ONTARIO HEALTH TECHNOLOGY ASSESSMENT SERIES

Percutaneous Vertebroplasty and Balloon Kyphoplasty for Painful Osteoporotic Vertebral Compression Fractures

A Health Technology Assessment

AUGUST 2025

Ontario Health

Key Messages

What Is This Health Technology Assessment About?

Vertebral compression fractures (breaks in the spine in which the broken bone has collapsed) are among the most common type of fracture in people with osteoporosis and can arise during activities of daily living without any specific impact or traumatic event. Osteoporotic vertebral compression fractures (OVCFs) are a common cause of both sudden and lasting back pain in older people (in addition, many OVCFs have no symptoms and may go undetected).

It is estimated that about 60% to 90% of people with painful OVCFs, the pain goes away within 4 to 8 weeks with treatment that may include rest, pain medication, and management of osteoporosis and other fracture risk factors. This is referred to as nonsurgical or conservative treatment. For severely painful OVCFs that do not respond to conservative treatment, doctors may use alternative procedures that involve injecting cement into the broken or collapsed bone to restore and harden it. We looked at 2 procedures: percutaneous vertebroplasty (PVP) and percutaneous balloon kyphoplasty (PBK).

This health technology assessment looked at how safe, effective, and cost-effective PVP and PBK are for adults with OVCFs that do not respond to conservative treatment. It also looked at the budget impact of publicly funding percutaneous vertebroplasty and percutaneous balloon kyphoplasty and at the experiences, preferences, and values of people with osteoporotic vertebral compression fractures.

What Did This Health Technology Assessment Find?

People with painful OVCFs that did not improve with conservative treatment, who then underwent PVP or PBK, showed significant short-term improvement in pain and physical function compared with people who continued with conservative treatment alone. No differences for either PVP or PBK compared to conservative treatment alone were found for mortality, subsequent fractures, or adverse events. Between 4% and 39% of people who underwent PVP or PBK experienced cement leakage, but a majority of these people did not experience any symptoms from the leaks.

Compared with conservative treatment, PVP and PBK may be cost-effective. We estimate that publicly funding PVP and PBK for people with painful OVCF in Ontario over the next 5 years would cost an additional $28 million.

Patients shared how OVCF negatively impacted their daily activities, work, social life, family relationships, and mental health. The 3 people we spoke with who underwent vertebroplasty all reported positive improvements in pain symptoms and quality of life. Transportation, cost of medication, and longer time for diagnosis were highlighted as barriers for accessing treatment.

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Abstract

Background

Vertebral compression fractures are among the most common types of fracture in patients with osteoporosis and they can arise during activities of daily living without any specific trauma event. For severely painful osteoporotic vertebral compression fractures (OVCFs) that do not respond to conservative treatment, minimally invasive percutaneous vertebroplasty (PVP) and percutaneous balloon kyphoplasty (PBK) may be used. We conducted a health technology assessment of PVP and PBK for people with painful OVCFs refractory to nonsurgical treatment that included an evaluation of effectiveness, safety, cost-effectiveness, the budget impact of publicly funding PVP and PBK, and patient preferences and values.

Methods

We performed a systematic literature search of the clinical evidence. We assessed the risk of bias of each included study using the ROBIS tool for systematic reviews, the Cochrane Risk of Bias tool for RCTs, and the ROBINS-I tool for observational studies and the quality of the body of evidence according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. We performed a systematic economic literature search and conducted a cost–utility analysis with a 3-year time horizon from a public payer perspective. We also analyzed the budget impact of publicly funding PVP and PBK in adults with painful OVCFs in Ontario. To contextualize the potential value of PVP and PBK, we spoke with people with OVCF.

Results

We included 10 studies in the clinical evidence review. Compared to conservative treatment (CT), there was significant (statistical and clinical) improvement in pain (up to 3 months follow-up, GRADE Low) and physical function (up to 6 months follow-up, GRADE Very low) for patients who underwent PVP. For PBK, there was significant (statistical and clinical) improvement in pain in the short term (up to 3 months follow-up, GRADE Very low) compared with CT. Overall, there were no significant differences for either PVP or PBK compared to conservative treatment for mortality, subsequent fractures or adverse events (GRADE Low to Very low). Cement leakage occurred in 4% to 39% of treated patients (PVP vs. CT, 4.0% [8/200 patients]; PVP vs. sham, 39.4% [9/99 patients]; PBK vs. CT, 4.5% [30/731 patients]) and most leakages were asymptomatic. The incremental cost-effectiveness ratio (ICER) of PVP compared with CT is $43,324 per quality-adjusted life-year (QALY) gained. The ICER of PBK compared with CT is $65,921 per QALY gained. The annual budget impact of publicly funding PVP and PBK in Ontario over the next 5 years ranges from an additional $0.5 million in Year 1 to $11.0 million in Year 5. The people we spoke to reported that their daily activities, work, social life, family relationships, and mental health were negatively impacted by OVCF. Those who underwent vertebroplasty reported a positive impact on pain relief and quality of life.

Conclusions

People who are refractory to first-line conservative treatment and who underwent PVP showed significant short-term clinical improvement in pain (GRADE Low) and physical function (GRADE Very low) compared to conservative treatment. Similarly, people who underwent PBK experienced significant short-term clinical improvement in pain (GRADE Very low) compared to conservative treatment. PVP and PBK were consistently more costly and more effective than CT. We estimate that publicly funding PVP and PBK in Ontario would result in additional costs of $28 million over the next 5 years. The insights shared by participants underscore the significant challenges individuals with OVCF face in managing their condition, with notable impacts on daily activities, work, social interactions, and mental health. Despite these challenges, participants highlighted the positive outcomes of vertebroplasty for those who underwent the procedure, particularly in terms of pain relief and improved quality of life.

Table of Contents

List of Tables

List of Figures

Objective

This health technology assessment evaluates the effectiveness, safety, and cost-effectiveness of percutaneous vertebroplasty and percutaneous balloon kyphoplasty for adults with painful osteoporotic vertebral compression fractures. It also evaluates the budget impact of publicly funding percutaneous vertebroplasty and balloon kyphoplasty and the experiences, preferences, and values of people with painful osteoporotic vertebral compression fractures.

Background

Health Condition

Osteoporosis is a skeletal condition characterized by decreased density (mass/volume) of normally mineralized bone.[1] The reduced bone density leads to decreased mechanical strength, making the skeleton more likely to fracture. Postmenopausal osteoporosis (Type I) and age-related osteoporosis (Type II) are the most common primary forms of bone loss seen in clinical practice.[1]

Vertebral compression fractures are among the most common type of fracture in people with osteoporosis and are almost twice as common as other fractures typically linked to osteoporosis, such as broken hips and wrists.[2] Osteoporotic vertebral compression fractures (OVCFs) can arise during activities of daily living without any specific trauma event, primarily occurring in the thoracic/lumbar region, and less frequently in the sacral and cervical regions. People with osteoporosis can suffer an OVCF even when doing everyday things**,** such as reaching, twisting, coughing, and sneezing.

Osteoporotic vertebral compression fractures are a common cause of both acute and chronic back pain in older populations, although many of these fractures can go undetected (only about one-third are clinically diagnosed).[3] Both symptomatic and asymptomatic OVCFs can lead to substantial spinal deformity, functional limitation, pulmonary compromise, gastrointestinal problems, sleep disturbances, difficulties in performing activities of daily living, and decreased quality of life. They are also associated with an increased risk of further vertebral fractures and increased mortality.[4]

While most fractures generally heal within a few months, some people have persistent pain and disability and require hospitalization, long-term care, or both.[5]

Clinical Need and Population of Interest

International

The incidence of OVCFs in individuals aged 50 years or older is estimated to be 307 per 100,000 person years based on a study of people in Germany, where the rate in women aged 85 to 89 years was found to be almost 8-fold higher than in women aged 60 to 64 years.[6] A study of people in Sweden estimated that the lifetime risk for a symptomatic OVCF for a person aged 45 years is 15% for a woman and 8% for a man.[5] In the United States, approximately 750,000 new osteoporotic vertebral fractures occur each year.[7]

Ontario

In fiscal year 2015/16, the age-standardized prevalence and incidence of diagnosed osteoporosis among Canadians 40 years and older in Ontario was 11.0 per 1,000 people and 6.5 per 1,000 people, respectively.[8] The age-standardized annual rate of osteoporosis-related spinal fractures among Canadians aged 40 years and older in Ontario was 116.6 per 100,000 during this period.[8]

Current Treatment Options

First Line Conservative (Nonsurgical) Treatment

The majority of people with OVCFs experience resolution of pain within 4 to 8 weeks after a period of rest, pain medication (e.g., acetaminophen, opioids, nonsteroidal anti-inflammatory drugs), and management of osteoporosis and risk factors for further fractures (e.g., anti-osteoporotic medications, falls prevention).[9] In some cases, patients may wear a brace to restrict movement and allow the OVCF to heal.[10] However, high doses of pain medication can have significant adverse effects and further worsen quality of life.[3] Impaired mobility in osteoporotic patients may further accelerate bone loss.[11]

There are variable estimates as to how many people with painful OVCFs will experience resolution of their pain after first line, conservative (nonsurgical) treatment. It is estimated that 66%,[12] 82%,[13] or 90% (James Waddell, MD, personal communication, March 27, 2024) of people with symptomatic OVCFs will be pain-free after a course of conservative treatment.

Health Technology Under Review

For severe pain not responding to conservative treatment, minimally invasive, vertebral augmentation methods may be used (i.e., percutaneous vertebroplasty [PVP] and percutaneous balloon kyphoplasty [PBK]).[14]

Percutaneous vertebroplasty may be performed by an interventional radiologist, neurosurgeon or orthopedic surgeon using imaging guidance on a patient who is under intravenous sedation or general anaesthesia. Under imaging guidance, most often fluoroscopy, a needle is inserted into the affected vertebral body, and bone cement, usually polymethylmethacrylate (PMMA), is injected.[15,16]

Percutaneous balloon kyphoplasty is a modified technique of traditional vertebroplasty implemented to address spinal deformity and help realign the spine.[17] Performed under fluoroscopic guidance, kyphoplasty involves the percutaneous placement of an inflatable bone tamp (or pump) into a vertebral body. Once inflated, a bone tamp restores the vertebral body back toward its original height while creating a cavity that can be filled with bone cement after deflation.[18] Similar to PVP, interventional radiologists, orthopedic surgeons, and neurosurgeons may perform PBK. The specifics of the technique used are largely dependent on the training of the provider (Stefano Priola, MD, personal communication, March 19, 2024).

In people with severe OVCF with kyphosis (rounding of the spine) and neurological deficits, vertebral augmentation usually neither corrects the deformity nor restores the stability of the fractured segment. As such, it is difficult to relieve refractory low back pain and neurological compression. Open surgery is often the best treatment option for such patients.[19]

Regulatory Information

The PVP and PBK delivery systems (including such components as inflatable balloon, balloon catheter, cement delivery gun, bone filler device, access needle, cannula, curette, inflation syringe) are licensed by Health Canada and classified as Class 2 devices.[20] These include:

- Synthes GMBH
  - SYNFLATE System (licence no. 91718), Class 2 device
- Medtronic Canada
  - KYPHX Osteointroducers (licence no. 24649), Class 2 device
  - One-Step Osteointroducer Bone Access Devices (licence no. 61350), Class 2 device
  - KYPHON Xpander II Inflatable Bone Tamp (licence no. 86203), Class 2 device
  - Kyphon digital inflation syringe (licence no. 61350), Class 2 device
  - Kyphon cement-delivery system (licence no. 85127), Class 2 device
  - Kyphon bone-filler device (licence no. 24739), Class 2 device
- Stryker Canada
  - iVAS (licence no. 83722), Class II device

Several bone cement products for PVP and PBK received Health Canada licensing and are classified as Class III devices. Examples include:

- Heraeus Medical GMBH
  - Osteopal V Radiopaque Bone Cement for Vertebroplasty (licence no. 80703)
- Medtronic
  - Kyphon Xpede Bone Cement (licence no. 98501)

Ontario, Canadian, and International Context

Ontario

Percutaneous balloon kyphoplasty and PBK are publicly funded in Ontario with fee codes listed within the Schedule of Benefits: N570 and N583, respectively.[21] In 2010, the Ontario Health Technology Advisory Committee (OHTAC) made the following recommendations for PVP[22] and PBK[23] for the treatment of OVCFs (based on health technology assessments for PVP[24] and PBK,[25] conducted by the Medical Advisory Secretariat):

Percutaneous Vertebroplasty for Treatment of Painful Osteoporotic Vertebral Compression Fractures[22]

- PVP should not be considered as the standard treatment for patients with OVCFs
- Conservative treatment, which allows the fracture to heal naturally and is safer than PVP, is preferred as the first line of treatment in these patients

Balloon Kyphoplasty for Treatment of Painful Osteoporotic Vertebral Compression Fractures[23]

- Conservative treatment, including appropriate pain control, which allows the fracture to heal naturally, is preferred for patients as the first line of treatment
- Management of the underlying condition that weakens the vertebral bodies should be initiated and the patient monitored appropriately, including bone mineral density testing
- People require education about the course of natural healing of such fractures in the majority of patients and that alternative treatment options such as kyphoplasty are available if they fail to respond to conservative treatment within an appropriate time.

People are considered refractory to a course of conservative treatment if they are still experiencing pain after approximately 6 to 8 weeks.[12]

In Ontario during fiscal years 2021/22 and 2022/23, an average of 1,061 procedures (PVP and PBK) for OVCFs were performed per year (IntelliHealth Ontario, intellihealth.moh.gov.on.ca; September 21, 2024). We estimate that there are approximately 2,200 people per year (people with painful OVCFs that are not responsive to conservative treatment) in Ontario that may need PVP or PBK (see population of interest in Table 41, below). Furthermore, PVP or PBK is funded through global budgets in some, but not all, hospitals in Ontario. For this reason, additional funding from the Ministry of Health is being sought. In 2016, OHTAC recommended[26] that vertebral augmentation (either PVP or PBK) be publicly funded and made accessible for appropriately selected cancer patients with vertebral compression fractures.

Patients may experience long wait times to receive PVP or PBK for painful OVCFs refractory to conservative treatment for reasons including a waitlist to receive magnetic resonance imaging (MRI) and long wait times to see a specialist (orthopedic or spinal surgeon or interventional radiologist; Typically, people who present to the emergency department and become inpatients with painful OVCFs refractory to conservative treatment receive PVP or PBK in a timely fashion. Patients with cancer and painful vertebral compression fractures are generally better triaged than patients without cancer and are better aligned with spinal surgeons at cancer centres (James Waddell MD, personal communication, March 27, 2024).

Canada

Percutaneous vertebroplasty (but not PBK) is listed in the 2024 Physician Schedule of Benefits in British Columbia[27] and states that PVP is payable only when performed on an inpatient or day-care basis in an acute care facility and payable for OVCFs only if conservative treatment shows no or minimal improvement after 4 to 6 weeks and pain remains incapacitating.

Percutaneous vertebroplasty and PBK are explicitly mentioned in physician fee codes for New Brunswick[28] and Saskatchewan,[29] while Manitoba[30] lists PVP only. The physician fee codes for these 3 provinces do not provide the specific criteria required for payment.

Physician fee codes in other provinces neither list nor explicitly mention PVP or PBK. For example, the Alberta Schedule of Medical Benefits[31] lists a procedure called “repair of vertebral fracture.”

International

United Kingdom

In 2013, the National Institute for Health and Care Excellence (NICE) recommended PVP and PBK[32] as options for treating OVCFs only in people who have severe ongoing pain after a recent, unhealed vertebral fracture despite optimal pain management where the pain has been confirmed to be at the level of the fracture by physical examination and imaging.

Australia

In 2020, the Medical Services Advisory Committee (MSAC)[33] supported public funding for PVP for severely painful thoracolumbar osteoporotic fractures of 3 weeks duration or less. The committee recommended that a prospective registry be developed to monitor this listing that includes the centre and state where the procedure was performed, whether the patient was hospitalized at the time the decision to perform procedure was made, and what (if any) associated adverse events required further medical or hospital attention.[33] Percutaneous vertebroplasty performed by an interventional radiologist for the treatment of painful thoracolumbar OVCFs is publicly funded in Australia where all of the following conditions are met[33]:

- Pain is severe
- Symptoms are poorly controlled by analgesic therapy (i.e., opiates)
- Fracture duration is ≤ 3 weeks
- There is magnetic resonance imaging (MRI, or SPECT-CT if an MRI is unavailable) evidence of acute vertebral fracture

Organizational Guidelines

American Society for Bone and Mineral Research (ASBMR), 2019[34]

- PVP provides no demonstrable clinically significant benefit over placebo or sham procedure. Results did not differ according to duration of pain (Quality of Evidence [QoE]: Low; Strength of Recommendation [SoR]: Weak).
- It is uncertain whether PVP increases risk of incident or radiographic vertebral fractures or related serious adverse events (QoE: Moderate; SoR: Moderate).
- PBK provides a small clinical benefit over conservative management, percutaneous vertebroplasty (QoE: High to Moderate; SoR: High to Moderate).
- It is uncertain whether PBK increases risk of incident or radiographic vertebral fractures or serious adverse events related to kyphoplasty (QoE: Low; SoR: Weak).

Society of Interventional Radiology (SIR), American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS), American College of Radiology (ACR), American Society of Neuroradiology (ASNR), American Society of Spine Radiology (ASSR), Canadian Interventional Radiology Association (CIRA), and the Society of NeuroInterventional Surgery (SNIS), 2014[35]

- The benefits of PVP outweigh its risks as well as the risks of non-operative medical therapy; the success rate in appropriately selected patients is consistently high

American Academy of Orthopaedic Surgeons, 2011[36]

- Recommends against vertebroplasty for people who present with an OVCF on imaging with correlating clinical signs and symptoms and who are neurologically intact
- Kyphoplasty is an option for people who present with an OVCF on imaging with correlating clinical signs and symptoms and who are neurologically intact

Equity Context

We use the PROGRESS-Plus framework[37] to help explicitly consider health equity in our health technology assessments. PROGRESS-Plus is a health equity framework used to identify population and individual characteristics across which health inequities may exist.[37] These characteristics include place of residence; race or ethnicity, culture or language; gender or sex; disability; occupation; religion; education; socioeconomic status; social capital; and other key characteristics that stratify health opportunities and outcomes.

Some people living in remote or rural geographic areas of Ontario may not have access to hospitals offering PVP or PBK, which may cause inequity. People with a lower socioeconomic status and people without primary care may have more difficulty accessing PVP or PBK.

In Ontario, PVP and PBK are funded by global budgets in some hospitals. However, this is inconsistent across the province.

People with cancer and painful vertebral compression fractures are generally better triaged than people without cancer and better aligned with spinal surgeons at cancer centres in Ontario.

Expert Consultation

We engaged with experts in the specialty areas of interventional radiology, neurosurgery, orthopedic surgery, and family medicine to help inform our understanding of aspects of the health technology and our methodologies and to contextualize the evidence.

PROSPERO Registration

This health technology assessment has been registered in PROSPERO, the international prospective register of systematic reviews (CRD42024557272), available at crd.york.ac.uk/PROSPERO.

Clinical Evidence

Research Question

What are the effectiveness and safety of percutaneous vertebroplasty (PVP) or percutaneous balloon kyphoplasty (PBK) compared with a) conservative treatment (CT), b) sham treatment (where the medical professional goes through the motions of a treatment without actually performing the treatment), and c) each other for the treatment of adults with painful osteoporotic vertebral compression fractures (OVCFs)?

Methods

Review Approach

To be expedient yet comprehensive in addressing the scope of our research question, we leveraged existing information by seeking systematic reviews that, in whole or in part, focused on the clinical populations of interest of this HTA. During scoping of this topic, which included a search of publications from international health technology assessment (HTA) agencies, we identified a comprehensive systematic review on PVP and PBK for the treatment of OVCFs conducted by Jacobsen et al.[38] Based on its recency and comprehensiveness, we planned to leverage and update this review.

Jacobsen et al[38] used a definition of the comparator that suited our purposes – conservative treatment or sham treatments – however, they did not include a direct comparison of PVP with PBK. We also identified a systematic review by Liu et al[39] that compared PVP with PBK as part of a much broader network meta-analysis of surgical procedures for OVCFs. Therefore, we also included this review[39] as a source for PVP versus PBK studies.

Clinical Literature Search

We performed a clinical literature search on May 29, 2024, to retrieve studies published from January 1, 2019, until the search date. The date limit reflects our plan to leverage and update the Swiss HTA by Jacobsen et al[38] (the end date for their literature search was December 13, 2019). We used the Ovid interface in the following databases: MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, and the National Health Service Economic Evaluation Database (NHS EED).

A medical librarian developed the search strategies using controlled vocabulary (e.g., Medical Subject Headings) and relevant keywords. The final search strategy was peer-reviewed using the PRESS Checklist.[40]

We created database auto-alerts in MEDLINE and Embase and monitored them until August 14, 2024. We also performed a targeted grey literature search of the International HTA Database, the websites of health technology assessment organizations and regulatory agencies, and clinical trial and systematic review registries, following a standard list of sites developed internally. See Appendix 1 for our literature search strategies, including all search terms.

Eligibility Criteria

Studies

Inclusion Criteria

- English-language full-text publications
- Studies published since December 2019
- Types of studies for clinical effectiveness
  - Randomized controlled trials (RCTs)
  - In the absence of RCTs, other comparative, prospective study designs will be considered
- Types of studies for safety
  - RCTs
  - Prospective comparative non-RCTs with at least 10 patients in each study arm
  - Prospective single-arm studies with at least 50 patients
  - Registry/database studies

Exclusion Criteria

- For clinical effectiveness studies:
  - Editorials, commentaries, case reports, conferences abstracts, letters, single-arm studies
- For safety studies:
  - Editorials, commentaries, case reports, conferences abstracts, letters
- Animal and in vitro studies

Participants

Inclusion Criteria

- Adults (≥ 18 years) with a diagnosis of symptomatic (i.e., painful) OVCF refractory to conservative (nonsurgical) treatment

Exclusion Criteria

- Adults with vertebral fractures due to other causes such as major trauma or cancer, patients who did not first undergo conservative treatment

Interventions

Inclusion Criteria

- PVP or PBK

Exclusion Criteria

- Vertebral body stenting, pedicle screw fixation, prophylactic augmentation (i.e., before a fracture occurs), KIVA VCF system (insertion of an implant combined with cement), SpineJack system (insertion of a retractable titanium expander). According to the experts we consulted, these devices

are rarely used in Ontario and are therefore not considered appropriate as either an intervention or comparator for the purposes of this HTA.

Comparators

Inclusion Criteria

- Sham; conservative treatment (e.g., pain medication, bed rest, braces); PBK (when intervention is PVP), PVP (when intervention is PBK)

Exclusion Criteria

- Vertebral body stenting; pedicle screw fixation; prophylactic augmentation (i.e., before a fracture occurs); KIVA VCF system (insertion of an implant combined with cement); SpineJack system (insertion of a retractable titanium expander). According to experts we consulted, these devices are rarely used in Ontario and are therefore not considered appropriate as either an intervention or comparator for the purposes of this HTA
- Open surgery

Outcome Measures

- Pain
- Physical function
- Quality of life
- Analgesia use
- Proportion of people able to return to independent living versus requiring assisted accommodation
- Mortality
- Serious adverse events (a serious adverse event is characterised as an event that is life-threatening, requires hospitalisation, is disabling or permanently damaging, requires intervention, or causes death, or any other event deemed serious by the study investigators[38])
- Any adverse events
- New symptomatic or radiographic vertebral fractures and location (adjacent or nonadjacent)
- Cement leakage
- Patient/physician exposure to radiation

Literature Screening

Two reviewers screened titles and abstracts to assess the eligibility of a sample of 100 citations to validate the inclusion and exclusion criteria. A single reviewer then screened all remaining citations using Covidence[41] and obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The same reviewer then examined the full-text articles and selected studies eligible for inclusion.

Data Extraction

We extracted relevant data on study characteristics and risk-of-bias items using a data form to collect information on the following:

- Source (e.g., citation information, study type)
- Methods (e.g., study design, study duration and years, participant allocation, allocation sequence concealment, blinding, reporting of missing data, reporting of outcomes, whether the study compared 2 or more groups)
- Outcomes (e.g., outcomes measured, number of participants for each outcome, number of participants missing for each outcome, outcome definition and source of information, unit of measurement, time points at which the outcomes were assessed)

We contacted study authors to provide clarification as needed.

Equity Considerations

Potential equity issues related to the research question (or the use of PVP or PBK in adults with painful OVCFs) were not evident during scoping. However, we report the available characteristics of participants in the included studies (e.g., PROGRESS-Plus categories[37]).

Statistical Analysis

We performed a meta-analysis of outcomes with updated studies as a continuum of the systematic review and meta-analysis[38] that we identified during scoping. Specifically, we extracted data from the systematic reviews and then added new data that we found from more recent studies published after the literature search in the included systematic reviews.

We performed a quantitative synthesis of the individual studies using Review Manager.[42]

We conducted subgroup analyses for people who had had OVCFs for less than 8 weeks, 8 weeks or more, and outcomes (e.g., pain) for people who underwent a sham procedure versus conservative treatment and inpatient versus outpatient procedures.

Critical Appraisal of Evidence

We assessed risk of bias using the ROBIS tool for systematic reviews,[43] the Cochrane Risk of Bias tool for RCTs,[44] and the ROBINS-I tool for observational studies[45] (Appendix 2). For studies included in the systematic reviews, we reported the risk of bias as assessed by the authors. We assessed the risk of bias for the additional recent studies that met our inclusion criteria.

We evaluated the quality of the body of evidence for each outcome according to the *Grading of Recommendations Assessment, Development, and Evaluation* (GRADE) *Handbook*.[46] The body of evidence was assessed based on the following considerations: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The overall rating reflects our certainty in the evidence.

Results

Clinical Literature Search

The clinical literature search yielded 1,459 citations, including grey literature results and after removing duplicates, published between January 1, 2019, and May 29, 2024. We identified 6 additional eligible studies from other sources, including database alerts (monitored until August 14, 2024). In total, we identified 10 publications (2 systematic reviews,[38,39] 4 RCTs,[47-50] and 4 observational studies[51-54]) that met our inclusion criteria. See Appendix 4 for a list of selected studies excluded after full-text review. Figure 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the clinical literature search.

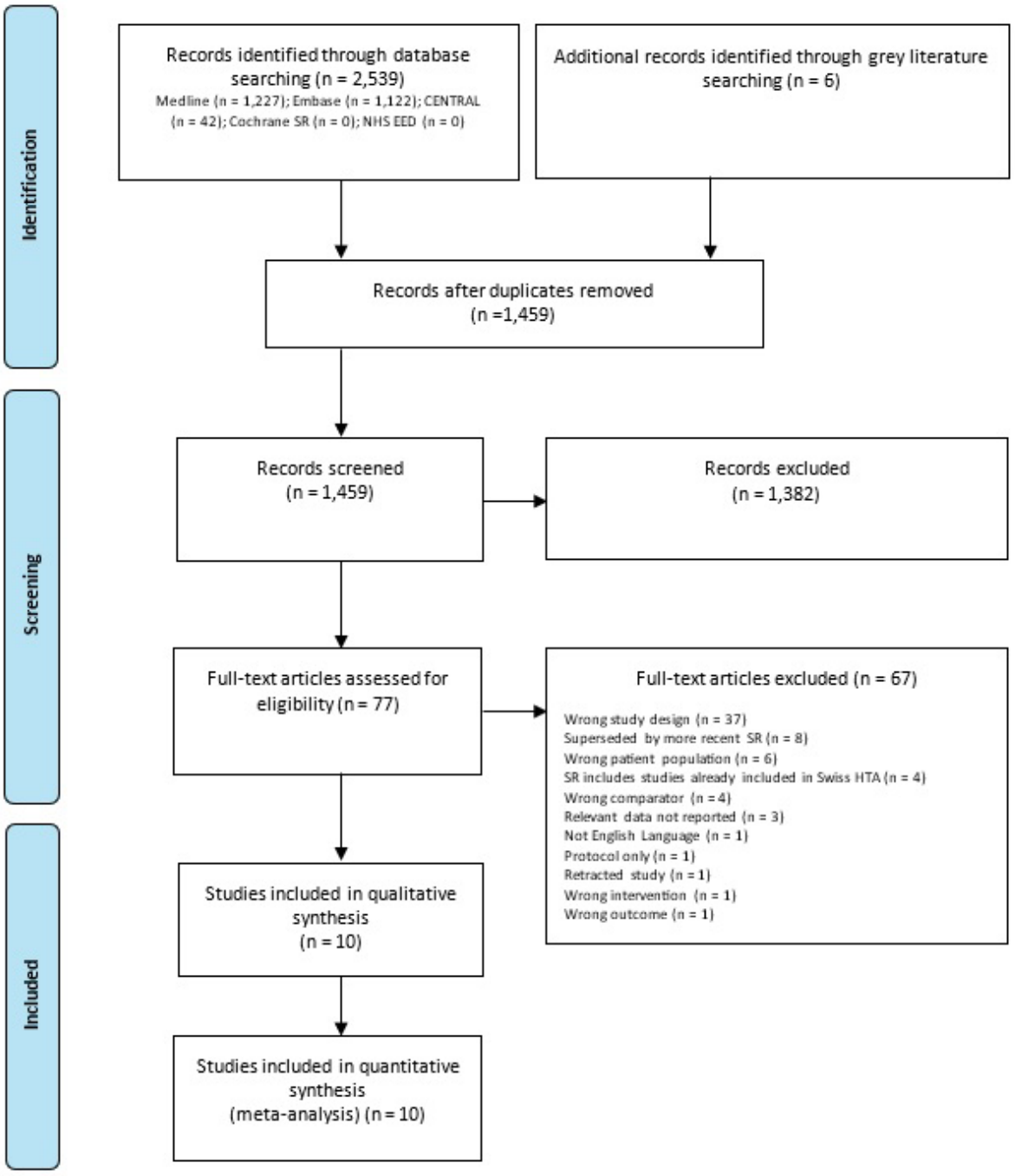


Figure 1: PRISMA Flow Diagram – Clinical Systematic Review

PRISMA flow diagram showing the clinical systematic review. The clinical literature search yielded 1,459 citations, including grey literature results and after removing duplicates, published between January 1, 2019, and May 29, 2024. We screened the abstracts of the 1,459 identified studies and excluded 1,382. We assessed the full text of 77 articles and excluded a further 67. In the end, we included 10 articles in the quantitative synthesis.
Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses; SR, systematic review.
Source: Adapted from Page et al.[55]

Characteristics of Included Studies

The 2020 systematic review by Jacobsen et al[38] reported the effectiveness and safety of PVP versus sham/conservative treatment and PBK versus sham/conservative treatment. We updated the literature search by Jacobsen et al,[38] adding another 4 RCTs[47-50] to our analysis for effectiveness outcomes (e.g., pain quality of life, physical function) and 4 observational studies[51,53,54,56] to our analysis of safety (e.g., mortality, cement leakage).

Jacobsen et al[38] did not compare the effectiveness of PVP with PBK; however, we identified a 2023 systematic review by Liu et al[39] that directly compared PVP with PBK. Our literature search further identified a recent RCT by Wang et al[50] that was not included this systematic review.[39] We updated the analysis by Liu et al[39] to include it.

Information about the characteristics of the included studies is reported in Table 1.

Table 1: Characteristics of Studies Included in the Clinical Literature Review

Author, year, country	Study design, length of follow-up	Participants	Intervention	Comparator	Outcomes
Systematic reviews					
Jacobsen et al 2020[38] Switzerland	Systematic review RCTs for effectiveness outcomes RCTs, prospective observational studies and registry studies for safety outcomes Literature search from inception to December 2019	Adults (age not specified) with OVCFs not responsive to conservative treatment	PVP, PBK	Sham, CT	Pain via VAS or NRS Physical function via ODI or RMDQ Quality of life via generic scales (e.g., SF-36, EQ-5D) and disease-specific scales (e.g., QUALEFFO) Refracture Adverse events (e.g., mortality, cement leakage, infection)
Liu et al, 2023[39] Korea	Systematic review of RCTs Literature search from inception to September 2023.	Adults ≥ 18 y diagnosed with OVCF	PVP	PBK	VAS ODI New fractures
RCTs					
Carli et al, 2023[48] Netherlands	RCT Double blinded Single centre 12 months	Adults ≥ 50 y, focal back pain at the level of OVCF for at least 3 mo at time of spinal radiography, bone edema of fractured vertebra at MRI N = 80	PVP	Sham	VAS QUALEFFO RMDQ score New fractures Use of analgesics Adverse events
Tantawy, 2022[47] Egypt	RCT Blinding not reported Single centre 3 months	Adults (age not specified) with painful OVCF diagnosed by "clinical means," CT and MRI. Location of pain consistent with anatomical site of fracture in MRI. Bone marrow edema on MRI present in all cases	PVP	CT (physical therapy, pain medication, osteoporosis medication, topical	VAS ODI New fractures

Author, year, country	Study design, length of follow-up	Participants	Intervention	Comparator	Outcomes
		All patients within the intervention group had PVP within 1 mo from pain onset. (Authors do not report how long patients in the control group had painful OVCF) N = 70		analgesics, and bracing)	
Wang et al, 2020[50] China	RCT Blinding not reported Single centre Length of follow-up not reported	Adults > 60 y diagnosed with OVCF based on clinical manifestations and frontal and lateral x-ray of thoracolumbar spine N = 80	PVP	PBK	VAS ODI Barthel Index (i.e., activities of daily living) Blood loss Operation time
Hansen et al, 2019[49] Denmark	RCT Double blinded Single centre 3 and 12 months	Adults with OVCFs who had ≤ 8 wk of back pain and MRI-indicated edema N = 52	PVP	Sham	VAS Quality of life: EQ-5D and SSF-36 physical composite summary score
Observational Studies					
Aregger et al, 2024[51] Switzerland	Prospective case series Single centre 10 years	Adults > 18 y with OVCFs who, despite receiving adequate analgesia, required hospitalization due to being immobile for over 1 wk N = 49	PVP	—	Pain (VAS and NRS) Quality of life (EQ-5D and NASS score) New fractures Mortality
Gold et al, 2023[56]	Retrospective registry cohort study 30 days, 6 and 12 months	Adults (age not specified) who were US Medicare enrollees with thoracic or lumbar OVCFs. Patients had at least 1 diagnosis code for osteoporosis within a year prior through the first 6 mo after their index fractures N = 38,034	PBK	—	Mortality
Nguyen et al, 2020[53] Vietnam	Prospective case series Single centre 24 hours and 3 months	Adults (age not specified) diagnosed with OVCFs based on spinal x-ray and vertebral stem edema on MRI N = 65	PBK	—	VAS Adverse events
Tuan et al, 2020[54] Vietnam	Prospective case series Single centre 24 hours	Adults (age not specified) with painful OVCFs of at least 2 vertebrae with evidence of a “fresh fracture” on MRI N = 32	PVP	—	Cement leakage

Abbreviations: CT, conservative treatment; EQ-5D, Euroqol -5 dimension; MRI, magnetic resonance imaging; NASS, North American Spine Society; NRS, numerical rating score; PODI, Oswestry Disability Index; BK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QUALEFFO, Quality of Life Questionnaire of the European Foundation for Osteoporosis; RCT, randomized controlled trial; RMDQ, Roland Morris Disability Questionnaire; SF-36, short form 36; VAS, visual analogue score.

Characteristics of the 12 PVP (compared to conservative treatment or sham) or 4 PBK (compared to conservative treatment only) RCTs and 31 observational studies (for safety outcomes, e.g., comparative or single arm trials) that were included in the systematic review by Jacobsen et al[38] are reported in Table 2.

No studies were identified that compared PBK to sham.

The characteristics of the 5 RCTs included in the systematic review by Liu et al[39] (PVP compared with PBK) are reported in Table 3.

Table 2: Characteristics of Studies Included in the Systematic Review by Jacobsen et al[38]

Author, year, country	Study design and follow-up period	Participants	Intervention	Comparator	Outcomes
PVP Versus CT RCTs					
Blasco et al, 2012[57] Spain	RCT Open label Single centre 12 months	Adults with OVCF clinical onset < 12 mo, confirmed by x-ray and presence of edema on MRI N = 125	PVP	CT (analgesics)	Pain (VAS) Quality of life (QUALEFFO) Analgesic use Cement leakage New vertebral fracture Mortality
Chen et al, 2014[58] China	RCT Open label Single centre 12 months	Adults with OVCF confirmed with MRI, persistent back pain for > 3 mo N = 96	PVP	CT (bracing, analgesia, physiotherapy, and anti-osteoporotic medication)	Pain (VAS) Function (ODI, RMDQ) Analgesic use New fractures
Farrokhi et al 2011[59] Iran	RCT Single blinded Single centre 36 months	Adults with OVCF, severe back pain refractory to analgesics for ≥ 4 wk to 1 y, focal tenderness on clinical exam related to fracture level and edema on MRI, unresponsive to medical therapy N = 82	PVP	CT (optimal medical management; i.e., mix of paracetamol, codeine, ibuprofen, calcium, vitamin D, alendronate, and calcitonin)	Pain (VAS) Functional (ODI) Cement leakage New vertebral fracture Mortality
Klazen et al, 2010[60,61] Venmans et al 2011[62] Netherlands	RCT (VERTOS II) Open label Multicentre 12 months	Adults with OVCF, back pain for ≤ 6 wk, edema on MRI, focal tenderness on physical examination N = 202	PVP	CT (analgesics: paracetamol, tramadol, tramadol and paracetamol, morphine, osteoporosis medication)	Pain (VAS) Function (RMDQ) Quality of life (QUALEFFO, EQ-5D) Analgesic usage Adverse events Cement leakage New vertebral fracture Mortality
Leali et al 2016[63] Italy, France	RCT Unclear blinding Multicentre 6 months	Post-menopausal women with OVCF, acute pain, edema present on MRI N = 400	PVP	CT (pain medication, osteoporosis medication, physiotherapy, or bracing)	Adverse events Mortality
Rousing et al, 2009[64] 2010[65] Denmark	RCT Open label Single centre 12 months	Adults with OVCF, intractable pain < 8 wk, MRI confirmed OVCF N = 49	PVP	CT (brace treatment, pain medication, general mobilising physiotherapy)	Pain (VAS) Function (TUG) Quality of life (SF-36, EQ-5D) Adverse events Mortality New vertebral fracture
Voormolen et al, 2007[66] Netherlands	RCT Open label Multicentre 12 months	Adults ≥ 50 y with OVCF, debilitating back pain relating to the fracture with 6 wk to 6 mo duration refractory to medical therapy, edema at fracture on spinal MRI N = 34	PVP	CT (optimal pain medication; i.e., paracetamol, NSAIDs, or opiate derivatives)	Pain (VAS) Function (RMDQ) Quality of life (QUALEFFO) Analgesic use Adverse events

Author, year, country	Study design and follow-up period	Participants	Intervention	Comparator	Outcomes
Yang et al, 2016[67] China	RCT Unclear blinding Multicentre 12 months	Adults with OVCF, back pain, MRI-confirmed, living independently without need for wheelchair prior to trauma N = 107	PVP	CT (bed rest, bracing, physiotherapy, & NSAIDs; tramadol and morphine, if needed)	Quality of life (ODI, QUALEFFO) Adverse events Cement leakage New vertebral fractures
PVP Versus Sham RCTs					
Buchbinder et al, 2009[68] Kroon et al, 2014[69] Staples et al, 2015[70] Australia	RCT Double blinded Multicentre 24 months	Adults with back pain < 12 mo, MRI-confirmed acute OVCF (edema or fracture line) N = 78	PVP	Sham	Pain (NRS/VAS) Function (RMDQ) Quality of life (QUALEFFO, EQ-5D) Analgesic use Any adverse events Mortality New vertebral fracture
Clark et al, 2016[71] Australia	RCT (VAPOUR trial) Double blinded Multicentre 6 months	Adult osteoporotic patients, 1 or 2 OVCF < 6 wk, MRI confirmed VCF N = 120	PVP	Sham	Pain (NRS, VAS) Function (RMDQ) Quality of life (QUALEFFO, SF-36, EQ-5D) Analgesic use Any adverse events Cement leakage Mortality New vertebral fracture Length of stay
Firanescu et al, 2011,[72] 2018,[73] 2019[74] Netherlands	RCT (VERTOS IV trial) Double blinded Multicentre 12 months	Adults with OVCF of up to 6 wk duration, bone edema on MRI N = 180	PVP	Sham	Pain (VAS) Function (RMDQ) Quality of life (QUALEFFO) Analgesic use Any adverse events New vertebral fracture Mortality
Kallmes et al, 2009[75] Comstock et al, 2013[76] United States, Australia, United Kingdom	RCT Double blinded Multicentre 12 months	Adults >50 y of age with OVCFs < 12 mo, refractory to medical therapy, pain score at least 3/10 N = 131	PVP	Sham	Pain (NRS/VAS) Function (SOF-ADL, RMDQ) Quality of life (EQ-5D, SF-36) Analgesic use Adverse events Mortality
PVP Observational Studies					
Andrei et al, 2017[77] Romania	Prospective Single centre 12 months	Adults with OVCF N = 66	PVP	CT (details not reported)	Adverse events
Diamond et al, 2003,[78] 2006[79] Australia	Prospective Single centre 24 months	Adults with severe OVCF pain lasting 1–6 wk, unresponsive to non-opiate analgesia n = 126	PVP	CT (paracetamol, opiates, COX inhibitors, hot packs, gentle mobilization)	Any severe adverse events Cement leakage Mortality New fractures
Chen et al, 2013[80] United States	US Medicare & Medicaid database 30 days–6 months	Adults > 65 y who did not have end-stage renal disease or malignant neoplasm N = 68,752	PVP PBK	CT ("nonsurgical management")	Adverse events Mortality Readmissions Length of stay Discharge to home Additional vertebral procedures
Ong et al, 2018[81] United States	US Medicare & Medicaid claims database 1–10 years	Adults > 65 y with OVCF, hospital record extending 12 mo before OVCF N = 2,077,944	PVP PBK	CT ("nonsurgical management")	Adverse events Mortality Readmissions Length of stay Discharge to home

Author, year, country	Study design and follow-up period	Participants	Intervention	Comparator	Outcomes
Al-Ali et al, 2009[82] United States	Prospective case series Single centre 1 year	Adults with painful OVCF who failed CT N = 357	PVP	—	Cement leak
Bae et al, 2012[83] United States	Compared 2 types of cement Multicentre 24 months	Adults with painful OVCFs who failed CT (4–52 wk) N = 256	PVP	—	Cement leak
DePalma et al, 2011[84] United States	Prospective case series Single centre 24 months	Adults with painful OVCFs who failed CT N = 123	PVP	—	Cement leak
Dohm et al, 2014[85] United States	PVP vs. PBK Multicentre 24 months	Adults with acute painful OVCF who failed CT N = 404	PVP	—	Cement leak
Fenoglio et al, 2008[86] Italy	Prospective case series Single centre Median follow up: 20.4 months (range 6–24 months)	Adults with painful OVCFs who failed CT (at least 1 mo) N = 52	PVP	—	Cement leak
Kotwica et al, 2011[87] Poland	Prospective case series Single centre Minimum 12 months	Adults with acute painful OVCF who failed CT N = 200	PVP	—	Cement leak
Masala et al, 2012[88] Italy	Prospective case series Single centre 1 year	Adults with symptomatic OVCFs who failed CT N = 80	PVP	—	Cement leak
Masala et al, 2009[89] Italy	Prospective case series Single centre 3 years	Patients with painful vertebral fractures who failed CT (at least 2 mo) N = 308	PVP	—	Cement leak
Nieuwenhuijse et al, 2012[90] Netherlands	Prospective case series Single centre 1 year	Adults with painful OVCF who failed CT (at least 2 mo) N = 115	PVP	—	Cement leak
Niuewenhuijse et al, 2010[91] Netherlands	Low vs. medium viscosity cement Single centre 1 year	Adults with painful OVCF who failed CT (at least 6 wk) N = 64	PVP	—	Cement leak
Pitton et al, 2008[92] Germany	Prospective case series Single centre Mean: 19.7 months	Adults with painful OVCF who failed CT N = 191	PVP	—	Cement leak
Santiago et al, 2010[93] Spain	PVP vs. PBK study Single centre 1 year	Adults with OVCF who failed CT N = 60	PVP	—	Cement leak
Saracen et al, 2014[94] Poland	Prospective case series Single centre 24 months	Adults with OVCFs N = 160	PVP	—	Cement leak
Voormolen et al, 2006[95] Netherlands	Prospective case series Single centre	Adults with OVCF who failed CT (at least 6 wk) N = 77	PVP	—	Cement leak

Author, year, country	Study design and follow-up period	Participants	Intervention	Comparator	Outcomes
	6 months				
Voormolen et al, 2006[96] Netherlands	Prospective case series Single centre Mean: 10.4 months	Adults with OVCF who failed CT (at least 6 wk) N = 112	PVP	—	Cement leak
PBK Versus CT RCTs					
Jin et al, 2018[97] China	RCT, open-label Single centre 12 months	Adults ≥ 60 y with OVCF local pain and injured vertebra on clinical exam and MRI confirmed N = 41	PBK	CT (analgesics and osteoporosis treatment)	Pain (VAS) Quality of life (SF-36)
Li et al, 2017[98] China	RCT, open-label Single centre 6 months	Adults ≥ 65 y with OVCF of duration 2 h to 2 wk, fracture confirmed with x-ray, computed tomography, or MRI scan N = 80	PBK	CT (physiotherapy and bed rest)	Pain (VAS) Function (ODI) Any adverse event
Liu et al, 2019[99] China	RCT, open-label Single centre Length of follow-up not reported	Adults with OVCF confirmed with x-ray and computed tomography scans N = 116	PBK	CT (analgesics, physiotherapy, fixation, and bed rest)	Any adverse event Cement leak
Wardlaw et al, 2009[100] Van Meirhaeghe et al, 2013[101] Austria, Netherlands, France, United Kingdom, Germany, Sweden, Italy	RCT, open-label Multicentre 24 months	Adults with OVCF, bone marrow signal changes on MRI N = 300	PBK	CT (analgesics, bed rest, bracing, physiotherapy, rehabilitation programs and walking aids, calcium, and vitamin D)	Pain (VAS) Function (RMDQ) Quality of Life (SF-36, EQ-5D) Any severe adverse event Cement leak Mortality New vertebral fracture
PBK Versus CT Observational Studies					
Eidt-Koch et al, 2011[102] Germany	Prospective Multicentre 12 months	Adults > 50 y with painful OVCF < 3 mo N = 124	PBK	CT (not reported)	Quality of life (EQ-5D, RMDQ) Mortality
Giannotti et al, 2012[103] Italy	Prospective Single centre 12 months	Adults with OVCF N = 50	PBK	CT (not reported)	Cement leakage New fractures
Kasperk et al, 2005,[104] 2010[105] Grafe et al, 2005[106] Germany	Prospective Single centre 36 months	Adults with painful OVCFs > 12 mo, chronic back pain > 1 y N = 60	PBK	CT (analgesic medication, physiotherapy)	Pain (VAS) Adverse events Cement leakage New and adjacent fractures Mortality
Movrin et al, 2010[107] Slovenia	Prospective Single centre 12 months	Adults with painful OVCF < 6 wk, able to tolerate general anaesthesia n = 107	PBK	CT (bed rest, analgesic medication)	Pain (VAS) New and adjacent fracture Cement leakage
Chen et al, 2013[80] United States	US Medicare & Medicaid database (registry) 30 days–3 years	Adults > 65 y who did not have end-stage renal disease or malignant neoplasm N = 68,752	PVP PBK	CT (nonsurgical management)	Adverse events Mortality Readmissions Length of stay Discharge to home Additional vertebral procedures

Author, year, country	Study design and follow-up period	Participants	Intervention	Comparator	Outcomes
Ong et al, 2018[81] United States	US Medicare & Medicaid claims database (registry) 1–10 years	Adults > 65 y with OVCF, hospital record extending 12 mo before OVCF. N = 2,077,944	PVP PBK	CT (nonsurgical management)	Adverse events Mortality Readmissions Length of stay Discharge to home
Dohm et al, 2014[85] United States	PVP vs. PBK (Jacobsen et al[38] focused on PBK arm only) Multicentre 24 months	Adults with acute painful OVCF who failed CT N = 404	PBK	—	Cement leak
Hillmeier et al, 2004[108] Germany	Prospective comparative study of 2 different cements Multicentre 6–12 months	Adults with painful OVCF N = 102	PBK	—	Cement leak
Hübschle et al, 2014[109] Switzerland	Retrospective case series (registry) Multicentre 12 months	Adults with osteoporosis, trauma and cancer diagnoses (osteoporosis accounted for the majority of fractures – 84%, n = 522/625 N = 625	PBK	—	Cement leak
Prokop et al, 2012[110] Germany	Case series Single centre Follow-up duration not reported	Details not reported N = 564	PBK	—	Cement leak
Robinson et al, 2008[111] United States	Prospective case series Single centre 6 months	Adults with painful OVCF who failed CT (12 wk) N = 102	PBK	—	Cement leak
Santiago et al, 2010[93] Spain	Prospective comparative study of PVP vs. PBK	Adults with non-traumatic or low-energy fractures with primary osteoporosis who failed CT N = 60	PBK	—	Cement leak

Abbreviations: COX, cyclooxygenase; CT, conservative treatment; EQ-5D, Euroqol -5 dimension; MRI, magnetic resonance imaging; NRS, numerical rating score; NSAID, nonsteroidal anti-inflammatory drugs; ODI, Oswestry disability index; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QUALEFFO, quality of life questionnaire of the European Foundation for Osteoporosis; RCT, randomized controlled trial; RMDQ, Roland-Morris Disability Questionnaire; SF-36, Short Form 36; SOF-ADL, study of osteoporotic fractures–activities of daily living questionnaire; VAS, visual analogue scale.

Table 3: Characteristics of Studies Included in the Systematic Review by Liu et al[39]

Author, year, country	Study design, length of follow-up	Participants	Intervention	Comparator	Outcomes
Evans et al, 2016[112] United States	RCT Multicentre 3 and 30 days, 6 and 12 months	Adults with OVCF N = 197	PVP	PBK	Pain (VAS) Function (RMDQ, SOF-ADL, EQ-5D, SF-36, OPAQ)
Wang et al, 2015[113] China	RCT Single centre 1 day, 3 and 12 months	Adults with OVCF N = 188	PVP	PBK	Pain (VAS) Function (ODI) Cement leakage
Dohm et al, 2014[85] United States	RCT Multicentre 1 day, 2, 12, and 24 months	Adults with OVCF N = 641	PVP	PBK	Pain (VAS) Function (ODI, SF-36, EQ-5D) Cement leakage New radiographic OVCF
Liu et al, 2010[114] China	RCT Single centre 3 days, 6 months	Adults with OVCF N = 177	PVP	PBK	Pain (VAS)
Bae et al, 2010[115] United Kingdom	RCT Multicentre 1 week, 1, 3, 6, 12, 24, and 36 months	Adults with OVCF N = 66	PVP	PBK	Pain (VAS) Function (ODI, SF-12)

Abbreviations: EQ-5D, European Quality of Life–5 Dimensions; ODI, Oswestry disability index; OPAQ, osteoporosis assessment questionnaire; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial; RMDQ, Roland Morris disability questionnaire; SF-12, 12-item short form health survey; SF-36, 36-item short form health survey; SOF ADL, study of osteoporotic fractures index scoring activities of daily living; VAS, visual analogue scale.

Risk of Bias in the Included Studies

Detailed information about the risk of bias in the included studies is found in Tables A1–A3 (Appendix 2). The two systematic reviews[38,39] were rated as low risk of bias using the ROBIS tool (Table A1, Appendix 2).

In the systematic review by Jacobsen et al,[38] the evidence base for the effectiveness and safety of PVP came from 12 RCTs, 2 observational studies, 2 database/registry studies, and 15 single-arm studies. According to the authors, the included RCTs ranged from low to high risk of bias (based on the Cochrane risk of bias tool).[38] The main concern in the majority of RCTs comparing PVP to CT was the absence of blinding.[38] Patients and outcome assessors were both aware of which treatment was received. Knowledge of the intervention can potentially influence the reporting of subjective outcomes such as pain and quality of life measures.[38] Concerns around blinding were addressed in the sham comparison in which patient and outcome assessor were both unaware of which intervention the individual received.[38] However, radiologists or neurosurgeons performing the procedure were necessarily unblinded and it was often unclear whether they were involved with recording subjective outcomes such as pain or quality of life in sham trials.[38]

The majority of RCTs comparing PVP to CT had unclear risk of bias in terms of completeness of outcome data (attrition bias).[38] There were significant baseline differences in Euroqol -5 dimension (EQ-5D) in the RCTs by Rousing et al[64] and Klazen et al.[60] Klazen et al[60] attempted to correct for baseline differences via regression analysis, whereas Rousing et al[64] did not. Baseline imbalances were a cause of bias in the effect estimate and may have led to over- or under-estimation of the true effect.[38] For safety-related outcomes, adverse events were frequently not defined and often not listed in the trial's protocol.[38] The overall risk of bias was moderate to serious for non-RCTs and serious for database analyses (based on ROBINS-I tool) comparing PVP to CT.[38] The selection of participants may have been biased as allocation to the control group was based on refusal to undergo PVP rather than demographic factors. However,

reasons for refusal of PVP were not reported and consequently the effect on selection cannot be fully determined.[38]

The main concern for non-RCTs were losses to follow-up.[38] Data were available for 77% of participants in Diamond et al[78] and 91% of participants in Andrei et al.[77] Due to the under-reporting of safety outcomes and the relatively small sample sizes, losses to follow-up may have disproportionally influenced the event rate.[38] The main risk of bias concern in the database analyses was related to patient selection (bias due to confounding).[38] Patients were identified using ICD-9-CM codes, with codes specific to the diagnosis and intervention. However, the codes did not provide information regarding how the vertebral fractures arose. In an attempt to limit the results to those patients with osteoporotic vertebral fractures, the studies excluded younger adults (< 65 years) and those with neoplasms.[38] However, patients with non-OVCFs may have been part of the cohort, which may have influenced the results if those patients were comparatively healthier or sicker.[38] Furthermore, the conservative treatment cohort was poorly defined.[38]

For PBK, Jacobsen et al[38] stated that the evidence base for effectiveness and safety came from 4 RCTs, 4 observational studies, 2 database/registry studies, and 6 single-arm studies. The authors reported that the included RCTs were generally moderate to high risk of bias (Cochrane Risk of Bias tool[44]). For RCTs, assessment of bias was hampered by underreporting of study methodology, which limited the ability to accurately evaluate each bias domain, an effect particularly apparent in Liu et al.[99] Lack of blinding likely influenced subjective outcomes such as pain and quality of life. This was the main concern among PBK trials.[38] All studies reported substantial losses to follow-up.[38] Owing to the limited reporting, it was unclear whether patients lost to follow-up were included in the results. Losses to follow-up were particularly important for safety-related outcomes given that most studies were already under-powered to detect differences. Wardlaw et al[100] noted that not all vertebrae were able to be read by radiologists. Consequently, the incidence of new fractures was analysed in patients with images of at least 7 vertebrae at baseline and 12 months, corresponding to 81% of PBK patients and 68% of CT patients.[38] This may have enriched or diminished the actual fracture rate. Other concerns related to the lack of published protocols, which limits our ability to accurately assess publication bias.[38] Two RCTs[100,101] reported that the sponsor had a role in study design, data monitoring, reporting or results, and paid for the statistical analysis.

The observational studies comparing PBK to CT ranged from low to mostly serious risk of bias (ROBINS-I).[38] Edit-Kock et al[102] failed to appropriately define the comparator group and had significant losses to follow-up. Key concerns in the study by Movrin et al[107] related to significant baseline differences in age, pain, and kyphotic treatment angle between patients undergoing PBK and those undergoing CT.[38] The authors corrected for this when evaluating adjacent fractures, but not for any other outcome. Therefore, it was unclear whether the differences observed at later timepoints reflect the interventions or patient demographics. The patient and the outcome assessor were unblinded to the intervention across all the non-RCTs.[38] This was not a concern for objective outcomes such as new fractures; however, for subjective outcomes such as the perception of pain, knowledge of the intervention can introduce bias. Consequently, studies evaluating pain and quality of life measures were considered to have a serious risk of bias. Kasperk et al[104] modified the visual analogue scale questionnaire as patients were deemed too old or fragile to answer questions regarding sex life, jogging, weight lifting, and traveling. It was unclear whether this modified questionnaire was administered to all patients or just those deemed too old or fragile.[38] Giannotti et al[103] provided limited methodological information, consequently an accurate assessment of risk of bias could not be obtained.

Liu et al[39] reported that the risk of bias in the 5 RCTs included their systematic review was low,[112,115] moderate,[113,114] and high,[85] based on the Cochrane risk of bias tool.[44]

The risk of bias in the RCTs we identified in our updated literature search was low for 2 trials[48,49] and a mix of low to high for 2 trials (Table A2, Appendix 2).[47,116] The risk of bias for the 5 observational studies[51,53,54,56] ranged from moderate to serious, based on the ROBINS-I tool (Table A3, Appendix 2).

PVP Compared With Conservative Treatment

Pain

We included 8 RCTs[38,47,57-60,64,66,67] in our meta-analysis for pain as measured by a VAS, from 1 day to 36 months post-intervention (7 from the review by Jacobsen et al[38] and 1 identified through the updated literature search[47]). Overall, there were statistically significant differences favouring PVP at 1 day, 1 week, and 1 and 3 months follow-up. While there were also statistically significant differences at 6, 12, 24, and 36 months follow-up, the clinical significance related to these later follow-ups is uncertain based on published values for the minimal clinically important difference (MCID) (Table A8, Appendix 3).[38] The estimates for 24 and 36 months follow-up were based on 1 RCT.[59] At 1 month, the mean difference was −2.00 (95% confidence interval [CI]: −2.86 to −1.15) and at 12 months the mean difference was −1.35 (95% CI: −1.70 to −1.00; Figure 2).

Six studies[57,58,60,64,66,67] used a 10-point VAS (10 representing the worst pain) and 1[59] used a 9-point scale.[59] Tantawy[47] did not explicitly report details of the VAS used in his trial (in which he was the sole person who performed the procedures and assessed all outcomes). While the studies differed slightly in scale, Jacobsen et al[38] reported that it was unlikely to significantly impact overall results when included in a meta-analysis. Of note, none of the studies reported the context in which the pain was felt (e.g., spontaneous pain or pain during activity) or who completed the VAS measurement.[38]

Subanalyses of the results for duration of painful OVCF (beginning more or less than 8 weeks) before the start of the study are presented in Figures A1 and A2 (Appendix 3), as reported by Jacobsen et al.[38] Subgroup analysis of OVCFs beginning less than 8 weeks before the study showed significant differences in pain scores between PVP and CT groups at all follow-up timepoints. For OVCFs older than 8 weeks, there were statistically significant differences at 1 week and 1, 3 and 12 months posttreatment, but not at 2 weeks, or 2 or 6 months posttreatment. Of note, Jacobsen et al[38] identified considerable statistical heterogeneity and inconsistency at most timepoints.

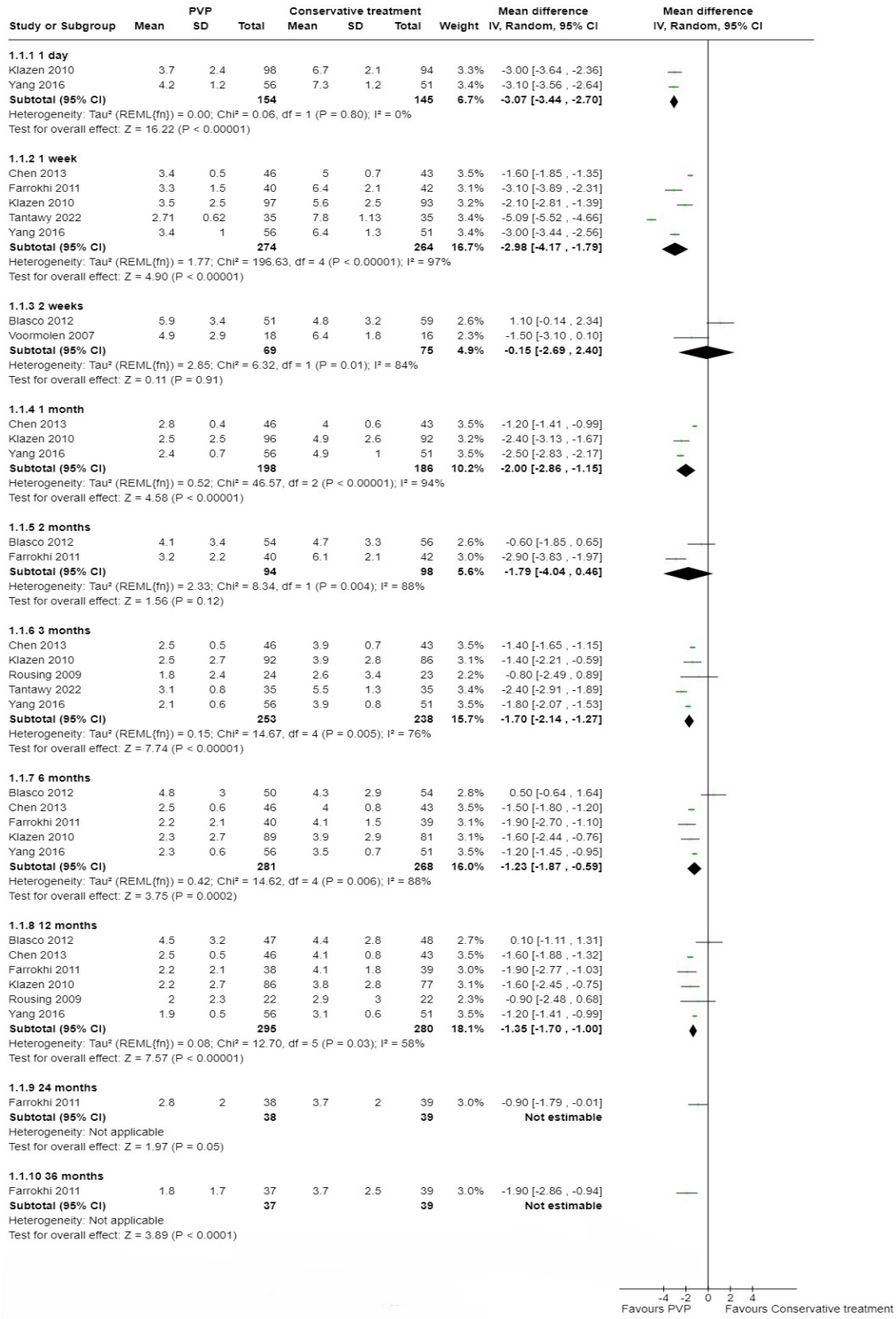


Figure 2: Mean Difference in Pain (VAS) for PVP Versus CT

Figure shows the mean difference (95% CI) in pain as measured by the visual analogue scale for PVP compared to CT at follow-up timepoints ranging from 1 day to 36 months. Overall, there were significant differences favouring PVP at 1 day, 1 week, and 1 and 3 months follow-up. While there were also significant differences at 6, 12, 24, and 36 months follow-up, the clinical significance related to these later follow-ups is uncertain based on published values for the minimal clinically important difference.

Abbreviations: CI, Confidence Interval; CT, conservative treatment; PVP, percutaneous vertebroplasty; SD, standard deviation; VAS, visual analogue scale.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A4, Appendix 3).

Use of Analgesics

Jacobsen et al[38] identified 4 RCTs reporting the number of patients using analgesics; follow-up ranged from 1 week to 6 months posttreatment. Two trials[57,58] were meta-analyzed by the Jacobsen authors, while the other 2[60,66] were not included in a meta-analysis because the study authors reported the range or described their results narratively.

Jacobsen et al[38] reported that there were no statistically significant differences at 1 week (risk ratio [RR]: 0.62; 95% CI: 0.20–1.89), 1 month (RR: 0.53; 95% CI: 0.10–2.69) or 6 months (RR: 0.48; 95% CI: 0.10–2.42) (Table 4). There was statistically significant heterogeneity associated with the summary estimates. The types of analgesics used by patients were not specified in the trial by Chen et al.[58] Blasco et al[57] reported that the analgesics included minor analgesic, minor opioid, and major opioid.[57]

Table 4: PVP Versus CT: Analgesic Use Posttreatment for Pain

Follow-up	No. of RCTs	PVP, n/N (%)	CT, n/N (%)	RR (95% CI)	Heterogeneity
1 week	2[57,58]	64/110 (58.2%)	82/104 (78.9%)	0.62 (0.20 to 1.89) *P* = 0.40	χ2 = 18.60 *P* < 0.00001 I^2 = 95%
1 month	2[57,58]	56/110 (50.9%)	71/104 (68.3%)	0.53 (0.10 to 2.69) *P* = 0.44	χ2 = 18.80 *P* < 0.0001 I^2 = 95%
6 months	2[57,58]	54/110 (49.1%)	76/104 (73.1%)	0.48 (0.10 to 2.42) *P* = 0.38	χ2 = 18.90 *P* < 0.0001 I^2 = 95%

Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial; RR, risk ratio.

The 2 RCTs[60,66] that were not meta-analyzed by Jacobsen et al[38] concluded that there were statistically significant differences in analgesic use in the short-term between the treatment groups. Voormolen et al[66] did not report a *P* value and Klazen et al[60] reported that the differences were not significant at later timepoints (3–12 months follow-up; Table 5). Jacobsen et al[38] did not meta-analyze subgroups (i.e., < or > 8 weeks after onset of painful OVCFs) due to the small number of available studies.

Table 5: PVP Versus CT: Analgesic Use Posttreatment for Pain (Studies Not Meta-Analyzed by Jacobsen et al[38])

Author, year	Length of follow-up	PVP (mean [range] or n/N)	CT (mean [range] or n/N)	Mean difference (95% CI)	*P* value
Voormolen et al, 2007[66]	Baseline 1 day 2 weeks	1.9 (0–3) 1.1 (0–3) 1.2 (0–3)	1.7 (0–3) 2.5 (1–3) 2.6 (2–3)	NR −1.4 (−2.1 to −0.8) −1.5 (−2.3 to −0.8)	NR < 0.05 < 0.05
Klazen et al, 2010[60]	Baseline 1 day 1 week 1 month	96/101 NR NR NR	94/101 NR NR NR	NR NR NR NR	> 0.05 < 0.001 = 0.001 0.033

Abbreviations: CI, confidence interval; CT, conservative treatment; NR, not reported; PVP, percutaneous vertebroplasty.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, indirectness, and imprecision (Table A4, Appendix 3).

Physical Function

Four RCTs[47,58,59,67] provided evidence on function, as measured by the Oswestry Disability Index (ODI), with follow-up ranging from 1 day to 36 months. For the ODI, 0% to 20% represents minimal disability, 21% to 40% is moderate disability, 41% to 60% is severe disability, 61% to 80% is crippling back pain, and 81% to 100% is bed-bound. Overall, there were statistically significant differences favouring PVP compared with CT at follow-up periods of 1 day to 6 months (Figure 3). These differences were also clinically significant based on published MCID values (Table A8, Appendix 3). At 3 months, the mean difference was −18.08 (95% CI: −23.84 to −12.31). There were also statistically significant (albeit likely not clinically significant) differences favouring PVP at 12, 24, and 36 months; these results are all based on 1 RCT.[59] At 12 months, the mean difference was −10.14 (95% CI: −14.14 to −6.14) (Figure 3).

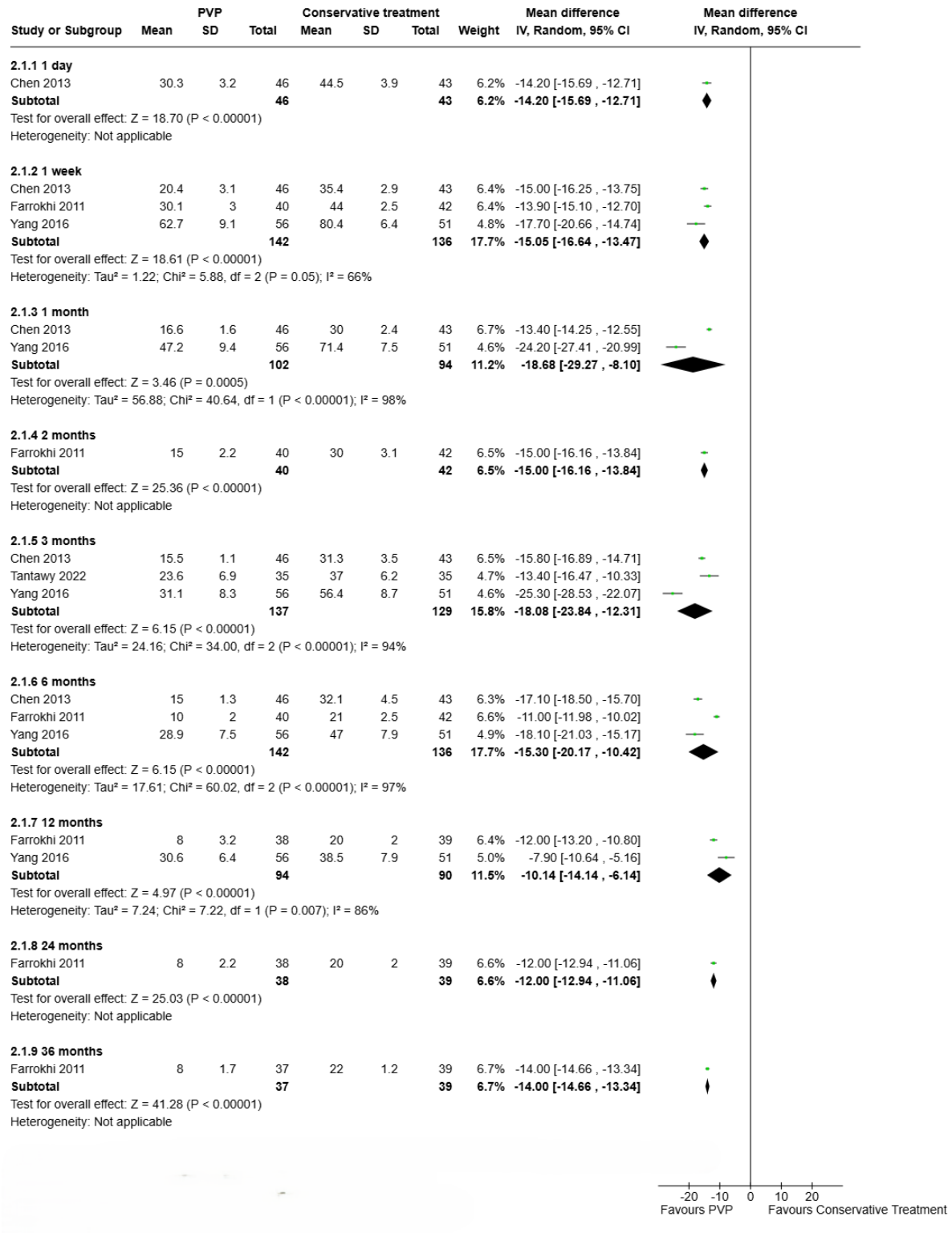


Figure 3: Mean Difference in Oswestry Disability Index for PVP Compared to CT

Figure shows the mean difference (95% CI) in physical function as measured by the Oswestry Disability Index for PVP compared to CT at follow-up timepoints ranging from 1 day to 36 months. Overall, there were significant differences favouring PVP over CT at follow-up periods of 1 day to 6 months. These differences were also clinically significant based on published MCID values.

Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty; SD, standard deviation.

Subgroup analysis of the results for duration of painful OVCFs that are less than or more than 8 weeks since onset are presented in Figures A3 and A4 (Appendix 3). Analysis showed significant differences in ODI between PVP and CT groups at all follow-up timepoints.

Jacobsen et al[38] identified 3 RCTs[58,60,66] that provided evidence on function, as measured by the Roland Morris Disability Questionnaire (RMDQ), from 1 day to 12 months post-intervention. The RMDQ measure has 0 to 24 points, with higher scores indicating decreasing physical functioning and increasing disability. Two RCTs[58,60] were included in the meta-analysis. A third[66] reported range rather than standard deviation and is described narratively. Overall, there were statistically significant differences favouring PVP over CT from 1 day to 6 months follow-up; these were also likely clinically significant based on published MCID values (Table A8, Appendix 3).[38] However, there was no statistically significant difference at 12 months follow-up. The mean difference was −2.37 (95%CI: −3.25 to −1.50) at 1 month and −1.90 (95%CI: −4.01 to 0.21) at 12 months.

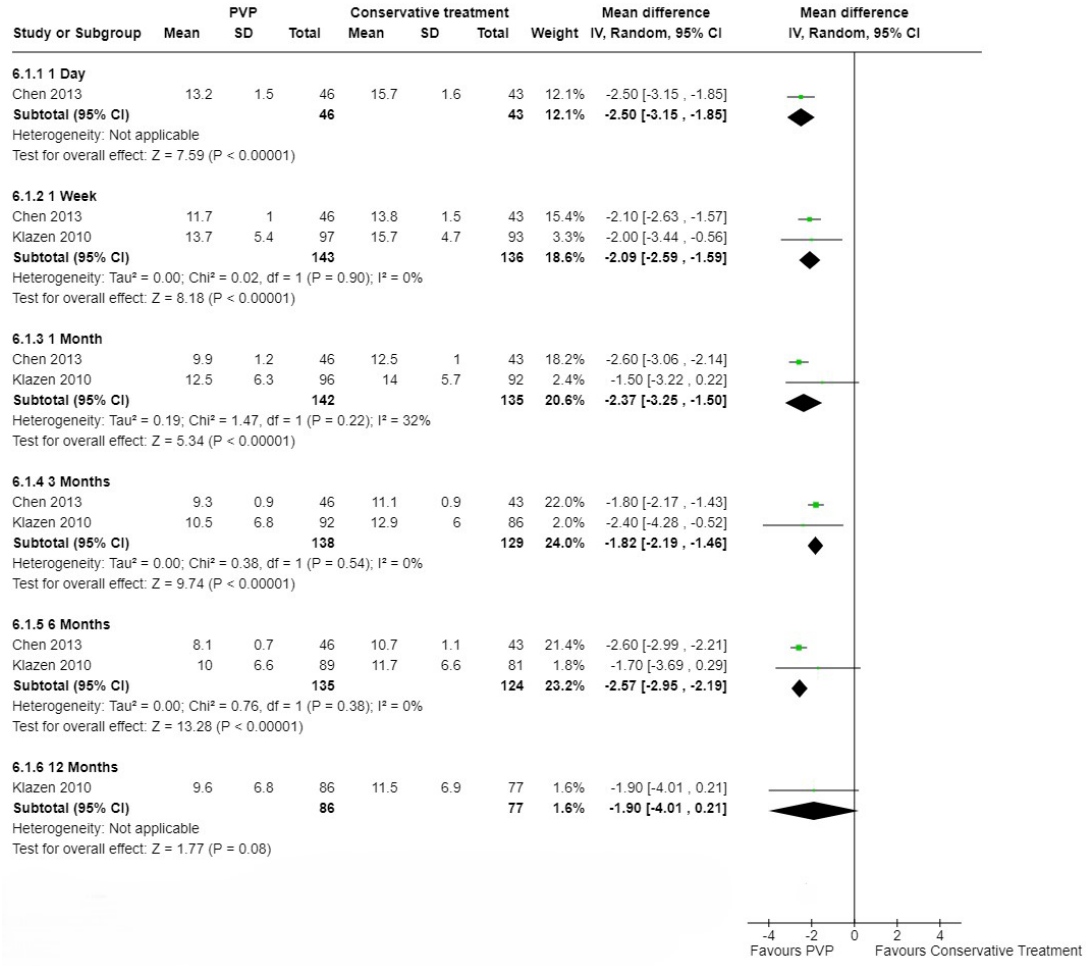


Figure 4: Mean Difference in Roland Morris Disability Questionnaire for PVP Compared to CT

Figure shows the mean difference (95% CI) in physical function as measured by the Roland Morris Disability Questionnaire for PVP compared to CT at follow-up timepoints ranging from 1 day to 12 months. Overall, there were significant differences favouring PVP over CT from 1 day to 6 months follow-up; these were also likely clinically significant based on published minimum clinically important differences.
Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty; SD, standard deviation.

