THE TREATMENT OF SYMPTOMATIC OSTEOPOROTIC SPINAL COMPRESSION FRACTURES

GUIDELINE AND EVIDENCE REPORT

Adopted by the American Academy of Orthopaedic Surgeons
Board of Directors
September 24, 2010

Disclaimer
This Clinical Practice Guideline was developed by an AAOS physician volunteer Work Group based on a systematic review of the current scientific and clinical information and accepted approaches to treatment and/or diagnosis. This Clinical Practice Guideline is not intended to be a fixed protocol, as some patients may require more or less treatment or different means of diagnosis. Clinical patients may not necessarily be the same as those found in a clinical trial. Patient care and treatment should always be based on a clinician's independent medical judgment, given the individual patient's clinical circumstances.

Disclosure Requirement
In accordance with AAOS policy, all individuals whose names appear as authors or contributors to Clinical Practice Guideline filed a disclosure statement as part of the submission process. All panel members provided full disclosure of potential conflicts of interest prior to voting on the recommendations contained within this Clinical Practice Guidelines.

Funding Source
This Clinical Practice Guideline was funded exclusively by the American Academy of Orthopaedic Surgeons who received no funding from outside commercial sources to support the development of this document.

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Published 2010 by the American Academy of Orthopaedic Surgeons
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Rosemont, IL 60018
First Edition
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Summary of Recommendations

The following is a summary of the recommendations in the AAOS' clinical practice guideline, The Treatment of Symptomatic Osteoporotic Spinal Compression fractures. This summary does not contain rationales that explain how and why these recommendations were developed nor does it contain the evidence supporting these recommendations. All readers of this summary are strongly urged to consult the full guideline and evidence report for this information. We are confident that those who read the full guideline and evidence report will see that the recommendations were developed using systematic evidence-based processes designed to combat bias, enhance transparency, and promote reproducibility.

This summary of recommendations is not intended to stand alone. Treatment decisions should be made in light of all circumstances presented by the patient. Treatments and procedures applicable to the individual patient rely on mutual communication between patient, physician, and other healthcare practitioners.

1. We suggest patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms suggesting an acute injury (0-5 days after identifiable event or onset of symptoms) and who are neurologically intact be treated with calcitonin for 4 weeks.

   Strength of Recommendation: Moderate

   Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.

   Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

2. Ibandronate and strontium ranelate are options to prevent additional symptomatic fractures in patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms.

   Strength of Recommendation: Limited

   Description: Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single "Moderate" quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

   Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.

3. We are unable to recommend for or against bed rest, complementary and alternative medicine, or opioids/analgesics for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

   Strength of Recommendation: Inconclusive

   Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

   Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

4. It is an option to treat patients who present with an osteoporotic spinal compression fracture at L3 or L4 on imaging with correlating clinical signs and symptoms suggesting an acute injury and who are neurologically intact with an L2 nerve root block.

   Strength of Recommendation: Limited

   Description: Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single "Moderate" quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

   Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.

5. We are unable to recommend for or against treatment with a brace for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

   Strength of Recommendation: Inconclusive

   Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

   Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

6. We are unable to recommend for or against a supervised or unsupervised exercise program for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

   Strength of Recommendation: Inconclusive

   Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

   Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

7. We are unable to recommend for or against electrical stimulation for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

   Strength of Recommendation: Inconclusive

   Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

   Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

8. We recommend against vertebroplasty for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

   Strength of Recommendation: Strong

   Description: Evidence is based on two or more “High” strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a strong negative recommendation), and that the strength of the supporting evidence is high.

   Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

9. Kyphoplasty is an option for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

   Strength of Recommendation: Limited

   Description: Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single "Moderate" quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

   Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.

10. We are unable to recommend for or against improvement of kyphosis angle in the treatment of patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms.

    Strength of Recommendation: Inconclusive

    Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

    Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

11. We are unable to recommend for or against any specific treatment for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are not neurologically intact.

    Strength of Recommendation: Inconclusive

    Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

    Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

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Peer Review

Participation in the AAOS peer review process does not constitute an endorsement of this guideline by the participating organization.

The following seven organizations participated in peer review of this clinical practice guideline and gave their explicit consent to have their names listed in this document:

American Academy of Physical Medicine and Rehabilitation (AAPMR)

American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS Joint Section)

American College of Radiology (ACR)

AO Spine International

International Spine Intervention Society (ISIS)

National Osteoporosis Foundation (NOF)

North American Spine Association (NASS)

Participation in the AAOS peer review process does not constitute an endorsement of this guideline by the participating organization.

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I. INTRODUCTION

OVERVIEW

This clinical practice guideline is based on a systematic review of published studies on the treatment of symptomatic osteoporotic spinal compression fractures in adults. In addition to providing practice recommendations, this guideline also highlights gaps in the literature and areas that require future research.

This guideline is intended to be used by all appropriately trained surgeons and all qualified physicians managing the treatment of symptomatic osteoporotic spinal compression fractures. It is also intended to serve as an information resource for decision makers and developers of practice guidelines and recommendations.

GOALS AND RATIONALE

The purpose of this clinical practice guideline is to help improve treatment based on the current best evidence. Current evidence-based medicine (EBM) standards demand that physicians use the best available evidence in their clinical decision making. To assist in this, this clinical practice guideline consists of a systematic review of the available literature regarding the treatment of symptomatic osteoporotic spinal compression fractures. The systematic review detailed herein was conducted between March 2009 and February 2010 and demonstrates where there is good evidence, where evidence is lacking, and what topics future research must target in order to improve the treatment of patients with symptomatic osteoporotic spinal compression fractures. AAOS staff and the physician work group systematically reviewed the available literature and subsequently wrote the following recommendations based on a rigorous, standardized process.

Musculoskeletal care is provided in many different settings by many different providers. We created this guideline as an educational tool to guide qualified physicians through a series of treatment decisions in an effort to improve the quality and efficiency of care. This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

INTENDED USERS

This guideline is intended to be used by orthopaedic surgeons and all qualified physicians managing patients with symptomatic osteoporotic spinal compression fractures. Typically, orthopaedic surgeons will have completed medical training, a qualified residency in orthopaedic surgery, and some may have completed additional sub-specialty training. Insurance payers, governmental bodies, and health-policy decision-makers may also find this guideline useful as an evolving standard of evidence regarding treatment of symptomatic osteoporotic spinal compression fractures.

Treatment for symptomatic osteoporotic spinal compression fractures is based on the assumption that decisions are predicated on patient and physician mutual communication with discussion of available treatments and procedures applicable to the individual patient. Once the patient has been informed of available therapies and has discussed these options with his/her physician, an informed decision can be made. Clinician input based on experience with conservative management and the clinician's surgical experience and skills increases the probability of identifying patients who will benefit from specific treatment options.

PATIENT POPULATION

This document addresses the treatment of symptomatic osteoporotic spinal compression fractures in adults (defined as patients 18 years of age and older).

ETIOLOGY

Symptomatic osteoporotic spinal compression fractures are a result of osteoporosis.

INCIDENCE

Symptomatic osteoporotic spinal compression fractures are a common occurrence. About 750,000 new vertebral fractures occur each year in the United States.[1]

BURDEN OF DISEASE

The economic burden of treating incident osteoporotic fractures was estimated at $17 billion in 2005.[2]

EMOTIONAL AND PHYSICAL IMPACT

Symptomatic osteoporotic spinal compression fractures cause pain, loss of physical function, and are associated with increased mortality.

POTENTIAL BENEFITS, HARMS, AND CONTRAINDICATIONS

The aim of treatment is pain relief and recovery of mobility. Most treatments are associated with some known risks, especially invasive and operative treatments. In addition, contraindications vary widely based on the treatment administered. Therefore, discussion of available treatments and procedures applicable to the individual patient rely on mutual communication between the patient and physician, weighing the potential risks and benefits for that patient.

II. METHODS

This clinical practice guideline and the systematic review upon which it is based evaluate the effectiveness of treatments for symptomatic osteoporotic spinal compression fractures. This section describes the methods used to prepare this guideline and systematic review, including search strategies used to identify literature, criteria for selecting eligible articles, determining the strength of the evidence, data extraction, methods of statistical analysis, and the review and approval of the guideline. The methods used to perform this systematic review were employed to minimize bias in the selection, appraisal, and analysis of the available evidence.[3, 4] These processes are vital to the development of reliable, transparent, and accurate clinical recommendations for treating symptomatic osteoporotic spinal compression fractures.

This guideline and systematic review were prepared by the AAOS Treatment of Symptomatic Osteoporotic Spinal Compression Fractures guideline work group with the assistance of the AAOS Clinical Practice Guidelines Unit in the Department of Research and Scientific Affairs at the AAOS (Appendix I).

To develop this guideline, the work group held an introductory meeting to develop the scope of the guideline on March 28, 2009. Upon completion of the systematic review, the work group met again on February 27 and 28, 2010 to write and vote on the final recommendations and rationales for each recommendation. The resulting draft guidelines were then peer-reviewed, subsequently sent for public commentary, and then sequentially approved by the AAOS Evidence Based Practice Committee, AAOS Guidelines and Technology Oversight Committee, AAOS Council on Research, Quality Assessment, and Technology, and the AAOS Board of Directors (see Appendix II for a description of the AAOS bodies involved in the approval process)

FORMULATING PRELIMINARY RECOMMENDATIONS

The work group began work on this guideline by constructing a set of preliminary recommendations. These recommendations specify [what] should be done in [whom], [when], [where], and [how often or how long]. They function as questions for the systematic review, not as final recommendations or conclusions. Preliminary recommendations are almost always modified on the basis of the results of the systematic review. Once established, these *a priori* preliminary recommendations cannot be modified until the final work group meeting, they must be addressed by the systematic review, and the relevant review results must be presented in the final guideline.

STUDY SELECTION CRITERIA

We developed *a priori* article inclusion criteria for our review. These criteria are our "rules of evidence" and articles that do not meet them are, for the purposes of this guideline, not evidence.

To be included in our systematic reviews (and hence, in this guideline) an article had to be a report of a study that:

Investigates osteoporotic spinal compression fracture patients

- is a full article report of a clinical study (i.e., retrospective case series, medical records review, meeting abstracts, historical articles, editorials, letters, and commentaries are excluded)
- was published in English
- was published in or after 1966
- appeared in a peer-reviewed publication
- enrolled 10 or more patients per group
- presented results quantitatively
- enrolled patients 18 years of age or older (100% of study population)
- is not an in vitro, biomechanical, or cadaver study
- excluded the following patients (unless results were reported separately):
  osteogenesis imperfecta (OI)
  solid metastatic tumors of the spine
- for any given follow-up time point in any included study, there must be ≥ 50% patient follow-up (if the follow-up is >50% but <80%, the study quality will be downgraded by one Level)
- results reported as "post-hoc subgroup analyses" will be excluded [5]

When a study's "duration of symptoms" is not the same as those examined by the work group (i.e. 0-2 weeks, 2-6 weeks, etc.) the study will be assigned to the appropriate "duration of symptoms" group based upon the mean duration of symptoms. If a range rather than mean is provided, the higher end of the range will dictate which "duration of symptoms" group the study will be assigned to. For example, a study reporting patient symptoms of 0-4 weeks would be included in the time frame "2-6 weeks" created by the work group.

When considering studies for inclusion, we included only the best available evidence. Accordingly, we first included Level I evidence. In the absence of two or more studies of this Level, we sequentially searched for and included Level II through Level IV evidence, and did not proceed to a lower level if there were two or more studies of a higher level. For example, if there were two Level II studies that addressed a recommendation, we did not include Level III or IV studies.

OUTCOMES CONSIDERED

Clinical studies often report many different outcomes. For this guideline, patient-oriented outcomes are included wherever possible. If patient-oriented outcomes were not available surrogate/intermediate outcomes were considered. Surrogate outcome measures are laboratory measurements or another physical sign used as substitutes for a clinically meaningful end point that measures directly how a patient feels, functions, or survives.[6] Radiographic results are an example of a surrogate outcome.

For outcomes measured using "paper and pencil" instruments (e.g. the visual analogue scale), the results using validated instruments are considered the best available evidence. In the absence of results using validated instruments, results using non-validated instruments are considered as the best available evidence and the strength of the recommendation is lowered. For this guideline, all outcomes we reported were validated in a spine patient population.

MINIMAL CLINICALLY IMPORTANT IMPROVEMENT

Wherever possible, we considered the effects of treatments in terms of the minimal clinically important improvement (MCII) in addition to whether their effects were statistically significant. The MCII is the smallest clinical change that is important to patients, and recognizes the fact that there are some treatment-induced statistically significant improvements that are too small to matter to patients. The values we used for MCIIs are derived from a published study investigating the Visual Analogue Scale, the Numerical Rating Scale, the Oswestry Disability Index, and the Roland Disability Questionnaire;[7] a study investigating the Physical Component Summary of the SF-36;[8] a study investigating the Assessment of Quality of Life instrument (AQoL);[9] and a study investigating the EQ-5D instrument.[10]

Table 1 MCII of outcomes

Outcome Measure	MCII (points)
Pain – VAS (0-100)	15
Pain – NRS (0-10)	2
Oswestry Disability Index	10
Roland-Morris Disability Questionnaire	5
SF-36 Physical Component Summary	4.9
AQoL	0.06
EQ-5D	0.074

When possible we describe the results of studies using terminology based on that of Armitage, et al.[11] The associated descriptive terms in this guideline and the conditions for using each of these terms, are outlined in Table 2.

Table 2 Descriptive terms for results with MCII

Descriptive Term	Condition for Use
Clinically Important	Statistically significant and lower confidence limit > MCII
Possibly Clinically Important	Statistically significant and confidence intervals contain the MCII
Not Clinically Important	Statistically significant and upper confidence limit < MCII
Negative	Not statistically significant and upper confidence limit < MCII
Inconclusive	Not statistically significant but confidence intervals contain the MCII

When MCII values from the specific guideline patient population was not available, we used values from the most closely related population that has published data available. We acknowledge that there can be variance in the MCII from disease to disease as well as what individual patients consider improvement. For this guideline, we included MCII values for pain and disability from studies including patients with low back pain, the MCII values cited for the SF-36 PCS are derived from patients who were treated with lumbar spine surgery and the MCII for the quality of life values are from studies that included a variety of conditions.[7,8,9,10]

LITERATURE SEARCHES

We attempted to make our searches for articles comprehensive. Using comprehensive literature searches ensures that the evidence we considered for this guideline is not biased for (or against) any particular point of view.

We searched for articles published from January 1966 to December 31, 2009. We searched four electronic databases; PubMed, EMBASE, CINAHL, and The Cochrane Central Register of Controlled Trials. Strategies for searching electronic databases were constructed by a Medical Librarian using previously published search strategies to identify relevant studies.[12-18]

We supplemented searches of electronic databases with manual screening of the bibliographies of all retrieved publications. We also searched the bibliographies of recent systematic reviews and other review articles for potentially relevant citations. Finally, work group members provided a list of potentially relevant studies that were not identified by our searches. All articles identified were subject to the study selection criteria listed above.

The study attrition diagram in Appendix III provides details about the inclusion and exclusion of the studies considered for this guideline. The search strategies used to identify these studies are provided in Appendix IV.

DATA EXTRACTION

Data elements extracted from studies were defined in consultation with the physician work group. The elements extracted are shown in Appendix V. Evidence tables were constructed to summarize the best evidence pertaining to each preliminary recommendation. Disagreements about the accuracy of extracted data were resolved by consensus and consulting the work group.

JUDGING THE QUALITY OF EVIDENCE

Determining the quality of the included evidence is vitally important when preparing any evidence-based work product. Doing so conveys the amount of confidence one can have in any study's results. One has more confidence in high quality evidence than in low quality evidence.

Assigning a level of evidence on the basis of study design plus other quality characteristics ties the levels of evidence we report more closely to quality than levels of evidence based only on study design. Because we tie quality to levels of evidence, we are able to characterize the confidence one can have in their results. Accordingly, we characterize the confidence one can have in Level I evidence as high, the confidence one can have in Level II and III evidence as moderate, and the confidence one can have in Level IV and V evidence as low. Similarly, throughout the guideline we refer to Level I evidence as reliable, Level II and III evidence as moderately reliable, and Level IV and V evidence as not reliable.

TREATMENT STUDIES

In studies investigating the result of treatment, we assessed the quality of the evidence for each outcome at each time point reported in a study. We did not simply assess the overall quality of a study. Our approach follows the recommendations of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) working group[19] as well as others.[20]

We evaluated quality on a per outcome basis rather than a per study basis because quality is not necessarily the same for all outcomes and all follow-up times reported in a study. For example, a study might report results immediately after patients received a given treatment and after some period of time has passed. Often, nearly all enrolled patients contribute data at early follow-up times but, at much later follow-up times, only a few patients may contribute data. One has more confidence in the earlier data than in the later data. The fact that we would assign a higher quality score to the earlier results reflects this difference in confidence.

We assessed the quality of treatment studies using a two step process. First, we assigned a level of evidence to all results reported in a study based solely on that study's design. Accordingly, all data presented in randomized controlled trials were initially categorized as Level I evidence, all results presented in non-randomized controlled trials and other

prospective comparative studies were initially categorized as Level II, all results presented in retrospective comparative and case-control studies were initially categorized as Level III, and all results presented in prospective case-series reports were initially categorized as Level IV. We next assessed each outcome at each reported time point using a quality questionnaire and, when quality standards were not met, downgraded the level of evidence (for this outcome at this time point) by one level (see Appendix VI).

DEFINING THE STRENGTH OF THE RECOMMENDATIONS

Judging the quality of evidence is only a stepping stone towards arriving at the strength of a guideline recommendation. Unlike Levels of Evidence (which apply only to a given result at a given follow-up time in a given study) strength of recommendation takes into account the quality, quantity, and applicability of the available evidence. Strength also takes into account the trade-off between the benefits and harms of a treatment or diagnostic procedure, and the magnitude of a treatment's effect.

Strength of recommendation expresses the degree of confidence one can have in a recommendation. As such, the strength expresses how possible it is that a recommendation will be overturned by future evidence. It is very difficult for future evidence to overturn a recommendation that is based on many high quality randomized controlled trials that show a large effect. It is much more likely that future evidence will overturn recommendations derived from a few small case series. Consequently, recommendations based on the former kind of evidence are given a high strength of recommendation and recommendations based on the latter kind of evidence are given a low strength.

To develop the strength of a recommendation, AAOS staff first assigned a preliminary strength for each recommendation that took only the quality and quantity of the available evidence into account (see Table 3). Work group members then modified the preliminary strength using the 'Form for Assigning Strength of Recommendation (Interventions)' shown in Appendix VII.

Table 3 Strength of Recommendation Descriptions

Statement Rating	Description of Evidence Strength	Implication for Practice
Strong	Evidence is based on two or more "High" strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a strong negative recommendation), and that the strength of the supporting evidence is high.	Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.
Moderate	Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.	Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.
Limited	Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single Moderate quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.	Practitioners should be cautious in deciding whether to follow a recommendation classified as **Limited**, and should exercise judgment and be alert to emerging publications that report evidence. Patient preference should have a substantial influencing role.
Inconclusive	Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.	Practitioners should feel little constraint in deciding whether to follow a recommendation labeled as **Inconclusive** and should exercise judgment and be alert to future publications that clarify existing evidence for determining balance of benefits versus potential harm. Patient preference should have a substantial influencing role.
Consensus[1]	The supporting evidence is lacking and requires the work group to make a recommendation based on expert opinion by considering the known potential harm and benefits associated with the treatment. A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria.	Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus,** although they may set boundaries on alternatives. Patient preference should have a substantial influencing role.

[1] The AAOS will issue a consensus-based recommendation only when the service in question has virtually no associated harm and is of low cost (e.g. a history and physical) or when not establishing a recommendation could have catastrophic consequences.

Each recommendation was written using language that accounts for the final strength of the recommendation. This language, and the corresponding strength, is shown in Table 4.

Table 4 AAOS guideline language

Guideline Language	Strength of Recommendation
We ***recommend***	Strong
We ***suggest***	Moderate
option	Limited
We are ***unable to recommend for or against***	Inconclusive
In the absence of reliable evidence, it is the ***opinion*** of this work group*	Consensus*

* *Consensus based recommendations are made according to specific criteria. These criteria can be found in Appendix VI.

CONSENSUS DEVELOPMENT

The recommendations and their strength were voted on using a structured voting technique known as the nominal group technique.[21] We present details of this technique in Appendix VIII. Voting on guideline recommendations was conducted using a secret ballot and work group members were blinded to the responses of other members. If disagreement between work group members was significant, there was further discussion to see whether the disagreement(s) could be resolved. Up to three rounds of voting were held to attempt to resolve disagreements. If disagreements were not resolved following three voting rounds, no recommendation was adopted. Lack of agreement is a reason that the strength for some recommendations is labeled "Inconclusive."

STATISTICAL METHODS

When possible the results of statistical analysis conducted by the AAOS Clinical Practice Guidelines Unit using STATA 10.0 (StataCorp LP, College Station, Texas) are reported. The program was used to determine the magnitude of the treatment effect. For data reported as means (and associated measures of dispersion) the mean difference between groups was calculated. For proportions, the odds ratio was calculated as a measure of treatment effect. When no events occur ("zero event") in a proportion, the variance of the arcsine difference was used to determine statistical significance ($p < 0.05$).[22]

To compare recurrent and adjacent fracture rates we report the proportion of patients that experienced a fracture and percentage of patients that experienced a fracture. The variance of the arcsine difference was used to determine statistical significance ($p < 0.05$) of fracture rates.[22]

We performed meta-analyses using the random effects method of DerSimonian and Laird.[23] Heterogeneity was assessed with the I-squared statistic.[24] All meta-analyses were performed using STATA 10.0 (StataCorp LP, College Station, Texas) and the "metan" command.

To assess the power of an outcome to detect a statistically significant difference we determined whether the number of patients in the study was sufficient to detect a small, medium, or large effect, while assuming an alpha of 0.05 as the significance level, 80% power, and Cohen's definitions of small, medium, and large effects (a small effect is d = 0.2, a medium effect is d = 0.5, and a large effect is d = 0.8).[25] When a study with a non-significant difference that was unable to detect a large effect it was categorized as low power. Studies able to detect medium effects or with statistically significant differences were categorized as high power.

When published studies report measures of dispersion other than the standard deviation the value was estimated to facilitate calculation of the treatment effect. In studies that report standard errors or confidence intervals the standard deviation was back-calculated. In studies that only report the median, range, and size of the trial, we estimated the means and variances according to a published method.[26] Studies that report results in graphical form were analyzed with TechDig 2.0 (Ronald B. Jones, Mundelein, Illinois) to estimate the mean and variance.

In some circumstances statistical testing was conducted by the authors and measures of dispersion were not reported. In the absence of measures of dispersion, the results of the statistical analyses conducted by the authors are included in the analysis and are identified as those of the study authors.

PEER REVIEW

The draft of the guideline and evidence report was peer reviewed by an external, outside specialty panel that was nominated *a priori* by the physician work group prior to the development of the guideline. The physician members of the AAOS Guidelines and Technology Oversight Committee and the Evidence Based Practice Committee also provided peer review of the draft document. Peer review was accomplished using a structured peer review form (see Appendix IX). The draft guideline was sent to a total of 32 reviewers and 11 returned reviews (see Appendix X). The disposition of all non-editorial peer review comments was documented and accompanied this guideline through the public commentary and the AAOS guideline approval process.

PUBLIC COMMENTARY

After modifying the draft in response to peer review, the guideline was subjected to a thirty day period of "Public Commentary." Commentators consist of members of the AAOS Board of Directors (BOD), members of the Council on Research, Quality Assessment, and Technology (CORQAT), members of the Board of Councilors (BOC), and members of the Board of Specialty Societies (BOS). Based on these bodies, over 200 commentators had the opportunity to provide input into this guideline development process. Of these, forty-nine members received the document for review and one member returned public comments (see Appendix X).

THE AAOS GUIDELINE APPROVAL PROCESS

Following public commentary, the draft was again modified by the AAOS Clinical Practice Guidelines Unit and work group members. This final guideline draft was approved by the AAOS Guidelines Oversight Committee, the AAOS Evidence Based

Practice Committee, the AAOS Council on Research, Quality Assessment, and Technology, and the AAOS Board of Directors. Descriptions of these bodies are provided in Appendix II.

REVISION PLANS

This guideline represents a cross-sectional view of current treatment and/or diagnosis and may become outdated as new evidence becomes available. This guideline will be revised in accordance with new evidence, changing practice, rapidly emerging treatment options, new technology. This guideline will be updated or withdrawn in five years in accordance with the standards of the National Guideline Clearinghouse.

GUIDELINE DISSEMINATION PLANS

The primary purpose of the present document is to provide interested readers with full documentation about not only our recommendations, but also about how we arrived at those recommendations. This document is also posted on the AAOS website at http://www.aaos.org/research/guidelines/guide.asp.

Shorter versions of the guideline are available in other venues. Publication of most guidelines is announced by an Academy press release, articles authored by the work group and published in the Journal of the American Academy of Orthopaedic Surgeons, and articles published in AAOS *Now*. Most guidelines are also distributed at the AAOS Annual Meeting in various venues such as on Academy Row and at Committee Scientific Exhibits.

Selected guidelines are disseminated by webinar, an Online Module for the Orthopaedic Knowledge Online website, Radio Media Tours, Media Briefings, and by distributing them at relevant Continuing Medical Education (CME) courses and at the AAOS Resource Center.

Other dissemination efforts outside of the AAOS will include submitting the guideline to the National Guideline Clearinghouse and distributing the guideline at other medical specialty societies' meetings.

III. RECOMMENDATIONS AND SUPPORTING DATA

RECOMMENDATION 1

We suggest patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms suggesting an acute injury (0-5 days after identifiable event or onset of symptoms) and who are neurologically intact be treated with calcitonin for 4 weeks.

Quality of Evidence	Quantity of Evidence	Applicability Downgrade	Critical Outcome(s)
Level II	4 studies	No	Pain

Strength of Recommendation: Moderate

Description: Evidence from two or more "Moderate" strength studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. A **Moderate** recommendation means that the benefits exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a negative recommendation), but the strength of the supporting evidence is not as strong.

Implications: Practitioners should generally follow a **Moderate** recommendation but remain alert to new information and be sensitive to patient preferences.

Rationale

This recommendation is based on two Level II studies which showed benefit in reducing pain at 4 weeks using salmon calcitonin administered within 5 days of a fracture event.[27, 28] In one study, 100 patients were treated with 200 IU nasal calcitonin or placebo. Calcitonin reduced pain in 4 positions (bedrest, sitting, standing, and walking) and the number of bedridden patients at 1, 2, 3, and 4 weeks in a clinically important manner. In a second study with 36 patients, similar results were found with calcitonin suppositories 200 IU. Side effects of calcitonin include mild dizziness.[28]

Two additional Level II studies with calcitonin showed benefit at longer periods of time (3-12) months but were not as well designed.[29, 30] In one, possibly clinically important benefit was shown in pain reduction using nasal calcitonin in a two-month on and two month off fashion for 12 months compared to calcium 500 mg with vitamin D 200 IU.[29] In another study, 200 IU nasal calcitonin led to possibly clinically important improvement in pain at 3 months when compared to 1000 mg calcium.[30]

The effect of subcutaneous administration of calcitonin is undetermined in a rigorous scientific manner.

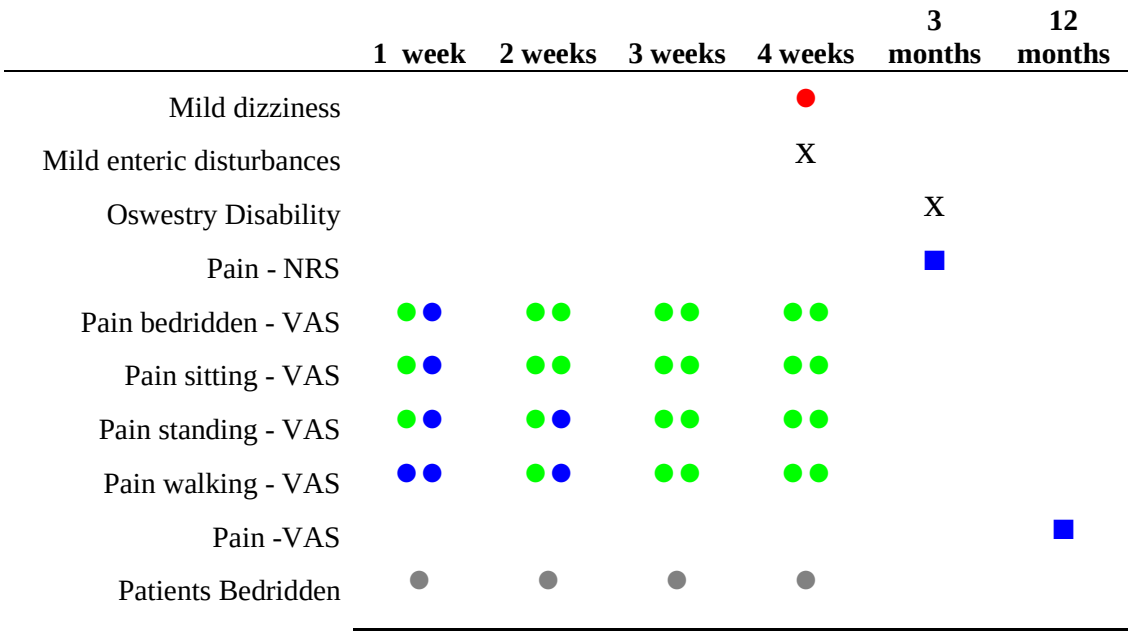
Supporting Evidence

Two studies with moderately reliable data enrolling a total of 136 patients compared calcitonin against placebo among patients with an acute injury (0-5 days after injury).[27, 28] In each study, only paracetamol was permitted as a rescue analgesic. Calcitonin reduced pain more than placebo at clinically important or possibly clinically important levels in both studies from 1-4 weeks (results presented in Table 7 - Table 9).

Two additional studies with moderately reliable data enrolling a total of 82 patients compared calcitonin to non-placebo control.[29, 30] As opposed to the two calcitonin vs. placebo studies, the time since injury was greater than 3 months in one study[30] and not specified in the other.[29] In each study, the calcitonin group also received calcium. The control group was calcium in the first study and calcium and vitamin D in the second study. A possibly clinically important improvement in pain occurred in the calcitonin group at 3 and 12 months, respectively, but there was no difference in function at 3 months (Table 10).

SUMMARY OF EVIDENCE

Table 5 Summary of Calcitonin Outcomes



circle-calcitonin compared to placebo; square-calcitonin compared to no calcitonin
green-clinically important in favor of calcitonin; **blue**-possibly clinically important in favor of Calcitonin; **red**-statistically significant in favor of placebo
grey-statistically significant; open-not statistically significant, X-underpowered study

Pain –VAS =Pain measured using the visual analog scale.

Pain-NRS = Pain measured with the numerical rating scale.

Please see Appendix XI for a list of all abbreviations used in this report.

STUDY QUALITY

Table 6 Quality of Included Studies for Recommendation 1 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Lyritis 1997	Pain - VAS	1 Week	100	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1997	Pain - VAS	2 Weeks	100	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1997	Pain - VAS	3 Weeks	100	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1997	Pain - VAS	4 Weeks	100	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1997	Number of bedridden patients	1 Week	100	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1997	Number of bedridden patients	2 Weeks	100	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1997	Number of bedridden patients	3 Weeks	100	Calcitonin vs. placebo	Level II	×	×	●	●	●	●

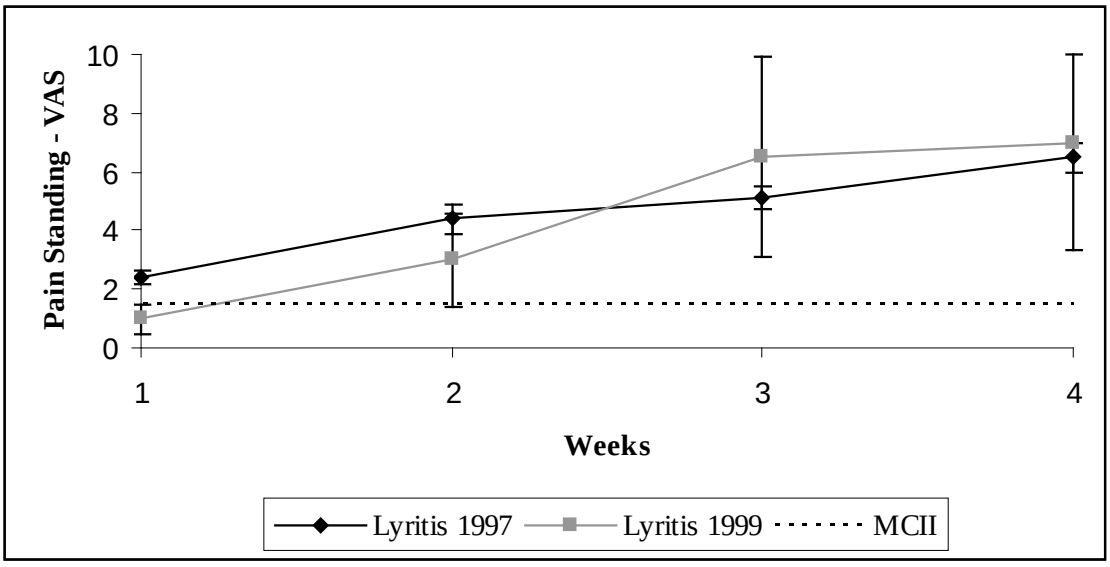
Table 6 Quality of Included Studies for Recommendation 1 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Lyritis 1997	Number of bedridden patients	4 Weeks	100	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1999	Pain - VAS	1 Week	36	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1999	Pain - VAS	2 Weeks	36	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1999	Pain - VAS	3 Weeks	36	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Lyritis 1999	Pain - VAS	4 Weeks	36	Calcitonin vs. placebo	Level II	×	×	●	●	●	●
Peichl	Pain - VAS	12 Months	42	Calcitonin vs. control	Level II	×	×	○	○	●	●
Papadokostakis	Pain - NRS	3 Months	40	Calcitonin vs. control	Level II	●	×	○	○	●	●
Papadokostakis	Oswestry score	3 Months	40	Calcitonin vs. control	Level II	●	×	○	○	●	●

CALCITONIN VS. PLACEBO

Figure 1 Calcitonin vs. Placebo – Difference in Pain



Interpreting the Graphs

Throughout the guideline we use line graphs to illustrate the differences in efficacy between the experimental and control groups of a study. Each point represents the difference between the two study groups for the designated outcome at that particular time point. A positive value indicates a better outcome (e.g., less pain) in the experimental group. The error bars represent the 95% Confidence Interval. The dotted line represents the Minimally Clinically Important Improvement (MCII) for the outcome.

