42	Oct 2020
NCT02700308	A Randomized, Multicenter, Open-label, Bayesian-based Phase II Study of the Feasibility of Kyphoplasty in the Local Treatment of Spine Metastases From Solid Tumors	60	Sep 2022
NCT04581707	Evaluation of Surgical Therapy of Vertebral Compression Fractures With the Kyphoplasty Single Balloon Catheter	80	Oct 2021

	Allevo (Joline®) and the Quattroplasty Double Balloon Catheter Stop'n GO (Joline®) With BonOs® Inject Bone Cement		

NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	22510, 22511, 22512, 22513, 22514, 22515, 0200T, 0201T
HCPCS Codes	C1062, C7504, C7505, C7507, C7508

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
01/01/2025	Document updated with literature review. The following changes were made to Coverage: Added coverage criteria for percutaneous vertebroplasty and sacroplasty, previously addressed on RAD601.056 Percutaneous Vertebroplasty and Sacroplasty. References 1-8, 15-19, 21-22, 24-29, 31-34, 36-41, 44-46, 66-68, 70-71 added. Title changed from Percutaneous Balloon

	Kyphoplasty, Radiofrequency Kyphoplasty, and Mechanical Vertebral Augmentation.
02/01/2024	Reviewed. No changes.
06/01/2023	Document updated with literature review. The following change was made to Coverage: Modified conditional coverage criteria for percutaneous balloon kyphoplasty or mechanical vertebral augmentation. Added the following references: 7, 9-11, and 21.
09/15/2021	Reviewed. No changes.
01/01/2021	Document updated with literature review. The following changes were made to Coverage: 1) Clarified that the medically necessary statements on compression fractures apply to the thoracolumbar spine; and 2) Removed tradename "Kiva" to describe mechanical vertebral augmentation and replaced with "with an FDA cleared device". Added/updated the following references: 15, 21, 24, 29 and 32.
11/15/2019	Document updated with literature review. The following change was made to Coverage: Added "Symptomatic osteoporotic vertebral compression fractures that are less than 6 weeks in duration that have led to hospitalization or persist at a level that prevents ambulation" as a conditional criterion for percutaneous balloon kyphoplasty or mechanical vertebral augmentation (i.e., with Kiva®). The following references were added: 19-20, 23 and 30.
06/01/2018	Document updated with literature review. The following changes were made to Coverage. 1) added "compression" to state "The treatment of symptomatic osteoporotic vertebral compression fractures that have failed to respond to conservative treatment (e.g., analgesics, physical therapy, rest) for at least 6 weeks" 2) Editorial change" for immediate" changed to "including" in the experimental, investigational and/or unproven coverage statement. 3) Added "Radiofrequency" and maintained language "including but not limited to vertebral body stenting" to the experimental, investigational and/or unproven coverage statement for devices. Title changed from Percutaneous Balloon Kyphoplasty and Mechanical Vertebral Augmentation.
12/01/2016	Reviewed. No changes.
02/01/2016	Document updated with literature review. 1) mechanical vertebral augmentation with Kiva was changed to medically necessary for a) the treatment of symptomatic osteoporotic vertebral fractures that have failed to respond to conservative treatment (e.g., analgesics, physical therapy, rest) for at least 6 weeks; and b) for the treatment of severe pain due to osteolytic lesions of the spine related to multiple myeloma or metastatic malignancies. 2) Percutaneous balloon kyphoplasty and mechanical vertebral augmentation with Kiva® is considered experimental, investigational, and/or unproven for immediate use in acute vertebral fractures due to osteoporosis or trauma. 3)Percutaneous balloon kyphoplasty and mechanical vertebral

	augmentation with Kiva® is considered experimental, investigational, and/or unproven for all other indications.4) Percutaneous mechanical vertebral augmentation using any other device, including but not limited to vertebral body stenting, is considered experimental, investigational, and/or unproven.
02/15/2015	Document updated with literature review. The following was added to Coverage: Percutaneous mechanical vertebral augmentation using any other device, including but not limited to Kiva® and vertebral body stenting, is considered experimental, investigational and/or unproven. In addition, "Percutaneous Vertebroplasty and Sacroplasty" were removed from this policy and are now on Medical Policy RAD601.056 Percutaneous Vertebroplasty and Sacroplasty. The title of this document changed from "Percutaneous Vertebroplasty, Percutaneous Kyphoplasty, and Percutaneous Sacroplasty."0
09/15/2012	Document updated with literature review. Title changed to include "Percutaneous Sacroplasty". The following change was made to coverage: Percutaneous sacroplasty is considered experimental, investigational and unproven for all indications, including use in sacral insufficiency fractures due to osteoporosis and spinal lesions due to metastatic malignancies or multiple myeloma.
09/01/2010	Document updated with literature review. Title changed from "Percutaneous Polymethylmethacrylate Vertebroplasty, Percutaneous Kyphoplasty". The following changes were made 1) Percutaneous Polymethylmethacrylate Vertebroplasty (PPV) or Percutaneous Kyphoplasty (PK) may be considered medically necessary for the treatment of symptomatic osteoporotic vertebral fractures that have failed to respond to conservative treatment, or for the treatment of severe pain due to osteolytic lesions of the spine related to multiple myeloma or metastatic malignancies. 2) PPV and PK are considered experimental, investigational and unproven for all other indications. 3). Sacroplasty is considered experimental, investigational and unproven for all indications.
02/15/2008	Revised/Updated Entire Document
01/01/2007	Codes Revised/Added Deleted
02/01/2006	Revised/Updated Entire Document
01/01/2006	Codes Revised/Added Deleted
03/30/2004	Revised/Updated Entire Document
03/01/2002	New Medical Document