Subgroup analysis of the results for duration of painful OVCFs that are less than or more than 8 weeks since onset are presented in Figures A5 and A6 (Appendix 3). Analysis of OVCFs of less than 8 weeks (1 RCT[60]) showed significant differences in RMDQ favouring PVP over CT at 1 day and at 3 months follow-up. For OVCFs of more than 8 weeks (1 RCT[58]), there were significant differences favouring PVP over CT at all follow-up assessments.

The RCT by Voormolen et al[66] reported range rather than standard deviation. There was a significant difference favouring PVP over CT at 2 weeks follow-up (Table 6).

Table 6: PVP Versus CT: Function (Roland Morris Disability Questionnaire)

Author, year	Length of follow-up	PVP, mean (range)	CT, mean (range)	Mean difference (95% CI)	*P* value
Voormolen et al, 2007[66]	Baseline	1.9 (0–3)	1.7 (0–3)	NA	NA
	1 day	1.2 (0–3)	2.6 (2–3)	1.4 (−2.0 to −0.8)	< .05
	2 weeks	1.2 (0–3)	2.6 (2–3)	1.4 (−2.0 to −0.8)	< .05

Abbreviations: CI, confidence interval; CT, conservative treatment; NA, not applicable; PVP, percutaneous vertebroplasty.

Jacobsen et al[38] identified 1 RCT[64] that reported timed up-and-go scores at 3 and 12 months follow-up. There was no significant difference between PVP and CT groups at either timepoint (*P* > .05) (Table 7). The test involved patients rising from a chair, walking 3 metres, returning, and resitting in the chair. A reduction in time corresponded to improved function.[64]

Table 7: PVP Versus CT: Function (Timed Up-And-Go Scores)

Author, year	Length of follow-up	PVP, (mean ± SD)	CT, (mean ± SD)	*P* value
Rousing et al, 2009[64]	Baseline	NR	NR	—
	3 months	16.0 ± 5.5 s	17.0 ± 9.7 s	.75
	12 months	16.1 ± 7.9 s	17.3 ± 9.2 s	.67

Abbreviations: CT, conservative treatment; NR, not reported; PVP, percutaneous vertebroplasty; SD, standard deviation.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A4, Appendix 3).

Quality of Life

Jacobsen et al[38] identified 2 studies[60,64] that provided evidence for quality of life, as measured by EQ-5D (where 0 indicates death and 1 indicates perfect health) from 1 week to 12 months follow-up. Overall, there were small statistically significant differences favouring PVP at 1 week, and at 1, 6, and 12 months follow-up. However, based on published MCIDs (Table A8, Appendix 3), these are unlikely to be clinically significant.[38] The estimates at 1 week, and at 1 and 6 months are based on 1 RCT.[60] The mean difference was 0.10 (95% CI: 0.03–0.17) at 1 month and 0.10 (95% CI: 0.02–0.18) at 12 months (Figure 5).

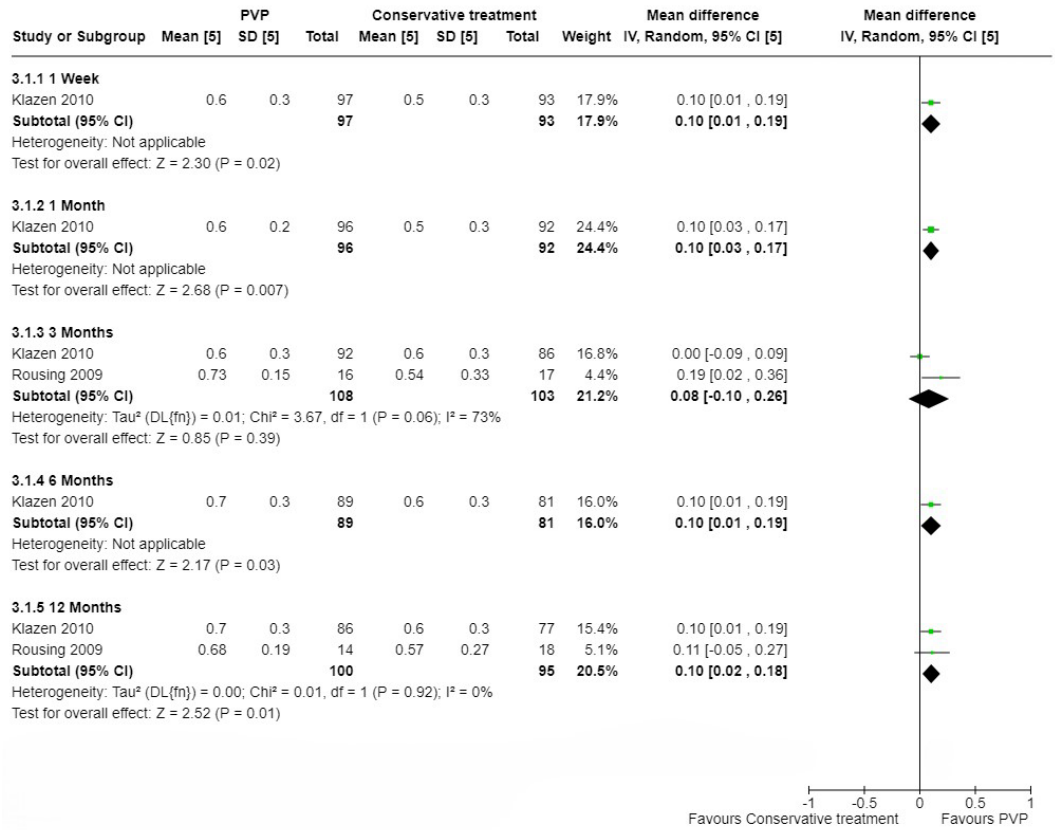


Figure 5: Mean Difference in Quality of Life (EQ-5D) for PVP Compared to CT

Figure shows the mean difference (95% CI) in quality of life as measured by EQ-5D for PVP compared to CT at follow-up timepoints ranging from 1 week to 12 months. Overall, there were small statistically significant differences favouring PVP at 1 week and at 1, 6, and 12 months follow-up. However, based on published minimal clinically important differences, these are unlikely to be clinically significant.

Abbreviations: CI, confidence interval; CT, conservative treatment; EQ-5D, EuroQol- 5 Dimension; PVP, percutaneous vertebroplasty; SD, standard deviation.

Jacobsen et al[38] noted that the baseline EQ-5D score significantly differed in Rousing et al,[64] with patients in the PVP group reporting higher EQ-5D scores compared to the CT group ($P < .05$). Baseline EQ-5D scores also differed in the trial by Klazen et al,[60] with patients in the PVP group reporting lower EQ-5D scores compared to the CT group ($P < .05$). Subgroup analyses were not performed by Jacobsen et al[38] because both studies[60,64] enrolled participants with OVCFs that were less than 8 weeks from onset.

Jacobsen et al[38] identified 4 RCTs[57,60,66,67] that used the quality of life questionnaire of the European Foundation for Osteoporosis (QUALEFFO), which ranges from 0 to 100, with 0 indicating a high quality of life and 100 indicating a poor quality of life. Overall, there was a significant difference in QUALEFFO scores at 1 week and 3 months follow-up (Figure 6). For all other follow-up times (2 weeks and 1, 2, 6, and 12 months), there were no significant differences in QUALEFFO scores between PVP and CT. Of note, there were considerable levels of heterogeneity ($I^2 \geq 80\%$) at all follow-up timepoints.[38]

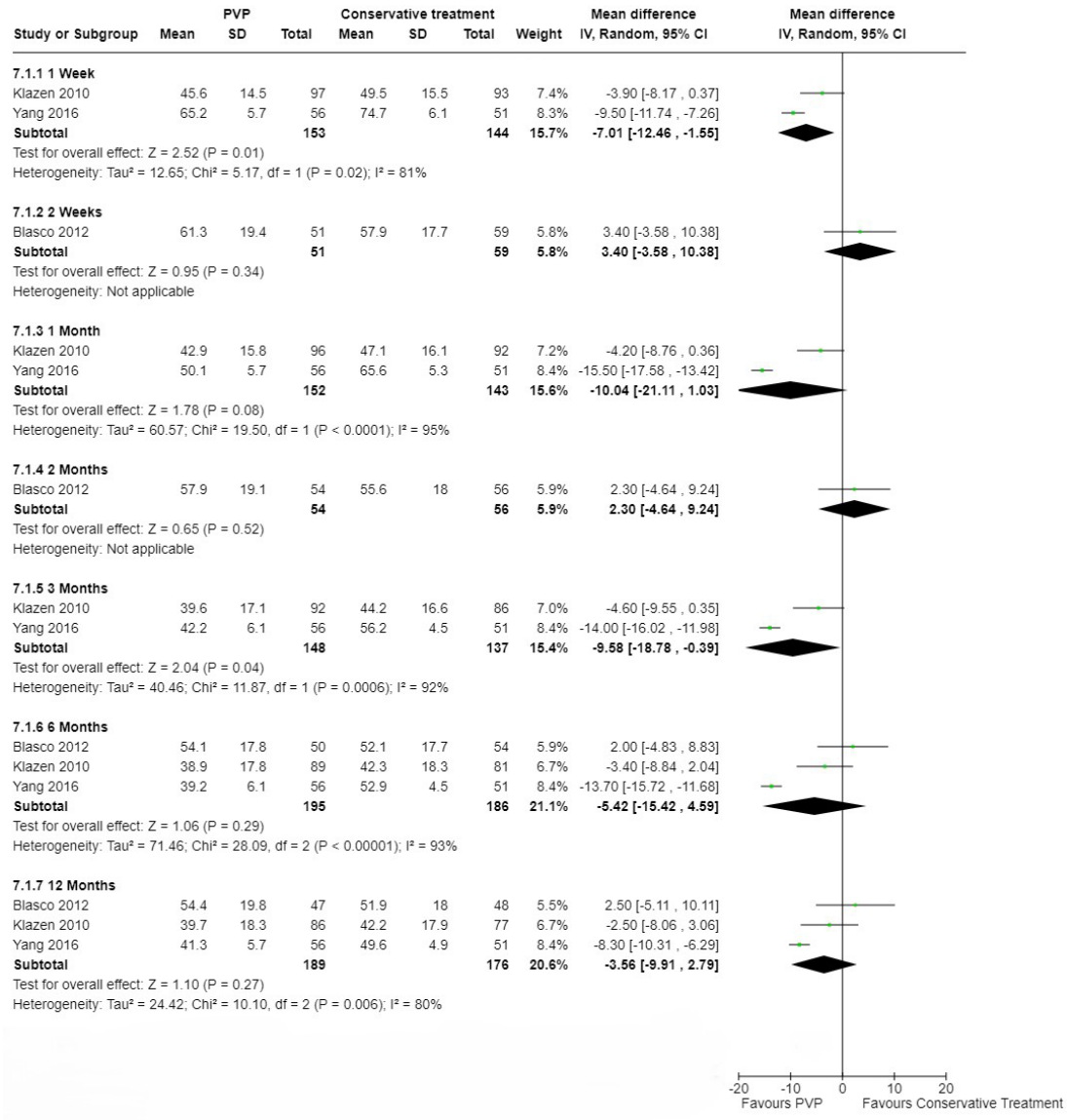


Figure 6: Mean Difference in Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) for PVP Compared to CT

Figure shows the mean difference (95% CI) in quality of life as measured by QUALEFFO for PVP compared to CT at follow-up timepoints ranging from 1 week to 12 months. Overall, there was a significant difference in QUALEFFO scores at 1 week and 3 months follow-up. For all other follow-up times (2 weeks and 1, 2, 6, and 12 months), there were no significant differences in QUALEFFO scores between PVP and CT.
Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty; QUALEFFO, quality of life questionnaire of the European Foundation for Osteoporosis; SD, standard deviation.

Subgroup analysis of the results for duration of painful OVCFs that are less than or more than 8 weeks since onset are presented in Figures A7 and A8 (Appendix 3). Analysis of OVCFs of less than 8 weeks (2 RCTs[60,67]) showed significant differences in QUALEFFO scores favouring PVP over CT at 1 week (mean difference [MD]: −7.01; 95% CI: −12.46 to −1.55) and at 3 (MD: −9.58; 95% CI: −18.78 to −0.39) and 12 (MD: −8.87; 95% CI: −18.95 to 1.20) months follow-up. For OVCFs of more than 8 weeks (1 RCT[57]), there were no significant differences favouring PVP over CT at any follow-up assessment.

One RCT[66] was not included in the meta-analysis by Jacobsen et al[38] because range was reported instead of standard deviation. The authors reported a significant difference between the PVP and CT groups at 2 weeks follow-up (Table 8).

Table 8: PVP Versus CT: Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO)

Author, year	Length of follow-up	PVP, mean (range)	CT, mean (range)	Mean difference (95% CI)	*P* value
Voormolen et al, 2007[66]	Baseline 2 weeks	60 (37–86) 53 (28–79)	67 (38–86) 67 (40–88)	— −14 (−24.7 to −3.4)	— < .05

Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty.

Jacobsen et al[38] identified 1 RCT[64] that compared results from the short form 36 questionnaire (SF-36) for patients who underwent PVP versus CT. The SF-36 covers 8 domains (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health), with higher scores indicating better health and functioning.[38]

Overall, there was no significant difference between PVP and CT groups for the physical or mental domains ($P > .05$) (Table 9).

Table 9: PVP Versus CT: Quality of Life (SF-36)

Author, year	Length of follow-up	PVP, mean (95% CI)	CT, mean (95% CI)	*P* value
Physical domain				
Rousing et al, 2009[64]	Baseline	36.7 (30.0–43.4)	33.4 (26.2–40.7)	—
	3 months	34.0 (30.1–37.9)	20.3 (24.5– 34.1)	.12
	12 months	32.1 (27.8–36.3)	30.5 (25.2–35.7)	.63
Mental domain				
Rousing et al, 2009[64]	Baseline	49.7 (43.6–55.8)	49.6 (41.9–57.3)	—
	3 months	48.9 (43.8– 54.0)	46.2 (39.2–53.2)	.51
	12 months	46.2 (39.2–53.2)	49.0 (43.9–54.1)	.93

Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty; SF-36, short form 36 questionnaire.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A4, Appendix 3).

All Cause Mortality

Five RCTs[57,59,60,63,64] reported all cause mortality. Overall, there was no statistically significant difference between the PVP and CT groups (RR = 0.72; 95% CI: 0.36–1.48) (Figure 7). The absolute risk for patients undergoing PVP was 3.1% (13/412) and 4.2% (18/424) for those who received CT. Jacobsen et al[38] reported that all deaths were deemed unrelated to PVP.

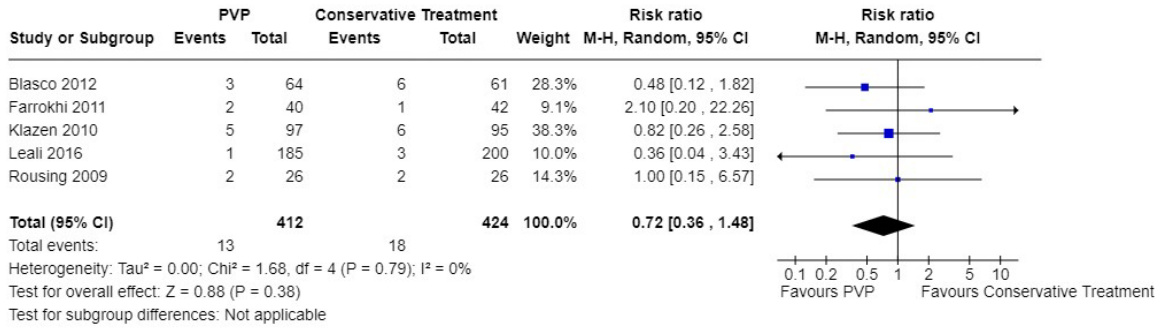


Figure 7: Meta-analysis of RCTs for All-Cause Mortality: PVP Compared to CT

Figure shows the risk ratio (95% CI) for all cause mortality for PVP compared to CT. Overall, there was no significant difference between the PVP and CT groups (RR = 0.72; 95% CI: 0.361.48).

Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty.

Jacobsen et al[38] identified 1 prospective, comparative observational study[79] that reported all cause and fracture-related mortality. There was no difference in mortality between the PVP and CT arms (*P* = .89); however, 1 fracture-related death was reported in the PVP arm and 4 fracture-related deaths in the CT arm (*P* = .05) (Table 10). The authors[38] concluded that the remaining deaths were unrelated to the intervention.

Table 10: PVP Versus CT: All-Cause and Fracture-Related Mortality (Observational Study)

Author, year	Length of follow-up	Mortality type	PVP, n/N (%)	CT, n/N (%)	Hazard ratio (95% CI)
Diamond et al, 2006[79]	24 months	All cause	15/88 (17.0%)	6/38 (15.8%)	1.07 (0.42–2.76) *P* = .89
Diamond et al, 2006[79]	24 months	Fracture related	1/15 (6.7%)	4/6 (66.7%)	0.11 (0.01–0.96) *P* = .05

Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty.

We identified 1 additional prospective, noncomparative observational study[51] that reported 66.4% (186/280) of patients died within 10 years after receiving PVP. Aregger et al[51] reported a mortality rate of 30% at 4 years and 50% at 6 years.[51]

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A4, Appendix 3).

Adverse Events

In the RCT by Klazen et al,[60] there were no serious adverse events in the PVP (0/101) or the CT (0/101) groups. One observational study reported on serious adverse events at 24 months follow-up, also finding no significant difference between PVP (0/88 patients) and CT (0/38 patients).[79]

Six RCTs[47,59,60,63,66,67] reported on adverse events in people who underwent PVP compared with CT. Overall, there was no significant difference between the treatment groups (RR: 1.28; 95% CI: 0.30–5.51)

(Figure 8). The absolute risk was 3.9% (13/330 patients) for PVP and 5.2% (18/344 patients) for CT. One RCT, by Klazen et al,[60] reported adverse events in the PVP trial arm but not in the CT arm and was not included in the meta-analysis. The authors did report 3 perioperative adverse events: pain-induced vasovagal reaction (n = 2) and an asthma exacerbation (n = 1). PVP was successfully completed in all patients who experienced these adverse events.[60]

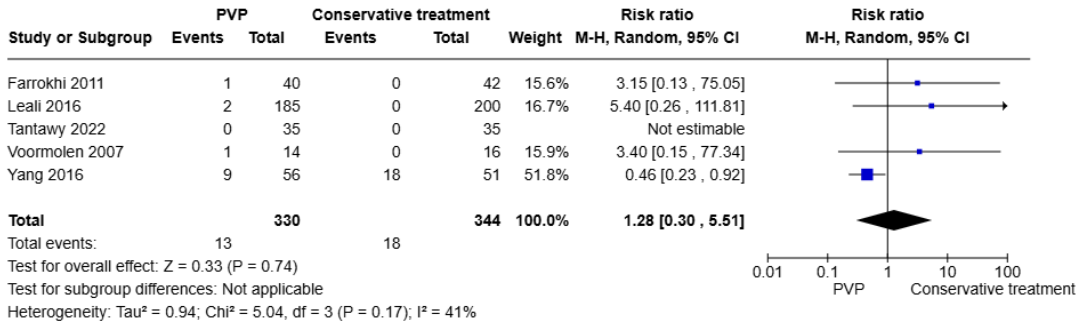


Figure 8: Meta-analysis of RCTs for Any Adverse Events: PVP Compared to CT

Figure shows the risk ratio (95% CI) for any adverse events for PVP compared to CT. Overall, there was no significant difference between the treatment groups (RR: 1.28; 95% CI: 0.30–5.51).
Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty.

Jacobsen et al[38] identified 2 prospective observational studies[77,79] comparing PVP and CT that reported on adverse events. The absolute rate of adverse events was 2.5% (n = 3/118) in the PVP trial arm and 0.0% (n = 0/68) in the CT arm (Table 11). The adverse events included a fracture of transverse processes (n = 2) and a psoas muscle hematoma (n = 1).

Table 11: PVP Versus CT: Any Adverse Events (Observational Studies)

Author, year	Length of follow-up	PVP, n/N (%)	CT, n/N (%)	*P* value
Andrei et al, 2017[77]	12 months	0/30 (0.0%) patients	0/30 (0.0%) patients	NR
Diamond et al, 2006[79]	24 months	3/88 (3.4%) patients	0/38 (0.0%) patients	NR
Absolute rate	**12–24 months**	**3/118 (2.5%) patients**	**0/68 (0.0%) patients**	**—**

Abbreviations: CT, conservative treatment; NR, not reported; PVP, percutaneous vertebroplasty.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A4, Appendix 3).

New Fractures

Symptomatic Fractures

Jacobsen et al[38] identified 5 RCTs[57-59,63,67] that reported evidence on new, symptomatic OVCFs. Overall, there was no statistically significant difference between PVP and CT groups (RR: 1.50; 95% CI: 0.32–7.10) (Figure 9). The absolute risk was 8.7% (34/389) for PVP and 7.8% (18/394) for CT. Two studies noted that the new symptomatic fracture was adjacent to the initial fracture.[59,63] Three studies did not specify location of the new fracture in relation to the old fracture.[57,58,67]

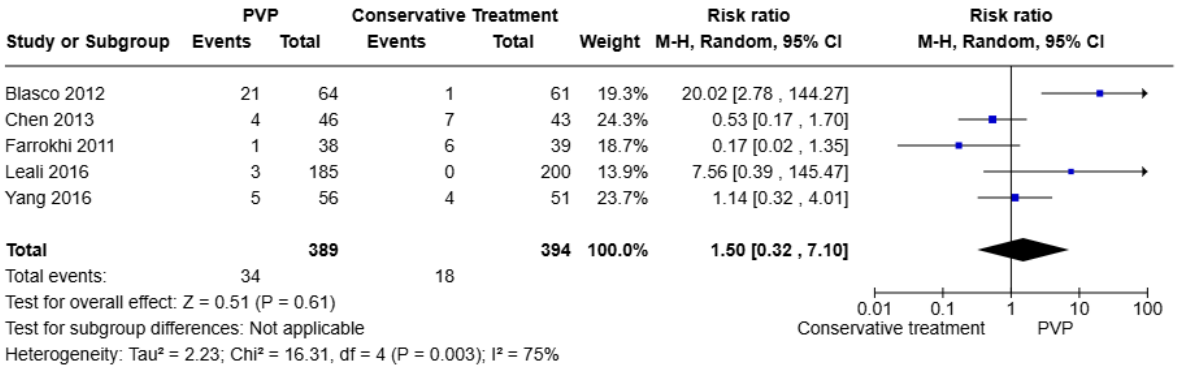


Figure 9: Meta-analysis of RCTs for Symptomatic New Fractures: PVP Compared to Conservative Treatment

Figure shows the risk ratio (95% CI) for symptomatic new fractures for PVP compared to CT. Overall, there was no statistically significant difference between the PVP and CT groups.

Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty.

Jacobsen et al[38] identified 1 prospective, comparative observational study[78] that provided evidence on new symptomatic fractures. At 6 weeks follow-up, 3 patients in the PVP group (3.4%) reported recurrent back pain attributable to new fractures; however, Jacobsen et al[38] stated new fractures in the CT group were not reported by the primary study authors. By 24 months, 18 new symptomatic fractures were reported in the PVP group, 11 of which were treated with PVP. According to Jacobsen et al,[38] the number of patients per treatment arm and location of the new fractures relative to the original fracture were not reported.

Radiographic Fractures

Jacobsen et al[38] identified 4 RCTs[57,60,64,67] that reported evidence on new radiographic OVCFs. Overall, there was no statistically significant difference between PVP and CT groups (RR: 1.46; 95% CI: 0.46–4.58) (Figure 10). The absolute risk was 23.4% (55/235) for PVP and 19.5% (43/220) for CT.

Three RCTs[57,60,64] noted that the new symptomatic fracture was adjacent to the initial fracture. One RCT[67] did not specify the new fracture location in relation to the old fracture.

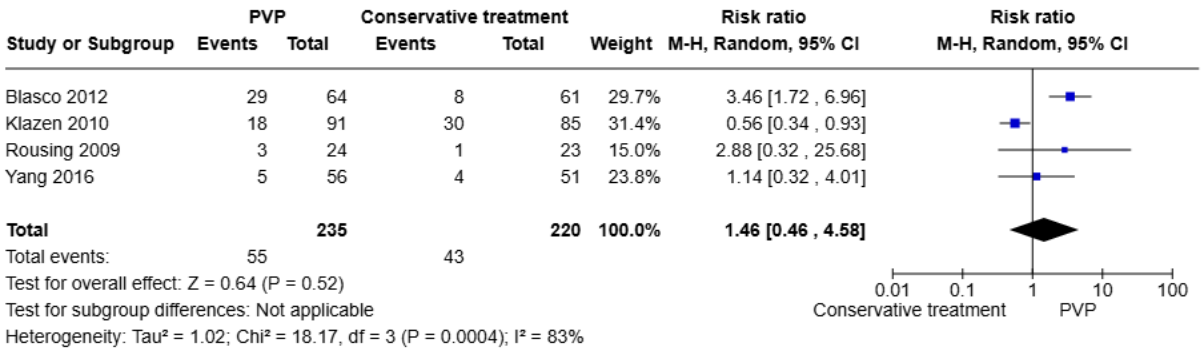


Figure 10: Meta-analysis of RCTs for Radiographic New Fractures: PVP Compared to CT

Figure shows the risk ratio (95% CI) for radiographic new fractures for PVP compared to CT. Overall, there was no significant difference between the PVP and CT groups.

Abbreviations: CI, confidence interval; CT, conservative treatment; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

The RCT by Tantawy et al[47] did not explicitly report whether new fractures were determined by symptoms or radiography. The authors stated that 2/35 PVP patients and 0/35 CT patients experienced new fractures during the 3 month follow-up period.

Comparative Observational Studies

Jacobsen et al[38] identified 1 prospective, comparative observational study (Diamond et al[79]), which found no significant difference between PVP (9/88 [10.2%]) and CT (4/38 [10.5%]) groups (*P* = .52) regarding new radiographic OVCFs at 24 months follow-up.

Single Arm Observational Studies

Our updated literature search identified 1 single arm case series study of people who underwent PVP. Aregger et al[51] conducted a prospective case series and reported that 26/49 patients (53%) experienced new OVCFs within 10 years after PVP. We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A4, Appendix 3).

Cement Leakage

Jacobsen et al[38] found 6 RCTs[57-59,61,64,67] that reported cement leakage following PVP. Five reported the incidence of cement leak per vertebrae treated,[57-59,61,67] and 1 reported no symptomatic leaks.[64] The absolute rate of cement leaks per treated vertebrae was 36.7% (238/648) and the range varied from 14.0% (n = 14/100) to 72.0% (97/134) (Table 12). One RCT reported a symptomatic leak that resulted in extremity pain and weakness.[59]

Table 12: PVP Versus CT: Cement Leakage (RCTs)

Author, year	Length of follow-up	Cement leakage per vertebra	Symptomatic or asymptomatic
Blasco et al, 2012[57]	12 months	69/140 (49.0%) treated vertebrae	Asymptomatic
Chen et al, 2014[58]	12 months	36/69 (52.0%) treated vertebrae	Asymptomatic
Farrokhi et al, 2011[59]	36 months	14/100 (14.0%) treated vertebrae	1 symptomatic patient 13 asymptomatic patients
Klazen et al, 2010[61]	12 months	97/134 (72.0%) treated vertebrae	Asymptomatic
Rousing et al, 2009[64]	12 months	Not reported	Asymptomatic
Yang et al, 2016[67]	12 months	22/65 (33.8%) treated vertebrae	Asymptomatic
Absolute estimate	12 to 36 months	238/648 (36.7%) treated vertebrae	

Abbreviations: CT, conservative treatment; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

No comparative observational studies were identified that reported on cement leakage. Sixteen single-arm observational studies reported cement leakage following PVP (Table A3, Appendix 3). This includes 15 studies from the systematic review by Jacobsen et al[38] and 1 additional study[54] identified in our updated literature search. Most studies reported cement leak per vertebrae treated. The absolute rate of cement leaks per treated vertebrae was 38.6% (1,145/2,968) (Table A3, Appendix 3). On a per-patient basis, 4.0% (8/200) of patients reported cement leaks. There were 4 symptomatic cement leaks, which caused nerve root irritation and cement embolism. The remaining cement leaks were asymptomatic (Table A4, Appendix 3).

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A5, Appendix 3).

PVP Compared With Sham

Pain

Six RCTs[48,49,68,71,73,75] provided evidence on pain, as measured by the numerical rating score (NRS) or VAS, from 1 day to 24 months posttreatment. The RCTs used different methods of assessing pain, although all trials measured pain on a 10-point scale, with 0 representing no pain and 10 representing the worst pain. Three RCTs[48,49,73] measured pain using the VAS and 3[68,71,75] used the NRS scale.

There were statistically significant differences favouring PVP at 1 month (MD: −0.61; 95% CI: −1.04 to −0.18), 3 months (MD: −0.62; 95% CI: −1.09 to −0.14), 6 months (MD: −0.69; 95% CI: −1.18 to −0.20), and 12 months (MD: −0.61; 95% CI: −1.11 to −0.12) follow-up (Figure 11). The clinical significance of these results is uncertain based on published MCIDs (Table A9, Appendix 3).[38]

Subgroup analysis of the results for duration of painful OVCF that are less than or more than 8 weeks since onset are presented in Figures A9 and A10 (Appendix 3). Analysis of OVCFs of less than 8 weeks (3 RCTs[49,71,73]) showed significant differences in pain scores favouring PVP over sham at 3 days (MD: −1.70; 95% CI: −2.60 to −0.80) and 2 weeks (MD: −1.20; 95% CI: −2.26 to −0.14) follow-up. For OVCFs of more than 8 weeks (3 RCTs[48,68,75]), there were significant differences in pain scores favouring PVP at 1 month (MD: −0.76; 95% CI: −1.47 to −0.04), 3 months (MD: −0.99; 95% CI: −1.72 to −0.26), and 12 months (MD: −0.92; 95% CI: −1.66 to −0.18) follow-up.

Subgroup analysis for the use of VAS or NRS are presented in Figures A11 and A12 (Appendix 3). Subgroup analysis of RCTs[48,49,73] that used VAS[48,49,73] showed no significant difference at any of the

follow-up timepoints. There were significant differences in RCTs[68,71,75] that used NRS[68,71,75] at the 1 month (MD: −0.98; 95% CI: −1.69 to −0.28), 3 month (MD: −0.92; 95% CI: −1.68 to −0.16), and 6 month (MD: −0.83; 95% CI: −1.62 to −0.05) follow-ups.

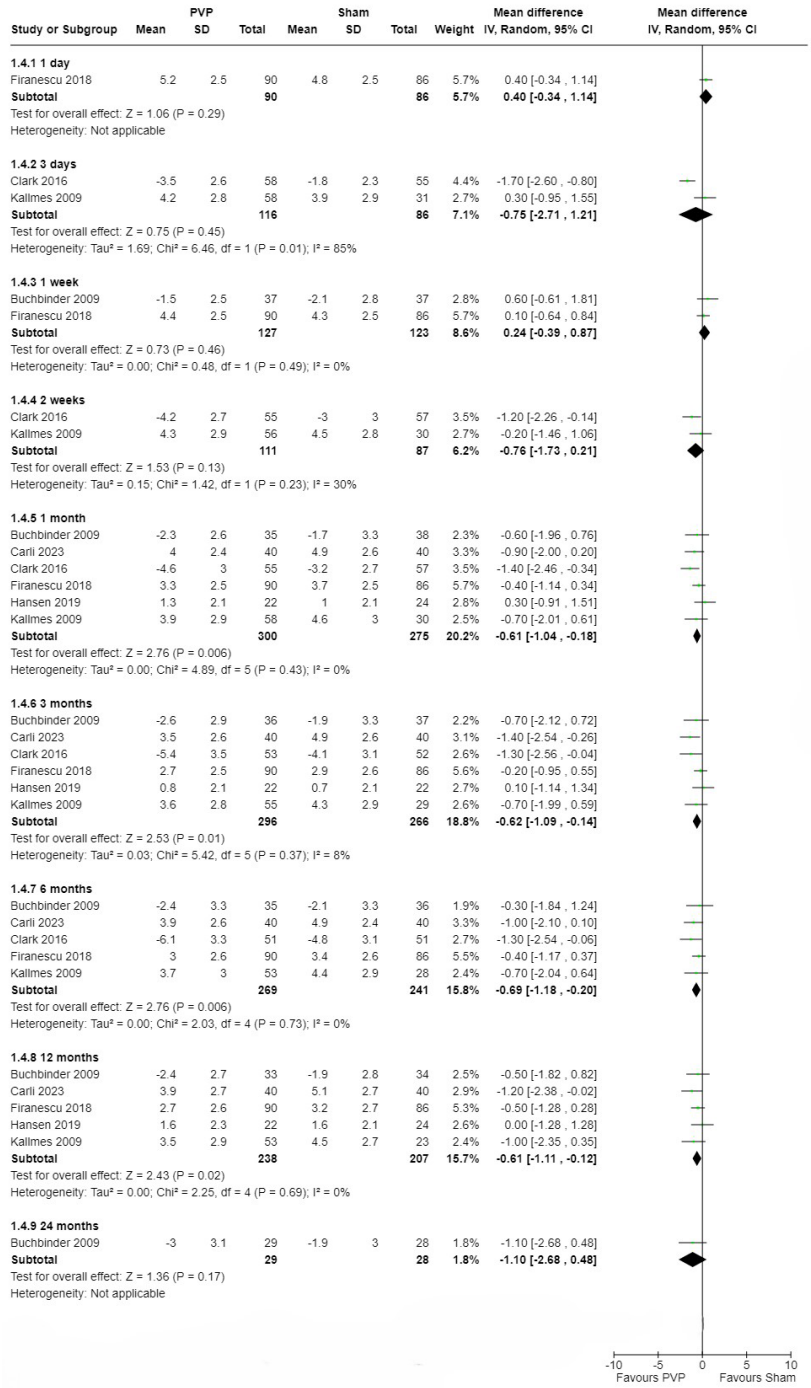


Figure 11: Meta-analysis of RCTs for Pain (VAS or NRS): PVP Compared to Sham

Figure shows the mean difference (95% CI) for pain as measured by VAS or NRS for PVP compared to sham at follow-up timepoints ranging from 1 day to 24 months. There were significant differences favouring PVP at 1, 3, 6, and 12 months follow-up. The clinical significance of these results is uncertain based on published minimum clinically important differences.

Abbreviations: CI, confidence interval; NRS, numerical rating score; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial; SD, standard deviation; VAS, visual analogue scale.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and inconsistency (Table A6, Appendix 3).

Use of Analgesics

Six RCTs[48,49,68,71,73,75] provided evidence on the number of patients using analgesics, from 1 day to 12 months posttreatment. Four RCTs[48,71,73,75] were included in the meta-analysis and 2[49,68] were not. Hansen et al[49] stated "at 0–12 weeks and at 12 month follow-up there were a similar amount and frequency of opioids in the two groups"; no further data were reported. Buchbinder et al[68] did not report explicit data (numerator and denominator) for each follow-up timepoint.

There were no statistically significant differences between PVP and the sham groups at any follow-up timepoint (Figure 12).

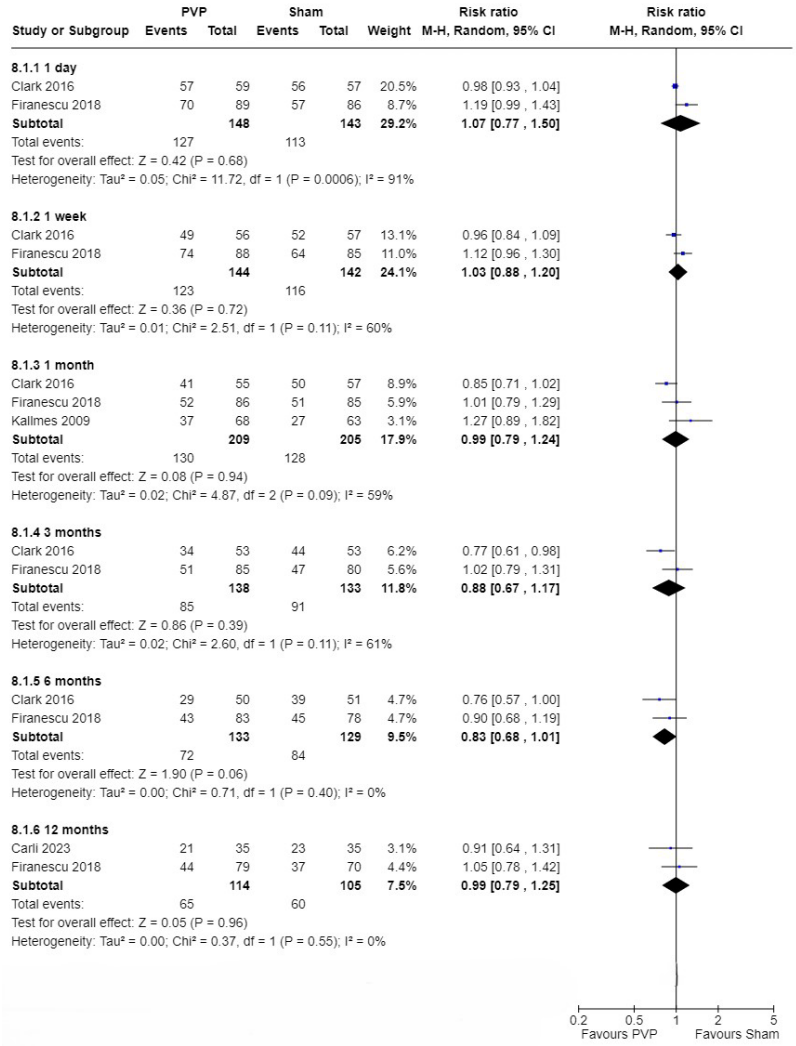


Figure 12: Meta-analysis of RCTs for Use of Analgesics: PVP Compared to Sham

Figure shows the mean difference (95% CI) for use of analgesics for PVP compared to sham at follow-up timepoints ranging from 1 day to 12 months. There were no statistically significant differences between the PVP and sham groups at any follow-up timepoint.
Abbreviations: CI, Confidence Interval; PVP, Percutaneous Vertebroplasty; RCT, randomized controlled trial.

Subgroup analysis of the results for duration of painful OVCFs that are less than or more than 8 weeks since onset are presented in Figures A13 and A14 (Appendix 3). No significant differences were observed between PVP and sham. We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, indirectness, and imprecision (Table A6, Appendix 3).

Physical Function

Four RCTs[48,68,73,75] provided evidence on function, as measured by RMDQ, from 1 day to 24 months follow-up. Two[68,75] used the modified 0 to 23 point RMDQ scale and one[73] used the 0 to 24 point RMDQ scale. In contrast, Carli et al[48] used a RMDQ scale that ranged from 0 to 100. For all scales, higher scores indicated decreasing physical functioning and increasing physical impairment.

Overall, there were no statistically significant differences between PVP and sham groups at all follow-up timepoints except at 3 months posttreatment (standardized mean difference [SMD] −0.21; 95% CI: −0.41 to −0.02) (Figure 13). Based on published MCIDs, the clinical significance is uncertain (Table A9, Appendix 3).[38]

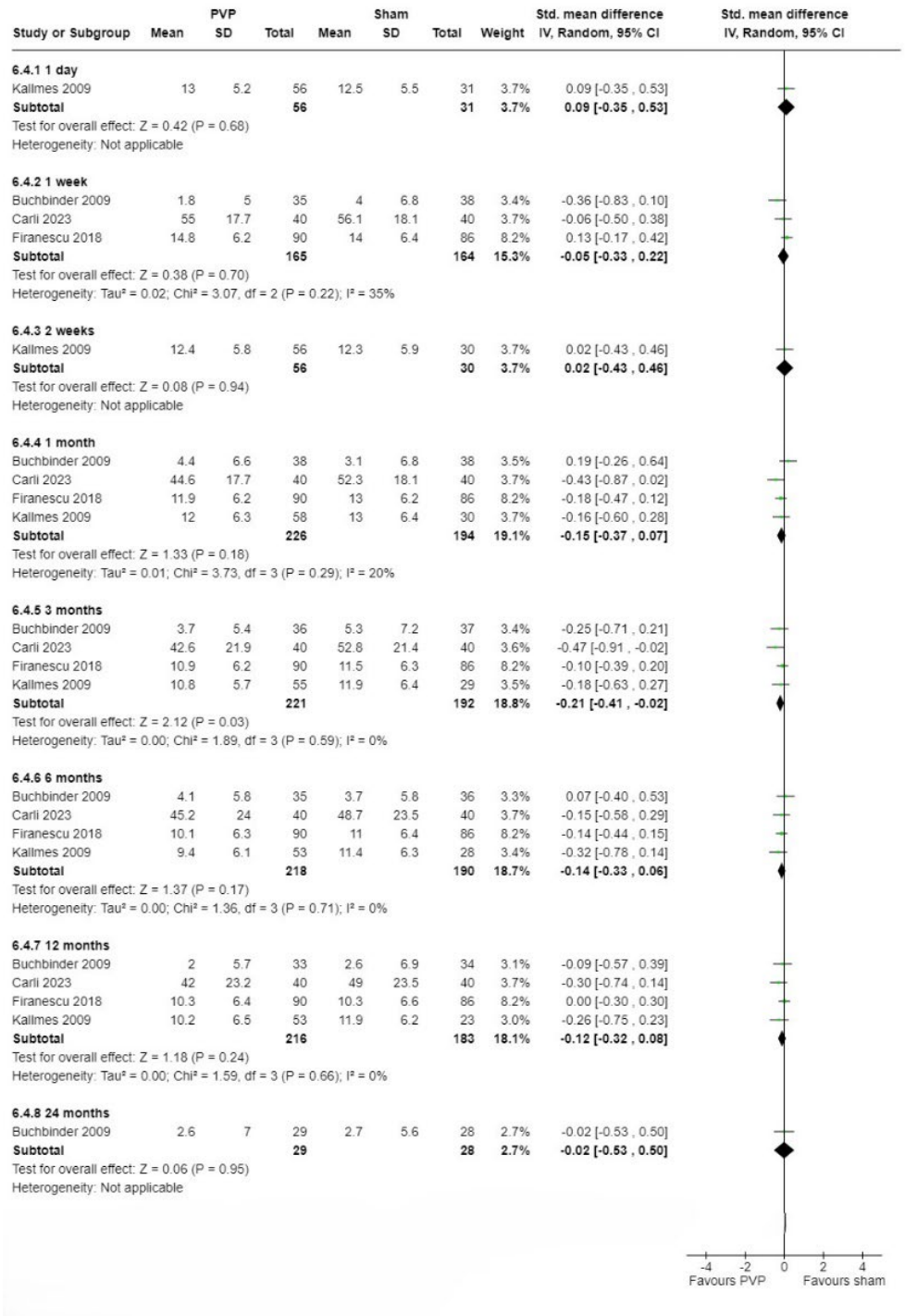


Figure 13: Meta-analysis of RCTs for Roland-Morris Disability Questionnaire: PVP Compared to Sham

Figure shows the standardized mean difference (95% CI) for physical function as measured by the Roland-Morris Disability Questionnaire for PVP compared to sham at follow-up timepoints ranging from 1 day to 24 months. Overall, there were no significant differences between PVP and sham groups at all follow-up timepoints except at 3 months posttreatment. Based on published minimum clinically important differences, the clinical significance is uncertain.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

Subgroup analysis of the results for duration of painful OVCFs that are less than or more than 8 weeks since onset are presented in Figures A15 and A16 (Appendix 3). There was no significant difference in the mean difference of RMDQ scores between PVP and sham for OVCFs that were less than 8 weeks old. No significant differences in the SMD were observed in RMDQ scores between PVP and sham for OVCFs more than 8 weeks old, except at the 3-month follow-up timepoint, which favoured PVP (SMD: −0.30; 95% CI: −0.56 to −0.04).

One RCT[68] provided evidence on "timed up-and-go" scores at 12 and 24 months follow-up.[68] However, the authors did not report statistical significance between the PVP and sham groups; therefore, it is unclear whether the groups differed (Table 13).

Table 13: PVP Versus Sham: Timed Up and Go Scores (RCTs)

Author, year	Length of follow-up	PVP, mean ± SD	Sham, mean ± SD	*P* value
Buchbinder et al, 2009[68]	Baseline	20.5 ± 8.8 s	29.0 ± 15.0 s	NR
	12 months	−2.6 ± 12.2 s	4.3 ± 13.4 s	NR
	24 months	3.5 ± 17.1 s	4.7 ± 9.7 s	NR

Abbreviations: NR, not reported; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial; SD, standard deviation.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A6, Appendix 3).

Quality of Life

Four studies[49,68,71,75] (including 1 RCT[49] that we identified in our literature search) provided evidence on EQ-5D scores from 1 month to 24 months follow-up. [38]

Overall, there was no statistically significant difference between PVP and sham at 3, 12, and 24 months follow-up (Figure 14). However, there was a statistically significant difference between PVP and sham at 1 and 6 months favouring PVP (MD: 0.05; 95% CI: 0.01–0.08, and MD: 0.06; 95% CI: 0.01–0.10, respectively). These results do not surpass the lower bounds of published MCIDs (Table A9, Appendix 3).

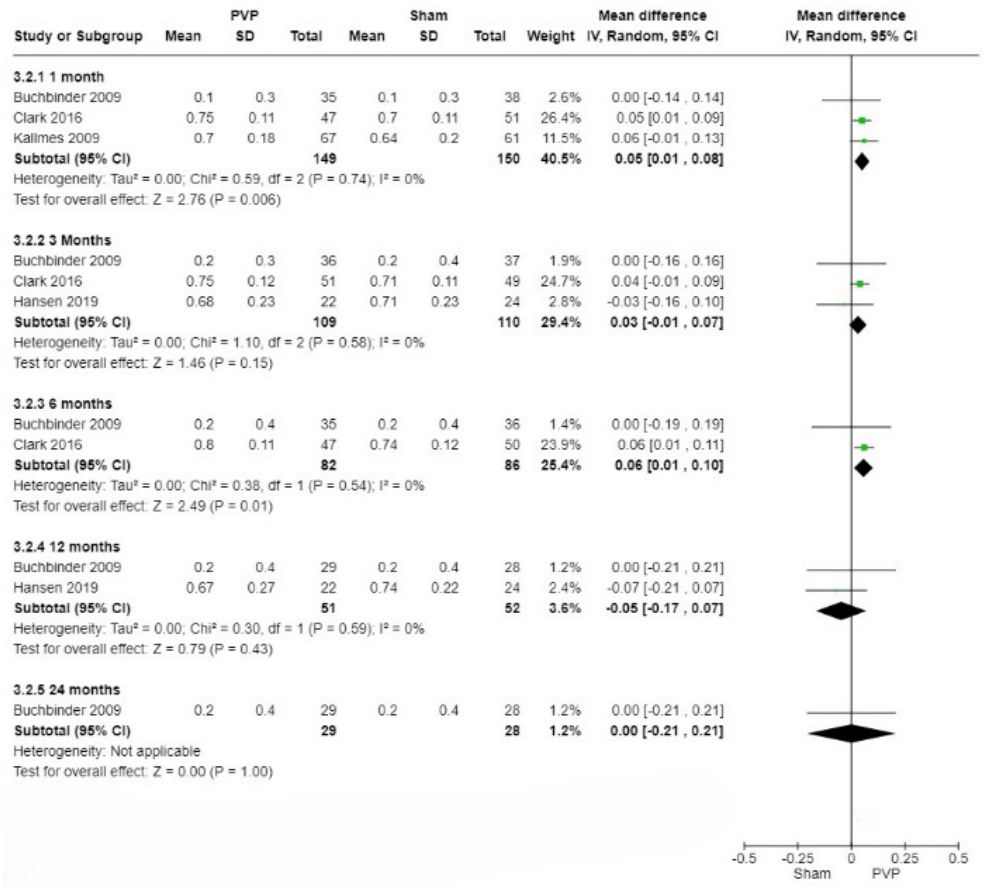


Figure 14: Meta-analysis of RCTs for Quality of Life (EQ-5D): PVP Versus Sham

Figure shows the mean difference (95% CI) for quality of life as measured by EQ-5D for PVP compared to sham at follow-up timepoints ranging from 1 to 24 months. Overall, there was no significant difference between PVP and sham at 3, 12, and 24 months follow-up. However, there was a significant difference between PVP and sham at 1 and 6 months favouring PVP. However, these results do not surpass the lower bounds of published minimum clinically important differences.

Abbreviations: CI, confidence interval; EQ-5D, EuroQol- 5-dimension; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial; SD, standard deviation.

The RCTs differed with regard to the mean age of fractures (<[49,71] or >[68,75] 8 weeks). Subgroup analysis related to the age of the OVCFs (< or > 8 weeks) are presented in Figures A17 and A18 (Appendix 3). For fractures less than 8 weeks since onset, there was a statistically significant difference between PVP and sham at 1 and 6 months favouring PVP. For fractures of more than 8 weeks, no statistically significant differences were observed in the mean difference of EQ-5D scores between PVP and the sham groups.

Four RCTs[48,68,71,73] reported evidence on quality of life as measured by QUALEFFO from 1 day to 24 months follow-up. Overall, there were no statistically significant differences between PVP and sham groups at any timepoint except the 2 week follow-up (MD: −6.00; 95% CI: −11.24 to −0.76), which was based on 1 RCT[71] with wide confidence intervals (Figure 15).

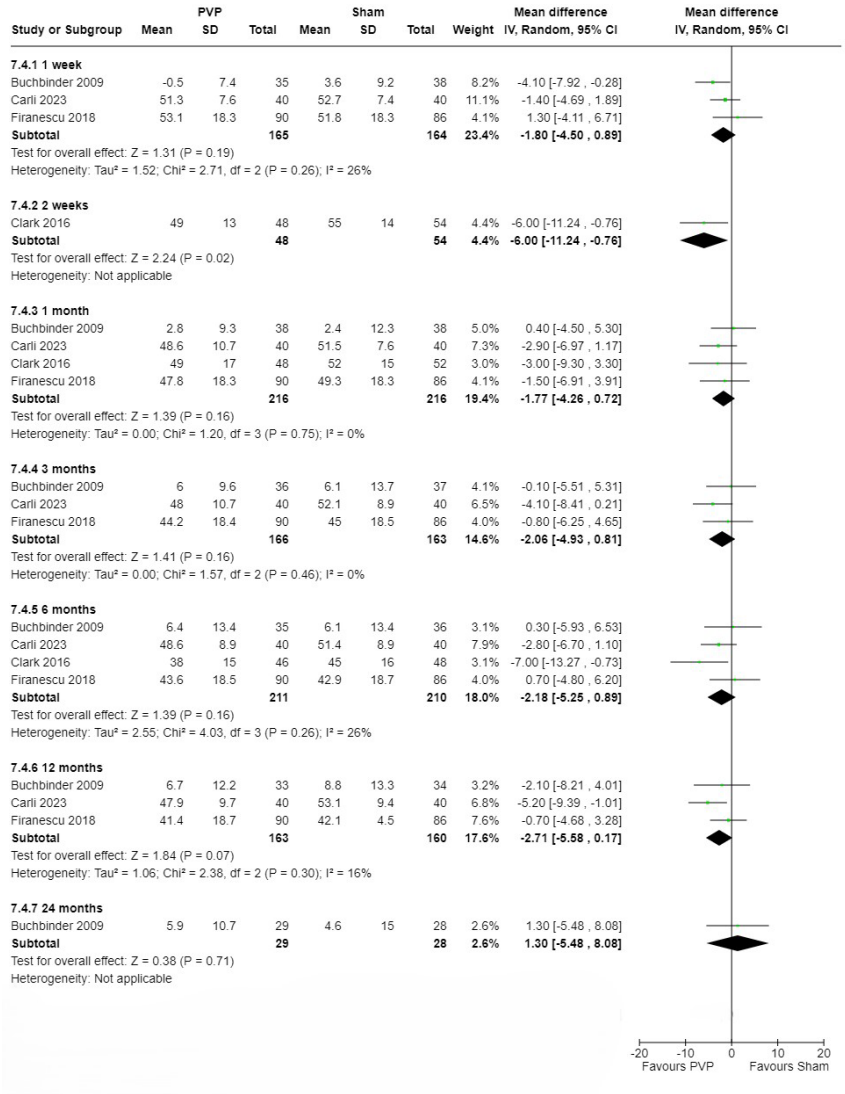


Figure 15: Meta-analysis of RCTs for QUALEFFO: PVP Compared to Sham

Figure shows the mean difference (95% CI) for quality of life as measured by QUALEFFO for PVP compared to sham at follow-up timepoints ranging from 1 week to 24 months. Overall, there were no significant differences between PVP and sham groups at any timepoint except the 2 week follow-up, which was based on 1 RCT with wide confidence intervals.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; QUALEFFO, International Osteoporosis Foundation Quality of Life Questionnaire; RCT, randomized controlled trial; SD, standard deviation.

Subgroup analysis related to the age of the OVCFs that are less than or more than 8 weeks since onset are presented in Figures A19 and A20 (Appendix 3). For fractures less than 8 weeks, there was a statistically significant difference between PVP and sham at 2 weeks follow-up favouring PVP. However, no statistically significant differences were observed at any other follow-up timepoints. For fractures more than 8 weeks, no statistically significant differences were observed in the mean difference of QUALEFFO scores between PVP and the sham groups.

One RCT[75] reported the Study of Osteoporotic Fractures–Activities of Daily Living questionnaire (SOF-ADL) scores at 1 month follow-up for PVP compared with sham; no statistically significant difference was observed ($P > .05$) (Table 14).

Table 14: PVP Versus Sham: Study of Osteoporotic Fractures–Activities of Daily Living Questionnaire

Author, year	Length of follow-up	PVP, mean ± SD	Sham, mean ± SD	*P* value
Kallmes et al, 2009[75]	Baseline 1 month	10.0 ± 3.6 7.7 ± 3.7	10.3 ± 2.8 8.2 ± 3.6	NR 0.51

Abbreviations: NR, not reported; PVP, percutaneous vertebroplasty; SD, standard deviation.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A6, Appendix 3).

Mortality

Jacobsen et al[38] identified 4 RCTs that reported all cause mortality.[68,71,73,75] Overall, there was no statistically significant difference in all cause mortality between patients who underwent PVP compared to sham (RR: 0.94; 95% CI: 0.50–1.76) (Figure 16).

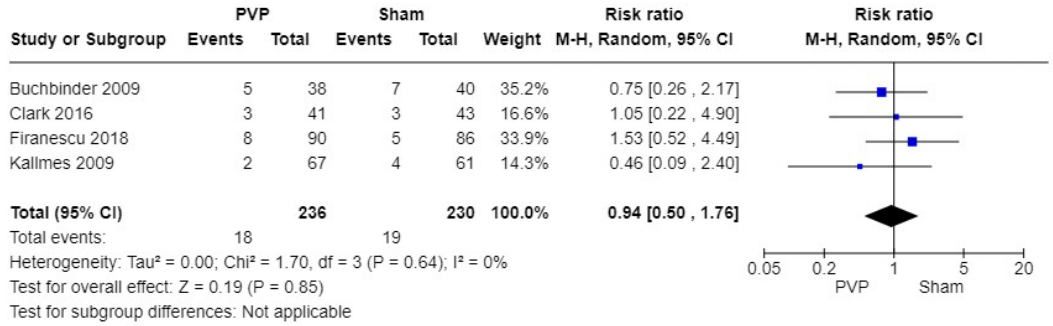


Figure 16: Meta-analysis of RCTs for All-Cause Mortality: PVP Compared to Sham

Figure shows the risk ratio (95% CI) for all-cause mortality for PVP compared to sham. There was no significant difference in all-cause mortality between patients who underwent PVP compared to sham

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

We rated the overall quality of evidence (GRADE) as Low, downgrading for inconsistency and imprecision (Table A6, Appendix 3).

Adverse Events

Four RCTs[48,68,71,75] reported data specifically for severe adverse events. Overall, there was no statistically significant difference between PVP and sham groups (RR: 0.86; 95% CI: 0.28–2.69) (Figure 17). The absolute risk was 2.4% (n = 5/207) for PVP and 2.9% (n = 6/202) for the sham group.

The reporting of severe adverse events differed between the included studies. Only 1 study provided a definition of a severe adverse event.[71] Two RCTs[48,75] reported the number of events per patient. Buchbinder et al[68] did not specify whether the events were per patient or total events.

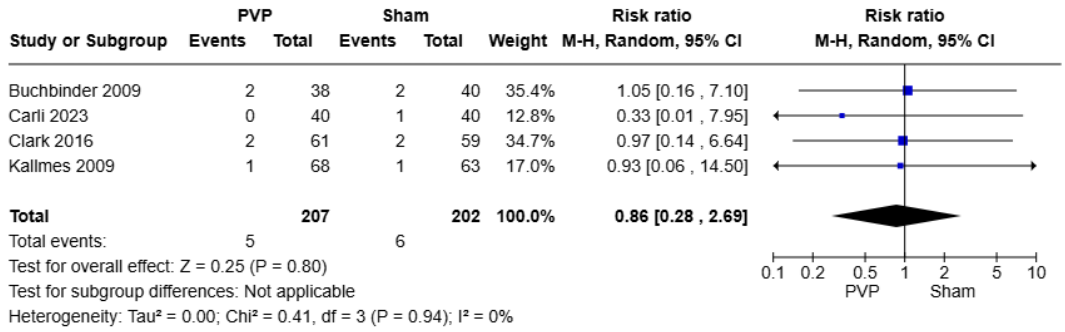


Figure 17: Meta-analysis of RCTs for Severe Adverse Events: PVP Compared to Sham

Figure shows the risk ratio (95% CI) for severe adverse events for PVP compared to sham. There was no significant difference between PVP and sham groups.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

Serious adverse events in the PVP group included injury to the thecal sac,[75] osteomyelitis,[68] tightness in the back or rib cage,[68] respiratory arrest, and humerus fracture.[71] Serious adverse events in the sham group included tightness in the back or rib cage,[68] tachycardia and rigors of unknown cause,[75] and spinal cord compression.[48,71]

Jacobsen et al[38] identified 2 RCTs[68,73] that reported any adverse events. Overall, there was a statistically significant increase in adverse events in the PVP group compared with the sham group (RR: 2.41; 95% CI: 1.06–5.52) (Figure 18). Of note, the 95% CI of the risk ratio for the RCT by Firanescu et al[73] was very broad (RR: 4.89; 95% CI: 0.24–100.47).

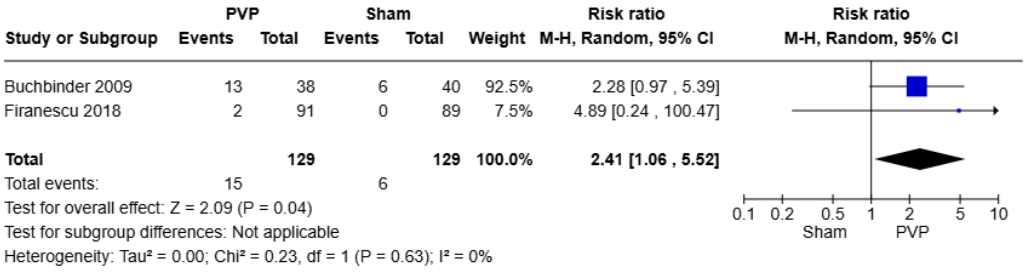


Figure 18: Meta-analysis of RCTs for Any Adverse Events: PVP Versus Sham

Figure shows the risk ratio (95% CI) for any adverse events for PVP compared to sham. There was a significant increase in adverse events in the PVP group compared with the sham group. Of note, the 95% CI of the risk ratio for one of the 2 RCTs was very broad.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

Adverse events reported by Buchbinder et al[68] in both study arms were pain (leg, chest, stomach), muscle cramping near the puncture site, and tightness in the back or ribcage.[68] Chest pain and osteomyelitis were reported only in the PVP arm.[68] Firanescu et al[73] reported respiratory insufficiency related to underlying severe chronic obstructive pulmonary disease and a vasovagal reaction in the PVP arm and no adverse events in the sham arm.[73]

We rated the overall quality of evidence (GRADE) as Low, downgrading for inconsistency and imprecision (Table A6, Appendix 3).

New Fractures

Symptomatic Fractures

Two RCTs[48,68] reported new OVCFs after patients received PVP or a sham procedure. There was no statistically significant difference in new OVCFs between patients who underwent PVP or sham (RR: 1.07; 95% CI: 0.66–1.73) (Figure 19). Carli et al[48] did not explicitly state whether the new OVCFs were identified via symptoms alone or radiography. Neither RCT explicitly stated the location of the new OVCF relative to the index OVCF.

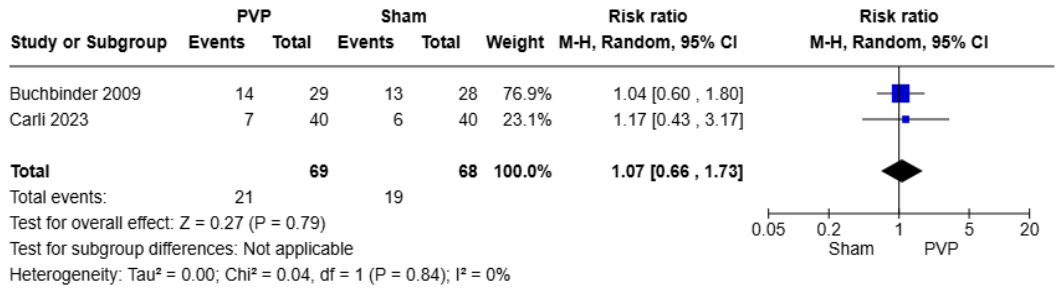


Figure 19: Meta-analysis of RCTs for Symptomatic New Fractures: PVP Compared to Sham

Figure shows the risk ratio (95% CI) for symptomatic new fractures for PVP compared to sham. There was no significant difference in new OVCFs between patients who underwent PVP or sham.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

Radiographic Fractures

Three RCTs[68,71,73] provided evidence regarding new radiographic fractures for people who received PVP compared with sham treatment. Overall, there was no statistically significant difference in new radiographic fractures between PVP and the sham group (RR: 1.11; 95% CI: 0.70–1.74) (Figure 20).

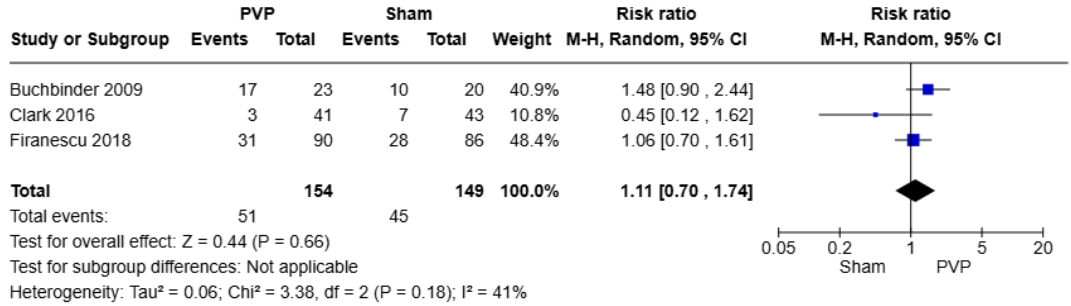


Figure 20: Meta-analysis of RCTs for Radiographic New Fractures: PVP Compared to Sham

Figure shows the risk ratio (95% CI) for radiographic new fractures for PVP compared to sham. There was no significant difference in new radiographic fractures between the PVP and sham groups.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

We rated the overall quality of evidence (GRADE) as Low, downgrading for inconsistency and imprecision (Table A6, Appendix 3).

Cement Leakage

Jacobson et al[38] identified 3 RCTs[68,71,73] comparing PVP with sham that reported cement leakage. We identified 1 additional RCT[48] in our updated literature search (Table 15). The absolute rate of cement leaks per treated vertebrae was 61.8% (149/241). The range varied from 69.8% (44/63) to 91.3% (105/115). When assessed on a per patient basis, cement leakage was 39.4% (39/99). The range varied from 34.4% (21/61) to 37.0% (18/38). Patients in 3 RCTs[68,71,73] were asymptomatic[68,71,73] and 1 RCT[48] did not report whether leakage was asymptomatic or symptomatic.

Table 15: PVP Versus Sham: Cement Leakage

Author, year	Length of follow-up	Cement leakage per vertebra	Symptomatic or asymptomatic
Buchbinder et al, 2009[68]	24 months	18/38 (37.0%) patients	Asymptomatic
Clark et al, 2016[71]	6 months	21/61 (34.4%) patients	Asymptomatic
Firanescu et al, 2018[73]	12 months	105/115 (91.3%) treated vertebrae	Asymptomatic
Carli et al, 2023[48]	12 months	(44/63) 69.8% treated vertebrae	NR
Absolute estimate	6–12 months	149/241 (61.8%) treated vertebrae 39/99 (39.4%) patients	—

Abbreviation: NR, Not Reported; PVP, percutaneous vertebroplasty.

We rated the overall quality of evidence (GRADE) as Low, downgrading for inconsistency and imprecision (Table A6, Appendix 3).

PBK Compared With Conservative Treatment

Pain

Jacobsen et al[38] identified 3 RCTs[97,98,100] that provided data on pain, as measured by VAS, from 1 day to 24 months posttreatment. Overall, there were statistically significant differences favouring PBK at 1 and 3 days, 1 week, and at 3, 6, 12, and 24 months (Figure 21). However, there was no statistically significant difference between PBK and CT in pain improvement via VAS scores at 1 month. Based on published MCIDs, the summary estimates at 1 day, 3 days, 1 week, and 3 months likely translate into clinically significant improvements in pain (Table A9, Appendix 3).[38]

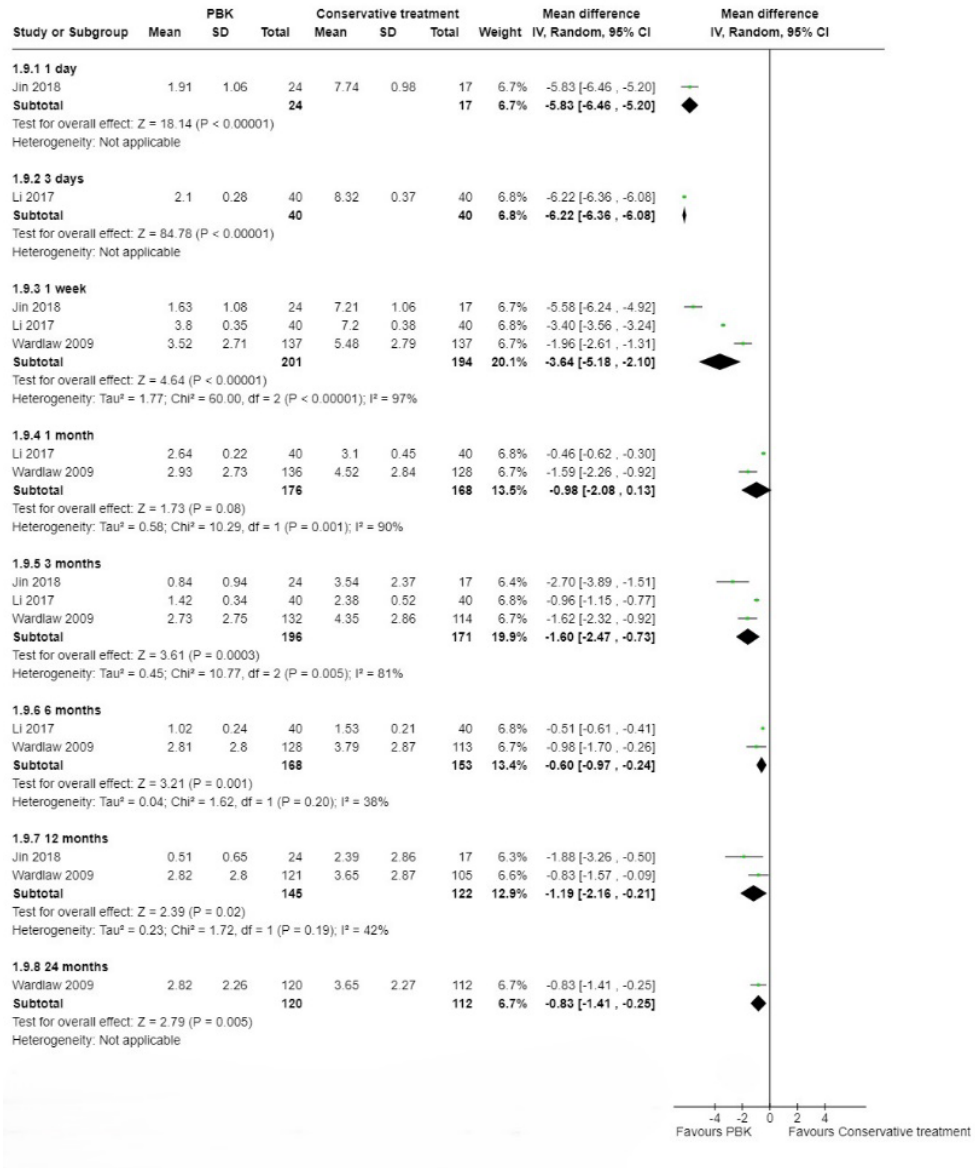


Figure 21: Meta-analysis of RCTs for Pain (Visual Analogue Scale): PBK Compared to CT

Figure shows the mean difference (95% CI) for pain as measured by the visual analogue scale for PBK compared to CT at follow-up timepoints ranging from 1 day to 24 months.

Abbreviations: CI, confidence interval; CT, conservative treatment; PBK, percutaneous balloon kyphoplasty; RCT, randomized controlled trial; SD, standard deviation.

While observational studies were not included in effectiveness outcomes for PVP versus CT or PVP versus sham, it appears Jacobsen et al[38] included observational studies for PBK versus CT due to the few RCTs that assessed effectiveness of PBK versus CT. The authors identified 2 prospective comparative observational studies[104,107] that measured VAS in patients who underwent PBK or CT from 3 to 12 months postintervention.

Overall, both observational studies concluded that there were statistically significant differences between PBK and CT groups at 12 months (Table 16). Kasperk et al[104] used an inverted VAS scale where

a score of 0 indicates maximal pain, while Movrin et al[107] used a scale where a score of 10 corresponds to maximal pain.[107] Of note, there was a significant difference in the mean baseline VAS scores (Table 16) between arms in the study by Movrin et al.[107] Kasperk et al[104] did not report whether the mean baseline scores for the study arms were significantly different.

Table 16: PBK Versus CT: Pain (Visual Analogue Scale)

Author, year	Length of follow-up	PBK, mean ± SD	CT, mean ± SD	*P* value
Kasperk et al, 2005[104]	Baseline	26.2 ± 12.6	33.6 ± 18.3	NR
	3 months	42.4 ± 17.9	33.9 ± 18.4	.012
	6 months	44.2 ± 20.9	35.6 ± 18.3	.019
	12 months	44.4 ± 19.7	34.3 ± 19.5	.008
Movrin et al, 2010[107]	Baseline	8.8 ± 8.1	6.7 ± 7.8	< .001
	12 months	2.0 ± 1.2	3.8 ± 1.5	< .001

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty; SD, standard deviation.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A7, Appendix 3).

Use of Analgesics

Jacobsen et al[38] identified 1 RCT (Wardlaw et al[100]) that provided evidence on pain assessed by use of analgesics from 1 to 12 months. Overall, the number of people taking any analgesic or a combination of analgesics (non-opioid and opioid) was smaller in the PBK group compared to the CT group (Table 17).[38] The number of people using non-opioid and strong-opioid analgesics did not change greatly throughout the follow-up period;[38] however, the authors did not report statistical significance, which limits the conclusions of the study.[38]

Table 17: PBK Versus CT: Analgesic Use at 1 and 12 Months Follow-Up Reported in RCT by Wardlaw et al[100]

Follow-up timepoints	Type of analgesic	PBK, n/N	CT, n/N	*P* value
Baseline	Any analgesic	132/140 (94%)	135/146 (92%)	NR
	Non-opioid	29/140 (21%)	36/146 (25%)	
	Combination	81/140 (58%)	82/146 (56%)	
	Strong opioid	22/140 (16%)	17/146 (12%)	
1 month	Any analgesic	81/114 (71%)	105/115 (91%)	NR
	Non-opioid	28/114 (25%)	31/115 (27%)	
	Combination	47/114 (41%)	65/115 (57%)	
	Strong opioid	6/114 (5%)	9/115 (8%)	
12 months	Any analgesic	61/117 (52%)	69/101 (68%)	NR
	Non-opioid	28/117 (24%)	32/101 (32%)	
	Combination	28/117 (24%)	35/101 (35%)	
	Strong opioid	5/117 (4%)	5/101 (5%)	

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty; RCT, randomized controlled trial.

Jacobsen et al[38] identified 1 prospective comparative observational study[104] that assessed the use of analgesics. People in the PBK group reduced opioid use more than people in the CT group; however, neither statistical significance between study arms nor the follow-up time were reported (Table 18).[38]

Table 18: PBK Versus CT: Analgesic Use Reported in Observational Study by Kasperk et al[104]

Follow-up timepoints	PBK, n/N	CT, n/N	*P* value
Baseline	27/40 (67.0%)	14/20 (70%)	NR
NR	22/40 (55.0%)	13/20 (65%)	NR

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, indirectness, and imprecision (Table A7, Appendix 3).