In the figure above, the difference in pain between the calcitonin and placebo groups is compared at 4 time points in two separate studies (Lyritis 1997 and Lyritis 1999). For instance, at 4 weeks the pain on VAS in the calcitonin group is about 7 units less than the pain in the placebo group in both studies. The difference is statistically significant because the confidence intervals do not cross 0, and the difference is clinically important because the lower confidence interval is greater than the MCII value.

Table 7 Calcitonin vs. Placebo - Pain

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Lyritis 1997	100	II	0-5 days	Pain bedridden - VAS	1 week	3.9 (3.1, 4.7)	Calcitonin	Yes
Lyritis 1999	36					3.0 (1.4, 4.6)	Calcitonin	Possibly
Lyritis 1997	100				2 weeks	4.5 (3.9, 5.1)	Calcitonin	Yes
Lyritis 1999	36					5.0 (2.4, 7.6)	Calcitonin	Yes
Lyritis 1997	100				3 weeks	5.0 (4.1, 5.9)	Calcitonin	Yes
Lyritis 1999	36					5.0 (2.4, 7.6)	Calcitonin	Yes
Lyritis 1997	100				4 weeks	4.9 (4.3, 5.5)	Calcitonin	Yes
Lyritis 1999	36					5.5 (2.6, 8.4)	Calcitonin	Yes
Lyritis 1997	100			Pain sitting - VAS	1 week	2.5 (2.2, 2.8)	Calcitonin	Yes
Lyritis 1999	36					2.0 (0.9, 3.1)	Calcitonin	Possibly
Lyritis 1997	100				2 weeks	3.9 (3.4, 4.4)	Calcitonin	Yes
Lyritis 1999	36					4.0 (1.9, 6.1)	Calcitonin	Yes
Lyritis 1997	100				3 weeks	4.0 (3.6, 4.4)	Calcitonin	Yes
Lyritis 1999	36					6.5 (3.1, 9.9)	Calcitonin	Yes
Lyritis 1997	100				4 weeks	5.0 (4.4, 5.6)	Calcitonin	Yes
Lyritis 1999	36					7.0 (3.3, 10)	Calcitonin	Yes
Lyritis 1997	100			Pain standing - VAS	1 week	2.4 (2.2, 2.6)	Calcitonin	Yes
Lyritis 1999	36					1.0 (0.5, 1.5)	Calcitonin	Possibly
Lyritis 1997	100				2 weeks	4.4 (3.9, 4.9)	Calcitonin	Yes
Lyritis 1999	36					3.0 (1.4, 4.6)	Calcitonin	Possibly
Lyritis 1997	100				3 weeks	5.1 (4.7, 5.5)	Calcitonin	Yes
Lyritis 1999	36					6.5 (3.1, 9.9)	Calcitonin	Yes
Lyritis 1997	100				4 weeks	6.5 (6.0, 7.0)	Calcitonin	Yes
Lyritis 1999	36					7.0 (3.3, 10)	Calcitonin	Yes

Table 7 Calcitonin vs. Placebo - Pain

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Lyritis 1997	100	II	0-5 days	Pain walking - VAS	1 week	0.8 (0.7, 0.9)	Calcitonin	Possibly
Lyritis 1999	36					1.0 (0.4, 1.6)	Calcitonin	Possibly
Lyritis 1997	100				2 weeks	3.8 (3.5, 4.1)	Calcitonin	Yes
Lyritis 1999	36					3.0 (1.4, 4.6)	Calcitonin	Possibly
Lyritis 1997	100				3 weeks	4.5 (4.2, 4.8)	Calcitonin	Yes
Lyritis 1999	36					7.0 (3.3, 10)	Calcitonin	Yes
Lyritis 1997	100				4 weeks	6.4 (6.0, 6.8)	Calcitonin	Yes
Lyritis 1999	36					7.0 (3.3, 10)	Calcitonin	Yes

*95% Confidence Intervals estimated from medians and p-value (from Mann-Whitney test)

Table 8 Calcitonin vs. Placebo – Bedridden Patients

Study	Level of Evidence	Time After Injury	Outcome	Duration	Calcitonin n/N	Placebo n/N	p-value
Lyritis 1997	II	0-5 days	Patients Bedridden	1 week	3/50	50/50	<.0001
				2 weeks	0/50	50/50	<.0001
				3 weeks	0/50	38/50	<.0001
				4 weeks	0/50	26/50	<.0001

Shaded cell indicates favored treatment

Table 9 Calcitonin vs. Placebo – Adverse Events

Study	Level of Evidence	Time After Injury	Outcome	Duration	Calcitonin n/N	Placebo n/N	p-value
Lyritis 1999	II	0-5 days	Mild dizziness	4 weeks	7/19	1/16	0.02
			Mild enteric disturbances	4 weeks	11/19	7/16	0.40

Study lacked sufficient power to detect large effect for mild enteric disturbances; shaded cell indicates favored treatment

CALCITONIN VS. NO CALCITONIN

Table 10 Calcitonin vs. No Calcitonin – Pain and Function

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Papadokostakis	40	II	>3 months	Pain - NRS	3 months	2.5 (1.1, 3.9)*	Calcitonin	Possibly
Peichl	42	II	Not Specified	Pain - VAS	12 months	1.4 (0.6, 2.2)	Calcitonin	Possibly
Papadokostakis	40	II	>3 months	Oswestry Disability	3 months	3.2 (-7.1, 13.5)	○	Inconclusive

Papadokostakis study lacked sufficient power to detect large effect for Oswestry Disability; *Estimated from median and range;
○ = no statistically significant difference

RECOMMENDATION 2

Ibandronate and strontium ranelate are options to prevent additional symptomatic fractures in patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms.

Quality of Evidence	Quantity of Evidence	Applicability Downgrade	Critical Outcome(s)
Level I Level II	4 studies 33 studies	No	Symptomatic Fracture

Strength of Recommendation: Limited

Description: Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single "Moderate" quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.

Rationale

There have been numerous studies examining the effects of medical therapies for the treatment of osteoporosis to prevent radiographic fractures. The focus of this recommendation is not the use of medical therapies for treatment of osteoporosis (i.e. prevention of fragility fracture), but their use in patients with an existing fracture and the prevention of those patients experiencing symptomatic fractures (i.e. the critical outcome for this recommendation). Three studies of osteoporosis drugs exclusively enrolled symptomatic patients but none reported the critical outcome of a symptomatic fracture. Thirty-four additional studies were included that enrolled patients with symptomatic fractures or asymptomatic fractures (incident fracture determined by radiograph). Three of these studies reported the critical outcome of symptomatic fracture.

One Level II study[31] investigated daily (2.5 mg) and intermittent (20 mg every other day for 12 doses every 3 months) administration of ibandronate for symptomatic vertebral fractures compared to placebo. Daily and intermittent ibandronate treatment regimens reduced new symptomatic vertebral fractures in a statistically significant manner at 3 years. There were no statistically significant differences in adverse events between ibandronate and placebo groups including those in the upper gastrointestinal tract.

One Level II study[32]investigated daily strontium ranelate (2g) for vertebral fractures compared to placebo. Strontium ranelate reduced new symptomatic vertebral fractures in a statistically significant manner at 1 and 3 years. The occurrence of adverse events was

similar between patients assigned to placebo or strontium ranelate. The only statistically significant differences were diarrhea, which occurred more frequently in patients receiving strontium ranelate, and incidence of gastritis, which occurred more frequently in patients receiving placebo. Effective as of July 15, 2010, Strontium Ranelate is not approved for marketing or the treatment of any medical condition in the United States. The United States Food and Drug Administration's (FDA) current policy regarding disclosure of marketing applications can be found in "Current Disclosure Policies for Marketing Applications" on the FDA website.

One Level II study[33]investigated daily oral pamidronate (150 mg) for vertebral fractures compared to placebo. Oral pamidronate did not reduce new symptomatic vertebral fractures in a statistically significant manner at 3 years and adverse events were similar between patients receiving placebo or oral pamidronate.

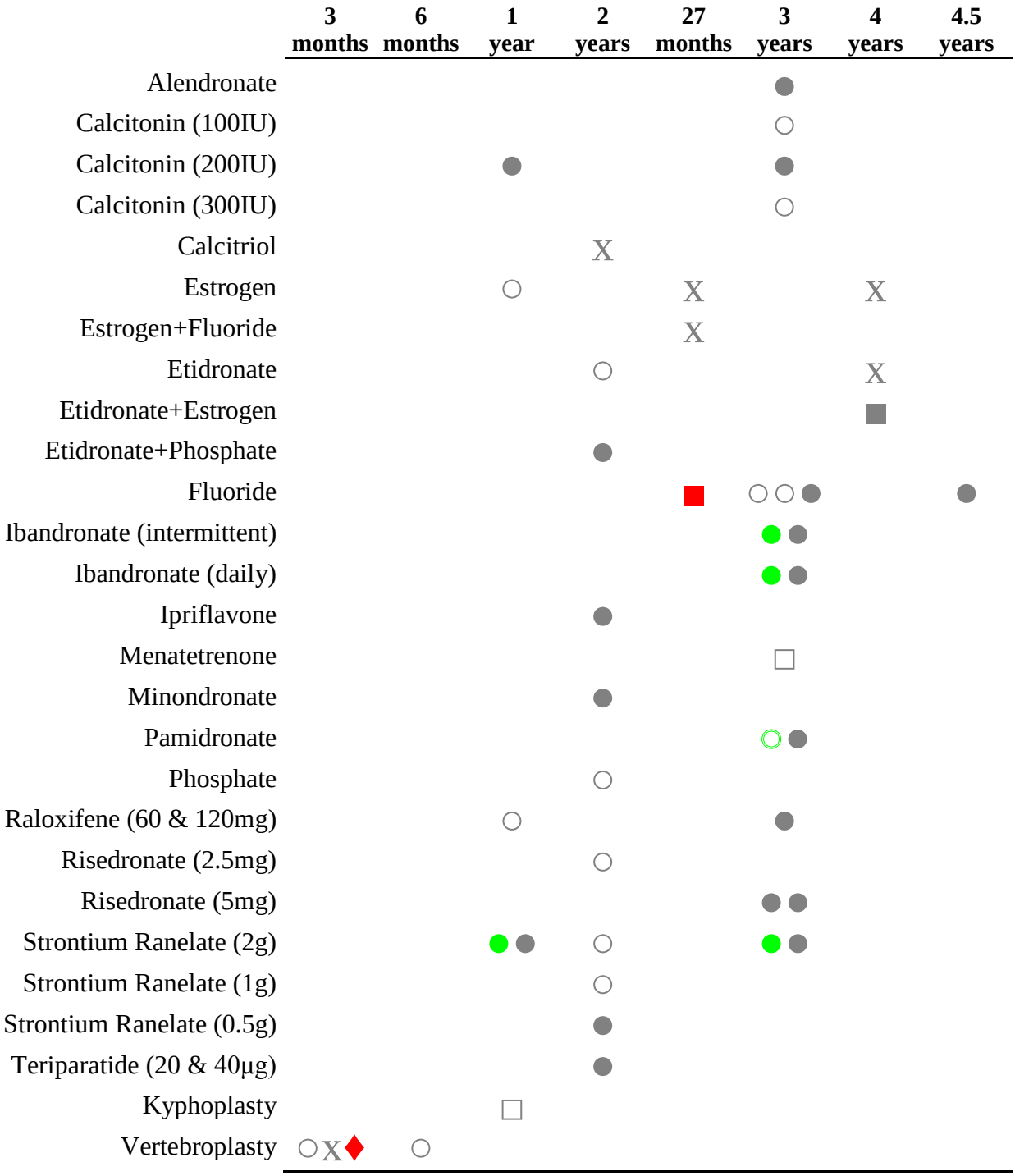
No recommendation is made *for or against* the use of any of the treatments considered not applicable to the reduction of future symptomatic vertebral fractures despite the large body of evidence for their use in osteoporosis.

Supporting Evidence

We have tabled data on radiographic and symptomatic fracture from 37 studies, analyzing 18,305 unique patients, with reliable or moderately reliable data that report the cumulative number of patients with an incident or recurrent fracture within the first 3 months up to 4.5 years following initiation of treatment. Three of the 35 studies enrolled patients who had symptoms of osteoporotic spinal compression fracture. None of these studies report recurrent or adjacent fractures as symptomatic. However, three different included studies (i.e. studies that enrolled symptomatic and asymptomatic patients) did report recurrent or adjacent fractures as symptomatic. Twenty nine of the 37 studies enroll an exclusively female population. Table 11 illustrates the symptomatic fractures and the radiographic fractures reported as outcomes in the included studies which compared the treatment to a placebo or control. Table 12 lists the comparisons from the included studies for this recommendation including direct comparisons of treatments (i.e. not placebo or control).

SUMMARY OF EVIDENCE

Table 11 Fracture Prevention Outcomes



circle-compared to placebo; square-compared to conservative treatment; diamond-reported as "adjacent fracture"; **green**-symptomatic fracture; **grey**-radiographic fracture; closed-statistically significant; open-not statistically significant, X-underpowered study; **red**-statistically significant in favor of placebo/conservative; not all treatments were investigated at different dosages; g-grams; mg-milligrams; mcg-micrograms IU-international unit

Table 12 Treatment Comparisons for Recommendation 2

Compared to Placebo or Control	
Alendronate [34]	Calcitonin [29, 35]
Estrogen [36-38]	Etidronate [38, 39]
Etidronate+Estrogen [38]	Etidronate+Phosphate [39]
Fluoride [36, 40-43]	Ibandronate [31†]
Ipriflavone [44]	Menatetrenone [45]
Minondronate [46]	Pamidronate [33†]
Phosphate [39]	Raloxifene [47, 48]
Risedronate [49-51]	Strontium Ranelate [32, 52†]
Teriparatide [53]	Kyphoplasty [54*]
	Vertebroplasty [1* 55]
Direct Comparisons	
Alendronate to Alfacalcidol [56]	
Estrogen to Estrogen+Calcitriol [57]	
Etidronate to Fluoride [58]	
Etidronate to Risedronate [59]	
Etidronate to Phosphate to Etidronate+Phosphate [39]	
Kyphoplasty to Vertebroplasty [60, 61]	
Underpowered Comparisons	
Alendronate to Etidronate [62*]	
Calcitriol to Placebo[63]	
Estrogen+Fluoride to Control [36]	
Estrogen to Etidronate to Etidronate+Estrogen [38]	
Estrogen to Fluoride to Estrogen+Fluoride [36]	
Nandrolone to 1α-OH D3 to Calcium infusion [64]	
Teriparatide to Teriparatide+Calcitonin [65]	

* study enrolls symptomatic patients; † study reports symptomatic recurrent or adjacent spinal compression fracture

STUDY QUALITY

Table 13 Quality of Included Studies for Recommendation 2 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Buchbinder	Fracture	3 Months	73	Vertebroplasty vs. placebo	Level I	●	●	●	●	●	●
Rousing	Fracture	3 Months	47	Vertebroplasty vs. conservative	Level II	×	●	○	○	●	●
Rousing	Adjacent Fracture	3 Months	47	Vertebroplasty vs. conservative	Level II	×	●	○	○	●	●
Buchbinder	Fracture	6 Months	71	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Inoue	Fracture	3 Years	1018	Menatetrenone vs. Control	Level II	×	×	○	○	○	●
Liu	Adjacent Fracture	6 Months	100	Kyphoplasty vs. Vertebroplasty	Level II	●	×	×	×	●	●
Wardlaw	Fracture	1 Year	210	Kyphoplasty vs. Conservative	Level II	●	×	○	○	●	●
Matsumoto	Fracture	2 Years	674	Minondronate vs. Placebo	Level I	●	●	●	●	●	●
Chesnut 2004	Symptomatic Fracture	3 Years	2929	Ibandronate vs. Placebo	Level II	×	×	●	●	●	●

Table 13 Quality of Included Studies for Recommendation 2 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Chesnut 2004	Fracture	3 Years	2929	Ibandronate vs. Placebo	Level II	×	×	●	●	●	●
Kushida 2004	Fracture	4 Years	433	Etidronate vs. Risedronate	Level II	×	×	●	●	○	●
Meunier 2004	Symptomatic Fracture	1 Year	1385	Strontium Ranelate vs. Placebo	Level II	×	×	●	●	●	●
Meunier 2004	Fracture	1 Year	1385	Strontium Ranelate vs. Placebo	Level II	×	×	●	●	●	●
Meunier 2004	Symptomatic Fracture	3 Years	1442	Strontium Ranelate vs. Placebo	Level II	×	×	●	●	●	●
Meunier 2004	Fracture	3 Years	1442	Strontium Ranelate vs. Placebo	Level II	×	×	●	●	●	●
Gutteridge 2003	Fracture	2 Years	70	Estrogen vs. Estrogen+Calcitriol	Level II	●	●	×	●	●	●
Iwamoto	Fracture	6 Months	50	Alendronate vs. Etidronate	Level II	×	×	×	×	●	●
Brumsen	Symptomatic Fracture	3 Years	91	Pamidronate vs. Placebo	Level II	×	×	●	●	●	●

Table 13 Quality of Included Studies for Recommendation 2 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Brumsen	Fracture	3 Years	91	Pamidronate vs. Placebo	Level II	×	×	●	●	●	●
Gutteridge 2002	Fracture	27 Months	75	Estrogen vs. Fluoride vs. Estrogen+Fluoride vs. Control	Level II	●	×	○	○	○	●
Kushida 2002	Fracture	2 Years	314	Alendronate vs. Alfacalcidol	Level II	×	×	●	●	●	●
Meunier 2002	Fracture	2 Years	338	Strontium Ranelate vs. Placebo	Level II	×	×	●	●	●	●
Neer	Fracture	2 Years	1326	Teriparatide vs. Placebo	Level II	×	×	●	●	●	●
Rubin	Fracture	3 Years	72	Fluoride vs. Placebo	Level II	×	×	●	●	●	●
Chesnut 2000	Fracture	3 Years	817	Calcitonin vs. Placebo	Level II	●	×	●	●	○	●
Guanabens	Fracture	3 Years	78	Etidronate vs. Fluoride	Level II	×	×	×	×	○	●
Reginster	Fracture	3 Years	690	Risedronate vs. Placebo	Level II	×	×	●	●	○	●

Table 13 Quality of Included Studies for Recommendation 2 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Ettinger	Fracture	3 Years	2304	Raloxifene vs. Placebo	Level II	×	×	●	●	●	●
Harris	Fracture	3 Years	1627	Risedronate vs. Placebo	Level II	●	●	●	●	○	●
Peichl	Fracture	1 Year	42	Calcitonin vs. Placebo	Level II	×	×	○	○	●	●
Ringe	Fracture	3 Years	123	Fluoride vs. Control	Level II	×	×	×	●	●	●
Lufkin 1998	Fracture	1 Year	133	Raloxifene vs. Placebo	Level II	×	×	●	×	●	●
Meunier 1998	Fracture	3 Years	354	Fluoride vs. Placebo	Level II	×	×	●	●	●	●
Wimalawansa	Fracture	4 Years	58	Estrogen vs. Etidronate vs. Etidronate+Estrogen vs. Control	Level II	●	×	×	●	●	●
Clemmesen	Fracture	2 Years	93	Risedronate vs. Placebo	Level II	×	×	●	●	○	●
Hodsman	Fracture	2 Years	24	Teriparatide vs. Teriparatide and	Level II	×	×	×	×	○	●

Table 13 Quality of Included Studies for Recommendation 2 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
				Calcitonin							
Black	Fracture	3 Years	1946	Alendronate vs. Placebo	Level I	×	●	●	●	●	●
Maugeri	Fracture	2 Years	84	Ipriflavone vs. Placebo	Level II	×	×	●	●	●	●
Pak	Fracture	4.5 Years	99	Fluoride vs. Placebo	Level II	×	×	●	×	●	●
Lufkin 1992	Fracture	1 Year	68	Estrogen vs. Placebo	Level II	×	×	●	×	●	●
Gallagher	Fracture	2 years	40	Calcitriol vs. Placebo	Level I	●	●	●	●	●	●
Watts	Fracture	2 Years	378	Etidronate vs. Phosphate vs. Etidronate+Phosphate vs. Placebo	Level II	●	×	●	●	●	●
Geusens	Fracture	2 Years	34	Nandrolone vs. 1α-OH D3 vs. Calcium infusion	Level II	×	×	●	●	○	●

Table 14 Quality of Included Studies for Recommendation 2 - Prospective Comparative Studies

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	All groups have similar characteristics at entry	All groups have similar outcome performance at entry	All groups concurrently treated	Follow Up - 80% or more	Same center for experimental and control group data
Grohs	Adjacent Fracture	4 Months	51	Vertebroplasty vs. Kyphoplasty	Level II	●	●	●	●	●

ALENDRONATE

One study with reliable data compared alendronate to placebo and reported the cumulative number of patients with an incident or recurring fracture within three years. [34]

Table 15 Alendronate vs. Placebo - Fractures

Study	Outcome	Duration	Alendronate n/N (%)	Placebo n/N (%)	p-value	Power
Black	Fracture	3 Years	78/981 (7.95%)	145/965 (15.03%)	0.000	High

shaded box indicates favored treatment

ALENDRONATE VS. ALFACALCIDOL

One study with moderately reliable data, which enrolled men and women, compared alendronate to alfacalcidol and reported the cumulative number of patients with an incident or recurring fracture within two years. [56]

Table 16 Alendronate vs. Alfacalcidol - Fractures

Study	Outcome	Duration	Alendronate n/N (%)	Alfacalcidol n/N (%)	p-value	Power
Kushida 2002	Fracture	2 Years	20/164 (12.20%)	25/150 (16.67%)	0.259	High

Study enrolled males and females

ALENDRONATE VS. ETIDRONATE

One study with moderately reliable data, which enrolled patients with symptoms of spinal compression fractures, compared alendronate to etidronate and reported the cumulative number of patients with an incident or recurring fracture within six months. [62]

Table 17 Alendronate vs. Etidronate - Fractures

Study	Outcome	Duration	Alendronate n/N (%)	Etidronate n/N (%)	p-value	Power
Iwamoto	Fracture	6 Months	0/25 (0%)	1/25 (4%)	0.154	Low

Patients were symptomatic at enrollment

CALCITONIN

Two studies with moderately reliable data compared salmon calcitonin to placebo and reported the cumulative number of patients with an incident or recurring fracture within one or three years. [29, 35] In both studies the 200 IU dosage resulted in statistically significant differences in cumulative fracture rates.

Table 18 Calcitonin vs. Placebo - Fractures

Study	Outcome	Dosage	Duration	Calcitonin n/N (%)	Placebo n/N (%)	p-value	Power
Peichl	Fracture	200 IU	1 Year	0/24 (0%)	3/18 (16.67%)	0.007	High
Chesnut 2000	Fracture	100 IU	3 Years	52/201 (25.87%)	60/203 (29.56%)	0.408	High
Chesnut 2000	Fracture	200 IU	3 Years	40/207 (19.32%)	60/203 (29.56%)	0.015	High
Chesnut 2000	Fracture	300 IU	3 Years	48/206 (23.30%)	60/203 (29.56%)	0.151	High

shaded box indicates favored treatment

CALCITRIOL

One study with reliable data compared calcitriol to placebo and reported the cumulative number of patients with an incident or recurring fracture within two years. [63]

Table 19 Calcitriol vs. Placebo - Fractures

Study	Outcome	Duration	Calcitriol n/N (%)	Placebo n/N (%)	p-value	Power
Gallagher	Fracture	2 Years	8/18 (44.44%)	9/22 (40.91%)	0.822	Low

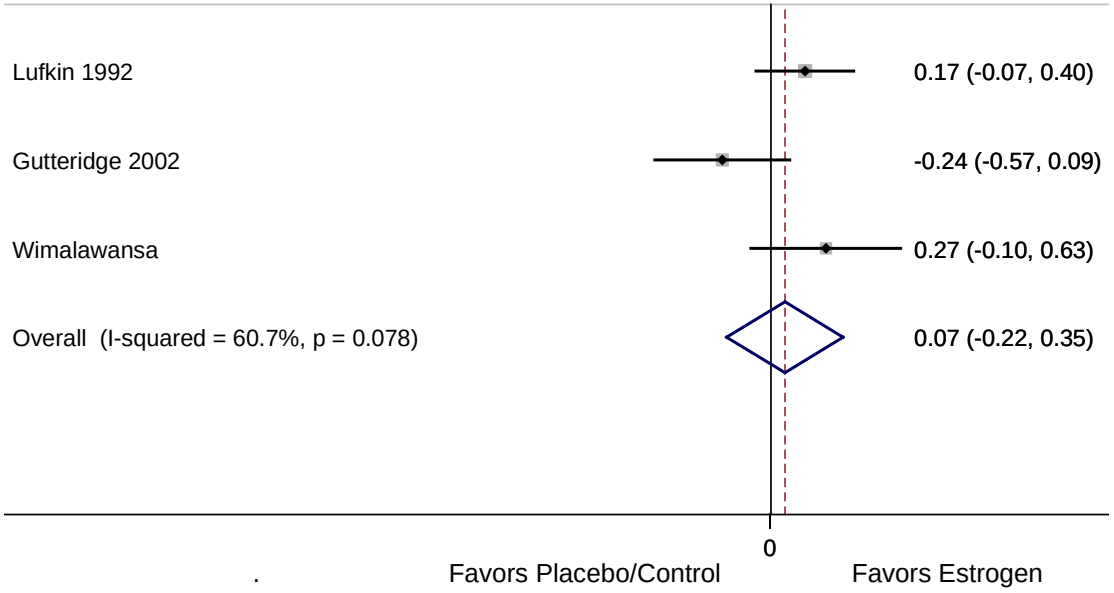
ESTROGEN

Three studies with moderately reliable data compared estrogen to a placebo or control group and reported the cumulative number of patients with an incident or recurring fracture within one year, twenty seven months, or four years. [36-38] We conducted a meta-analysis (using the arcsin difference [22]) of these three studies in an effort to improve the power of this analysis. Figure 2 illustrates a non-significant effect with substantial heterogeneity (I^2 = 60.7%).

Table 20 Estrogen vs. Placebo or Control - Fractures

Study	Outcome	Duration	Estrogen n/N (%)	Placebo/Control n/N (%)	p-value	Power
Lufkin 1992	Fracture	1 Year	7/34 (20.59%)	12/34 (35.29%)	0.173	High
Gutteridge 2002	Fracture	27 Months	5/15 (33.33%)	3/22 (13.64%)	0.156	Low
Wimalawansa	Fracture	4 Years	2/15 (13.33%)	5/14 (35.71%)	0.151	Low

Figure 2 Meta-analysis of Estrogen vs. Placebo or Control - Fractures



ESTROGEN VS. ESTROGEN+CALCITRIOL

One study with moderately reliable data compared the combination of estrogen and calcitriol to estrogen alone and reported the cumulative number of patients with an incident or recurring fracture within two years. [57]

Table 21 Estrogen vs. Estrogen+Calcitriol - Fractures

Study	Outcome	Duration	Estrogen n/N (%)	Estrogen+Calcitriol n/N (%)	p-value	Power
Gutteridge 2003	Fracture	2 Years	8/36 (22.22%)	4/34 (11.76%)	0.239	High

ESTROGEN+ETIDRONATE

One study with moderately reliable data compared the combination of estrogen and etidronate to a control group and reported the cumulative number of patients with an incident or recurring fracture within four years. [38]

Table 22 Estrogen+Etidronate vs. Control - Fractures

Study	Outcome	Duration	Estrogen+Etidronate n/N (%)	Control n/N (%)	p-value	Power
Wimalawansa	Fracture	4 Years	1/15 (6.67%)	5/14 (35.71%)	0.041	High

shaded box indicates favored treatment

ESTROGEN VS. ETIDRONATE VS. ESTROGEN+ ETIDRONATE

One study with moderately reliable data compared estrogen to etidronate to estrogen +etidronate and reported the cumulative number of patients with an incident or recurring fracture within four years. [38]

Table 23 Estrogen vs. Etidronate vs. Etidronate+Estrogen - Fractures

Study	Outcome	Duration	Estrogen n/N (%)	Etidronate n/N (%)	p-value	Power
Wimalawansa	Fracture	4 Years	2/15 (13.33%)	3/14 (21.43%)	0.563	Low

Estrogen n/N (%)	Estrogen+Etidronate n/N (%)	p-value	Power

Study	Outcome	Duration	Estrogen n/N (%)	Etidronate n/N (%)	p-value	Power
			2/15 (13.33%)	1/15 (6.67%)	0.537	Low

Etidronate n/N (%)	Estrogen+Etidronate n/N (%)	p-value	Power
3/14 (21.43%)	1/15 (6.67%)	0.236	Low

ESTROGEN+FLUORIDE

One study with moderately reliable data compared the combination of estrogen and fluoride to a control group and reported the cumulative number of patients with an incident or recurring fracture within twenty seven months. [36]

Table 24 Estrogen+Fluoride vs. Placebo - Fractures

Study	Outcome	Duration	Estrogen+Fluroide n/N (%)	Control n/N (%)	p-value	Power
Gutteridge 2002	Fracture	27 Months	4/14 (28.57%)	3/22 (13.64%)	0.277	Low

ESTROGEN VS. FLUORIDE VS. ESTROGEN+FLUORIDE

One study with moderately reliable data compared estrogen to fluoride to estrogen+fluoride and reported the cumulative number of patients with an incident or recurring fracture within twenty seven months. [36]

Table 25 Estrogen vs. Fluoride vs. Estrogen+Fluoride - Fractures

Study	Outcome	Duration	Estrogen n/N (%)	Fluoride n/N (%)	p-value	Power
Gutteridge 2002	Fracture	27 Months	5/15 (33.33%)	11/24 (45.83%)	0.436	Low

Estrogen n/N (%)	Estrogen+Fuoride n/N (%)	p-value	Power
5/15 (33.33%)	4/14 (28.57%)	0.781	Low

Fluoride n/N (%)	Estrogen+Fluoride n/N (%)	p-value	Power
11/24 (45.83%)	4/14 (28.57%)	0.285	Low

ETIDRONATE

Two studies with moderately reliable data compared etidronate to a placebo or control group and reported the cumulative number of patients with an incident or recurring fracture within two years or four years. [38, 39]

Table 26 Etidronate vs. Placebo or Control - Fractures

Study	Outcome	Duration	Etidronate n/N (%)	Placebo/Control n/N (%)	p-value	Power
Watts	Fracture	2 Years	5/98 (5.10%)	10/91 (10.99%)	0.131	High
Wimalawansa	Fracture	4 Years	3/14 (21.43%)	5/14 (35.71%)	0.399	Low

ETIDRONATE VS. ALENDRONATE

One study with moderately reliable data, which enrolled patients with symptoms of spinal compression fractures, compared etidronate to alendronate and reported the cumulative number of patients with an incident or recurring fracture within six months. [62]

Table 27 Etidronate vs. Alendronate - Fractures

Study	Outcome	Duration	Etidronate n/N (%)	Alendronate n/N (%)	p-value	Power
Iwamoto	Fracture	6 Months	1/25 (4%)	0/25 (0%)	0.154	Low

Patients were symptomatic at enrollment

ETIDRONATE VS. RISEDRONATE

One study with moderately reliable data compared etidronate to risedronate and reported the cumulative number of patients with an incident or recurring fracture within four years. [59]

Table 28 Etidronate vs. Risedronate - Fractures

Study	Outcome	Duration	Etidronate %	Risedronate %	p-value	Power
Kushida 2004	Fracture	4 Years	14.19 %	12.27 %	0.554	High

Percentages reported by study authors, authors do not report sufficient information for n/N

ETIDRONATE VS. FLUORIDE

One study with moderately reliable data compared etidronate to fluoride and reported the cumulative number of patients with an incident or recurring fracture within three years. [58]

Table 29 Etidronate vs. Fluoride - Fractures

Study	Outcome	Duration	Etidronate n/N (%)	Fluoride n/N (%)	p-value	Power
Guanabens	Fracture	3 Years	8/47 (17.02%)	5/31 (16.13%)	0.917	High

ETIDRONATE+ESTROGEN

One study with moderately reliable data compared the combination of etidronate and estrogen to a control group and reported the cumulative number of patients with an incident or recurring fracture within four years. [38]

Table 30 Etidronate+Estrogen vs. Control - Fractures

Study	Outcome	Duration	Etidronate+Estrogen n/N (%)	Control n/N (%)	p-value	Power
Wimalawansa	Fracture	4 Years	1/15 (6.67%)	5/14 (35.71%)	0.041	High

shaded box indicates favored treatment

ETIDRONATE VS. ESTROGEN VS. ETIDRONATE+ESTROGEN

One study with moderately reliable data compared etidronate to estrogen to etidronate+estrogen and reported the cumulative number of patients with an incident or recurring fracture within four years. [38]

Table 31 Etidronate vs. Estrogen vs. Etidronate+Estrogen - Fractures

Study	Outcome	Duration	Etidronate n/N (%)	Estrogen n/N (%)	p-value	Power
Wimalawansa	Fracture	4 Years	3/14 (21.43%)	2/15 (13.33%)	0.563	Low

Etidronate n/N (%)	Estrogen+Etidronate n/N (%)	p-value	Power

Study	Outcome	Duration	Etidronate n/N (%)	Estrogen n/N (%)	p-value	Power
			3/14 (21.43%)	1/15 (6.67%)	0.236	Low

Estrogen n/N (%)	Estrogen+Etidronate n/N (%)	p-value	Power
2/15 (13.33%)	1/15 (6.67%)	0.537	Low

ETIDRONATE+PHOSPHATE

One study with moderately reliable data compared the combination of etidronate and phosphate to a placebo group and reported the cumulative number of patients with an incident or recurring fracture within two years. [39]

Table 32 Etidronate+Phosphate vs. Placebo - Fractures

Study	Outcome	Duration	Etidronate+Phosphate n/N (%)	Placebo n/N (%)	p-value	Power
Watts	Fracture	2 Years	3/97 (3.09%)	10/91 (10.99%)	0.027	High

shaded box indicates favored treatment

ETIDRONATE VS. PHOSPHATE VS. ETIDRONATE+PHOSPHATE

One study with moderately reliable data compared etidronate to phosphate to etidronate+phosphate and reported the cumulative number of patients with an incident or recurring fracture within two years. [39]

Table 33 Etidronate vs. Phosphate vs. Etidronate+Phosphate - Fractures

Study	Outcome	Duration	Etidronate n/N (%)	Phosphate n/N (%)	p-value	Power
Watts	Fracture	2 Years	5/98 (5.10%)	7/92 (7.61%)	0.477	High

Etidronate n/N (%)	Etidronate+Phosphate n/N (%)	p-value	Power
5/98 (5.10%)	3/97 (3.09%)	0.476	High

Phosphate n/N (%)	Etidronate+Phosphate n/N (%)	p-value	Power
7/92 (7.61%)	3/97 (3.09%)	0.158	High

FLUORIDE

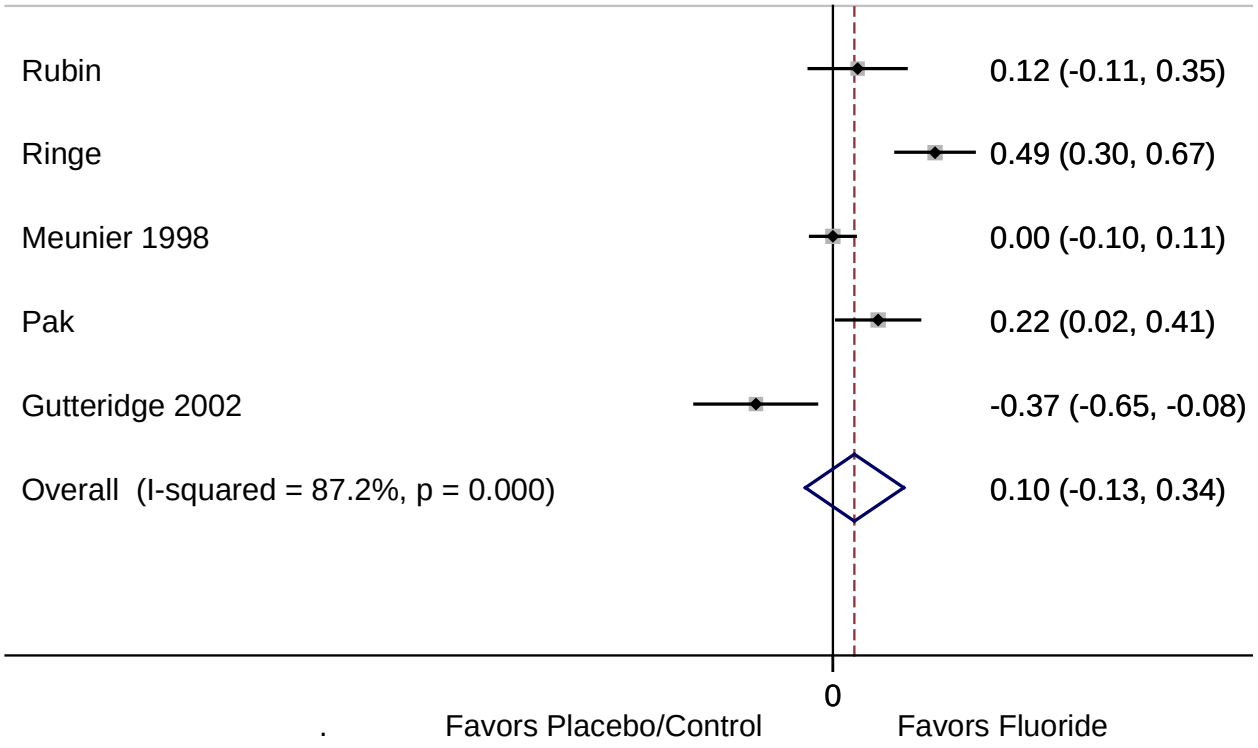
Five studies with moderately reliable data compared fluoride to a placebo or control group and reported the cumulative number of patients with an incident or recurring fracture within twenty seven months, three years or four and a half years. [36, 40-43] We conducted a meta-analysis (using the arcsin difference [22]) of these five studies in an effort to address the differences in the direction of the effect in different trials. Figure 3 illustrates a non-significant effect with substantial heterogeneity (I^2 = 87.2%).