Physical Function

Jacobsen et al[38] identified 1 RCT that provided evidence on function as measured by RMDQ from 1 week to 24 months posttreatment. Wardlaw et al[100] reported statistically significant differences between the PBK and CT groups at 1 week and 1, 3, 6, and 12 months follow-up. However, there was no significant difference at 24 months posttreatment (Table 19). Jacobsen et al[38] stated that the clinical impact is uncertain.

Table 19: PBK Versus CT: Results for Function (Roland Morris Disability Questionnaire) Reported in RCT by Wardlaw et al[100]

Author, year	Length of follow-up	PBK, mean ± SD	CT, mean ± SD	*P* value
Wardlaw et al, 2009[100]	Baseline	16.9 ± 5.1	17.0 ± 4.3	NS
	1 week	16.9 ± 4.2	17.0 ± 4.3	NR
	1 month	10.9 ± 4.3	15.1 ± 4.3	< 0.0001
	3 months	9.2 ± 4.4	12.9 ± 4.4	< 0.0001
	6 months	8.5 ± 4.4	11.5 ± 4.5	< 0.0001
	12 months	8.6 ± 4.5	11.5 ± 4.5	< 0.001
	24 months	8.9 ± 4.5	10.3 ± 4.5	.06

Abbreviations: CT, conservative treatment; NR, not reported; NS, not significant; PBK, percutaneous balloon kyphoplasty; RCT, randomized controlled trial; SD, standard deviation.

Jacobsen et al[38] also identified a prospective, comparative observational study that measured RMDQ from 3 to 12 months posttreatment. Overall, Eidt-Koch et al[102] reported significant differences between the mean scores of the PBK and CT groups at all follow-up timepoints, but standard deviation was not reported for any of the mean scores (Table 20).

Table 20: PBK Versus CT: Results for Function (Roland Morris Disability Questionnaire) Reported in Observational Study by Eidt-Koch et al[102]

Author, year	Length of follow-up	PBK, mean ± SD	CT, mean ± SD	*P* Value
Eidt-Koch et al, 2011[102]	Baseline	15.2 ± NR	14.4 ± NR	.31
	3 months	10.3 ± NR	14.4 ± NR	.004
	6 months	8.8 ± NR	14.4 ± NR	.000
	12 months	8.9 ± NR	13.7 ± NR	.001

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty; SD, standard deviation.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A7, Appendix 3).

Quality of Life

Jacobsen et al[38] identified 1 study that provided evidence related to the EQ-5D, from 1 month to 24 months postintervention. Wardlaw et al[100] reported a statistically significant difference between PBK and CT groups from 1 to 24 months (Table 21). Statistical differences at 1 week were not reported in the study. The authors stated that the clinical impact is uncertain.[38]

Table 21: PBK Versus CT: Results for Quality of Life (EQ-5D)

Author, year	Length of follow-up	PBK (n = 149), mean ± SD	CT (n = 151), mean ± SD	*P* value
Wardlaw et al, 2009[100]	Baseline	0.16 ± 1.03	0.17 ± 0.99	NS
	1 month	0.54 ± 1.03	0.37 ± 1.04	< .0001
	3 months	0.59 ± 1.07	0.49 ± 1.04	.002
	6 months	0.63 ± 1.03	0.50 ± 1.04	.0009
	12 months	0.61 ± 1.03	0.51 ± 1.09	.006
	24 months	0.61 ± 0.30	0.53 ± 0.32	.04

Abbreviations: CT, conservative treatment; EQ-5D, EuroQol 5 dimensions questionnaire; NS, not significant; PBK, percutaneous balloon kyphoplasty; SD, standard deviation.

Jacobsen et al[38] identified 2 RCTs that assessed the physical domain of the SF-36 questionnaire from 1 to 24 months follow-up (Table 22). Jin et al[97] found significant differences between PBK and CT groups at 12 months follow-up (*P* = .02). Wardlaw et al[100] noted significant differences between PBK and CT at 1, 3, and 6 months, but not at 12 and 24 months (Table 22).

Table 22: PBK Versus CT: Results for Quality of Life (SF-36)

Author, year	Length of follow-up	PBK, mean ± SD	CT, mean ± SD	*P* value
Jin et al, 2018[97]	12 months	78.1 ± 11.5	64.5 ± 20.3	.02
Wardlaw et al, 2009[100]	Baseline	26.0 ± 5.5	25.5 ± 5.0	NS
	1 month	33.4 ± 5.6	27.5 ± 5.6	< .0001
	3 months	35.6 ± 5.6	31.1 ± 5.8	< .0001
	6 months	36.4 ± 5.6	32.6 ± 5.7	.001
	12 months	35.9 ± 5.6	33.8 ± 5.8	.1
	24 months	35.8 ± 5.6	33.8 ± 5.8	.1

Abbreviations: CT, conservative treatment; SF-36, short-form 36 questionnaire; NS, not significant; PBK, percutaneous balloon kyphoplasty; SD, standard deviation.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A7, Appendix 3).

Mortality

Jacobsen et al[38] identified 1 RCT that provided evidence on all-cause mortality. Wardlaw et al[100] reported that, by 12 months, there were 9 deaths (out of 149 patients, 6.0%) in the PBK arm and 7 deaths (out of 151, 4.6%) in the CT arm (*P* value not reported). All deaths were deemed unrelated to the

intervention. The authors[38] identified 1 observational study that provided evidence on all-cause mortality. Kasperk et al[105] reported 1 death (out of 40 patients, 2.5%) in the PBK arm and 3 deaths (out of 20, 15.0%) in the CT arm by 36 months follow-up (*P* value not reported). All deaths were deemed unrelated to the intervention.[38]

We identified an additional observational registry study[52] of 38,034 US Medicare enrollees (median age: 80.5 years; interquartile range: 74.4–86.4 years) who had PBK within 180 days of an OVCF. Within 30 days post-PBK, 278 patients died (0.7%). Within 6 months post-PBK, 2,291 patients died (6.0%), and within 1 year, 3,781 patients died (9.9%).[117]

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A7, Appendix 3).

Adverse Events

Jacobsen et al[38] identified 1 RCT that reported data on severe adverse events (Table 23). Wardlaw et al[100] reported that, at 12 months follow-up, there were 58 severe adverse events in the PBK group and 54 in the CT group. It is unclear whether any individual person experienced more than 1 adverse event. The most common severe adverse events were cardiovascular, vascular, and respiratory disorders and back pain, while infection, anaemia, neoplasms, and nervous system and psychiatric disorders were infrequent adverse events.[38] Wardlaw et al[100] reported that 2 severe events were attributed to PBK: a surgical site hematoma and a urinary tract infection. No severe adverse events were attributed to CT.[38]

Table 23: PBK Versus CT: Severe Adverse Events

Author, year	Severe adverse event	PBK, n/N (%)	CT, n/N (%)	*P* value
Wardlaw et al, 2009[100]	All events	58/NR	54/NR	NR
	Procedure-related events	2/149 (1.3%)	0/151 (0.0%)	

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty.

Jacobsen et al[38] identified 3 RCTs[98-100] that reported data on any adverse events. The RCTs were not meta-analyzed since it is unclear whether they reported the number of people experiencing an adverse event or the total number of adverse events.[38] One RCT[98] reported that there were no events in either trial arm, while another[99] reported a statistically significant difference in adverse events; however, the length of follow-up was not reported (Table 24). The third RCT[100] reported no statistically significant difference between PBK and CT.

Table 24: PBK Versus CT: Any Adverse Events

Author, year	Length of follow-up	PBK, n	CT, n	*P* value
Li et al, 2017[98]	6 months	0	0	NR
Liu et al, 2019[99]	NR	1	9	< .05
Wardlaw et al, 2009[100]	12 months	130	122	> .05
Total		**131**	**131**	

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty.

Jacobsen et al[38] identified 1 prospective, comparative observational study that provided data on severe adverse events at 36 months follow-up. Overall, Kasperk et al[105] reported no statistically significant difference in the number of adverse events between the PBK (0/40 patients) and CT (0/20 patients) groups (*P* value not reported). We identified 1 prospective case series that reported adverse events after PBK. Nguyen et al[53] reported that intercostal neuralgia occurred in 2/65 patients (3.1%), but they did not report length of follow-up.[53]

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A7, Appendix 3).

New Fractures

Symptomatic Fractures

Jacobsen et al[38] identified 1 RCT that provided evidence on new symptomatic OVCFs at 12 months follow-up. Wardlaw et al[100] found that 14% percent of patients (21/149) in the PBK group reported new symptomatic fractures. The incidence of new symptomatic fractures in the CT group was not reported. It was unclear whether the fractures were adjacent to the initial fracture. A 24 month follow-up reported no statistically significant difference in the number of subsequent painful OVCFs between the PBK and CT groups (26/149 [17.4%] and 17/151 [11.3%], respectively, *P* = .12).[100]

Jacobsen et al[38] identified 1 observational study that provided evidence on new symptomatic OVCFs. Kasperk et al[105] reported that there were 7 new symptomatic fractures in 3/34 (8.8%) PBK patients by the end of 36 months of follow-up. It was unclear whether the fractures were adjacent to the initial fracture. The Kasperk authors did not report data for patients who received conservative treatment.

Radiographic Fractures

Jacobsen et al[38] found 1 RCT that provided evidence on new radiographic OVCFs at 12 months follow-up. Wardlaw et al[100] reported no statistically significant difference in new radiographic OVCFs between the PBK (38/115 [33.0%] patients) and CT (24/95 [25.2%] patients) groups (*P* = .20). It was unclear whether fractures were adjacent to the initial fracture. A 24 month follow-up reported no statistically significant difference in the number of subsequent OVCFs identified by radiographs between the PBK and CT groups (56/118 [47.5%] and 45/102 [44.1%], respectively, *P* = .24).[118] At 24 months, 28 of 118 patients (23.7%) in the PBK group and 17 of 102 (16.7%) in the CT group had fractures adjacent to the index fracture (*P* = .24).[118] Of note, at 24 months, data were available for a total of 232 patients (120 PBK and 112 CT). Sixty-eight patients were no longer participating in the study.[118]

Jacobsen et al[38] identified 2 observational studies[105,107] that provided evidence on new radiographic OVCFs (Table 25). There were no statistically significant differences between PBK and CT groups in terms of new radiographic fractures when assessed on a per-treated vertebrae[105] (*P* = .59) or a per patient[107] (*P* = .12) basis.[107]

Table 25: PBK Versus CT: Radiographic New Fractures in Observational Studies

Author, year	Length of follow-up	PBK, n/N (%)	CT, n/N (%)	*P* value
Kasperk et al, 2010[105]	36 months	7/72 (9.7%) treated vertebrae	4/29 (13.8%) treated vertebrae	.59
Movrin et al, 2010[107]	12 months	3/46 (6.5%) patients	10/61 (16.4%) patients	.12

Abbreviations: CT, conservative treatment; PBK, percutaneous balloon kyphoplasty.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A7, Appendix 3).

Cement Leakage

Jacobsen et al[38] stated 2 RCTs reported cement leakage after PBK (Table 26).[99,100] The absolute rate per treated vertebrae was 27.1% (51/188). The rate of cement leakage per patient was 23.7% (49/207), ranging from 1.7% (1/58)[99] to 32.2% (48/149).[100] Wardlaw et al[100] stated that all the cement leaks were asymptomatic. However, Liu et al[99] did not report whether cement leaks were symptomatic or asymptomatic.

Table 26: PBK Versus CT: Cement Leakage in RCTs

Author, year	Length of follow-up	PBK, n/N (%)	Symptomatic or asymptomatic
Liu et al, 2019[99]	NR	1/58 (1.7%) patients	NR
Wardlaw et al, 2009[100]	12 months	51/188 (27.1%) treated vertebrae 48/149 (32.2%) patients	Asymptomatic
Absolute estimate		49/207 (23.7%) patients 51/188 (27.1%) treated vertebrae	—

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty.

Jacobsen et al[38] reported that 3 comparative observational studies[103,105,107] reported cement leakage after PBK by either the incidence per vertebrae treated or per patient (Table 27). The absolute rate per treated vertebrae was 11.3% (11/97), ranging from 9.7% (7/72)[105] to 16.0% (4/25).[103] The rate per patient was 8.7% (4/46).[107] The leaks were asymptomatic in 2 studies[103,105]; however, the third (Movrin et al[107]) did not report whether the leaks were symptomatic or asymptomatic.

Table 27: PBK Versus CT: Cement Leakage in Observational Studies

Author, year	Length of follow-up	PBK, n/N (%)	Symptomatic or asymptomatic
Kasperk et al, 2010[105]	36 months	7/72 (9.7%) treated vertebrae	Asymptomatic
Giannotti et al, 2012[103]	24 months	4/25 (16.0%) treated vertebrae	Asymptomatic
Movrin et al,2010[107]	12 months	4/46 (8.7%) patients	NR
Absolute estimate	12–36 months	11/97 (11.3%) treated vertebrae 4/46 (8.7%) patients	—

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty.

Seven single arm studies[53,85,93,108-111] reported cement leakage after PBK by either the incidence of cement leak per vertebrae treated, per patient, or both (Table 28). The absolute rate per treated vertebrae was 27.5% (385/1,402), ranging from 5.2% (7/135) to 73.4% (157/214). The rate per patient was 4.5% (30/731), ranging from 0.5% (3/564) to 30.8% (20/65).

Four leaks led to cement embolism, hemiparesis, heart perforation, and emergency surgery. The remaining cases were asymptomatic (Table 28).

Table 28: PBK Versus CT: Cement Leakage in Single Arm Studies

Author, year	Length of follow-up	PBK, n/N (%)	Symptomatic or asymptomatic
Dohm et al, 2014[85]	24 months	157/214 (73.4%) treated vertebrae	1 symptomatic (cement embolism), remaining asymptomatic
Hillmeier et al, 2004[108]	12 months	13/192 (6.8%) treated vertebrae	Asymptomatic
Hubschle et al, 2014[109]	12 months	201/819 (24.5%) treated vertebrae	4 symptomatic, remaining asymptomatic
Prokop et al, 2012[110]	6 months	3/564 (0.5%) patients 16% (not reported whether per patient or per vertebrae)	3 symptomatic (hemiparesis, cement embolism leading to heart perforation, and cement-filled stents requiring emergency surgery)
Robinson et al, 2008[111]	6 months	7/102 (6.9%) patients 7/135 (5.2%) treated vertebrae	Asymptomatic
Santiago et al, 2010[93]	12 months	7/42 (16.7%) treated vertebrae	Asymptomatic
Nguyen et al, 2020[53]	3 months	20/65 (30.8%) patients	NR
Absolute estimate	3–24 months	385/1,402 (27.5%) treated vertebrae 30/731 (4.5%) patients	—

Abbreviations: CT, conservative treatment; NR, not reported; PBK, percutaneous balloon kyphoplasty.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias and imprecision (Table A7, Appendix 3).

PVP Compared With PBK

Pain

We identified 6 RCTs that reported on pain (VAS or NRS) in people who underwent PVP or PBK. We included 5 of these RCTs[85,112-115] in our meta-analysis. Overall, there was no statistically significant difference in pain between PVP and PBK at 1, 3, 6, 12, and 24 months follow-up (Figure 22). There was a statistically significant difference at 3 days posttreatment favouring PVP (mean difference: −0.31; 95% CI: −0.52 to −0.10) (Figure 22).

We excluded the RCT by Wang et al[50] because it did not report any information about the time of follow-up, whether patients failed conservative treatment, or the time interval between initial pain onset and time of PVP or PBK. The authors did report a significant difference in pain scores (VAS) favouring PBK (mean: 4.21; SD: 1.01) compared with PVP (mean: 6.98; SD: 1.03), $P < .05$. [50]

Subgroup analysis by duration of pain from onset to time of PVP or PBK was not undertaken due to unclear reporting by all the primary studies except for the RCT by Liu et al.[114] This study included people who underwent PVP or PBK within 43 days of injury. The authors reported that there was a significant difference in pain at 3 days posttreatment (favouring PVP), but no significant difference in pain between patients who had PVP compared with those who had PBK at the 6 month follow-up (Figure 22).

Dohm et al[85] included patients who had OVCFs within 6 months of enrolment. Evans et al[112] included patients who experienced pain within the last 12 months. Bae et al[115] included patients who failed conservative management for at least 6 weeks, but not longer than 1 year. Wang et al[113] included patients who had unsatisfactory pain relief after at least 4 weeks of conservative treatment.

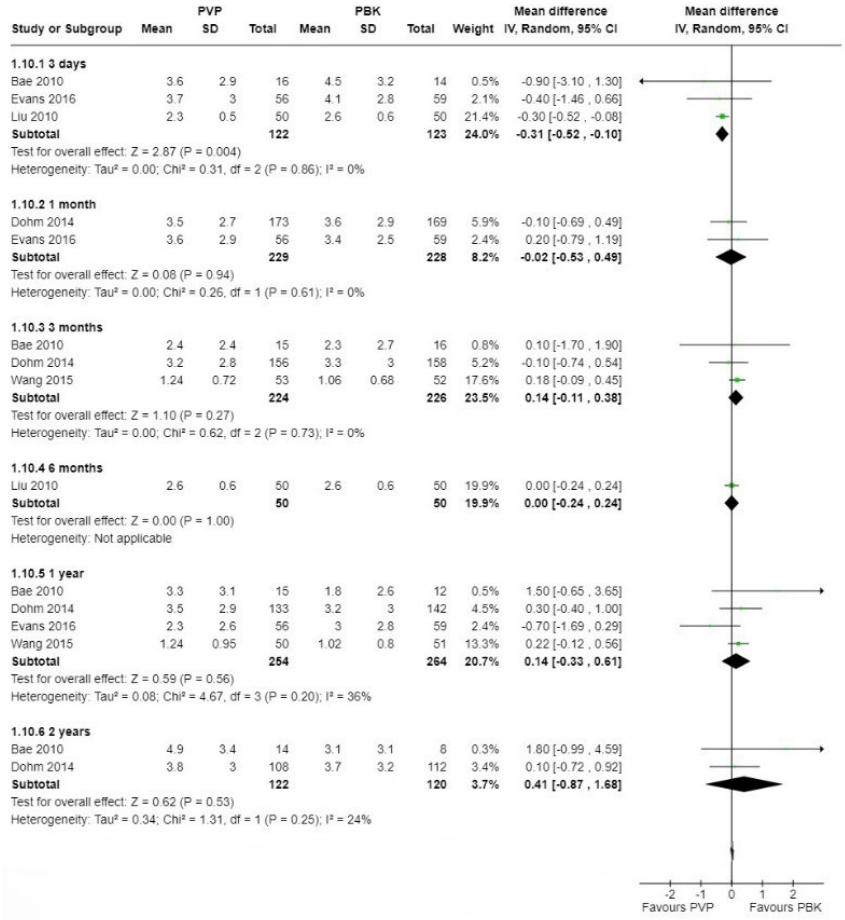


Figure 22: Meta-analysis of RCTs for Pain (Visual Analogue Scale or Numerical Rating Score): PVP Compared to PBK

Figure shows the mean difference (95% CI) for pain as measured by the visual analogue scale or the numerical rating score for PVP compared to PBK at follow-up timepoints ranging from 3 days to 2 years. Overall, there was no significant difference in pain between PVP and PBK at 1, 3, 6, 12, and 24 months follow-up. There was a significant difference at 3 days posttreatment favouring PVP.
Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SD, standard deviation; RCT, randomized controlled trial.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A8, Appendix 3).

Use of Analgesics

One RCT, Dohm et al,[85] compared the use of opioids in patients who underwent PVP with those who underwent PBK.[85] The authors reported that, at 6 months follow-up, there was no statistically significant difference in the number of patients using opioids posttreatment (34/142 PVP patients, compared with 25/142 PBK patients) (RR: 1.36; 95% CI: 0.86–2.16).

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, indirectness and imprecision (Table A8, Appendix 3).

Physical Function

We identified 4 RCTS that reported physical function (ODI). Three[85,113,115] were included in the meta-analysis because they provided follow-up timepoints (Figure 23). Overall, there was no statistically significant difference in improvement of ODI scores between patients who underwent PVP versus PBK at 1, 3, 12, or 24 months follow-up (Figure 23).

Wang et al[50] reported a statistically significant improvement in ODI score for patients who received PBK (mean: 23.3 ± SD 3.3) compared with PVP (mean: 35.9 ± SD 6.3), $P < .05$. However, the authors did not report the follow-up time for this assessment.

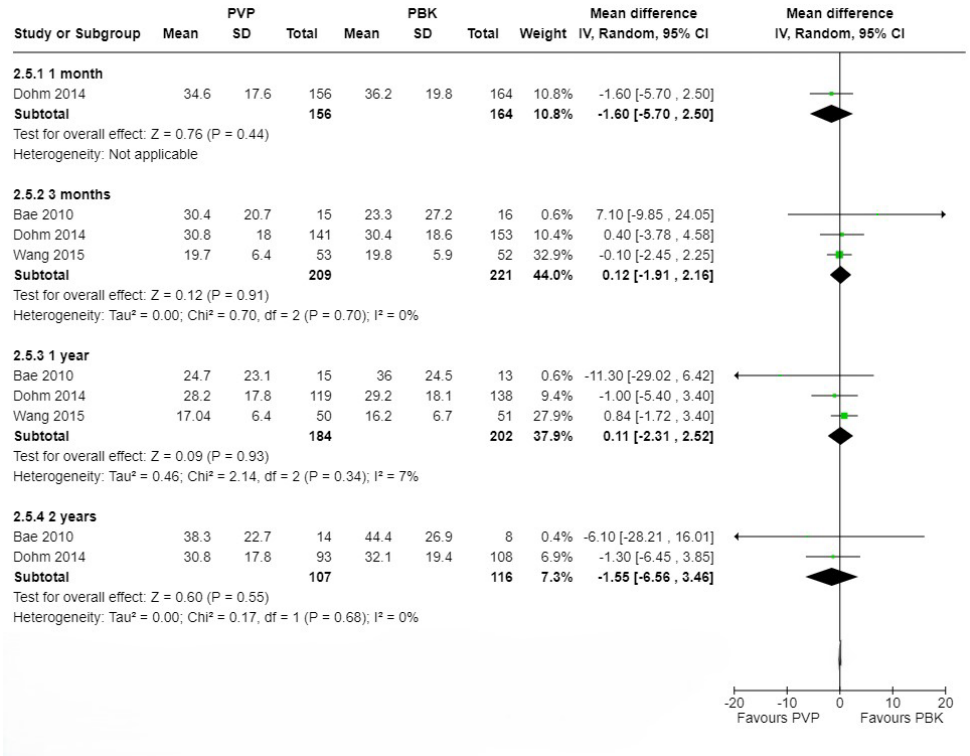


Figure 23: Meta-analysis of RCTs for Physical Function (Oswestry Disability Index): PVP Versus PBK

Figure shows the mean difference (95% CI) for physical function as measured by the Oswestry Disability Index for PVP compared to PBK at follow-up timepoints ranging from 1 month to 2 years. Overall, there was no significant difference in improvement of ODI scores between patients who underwent PVP versus PBK at 1, 3, 12, or 24 months follow-up.
Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial; SD, standard deviation.

Evans et al[112] assessed physical function using RMDQ and reported no statistically significant difference in improvement of function between PVP and PBK at 3 or 30 days, 6 months, or 1 year (Figure 24).

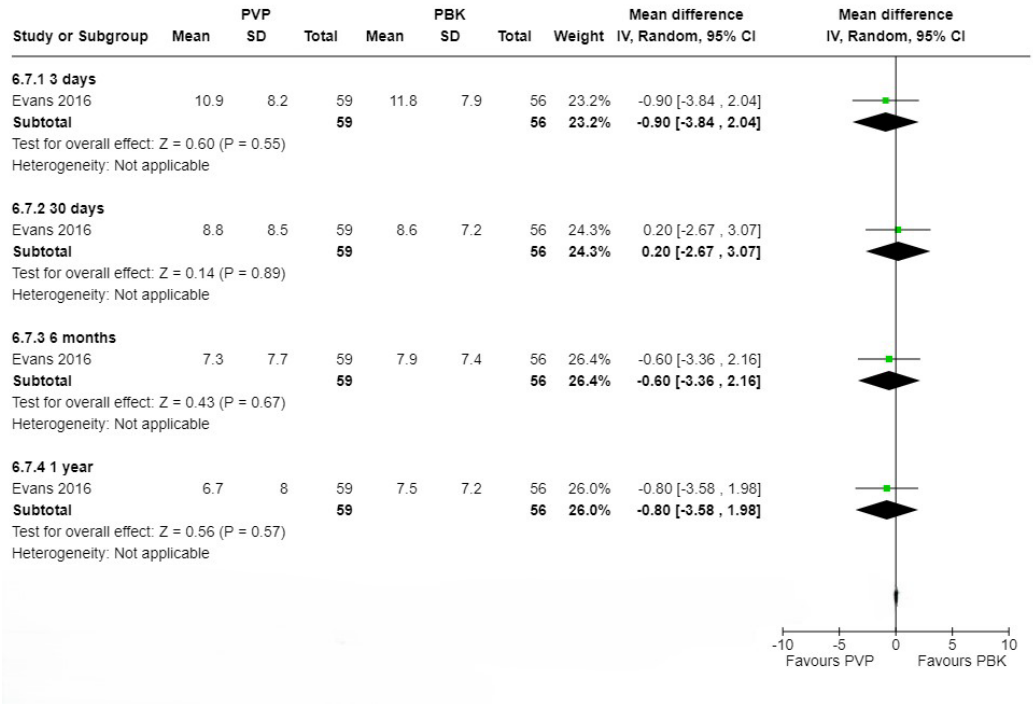


Figure 24: Meta-analysis of RCTs for Physical Function (Roland Morris Disability Questionnaire): PVP Versus PBK

Figure shows the mean difference (95% CI) for physical function as measured by the Roland Morris Disability Questionnaire for PVP compared to PBK at follow-up timepoints ranging from 3 days to 1 year. There was no significant difference in improvement of function between PVP and PBK at 3 or 30 days, 6 months, or 1 year.
Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial; SD, standard deviation.

Evans et al[112] also measured function using the SOF-ADL scale; however, data (mean and SD) were not reported for each treatment group at the follow-up timepoints.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias, inconsistency, and imprecision (Table A8, Appendix 3).

Quality of Life

We identified 1 RCT that provided data for EQ-5D. There was no statistically significant difference between PVP and PBK groups in improvement of quality of life at any follow-up timepoint (Figure 25).[85]

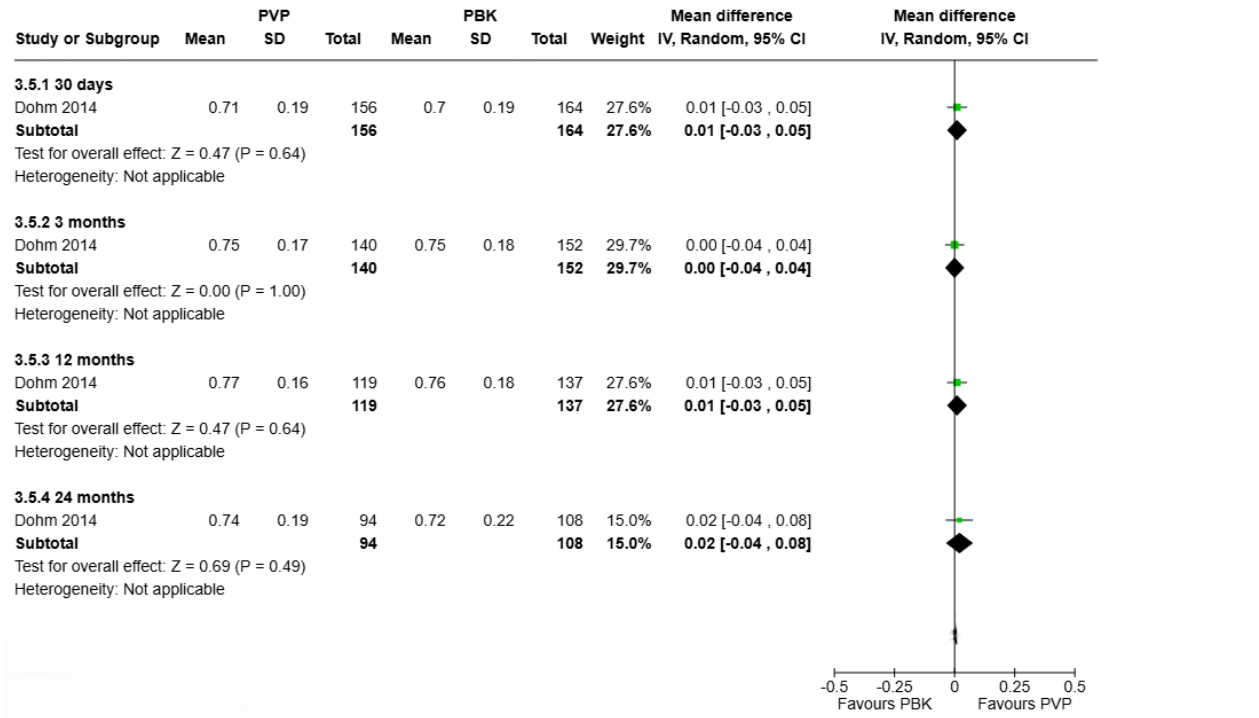


Figure 25: Results of RCT for EQ-5D: PVP Versus PBK

Figure shows the mean difference (95% CI) for quality of life as measured by EQ-5D for PVP compared to PBK at follow-up timepoints ranging from 30 days to 2 years. There was no significant difference between PVP and PBK groups in improvement of quality of life at any follow-up timepoint.

Abbreviations: CI, confidence interval; EQ-5D, EuroQol 5 dimensions questionnaire; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SD, standard deviation.

Dohm et al[85] reported the SF-36 physical component score (PCS) and mental component score (MCS). Overall, there was no significant difference in improvement in quality of life (SF-36 PCS or MCS) between PVP and PBK at 1, 3, 12, or 24 month follow-ups (Figures A21 and A22, Appendix 3). Bae et al[115] assessed SF-12 PCS and MCS scores and reported no significant difference in improvement in quality of life between PVP and PBK at 3, 12, or 24 month follow-ups (Figures A23 and A24, Appendix 3). Evans et al[112] also measured quality of life using the SF-36 PCS and MCS; however, data (mean and SD) were not reported for either treatment group at any of the follow-up timepoints.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias and imprecision (Table A8, Appendix 3).

Mortality

Two RCTs were identified that reported mortality. Both stated that there were no deaths in either the PVP or PBK arms of the trials. Dohm et al[85] reported 0 deaths in 190 patients in the PVP arm and 191 in the PBK arm at 2 years follow-up. Similarly, Wang et al[113] reported 0 deaths in 52 patients in the PVP group and 54 in the PBK group at 1 year follow-up.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias and imprecision (Table A8, Appendix 3).

Adverse Events

Three RCTs reported adverse events. Bae et al[115] reported that 1/20 patients who underwent PBK had a soft disc herniation at 3 months follow-up. No adverse events were reported in the PVP group (20 patients). Wang et al[113] reported no neurological deficit or embolism in the PVP arm (0/53 patients). In the PBK group, 2/54 patients had severe adverse events. One person experienced severe discogenic back pain related to a disc leak and underwent discectomy with posterior spinal fusion. A second patient had an asymptomatic cement emboli in the right lung related to venous leakage. A summary of the adverse events reported by Dohm et al[85] are shown in Table 29. There were 12 serious adverse events in patients who underwent PVP and 11 in those who underwent PBK. Of note, patients may have had multiple adverse events. In terms of any adverse events, 15 reported in the PVP group and 12 in the PBK group.

Table 29: PVP Versus PBK: Adverse Events Reported in Dohm et al[85]

Adverse event	PVP (n = 190 patients)	PBK (n = 191 patients)
Bone marrow edema	1	0
Constipation	0	1[a]
Hypersensitivity	1[a]	0
Procedural hypotension	0	1[a]
Procedural pain	3[a]	3[b]
Implant site extravasation	1	0
Cement embolism	1[a]	1[a]
Spinal fracture	0	1[a]
Arthralgia	0	1[a]
Back pain	3[a]	2[a]
Muscle spasm	0	1[a]
Symptomatic vertebral fracture	2[a]	1[a]
Hypoxia	1[a]	0
Respiratory failure	1[a]	0
Hematoma	1	0

Abbreviations: PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.
[a]Adverse event was classified as serious in original study.
[b]Two of the 3 events were classified as serious in the original study.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias and imprecision (Table A8, Appendix 3).

New Fractures

Four RCTs reported on new vertebral fractures after patients underwent PVP or PBK. Overall, there was no statistically significant difference in new fractures between patients who received PVP compared with PBK (RR: 0.84; 95% CI: 0.66–1.07) (Figure 26). Bae et al[115] reported that additional fractures occurred at the same rate in both trial groups through up to 2 years follow-up. A total of 20 new fractures (10 adjacent and 10 nonadjacent) occurred in 12 patients (6 in the PVP group and 6 in the PBK group). Wang et al[113] stated there was 1 new adjacent vertebral fracture in the PVP group (2%), and 4 new nonadjacent vertebral fractures in the PBK group (7.8%) over a 1 year follow-up. Liu et al[114]

reported 2 patients in the PKB group with adjacent fractures that occurred 41 and 50 days after surgery. Dohm et al[85] did not report whether the new radiographic vertebral fractures were adjacent or nonadjacent. The authors stated that new vertebral fractures were determined radiographically after up to 24 months follow-up. However, the other RCTs[113-115] did not explicitly state whether new fractures were determined symptomatically, radiographically, or both.

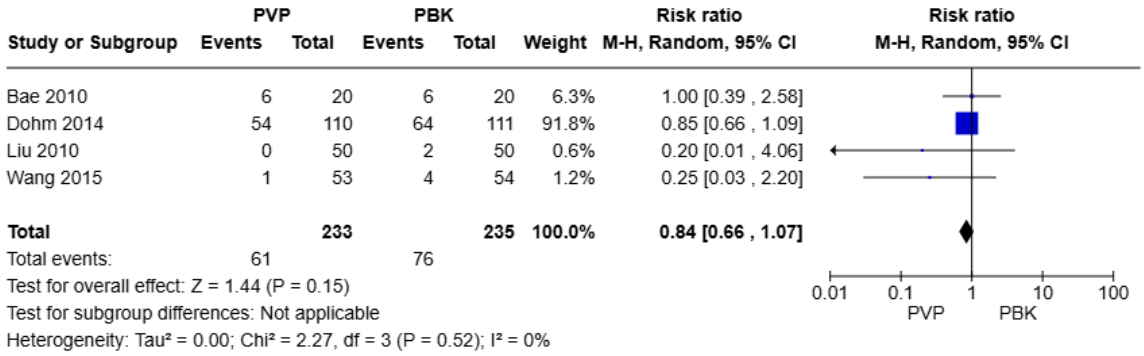


Figure 26: Meta-analysis of RCTs for New Fractures: PVP Compared to PBK

Figure shows the risk ratio (95% CI) for new fractures for PVP compared to PBK. Overall, there was no significant difference in new fractures between patients who received PVP compared with PBK.
Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias and imprecision (Table A8, Appendix 3).

Cement Leakage

Three RCTs[85,113,115] reported cement leakages per vertebrae (Table 30). Overall, there was no statistically significant difference in cement leakage between PVP and PBK (RR: 0.87; 95% CI: 0.54–1.39) (Figure A25, Appendix 3). However, 1 RCT (Wang et al[113]) used high viscosity cement in the PVP arm and low viscosity cement in the PBK arm.

Table 30: PVP Versus PBK: Cement Leakage in RCTs

Author, year	Length of follow-up	PVP, n/N (%)	PBK, n/N (%)	Symptomatic or asymptomatic
Bae et al, 2010[115]	24 months	15/26 (57.7%) vertebrae	15/26 (57.7%) vertebrae	Asymptomatic
Wang et al, 2015[113,a]	12 months	9/68 (13.24%) vertebrae	22/72 (30.56%) vertebrae	All patients asymptomatic in PVP group 1 patient symptomatic in PBK group
Dohm et al, 2014[85]	24 months	164/201 (82%) vertebrae	157/214 (73%) vertebrae	1 patient symptomatic in PVP group (cement embolism) 1 patient symptomatic in PBK group (cement embolism)

Abbreviations: PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.
[a]Two different types of cement were used: patients randomly underwent either PVP with a high viscosity cement or PBK with a low-viscosity cement.

Therefore, we performed a sensitivity analysis and removed the RCT by Wang et al[113] from the meta-analysis (Figure A26, Appendix 3). Overall, there was a significant difference in cement leakage favouring PBK (RR 1.11; 95% CI: 1.00 to 1.22).

We rated the overall quality of evidence (GRADE) as Very low, downgrading for risk of bias and imprecision (Table A8, Appendix 3).

Radiation Exposure

Jacobsen et al[38] included one series case study that reported on radiation exposure to the operator during PVP and PBK procedures.[119] Most of the radiation exposure during PVP occurred during needle/device placement rather than cement delivery.[38] Radiation exposure during PBK was attributable to both needle/device placement and cement delivery.[38] Overall, operators of PVP were exposed to less radiation than were operators of PBK ($P < .0001$) (Table 31).[38] This was likely attributable to the different procedure times.[38] For reference, Jacobsen et al[38] stated that a dental x-ray results in an exposure of 4 to 10 µSv per procedure.

Table 31: PVP Versus PBK: Radiation Exposure

Author, year	Outcome	PVP, mean ± SD	PBK, mean ± SD	*P* value
Ortiz et al, 2006[119]	Needle/device placement Duration	1.25 ± 1.3 µSv 3.9 ± 2.4 min	4.1 ± 5.5 µSv 4.4 ± 1.4 min	.02 NS
	Cement delivery Duration	0.45 ± 0.94 µSv 1.5 ± 0.6 min	4.5 ± 11.8 µSv 2.1 ± 0.9 min	NS < .0001
	Total exposure Duration	1.7 ± 1.9 µSv 39.3 ± 8 min	8.6 ± 13.9 µSv 55.7 ± 13min	< .0001 < .0001

Abbreviations: NS, not significant; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SD, standard deviation.

We rated the overall quality of evidence (GRADE) as Low, downgrading for risk of bias (Table A8, Appendix 3).

Ongoing Studies

We are aware of the following ongoing studies that have potential relevance to/other studies that may affect this review/our research question:

- Effect and Essentiality of Vertebroplasty Surgery in Acute Vertebral Compression Fractures ClinicalTrials.gov ID NCT03360383
- Early Percutaneous Vertebroplasty Versus Standard Conservative Treatment in Thoracolumbar Vertebral Fractures (AGIL11) ClinicalTrials.gov ID NCT03617094
- Percutaneous Vertebroplasty vs. Sham for Osteoporotic Vertebral Compression Fractures Focusing on Pain and Economy. (VOPE2) ClinicalTrials.gov ID NCT06141187

Discussion

Similar to Jacobsen et al,[38] the studies included in our HTA varied with respect to eligibility requirements (e.g., duration of OVCF pain < 6 weeks, < 6 months, or < 1 year), length of follow-up (e.g., 6, 12, or 24 months), and risk of bias (e.g., details regarding randomization, lack of intent-to-treat analysis, extent of patient/provider blinding, accounting for patients and outcomes, justification for sample sizes, and low patient enrollment). Percutaneous vertebroplasty compared to conservative treatment was the most commonly studied comparison, with fewer studies comparing PVP to sham and PBK to conservative treatment. No studies were identified that compared PBK to sham. Most of the included RCTs stipulated in their inclusion criteria that the OVCF was confirmed via imaging, specifically magnetic resonance imaging (MRI) to identify edema. While some studies reported that included patients must have failed conservative treatment prior to PVP or PBK, it is unclear whether this was a requirement in many RCTs. The certainty of the evidence (GRADE) ranged from Very low to Low. Common sources of downgrading in PVP trials related to risk of bias and inconsistency.[38] The main bias concerns include the lack of blinding in PVP versus conservative treatment trials and losses to follow-up.[38] The considerable level of heterogeneity and inconsistency added to the uncertainty.[38] The inconsistency of effects relates to the small sample sizes (particularly at later follow-up timepoints) and the opposing direction of effect in a quality of life outcome (QUALEFFO at 6 months follow-up) (Figure 15) in 2 key sham trials.[68,71]

No studies were identified that reported on the number of patients who underwent PVP or PBK who were then able to return to independent living or admission to specialized care accommodation (e.g., long-term care residence).

Jacobsen et al[38] noted that the clinical interpretation of the evidence is limited by the general absence of vertebral fracture–specific MCIDs in the literature. The authors identified 2 vertebral fracture-specific MCIDs[120,121]; however, both related specifically to a functional outcome (RMDQ) (Table A9, Appendix 3).[38] The remaining MCIDs that they identified in their systematic review generally pertained to chronic back pain requiring surgery (Table A9, Appendix 3). Back pain has a different clinical profile to OVCFs with respect to patient demographics, symptomology, and treatment expectations. Therefore, they cautioned that the applicability of MCIDs is uncertain, as those specific to chronic back pain may over- or underestimate clinically meaningful thresholds that are specific to OVCFs. [38]

PVP Versus Conservative Treatment

Overall, there were significant (statistical and clinical) differences in pain scores favouring PVP over conservative treatment in the short term. The reduction in pain was greatest at the earliest follow-up timepoints (e.g., 1 day, 1 week, and 1 month posttreatment). There were no significant differences at 2 weeks or 2 months, while pain scores reported at 3, 6, and 12 months favoured PVP over conservative treatment. Jacobsen et al[38] suggested that by 12 months, the clinical significance was uncertain. At 24 and 36 months, pain scores were uncertain because they were based on 1 RCT[59] with limited patient numbers. Of note, there was significant statistical heterogeneity (I^2 ranging from 58% to 97%) at all follow-up timepoints (except 1 day posttreatment) (Figure 2).

The use of analgesic drugs generally did not differ between PVP and conservative treatment, suggesting that while subjective measures (e.g., VAS) of pain decreased, more objective measures did not.[38] This may be related to the lack of blinding among the RCTs, which predisposes them to outcome bias because participants have knowledge of the assigned intervention.[38]

Similar to pain scores, there were significant differences (statistical and clinical) in the short term for function-related (ODI and RMDQ) outcomes favouring PVP over conservative treatment.[38] The reduction in scores was generally consistent across most timepoints, but Jacobsen et al[38] suggested that by 12 months (Figure 4), the results may not have been clinically significant. Also similar to pain scores, there was significant statistical heterogeneity at follow-up timepoints (Figure 3) and wide confidence intervals for the summary statistics (Figure 4).

The effect of PVP compared to conservative treatment on quality of life outcomes (e.g., EQ-5D, QUALEFFO) was inconsistent (Figure 5) and was associated with considerable statistical heterogeneity (Figure 6).

The comparative safety of PVP suggests the incidence of mortality, serious adverse events, any adverse events, and new fractures was similar to CT.[38] However, there was uncertainty since the RCTs were likely underpowered to detect these group differences and generally had short follow-up timeframes. The absolute estimate for cement leakage from 6 RCTs was 36.7% of treated vertebrae (Table 12). Most instances of cement leakage were asymptomatic, although a very small number of cement embolism cases, a serious adverse event, were reported for both PVP and PBK.

Subgroup analyses suggested acute fractures appear more responsive to PVP at earlier timepoints as reductions in pain were greater than for older fractures (Figures A1 and A2).

PVP Versus Sham

There were significant differences (with small effect sizes) between PVP and sham groups for pain (VAS/NRS) from 1 to 12 months posttreatment, but not at 24 months posttreatment (Figure 11). However, the use of analgesic drugs did not differ between PVP and sham at most timepoints. This lack of difference may reflect the pooling of different analgesic classes (NSAIDs and opioids).[38] It is unclear whether NSAIDs or opioids are differentially reduced following PVP because several studies did not report this information.[38] Inconsistent statistical differences were observed for quality of life (QUALEFFO, EQ-5D) (Figures 14 and 15) and no significant differences were observed between PVP and sham at most follow-up assessments for function (RMDQ) (Figure 13). Overall, the effect sizes for most outcomes were small, subject to statistical heterogeneity, and unlikely to translate to clinically meaningful differences.[38]

No significant differences were observed between PVP and sham for mortality, new fractures, or severe adverse events; however, there was a significant difference favouring sham for the occurrence of any adverse events based on 2 RCTs with very wide confidence intervals (Figure 18).[68,73] The absolute estimate for cement leakage was 61.8% of treated vertebrae and 39.4% of patients (Table 15).

Subgroup analyses suggested acute fractures appear more responsive to PVP at earlier timepoints as improvement in quality of life (EQ-5D) was greater for newer than for older fractures (Figures A17 and A18).

PBK Versus Conservative Treatment

A small number of RCTs informed the evidence base comparing PBK to conservative treatment. Overall, there were statistically and clinically meaningful differences between PBK and conservative treatment in the short-term (up to around 1 week). However, similar to PVP, the improvement in pain decreases over time and the difference between groups is not clinically meaningful by around 12 months (Figure 21).[38]

A function outcome (RMDQ) (Table 19) and quality of life (EQ-5D) (Table 21) differed statistically between PBK and conservative treatment; however, most of the outcomes were informed by only 1 RCT, adding uncertainty to the results. The differences between groups persisted from 1 to 12 months, although whether they translated to clinical improvements is uncertain.[38] Like PVP, the PBK analysis is subject to outcome bias since participants knew which treatment they received.

Similar to PVP, the comparative safety of PBK suggests the incidence of mortality, serious adverse events (Table 23), any adverse events (Table 24), and new fractures is similar to CT.[38] However, the RCTs were likely underpowered to detect these group differences and the studies reported limited follow-up timeframes (e.g., up to 36 months).[38] The absolute estimate for cement leakage was 27.1% of treated vertebrae and 23.7% of patients.

Subgroup analysis based on fracture age was not performed due to the small number of studies identified. The pivotal PBK trial (FREE trial)[100] noted that the sponsor had input into the design, monitoring, and reporting of results.[38]

Overall, when compared to conservative treatment, PVP and PBK may have resulted in an immediate, clinically relevant short-term improvement in pain, function, and some quality of life measures.[38] The clinical relevancy may have attenuated at later timepoints, but the results remained statistically significant. When compared to sham treatments, PVP statistically differed with respect to pain and some quality of life measures; however, there was uncertainty regarding clinical relevance, inconsistency, and general lack of functional improvements.[38]

PVP Versus PBK

In general, there was inconsistent reporting in the RCTs about the age of the OVCF in the included patients. For example, different studies followed different methodology, reporting that patients underwent PVP or PBK either:

- Within 43 days of injury,[114]
- Had OVCFs within 6 months prior to enrolment,[85]
- If they experienced pain within the last 12 months,[112]
- If they failed conservative management for at least 6 weeks but not longer than 1 year,[115] or
- If they had unsatisfactory pain relief after at least 4 weeks of conservative treatment[113]

No significant differences between PVP and PBK were observed in improvement of pain scores at 1, 3, 6, 12, or 24 months posttreatment. At 3 days follow-up, there was a significant improvement in pain favouring PVP (with a small effect size and unlikely clinical significance) (Figure 22). No significant differences were reported for physical function (ODI, RMDQ) (Figures 23 and 24) or quality of life (EQ-5D, SF-36) (Figures 25, A21, and A22).

While there were no significant differences observed between PVP and PBK for mortality, adverse events, or new fractures, there was a significant difference in cement leakage favouring PBK (Figure A26). The lower incidence of cement leakage after PBK is thought to reflect the lower injection pressure required to perform the procedure, since space for the cement within the vertebral bone is created with the balloon prior to cement injection.[122] This may enable more precise placement of cement compared to PVP.[122]

One study assessed radiation exposure by physicians who delivered PVP or PBK. Overall, operators of PVP were exposed to significantly less radiation than operators of PBK (Table 31). This was likely attributable to the different procedure times (procedure time was lower for PVP).

We were unable to perform a subanalysis for inpatient versus outpatient outcomes due to scant reporting of this information within the systematic review by Jacobsen et al,[38] as well as in the additional studies. We were unable to subanalyze for sham versus conservative treatment as no studies included both of these arms within their assessments.

Strengths and Limitations

Strengths include:

- We updated the systemic review by Jacobsen et al[38] and included additional studies
- Our systematic review included comparisons of PVP to conservative treatment and sham, PBK to conservative treatment, and an additional direct comparison of PVP with PBK

Limitations include:

- Similar to Jacobsen et al,[38] we did not identify any RCTs that compared PBK with sham treatment

Conclusions

Compared to conservative treatment in people with painful OVCFs, PVP:

- May demonstrate clinically and statistically significant improvements in pain in the short-term (GRADE: Low)
- May demonstrate clinically and statistically significant improvements in physical function in the short term, but the evidence is very uncertain (GRADE: Very Low)
- May improve quality of life, but the evidence is very uncertain (GRADE: Very Low)
- May have little to no effect on use of analgesics, mortality, adverse events, and new fractures (GRADE: Very Low)

Not applicable for comparison with CT since cement leakage is not an outcome for CT:

- Cement leakage (GRADE Very Low)

Compared to sham in people with painful OVCFs, PVP:

- May reduce pain slightly (GRADE: Low)
- May increase adverse events (GRADE: Low)
- May have little to no effect on the use of analgesics but the evidence is very uncertain (GRADE: Very Low)
- May result in little to no difference in physical function, quality of life, mortality, or new fractures (GRADE: Low)

Not applicable for comparison with sham since cement leakage is not an outcome for sham:

- Cement leakage (GRADE: Low)

Compared to conservative treatment in people with painful OVCFs, PBK:

- May improve physical function and quality of life (GRADE: Low)
- May demonstrate clinically and statistically significant improvements in pain in the short term, but the evidence is very uncertain (GRADE: Very Low)
- May have little to no effect on use of analgesics, but the evidence is very uncertain (GRADE: Very Low)
- May result in little to no difference in mortality, adverse events, or new fractures (GRADE: Low)

Not applicable for comparison with CT since cement leakage is not an outcome for CT:

- Cement leakage (GRADE: Low)

Compared with PBK in people with painful OVCFs, PVP:

- May increase cement leakage, but the evidence is very uncertain (GRADE: Very Low)
- May have little to no effect on pain, use of analgesics, physical function, quality of life, mortality, adverse events, or new fractures, but the evidence is very uncertain (GRADE: Very Low)
- Likely reduces radiation exposure to the provider/operator slightly (GRADE: Low)

Economic Evidence

Research Question

What is the cost-effectiveness of percutaneous vertebroplasty (PVP) or percutaneous balloon kyphoplasty (PBK) combined with conservative treatment (CT) compared with CT alone for the treatment of adults with painful osteoporotic vertebral compression fractures (OVCFs)?

Methods

Economic Literature Search

We performed an economic literature search on May 29, 2024, to retrieve studies published from January 1, 2019, until the search date. This date limit reflects our plan to leverage and update the Swiss Health Technology Assessment (HTA) by Jacobsen et al,[38] which had an end date of January 22, 2020. To retrieve relevant studies, we developed a search using the clinical search strategy with an economic and costing filter applied.

We created database auto-alerts in MEDLINE and Embase and monitored them until October 1, 2024. We also performed a targeted grey literature search following a standard list of websites developed internally, which includes the International HTA Database and the Tufts Cost-Effectiveness Analysis Registry. See Clinical Literature Search, above, for further details on methods used. See Appendix 1 for our literature search strategies, including all search terms.

Eligibility Criteria

Studies

Inclusion Criteria

- English-language full-text publications
- Studies published since January 1, 2019
- Cost–benefit analyses, cost-effectiveness analyses, or cost–utility analyses

Exclusion Criteria

- Editorials, commentaries, case reports, and abstracts

Participants

Inclusion Criteria

- Adults (≥ 18 years) with a diagnosis of symptomatic (i.e., painful) OVCF refractory to conservative (nonsurgical) treatment

Exclusion Criteria

- Adults with vertebral fractures due to other causes such as major trauma or cancer, people who did not first undergo conservative (nonsurgical) treatment (CT)

Interventions

Inclusion Criteria

- PVP or PBK with CT

Exclusion Criteria

- Vertebral body stenting, pedicle screw fixation, prophylactic augmentation (i.e., before a fracture occurs), KIVA VCF system (insertion of an implant combined with cement), SpineJack system (insertion of a retractable titanium expander). According to experts, these devices are rarely used in Ontario and are therefore not considered appropriate as either an intervention or comparator for the purposes of this HTA

Comparators

Inclusion Criteria

- CT

Exclusion Criteria

- Vertebral body stenting, pedicle screw fixation, prophylactic augmentation (i.e., before a fracture occurs), KIVA VCF system (insertion of an implant combined with cement), SpineJack system (insertion of a retractable titanium expander). According to experts, these devices are rarely used in Ontario and are therefore not considered appropriate as either an intervention or comparator for the purposes of this HTA

Outcome Measures

- Costs
- Health outcomes (e.g., quality-adjusted life-years)
- Incremental costs
- Incremental effectiveness
- Incremental cost-effectiveness ratios

Literature Screening

A single reviewer conducted an initial screening of titles and abstracts using Covidence[55] and then obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The same reviewer then examined the full-text articles and selected studies eligible for inclusion.

Data Extraction

We extracted relevant data on study characteristics and outcomes to collect information about the following:

- Source (e.g., citation information, study type)
- Methods (e.g., study design, analytic technique, perspective, time horizon, population, intervention[s], comparator[s])
- Outcomes (e.g., health outcomes, costs, incremental cost-effectiveness ratios)

Study Applicability and Limitations

We determined the usefulness of each identified study for decision-making by applying a modified quality appraisal checklist for economic evaluations originally developed by the National Institute for Health and Care Excellence (NICE) in the United Kingdom.[123] The NICE checklist has 2 sections: the first is for assessing study applicability and the second is for assessing study limitations. We modified the wording of the questions of the first section to make it specific to Ontario. Using this checklist, we assessed the applicability of each study to the research question (directly, partially, or not applicable). Next, we assessed the limitations (minor, potentially serious, or very serious) of the studies that we found to be applicable.

Results

Economic Literature Search

The economic literature search yielded 132 citations, including grey literature results and after removing duplicates, published between January 1, 2019, and May 29, 2024. We identified 7 additional eligible studies from other sources, including database alerts (monitored until October 1, 2024). In total, we identified 11 studies that met our inclusion criteria. Figure 27 presents the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the economic literature search.

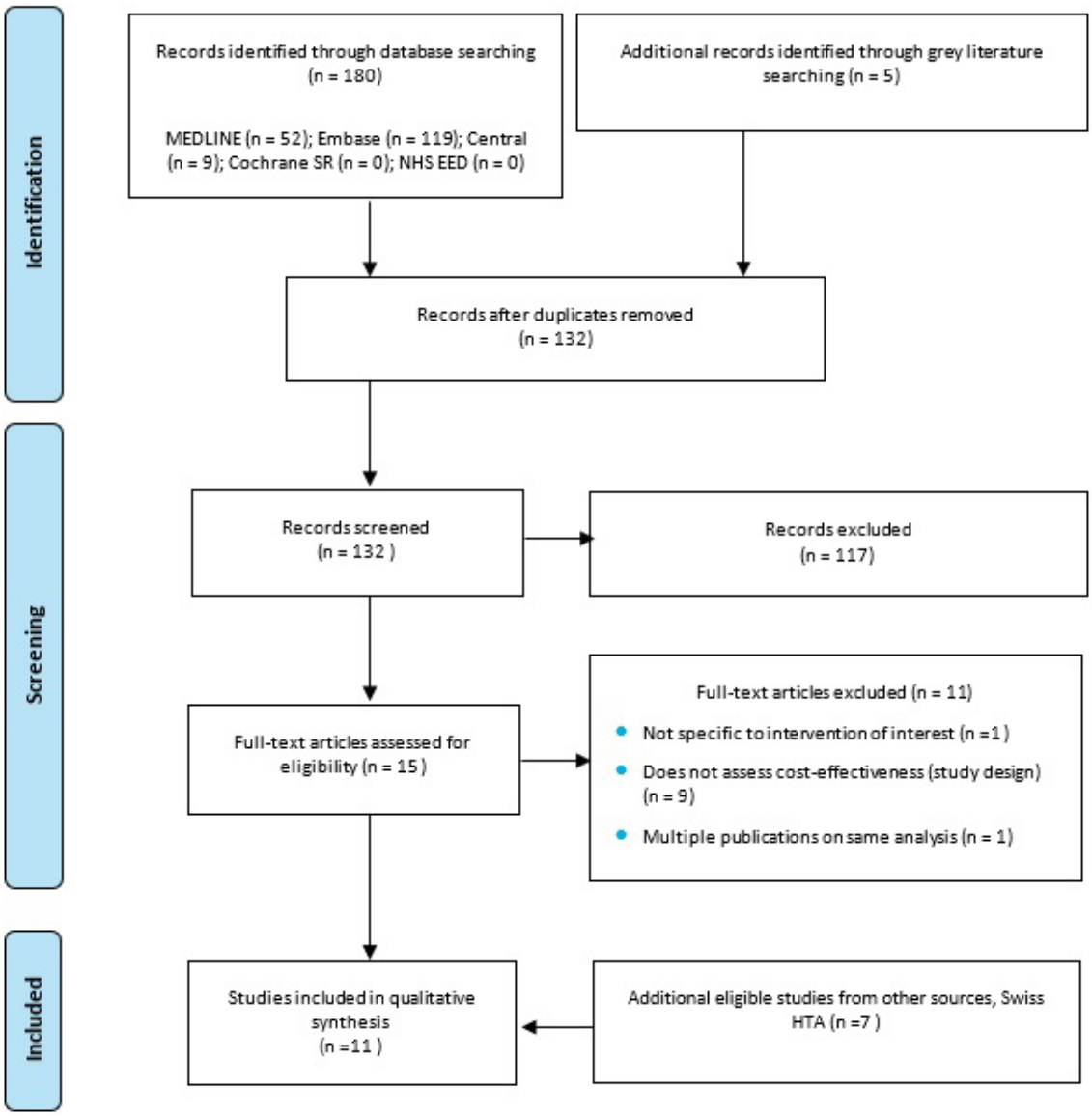


Figure 27: PRISMA Flow Diagram – Economic Systematic Review

PRISMA flow diagram showing the economic systematic review. The economic literature search yielded 132 citations, including grey literature results and after removing duplicates, published between January 1, 2019, and May 29, 2024. We screened the abstracts of 132 identified studies and excluded 117. We assessed the full text of 15 articles and excluded a further 11. In the end, we included 11 articles in the qualitative synthesis (including 7 from other sources).

Abbreviations: HTA, health technology assessment; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Source: Adapted from Page et al.[55]

Overview of Included Economic Studies

We included 11 relevant studies published between 2008 and 2021. We identified 4 studies published since January 1, 2019, in the literature review and an additional 7 studies in the economic literature review by Jacobsen et al.[38] Table 32 describes the study design, population, interventions, comparators, and results of the included studies. Of the 11 studies included in our review, 8 were cost-utility analyses

(CUA),[38,124-130] 2 were cost-effectiveness analyses (CEA),[131,132] and 1 included both a CUA and CEA.[60] The studies were mainly conducted in Europe: 1 from Italy,[131] 3 from the United Kingdom,[124,125,127] 1 from the Netherlands,[60] 1 from Switzerland,[38] and 1 from Sweden.[126] Additionally, there were 2 US studies,[128,132] 1 from Australia,[129] and 1 from Japan.[130] No Canadian studies were identified.

We also identified 3 publications on 2 prior systematic reviews of economic evaluations.[133-135] The more recent systematic review used a literature search dated up to May 2021. Two HTAs also included economic literature reviews, 1 with a literature search dated up to November 2011[127] and the other to January 2020.[38] Our economic literature search was an extension of the latter literature review. The earliest of the systematic reviews concluded that more clinical data is needed and no definitive conclusion could be made on the cost-effectiveness of vertebral augmentation procedures.[135] The most recent systematic review concluded that PVP and PBK have been shown to be cost-effective compared with CT.[133,134] All of our identified studies were included in the previous systematic reviews; however, we excluded some of the studies included in prior reviews. The studies and reasons for exclusion are listed in Table A10 (Appendix 5).

Most studies conducted pairwise comparisons, either PVP or PBK compared with CT.[38,60,125,126,128-131] Three studies compared more than 2 strategies. Svedbom et al[124] compared PBK, PVP, and CT using results from 2 different clinical trials. Edidin et al[132] used US Medicare claims data to compare PBK, PVP, and CT. NICE[127] compared PVP, PBK, CT, and operative placebo with local anesthesia using multiple sources.

Terms used for the comparator varied across studies, but typically included pain management. The terms used by authors and descriptions provided in economic studies is provided in Table A11 (Appendix 6).

PVP Compared With Conservative Treatment

Five studies conducted analyses comparing PVP with CT.[38,60,128,129,131] The clinical data sources of these studies varied. The study by Klazen et al[60] was conducted alongside the randomized trial, VERTOS II, while Jacobsen et al[38] used the findings of that trial in their CUA. Australia's MSAC[129] used clinical effectiveness data from a different randomized trial, Masala et al[131] used observational (non-randomized) patient-level data to inform their effectiveness measures, and Hopkins et al[128] assumed that PVP would have the same effectiveness as PBK. The first four studies used a 1-year time horizon and took a health care payer perspective, while Hopkins et al[128] used a lifetime time horizon and a US Medicare payer perspective. All studies concluded that PVP was cost-effective compared with CT.

Klazen et al[60] conducted a CUA alongside the clinical trial of PVP compared with CT for people with OVCF with acute (≤ 6 weeks) back pain. Quality-adjusted life years (QALYs) were measured in the trial using the Euroqol -5 dimension (EQ-5D) questionnaire; however, there were baseline differences between the PVP and CT groups. The authors stated that differences were due to chance and reported the mean difference in QALYs at 1 month and 1 year, adjusted for the baseline differences using regression analyses. The incremental cost-effectiveness ratio (ICER) of PVP compared with CT was €22,685 EUR/QALY and, in a probabilistic sensitivity analysis, there was a 70% probability that PVP was cost-effective at a willingness-to-pay (WTP) value of €30,000 EUR/QALY.

A CUA conducted as part of an HTA in Switzerland by Jacobsen et al[38] compared PVP with CT for patients with acute (< 8 weeks) fractures. Percutaneous vertebroplasty is mainly performed for inpatients in Switzerland. Utility differences between PVP and CT from the previously mentioned RCT were used.[60] No

treatment effects on mortality were included. The ICER of PVP compared with CT over 1 year from a public payer perspective was $19,669 CHF/QALY. There was an 85% probability that PVP is cost-effective at 1 year compared with CT at a WTP value of $100,000 CHF/QALY. In sensitivity analyses, results were most affected by costs of CT, cost of inpatient PVP, and utility gains.

Australia's MSAC[129] conducted a CUA as part of an HTA for people with acute (< 6 weeks) OVCF compared PVP with CT using results from an Australian RCT that compared PVP to sham treatment.[71] Only a public summary document was available, limiting our ability to critique the analysis. Deterministic results at 12 months concluded that if CT does include magnetic resonance imaging (MRI), PVP would be dominant, and if CT does not include an MRI, the ICER would be $5,331.51 AUD/QALY. The summary document reported a multiway sensitivity analysis that estimated the ICER to be $71,000 AUD/QALY and stated that results were sensitive to assumptions about use of hospital services (e.g., hospital length of stay).

Masala et al[131] was the only study to compare PVP with CT using non-randomized data. The study was conducted in Italy among patients who were refractory to 2 weeks of analgesic therapy and either accepted or refused PVP, potentially resulting in baseline differences between groups. Health outcomes used for the analyses were pain, as measured by the visual analogue scale (VAS), an ambulation scale, and an activities of daily living (ADL) scale. The authors calculated the ratio of average cost to change in health outcome at 1, 3, and 12 months for each treatment arm. We used the average costs and changes in health outcomes to calculate an ICER ([cost of intervention – cost of comparator] ÷ [health outcome of intervention – health outcome of comparator]) for each health outcome at 12 months and reported our results in Table 32. PVP was less costly and more effective than CT in all comparisons. No sensitivity analyses were reported.

Hopkins et al[128] compared PVP with CT over a lifetime horizon. The analysis also included a comparison of PBK with CT, but no comparisons between PVP and PBK were made. The treatment effect of PVP was assumed to be the same as PBK, which was taken from the FREE trial.[100,118] The authors did not incorporate the treatment effect on subsequent OVCF. Two-year costs were estimated from Medicare claim payments in the United States. Medicare claims data were also used to estimate survival outcomes and a treatment effect on mortality was estimated and incorporated in the model over a 2-year period. Groups were matched on age, sex, Charlson Comorbidity Index, and hospitalization status. The ICERs comparing PVP to CT were $39,774 USD/QALY in the inpatient setting and $12,293 USD in the outpatient setting. Probabilistic sensitivity analyses were not reported for PVP compared with CT, but were stated to be similar to the results of PBK compared with CT, which found that PBK had an 80% and 100% probability of being cost-effective in the inpatient and outpatient settings, respectively, at a $50,000 USD WTP value. In a one-way sensitivity analysis, the results were sensitive to the mortality assumptions.

PBK Compared With Conservative Treatment

There were 5 studies that conducted analyses comparing PBK with conservative treatment.[38,125,126,128,130] Three used clinical effectiveness results from the FREE trial[38,125,128] and another used only a subset of Swedish participants from the FREE trial.[126] One used observational (non-randomized) patient-level data to inform their effectiveness measures.[130] Two used a 2-year time horizon, the duration of the FREE trial,[38,126] while the other 3 used a lifetime time horizon.[125,128,130] Three studies used a health care payer perspective,[38,125,130] 1 used a societal perspective,[126] and 1 used a US Medicare payer perspective.[128] Four of the studies[38,125,128,130] concluded that PBK was cost-effective compared with CT.

Strom et al[125] conducted a lifetime CUA of PBK compared with CT for hospitalized patients with OVCF. The treatment effect of PBK on quality of life was taken from the first-year results of the FREE trial. Adverse events were not included in the analysis, nor was treatment effect on mortality or subsequent OVCF. The analysis assumed that PBK led to a shorter hospital stay (reduction of 6 days). The ICER comparing PBK with CT was £8,940 GBP/QALY. In a probability sensitivity analysis, there was a 13% chance that PBK is cost-saving (less costly and more effective) compared with CT. In one-way sensitivity analyses, the results were sensitive to assumptions about the duration of treatment effect on utility, the reduction in hospital length of stay, and the patient start age.

Fritzell et al[126] conducted a CUA that compared PBK with CT over a 2-year time horizon for hospitalized patients. A person-level CUA was conducted using cost and quality of life results for the Swedish participants of the FREE trial. A societal perspective was used and costs of travel and support (including shopping and house cleaning) were included. Costs due to missed work were insignificant as all participants were on pensions due to age. The ICER was 884,682 SEK/QALY and the probabilistic sensitivity analysis found that there was a less than 40% probability that PBK is cost-effective at a WTP threshold of 600,000 SEK. In a one-way sensitivity analysis, results were sensitive to the quality of life estimates. When results from the trial for all patients were used, the new ICER could be considered cost-effective.

Takahashi et al[130] conducted CUAs that compared PBK with CT over 3- and 20-year time horizons. Data on cost and quality of life were collected over 6-months from patients. The PBK cohort was created from hospital inpatients undergoing PBK. The CT cohort was created from a historical cohort of conservatively treated patients, 66% of whom were hospitalized. One-to-one propensity score matching on age, sex, number of baseline old fractures, fracture level, and baseline Short-Form–Six Dimensions (SF-6D) score was used for the analysis. The treatment effect on quality of life was assumed to last for 3 years. The 3-year ICER was ¥4,404,158 JPY/QALY and the 20-year ICER was ¥2,416,406 JPY/QALY. A probabilistic sensitivity analysis was conducted and found at 50% probability of PBK being cost-effective, the ICER was ¥1,121,453 JPY/QALY. In one-way sensitivity analyses, incorporating a mortality benefit significantly reduced the ICER.

Hopkins et al[128] conducted a CUA that compared PBK with CT over a lifetime horizon. The treatment effect of PBK on quality of life was taken from the FREE trial. Cost data on PBK came from Medicare claim payments in the United States. Medicare claims data were also used to estimate survival outcomes and a treatment effect on mortality was estimated and incorporated in the model over a 2-year period. Groups were matched on age, sex, Charlson Comorbidity Index, and hospitalization status. The ICERs comparing PBK to CT were $43,455 USD/QALY in the inpatient setting and $10,922 USD/QALY in outpatient settings. The probabilistic sensitivity analyses found that PBK had an 80% and 100% probability of being cost-effective in the inpatient and outpatient settings, respectively, at a $50,000 USD WTP value. In a one-way sensitivity analysis, the results were sensitive to the mortality assumptions.

In a CUA as part of an HTA conducted in Switzerland, Jacobsen et al[38] compared PBK with CT for patients with acute (< 3 months) fractures over a 2-year time horizon. Utility differences between PBK and CT were taken from the FREE trial. No treatment effects on mortality were included. The ICER comparing PBK and CT from a public payer perspective was 18,405 CHF/QALY. There was an 87% probability that PVP is cost-effective at 1 year compared with conservative treatment at a WTP value of 100,000 CHF/QALY. In sensitivity analyses, results were most affected by costs of CT, cost of inpatient PVP, and utility gains.

Comparison of PVP, PBK, and CT

Three studies conducted analyses comparing PVP, PBK, and CT.[124,127,132] Two used a lifetime time horizon and 1 used different time horizons for costs (3 years) and benefits (lifetime). The studies had mixed results. Two concluded that PBK was cost-effective when compared with PVP and CT[124,132] and 1 did not make any definitive conclusions because the results were sensitive to the assumptions made.[127]

Svedbom et al[124] conducted a lifetime cost–utility analysis of PBK compared with PVP and CT for hospitalized patients with OVCF. The analysis built on the previous CUA by Strom et al,[125] but with 2-year quality of life results from the FREE trial. Quality of life for the first year of PVP was taken from the VERTOS II trial.[60] For the second year of PVP, it was assumed that PVP would result in the same percentage change in quality of life as PBK. Adverse events and treatment effect on subsequent OVCF were not included, but a treatment effect on mortality was assumed for 4 years. The analysis leveraged Strom et al's[125] assumption about the reduction in hospital length of stay for PBK compared with CT and assumed the same reduction with PVP. The ICERs were £2,706 GBP/QALY and £15,982 GBP for PBK compared with CT and PBK compared with PVP, respectively. The probabilistic sensitivity analysis found that PBK had a 60% chance of being the optimal strategy for a WTP value of £20,000 GBP/QALY. In one-way sensitivity analyses, the results were sensitive to assumptions about treatment effects on subsequent OVCF and mortality.

Edidin et al[132] conducted a CEA using observational (non-randomized), patient-level data from US Medicare claims to inform the clinical effectiveness (mortality estimates). The authors concluded that, among patients for whom surgical treatment was indicated, PBK was cost-effective and perhaps even cost saving compared with PVP. PVP and PBK were cost-effective compared with CT.

Stevenson et al[127] conducted an economic evaluation as part of an HTA for NICE in the United Kingdom. The authors compared four alternatives over a lifetime time horizon: PBK, PVP, optimal pain management (i.e., CT), and operative placebo with local anesthesia. Using sensitivity analyses, it was determined that results were sensitive to assumptions about the treatment effect on mortality and the source used for quality of life (utility) estimates. Rather than defining a reference case, 6 scenarios were presented using varying assumptions about the mortality benefit and differing sources for utility. The first approach to estimate treatment effect on utility was to use trial data for the PBK and CT comparison and assume that the same would apply to PVP. This was repeated with 3 different trial results. In the second approach, they conducted a network meta-analysis (NMA) on the mean difference in VAS scores, as this was a more commonly measured outcome in trials. The VAS scores were converted to EQ-5D scores using a mapping algorithm calculated using trial data that measured both VAS and EQ-5D scores. No definitive conclusion was provided because results were dependent on the assumptions made.