Table 34 Fluoride vs. Placebo or Control - Fractures

Study	Outcome	Duration	Fluoride n/N (%)	Placebo/Control n/N (%)	p-value	Power
Rubin	Fracture	3 Years	8/34 (23.53%)	13/38 (34.21%)	0.316	High
Ringe	Fracture	3 Years	20/81 (24.69%)	30/42 (71.43%)	0.000	High
Meunier 1998	Fracture	3 Years	71/208 (34.13%)	50/146 (34.25%)	0.983	High
Pak	Fracture	4.5 Years	8/48 (16.67%)	18/51 (35.29%)	0.032	High
Gutteridge 2002	Fracture	27 Months	11/24 (45.83%)	3/22 (13.64%)	0.013	High

shaded box indicates favored treatment

Figure 3 Meta-analysis of Fluoride vs. Placebo or Control - Fractures



FLUORIDE VS. ETIDRONATE

One study with moderately reliable data compared fluoride to etidronate and reported the cumulative number of patients with an incident or recurring fracture within three years. [58]

Table 35 Fluoride vs. Etidronate - Fractures

Study	Outcome	Duration	Fluoride n/N (%)	Etidronate n/N (%)	p-value	Power
Guanabens	Fracture	3 Years	5/31 (16.13%)	8/47 (17.02%)	0.917	High

FLOURIDE+ESTROGEN

One study with moderately reliable data compared the combination of fluoride and estrogen to a placebo and reported the cumulative number of patients with an incident or recurring fracture within twenty seven months. [36]

Table 36 Fluoride+Estrogen vs. Placebo - Fractures

Study	Outcome	Duration	Fluroide+Estrogen n/N (%)	Placebo n/N (%)	p-value	Power
Gutteridge 2002	Fracture	27 Months	4/14 (28.57%)	3/22 (13.64%)	0.277	Low

FLUORIDE VS. ESTROGEN VS. FLUORIDE+ESTROGEN

One study with moderately reliable data compared fluoride to estrogen to estrogen+fluoride and reported the cumulative number of patients with an incident or recurring fracture within twenty seven months. [36]

Table 37 Fluoride vs. Estrogen vs. Fluoride+Estrogen - Fractures

Study	Outcome	Duration	Fluoride n/N (%)	Estrogen n/N (%)	p-value	Power
Gutteridge 2002	Fracture	27 Months	11/24 (45.83%)	5/15 (33.33%)	0.436	Low

Fluoride n/N (%)	Fluoride+Estrogen n/N (%)	p-value	Power

Study	Outcome	Duration	Fluoride n/N (%)	Estrogen n/N (%)	p-value	Power
			11/24 (45.83%)	4/14 (28.57%)	0.285	Low

Estrogen n/N (%)	Fluoride+Estrogen n/N (%)	p-value	Power
5/15 (33.33%)	4/14 (28.57%)	0.781	Low

IBANDRONATE

One study with moderately reliable data compared ibandronate intermittent or daily to placebo and reported the cumulative number of patients with an incident or recurring fracture within three years. [31] Additionally, this study reports the proportion of fractures that were symptomatic.

Table 38 Ibandronate vs. Placebo - Fractures

Study	Outcome	Duration	Ibandronate (intermittent) n/N (%)	Placebo n/N (%)	p-value	Power
Chesnut 2004	Symptomatic Fracture	3 Years	22/977 (2.25%)	41/975 (4.21%)	0.014	High
Chesnut 2004	Fracture	3 Years	39/977 (3.99%)	73/975 (7.49%)	0.001	High

Study	Outcome	Duration	Ibandronate (daily) n/N (%)	Placebo n/N (%)	p-value	Power
Chesnut 2004	Symptomatic Fracture	3 Years	22/977 (2.25%)	41/975 (4.21%)	0.014	High
Chesnut 2004	Fracture	3 Years	37/977 (3.79%)	73/975 (7.49%)	0.000	High

shaded box indicates favored treatment

IPRIFLAVONE

One study with moderately reliable data compared ipriflavone to placebo and reported the cumulative number of patients with an incident or recurring fracture within two years. [44]

Table 39 Ipriflavone vs. Placebo - Fractures

Study	Outcome	Duration	Ipriflavone n/N (%)	Placebo n/N (%)	p-value	Power
Maugeri	Fracture	2 Years	2/41 (4.88%)	11/43 (15.03%)	0.005	High

shaded box indicates favored treatment

MENATETRENONE

One study with moderately reliable data compared menatetrenone to a control group and reported the cumulative number of patients with an incident or recurring fracture within three years. [45]

Table 40 Menatetrenone vs. Control - Fractures

Study	Outcome	Duration	Menatetrenone n/N (%)	Control n/N (%)	p-value	Power
Inoue	Fracture	3 Years	152/516 (29.46%)	151/502 (30.08%)	0.828	High

MINONDRONATE

One study with reliable data compared minondronate to placebo and reported the cumulative number of patients with an incident or recurring fracture within two years.

Table 41 Minondronate vs. Placebo - Fractures

Study	Outcome	Duration	Minondronate n/N (%)	Placebo n/N (%)	p-value	Power
Matsumoto	Fracture	2 Years	31/343 (9.04%)	69/331 (20.85%)	0.000	High

shaded box indicates favored treatment

NANDROLONE VS. 1A-OH D3 VS. CALCIUM INFUSION

One study with moderately reliable data, which enrolled men and women, compared nandrolone to 1α-hydroxyvitaman D3 to calcium infusion and reported the cumulative number of patients with an incident or recurring fracture within two years. [64]

Table 42 Nandrolone vs. 1α-hydroxyvitaman D3 vs. Calcium Infusion - Fractures

Study	Outcome	Duration	Nandrolone n/N (%)	1α-OH D3 n/N (%)	p-value	Power
Geusens	Fracture	2 Years	5/11 (45.45%)	7/11 (63.64%)	0.389	Low
Study enrolled males and females						
			Nandrolone n/N (%)	**Calcium Infusion**	**p-value**	**Power**

Study	Outcome	Duration	Nandrolone n/N (%)	1α-OH D3 n/N (%)	p-value	Power
				n/N (%)		
			5/11 (45.45%)	8/12 (66.67%)	0.302	Low

1α-OH D3 n/N (%)	Calcium Infusion n/N (%)	p-value	Power
7/11 (63.64%)	4/14 (28.57%)	0.879	Low

PAMIDRONATE

One study with moderately reliable data, which enrolled men and women, compared pamidronate to placebo and reported the cumulative number of patients with an incident or recurring fracture within three years. [33] Additionally, this study reports the proportion of fractures that were symptomatic.

Table 43 Pamidronate vs. Placebo - Fractures

Study	Outcome	Duration	Pamidronate n/N (%)	Placebo n/N (%)	p-value	Power
Brumsen	Symptomatic Fracture	3 Years	3/46 (6.52%)	6/45 (13.33%)	0.270	High
Brumsen	Fracture	3 Years	5/46 (10.87%)	15/45 (33.33%)	0.008	High

Study enrolled males and females, shaded box indicates favored treatment

PHOSPHATE

One study with moderately reliable data compared phosphate to placebo and reported the cumulative number of patients with an incident or recurring fracture within two years. [39]

Table 44 Phosphate vs. Placebo - Fractures

Study	Outcome	Duration	Phosphate n/N (%)	Placebo n/N (%)	p-value	Power
Watts	Fracture	2 Years	7/92 (7.61%)	10/91 (10.99%)	0.429	High

PHOSPHATE VS. ETIDRONATE VS. PHOSPHATE+ETIDRONATE

One study with moderately reliable data compared phosphate to etidronate to etidronate+phosphate and reported the cumulative number of patients with an incident or recurring fracture within two years. [39]

Table 45 Phosphate vs. Etdironate vs. Phosphate+Etidronate - Fractures

Study	Outcome	Duration	Phosphate n/N (%)	Etidronate n/N (%)	p-value	Power
Watts	Fracture	2 Years	7/92 (7.61%)	5/98 (5.10%)	0.477	High

Study	Outcome	Duration	Phosphate n/N (%)	Etidronate n/N (%)	p-value	Power

Phosphate n/N (%)	Etidronate+Phosphate n/N (%)	p-value	Power
7/92 (7.61%)	3/97 (3.09%)	0.158	High

Etidronate n/N (%)	Etidronate+Phosphate n/N (%)	p-value	Power
5/98 (5.10%)	3/97 (3.09%)	0.476	High

RALOXIFENE

Two studies with moderately reliable data compared raloxifene to placebo and reported the cumulative number of patients with an incident or recurring fracture within one or three years. [47, 48]

Table 46 Raloxifene vs. Placebo - Fractures

Study	Outcome	Dosage	Duration	Raloxifene n/N (%)	Placebo n/N (%)	p-value	Power
Ettinger	Fracture	60 mg	3 Years	113/769 (14.69%)	163/770 (21.17%)	0.001	High
Lufkin 1998	Fracture	60 mg	1 Year	21/43 (48.84%)	18/45 (40.00%)	0.404	High
Ettinger	Fracture	120 mg	3 Years	82/765 (10.72%)	163/770 (21.17%)	0.000	High
Lufkin 1998	Fracture	120 mg	1 Year	20/45 (44.44%)	18/45 (40.00%)	0.669	High

Lufkin 1998: baseline differences in age, shaded box indicates favored treatment

RISEDRONATE

Three studies with moderately reliable data compared risedronate to placebo and reported the cumulative number of patients with an incident or recurring fracture within two or three years. [49-51]

Table 47 Risedronate vs. Placebo - Fractures

Study	Outcome	Dosage	Duration	Risedronate n/N (%)	Placebo n/N (%)	p-value	Power
Regnister	Fracture	5 mg daily	3 Years	53/344 (15.41%)	89/346 (25.72%)	0.001	High
Harris	Fracture	5 mg daily	3 Years	33/812 (4.06%)	52/815 (6.38%)	0.035	High
Clemmesen	Fracture	2.5 mg continuous	2 Years	13/29 (44.83%)	20/31 (64.52%)	0.123	High
Clemmesen	Fracture	2.5 mg cyclical	2 Years	15/33 (45.45%)	20/31 (64.52%)	0.123	High

shaded box indicates favored treatment

RISEDRONATE VS. ETIDRONATE

One study with moderately reliable data compared risedronate to etidronate and reported the cumulative number of patients with an incident or recurring fracture within four years. [59]

Table 48 Risedronate vs. Etidronate - Fractures

Study	Outcome	Duration	Risedronate %	Etidronate %	p-value	Power
Kushida 2004	Fracture	4 Years	12.27 %	14.19 %	0.554	High

Percentages reported by study authors, do not report sufficient information for n/N

STRONTIUM RANELATE

Two studies with moderately reliable data compared strontium ranelate to placebo and reported the cumulative number of patients with an incident or recurring fracture within one, two, or three years. [32, 52] Additionally, one study reports the proportion of fractures that were symptomatic. [70]

Table 49 Strontium Ranelate vs. Placebo - Fractures

Study	Outcome	Dosage	Duration	Strontium Ranelate n/N (%)	Placebo n/N (%)	p-value	Power
Meunier 2004	Symptomatic Fracture	2 g daily	1 Year	21/686 (3.06%)	45/699 (6.44%)	0.003	High
Meunier 2004	Symptomatic Fracture	2 g daily	3 Year	81/719 (11.27%)	126/723 (17.43%)	0.001	High
Meunier 2004	Fracture	2 g daily	1 Year	44/686 (6.41%)	85/699 (12.16%)	0.000	High
Meunier 2004	Fracture	2 g daily	3 Year	150/719 (20.86%)	237/723 (32.78%)	0.000	High
Meunier 2002	Fracture	0.5 g daily	2 years	31/80 (38.75%)	47/87 (54.02%)	0.047	High
Meunier 2002	Fracture	1 g daily	2 years	49/86 (56.98%)	47/87 (54.02%)	0.696	High
Meunier 2002	Fracture	2 g daily	2 years	36/85 (42.35%)	47/87 (54.02%)	0.125	High

shaded box indicates favored treatment

TERIPARATIDE

One study with moderately reliable data compared teriparatide to placebo and reported the cumulative number of patients with an incident or recurring fracture within two years. [53]

Table 50 Teriparatide vs. Placebo - Fractures

Study	Outcome	Dosage	Duration	Teriparatide n/N (%)	Placebo n/N (%)	p-value	Power
Neer	Fracture	20 mcg	2 Years	22/444 (4.95%)	64/448 (14.29%)	0.000	High
Neer	Fracture	40 mcg	2 Years	19/434 (4.38%)	64/448 (14.29%)	0.000	High

shaded box indicates favored treatment

TERIPARATIDE VS. TERIPARATIDE+CALCITONIN

One study with moderately reliable data compared teriparatide to teriparatide with calcitonin and reported the cumulative number of patients with an incident or recurring fracture within two years. [65]

Table 51 Teriparatide vs. Teriparatide+Calcitonin - Fractures

Study	Outcome	Duration	PTH n/N (%)	PTH+Calcitonin n/N (%)	p-value	Power
Hodsman	Fracture	2 Years	1/11 (9.09%)	4/13 (30.77%)	0.169	Low

KYPHOPLASTY

One study with moderately reliable data, which enrolled men and women with symptoms of spinal compression fractures, compared kyphoplasty to conservative treatment and reported the cumulative number of patients with an incident or recurring fracture within one year. [54]

Table 52 Kyphoplasty vs. Conservative Treatment - Fractures

Study	Outcome	Duration	Kyphoplasty n/N (%)	Conservative n/N (%)	p-value	Power
Wardlaw	Fracture	1 Year	38/115 (33.04%)	24/95 (25.26%)	0.216	High

Study enrolled males and females, patients were symptomatic at enrollment

VERTEBROPLASTY VS. PLACEBO

One study with reliable data, which enrolled men and women with symptoms of spinal compression fractures, compared vertebroplasty to placebo and reported the cumulative number of patients with an incident or recurring fracture within three and six months. [1]

Table 53 Vertebroplasty vs. Placebo - Fractures

Study	Outcome	Duration	Vertebroplasty n/N (%)	Placebo n/N (%)	p-value	Power
Buchbinder	Fracture	3 months	2/36 (5.56%)	4/37 (10.81%)	0.407	High
Buchbinder	Fracture	6 Months	3/35 (8.57%)	4/36 (11.11%)	0.719	High

Study enrolled males and females, patients were symptomatic at enrollment

VERTEBROPLASTY VS. CONSERVATIVE

One study with moderately reliable data compared vertebroplasty to conservative treatment and reported the cumulative number of patients with an incident or recurring fracture within the first three months.[55] Additionally, this study reports the number of these fractures that occurred on adjacent vertebrae.

Table 54 Vertebroplasty vs. Conservative - Fractures

Study	Outcome	Duration	Vertebroplasty n/N (%)	Conservative n/N (%)	p-value	Power

Study	Outcome	Duration	Vertebroplasty n/N (%)	Conservative n/N (%)	p-value	Power
Rousing	Fracture	3 months	3/24 (12.5%)	1/23 (4.35%)	0.300	Low
Rousing	Adjacent Fracture	3 months	2/24 (8.33%)	0/23 (0%)	0.045	High

KYPHOPLASTY VS. VERTEBROPLASTY

One study with reliable data, which enrolled men and women, compared kyphoplasty to vertebroplasty and reported the cumulative number of patients with an incident or recurring fracture within six months. [61] Another study with moderately reliable data compared kyphoplasty to vertebroplasty and reported the cumulative number of adjacent fractures within the first four months.[60]

Table 55 Kyphoplasty vs. Vertebroplasty - Fractures

Study	Outcome	Duration	Kyphoplasty n/N (%)	Vertebroplasty n/N (%)	p-value	Power
Grohs	Adjacent Fracture	4 months	6/28 (21.43%)	1/23 (4.35%)	0.054	Low
Liu	Adjacent Fracture	6 Months	2/50 (4.00%)	0/50 (0%)	0.044	High

Study enrolled males and females, shaded box indicates favored treatment

RECOMMENDATION 3

We are unable to recommend for or against bed rest, complementary and alternative medicine, or opioids/analgesics for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

Strength of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

Rationale

There are no existing adequate data to address the use of the following potential conservative, nonoperative therapies for a spinal compression fracture in patients who are neurologically intact: bed rest or complementary, alternative medicines and opioids/analgesics.

RECOMMENDATION 4

It is an option to treat patients who present with an osteoporotic spinal compression fracture at L3 or L4 on imaging with correlating clinical signs and symptoms suggesting an acute injury and who are neurologically intact with an L2 nerve root block.

Quality of Evidence	Quantity of Evidence	Applicability Downgrade	Critical Outcome(s)
Level II	1 study	No	Pain, Function

Strength of Recommendation: Limited

Description: Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single "Moderate" quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.

Rationale

The role of L2 selective nerve root blocks as a non-operative treatment for back pain associated with mid-lumbar compression fracture has been studied.[66] In this trial, two groups of 30 acute fracture patients received unilateral L2 root block or subcutaneous injection as a control. A possibly clinically important benefit was seen with the treatment at two weeks but became nonsignificant at one month. The effect of bilateral L2 injection was not addressed in this study or the literature. Based on this single study, support for L2 root injection for treating new onset back pain associated with L3 or L4 compression fractures is weak and is therefore only an option for temporary pain relief.

Supporting Evidence

One study with moderately reliable data enrolling 60 patients compared nerve block to a control group of subcutaneous injection.[66] The study occurred with "acute" injury patients. All patients received nonsteroidal anti-inflammatory drugs (NSAIDs) and soft lumbar support belts. Patients were allowed a maximum of 7 days of bed rest. Pain was reduced more in the nerve block group for two weeks at possibly clinically significant levels. The effects were no longer significant after two weeks, and there were no differences in function at any duration (

Table 57 - Table 59).

STUDY QUALITY

Table 56 Quality of Included Study for Recommendation 4 - Randomized Trial

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Ohtori	Pain - VAS	1 Hour	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Pain - VAS	1 Week	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Pain - VAS	2 Weeks	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Pain - VAS	1 Month	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Pain - VAS	2 Months	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Pain - VAS	3 Months	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Pain - VAS	4 Months	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Roland-Morris score	1 Month	60	Nerve block vs. control	Level II	×	×	×	×	●	●

Table 56 Quality of Included Study for Recommendation 4 - Randomized Trial

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Ohtori	Roland-Morris score	2 Months	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Roland-Morris score	3 Months	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	Roland-Morris score	4 Months	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	SF-36	1 Month	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	SF-36	2 Months	60	Nerve block vs. control	Level II	×	×	×	×	●	●
Ohtori	SF-36	4 Months	60	Nerve block vs. control	Level II	×	×	×	×	●	●

NERVE BLOCK VS. SUBCUTANEOUS INJECTION

Figure 4 Nerve Block vs. Subcutaneous Injection - Difference in Pain

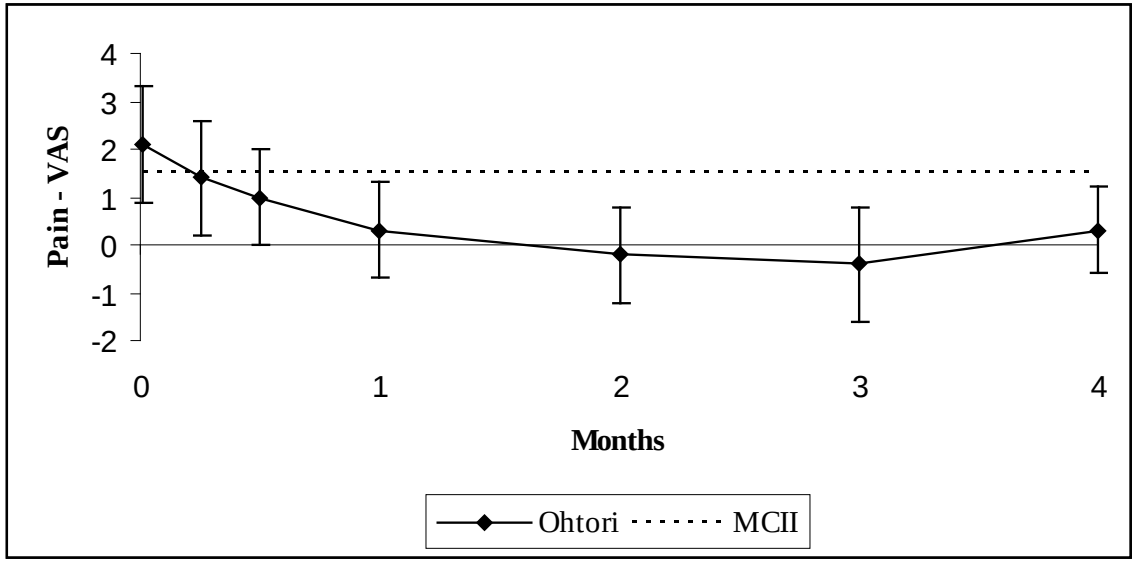


Table 57 Nerve block vs. Subcutaneous Injection - Pain

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Ohtori	60	II	"acute"	Pain - VAS	1 hour	2.1 (0.9, 3.3)	Nerve block	Possibly
					1 week	1.4 (0.2, 2.6)	Nerve block	Possibly
					2 weeks	1.0 (-0.01, 2.0)	○*	Inconclusive
					1 month	0.3 (-0.7, 1.3)	○	No
					2 months	-0.2 (-1.2, 0.8)	○	No
					3 months	-0.4 (-1.6, 0.8)	○	Inconclusive
					4 months	0.3 (-0.6, 1.2)	○	No

*Authors reported the difference at 2 weeks was statistically significant according to the Wilcoxon signed rank test (results presented in this table are based on an independent t-test)

Table 58 Nerve block vs. Subcutaneous Injection – Physical Function

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Ohtori	60	II	"acute"	Roland-Morris Disability	1 month	1.0 (-1.5, 3.5)	○	No
					2 months	0.0 (-2.5, 2.5)	○	No
					3 months	-0.5 (-2.8, 1.8)	○	No
					4 months	0.0 (-1.8, 1.8)	○	No

Table 59 Nerve block vs. Control – SF-36

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Ohtori	60	II	"acute"	SF-36 Physical Functioning	1 month	1.2 (-6.2, 8.6)	○	n/a
					2 months	-0.5 (-7.2, 6.2)	○	
					4 months	1.4 (-5.6, 8.4)	○	
				SF-36 Physical Role	1 month	4.6 (-1.7, 11.0)	○	
					2 months	2.2 (-5.0, 9.4)	○	
					4 months	0.3 (-5.9, 6.5)	○	
				SF-36 Bodily Pain	1 month	-0.2 (-3.9, 3.5)	○	
					2 months	3.3 (-0.2, 6.8)	○	
					4 months	-0.6 (-7.3, 6.1)	○	
				SF-36 Health Perception	1 month	3.3 (-2.5, 9.1)	○	
					2 months	5.0 (-1.9, 11.9)	○	
					4 months	3.0 (-2.9, 8.9)	○	
				SF-36 Vitality	1 month	4.0 (-2.5, 10.5)	○	
					2 months	-4.5 (-8.8, -0.2)	Control	
					4 months	2.2 (-3.5, 7.9)	○	
				SF-36 Social Functioning	1 month	5.8 (2.7, 8.9)	Nerve block	
					2 months	-1.0 (-6.2, 4.2)	○	
					4 months	27.2 (22.0, 32.4)	Nerve block*	
				SF-36 Emotional Role	1 month	-0.4 (-6.1, 5.3)	○	
					2 months	-1.1 (-6.9, 4.7)	○	
					4 months	-1.9 (-7.1, 3.3)	○	
				SF-36 Mental Health	1 month	-5.2 (-9.8, -0.6)	Control	
					2 months	0.0 (-4.8, 4.8)	○	
					4 months	-1.6 (-6.6, 3.4)	○	

*Authors report this as not significant; possibly a typo in the reported results

RECOMMENDATION 5

We are unable to recommend for or against treatment with a brace for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

Quality of Evidence	Quantity of Evidence	Applicability Downgrade	Critical Outcome(s)
Level II	1 study	Yes	Pain, Function

Strength of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

Rationale

There was only one Level II article studying the effect of bracing.[67] This recommendation was downgraded to inconclusive because neither the age nor the level of the fracture being treated was reported. Additionally, this study investigated only a single specific type of brace for all fractures which call into question the generalizability of these results to all braces. While the results were statistically significant, we do not know if they were clinically important (MCII unknown). Based on this single study, there is insufficient evidence to recommend for or against the use of bracing.

Supporting Evidence

One study with moderately reliable data enrolling 62 patients investigated brace vs. no brace among patients whose time after injury was not specified.[67] Patients wore the back orthosis for 6 months. Pain, function, and well-being measures favored the brace group at 6 months (Table 61).

STUDY QUALITY

Table 60 Quality of Included Study for Recommendation 5 - Randomized Trial

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Pfeifer	LDL disability	6 Months	62	Brace vs. control	Level II	×	×	○	○	●	●
Pfeifer	LDL self care	6 Months	62	Brace vs. control	Level II	×	×	○	○	●	●
Pfeifer	Pain	6 Months	62	Brace vs. control	Level II	×	×	○	○	●	●
Pfeifer	Well being	6 Months	62	Brace vs. control	Level II	×	×	○	○	●	●

BRACE VS. NO BRACE

Table 61 Brace vs. No Brace – Pain and Limitations of Daily Living

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)*	Favors	Clinically Important?
Pfeifer	62	II	Not Specified	Pain – Miltner's rating scale	6 months	1.6 (1.1, 2.1)	Brace	n/a
				Limitations of daily living – Disability	6 months	2.3 (1.7, 2.9)	Brace	
				Limitations of daily living – Self-care	6 months	1.1 (0.7, 1.5)	Brace	
				Well-being	6 months	12.7 (9.7, 15.7)	Brace	

*Difference in change scores

RECOMMENDATION 6

We are unable to recommend for or against a supervised or unsupervised exercise program for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

Quality of Evidence	Quantity of Evidence	Applicability Downgrade	Critical Outcome(s)
Level II	1 study	Yes	Pain, Function

Strength of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

Rationale

A single Level II study evaluated fractures with low back pain of greater than 3 months' duration using a home-based exercise program compared to a control group continuing usual activities using the Osteoporosis Quality of Life Questionnaire, which evaluates 5 domains.[68] We downgraded this recommendation to inconclusive because the low back pain experienced by patients in this study may not be the direct result of a specific spinal compression fracture. Results did favor exercise to improve the symptom domain at 6 and 12 months and the emotion domain at 6 months but not at 12 months. There was no difference in the physical function domain at 6 or 12 months. When evaluating the domain of activities of daily living there was no difference at 6 months but there was evidence favoring exercise at 12 months. In evaluating the leisure/social domain there was evidence to support exercise at the 6 month level but no difference at the 12 month level. The clinical importance of these outcomes is unknown. There was no documentation that the back pain measured was a direct result of the fracture.

Supporting Evidence

One study with moderately reliable data enrolling 60 patients compared a home-based exercise program vs. a control group continuing usual activities.[68] The patients had a chronic injury (>3 months since fracture). Several domains of the Osteoporosis Quality of Life Questionnaire favored the exercise group at either 6 or 12 months, but the Sickness Impact Profile showed no significant difference (Table 63 - Table 64).

STUDY QUALITY

Table 62 Quality of Included Study for Recommendation 6 - Randomized Trial

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Papaioannou	Osteoporosis Quality of Life Questionnaire	6 Months	60	Exercise vs. control	Level II	●	×	○	○	●	○
Papaioannou	Osteoporosis Quality of Life Questionnaire	12 Months	57	Exercise vs. control	Level II	●	×	○	○	●	○
Papaioannou	Sickness Impact Profile	6 Months	60	Exercise vs. control	Level II	●	×	○	○	●	○
Papaioannou	Sickness Impact Profile	12 Months	57	Exercise vs. control	Level II	●	×	○	○	●	○

EXERCISE VS. NO EXERCISE

Table 63 Exercise vs. Control - Osteoporosis Quality of Life Questionnaire (OQLQ)

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors*	Clinically Important?
Papaioannou	6 months:60 12 months:57	II	>3 months	OQLQ Symptoms	6 months	0.44 (0.16, 0.73)	Exercise	n/a
					12 months	0.38 (-0.05, 0.81)	Exercise	
				OQLQ Emotions	6 months	0.34 (0.02, 0.66)	Exercise	
					12 months	0.30 (-0.21, 0.81)	○	
				OQLQ Physical Function	6 months	0.22 (-0.08, 0.52)	○	
					12 months	0.16 (-0.35, 0.68)	○	
				OQLQ Activities of Daily Living	6 months	0.17 (-0.09, 0.43)	○	
					12 months	0.34 (-0.11, 0.79)	Exercise	
				OQLQ Leisure/Social Activities	6 months	0.39 (-0.02, 0.81)	Exercise	
					12 months	0.26 (-0.22, 0.74)	○	

*Baseline-adjusted p-values

Table 64 Exercise vs. Control - Sickness Impact Profile (SIP)

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors*	Clinically Important?
Papaioannou	60	II	>3 months	SIP Physical Domain	6 months	0.80 (-1.52, 3.13	○	n/a
				SIP Psychosocial Domain		0.09 (-3.21, 3.41)	○	
				SIP Total		0.55 (-1.81, 2.91)	○	

*Baseline-adjusted p-values

RECOMMENDATION 7

We are unable to recommend for or against electrical stimulation for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

Quality of Evidence	Quantity of Evidence	Applicability Downgrade	Critical Outcome(s)
Level I	1 study	Yes	Pain, Function

Strength of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

Rationale

One Level I study addressed the use of electrical stimulation limited to symptomatic patients with chronic vertebral compression fractures, with short term follow up of three months.[69] This study had insufficient power to find a difference in this treatment when compared to a control group for the critical outcome measure of pain relief as well as quality of life. A surrogate outcome measure of change in use of NSAIDs was reported but the change in use was based on percentage of patients using less NSAIDs with electrical stimulation as opposed to the actual amount of NSAIDs used by individual patients. This outcome measure has little clinical significance and no quantitative measure to gauge pre vs. post treatment effect. Because of the inability to detect a difference in pain (an outcome that is critical to understand treatment effectiveness) or quality of life ,the evidence is inconclusive and we are unable to recommend for or against this treatment.

Supporting Evidence

One study with reliable data from 41 patients compared CCEF stimulation vs. placebo stimulation.[69] Patients had had a fracture for greater than 6 months, and all patients began the study taking analgesic medication. The study lacked power to detect a significant difference in pain or quality of life between the two groups. At 10 and 11 weeks only, the active treatment group had significantly fewer patients continuing NSAID usage (Table 66 -

Table 68).

STUDY QUALITY

Table 65 Quality of Included Study for Recommendation 7 - Randomized Trial

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Rossini	Analgesic Usage	1 Week	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	2 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	3 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	4 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	5 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	6 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	7 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	8 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●

Table 65 Quality of Included Study for Recommendation 7 - Randomized Trial

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Rossini	Analgesic Usage	9 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	10 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	11 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Analgesic Usage	12 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Pain - VAS	2 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Pain - VAS	4 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Pain - VAS	8 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	Pain - VAS	12 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	QUALEFFO	2 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●

Table 65 Quality of Included Study for Recommendation 7 - Randomized Trial

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Rossini	QUALEFFO	4 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	QUALEFFO	8 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●
Rossini	QUALEFFO	12 Weeks	41	CCEF stimulation vs. placebo	Level I	●	×	●	●	●	●

ELECTRICAL STIMULATION VS. PLACEBO

Figure 5 CCEF Stimulation vs. Placebo - Difference in Pain

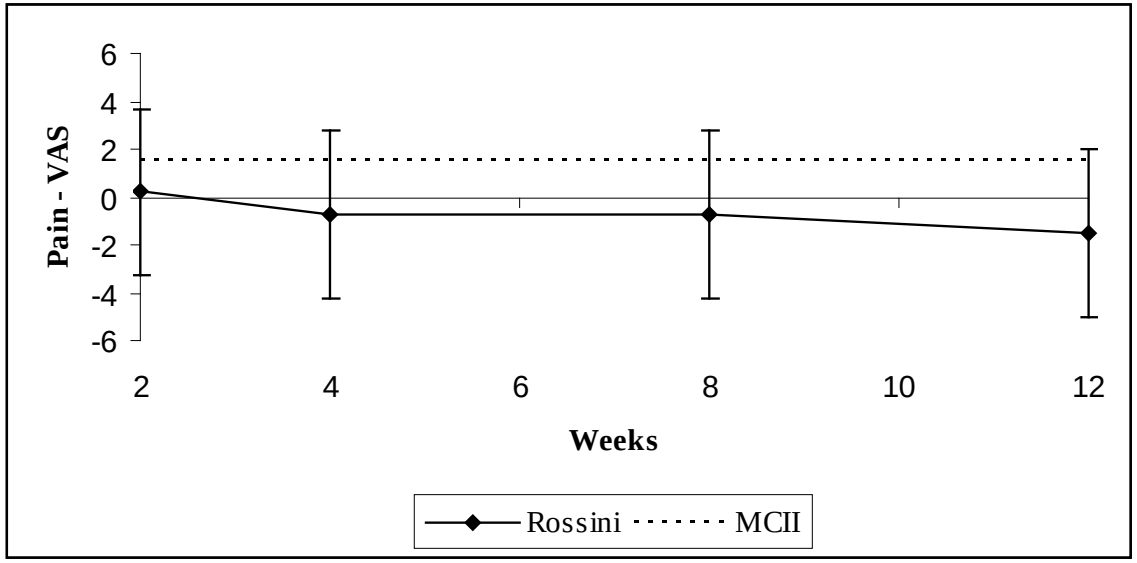


Table 66 CCEF Stimulation vs. Placebo - Pain

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Rossini	41	I	>6 months	Pain – VAS	2 weeks	0.2 (-3.3, 3.7)	○	Inconclusive
					4 weeks	-0.7 (-4.2, 2.8)	○	Inconclusive
					8 weeks	-0.7 (-4.2, 2.8)	○	Inconclusive
					12 weeks	-1.5 (-5.0, 2.0)	○	Inconclusive

Study lacked sufficient power to detect large effect

Table 67 CCEF Stimulation vs. Placebo - Quality of Life

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Rossini	41	I	>6 months	QUALEFFO*	2 weeks	-1.8 (-11.0, 7.4)	○	n/a
					4 weeks	-6.4 (-15.6, 2.8)	○	
					8 weeks	-4.8 (-14.0, 4.4)	○	
					12 weeks	-4.2 (-13.4, 5.0)	○	

*Quality of life questionnaire of the European Foundation for Osteoporosis; study lacked sufficient power to detect large effect

Table 68 CCEF Stimulation vs. Placebo - Patients continuing NSAID usage

Study	Level of Evidence	Time After Injury	Outcome	Duration	CCEF n/N	Placebo n/N	OR (95% CI)
Rossini	I	>6 months	NSAID Use	1 week	6/20	12/21	0.32 (0.07, 1.38)
				2 weeks	5/20	11/21	0.30 (0.06, 1.35)
				3 weeks	5/20	7/21	0.67 (0.13, 3.15)
				4 weeks	2/20	6/21	0.28 (0.02, 1.91)
				5 weeks	3/20	5/21	0.56 (0.08, 3.52)
				6 weeks	1/20	4/21	0.22 (0.004, 2.64)
				7 weeks	2/20	5/21	0.36 (0.03, 2.61)
				8 weeks	3/20	6/21	0.44 (0.06, 2.56)
				9 weeks	1/20	6/21	0.13 (0.003, 1.32)
				10 weeks	1/20	9/21	0.07 (0.002, 0.65)
				11 weeks	1/20	8/21	0.09 (0.002, 0.81)
				12 weeks	2/20	8/21	0.18 (0.02, 1.16)

Study lacked sufficient power to detect large effect for each non-significant outcome; shaded cell indicates favored treatment

RECOMMENDATION 8

We recommend against vertebroplasty for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

Quality of Evidence	Quantity of Evidence	Applicability Downgrade	Critical Outcome(s)
Level I Level II	2 studies 3 studies	No	Pain, Function

Strength of Recommendation: Strong

Description: Evidence is based on two or more "High" strength studies with consistent findings for recommending for or against the intervention. A **Strong** recommendation means that the benefits of the recommended approach clearly exceed the potential harm (or that the potential harm clearly exceeds the benefits in the case of a strong negative recommendation), and that the strength of the supporting evidence is high.

Implications: Practitioners should follow a **Strong** recommendation unless a clear and compelling rationale for an alternative approach is present.

Rationale

There are two Level I studies that compare vertebroplasty to a sham procedure.[1, 70] These studies report no statistically significant difference between the two procedures in pain using the VAS and function using the Roland Morris Disability scale (up to one month and six months respectively).

These studies have been criticized for a variety of reasons. It has been argued that one of the trials[1] was underpowered. However, this study did have sufficient power to detect the minimally clinically important (MCII) difference in pain (see Supporting Evidence section for details). Although crossover of patients after one month may have influenced the results in one of these studies,[70] there was no crossover in the other study[1] which also found no statistically significant or clinically important differences. Furthermore, crossover does not affect the lack of benefit for pain and function that the authors measured at one month.

Another concern was the low participation rate of eligible patients. This is an issue of external validity (generalizability) and not internal validity. The work group discussed this flaw, but chose not to downgrade this study for applicability because the trial authors noted that the enrolled patients were comparable to patients seen in routine care.[ref]

Furthermore, it has been proposed that vertebroplasty works better with certain fracture types than others. There are no prospective studies that report significant differences in outcomes based on fracture type.

It has also been proposed that vertebroplasty works better in patients that have more pain than those that were included in these trials. The baseline pain in both these trials was approximately 7 on a scale from 0 to 10. Other comparative studies had a baseline pain of about 8 and also had a mainly negative outcome.[55, 71, 72]

We recognize that a sham procedure may still introduce bias in the results (e.g. surgeons who know they are performing a sham procedure can unintentionally convey expectations to their patients) but there are also three other Level II studies that do not use a sham procedure as a control and they report similar results. One of these studies found clinically important pain relief at 24 hours.[72] At six weeks pain relief was still statistically significant but not clinically important. After six weeks the effect was not statistically or clinically important (observations to two years). One study reported results for pain that were statistically significant and possibly clinically important at one day but inconclusive at two weeks.[71] Another study found inconclusive results at three months.[55]

By making a strong recommendation against the use of vertebroplasty we are expressing our confidence that future evidence is unlikely to overturn the results of these trials.

Supporting Evidence

Two studies with reliable data enrolling a total of 209 patients compared vertebroplasty to placebo.[1, 70] One study included patients with subacute fractures (9 weeks since injury),[1] while the other included chronic fractures (18 weeks).[70] In the study of patients with subacute fractures, after the surgery all participants received usual care according to the discretion of the treating physician.[1] In the study of patients with chronic fractures, patients were allowed to cross over to the alternative treatment after one month.[70] There were no significant differences in pain, function, or quality of life in either study (Table 72 -Table 77).

Three additional studies with moderately reliable data enrolling a total of 210 patients compared vertebroplasty to conservative treatment.[55, 71, 72] Two studies were of patients with acute injuries, [55, 72] while the other included patients with subacute injuries (mean time after injury 11.6 weeks).[71] In the randomized trial of patients with acute injuries, patients in both groups were offered pain medication and physiotherapy, while only patients in the conservative group were offered brace treatment.[55] In the non-randomized trial of patients with acute injuries, all patients were offered similar analgesia and osteoporosis medications.[72] In the randomized trial of patients with subacute injuries, patients were treated with pain medication according to individual needs.[71] Pain was significantly reduced for one day in the vertebroplasty group, but not for longer durations (the significant result at 6 weeks is not clinically important). Function was improved for 2 weeks in one study and 6 weeks in another, but was no longer significant beyond 6 months. Quality of life and analgesic use favored the vertebroplasty group at 2 weeks. Fracture-related mortality was significantly reduced in the vertebroplasty group, but overall mortality was not (Table 78 - Table 83).

*Power calculations referenced in Rationale:*While the study's *a priori* power analysis indicated that the study was powered to detect a between-group difference in pain of 2.5 units on VAS, further analysis indicated that the study was also powered sufficiently to detect the minimally clinically important difference of 1.5 units on VAS. Using the study's baseline standard deviation of 2.2 units, the minimum sample size required to have sufficient power to detect a 1.5 unit difference was 35 patients per group. The study enrolled 38 patients in the vertebroplasty group and 40 patients in the placebo group.

SUMMARY OF EVIDENCE

Table 69 Summary of Vertebroplasty Outcomes

	1 day	3 days	1 week	2 weeks	1 month	6 weeks	3 months	6 months	6-12 months	24 months
ADL					○					
Adverse Events							○	○		
Analgesic Use	■			■	○					
AQoL			○		○		○	○		
Barthel Index	■					■			□	□
Dallas Pain Questionnaire (all subtests)							X			
EQ-5D			○		○○		○	○		
Mortality								■		□
Pain at rest			○		○		○	○		
Pain Bothersome Index					○					
Pain Frequency Index					○					
Pain in bed at night			○		○		○	○		
Pain-VAS	■■	○	○	○X	○○	■	○X	○	□	□
QUALEFFO			●	■	○		○	○		
Roland Morris Disability		○	○	○■	○○		○	○		
SF-36 MCS					○		X			
SF-36 PCS					○		X			

circle-vertebroplasty compared to placebo w/usual care; square-vertebroplasty compared to conservative treatment
green-clinically important in favor of vertebroplasty; **blue**-possibly clinically important in favor of vertebroplasty;
yellow-not clinically important in favor of vertebroplasty; **red**-statistically significant in favor of placebo/conservative;
grey-statistically significant; open-not statistically significant, X-underpowered study

STUDY QUALITY

Table 70 Quality of Included Studies for Recommendation 8 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Rousing	Pain - VAS	3 Months	43	Vertebroplasty vs. conservative	Level II	×	●	○	○	●	●
Rousing	SF-36 (mental)	3 Months	43	Vertebroplasty vs. conservative	Level II	×	●	○	○	●	●
Rousing	SF-36 (physical)	3 Months	43	Vertebroplasty vs. conservative	Level II	×	●	○	○	●	●
Rousing	DPQ (anxiety and depression)	3 Months	33	Vertebroplasty vs. conservative	Level II	×	●	○	○	○	●
Rousing	DPQ (daily activities)	3 Months	42	Vertebroplasty vs. conservative	Level II	×	●	○	○	●	●
Rousing	DPQ (social interest)	3 Months	45	Vertebroplasty vs. conservative	Level II	×	●	○	○	○	●
Rousing	DPQ (work and leisure)	3 Months	43	Vertebroplasty vs. conservative	Level II	×	●	○	○	●	●
Voormolen	Analgesic Usage	1 Day	34	Vertebroplasty vs. conservative	Level II	×	×	○	○	●	●

Table 70 Quality of Included Studies for Recommendation 8 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Voormolen	Analgesic Usage	2 Weeks	34	Vertebroplasty vs. conservative	Level II	×	×	○	○	●	●
Voormolen	Pain - VAS	1 Day	34	Vertebroplasty vs. conservative	Level II	×	×	○	○	●	●
Voormolen	Pain - VAS	2 Weeks	34	Vertebroplasty vs. conservative	Level II	×	×	○	○	●	●
Voormolen	QUALEFFO	2 Weeks	34	Vertebroplasty vs. conservative	Level II	×	×	○	○	●	●
Voormolen	Roland-Morris score	2 Weeks	34	Vertebroplasty vs. conservative	Level II	×	×	○	○	●	●
Buchbinder	AQoL	1 Week	74	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	AQoL	1 Month	73	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	AQoL	3 Months	73	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	AQoL	6 Months	71	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●

Table 70 Quality of Included Studies for Recommendation 8 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Buchbinder	EQ-5D	1 Week	59	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	EQ-5D	1 Month	59	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	EQ-5D	3 Months	59	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	EQ-5D	6 Months	59	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	Pain - VAS	1 Week	74	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	Pain - VAS	1 Month	73	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	Pain - VAS	3 Months	73	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	Pain - VAS	6 Months	71	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	QUALEFFO	1 Week	74	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●

Table 70 Quality of Included Studies for Recommendation 8 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Buchbinder	QUALEFFO	1 Month	73	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	QUALEFFO	3 Months	73	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	QUALEFFO	6 Months	71	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	Roland-Morris score	1 Week	59	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	Roland-Morris score	1 Month	59	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	Roland-Morris score	3 Months	59	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Buchbinder	Roland-Morris score	6 Months	59	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	EQ-5D	1 Month	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	Opioid Use	1 Month	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●

Table 70 Quality of Included Studies for Recommendation 8 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Kallmes	Pain - VAS	3 Days	131	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	Pain - VAS	2 Weeks	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	Pain - VAS	1 Month	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	Pain Bothersomeness Index	1 Month	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	Pain Frequency Index	1 Month	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	Roland-Morris score	3 Days	131	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	Roland-Morris score	2 Weeks	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	Roland-Morris score	1 Month	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	SF-36	1 Month	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●
Kallmes	SOF-ADL	1 Month	125	Vertebroplasty vs. Placebo	Level I	●	●	●	●	●	●

Table 71 Quality of Included Studies for Recommendation 8 - Prospective Comparative Study

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	All groups have similar characteristics at entry	All groups have similar outcome performance at entry	All groups concurrently treated	Follow Up - 80% or more	Same center for experimental and control group data
Diamond	Pain - VAS	1 Day	126	Vertebroplasty vs. conservative	Level II	●	●	●	●	●
Diamond	Pain - VAS	6 Weeks	126	Vertebroplasty vs. conservative	Level II	●	●	●	●	●
Diamond	Pain - VAS	12 Months	126	Vertebroplasty vs. conservative	Level II	●	●	●	●	●

VERTEBROPLASTY VS. PLACEBO

Figure 6 Vertebroplasty vs. Placebo – Difference in Pain

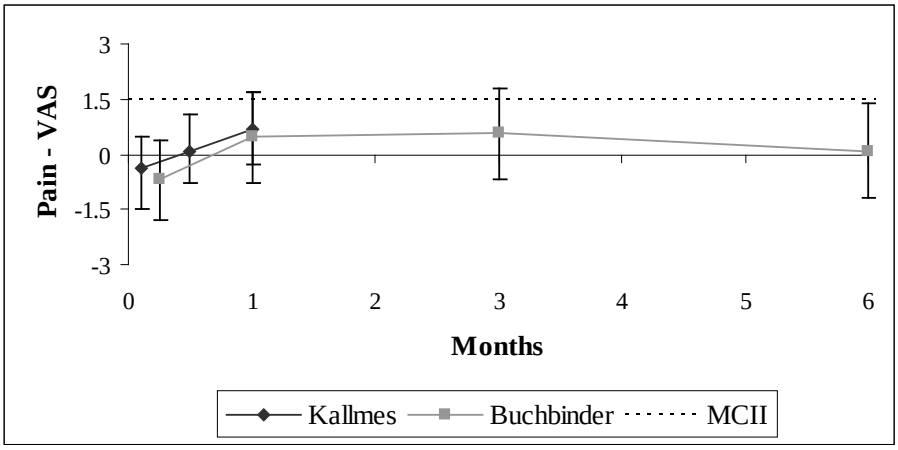


Figure 7 Vertebroplasty vs. Placebo – Difference in Physical Function

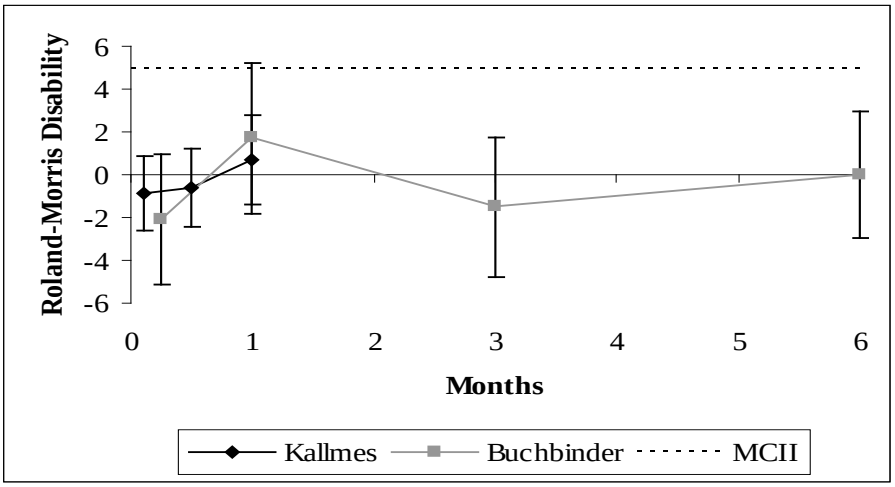


Table 72 Vertebroplasty vs. Placebo - Pain

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)*	Favors	Clinically Important?
Kallmes	131	I	18 weeks	Pain - VAS	3 days	-0.4 (-1.5, 0.5)	○	No
Buchbinder	74		9 weeks		1 week	-0.7 (-1.8, 0.4)	○	Inconclusive
Kallmes	125		18 weeks		2 weeks	0.1 (-0.8, 1.1)	○	No
Buchbinder	73		9 weeks		1 month	0.5 (-0.8, 1.7)	○	Inconclusive
Kallmes	125		18 weeks			0.7 (-0.3, 1.7)	○	Inconclusive
Buchbinder	73		9 weeks		3 months	0.6 (-0.7, 1.8)	○	Inconclusive
	71				6 months	0.1 (-1.2, 1.4)	○	No
Kallmes	125		18 weeks	Pain Frequency Index	1 month	0.2 (-0.2, 0.6)	○	No
				Pain Bothersomeness Index	1 month	0.2 (-0.2, 0.6)	○	No
Buchbinder	74		9 weeks	Pain at rest	1 week	-0.2 (-1.5, 1.1)	○	No
	73				1 month	0.5 (-0.9, 1.8)	○	Inconclusive
	73				3 months	0.1 (-1.1, 1.4)	○	No
	71				6 months	0.3 (-0.9, 1.5)	○	No
	74			Pain in bed at night	1 week	-0.1 (-1.3, 1.1)	○	No
	73				1 month	0.8 (-0.5, 2.1)	○	Inconclusive
	73				3 months	0.2 (-0.9, 1.3)	○	No
	71				6 months	-0.2 (-1.6, 1.1)	○	No

*Baseline-adjusted differences

Table 73 Vertebroplasty vs. Placebo – Physical Function

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)*	Favors	Clinically Important?
Kallmes	131	I	18 weeks	Roland-Morris Disability (RMD)	3 days	-0.9 (-2.7, 0.8)	○	No
Buchbinder	74		9 weeks		1 week	-2.1 (-5.2, 0.9)	○	Inconclusive
Kallmes	125		18 weeks		2 weeks	-0.6 (-2.4, 1.2)	○	No
Buchbinder	73		9 weeks		1 month	1.7 (-1.8, 5.2)	○	Inconclusive
Kallmes	125		18 weeks			0.7 (-1.3, 2.8)	○	No
Buchbinder	73		9 weeks		3 months	-1.5 (-4.8, 1.7)	○	No
	71				6 months	0.0 (-3.0, 2.9)	○	No
Kallmes	125		18 weeks	Activities of Daily Living (SOF-ADL)	1 month	0.4 (-0.8, 1.6)	○	n/a

*Baseline-adjusted differences

Table 74 Vertebroplasty vs. Placebo – Physical and Mental Health

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)*	Favors	Clinically Important?
Kallmes	125	I	18 weeks	SF-36 Physical Component	1 month	1.0 (-1.7, 3.7)	○	No
				SF-36 Mental Component		1.0 (-3.7, 4.6)	○	n/a

*Baseline-adjusted differences

Table 75 Vertebroplasty vs. Placebo – Analgesic Use

Study	Level of Evidence	Time After Injury	Outcome	Duration	Vertebroplasty n/N	Placebo n/N	OR (95% CI)*
Kallmes	I	18 weeks	Opioid Use	1 month	37/68	27/63	1.15 (0.98, 1.35)

*Baseline-adjusted differences

Table 76 Vertebroplasty vs. Placebo – Quality of Life

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)*	Favors	Clinically Important?
Buchbinder	74	I	9 weeks	EQ-5D	1 week	0.0 (-0.1, 0.2)	○	Inconclusive
Kallmes	125		18 weeks		1 month	0.05 (-0.01, 0.11)	○	
Buchbinder	73		9 weeks		1 month	0.0 (-0.1, 0.1)	○	
	73				3 months	0.0 (-0.1, 0.2)	○	
	71				6 months	0.0 (-0.1, 0.2)	○	
Buchbinder	74		9 weeks	AQoL (Assessment of Quality of Life)	1 week	0.0 (-0.1, 0.1)	○	
	73				1 month	0.0 (-0.1, 0.1)	○	
	73				3 months	0.0 (-0.1, 0.1)	○	
	71				6 months	0.1 (-0.1, 0.2)	○	
Buchbinder	74		9 weeks	QUALEFFO	1 week	-4.0 (-7.8, -0.2)	Placebo	n/a
	73				1 month	0.9 (-4.2, 6.0)	○	
	73				3 months	0.7 (-4.4, 5.7)	○	
	71				6 months	0.6 (-5.1, 6.2)	○	

*Baseline-adjusted differences

Table 77 Vertebroplasty vs. Placebo – Adverse Events

Study	Level of Evidence	Time After Injury	Outcome	Duration	Vertebroplasty n/N	Placebo n/N	p-value
Kallmes	I	18 weeks	Adverse Events	3 months	1/68	1/63	0.96
Buchbinder		9 weeks	Adverse Events (other than incident fractures)	6 months	13/38	6/40	0.066

VERTEBROPLASTY VS. CONSERVATIVE

Figure 8 Vertebroplasty vs. Conservative – Difference in Pain

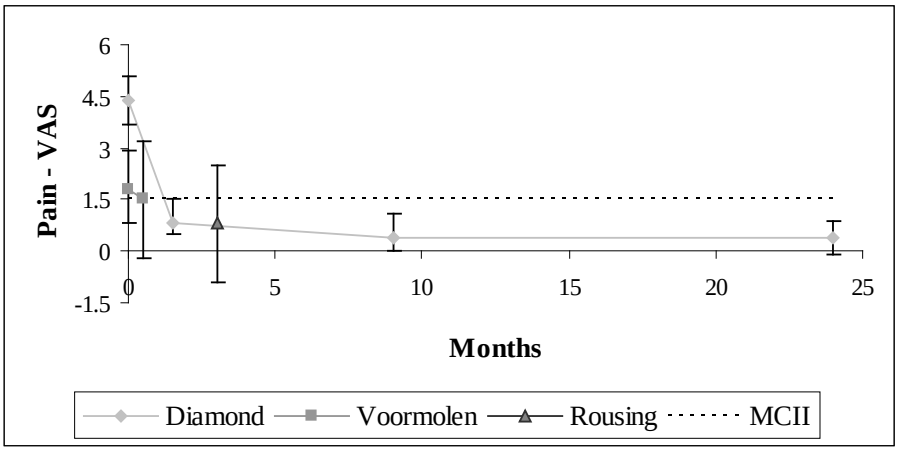


Figure 9 Vertebroplasty vs. Conservative – Difference in Physical Function (Barthel Index)

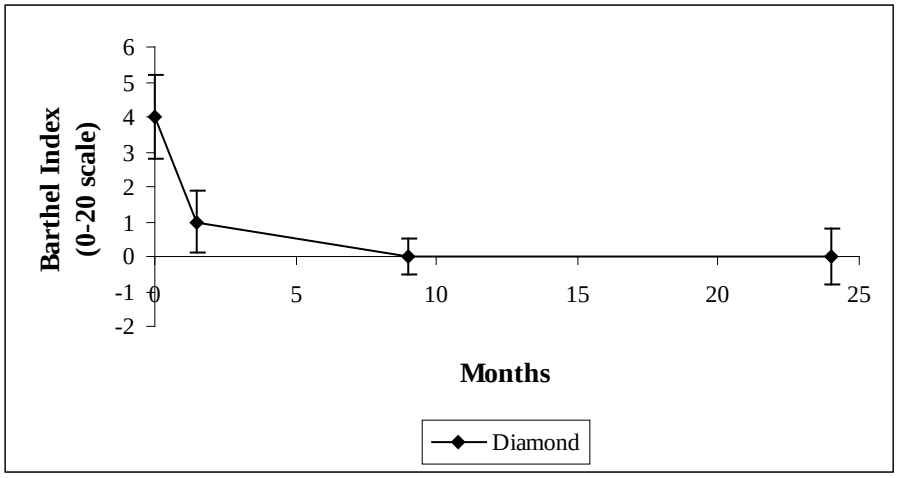


Table 78 Vertebroplasty vs. Conservative - Pain

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Diamond	126	II	1-6 weeks	Pain – VAS	1 day	4.4 (3.7, 5.1)*	Vertebroplasty	Yes
Voormolen	34		11.6 weeks			1.8 (0.8, 2.9)	Vertebroplasty	Possibly
					2 weeks	1.5 (-0.2, 3.2)	○	Inconclusive
Diamond	126		1-6 weeks		6 weeks	0.8 (0.5, 1.5)*	Vertebroplasty	No
Rousing	46		1 week		3 months	0.8 (-0.9, 2.5)	○	Inconclusive
Diamond	126		1-6 weeks		6-12 months	0.4 (-0.3, 1.1)*	○	No
					24 months	0.4 (-0.1, 0.9)*	○	No

*Study used 0-25 scale; data has been normalized to 0-10 scale; Voormolen and Rousing studies lacked sufficient power to detect large effect for each non-significant outcome

Table 79.Vertebroplasty vs. Conservative – Physical Function

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Diamond	126	II	1-6 weeks	Barthel Index	1 day	4.0 (2.8, 5.2)	Vertebroplasty	n/a
					6 weeks	1.0 (0.1, 1.9)	Vertebroplasty	
					6-12 months	0.0 (-0.5, 0.5)	○	
					24 months	0.0 (-0.8, 0.8)	○	
Voormolen	34	II	11.6 weeks	Roland-Morris Disability	2 weeks	5.0 (1.2, 8.4)	Vertebroplasty	Possibly

Table 80 Vertebroplasty vs. Conservative – Quality of Life

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Voormolen	34	II	11.6 weeks	QUALEFFO	2 weeks	14 (3.4, 24.7)	Vertebroplasty	n/a

Table 81 Vertebroplasty vs. Conservative – Physical and Mental Health

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Rousing	43	II	1 week	SF-36 Physical Component	3 months	4.7 (-1.2, 10.6)	○	Inconclusive
				SF-36 Mental Component		2.7 (-5.6, 11.0)	○	n/a
				Dallas Pain Questionnaire (DPQ) daily activities		-10.3 (-32.9, 12.3)	○	
				DPQ work and leisure		-20.7 (-41.9, 0.5)	○	
				DPQ anxiety and depression		-11.3 (-35.1, 12.5)	○	
				DPQ social interest		-6.6 (-25.4, 12.2)	○	

Study lacked sufficient power to detect large effect for each outcome

Table 82 Vertebroplasty vs. Conservative – Analgesic Use

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Voormolen	34	II	11.6 weeks	Analgesic Use	1 day	1.4 (0.8, 2.1)	Vertebroplasty	n/a
					2 weeks	1.4 (0.8, 2.0)	Vertebroplasty	

Table 83 Vertebroplasty vs. Conservative – Adverse Events

Study	Level of Evidence	Time After Injury	Outcome	Duration	Vertebroplasty n/N	Conservative n/N	Hazard Ratio (95% CI)
Diamond	II	1-6 weeks	Mortality	6 months	1/88	4/38	0.11 (0.01, 0.96)
				2 years	15/88	6/38	1.07 (0.42, 2.76)

Shaded cell indicates favored treatment

RECOMMENDATION 9

Kyphoplasty is an option for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

Quality of Evidence	Quantity of Evidence	Applicability Downgrade	Critical Outcome(s)
Level II	5 studies	Yes	Pain, Function

Strength of Recommendation: Limited

Description: Evidence from two or more "Low" strength studies with consistent findings, or evidence from a single "Moderate" quality study recommending for or against the intervention or diagnostic. A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

Implications: Practitioners should exercise clinical judgment when following a recommendation classified as **Limited**, and should be alert to emerging evidence that might negate the current findings. Patient preference should have a substantial influencing role.

Rationale

Two Level II studies examined the use of kyphoplasty compared to conservative treatment.[54, 73] One study examined subacute fractures[54] while the other study examined chronic fractures.[73] In the study of patients with subacute fractures, clinically important benefits in pain were found at 1 week and 1 month, with possibly important effects at 3 and 6 months. There was no clinically important benefit in pain at 12 months. The study also found possibly clinically important benefits in physical function (at 1 and 3 months only) and the SF-36 physical component score (at 1, 3, and 6 months only). Clinically important improvement in quality of life was present at 1 month, and it was possibly clinically important at 3, 6, and 12 months.

In the chronic fractures study, all patients had fractures that were greater than one year old, raising the question as to whether the fracture was responsible for all of the pain. There was a statistically significant and possibly clinically important improvement in pain at 3, 6 and 12 months.

There were also three Level II studies which compared kyphoplasty to vertebroplasty.[60, 61, 74] These studies were inconsistent in design and outcome. In the first study, patients were treated at a median of 8 weeks after a fracture.[60] No conservative treatment control group was included. Kyphoplasty was favored over vertebroplasty when pain was measured out to two years. Repeat kyphoplasty in this study was a confounding factor. In

the second study 21 patients were treated.[74] Both groups experienced similar pain relief at 6 months, although there was insufficient power to find a difference. In the third and most recent study, 100 patients received either kyphoplasty or vertebroplasty within 43 days of fracture.[61] There was no difference in pain outcomes between the treatment groups at 3 days and 6 months.

When considering the technical similarities between kyphoplasty and vertebroplasty and the unique recommendations for their use within this guideline, several points deserve mention.

- The comparison of vertebroplasty to a sham procedure confirms the lack of benefit from vertebroplasty for critical outcomes.

- Both procedures were compared to similar control groups. In the case of kyphoplasty the comparison to conservative treatment resulted in possible clinically important differences for critical outcomes up to 12 months whereas vertebroplasty compared to conservative treatment showed only possible clinically important differences for critical outcomes at 1 day.

- The direct comparison between vertebroplasty and kyphoplasty is logically consistent with the previous two points in as much as it shows a possibly clinically important advantage in critical outcomes for kyphoplasty at durations up to 2 years.

These points alone merit a moderate strength recommendation for kyphoplasty due to the two Level II studies which compared kyphoplasty to conservative treatment. However, the comparisons between vertebroplasty and kyphoplasty are important. The results of the direct comparisons between kyphoplasty and vertebroplasty are not repeated across all studies which lowers our confidence that future studies will confirm the results of the current evidence. Thus, the recommendation is downgraded from moderate to limited and kyphoplasty is an option, for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact.