Table 32: Characteristics of Studies Included in the Economic Literature Review

Author, year, country	Analytic technique, study design, perspective, time horizon (discount rate)	Population	Intervention(s) and comparator(s)	Results		
				Health outcomes	Costs	Cost-effectiveness
PVP compared with CT						
Masala et al, 2008[131] Italy	CEA Observational data, person-level analysis Hospital perspective 1 y (NA)	Mean age: 72 y Single symptomatic acute (within last 3 mo); amyelic (no spinal cord involvement) osteoporotic vertebral fracture following 2 wk analgesic therapy	**I:** PVP acceptors, PVP and 1 wk drug therapy (N = 54) **C:** PVP refusers, CT (N = 86)	12-mo baseline mean score: **I:** VAS: 1.1–8.70 Ambulation: 1.4–3.6 ADL scale: 1.5-3.9 **C:** VAS: 1.8–8.6 Ambulation: 1.6–3.6 ADL scale: 1.7–4.0	EUR[a] 12 mo. cost: **I:** €4,101.05 (€755.41) **C:** €4,299.55 (€3,211.53)	ICERs reported as cost per one unit decrease in scale at 12 months VAS: dominant[b] Ambulation: dominant[b] ADL scale: dominant[b] PSA: NR
Klazen et al, 2010[60] The Netherlands and Belgium	CEA, CUA Trial-based analysis Health care payer perspective 1 y (NA)	Mean age 75 y 69% female Patients with acute (≤ 6 weeks) painful (VAS ≥ 5) OVCF	**I:** PVP + optimum pain treatment (N = 86) **C:** CT (N = 77)	QALYs (EQ-5D) The total QALYs for each group were not reported. IE at 1 y (PVP vs CT): 0.108 QALYs (after adjusting for baseline differences using regression analysis) Pain-free days (defined as VAS score ≤ 3) 120.3 pain-free days gained at 1 year	Euros, 2008 The total cost for each group was not reported. IC at 1 y (PVP vs. CT): €2,450 in favour of CT	€22,685/QALY €20/pain-free day PSA: There is a greater than 70% probability that PVP is cost-effective at a WTP value of €30,000/QALY
MASC, 2019[129] Australia	CUA Decision tree model Health care payer perspective 6 mo and 1 y (5%)	Patients with OVCF, fracture age < 6 wk old	**I:** PVP **C:** CT	PVP 6 mo: 0.37 QALYs 1 y: 0.73 QALYs CT 6 mo: 0.35 QALYs 1 y: 0.70 QALYs	Currency NR but assumed AUD[a] PVP 6 mo: $10,118.32 1 y: $10,574.09 CT at 6 mo with MRI: $10,282.54 without MRI: $9,765.44 CT at 1 y: with MRI: $10,737.14 without MRI: $10,378.74	6 mo: PVP vs CT with MRI: Dominant PVP vs CT without MRI: $16,104.57/QALY 1 y: PVP vs. CT with MRI: Dominant PVP vs. CT without MRI: $5,331.51/QALY Multiway sensitivity analysis: $71,000/QALY PSA: NR

Author, year, country	Analytic technique, study design, perspective, time horizon (discount rate)	Population	Intervention(s) and comparator(s)	Results		
				Health outcomes	Costs	Cost-effectiveness
Hopkins et al, 2020[128] United States	CUA Markov microsimulation model US Medicare payer perspective Lifetime (3%)	Patients with OVCF Reference case demographic characteristics based on Medicare and Medicaid Services claims data (mean age 79–82 y)	**I:** PVP (N = 720 inpatient; 1,042 outpatient) **C:** CT (N = matched one-to-one)	PVP Inpatient 2.23 QALYs, Outpatient 3.71 QALYs C Inpatient 1.47 QALYS, Outpatient 3.02 QALYs	USD, 2016 PVP Inpatient $32,301, Outpatient $32,972 C Inpatient $31,005, Outpatient $23,789	Inpatient, $39,774/QALY Outpatient, $12,293/QALY PSA: NR, authors stated that results were similar to PBK vs. CT results
Jacobsen et al, 2020[38] Switzerland	CUA Decision tree model Swiss public payer perspective 1 y (NA)	Patients with OVCF, fracture age < 8 wk	**I:** PVP **C:** CT	The total QALYs for each group were not reported IE at 1 y: 0.11 QALYs	CHF, year NR PVP: 11,163 CT: 9,039	CHF 19,669 per QALY PSA: At WTP value of CHF 100,000 per QALY, there was an 85% probability that PVP is cost-effective compared with CT at 12 mo
PBK compared with CT						
Strom et al, 2010[125] United Kingdom	CUA Markov cohort model Healthcare payer perspective Lifetime (3.5%)	Mean age: 70 y Patients hospitalized with painful OVCF	**I:** PBK + CT **C:** CT	I: 3.842 QALYs **C:** 3.673 QALYs	GBP, 2008 I: £10,420 C: £8,926	£8,840/QALY PSA: There was a 13% probability that PBK is cost-saving (less costly and more effective) compared with NSM
Fritzell et al, 2011[126] Sweden	CUA Trial-based analysis (subset of FREE trial) Societal perspective 2 y (NR)	Hospitalized patients with acute/subacute (< 3 mo) painful OVCF PBK: mean age 72 y; 71% female CT: mean age 75 y; 78% female	**I:** PBK + CT (N = 32) **C:** CT (N = 31)	The total QALYs for each group were not reported IE at 2 y (PBK vs. CT): 0.085 QALYs (after adjusting for baseline differences using regression analysis)	SEK, 2008[c] I: 160,017 kr (SD = 151,082 kr) C: 84,818 kr (SD = 40,953 kr)	884,682 kr/QALY PSA: There is a < 40% probability that PBK is cost-effective at a WTP value of 600,000 kr
Takahashi et al, 2019[130] Japan	CUA Markov cohort and propensity score matching study, non-randomized Health care payer perspective 3 and 20 y (3.5%)	Patients 65 and older with painful OVCF Mean age 78 y, 87% female All patients in PBK group were hospitalized, 66% of patients in NSM group were hospitalized	**I:** PBK + CT (N = 100) **C:** CT (N = 420)	At 6 mo PBK: 0.153 QALYs C: 0.120 QALYs	Yen, year NR PBK: ¥1,329,629 C: ¥926,642[c]	3 y: ¥4,404,158/QALY 20 y: ¥2,416,406/QALY PSA: when the probability of cost-effectiveness is 50%, the WTP value must be ¥1,121,453 JPY/QALY to be cost effective

Author, year, country	Analytic technique, study design, perspective, time horizon (discount rate)	Population	Intervention(s) and comparator(s)	Results		
				Health outcomes	Costs	Cost-effectiveness
Hopkins et al, 2020[128] United States	CUA Markov microsimulation model US Medicare payer perspective Lifetime (3%)	Patients with OVCF Reference case demographic characteristics based on Medicare and Medicaid Services claims data (mean age 79–82 y)	**I:** PBK (N = 2,071 inpatient; N = 3,708 outpatient) **C:** CT (N = matched one-to-one)	PBK: Inpatient 2.08 QALYs, Outpatient 3.88 QALYs C: Inpatient 1.47 QALYs, Outpatient 3.08 QALYs	USD, 2016 PBK: Inpatient $58,986 Outpatient $32,972 C: Inpatient $32,324, Outpatient $24,234	Inpatient, $43,455/QALY Outpatient, $10,922/QALY PSA: At a US WTP value of $50,000/QALY, PBK inpatient and PBK outpatient had an 80% and 100% probability of being cost-effective, respectively
Jacobsen et al, 2020[38] Switzerland	CUA Decision tree model Swiss public payer perspective PVP: 1 y (NA) PBK: 2 y (NR)	Patients with OVCF, fracture age < 3 mo for PBK	**I:** PBK **C:** CT	The total QALYs for each group were not reported IE at 2 y: 0.21 QALYs	CHF, year NR PBK: CHF 11,163 CT: CHF 9,039	At 12 mo.: CHF 18,405 per QALY At 24 mo.: CHF 10,341 PSA: At WTP value of CHF 100,000 per QALY, there was an 87% probability that PVP is cost-effective compared with CT at 12 mo
Comparison of PVP, PBK, and CT						
Edidin et al, 2012[132] United States	CEA Longitudinal administrative data claims and statistical (Weibull survival) modeling US Medicare perspective Costs: 3 y (3%) Health outcomes: lifetime (3%)	Medicare patients ≥ 65 with outpatient claim for newly diagnosed VCF	**I:** PBK (N = 119,253; 5,670 for costing analysis) **I:** PVP (N = 63,693; 3,539 for costing analysis) **C:** CT (N = 676,032; 57,809 for costing analysis)	The predicted life expectancy for each group was not reported The range of median increase in predicted life expectancy for all age–sex groups was: PBK vs. non-operated: 3.0–9.5 y PVP vs. non-operated: 1.0–4.3 y PBK vs. PVP: 2.0–5.2 y	2010, USD Range of median costs for all age-sex groups: PBK: $57,770–$89,670 PVP: $45,220–$94,240 Non-operated: $19,950–$37,100	Range of cost per life year gained for all age-sex groups: PBK vs. non-operated: $1,863–$6,687 PVP vs. non-operated: $2,452–$13,543 PBK vs. PVP: dominant (i.e., less costly and more effective) to $2,763 PSA: NR
Svedbom et al, 2013[124] United Kingdom	CUA Markov cohort model Health care payer perspective Lifetime (3.5%)	Patients hospitalized with acute, symptomatic OVCF Modelled mean age 70 y, all female population	**I:** PBK **I:** PVP **C:** CT	PBK: 5.473 QALYs PVP: 5.338 QALYs CT: 4.976 QALYs	GBP, 2009 PBK: £9,313 PVP: £7,157 CT: £7,969	PBK vs. PVP: £15,982/QALY PBK vs. CT £2,706/QALY PSA: PBK had a 60% probability of being optimal strategy at a WTP value of £20,000 and a 75% probability at a threshold of £30,000

Author, year, country	Analytic technique, study design, perspective, time horizon (discount rate)	Population	Intervention(s) and comparator(s)	Results		
				Health outcomes	Costs	Cost-effectiveness
Stevenson et al, 2014[127] United Kingdom	CUA State transition model United Kingdom public health care payer perspective 50 y (3.5%)	Patients with OVCF Modelled mean age 70 y, all female population	**I:** PBK **I:** PVP **C:** CT (optimal pain management) **C:** OPLA	Results were presented for different utility data sources within 6 scenarios. The relative number of QALYs for each intervention changed in the different scenarios	GBP, 2009/10 There was less variation in costs for the 6 scenarios PBK was consistently highest with range £8,100–£8,400 PVP, OPLA, and CT had similar costs in all scenarios, about £6,100	Results varied depending on the scenario: If differential mortality effects, where PBK is more effective than PVP are assumed, PBK had the highest QALYs and an ICER < £20,000 If differential mortality effects where PBK and PVP have the same effect, which is twice the effect of OPLA, are assumed, then PBK was dominated by PVP; PVP had an ICER < £10,000 when compared with CT and OPLA If identical mortality effects were assumed for PBK, PVP, and OPLA, then OPLA dominated PVP and PBK If no mortality benefits were assumed for any intervention, the results depended on other assumptions; particularly hospitalization costs. PVP was often the dominant procedure PSA: All scenarios were run probabilistically; therefore, the results represent PSA results

Abbreviations: ADL, activities of daily living; CEA, cost-effectiveness analysis; CT, conservative treatment; CUA, cost–utility analysis; IC, incremental cost; ICER, incremental cost-effectiveness ratio; IE, incremental effect (health outcomes); mo, months; MRI, magnetic resonance imaging; NA, not applicable; NR, not reported; OPLA, operative placebo with local anaesthesia; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PSA, probabilistic sensitivity analysis; PVP, percutaneous vertebroplasty; QALY, quality-adjusted life year; VAS, visual analogue scale; VCF, vertebral compression fracture; WTP, willingness to pay; y, years.

[a]Year not reported.

[b]Dominant indicates the intervention was less costly and more effective than the comparator.

[c]Adjusted to 2008, 1 Euro = 9,6 kr and 1 USD = 6.6 kr. In May 2008 1 GBP = ¥147.63

Applicability and Limitations of the Included Studies

Table A12 (Appendix 7) provides the results of the quality appraisal checklist for economic evaluations applied to the included studies. No studies were deemed directly applicable to the research question, 8 were deemed partially applicable, and the remaining 3 were deemed not applicable. We assessed the limitations of the studies deemed partially applicable (Table A13). Seven studies had minor limitations, and 1 had potentially serious limitations. No studies were relevant to the Ontario setting.

Discussion

We identified 11 economic studies that evaluated the cost-effectiveness of vertebral augmentation (PVP or PBK) compared with CT for people with OVCF.

All studies that compared PVP with CT concluded that PVP was a cost-effective strategy for treating people with painful OVCF. Only 1 study reported a requirement that patients were refractory to CT (analgesic therapy); however, the duration of CT treatment required to determine refractoriness was 2 weeks.[131] All studies required patients to have acute, symptomatic (i.e., painful) OVCF.[38,60,128,129] Acute was defined in 2 studies as less than 6 weeks,[60,129] another as less than 8 weeks,[38] and 2 as less than 3 months.[128,131]

Four of 5 studies that compared PBK with CT considered PBK to be cost-effective[38,125,128,130]; the fifth found the opposite and concluded that PBK would not be considered cost-effective compared with CT.[126]

Most studies conducted CUAs and included treatment effects on quality of life (utility). There were differences across studies on whether treatment effects on mortality, subsequent OVCF, and length of hospital stay were included. Studies that did include these effects found that results were sensitive to assumptions about their values.[124,125,127,128,130]

Strengths and Limitations

We conducted a thorough literature search of the economic evidence and found 11 studies relevant to our research question. We assessed the applicability and limitations of the evidence to determine that none of the studies were directly applicable to the Ontario context. The PVP and PBK procedures were generally well-described in the studies; however, the composition of CT was less clear.

Guidelines have been mixed on the appropriateness of PVP and PBK. Some guidelines focus on specific patient populations (e.g., acute fractures, refractory to CT). Factors such as age of fracture and whether CT had been tried prior to PVP or PBK were rarely specified by studies. Where available, we drew information from the RCTs that informed the economic evaluations, but refractoriness to CT was almost never described. PVP and PBK can be performed as inpatient or outpatient procedures. It was also not always indicated whether the populations in the economic evaluations were inpatient, outpatient, or mixed.

Conclusions

We identified 11 economic studies. All studies that compared PVP with CT concluded that PVP was a cost-effective strategy for treating people with painful OVCFs. Of 5 studies that compared PBK with CT, 4 considered PBK to be a cost-effective option. However, the results may not be generalizable to Ontario because none of the studies were directly applicable to our research question and none were based on a Canadian setting.

Primary Economic Evaluation

We found several published economic evaluations evaluating the cost-effectiveness of percutaneous vertebroplasty (PVP) and percutaneous balloon kyphoplasty (PBK) for adults with painful osteoporotic vertebral compression fractures (OVCFs). However, none of the studies were directly applicable to the Ontario context. Therefore, we conducted a primary economic evaluation.

Research Question

What is the cost-effectiveness of PVP or PBK with conservative treatment (CT) compared with CT alone for the treatment of adults with painful osteoporotic vertebral compression fractures (OVCFs) from the perspective of the Ontario Ministry of Health?

Methods

The information presented in this report follows the reporting standards set out by the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.[136] The content of this report is based on a previously developed economic project plan.

Type of Analysis

We conducted a cost–utility analysis (CUA), as recommended by Canada's Drug Agency (CDA) (formerly the Canadian Agency for Drugs and Technologies in Health [CADTH]) guidelines for economic evaluations.[15] The results are reported as the incremental cost per quality-adjusted life years (QALYs) gained.

Population of Interest

Our population of interest was adults (≥ 40 years of age) with a diagnosis of symptomatic (i.e., painful) OVCF refractory to CT. We modelled a population of people 72 years of age and 60% female, based on characteristics of people currently receiving the procedure in Ontario (IntelliHealth data accessed Aug 22, 2024).

Perspective

We conducted this analysis from the perspective of the Ontario Ministry of Health.

Interventions and Comparators

We conducted evaluations of vertebral augmentation (PVP or PBK) combined with CT, compared with CT alone. Table 33 summarizes the interventions evaluated in the economic model.

Table 33: Disease Interventions and Comparators Evaluated in the Primary Economic Model

Interventions	Comparator	Population	Outcome
PBK with CT PVP with CT	CT	Adults (≥ 40 years) with a diagnosis of symptomatic (i.e., painful) OVCF refractory to conservative (nonsurgical) treatment	Total costs, QALYs, ICER estimated as cost per QALY gained

Abbreviations: CT, conservative treatment; ICER, incremental cost-effectiveness ratio; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QALYs, quality-adjusted life years.

Conservative Treatment

In Ontario, CT consists of pain medication (e.g., acetaminophen, opioids, nonsteroidal anti-inflammatory drugs), advice to stay active as tolerated, exercise, physiotherapy, and in some cases use of a back brace (E. Wai, MD, video communication, May 9, 2024). A systematic review of international clinical guidelines for the treatment of vertebral compression fractures found 3 guidelines that included descriptions of CT published between 2010 and 2016.[137] Descriptions of CT varied across the guidelines, though each included a pharmacologic component (calcitonin and opioids, pain medication, or nonsteroidal anti-inflammatory drugs) and at least 1 other component (brace, bed rest, exercise, electrical stimulation, or methods of immobility).[127,138,139] Note that bed rest is no longer considered an appropriate treatment (E. Wai, MD, video communication, May 9, 2024).

The details of CT assumed in our CUA are included in the cost section and were developed with clinical experts to reflect current practice in Ontario.

Vertebral Augmentation

Two types of vertebral augmentation are considered in this report: PVP and PBK. Both procedures consist of injecting bone cement, usually polymethylmethacrylate (PMMA), into the fracture; however, PBK includes an additional step of inflating a balloon to increase the space in the fracture. PVP and PBK can be performed by an interventional radiologist, neurosurgeon (spinal surgeon), or orthopedic surgeon and may be provided as an inpatient or an outpatient (day) procedure. It can be performed in an operating room or an interventional radiology suite. The type of procedure used (PVP or PBK) depends on physician preference and experience (S. Priola, MD, video communication, March 19, 2024; J. Waddell, MD, video communication, March 27, 2024).

Time Horizon and Discounting

We used a 3-year time horizon in our reference case analysis. Based on the conclusions of the Clinical Review, PVP and PBK may improve physical function and quality of life and increase risk of cement leakage. A 3-year horizon allows us to capture those differences and incorporate the longest available randomized controlled trial (RCT) data. Scenario analyses were used to explore the impact of longer time horizons and impacts that were less certain, such as treatment effect on mortality, subsequent OVCFs, and adverse events. In accordance with the CDA guidelines,[140] we applied an annual discount rate of 1.5% to both costs and QALYs incurred after the first year.

Main Assumptions

The model's main assumptions were as follows:

- For the treatment effect on quality of life (utility), we assumed that after the 2-year follow-up there was a 1-year offset period in which the mean difference in utility among all interventions declines to zero. This assumption has been used by previous economic evaluations.[32,124,126,127,130] We assumed that during the 1-year offset period all utilities increase to the highest intervention's utility. We chose to assume that the intervention utilities would increase rather than decrease to no difference because the main trial for PBK compared with CT reported that although quality of life (utility) was fairly stable for the trial duration, the CT arm gradually improved physical function and disability over time[22]
- The Clinical Review concluded that PVP and PBK each compared with CT may have little to no effect on mortality, adverse events, or new fractures; therefore, we did not consider treatment effects on these outcomes in the reference case
- The Clinical Review concluded that PVP and PBK each compared with CT may have little to no effect on analgesic use, consequently we assumed that people who receive PVP or PBK still receive CT and that costs for CT would be the same in all treatment arms
- We assumed that subsequent OVCFs were treated using the same intervention as the initial OVCF, in accordance with RCT protocols, where stated, and would incur the same costs and benefits as the initial OVCF[60,118]
- We assumed that subsequent OVCFs resulted in the same costs and utility as the initial OVCF. We used the intervention costs and the utility values from the RCTs at baseline to reset the utility
- We assumed that the increased risk of death for people with an OVCF compared with people without an OVCF lasted 1 year for men and 10 years for women[141]
- We assumed that the increased risk of subsequent OVCFs following an initial OVCF compared with people without an OVCF lasted 8 years[142]

Model Structure

We developed a decision-analytic model (decision tree and Markov state transition model) using TreeAge Pro software[143] with a 1-month cycle length (using 365/12, 1 month = 30.42 days) and 3-year time horizon to which we applied a half-cycle correction. The decision tree allocates people to one of our interventions, after which they enter the Markov model (Figure 28). The Markov model consisted of 3 health states: post-treatment, subsequent OVCF, and dead. The model was informed by the model used by Strom et al,[125] which has also been used in adapted form by others.[124,128,130] All patients began in the post-treatment health state. From the post-treatment health state, transitions to subsequent OVCF or dead were allowable. From the subsequent OVCF state, someone may experience another OVCF or die. Because quality of life and treatment effects depended on how much time had passed since the fracture event, we used tunnel states to track the time-in-state.

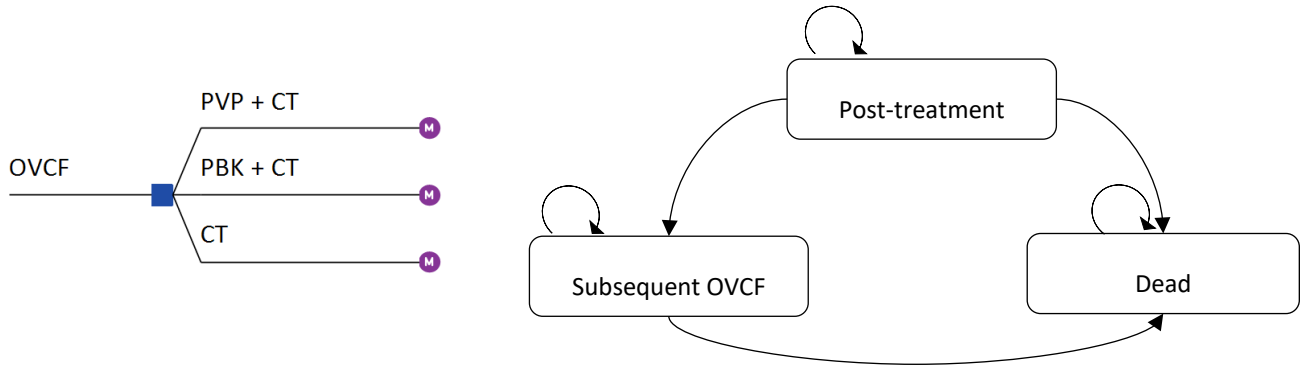


Figure 28: Model Structure

The left side of the figure depicts a decision tree for people with OVCF following which a decision node branches out to the 3 treatment options: PVP + CT, PBK + CT, and CT alone. The right side of figure depicts the Markov state transition model as a bubble diagram with 3 health states as rectangles (bubbles) and arrows indicating the allowable transitions between health states. The health states are: (1) post-treatment, in which a person can remain or proceed to the subsequent OVCF or the dead state, (2) Subsequent OVCF, in which a person can remain or proceed to the dead state, and (3) the Dead state.

Abbreviations: CT, conservative treatment; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

Clinical Outcomes and Utility Parameters

Natural History

We modeled the natural history of patients with osteoporosis who have had an OVCF. Based on our model structure, people could have a subsequent OVCF or die. Our approaches to estimating the transition probabilities are described below and in Table 34.

Probability of Subsequent OVCF

The probability of a subsequent OVCF depended on patient age and sex. Annual rates of osteoporosis-related vertebral fractures by age and sex were taken from the Canadian Chronic Disease Surveillance System (CCDSS) based on 2019–2020 data and converted to 1-month probabilities.[144] In a 3-year prospective Canadian study in postmenopausal women, an adjusted model found that low bone mineral density (BMD) and a prior vertebral fracture were associated with an increased risk in subsequent clinical vertebral fractures.[145] Osteoporosis is characterized as BMD that is 2.5 or more standard deviations below peak bone mass.[146] We assumed an average reduction in BMD by 2.5 standard deviations for our population of interest and calculated the associated relative risk using the results of this study.[145] Because osteoporosis is a chronic condition, we assumed the increased risk of subsequent OVCF due to osteoporosis lasted a lifetime.[147] We further assumed that the increased risk due to prior vertebral fracture lasted 8 years, which was the average follow-up time in a meta-analysis.[142] This is relevant for the scenario analyses in which we used lifetime time horizons. A sample calculation is presented in Appendix 9.

Mortality

People with osteoporosis are at an increased risk of death compared with the general population, which we accounted for by multiplying the mortality rate for the general Canadian population from Canadian life tables[148] by the mortality rate ratios comparing people with and without osteoporosis reported in Canada.[147] A Canadian study found that people with a prior fracture are at an increased risk of death.[141] The increased risk of death lasted 10 years for women and 1 year for men (Table 34).[141] Although accounting for both osteoporosis and vertebral fracture may be expected to overestimate the mortality risk, a study among only people with osteoporosis found that the increased risk of mortality with vertebral fracture still held.[149] A sample calculation is presented in Appendix 9.

Table 34: Natural History Inputs Used in the Economic Model

Model parameter	Value		Distribution	Reference
Subsequent OVCF				
Annual rate of OVCF per 100,000[a,b]	**Women** 40–49: 30 50–64: 67 65–79: 184 ≥ 80: 557	**Men** 40–49: 42 50–64: 74 65–79: 146 ≥ 80: 382	Fixed	CCDSS[144]
Relative risk of OVCF with 2.5 SD decrease in BMD[c]	6.86 (1.24–38.1)[c]		Log-normal	Papaioannou et al, 2005[145]
Relative risk of OVCF given prior OVCF	2.34 (0.90–6.09)		Fixed[d]	Papaioannou et al, 2005[145]
Mortality				
Annual probability of death[a,b]	Life tables		Fixed	Statistics Canada[148]
Rate ratio of death for those with vs. without osteoporosis	**Women** 40–49: 2.8 50–64: 1.5 65–79: 1.1 ≥ 80: 1.1	**Men** 40–49: 3.9 50–64: 2.3 65–79: 1.6 ≥ 80: 1.3	Fixed	CCDSS[147]
Hazard ratio of death given prior OVCF vs. none	**Women** Year 1: 1.27 (1.11–1.46) Years 2–5: 1.39 (1.18–1.64) Years 6–10: 1.35 (1.13–1.61)	**Men** Year 1: 1.26 (1.04–1.53)	Log-normal	Ye et al, 2022[141]

Abbreviations: BMD, bone mineral density; CCDSS, Canadian Chronic Disease Surveillance System; OVCF, osteoporotic vertebral compression fracture; SD, standard deviation.

[a]Annual rates were converted to monthly rates by dividing 365 by 12 (30.4 d/mo).

[b]Rates and probabilities were converted using the following formula p = 1 – exp(−rt), where p is the probability, r is the rate, and t is the unit of time (in our case 1/12 to convert annual to monthly).

[c]Calculated from Papaioannou et al,[145] who reported the relative risk for 1 SD decrease in BMD. Details in Appendix 9.

[d]Fixed value was used instead of a distribution to avoid potential bias due to wide confidence interval.[150]

Health State Utilities

A health state utility represents a person's preference for a certain health state or outcome, such as vertebral fracture. Utilities are often measured on a scale ranging from 0 (death) to 1 (full health). One method of determining a health state utility value is using questionnaires such as the EuroQol-5D (EQ-5D). Some of the clinical trials collected EQ-5D values at baseline and at various timepoints for each intervention and comparator group (Figures 5 and 25 and Table 21, above).

The overall quality of the clinical evidence (Grading of Recommendations Assessment, Development, and Evaluation [GRADE]) for quality of life was Very low, Low, and Very low for the comparisons PVP with CT, PBK with CT, and PVP with PBK, respectively. We derived utilities for the CT post-treatment state from the comparison of PBK with CT, which had the highest quality of evidence (Low) and longest follow-up time (24 months). Utilities for CT are reported for 1, 3, 6, 12, and 24 months in Table 21, which came from 1 RCT.[85,101] We imputed missing months using linear interpolation. Utilities were weighted by time by taking an average of the current month and 1 month prior to use in the model. The utilities for CT were defined as beta distributions to use in the probabilistic analysis (Appendix 8, Table A14). We adjusted for age and sex using the utilities for the general population measured by Guertin et al[151] (Appendix 8, Table A15). The utilities were adjusted using the multiplicative method described in the National Institute of Health and Care Excellence (NICE) technical support document (Appendix 9).[152]

For the PBK and PVP post-treatment health states, we applied treatment effects measured as mean difference in utility from the Clinical Review, which were sourced from the same RCT as the CT values.[101] We used the same methods that we used for the CT utilities to calculate the weighted mean difference in utility between PBK and CT. The monthly weighted mean differences in utilities were defined as normal distributions (Appendix 8, Table A16). PBK had statistically significant higher values at all timepoints. These values were added to the CT post-treatment arm utilities to estimate the PBK post-treatment utility.

No RCTs were identified that compared all 3 treatment approaches – CT, PBK, and PVP – therefore, for PVP, we calculated the monthly mean difference in utility between PVP and PBK from a trial that compared PBK with PVP using the same methods as above. We defined the weighted mean differences as normal distributions and applied the results to the PBK utilities we obtained (Appendix 8, Table A17).[85] Utilities for 1, 3, 12, and 24 months were not statistically significant, and the quality of evidence was rated Very low (Figure 25).

For the subsequent OVCF health state, we assumed that everyone would receive the same intervention that they received for their initial OVCF and thus applied the corresponding post-treatment utilities described above.

Table 35: Utilities Used in the Economic Model

Health state or treatment state	Utility	Distribution	Reference
Age- and sex-adjusted utility values of the Canadian population	See Appendix 8, Table A15	Fixed	Guertin et al, 2018[151]
Post-treatment, CT	See Appendix 8, Table A14	Beta	Clinical review, Table 21; Van Meirhaeghe et al, 2013[101]
Weighted mean difference of PBK + CT vs. CT	See Appendix 8, Table A16	Normal	Clinical review, Table 21; Van Meirhaeghe et al, 2013[101]
Weighted mean difference of PVP + CT vs. PBK + CT	See Appendix 8, Table A17	Normal	Clinical review, Figure 25; Dohm et al, 2014[85]
Post-treatment, PBK	Post-treatment, CT utilities plus weighted mean difference of PBK vs. CT	NA	Clinical review, Table 21; Van Meirhaeghe et al, 2013[101]
Post-treatment, PVP	Post-treatment, CT utilities plus weighted mean difference of PBK vs. CT plus weighted mean difference of PVP vs. PBK	NA	Clinical review, Table 21, Figure 25; Van Meirhaeghe et al, 2013[101]; Dohm et al, 2014[85]
Subsequent OVCF	Same as initial OVCF	NA	Assumption
Dead	0	Fixed	

Abbreviations: CT, conservative treatment; NA, not applicable; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

Impact of Vertebral Augmentation on Natural History

In addition to the impact of vertebral augmentation (PVP and PBK) on quality of life (utility), the Clinical Review assessed the potential impact of the intervention on mortality, serious adverse events, cement leakage, and new OVCFs. Clinical events such as mortality and new OVCFs can impact how people move through the Markov model (i.e., from post-treatment health state to death or subsequent OVCF). Clinical events such as serious adverse events and symptomatic cement leakage are associated with increased costs. The Clinical Review found that mortality, serious adverse events and new OVCFs were similar between PVP and CT as well as between PBK and CT, though there was uncertainty due to studies likely being underpowered to detect such differences. The quality of the evidence (GRADE) for PVP compared with CT was Very low, while the quality of evidence for PBK compared with CT was Low. Our clinical review concluded that PVP and PBK may have little to no effect on mortality, new fractures, or adverse events. Therefore, we included these outcomes only in scenario analyses. The clinical review concluded that the interventions may increase cement leakage. Symptomatic cement leakage was included in our reference case.

Cement Leakage

Cement leakage was categorized in the clinical review as symptomatic or asymptomatic. For the purposes of the economic evaluation, we were only interested in symptomatic cement leakage.

For PVP, there was 1 case of symptomatic cement leakage reported among 648 patients from 6 trials that ranged in follow-up from 12 to 36 months (Table 12). The timing of the symptomatic cement

leakage was not included in the RCT that reported it, only that it was a post-operative complication.[59] We used these results in our reference case.

For PBK, our clinical review identified 1 RCT that reported no symptomatic cases of cement leakage and another that did not distinguish symptomatic and asymptomatic cement leakage (Table 26). Similarly in observational trials, reports were either of only asymptomatic cases of cement leakage or not distinguished between asymptomatic and symptomatic cases (Table 27).

We used the results from the single arm trials, where there were 8 reports of symptomatic cement leakage among 731 patients ranging from 3 to 24 months follow-up (Table 28). Some of the cement leakages were reported by vertebrae and not by the patient, so it is possible that some patients experienced more than 1 cement leakage. The upper bound for the number of patients affected is 8. There were 3 trials that contributed to the 8 reports of symptomatic cement leakage. If each trial's reported cement leakage occurred in the same patient, the lower bound on the number of people affected is 3. We used the former estimate in our reference case.

Table 36: Summary Estimates Used in the Economic Model

Intervention	Variable	Estimate	Duration	Distribution	Reference
PVP	Probability of symptomatic cement leakage	0. 00154 (1/648)[59]	One-time event	Fixed	Table 12
PBK	Probability of symptomatic cement leakage	0.0109 (8/731)	One-time event	Fixed	Table 28

Abbreviations: PBK, balloon kyphoplasty; PVP, percutaneous vertebroplasty.

Cost Parameters

For each treatment, we costed the inpatient and outpatient settings from the Ontario Ministry of Health perspective. Health service utilization was informed by clinical experts and unit costs were sourced from the IntelliHealth Ontario portal (intellihealth.moh.gov.on.ca), the Ontario Schedule of Benefits for Physician Services,[153] and the Ontario Drug Formulary.[154] The cost of subsequent OVCF comprised emergency department visit costs and intervention costs again. Costs were applied one-time at the time of the event. Table 37 displays a breakdown of the costs included for each intervention in the inpatient or outpatient setting. All costs were reported in 2024 Canadian dollars (Table 37). For costs taken from sources not reported in 2024 dollars, we used the all-items Statistics Canada Consumer Price Index (CPI) to adjust costs to 2024 CAD.[155] No conversions between currencies were required as all costs were sourced from Canadian data. Detailed costing is provided in Table A18 (Appendix 8).

Table 37: Costs Included for Each Intervention[a]

	CT outpatient[b]	CT inpatient[b]	PVP + CT outpatient[b]	PVP + CT inpatient[b]	PBK + CT outpatient[b]	PBK + CT inpatient[b]
Outpatient costs: $364	X	X	X	X	X	X
Hospitalization for OVCF – no procedure: $16,366		X				
Hospitalization for OVCF: PVP: $35,508; PBK: $39,128				X		X
Outpatient procedure costs (PVP or PBK): PVP $5,747, PBK $8,995			X		X	
Pre- and post-procedure costs: PVP $318, PBK $299			X	X	X	X
Cost of symptomatic cement leakage: $35,574[b]			X	X	X	X
Total	$364	$16,729	$6,483	$36,244	$10,046	$40,180

Abbreviations: CT, conservative treatment; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]All costs in 2024 CAD.

[b]31% of the population of interest were inpatient and 69% were outpatient from IntelliHealth data on people with spine fractures accessed September 19, 2024. Data shown in Appendix 8, Tables A20 and A21.

[c]Cost was multiplied by the percentage of people who experienced the event: 0.154% for PVP and 1.09% for PBK. Results may appear inexact due to rounding.

Outpatient Conservative Treatment Costs

We estimated the health care resource use for CT to be $363.50 after input from clinical experts about current practice in Ontario (Tables 37 and A18, Appendix 8). We assumed that everyone had an average of 2 visits with their family doctor and 1 visit with an orthopedic surgeon and received 1,000 mg of acetaminophen 3 times per day for 6 weeks. 50% of people received 1 mg hydromorphone per day for 6 weeks and 50% would attend government-funded physiotherapy. Government-funded physiotherapy is available to people 65 years or older and is recommended after a recent illness, injury, accident, or surgery that led to a decline in function or movement.[40] We assumed that people receiving PVP or PBK would have received the same CT for the same duration as those who received CT alone.

Emergency Department Costs

We assumed that 50% of people with a subsequent OVCF visited the emergency department (ED) (D. Tannenbaum, MD, email communication, September 7, 2024). We estimated the cost of an ED visit for a vertebral fracture using ambulatory (NACRS) data from IntelliHealth Ontario. We identified cases of osteoporosis-related vertebral fractures using the same case definition as the chronic disease surveillance system in which only people aged 40 and older with an osteoporosis-related vertebral fracture diagnosis (Appendix 8, Table A19) were included.[147] In fiscal year 2022, there were 3,625 ED visits for osteoporosis-related vertebral fractures, with a mean cost of $845.00 (Appendix 8, Table A18). We added the physician fee for 1 ED consultation to this estimate, for a total cost of $954.88.

Hospitalization for OVCF

We estimated the percentage of people with an OVCF who would be admitted to hospital using ambulatory data from IntelliHealth for fiscal years 2021 to 2023. Disposition status was dichotomized into admitted and not admitted (Appendix 8, Table A20). Over fiscal years 2021 to 2023, an average of 31% of people with a spinal fracture were admitted to hospital (Appendix 8, Table A21).

No Procedure (CT Only)

We estimated the cost of a hospitalization for an OVCF using inpatient discharge data (Discharge Abstract Database) from IntelliHealth Ontario. We used the same age and diagnostic criteria as the ED visits, but included only cases where the main intervention was empty or was diagnostic imaging. We used the following estimated inpatient OVCF costs per patient who received CT only (inpatient hospitalization costs for patients who received PVP or PBK are described later). In fiscal years 2020 to 2022, there were 2,943 hospitalizations with a mean hospital cost of $13,944.66 for people aged 40 or older with an osteoporosis-related vertebral fracture diagnosis. To estimate physician costs, we adopted the method used in a previously published HTA in which the ratio of the physician costs to hospital costs was estimated using the CIHI patient cost estimator.[156,157] Physician costs were then obtained by multiplying the calculated ratio by the hospital costs obtained from IntelliHealth Ontario. We used the ratio of physician to hospital costs for patients with spinal injury (case mix group 771) and obtained physician costs of $2,420.91, bringing the total cost to $16,365.56.

PVP or PBK Procedure

The hospital costs for the procedure were obtained from the Ontario Case Costing Initiative[158] using the inpatient (DAD) dataset (IntelliHealth Ontario data accessed August 28, 2024). We identified procedures in the data using the Canadian Classification of Health Interventions procedure codes for PVP and PBK (Appendix 8, Table A22) for fiscal years 2020 to 2022. To obtain accurate cost estimates for an inpatient procedure for PVP or PBK, we limited our search to cases with PVP or PBK in the main intervention field. It is possible that more patients received PVP or PBK in hospital, but the intervention was secondary to another main intervention. There were 98 cases of PVP between fiscal years 2020 and 2022 with an estimated mean hospital cost of $27,884.64. There were 39 cases of PBK between fiscal years 2020 and 2022 with an estimated mean hospital cost of $30,727.28. We used the ratio of physician costs to hospital costs from the CIHI patient cost estimator for patients with a spinal intervention with trauma/complication of treatment (CMG 731). The physician costs were $7,623.56 and $8,400.73 and the total costs were $35,508.20 and $39,128.02 for PVP and PBK, respectively.

Outpatient (Day) Procedure

We assumed that the remaining patients who are not hospitalized would receive the intervention as a day procedure. The hospital costs for the procedure were obtained from the Ontario Case Costing Initiative using the ambulatory dataset (National Ambulatory Care Reporting System) and selecting day procedures only (IntelliHealth Ontario data accessed October 15, 2024). We identified procedures in the data using the Canadian Classification of Health Interventions procedure codes for PVP and PBK for fiscal years 2018 to 2022, excluding people with a main cancer diagnosis (ICD-10 code beginning with “C”). We estimated hospital costs of about $4,580.21 and $6,666.79 for PVP and PBK, respectively (IntelliHealth Ontario, accessed October 15, 2024). We estimated physician fees for the procedures by calculating the physician, anesthesiologist, and surgical assistant fees associated with relevant Ontario Health Insurance

Plan (OHIP) fee codes (Appendix 8, Table A23). We estimated physician costs of $1,167.20 and $2,327.86 for PVP and PBK, respectively. We estimated the average number of levels operated on per patient for each procedure and the percentage of time an anesthesiologist or surgical assistant was present for the procedure using OHIP billing data from fiscal years 2018 to 2022 (IntelliHealth, accessed September 11, 2024). We identified extra levels billed per patient from the OHIP fee code for extra levels, E391 and E393 for PVP and PBK, respectively. We identified anesthesiologist and surgical assistant fees using fee schedule code suffixes C and B, respectively. We assumed that the number of levels operated on and the percentage of time anesthesiologists or surgical assistants are involved would remain constant.

Pre- and Post-Procedure Costs

We costed the physician appointments and scans that would occur pre- and post-procedure. We assumed that all patients would receive magnetic resonance imaging (MRI) before their procedure (S. Priola, MD, video communication, March 19, 2024). We assumed that all patients have 1 visit with a specialist (interventional radiologist or neurosurgeon) before and after their PVP or PBK procedure. The total pre- and post-procedure costs for PVP and PBK were $317.54 and $298.92, respectively.

Costs of Symptomatic Cement Leakage

We costed symptomatic cement leakage in the same manner as serious adverse events. We multiplied the treatment costs by the percentage of people who experienced symptomatic cement leakage to obtain an average per person cost of symptomatic cement leakage. The percentages of symptomatic cement leakage are presented in Table 36, and the cost of treatment is presented in Table 37 and Appendix 8, Table A18.

There was 1 report of a symptomatic cement leak that included information on the treatment provided. Farrokhi et al[59] reported an epidural cement leakage that caused severe lower-extremity pain and weakness on the right side that was treated with immediate decompression through a bilateral laminectomy and evacuation of bone cement. We estimated the cost of treatment using inpatient data from IntelliHealth Ontario accessed October 16, 2024. We identified cases for which the main intervention was spinal vertebrae fixation including laminectomy (CCI code 1SC74), with additional intervention release spinal code (CCI codes for 1AW72). There were 79 cases in fiscal year 2022, with an average cost of $35,573.98. We used this estimate as the average cost per symptomatic cement leak.

Internal Validation

The secondary health economist conducted formal internal validation. This process included testing the mathematical logic of the model, checking for errors, and ensuring the accuracy of parameter inputs and equations.

Equity Considerations

Economic evaluations inherently focus on horizontal equity (i.e., people with similar characteristics are treated in a similar way). Where possible, we conduct subgroup or scenario analyses to best address vertical equity (which allows for people with different characteristics to be treated differently according to their needs).

In our economic evaluation, the use of QALYs reflects horizontal equity because equal social value is assigned to each unit of health effect, regardless of the characteristics of the people who receive those effects or the condition being treated.

We considered equity in terms of access to the technology by conducting a scenario analysis that included costs for the Northern Health Travel Grant. We also considered a scenario analysis from a societal perspective to capture out-of-pocket costs not included in the Ontario Ministry of Health perspective.

Analysis

Our reference case and scenario analyses adhered to Canada's Drug Agency guidelines[140] when appropriate. The reference case represents the analysis with the most likely set of input parameters and model assumptions relevant to Ontario. Our scenario analyses explored how the results would be affected by varying input parameters and model assumptions.

For the reference case, we conducted a probabilistic analysis to capture the uncertainty in model parameters. When possible, we specified distributions around input parameters using the mean and standard error. Selected cost parameters were characterized by gamma distributions, probabilities and utilities by beta distributions, mean differences in utilities by normal distributions, and relative risks by log-normal distributions. We ran 5,000 simulations and calculated mean total costs and mean QALYs with credible intervals for each intervention assessed. Following the CDA guidelines,[140] we reported the sequential incremental cost-effectiveness ratios (ICERs) and an ICER produced from a common comparator (conventional treatment). We ordered treatments by mean total costs, from lowest to highest. For sequential ICERs, after excluding treatments that were either dominated or subject to extended dominance, we calculated the ICER for a less costly comparator compared with the next more costly comparator. In addition to estimating the ICER for each comparison, we also used net monetary benefit (NMB) to evaluate the cost-effectiveness of the 3 included treatments (incremental net benefit).

The results of the probabilistic analysis are presented in a cost-effectiveness acceptability curve. Although not used as definitive willingness-to-pay (WTP) thresholds, including graphical indications of the location of the results relative to guideposts of $50,000 and $100,000 per QALY facilitates interpretation of the findings and comparison with historical decisions. We also present uncertainty quantitatively as the probability that an intervention is cost-effective at previously mentioned WTP guideposts. For each simulation, treatment with the maximum NMB at the given WTP was considered the most cost-effective among the 3 treatments we compared.[159] The probability of being cost-effective for each treatment was equal to the proportion of the 5,000 simulations for which this treatment had the highest NMB.

Scenario Analyses

We conducted scenario analyses to assess the impact of key assumptions on model results. Table 38 summarizes the values used in scenario analyses.

Treatment Effects

- **Scenario 1:** we explored the impact of using the utility data from the PVP versus CT trials using the results from our clinical review on PVP compared with CT. We identified 2 RCTs that reported EQ-5D

from 1 week to 12 months (Figure 5).[60,65] These were not used for the reference case as both studies reported statistically significantly different EQ-5D between groups at baseline. For this scenario analysis, we calculated monthly weighted mean differences in utility between PVP and CT for the first 12 months (Appendix 8, Table A27). These values were applied to the post-treatment CT utilities calculated from the FREE trial[101] rather than from the trials of PVP compared with CT because of the imbalances in utility between groups at baseline in both trials. Because both trials had only 12-month follow-up data, we applied the method used by Svedbom et al[124] to derive a 24-month utility for PVP. We assumed that the percentage change in utility from 12 to 24 months for PBK compared with CT in the FREE trial would apply to the comparison of PVP with CT as well. We used the same assumption about duration of treatment effect and applied a 1-year offset period to all interventions, during which time the difference in utilities decreased to no difference. In Scenario 1-1, we used a 3-year time horizon; in Scenario 1-2 we used a lifetime time horizon

- **Scenario 2:** We explored the assumptions around treatment effect on utility. In Scenarios 2-1 and 2-2, we varied the duration of the offset period. As suggested by Canadian guidelines, we varied the 1-year offset period to 0 years, representing no effect beyond the trial duration (Scenario 2-1). In Scenario 2-2, we assumed the offset period was infinite, representing no waning of treatment effect.[160] In Scenario 2-3, we used the 1-year offset period but assumed that all utilities go down to the lowest 2-year value. Scenarios 2-1 and 2-2 used a lifetime time horizon, while Scenario 2-3 used a 3-year time horizon
- **Scenario 3**: We included a treatment effect on mortality from the clinical review. For PVP compared with CT, our review found a risk ratio for all-cause mortality based on 5 RCTs that favoured PVP (though it was not statistically significant; relative risk [RR] = 0.72; 95% confidence interval [CI]: 0.36–1.48) (Figure 7). Four of the RCTs had a 1-year follow-up, while 1 had a 3-year follow-up. For PBK compared with CT, the clinical review described all-cause mortality from 1 RCT comparing PBK to CT.[100] By 12 months, there were 9/149 (6.0%) deaths in the PBK arm and 7/151 (4.6%) in the CT arm. We used these estimates to calculate an RR and 95% CI. We applied the relative risks in our scenario analyses. In Scenario 3-1, we ran a 3-year time horizon and applied this treatment effect for the duration of our model. In Scenario 3-2, we ran a lifetime time horizon and applied the treatment effect for 3 years to reflect the longest available comparative data
- **Scenario 4:** We explored using different estimates for the treatment effects on mortality. We used results from a published meta-analysis of observational studies.[161] In Scenario 4-1, we used a time horizon of 3-years for comparison with our reference case and applied the treatment effect for the duration of the model. In Scenario 4-2, we used a lifetime time horizon and applied the treatment effect for 5 years to align with the study findings[161]
- **Scenario 5:** We explored the treatment effect on mortality using results from a retrospective analysis of Medicare claims data in the United States.[162] Although not part of our review, this study was used in other economic evaluations[124,127]; therefore, these scenario analyses will allow us to more directly compare our cost-effectiveness results to others. In Scenario 5-1, we used a 3-year time horizon for comparison with our reference case and applied the treatment effect for the

duration of the model. In Scenario 5-2, we used a lifetime time horizon and applied the treatment effect for 4 years

- **Scenario 6:** We included a treatment effect on subsequent OVCF from our clinical review. For PVP compared with CT, we did not find a statistically significant difference in subsequent (new, symptomatic) OVCF in a meta-analysis of 5 RCTs (RR: 1.50; 95% CI: 0.32–7.10) (Figure 9). We applied the point estimate result in our scenario analysis to avoid biasing the results because of the wide confidence interval.[150] The follow-up of the RCTs ranged from 6 to 24 months, though the majority had a 12-month follow-up. We assumed that the treatment effect of PVP on subsequent OVCF would last 2 years as that was the longest available comparative data. For PBK compared with CT, 1 trial reported clinically recognized vertebral fractures at 24 months.[118] There were 26/149 (17.4%) fractures in the PBK arm and 17/151 (11.3%) in the CT arm (see New Fractures, Symptomatic Fractures, above). We used these values to calculate an RR and 95% CI for subsequent OVCF for PBK compared with CT. We assumed the treatment effect of PBK on subsequent OVCF would last 2 years to reflect the longest available comparative data. We applied these treatment effects using our model with a 3-year time horizon (Scenario 6-1) and lifetime time horizon (Scenario 6-2)
- **Scenario 7:** We used the results of a meta-analysis that compared the incidence of clinical adjacent fractures between people who received PVP or PBK with CT.[163] Follow-up for the included studies varied, with a maximum of up to 4 years. In Scenario 7-1, we ran a 3-year model and applied the treatment effect for the duration of the model. In Scenario 7-2, we ran a lifetime model and applied the treatment effect for 4 years
- **Scenario 8:** We used results from our clinical review on subsequent OVCF comparing PVP with PBK. Based on 4 RCTs, there was a non-significant difference in new fractures between patients who received PVP compared with PBK (RR: 0.84; 95% CI: 0.66–1.07) (Figure 26). In Scenario 8-1, we ran a 3-year model and applied the treatment effect for 2 years. In Scenario 8-2, we ran a lifetime model and applied the treatment effect for 2 years
- **Scenario 9:** We considered the impact of treatment effects on both OVCF and mortality simultaneously, using the estimates from our clinical review. In Scenario 9-1, we used a 3-year time horizon. In Scenario 9-2, we used a lifetime time horizon
- **Scenario 10:** We included a treatment effect on serious adverse events from our clinical review. We calculated a cost per serious adverse event for PVP and PBK by multiplying their respective probabilities of a serious adverse event by the average cost per serious adverse event. We estimated the average cost per serious adverse event by estimating the cost of serious adverse events identified in our review. We found 2 types of serious adverse event: surgical site hematoma and urinary tract infection

  We assumed that a surgical site hematoma would be treated in the ED and we identified cases using a main diagnosis code: T81.0, haemorrhage and haematoma complicating a procedure, not elsewhere classified. We found 7,984 cases of haemorrhage and haematoma in fiscal year 2022, with an average cost of $371.63 (IntelliHealth data accessed October 16, 2024). For the cost of treating a urinary tract infection, we used a published cost-effectiveness analysis that reported the

cost of an ED-managed urinary tract infection including health care professional and medication costs for initial treatment and subsequent treatment for those who do not initially respond.[164] The cost for treatment was $445.16

We used the average of these 2 costs – $408.39- –as the cost per treatment of serious adverse events. We estimated the percentage of serious adverse events using 2 different sources. In Scenario 10-1 we used results from an RCT[100] that compared PBK with CT at 12 months follow-up (Table 23). There were 2 procedure-related serious adverse events (2/149 = 1.3%) in the PBK group and no serious adverse events (0/151 = 0.0%) in the CT group. In Scenario 10-2, we used the probability of serious adverse events by using the results from the trial by Dohm et al[85] comparing PBK with PVP. There were 6.3% (12/191) and 5.8% (11/190) serious device/procedure/anesthesia-related adverse events, not including symptomatic vertebral fractures in the PBK and PVP arms, respectively (Table 29). We assumed that they would occur within 1 model cycle (i.e., within the first month after the procedure). We did not apply disutilities for serious adverse events because the utilities were taken directly from trials and therefore any utility decrements due to adverse events would already be accounted for in that data and those estimates[152]

- **Scenario 11:** For Scenario 11-1, we varied the probability of symptomatic cement leakages in the PVP arm using the results of observational studies from our clinical review, in which we found 4 symptomatic cement leaks among 200 patients (Table A3, Appendix 3). In Scenario 11-2, we used the lower bound (3/731) on the possible number of people with symptomatic cement leaks
- **Scenario 12**: We considered scenarios in which there are changes in the use of CT for people who received PVP or PBK. We estimated the absolute risk reduction of analgesic use at 1 month (Tables 4 and 17) and assumed that the total cost of CT (doctor's visits, pharmacological treatment, other non-pharmacological components) would decrease proportionally

Clinical Pathway

- **Scenario 13:** We assumed that all subsequent OVCF would be treated with CT
- **Scenario 14:** We assumed that everyone would start osteoporosis medication after their initial OVCF and therefore applied the costs (Appendix 8, Table A28) and treatment effects (Table A29) for osteoporosis medication to everyone
- **Scenario 15:** We considered a scenario to represent some variation in clinical practice around the type of imaging used to diagnose OVCF. We assumed that, rather than an MRI, everyone would receive a computed tomography scan (OHIP fee code X415, computed tomography scan, spine without IV contrast) and a bone scan (OHIP fee claim J851, bone scintigraphy single site)
- **Scenario 16:** We considered a scenario where people receiving CT only would still receive the pre-procedure MRI scan

Composition of Population

- **Scenario 17:** We varied the percentage of people with OVCF who are hospitalized to 10% for Scenario 17-1 and 50% for Scenario 17-2. In Scenario 17-3, we assumed 0% hospitalization (i.e., all outpatient)
- **Scenario 18:** We explored the effect of using a different age for our cohort. In Scenario 18-1, we assumed everyone had a starting age of 60 years. In Scenario 18-2, we assumed everyone had a starting age of 80 years
- **Scenario 19:** We increased the percentage of females in the cohort to 75%, which more closely aligned with the percentage of females in RCTs[60,100]
- **Scenario 20:** We decreased the percentage of people with OVCF who visit the ED to 10% for Scenario 20-1 and increased it to 100% for Scenario 20-2

Costs

- **Scenario 21:** We varied the cost of CT in all treatment arms. In Scenario 21-1, we assumed that the duration of analgesic use in CT was 6 months rather than 6 weeks. In Scenario 21-2, we lowered the cost of CT by assuming there was only 1 physician visit, no orthopedic surgery consultation, no government-funded physiotherapy for anyone, and 2 weeks of analgesics. In Scenario 21-3, we increased the cost of CT by assuming 3 physician visits, an orthopedic surgery consultation, 8 weeks of analgesics, and 1 episode of government-funded physiotherapy for everyone
- **Scenario 22**: We varied the costs of outpatient procedures for PVP and PBK by assuming a 20% decrease in hospital costs for day surgeries in Scenario 22-1 and a 20% increase for Scenario 22-2
- **Scenario 23:** We varied the costs of inpatient procedures for PVP and PBK by assuming a 20% decrease in inpatient hospital costs in Scenario 23-1 and a 20% increase for Scenario 23-2
- **Scenario 24**: We varied the cost of hospitalization for OVCF without a procedure using the CIHI patient cost estimator for CMG 771, spinal injury[156] (Scenario 24-1) and Ontario administrative data on inpatient discharges for people age 40 and older with a main diagnosis of spinal fracture and any intervention except therapeutic spinal interventions using CCI code 1SC (Scenario 24-2)

Natural History Parameters

- **Scenario 25:** We considered an alternate relative risk of OVCF given prior OVCF using a Meta-analysis by Warriner et al[142]
- **Scenario 26:** We varied the relative risk of mortality given a prior OVCF compared with no prior OVCF using a study conducted among women and men with osteoporosis and applied the effect for the duration of the model.[149] This relative risk was selected because it was used in the previous HTA conducted by NICE[127]
- **Scenario 27:** We tested a different annual rate of vertebral fractures using a different Canadian data source[165]

Additional Scenarios

- **Scenario 28:** We conducted a scenario analysis that included the costs of the Northern Health Travel Grant (NHTG). The NHTG is available to eligible Northern Ontario residents who travel long distances for medical specialist services.[166] In 2021, 5.3% of the Ontario population lived in the North East or North West regions.[167] We assumed that people travel an average of 150 km each way (300 km total) and stay overnight in a hotel for 1 night, which is reimbursed for $175. The total cost reimbursed by the NHTG would be $298 ($0.41/km × 300 km + $175). This cost was applied to the PVP and PBK strategies only
- **Scenario 29:** We estimated additional costs from the societal perspective using a Canadian trial that collected societal costs from women who had experienced vertebral fractures and were assigned to the control group.[168] The average annual cost was $14,892. We assumed that the costs were evenly distributed throughout the first year and applied them to the monthly cycle costs for the post-treatment health state (all interventions) and the subsequent OVCF health state

Table 38: Variables Varied in Scenario Analyses

Scenario[a,b]	Parameter	Reference case value	Scenario analysis value[c]
Treatment effects			
Scenario 1-1	Source of treatment effect data of PVP on quality of life, 3-year time horizon	PVP vs. PBK trial data (Appendix 8, Table A17)	PVP + CT vs. CT trial data (Appendix 8, Table A27)
Scenario 1-2	Source of treatment effect data of PVP on quality of life, lifetime time horizon	PVP vs. PBK trial data (Appendix 8, Table A17)	PVP + CT vs. CT trial data (Appendix 8, Table A27)
Scenario 2-1	Duration of treatment effect, 0-year offset period, lifetime time horizon	1-year offset period	0-year offset period (i.e., after 2-years, all utilities immediately reach the highest 2-year value)
Scenario 2-2	Duration of treatment effect, infinite offset period, lifetime time horizon	1-year offset period	Infinite offset period (i.e., all utilities remain at their own 2-year period for duration of model)
Scenario 2-3	Treatment offset period	1-year offset period, utilities for all interventions go up to highest 2-year value	1-year offset period, utilities for all interventions go down to lowest 2-year value
Scenario 3-1	Treatment effect of PVP and PBK on mortality, 3-year time horizon, relative risk (95% CI)	None	PVP: 0.72 (0.36–1.48) PBK: 1.30 (0.49–3.41) Applied for 3 years
Scenario 3-2	Treatment effect of PVP and PBK on mortality, lifetime time horizon, relative risk (95% CI)	None	PVP: 0.72 (0.36–1.48) PBK: 1.30 (0.49–3.41) Applied for 3 years
Scenario 4-1	Treatment effect of PVP and PBK on mortality 3-year time horizon, relative risk (95% CI)	None	PVP and PBK vs. CT: 0.78 (0.66–0.92)[161] Applied for 2 years

Scenario[a,b]	Parameter	Reference case value	Scenario analysis value[c]
Scenario 4-2	Treatment effect of PVP and PBK on mortality, lifetime time horizon, relative risk (95% CI)	None	PVP and PBK vs. CT: 0.78 (0.66–0.92)[161] Applied for 5 years
Scenario 5-1	Treatment effect of PVP and PBK on mortality, 3-year time horizon, relative risk (95% CI)	None	PBK vs. CT: 0.56 (0.55–0.57)[162] PVP vs. CT: 0.76 (0.75–0.77)[162] Applied for 2 years
Scenario 5-2	Treatment effect of PVP and PBK on mortality, lifetime time horizon, relative risk (95% CI)	None	PBK vs. CT: 0.56 (0.55–0.57)[162] PVP vs. CT: 0.76 (0.75–0.77)[162] Applied for 4 years
Scenario 6-1	Treatment effect of PVP and PBK on subsequent OVCF, 3-year time horizon, relative risk (95% CI)	None	PVP vs. CT: 1.50 (0.32–7.10)[d] PBK vs. CT: 1.55 (0.88–2.73) Applied for 2 years
Scenario 6-2	Treatment effect of PVP and PBK on subsequent OVCF, lifetime time horizon, relative risk (95% CI)	None	PVP vs. CT: 1.50 (0.32–7.10)[c] PBK vs. CT: 1.55 (0.88–2.73) Applied for 2 years
Scenario 7-1	Treatment effect of PVP and PBK on subsequent OVCF, 3-year time horizon, relative risk (95% CI)	None	PVP and PBK: 0.67 (0.38–1.19)[163] Applied for 2 years
Scenario 7-2	Treatment effect of PVP and PBK on subsequent OVCF, lifetime time horizon, relative risk (95% CI)	None	PVP and PBK: 0.67 (0.38–1.19)[163] Applied for 4 years
Scenario 8-1	Treatment effect on subsequent OVCF, 3-year time horizon, relative risk (95% CI)	None	PBK vs. CT: 1.55 (0.88–2.73) PVP vs. PBK: 0.84 (0.66–1.07)
Scenario 8-2	Treatment effect on subsequent OVCF, lifetime time horizon, relative risk (95% CI)	None	PBK vs. CT: 1.55 (0.88–2.73) PVP vs. PBK: 0.84 (0.66–1.07)
Scenario 9-1	Treatment effect on mortality and OVCF simultaneously, 3-year time horizon	None	Mortality: see Scenario 3-1 Subsequent OVCF: see Scenario 6-1
Scenario 9-2	Treatment effect on mortality and OVCF simultaneously, lifetime time horizon	None	Mortality: see Scenario 3-2 Subsequent OVCF: see Scenario 6-2
Scenario 10-1	Treatment effect on serious adverse events, probability	None	PVP: 0.0 PBK: 0.013 (2/149)
Scenario 10-2	Treatment effect on serious adverse events, probability	None	PVP: 0.058 (11/190) PBK: 0.063 (12/191)
Scenario 11-1	Treatment effect on symptomatic cement leakage, probability	PVP: 1/648 PBK: 8/731	PVP: 4/200 PBK: 8/731
Scenario 11-2	Treatment effect on symptomatic cement leakage, probability	PVP: 1/648 PBK: 8/731	PVP: 1/648 PBK: 3/731
Scenario 12	Reduction in use of CT with PVP and PBK	No change	PVP: CT use reduced by 17%[e] PBK: CT use reduced by 20%[f]
Clinical pathway			
Scenario 13	Subsequent OVCF all treated with CT	Treated same as initial OVCF	Treated with CT
Scenario 14	Osteoporosis treatment	Cost of osteoporosis treatment: NA Relative risk of vertebral fracture while on osteoporosis treatment: NA	Cost of osteoporosis treatment: $226.18 (Appendix 8, Table A28) Relative risk of vertebral fracture while on osteoporosis treatment (Appendix 8, Table A29)

Scenario[a,b]	Parameter	Reference case value	Scenario analysis value[c]
Scenario 15	Pre-procedure scans	Everyone gets an MRI	Everyone gets a computed tomography scan and a bone scan
Scenario 16	Pre-procedure scans in CT arm	None	Everyone gets an MRI
Composition of population of interest			
Scenario 17-1	Percentage of people with OVCF who are hospitalized	31%	10%
Scenario 17-2	Percentage of people with OVCF who are hospitalized	31%	50%
Scenario 18-1	Starting age of cohort	72 years	65 years
Scenario 18-2	Starting age of cohort	72 years	80 years
Scenario 19	Percentage of females in cohort	60%	75%
Scenario 20-1	Percentage of people with subsequent OVCF who visit emergency department	50%	10%
Scenario 20-2	Percentage of people with subsequent OVCF who visit emergency department	50%	100%
Costs			
Scenario 21-1	Cost of outpatient CT (duration of analgesic use)	6 weeks, cost of CT: $363.50	6 months, cost of CT: $386.67
Scenario 21-2	Cost of outpatient CT, low estimate	$363.50	$61.21
Scenario 21-3	Cost of outpatient CT, high estimate	$363.50	$751.06
Scenario 22-1	Hospital day procedure cost of PVP and PBK, low estimate	PVP: $4,580.21 PBK: $6,666.79	20% decrease in hospital costs
Scenario 22-2	Hospital day procedure cost of PVP and PBK, high estimate	PVP: $4,580.21 PBK: $6,666.79	20% increase in hospital costs
Scenario 23-1	Inpatient costs of PVP and PBK, mean (SE)	PVP: $35,508.20 ($4,604.60) PBK: $39,128.02 ($8,027.60)	20% decrease in hospital costs
Scenario 23-2	Inpatient costs of PVP and PBK, mean (SE)	PVP: $35,508.20 ($4,604.60) PBK: $39,128.02 ($8,027.60)	20% increase in hospital costs
Scenario 24-1	Cost of hospitalization for OVCF, no procedure	$16,365.56 ($1,379.82)	$11,423.28 ($963.12)[156]
Scenario 24-1	Cost of hospitalization for OVCF, no procedure	$16,365.56 ($1,379.82)	$41,849.54 ($5,640.49) (IntelliHealth data accessed Dec 10, 2024)[g]
Natural history parameters			
Scenario 25	Relative risk of OVCF given prior OVCF	2.34	4.9 (2.4–9.8)[142]
Scenario 26	Relative risk of mortality given prior OVCF	See Table 34	4.4 (1.85–10.6)[149]
Scenario 27	Annual rate of vertebral fractures per 100,000	See Table 34	Women[165] 50–59: 176.3 60–69: 152.3 70–79: 394.1 ≥ 80: 763.3 Men[165] 50–59: 164.9 60–69: 115.9 70–79: 207.2 ≥ 80: 304.1
Additional parameters			
Scenario 28	Northern Health Travel Grant costs	Not included	Included, $298 per eligible patient

Scenario[a,b]	Parameter	Reference case value	Scenario analysis value[c]
Scenario 29	Societal perspective	Public health care payer perspective	Societal perspective, additional $14,891.84 for first year after OVCF

Abbreviations: CI, confidence interval; CT, conservative treatment; ICD-10, international classification of diseases, tenth revision; MRI, magnetic resonance imaging; NA, not applicable; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SA, scenario analysis; SE, standard error; vs. versus.

[a]Scenario analyses used a 3-year time horizon unless otherwise stated.

[b]Lifetime horizon was 28 years (i.e., until age 100 or death, whichever came first).

[c]Relative risks were described as log-normal distributions, costs were described as gamma distributions, unless stated otherwise.

[d]Fixed value was used instead of a distribution to avoid potential bias due to wide confidence interval.[150]

[e]Calculated from clinical review, Table 4, Use of analgesics at 1 month; absolute risk reduction = 68.3% − 50.9% = 17.4%

[f]Calculated from clinical review, Table 17, Use of any analgesic at 1 month; absolute risk reduction = 91% − 71% = 20%

[g]IntelliHealth hospital inpatient data, limited to patients aged 40 or older with an ICD-10 code for spine fracture and any intervention except CCI code 1SC – Therapeutic Interventions on the Spinal Vertebrae.

Results

Reference Case Analysis

Table 39 presents the reference case results, from lowest to highest total costs. Conservative treatment had the lowest expected costs ($6,101) and lowest expected QALYs (1.470), followed by PVP with $17,501 expected costs and 1.733 expected QALYs. PBK had the highest expected costs ($21,675) and 1.706 expected QALYs.

The ICER comparing PVP with CT was $43,324/QALY and the ICER comparing PBK with CT was $65,921/QALY. In our sequential analysis, PBK was dominated by PVP because it has higher expected costs and lower expected QALYs than PVP.

Detailed results of the reference case are presented in Table A31 (Appendix 8).

Table 39: Reference Case Analysis Results for OVCF Treatments

Strategy[a]	Average total costs (95% CrI), $	Average total effects (95% CrI), QALYs	ICER vs. CT (95% CrI), $/QALY	Sequential ICER (95% CrI), $/QALY
CT	6,101 (4,938–8,299)	1.470 (1.435–1.497)	NA	NA
PVP + CT	17,501 (13,905–23,445)	1.733 (1.688–1.777)	43,324 (35,008–53,273)	43,324 (35,008–53,273)
PBK + CT	21,675 (15,920–30,245)	1.706 (1.665–1.747)	65,921 (49,634–84,382)	Dominated[b]

Note: Some numbers may appear inexact due to rounding.

Abbreviations: CrI, credible interval; CT, conservative treatment; ICER, incremental cost-effectiveness ratio; NA, not applicable; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QALY, quality-adjusted life-year.

[a]Treatment strategies are ordered by average total costs, from lowest to highest.

[b]Dominated indicates PBK is more costly and less effect than PVP.

Cost-Effectiveness Acceptability Curve

The results of the probabilistic analysis in the reference case are presented in Figure 29. At a WTP value of $50,000/QALY, the probability of being cost-effective for PVP, PBK, and CT were approximately 79%, 3%, and 18%, respectively. At a WTP value of $100,000/QALY, the probabilities of being cost-effective for PVP, PBK, and CT were 98%, 2%, and 0% respectively.

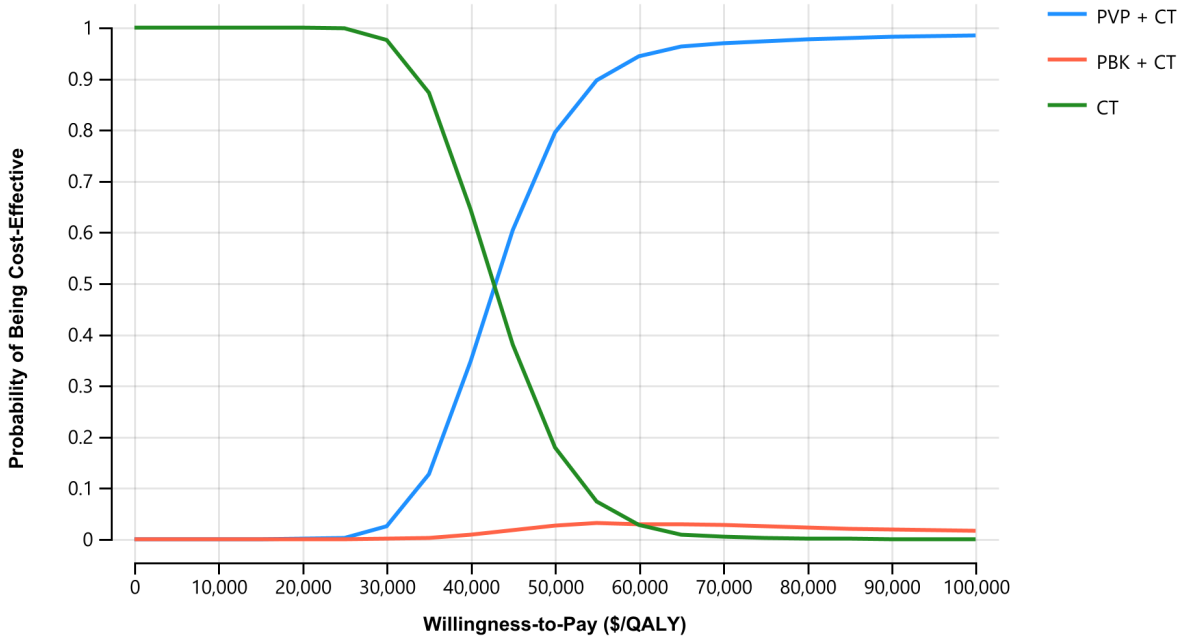


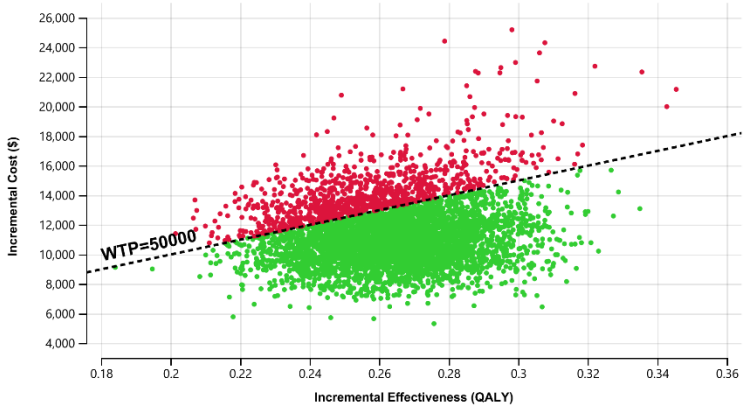
Figure 29: Cost-Effectiveness Acceptability Curve of Treatments for OVCF

A cost-effectiveness acceptability curve showing the results of the probabilistic analysis from 5,000 model simulations. Willingness-to-pay values from $0 to $100,000 per QALY are shown along the horizontal x-axis and the probability of being cost-effective from 0 to 1 on the vertical y-axis. A curve depicting the probability of being cost-effective for a given willingness-to-pay value is shown for each intervention. At lower willingness-to-pay values, CT alone has the highest probability of being cost-effective. As willingness-to-pay values increase, PVP + CT becomes more likely to be cost-effective while CT alone becomes less likely, with PVP + CT becoming the most likely option at a willingness-to-pay value of $43,324. There is no willingness-to-pay value at which PBK + CT has the highest probability of being cost-effective.

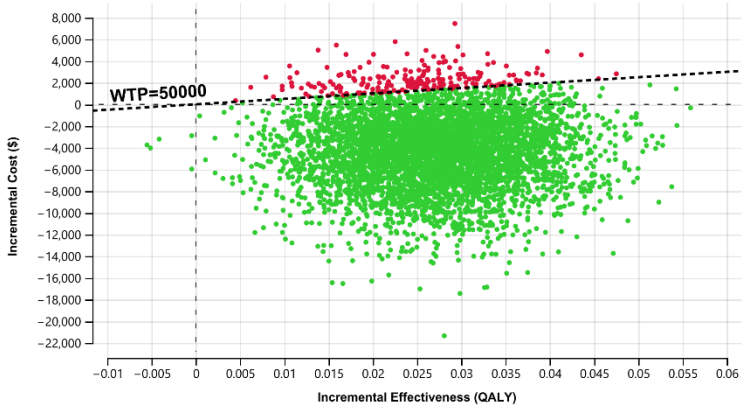
Abbreviations: CT, conservative treatment; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QALY, quality-adjusted life year.

Incremental Cost-Effectiveness Scatterplot

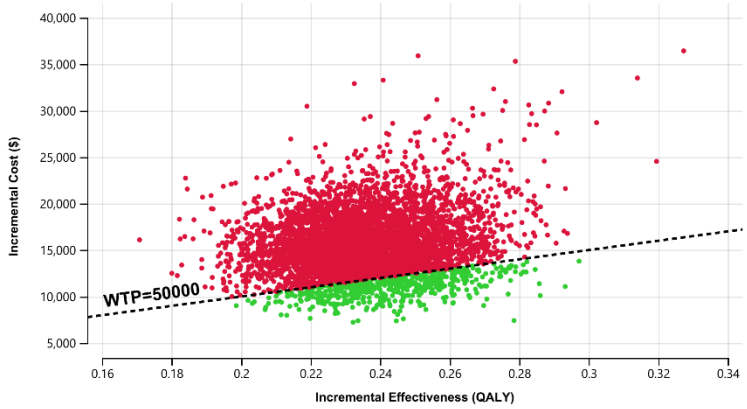
The results of the reference case probabilistic analysis for 5,000 simulations are also presented on an incremental cost-effectiveness scatterplot in Figure 30, which illustrates the incremental cost and incremental effect differences for pairs of interventions. The dashed line depicts a WTP value of $50,000/QALY gained. Points that fall below the line are considered cost-effective (optimal, shown in green) and points that fall above the line are considered sub-optimal (shown in red).



A: PVP + CT compared with PBK + CT



B: PVP + CT compared with CT



C: PBK + CT compared with CT

Figure 30: Incremental Cost-Effectiveness Scatterplot of Treatments for OVCF

Three scatterplots of probabilistic results from 5,000 model simulations showing the incremental effectiveness (QALYs) along the horizontal x-axis and incremental cost ($) along the vertical y-axis for each treatment comparison pair. A dashed line on each scatterplot is shown to represent the WTP value $50,000 per QALY gained. Points below the WTP line are considered cost-effective and points above the WTP line are considered not cost-effective. Figure A shows the comparison of PVP + CT and PBK + CT, in which over half of the points fall below the WTP line, indicating that PVP + CT is cost-effective compared with PBK + CT. Figure B shows the comparison of PVP + CT with CT, in which most of the points fall below the WTP line, indicating that PVP + CT is cost-effective. Figure C shows the comparison of PBK + CT with CT, in which most of the points fall above the WTP, indicating the PBK + CT is not the cost-effective option.

Abbreviations: CT, conservative treatment; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QALY, quality-adjusted life year; WTP, willingness-to-pay.

Scenario Analysis

The results of the scenario analyses are presented in Table 40. A detailed table of scenario analysis results is presented in Table A32 (Appendix 8). The results were most sensitive to the source for PVP utility data (Scenarios 1-1, 1-2), assumptions about the duration of treatment effect on utility (Scenario 2-2), treatment effect on mortality (Scenarios 5-2, 8-1), and cost of hospitalization for OVCF without PVP or PBK procedure (Scenario 24-2).

The ICER for PVP compared with CT was $43,324/QALY in our reference case. The minimum ICER for PVP compared with CT was $10,033 (Scenario 24-2), which suggests more favourable results for PVP occurred when we used a higher estimate for the cost of hospitalization for CT. The maximum ICER was $78,200/QALY and occurred when we incorporated treatment effects on subsequent OVCF using the PVP compared with PBK findings from our clinical review (Scenario 8-1).