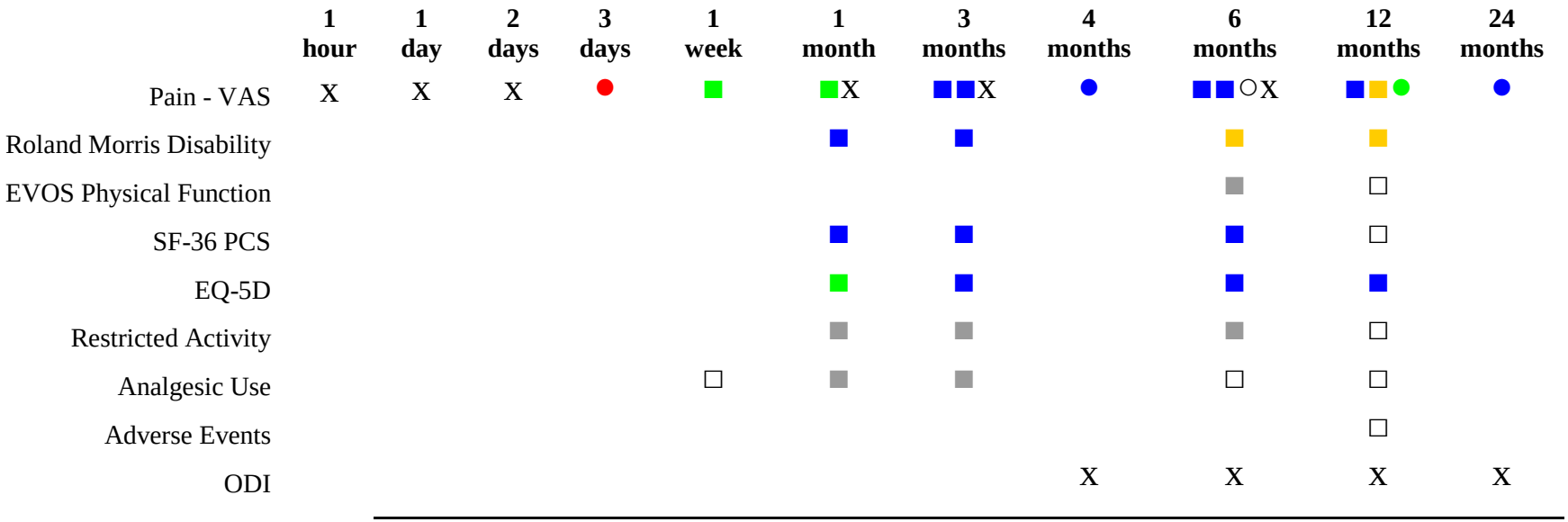
Supporting Evidence

Two studies with moderately reliable data enrolling a total of 360 patients compared kyphoplasty to conservative treatment.[54, 73] One study was of patients with 6 weeks since injury,[54] while the other study was of patients with a chronic injury (>12 months).[73] In the study of patients with an acute injury, all participants received analgesics, bed rest, braces, physiotherapy, rehabilitation programs, and walking aids according to each hospital's standard practice.[54] In the study of patients with a chronic injury, all patients received calcium, vitamin D, an oral amino-bisphosphonate, regular physiotherapy, and pain medication.[73] In both studies, pain was reduced significantly more in the kyphoplasty group for 12 months, while function was improved for at least 6 months. Quality of life was measured in one study, and it was improved for 12 months in the kyphoplasty group (Table 87- Table 93).

Three additional studies with moderately reliable data enrolling a total of 172 patients compared kyphoplasty with vertebroplasty.[60, 61, 74] One study included patients with acute fractures (2 weeks since injury),[61] another included patients with subacute fractures (8 weeks),[60] and the third included patients with time to injury of less than 6 months.[74] Only one study reported clinically important differences in pain (subacute fractures study), and the results favored kyphoplasty. There were no significant differences in function (Table 94 - Table 95).

SUMMARY OF EVIDENCE

Table 84 Summary of Kyphoplasty Outcomes



square-kyphoplasty compared to conservative treatment; circle-kyphoplasty compared to vertebroplasty;
green-clinically important in favor of kyphoplasty; **blue**-possibly clinically important in favor of kyphoplasty;
yellow-not clinically important in favor of kyphoplasty;
red-not clinically important in favor of vertebroplasty
grey-statistically significant; open-not statistically significant, X-underpowered study

STUDY QUALITY

Table 85 Quality of Included Studies for Recommendation 9 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Wardlaw	Analgesic Usage	1 Week	234	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Analgesic Usage	1 Month	229	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Analgesic Usage	3 Months	226	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Analgesic Usage	6 Months	236	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Analgesic Usage	12 Months	216	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Back Pain	1 Week	274	Kyphoplasty vs. conservative	Level II	●	×	○	○	●	●
Wardlaw	Back Pain	1 Month	264	Kyphoplasty vs. conservative	Level II	●	×	○	○	●	●

Table 85 Quality of Included Studies for Recommendation 9 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Wardlaw	Back Pain	3 Months	246	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Back Pain	6 Months	241	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Back Pain	12 Months	226	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Days of Restricted Activity	1 Month	246	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Days of Restricted Activity	3 Months	233	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Days of Restricted Activity	6 Months	234	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Days of Restricted Activity	12 Months	222	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●

Table 85 Quality of Included Studies for Recommendation 9 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Wardlaw	EQ-5D	1 Month	261	Kyphoplasty vs. conservative	Level II	●	×	○	○	●	●
Wardlaw	EQ-5D	3 Months	242	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	EQ-5D	6 Months	238	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	EQ-5D	12 Months	226	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Roland-Morris score	1 Month	253	Kyphoplasty vs. conservative	Level II	●	×	○	○	●	●
Wardlaw	Roland-Morris score	3 Months	225	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Roland-Morris score	6 Months	220	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	Roland-Morris score	12 Months	204	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	SF-36 (physical)	1 Month	261	Kyphoplasty vs. conservative	Level II	●	×	○	○	●	●

Table 85 Quality of Included Studies for Recommendation 9 - Randomized Trials

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	Stochastic Randomization	Allocation Concealment	Patients Blinded	Those rating outcome Blinded	Follow Up - 80% or more	All groups have similar outcome performance at entry
Wardlaw	SF-36 (physical)	3 Months	241	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	SF-36 (physical)	6 Months	237	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Wardlaw	SF-36 (physical)	12 Months	225	Kyphoplasty vs. conservative	Level II	●	×	○	○	○	●
Liu	Pain - VAS	3 Days	100	Kyphoplasty vs. Vertebroplasty	Level II	●	×	×	×	●	●
Liu	Pain - VAS	6 Months	100	Kyphoplasty vs. Vertebroplasty	Level II	●	×	×	×	●	●

Table 86 Quality of Included Studies for Recommendation 9 - Prospective Comparative Studies

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	All groups have similar characteristics at entry	All groups have similar outcome performance at entry	All groups concurrently treated	Follow Up - 80% or more	Same center for experimental and control group data
Grafe	EVOS	6 Months	60	Kyphoplasty vs. conservative	Level II	●	●	●	●	●
Grafe	EVOS	12 Months	60	Kyphoplasty vs. conservative	Level II	●	●	●	●	●
Kasperk (interim report of Grafe study)	Pain - VAS	3 Months	54	Kyphoplasty vs. conservative	Level II	●	●	●	●	●
Grafe	Pain - VAS	6 Months	60	Kyphoplasty vs. conservative	Level II	●	●	●	●	●
Grafe	Pain - VAS	12 Months	60	Kyphoplasty vs. conservative	Level II	●	●	●	●	●
De Negri	Oswestry score	6 Months	21	Vertebroplasty vs. kyphoplasty	Level II	×	●	●	●	●
De Negri	Pain - VAS	1 Hour	21	Vertebroplasty vs. kyphoplasty	Level II	×	●	●	●	●
De Negri	Pain - VAS	2 Days	21	Vertebroplasty vs. kyphoplasty	Level II	×	●	●	●	●

Table 86 Quality of Included Studies for Recommendation 9 - Prospective Comparative Studies

● = Yes ○ = No
× = Not Reported

Author	Outcome	Duration	N	Treatments	Level of Evidence	All groups have similar characteristics at entry	All groups have similar outcome performance at entry	All groups concurrently treated	Follow Up - 80% or more	Same center for experimental and control group data
De Negri	Pain - VAS	1 Month	21	Vertebroplasty vs. kyphoplasty	Level II	×	●	●	●	●
De Negri	Pain - VAS	3 Months	21	Vertebroplasty vs. kyphoplasty	Level II	×	●	●	●	●
De Negri	Pain - VAS	6 Months	21	Vertebroplasty vs. kyphoplasty	Level II	×	●	●	●	●
Grohs	Oswestry score	4 Months	51	Vertebroplasty vs. kyphoplasty	Level II	●	●	●	●	●
Grohs	Oswestry score	1 Year	51	Vertebroplasty vs. kyphoplasty	Level II	●	●	●	●	●
Grohs	Oswestry score	2 Years	51	Vertebroplasty vs. kyphoplasty	Level II	●	●	●	●	●
Grohs	Pain - VAS	1 Day	51	Vertebroplasty vs. kyphoplasty	Level II	●	●	●	●	●
Grohs	Pain - VAS	4 Months	51	Vertebroplasty vs. kyphoplasty	Level II	●	●	●	●	●
Grohs	Pain - VAS	1 Year	51	Vertebroplasty vs. kyphoplasty	Level II	●	●	●	●	●
Grohs	Pain - VAS	2 Years	51	Vertebroplasty vs. kyphoplasty	Level II	●	●	●	●	●

KYPHOPLASTY VS. CONSERVATIVE

Figure 10 Kyphoplasty vs. Conservative – Difference in Pain

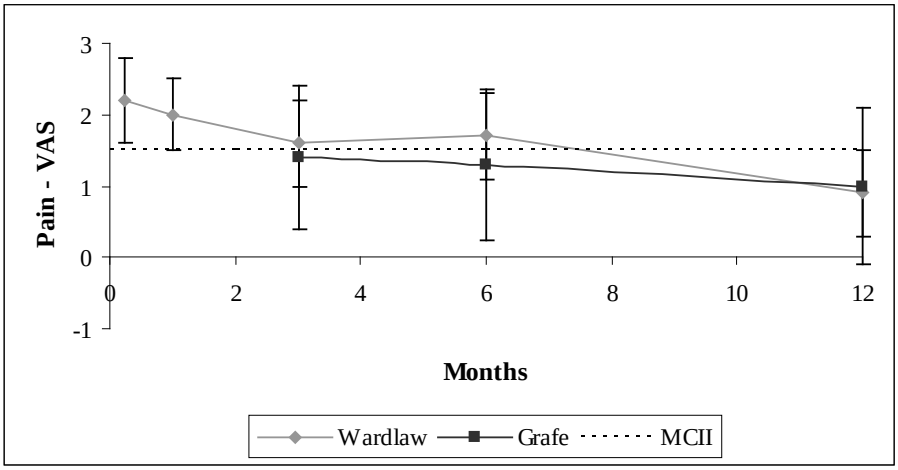


Figure 11 Kyphoplasty vs. Conservative – Difference in Physical Function (Roland-Morris Disability)

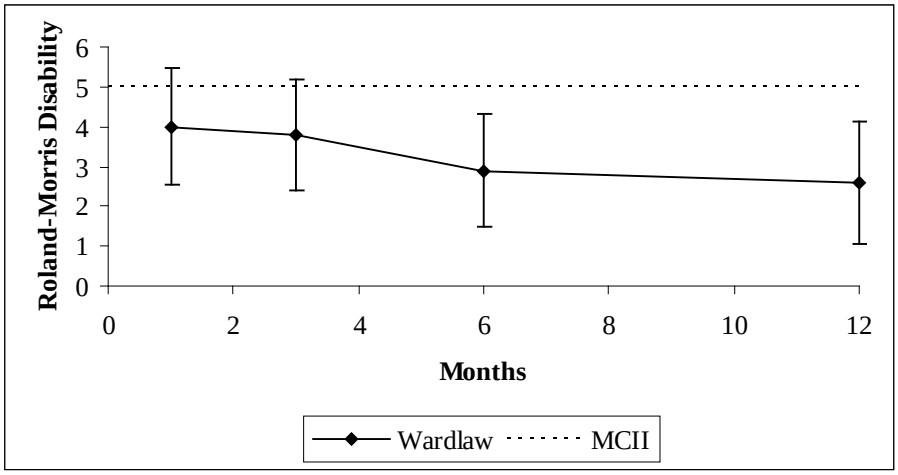


Table 87 Kyphoplasty vs. Conservative - Pain

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Wardlaw	274	II	6 weeks	Pain - VAS	1 week	2.2 (1.6, 2.8)*	Kyphoplasty	Yes
	264				1 month	2.0 (1.5, 2.5)	Kyphoplasty	Yes
	246				3 months	1.6 (1.0, 2.2)	Kyphoplasty	Possibly
Grafe	60		>12 months			1.4 (0.4, 2.4)*	Kyphoplasty*	Possibly
Wardlaw	241		6 weeks		6 months	1.7 (1.1, 2.3)	Kyphoplasty	Possibly
Grafe	60		>12 months			1.3 (0.3, 2.4)*	Kyphoplasty*	Possibly
Wardlaw	226		6 weeks		12 months	0.9 (0.3, 1.5)*	Kyphoplasty	No
Grafe	60		>12 months			1.0 (-0.1, 2.1)	Kyphoplasty*	Possibly

*Baseline-adjusted difference; 3 month data from Grafe study is from interim report[75]

Table 88 Kyphoplasty vs. Conservative - Physical Function

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Wardlaw	253	II	6 weeks	Roland-Morris Disability	1 month	4.0 (2.6, 5.5)*	Kyphoplasty	Possibly
	225				3 months	3.8 (2.4, 5.2)	Kyphoplasty	Possibly
	220				6 months	2.9 (1.5, 4.3)	Kyphoplasty	No
	204				12 months	2.6 (1.0, 4.1)*	Kyphoplasty	No
Grafe	60	II	>12 months	EVOS Physical Function	6 months	10.6 (0.9, 20.3)	Kyphoplasty	n/a
					12 months	10.2 (-1.0, 21.4)	○	

*Baseline-adjusted difference

Table 89 Kyphoplasty vs. Conservative - SF-36 Physical Component Score (PCS)

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Wardlaw	261	II	6 weeks	SF-36 PCS	1 month	5.2 (2.9, 7.4)*	Kyphoplasty	Possibly
	241				3 months	4.0 (1.6, 6.3)*	Kyphoplasty	Possibly
	237				6 months	3.2 (0.9, 5.6)*	Kyphoplasty	Possibly
	225				12 months	1.5 (-0.8, 3.9)*	○	No

*Baseline-adjusted difference

Table 90 Kyphoplasty vs. Conservative – Quality of Life

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Wardlaw	261	II	6 weeks	EQ-5D	1 month	0.18 (0.08, 0.28)*	Kyphoplasty	Yes
	241				3 months	0.10 (0.02, 0.18)	Kyphoplasty	Possibly
	237				6 months	0.12 (0.04, 0.20)	Kyphoplasty	Possibly
	225				12 months	0.12 (0.01, 0.22)*	Kyphoplasty	Possibly

*Baseline-adjusted difference

Table 91 Kyphoplasty vs. Conservative – Restricted Activity

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Wardlaw	246	II	6 weeks	Days of Restricted Activity per 2 weeks	1 month	2.9 (1.3, 4.6)*	Kyphoplasty	n/a
	233				3 months	4.0 (2.6, 5.4)	Kyphoplasty	
	234				6 months	2.5 (1.1, 3.9)	Kyphoplasty	
	222				12 months	1.6 (-0.1, 3.3)*	○*	

*Baseline-adjusted difference

Table 92 Kyphoplasty vs. Conservative – Opioid Use

Study	Level of Evidence	Time After Injury	Outcome	Duration	Kyphoplasty n/N	Conservative n/N	OR (95% CI)
Wardlaw	II	6 weeks	Opioid Use	1 week	60/103	89/131	0.66 (0.37, 1.17)
				1 month	53/114	74/115	0.48 (0.27, 0.85)
				3 months	39/120	56/106	0.43 (0.24, 0.76)
				6 months	38/124	48/112	0.59 (0.33, 1.04)
				12 months	32/115	34/101	0.76 (0.40, 1.41)

Shaded cell indicates favored treatment

Table 93 Kyphoplasty vs. Conservative – Adverse Events

Study	Level of Evidence	Time After Injury	Outcome	Duration	Kyphoplasty n/N	Conservative n/N	OR (95% CI)
Wardlaw	II	6 weeks	Adverse Events	12 months	130/149	122/151	1.63 (0.83, 3.24)
			Serious Adverse Events	12 months	58/149	54/151	1.14 (0.70, 1.88)

KYPHOPLASTY VS. VERTEBROPLASTY

Figure 12 Kyphoplasty vs. Vertebroplasty - Difference in Pain

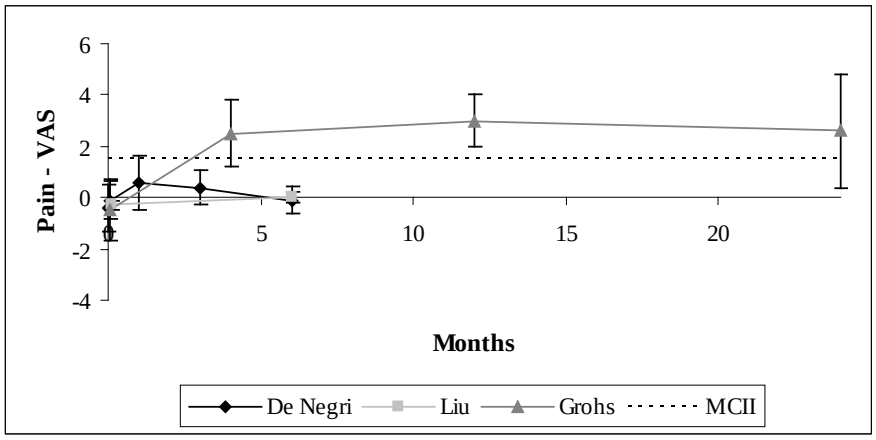


Figure 13 Kyphoplasty vs. Vertebroplasty - Difference in Physical Function

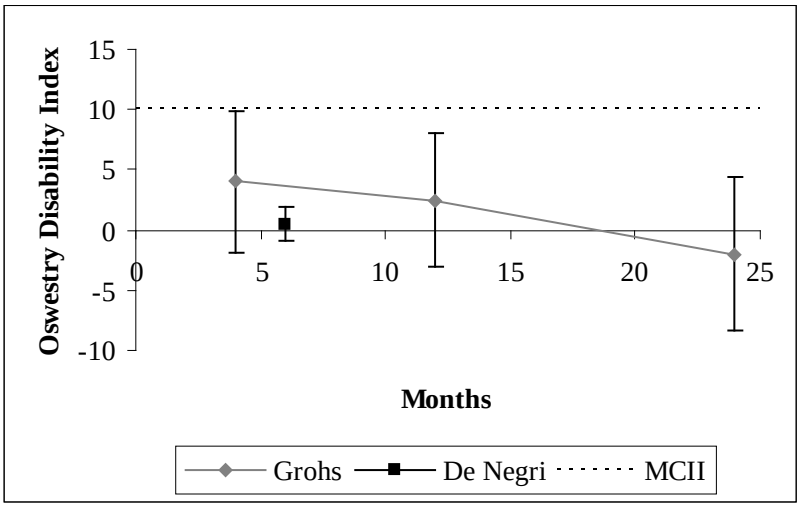


Table 94 Kyphoplasty vs. Vertebroplasty - Pain

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
De Negri	21	II	<6 months	Pain - VAS	1 hour	-0.4 (-1.3, 0.5)	○	No
Grohs	51		8.5 weeks		1 day	-0.5 (-1.7, 0.7)*	○	Inconclusive
De Negri	21		<6 months		2 days	-0.1 (-0.8, 0.7)	○	No
Liu	100		2.3 weeks		3 days	-0.3 (-0.5, -0.1)	Vertebroplasty	No
De Negri	21		<6 months		1 month	0.6 (-0.4, 1.7)	○	Inconclusive
					3 months	0.4 (-0.3, 1.1)	○	No
Grohs	51		8.5 weeks		4 months	2.5 (1.2, 3.8)*	Kyphoplasty	Possibly
Liu	100		2.3 weeks		6 months	0.0 (-0.2, 0.2)	○	No
De Negri	21		<6 months			-0.1 (-0.7, 0.4)	○	No
Grohs	51		8.5 weeks		1 year	3.0 (2.0, 4.0)*	Kyphoplasty	Yes
					2 years	2.6 (0.4, 4.8)*	Kyphoplasty	Possibly

Both the De Negri and Grohs studies lacked sufficient power to detect a large effect for each non-significant outcome; *from median and range

Table 95 Kyphoplasty vs. Vertebroplasty – Physical Function

Study	n	Level of Evidence	Time After Injury	Outcome	Duration	Difference between groups (95% CI)	Favors	Clinically Important?
Grohs	51	II	8.5 weeks	Oswestry Disability Index	4 months	4.0 (-1.9, 9.9)*	○	No
De Negri	21		<6 months		6 months	0.5 (-1.0, 1.9)	○	
Grohs	51		8.5 weeks		1 year	2.5 (-3.0, 8.0)*	○	
					2 years	-2.0 (-8.4, 4.4)*	○	

Both studies lacked sufficient power to detect a large effect for each outcome; *from median and range

RECOMMENDATION 10

We are unable to recommend for or against improvement of kyphosis angle in the treatment of patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms.

Strength of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

Rationale

We found no study which addressed sagittal balance correction and properly correlated kyphosis angle with any patient-oriented outcome. All studies retrieved for this recommendation either examined only a single vertebrae as opposed to regional kyphosis or did not report the correlation between a change in kyphosis angle and a change in any patient-oriented outcome.

Supporting Evidence

We found no studies which examined the correlation between a change in regional kyphosis angle and any patient-oriented outcome.

RECOMMENDATION 11

We are unable to recommend for or against any specific treatment for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are not neurologically intact.

Strength of Recommendation: Inconclusive

Description: Evidence from a single low quality study or conflicting findings that do not allow a recommendation for or against the intervention. An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Implications: Practitioners should feel little constraint in following a recommendation labeled as **Inconclusive,** exercise clinical judgment, and be alert for emerging evidence that clarifies or helps to determine the balance between benefits and potential harm. Patient preference should have a substantial influencing role.

Rationale

Patients who present with neurological symptoms and osteoporotic spinal compression fractures clearly require treatment because they face pain, diminished function, and increased mortality.[68] However, despite the need to treat such patients, there is an absence of studies that examine which treatments are most effective for these patients. Therefore, we are unable to recommend for or against any specific treatment.

Supporting Evidence

No studies met the inclusion criteria for this guideline.

FUTURE RESEARCH

The work group realizes that the paucity of good quality research studies has limited the strength of the recommendations. This underscores the necessity for further work in this area. In particular, we hope that Level I studies are carried out to determine the effectiveness of modalities such as bracing, physical therapy/exercise, and kyphoplasty in the treatment of these fractures.

Our review suggests that radiographic fracture is not a reliable surrogate measure of symptomatic fracture. In many of the studies we reviewed the presence of a radiographic fracture, even if chronic, was postulated to be the source of back pain symptoms with no clear rational for that determination. This emphasizes the need for long term prospective studies on the natural history of osteoporotic spinal insufficiency fractures. There are comments in the literature about various fracture parameters such as type, location, degree of kyphosis, etc. as being clinically important. Unfortunately, this has not been adequately studied.

Guidelines are living documents. Based on the fluid nature of guidelines, the work group anticipates that future research will address some of the recommendations in this guideline. We welcome further well-designed high quality research that will help clarify the recommendations in this guideline. We also welcome the opportunity to review the literature again in the future. The work group hopes that additional good quality studies will become available to address some of the many inadequately and unanswered questions in this guideline.

IV. **APPENDIXES**

APPENDIX I
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APPENDIX II
AAOS BODIES THAT APPROVED THIS CLINICAL PRACTICE GUIDELINE

Guidelines and Technology Oversight Committee
The AAOS Guidelines and Technology Oversight Committee (GTOC) consists of sixteen AAOS members. The overall purpose of this Committee is to oversee the development of the clinical practice guidelines, performance measures, health technology assessments and utilization guidelines.

Evidence Based Practice Committee
The AAOS Evidence Based Practice Committee (EBPC) consists of ten AAOS members. This Committee provides review, planning and oversight for all activities related to quality improvement in orthopaedic practice, including, but not limited to evidence-based guidelines, performance measures, and outcomes.

Council on Research, Quality Assessment, and Technology
To enhance the mission of the AAOS, the Council on Research, Quality Assessment, and Technology promotes the most ethically and scientifically sound basic, clinical, and translational research possible to ensure the future care for patients with musculoskeletal disorders. The Council also serves as the primary resource to educate its members, the public, and public policy makers regarding evidenced-based medical practice, orthopaedic devices and biologics, regulatory pathways and standards development, patient safety, occupational health, technology assessment, and other related areas of importance.

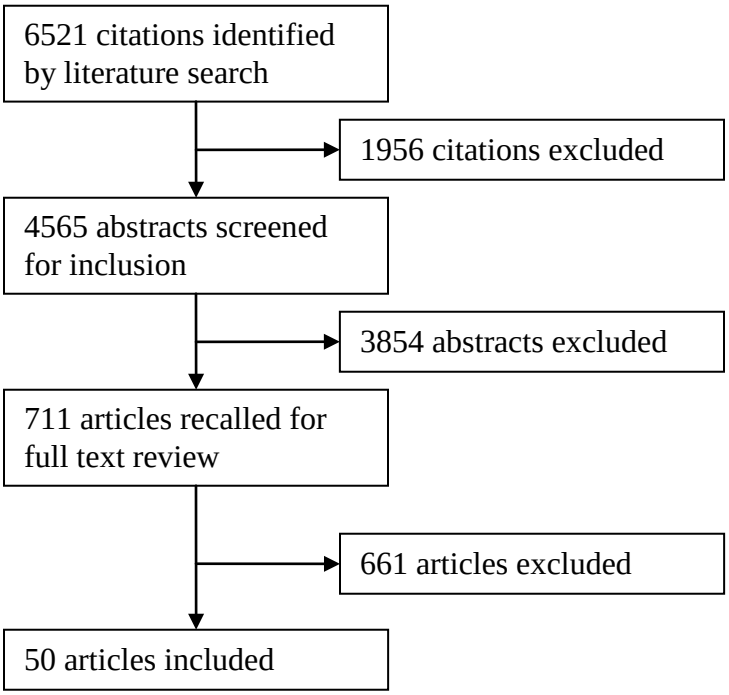
The Council is comprised of the chairs of the AAOS Biological Implants, Biomedical Engineering, Evidence Based Practice, Guidelines and Technology Oversight, Occupational Health and Workers' Compensation, Patient Safety, Research Development, and US Bone and Joint Decade committees. Also on the Council are the AAOS second vice-president, representatives of the Diversity Advisory Board, the Women's Health Issues Advisory Board, the Board of Specialty Societies (BOS), the Board of Councilors (BOC), the Communications Cabinet, the Orthopaedic Research Society (ORS), the Orthopedic Research and Education Foundation (OREF), and three members at large.

Board of Directors
The 17 member AAOS Board of Directors manages the affairs of the AAOS, sets policy, and determines and continually reassesses the Strategic Plan.

DOCUMENTATION OF APPROVAL

AAOS Work Group Draft Completed	March 30, 2010
Peer Review Completed	April 30, 2010
Public Commentary Completed	August 27, 2010
AAOS Guidelines and Technology Oversight Committee	September 3, 2010
AAOS Evidence Based Practice Committee	September 3, 2010
AAOS Council on Research Quality Assessment and Technology	September 7, 2010
AAOS Board of Directors	September 24, 2010

APPENDIX III
STUDY ATTRITION FLOWCHART



APPENDIX IV
LITERATURE SEARCHES

Search Strategy for PubMed/MEDLINE

#1 "Fractures, Compression"[mh] OR ((compression[tiab] OR insufficiency[tiab] OR collaps*[tiab] OR osteoporo*[tiab] OR pathologic*[tiab]) AND (fracture*[tiab] OR "Spinal Fractures"[mh]) AND (spine[tiab] OR spinal[tiab] OR vertebr*[tiab] OR dorsolumbar[tiab] OR lumbar[tiab] OR "Lumbar Vertebrae"[mh] OR thoracic[mh] OR "Thoracic Vertebrae"[mh] OR "spinal injuries"[mh]))

#2 "Bed rest"[mh] OR (bed[tiab] AND rest[tiab]) OR "Physical Therapy Modalities"[mh] OR "physical therapy" OR physiotherap*[tiab] OR brace[tiab] OR bracing[tiab] OR "Complementary Therapies"[mh] OR acupuncture[tiab] OR magnet[tiab] OR magnets[tiab] OR "Electric stimulation"[mh] OR (electric*[tiab] AND stimulat*[tiab]) OR complementary[tiab] OR alternative[tiab] OR drug therapy[sh] OR Analgesics[mh] OR analgesics[pa] OR NSAID[tiab] OR opioid*[tiab] OR (muscle[tiab] AND relax*[tiab]) OR "Muscle Relaxants, Central"[mh] OR acetaminophen[tiab] OR naproxen[tiab] OR ibuprofen[tiab] OR hydrocodone[tiab] OR oxycodone[tiab] OR oxycontin[tiab] OR morphine[tiab] OR benzodiazepine*[tiab] OR tramadol[tiab] OR Steroids[mh] OR steroid*[tiab] OR prednisone[tiab] OR Glucocorticoids[mh] OR Glucocorticoids[pa] OR solumedrol[tiab] OR fentanyl[tiab] OR lidoderm[tiab] OR aspirin[tiab] OR codeine[tiab] OR "Bone Density Conservation Agents"[mh] OR "Bone Density Conservation Agents"[pa] OR Diphosphonates[mh] OR bisphosphonate*[tiab] OR alendronate[tiab] OR fosamax[tiab] OR calcitonin[tiab] OR surgery[sh] OR surgical[tiab] OR surgery[tiab] OR repair*[tiab] OR "Orthopedic procedures"[mh] OR (percutaneous[tiab] AND vertebral[tiab] AND augmentation[tiab]) OR PMMA[tiab] OR " Polymethyl Methacrylate"[substance] OR (polymethyl[tiab] AND methacrylate[tiab]) OR Vertebroplasty[mh] OR vertebroplasty[tiab] OR kyphoplasty[tiab] OR "Bone Cements"[mh] OR "Bone Cements"[pa] OR BMP[tiab] OR (bone[tiab] AND morphogenic[tiab] AND (protein[tiab] OR proteins[tiab]))

#3 English[lang] AND 1966:2009[pdat] NOT (animal[mh] NOT human[mh]) NOT ((child[mh] OR infant[mh] OR adolescent[mh]) NOT adult[mh]) NOT (cadaver[mh] OR "in vitro"[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR addresses[pt] OR news[pt] OR "newspaper article"[pt] OR “historical article”[pt] OR "case report"[title])

#4 #1 AND #2 AND #3

#5 Medline[tw] OR systematic review[tiab] OR Meta-analysis[pt]

#6 #4 AND #5

#7 "Clinical Trial"[pt] OR (clinical[tiab] AND trial[tiab]) OR random*[tw] OR "Therapeutic use"[sh]

#8 (#4 AND #7) NOT #5

#9 #4 NOT (#7 OR #5)

Search strategy for EMBASE

#1 'Compression fracture'/de OR ((compression OR insufficiency OR collaps* OR osteoporo* OR pathologic*) AND (fracture* OR 'Spine fracture'/de) AND (spine OR spinal OR vertebr* OR dorsolumbar OR lumbar OR 'lumbar vertebra'/de OR thoracic OR vertebra/de OR 'spine injury'/de))

#2 'bed rest'/de OR (bed AND rest) OR 'physical medicine'/exp OR 'physical therapy' OR physiotherap* OR brace OR bracing OR 'alternative medicine'/de OR acupuncture/de OR acupuncture OR magnet OR 'nonsteroid antiinflammatory agent'/exp OR 'narcotic analgesic agent'/exp OR opioid* OR 'muscle relaxant agent'/exp OR (muscle AND relax*) OR acetaminophen OR naproxen OR ibuprofen OR hydrocodone OR oxycodone OR oxycontin OR morphine OR benzodiazepine* OR tramadol OR steroid* OR prednisone OR steroid/exp OR solumedrol OR fentanyl OR lidoderm OR aspirin OR codeine OR 'bone density conservation agent'/de OR bisphosphonate* OR 'bisphosphonic acid derivative'/exp OR alendronate OR fosamax OR calcitonin OR surgical OR surgery OR repair* OR 'orthopedic surgery'/exp OR 'percutaneous vertebral augmentation' OR PMMA OR 'poly(methyl methacrylate)'/de OR 'polymethyl methacrylate' OR 'percutaneous vertebroplasty'/de OR vertebroplasty OR kyphoplasty/de OR kyphoplasty OR 'bone cement'/exp OR BMP OR 'bone morhpogenic protein*' OR 'bone morphogenetic protein'/de

#3 [english]/lim AND [humans]/lim AND [embase]/lim NOT (cadaver/de OR 'in vitro study'/exp OR ‘case report’:ti OR 'abstract report'/de OR book/de OR editorial/de OR letter/de OR note/de)

#4 #1 AND #2 AND #3

#5 ('meta analysis' OR 'systematic review' OR medline)

#6 #4 AND #5

#7 random* OR 'clinical trial' OR 'health care quality'/exp

#8 (#4 AND #7) NOT #5

#9 #4 NOT (#7 OR #5)

Search Strategy for CINAHL

S1 (compression OR insufficiency OR collaps* OR osteoporo* OR pathologic*) and (fracture* OR MH "Spinal Fractures") and (spine OR spinal OR vertebr* OR dorsolumbar OR lumbar OR MH "Lumbar Vertebrae" OR MH "Thoracic Vertebrae" OR thoracic OR MH "Spinal Injuries")

S2 MH "Fractures, Compression"

S3 S1 OR S2

S4 MH "bed rest" OR "bed rest" OR MH "Bed Rest Care (Iowa NIC)" OR MH "Physical Therapy +" OR "physical therapy" OR physiotherapy* OR MH "Orthoses" OR brace OR bracing OR MH "Alternative Therapies +" OR acupuncture OR magnet OR magnets OR MH "Electric Stimulation" OR "electric stimulat*" OR MH "acupuncture +" OR MH "Analgesics, Opioid +" OR NSAID OR opioid* OR MH "Antiinflammatory Agents, Non-Steroidal +" OR MH "Muscle Relaxants, Central +" OR "muscle relax*" OR acetaminophen OR naproxen OR ibuprofen OR hydrocodone OR oxycodone OR oxycontin OR morphine OR benzodiazepine* OR tramadol OR MH "Steroids" OR steroid* OR prednisone OR solumedrol OR fentanyl OR lidoderm OR aspirin OR codeine OR MH "Diphosphonates +" OR fosamax OR alendronate OR calcitonin OR surgical OR surgery OR repair* OR MH "Orthopedic Surgery +" OR "percutaneous vertebral augmentation" OR PMMA OR "polymethyl methacrylate" OR vertebroplasty OR kyphoplasty OR MH "Bone Cements" OR BMP OR "bone morphogenic protein*"

S5 LA English not (PT "editorial" or PT "letter" or PT "case study" or TI "case report")

S6 S3 and S4 and S5

S7 "meta analysis" or PT "review" or PT "systematic review"

S8 S6 AND S7

S9 MH "treatment outcomes+" OR MH "experimental studies" OR random*

S10 (S6 AND S9) not S7

S11 S6 not (S7 or S9)

Search strategy for Cochrane Library

(spine OR spinal OR vertebr*) AND (compression OR insufficiency) AND fracture AND (surgery OR surgical OR repair OR treat* OR therap*)

APPENDIX V
DATA EXTRACTION ELEMENTS

The data elements below were extracted into electronic forms in Microsoft® Access. The extracted information includes:

Study Characteristics

- methods of randomization and allocation
- blinding of patients and evaluators
- loss to follow-up
- study design

Patient Characteristics

- patient inclusion/exclusion criteria
- age
- gender
- fracture classification

Results (for all relevant outcomes in a study)

- outcome measure
- duration of follow up
- mean or median
- measure of dispersion
- results of hypothesis testing

APPENDIX VI
JUDGING THE QUALITY OF TREATMENT STUDIES

RANDOMIZED CONTROLLED TRIALS

Did the study employ stochastic randomization?

Was there concealment of allocation?

Were subjects blinded to the treatment they received?

Were those who assessed/rated the patient's outcomes blinded to the group to which the patients were assigned?

Was there more than 80% follow-up for all patients in the control group and the experimental group on the outcome of interest?

Did patients in the different study groups have similar levels of performance on ALL of the outcome variables at the time they were assigned to groups?

For randomized crossover studies, was there evidence that the results obtained in the study's two experimental groups (in period 1 and 2) did not differ?

For randomized crossover studies, was there evidence that the results of the two control groups (in period 1 and 2) did not differ?

PROSPECTIVE NON- RANDOMIZED CONTROLLED STUDIES

Were the characteristics of patients in the different study groups comparable at the beginning of the study?

Did patients in the different study groups have similar levels of performance on ALL of the outcome variables at baseline?

Were all of the study's groups concurrently treated?

Was there more than 80% follow-up for all patients in the control group and the experimental group on the outcome of interest?

Did the study avoid collecting control group data from one center and experimental group data from another?

For crossover studies, was there evidence that the results obtained in the study's two experimental groups (in period 1 and 2) did not differ?

For crossover studies, was there evidence that the results of the two control groups (in period 1 and 2) did not differ?

RETROSPECTIVE COMPARATIVE STUDIES

Was there less than 20% difference in completion rates in the study's groups?

Were all of the study's groups concurrently treated?

Was the same treatment given to all patients enrolled in the experimental and

Were the same laboratory tests, clinical findings, psychological instruments, etc. used to measure the outcomes in all of the study's groups?

Were the follow-up times in all of the study's relevant groups approximately equal?

Was there more than 80% follow-up for all patients in the control group and the experimental group on the outcome of interest?

Did the study avoid collecting control group data from one center and experimental group data from another?

Did patients in the different study groups have similar levels of performance on ALL of the outcome variables at the time they were assigned to groups?

Were the characteristics of patients in the different study groups comparable at the beginning of the study?

CASE SERIES

Was enrollment in the study consecutive?

Was there more than 80% follow-up for all patients on the outcome of interest?

Were the same laboratory tests, clinical findings, psychological instruments, etc. used to measure the outcomes in all patients?

Were the patients instructed/not given concomitant or adjuvant treatments?

Were the follow-up times for all patients approximately equal?

OPINION-BASED RECOMMENDATIONS

A guideline can contain recommendations that are backed by little or no data. Under such circumstances, work groups often issue opinion-based recommendations. Although doing so is sometimes acceptable in an evidence-based guideline (expert opinion is a form of evidence), it is also important to avoid constructing a guideline that liberally uses expert opinion; research shows that expert opinion is often incorrect.

Opinion-based recommendations are developed only if they address a vitally important aspect of patient care. For example, constructing an opinion-based recommendation in favor of taking a history and physical is warranted. Constructing an opinion-based recommendation in favor of a specific modification of a surgical technique is seldom warranted. To ensure that an opinion-based recommendation is absolutely necessary, the AAOS has adopted rules to guide the content of the rationales that underpin such recommendations. These rules are based on those outlined by the US Preventive Services Task Force (USPSTF).[76] Specifically, rationales based on expert opinion must:

- Not contain references to or citations from articles not included in the systematic review that underpins the recommendation.

- Not contain the AAOS guideline language “We Recommend”, “We suggest” or “treatment x is an option”.

- Contain an explanation of the potential preventable burden of disease. This involves considering both the incidence and/or prevalence of the disease, disorder, or condition and considering the associated burden of suffering. To paraphrase the USPSTF, when evidence is insufficient, provision of a treatment (or diagnostic) for a serious condition might be viewed more favorably than provision of a treatment (or diagnostic) for a condition that does not cause as much suffering. The AAOS (like the USPSTF) understand that evaluating the “burden of suffering” is subjective and involves judgment. This evaluation should be informed by patient values and concerns. The considerations outlined in this bullet make it difficult to recommend new technologies. It is not appropriate for a guideline to recommend widespread use of a technology backed by little data and for which there is limited experience. Such technologies are addressed in the AAOS’ Technology Overviews.

- Address potential harms. In general, “When the evidence is insufficient, an intervention with a large potential for harm (such as major surgery) might be viewed less favorably than an intervention with a small potential for harm (such as advice to watch less television).”[76]

- Address apparent discrepancies in the logic of different recommendations. Accordingly, if there are no relevant data for several recommendations and the work group chooses to issue an opinion-based recommendation in some cases

but chooses not to make a recommendation in other cases, the rationales for the opinion-based recommendations must explain why this difference exists. Information garnered from the previous bullet points will be helpful in this regard.

- Consider current practice. The USPSTF specifically states that clinicians justifiably fear that not doing something that is done on a widespread basis will lead to litigation.[76] The consequences of not providing a service that is neither widely available nor widely used are less serious than the consequences of not providing a treatment accepted by the medical profession and thus expected by patients. Discussions of available treatments and procedures rely on mutual communication between the patient's guardian and physician, and on weighing the potential risks and benefits for a given patient. The patient's "expectation of treatment" must be tempered by the treating physician's guidance about the reasonable outcomes that the patient can expect.

- Justify, why a more costly device, drug, or procedure is being recommended over a less costly one whenever such an opinion-based recommendation is made.

Work group members write the rationales for opinion based recommendations on the first day of the final work group meeting. When the work group re-convenes on the second day of its meeting, it will vote on the rationales. The typical voting rules will apply. If the work group cannot adopt a rationale after three votes, the rationale and the opinion-based recommendation will be withdrawn, and a "recommendation" stating that the group can neither recommend for or against the recommendation in question will appear in the guideline.

Discussions of opinion-based rationales may cause some members to change their minds about whether to issue an opinion-based recommendation. Accordingly, at any time during the discussion of the rationale for an opinion-based recommendation, any member of the work group can make a motion to withdraw that recommendation and have the guideline state that the work group can neither recommend for or against the recommendation in question.

CHECKLIST FOR VOTING ON OPINION-BASED RECOMMENDATIONS

When voting on the rationale, please consider the following:

1. Does the recommendation affect a substantial number of patients or address treatment (or diagnosis) of a condition that causes death and/or considerable suffering?

2. Does the recommendation address the potential harms that will be incurred if it is implemented and, if these harms are serious, does the recommendation justify;

    a. why the potential benefits outweigh the potential harms and/or

b. why an alternative course of treatment (or diagnostic workup) that involves less serious or fewer harms is not being recommended?

3. Does the rationale explain why the work group chose to make a recommendation in the face of minimal evidence while, in other instances, it chose to make no recommendation in the face of a similar amount of evidence?

4. Does the rationale explain that the recommendation is consistent with current practice?

5. If relevant, does the rationale justify why a more costly device, drug, or procedure is being recommended over a less costly one?

APPENDIX VII
FORM FOR ASSIGNING STRENGTH OF RECOMMENDATION (INTERVENTIONS)

GUIDELINE RECOMMENDATION_____

PRELIMINARY STRENGTH OF RECOMMENDATION: _____

STEP 1: LIST BENEFITS AND HARMS

Please list the benefits (as demonstrated by the systematic review) of the intervention.

Please list the harms (as demonstrated by the systematic review) of the intervention.

Please list the benefits for which the systematic review is not definitive.

Please list the harms for which the systematic review is not definitive.

STEP 2: IDENTIFY CRITICAL OUTCOMES

Please circle the above outcomes that are critical for determining whether the intervention is beneficial and whether it is harmful.

Are data about critical outcomes lacking to such a degree that you would lower the preliminary strength of the recommendation?

What is the resulting strength of recommendation?

STEP 3: EVALUATE APPLICABILITY OF THE EVIDENCE

Is the applicability of the evidence for any of the critical outcomes so low that substantially worse results are likely to be obtained in actual clinical practice?

Please list the critical outcomes backed by evidence of doubtful applicability.

Should the strength of recommendation be lowered because of low applicability?

What is the resulting strength of recommendation?

STEP 4: BALANCE BENEFITS AND HARMS

Are there trade-offs between benefits and harms that alter the strength of recommendation obtained in STEP 3?

What is the resulting strength of recommendation?

STEP 5 CONSIDER STRENGTH OF EVIDENCE

Does the strength of the existing evidence alter the strength of recommendation obtained in STEP 4?

What is the resulting strength of recommendation?

NOTE: Because we are not performing a formal cost analyses, you should only consider costs if their impact is substantial.

APPENDIX VIII
VOTING BY THE NOMINAL GROUP TECHNIQUE

Voting on guideline recommendations will be conducted using a modification of the nominal group technique (NGT), a method previously used in guideline development.[21] Briefly each member of the guideline work group ranks his or her agreement with a guideline recommendation on a scale ranging from 1 to 9 (where 1 is "extremely inappropriate" and 9 is "extremely appropriate"). Consensus is obtained if the number of individuals who do not rate a measure as 7, 8, or 9 is statistically non-significant (as determined using the binomial distribution). Because the number of work group members who are allowed to dissent with the recommendation depends on statistical significance, the number of permissible dissenters varies with the size of the work group. The number of permissible dissenters for several work group sizes is given in the table below:

Work group Size	Number of Permissible Dissenters
≤ 3	Not allowed, statistical significance cannot be obtained
4-5	0
6-8	1
9	1 or 2

The NGT is conducted by first having members vote on a given recommendation without discussion. If the number of dissenters is "permissible", the recommendation is adopted without further discussion. If the number of dissenters is not permissible, there is further discussion to see whether the disagreement(s) can be resolved. Three rounds of voting are held to attempt to resolve disagreements. If disagreements are not resolved after three voting rounds, no recommendation is adopted.

APPENDIX IX
STRUCTURED PEER REVIEW FORM

Review of any AAOS confidential draft allows us to improve the overall guideline but <u>does not imply endorsement</u> by any given individual or any specialty society who participates in our review processes. The AAOS review process may result in changes to the documents; therefore, endorsement cannot be solicited until the AAOS Board of Directors officially approves the final guideline.

Reviewer Information:

Name of Reviewer_____

Address_____

City_____ State_____ Zip Code_____

Phone _____Fax _____E-mail_____

Specialty Area/Discipline: _____

Work setting: _____Credentials: _____

May we list you as a Peer Reviewer in the final Guidelines (GL)? ☐ Yes ☐ No
If you do not wish to be listed, your name will be removed for identification purposes. However, your COI will still be available for review with the comments you have made.

Are you reviewing this guideline as a representative of a professional society? ☐ Yes ☐ No

If yes, may we list your society as a reviewer of this guideline? ☐ Yes ☐ No

Society Name: _____
(Listing the specialty society as a reviewing society does not imply or otherwise indicate endorsement of this guideline.)

Conflicts of Interest (COI): All Reviewers must declare their conflicts of interest.

If the boxes below are not checked and/or the reviewer does not attach his/her conflicts of interest, the reviewer's comments will not be addressed by the AAOS nor will the reviewer's name or society be listed as a reviewer of this GL. If a committee reviews the guideline, only the chairperson/or lead of the review must declare their relevant COI.

☐ **I have declared my conflicts of interest on page 2 of this form.**

☐ **I have declared my conflicts of interest in the AAOS database; my customer # is** _____

☐ **I understand that the AAOS will post my declared conflicts of interest with my comments concerning review of this guideline or technology overview on the AAOS website.**

REVIEWER CONFLICT OF INTEREST - The Orthopaedic Disclosure Program

Each item below requires an answer. Please report information for the last 12-months as required by the Accreditation Council for Continuing Medical Education (ACCME) guidelines.

Do you or a member of your immediate family receive royalties for any pharmaceutical, biomaterial or orthopaedic product or device? If YES, please identify product or device:	☐ Yes ☐ No
Within the past twelve months, have you or a member of your immediate family served on the speakers bureau or have you been paid an honorarium to present by any pharmaceutical, biomaterial or orthopaedic product or device company? If YES, please identify company:	☐ Yes ☐ No
Are you or a member of your immediate family a PAID EMPLOYEE for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Are you or a member of your immediate family a PAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Are you or a member of your immediate family an UNPAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family own stock or stock options in any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier (excluding mutual funds) If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive research or institutional support as a principal investigator from any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive any other financial or material support from any pharmaceutical, biomaterial or orthopaedic device and equipment company or supplier? If YES, please identify company or supplier:	☐ Yes ☐ No
Do you or a member of your immediate family receive any royalties, financial or material support from any medical and/or orthopaedic publishers? If YES, please identify publisher:	☐ Yes ☐ No
Do you or a member of your immediate family serve on the editorial or governing board of any medical and/or orthopaedic publication? If YES, please identify:	☐ Yes ☐ No
Do you or a member of your immediate family serve on the Board of Directors or a committee of any medical and/or orthopaedic professional society? If YES, please identify:	☐ Yes ☐ No

Reviewer Instructions

Please read and review this Draft Clinical Practice Guideline and its associated Technical Report with particular focus on your area of expertise. Your responses are confidential and will be used only to assess the validity, clarity and accuracy of the interpretation of the evidence. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the guideline and Technical Report. If you need more space than is provided, please attach additional pages.

Please complete and return this form electronically to wies@aaos.org or fax the form back to Jan Wies at (847) 823-9769. Thank you in advance for your time in completing this form and giving us your feedback. We value your input and greatly appreciate your efforts. Please send the completed form and comments by end of day **DATE**.

Please indicate your level of agreement with each of the following statements by placing an "X" in the appropriate box.

	Disagree	Somewhat Disagree	Somewhat Agree	Agree
1. The recommendations are clearly stated	☐	☐	☐	☐
2. There is an explicit link between the recommendations and the supporting evidence	☐	☐	☐	☐
3. Given the nature of the topic and the data, all clinically important outcomes are considered	☐	☐	☐	☐
4. The guideline's target audience is clearly described	☐	☐	☐	☐
5. The patients to whom this guideline is meant to apply are specifically described	☐	☐	☐	☐
6. The criteria used to select articles for inclusion are appropriate	☐	☐	☐	☐
7. The reasons why some studies were excluded are clearly described	☐	☐	☐	☐
8. All important studies that met the article inclusion criteria are included	☐	☐	☐	☐
9. The validity of the studies is appropriately appraised	☐	☐	☐	☐
10. The methods are described in such a way as to be reproducible.	☐	☐	☐	☐
11. The statistical methods are appropriate to the material and the objectives of this guideline	☐	☐	☐	☐
12. Important parameters (e.g., setting, study population, study design) that could affect study results are systematically addressed	☐	☐	☐	☐
13. Health benefits, side effects, and risks are adequately addressed	☐	☐	☐	☐
14. The writing style is appropriate for health care professionals.	☐	☐	☐	☐
15. The grades assigned to each recommendation are appropriate	☐	☐	☐	☐

COMMENTS

Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the guideline and Technical Report

---

OVERALL ASSESSMENT

Would you recommend these guidelines for use in practice? (check one)

☐ Strongly recommend

☐ Recommend (with provisions or alterations)

☐ Would not recommend

☐ Unsure

APPENDIX X
PEER REVIEW PANEL

Participation in the AAOS peer review process does not constitute an endorsement of this guideline by the participating organization.

Peer review of the draft guideline is completed by an outside Peer Review Panel. Outside peer reviewers are solicited for each AAOS guideline and consist of experts in the guideline's topic area. These experts represent professional societies other than AAOS and are nominated by the guideline work group prior to beginning work on the guideline. For this guideline, 23 outside peer review organizations were invited to review the draft guideline and all supporting documentation. Eight societies participated in the peer review of the Treatment of Symptomatic Osteoporotic Spinal Compression Fractures guideline draft and seven explicitly consented to be listed as a peer review organization in this appendix.

The organizations that reviewed the document and consented to be listed as a peer review organization are listed below:

American Academy of Physical Medicine and Rehabilitation (AAPMR)

American College of Radiology (ACR)

AO Spine International

International Spine Intervention Society (ISIS)

National Osteoporosis Foundation (NOF)

North American Spine Association (NASS)

Neurosurgery Washington Committee, American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS)

Individuals who participated in the peer review of this document and gave their consent to be listed as reviewers of this document are:

Professor Nikolai Bogduk MD ISIS

Christopher M. Bono MD NASS

Gary Ghiselli MD NASS

Bradford J Richmond MD ACR

Charles A. Reitman, MD AAOS GTOC

Paul Heini MD AO Spine

John Kirkpatrick MD AAOS EBPC

Michael R. McClung, MD NOF

Ariz R. Mehta MD AAPMR

Mark E. Linskey, M.D. (as Chairman of the AANS/CNS Joint Guidelines Committee)

Participation in the AAOS guideline peer review process does not constitute an endorsement of the guideline by the participating organizations or the individuals listed above nor does it is any way imply the reviewer supports this document.

PUBLIC COMMENTARY

A period of public commentary follows the peer review of the draft guideline. If significant non-editorial changes are made to the document as a result of public commentary, these changes are also documented and forwarded to the AAOS bodies that approve the final guideline.

Public commentators who gave explicit consent to be listed in this document include the following:

None

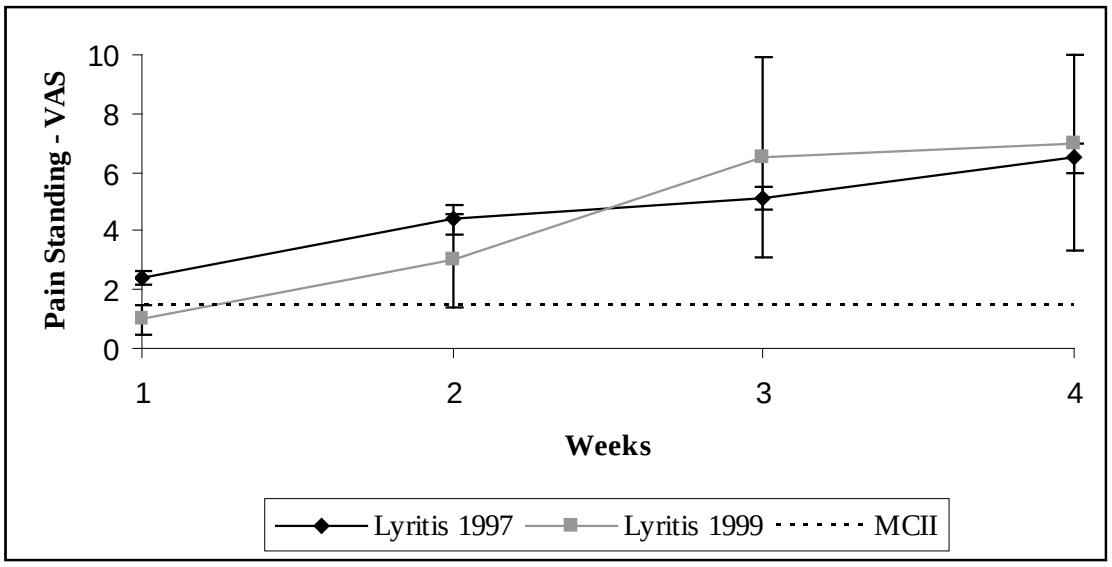
Participation in the AAOS guideline public commentary review process does not constitute an endorsement of the guideline by the participating organizations or the individual listed nor does it in any way imply the reviewer supports this document.

APPENDIX XI
INTERPRETING THE GRAPHS
LINE GRAPHS

Throughout the guideline we use line graphs to illustrate the differences in efficacy between the experimental and control groups of a study. Each point represents the difference between the two study groups for the designated outcome at that particular time point. A positive value indicates a better outcome (e.g., less pain) in the experimental group. The error bars represent the 95% Confidence Interval. The dotted line represents the Minimally Clinically Important Improvement (MCII) for the outcome.

In the example below, the difference in pain between the calcitonin and placebo groups is compared at 4 time points in two separate studies (Lyritis 1997 and Lyritis 1999). For instance, at 4 weeks the pain on VAS in the calcitonin group is about 7 units less than the pain in the placebo group. The difference is statistically significant because the confidence intervals do not cross 0, and the difference is clinically important because the lower confidence interval is greater than the MCII value.

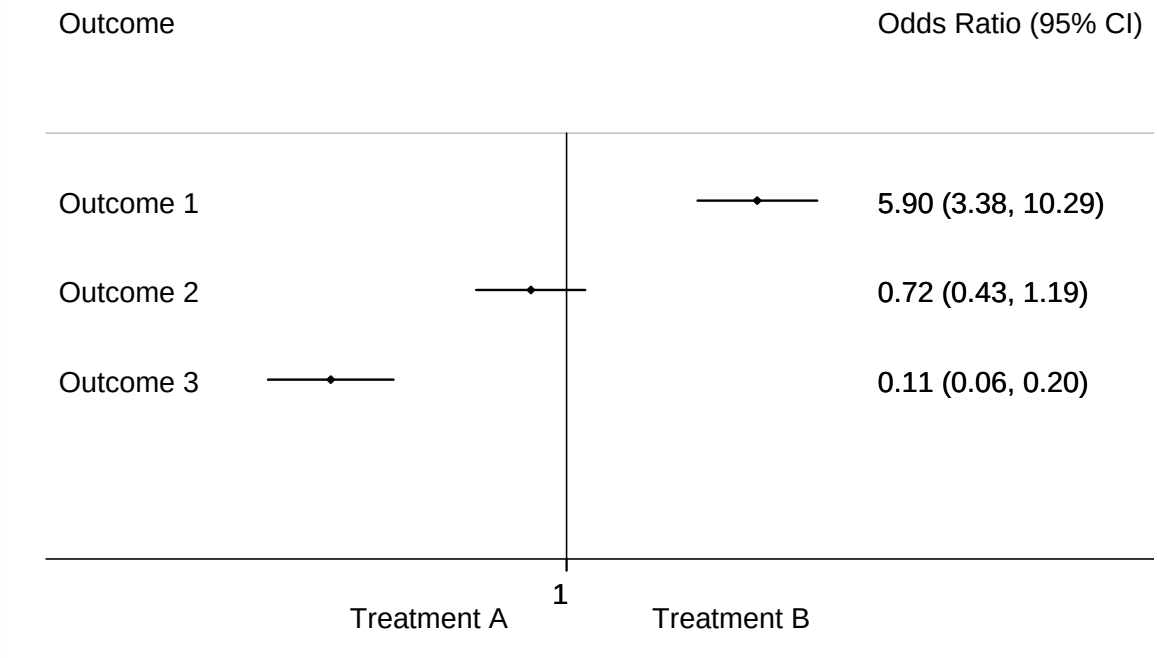
Calcitonin vs. Placebo – Difference in Pain



FOREST PLOTS

In Recommendation 2 we use descriptive diagrams known as forest plots to present data from studies comparing the differences in outcomes between two treatment groups. In cases where a meta-analysis has been performed (combining combining results of multiple studies into a single estimate of overall effect), the estimate of overall effect is presented at the bottom of the graph using a diamond to illustrate the confidence intervals of the estimated overall effect. In cases where a meta-analysis has not been performed, each point and corresponding horizontal line on a sample plot should be viewed independently. In the example below, the odds ratio is the effect measure used to depict differences in outcomes between the two treatment groups of a study. In other forest plots, the point can refer to other summary measures (such as the mean difference or relative risk). The horizontal line running through each point represents the 95% confidence interval for that point. In this graph, the solid vertical line represents "no effect" where the Odds Ratio, OR, is equal to one. When mean differences are portrayed, the vertical line of no effect is at zero.

For example, in the figure below the odds of a patient experiencing Outcome 1 are 5.9 times greater for patients who received Treatment B than for patients who received Treatment A.. This result is statistically significant because the 95% Confidence Interval does not cross the "no effect" line. In general, the plots are arranged such that results to the left of the "no effect" line favor Treatment A while results to the right favor Treatment B. In the example below, the odds ratio for Outcome 1 favors Treatment B, the odds ratio for Outcome 3 favors Treatment A, and the odds ratio for Outcome 2 does not favor either treatment because the 95% CI crosses the "no effect" line (i.e. the difference is not statistically significant).



ABBREVIATIONS USED IN THIS REPORT

95% CI	95% confidence interval
AAOS	American Academy of Orthopaedic Surgeons
ADL	activities of daily living
AQoL	Assessment of Quality of Life
BOC	AAOS Board of Councilors
BOD	AAOS Board of Directors
BOS	AAOS Board of Specialty Societies
CCEF	capacatively coupled electric field
CI	confidence interval
CME	Continuing Medical Education
CORQAT	AAOS Council on Research, Quality Assessment, and Technology
DPQ	Dallas Pain Questionnaire
EBM	evidence based medicine
EBPC	AAOS Evidence Based Practice Committee
EQ-5D	European Quality of Life – Five Dimensions
EVOS	European Vertebral Osteoporosis Study
g	gram
GRADE	Grading of Recommendations, Assessment, Development, and
GTOC	AAOS Guidelines and Technology Oversight Committee
IU	International Unit
LDL	limitations of daily living
mcg	microgram
MCID	minimal clinically important difference
MCII	minimal clinically important improvement
mg	milligram
MRI	magnetic resonance imaging
n/a	not applicable
NGT	Nominal Group Technique
NRS	numerical rating scale
NSAID	non-steroidal anti-inflammatory drug
ODI	Oswestry Disability Index
OQLQ	Osteoporosis Quality of Life Questionnaire
OR	odds ratio
OREF	Orthopedic Research and Education Foundation
ORS	Orthopaedic Research Society
QUALEFFO	Quality of Life of the European Foundation for Osteporosis
RDQ	Roland-Morris Disability Questionnaire
SD	standard deviation
SF-36	36-Item Short Form Survey Instrument
SF-36 MCS	36-Item Short Form Survey Instrument Mental Component Score
SF-36 PCS	36-Item Short Form Survey Instrument Physical Component Score

SIP	sickness impact profile
SOF-ADL	Study of Osteoporotic Fractures-Activities of Daily Living
VAS	visual analog scale
WMD	weighted mean difference
μg	microgram

APPENDIX XII
CONFLICT OF INTEREST

All members of the AAOS work group disclosed any conflicts of interest prior to the development of the recommendations for this guideline. Conflicts of interest are disclosed in writing with the American Academy of Orthopaedic Surgeons via a private on-line reporting database and also verbally at the recommendation approval meeting.

Stephen I Esses, MD (Houston, TX): 2 (Orthopedics; Spine; THE SPINE JOURNAL). Submitted on: 10/23/2009 and last confirmed as accurate on 01/22/2010.

Joel A Finkelstein, MD (Toronto, ON Canada): 7 (Stryker; Synthes). Submitted on: 02/03/2009.

John Jenkins (Jackson, TN): 4 (Norvartis; Procter & Gamble; Roche). Submitted on: 03/11/2009.

Robert A McGuire, Jr MD (Jackson, MS): 1 (AOSpine North America chairman); 2 (Journal of Spinal Disorders); 3 (DePuy, A Johnson & Johnson Company); 5A (Synthes); 7 (AO; Stryker). Submitted on: 02/16/2009.

Eric John Woodard, MD (Boston, MA): 1 (AOSpine); 4 (DePuy, A Johnson & Johnson Company; Stryker; Synthes); 5A (invivo therapeutics); 7 (Synthes; AOSpine); 8 (Medtronic); 10 (Nanoventures). Submitted on: 03/24/2009.

William Charles Watters III, MD (Houston, TX): 1 (North American Spine Society; American Board of Spine Surgery; Board of Advisoer Official Disability Guidelines; Associate Member of The Editorial Board, The Spine Journal; Med Center Ambulatory Surgery Center); 2 (The Spine Journal); 4 (Stryker; Synthes); 5A (Orthofix, Inc.; Stryker); 8 (Intrisic Therapeutics). Submitted on: 08/14/2009.

Disclosure Items: (n) = Respondent answered 'No' to all items indicating no conflicts. 1=Board member/owner/officer/committee appointments; 2= Medical/Orthopaedic Publications; 3= Royalties; 4= Speakers bureau/paid presentations;5A= Paid consultant; 5B= Unpaid consultant; 6= Research or institutional support from a publisher; 7= Research or institutional support from a company or supplier; 8= Stock or Stock Options; 9= Other financial/material support from a publisher; 10= Other financial/material support from a company or supplier.