The ICER for PBK compared with CT was $65,921/QALY in our reference case. The most favourable ICER (lower incremental costs and higher incremental QALYs) for PBK compared with CT was $25,647/QALY, which occurred in Scenario 2-2, where we assumed that there was no waning of treatment effect. However, it is unlikely that treatment effects could be sustained for a lifetime.[160] The least favourable ICER (higher incremental costs and lower incremental QALYs) for PBK compared with CT was $2,630,894 (Scenario 9-2). This ICER occurred when we incorporated the treatment effects of PBK on mortality and on subsequent OVCF from the clinical review. There was a lot of uncertainty around these parameters. Other studies found opposite results for the mortality effect of PBK and PVP.[161,162] Studies on subsequent OVCF were mixed – the clinical review found that PBK or PVP increased the risk of subsequent OVCF, while another meta-analysis found that it decreased the risk.[163]

Table 40: Scenario Analysis Results

Scenario	ICER, PVP vs. CT, $/QALY	ICER, PBK vs. CT, $/QALY	Sequential ICER, PVP vs. CT, $/QALY	Sequential ICER, PBK vs. PVP, $/QALY
Reference case	43,324	65,921	43,324	Dominated[a]
Reference case, 2-year time horizon	50,870	75,974	50,870	Dominated[a]
Reference case, lifetime time horizon	46,844	71,176	46,844	Dominated[a]
Scenario 1-1: source of PVP utility, 3-year time horizon	53,118	65,921	53,118	192,874
Scenario 1-2: source of PVP utility, lifetime time horizon	57,321	71,176	57,321	208,122
Scenario 2-1: duration of treatment effect, no offset period, lifetime time horizon	55,387	82,484	55,387	Dominated[a]
Scenario 2-2: duration of treatment effect, no waning of treatment effect, lifetime time horizon	15,631	25,647	15,631	Dominated[a]
Scenario 2-3: 1-year treatment offset, all utilities go down to lowest 2-year value	43,324	65,921	43,324	Dominated[a]
Scenario 3-1: treatment effect on mortality, 3-year time horizon	40,633	76,706	40,633	Dominated[a]

Scenario	ICER, PVP vs. CT, $/QALY	ICER, PBK vs. CT, $/QALY	Sequential ICER, PVP vs. CT, $/QALY	Sequential ICER, PBK vs. PVP, $/QALY
Scenario 3-2: treatment effect on mortality, lifetime time horizon	31,144	1,117,017	31,144	Dominated[a]
Scenario 4-1: treatment effect on mortality, 3-year time horizon	40,823	61,764	40,823	Dominated[a]
Scenario 4-2: treatment effect on mortality, lifetime time horizon	27,980	40,442	27,980	Dominated[a]
Scenario 5-1: treatment effect on mortality, 3-year time horizon	40,578	57,973	40,578	Dominated[a]
Scenario 5-2: treatment effect on mortality, lifetime time horizon	26,900	31,161	26,900	50,370
Scenario 6-1: treatment effect on subsequent OVCF, 3-year time horizon	46,154	70,900	46,154	Dominated[a]
Scenario 6-2: treatment effect on subsequent OVCF, lifetime time horizon	53,409	83,266	53,409	Dominated[a]
Scenario 7-1: treatment effect on subsequent OVCF, 3-year time horizon	41,052	62,771	41,052	Dominated[a]
Scenario 7-2: treatment effect on subsequent OVCF, lifetime time horizon	41,190	63,080	41,190	Dominated[a]
Scenario 8-1: treatment effect on subsequent OVCF, 3-year time horizon	45,487	70,900	45,487	Dominated[a]
Scenario 8-2: treatment effect on subsequent OVCF, lifetime time horizon	51,947	83,266	51,947	Dominated[a]
Scenario 9: treatment effect on OVCF and mortality simultaneously, 3-year time horizon	43,287	82,531	43,287	Dominated[a]
Scenario 9: treatment effect on OVCF and mortality simultaneously, lifetime time horizon	35,326	2,630,894	35,326	Dominated[a]
Scenario 10-1: treatment effect on serious adverse events	43,324	65,947	43,324	Dominated[a]
Scenario 10-2: treatment effect on serious adverse events	43,424	66,042	43,424	Dominated[a]
Scenario 11-1: treatment effect on symptomatic cement leakage	46,100	65,921	46,100	Dominated[a]
Scenario 11-2: treatment effect on symptomatic cement leakage	43,324	64,775	43,324	Dominated[a]
Scenario 12: reduction in use of CT reduced with PVP and PBK	43,074	65,619	43,074	Dominated[a]
Scenario 13: all subsequent OVCF treated with CT	40,909	62,443	40,909	Dominated[a]
Scenario 14: everyone starts osteoporosis medication	42,677	65,002	42,677	Dominated[a]
Scenario 15: computed tomography and bone scans used instead of MRI	43,975	66,647	43,975	Dominated[a]
Scenario 16: people in CT arm receive pre-procedure scans	43,065	65,633	43,065	Dominated[a]

Scenario	ICER, PVP vs. CT, $/QALY	ICER, PBK vs. CT, $/QALY	Sequential ICER, PVP vs. CT, $/QALY	Sequential ICER, PBK vs. PVP, $/QALY
Scenario 17-1: percentage of people with OVCF who are hospitalized, 10%	31,501	52,192	31,501	Dominated[a]
Scenario 17-2: percentage of people with OVCF who are hospitalized, 50%	54,021	78,342	54,021	Dominated[a]
Scenario 17-3: percentage of people with OVCF who are hospitalized, 0% (all outpatients)	25,871	45,655	25,871	Dominated[a]
Scenario 18-1: starting age of cohort, 65 years	42,354	64,493	42,354	Dominated[a]
Scenario 18-2: starting age of cohort, 80 years	57,858	87,323	57,858	Dominated[a]
Scenario 19: percentage of females in cohort, 75%	43,302	65,888	43,302	Dominated[a]
Scenario 20-1: percentage of people with subsequent OVCF who visit ED, 10%	43,324	65,921	3,121	Dominated[a]
Scenario 20-2: percentage of people with subsequent OVCF who visit ED, 100%	43,324	65,921	43,324	Dominated[a]
Scenario 21-1: cost of outpatient CT (6-month duration of analgesic use)	43,337	65,954	43,337	Dominated[a]
Scenario 21-2: cost of outpatient CT (low estimate)	43,324	65,921	43,324	Dominated[a]
Scenario 21-3: cost of outpatient CT (high estimate)	43,324	65,921	43,324	Dominated[a]
Scenario 22-1: hospital day procedure cost of PVP and PBK	40,652	61,580	40,652	Dominated[a]
Scenario 22-2: hospital day procedure cost of PVP and PBK	45,996	70,261	45,996	Dominated[a]
Scenario 23-1: inpatient costs of PVP and PBK	34,037	54,461	34,037	Dominated[a]
Scenario 23-2: inpatient costs of PVP and PBK	52,610	77,381	52,610	Dominated[a]
Scenario 24-1: cost of hospitalization for OVCF, no procedure	49,792	73,125	49,792	Dominated[a]
Scenario 24-2: cost of hospitalization for OVCF, no procedure	10,033	28,843	10,033	Dominated[a]
Scenario 25: relative risk of OVCF given prior OVCF	47,635	72,193	47,635	Dominated[a]
Scenario 26: relative risk of mortality given prior OVCF	47,164	71,459	47,164	Dominated[a]
Scenario 27: different annual rate of OVCF	46,459	70,487	46,459	Dominated[a]
Scenario 28: Northern Health Travel Grant	43,391	65,995	43,391	Dominated[a]
Scenario 29: societal perspective	43,324	65,921	43,324	Dominated[a]

Abbreviations: CT, conservative treatment; ED, emergency department; ICER, incremental cost-effectiveness ratio; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QALY, quality-adjusted life year.

[a]Dominated indicates PBK is more costly and less effective than PVP.

Discussion

We conducted a CUA comparing PVP, PBK, and CT for people with painful OVCFs from the perspective of the Ontario Ministry of Health. Results showed that PVP and PBK were each consistently more costly and more effective than CT.

In our reference case and most scenario analyses, PVP was less costly and more effective than PBK. For these analyses, the effectiveness was taken from Dohm et al.[85].The Dohm authors compared PVP with PBK and found that PVP was more effective and therefore dominated PBK (was less costly and more effective). However, when the results from an alternative trial that compared PVP with CT were incorporated, we found that PBK was more effective than PVP, introducing some uncertainty into our results.[60 124]

The HTA published by NICE in 2014 did not include a reference case because of the uncertainty around the treatment effect on mortality and sources of utility estimates.[127] The authors chose instead to run multiple scenarios with different mortality assumptions and utility sources and found that the results changed depending on the scenario. Because of this, they made no definitive conclusions around mortality and utility for PVP versus PBK.

Similarly, our clinical review was not able to establish a treatment effect on mortality. We ran a few scenarios to explore the impact of a treatment effect on mortality. The estimates varied widely, with some sources[161,162] showing an increase in mortality with PVP and PBK while others showed a reduction. In all but 1 scenario, PVP had the highest QALY gains compared with CT and PBK; however, when estimates from Edidin et al[162] were used, PBK had the highest QALY gains and had the potential to be cost-effective, depending on the WTP value.

Some economic evaluations incorporated a treatment effect on the length of hospitalization in their reference cases or scenario analyses.[124,125,129] We did not explore this outcome in our analyses as our clinical review did not uncover any data on treatment effects on length of hospital stay. However, we costed the hospitalization from Ontario data. The Swiss HTA[38] found that hospital length of stay was shorter for people with procedures, but the overall hospital costs were still higher. We explored a scenario analysis using an alternative estimate for the cost of hospitalization for CT that was over twice our reference case estimate. The cost of CT was still lower than the inpatient costs of PVP and PBK.

Another suggested benefit of PVP and PBK interventions was a reduction in caregiver time or lost productivity. We did not find any evidence on treatment effect on these other components so, although we ran a scenario analysis that included total costs from a societal perspective – including items such as unpaid caregiver time and lost productivity (estimated by Hassan et al[168]) (Scenario 29) – the costs cancelled out because we could not establish whether there were differences in the costs among interventions.

Although clinical guidelines suggest first trying CT, which is consistent with practice in Ontario, type and duration of CT use was not consistently reported in the clinical trials from which we derived our clinical parameters. Our review found that, while some studies' inclusion criteria required that patients failed conservative treatment prior to PVP or PBK, it is unclear whether this was a requirement in many RCTs. Therefore, it is possible that the patients in the RCTs do not reflect patients in Ontario who would be eligible for these interventions. For example, in the VERTOS II trial, 431 patients were identified as eligible for randomization and 229 (53%) had spontaneous pain relief prior to randomization, making

them ineligible for the trial.[60] The time from identification to pain relief for these patients was not provided.

All our results need to be interpreted with caution given that the clinical evidence that informed our economic modeling—while not sparse or very limited—was of low to very low quality and therefore uncertain.

Strengths and Limitations

Our study had the following strengths:

- We engaged with multiple clinical experts to validate our assumptions
- Our cost parameters were informed by Ontario administrative data for procedures already occurring in Ontario hospitals
- Our clinical effectiveness parameters were informed by the clinical review, which included a systematic review and meta-analyses
- We conducted numerous scenario analyses to test the robustness of the results

The following limitations should be noted when interpreting the findings of our analyses:

- Subgroup analyses by fracture age were not possible because the RCT that informed the utility parameters for CT and PBK was conducted in patients who had OVCFs less than 3 months old and the authors did not report subgroups.[100] All the RCTs included in our clinical review of EQ-5D for PVP compared with CT enrolled participants with OVCF less than 8 weeks from onset[60,65]
- A previous systematic review highlighted differing cost-effectiveness results for inpatients compared with outpatients.[133] Although we incorporated different costs for inpatients and outpatients, the treatment effects were not available by hospitalization status. The treatment effect of PBK on quality of life was taken from an RCT that included only hospitalized participants.[100,101] We assumed that people who are treated as outpatients would receive the same benefits as inpatients. Dohm et al[85] conducted their analysis comparing PVP and PBK on both inpatients and outpatients
- Much of the osteoporosis literature is conducted in women. Although we attempted to find parameter values that represented our population of interest, which included men and women, there were some values where we were limited to studies that focussed on women (e.g., relative risk of vertebral fracture after prior vertebral fracture, relative risk of vertebral fracture in people with low BMD).[145] Some of the parameters that were applied to our whole population may have different values for men and women. We ran scenario analyses on these parameters, and they were not found to be impactful on the ICERs
- Our costs for hospitalization with PVP or PBK represented the full cost of the hospital stay. Patients may have received other interventions while in hospital, so the costs of inpatient PVP and PBK may be overestimated. We included costs of hospital stays for people without the procedure to minimize the incremental overestimate and conducted sensitivity analyses on the hospital costs for PVP and PBK

- Our cost for hospitalization without procedure was based on all vertebral fractures. We excluded people who received interventions in hospital to avoid overestimating costs by including people who received major surgeries; however, we may have underestimated costs by unintentionally excluding people who received other unrelated procedures. We ran a scenario analysis in which we estimated the mean cost for everyone who did not receive a therapeutic spinal intervention. Although the estimated cost was higher than the reference case estimate for hospitalization without the procedure, it was still higher than the costs of inpatient PVP and PBK

Conclusions

We found that PVP and PBK consistently produced higher QALYS at higher costs compared with CT. The ICERs comparing PVP with CT and PBK with CT were $43,324 and $65,921 per QALY, respectively, from the perspective of the Ontario Ministry of Health, over 3 years. PVP was less costly and more effective than PBK, but results were uncertain.

Budget Impact Analysis

Research Question

What is the potential 5-year budget impact for the Ontario Ministry of Health of publicly funding percutaneous vertebroplasty [PVP] or percutaneous balloon kyphoplasty [PBK] for the treatment of adults with painful osteoporotic vertebral compression fractures (OVCF)?

Methods

Analytic Framework

We estimated the budget impact of publicly funding vertebral augmentation using the cost difference between 2 scenarios: (1) current clinical practice in which vertebral augmentation for the treatment of painful OVCFs is funded through global hospital budgets (the current scenario), and (2) anticipated clinical practice with increased uptake of vertebral augmentation (the new scenario). Figure 31 presents the model schematic.

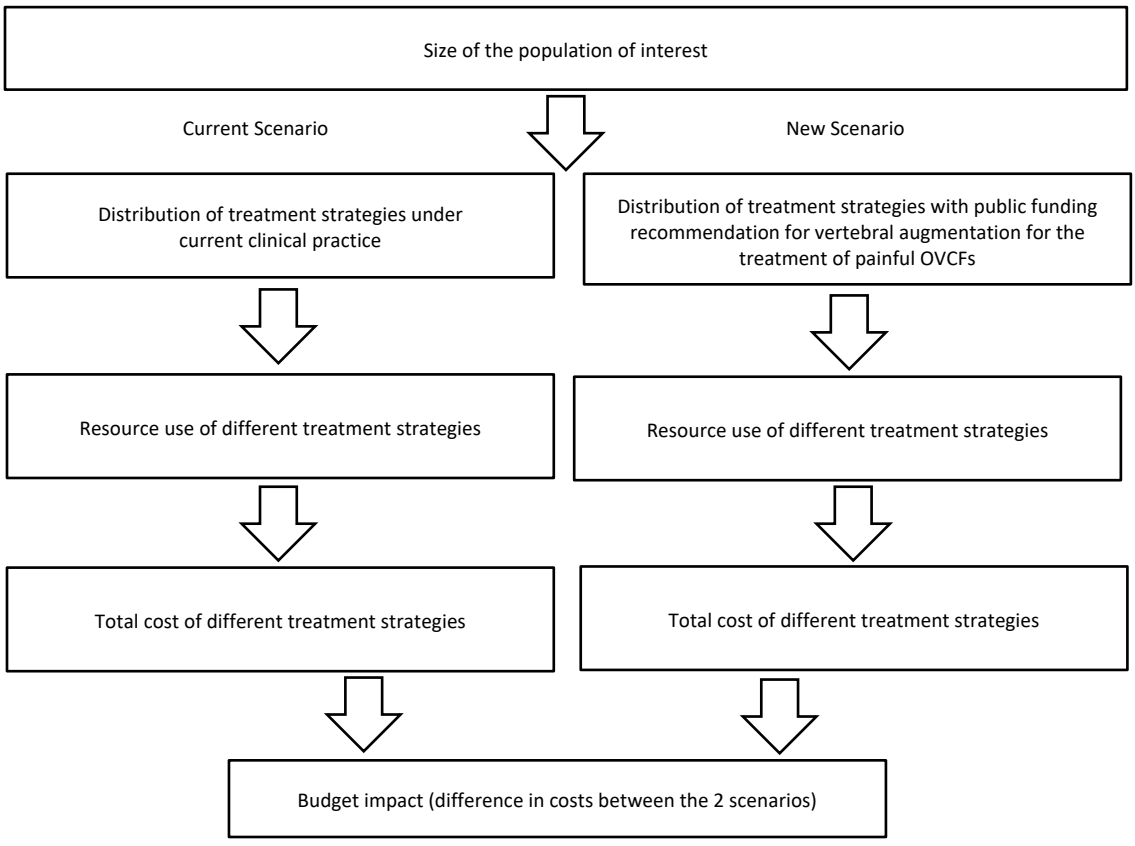


Figure 31: Schematic Model of Budget Impact

Flow chart describing the model for the budget impact analysis. Based on the size of the population of interest, we created 2 scenarios: the current scenario, which would explore the distribution of treatment strategies, resource use and total costs under current clinical practice and the new scenario, which would explore the distribution of treatment strategies, resource use, and total costs with a public funding recommendation for PVP and PBK for the treatment of painful OVCFs. The budget impact would represent the difference in costs between the 2 scenarios.

Key Assumptions

The budget impact used the costs from the primary economic evaluation; therefore, all the assumptions in the primary economic evaluation apply to the budget impact analysis. In addition, we assumed the following:

- The proportion of PVP and PBK usage would remain stable at current levels for the current scenario
- In the new scenario, the uptake of PVP and PBK collectively increase, but the proportion of PVP usage relative to PBK would increase over time

Population of Interest

The size of the population of interest was estimated based on published publicly available epidemiological data and literature estimates (Table 41).

We used Ontario Ministry of Finance population projections to estimate the adult (age ≥ 40) population of Ontario from 2025 to 2029.[169] We selected people aged 40 and older to align with the age group used by the Canadian Chronic Disease Surveillance System[144,147] (based on Ontario data from fiscal years 2018 to 2022, < 2% of all cases were people < 40) (IntelliHealth, accessed September 11, 2024). This aligns with reporting by consulted experts (M Baerlocher, MD, video communication, March 13, 2024). We applied the incidence of osteoporotic spine fractures per 100,000 people from the Canadian Chronic Disease Surveillance System (CCDSS) in 2021–2022 (138/100,000; 95% confidence interval [CI]: 136–141) to estimate the annual incidence of OVCF in Ontario[144] Vertebral fractures may be asymptomatic or symptomatic (i.e., painful). Asymptomatic vertebral fractures may come to clinical attention when diagnosed incidentally (e.g., through radiographic imaging performed for unrelated health concerns). When a vertebral fracture is diagnosed due to clinical symptoms (e.g., reported pain) and using a radiographic image, it is called a clinical vertebral fracture. Our population of interest is those with painful OVCF; i.e., clinical vertebral fractures. The CCDSS case definition of vertebral fracture does not specify whether the fractures are symptomatic (clinical) or asymptomatic (radiographic) since the diagnosis field used to capture the fracture does not indicate whether the patient was experiencing pain. However, [165] one of the papers on which the algorithm for the case definition is based, referred to the vertebral fractures as "clinical vertebral fractures." We assumed that all vertebral fractures in the CCDSS were painful and included in our population of interest.

First-line treatment for OVCF is conservative treatment (CT). Vertebral augmentation is reserved for people who do not respond to 6 weeks of CT or who have severe pain such that they are hospitalized and immobile (E. Wai, MD, video communication, May 9, 2024). The amount of time CT must be tried varies with guidelines. A consensus statement by American and Canadian radiology and neurological surgery organizations focuses on pain, unwanted side effects, and mobility in determining failure of CT.[35] Other guidelines range from 3 to 6 weeks of CT.[3,170,171] Estimates for the percentage of people who do not respond to CT ranged widely, from 10% (S. Priola, MD, J. Waddell, MD, E. Wai, MD, video communication, March to May 2024) to 47%.[60] We used an estimate of 20% for our reference case.[172,173]

Table 41: Population of Interest

Criteria	Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)
Ontario population (age ≥ 40)[169]	8,016,202	8,134,503	8,248,847	8,369,044	8,496,795
OVCF, 0.138%[144]	11,062	11,226	11,383	11,549	11,726
Symptomatic (painful), 100%	11,062	11,226	11,383	11,549	11,726
No response to conservative treatment, 20%	2,212	2,245	2,277	2,310	2,345

Abbreviation: OVCF, osteoporotic vertebral compression fracture.

Current Intervention Mix

Currently, vertebral augmentation procedures for OVCFs are offered in Ontario and funded through hospital global budgets, meaning that it is up to each hospital to decide how much funding, if any, to allocate to PVP and PBK. Ontario Health Insurance Plan (OHIP) fee claim codes exist for both procedures (Appendix 8, Table A23). We estimated the current volume of procedures in Ontario using OHIP fee claim data (IntelliHealth Ontario, intellihealth.moh.gov.on.ca; September 21, 2024). We removed cancer patients by excluding cases with any of the terms malignant, myeloma, lymphoma, leukemia, or carcinoma in the OHIP diagnosis description field. In Ontario, during fiscal years 2021 and 2022, an average of 1,061 procedures were performed per year (Table 42).

Table 42: Total Volume of Vertebral Augmentation Procedures in the Current Scenario

Procedure	FY 2021/22[a,b]	FY 2022/23[a,b]
PVP	**753**	**901**
E388, vertebroplasty combined with any other procedure	281	409
N570, vertebroplasty, sole procedure	472	492
PBK	**210**	**257**
E392, kyphoplasty combined with any other procedure	32	52
N583, kyphoplasty, sole procedure	178	205
Total number of PVP and PBK procedures	**963**	**1,158**

Abbreviations: FY, fiscal year; PBK, balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]OHIP fee claims data accessed via IntelliHealth, September 21, 2024. All claims for E388, E392, N570, N583 with an A suffix were included.

[b]Cancer diagnoses identified by the terms malignant, myeloma, lymphoma, leukemia, carcinoma in OHIP diagnosis description field.

Uptake of the New Intervention and New Intervention Mix

Currently, the volume of procedures represents 48% of the estimated population of interest. We assumed that this value would sightly increase in Year 1 to 50% and then by an additional 10% each subsequent year, resulting in 90% coverage in Year 5 (Table 43). In fiscal years 2021 and 2022, approximately 78% of vertebral augmentation procedures were PVP and the remaining were PBK. We assumed this distribution of PVP and PBK would continue in the current scenario. For the new scenario, we used this distribution of procedures in the first year, based on information from clinical experts that PVP would likely be the dominant procedure over time because it takes less time and is less costly than PBK. We assumed that the proportion of PVP procedures would increase from 78% in Year 1 to 82.5%,

85%, 87.5%, and 90% in Years 2 to 5, respectively (M. Baerlocher, MD, email communication, January 7, 2025; J. Waddell, MD, email communication, September 23, 2024). This results in 46 additional people receiving PVP or PBK in Year 1 (i.e., 863 + 243 – 827 – 233), increasing to 986 additional people in Year 5, for a total of 2,546 additional people treated with PVP or PBK over 5 years.

Table 43: Volume of Interventions in the Current and New Scenarios

	Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)	Total
Current scenario	**2,212**	**2,245**	**2,277**	**2,310**	**2,345**	**11,389**
Uptake rate for VA	48%	48%	48%	48%	48%	
Conservative treatment only	1,152	1,169	1,185	1,203	1,221	**5,930**
PVP	827	839	851	864	877	**4,258**
PBK	233	237	241	243	247	**1,201**
New scenario[a]	**2,212**	**2,245**	**2,277**	**2,310**	**2,345**	**11,389**
Uptake rate for VA	50%	60%	70%	80%	90%	
Conservative treatment only	1,106	898	683	462	235	**3,384**
PVP	863	1,111	1,355	1,617	1,900	**6,846**
PBK	243	236	239	231	210	**1,159**

Abbreviations: PBK, balloon kyphoplasty; PVP, percutaneous vertebroplasty, VA, vertebral augmentation.

[a]The volume of interventions was calculated from the total number multiplied by the market distribution of the corresponding treatment. For example, in the New Scenario, the total volume in Year 1 is 2,212. The uptake of any vertebral augmentation (PVP or PBK) is 50%, and the market distribution of PVP is 78%, so the volume of PVP in Year 1 is 863 (2,212 × 50% × 78%).

Some numbers may appear inexact due to rounding.

Resources and Costs

We derived costs for the budget impact analysis by running the primary economic evaluation with a 5-year time horizon and a 0% discount rate (Table 44). Table A33 (Appendix 8) presents a version of the table with intervention costs broken down into the following component costs: physician fees, hospital costs, medications costs, physiotherapy costs, materials and supply costs, and adverse event costs.

Table 44: Average Per-Person Annual Cost Estimates

	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $	Total, $[a]
CT	**5,669.96**	**227.12**	**219.52**	**211.90**	**204.58**	**6,533.08**
Intervention costs	5,435.31	0.00	0.00	0.00	0.00	**5,435.31**
Subsequent OVCF costs	234.65	227.12	219.52	211.90	204.58	**1,097.77**
PVP	**16,323.89**	**619.75**	**598.94**	**578.44**	**558.18**	**18,679.20**
Intervention costs	15,683.52	0.00	0.00	0.00	0.00	**15,683.52**
Subsequent OVCF costs	640.38	619.75	598.94	578.44	558.18	**2,995.68**
PBK	**20,223.22**	**764.16**	**739.32**	**713.64**	**688.76**	**23,129.10**
Intervention costs	19,433.16	0.00	0.00	0.00	0.00	**19,433.16**
Subsequent OVCF costs	790.06	764.16	739.32	713.64	688.76	3,695.94

Abbreviations: CT, conservative treatment; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Some numbers may appear inexact due to rounding.

Internal Validation

The secondary health economist conducted formal internal validation. This process included checking for errors and ensuring the accuracy of parameter inputs and equations in the budget impact analysis.

Analysis

We conducted a reference case analysis and sensitivity analyses. Our reference case analysis represents the analysis with the most likely set of input parameters and model assumptions. We will also present total costs as well as disaggregated costs by cost categories. Our sensitivity analyses explored how the results are affected by varying input parameters and model assumptions. A summary of sensitivity analyses is shown in Table 45.

Table 45: Summary of Sensitivity Analyses

Scenario	Parameter	Reference case value	Scenario analysis value
Scenario 1	Population of interest	Table 41	Low population estimate (Table A34, Appendix 8)
Scenario 2	Population of interest	Table 41	High population estimate (Table A35, Appendix 8)
Scenario 3	Uptake of vertebral augmentation	50% in Year 1, increasing linearly to 90% in Year 5	Lower uptake 48%, 50%, 55%, 60%, 65% in Years 1–5, respectively (Table A36, Appendix 8)
Scenario 4	Uptake of vertebral augmentation	50% in Year 1, increasing linearly to 90% in Year 5	Higher uptake 50%, 75%, 100%, 100%, 100%, in Years 1–5, respectively (Table A37, Appendix 8)
Scenario 5	Proportion of vertebral augmentation procedures that are PVP procedures in the new scenario	78% PVP in Year 1 increasing linearly to 90% in Year 5	78% PVP in Years 1–5 (Table A38, Appendix 8)
Scenario 6	Treatment of subsequent OVCF	Same as initial OVCF	All subsequent OVCF treated with CT (Scenario 13; Table A39, Appendix 8)
Scenario 7	Treatment effect on subsequent OVCF	PEE reference case, none	Treatment effect on subsequent OVCF from clinical review
Scenario 8	Cost of hospitalization without a procedure	PEE reference case	PEE Scenario 24-2, higher cost
Scenario 9	Proportion of people with OVCF hospitalized	PEE reference case, 31%	PEE Scenario 17-3, 0%; i.e., all outpatients
Scenario 10	Current usage of PVP and PBK	1,060 procedures per year, calculated as the average of all years in Table 42	1,158 procedures per year, calculated using fiscal year 2022/23 only (Table 42)

Abbreviations: CT, conservative treatment; OVCF, osteoporotic vertebral compression fracture; PBK, balloon kyphoplasty; PEE, primary economic evaluation; PVP, percutaneous vertebroplasty.

Results

Reference Case

Increased clinical practice with a positive public funding recommendation for PVP and PBK for painful, OVCFs would incur an additional $0.5 million in Year 1, increasing to a maximum of an additional $11 million in Year 5, for a total budget impact of an additional $28 million over the next 5 years (Table 46). For a detailed breakdown of the intervention costs, see Table A40 (Appendix 8).

Almost all the 5-year budget impact was attributed to the additional cost of the PVP and PBK procedures. Approximately $2 million was attributed to increased costs for subsequent OVCF.

Table 46: Budget Impact Analysis Results

	Budget impact, $ million[a,b]					
Scenario	**Year 1 (2025)**	**Year 2 (2026)**	**Year 3 (2027)**	**Year 4 (2028)**	**Year 5 (2029)**	**Total[a]**
Current scenario	**24.8**	**26.1**	**27.4**	**28.6**	**29.9**	**136.8**
Intervention costs	23.8	24.1	24.5	24.8	25.2	**122.4**
Cost of subsequent OVCF	1.0	2.0	2.9	3.8	4.7	**14.4**
New scenario	**25.3**	**29.0**	**32.8**	**36.8**	**40.9**	**164.8**
Intervention costs	24.3	26.9	29.6	32.4	35.2	**148.3**
Cost of subsequent OVCF	1.0	2.1	3.2	4.4	5.7	**16.5**
Budget impact	**0.5**	**2.9**	**5.5**	**8.2**	**11.0**	**28.0**
Intervention costs	0.5	2.8	5.1	7.5	10.0	**25.9**
Cost of subsequent OVCF	0.0	0.1	0.3	0.6	1.0	**2.1**

Abbreviation: OVCF, osteoporotic vertebral compression fracture.

[a]Results may appear inexact due to rounding.

[b]All costs were calculated using the mean cost from the probabilistic results in our Primary Economic Evaluation.

Sensitivity Analysis

The results of the scenario analyses are presented in Table 47. Detailed tables are presented for selected scenarios in Tables A41 – A44 (Appendix 8). The budget impact was most affected by changing the population of interest; i.e., the potential number of people receiving PVP and PBK. The assumptions (1) a lower population of interest, (2) a lower uptake of PVP and PBK in the new scenario, (3) treating all subsequent OVCF with CT, (4) using a higher estimate for the cost of hospitalization without procedure, and (5) everyone is an outpatient resulted in lower budget impacts. The assumptions (1) a higher population of interest, (2) a higher uptake of PVP and PBK, and (3) keeping the distribution of PVP at 78% in the new scenario resulted in higher budget impacts.

In Scenario 5, where the distribution of PVP and PBK remains stable over time, there was a 5% increase in the budget impact. This was because our reference case assumed that, over time, more PVP would be used instead of PBK and PVP was less costly than PBK.

In the reference case, where we assumed no treatment effect on subsequent OVCF, the number of subsequent OVCF was the same for all interventions (CT, PVP, PBK). The difference in cost arose from the assumption that subsequent OVCF were treated using the same strategy as the initial OVCF. Because PBK and PVP are more expensive than CT, there were increased costs for treating subsequent OVCF. In Scenario 6, where we assumed that all subsequent OVCF were treated using CT, the budget impact for subsequent OVCF decreased to $0 (Table A41, Appendix 8).

Additionally, when we included a treatment effect on subsequent OVCF (Scenario 7), we saw a budget impact for subsequent OVCF due to differences in the number of subsequent OVCF that occurred. Using data from the clinical review, PVP and PBK increased the risk of subsequent OVCF, resulting in a total budget impact of $29.4 million over 5 years, with $3.4 million attributed to subsequent OVCF (Table A42, Appendix 8).

In Scenario 9, all outpatient treatment, the budget impact over 5 years decreased to $16.7 million. This estimate would be the upper bound on the cost to treat outpatients since we used the same population size as our reference case, which contained both inpatient and outpatient treatment.

Table 47: Budget Impact Analysis Results – Scenario Analyses

	Budget impact, $ million						
Scenario	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Total[a]**	**% Change[b]**
Reference case	0.5	2.9	5.5	8.2	11.0	28.0	—
Scenario 1, low population estimate	0.4	0.3	0.4	0.4	0.5	2.0	−93%
Scenario 2, high population estimate	1.3	7.1	13.4	20.0	27.0	68.7	145%
Scenario 3, lower uptake	0.0	0.3	1.5	2.8	4.1	8.7	−69%
Scenario 4, higher uptake	0.5	6.7	13.3	13.7	14.1	48.4	73%
Scenario 5, distribution of PVP and PBK remain stable over time	0.5	3.1	5.9	8.9	12.0	30.4	9%
Scenario 6, all subsequent OVCF treated with CT	0.5	2.8	5.1	7.6	10.0	25.9	−7%
Scenario 7, treatment effect on subsequent OVCF	0.5	3.0	5.7	8.6	11.5	29.4	5%
Scenario 8, higher cost of hospitalization without procedure	0.5	2.8	5.2	7.7	10.2	26.4	−6%
Scenario 9, all outpatients	0.3	1.7	3.3	4.9	6.5	16.7	−40%
Scenario 10, higher PVP and PBK use in current scenario	0.7	1.8	4.3	6.9	9.7	23.3	−17%

Abbreviations: CT, conservative treatment; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Results may appear inexact due to rounding.

[b]Percent change calculated as the difference in the total budget impact of the scenario analysis and the total budget impact of the reference case divided by the total budget impact of the reference case.

Discussion

We estimated the budget impact of increased clinical use of PVP and PBK with a positive funding recommendation. We found that there would be additional costs of $28 million over the next 5 years. Most of the budget impact (> 90%) was a result of costs of the PVP and PBK procedures. The results

were most sensitive to the size of the population of interest as the cost and number of procedures was driving the budget impact.

We estimated that an additional 46 people would be treated in Year 1, increasing to 986 people in Year 5, for a total of 2,546 additional people over 5 years. This implies an equivalent number of additional MRI scans would be required as part of the PVP and PBK procedures. Wait times for MRI in Ontario vary depending on priority level and geography. The provincial average wait time ranges from 3 to 101 days, depending on priority level.[174] Imaging wait times were already a barrier to receiving the procedures in a timely manner (see Ontario Context, above).

Wait times for this procedure are not reported by Ontario Health. There were 30 sites that performed PVP or PBK for inpatients or outpatients between fiscal years 2020 and 2023, so there may be a sufficient number of trained providers in the province; however, the procedures are done in an IR or OR suite and would compete for those resources with other surgeries (IntelliHealth, accessed June 13, 2024).

There has been some research on the predictors of failure of CT.[175] Future research may assist with scheduling patients likely to have refractory pain after CT within the recommended time for the procedure.

Strengths and Limitations

We estimated costs for our budget impact analysis using Ontario administrative data. Because PVP and PBK are already being performed in Ontario hospitals for painful OVCFs using hospital global budgets and have associated procedure and fee claim codes, we were able to identify cases in the administrative data and confidently estimate the costs of day procedures for PVP and PBK. We are less confident in the estimates for the inpatient procedure costs because those costs represent the cost of the hospital stay and not just the procedure of interest. We conducted scenario analyses allowing for a range of population and uptake estimates to explore the uncertainty in the budget impact estimates.

There were some other limitations to consider in our budget impact analysis. This analysis was developed from the results of our primary economic evaluation and any uncertainties were carried forward into this analysis. The uptake of PVP and PBK with a positive funding recommendation is based on historical data and expert opinion. We conducted scenario analyses to explore the impact of these uncertainties.

Conclusions

We estimated that publicly funding PVP and PBK for painful OVCFs would result in an additional budget impact of $28 million over the next 5 years.

Preferences and Values Evidence

Objective

The objective of this analysis was to explore the underlying values, needs, and priorities of those who have lived experience with osteoporotic vertebral compression fractures (OVCFs), as well as the preferences and perceptions of patients, family, and care partners of percutaneous vertebroplasty (PVP) and balloon kyphoplasty (PBK).

Background

Exploring patient preferences and values provides a unique source of information about people's experiences of a health condition and the health technologies or interventions used to manage or treat that health condition. It includes the impact of the condition and its treatment on the person with the health condition, their family and other care partners, and the person's personal environment. Engagement also provides insights into how a health condition is managed by the province's health system.

Information shared from lived experience can also identify gaps or limitations in published research (e.g., outcomes important to those with lived experience that are not reflected in the literature).[176-178] Additionally, lived experience can provide information and perspectives on the ethical and social values implications of health technologies or interventions.

Because the needs, preferences, priorities, and values of those with lived experience in Ontario are important to consider to understand the impact of a technology or intervention in people's lives, we may speak directly with people who live with a given health condition, including those with experience of the technology or intervention we are exploring.

For this analysis, we examined the preferences and values of people with lived experience of OVCF in two ways:

- A review by Ontario Health of the quantitative evidence on patient preferences and values
- Direct engagement by the Patient and Public Partnering team at Ontario Health with eligible participants through telephone interviews.

Quantitative Evidence

Research Questions

- What is the relative preference of patients for PVP or PBK compared with conservative treatment?
- What is the relative importance of key attributes of PVP or PBK, and what trade-offs between attributes are patients willing to make?

Methods

Literature Search

We performed a literature search for quantitative evidence of preferences and values on June 21, 2024, to retrieve studies published from database inception until the search date. We used the Ovid interface to search MEDLINE and the EBSCOhost interface to search the Cumulative Index to Nursing & Allied Health (CINAHL).

The search was based on the population and intervention of the clinical search strategy with a methodological filter applied to limit retrieval to quantitative evidence of preferences and values (modified from Selva et al[179]). The final search strategy was peer reviewed using the PRESS Checklist.[40]

We created database auto-alerts in MEDLINE and CINAHL and monitored them until August 14, 2024. See Appendix 1 for our literature search strategies, including all search terms.

Eligibility Criteria

Studies

Inclusion Criteria

- English-language full-text publications
- Studies published from inception to June 21, 2024
- Randomized controlled trials, cohort studies, cross-sectional studies that examined:
  - Patients' preferences for PVP or PBK treatment decision-making for OVCFs, and
  - Utility measures: direct techniques (standard gamble, time trade-off, rating scales) or conjoint analysis (discrete choice experiment, contingent valuation and willingness-to-pay, probability trade-off), or
  - Non-utility quantitative measures: direct-choice techniques, decision aids, surveys, questionnaires

Exclusion Criteria

- Animal and in vitro studies
- Nonsystematic reviews, narrative reviews, abstracts, editorials, letters, case reports, commentaries, and qualitative studies

Participants

Inclusion Criteria

- Adults (≥ 18 years of age) with a diagnosis of symptomatic (i.e., painful) OVCF refractory to conservative (nonsurgical) treatment

Exclusion Criteria

- Adults with vertebral fractures due to other causes, such as major trauma or cancer
- Patients who did not first undergo conservative (nonsurgical) treatment

Interventions

Inclusion Criteria

- PVP or PBK

Exclusion Criteria

- Vertebral body stenting; pedicle screw fixation; prophylactic augmentation (i.e., before a fracture occurs); KIVA VCF system (insertion of an implant combined with cement); SpineJack system (insertion of a retractable titanium expander). According to experts whom we consulted, these devices are rarely used in Ontario to date and are therefore not considered appropriate as either an intervention or comparator for the purposes of this health technology assessment (HTA)

Comparators

Inclusion Criteria

- Sham; conservative (nonsurgical) treatment (e.g., pain medication, bed rest, braces); PBK (when intervention is PVP), PVP (when intervention is PBK)

Exclusion Criteria

- Vertebral body stenting; pedicle screw fixation; prophylactic augmentation (i.e., before a fracture occurs); KIVA VCF system (insertion of an implant combined with cement); SpineJack system (insertion of a retractable titanium expander). According to experts whom we consulted, these devices are rarely used in Ontario to date and are therefore not considered appropriate as either an intervention or comparator for the purposes of this HTA

Outcome Measures

- Patients' preference or values

Literature Screening

A single reviewer conducted an initial screening of titles and abstracts using Covidence[41] and then obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The same reviewer then examined the full-text articles and selected studies eligible for inclusion.

Data Extraction

We extracted relevant data on study characteristics using a data form to collect information about the following:

- Source (e.g., citation information, contact details, study type)
- Methods (e.g., study design, study duration, participant recruitment)

- Outcomes (e.g., outcomes measured, outcome definition and source of information, unit of measurement, time points at which the outcomes were assessed)

Statistical Analysis

Results are summarized narratively. No additional statistical analyses were conducted beyond those reported in the primary studies.

Critical Appraisal of Evidence

We did not undertake a formal critical appraisal of the included studies.

Results

Literature Search

The literature search of the quantitative evidence of preferences and values yielded 153 citations published between database inception and June 21, 2024, after duplicates were removed. We identified no additional studies from other sources, including database alerts (monitored until August 14, 2024). In total, we identified 0 studies that met our inclusion criteria.

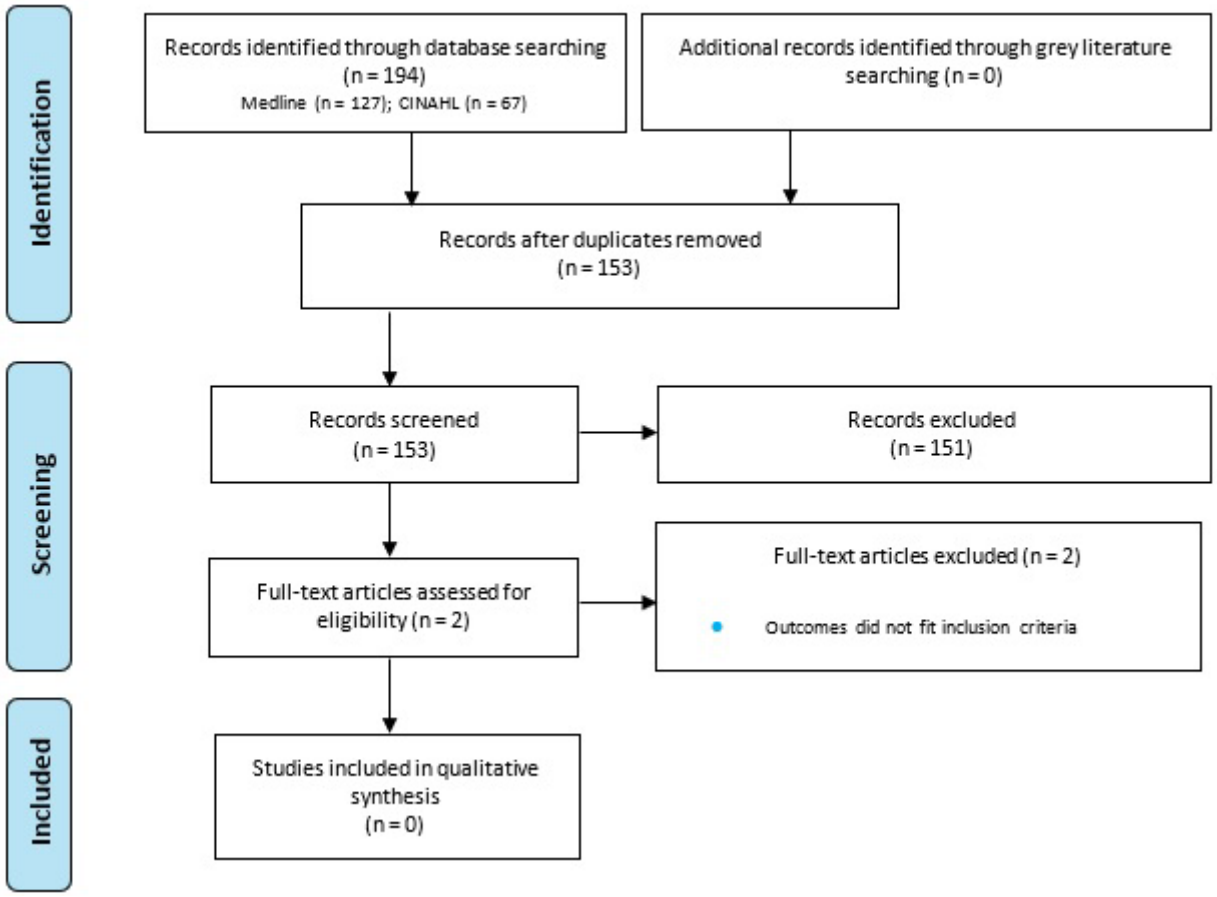


Figure 32: PRISMA Flow Diagram – Quantitative Evidence of Preferences and Values Review

PRISMA flow diagram showing the quantitative evidence of preferences and values review. The literature search for quantitative evidence of preferences and values yielded 153 citations, including grey literature results and after removing duplicates, published between database inception and June 21, 2024. We screened the abstracts of the 153 identified studies and excluded 151. We assessed the full text of 2 articles and excluded a further 2. In the end, we included 0 articles in the qualitative synthesis.

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

Source: Adapted from Page et al.[55]

Conclusions

No studies assessing patient preferences or values were identified that matched our inclusion criteria.

Direct Patient Engagement

Methods

Partnership Plan

The partnership plan for this HTA focused on consultation to examine the experiences of people with OVCF and those of their families or care partners. We engaged people via telephone interviews and distributed a survey throughout clinics in Ontario.

We used a qualitative interview, as this method of engagement allowed us to explore the meaning of central themes in the experiences of people with OVCF, their journey to diagnosis, and the experiences of their families or care partners.[126] The sensitive nature of exploring people's experiences of a health condition and their quality of life further supported our choice of methodology. We also designed a survey to provide an alternative method of engagement.

Participant Outreach

We used an approach called purposive sampling,[127-130] which involves actively reaching out to people with direct experience of the health condition and health technology or intervention being reviewed. We approached clinical experts in an effort to engage with patients who have undergone PVP or PBK. Our interview recruitment poster and survey was distributed to 1,000 interventional radiologists across Ontario through an email blast. We also reached out to potential participants through back pain clinics and the Ontario Health's patient, family, and advisors (PFA) network.

Inclusion Criteria

We sought to speak with adults with lived experience of OVCF who underwent or may undergo PVP or PBK. People did not need to have direct experience with PVP or PBK to participate.

Exclusion Criteria

We did not set exclusion criteria for participants who otherwise met the inclusion criteria.

Participants

For this project, we spoke to a total of 7 participants. Of the 7 who were interviewed, 2 had experience with PVP and 1 had experience with PBK, 3 received conservative treatment. One was a care partner of a patient with osteoporosis.

Approach

At the beginning of the interview, we explained the role of our organization, the purpose of this health technology assessment, the risks of participation, and how participants' personal health information would be protected. We gave this information to participants both verbally and in a letter of information (Appendix 9) if requested. We then obtained participants' verbal consent before starting the interview. With participants' consent, we audio-recorded and then transcribed the interviews.

Interviews lasted approximately 30 to 60 minutes. The interview was semi structured and consisted of a series of open-ended questions. Questions were based on a list developed by the Health Technology Assessment International Interest Group on Patient and Citizen Involvement in Health Technology Assessment.[131] Questions focused on the impact of OVCF on quality of life, the journey to diagnosis, and experience with PVP or PBK. See Appendix 10 for our interview guide.

Data Extraction and Analysis

We used a modified version of a grounded-theory methodology to analyze interview transcripts. This approach allowed us to organize and compare information on experiences across participants. This method consists of a repetitive process of obtaining, documenting, and analyzing responses while

simultaneously collecting, analyzing, and comparing information.[132,133] We used the qualitative data analysis software program NVivo[134] to identify and interpret patterns in the data. The patterns we identified allowed us to describe the impact of OVCF on the patient's life and decision-making factors for PVP and PBK.

Results

Living With OVCF

Patients with OVCF described experiencing a range of debilitating symptoms that significantly impact their quality of life. Chronic back pain is the most common symptom, with patients reporting a pain that worsens with movement, making even simple tasks like walking challenging. In addition to back pain, participants mentioned experiencing limited mobility, sleep disturbances, and breathing issues. These symptoms are persistent and chronic, causing ongoing discomfort that interferes with daily activities.

> *The main problem I have with osteoporosis is the pain that I've had in my back.*
>
> *I was not mobile at all. I spent 24/7 in bed, writhing in pain. No medication would help.*
>
> *Couldn't walk 2 or 3 feet without the pain, I was almost throwing up. It was quite intensive.*
>
> *Whenever I lie down, I have very rapid breathing. It is hard for my lungs to expand because of the fractures in my back and that is very burdensome.*
>
> *The pain increases the more tired I get and night is my worst. I'm having total sleeplessness.*
>
> *I'm up almost every single night until maybe five or six in the morning, and then I try to get a couple of hours sleep. So I'm having constant discomfort.*

Impact on Day-to-Day Life

Participants explained that the pain associated with OVCF caused significant mobility issues that affect their ability to perform everyday tasks. The pain negatively impacted their day-to-day life, including difficulty performing activities such as showering, walking, leaving the house, and doing household chores. Some participants expressed feeling distressed by the limitations on their mobility and experienced guilt for not being able to contribute to their household as much as they would have liked.

> *I'll get in the shower and then by the time I'm getting out, I'm basically almost crawling to get out. I can't wait to go lie down before I get dressed.*
>
> *I used to walk every day for an hour and a half in the morning and I can't do that. So that certainly affected my mobility.*
>
> *I can't walk the way I used to and that is very upsetting for me. If I don't use a cane or sticks, I have pain when I'm walking.*

I'm no longer able to get out. My community has arranged for a private taxi to take me to medical appointments, but other than that, we go nowhere.

I can't do laundry and housework and make meals and try to go to the grocery store…I feel useless. I'm always apologizing.

Impact on Work

Participants reported that their symptoms significantly impacted their ability to maintain productivity at work and, in some cases, led to unemployment. They explained that jobs requiring prolonged sitting, such as working at a desk or facilitating a group, caused severe discomfort and physical strain, making it difficult to perform their duties. Some people mentioned they could only sit for a limited time before needing to move or adjust their position due to back pain. For others, the physical challenges were so debilitating that they were unable to work at all, with some even being unable to perform basic self-care tasks. As a result, many were either unable to continue in their previous jobs or had to rely on disability benefits.

I work on a computer and if I'm facilitating a group or something I have to sit down, but I can't sit down for a long time, so I start moving my back, touching it and stuff.

I'm unemployed. And the reason why I'm unemployed is because of my health conditions, including that I can't really sit longer than maybe 3 hours at a desk.

I'm on disability. I thank God I don't have to go to work because there's no way… I could barely get myself in and out of the bathtub.

I could do zero work.

Impact on Social Life and Family Relationships

Participants shared that their OVCF symptoms greatly restricted their social lives, leaving them with little opportunity for meaningful interaction outside the home. They reported being largely homebound, with limited contact with friends and family, mostly through phone or email. They also expressed that social activities, such as attending gatherings, church, or other events, were no longer possible due to their physical limitations. Some participants described feeling isolated, with 1 person mentioning that they spent the majority of their time in bed, leaving only occasionally for necessities. Even when able to attend social events, they often faced physical discomfort, such as difficulty sitting for long periods or maintaining posture, which further hindered their ability to engage fully with others. This isolation left many feeling disconnected from their loved ones.

We [participant and spouse] have no social life. We have 1 or 2 friends that we keep in touch with by phone and e-mail. But as far as getting out to other people's places or to church or social activities, we are unable. Me particularly. I do have company once in a while for coffee or a light meal, but other than that, I'm homebound.

I was in bed 24 hours a day except to go out every 3rd day or to take a shower. I had zero social life.

It's limited what I can do, like [not being able to] go to a concert, sitting down on hard surfaces longer than an hour. I always have to remind myself not to slouch and sit up straight. I always sit at the edge of a seat and not really sitting with the people.

Impact on Care Partners

Care partners, typically family members of people with OVCF, expressed a sense of helplessness as they watched their loved ones endure pain and struggle with daily activities. They shared the emotional difficulty of wanting to help while feeling limited in what they could do to alleviate their family member's suffering. Some care partners highlighted the logistical challenges of caregiving, such as the physical distance between them and their loved ones, which made it harder to offer consistent support. These family members often had to travel long distances to provide the help needed, which added to the emotional and physical burden of caregiving.

It's difficult because, as a family member, you wish you could do something, but [you] can't.

She complains about [the pain] a lot, which I understand. But you know, I always have to contend with this feeling of wanting to help and I wish I could help, but there is really not a lot that I that I can do.

I have to provide her with a lot of help, which is kind of difficult for me because we live in different cities .I have to drive about an hour to get there and then I have to help her with whatever needs helping.

Impact on Mental Health

Participants reported that their mental health was significantly impacted by OVCF, with many describing feelings of anxiety, depression, and irritability. The chronic pain and discomfort associated with the condition contributed to these emotional struggles, often leaving participants feeling discouraged and helpless. Some people described how the constant physical strain led to a deep sense of frustration and sadness as they were unable to participate in daily activities or contribute to their families. The persistent nature of the pain also created a sense of isolation, with patients feeling there was no escape from their suffering, further worsening their mental health.

It affects your mood and sometimes when it [my back] is really sore, it irritates [me]. I already have anxiety and I take medication for depression.

It has a fairly significant negative impact on her mental health. I think just the chronic discomfort is very discouraging for her.

It makes you depressed. I mean, how could it not when you feel like you can't do anything to help contribute?

I definitely think that mental health is something that is impacted by the constant pain. And there's nowhere to turn with pain.

However, they also emphasized that maintaining a positive attitude and mindset played a crucial role in helping them cope with their health challenges. One participant mentioned using cognitive behavioral therapy as an effective strategy to enhance their mental well-being.

> *I don't let it impact my mental health. I am exhausted and that can easily pull someone down, but I have a strong faith and a very positive attitude and I believe that your mindset and your mental health determines how you progress ahead and your physical healing.*

> *I deal with cognitive behavioral therapy, that has allowed me to become more clear in regards to being action oriented and becoming realistic of my limitations and being ok with it, but it's a lot of mental health work.*

Treatment

Participants shared their experiences of exploring various treatment options for OVCF, including medications. While some noted experiencing temporary pain relief from medication, the majority reported that their symptoms persisted despite taking their medication.

> *No medication would help. I had oxycodone, I had hydromorphone, I had Toradol [ketorolac]. Nothing would help.*

> *When I take the oxy [codone], the pain's not gone, but I can tolerate it and lay down.*

> *When I take the pill [pain medication], I lay down. I have some relief, but the pain is still there.*

> *They gave me injections in the spine with Toradol [ketorolac], with cortisone. I was taking oral cortisone as well as all these pain medications and nothing worked at all. It was just like 10 out of 10 pain and it was very hard to deal with this.*

Patients with other comorbidities explained that they were unable to take medication for osteoporosis because it would interfere with the other medications they were already using. Some also mentioned experiencing side effects from the medications they were prescribed.

> *I'm on blood thinners, so I cannot take anti-inflammatory drugs, which would certainly help my osteoporosis. So that treatment is not available to me.*

> *I was going for ketamine injections at a hospital, I didn't like what it was doing to my brain, it was also causing breathing problems for me, so I voluntarily stopped going there.*

Some patients described alternative treatment options that they used to manage their symptoms, such as physiotherapy, massage, and cannabidiol (CBD) oil.

> *I think she did physiotherapy, but that was quite some time ago.*
>
> *She tried CBD oil a couple of years ago and she wasn't overly fond of it. She felt like it was sort of clouding her judgement.*
>
> *I do massage and I was told that that's probably a good thing that I do a monthly massage to keep my muscles blood flowing to them.*

PVP and PBK

Awareness of PVP and PBK

People highlighted a significant lack of awareness about PVP and PBK as treatment options for OVCF. Many expressed frustration that they were not informed about these procedures by their health care providers and had to rely on online resources to learn about them. Some participants mentioned researching the treatments on their own to understand the procedure. They stressed the importance of educating patients, particularly those with osteoporosis, about these options, so they aren't left to discover them through independent searches or by chance.

> *Nobody contacted me, I didn't know what it [vertebroplasty] was. I had to look it up online.*
>
> *I was never offered vertebroplasty, which is the obvious treatment for this, which should be done basically immediately when your fractures are diagnosed. I think that people should be educated that this type of surgery exists and that people with osteoporosis should be aware of it. Not finding out by recommendation or just by looking up on Google or something like that.*
>
> *I looked it [vertebroplasty] up, I saw on YouTube a mock operation that was done on the cadaver, so I knew what was going to be done.*

Some participants shared that vertebroplasty was discussed as a treatment option with their health care provider, but they were unable to undergo the procedure due to medical ineligibility.

> *I explored with my family doctor and other people [who] knew about vertebroplasty. They all told me it was way too late. It can't help you. It has to be done immediately.*
>
> *My doctor said that I would never be able to go through any kind of surgery because my osteoporosis has made my bones like chalk*

Decision-Making for PVP or PBK

People who underwent PVP and PBK were driven to seek treatment primarily due to the severe pain caused by their fractures. Many expressed a sense of desperation to find relief, viewing the procedure as a worthwhile option despite the risks. They considered vertebroplasty to be a relatively low-risk

procedure, with the primary focus being pain relief, even if it meant accepting certain physical changes, such as becoming shorter due to compression.

> *I did [PVP] because, if there was even an ounce of help, it [would be] worth it. It was no difficulty for me to have the procedure.*

> *I don't care if I'm shorter now. Apparently, I'm going to be shorter because of the compression, but it's all about pain relief. The main factor is trying to get some relief.*

> *There were risks, but very minor. But I was prepared to get rid of the pain any way I could.*

Some participants expressed a preference for minimally invasive treatment options, citing concerns about the limitations and side effects of pharmacological pain management. They mentioned that certain medications, like stronger pain relievers, were not suitable for them due to issues like stomach sensitivity or the risk of dependency.

> *I can only take Tylenol, not Advil or anything stronger, because my stomach's been weak. So I gather that [vertebroplasty] treatment would [leave me] better off.*

> *The hydromorphone is kind of addicting. She has to keep taking it, which I don't think she really wants to. I don't think she wants to be dependent on pharmacological treatment*

Experience With PVP or PBK

All participants who underwent PVP and PBK reported having a positive experience with the procedure, describing it as life-changing. Many noted that the surgery was quick, with minimal sedation required. Recovery was generally brief, with most people resuming normal activities within a few days, though some took precautions for a few months to avoid lifting heavy objects. They emphasized the significant pain relief they experienced, with some even describing it as a “miracle” that they were able to walk without pain.

> *The procedure was half hour to 45 minutes long. I was really nervous because I thought I was going to go to sleep, but apparently I'm kind of awake but sedated. The gentleman who did the procedure came and spoke to me beforehand and I felt my anxiety calm down. And then in my recovery I was there 3 to 4 hours afterwards.*

> *I just took it easy for a couple of days. And then I kind of went about my life. The cement hardens quickly; it stabilizes the pieces of the fracture that are moving about or that aren't solid.*

> *I was booked for surgery within days. I had the surgery done in an outpatient clinic. The surgery was successful, and I walked without pain. A miracle suddenly. Now I have no pain.*

> *It was a fantastic experience. No drugs were required after the surgery, I walked freely.*
>
> *I had to take precautions for 3 months not to lift anything heavy, but it was a life changing experience… unbelievable to have this pain go away all of a sudden.*

One participant who underwent PVP mentioned losing a few inches of height as a side effect of the procedure.

> *The problem is, I lost 4 inches in height from the procedure and I don't like that happening to me, but in terms of pain I'm not worse than I was. So, I feel the vertebroplasty helped to stabilize my back at that point.*

Impact of PVP and PBK

People who underwent PVP and PBK shared positive experiences regarding the significant pain relief and improvements in their overall quality of life. Many reported feeling immediate relief from pain, with some even walking out of the procedure with little to no discomfort. They noted that the procedure helped restore their condition to pre-fracture levels, alleviating the chronic pain that had been affecting their daily lives. The ability to wake up and go through the day without constant pain was described as a major improvement in their overall well-being.

> *[The treatment] definitely gave me relief from the pain that I was having. My pain wasn't the same. [After] I received vertebroplasty, my pain wasn't as severe.*
>
> *I asked him [my doctor] how quickly I would return to normal and he said within hours, and he was right. When the surgery was over, I walked out without pain.*
>
> *I will say that it [PVP] definitely did help and that I didn't get any worse. I returned to where I was in terms of my back issues and my back pain before the fractures.*
>
> *It [PVP] helped my pain at the time. Any pain that you can release for anybody is definitely an improvement in the quality of life because it's not great to wake up and go to sleep in pain.*

Barriers

Lack of Access to Treatment

Patients discussed several challenges in accessing treatment for OVCF, particularly highlighting transportation and out-of-pocket costs as major barriers. They mentioned difficulties in getting to and from medical appointments, especially when they lacked the means to drive or had to rely on expensive taxi services. Additionally, many patients faced financial obstacles, such as the high cost of medications and treatments not covered by insurance, like Prolia injections, which added a significant financial burden. For those who were self-employed or had private insurance, they often encountered caps on coverage, further complicating access to necessary care.

Getting to and from her hospital or to the physio was kind of difficult because I wasn't old enough to drive and my father had to work.

The pain clinic was just out of the area and my family doctor is at a distance, so I have to take a taxi, which costs me $125 to see my GP.

My prolia injection is not covered by my drug plan, it costs about $500 a shot. I'm self-employed, so I have private insurance and, you know, all of a sudden you realize that there's a cap on things.

Longer Wait Times for Diagnosis

People identified long wait times for diagnosis as a major obstacle to receiving timely treatment. Many shared that they had to advocate for themselves to secure essential diagnostic tests, such as x-rays or MRIs, often facing weeks of delays before receiving a proper diagnosis. Some patients expressed frustration with the lack of communication from their health care providers, feeling isolated and unsupported as they struggled with intense pain. Additionally, there were concerns about the insufficient support for seniors within the health care system, with patients noting that long wait times and a lack of attention from clinics made it particularly difficult for older individuals to access the care they needed.

I was hospitalized last year when I had the terrible fracture. It seemed to be around the waist area and I could not move any part of my body. The pain was so severe I was in bed for months after the hospitalization, but the doctors in the hospital would not give me an MRI. Finally, I got an MRI, but with the long wait for those tests, I had to wait another 6 to 8 weeks just for a diagnosis.

My doctor couldn't get me an appointment for weeks. I finally got an appointment on my own through somebody. But at that point, I had asked my family doctor to x-ray my back because I was in such pain and the x-rays came back that I had 4 fractures.

There was really a lack of communication. I actually felt all alone in the world because I'm suffering at home, phoning my family doctor, and then they are like "you have to wait. You have to wait."

We just don't have the same support anymore and I will say particularly for seniors. It's almost as if seniors these days are disposable with the long wait times and the lack of interest in new clinics taking on seniors.

Some people also reported being misdiagnosed, which not only caused additional distress but also contributed to further delays in receiving the appropriate treatment.

> *It was 8 weeks with horrible pain in my back, which they kept thinking was a problem with my stomach. So I was misdiagnosed.*

> *The first doctor who saw me said I had peritonitis and he just went on with that diagnosis and didn't explore any further. Had I had x-rays at the time, then maybe I would have had the experience with vertebroplasty at the correct time. So that was a barrier to my treatment*

Lack of Awareness About Vertebroplasty

Other people expressed frustration with the lack of awareness about vertebroplasty among health care providers, sharing that they had to advocate for themselves to access this treatment. They also voiced concerns for others who might not have the same ability to advocate for themselves and thus could struggle to access the care they need.

> *I wonder how much family doctors in training are aware of the procedure. Orthopedic doctors would be aware of the procedure, but you wouldn't necessarily get to [see] an orthopedic doctor if you have a fracture, you could wait 6 months to see somebody. So my question would be how would somebody in my position have access to this procedure?*

> *I cannot get information out of my specialist. And it's as if I'm challenging them by asking any questions about my treatment, the last 3 appointments have been very discouraging … to have the doctor say angrily that there's nothing more she can do for me. I will continue to advocate for myself.*

> *I think it would be a big issue for somebody who did not have access to treatment [PVP] the way I did, because I already know the doctor who does vertebroplasty [and can easily contact them]. But I'm not sure how someone else can access this treatment when they are diagnosed with vertebral fractures. Do they have the opportunity immediately to have vertebroplasty and, if they don't, that's what we should be fighting for.*

Discussion

All participants had either lived experience with OVCF or were family members or care partners of someone affected by the condition. They shared how OVCF negatively impacted their daily activities, work, social life, family relationships, and mental health. Participants discussed their journeys in managing the condition, exploring various treatment options, and their experiences with vertebroplasty. Of the 3 participants who underwent vertebroplasty, all reported positive improvements in pain symptoms and quality of life. Transportation, cost of medication, and longer time for diagnosis were highlighted as barriers for accessing treatment. Additionally, participants emphasized the need to expand access to minimally invasive treatment options like vertebroplasty for individuals with OVCF.

However, our analysis was limited by a small sample size, despite considerable recruitment efforts. We collaborated with clinical experts who helped distribute our recruitment posters to a wide network of

interventional radiologists across Ontario. We also reached out to back pain clinics and offered surveys as an alternative means of engagement. Despite these efforts, we were unable to recruit additional participants

Conclusions

The insights shared by participants underscore the significant challenges individuals with OVCF face in managing their condition, with notable impacts on daily activities, work, social interactions, and mental health. Despite these challenges, participants highlighted the positive outcomes of vertebroplasty for those who underwent the procedure, particularly in terms of pain relief and improved quality of life. However, barriers such as transportation, medication costs, and longer wait times for diagnosis remain significant obstacles to accessing timely treatment. Participants also emphasized the importance of expanding access to minimally invasive treatment options like vertebroplasty to improve the care and outcomes for people living with OVCF.

Conclusions of the Health Technology Assessment

Compared to conservative treatment in people with painful OVCFs, PVP may improve physical function and quality of life (GRADE: Very low) and may reduce pain in the short term (i.e., ≤ 3 months) (GRADE: Low), but it may have little to no effect on use of analgesics, mortality, adverse events, and new fractures (GRADE: Very low).

Compared to sham in people with painful OVCFs, PVP may increase adverse events and may reduce pain slightly (GRADE: Low), but it may have little to no effect on use of analgesics (GRADE: Very low). It also probably results in little to no difference in physical function, quality of life, mortality, and new fractures (GRADE: Low).

Compared to conservative treatment in people with painful OVCFs, PBK may improve physical function and quality of life (GRADE: Low) and may reduce pain in the short term (i.e., ≤ 3 months) (GRADE: Very low), but it may have little to no effect on use of analgesics (GRADE: Very low). It probably results in little to no difference in mortality, adverse events and new fractures (GRADE: Low).

Compared to PBK in people with painful OVCFs, PVP may increase cement leakage (GRADE: Very low) and may have little to no effect on pain, use of analgesics, physical function, quality of life, mortality, adverse events, and new fractures (GRADE: Very low).

PVP likely reduces radiation exposure to the provider/operator slightly (GRADE: Low).

PVP and PBK consistently produced higher QALYS at higher costs compared with CT. The ICERs comparing PVP with CT and PBK with CT were $43,324 and $65,921 per QALY, respectively, from the perspective of the Ontario Ministry of Health over 3 years. We estimated that publicly funding PVP and PBK for painful OVCFs would cost an additional $28 million over the next 5 years.

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Abbreviations

BMD: bone mineral density

CDA: Canada's Drug Agency

CI: confidence interval

CT: conservative treatment

CUA: cost-utility analysis

ED: emergency department

EQ-5D: Euroqol -5 dimension

GRADE: Grading of Recommendations Assessment, Development, and Evaluation

HTA: health technology assessment

ICER: incremental cost-effectiveness ratio

MCID: minimal clinically important difference

MD: mean difference

MRI: magnetic resonance imaging

NICE: National Institute for Health and Care Excellence

NMB: net monetary benefit

NRS: numerical rating score

ODI: Oswestry Disability Index

OHIP: Ontario Health Insurance Plan

OR: odds ratio

OVCF: osteoporotic vertebral compression fracture

PBK: percutaneous balloon kyphoplasty

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

PVP: percutaneous vertebroplasty

QALY: quality-adjusted life year

QUALEFFO: quality of life questionnaire of the European Foundation for Osteoporosis

RCT: randomized controlled trial

RMDQ: Roland Morris disability questionnaire

RR: relative risk

SD: standard deviation

SF-36: short form 36 questionnaire

SMD: standardized mean difference

SOF-ADL: study of osteoporotic fractures–activities of daily living questionnaire

SoR: study of osteoporotic fractures–activities of daily living questionnaire

VAS: visual analogue score

WTP: willingness to pay

Glossary

Adverse event: An adverse event is an unexpected medical problem that happens during treatment for a health condition. Adverse events may be caused by something other than the treatment.

Cohort model: In economic evaluations, a cohort model is used to simulate what happens to a homogeneous cohort (group) of patients after receiving a specific health care intervention. The proportion of the cohort who experiences certain health outcomes or events is estimated, along with the relevant costs and benefits. In contrast, a microsimulation model follows the course of individual patients.

Cost-effective: A health care intervention is considered cost-effective when it provides additional benefits, compared with relevant alternatives, at an additional cost that is acceptable to a decision-maker based on the maximum willingness-to-pay value.

Cost-effectiveness acceptability curve: In economic evaluations, a cost-effectiveness acceptability curve is a graphical representation of the results of a probabilistic analysis. It illustrates the probability of health care interventions being cost-effective over a range of willingness-to-pay values. Willingness-to-pay values are plotted on the horizontal axis of the graph, and the probability of the intervention of interest and its comparator(s) being cost-effective at corresponding willingness-to-pay values is plotted on the vertical axis.

Cost-effectiveness analysis: Used broadly, "cost-effectiveness analysis" may refer to an economic evaluation used to compare the benefits of two or more health care interventions with their costs. It may encompass several types of analysis (e.g., cost-effectiveness analysis, cost–utility analysis). Used more specifically, "cost-effectiveness analysis" may refer to a type of economic evaluation in which the main outcome measure is the incremental cost per natural unit of health (e.g., life-year, symptom-free day) gained.

Cost–utility analysis: A cost–utility analysis is a type of economic evaluation used to compare the benefits of two or more health care interventions with their costs. The benefits are measured using quality-adjusted life-years, which capture both the quality and quantity of life. In a cost–utility analysis, the main outcome measure is the incremental cost per quality-adjusted life-year gained.

Decision tree: A decision tree is a type of economic model used to assess the costs and benefits of two or more alternative health care interventions. Each intervention may be associated with different outcomes, which are represented by distinct branches in the tree. Each outcome may have a different probability of occurring and may lead to different costs and benefits.

Discounting: Discounting is a method used in economic evaluations to adjust for the differential timing of the costs incurred and the benefits generated by a health care intervention over time. Discounting reflects the concept of positive time preference, whereby future costs and benefits are reduced to reflect their present value. The health technology assessments conducted by Ontario Health use an annual discount rate of 1.5% for both future costs and future benefits.

Disutility: A disutility is a decrease in utility (i.e., a decrease in preference for a particular health outcome) typically resulting from a particular health condition (e.g., experiencing a symptom or complication).

Dominant: A health care intervention is considered dominant when it is more effective and less costly than its comparator(s).

EQ-5D: The EQ-5D is a generic health-related quality-of-life classification system widely used in clinical studies. In economic evaluations, it is used as an indirect method of obtaining health state preferences (i.e., utility values). The EQ-5D questionnaire consists of five questions relating to different domains of quality of life: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. For each domain, there are three response options: no problems, some problems, or severe problems. A newer instrument, the EQ-5D-5L, includes five response options for each domain. A scoring table is used to convert EQ-5D scores to utility values.

Equity: Unlike the notion of equality, equity is not about treating everyone the same way.[180] It denotes fairness and justice in process and in results. Equitable outcomes often require differential treatment and resource redistribution to achieve a level playing field among all individuals and communities. This requires recognizing and addressing barriers to opportunities for all to thrive in our society.

Extended dominance: A health care intervention is considered to be extendedly dominated when it has an incremental cost-effectiveness ratio higher than that of the next most costly or effective comparator. Interventions that are extendedly dominated are ruled out.

Health inequity: Health inequities are avoidable inequalities in health between groups of people within countries and between countries.[181] These inequities arise from inequalities within and between societies. Social and economic conditions and their effects on people's lives determine their risk of illness and the actions taken to prevent them becoming ill or treat illness when it occurs.

Health-related quality of life: Health-related quality of life is a measure of the impact of a health care intervention on a person's health. It includes the dimensions of physiology, function, social life, cognition, emotions, sleep and rest, energy and vitality, health perception, and general life satisfaction.

Health state: A health state is a particular status of health (e.g., sick, well, dead). A health state is associated with some amount of benefit and may be associated with specific costs. Benefit is captured through individual or societal preferences for the time spent in each health state and is expressed in quality-adjusted weights called utility values. In a Markov model, a finite number of mutually exclusive health states are used to represent discrete states of health.

Incremental cost: The incremental cost is the additional cost, typically per person, of a health care intervention versus a comparator.

Incremental cost-effectiveness ratio (ICER): The incremental cost-effectiveness ratio (ICER) is a summary measure that indicates, for a given health care intervention, how much more a health care consumer must pay to get an additional unit of benefit relative to an alternative intervention. It is obtained by dividing the incremental cost by the incremental effectiveness. Incremental cost-effectiveness ratios are typically presented as the cost per life-year gained or the cost per quality-adjusted life-year gained.

Incremental net benefit: Incremental net benefit is a summary measure of cost-effectiveness. It incorporates the differences in cost and effect between two health care interventions and the willingness-to-pay value. Net health benefit is calculated as the difference in effect minus the difference in cost divided by the willingness-to-pay value. Net monetary benefit is calculated as the willingness-to-pay value multiplied by the difference in effect minus the difference in cost. An intervention can be considered cost-effective if either the net health or net monetary benefit is greater than zero.

Market distribution: When evaluating more than two technologies, the market distribution is the proportion of the population that uses each technology.

Markov model: A Markov model is a type of decision-analytic model used in economic evaluations to estimate the costs and health outcomes (e.g., quality-adjusted life-years gained) associated with using a particular health care intervention. Markov models are useful for clinical problems that involve events of interest that may recur over time (e.g., stroke). A Markov model consists of mutually exclusive, exhaustive health states. Patients remain in a given health state for a certain period of time before moving to another health state based on transition probabilities. The health states and events modelled may be associated with specific costs and health outcomes.

Ministry of Health perspective: The perspective adopted in economic evaluations determines the types of costs and health benefits to include. Ontario Health develops health technology assessment reports from the perspective of the Ontario Ministry of Health. This perspective includes all costs and health benefits attributable to the Ministry of Health, such as treatment costs (e.g., drugs, administration, monitoring, hospital stays) and costs associated with managing adverse events caused by treatments. This perspective does not include out-of-pocket costs incurred by patients related to obtaining care (e.g., transportation) or loss of productivity (e.g., absenteeism).

One-way sensitivity analysis: A one-way sensitivity analysis is used to explore uncertainty in the results of an economic evaluation. It is done by varying one model input (i.e., a parameter) at a time between its minimum and maximum values to observe the potential impact on the cost-effectiveness of the health care intervention of interest.