APPENDIX XIII
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EXCLUDED ARTICLES AND REASON FOR EXCLUSION

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Adachi 2009	Treating osteoporosis in Canada: What clinical efficacy data should be considered by policy decision makers?	Systematic review, bibliography screened
Adachi 2007	Assessing compliance, acceptance, and tolerability of teriparatide in patients with osteoporosis who fractured while on antiresorptive treatment or were intolerant to previous antiresorptive treatment: an 18-month, multicenter, open-label, prospective stu	Does not investigate efficacy of treatment
Adachi 2005	Vertebral fracture risk reduction with risedronate in post-menopausal women with osteoporosis: a meta-analysis of individual patient data	Systematic review, bibliography screened
Adami 2008	Effect of raloxifene after recombinant teriparatide [hPTH(1-34)] treatment in postmenopausal women with osteoporosis	Incorrect patient population
Adami 2006	Protelos: nonvertebral and hip antifracture efficacy in postmenopausal osteoporosis	Not specific to fracture patients
Adami 2001	Alendronate for the treatment of osteoporosis in men	Narrative review, bibliography screened
Adelaide Health Technology 2006	Vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture (Brief record)	Systematic review, bibliography screened
Afzal 2007	Percutaneous vertebroplasty for osteoporotic fractures	Not best available evidence
Agnusdei 1997	Efficacy of ipriflavone in established osteoporosis and long-term safety	Narrative review, bibliography screened
Agnusdei 1992	Effects of ipriflavone on bone mass and calcium metabolism in postmenopausal osteoporosis	Not specific to fracture patients
Alanay 2001	Short-segment pedicle instrumentation of thoracolumbar burst fractures: does transpedicular intracorporeal grafting prevent early failure?	Incorrect patient population
Alexandersen 2001	Ipriflavone in the treatment of postmenopausal osteoporosis: a randomized controlled trial	Incorrect patient population
Almqvist 2004	Early parathyroidectomy increases bone mineral density in patients with mild primary hyperparathyroidism: a prospective and randomized study	Incorrect patient population
Alvarez 2006	Percutaneous vertebroplasty: functional improvement in patients with osteoporotic compression fractures	Not best available evidence
Alvarez 2005	Predictors of outcomes of percutaneous vertebroplasty for osteoporotic vertebral fractures	Retrospective case series
Amar 2003	Use of a screw-syringe injector for cement delivery during kyphoplasty: technical report	Surgical Technique
Amar 2001	Percutaneous transpedicular polymethylmethacrylate vertebroplasty for the treatment of spinal compression fractures	Retrospective case series
Ambrosanio 2005	Vertebroplasty in the treatment of spine disease	Not best available evidence

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Anderson 1997	Effect of intermittent cyclical disodium etidronate therapy on bone mineral density in men with vertebral fractures	Does not report patient oriented outcomes
Anonymous 2008	Zoledronic acid improves bone density and reduces fractures	Commentary
Anonymous 2005	Strontium: new drug. Postmenopausal osteoporosis: too many unknowns	Narrative review, bibliography screened
Anonymous 2005	Teriparatide: new preparation. Osteoporosis: less well evaluated than alendronic acid	Narrative review, bibliography screened
Anonymous 1998	Fluoride and bone: a second look. No use in osteoporosis	Narrative review, bibliography screened
Anonymous 1997	Measuring quality of life in women with osteoporosis. Osteoporosis Quality of Life Study Group	Does not investigate efficacy of treatment
Anselmetti 2008	Percutaneous vertebroplasty and bone cement leakage: clinical experience with a new high-viscosity bone cement and delivery system for vertebral augmentation in benign and malignant compression fractures	Does not compare two treatments; compares techniques of a treatment
Anselmetti 2007	Pain relief following percutaneous vertebroplasty: results of a series of 283 consecutive patients treated in a single institution	Not best available evidence
Anselmetti 2005	Treatment of painful compression vertebral fractures with vertebroplasty: results and complications	Not best available evidence
Antoniucci 2005	Postmenopausal bilateral oophorectomy is not associated with increased fracture risk in older women	Does not investigate efficacy of treatment
Armbrecht 2008	Vertebral fracture diagnosis in the multinational BONE study of oral ibandronate: quality management in radiology	Does not investigate efficacy of treatment
Armingeat 2006	Intravenous pamidronate for pain relief in recent osteoporotic vertebral compression fracture: a randomized double-blind controlled study	Treatment comparison not relevant
Aslam 2008	Percutaneous vertebroplasty in osteoporotic vertebral compression fractures: our initial experience	Not best available evidence
Aursnes 2000	A Bayesian analysis of bisphosphonate effects and cost-effectiveness in post-menopausal osteoporosis	Systematic review, bibliography screened
Avenell 2009	Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis	Systematic review, bibliography screened
Aydin 1999	Z-plate instrumentation in thoracolumbar spinal fractures	Incorrect patient population
Aydogan 2009	The pedicle screw fixation with vertebroplasty augmentation in the surgical treatment of the severe osteoporotic spines	Not best available evidence

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Bailey 2009	Comparison of thoracolumbosacral orthosis and no orthosis for the treatment of thoracolumbar burst fractures: interim analysis of a multicenter randomized clinical equivalence trial	Incorrect patient population, non-osteoporotic patients
Banerjee 2007	Back stab: percutaneous vertebroplasty for severe back pain	Systematic review, bibliography screened
Barbagallo 2007	Quality of life in osteoporotic women with inadequate clinical response to antiresorptive drugs: results from the ICARO study	Insufficient data
Barbero 2008	Percutaneous vertebroplasty: the follow-up	Not best available evidence
Baroud 2006	Biomechanical impact of vertebroplasty. Postoperative biomechanics of vertebroplasty	Narrative review, bibliography screened
Barrocas 2007	Vertebral augmentation in osteoporotic fractures	Narrative review, bibliography screened
Bauer 2006	Short-term changes in bone turnover markers and bone mineral density response to parathyroid hormone in postmenopausal women with osteoporosis	Not specific to fracture patients
Beattie 2003	Kyphoplasty and vertebroplasty for the treatment of osteoporotic vertebral compression fractures	Narrative review, bibliography screened
Becker 2007	Is there an indication for prophylactic balloon kyphoplasty? A pilot study	Does not compare two treatments; compares techniques of a treatment
Berlemann 2004	Kyphoplasty for treatment of osteoporotic vertebral fractures: a prospective non-randomized study	Not best available evidence
Bhatia 2006	Cement leakage in percutaneous vertebroplasty: effect of preinjection gelfoam embolization	Not best available evidence
Bierschneider 2005	Minimally invasive vertebral augmentation techniques in osteoporotic fractures	Narrative review, bibliography screened
Bjarnason 2001	Six and twelve month changes in bone turnover are related to reduction in vertebral fracture risk during 3 years of raloxifene treatment in postmenopausal osteoporosis	Not specific to fracture patients
Black 2007	Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis	Not specific to fracture patients
Black 2000	Fracture risk reduction with alendronate in women with osteoporosis: the Fracture Intervention Trial. FIT Research Group	Subgroup analysis of included RCT
Black 1999	The effect of alendronate therapy on osteoporotic fracture in the vertebral fracture arm of the Fracture Intervention Trial	Commentary
Black 1993	Design of the Fracture Intervention Trial	Description of study design
Blake 2007	A review of strontium ranelate and its effect on DXA scans	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Blake 2006	Strontium ranelate: a novel treatment for postmenopausal osteoporosis: a review of safety and efficacy	Narrative review, bibliography screened
Blattert 2009	Suitability of a calcium phosphate cement in osteoporotic vertebral body fracture augmentation: a controlled, randomized, clinical trial of balloon kyphoplasty comparing calcium phosphate versus polymethylmethacrylate	Does not compare two treatments; compares techniques of a treatment
Blau 2003	Analgesic efficacy of calcitonin for vertebral fracture pain	Systematic review, bibliography screened
Blouin 2009	Comparison of direct health care costs related to the pharmacological treatment of osteoporosis and to the management of osteoporotic fractures among compliant and noncompliant users of alendronate and risedronate: A population-based study	Cost-effectiveness study
Body 2002	Calcitonin for the long-term prevention and treatment of postmenopausal osteoporosis	Narrative review, bibliography screened
Body 2002	A randomized double-blind trial to compare the efficacy of teriparatide [recombinant human parathyroid hormone (1-34)] with alendronate in postmenopausal women with osteoporosis	Not specific to fracture patients
Bonnick 2009	Patient satisfaction in postmenopausal women treated with a weekly bisphosphonate transitioned to once-monthly ibandronate	Not specific to fracture patients
Bonnick 2007	Treatment with alendronate plus calcium, alendronate alone, or calcium alone for postmenopausal low bone mineral density	Not specific to fracture patients
Boonen 2009	Once-weekly risedronate in men with osteoporosis: Results of a 2-Year, placebo-controlled, double-blind, multicenter study	Not specific to fracture patients
Boonen 2004	Safety and efficacy of risedronate in reducing fracture risk in osteoporotic women aged 80 and older: implications for the use of antiresorptive agents in the old and oldest old	Systematic review, bibliography screened
Borgstrom 2004	Cost effectiveness of raloxifene in the treatment of osteoporosis in Sweden: an economic evaluation based on the MORE study	Cost-effectiveness study
Boszczyk 2004	Microsurgical interlaminary vertebro- and kyphoplasty for severe osteoporotic fractures	Retrospective case series
Bouxsein 2009	Teriparatide and raloxifene reduce the risk of new adjacent vertebral fractures in postmenopausal women with osteoporosis: Results from two randomized controlled trials	Narrative review, bibliography screened
Bouza 2006	Efficacy and safety of balloon kyphoplasty in the treatment of vertebral compression fractures: a systematic review	Systematic review, bibliography screened
Bradbeer 1992	Treatment of osteoporosis with parathyroid peptide (hPTH 1-34) and oestrogen: increase in volumetric density of iliac cancellous bone may depend on reduced trabecular spacing as well as increased thickness of packets of newly formed bone	Does not report patient oriented outcomes
Braun 2008	Outcome of CT-guided vertebroplasty in outpatients with severe vertebral compression fractures	Retrospective case series

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Bravenboer 1999	Bone histomorphometric evaluation of pamidronate treatment in clinically manifest osteoporosis	Does not report patient oriented outcomes
Brecht 2004	Health-economic comparison of three recommended drugs for the treatment of osteoporosis	Cost-effectiveness study
Briot 2007	How long should patients take medications for postmenopausal osteoporosis?	Narrative review, bibliography screened
Brook 2008	Vertebral augmentation with a flexible curved needle: preliminary results in 17 consecutive patients	Not best available evidence
Brookhart 2007	Gaps in Treatment Among Users of Osteoporosis Medications: The Dynamics of Noncompliance	Does not investigate efficacy of treatment
Brown 2005	Correlation between preprocedural MRI findings and clinical outcomes in the treatment of chronic symptomatic vertebral compression fractures with percutaneous vertebroplasty	Retrospective case series
Brown 2004	Treatment of chronic symptomatic vertebral compression fractures with percutaneous vertebroplasty	Retrospective case series
Brown 2002	The efficacy and tolerability of risedronate once a week for the treatment of postmenopausal osteoporosis	Not specific to fracture patients
Bruyere 2008	Effects of strontium ranelate on spinal osteoarthritis progression	Incorrect patient population
Bundred 2008	Effective inhibition of aromatase inhibitor-associated bone loss by zoledronic acid in postmenopausal women with early breast cancer receiving adjuvant letrozole: ZO-FAST study results	Not specific to fracture patients
Burckhardt 1993	The effect of treatment with calcitonin on vertebral fracture rate in osteoporosis	Systematic review, bibliography screened
Butler 2005	Percutaneous sacroplasty for the treatment of sacral insufficiency fractures	Less than 10 patients per group
Campbell 2004	Five year study of etidronate and/or calcium as prevention and treatment for osteoporosis and fractures in patients with asthma receiving long term oral and/or inhaled glucocorticoids	Not specific to fracture patients
Caplan 1994	Pathogenesis of vertebral crush fractures in women	Does not investigate efficacy of treatment
Carlier 2004	Osteoporotic vertebral collapse: percutaneous vertebroplasty and local kyphosis correction	Not best available evidence
Caudana 2008	CT-guided percutaneous vertebroplasty: personal experience in the treatment of osteoporotic fractures and dorsolumbar metastases	Not best available evidence
Cengiz 2008	Timing of thoracolomber spine stabilization in trauma patients; impact on neurological outcome and clinical course. A real prospective (rct) randomized controlled study	Incorrect patient population
Cesareo 2007	Evidence based medicine and effective interventions of pharmacological therapy for the prevention of osteoporotic fractures	Systematic review, bibliography screened
Chang 2007	Unipedicular vertebroplasty for osteoporotic compression fracture using an individualized needle insertion angle	Not best available evidence

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Chapurlat 2008	Single annual injectable treatment for postmenopausal osteoporosis	Narrative review, bibliography screened
Che 2006	Outcomes of a disease-management program for patients with recent osteoporotic fracture	Does not investigate efficacy of treatment
Chen 2009	Kyphoplasty for chronic painful osteoporotic vertebral compression fractures via unipedicular versus bipedicular approachment: A comparative study in early stage	Not relevant, comparison not considered for this guideline
Chen 2004	Intracorporal bone grafting for vertebral compression fractures with intraosseous vacuum phenomenon	Not best available evidence
Chen 2003	Percutaneous vertebroplasty for the treatment of osteoporotic vertebral compression fractures	Not best available evidence
Chen 2002	Percutaneous vertebroplasty for the treatment of osteoporotic vertebral compression fractures: a preliminary report	Not best available evidence
Chesnut 2005	Ibandronate produces significant, similar antifracture efficacy in North American and European women: new clinical findings from BONE	Duplicate study data, subgroup analysis
Chesnut 1983	Stanozolol in postmenopausal osteoporosis: therapeutic efficacy and possible mechanisms of action	Insufficient data
Cheung 2005	Vertebroplasty by use of a strontium-containing bioactive bone cement	Narrative review, bibliography screened
Chevalley 2002	An osteoporosis clinical pathway for the medical management of patients with low-trauma fracture	Incorrect patient population
Cho 2007	Vertebroplasty utilizing percutaneous vertebral body access (PVBA) technique for osteoporotic vertebral compression fractures in the middle thoracic vertebrae	Retrospective case series
Chow 2004	Successful salvage using percutaneous vertebroplasty in cancer patients with painful spinal metastases or osteoporotic compression fractures	Incorrect patient population
Chrischilles 2001	The effect of alendronate on fracture-related healthcare utilization and costs: The fracture intervention trial	Cost-effectiveness study
Christodoulou 2005	Vertebral body reconstruction with injectable hydroxyapatite cement for the management of unstable thoracolumbar burst fractures: a preliminary report	Incorrect patient population
Chung 2008	Comparative study of balloon kyphoplasty with unilateral versus bilateral approach in osteoporotic vertebral compression fractures	Does not compare two treatments; compares techniques of a treatment
Colon Emeric 2006	Osteoporotic fractures in older adults	Narrative review, bibliography screened
Combe 1997	Equivalence of nasal spray and subcutaneous formulations of salmon calcitonin	Does not compare two treatments; compares techniques of a treatment
Comite d'Evaluation 2006	Kyphoplasty - systematic review, expert panel (Brief record)	Commentary

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Compston 2009	Guidelines for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK	Guideline summary
Compston 2005	Prevention of vertebral fractures by strontium ranelate in postmenopausal women with osteoporosis	Narrative review, bibliography screened
Cortet 2002	Evaluation of spinal curvatures after a recent osteoporotic vertebral fracture	Does not investigate efficacy of treatment
Cortet 1999	Percutaneous vertebroplasty in the treatment of osteoporotic vertebral compression fractures: an open prospective study	Not best available evidence
Coumans 2003	Kyphoplasty for vertebral compression fractures: 1-year clinical outcomes from a prospective study	Not best available evidence
Coyle 2001	Cost effectiveness of nasal calcitonin in postmenopausal women: use of Cochrane Collaboration methods for meta-analysis within economic evaluation	Systematic review, bibliography screened
Crans 2004	Association of severe vertebral fractures with reduced quality of life: reduction in the incidence of severe vertebral fractures by teriparatide	Post hoc subgroup analysis of included RCT
Crisp 1984	Combined treatment of post-menopausal osteoporosis: effect on muscle function and a new radiological method for assessing trabecular bone	Not best available evidence
Cummings 2009	Denosumab for prevention of fractures in postmenopausal women with osteoporosis	Not specific to fracture patients
Cummings 2008	The effects of tibolone in older postmenopausal women	Incorrect patient population
Curtis 2008	Benefit of adherence with bisphosphonates depends on age and fracture type: Results from an analysis of 101,038 new bisphosphonate users	Not specific to fracture patients
Curtis 2007	Prevention and treatment of glucocorticoid-induced osteoporosis	Narrative review, bibliography screened
Cyteval 1999	Acute osteoporotic vertebral collapse: open study on percutaneous injection of acrylic surgical cement in 20 patients	Not best available evidence
DalCanto 2009	Double cement-application cavity containment kyphoplasty: technique description and efficacy	Retrospective case series
Dansie 2005	MRI findings after successful vertebroplasty	Retrospective case series
Dawson Hughes 2007	Response to teriparatide in patients with baseline 25-hydroxyvitamin D insufficiency or sufficiency	Post hoc subgroup analysis
De 1999	Incremental cost of medical care after hip fracture and first vertebral fracture: The Rotterdam Study	Does not investigate efficacy of treatment
Deal 2005	Combination teriparatide and raloxifene therapy for postmenopausal osteoporosis: results from a 6-month double-blind placebo-controlled trial	Not specific to fracture patients
Deen 2006	Balloon kyphoplasty for vertebral compression fractures in solid organ transplant recipients: results of treatment and comparison with primary osteoporotic vertebral compression fractures	Not best available evidence

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Delmas 2008	Monthly dosing of 75 mg risedronate on 2 consecutive days a month: efficacy and safety results	Not specific to fracture patients
Delmas 2008	Efficacy and safety of risedronate 150 mg once a month in the treatment of postmenopausal osteoporosis	Not specific to fracture patients
Delmas 2005	Clinical effects of strontium ranelate in women with postmenopausal osteoporosis	Narrative review, bibliography screened
Delmas 2003	Severity of prevalent vertebral fractures and the risk of subsequent vertebral and nonvertebral fractures: results from the MORE trial	Post hoc subgroup analysis
Delmas 2002	Efficacy of raloxifene on vertebral fracture risk reduction in postmenopausal women with osteoporosis: four-year results from a randomized clinical trial	Subgroup analysis of included RCT
Delmas 1990	Treatment of vertebral osteoporosis with disodium monofluorophosphate: comparison with sodium fluoride	Not best available evidence
Deprez 2003	Nonpharmacological prevention of osteoporotic fractures	Narrative review, bibliography screened
Diamond 2006	Clinical outcomes after acute osteoporotic vertebral fractures: a 2-year non-randomised trial comparing percutaneous vertebroplasty with conservative therapy	Not best available evidence
Diamond 2003	Management of acute osteoporotic vertebral fractures: a nonrandomized trial comparing percutaneous vertebroplasty with conservative therapy	Interim Analysis
Diamond 2001	Guidelines for treatment of osteoporosis in men	Systematic review, bibliography screened
Dixon 2004	Vertebroplasty and kyphoplasty: rapid pain relief for vertebral compression fractures	Narrative review, bibliography screened
Do 2005	Prospective analysis of clinical outcomes after percutaneous vertebroplasty for painful osteoporotic vertebral body fractures	Not best available evidence
Do 2003	Percutaneous vertebroplasty: rationale, clinical outcomes, and future directions	Narrative review, bibliography screened
Donggrell 2008	New horizons for zoledronic acid: Results of the HORIZON trials in postmenopausal women with osteoporosis and after hip fracture	Commentary
Donovan 2004	Multiple adjacent vertebral fractures after kyphoplasty in a patient with steroid-induced osteoporosis	Case report
Doo 2008	Clinical relevance of pain patterns in osteoporotic vertebral compression fractures	Not best available evidence
Doren 2000	Prevention of postmenopausal osteoporosis with oestrogen replacement therapy and associated compounds: update on clinical trials since 1995	Systematic review, bibliography screened
Downs 1999	An open-label extension study of alendronate treatment in elderly women with osteoporosis	Not specific to fracture patients

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Duque 2001	Anabolic agents to treat osteoporosis in older people: is there still place for fluoride? Fluoride for treating postmenopausal osteoporosis	Systematic review, bibliography screened
Duran 2007	Pulmonary cement embolism: a complication of percutaneous vertebroplasty	Retrospective case series
Dure Smith 1991	Fluoride therapy for osteoporosis: a review of dose response, duration of treatment, and skeletal sites of action	Narrative review, bibliography screened
Earnshaw 2007	Cost-effectiveness of bisphosphonate therapies for women with postmenopausal osteoporosis: implications of improved persistence with less frequently administered oral bisphosphonates	Cost-effectiveness study
Eastell 2009	Effect of once-yearly zoledronic acid five milligrams on fracture risk and change in femoral neck bone mineral density	Post hoc subgroup analysis
Eastell 2009	Sequential treatment of severe postmenopausal osteoporosis after teriparatide: final results of the randomized, controlled european study of forsteo (EUROFORS)	Not relevant, sequential treatment not considered for this guideline
Eck 2008	Comparison of vertebroplasty and balloon kyphoplasty for treatment of vertebral compression fractures: a meta-analysis of the literature	Systematic review, bibliography screened
Eck 2002	Vertebroplasty: a new treatment strategy for osteoporotic compression fractures	Surgical Technique
Edelman 2005	Percutaneous vertebroplasty: a review for the primary care physician	Commentary
Ensrud 2008	Effects of raloxifene on fracture risk in postmenopausal women: the Raloxifene Use for the Heart Trial	Incorrect patient population
Ensrud 2000	Prevalent vertebral deformities predict mortality and hospitalization in older women with low bone mass	Does not investigate efficacy of treatment
Ensrud 1998	Alendronate reduced new fractures in postmenopausal women who had low bone-mineral density and existing vertebral fractures	Commentary
Ensrud 1997	Correlates of kyphosis in older women. The Fracture Intervention Trial Research Group	Does not investigate efficacy of treatment
Ensrud 1997	Treatment with alendronate prevents fractures in women at highest risk: results from the Fracture Intervention Trial	subgroup analysis of included RCT
Epstein 2009	Update on monthly oral bisphosphonate therapy for the treatment of osteoporosis: focus on ibandronate 150 mg and risedronate 150 mg	Systematic review, bibliography screened
Epstein 2006	The problem of low levels of vitamin D and osteoporosis: use of combination therapy with alendronic acid and colecalciferol (vitamin D3)	Narrative review, bibliography screened
Epstein 2000	Postmenopausal osteoporosis: fracture consequences and treatment efficacy vary by skeletal site	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Eriksen 2004	Teriparatide: A bone formation treatment for osteoporosis	Narrative review, bibliography screened
Ettinger 2005	Simple computer model for calculating and reporting 5-year osteoporotic fracture risk in postmenopausal women	Does not investigate efficacy of treatment
Evans 2003	Vertebral compression fractures: pain reduction and improvement in functional mobility after percutaneous polymethylmethacrylate vertebroplasty retrospective report of 245 cases	Retrospective case series
Eyheremendy 2004	Percutaneous pediculoplasty in osteoporotic compression fractures	Less than 10 patients per group
Fadanelli 2004	Combining bisphosphonates with hormone therapy for postmenopausal osteoporosis	Narrative review, bibliography screened
Fairney 1998	The use of cyclical etidronate in osteoporosis: changes after completion of 3 years treatment	Does not report patient oriented outcomes
Falch 1987	Postmenopausal osteoporosis: no effect of three years treatment with 1,25-dihydroxycholecalciferol	Incorrect patient population
Farley 1992	Spinal fractures during fluoride therapy for osteoporosis: relationship to spinal bone density	Retrospective case series
Farley 1989	Efficacy of long-term fluoride and calcium therapy in correcting the deficit of spinal bone density in osteoporosis	Not best available evidence
Farrerons 1997	Sodium fluoride treatment is a major protector against vertebral and nonvertebral fractures when compared with other common treatments of osteoporosis: a longitudinal, observational study	Not best available evidence
Feldstein 2003	Bone mineral density measurement and treatment for osteoporosis in older individuals with fractures: A gap in evidence-based practice guideline implementation	Does not investigate efficacy of treatment
Felsenberg 2005	Oral ibandronate significantly reduces the risk of vertebral fractures of greater severity after 1, 2, and 3 years in postmenopausal women with osteoporosis	Post hoc subgroup analysis
Fernandes 2009	Effects of Short-Term Risedronate on Bone Resorption and Patient Satisfaction in Postmenopausal Osteoporosis Patients	Not specific to fracture patients
Ferrer 2006	Validation of a minimum outcome core set in the evaluation of patients with back pain	Does not investigate efficacy of treatment
Figueiredo 2009	Percutaneous vertebroplasty: a comparison between the procedure using the traditional and the new side-opening cannula for osteoporotic vertebral fracture	Not relevant, comparison not considered for this guideline
Filip 2005	Osteoporosis risk factors in rural and urban women from the Lublin Region of Poland	Does not investigate efficacy of treatment
Filipponi 1996	Cyclical intravenous clodronate in postmenopausal osteoporosis: results of a long-term clinical trial	Not specific to fracture patients
Finkelstein 2004	Diagnosis and management of pathological fractures of the spine	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Fisher 2002	Percutaneous vertebroplasty: a bone cement procedure for spinal pain relief	Narrative review, bibliography screened
Fleurence 2007	The cost effectiveness of bisphosphonates for the prevention and treatment of osteoporosis: a structured review of the literature	Cost-effectiveness study
Flicker 1997	Nandrolone decanoate and intranasal calcitonin as therapy in established osteoporosis	Does not report relevant outcome
Flors 2009	Vesselplasty: a new technical approach to treat symptomatic vertebral compression fractures	Not best available evidence
Fogelman 2008	Parathyroid hormone(1-84) treatment of postmenopausal women with low bone mass receiving hormone replacement therapy	Not specific to fracture patients
Foley 1983	Thoracic and lumbar spine fusion: postoperative radiologic evaluation	Retrospective case series
Frampton 2009	Risedronate on two consecutive days per month	Narrative review, bibliography screened
Francis 2008	Back pain in osteoporotic vertebral fractures	Narrative review, bibliography screened
Francis 2004	Acute and long-term management of patients with vertebral fractures	Systematic review, bibliography screened
Francis 2001	Androgen replacement in aging men	Incorrect patient population
Francis 1996	A comparison of the effects of alfacalcidol treatment and vitamin D2 supplementation on calcium absorption in elderly women with vertebral fractures	Does not report patient oriented outcomes
Franck 2003	Interdisciplinary approach to balloon kyphoplasty in the treatment of osteoporotic vertebral compression fractures	Narrative review, bibliography screened
Frankel 2007	Percutaneous vertebral augmentation: an elevation in adjacent-level fracture risk in kyphoplasty as compared with vertebroplasty	Not best available evidence
Frey 2008	Percutaneous sacroplasty for osteoporotic sacral insufficiency fractures: a prospective, multicenter, observational pilot study	Incorrect patient population
Frey 2007	Efficacy and safety of percutaneous sacroplasty for painful osteoporotic sacral insufficiency fractures: a prospective, multicenter trial	Incorrect patient population
Fribourg 2004	Incidence of subsequent vertebral fracture after kyphoplasty	Retrospective case series
Fujita 2007	Clinical effect of bisphosphonate and vitamin D on osteoporosis: reappraisal of a multicenter double-blind clinical trial comparing etidronate and alfacalcidol	Post hoc subgroup analysis
Fujita 2004	Reappraisal of Katsuragi calcium study, a prospective, double-blind, placebo-controlled study of the effect of active absorbable algal calcium (AAACa) on vertebral deformity and fracture	Not specific to fracture patients

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Fukunaga 2002	A comparison of the effect of risedronate and etidronate on lumbar bone mineral density in Japanese patients with osteoporosis: a randomized controlled trial	Not specific to fracture patients
Gahr 2006	Percutaneous internal fixation of thoracolumbar spine fractures	Less than 50% follow-up
Gallagher 2005	Teriparatide reduces the fracture risk associated with increasing number and severity of osteoporotic fractures	Post hoc subgroup analysis of included RCT
Gangji 1999	Analgesic effect of intravenous pamidronate on chronic back pain due to osteoporotic vertebral fractures	Retrospective case series
Gardner 2005	Thoracic and lumbar spine fractures	Narrative review, bibliography screened
Gardner 2005	Prevention and treatment of osteoporotic fractures	Narrative review, bibliography screened
Garfin 2006	Balloon kyphoplasty for symptomatic vertebral body compression fractures results in rapid, significant, and sustained improvements in back pain, function, and quality of life for elderly patients	Not best available evidence
Garfin 2001	New technologies in spine: kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures	Narrative review, bibliography screened
Gaughen 2002	Lack of preoperative spinous process tenderness does not affect clinical success of percutaneous vertebroplasty	Retrospective case series
Gaughen 2002	Relevance of antecedent venography in percutaneous vertebroplasty for the treatment of osteoporotic compression fractures	Does not compare two treatments; compares techniques of a treatment
Genant 2005	Reduction in vertebral fracture risk in teriparatide-treated postmenopausal women as assessed by spinal deformity index	Post hoc subgroup analysis of included RCT
Gennari 2002	Analgesic effect of calcitonin in osteoporosis	Narrative review, bibliography screened
Gerszten 2005	Combination kyphoplasty and spinal radiosurgery: a new treatment paradigm for pathological fractures	Incorrect patient population
Gertzbein 1992	Scoliosis Research Society. Multicenter spine fracture study	Incorrect patient population
Geusens 2001	Review of risedronate in the treatment of osteoporosis	Narrative review, bibliography screened
Geusens 1998	Cyclical etidronate increases bone density in the spine and hip of postmenopausal women receiving long term corticosteroid treatment. A double blind, randomised placebo controlled study	Incorrect patient population
Geusens 1986	Bone mineral content, cortical thickness and fracture rate in osteoporotic women after withdrawal of treatment with nandrolone decanoate, 1-alpha hydroxyvitamin D3, or intermittent calcium infusions	Less than 10 patients per group

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Gill 2007	Comparing pain reduction following kyphoplasty and vertebroplasty for osteoporotic vertebral compression fractures	Systematic review, bibliography screened
Goh 2002	Advances in surgical treatment of osteoporotic fractures of the spine	Narrative review, bibliography screened
Gold 2007	Do estrogen or selective estrogen receptor modulators improve quality of life for women with postmenopausal osteoporosis?	Narrative review, bibliography screened
Grados 2000	Long-term observations of vertebral osteoporotic fractures treated by percutaneous vertebroplasty	Retrospective case series
Grafe 2008	Calcium-phosphate and polymethylmethacrylate cement in long-term outcome after kyphoplasty of painful osteoporotic vertebral fractures	Does not compare two treatments; compares techniques of a treatment
Grafe 2005	Reduction of pain and fracture incidence after kyphoplasty: 1-year outcomes of a prospective controlled trial of patients with primary osteoporosis	Not best available evidence
Gray 2007	INvestigational Vertebroplasty Efficacy and Safety Trial (INVEST): a randomized controlled trial of percutaneous vertebroplasty	Description of study design
Greenspan 2002	Alendronate improves bone mineral density in elderly women with osteoporosis residing in long-term care facilities: A randomized, double-blind, placebo-controlled trial	Not specific to fracture patients
Grohs 2005	Minimal invasive stabilization of osteoporotic vertebral fractures: a prospective nonrandomized comparison of vertebroplasty and balloon kyphoplasty	Not best available evidence
Grieg 2008	Postural taping decreases thoracic kyphosis but does not influence trunk muscle electromyographic activity or balance in women with osteoporosis	Does not report patient oriented outcomes
Grove 1981	Relief of osteoporotic backache with fluoride, calcium, and calciferol	Does not report recurrent and/or adjacent fractures
Guarnieri 2009	Management of vertebral re-fractures after vertebroplasty in osteoporotic patients	Not best available evidence
Gunter 2003	Management of osteoporosis in women aged 50 and older with osteoporosis-related fractures in a managed care population	Does not investigate efficacy of treatment
Ha 2006	Percutaneous vertebroplasty for vertebral compression fractures with and without intravertebral clefts	Not best available evidence
Haczynski 2001	Vertebral fractures: a hidden problem of osteoporosis	Narrative review, bibliography screened
Hadjipavlou 2005	Percutaneous vertebroplasty and balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures and osteolytic tumours	Systematic review, bibliography screened
Hagino 2009	A double-blinded head-to-head trial of minodronate and alendronate in women with postmenopausal osteoporosis	Not specific to fracture patients

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Hanley 2000	Etridronate therapy in the treatment and prevention of osteoporosis	Narrative review, bibliography screened
Hanna 2007	Kyphoplasty. A treatment for osteoporotic vertebral compression fractures	Narrative review, bibliography screened
Harrington 2007	Osteoporosis disease management for fragility fracture patients: New understandings based on three years' experience with an osteoporosis care service	Does not investigate efficacy of treatment
Harris 2001	Bisphosphonates for the treatment of postmenopausal osteoporosis: clinical studies of etidronate and alendronate	Narrative review, bibliography screened
Harris 1993	Four-year study of intermittent cyclic etidronate treatment of postmenopausal osteoporosis: three years of blinded therapy followed by one year of open therapy	Follow-up study to included RCT
Harrop 2004	Primary and secondary osteoporosis' incidence of subsequent vertebral compression fractures after kyphoplasty	Retrospective case series
Hart 2003	Percutaneous treatment of osteoporotic spinal compression fractures	Commentary
Hasling 1987	Safety of osteoporosis treatment with sodium fluoride, calcium phosphate and vitamin D	Not best available evidence
Hassager 1989	Changes in soft tissue body composition and plasma lipid metabolism during nandrolone decanoate therapy in postmenopausal osteoporotic women	Does not report relevant outcome
Hayne 2003	Vertebroplasty and kyphoplasty: new treatments for painful osteoporotic vertebral fractures	Narrative review, bibliography screened
Heaney 2002	Risedronate reduces the risk of first vertebral fracture in osteoporotic women	Incorrect patient population
Heijckmann 2002	Intravenous pamidronate compared with oral alendronate for the treatment of postmenopausal osteoporosis	Insufficient data
Heini 2000	Percutaneous transpedicular vertebroplasty with PMMA: operative technique and early results. A prospective study for the treatment of osteoporotic compression fractures	Not best available evidence
Hillmeier 2003	Minimally invasive reduction and internal stabilization of osteoporotic vertebral body fractures (Balloon Kyphoplasty)	Not best available evidence
Hitz 2007	Bone mineral density and bone markers in patients with a recent low-energy fracture: effect of 1 y of treatment with calcium and vitamin D	Incorrect patient population
Hiwatashi 2007	Vertebroplasty for osteoporotic fractures with spinal canal compromise	Retrospective case series
Hiwatashi 2007	Patients with osteoporosis on steroid medication tend to sustain subsequent fractures	Retrospective case series
Hiwatashi 2003	Increase in vertebral body height after vertebroplasty	Does not report patient oriented outcomes

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Ho 2000	Effects of alendronate on bone density in men with primary and secondary osteoporosis	Does not report patient oriented outcomes
Hochberg 2000	Preventing fractures in postmenopausal women with osteoporosis. A review of recent controlled trials of antiresorptive agents	Systematic review, bibliography screened
Hochmuth 2006	Percutaneous vertebroplasty in the therapy of osteoporotic vertebral compression fractures: a critical review	Narrative review, bibliography screened
Hodsman 1989	Effects of cyclical therapy for osteoporosis using an oral regimen of inorganic phosphate and sodium etidronate: a clinical and bone histomorphometric study	Not best available evidence
Holick 2005	PTH (1-34): a novel anabolic drug for the treatment of osteoporosis	Narrative review, bibliography screened
Hollingworth 2006	Evidence on the effectiveness and cost-effectiveness of vertebroplasty: A review of policy makers' responses	Narrative review, bibliography screened
Holzherr 2000	Calcium absorption in postmenopausal osteoporosis: benefit of HRT plus calcitriol, but not HRT alone, in both malabsorbers and normal absorbers	Does not report patient oriented outcomes
Hongo 2007	Effect of low-intensity back exercise on quality of life and back extensor strength in patients with osteoporosis: a randomized controlled trial	Not specific to fracture patients
Hsieh 2008	Pain relief in patients treated with percutaneous vertebroplasty: An evaluation cement volume	Not best available evidence
Hu 2007	Complications of vertebroplasty and kyphoplasty	Narrative review, bibliography screened
Huet 2005	Burst-fractures and cementoplasty	Incorrect patient population
Hulme 2006	Vertebroplasty and kyphoplasty: a systematic review of 69 clinical studies	Systematic review, bibliography screened
Huntoon 2004	Complications related to vertebroplasty and kyphoplasty	Narrative review, bibliography screened
Institute for Clinical Systems Improvement 2004	Vertebroplasty and balloon-assisted vertebroplasty for the treatment of osteoporotic compression fractures (Structured abstract)	Systematic review, bibliography screened
Ishida 2004	Comparative efficacy of hormone replacement therapy, etidronate, calcitonin, alfacalcidol, and vitamin K in postmenopausal women with osteoporosis: The Yamaguchi Osteoporosis Prevention Study	Not specific to fracture patients
Ismail 2000	Risk factors for vertebral deformities in men: relationship to number of vertebral deformities. European Vertebral Osteoporosis Study Group	Does not investigate efficacy of treatment
Iwamoto 2007	Effects of antifracture drugs in postmenopausal, male and glucocorticoid-induced osteoporosis--usefulness of alendronate and risedronate	Review of systematic reviews

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Iwamoto 2005	Comparison of effect of treatment with etidronate and alendronate on lumbar bone mineral density in elderly women with osteoporosis	Insufficient data
Iwamoto 2004	Effects of alendronate on metacarpal and lumbar bone mineral density, bone resorption, and chronic back pain in postmenopausal women with osteoporosis	Not best available evidence
Iwamoto 2004	Determinants of one-year response of lumbar bone mineral density to alendronate treatment in elderly Japanese women with osteoporosis	Not specific to fracture patients
Iwamoto 2002	Effects of 5-year treatment with elcatonin and alfacalcidol on lumbar bone mineral density and the incidence of vertebral fractures in postmenopausal women with osteoporosis: a retrospective study	Not specific to fracture patients
Iwamoto 2001	Effect of menatetrenone on bone mineral density and incidence of vertebral fractures in postmenopausal women with osteoporosis: a comparison with the effect of etidronate	Not specific to fracture patients
Jalava 2003	Association Between Vertebral Fracture and Increased Mortality in Osteoporotic Patients	Does not investigate efficacy of treatment
Jansen 2009	Prevention of vertebral fractures in osteoporosis: mixed treatment comparison of bisphosphonate therapies	Systematic review, bibliography screened
Jay 2005	Treatment of osteoporosis in old age	Narrative review, bibliography screened
Jensen 2007	Position statement on percutaneous vertebral augmentation: a consensus statement developed by the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology, American Association of Neurological Surgeons/Congres	Consensus statement
Johansen 1989	Treatment of postmenopausal osteoporosis: is the anabolic steroid nandrolone decanoate a candidate?	Does not report patient oriented outcomes
Johansson 1994	Community-based population study of vertebral fractures in 85-year-old men and women	Does not investigate efficacy of treatment
Johnell 2003	Cost effectiveness of alendronate (fosamax) for the treatment of osteoporosis and prevention of fractures	Cost-effectiveness study
Jung 2006	Leakage of polymethylmethacrylate in percutaneous vertebroplasty: comparison of osteoporotic vertebral compression fractures with and without an intravertebral vacuum cleft	Not best available evidence
Kang 2003	Cement augmentation of osteoporotic compression fractures and intraoperative navigation: summary statement	Commentary
Kanis 2009	Bazedoxifene reduces vertebral and clinical fractures in postmenopausal women at high risk assessed with FRAX((registered trademark))	Not specific to fracture patients
Kanis 2005	Risedronate decreases fracture risk in patients selected solely on the basis of prior vertebral fracture	Post hoc subgroup analysis
Kanis 2005	Cost-effectiveness of raloxifene in the UK: an economic evaluation based on the MORE study	Cost-effectiveness study