Probabilistic analysis: A probabilistic analysis (also known as a probabilistic sensitivity analysis) is used in economic models to explore uncertainty in several parameters simultaneously and is done using Monte Carlo simulation. Model inputs are defined as a distribution of possible values. In each iteration, model inputs are obtained by randomly sampling from each distribution, and a single estimate of cost and effectiveness is generated. This process is repeated many times (e.g., 10,000 times) to estimate the number of times (i.e., the probability) that the health care intervention of interest is cost-effective.

Quality-adjusted life-year (QALY): The quality-adjusted life-year (QALY) is a generic health outcome measure commonly used in cost–utility analyses to reflect the quantity and quality of life-years lived. The life-years lived are adjusted for quality of life using individual or societal preferences (i.e., utility values) for being in a particular health state. One year of perfect health is represented by one quality-adjusted life-year.

Reference case: The reference case is a preferred set of methods and principles that provide the guidelines for economic evaluations. Its purpose is to standardize the approach of conducting and reporting economic evaluations, so that results can be compared across studies.

Scenario analysis: A scenario analysis is used to explore uncertainty in the results of an economic evaluation. It is done by observing the potential impact of different scenarios on the cost-effectiveness of a health care intervention. Scenario analyses involve varying structural assumptions from the reference case.

Sensitivity analysis: Every economic evaluation contains some degree of uncertainty, and results can vary depending on the values taken by key parameters and the assumptions made. Sensitivity analysis allows these factors to be varied and shows the impact of these variations on the results of the evaluation. There are various types of sensitivity analysis, including deterministic, probabilistic, and scenario.

Sham treatment: Similar in concept to a placebo, in a sham treatment, the medical professional goes through the motions of a treatment without actually performing the treatment.

Short-Form–Six Dimensions (SF-6D): The SF-6D is a generic health-related quality-of-life classification system widely used in clinical studies. In economic evaluations, it is used as an indirect method of obtaining health state preferences (i.e., utility values). The classification system consists of six attributes (physical functioning, role limitations, social functioning, pain, mental health, and vitality), each associated with four to six levels, thus producing a total of 18,000 possible unique health states. A scoring table is used to convert SF-6D scores to health state values.

Societal perspective: The perspective adopted in an economic evaluation determines the types of costs and health benefits to include. The societal perspective reflects the broader economy and is the aggregation of all perspectives (e.g., health care payer and patient perspectives). It considers the full effect of a health condition on society, including all costs (regardless of who pays) and all benefits (regardless of who benefits).

Time horizon: In economic evaluations, the time horizon is the time frame over which costs and benefits are examined and calculated. The relevant time horizon is chosen based on the nature of the disease and health care intervention being assessed, as well as the purpose of the analysis. For instance, a lifetime horizon would be chosen to capture the long-term health and cost consequences over a patient's lifetime.

Uptake rate: In instances where two technologies are being compared, the uptake rate is the rate at which a new technology is adopted. When a new technology is adopted, it may be used in addition to an existing technology, or it may replace an existing technology.

Utility: A utility is a value that represents a person's preference for various health states. Typically, utility values are anchored at 0 (death) and 1 (perfect health). In some scoring systems, a negative utility value indicates a state of health valued as being worse than death. Utility values can be aggregated over time to derive quality-adjusted life-years, a common outcome measure in economic evaluations.

Visual analogue scale (VAS): The visual analogue scale (VAS) is a direct method of measuring people's preferences for various health states. Respondents are first asked to rank a series of health states from least to most preferable. Then, they are asked to place the health states on a scale with intervals reflecting the differences in preference among the given health states. The scale ranges from 0 (worst imaginable health) to 100 (best imaginable health). The value of a respondent's preference for each health state is given by their placement of each health state on the scale.

Willingness-to-pay value: A willingness-to-pay value is the monetary value a health care consumer is willing to pay for added health benefits. When conducting a cost–utility analysis, the willingness-to-pay value represents the cost a consumer is willing to pay for an additional quality-adjusted life-year. If the incremental cost-effectiveness ratio is less than the willingness-to-pay value, the health care intervention of interest is considered cost-effective. If the incremental cost-effectiveness ratio is more than the willingness-to-pay value, the intervention is considered not to be cost-effective.

Appendices

Appendix 1: Literature Search Strategies

Clinical Evidence Search

Search date: May 29, 2024
Databases searched: Ovid MEDLINE, Embase, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, NHS Economic Evaluation Database

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <April 2024>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to May 22, 2024>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2024 Week 21>, Ovid MEDLINE(R) ALL <1946 to May 24, 2024>

Search Strategy:

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1 spinal fractures/ (34896)
2 osteoporotic fractures/ (25094)
3 Fractures, Compression/ (9724)
4 (((spine* or spinal or thoracolumbar* or compression* or osteopor* or vertebr*) adj3 (fractur* or break* or broke*)) or OVCF or VCF).ti,ab,kf. (108003)
5 or/1-4 (129133)
6 exp vertebroplasty/ (12842)
7 (vertebr#plast* or kyphoplast* or PVP or PBK).ti,ab,kf. (39641)
8 ((osteoplast* or augment* or balloon*) adj3 (vertebr* or spine* or spinal)).ti,ab,kf. (4530)
9 (synflate* or kyphon* or iVAS* or KYPHX* or osteointroducer* or Osteopal*).ti,ab,kf. (865)
10 (one step* adj3 (osteo* or bone access* or device* or fill* or inflation* or inject* or cement* or paste* or glue*)).ti,ab,kf. (420)
11 or/6-10 (44813)
12 5 and 11 (12201)
13 exp Animals/ not Humans/ (16520211)
14 12 not 13 (9942)
15 Case Reports/ or Comment.pt. or Editorial.pt. or (Letter not (Letter and Randomized Controlled Trial)).pt. or Congress.pt. (6686707)
16 14 not 15 (8847)
17 limit 16 to english language [Limit not valid in CDSR; records were retained] (7698)
18 limit 17 to yr="2019 -Current" (3114)
19 18 use medall,coch,cleed (1179)
20 ((Letter not (Letter and Randomized Controlled Trial)) or Conference proceeding or Editorial or Comment or Trial registry record).pt. (5098164)
21 18 not 20 (3042)
22 21 use cctr (127)
23 19 or 22 (1306)
24 spine fracture/ (25709)
25 fragility fracture/ (24848)

26 compression fracture/ (12390)
27 (((spine* or spinal or thoracolumbar* or compression* or osteopor* or vertebr*) adj3 (fractur* or break* or broke*)) or OVCF or VCF).tw,kw,kf. (112842)
28 or/24-27 (130781)
29 exp percutaneous vertebroplasty/ (9082)
30 (vertebr#plast* or kyphoplast* or PVP or PBK).tw,kw,kf,dv. (39733)
31 ((osteoplast* or augment* or balloon*) adj3 (vertebr* or spine* or spinal)).tw,kw,kf,dv. (4838)
32 (synflate* or kyphon* or iVAS* or KYPHX* or osteointroducer* or Osteopal*).tw,kw,kf,dv. (1086)
33 (one step* adj3 (osteo* or bone access* or device* or fill* or inflation* or inject* or cement* or paste* or glue*)).tw,kw,kf,dv. (440)
34 or/29-33 (44865)
35 28 and 34 (12025)
36 (exp animal/ or nonhuman/) not exp human/ (12148690)
37 35 not 36 (11880)
38 Case Report/ or Comment/ or Editorial/ or (letter.pt. not (letter.pt. and randomized controlled trial/)) or conference abstract.pt. or conference review.pt. (11772183)
39 37 not 38 (9304)
40 limit 39 to english language [Limit not valid in CDSR; records were retained] (7867)
41 limit 40 to yr="2019 -Current" (2710)
42 41 use emez (1233)
43 23 or 42 (2539)
44 43 use medall (1179)
45 43 use coch (0)
46 43 use cctr (127)
47 43 use cleed (0)
48 43 use emez (1233)
49 remove duplicates from 43 (1453)
50 49 use medall,emez (1443)

Economic Evidence Search

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <April 2024>, EBM Reviews - Cochrane Database of Systematic Reviews <2005 to May 29, 2024>, EBM Reviews - NHS Economic Evaluation Database <1st Quarter 2016>, Embase <1980 to 2024 Week 21>, Ovid MEDLINE(R) ALL <1946 to May 28, 2024>

Search date: May 29, 2024

Search Strategy:

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1 spinal fractures/ (34899)
2 osteoporotic fractures/ (25096)
3 Fractures, Compression/ (9725)
4 (((spine* or spinal or thoracolumbar* or compression* or osteopor* or vertebr*) adj3 (fractur* or break* or broke*)) or OVCF or VCF).ti,ab,kf. (108029)
5 or/1-4 (129161)
6 exp vertebroplasty/ (12843)
7 (vertebr#plast* or kyphoplast* or PVP or PBK).ti,ab,kf. (39650)

8 ((osteoplast* or augment* or balloon*) adj3 (vertebr* or spine* or spinal)).ti,ab,kf. (4531)
9 (synflate* or kyphon* or iVAS* or KYPHX* or osteointroducer* or Osteopal*).ti,ab,kf. (866)
10 (one step* adj3 (osteo* or bone access* or device* or fill* or inflation* or inject* or cement* or paste* or glue*)).ti,ab,kf. (420)
11 or/6-10 (44823)
12 5 and 11 (12203)
13 exp Animals/ not Humans/ (16521556)
14 12 not 13 (9944)
15 Case Reports/ or Comment.pt. or Editorial.pt. or (Letter not (Letter and Randomized Controlled Trial)).pt. or Congress.pt. (6688569)
16 14 not 15 (8849)
17 limit 16 to english language [Limit not valid in CDSR; records were retained] (7700)
18 limit 17 to yr="2019-current" (3116)
19 18 use coch,cleed (0)
20 economics/ (265270)
21 economics, medical/ or economics, pharmaceutical/ or exp economics, hospital/ or economics, nursing/ or economics, dental/ (1099971)
22 economics.fs. (473423)
23 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).ti,ab,kf. (1362247)
24 exp "costs and cost analysis"/ (712150)
25 (cost or costs or costing or costly).ti. (347251)
26 cost effective*.ti,ab,kf. (483848)
27 (cost* adj2 (util* or efficacy* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog* or increment*)).ab,kf. (327839)
28 models, economic/ (16515)
29 markov chains/ or monte carlo method/ (112582)
30 (decision adj1 (tree* or analy* or model*)).ti,ab,kf. (73310)
31 (markov or markow or monte carlo).ti,ab,kf. (189323)
32 quality-adjusted life years/ (59309)
33 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).ti,ab,kf. (120329)
34 ((adjusted adj1 (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).ti,ab,kf. (214087)
35 or/20-34 (3565139)
36 18 and 35 (180)
37 19 or 36 (180)
38 spine fracture/ (25709)
39 fragility fracture/ (24848)
40 compression fracture/ (12391)
41 (((spine* or spinal or thoracolumbar* or compression* or osteopor* or vertebr*) adj3 (fractur* or break* or broke*)) or OVCF or VCF).tw,kw,kf. (112869)
42 or/38-41 (130808)
43 exp percutaneous vertebroplasty/ (9082)
44 (vertebr#plast* or kyphoplast* or PVP or PBK).tw,kw,kf,dv. (39742)
45 ((osteoplast* or augment* or balloon*) adj3 (vertebr* or spine* or spinal)).tw,kw,kf,dv. (4839)
46 (synflate* or kyphon* or iVAS* or KYPHX* or osteointroducer* or Osteopal*).tw,kw,kf,dv. (1087)
47 (one step* adj3 (osteo* or bone access* or device* or fill* or inflation* or inject* or cement* or paste* or glue*)).tw,kw,kf,dv. (440)
48 or/43-47 (44875)

49 42 and 48 (12027)
50 (exp animal/ or nonhuman/) not exp human/ (12150035)
51 49 not 50 (11882)
52 Case Report/ or Comment/ or Editorial/ or (letter.pt. not (letter.pt. and randomized controlled trial/)) or conference abstract.pt. or conference review.pt. (11773133)
53 51 not 52 (9306)
54 limit 53 to english language [Limit not valid in CDSR; records were retained] (7869)
55 limit 54 to yr="2019-current" (2712)
56 Economics/ (265270)
57 Health Economics/ or Pharmacoeconomics/ or Drug Cost/ or Drug Formulary/ (153920)
58 Economic Aspect/ or exp Economic Evaluation/ (574650)
59 (econom* or price or prices or pricing or priced or discount* or expenditure* or budget* or pharmacoeconomic* or pharmaco-economic*).tw,kw,kf. (1382818)
60 exp "Cost"/ (712150)
61 (cost or costs or costing or costly).ti. (347251)
62 cost effective*.tw,kw,kf. (492807)
63 (cost* adj2 (util* or efficac* or benefit* or minimi* or analy* or saving* or estimate* or allocation or control or sharing or instrument* or technolog* or increment*)).ab,kw,kf. (338116)
64 Monte Carlo Method/ (87183)
65 (decision adj1 (tree* or analy* or model*)).tw,kw,kf. (76752)
66 (markov or markow or monte carlo).tw,kw,kf. (192815)
67 Quality-Adjusted Life Years/ (59309)
68 (QOLY or QOLYs or HRQOL or HRQOLs or QALY or QALYs or QALE or QALEs).tw,kw,kf. (123699)
69 ((adjusted adj1 (quality or life)) or (willing* adj2 pay) or sensitivity analys*s).tw,kw,kf. (235145)
70 or/56-69 (3068733)
71 55 and 70 (136)
72 71 use emez (74)
73 37 or 72 (180)
74 73 use medall (52)
75 73 use coch (0)
76 73 use cctr (9)
77 73 use cleed (0)
78 73 use emez (119)
79 remove duplicates from 73 (127)
80 79 use medall,emez (125)
81 79 use cctr (2)

Quantitative Evidence of Preferences and Values Search

Search Date: June 21, 2024
Database: Ovid MEDLINE(R) ALL <1946 to June 21, 2024>
Search Strategy:

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1 spinal fractures/ (18456)
2 osteoporotic fractures/ (8592)
3 Fractures, Compression/ (3456)

4 (((spine* or spinal or thoracolumbar* or compression* or osteopor* or vertebr*) adj3 (fractur* or break* or broke*)) or OVCF or VCF).ti,ab,kf. (41513)
5 or/1-4 (50344)
6 exp vertebroplasty/ (3510)
7 (vertebr#plast* or kyphoplast* or PVP or PBK).ti,ab,kf. (16408)
8 ((osteoplast* or augment* or balloon*) adj3 (vertebr* or spine* or spinal)).ti,ab,kf. (1883)
9 (synflate* or kyphon* or iVAS* or KYPHX* or osteointroducer* or Osteopal*).ti,ab,kf. (283)
10 (one step* adj3 (osteo* or bone access* or device* or fill* or inflation* or inject* or cement* or paste* or glue*)).ti,ab,kf. (193)
11 or/6-10 (18087)
12 5 and 11 (4788)
13 Attitude to Health/ (85479)
14 Health Knowledge, Attitudes, Practice/ (129485)
15 Patient Participation/ (30084)
16 Patient Preference/ (11087)
17 Attitude of Health Personnel/ (133520)
18 *Professional-Patient Relations/ (12546)
19 *Physician-Patient Relations/ (37561)
20 Choice Behavior/ (35383)
21 (choice or choices or value* or valuation* or knowledg*).ti. (339334)
22 (preference* or expectation* or attitude* or acceptab* or point of view).ti,ab,kf. (789554)
23 ((clinician* or doctor* or surgeon* or radiologist* or (health* adj2 worker*) or patient*1 or personal or physician* or practitioner* or professional*1 or provider* or user*1 or women or men) adj2 (participation or perspective* or perception* or misperception* or perceiv* or view* or understand* or misunderstand* or value*1 or knowledg*)).ti,ab,kf. (204765)
24 health perception*.ti,ab,kf. (3533)
25 *Decision Making/ (47237)
26 (clinician* or doctor* or surgeon* or radiologist* or (health* adj2 worker*) or patient*1 or personal or physician* or practitioner* or professional*1 or provider* or user*1 or women or men).ti. (3163803)
27 25 and 26 (8750)
28 (decision* and mak*).ti. (40475)
29 (decision mak* or decisions mak*).ti,ab,kf. (234389)
30 28 or 29 (236101)
31 (clinician* or doctor* or surgeon* or radiologist* or (health* adj2 worker*) or patient*1 or personal or physician* or practitioner* or professional*1 or provider* or user*1 or women or men).ti,ab,kf. (10518465)
32 30 and 31 (149839)
33 (discrete choice* or decision board* or decision analy* or decision-support or decision tool* or decision aid* or latent class* or decision* conflict* or decision* regret*).ti,ab,kf. (56622)
34 Decision Support Techniques/ (22797)
35 (health and utilit*).ti. (2100)
36 (gamble* or prospect theory or health utilit* or utility value* or utility score* or utility estimate* or health state or feeling thermometer* or best-worst scaling or time trade-off or TTO or probability trade-off).ti,ab,kf. (18192)
37 (preference based or preference score* or preference elicitation or multiattribute or multi attribute).ti,ab,kf. (4180)
38 or/13-24,27,32-37 (1678885)

39 12 and 38 (157)
40 Case Reports/ or Comment.pt. or Editorial.pt. or (Letter not (Letter and Randomized Controlled Trial)).pt. or Congress.pt. (4497522)
41 39 not 40 (140)
42 limit 41 to english language (127)

Database: CINAHL

Search Date: June 21, 2024
Search Strategy:

#	Query	Results
S1	(MH "Fractures, Vertebral Compression")	392
S2	(MH "Osteoporotic Fractures")	1,212
S3	(MH "Fractures, Compression+")	1,651
S4	TI((((spine* or spinal or thoracolumbar* or compression* or osteopor* or vertebr*) n3 (fractur* or break* or broke*)) or OVCF or VCF)	5,963
S5	AB((((spine* or spinal or thoracolumbar* or compression* or osteopor* or vertebr*) n3 (fractur* or break* or broke*)) or OVCF or VCF)	10,322
S6	(MH "Vertebroplasty+")	1,721
S7	TI((vertebr#plast* or kyphoplast* or PVP or PBK)	2,065
S8	AB((vertebr#plast* or kyphoplast* or PVP or PBK)	1,896
S9	TI((osteoplast* or augment* or balloon*) n3 (vertebr* or spine* or spinal))	399
S10	AB((osteoplast* or augment* or balloon*) n3 (vertebr* or spine* or spinal))	531
S11	TI(synflate* or kyphon* or iVAS* or KYPHX* or osteointroducer* or Osteopal*)	5
S12	AB(synflate* or kyphon* or iVAS* or KYPHX* or osteointroducer* or Osteopal*)	60
S13	TI(one step* N3 (osteo* or bone access* or device* or fill* or inflation* or inject* or cement* or paste* or glue*))	15
S14	AB(one step* N3 (osteo* or bone access* or device* or fill* or inflation* or inject* or cement* or paste* or glue*))	15
S15	S1 OR S2 OR S3 OR S4 OR S5	13,920
S16	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	3,690
S17	S15 AND S16	1,766
S18	(MH "Attitude to Health")	49,378
S19	(MH "Health Knowledge")	40,120
S20	(MH "Consumer Participation")	24,767
S21	(MH "Patient Preference")	3,264
S22	(MH "Attitude of Health Personnel")	56,525
S23	(MM "Professional-Patient Relations")	14,612
S24	(MM "Physician-Patient Relations")	17,561
S25	(MM "Nurse-Patient Relations")	13,608
S26	TI (choice or choices or value* or valuation* or knowledg*)	121,665
S27	(preference* or expectation* or attitude* or acceptab* or point of view)	576,816
S28	((clinician* or doctor* or surgeon* or radiologist* or (health* N2 worker*) or nurse or nurses or patient or patients or personal or physician* or practitioner* or professional or professionals or provider* or user or users or women or men) N2 (knowledg* or misperception* or misunderstand* or participation or perceiv* or perception* or perspective* or understand* or value or values or view*))	187,060

S29 health perception* 1,838
S30 (MH "Decision Making, Shared") 4,233
S31 (MH "Decision Making, Patient") 15,833
S32 (MH "Decision Making, Family") 4,307
S33 (MM "Decision Making") 26,243
S34 TI (clinician* or doctor* or surgeon* or radiologist* or (health* N2 worker*) or nurse or nurses or patient or patients or personal or physician* or practitioner* or professional or professionals or provider* or user or users or women or men) 1,447,908
S35 S33 AND S34 5,643
S36 TI (decision* and mak*) 22,583
S37 (decision mak* or decisions mak*) 177,628
S38 S36 OR S37 178,191
S39 (clinician* or doctor* or (health* N2 worker*) or surgeon or radiologist or nurse or nurses or patient or patients or personal or physician* or practitioner* or professional or professionals or provider* or user or users or women or men) 3,841,107
S40 S38 AND S39 125,550
S41 (discrete choice* or decision board* or decision analy* or decision support or decision tool* or decision aid* or latent class* or decision* conflict* or decision* regret*) 31,167
S42 (MH "Decision Support Techniques") 7,824
S43 TI (health and utilit*) 1,244
S44 (gamble* or prospect theory or health utilit* or utility value* or utility score* or utility estimate* or health state or feeling thermometer* or best worst scaling or time trade off or TTO or probability trade off) 7,798

S45 (preference based or preference score* or preference elicitation or multiattribute or multi attribute) 1,551
S46 S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S35 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 934,602
S47 S17 AND S46 69
S48 S17 AND S46 69
Limiters - English Language 67

Grey Literature Search

Performed on: June 3 – June 11

Websites searched:
Alberta Health Evidence Reviews, BC Health Technology Assessments, Canada's Drug Agency (CDA), Institut national d'excellence en santé et en services sociaux (INESSS), Institute of Health Economics (IHE), University Of Calgary Health Technology Assessment Unit, Ontario Health Technology Assessment Committee (OHTAC), McGill University Health Centre Health Technology Assessment Unit, Centre Hospitalier de l'Universite de Quebec-Universite Laval, Contextualized Health Research Synthesis Program of Newfoundland (CHRSP), Health Canada Medical Device Database, International HTA Database (INAHTA), Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Centers, Centers for Medicare & Medicaid Services Technology Assessments, Veterans Affairs Health Services Research and Development, Institute for Clinical and Economic Review, Oregon Health Authority Health Evidence Review Commission, Washington State Health Care Authority Health Technology Reviews, National Institute for Health and Care Excellence (NICE), National Health Service

England (NHS), Healthcare Improvement Scotland, Health Technology Wales, Ireland Health Information and Quality Authority Health Technology Assessments, Adelaide Health Technology Assessment, Australian Government Medical Services Advisory Committee, Monash Health Centre for Clinical Effectiveness, The Sax Institute, Australian Government Department of Health and Aged Care, Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S), Pharmac, Italian National Agency for Regional Health Services (Aegnas), Belgian Health Care Knowledge Centre, Ludwig Boltzmann Institute for Health Technology Assessment (Austria), The Regional Health Technology Assessment Centre (HTA-centrum), Swedish Agency for Health Technology Assessment and Assessment of Social Services, Norwegian Institute of Public Health - Health Technology Assessments, The Danish Health Technology Council, Ministry of Health Malaysia - Health Technology Assessment Section, Tuft's Cost-Effectiveness Analysis Registry, Sick Kids PEDE Database, PROSPERO, EUnetHTA, clinicaltrials.gov

Keywords Used: compression fracture, spinal fracture, thoracolumbar fracture, OVCF, VCF, osteoporotic fracture, insufficiency fracture, vertebroplasty, kyphoplasty, PVP, PBK, vertebral osteoplasty, spinal osteoplasty, vertebral augmentation, spinal augmentation, balloon spinal, balloon vertebral, cement spinal, cement vertebral, synflate, kyphon, osteopal, osteointroducer, one step
Clinical results (included in PRISMA):5
Economic results (included in PRISMA):5
Ongoing HTAs (PROSPERO/EUnetHTA/Washington State Health Care): 35
Ongoing clinical trials: 95

Appendix 2: Critical Appraisal of Clinical Evidence

Table A1: Risk of Bias[a] Among Systematic Reviews (ROBIS Tool)

	Phase 2				Phase 3
Author, year	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias in the review
Jacobsen et al,[38] 2020	Low	Low	Low	Low	Low
Liu et al,[39] 2023	Low	Low	Low	Low	Low

Abbreviation: ROBIS, Risk of Bias in Systematic Reviews.

[a]Possible risk-of-bias levels: low, high, unclear.

Table A2: Risk of Bias[a] Among Randomized Controlled Trials (Cochrane Risk-of-Bias Tool)

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Incomplete outcome data	Selective reporting	Other bias
Carli et al,[48] 2023	Low	Low	Low	Low	Low	High[b]
Hansen et al,[49] 2019	Low	Low	Low	High[c]	Low	—
Tantawy,[47] 2022	Low	High[d]	High[e]	Low	Low	—
Wang et al,[50] 2020	Low	High[d]	High	Low	low	High[f]

[a]Possible risk-of-bias levels: low, high, and unclear.

[b]No statistical testing reported between treatment groups in baseline characteristics (e.g., age, number of days with pain before procedure).

[c]Attrition was > 10%. Authors did not do imputation or other method for handling missing data. Envelop probably ok for allocation concealment.

[d]No details reported.

[e]No details about whether physician or patients were blinded (all procedures and analyses were performed by 1 physician).[47]

[f]Baseline characteristics not reported. Authors[50] stated "[t]here was no significant difference in general clinical information in terms of age, gender and other data between the two groups ($P > 0.05$)."

Table A3: Risk of Bias[a] Among Nonrandomized Trials (ROBINS-I Tool)

	Pre-intervention		At intervention		Post-intervention		
Author, year	Confounding	Study participation selection	Classification of interventions	Deviations from intended intervention	Missing data	Measurement of outcomes	Selection of reported results
Aregger et al,[51] 2024	Serious[b]	Low	Low	Low	Serious[c]	Serious[d]	Low
Gold et al,[56] 2023	Moderate[e]	Low	Low	Low	Low	Low	Low
Nguyen et al,[53] 2020	Serious[b]	Serious[f]	Low	Low	Low	Serious[g]	Low
Tuan et al,[54] 2020	Serious[b]	Serious[f]	Low	Low	Low	Low	Low

Abbreviation: ROBINS-I, Risk of Bias in Non-randomized Studies – of Interventions.

[a]Possible risk-of-bias levels: low, moderate, serious, critical, and no information.

[b]Scant details reported for baseline characteristics of patients. No analysis/discussion related to any baseline characteristics.

[c]Out of the initial cohort of 94 patients, 45 individuals were excluded from the follow-up assessment for the following reasons: 27 (9.6%) declined to participate in the follow-up, 8 (2.9%) were unable to undergo assessment due to cognitive impairment, and 4 (1.4%) had insufficient imaging data available. Additionally, 6 patients were deemed "lost to follow-up."

[d]Some patients underwent complete (clinical and radiological) follow-up, while others followed up via a written form or by phone only.

[e]Retrospective cohort study of US Medicare enrollees compared with propensity-matched patients on demographic and clinical variables.

[f]Prospective single arm study. No information reported about how many patients were screened and subsequently met inclusion criteria.

[g]No information related to when refractures occurred when discovered during follow-up (or total follow-up duration).

Appendix 3: Additional Results

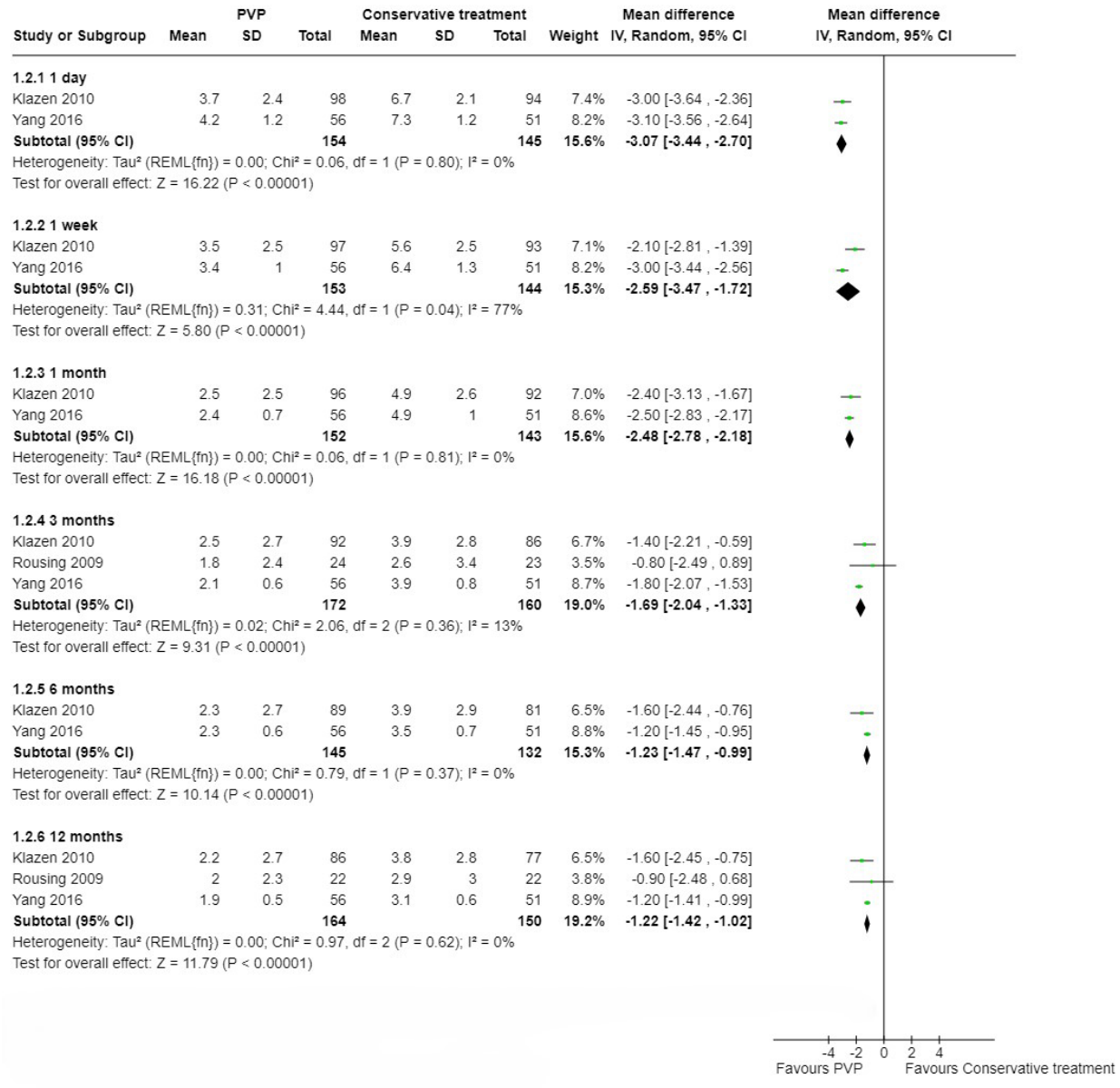

Figure A1: Percutaneous Vertebroplasty Versus Conservative Treatment: Subgroup Analysis of the Visual Analogue Scale Less Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for pain as measured by the visual analogue scale for PVP compared to CT at follow-up timepoints ranging from 1 day to 12 months. Fractures were less than 8 weeks old. There were significant differences favouring PVP at all follow-up timepoints.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

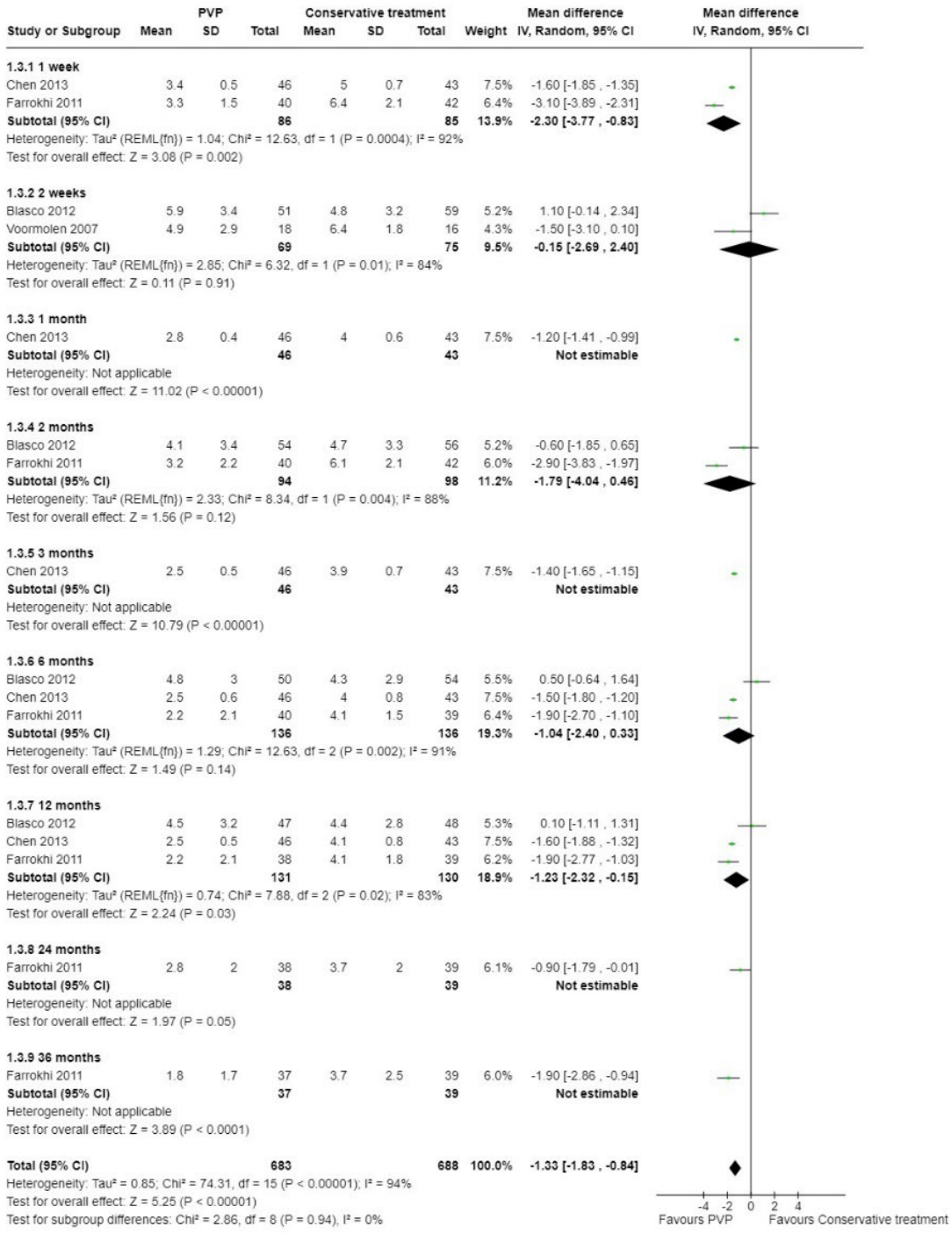

Figure A2: Percutaneous Vertebroplasty Versus Conservative Treatment: Subgroup Analysis of the Visual Analogue Scale More Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for pain as measured by the visual analogue scale for PVP compared to CT at follow-up timepoints ranging from 1 week to 36 months. Fractures were greater than 8 weeks old. There were statistically significant differences favouring PVP at 1 week and 1, 3, and 12 months posttreatment, but not at 2 weeks, or 2 or 6 months posttreatment.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

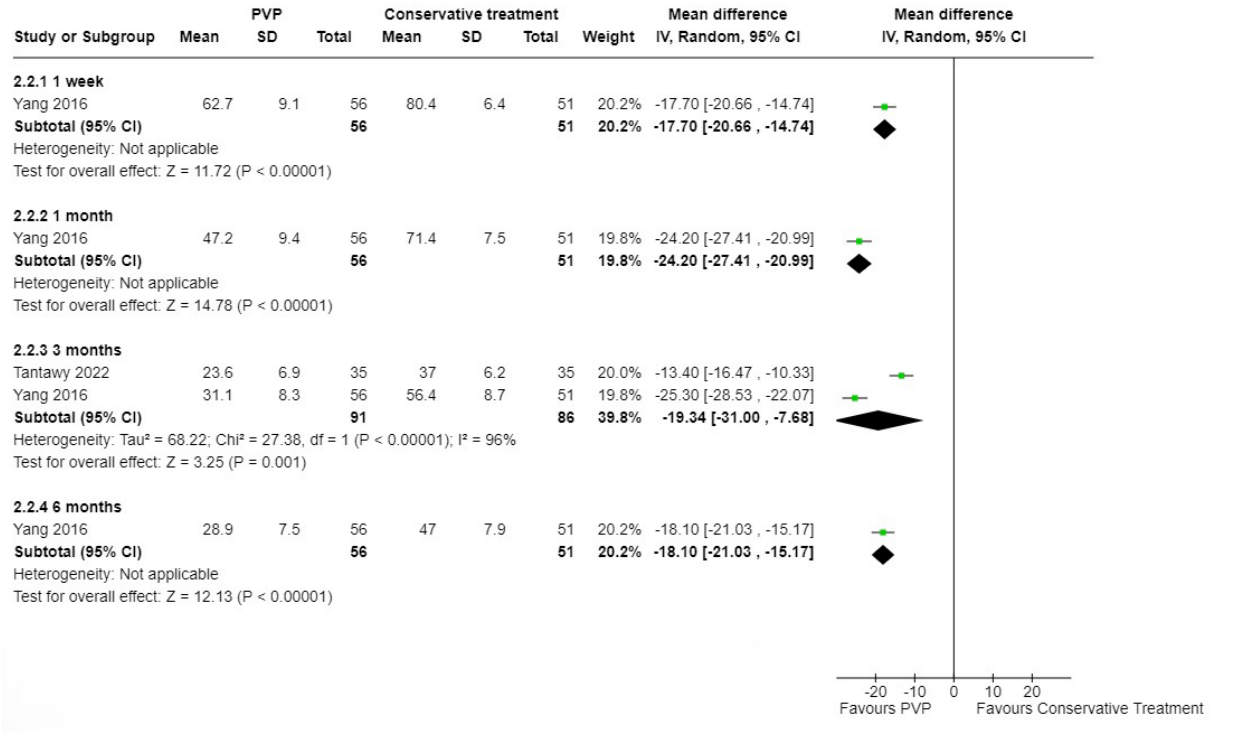

Figure A3: Percutaneous Vertebroplasty Versus Conservative Treatment: Subgroup Analysis of the Oswestry Disability Index Less Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for physical function as measured by the Oswestry Disability Index for PVP compared to CT at follow-up timepoints ranging from 1 week to 6 months. Fractures were less than 8 weeks old. There were significant differences in ODI favouring PVP at all follow-up timepoints.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

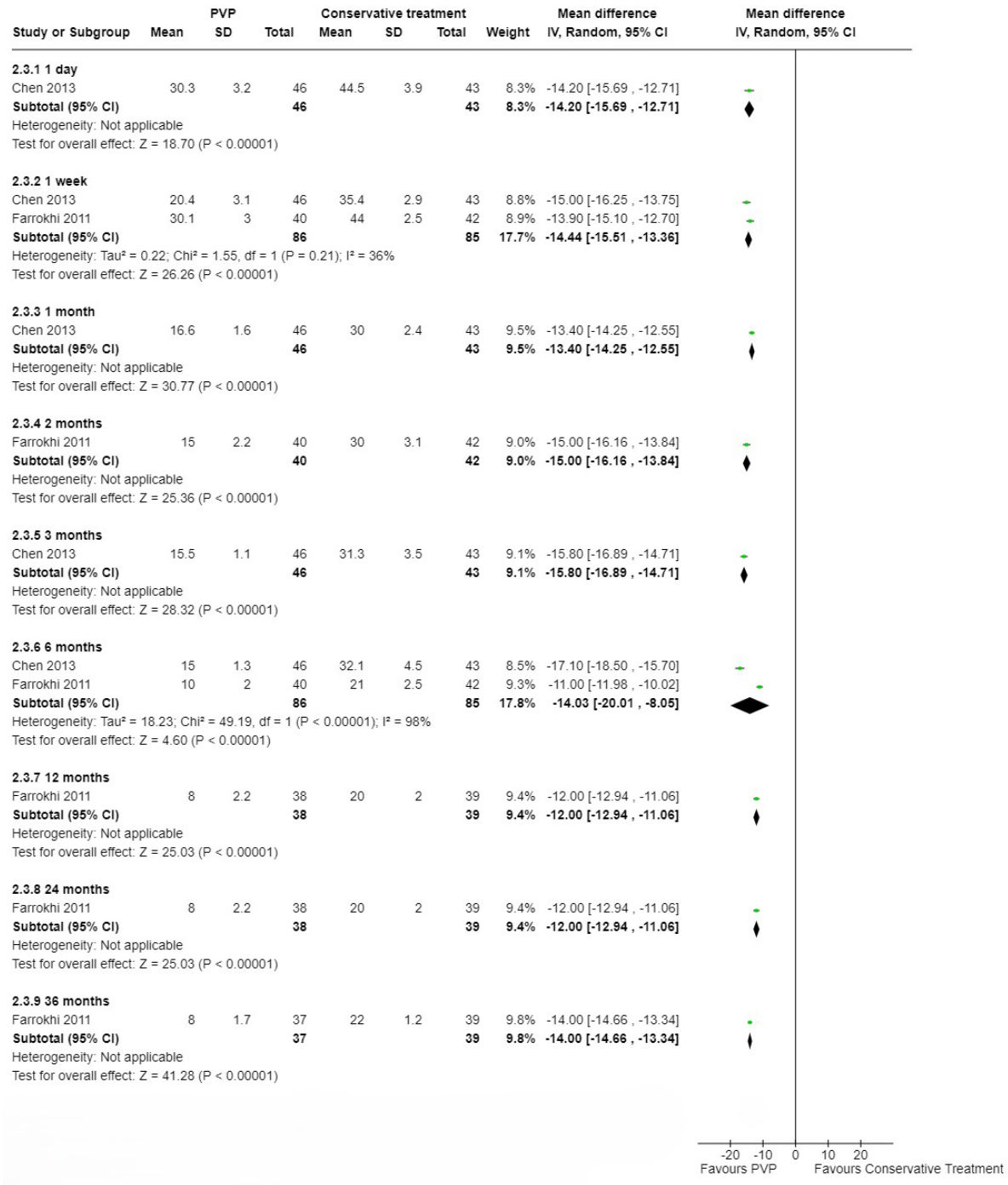

Figure A4: Percutaneous Vertebroplasty Versus Conservative Treatment: Subgroup Analysis of the Oswestry Disability Index More Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for physical function as measured by the Oswestry Disability Index for PVP compared to CT at follow-up timepoints ranging from 1 day to 36 months. Fractures were greater than 8 weeks old. There were significant differences in ODI favouring PVP at all follow-up timepoints.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

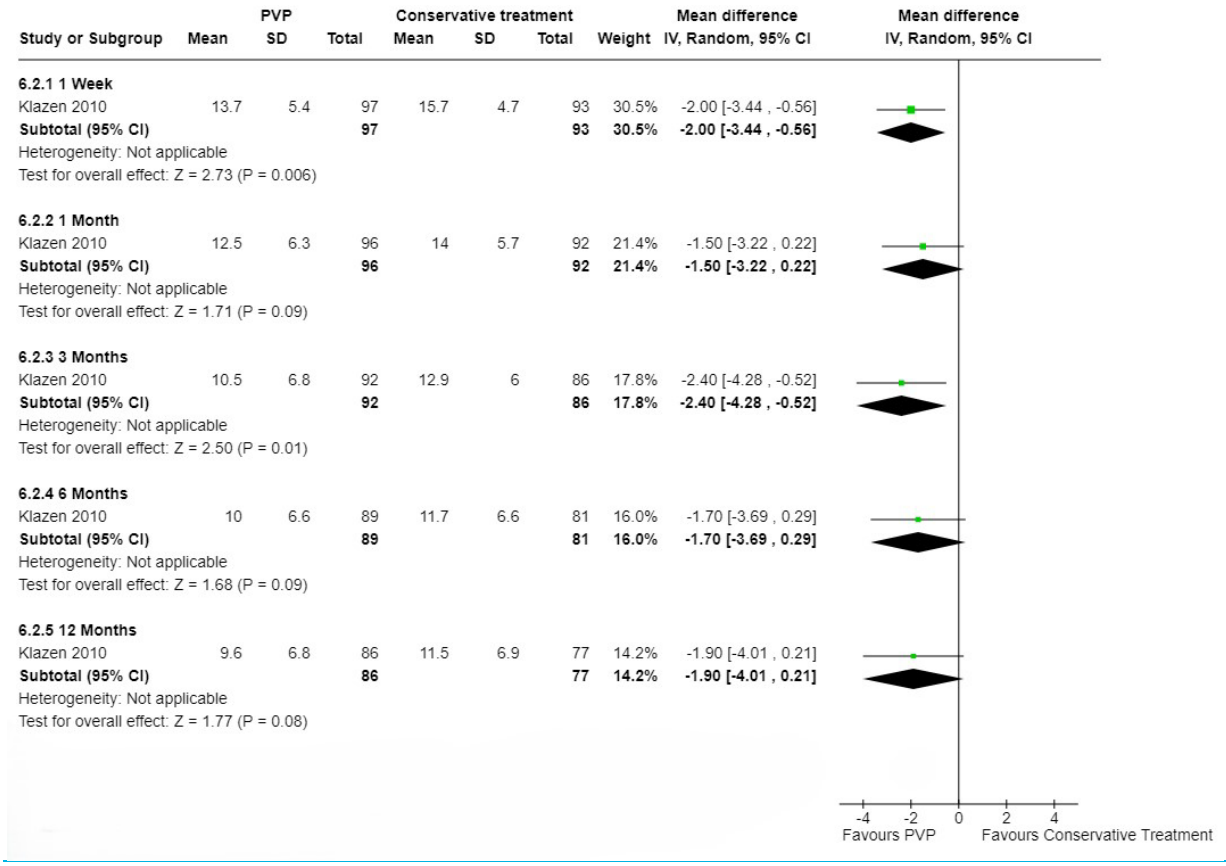

Figure A5: Percutaneous Vertebroplasty Versus Conservative Treatment: Subgroup Analysis of the Roland-Morris Disability Questionnaire Less Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for physical function as measured by the RMDQ for PVP compared to CT at follow-up timepoints ranging from 1 week to 12 months. Fractures were less than 8 weeks old. There were significant differences in RMDQ favouring PVP over CT at 1 day and at 3 months follow-up.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; RMDQ, Roland-Morris Disability Questionnaire; SD, standard deviation.

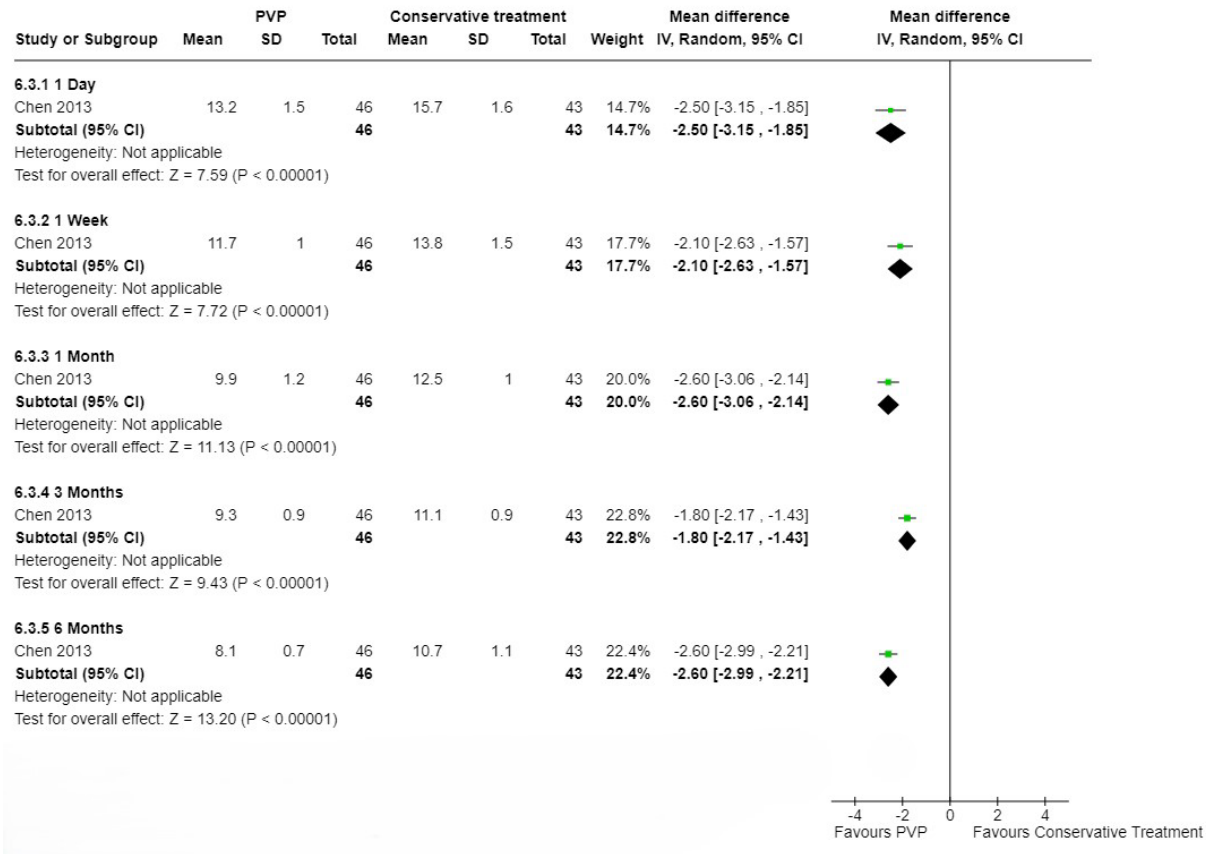

Figure A6: Percutaneous Vertebroplasty Versus Conservative Treatment: Subgroup Analysis of the Roland-Morris Disability Questionnaire More Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for physical function as measured by the RMDQ for PVP compared to CT at follow-up timepoints ranging from 1 day to 6 months. Fractures were greater than 8 weeks old. There were significant differences favouring PVP over CT at all follow-up assessments.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; RMDQ, Roland-Morris Disability Questionnaire; SD, standard deviation.

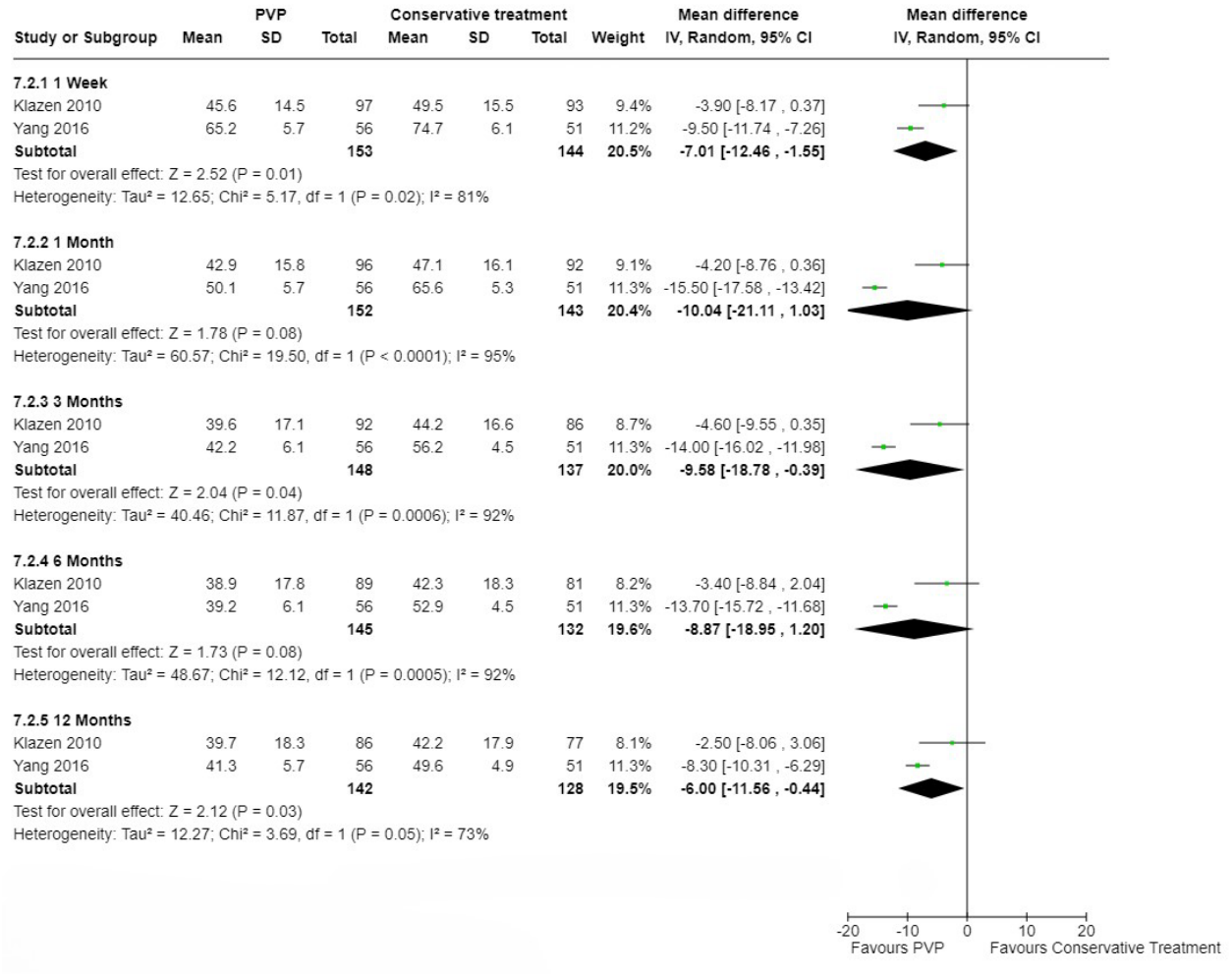

Figure A7: Percutaneous Vertebroplasty Versus Conservative Treatment: Subgroup Analysis of Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) Less Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for quality of life as measured by QUALEFFO for PVP compared to CT at follow-up timepoints ranging from 1 week to 12 months. Fractures were less than 8 weeks old. There were significant differences in QUALEFFO scores favouring PVP over CT at 1 week and at 3 and 12 months follow-up.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

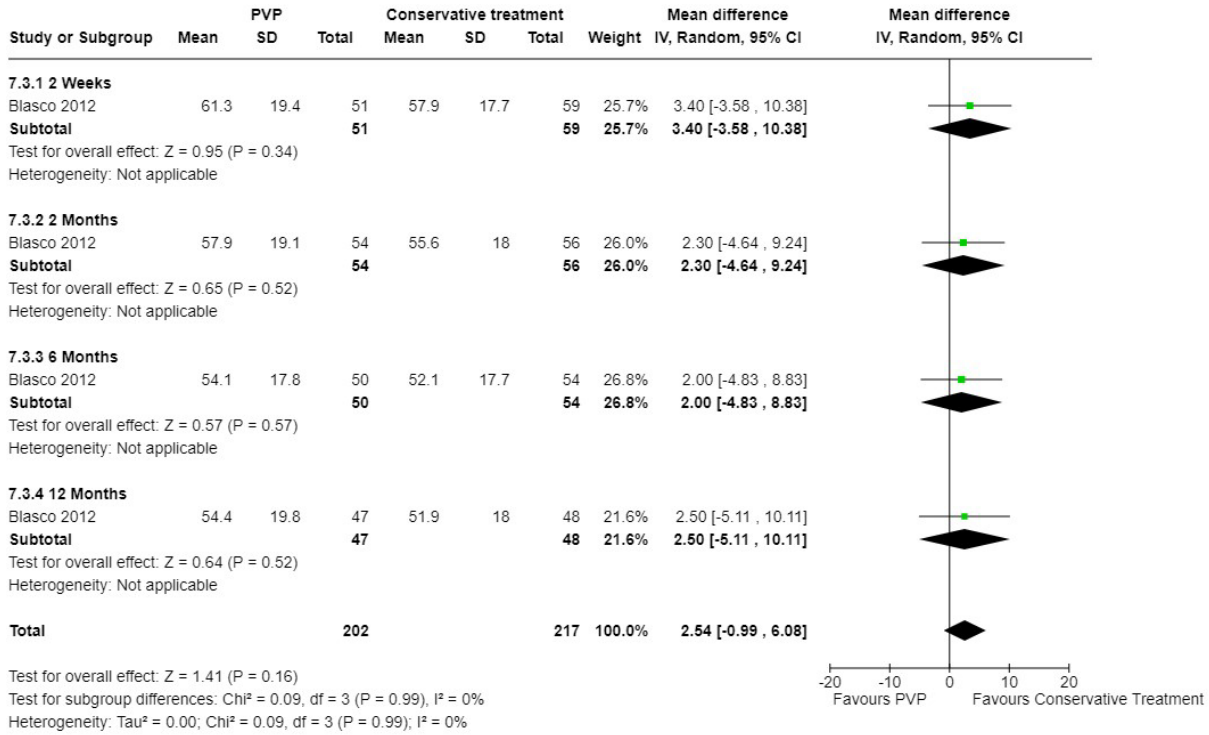

Figure A8: Percutaneous Vertebroplasty Versus Conservative Treatment: Subgroup Analysis of Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) More Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for quality of life as measured by QUALEFFO for PVP compared to CT at follow-up timepoints ranging from 2 weeks to 12 months. Fractures were greater than 8 weeks old. There were no significant differences favouring PVP over CT at any follow-up assessment.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

Table A4: PVP Versus Conservative Treatment: Cement Leakage (Single Arm Observational Studies)

Author, year	Length of follow-up	Cement Leakage per vertebral bodies treated or per patient, n/N (%)	Symptomatic or asymptomatic
Al-Ali et al,[82] 2009	12 months	219/660 (33.2%) treated vertebrae	Asymptomatic
Bae et al,[83] 2012[a]	24 months	63.8% treated vertebrae	3 symptomatic patients (nerve root irritation), remaining asymptomatic
De Palma et al,[84] 2011	24 months	29/163 (17.8%) treated vertebrae	Asymptomatic
Dohm et al,[85] 2014	24 months	164/201 (81.6%) treated vertebrae	1 symptomatic (cement embolism), remaining asymptomatic
Fenoglio et al,[86] 2008	20.4 months	7/52 (13.5%) treated vertebrae	NR
Kotwica et al,[87] 2011[b]	24 months	8/200 (4.0%) patients	Asymptomatic
Masala et al,[88] 2012	12 months	15/128 (11.7%) treated vertebrae	NR
Masala et al,[89] 2009	36 months	4.8% [c]	Asymptomatic
Nieuwenhuijse et al,[90] 2012	12 months	155/216 (71.8%) treated vertebrae	Asymptomatic
Nieuwenhuijse et al,[91] 2010	12 months	99/125 (79.2%) treated vertebrae[d]	Asymptomatic (1 asymptomatic pulmonary cement embolism and cement spur)
Pitton et al,[92] 2008	19.7 months	214/385 (55.6%) treated vertebrae	Asymptomatic
Santiago et al,[93] 2010	12 months	14/69 (20.2%) treated vertebrae	NR
Saracen et al,[94] 2014	24 months	83/594 (14.0%) treated vertebrae	NR
Voormolen et al,[95] 2006	12 months	79/168 (47.0%) treated vertebrae	Asymptomatic
Voormolen et a,l[96] 2006	12 months	31/102 (30.4%) treated vertebrae	NR
Tuan et al,[54] 2020	Postprocedure	36/105 (34.3%) treated vertebrae	Asymptomatic
Absolute rate		**1,145/2,968 (38.6%) treated vertebrae** **8/200 (4.0%) patients**	

Abbreviation: NR, not reported.

[a]Results of polymethylmethacrylate (PMMA) arm reported, absolute number of adjacent fractures could not be determined.

[b]200 patients assessed postoperatively and 80 patients assessed at 24 months.

[c]Not reported whether per patient or per vertebra.

[d]Low and medium viscosity cement arms pooled.

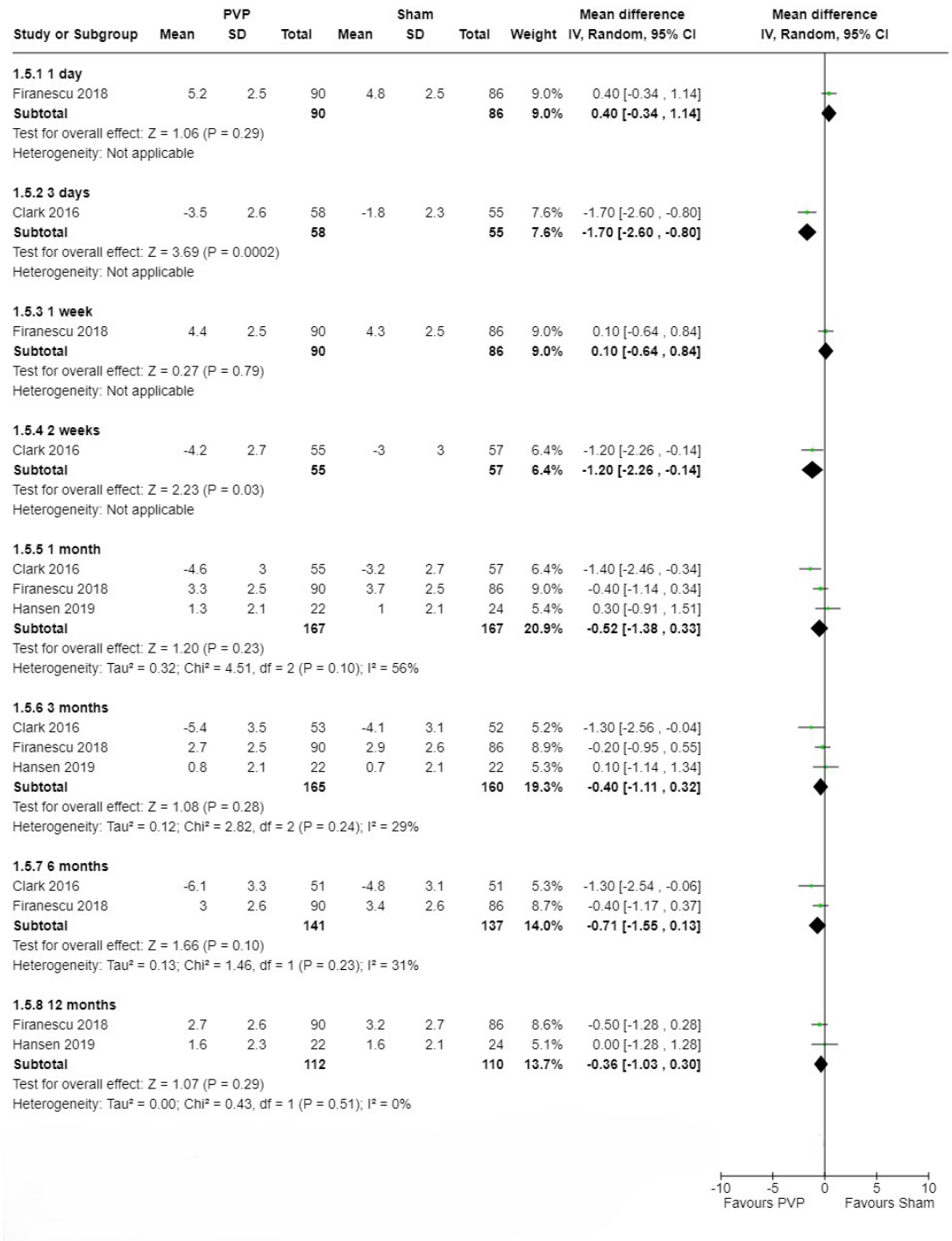

Figure A9: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Visual Analogue Scale or Numerical Rating Score Less Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for pain as measured by the Visual Analogue Scale or the Numerical Rating Score for PVP compared to sham at follow-up timepoints ranging from 1 day to 12 months. Fractures were less than 8 weeks old. There were significant differences in pain scores favouring PVP over sham at 3 days and 2 weeks follow-up.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

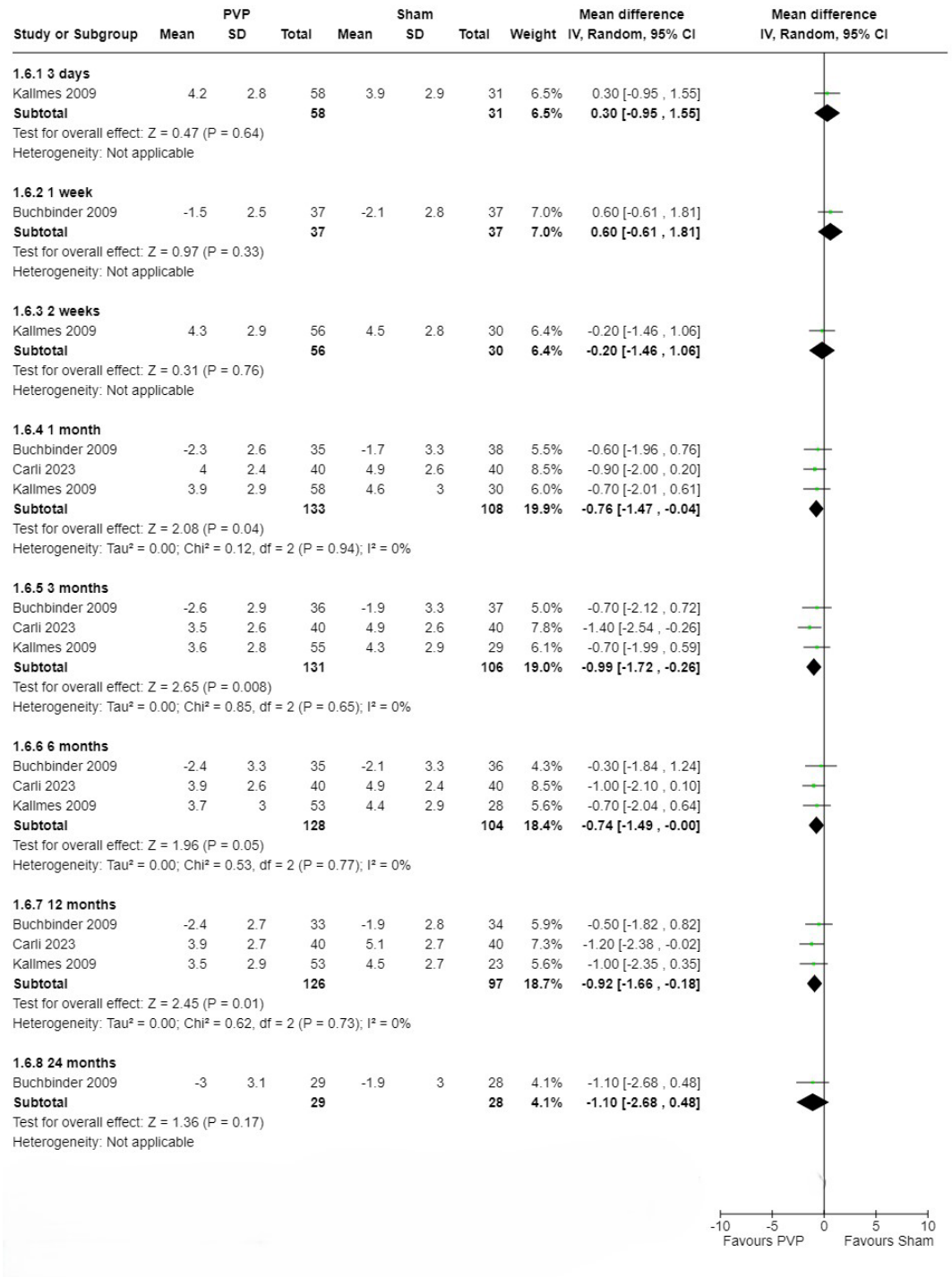

Figure A10: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Visual Analogue Scale or Numerical Rating Score More Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for pain as measured by the Visual Analogue Scale or the Numerical Rating Score for PVP compared to sham at follow-up timepoints ranging from 3 days to 24 months. Fractures were greater than 8 weeks old. There were significant differences in pain scores favouring PVP at 1, 3, and 12 months follow-up.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

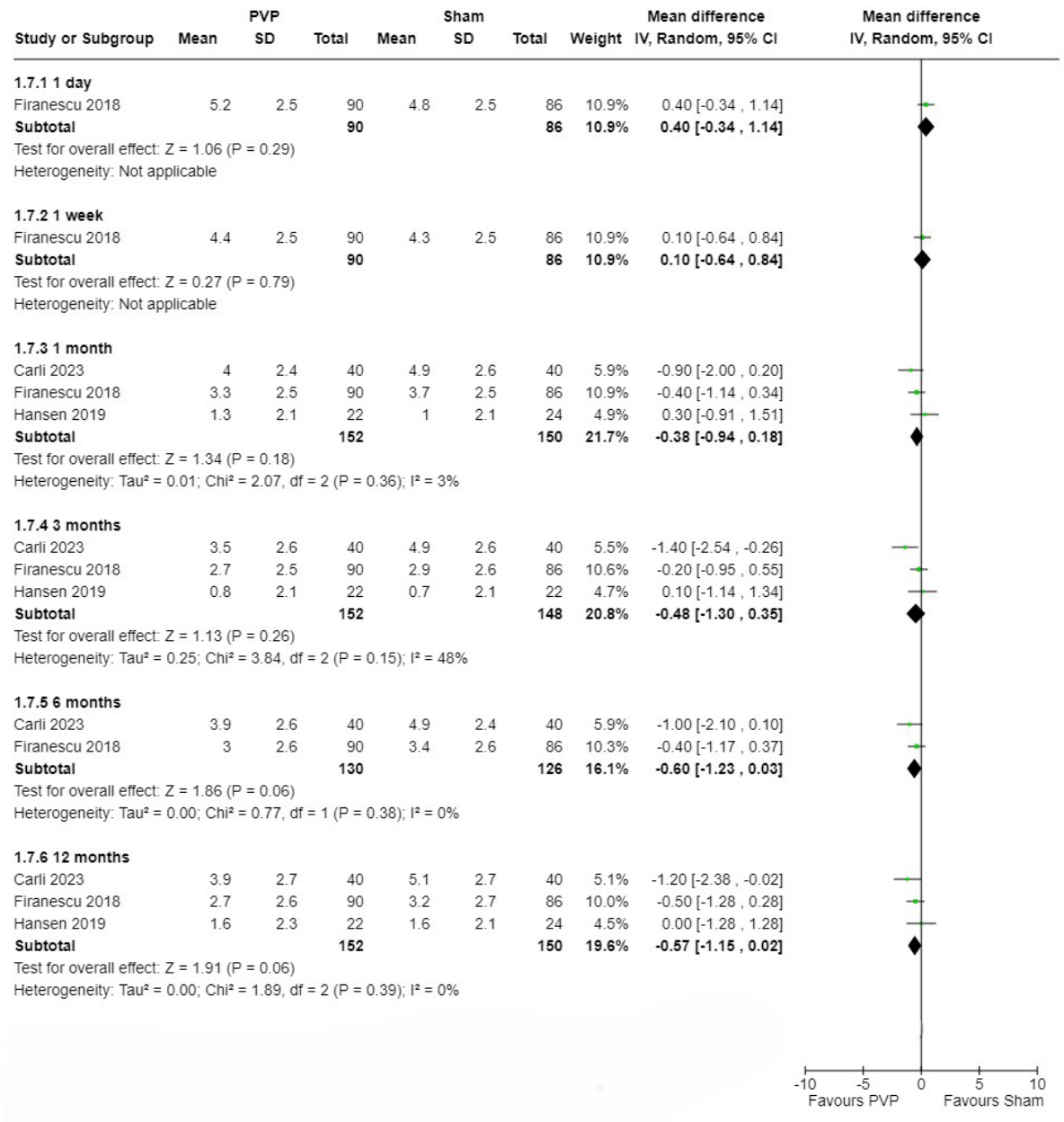

Figure A11: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Visual Analogue Scale

Figure shows the mean difference (95% CI) for pain as measured by the Visual Analogue Scale for PVP compared to sham at follow-up timepoints ranging from 1 day to 12 months. There were no significant differences between PVP and sham at any follow-up timepoint.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

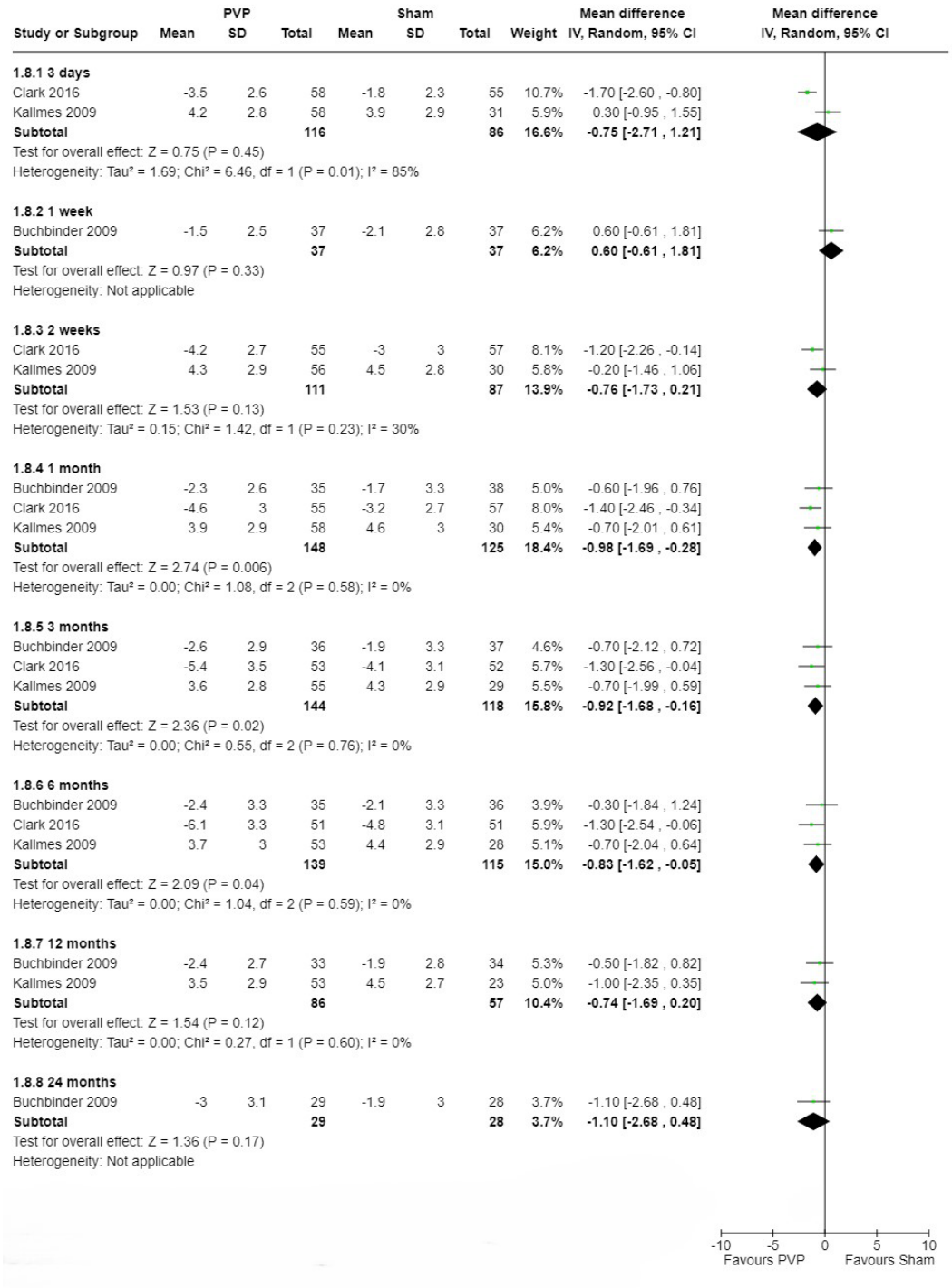

Figure A12: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Numerical Rating Score

Figure shows the mean difference (95% CI) for pain as measured by the Numerical Rating Score for PVP compared to sham at follow-up timepoints ranging from 3 days to 24 months. There were significant differences favouring PVP at the 1, 3, and 6 month follow-ups.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

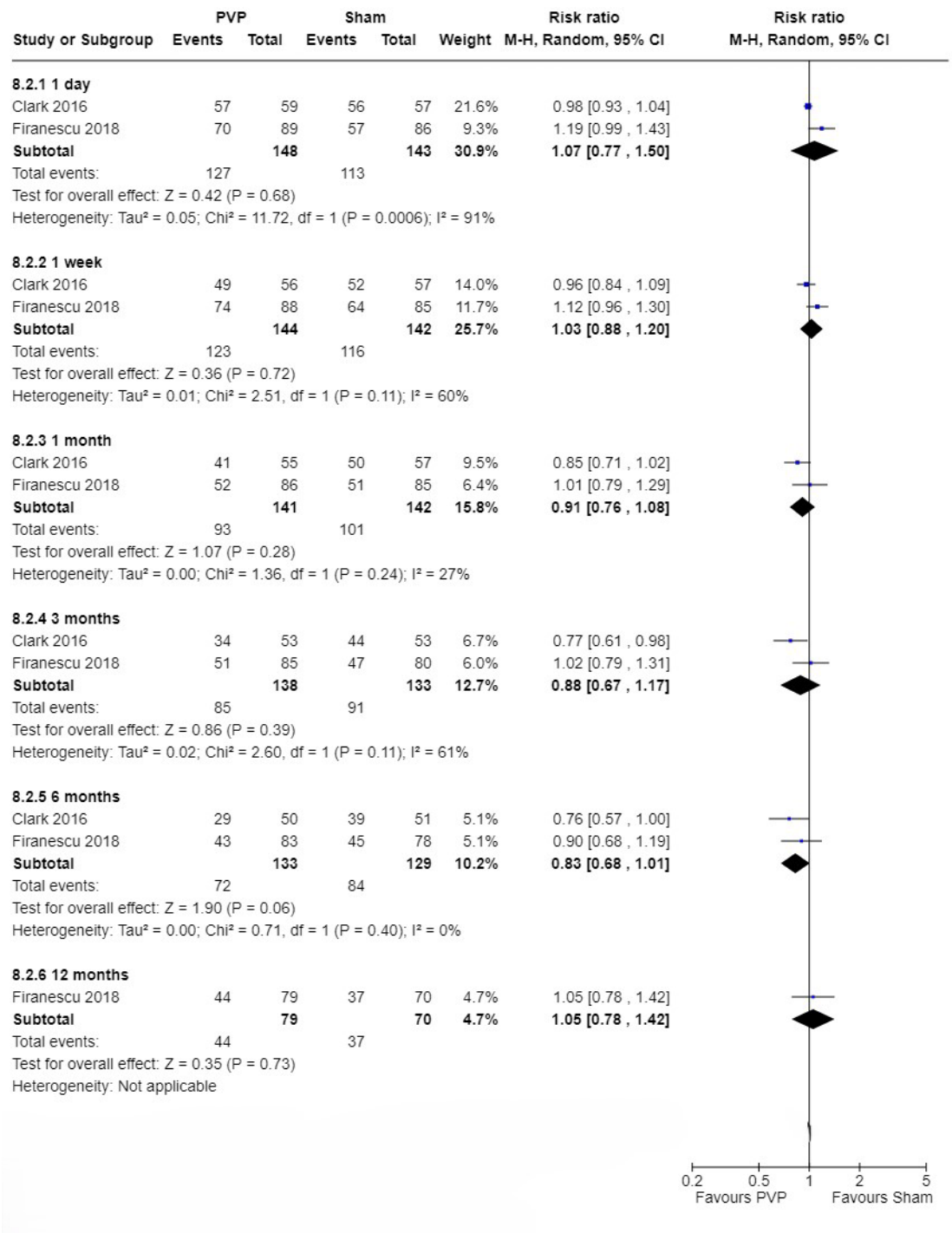

Figure A13: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Use of Analgesics Less Than 8 weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the risk ratio (95% CI) for use of analgesics for PVP compared to sham at follow-up timepoints ranging from 1 day to 12 months. Fractures were less
than 8 weeks old. No significant differences were observed between PVP and sham.
Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty.

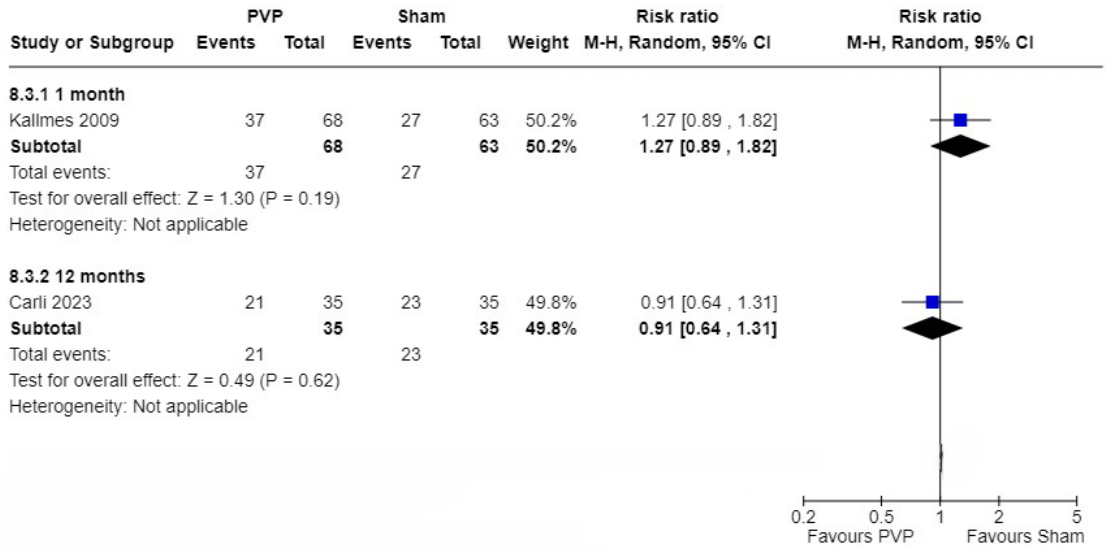

Figure A14: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Use of Analgesics More Than 8 weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the risk ratio (95% CI) for use of analgesics for PVP compared to sham at follow-up timepoints ranging from 1 to 12 months. Fractures were greater than 8 weeks old. No significant differences were observed between PVP and sham.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty.

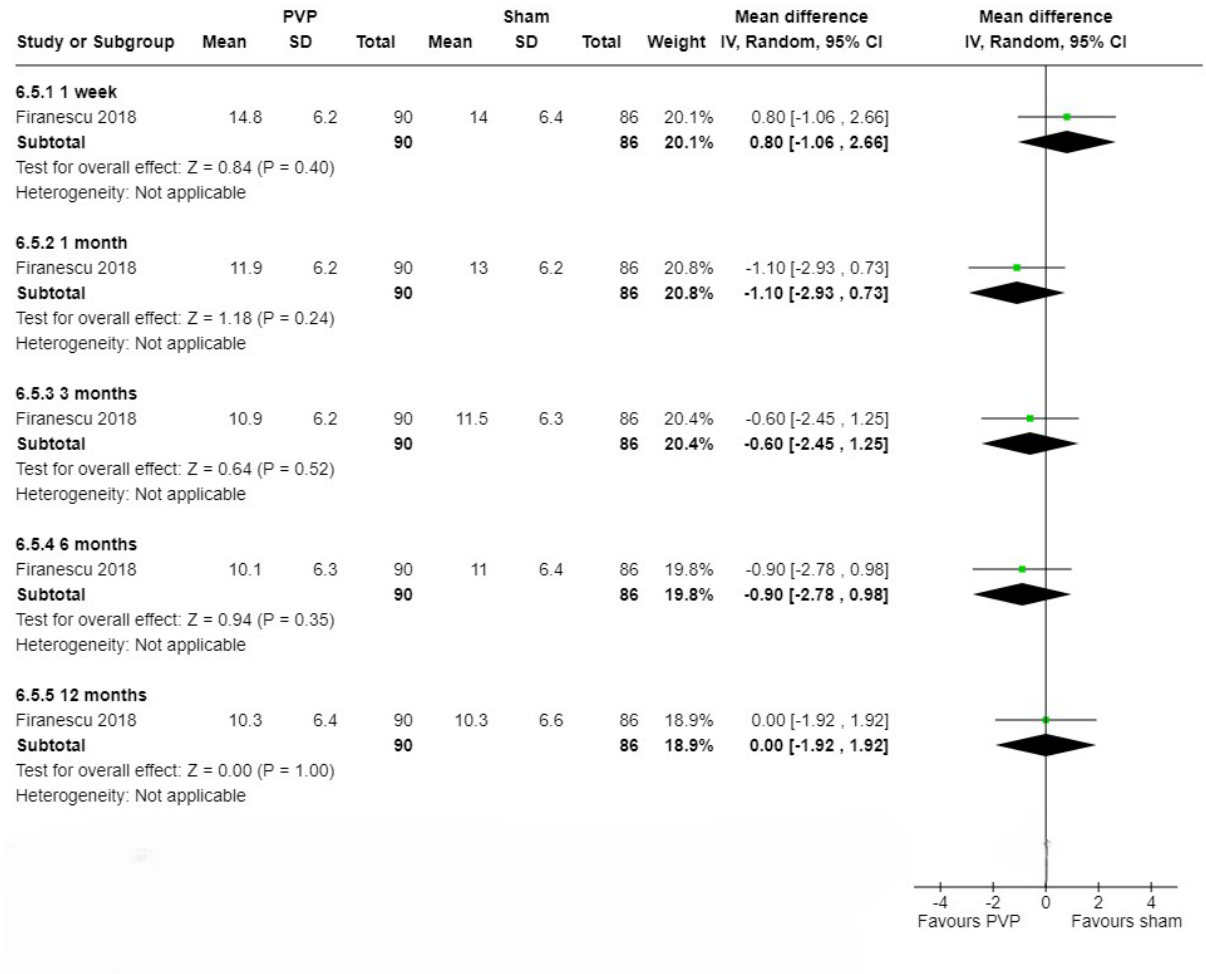

Figure A15: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Roland-Morris Disability Questionnaire Less Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for physical function as measured by the RMDQ for PVP compared to sham at follow-up timepoints ranging from 1 week to 12 months. Fractures were less than 8 weeks old. There was no significant difference in the mean difference of RMDQ scores between PVP and sham.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; Roland-Morris Disability Questionnaire; SD, standard deviation.

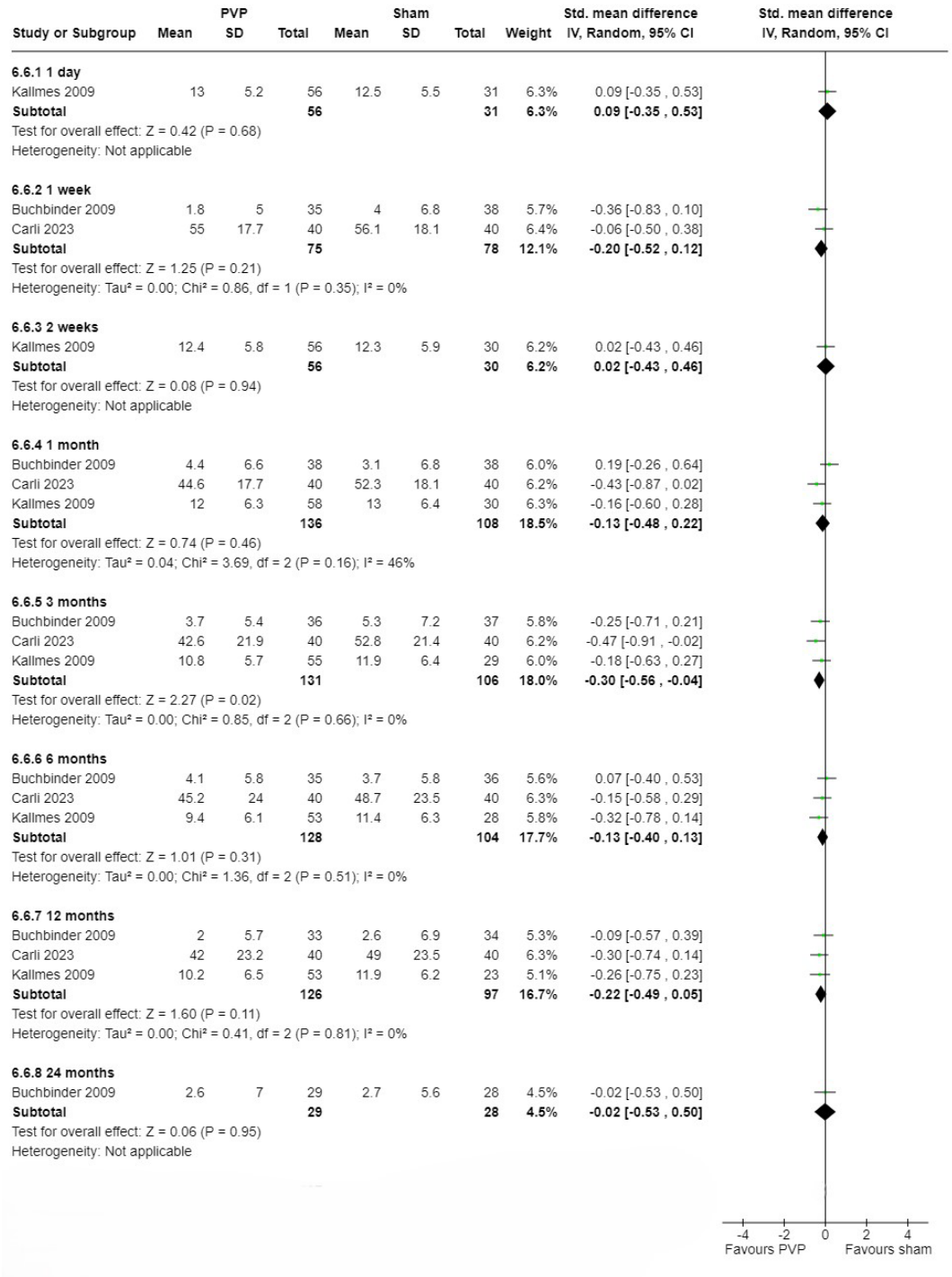

Figure A16: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Roland-Morris Disability Questionnaire More Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the standardized mean difference (95% CI) for physical function as measured by the RMDQ for PVP compared to sham at follow-up timepoints ranging from 1 day to 24 months. Fractures were greater than 8 weeks old. No significant differences were observed in RMDQ scores between PVP and sham except at the 3-month follow-up timepoint, which favoured PVP.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; Roland-Morris Disability Questionnaire; SD, standard deviation.

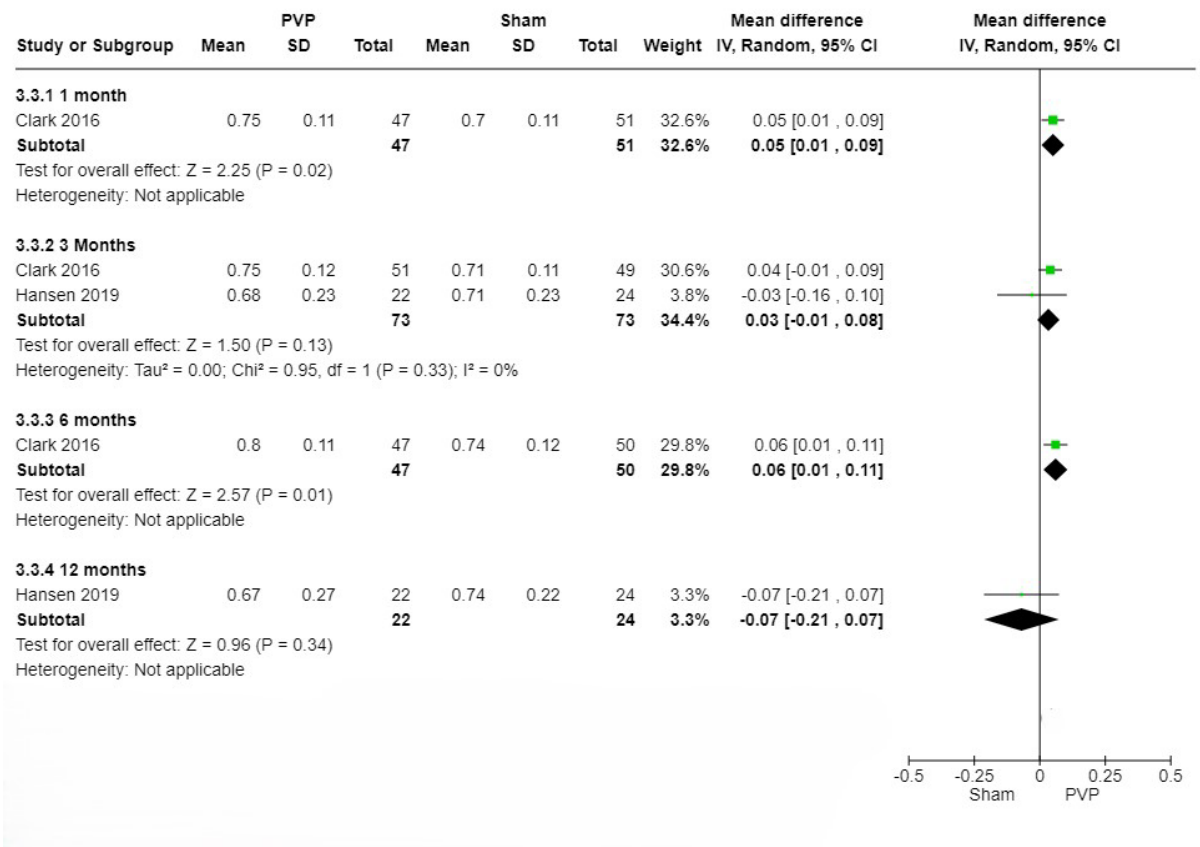

Figure A17: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of EQ-5D Less Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for quality of life as measured by EQ-5D for PVP compared to sham at follow-up timepoints ranging from 1 to 12 months. Fractures were less than 8 weeks old. There was a significant difference between PVP and sham at 1 and 6 months favouring PVP.

Abbreviations: CI, confidence interval; EQ-5D, EuroQol- 5 dimension; PVP, percutaneous vertebroplasty; SD, standard deviation.

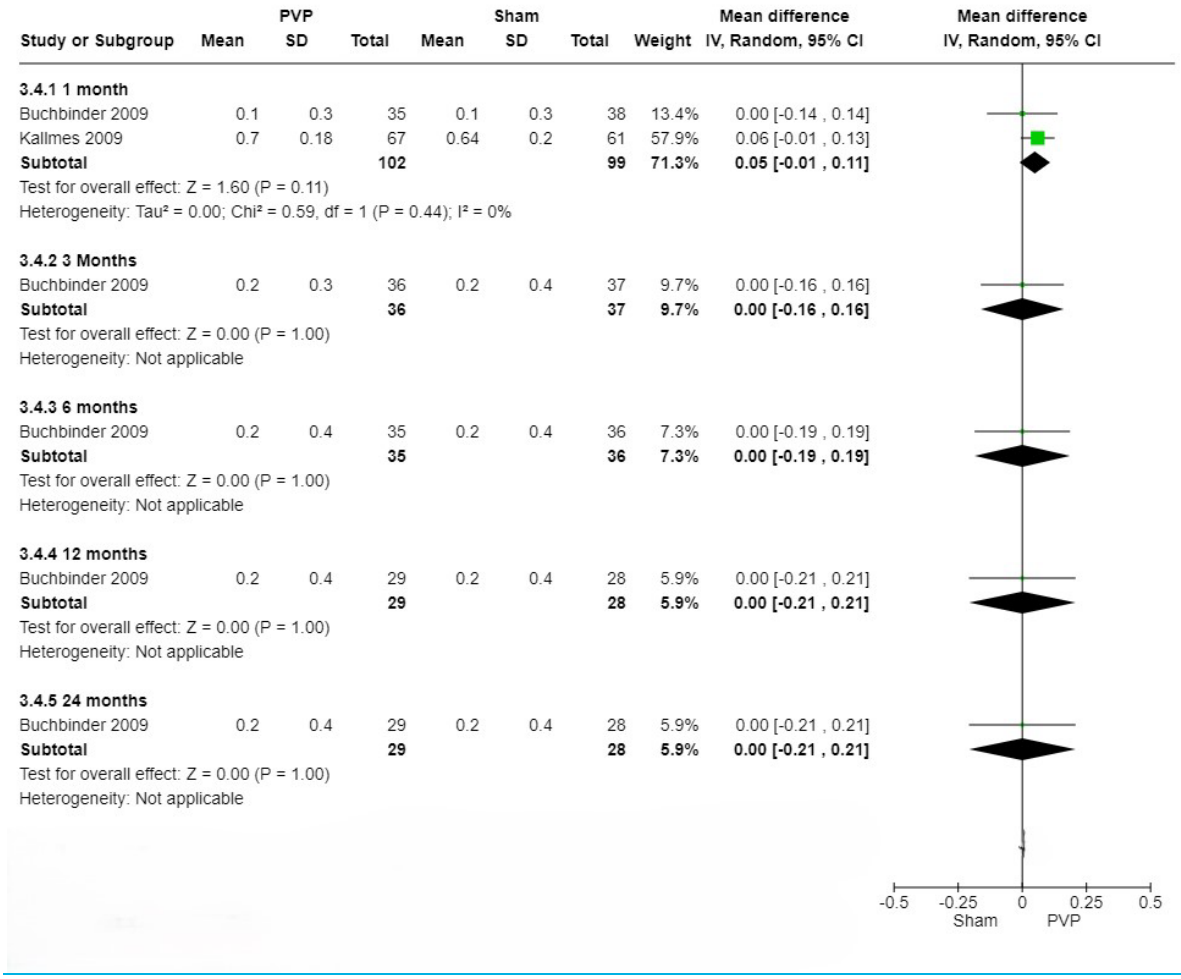

Figure A18: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of EQ-5D More Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for quality of life as measured by EQ-5D for PVP compared to sham at follow-up timepoints ranging from 1 to 24 months. Fractures were greater than 8 weeks old. No significant differences were observed in the mean difference of EQ-5D scores between PVP and the sham groups.

Abbreviations: CI, confidence interval; EQ-5D, EuroQol- 5 dimension; PVP, percutaneous vertebroplasty; SD, standard deviation.

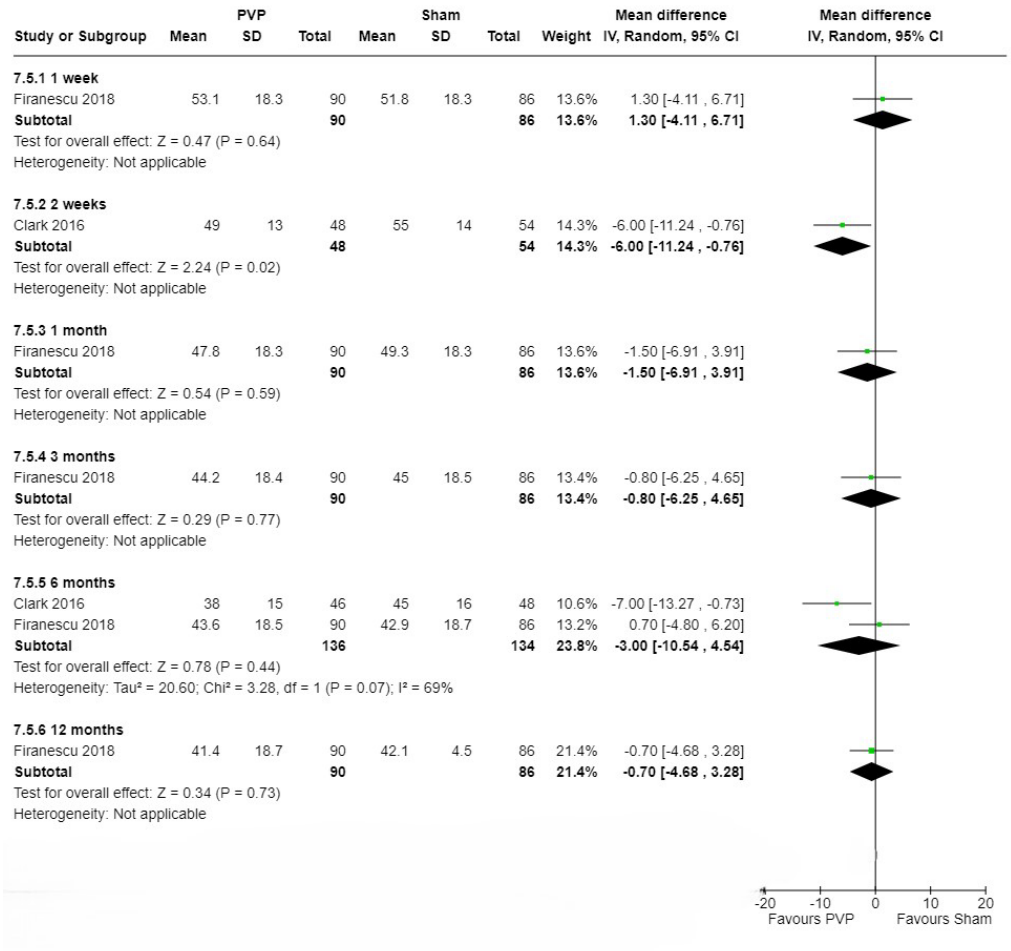

Figure A19: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) Less Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for quality of life as measured by QUALEFFO for PVP compared to sham at follow-up timepoints ranging from 1 week to 12 months. Fractures were less than 8 weeks old. There was a significant difference between PVP and sham at 2 weeks follow-up favouring PVP, however, no significant differences were observed at any other follow-up timepoints.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

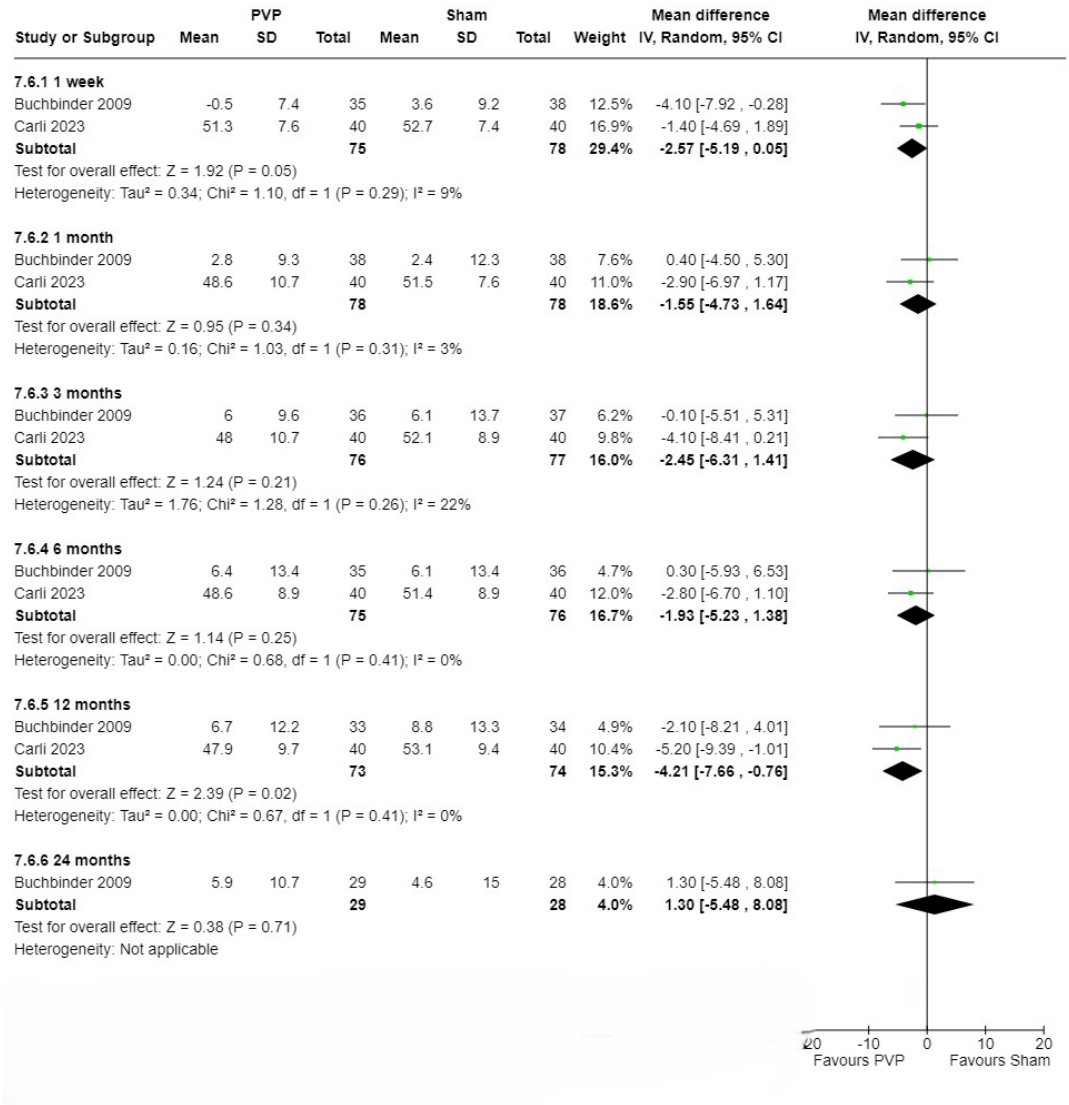

Figure A20: Percutaneous Vertebroplasty Versus Sham: Subgroup Analysis of Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) More Than 8 Weeks From Start of Painful Osteoporotic Vertebral Compression Fracture

Figure shows the mean difference (95% CI) for quality of life as measured by QUALEFFO for PVP compared to sham at follow-up timepoints ranging from 1 week to 24 months. Fractures were greater than 8 weeks old. No significant differences were observed in the mean difference of QUALEFFO scores between PVP and the sham groups.

Abbreviations: CI, confidence interval; PVP, percutaneous vertebroplasty; SD, standard deviation.

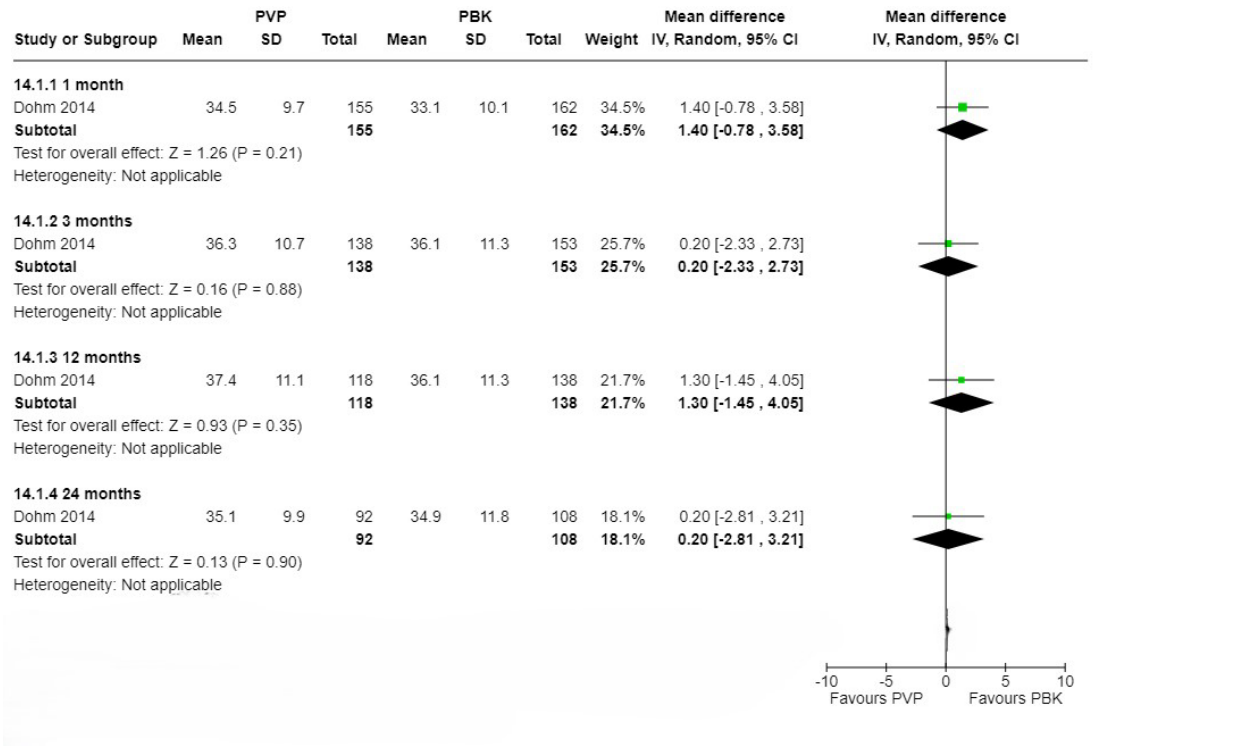

Figure A21: Percutaneous Vertebroplasty Versus Percutaneous Balloon Kyphoplasty: SF-36 PCS

Figure shows the mean difference (95% CI) for quality of life as measured by SF-36 PCS for PVP compared to PBK at follow-up timepoints ranging from 1 to 24 months. There was no significant difference in improvement in quality of life between PVP and PBK at 1, 3, 12, or 24 month follow-ups.

Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SF-36 PCS, 36-item short form health survey physical component summary; SD, standard deviation.

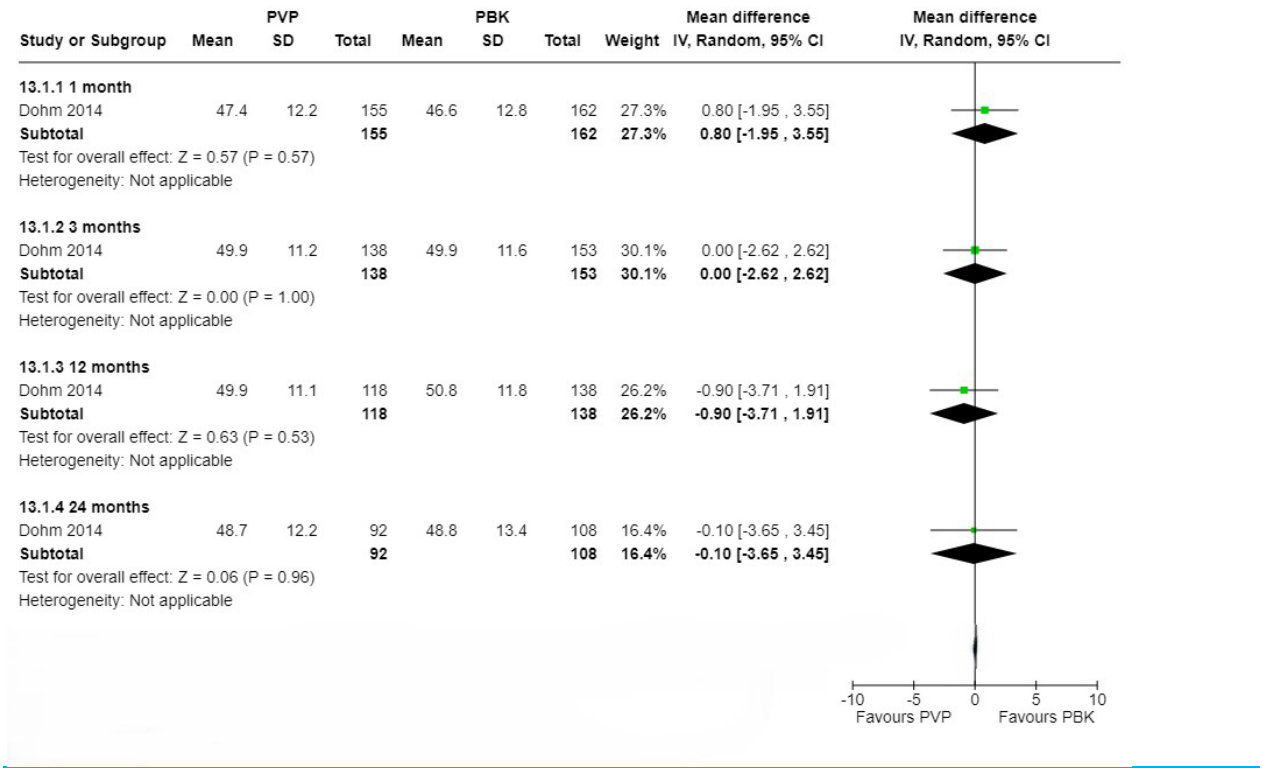

Figure A22: Percutaneous Vertebroplasty Versus Percutaneous Balloon Kyphoplasty: SF-36 MCS

Figure shows the mean difference (95% CI) for quality of life as measured by SF-36 MCS for PVP compared to PBK at follow-up timepoints ranging from 1 to 24 months. There was no significant difference in improvement in quality of life between PVP and PBK at 1, 3, 12, or 24 month follow-ups.

Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SF-36 MCS, 36-item short form health survey mental component summary; SD, standard deviation.

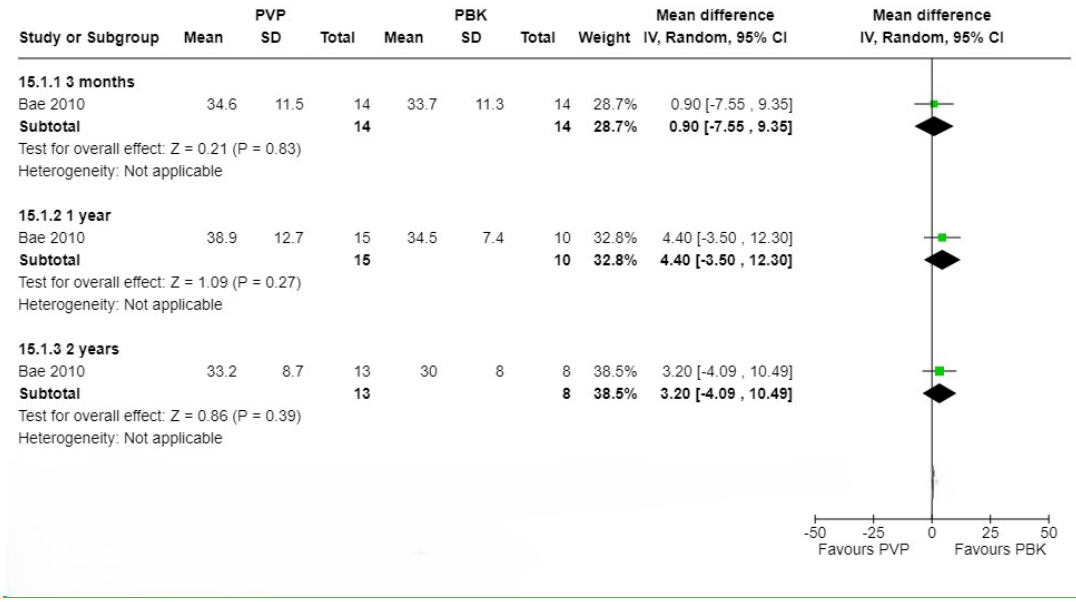

Figure A23: Percutaneous Vertebroplasty Versus Percutaneous Balloon Kyphoplasty: SF-12 PCS

Figure shows the mean difference (95% CI) for quality of life as measured by SF-12 PCS for PVP compared to PBK at follow-up timepoints ranging from 3 months to 2 years. There was no significant difference in improvement in quality of life between PVP and PBK at 3, 12, or 24 month follow-ups.

Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SF-12 PCS, 12-item short form health survey physical component summary; SD, standard deviation.

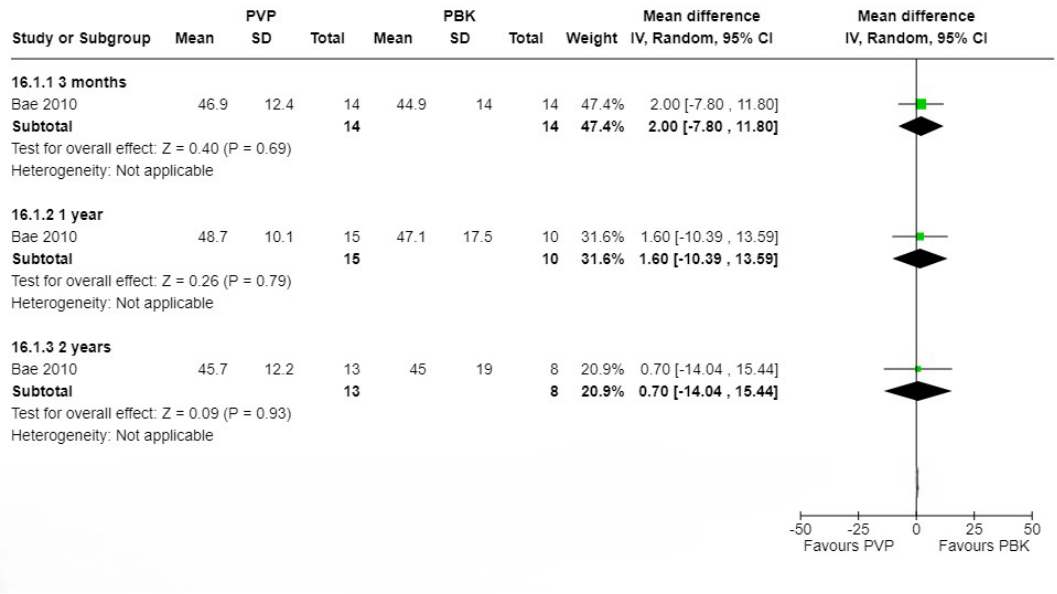

Figure A24: Percutaneous Vertebroplasty Versus Percutaneous Balloon Kyphoplasty: SF-12 MCS

Figure shows the mean difference (95% CI) for quality of life as measured by SF-12 MCS for PVP compared to PBK at follow-up timepoints ranging from 3 months to 2 years. There was no significant difference in improvement in quality of life between PVP and PBK at 3, 12, or 24 month follow-ups.

Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SF-12 MCS, 12-item short form health survey mental component summary; SD, standard deviation.

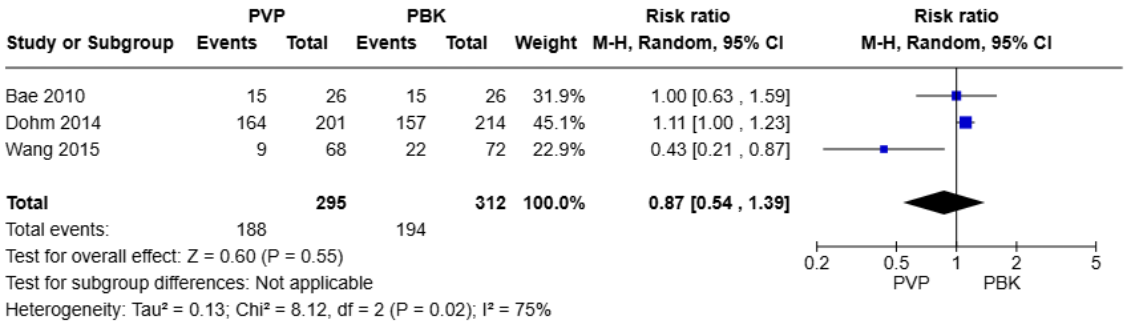

Figure A25: Percutaneous Vertebroplasty Versus Percutaneous Balloon Kyphoplasty: Cement Leakage[a]

Figure shows the risk ratio (95% CI) for cement leakage for PVP compared to PBK. The figure shows that there was no significant difference in cement leakage between PVP and PBK.

Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]In the RCT by Wang et al,[113] 2 different types of cement were used. Patients randomly underwent either high viscosity PVP (Confidence Spinal Cement System, DePuy Spine Inc, Raynham, MA, USA) or PBK with a low-viscosity cement, OSTEOPAL V (Heraeus Medical GmbH, Wehrheim, Germany).

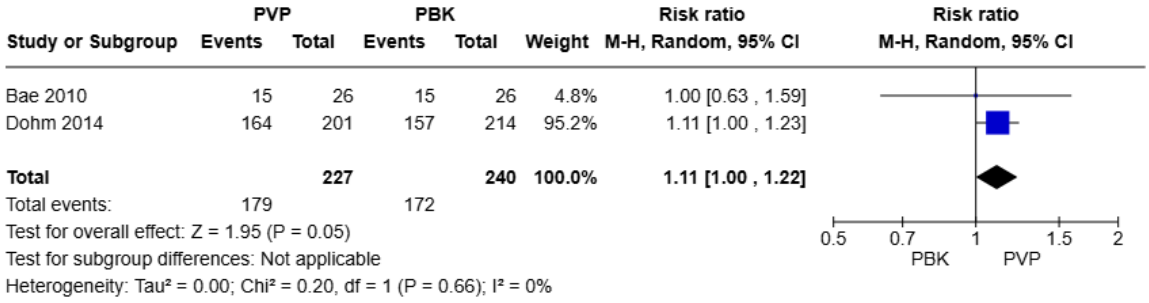

Figure A26: Percutaneous Vertebroplasty Versus Percutaneous Balloon Kyphoplasty: Cement Leakage[a]

Figure shows the risk ratio (95% CI) for cement leakage for PVP compared to PBK. Overall, there was a significant difference in cement leakage favouring PBK.

Abbreviations: CI, confidence interval; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Sensitivity analysis where the RCT by Wang et al[113] is removed since it used high viscosity cement in the PVP arm and low viscosity cement in the PBK arm.

Table A5: GRADE Evidence Profile for the Comparison of PVP and CT[a]

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Pain							
8 RCTs[47,57-60,66,67]	Serious limitations[b]	Serious limitations[c]	No serious limitations	Serious limitations[d,e]	Undetected	—	⨁⨁ Low
Use of analgesics							
2 RCTs[57,58]	Serious limitations[b]	Serious limitations[c]	Serious limitations[f]	Serious limitations[g]	Undetected	—	⨁ Very low
Physical function							
6 RCTs[47,58-60,64,67]	Serious limitations[b]	Serious limitations[c]	No serious limitations	Serious limitations[d]	Undetected	—	⨁ Very low
Quality of life							
4 RCTs[57,60,64,67]	Serious limitations[b]	Serious limitations[c]	No serious limitations	Serious limitations[d,f]	Undetected	—	⨁ Very low
All cause mortality							
5 RCTs[57,59,60,63,64]	Serious limitations[h]	Serious limitations[g]	No serious limitations	Serious limitations[d,i]	Undetected	—	⨁ Very low
Adverse events							
6 RCTs[47,59,63,66,67]	Serious limitations[h]	Serious limitations[g]	No serious limitations	Serious limitations[d,i]	Undetected	—	⨁ Very low
New fractures							
6 RCTs[57-59,63,64,67]	Serious limitations[h]	Serious limitations[g]	No serious limitations	Serious limitations[d,i]	Undetected	—	⨁ Very low
Cement leakage							
6 RCTs[57-59,61,64,67]	Serious limitations[h]	Serious limitations[g]	No serious limitations	Serious limitations[d]	Undetected	—	⨁ Very low

Abbreviations: CT, conservative treatment; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

[a]As reported by Jacobsen et al[38] and modified, if applicable, where RCTs identified in our updated literature search were included.

[b]Lack of blinding, incomplete accounting of patients and outcome events.

[c]Considerable levels of statistical heterogeneity as inferred by I^2.

[d]Low number of patients at evaluated follow-up timepoints.

[e]Indirect marker of pain.

[f]Wide confidence intervals.

[g]Inconsistency in direction of individual study results.

[h]Incomplete accounting of patients and outcome events, may influence event rate.

[i]Very wide confidence intervals.

Table A6: GRADE Evidence Profile for the Comparison of PVP and Sham Control

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Pain							
6 RCTs[48,49,68,71,73,75]	Serious limitations[a,b]	Serious limitations[c]	No serious limitations	No serious limitations	Undetected	—	⨁⨁ Low
Use of analgesics							
4 RCTs[48,71,73,75]	Serious limitations[b]	Serious limitations[d]	Serious limitations[e]	Serious limitations[f]	Undetected	—	⨁ Very low
Physical function							
4 RCTs[48,68,73,75]	Serious limitations[b]	No serious limitations	No serious limitations	Serious limitations[g]	Undetected	—	⨁⨁ Low
Quality of life							
5 RCTs[49,68,71,73,75]	Serious limitations[a,b]	No serious limitations	No serious limitations	Serious limitations[c,f]	Undetected	—	⨁⨁ Low
Mortality							
4 RCTs[68,71,73,75]	No serious limitations	Serious limitations[c]	No serious limitations	Serious limitations[f,h]	Undetected	—	⨁⨁ Low
Adverse events							
5 RCTs[48,68,71,73,75]	No serious limitations	Serious limitations[c]	No serious limitations	Serious limitations[f,h]	Undetected	—	⨁⨁ Low
New fractures							
4 RCTs[48,68,71,73]	No serious limitations	Serious limitations[c]	No serious limitations	Serious limitations[f,h]	Undetected	—	⨁⨁ Low
Cement leakage							
4 RCTs[48,68,71,73]	No serious limitations	Serious limitations[c]	No serious limitations	Serious limitations[f]	Undetected	—	⨁⨁ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

[a]For the RCT by Hansen et al,[49] attrition was > 10% and did not do intent-to-treat for handling missing data.

[b]In the RCT by Carli et al,[48] there was no statistical testing reported nor discussion of baseline characteristics of study arms (e.g., age, number of days with pain before procedure). For the RCTs by Buchbinder et al,[68] Clark et al,[71] and Firanescu et al,[73] there were concerns around blinding. The individual radiologists or neurosurgeons performing the procedure were inherently unblinded and it was often unclear whether they were involved with recording subjective outcomes such as pain or quality of life in sham trials. Jacobsen et al[38] noted a lack of clarity regarding completeness of outcome data for Buchbinder et al,[68] Clark et al,[71] and Firanescu et al[73].

[c]Inconsistency in direction of individual study results. For the outcome of pain there was inconsistency in the results of studies using visual rating scale versus numerical rating scale.

[d]Moderate levels of statistical heterogeneity as inferred by I^2.

[e]Indirect measure of pain.

[f]Low number of patients.

[g]One RCT[68] for timed-up-and-go scores.

[h]Wide confidence intervals.

Table A7: GRADE Evidence Profile for the Comparison of PBK and CT

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Pain							
2 RCTs[97,100]	Serious limitations[a]	Serious limitations[b]	No serious limitations	Serious limitations[c]	Undetected	—	⊕ Very low
Use of analgesics							
1 RCT[100]	Serious limitations[a]	No serious limitations	Serious limitations[d]	Serious limitations[c]	Undetected	—	⊕ Very low
Physical function							
1 RCT[100]	Serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[c]	Undetected	—	⊕⊕ Low
Quality of life							
2 RCTs[97,100]	Serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[c]	Undetected	—	⊕⊕ Low
Mortality							
1 RCT[100]	Serious limitations[a]	No serious limitations	No serious limitations	Serious limitations[c]	Undetected	—	⊕⊕ Low
Adverse events							
3 RCTs[98-100]	Serious limitations[e]	No serious limitations	No serious limitations	Serious limitations[c]	Undetected	—	⊕⊕ Low
New fractures							
1 RCT[100]	Serious limitations[e]	No serious limitations	No serious limitations	Serious limitations[c]	Undetected	—	⊕⊕ Low
Cement leakage							
2 RCTs[99,100]	Serious limitations[e]	No serious limitations	No serious limitations	Serious limitations[c]	Undetected	—	⊕⊕ Low

Abbreviations: CT, conservative treatment; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial.

[a]Lack of blinding and concealment, and complete accounting of patients or outcome events (e.g., the RCT by Wardlaw et al[100] had > 10% difference in loss to follow-up between study arms at 3 months follow-up).

[b]Considerable levels of heterogeneity as inferred by I^2.

[d]Low number of patients.

[d]Indirect marker of pain.

[e]Incomplete accounting of patients and outcome events.

Table A8: GRADE Evidence Profile for the Comparison of PVP and PBK

Number of studies (design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Upgrade considerations	Quality
Pain							
6 RCTs[50,85,112-115]	Serious limitations[a,b,c]	Serious limitations[d]	No serious limitations	Serious limitations[e,f]	Undetected	—	⨁ Very low
Use of analgesics							
1 RCT[85]	Serious limitations[a]	No serious limitations	Serious limitations[g]	Serious limitations[f]	Undetected	—	⨁ Very low
Physical function							
4 RCTs[50,85,113,115]	Serious limitations[a,b,c]	Serious limitations[d]	No serious limitations	Serious limitations[e,f]	Undetected	—	⨁ Very low
Quality of life							
3 RCTs[85,112,115]	Very serious limitations[a,b,c]	No serious limitations	No serious limitations	Serious limitations[e,f]	Undetected	—	⨁ Very low
Mortality							
2 RCTs[85,113]	Very serious limitations[a,c]	No serious limitations	No serious limitations	Serious limitations[f]	Undetected	—	⨁ Very low
Adverse events							
3 RCTs[85,113,115]	Very serious limitations[a,c]	No serious limitations	No serious limitations	Serious limitations[e,f]	Undetected	—	⨁ Very low
New fractures							
4 RCTs[85,113-115]	Very serious limitations[a,c]	No serious limitations	No serious limitations	Serious limitations[e,f]	Undetected	—	⨁ Very low
Cement leakage							
3 RCTs[85,113,115]	Very serious limitations[a,c]	No serious limitations	No serious limitations	Serious limitations[f]	Undetected	—	⨁ Very low
Radiation exposure							
1 case series[119]	Serious limitations[h]	No serious limitations	No serious limitations	No serious limitations	Undetected	—	⨁⨁ Low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

[a]The original study design for the RCT by Dohm et al[85] required 1,234 randomized patients; however, the study was stopped early (with only 404 enrolled patients) due to low enrollment, difficulty in willingness to randomize patients, and a high proportion of early terminations.

[b]25% of patients in the RCT by Evans et al[112] did not complete follow-up.

[c]No information regarding process of randomization, use of intent-to-treat analysis, or loss to follow-up in RCTs by Bae et al,[115] Liu et al,[114] and Wang et al.[50,113] Incomplete accounting of patients and outcome events.

[d]Inconsistency in direction of individual study results.

[e]Wide confidence intervals.

[f]Low number of patients.

[g]Indirect marker of pain.

[h]Observational studies start at Moderate. No information if prospective or retrospective case series.

Table A9: Minimum Clinically Important Differences or Improvements for Outcomes of Interest Used by Jacobsen et al[38]

MIC, MCID, or MCII	Study type	Population	Reference
Roland-Morris disability questionnaire			
Distribution-based[a:] 2–8 MCID	Cohort study	OVCFs (PVP, PBK)	Lee et al,[120] 2017
2–3 (scoring range: 0–23) MCID	SR	OVCFs	Roland et al,[121] 2000
EuroQol 5 dimension questionnaire			
0.24 MCID	Cohort study	Patients with cervical radiculopathy	Parker et al,[182] 2013
0.17 MIC	Cohort study	Patients with chronic back pain undergoing surgery or rehabilitation	Johnsen et al,[183] 2013
Numerical rating scale			
Anchor-based: 4.0 Distribution-based: 0.86 MCID	Cohort study	Patients with chronic lower back pain undergoing physical therapy	Maughan et al,[184] 2010
2.0 or 30% from baseline:[b] 1–4.5[c] MIC	Systematic review and panel input	Patients with chronic lower back pain	Ostelo et al,[185] 2008
Average: 4 (95% CI, 3.4–5.0) (MDC) 1.5 MCII	Cohort study	Patients seeking treatment for neck pain	Kovacs et al,[186] 2008
Oswestry disability index			
Distribution-based: 12.81 (scoring range 0–50) MCID	Cohort study	Patients undergoing spinal surgery	Copay et al,[187] 2008
Anchor-based: 7.5 Distribution-based: 6.06 MCID	Cohort study	Patients with chronic lower back pain undergoing physical therapy	Maughan et al,[184] 2010
10 or 30% from baseline[b:] 4–15.0[c] MIC	Systematic review and panel input	Patients with chronic lower back pain	Ostelo et al,[185] 2008
Roland-Morris disability questionnaire			
Anchor-based: 3.5 Distribution-based: 1.78 MCID	Cohort study	Patients with chronic lower back pain undergoing physical therapy	Maughan et al,[184] 2010

MIC, MCID, or MCII	Study type	Population	Reference
5% or 30% from baseline[b]: 2.0–8.6[c] MIC	Systematic review and panel input	Patients with chronic lower back pain	Ostelo et al,[185] 2008
Short form 36 questionnaire			
3 MCID	Cohort study	Patients with chronic back pain	Lauridsen et al,[188] 2006
1.16 (scoring scale 1–10)	Cohort study	Patients undergoing spinal surgery	Copay et al,[187] 2008
Timed-up-and-go			
3.4 seconds MCID	Cohort study	Patients with lumbar degenerative disc disease undergoing microdiscectomy, fusion, or decompression	Gautschi et al,[189] 2017
Visual analogue scale			
15 points or 30% from baseline[b]: 2.0–29[c] MIC	Systematic review and panel input	Patients with chronic lower back pain	Ostelo et al,[185] 2008
2.6 MCID	Cohort study	Patients with cervical radiculopathy	Parker et al,[182] 2013
Back pain: 4–6 Leg pain: 3.9–6 MCID	Cohort study	Patients with lumbar degenerative disc disease undergoing laminectomy/foraminotomy	Parker et al,[190] 2012

Abbreviations: CI, confidence interval; OVCF, osteoporotic vertebral compression fracture; MDC, minimum detectable change; MIC, minimum important change; MCID, minimum clinically important difference; MCII, minimum clinically important improvements; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; SR, systematic review.

[a]Distribution-based refers to standard error of measurement as reported by Jacobsen et al.[38]

[b]Estimates based on literature search by Jacobsen et al.[38]

[c]Estimates derived from expert group in systematic review by Jacobsen et al.[38]

Appendix 4: Selected Excluded Studies – Clinical Evidence

For transparency, we provide a list of studies that readers might have expected to see but that did not meet the inclusion criteria, along with the primary reason for exclusion.

Citation	Primary reason for exclusion
Beall DP, Chambers MR, Thomas S, Amburgy J, Webb JR Jr, Goodman BS, et al. Prospective and multicenter evaluation of outcomes for quality of life and activities of daily living for balloon kyphoplasty in the treatment of vertebral compression fractures: the EVOLVE trial. Neurosurgery. 2019;84(1):169-178.	Case series. No safety data reoprted specifically for OVCFs
Gu Y, Hao K, Bai J, Hu J, Li Y. Effect of vertebroplasty with bone cement on osteoporotic compression fractures in elderly patients. Am J Transl Res. 2023;15(9):5921-5929.	Retrospective study
Liu Q, Cao J, Kong JJ. Clinical effect of balloon kyphoplasty in elderly patients with multiple osteoporotic vertebral fracture. Niger J Clin Pract. 2019;22(3):289-292.	Observational study – unclear whether prospective or retrospectve
Halvachizadeh S, Stalder AL, Bellut D, Hoppe S, Rossbach P, Cianfoni A, et al. Systematic review and meta-analysis of 3 treatment arms for vertebral compression fractures: a comparison of improvement in pain, adjacent-level fractures, and quality of life between vertebroplasty, kyphoplasty, and nonoperative management. JBJS Rev. 2021;9(10).	Includes same studies as Jacobsen et al.[33] Combines PVP and PBK as 1 group. Includes RCT by Korovessis et al[191] that used KIVA augmentation
Lou S, Shi X, Zhang X, Lyu H, Li Z, Wang Y. Percutaneous vertebroplasty versus non-operative treatment for osteoporotic vertebral compression fractures: a meta-analysis of randomized controlled trials. Osteoporos Int. 2019;30(12):2369-2380.	Superceded by more recent systematic review
Hinde K, Maingard J, Hirsch JA, Phan K, Asadi H, Chandra RV. Mortality outcomes of vertebral augmentation (vertebroplasty and/or balloon kyphoplasty) for osteoporotic vertebral compression fractures: a systematic review and meta-analysis. Radiology. 2020;295(1):96-103.	Superceded by more recent systematic review
Ding JK, Zhao B, Zhai YF. Subsequent fractures after vertebroplasty in osteoporotic vertebral fractures: a meta-analysis. Neurosurg Rev. 2022;45(3):2349-2359.	Included retrospective studies
Daher M, Kreichati G, Kharrat K, Sebaaly A. Vertebroplasty versus kyphoplasty in the treatment of osteoporotic vertebral compression fractures: a meta-analysis. World Neurosurg. 2023;171:65-71.	Superceded by more recent systematic review

Appendix 5: Economic Evidence

For transparency, we provide a list of studies that readers might have expected to see but that did not meet the inclusion criteria, along with the primary reason for exclusion.

Table A10: Selected Excluded Economic Studies

Citation	Primary reason for exclusion
Eidt D, Greiner W. PMS30 cost analysis of balloon kyphoplasty versus non surgical management for osteoporotic vertebral fractures in Germany. *Val Health* 2009;12(7):A438-A39.	Abstract only
Medical Advisory Secretariat. Percutaneous vertebroplasty for treatment of painful osteoporotic vertebral compression fractures: an evidence-based analysis. Ont Health Technol Assess Ser. 2010;10(19):1-45. Epub 2010 Oct 1.	Costs only
Takura T, Yoshimatsu M, Sugimori H, Takizawa K, Furumatsu Y, Ikeda H, et al. Cost-effectiveness analysis of percutaneous vertebroplasty for osteoporotic compression fractures. *Clin Spine Surg* 2017;30(3):E205-e10.	No comparator
Mehio AK, Lerner JH, Engelhart LM, Kozma CM, Slaton TL, Edwards NC, et al. Comparative hospital economics and patient presentation: vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture. *AJNR Am J Neuroradiol.* 2011;32(7):1290-4.	Costs only
Becker S, Pfeiffer KP, Ogon M. Comparison of inpatient treatment costs after balloon kyphoplasty and non-surgical treatment of vertebral body compression fractures. *Eur Spine J* 2011;20(8):1259-64.	Study design – cost consequence analysis
Goz V, Errico TJ, Weinreb JH, Koehler SM, Hecht AC, Lafage V, et al. Vertebroplasty and kyphoplasty: national outcomes and trends in utilization from 2005 through 2010. *Spine J* 2015;15(5):959-65.	Study design – cost consequence analysis
Lange A, Kasperk C, Alvares L, Sauermann S, Braun S. Survival and cost comparison of kyphoplasty and percutaneous vertebroplasty using German claims data. *Spine (Phila Pa 1976)* 2014;39(4):318-26.	Study design – cost consequence analysis
Chen C, Li DW, Wang Q, Xu XW, Ma YZ, Li Z, et al. The cost effectiveness analysis of minimally invasive surgery and conservative treatment in elderly osteoporotic spinal fracture. *Zhongguo Gu Shang* 2016;29(7):614-18.	Non-English article
Joestl J, Lang N, Bukaty A, Tiefenboeck TM, Platzer P.Osteoporosis associated vertebral fractures – health economic implications. *PloS one* 2017;12(5):e0178209.	Study design – cost consequence analysis

Appendix 6: Conservative Treatments

Table A11: Descriptions of Conservative Treatment

Author, year, country	Comparator name used by study authors	Comparator description by study authors
Masala et al,[131] 2008 Italy	PVP refusers, conservative medical therapy	Drug therapy (oral administration of 5–15 mg × 2/d of oxycodone, 50–200 mg × 2/d of tramadol, and 300–800 mg × 3/d of gabapentin for 30 weeks. If pain persisted, the same drug therapy was extended for 19 weeks), orthopedic brace, physical therapy (30–40 sessions of massotherapy and rehabilitation gymnastics, 20 sessions of postural restoration and hydrokinesitherapy in inpatients; 20 sessions of massotherapy, rehabilitation gymnastic, analgesic electrotherapy, and magnetotherapy in outpatients)
Strom et al,[125] 2010 United Kingdom	Non-surgical management	Analgesics, bed rest, back braces, physiotherapy, rehabilitation programs, and walking aids
Klazen et al,[60] 2010 The Netherlands and Belgium	Conservative treatment	Described in protocol for RCT only:[192] optimal pain management, physiotherapy, or bracing
Fritzell et al,[126] 2011 Sweden	Standard medical treatment	Reader directed to associated clinical trial publication:[100] all participants received analgesics, bed rest, back braces, physiotherapy, rehabilitation programmes, and walking aids according to the standard practices of participating hospitals
Edidin et al,[132] 2012 United States	Non-operated	No description provided, but notes in the discussion section indicate that the non-operated population may have received various types of conservative care
Svedbom et al,[124] 2013 United Kingdom	Non-surgical management	No description
Stevenson et al,[127] 2014 United Kingdom	Non-invasive management	Optimal pain management Background section of HTA includes further description of potential treatments, including bed rest, back bracing or casting, spine extension exercises, muscle relaxants and heat treatment for muscle spasm, massage and physiotherapy for kyphosis, walking aids, and education to avoid pain in activities of daily living
Hopkins et al,[128] 2020 United States	Conservative medical management	Inclusive of pharmaceutical pain management, bed rest, bracing, and physical therapy
Jacobsen et al,[38] 2021 Switzerland	Conservative treatment	Conventional treatment, or non-surgical treatments (including optimal medical therapy, physiotherapy or bracing)
MASC,[129] 2019 Australia	Conservative medical therapy	No description provided and clinical effectiveness estimate came from a sham-controlled trial[71]
Takahashi et al,[130] 2019 Japan	Non-surgical management	Bracing and medicine in conservative treatment group. All patients received appropriate medical support, including non-steroidal anti-inflammatory drugs, osteoporosis treatment, and a postoperative rehabilitation program

Abbreviations: HTA, health technology assessment; MASC, Medical Services Advisory Committee; PVP, percutaneous vertebroplasty; RCT, randomized controlled trial.

Appendix 7: Results of Applicability and Limitation Checklists for Studies Included in the Economic Literature Review

Table A12: Assessment of the Applicability of Studies Evaluating the Cost-Effectiveness of Vertebral Augmentation

Author, year, country	Is the study population appropriate for the review question?	Are the interventions appropriate for the review question?	Is the system in which the study was conducted sufficiently like the current Ontario context?	Is the perspective of the costs appropriate for the review question (e.g., Canadian public payer)?	Is the perspective of the outcomes appropriate for the review question?	Are all future costs and outcomes discounted appropriately (as per current CDA guidelines)?	Are QALYs derived using CDA's preferred methods, or is an appropriate social care–related equivalent used as an outcome? (If not, describe rationale and outcomes used in line with the analytical perspective taken)	Overall judgment[a]
Masala et al,[131] 2008 Italy	Yes	No	Yes	No	No	Yes	No (reduction in VAS pain score or ADL scale)	Not applicable
Strom et al,[125] 2010 United Kingdom	Partially (only hospitalized patients)	Yes	Yes	Yes	Yes	No (3.5%)	Yes	Partially applicable
Klazen et al,[60] 2010 The Netherlands and Belgium	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partially applicable
Fritzell et al,[126] 2011 Sweden	Partially (only hospitalized patients)	Yes	Yes	No	Yes	Unclear (NR)	Yes	Partially applicable
Edidin et al,[132] 2012 United States	Yes	Unclear	No	No	Yes	No (3%)	No (life years)	Not applicable
Svedbom et al,[124] 2013 United Kingdom	Partially (only hospitalized patients)	Yes	Yes	Yes	Yes	No (3.5%)	Yes	Partially applicable

Author, year, country	Is the study population appropriate for the review question?	Are the interventions appropriate for the review question?	Is the system in which the study was conducted sufficiently like the current Ontario context?	Is the perspective of the costs appropriate for the review question (e.g., Canadian public payer)?	Is the perspective of the outcomes appropriate for the review question?	Are all future costs and outcomes discounted appropriately (as per current CDA guidelines)?	Are QALYs derived using CDA's preferred methods, or is an appropriate social care–related equivalent used as an outcome? (If not, describe rationale and outcomes used in line with the analytical perspective taken)	Overall judgment[a]
Stevenson et al,[127] 2014 United Kingdom	Yes	Yes	Yes	Yes	Yes	No (3.5%)	Yes	Partially applicable
Hopkins et al,[128] 2020 United States	Yes	Yes	No	No	Yes	No (3%)	Yes	Partially applicable
Jacobsen et al,[38] 2021 Switzerland	Yes	Yes	Yes	Yes	Yes	Yes for PVP (1 year time horizon) Unclear for PBK (2 years, NR)	Yes	Partially applicable
MASC,[129] 2019 Australia	Yes	Yes	Yes	Yes	Yes	Unclear (time horizon is 6 mo, but states 5% discounting)	Unclear	Partially applicable
Takahashi et al,[130] 2019 Japan	Yes	Yes	No	Unclear	Yes	No (3.5%)	Yes	Not applicable

Note: Response options for all items were "yes," "partially," "no," "unclear," and "NA" (not applicable).

Abbreviations: ADL, activities of daily living; CDA, Canada's Drug Agency; NR, not reported; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; VAS, visual analogue score.

[a]Overall judgment may be "directly applicable," "partially applicable," or "not applicable."

Table A13: Assessment of the Limitations of Studies Evaluating the Cost-Effectiveness of Vertebral Augmentation

Author, year, country	Does the model structure adequately reflect the nature of the health condition under evaluation?	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Are all important and relevant health outcomes included?	Are the clinical inputs[a] obtained from the best available sources?	Do the clinical inputs[a] match the estimates contained in the clinical sources?	Are all important and relevant (direct) costs included in the analysis?	Are the estimates of resource use obtained from the best available sources?	Are the unit costs of resources obtained from the best available sources?	Is an appropriate incremental analysis presented, or can it be calculated from the reported data?	Are all important and uncertain parameters subjected to appropriate sensitivity analysis?	Is there a potential conflict of interest?	Overall judgment[b]
Strom et al,[125] 2010 United Kingdom	Yes	Yes	Uncertain. No treatment effect for mortality (study was before Edidin study came out), recurrent fracture risk, no AE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Minor limitations
Klazen et al,[60] 2010 The Netherlands and Belgium	NA	Uncertain	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Person-level, used bootstrapping didn't subject input parameters to uncertainty since there were none	No	Minor limitations
Fritzell et al,[126] 2011 Sweden	NA	Uncertain	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partially	No	Minor limitations

Author, year, country	Does the model structure adequately reflect the nature of the health condition under evaluation?	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Are all important and relevant health outcomes included?	Are the clinical inputs[a] obtained from the best available sources?	Do the clinical inputs[a] match the estimates contained in the clinical sources?	Are all important and relevant (direct) costs included in the analysis?	Are the estimates of resource use obtained from the best available sources?	Are the unit costs of resources obtained from the best available sources?	Is an appropriate incremental analysis presented, or can it be calculated from the reported data?	Are all important and uncertain parameters subjected to appropriate sensitivity analysis?	Is there a potential conflict of interest?	Overall judgment[b]
Svedbom et al,[124] 2013 United Kingdom	Yes	Yes	Uncertain. Mortality included. No treatment effect for recurrent fracture risk. AE not included	Yes	Partially	Yes	Yes	Yes	Yes	Yes	No	Minor limitations
Stevenson et al,[127] 2014 United Kingdom	Yes	Yes	Uncertain. Mortality is included. AE in sensitiivty analysis. Treatment benefit on recurrent fracture risk is not included.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Minor limitations

Author, year, country	Does the model structure adequately reflect the nature of the health condition under evaluation?	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Are all important and relevant health outcomes included?	Are the clinical inputs[a] obtained from the best available sources?	Do the clinical inputs[a] match the estimates contained in the clinical sources?	Are all important and relevant (direct) costs included in the analysis?	Are the estimates of resource use obtained from the best available sources?	Are the unit costs of resources obtained from the best available sources?	Is an appropriate incremental analysis presented, or can it be calculated from the reported data?	Are all important and uncertain parameters subjected to appropriate sensitivity analysis?	Is there a potential conflict of interest?	Overall judgment[b]
Hopkins et al,[128] 2020 United States	Yes	Yes	Uncertain. Mortality included. No treatment effect for recurrent fracture risk. AE not mentioned	Yes	Uncertain. Utilities were adjusted using US value set, whereas reported values from trial were adjusted using UK value set	Yes	Yes	Yes	Yes	Yes	Unclear	Minor limitations
Jacobsen et al,[38] 2021 Switzerland	Uncertain. Model can't capture potential difference with mortality	Uncertain. Model can't capture potential difference with mortality	Uncertain. Mortality is not included. AE and recurrent fracture in sensitivity analyses	Yes	PBK, yes PVP, unclear	Yes	Yes	Assumed same cost for PVP and PBK	Yes	Yes	No	Minor limitations

Author, year, country	Does the model structure adequately reflect the nature of the health condition under evaluation?	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Are all important and relevant health outcomes included?	Are the clinical inputs[a] obtained from the best available sources?	Do the clinical inputs[a] match the estimates contained in the clinical sources?	Are all important and relevant (direct) costs included in the analysis?	Are the estimates of resource use obtained from the best available sources?	Are the unit costs of resources obtained from the best available sources?	Is an appropriate incremental analysis presented, or can it be calculated from the reported data?	Are all important and uncertain parameters subjected to appropriate sensitivity analysis?	Is there a potential conflict of interest?	Overall judgment[b]
MASC,[129] 2019 Australia	Uncertain. Only states are alive and dead	Uncertain. Not sure if mortality needs to be accounted for yet	Uncertain. Very little information provided, but can tell that they included QoL benefits. Not sure about AE. Time horizon is short, so unlikely mortality or recurrent fracture included	Yes	Unclear (not enough detail reported)	Unclear	Unclear	Unclear	Yes	Unclear	Unclear	Potentially serious limitations

Note: Response options for all items were "yes," "partially," "no," "unclear," and "NA" (not applicable).

Abbreviations: AE, adverse event; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QoL, quality of life.

[a]Clinical inputs include relative treatment effects, natural history, and utilities.

[b]Overall judgment may be "minor limitations," "potentially serious limitations," or "very serious limitations."

Appendix 8: Supplementary Economic Tables

Table A14: Monthly Utilities for CT

Month	Utility[a]	95% CI	Source	Weighted utility[a,b]	95% CI	Source
Baseline	0.170	(0.120–0.220)	Van Meirhaeghe, 2013[101]	NA	NA	NA
1	0.370	(0.310–0.420)	Van Meirhaeghe, 2013[101]	0.270	(0.215–0.320)	Calculated[c]
2	0.430	(0.375–0.485)	Calculated[c]	0.400	(0.343–0.453)	Calculated[c]
3	0.490	(0.440–0.550)	Van Meirhaeghe, 2013[101]	0.460	(0.408–0.518)	Calculated[c]
4	0.493	(0.443–0.553)	Calculated[d]	0.492	(0.442–0.552)	Calculated[c]
~~5~~	0.497	(0.447–0.557)	Calculated[d]	0.495	(0.445–0.555)	Calculated[c]
6	0.500	(0.450–0.560)	Van Meirhaeghe, 2013[101]	0.498	(0.448–0.558)	Calculated[c]
7	0.502	(0.450–0.562)	Calculated[d]	0.501	(0.450–0.561)	Calculated[c]
8	0.503	(0.405–0.563)	Calculated[d]	0.503	(0.450–0.563)	Calculated[c]
9	0.505	(0.450–0.565)	Calculated[d]	0.504	(0.450–0.564)	Calculated[c]
10	0.507	(0.450–0.567)	Calculated[d]	0.506	(0.450–0.566)	Calculated[c]
11	0.508	(0.450–0.568)	Calculated[d]	0.508	(0.450–0.568)	Calculated[c]
12	0.510	(0.450–0.570)	Calculated[d]	0.509	(0.450–0.569)	Calculated[c]
13	0.512	(0.452–0.572)	Calculated[d]	0.511	(0.451–0.571)	Calculated[c]
14	0.513	(0.453–0.573)	Calculated[d]	0.513	(0.453–0.573)	Calculated[c]
15	0.515	(0.455–0.575)	Calculated[d]	0.514	(0.454–0.574)	Calculated[c]
16	0.517	(0.457–0.577)	Calculated[d]	0.516	(0.456–0.576)	Calculated[c]
17	0.518	(0.458–0.578)	Calculated[d]	0.518	(0.458–0.578)	Calculated[c]
18	0.520	(0.460–0.580)	Calculated[d]	0.519	(0.459–0.579)	Calculated[c]
19	0.522	(0.462–0.582)	Calculated[d]	0.521	(0.461–0.581)	Calculated[c]
20	0.523	(0.463–0.583)	Calculated[d]	0.523	(0.463–0.583)	Calculated[c]
21	0.525	(0.465–0.585)	Calculated[d]	0.524	(0.464–0.584)	Calculated[c]
22	0.527	(0.467–0.587)	Calculated[d]	0.526	(0.466–0.586)	Calculated[c]
23	0.528	(0.468–0.588)	Calculated[d]	0.528	(0.468–0.588)	Calculated[c]
24	0.530	(0.470–0.590)	Van Meirhaeghe, 2013[101]	0.529	(0.469–0.589)	Calculated[c]

Abbreviations: CI, confidence interval; CT, conservative treatment; NA, not applicable.

[a]Values from trial before adjustment for age and sex.

[b]Weighted utilities were defined as beta distributions.

[c]Weighted utilities were calculated as the average of the current month plus the previous month; e.g., weighted utility at month m = (utility at month m + utility at month [m − 1]/2).

[d]Missing monthly utilities were imputed using linear interpolation; e.g., utility at month 4 (u4) was imputed using the known values for month 3 (3, 0.490) and month 6 (6, 0.630) with the following formula: u4 = (4 − 3)(0.630 – 0.490)/(6 − 3) + 0.590.

Table A15: Mean Utilities for the Canadian Population by Age and Sex

	Mean utility[a]	
Age group, y	Male	Female
40–44	0.901	0.874
45–49	0.873	0.862
50–54	0.856	0.842
55–59	0.850	0.830
60–64	0.842	0.841
65–69	0.848	0.837
70–74	0.841	0.831
75–79	0.809	0.778
80–84	0.748	0.736
85+	0.682	0.616

[a]All values sourced from Guertin et al, 2018.[151]

Table A16: Monthly Mean Difference in Utilities for PBK + CT Compared With CT

Month	Mean difference in utility	95% CI	Source	Weighted mean difference in utility[a]	95% CI	Source
Baseline	−0.010	(−0.084 to 0.064)	Van Meirhaeghe, 2013[101]	NA	NA	NA
1	0.170	(0.092–0.248)	Van Meirhaeghe, 2013[101]	0.080	(0.004–0.156)	Calculated[b]
2	0.135	(0.055–0.215)	Calculated[c]	0.153	(0.074–0.231)	Calculated[b]
3	0.100	(0.019–0.181)	Van Meirhaeghe, 2013[101]	0.118	(0.037–0.198)	Calculated[b]
4	0.110	(−0.084 to 0.064)	Calculated[c]	0.105	(0.004–0.156)	Calculated[b]
~~5~~	0.120	(0.041–0.199)	Calculated[c]	0.115	(0.004–0.156)	Calculated[b]
6	0.130	(0.052–0.208)	Van Meirhaeghe, 2013[101]	0.125	(0.047–0.203)	Calculated[b]
7	0.125	(0.047–0.203)	Calculated[c]	0.128	(0.049–0.206)	Calculated[b]
8	0.120	(0.041–0.199)	Calculated[c]	0.123	(0.044–0.201)	Calculated[b]
9	0.115	(0.035–0.195)	Calculated[c]	0.118	(0.038–0.197)	Calculated[b]
10	0.110	(0.03–0.19)	Calculated[c]	0.113	(0.033–0.192)	Calculated[b]
11	0.105	(0.024–0.186)	Calculated[c]	0.108	(0.027–0.188)	Calculated[b]
12	0.100	(0.019–0.181)	Van Meirhaeghe, 2013[101]	0.103	(0.021–0.184)	Calculated[b]
13	0.098	(0.017–0.18)	Calculated[c]	0.099	(0.018–0.181)	Calculated[b]
14	0.097	(0.015–0.178)	Calculated[c]	0.098	(0.016–0.179)	Calculated[b]
15	0.095	(0.014–0.176)	Calculated[c]	0.096	(0.014–0.177)	Calculated[b]
16	0.093	(0.012–0.175)	Calculated[c]	0.094	(0.013–0.176)	Calculated[b]
17	0.092	(0.01–0.173)	Calculated[c]	0.093	(0.011–0.174)	Calculated[b]
18	0.090	(0.009–0.171)	Calculated[c]	0.091	(0.009–0.172)	Calculated[b]
19	0.088	(0.007–0.17)	Calculated[c]	0.089	(0.008–0.171)	Calculated[b]
20	0.087	(0.005–0.168)	Calculated[c]	0.088	(0.006–0.169)	Calculated[b]
21	0.085	(0.004–0.166)	Calculated[c]	0.086	(0.004–0.167)	Calculated[b]
22	0.083	(0.002–0.165)	Calculated[c]	0.084	(0.003–0.166)	Calculated[b]
23	0.082	(0–0.163)	Calculated[c]	0.083	(0.001–0.164)	Calculated[b]
24	0.080	(−0.001 to −0.161)	Van Meirhaeghe, 2013[101]	0.081	(−0.001 to 0.162)	Calculated[b]

Abbreviations: CI, confidence interval; CT, conservative treatment; NA, not applicable; PBK, percutaneous balloon kyphoplasty.

[a]Weighted mean difference in utilities were defined as normal distributions.

[b]Weighted utilities were calculated as the average of the current month and the previous month.

[c]Missing monthly mean difference in utilities were imputed using linear interpolation.

Table A17: Monthly Mean Difference in Utilities for PVP + CT Compared With PBK + CT

Month	Mean difference in utility	95% CI	Source	Weighted mean difference in utility[a]	95% CI	Source
Baseline	−0.020	(−0.07 to 0.03)	Dohm et al, 2014[85]	NA	NA	NA
1	0.010	(−0.032 to 0.052)	Dohm et al, 2014[85]	−0.005	(−0.051 to 0.041)	Calculated[b]
2	0.005	(−0.036 to 0.046)	Calculated[c]	0.008	(−0.034 to 0.049)	Calculated[b]
3	0.000	(−0.04 to 0.04)	Dohm et al, 2014[85]	0.003	(−0.038 to 0.043)	Calculated[b]
4	0.001	(−0.039 to 0.041)	Calculated[c]	0.001	(−0.04 to 0.041)	Calculated[b]
5	0.002	(−0.038 to 0.043)	Calculated[c]	0.002	(−0.039 to 0.042)	Calculated[b]
6	0.003	(−0.037 to 0.044)	Calculated[c]	0.003	(−0.038 to 0.043)	Calculated[b]
7	0.004	(−0.036 to 0.045)	Calculated[c]	0.004	(−0.037 to 0.045)	Calculated[b]
8	0.006	(−0.035 to 0.047)	Calculated[c]	0.005	(−0.036 to 0.046)	Calculated[b]
9	0.007	(−0.034 to 0.048)	Calculated[c]	0.006	(−0.035 to 0.047)	Calculated[b]
10	0.008	(−0.034to 0.049)	Calculated[c]	0.007	(−0.034 to 0.048)	Calculated[b]
11	0.009	(−0.033 to 0.05)	Calculated[c]	0.008	(−0.033 to 0.05)	Calculated[b]
12	0.010	(−0.032 to 0.052)	Dohm et al, 2014[85]	0.009	(−0.032to 0.051)	Calculated[b]
13	0.011	(−0.029 to 0.05)	Calculated[c]	0.010	(−0.03 to 0.051)	Calculated[b]
14	0.012	(−0.026 to 0.05)	Calculated[c]	0.011	(−0.027 to 0.05)	Calculated[b]
15	0.013	(−0.024 to 0.049)	Calculated[c]	0.012	(−0.025to 0.049)	Calculated[b]
16	0.013	(−0.023to 0.049)	Calculated[c]	0.013	(−0.023 to 0.049)	Calculated[b]
17	0.014	(−0.021to 0.05)	Calculated[c]	0.014	(−0.022 to 0.05)	Calculated[b]
18	0.015	(−0.021 to 0.051)	Calculated[c]	0.015	(−0.021 to 0.05)	Calculated[b]
19	0.016	(−0.021 to 0.053)	Calculated[c]	0.015	(−0.021 to 0.052)	Calculated[b]
20	0.017	(−0.021 to 0.055)	Calculated[c]	0.016	(−0.021 to 0.054)	Calculated[b]
21	0.018	(−0.022 to 0.057)	Calculated[c]	0.017	(−0.022 to 0.056)	Calculated[b]
22	0.018	(−0.024 to 0.06)	Calculated[c]	0.018	(−0.023 to 0.059)	Calculated[b]
23	0.019	(−0.025 to 0.064)	Calculated[c]	0.019	(−0.024 to 0.062)	Calculated[b]
24	0.020	(−0.037 to 0.077)	Dohm et al, 2014[85]	0.020	(−0.031 to 0.07)	Calculated[b]

Abbreviations: CI, confidence interval; CT, conservative treatment; NA, not applicable; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Weighted mean difference in utilities were defined as normal distributions.

[b]Weighted utilities were calculated as the average of the current month and the previous month

[c]Missing monthly mean difference utilities were imputed using linear interpolation.

Table A18: Costs Used in the Economic Model

Variable	Unit cost,[a] $	Quantity per patient	Total cost, $	Reference
Conservative treatment			**363.50**	
Doctor's visits				
Family doctor, intermediate assessment	37.95	2.5	94.72[a]	OSB 2023,[38] A007
Orthopedic surgery, consultation	83.85	1	86.20[a]	OSB 2023, A065
Pharmacological treatment (pain medication)				
Acetaminophen	0.0298 per two 500-mg tablets	Assume all patients receive 1,000 mg 3 times per day for 6 weeks	10.26[b,c]	ODB[154] Expert communication[d]
Hydromorphone	0.0959 per 1-mg tablet	Assume 50% of patients receive 1 tablet 3 times per day for 6 weeks	8.41[b,c]	Expert communication.[a] Percentage of patients taking weak or strong opiate derivatives from VERTOS II trial[60]
Other non-pharmacalogical components				
Physiotherapy	327.82 per episode of care	50%	163.91	Cost reference: MOH, email communication, July 16, 2024 Quantity per patient reference: Expert communication[d]
Exercise	0.00		0.00	No coverage from MOH
Back brace	0.00		0.00	No coverage from MOH
Emergency department costs			**477.44**	
Osteoporosis-related vertebral fracture ED visit	845.00 (8.91)	50%	422.50	IntelliHealth Ontario data, accessed August 28, 2024 Quantity per patient reference: expert communication[d]
ED physician fees, consultation	109.87	50%	54.94[a]	ODB 2023, H055
Hospitalization for OVCF				
Hospitalization without procedure (hospital and physician costs)	16,365.56 (1,379.82)	31%[e]	5,073.32	IntelliHealth Ontario data, accessed August 28, 2024, limited to patients 40 and older with an ICD-10-CA diagnosis for vertebral fracture CIHI patient cost estimator,[156] using a ratio of 0.17 for physician costs to hospital costs based on CMG 771, spinal injury

Variable	Unit cost,[a] $	Quantity per patient	Total cost, $	Reference
Hospitalization with PVP procedure (hospital and physician costs)	35,508.20 (4,604.60)	31% [e]	11,007.54	IntelliHealth Ontario data, accessed August 28, 2024 CIHI patient cost estimator,[156] using a ratio of 0.27 for physician costs to hospital costs based on CMG 731, spinal intervention with trauma/complication of treatment
Hospitalization with PBK procedure (hospital and physician costs)	39,128.02 (8,027.60)	31% [e]	12,129.68	IntelliHealth Ontario data, accessed August 28, 2024 CIHI patient cost estimator,[156] using a ratio of 0.27 for physician costs to hospital costs based on CMG 731, spinal intervention with trauma/complication of treatment
Pre-procedure scans, pre- and post-procedure appointments, PVP			**317.54**	
MRI, limited spine (1 segment)	59.50	100%	61.17[a]	OSB 2023, X493 multislice sequence
Special interventional radiological consultation	223.20	54%	123.90[a]	OSB 2023, A365 special interventional radiological consultation Percentage of PVP patients seen by interventional radiologist, from IntelliHealth Ontario (Table A24)
Special surgical consultation	163.20	46%	77.17[a]	OSB 2023, A935 consultation Percentage of PVP patients seen by surgeon, from IntelliHealth Ontario (Table A24)
Follow-up with interventional radiologist	50.00	54%	27.76[a]	OSB 2023, A335 consultation Percentage of PVP patients seen by interventional radiologist, from IntelliHealth Ontario (Table A24), assume all patients receive a follow-up appointment
Follow-up with surgeon, repeat consultation	58.25	46%	27.55[a]	OSB 2023, A046 Percentage of PVP patients seen by surgeon, from IntelliHealth Ontario (Table A24), assume all patients receive a follow-up appointment
Pre-procedure scans, pre- and post-procedure appointments, PBK			**298.92**	
MRI, limited spine (1 segment)	59.50	100%	61.17[a]	OSB 2023, X493 multislice sequence
Special interventional radiological consultation	223.20	19%	43.60[a]	OSB 2023, A365 special interventional radiological consultation Percentage of PBK patients seen by interventional radiologist, from IntelliHealth Ontario (Table A24)
Special surgical consultation	163.20	81%	135.89[a]	OSB 2023, A935 consultation Percentage of PBK patients seen by surgeon, from IntelliHealth Ontario (Table A24)

Variable	Unit cost,[a] $	Quantity per patient	Total cost, $	Reference
Follow-up with interventional radiologist	50.00	19%	9.77[a]	OSB 2023, A335 consultation Percentage of PBK patients seen by interventional radiologist, from IntelliHealth Ontario (Table A24), assume all patients receive a follow-up appointment
Follow-up with surgeon, repeat consultation	58.25	81%	48.50[a]	OSB 2023, A046 Percentage of PBK patients seen by surgeon, from IntelliHealth Ontario (Table A24), assume all patients receive a follow-up appointment
Outpatient procedure (day procedure), PVP			**5,747.41**	
Physician fees, first level	655.25	100%	673.60[a]	OSB 2023, N570
Physician fees, additional levels	252.95	1.6[f]	416.05[a]	OSB 2023, E391 IntelliHealth Ontario data, accessed September 11, 2024
Surgical assistant	141.46	4%[g]	5.60	OSB 2023, N570B Percentage of day procedures with surgical assistant, from IntelliHealth Ontario data, accessed September 11, 2024 (Table A16)
Anesthesiologist fees	206.96	35%[h]	71.95	OSB 2023, N570C Percentage of day procedures with anesthesia, from IntelliHealth Ontario data, accessed September 11, 2024 (Table A17)
Total physician fees, PVP procedure			**1,167.20**	
Hospital costs (outpatient), PVP	4,580.21 (378.07)	100%	4,580.21	IntelliHealth Ontario data (ambulatory visits), accessed October 15, 2024
Outpatient procedure (day procedure), PBK			**8,994.65**	
Physician fees, first level	1201.55	100%	1,235.19[a]	OSB 2023, N583
Physician fees, additional levels	510.00	1.5[f]	786.42[a]	OSB 2023, N393 IntelliHealth Ontario data, accessed September 11, 2024
Surgical assistant	154.32	44%[g]	67.88	OSB 2023, N570B Percentage of day procedures with surgical assistant, from IntelliHealth Ontario data, accessed September 11, 2024 (Table A25)
Anesthesiologist fees	238.80	99.8%[h]	238.37	OSB 2023, N570C Percentage of day procedures with anesthesia, from IntelliHealth Ontario data, accessed September 11, 2024 (Table A26)

Variable	Unit cost,[a] $	Quantity per patient	Total cost, $	Reference
Total physician fees, PBK procedure			**2,327.86**	
Hospital costs (outpatient)	6,666.79 (785.78)	100%	6,666.79	IntelliHealth Ontario data, accessed October 15, 2024
Symptomatic cement leakage				
Cost for treatment of symptomatic cement leakage	35,573.98			IntelliHealth Ontario data, accessed October 16, 2024
Total cost of symptomatic cement leakages, PVP	35,573.98	0.154% (1/648)	**54.90**	Farrokhi et al, 2011[59]
Total cost of symptomatic cement leakages, PBK	35,573.98	1.09% (8/731)	**389.32**	Clinical review

Abbreviations: CIHI, Canadian Institute for Health Information; CMG, case mix group; ED, emergency department; MOH, Ontario Ministry of Health; MRI, magnetic resonance imaging; ODB, Ontario drug benefit; OSB, Ontario Schedule of Benefit; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Includes a 2.8% increase applied to all OHIP fees[193] and a 15% age-based premium for 76% of people.

[b]Medication costs represent the cost paid by the Ontario Drug Benefit Program (MOH), including an 8% pharmacy mark-up and a 1-time $10 dispensing fee.[42]

[C]Represents the average cost to MOH, assuming 76% of people qualify for the Ontario Drug Benefit program.

[d]D. Tannenbaum, MD, email communication, September 7, 2024.

[e]Based on IntelliHealth Ontario data accessed September 19, 2024 (see Table A12 for more information).

[f]Calculated based on the ratio of extra levels billed for PVP (PBK) in fiscal years 2018 to 2022.

[g]Calculated based on the ratio of OHIP fee claims by a surgical assistant and the total number of procedures in fiscal years 2018 to 2022 for PVP (PBK).

[h]Calculated based on the ratio of OHIP billings by an anesthesiologist and the total number of procedures in fiscal years 2018 to 2022 for PVP (PBK).

Table A19: ICD-10-CA Codes for Vertebral Fracture Diagnosis

ICD-10-CA Code	ICD-10-CA Description
S22.0	Fracture of thoracic vertebra
S22.1	Multiple fractures of thoracic spine
S32.0	Fracture of lumbar vertebra

Abbreviation: ICD-10-CA, International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada.

Table A20: Admission Categories

Admitted	Not admitted
Client admitted as inpatient to critical care unit/operating room in reporting facility direct from ambulatory care visit functional centre	Died in facility
Client admitted as inpatient to other units in reporting facility direct from ambulatory care visit functional centre	Discharge to private home, condo, apartment with support service/referral
Transferred to another acute care facility directly from an ambulatory care visit functional centre	Discharge to private home, condo, apartment without support service/referral
	Intrafacility transfer to clinic
	Intrafacility transfer to day surgery
	Intrafacility transfer to the emergency department
	Left after initial assessment
	Left after triage
	Left at his/her own risk following registration
	Left at his/her own risk post initial treatment
	Transfer to correctional facility
	Transfer to group/supportive living
	Transfer to residential care
	Transferred to another non-acute care facility directly from an ambulatory care visit functional centre

Table A21: Admission to Hospital

Admission	FY 2021/22[a] (n = 6,427)	FY 2022/23[a] (n = 6,456)	FY 2023/24[a] (n = 6,804)
Admitted, %	30.0%	31.4%	31.7%

Abbreviations: FY, fiscal year; n, total number.

[a]Ambulatory visit data from IntelliHealth Ontario, accessed September 19, 2024. Includes emergency cases for people with a vertebral fracture diagnosis as the main diagnosis only.

Table A22: Vertebral Augmentation Procedure Codes

Intervention	CCI Code	Long description
PVP	1.SC.80.HA-XX-N	Repair, spinal vertebrae, using percutaneous approach and (injection of) synthetic material (e.g., bone cement). Includes vertebroplasty, percutaneous
PBK	1.SC.80.HA-BD-N	Repair, spinal vertebrae, using percutaneous approach with balloon and (injection of) synthetic material (e.g., bone cement). Includes balloon kyphoplasty

Abbreviations: CCI, Canadian Classification of Health Interventions; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

Table A23: Vertebral Augmentation Procedure OHIP Fee Codes

Intervention	OHIP fee code	OHIP fee code description
PVP	N570	Vertebroplasty (injection of bone cement) as sole procedure, first level
	E388	Vertebroplasty combined with any other procedure, first level, to other procedure
	E391	Vertebroplasty, each additional level, to N570 or E388
PBK	N583	Kyphoplasty (balloon tamp and injection of bone cement) as sole procedure, first level
	E392	Kyphoplasty combined with any other procedure, first level, to other procedure
	E393	Kyphoplasty, each additional level, to N583 or E392

Abbreviations: OHIP, Ontario Health Insurance Plan; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

Table A24: Specialists Performing PVP and PBK

Procedure	Interventional radiologist[a]	Surgeon[a,b]
PVP[c]	54%	46%
PBK[c]	19%	81%

Abbreviations: PBK, balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Specialist categorized according to fiscal specialty reported in OHIP fee claims data.

[b]Surgeons include neurosurgeons and orthopedic surgeons.

[c]OHIP fee claims data from IntelliHealth Ontario, accessed September 11, 2024, for fiscal years 2018 to 2022.

Table A25: Surgical Assistant Fees

Procedure	PVP	PBK	Source
Average procedure length, hours	1.0	1.0	M. Baerlocher, MD, email communication, March 13, 2024
Number of basic units	7	8	Schedule of Benefit (N570, N583)[38]
Number of time units[a]	4	4	Calculated based on average procedure length
Total number of units	11	12	Sum of basic and time units
Total billing[b]	**$141.46**	**$154.32**	

Abbreviations: PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Time units are calculated for every 15-minute period. During the first hour, each 15-minute period is equivalent to 1 time unit (the procedure typically can be performed within 1 hour).

[b]Unit price is $12.86 per unit, which includes the 2.8% increase to OHIP fees.

Table A26: Anesthesiologist Fees

Procedure	PVP	PBK	Source
Average procedure length, hours	1.0	1.0	M. Baerlocher, MD, email communication, March 13, 2024
Number of basic units	9	11	Schedule of Benefit (N570, N583)[38]
Number of time units[a]	4	4	Calculated based on average procedure length
Total number of units	13	15	Sum of basic and time units
Total billing[b]	**$206.96**	**$238.80**	

Abbreviations: PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Time units are calculated for every 15-minute period. During the first hour, each 15-minute period is equivalent to 1 time unit (the procedure typically can be performed within 1 hour).

[b]Unit price is $15.92 per unit, which includes the 2.8% increase to OHIP fees.

Table A27: Monthly Mean Difference in Utilities for PVP + CT Compared With CT

Month	Mean difference in utility	95% CI	Source	Weighted mean difference in utility[a]	95% CI	Source
Week 1	0.100	(0.01–0.19)	Figure 5	NA	NA	NA
1	0.100	(0.03–0.17)	Figure 5	0.100	(0.02–0.18)	Calculated[b]
2	0.090	(−0.035 to 0.215)	Calculated[c]	0.095	(−0.003 to 0.193)	Calculated[b]
3	0.080	(−0.1to 0.26)	Figure 5	0.085	(−0.068 to 0.238)	Calculated[b]
4	0.087	(−0.063 to 0.237)	Calculated[c]	0.083	(−0.082 to 0.248)	Calculated[b]
5	0.093	(−0.027 to 0.213)	Calculated[c]	0.090	(−0.045 to 0.225)	Calculated[b]
6	0.100	(0.01–0.19)	Figure 5	0.097	(−0.008 to 0.202)	Calculated[b]
7	0.100	(0.012–0.188)	Calculated[c]	0.100	(0.011–0.189)	Calculated[b]
8	0.100	(0.013–0.187)	Calculated[c]	0.100	(0.013–0.188)	Calculated[b]
9	0.100	(0.015–0.185)	Calculated[c]	0.100	(0.014–0.186)	Calculated[b]
10	0.100	(0.017–0.183)	Calculated[c]	0.100	(0.016–0.184)	Calculated[b]
11	0.100	(0.018–0.182)	Calculated[c]	0.100	(0.018–0.183)	Calculated[b]
12	0.100	(0.02–0.18)	Figure 5	0.100	(0.019–0.181)	Calculated[b]
13	0.098	(0.02–0.177)	Calculated[c]	0.099	(0.02–0.179)	Calculated[b]
14	0.097	(0.019–0.174)	Calculated[c]	0.098	(0.02–0.176)	Calculated[b]
15	0.095	(0.019–0.171)	Calculated[c]	0.096	(0.019–0.173)	Calculated[b]
16	0.093	(0.019–0.168)	Calculated[c]	0.094	(0.019–0.17)	Calculated[b]
17	0.092	(0.018–0.165)	Calculated[c]	0.093	(0.019–0.167)	Calculated[b]
18	0.090	(0.018–0.162)	Calculated[c]	0.091	(0.018–0.164)	Calculated[b]
19	0.088	(0.018–0.159)	Calculated[c]	0.089	(0.018–0.161)	Calculated[b]
20	0.087	(0.017–0.156)	Calculated[c]	0.088	(0.018–0.158)	Calculated[b]
21	0.085	(0.017–0.153)	Calculated[c]	0.086	(0.017–0.155)	Calculated[b]
22	0.083	(0.017–0.15)	Calculated[c]	0.084	(0.017–0.152)	Calculated[b]
23	0.082	(0.016–0.147)	Calculated[c]	0.083	(0.017–0.149)	Calculated[b]
24	0.080	(0.016–0.144)	Assumption[d], calculated[c]	0.081	(0.016–0.146)	Calculated[b]

Abbreviations: CI, confidence interval; CT, conservative treatment; NA, not applicable; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Weighted mean difference in utilities were defined as normal distributions.

[b]Weighted utilities were calculated as the average of the current month and the previous month.

[c]Missing monthly mean difference utilities were imputed using linear interpolation.

[d]Applied the same percentage change in mean difference in utility from 12 months to 24 months for PBK compared with CT in the FREE trial.

Table A28: Osteoporosis Medication Costs

Variable	Unit cost[a]	Quantity per patient	Total annual cost	Reference
Alendronate	$1.78	70 mg/wk	$92.58	Morin et al, 2023[146]; ODB formulary[154]
Risedronate	$11.19	150 mg/wk	$134.25	Morin et al, 2023[146]; ODB formulary[154]
Total annual cost of medications[a,b]			$226.18	Ontario Drug Programs reference manual[194]

[a]Medication costs include an 8% pharmacy mark-up and a 1-time $10 dispensing fee, assuming 4 dispensations per year.
[b]Represents the average cost to MOH assuming 76% of people qualify for the Ontario Drug Benefit program.

Table A29: Effect of Osteoporosis Medication on Subsequent OVCF

Model parameter	Value	Distribution	Reference
Relative risk of OVCF while on risedronate	0.61 (95% CI: 0.25–0.78)[a]	Log-normal	Barrioneuvo et al, 2019[195]
Relative risk of OVCF while on alendronate	0.57 (95% CI: 0.45–0.71)[a]	Log-normal	Barrioneuvo et al, 2019[195]

Abbreviations: CI, confidence interval; OVCF, osteoporotic vertebral compression fracture.
[a]Assume people stay on treatment for 5 years, after which there is a 5-year offset period in which the treatment effect diminishes to no effect.

Table A30: One-Year Societal Costs of OVCF for Scenario Analysis

Variable	Unit cost[a]	Quantity per patient	Total annual cost[a]	Reference
Unpaid caregiver time	NA	NA	$5,599.55	Hassan et al, 2020[168]
Lost productivity	NA	NA	$1,108.79	Hassan et al, 2020[168]
Out-of-pocket costs	NA	NA	$1,054.37	Hassan et al, 2020[168]
Medications	NA	NA	$2,204.27	Hassan et al, 2020[168]
Adverse events	NA	NA	$3,784.63	Hassan et al, 2020[168]
Physician visits and tests/procedures	NA	NA	$1,025.36	Hassan et al, 2020[168]
Allied health professional visits	NA	NA	$114.87	Hassan et al, 2020[168]
Total			**$14,891.84**	

Abbreviations: NA, not applicable; OVCF, osteoporotic vertebral compression fractures.
[a]Costs were converted from 2018 CAD to 2024 CAD using the Consumer Price Index.[155]

Table A31: Detailed Reference Case Analysis Results for OVCF Treatments

Strategy[a]	Average total costs (95% CrI)	Incremental costs[b]	Average total effects (95% CrI), QALYs	Incremental QALYs[b]	ICER vs. CT (95% CrI)/QALY	Sequential ICER (95% CrI)/QALY	Incremental NMB (95% CrI)[b,c,d] WTP $50,000/QALY	Incremental NMB (95% CrI)[b,c,d] WTP $100,000/QALY
CT	$6,101 ($4,938–$8,299)	NA	1.470 (1.435–1.497)	NA	NA	NA	NA	NA
PVP + CT	$17,501 ($13,905–$23,445)	$11,399 ($7,915–$16,096)	1.733 (1.688–1.777)	0.263 (0.226–0.302)	$43,324 ($35,008–$53,273)	$43,324 ($35,008–$53,273)	$1,757 (−$2,760 to $5,526)	$14,913 ($9,541–$19,927)
PBK + CT	$21,675 ($15,920–$30,245)	$15,574 ($10,066–$22,994)	1.706 (1.665–1.747)	0.236 (0.203–0.273)	$65,921 ($49,634–$84,382)	Dominated[e]	−$3,761 (−$10,977 to $1,833)	$8,051 ($735–$14,383)

Note: Some numbers may appear inexact due to rounding.

Abbreviations: CrI, credible interval; CT, conservative treatment; ICER, incremental cost-effectiveness ratio; NA, not applicable; NMB, net monetary benefit; OVCF, osteoporotic vertebral compression fractures; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QALY, quality-adjusted life-year; WTP, willingness to pay.

[a]Treatment strategies are ordered by average total costs, from lowest to highest.

[b]Incremental cost, QALYs, and NMB are compared with CT.

[c]Incremental NMB = incremental QALYs × WTP value – incremental cost.

[d]A positive increment NMB indicated the intervention can be considered cost-effective at that WTP value compared with the comparator.

[e]Dominated indicates PBK is more costly and less effective than PVP.

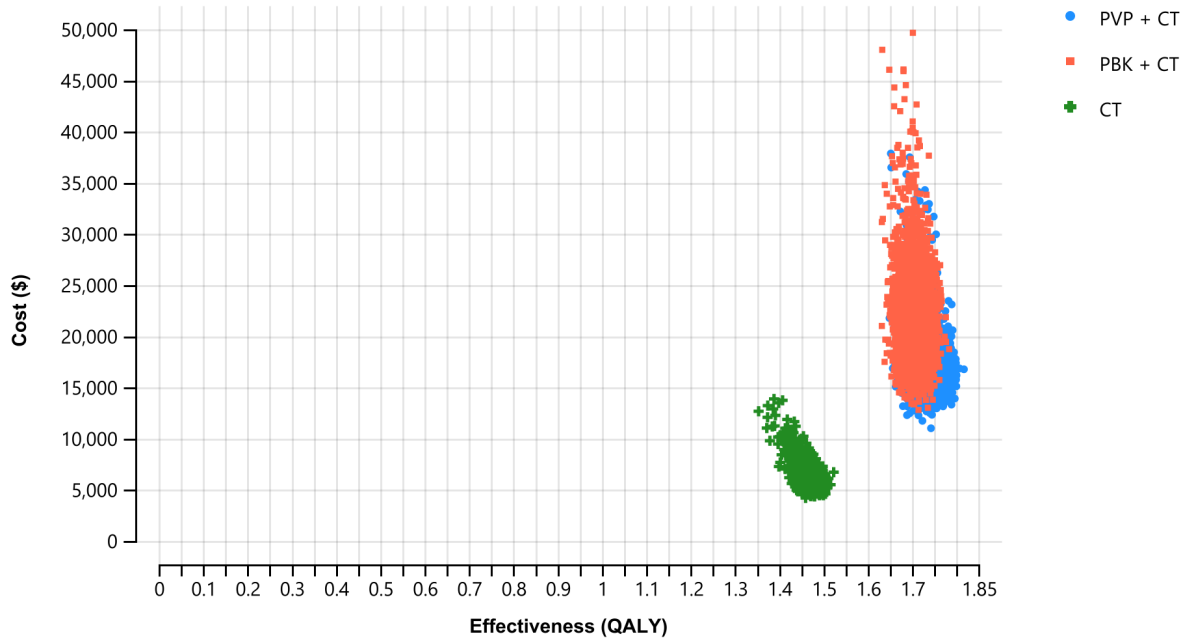

Figure A27: Cost-Effectiveness Scatterplot of Treatments for OVCF

A scatterplot of probabilistic results from 5,000 model simulations showing the average effectiveness (QALYs) on the horizontal x-axis from 0 to 1.85 QALYs and average cost ($) on the vertical y-axis from $0 to $50,000 per person for each treatment. The individual simulations for each PVP + CT and PBK + CT appear on the scatterplot as vertically elongated ovals with significant overlap on the right-middle of the scatterplot, indicating that they have similar costs and effectiveness. The simulations for CT appear as a smaller oval to the left and below PVP + CT and PBK + CT, indicating that is it less costly and less effective than the other interventions.

Abbreviations: CT, conservative treatment; OVCF, osteoporotic vertebral compression fractures; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QALY, quality-adjusted life year.

Table A32: Detailed Scenario Analysis Results

Scenario	Average total costs, $	Average total effects, QALYs	ICER vs. CT, $/QALY[a]	Sequential ICER, $/QALY[a]
Reference case				
CT	6,101	1.470	NA	NA
PVP + CT	17,501	1.733	43,324	43,324
PBK + CT	21,675	1.706	65,921	Dominated[b]
Reference case, 2-year time horizon				
CT	5,889	0.955	NA	NA
PVP + CT	16,922	1.172	50,870	50,870
PBK + CT	20,962	1.154	75,974	Dominated[b]
Reference case, lifetime time horizon				
CT	9,330	6.193	NA	NA
PVP + CT	26,308	6.556	46,844	46,844
PBK + CT	32,545	6.520	71,176	Dominated[b]
Scenario 1-1: source of PVP utility				

Scenario	Average total costs, $	Average total effects, QALYs	ICER vs. CT, $/QALY[a]	Sequential ICER, $/QALY[a]
CT	6,101	1.461	NA	NA
PVP + CT	17,501	1.675	53,118	53,118
PBK + CT	21,675	1.697	65,921	192,874
Scenario 1-2: source of PVP utility, lifetime time horizon				
CT	9,330	6.049	NA	NA
PVP + CT	26,308	6.345	57,321	57,321
PBK + CT	32,545	6.375	71,176	208,122
Scenario 2-1: duration of treatment effect, no offset period (benefits immediately end after 2 years)				
CT	9,330	6.249	NA	NA
PVP + CT	26,308	6.556	55,387	55,387
PBK + CT	32,545	6.531	82,484	Dominated[b]
Scenario 2-2: duration of treatment effect, infinite offset period (utilities stay at 2-year values indefinitely/no waning of treatment effect)				
CT	9,330	5.470	NA	NA
PVP + CT	26,308	6.556	15,631	15,631
PBK + CT	32,545	6.375	25,647	Dominated[b]
Scenario 2-3: 1-year treatment offset, all utilities go down to lowest 2-year value				
CT	6,101	1.425	NA	NA
PVP + CT	17,501	1.688	43,324	43,324
PBK + CT	21,675	1.662	65,921	Dominated[b]
Scenario 3-1: treatment effect on mortality, clinical review values, 3-year time horizon				
CT	6,101	1.470	NA	NA
PVP + CT	17,520	1.751	40,633	40,633
PBK + CT	21,631	1.672	76,706	Dominated[b]
Scenario 3-2: treatment effect on mortality, clinical review values, lifetime time horizon				
CT	9,330	6.193	NA	NA
PVP + CT	27,148	6.766	31,144	31,144
PBK + CT	31,498	6.213	1,117,017	Dominated[b]
Scenario 4-1: treatment effect on mortality, Hinde et al[161] values, 3-year time horizon				
CT	6,101	1.470	NA	NA
PVP + CT	17,518	1.749	40,823	40,823
PBK + CT	21,697	1.722	61,764	Dominated[b]
Scenario 4-2: treatment effect on mortality, Hinde et al[161] values, lifetime time horizon				
CT	9,330	6.193	NA	NA
PVP + CT	27,240	6.834	27,980	27,980
PBK + CT	33,699	6.796	40,442	Dominated[b]
Scenario 5-1: treatment effect on mortality, Edidin et al[162] value, 3-year time horizon				
CT	6,101	1.470	NA	NA
PVP + CT	17,520	1.751	40,578	40,578
PBK + CT	21,719	1.739	57,973	Dominated[b]
Scenario 5-2: treatment effect on mortality, Edidin et al[162] values, lifetime time horizon				
CT	9,330	6.193	NA	NA

Scenario	Average total costs, $	Average total effects, QALYs	ICER vs. CT, $/QALY[a]	Sequential ICER, $/QALY[a]
PVP + CT	27,343	6.863	26,900	26,900
PBK + CT	34,825	7.012	31,161	50,370
Scenario 6-1: treatment effect on subequent OVCF, clinical review values, 3-year time horizon				
CT	6,101	1.470	NA	NA
PVP + CT	18,173	1.731	46,154	46,154
PBK + CT	22,729	1.704	70,900	Dominated[b]
Scenario 6-2: treatment effect on subequent OVCF, clinical review values, lifetime time horizon				
CT	9,330	6.193	NA	NA
PVP + CT	28,402	6.551	53,409	53,409
PBK + CT	35,912	6.513	83,266	Dominated[b]
Scenario 7-1: treatment effect of PVP and PBK on subsequent OVCF, 3-year time horizon				
CT	6,101	1.470	NA	NA
PVP + CT	16,954	1.734	41,052	41,052
PBK + CT	21,001	1.707	62,771	Dominated[b]
Scenario 7-2: treatment effect of PVP and PBK on subsequent OVCF, lifetime time horizon				
CT	9,330	6.193	NA	NA
PVP + CT	24,480	6.561	41,190	41,190
PBK + CT	30,288	6.526	63,080	Dominated[b]
Scenario 8-1: treatment effect of PVP and PBK on subsequent OVCF, 3-year time horizon				
CT	6,101	1.470	NA	NA
PVP + CT	16,954	1.734	41,052	41,052
PBK + CT	21,001	1.707	62,771	Dominated[b]
Scenario 8-2: treatment effect of PVP and PBK on subsequent OVCF, lifetime time horizon				
CT	9,330	6.193	NA	NA
PVP + CT	27,943	6.552	51,947	51,947
PBK + CT	35,912	6.513	83,266	Dominated[a]
Scenario 9-1: treatment effect on mortality and subsequent OVCF, simultaneously, 3-year time horizon				
CT	6,101	1.470	NA	NA
PVP + CT	18,198	1.749	43,287	43,287
PBK + CT	22,669	1.670	82,531	Dominated[b]
Scenario 9-2: treatment effect on mortality and subsequent OVCF, simultaneously, lifetime time horizon				
CT	9,330	6.193	NA	NA
PVP + CT	29,509	6.765	35,326	35,326
PBK + CT	34,525	6.203	2,630,894	Dominated[b]
Scenario 10-1: treatment effect on serious adverse events				
CT	6,101	1.470	NA	NA
PVP + CT	17,501	1.733	43,324	43,324
PBK + CT	21,681	1.706	65,947	Dominated[b]
Scenario 10-2: treatment effect on serious adverse events				
CT	6,101	1.470	NA	NA
PVP + CT	17,527	1.733	43,424	43,424

Scenario	Average total costs, $	Average total effects, QALYs	ICER vs. CT, $/QALY[a]	Sequential ICER, $/QALY[a]
PBK + CT	21,704	1.706	66,042	Dominated[b]
Scenario 11-1: treatment effect on symptomatic cement leakage				
CT	6,101	1.470	NA	NA
PVP + CT	18,231	1.733	46,100	46,100
PBK + CT	21,675	1.706	65,921	Dominated[b]
Scenario 11-2: treatment effect on symptomatic cement leakage				
CT	6,101	1.470	NA	NA
PVP + CT	17,501	1.733	43,324	43,324
PBK + CT	21,404	1.706	64,775	Dominated[b]
Scenario 12: reduction in use of CT, reduced with PVP and PBK				
CT	6,101	1.469	NA	NA
PVP + CT	17,432	1.732	43,074	43,074
PBK + CT	21,594	1.705	65,619	Dominated[b]
Scenario 13: all subsequent OVCF treated with CT				
CT	6,116	1.503	NA	NA
PVP + CT	16,364	1.754	40,909	40,909
PBK + CT	20,113	1.728	62,443	Dominated[b]
Scenario 14: everyone starts osteoporosis medication				
CT	6,224	1.471	NA	NA
PVP + CT	17,408	1.733	42,677	42,677
PBK + CT	21,502	1.706	65,002	Dominated[b]
Scenario 15: computed tomography and bone scans used instead of MRI				
CT	6,101	1.470	NA	NA
PVP + CT	17,672	1.733	43,975	43,975
PBK + CT	21,847	1.706	66,647	Dominated[b]
Scenario 16: people in CT arm receive pre-procedure scans				
CT	6,169	1.470	NA	NA
PVP + CT	17,501	1.733	43,065	43,065
PBK + CT	21,675	1.706	65,633	Dominated[b]
Scenario 17-1: percentage of people with OVCF who are hospitalized, 10%				
CT	2,278	1.470	NA	NA
PVP + CT	10,567	1.733	31,501	31,501
PBK + CT	14,609	1.706	52,192	Dominated[b]
Scenario 17-2: percentage of people with OVCF who are hospitalized, 50%				
CT	9,560	1.470	NA	NA
PVP + CT	23,774	1.733	54,021	54,021
PBK + CT	28,068	1.706	78,342	Dominated[b]
Scenario 17-3: percentage of people with OVCF who are hospitalized, 0% (all outpatients)				
CT	458	1.470	NA	NA
PVP + CT	7,265	1.733	25,871	25,871
PBK + CT	11,244	1.706	45,655	Dominated[b]

Scenario	Average total costs, $	Average total effects, QALYs	ICER vs. CT, $/QALY[a]	Sequential ICER, $/QALY[a]
Scenario 18-1: starting age of cohort, 65 years				
CT	6,116	1.516	NA	NA
PVP + CT	17,541	1.785	42,354	42,354
PBK + CT	21,725	1.758	64,493	Dominated[b]
Scenario 18-2: starting age of cohort, 80 years				
CT	7,249	1.226	NA	NA
PVP + CT	20,633	1.458	57,858	57,858
PBK + CT	25,540	1.436	87,323	Dominated[b]
Scenario 19: percentage of females in cohort, 75%				
CT	6,127	1.476	NA	NA
PVP + CT	17,571	1.740	43,302	43,302
PBK + CT	21,761	1.713	65,888	Dominated[b]
Scenario 20-1: percentage of people with subsequent OVCF who visit the ED, 10%				
CT	6,058	1.470	NA	NA
PVP + CT	17,458	1.733	43,324	43,324
PBK + CT	21,632	1.706	65,921	Dominated[b]
Scenario 20-2: percentage of people with subsequent OVCF who visit the ED, 100%				
CT	6,155	1.470	NA	NA
PVP + CT	17,554	1.733	43,324	43,324
PBK + CT	21,729	1.706	65,921	Dominated[b]
Scenario 21-1: cost of outpatient CT (6-month duration of analgesic use)				
CT	6,127	1.469	NA	NA
PVP + CT	17,526	1.732	43,337	43,337
PBK + CT	21,701	1.706	65,954	Dominated[b]
Scenario 21-2: cost of outpatient CT (low estimate)				
CT	5,765	1.470	NA	NA
PVP + CT	17,164	1.733	43,324	43,324
PBK + CT	21,339	1.706	65,921	Dominated[b]
Scenario 21-3: cost of outpatient CT (high estimate)				
CT	6,532	1.470	NA	NA
PVP + CT	17,932	1.733	43,324	43,324
PBK + CT	22,106	1.706	65,921	Dominated[b]
Scenario 22-1: hospital day procedure cost of PVP and PBK				
CT	6,101	1.470	NA	NA
PVP + CT	16,798	1.733	40,652	40,652
PBK + CT	20,650	1.706	61,580	Dominated[b]
Scenario 22-2: hospital day procedure cost of PVP and PBK				
CT	6,101	1.470	NA	NA
PVP + CT	18,204	1.733	45,996	45,996
PBK + CT	22,700	1.706	70,261	Dominated[b]

Scenario	Average total costs, $	Average total effects, QALYs	ICER vs. CT, $/QALY[a]	Sequential ICER, $/QALY[a]
Scenario 23-1: inpatient costs of PVP and PBK, decreased				
CT	6,101	1.470	NA	NA
PVP + CT	15,057	1.733	34,037	34,037
PBK + CT	18,968	1.706	54,461	Dominated[b]
Scenario 23-2: inpatient costs of PVP and PBK, increased				
CT	6,101	1.470	NA	NA
PVP + CT	19,944	1.733	52,610	52,610
PBK + CT	24,383	1.706	77,381	Dominated[b]
Scenario 24-1: cost of hospitalization for OVCF, no procedure				
CT	4,399	1.470	NA	NA
PVP + CT	17,501	1.733	49,792	49,792
PBK + CT	21,675	1.706	73,125	Dominated[b]
Scenario 24-2: cost of hospitalization for OVCF, no procedure				
CT	14,861	1.470	NA	NA
PVP + CT	17,501	1.733	10,033	10,033
PBK + CT	21,675	1.706	28,843	Dominated[b]
Scenario 25: relative risk of subsequent OVCF given prior OVCF				
CT	6,912	1.459	NA	NA
PVP + CT	19,708	1.728	47,635	47,635
PBK + CT	24,404	1.701	72,193	Dominated[b]
Scenario 26: relative risk of mortality given prior OVCF				
CT	6,025	1.295	NA	NA
PVP + CT	17,292	1.534	47,164	47,164
PBK + CT	21,418	1.510	71,459	Dominated[b]
Scenario 27: applying a different rate of OVCF, 3-year time horizon				
CT	6,690	1.461	NA	NA
PVP + CT	19,108	1.729	46,459	46,459
PBK + CT	23,658	1.702	70,487	Dominated[b]
Scenario 28: Northern Health Travel Grant costs				
CT	6,101	1.470	NA	NA
PVP + CT	17,518	1.733	43,391	43,391
PBK + CT	21,693	1.706	65,995	Dominated[b]
Scenario 29: societal perspective				
CT	19,277	1.470	NA	NA
PVP + CT	30,676	1.733	43,324	43,324
PBK + CT	34,850	1.706	65,921	Dominated[b]

Abbreviations: CT, conservative treatment; ED, emergency department; ICER, incremental cost-effectiveness ratio; MRI, magnetic resonance imaging; NA, not applicable; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty; QALY, quality-adjusted life year.

[a]Results may appear inexact due to rounding.

[b]Dominated indicates PBK is more costly and less effective than PVP.

Table A33: Detailed average per-person annual cost estimates

	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $	Total, $[a]
CT	**5,669.96**	**227.12**	**219.52**	**211.90**	**204.58**	**6,533.08**
Physician fees	931.18	—	—	—	—	931.18
Hospital costs	4,321.55	—	—	—	—	4,321.55
Medication costs	18.67	—	—	—	—	18.67
Physiotherapy costs	163.91	—	—	—	—	163.91
Material & supplies[b]	—	—	—	—	—	—
Subsequent OVCF costs	234.65	227.12	219.52	211.90	204.58	1,097.77
PVP	**16,323.89**	**619.75**	**598.94**	**578.44**	**558.18**	**18,679.20**
Physician fees	3,661.75	—	—	—	—	3,661.75
Hospital costs	9,563.04	—	—	—	—	9,563.04
Medication costs[b]	18.67	—	—	—	—	18.67
Physiotherapy costs	163.91	—	—	—	—	163.91
Material & supplies	2,221.25	—	—	—	—	2,221.25
Adverse events costs	54.90	—	—	—	—	54.90
Subsequent OVCF costs	640.38	619.75	598.94	578.44	558.18	2,995.68
PBK	**20,223.22**	**764.16**	**739.32**	**713.64**	**688.76**	**23,129.10**
Physician fees	4,698.43	—	—	—	—	4,698.43
Hospital costs	11,533.59	—	—	—	—	11,533.59
Medication costs	18.67	—	—	—	—	18.67
Physiotherapy costs	163.91	—	—	—	—	163.91
Material & supplies[b]	2,629.23	—	—	—	—	2,629.23
Adverse events costs	389.32	—	—	—	—	389.32
Subsequent OVCF costs	790.06	764.16	739.32	713.64	688.76	3,695.94

Abbreviations: CT, conservative treatment; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Some numbers may appear inexact due to rounding.

[b]Material and supply costs were estimated by applying the ratio of the sum of direct costs of general supplies and direct patient costs specific to the total costs for PVP and PBK procedures in fiscal years 2020 – 2023 (IntelliHealth data accessed January 5, 2025).

Table A34: Population of Interest, Low Estimate for Scenario Analysis

Criteria	Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)
Ontario population (age ≥ 40 years)[a,169]	7,913,533	8,007,792	8,100,691	8,197,771	8,300,398
Osteoporotic spine fractures[b,147]	10,921	11,051	11,179	11,313	11,455
Symptomatic (painful), 100%	10,921	11,051	11,179	11,313	11,455
No response to conservative treatment, 10%	1,092	1,105	1,118	1,131	1,145

[a]Using low population projection estimate.

[b]Using lower 95% confidence interval.

Table A35: Population of Interest, High estimate for Scenario Analysis

Criteria	Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)
Ontario population (age ≥ 40 years)[a,169]	8,119,294	8,262,163	8,398,702	8,542,966	8,697,030
Osteoporotic spine fractures[b,147]	11,448	11,650	11,842	12,046	12,263
Symptomatic (painful), 100%	11,448	11,650	11,842	12,046	12,263
No response to conservative treatment, 47%	5,381	5,475	5,566	5,661	5,764

[a]Using high population projection estimate.
[b]Using upper 95% confidence interval.

Table A36: Lower Uptake of Vertebral Augmentation for Scenario Analysis

	Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)	Total
Current scenario						
Uptake	48%	48%	48%	48%	48%	
CT	1,152	1,169	1,185	1,203	1,221	**5,930**
PVP + CT	827	839	851	864	877	**4,258**
PBK + CT	233	237	241	243	247	**1,201**
Total population	2,212	2,245	2,277	2,310	2,345	**11,389**
New scenario						
Uptake (low)	48%	50%	55%	60%	65%	
CT	1,150	1,123	1,025	924	821	**5,043**
PVP + CT	828	926	1,064	1,213	1,372	**5,403**
PBK + CT	234	196	188	173	152	**943**
Total population	2,212	2,245	2,277	2,310	2,345	**11,389**

Abbreviations: CT, conservative treatment; PBK, balloon kyphoplasty; PVP, percutaneous vertebroplasty.

Table A37: Higher Uptake of Vertebral Augmentation for Scenario Analysis

	Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)	Total
Current scenario						
Uptake	48%	48%	48%	48%	48%	
CT	1,152	1,169	1,185	1,203	1,221	**5,930**
PVP + CT	827	839	851	864	877	**4,258**
PBK + CT	233	237	241	243	247	**1,201**
Total population	2,212	2,245	2,277	2,310	2,345	**11,389**
New scenario						
Uptake (high)	50%	75%	100%	100%	100%	
CT	1,106	561	0	0	0	**1,667**
PVP + CT	863	1,389	1,935	2,021	2,111	**8,319**
PBK + CT	243	295	342	289	234	**1,403**
Total population	2,212	2,245	2,277	2,310	2,345	**11,389**

Abbreviations: CT, conservative treatment; PBK, balloon kyphoplasty; PVP, percutaneous vertebroplasty.

Table A38: Distribution of PVP and PBK Remain Constant Over Time

	Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)	Total
Current scenario						
Uptake	48%	48%	48%	48%	48%	
CT	1,152	1,169	1,185	1,203	1,221	**5,930**
PVP + CT, 78%	827	839	851	864	877	**4,258**
PBK + CT, 22%	233	237	241	243	247	**1,201**
Total population	2,212	2,245	2,277	2,310	2,345	**11,389**
New scenario						
Uptake	50%	60%	70%	80%	90%	
CT	1,106	898	683	462	235	**3,384**
PVP + CT, 78%	863	1,051	1,243	1,441	1,646	**6,244**
PBK + CT, 22%	243	296	351	407	464	**1,761**
Total population	2,212	2,245	2,277	2,310	2,345	**11,389**

Abbreviations: CT, conservative treatment; PBK, balloon kyphoplasty; PVP, percutaneous vertebroplasty.

Table A39: Average Per-Person Annual Cost Estimates, All Subsequent OVCF Treated With CT

	Year 1, $	Year 2, $	Year 3, $	Year 4, $	Year 5, $	Total, $[a]
CT	**5,669.96**	**227.12**	**219.52**	**211.90**	**204.58**	**6,533.08**
Intervention costs	5,435.31	0.00	0.00	0.00	0.00	**5,435.31**
Subsequent OVCF costs	234.65	227.12	219.52	211.90	204.58	**1,097.77**
PVP + CT	**15,918.17**	**227.12**	**219.52**	**211.90**	**204.58**	**16,781.29**
Intervention costs	15,683.52	0.00	0.00	0.00	0.00	**15,683.52**
Subsequent OVCF costs	234.65	227.12	219.52	211.90	204.58	**1,097.77**
PBK + CT	**19,667.81**	**227.12**	**219.52**	**211.90**	**204.58**	**20,530.93**
Intervention costs	19,433.16	0.00	0.00	0.00	0.00	**19,433.16**
Subsequent OVCF costs	234.65	227.12	219.52	211.90	204.58	**1,097.77**

Abbreviations: CT, conservative treatment; OVCF, osteoporotic vertebral compression fracture; PBK, percutaneous balloon kyphoplasty; PVP, percutaneous vertebroplasty.

[a]Some numbers may appear inexact due to rounding.

Table A40: Detailed Budget Impact Analysis Results

	Budget impact, $[a,b]					
	Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)	Total[b]
Current scenario	24,753,206	26,071,900	27,365,383	28,640,129	29,938,922	136,769,538
Physician fees	5,197,931	5,274,856	5,350,418	5,424,998	5,509,373	26,757,576
Hospital costs	15,579,835	15,810,168	16,035,117	16,262,303	16,513,535	80,200,958
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,450,824	2,487,078	2,523,090	2,557,683	2,597,758	12,616,434
Adverse events costs	136,296	138,376	140,420	141,980	144,352	701,424
Cost of subsequent OVCF	984,367	1,951,507	2,900,661	3,831,431	4,745,731	14,413,697
New scenario	25,282,280	28,974,720	32,830,973	36,805,606	40,895,584	164,789,162
Physician fees	5,333,904	6,013,804	6,719,090	7,435,909	8,163,358	33,666,065
Hospital costs	15,840,649	17,228,641	18,662,404	20,122,600	21,608,734	93,463,028
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,557,081	3,088,628	3,637,341	4,198,732	4,772,813	18,254,594
Adverse events costs	142,165	152,919	167,310	178,647	186,108	827,149
Cost of subsequent OVCF	1,004,527	2,080,814	3,229,151	4,447,984	5,736,400	16,498,877
Budget impact	**529,074**	**2,902,821**	**5,465,590**	**8,165,477**	**10,956,662**	**28,019,624**
Physician fees	135,973	738,948	1,368,673	2,010,912	2,653,984	6,908,489
Medication costs	260,814	1,418,473	2,627,287	3,860,297	5,095,199	13,262,070
Physiotherapy costs	—	—	—	—	—	—
Material & supplies	—	—	—	—	—	—
Adverse events costs	106,257	601,550	1,114,250	1,641,048	2,175,054	5,638,160
Medication costs	5,870	14,543	26,890	36,666	41,756	125,725
Cost of subsequent OVCF	20,160	129,307	328,490	616,553	990,669	2,085,179

Abbreviation: OVCF, osteoporotic vertebral compression fracture.

[a]All costs in 2024 CAD.

[b]Results may appear inexact due to rounding.

Table A41: Detailed Budget Impact Analysis Results – Scenario 6

Scenario 6	Budget impact, $[a,b] Year 1 (2025)	Year 2 (2026)	Year 3 (2027)	Year 4 (2028)	Year 5 (2029)	Total[c]
Current scenario	**24,288,000**	**25,149,707**	**25,994,531**	**26,829,458**	**27,696,232**	**129,957,929**
Physician fees	5,197,931	5,274,856	5,350,418	5,424,998	5,509,373	26,757,576
Hospital costs	15,579,835	15,810,168	16,035,117	16,262,303	16,513,535	80,200,958
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,450,824	2,487,078	2,523,090	2,557,683	2,597,758	12,616,434
Adverse events costs	136,296	138,376	140,420	141,980	144,352	701,424
Cost of subsequent OVCF	519,162	1,029,314	1,529,810	2,020,760	2,503,042	7,602,088
New scenario	**24,796,914**	**27,923,221**	**31,131,631**	**34,378,382**	**37,662,226**	**155,892,374**
Physician fees	5,333,904	6,013,804	6,719,090	7,435,909	8,163,358	33,666,065
Hospital costs	15,840,649	17,228,641	18,662,404	20,122,600	21,608,734	93,463,028
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,557,081	3,088,628	3,637,341	4,198,732	4,772,813	18,254,594
Adverse events costs	142,165	152,919	167,310	178,647	186,108	827,149
Cost of subsequent OVCF	519,162	1,029,314	1,529,810	2,020,760	2,503,042	7,602,088
Budget impact	**508,914**	**2,773,514**	**5,137,100**	**7,548,924**	**9,965,993**	**25,934,445**
Physician fees	135,973	738,948	1,368,673	2,010,912	2,653,984	6,908,489
Hospital costs	260,814	1,418,473	2,627,287	3,860,297	5,095,199	13,262,070
Medication costs	—	—	—	—	—	—
Physiotherapy costs	—	—	—	—	—	—
Material & supplies	106,257	601,550	1,114,250	1,641,048	2,175,054	5,638,160
Adverse events costs	5,870	14,543	26,890	36,666	41,756	125,725
Cost of subsequent OVCF	—	—	—	—	—	—

Abbreviation: OVCF, osteoporotic vertebral compression fracture.

[a]All costs in 2024 CAD.

[b]All costs were calculated using the mean cost from Scenario 12, probabilistic results.

[c]Results may appear inexact due to rounding.

Table A42: Detailed Budget Impact Analysis Results – Scenario 7

	Budget impact, $[a,b]					
Scenario 7	**Year 1 (2025)**	**Year 2 (2026)**	**Year 3 (2027)**	**Year 4 (2028)**	**Year 5 (2029)**	**Total[c]**
Current scenario	**25,127,567**	**26,817,742**	**28,197,202**	**29,544,841**	**30,910,669**	**140,598,021**
Physician fees	5,197,931	5,274,856	5,350,418	5,424,998	5,509,373	26,757,576
Hospital costs	15,579,835	15,810,168	16,035,117	16,262,303	16,513,535	80,200,958
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,450,824	2,487,078	2,523,090	2,557,683	2,597,758	12,616,434
Adverse events costs	136,296	138,376	140,420	141,980	144,352	701,424
Cost of subsequent OVCF	1,358,729	2,697,349	3,732,480	4,736,143	5,717,478	18,242,180
New scenario	**25,672,859**	**29,821,782**	**33,907,604**	**38,115,456**	**42,444,361**	**169,962,061**
Physician fees	5,333,904	6,013,804	6,719,090	7,435,909	8,163,358	33,666,065
Hospital costs	15,840,649	17,228,641	18,662,404	20,122,600	21,608,734	93,463,028
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,557,081	3,088,628	3,637,341	4,198,732	4,772,813	18,254,594
Adverse events costs	142,165	152,919	167,310	178,647	186,108	827,149
Cost of subsequent OVCF	1,395,106	2,927,875	4,305,783	5,757,834	7,285,178	21,671,776
Budget impact	**545,291**	**3,004,039**	**5,710,402**	**8,570,615**	**11,533,693**	**29,364,041**
Physician fees	135,973	738,948	1,368,673	2,010,912	2,653,984	6,908,489
Hospital costs	260,814	1,418,473	2,627,287	3,860,297	5,095,199	13,262,070
Medication costs	—	—	—	—	—	—
Physiotherapy costs	—	—	—	—	—	—
Material & supplies	106,257	601,550	1,114,250	1,641,048	2,175,054	5,638,160
Adverse events costs	5,870	14,543	26,890	36,666	41,756	125,725
Cost of subsequent OVCF	36,377	230,526	573,303	1,021,691	1,567,699	3,429,596

Abbreviation: OVCF, osteoporotic vertebral compression fracture.

[a]All costs in 2024 CAD.

[b]All costs were calculated using the mean cost from Scenario 3-1, probabilistic results.

[c]Results may appear inexact due to rounding.

Table A43: Detailed Budget Impact Analysis Results – Scenario 8

	Budget impact, $[a,b]					
Scenario 8	**Year 1 (2025)**	**Year 2 (2026)**	**Year 3 (2027)**	**Year 4 (2028)**	**Year 5 (2029)**	**Total[c]**
Current scenario	**25,111,793**	**26,783,232**	**28,422,108**	**30,036,116**	**31,668,211**	**142,021,460**
Physician fees	5,197,931	5,274,856	5,350,418	5,424,998	5,509,373	26,757,576
Hospital costs	15,579,835	15,810,168	16,035,117	16,262,303	16,513,535	80,200,958
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,450,824	2,487,078	2,523,090	2,557,683	2,597,758	12,616,434
Adverse events costs	136,296	138,376	140,420	141,980	144,352	701,424
Cost of subsequent OVCF	1,342,955	2,662,839	3,957,386	5,227,418	6,475,020	19,665,619
New scenario	**25,626,549**	**29,587,823**	**33,636,314**	**37,727,726**	**41,859,676**	**168,438,088**
Physician fees	5,333,904	6,013,804	6,719,090	7,435,909	8,163,358	33,666,065
Hospital costs	15,840,649	17,228,641	18,662,404	20,122,600	21,608,734	93,463,028
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,557,081	3,088,628	3,637,341	4,198,732	4,772,813	18,254,594
Adverse events costs	142,165	152,919	167,310	178,647	186,108	827,149
Cost of subsequent OVCF	1,348,796	2,693,916	4,034,493	5,370,104	6,700,493	20,147,802
Budget impact	**514,755**	**2,804,591**	**5,214,206**	**7,691,610**	**10,191,465**	**26,416,628**
Physician fees	135,973	738,948	1,368,673	2,010,912	2,653,984	6,908,489
Hospital costs	260,814	1,418,473	2,627,287	3,860,297	5,095,199	13,262,070
Medication costs	—	—	—	—	—	—
Physiotherapy costs	—	—	—	—	—	—
Material & supplies	106,257	601,550	1,114,250	1,641,048	2,175,054	5,638,160
Adverse events costs	5,870	14,543	26,890	36,666	41,756	125,725
Cost of subsequent OVCF	5,842	31,077	77,107	142,686	225,472	482,183

Abbreviation: OVCF, osteoporotic vertebral compression fracture.

[a]All costs in 2024 CAD.

[b]All costs were calculated using the mean cost from Scenario 24-2, probabilistic results.

[c]Results may appear inexact due to rounding.

Table A44: Detailed Budget Impact Analysis Results – Scenario 9

	Budget impact, $[a,b]					
Scenario 9	**Year 1 (2025)**	**Year 2 (2026)**	**Year 3 (2027)**	**Year 4 (2028)**	**Year 5 (2029)**	**Total[c]**
Current scenario	**8,491,947**	**8,970,378**	**9,441,073**	**9,897,947**	**10,369,751**	**47,171,097**
Physician fees	2,241,439	2,274,754	2,307,629	2,338,644	2,375,513	11,537,980
Hospital costs	3,309,702	3,359,057	3,407,947	3,452,417	3,507,420	17,036,542
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,036,467	2,066,444	2,096,272	2,125,853	2,158,823	10,483,860
Adverse events costs	136,296	138,376	140,420	141,980	144,352	701,424
Cost of subsequent OVCF	364,091	721,833	1,073,129	1,417,318	1,755,471	5,331,842
New scenario	**8,821,746**	**10,702,785**	**12,702,310**	**14,757,421**	**16,860,680**	**63,844,941**
Physician fees	2,321,158	2,675,976	3,050,684	3,425,132	3,797,211	15,270,162
Hospital costs	3,452,951	4,054,607	4,696,017	5,331,325	5,955,473	23,490,373
Medication costs	41,307	41,916	42,506	43,125	43,783	212,637
Physiotherapy costs	362,646	367,998	373,171	378,609	384,388	1,866,812
Material & supplies	2,124,850	2,609,800	3,102,840	3,615,065	4,148,374	15,600,930
Adverse events costs	142,165	152,919	167,310	178,647	186,108	827,149
Cost of subsequent OVCF	376,668	799,568	1,269,782	1,785,518	2,345,342	6,576,878
Budget impact	**329,798**	**1,732,407**	**3,261,237**	**4,859,474**	**6,490,928**	**16,673,845**
Physician fees	79,718	401,222	743,055	1,086,488	1,421,698	3,732,182
Hospital costs	143,249	695,550	1,288,071	1,878,908	2,448,052	6,453,831
Medication costs	—	—	—	—	—	—
Physiotherapy costs	—	—	—	—	—	—
Material & supplies	88,384	543,356	1,006,568	1,489,212	1,989,551	5,117,071
Adverse events costs	5,870	14,543	26,890	36,666	41,756	125,725
Cost of subsequent OVCF	12,577	77,735	196,653	368,200	589,871	1,245,036

Abbreviation: OVCF, osteoporotic vertebral compression fracture.

[a]All costs in 2024 CAD.

[b]All costs were calculated using the mean cost from Scenario 17-3, probabilistic results.

[c]Results may appear inexact due to rounding.

Appendix 9: Sample Calculations

Transition Probability Calculations

Sample calculation of probability of subsequent OVCF for a 70-year-old woman in our population of interest in the first year after her initial OVCF:

$$Monthly\ rate\ of\ OVCF\ (general\ population) = \frac{184}{100{,}000}\ x\ \frac{1}{12} = 0.000153$$

$$Monthly\ rate\ of\ OVCF\ (population\ of\ interest) = Monthly\ rate\ of\ OVCF\ (general\ population) x\ RR_{osteo}\ x\ RR_{prior\ OVCF}$$

$$Monthly\ rate\ of\ OVCF\ (population\ of\ interest) = 0.000153\ x\ 6.86\ x\ 2.34 = 0.00246$$
$$Monthly\ probability\ of\ OVCF\ (population\ of\ interest) = 1 - \exp(-0.00246\ x\ 1) = 0.00246$$

Where:

- RR_{osteo} is the relative risk of an OVCF in people with osteoporosis compared to people without osteoporosis (2.5 SD reduction in BMD),
- $RR_{prior\ OVCF}$ is the relative risk of an OVCF in people with a prior OVCF compared to people without a prior OVCF,
- $RR_{osteo} = \exp(2.5\beta)$ where β = ln(2.16), the regression coefficient for 1 SD reduction in BMD at femoral neck from Papaioannou et al,[145] and
- $RR_{osteo} = 6.86$

Sample calculation of probability of death for a 70-year-old woman in our population of interest in the first year after her initial OVCF:

$$Annual\ probability\ of\ death\ (general\ population) = 0.01134$$

$$Annual\ rate\ of\ death\ (general\ population) = \frac{-\ln(1 - 0.01134)}{1} = 0.0114$$

$$Monthly\ rate\ of\ death\ (general\ population) = 0.0114\ x\ \frac{1}{12} = 0.00095$$

$$Monthly\ rate\ of\ death\ (population\ of\ interest) = 0.00095\ x\ 1.1\ x\ 1.27 = 0.00133$$

Where our population of interest are people with low BMD and a prior OVCF.

Health Utility Calculations

Health state utility values

Utility values from the RCTs were adjusted for age using the multiplicative method.[152]

$\frac{U_{T\_t}}{U_{T\_c}} = \frac{U_{G\_t}}{U_{G\_c}}$, then $U_{T\_c} = U_{T\_t}\ \frac{U_{G\_c}}{U_{G\_t}}$

Where:

- U_{T_t} is the utility of the trial participants at their age during the trial
- U_{T_c} is the utility of the trial participants at their current age
- U_{G_t} is the utility of the general population at their age during the trial
- U_{G_c} is the utility of the general population at their current age

Under the assumption of proportional changes in utility.

The baseline values reported in the trial represent people with a mean age between 70 and 74 years.[100]

A sample calculation using the utility value for CT from the FREE trial[100] (0.47) and the utility value for women between 70 and 74 years of age from Guertin et al[151] (0.831).

$$U_{T\_c} = \ 0.47\left(\frac{0.831}{0.831}\right) = 0.47$$

We obtained the value from the trial because we consider people the same age as those in the trial. We can apply this same formula for women between 80 and 84 years of age using the utility value 0.736 from Guertin et al.[151]

$$U_{T\_c} = \ 0.47\left(\frac{0.736}{0.831}\right) = 0.42$$

As anticipated, the utility is lower for women 10 years older.

Appendix 10: Letter of Information

LETTER OF INFORMATION

Ontario Health

Ontario Health is conducting a review of **Percutaneous Vertebroplasty and Balloon Kyphoplasty for Painful Osteoporotic Vertebral Compression Fractures (OVF).** The purpose is to better understand how this technique can be publicly funded in Ontario.

An important part of this review involves gathering perspectives of patients and caregivers of those who have been diagnosed and/or managed with OVCF and who may or may not have undergone PVP or PBK.

WHAT DO YOU NEED FROM ME

- ✓ Willingness to share your story
- ✓ 30-40 minutes of your time for a phone interview
- ✓ Permission to audio- (not video-) record the interview

What Your Participation Involves

If you agree to share your experiences, you will be asked to have an interview with Ontario Health (OH) staff. OH staff will contact interested participants by collecting contact information (i.e., email address and/or phone number) to set up an interview. The interview will last about 30-40 minutes. It will be held over the telephone. With your permission, the interview will be audio-taped. The interviewer will ask you questions about your or your loved one's condition and your perspectives about your cancer diagnosis and treatment options in Ontario. Participation is voluntary. You may refuse to participate, refuse to answer any questions or withdraw before or at any point during your interview. Withdrawal will in no way affect the care you receive.

Confidentiality

All information you share will be kept confidential and your privacy will be protected except as required by law. The results of this review will be published, however no identifying information will be released or published. Any records containing information from your interview will be stored securely until project completion. After completion of the project, the records will be destroyed. If you are sending us personal information by email, please be aware that electronic communication is not always secure and can be vulnerable to interception.

Ontario Health is designated an "institution" by the *Freedom of Information and Protection of Privacy Act* (FIPPA) and is collecting your personal information pursuant to FIPPA and the *Connecting Care Act, 2019* to support the Health Technology Assessment Program. If you have any questions regarding Ontario Health's collection and use of personal information for the purposes of this program, please contact Team Lead, Jigna Mistry noted below.

Risks to participation

There are no known physical risks to participating. Some participants may experience discomfort or anxiety after speaking about their experience.

DOCUMENTATION OF INFORMED CONSENT

We will give you a copy of this informed consent form after you and the OH staff have signed and dated it.

By signing this form, you confirm that:

- You agree to participate in this interview.
- You understand that your participation is voluntary.
- You understand the purpose, activities, risks and benefits of participating in this interview.
- You authorize the OH staff to use your data as explained in this form.
- OH staff have answered your questions to your satisfaction.

Please check the appropriate boxes:

- You give permission to the OH staff to audio record your interview: YES ☐ ☐ NO

Name of Participant (please print): _____

Signature of Participant (please sign): _____

Name of OH Staff: _____

Signature of OH Staff: _____

Place: _____ Date: _____

Note: For participants who are unable to electronically sign the consent form with their permission to participate in this interview, OH staff will audio-record participants' consent prior to their interview and retain a record of participants' verbal consent through OH's dedicated secure network drive.

Risks to participation

There are no known physical risks to participating. Some participants may experience discomfort or anxiety after speaking about their experience.

Appendix 11: Interview Guide

Interview Guide

Questions

1. Can you describe your diagnosis journey with osteoporosis?
2. What are your symptoms?
3. What is the impact of OVC on your day to day life, social life, work, relationships and quality of life?
4. What treatment options have you explored? (probe: government funded physiotherapy?)
5. Are you aware of vertebroplasty?
6. Do you have experience with vertebroplasty?

If yes,

1. Do you know if you had PVP or PBK?
2. What was the journey to get referral for this treatment?
3. What was your overall experience with the treatment? (probe: hospital stay, side effects, recovery time)
4. Were there any barriers for you to access this treatment? (probe: out-of-pocket cost for treatment)
5. What was the impact of this treatment on your symptoms?
6. What was the impact of treatment on your quality of life?

If no,

1. Would you be interested in getting this treatment? Why/why not?
2. What are your decision making factors for considering this treatment?

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