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Kanis 2003	Effect of raloxifene on the risk of new vertebral fracture in postmenopausal women with osteopenia or osteoporosis: a reanalysis of the Multiple Outcomes of Raloxifene Evaluation trial	Not specific to fracture patients
Kanis 1997	Treatment of osteoporosis with vitamin D	Narrative review, bibliography screened
Kapetanos 1997	A double blind study of intranasal calcitonin for established postmenopausal osteoporosis	Does not report patient oriented outcomes
Kaplan 1993	The cluster phenomenon in patients who have multiple vertebral compression fractures	Does not investigate efficacy of treatment
Kaplan 1993	Posture training support: Preliminary report on a series of patients with diminished symptomatic complications of osteoporosis	Not best available evidence
Kapuscinski 1996	An analgesic effect of synthetic human calcitonin in patients with primary osteoporosis	Not best available evidence
Karlsson 2005	Vertebroplasty and kyphoplasty: New treatment strategies for fractures in the osteoporotic spine	Narrative review, bibliography screened
Kaso 2008	Comparison of CT characteristics of extravertebral cement leakages after vertebroplasty performed by different navigation and injection techniques	Does not compare two treatments; compares techniques of a treatment
Kasperk 2005	Treatment of painful vertebral fractures by kyphoplasty in patients with primary osteoporosis: a prospective nonrandomized controlled study	Not best available evidence
Kaufman 2005	Teriparatide effects on vertebral fractures and bone mineral density in men with osteoporosis: treatment and discontinuation of therapy	Post hoc subgroup analysis
Kaufmann 2001	Age of fracture and clinical outcomes of percutaneous vertebroplasty	Retrospective case series
Kawanishi 2005	Percutaneous vertebroplasty for vertebral compression fracture: Indication, technique, and review of the literature	Retrospective case series
Kerr 2008	Percutaneous vertebral compression fracture management with polyethylene mesh-contained morcelized allograft bone	Systematic review, bibliography screened
Khanna 2006	Functional outcomes of kyphoplasty for the treatment of osteoporotic and osteolytic vertebral compression fractures	Not best available evidence
Kim 2009	Pulmonary cement embolism after percutaneous vertebroplasty in osteoporotic vertebral compression fractures: incidence, characteristics, and risk factors	Not best available evidence
Kim 2007	Radiofrequency neurotomy of the gray ramus communicans for lumbar osteoporotic compression fracture	Retrospective case series
Kim 2006	Osteoporotic compression fractures of the spine; current options and considerations for treatment	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Kim 2005	Percutaneous vertebroplasty and facet joint block	Not best available evidence
Kim 2004	Intravertebral vacuum phenomenon in osteoporotic compression fracture: report of 67 cases with quantitative evaluation of intravertebral instability	Retrospective case series
Kim 2004	Risk factors of new compression fractures in adjacent vertebrae after percutaneous vertebroplasty	Retrospective case series
Kim 2003	Nerve-root injections for the relief of pain in patients with osteoporotic vertebral fractures	Not best available evidence
Klazen 2007	VERTOS II: Percutaneous vertebroplasty versus conservative therapy in patients with painful osteoporotic vertebral compression fractures; rationale, objectives and design of a multicenter randomized controlled trial	Description of study design
Knavel 2009	Clinical outcomes with hemivertebral filling during percutaneous vertebroplasty	Does not compare two treatments; compares techniques of a treatment
Knop 2002	Fate of the transpedicular intervertebral bone graft after posterior stabilisation of thoracolumbar fractures	Retrospective case series
Knopp 2005	Calcitonin for treating acute pain of osteoporotic vertebral compression fractures: a systematic review of randomized, controlled trials	Systematic review, bibliography screened
Kobayashi 2009	Prophylactic vertebroplasty: cement injection into non-fractured vertebral bodies during percutaneous vertebroplasty	Does not compare two treatments; compares techniques of a treatment
Kobayashi 2005	Percutaneous vertebroplasty immediately relieves pain of osteoporotic vertebral compression fractures and prevents prolonged immobilization of patients	Not best available evidence
Koch 2007	Outcomes of patients receiving long-term corticosteroid therapy who undergo percutaneous vertebroplasty	Retrospective case series
Komemushi 2005	Percutaneous vertebroplasty for compression fracture: analysis of vertebral body volume by CT volumetry	Not best available evidence
Korovessis 2008	Minimal invasive short posterior instrumentation plus balloon kyphoplasty with calcium phosphate for burst and severe compression lumbar fractures	Not best available evidence
Korovessis 2008	Direct reduction of thoracolumbar burst fractures by means of balloon kyphoplasty with calcium phosphate and stabilization with pedicle-screw instrumentation and fusion	Incorrect patient population
Korovessis 2008	Evolution of bone mineral density after percutaneous kyphoplasty in fresh osteoporotic vertebral body fractures and adjacent vertebrae along with sagittal spine alignment	Not best available evidence
Krauss 2006	Kyphosis reduction and the rate of cement leaks after vertebroplasty of intravertebral clefts	Not best available evidence
Krueger 2009	Management of pulmonary cement embolism after percutaneous vertebroplasty and kyphoplasty: a systematic review of the literature	Systematic review, bibliography screened
Kulak 2004	Bone mineral density and serum levels of 25 OH vitamin D in chronic users of antiepileptic drugs	Incorrect patient population

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Kumar 2005	Vertebroplasty in osteoporotic spine fractures: a quality of life assessment	Not best available evidence
Kuntz 1986	Treatment of post-menopausal osteoporosis with phosphate and intermittent calcitonin	Does not report patient oriented outcomes
Kushida 2004	Alendronate reduced vertebral fracture risk in postmenopausal Japanese women with osteoporosis: a 3-year follow-up study	Less than 50% follow-up
Landin Wilhelmsen 2003	Growth hormone increases bone mineral content in postmenopausal osteoporosis: a randomized placebo-controlled trial	Not specific to fracture patients
Landman 1995	Skeletal metabolism in patients with osteoporosis after discontinuation of long-term treatment with oral pamidronate	Not best available evidence
Lane 2002	Intravertebral clefts opacified during vertebroplasty: pathogenesis, technical implications, and prognostic significance	Retrospective case series
Langdahl 2009	Teriparatide versus alendronate for treating glucocorticoid-induced osteoporosis: an analysis by gender and menopausal status	Not specific to fracture patients
Langsetmo 2009	Effectiveness of antiresorptives for the prevention of nonvertebral low-trauma fractures in a population-based cohort of women	Not specific to fracture patients
Laredo 2005	Complications of percutaneous vertebroplasty and their prevention	Narrative review, bibliography screened
Laroche 2006	Comparison of the analgesic efficacy of pamidronate and synthetic human calcitonin in osteoporotic vertebral fractures: a double-blind controlled study	Treatment comparison not relevant
Larsson 2002	Use of injectable calcium phosphate cement for fracture fixation: a review	Narrative review, bibliography screened
Lauro 1993	Effect of s-calcitonin on pain related to recent osteoporotic vertebral fractures: A single-blind controlled clinical study against ipriflavone	Treatment comparison not relevant
Lavelle 2007	Vertebroplasty and kyphoplasty	Narrative review, bibliography screened
Lavelle 2007	Vertebroplasty and kyphoplasty	Narrative review, bibliography screened
Layton 2007	Vertebroplasty, first 1000 levels of a single center: evaluation of the outcomes and complications	Retrospective case series
Lee 2008	Vertebroplasty using real-time, fluoroscopy-controlled, catheter-assisted, low-viscosity cement injection	Not best available evidence
Lee 2008	Clinical and radiographic results of unilateral transpedicular balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures	Not best available evidence

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Lee 2005	Vertebroplasty and kyphoplasty for vertebral compression fractures	Narrative review, bibliography screened
Lee 1996	The osteoporotic spine	Does not investigate efficacy of treatment
Legroux Gerot 2004	Long-term follow-up of vertebral osteoporotic fractures treated by percutaneous vertebroplasty	Not best available evidence
Leidig Bruckner 1994	Comparison of a semiquantitative and a quantitative method for assessing vertebral fractures in osteoporosis	Does not investigate efficacy of treatment
Leung 2005	The efficacy and tolerability of risedronate on bone mineral density and bone turnover markers in osteoporotic Chinese women: a randomized placebo-controlled study	Not specific to fracture patients
Levine 2006	Pharmacologic and nonpharmacologic management of osteoporosis	Narrative review, bibliography screened
Levine 2000	An evidence-based evaluation of percutaneous vertebroplasty	Systematic review, bibliography screened
Levis 2002	Alendronate reduces the risk of multiple symptomatic fractures: results from the fracture intervention trial	Subgroup analysis of included RCT
Lewiecki 2007	Bazedoxifene and bazedoxifene combined with conjugated estrogens for the management of postmenopausal osteoporosis	Commentary
Liaw 2009	Effects of Knight-Taylor brace on balance performance in osteoporotic patients with vertebral compression fracture	Does not report patient oriented outcomes
Liberman 1995	Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis	Not specific to fracture patients
Lieberman 2005	Surgical innovations: Kyphoplasty for women with compression fractures	Narrative review, bibliography screened
Lieberman 2004	Vertebral augmentation and the limits of interpreting complications reported in the food and drug administration manufacturer and user facility device experience database	Commentary
Lieberman 2001	Initial outcome and efficacy of 'kyphoplasty' in the treatment of painful osteoporotic vertebral compression fractures	Not best available evidence
Lifeso 1985	Fractures of the thoraco-lumbar spine	Incorrect patient population
Liliang 2005	Percutaneous vertebroplasty improves pain and physical functioning in elderly osteoporotic vertebral compression fracture patients	Not best available evidence
Lin 2007	New symptomatic compression fracture after percutaneous vertebroplasty at the thoracolumbar junction	Retrospective case series

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Lin 2004	Vertebroplasty: cement leakage into the disc increases the risk of new fracture of adjacent vertebral body	Retrospective case series
Lin 2004	The role of imaging studies of percutaneous vertebroplasty in 63 patients with osteoporotic compression fracture: Preliminary report	Not best available evidence
Lin 2002	Transpedicula PMMA vertebroplasty for the treatment of osteoporotic vertebral compression fracture	Not best available evidence
Lindholm 1978	Interim report on treatment of osteoporotic patients with 1 alpha-hydroxyvitamin D3 and calcium	Not best available evidence
Lindsay 2005	Longitudinal progression of fracture prevalence through a population of postmenopausal women with osteoporosis	Does not investigate efficacy of treatment
Lindsay 2004	Sustained vertebral fracture risk reduction after withdrawal of teriparatide in postmenopausal women with osteoporosis	Not best available evidence
Lindsay 2001	Risk of new vertebral fracture in the year following a fracture	Does not investigate efficacy of treatment
Lindsay 1999	Addition of alendronate to ongoing hormone replacement therapy in the treatment of osteoporosis: a randomized, controlled clinical trial	Not specific to fracture patients
Lindsay 1997	Randomised controlled study of effect of parathyroid hormone on vertebral-bone mass and fracture incidence among postmenopausal women on oestrogen with osteoporosis	Insufficient data
Lippuner 2003	Medical treatment of vertebral osteoporosis	Systematic review, bibliography screened
Liu 2004	Effects of raloxifene hydrochloride on bone mineral density, bone metabolism and serum lipids in Chinese postmenopausal women with osteoporosis: a multi-center, randomized, placebo-controlled clinical trial	Not specific to fracture patients
Lovi 2009	Vertebroplasty and kyphoplasty: Complementary techniques for the treatment of painful osteoporotic vertebral compression fractures. A prospective non-randomised study on 154 patients	Not best available evidence
Luengo 1991	Vertebral fractures in steroid dependent asthma and involutional osteoporosis: a comparative study	Does not investigate efficacy of treatment
Lundkvist 2006	Economic evaluation of parathyroid hormone (PTH) in the treatment of osteoporosis in postmenopausal women	Cost-effectiveness study
Lyritis 2002	Analgesic effects of calcitonin	Narrative review, bibliography screened
Maehara 2006	Gadolinium-enhanced magnetic resonance imaging after percutaneous vertebroplasty does not improve the short-term prediction of new compression fractures	Not best available evidence
Maestretti 2007	Prospective study of standalone balloon kyphoplasty with calcium phosphate cement augmentation in traumatic fractures	Not best available evidence

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Majd 2005	Preliminary outcomes and efficacy of the first 360 consecutive kyphoplasties for the treatment of painful osteoporotic vertebral compression fractures	Retrospective case series
Majima 2009	Effects of risedronate or alfacalcidol on bone mineral density, bone turnover, back pain, and fractures in Japanese men with primary osteoporosis: results of a two-year strict observational study	Not specific to fracture patients
Majima 2008	Efficacy of combined treatment with raloxifene and alfacalcidol on bone density and biochemical markers of bone turnover in postmenopausal osteoporosis	Not specific to fracture patients
Majima 2008	Association between baseline values of bone turnover markers and bone mineral density and their response to raloxifene treatment in Japanese postmenopausal women with osteoporosis	Not specific to fracture patients
Majima 2007	Clinical significance of 1-year treatment with raloxifene on bone and lipid metabolism in Japanese postmenopausal women with osteoporosis	Not specific to fracture patients
Majumdar 2005	Incidental vertebral fractures discovered with chest radiography in the emergency department: prevalence, recognition, and osteoporosis management in a cohort of elderly patients	Does not investigate efficacy of treatment
Maksymowych 1998	Managing acute osteoporotic vertebral fractures with calcitonin	Systematic review, bibliography screened
Malmros 1998	Positive effects of physiotherapy on chronic pain and performance in osteoporosis	Insufficient data
Mamelle 1988	Risk-benefit ratio of sodium fluoride treatment in primary vertebral osteoporosis	Insufficient data
Manson 2007	Minimally invasive techniques for the treatment of osteoporotic vertebral fractures	Narrative review, bibliography screened
Manson 2006	Minimally invasive techniques for the treatment of osteoporotic vertebral fractures	Narrative review, bibliography screened
Manuele 2007	The teriparatide in the treatment of severe senile osteoporosis	Does not report relevant outcome
Mao 2007	Effect of carbonated hydroxyapatite cement for filing vertebral body on the vertebral heights and pain in patients with osteoporotic vertebral compression fractures	Does not compare two treatments; compares techniques of a treatment
Marcus 2003	The skeletal response to teriparatide is largely independent of age, initial bone mineral density, and prevalent vertebral fractures in postmenopausal women with osteoporosis	Post hoc subgroup analysis of included RCT
Marcus 2002	Antiresorptive treatment of postmenopausal osteoporosis: comparison of study designs and outcomes in large clinical trials with fracture as an endpoint	Narrative review, bibliography screened
Maricic 2002	Early effects of raloxifene on clinical vertebral fractures at 12 months in postmenopausal women with osteoporosis	Subgroup analysis of included RCT
Marquis 2008	Strontium ranelate prevents quality of life impairment in post-menopausal women with established vertebral osteoporosis	Does not report relevant outcome
Martino 2005	Safety assessment of raloxifene over eight years in a clinical trial setting	Not specific to fracture patients

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Masala 2005	Kyphoplasty: indications, contraindications and technique	Less than 10 patients meeting inclusion criteria
Masud 1998	Effects of cyclical etidronate combined with calcitriol versus cyclical etidronate alone on spine and femoral neck bone mineral density in postmenopausal osteoporotic women	Not specific to fracture patients
Mathis 2004	Vertebroplasty versus kyphoplasty: A comparison and contrast	Commentary
Mazanec 2003	Vertebral compression fractures: manage aggressively to prevent sequelae	Narrative review, bibliography screened
McAfee 1985	Complications following Harrington instrumentation for fractures of the thoracolumbar spine	Retrospective case series
McArthur 2009	1150 kyphoplasties over 7 years: indications, techniques, and intraoperative complications	Not best available evidence
McCloskey 2001	Effects of clodronate on vertebral fracture risk in osteoporosis: a 1-year interim analysis	Not specific to fracture patients
McDonald 2009	The effect of operator variability and experience in vertebroplasty outcomes	Not relevant, comparison of surgeon experience
McGirt 2009	Vertebroplasty and kyphoplasty for the treatment of vertebral compression fractures: an evidenced-based review of the literature	Systematic review, bibliography screened
McGraw 2002	Predictive value of intraosseous venography before percutaneous vertebroplasty	Retrospective case series
McGraw 2002	Prospective evaluation of pain relief in 100 patients undergoing percutaneous vertebroplasty: results and follow-up	Not best available evidence
McKiernan 2004	Quality of life following vertebroplasty	Not best available evidence
McKiernan 2003	Reporting height restoration in vertebral compression fractures	Does not investigate efficacy of treatment
McLain 2006	The biomechanics of long versus short fixation for thoracolumbar spine fractures	Narrative review, bibliography screened
Mehbod 2003	Vertebroplasty for osteoporotic spine fracture: prevention and treatment	Narrative review, bibliography screened
Mellstrom 2004	Seven years of treatment with risedronate in women with postmenopausal osteoporosis	Not best available evidence
Melton 2006	Epidemiology of vertebral fractures: implications for vertebral augmentation	Does not investigate efficacy of treatment
Meunier 2004	Strontium ranelate prevented vertebral fractures in postmenopausal women with osteoporosis	Commentary
Meunier 2003	Design and methodology of the phase 3 trials for the clinical development of strontium ranelate in the treatment of women with postmenopausal osteoporosis	Description of study design
Migliore 2007	Combined use of teriparatide and TNFalpha blockade: safety	Less than 10 patients per group

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Miki 2003	Vitamin K(2) (menaquinone 4) reduces serum undercarboxylated osteocalcin level as early as 2 weeks in elderly women with established osteoporosis	Does not report patient oriented outcomes
Miller 2009	Denosumab: anti-RANKL antibody	Commentary
Miller 2008	Non-vertebral fracture risk reduction with oral bisphosphonates: challenges with interpreting clinical trial data	Systematic review, bibliography screened
Miller 2008	Once-monthly oral ibandronate compared with weekly oral alendronate in postmenopausal osteoporosis: Results from the head-to-head MOTION study	Not specific to fracture patients
Miller 2004	Weekly oral alendronic Acid in male osteoporosis	Not specific to fracture patients
Miller 1997	Cyclical etidronate in the treatment of postmenopausal osteoporosis: efficacy and safety after seven years of treatment	Follow-up study to included RCT
Mok 2008	Risedronate for prevention of bone mineral density loss in patients receiving high-dose glucocorticoids: A randomized double-blind placebo-controlled trial	Not specific to fracture patients
Molinari 2004	Vertebroplasty and kyphoplasty: Biomechanics, outcomes, and complications	Narrative review, bibliography screened
Moon 2003	Stabilisation of fractured thoracic and lumbar spine with Cotrel-Dubousset instrument	Incorrect patient population
Morabito 2003	Three-year effectiveness of intravenous pamidronate versus pamidronate plus slow-release sodium fluoride for postmenopausal osteoporosis	Incorrect patient population
Moreland 2001	Vertebroplasty: techniques to avoid complications	Retrospective case series
Moro 2007	Pharmacological treatment of osteoporosis for people over 70	Narrative review, bibliography screened
Muller 1999	Treatment of thoracolumbar burst fractures without neurologic deficit by indirect reduction and posterior instrumentation: bisegmental stabilization with monosegmental fusion	Retrospective case series
Murphy 2001	Effect of alendronate and MK-677 (a growth hormone secretagogue), individually and in combination, on markers of bone turnover and bone mineral density in postmenopausal osteoporotic women	Incorrect patient population
Muscoso 2004	Antiresorption therapy and reduction in fracture susceptibility in the osteoporotic elderly patient: open study	Not specific to fracture patients
Muto 2005	Vertebroplasty in the treatment of back pain	Does not report validated, patient oriented outcomes
Nagant 1990	Treatment of the vertebral crush fracture syndrome with enteric-coated sodium fluoride tablets and calcium supplements	Retrospective case series
Nakamura 1997	The importance of genetic and nutritional factors in responses to vitamin D and its analogs in osteoporotic patients	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Nakano 2006	Calcium phosphate cement-based vertebroplasty compared with conservative treatment for osteoporotic compression fractures: a matched case-control study	Not best available evidence
Nakano 2005	Calcium phosphate cement leakage after percutaneous vertebroplasty for osteoporotic vertebral fractures: risk factor analysis for cement leakage	Not best available evidence
Nakano 2002	Percutaneous transpedicular vertebroplasty with calcium phosphate cement in the treatment of osteoporotic vertebral compression and burst fractures	Retrospective case series
Need 1997	The response to calcitriol therapy in postmenopausal osteoporotic women is a function of initial calcium absorptive status	Does not report patient oriented outcomes
Neogi 2008	The effect of alendronate on progression of spinal osteophytes and disc-space narrowing	Does not report relevant outcome
Nevitt 2000	Effect of alendronate on limited-activity days and bed-disability days caused by back pain in postmenopausal women with existing vertebral fractures. Fracture Intervention Trial Research Group	Does not report relevant outcome
Nevitt 1999	Association of prevalent vertebral fractures, bone density, and alendronate treatment with incident vertebral fractures: effect of number and spinal location of fractures. The Fracture Intervention Trial Research Group	Post hoc analysis
Nguyen 2003	Osteoporotic vertebral burst fractures with neurologic compromise	Retrospective case series
Nolla 2001	Osteoporotic vertebral fracture in clinical practice. 669 Patients diagnosed over a 10 year period	Does not investigate efficacy of treatment
Nussbaum 2004	A review of complications associated with vertebroplasty and kyphoplasty as reported to the Food and Drug Administration medical device related web site	Narrative review, bibliography screened
Obermayer Pietsch 2008	Effects of two years of daily teriparatide treatment on BMD in postmenopausal women with severe osteoporosis with and without prior antiresorptive treatment	Not specific to fracture patients
Oglesby 2003	The impact of incident vertebral and non-vertebral fragility fractures on health-related quality of life in established postmenopausal osteoporosis: results from the teriparatide randomized, placebo-controlled trial in postmenopausal women	Does not investigate efficacy of treatment
Ohlin 2004	Vertebroplasty and kyphoplasty in the fractured osteoporotic spine	Narrative review, bibliography screened
Oka 2005	Intravertebral cleft sign on fat-suppressed contrast-enhanced MR: correlation with cement distribution pattern on percutaneous vertebroplasty	Retrospective case series
Oleksik 2000	Health-related quality of life in postmenopausal women with low BMD with or without prevalent vertebral fractures	Does not investigate efficacy of treatment
Olszynski 2008	Alendronate for the treatment of osteoporosis in men	Commentary
Oner 2006	Cement augmentation techniques in traumatic thoracolumbar spine fractures	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Oner 2005	Less invasive anterior column reconstruction in thoracolumbar fractures	Commentary
Oner 2002	Some complications of common treatment schemes of thoracolumbar spine fractures can be predicted with magnetic resonance imaging: prospective study of 53 patients with 71 fractures	Incorrect patient population
Ontario Ministry of Health 7 Long Term Care 2004	Balloon kyphoplasty (Brief record)	Systematic review, bibliography screened
Orimo 1994	Effects of 1 alpha-hydroxyvitamin D3 on lumbar bone mineral density and vertebral fractures in patients with postmenopausal osteoporosis	Not specific to fracture patients
Orimo 1987	Reduced occurrence of vertebral crush fractures in senile osteoporosis treated with 1 alpha (OH)-vitamin D3	Insufficient data
Orler 2006	Lordoplasty: report on early results with a new technique for the treatment of vertebral compression fractures to restore the lordosis	Not best available evidence
Ortolani 2006	Strontium ranelate: an increased bone quality leading to vertebral antifracture efficacy at all stages	Narrative review, bibliography screened
Ott 1994	Bone histomorphometric changes after cyclic therapy with phosphate and etidronate disodium in women with postmenopausal osteoporosis	Does not report patient oriented outcomes
Ott 1989	Calcitriol treatment is not effective in postmenopausal osteoporosis	Not best available evidence
Overgaard 1996	A new biochemical marker of bone resorption for follow-up on treatment with nasal salmon calcitonin	Not specific to fracture patients
Overgaard 1991	Long-term treatment of established osteoporosis with intranasal calcitonin	Incorrect patient population
Ozmen 2007	Influence of the selective oestrogen receptor modulator (raloxifene hydrochloride) on IL-6, TNF-alpha, TGF-beta1 and bone turnover markers in the treatment of postmenopausal osteoporosis	Not specific to fracture patients
Ozoran 1989	Calcitonin and calcium combined therapy in osteoporosis: effects on vertebra trabecular bone density	Not best available evidence
Pak 1997	Sustained-release sodium fluoride in the management of established postmenopausal osteoporosis	Insufficient data
Pak 1990	Effect of intermittent therapy with a slow-release fluoride preparation	Insufficient data
Pak 1989	Safe and effective treatment of osteoporosis with intermittent slow release sodium fluoride: augmentation of vertebral bone mass and inhibition of fractures	Not specific to fracture patients
Palmieri 1989	Effect of calcitonin and vitamin D in osteoporosis	Not best available evidence
Palomba 2008	Effectiveness of risedronate in osteoporotic postmenopausal women with inflammatory bowel disease: a prospective, parallel, open-label, two-year extension study	Not specific to fracture patients
Palussiere 2005	Clinical results of an open prospective study of a bis-GMA composite in percutaneous vertebral augmentation	Not best available evidence

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Papadopoulos 2008	Unipedicular balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures: early results	Not best available evidence
Papaioannou 2006	Determinants of health-related quality of life in women with vertebral fractures	Does not investigate efficacy of treatment
Papaioannou 2002	Diagnosis and management of vertebral fractures in elderly adults	Narrative review, bibliography screened
Pappagallo 2003	Treatment of chronic mechanical spinal pain with intravenous pamidronate: a review of medical records	Incorrect patient population
Parviainen 1999	Urinary bone resorption markers in monitoring treatment of symptomatic osteoporosis	Does not report patient oriented outcomes
Passeri 1992	Effect of ipriflavone on bone mass in elderly osteoporotic women	Insufficient reporting of outcomes
Pateder 2007	Vertebroplasty and kyphoplasty for the management of osteoporotic vertebral compression fractures	Narrative review, bibliography screened
Patel 2007	Neurologic deficit following percutaneous vertebral stabilization	Less than 10 patients per group
Pavlov 1999	Double-blind, placebo-controlled study of the effects of tibolone on bone mineral density in postmenopausal osteoporotic women with and without previous fractures	Insufficient data
Peh 2003	Percutaneous vertebroplasty: indications, contraindications, and technique	Narrative review, bibliography screened
Peh 2001	Percutaneous vertebroplasty: a new technique for treatment of painful compression fractures	Case report
Pepe 2008	The effects of alendronate treatment in osteoporotic patients affected by monoclonal gammopathy of undetermined significance	Not specific to fracture patients
Perez Higueras 2002	Percutaneous vertebroplasty: long-term clinical and radiological outcome	Not best available evidence
Pflugmacher 2009	Balloon kyphoplasty combined with posterior instrumentation for the treatment of burst fractures of the spine--1-year results	Not best available evidence
Pflugmacher 2006	Percutaneous balloon kyphoplasty in the treatment of pathological vertebral body fracture and deformity in multiple myeloma: a one-year follow-up	Incorrect patient population
Phillips 2003	Minimally invasive treatments of osteoporotic vertebral compression fractures	Narrative review, bibliography screened
Phillips 2003	Early radiographic and clinical results of balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures	Not best available evidence
Phillips 2003	Minimally invasive treatments of osteoporotic vertebral compression fractures: vertebroplasty and kyphoplasty	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Pippan 2006	Spinal body reconstruction in osteoporosis	Commentary
Pitton 2008	CT-guided vertebroplasty in osteoprotic vertebral fractures: incidence of secondary fractures and impact of intradiscal cement leakages during follow-up	Not best available evidence
Pitton 2008	CT-guided vertebroplasty: analysis of technical results, extraosseous cement leakages, and complications in 500 procedures	Not best available evidence
Ploeg 2006	Percutaneous vertebroplasty as a treatment for osteoporotic vertebral compression fractures: a systematic review	Systematic review, bibliography screened
Plosker 1996	Intranasal salcatonin (salmon calcitonin). A review of its pharmacological properties and role in the management of postmenopausal osteoporosis	Narrative review, bibliography screened
Pongsoipetch 2007	Pain reduction in patients with painful vertebral compression fractures undergoing percutaneous vertebroplasty	Retrospective case series
Power 1986	Sodium fluoride in the treatment of osteoporosis	Not best available evidence
Predey 2002	Percutaneous vertebroplasty: new treatment for vertebral compression fractures	Commentary
Prince 1997	The pathogenesis of age-related osteoporotic fracture: effects of dietary calcium deprivation	Does not report patient oriented outcomes
Pun 1989	Analgesic effect of intranasal salmon calcitonin in the treatment of osteoporotic vertebral fractures	Less than 10 patients per group
Qin 2007	Alendronate increases BMD at appendicular and axial skeletons in patients with established osteoporosis	Not specific to fracture patients
Qu 2005	The effect of raloxifene therapy on the risk of new clinical vertebral fractures at three and six months: a secondary analysis of the MORE trial	Not specific to fracture patients
Quandt 2005	Effect of alendronate on vertebral fracture risk in women with bone mineral density T scores of-1.6 to -2.5 at the femoral neck: the Fracture Intervention Trial	Post hoc subgroup analysis
Racewicz 2007	Monthly dosing with risedronate 50 mg on three consecutive days a month compared with daily dosing with risedronate 5 mg: a 6-month pilot study	Not specific to fracture patients
Radvany 2009	Research Reporting Standards for Percutaneous Vertebral Augmentation	Commentary
Rajzbaum 2008	Characterization of patients in the European Forsteo Observational Study (EFOS): postmenopausal women entering teriparatide treatment in a community setting	Does not investigate efficacy of treatment
Rapan 2009	Vertebroplasty for vertebral compression fracture	Not best available evidence
Recker 2009	Oral Ibandronate Preserves Trabecular Microarchitecture: Micro-Computed Tomography Findings From the Oral Ibandronate Osteoporosis Vertebral Fracture Trial in North America and Europe Study	Does not report relevant outcome
Recker 2007	Comparative effects of raloxifene and alendronate on fracture outcomes in postmenopausal women with low bone mass	Incorrect patient population

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Recker 2004	Histomorphometric evaluation of daily and intermittent oral ibandronate in women with postmenopausal osteoporosis: results from the BONE study	Does not report patient oriented outcomes
Reginster 2008	Effects of long-term strontium ranelate treatment on the risk of nonvertebral and vertebral fractures in postmenopausal osteoporosis: Results of a five-year, randomized, placebo-controlled trial	Not specific to fracture patients
Reginster 2006	Efficacy and tolerability of once-monthly oral ibandronate in postmenopausal osteoporosis: 2 year results from the MOBILE study	Does not investigate efficacy of treatment
Reginster 2006	Raloxifene reduces fractures in postmenopausal women with osteoporosis	Narrative review, bibliography screened
Reginster 2005	Importance of alfacalcidol in clinical conditions characterized by high rate of bone loss	Narrative review, bibliography screened
Reginster 2005	Strontium ranelate reduces the risk of nonvertebral fractures in postmenopausal women with osteoporosis: Treatment of Peripheral Osteoporosis (TROPOS) study	Post hoc subgroup analysis
Reginster 2004	Reduction in PINP, a marker of bone metabolism, with raloxifene treatment and its relationship with vertebral fracture risk	Not specific to fracture patients
Reginster 2003	Strontium ranelate phase 2 dose-ranging studies: PREVOS and STRATOS studies	Report of parallel studies, identical results for applicable study reported in another article
Reginster 2002	Strontium ranelate in osteoporosis	Narrative review, bibliography screened
Reginster 2001	Intermittent cyclic tiludronate in the treatment of osteoporosis	Insufficient data
Reginster 1998	The effect of sodium monofluorophosphate plus calcium on vertebral fracture rate in postmenopausal women with moderate osteoporosis. A randomized, controlled trial	Not specific to fracture patients
Reginster 1998	Efficacy and tolerability of calcitonin in the prevention and treatment of osteoporosis	Narrative review, bibliography screened
Reginster 1997	Design for an ipriflavone multicenter European fracture study	Does not investigate efficacy of treatment
Reid 2009	Zoledronic acid and risedronate in the prevention and treatment of glucocorticoid-induced osteoporosis (HORIZON): a multicentre, double-blind, double-dummy, randomised controlled trial	Not specific to fracture patients
Reid 2008	A comparison of the effect of alendronate and risedronate on bone mineral density in postmenopausal women with osteoporosis: 24-Month results from	Does not report relevant outcome
Reid 2007	Addition of monofluorophosphate to estrogen therapy in postmenopausal osteoporosis: a randomized controlled trial	Not specific to fracture patients
Reid 2002	Intermittent intravenous zoledronic acid increased bone mineral density in postmenopausal women	Incorrect patient population

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Resch 1989	Estimated long-term effect of calcitonin treatment in acute osteoporotic spine fractures	Does not report patient oriented outcomes
Rhyne 2004	Kyphoplasty: report of eighty-two thoracolumbar osteoporotic vertebral fractures	Retrospective case series
Rico 1992	Salmon calcitonin reduces vertebral fracture rate in postmenopausal crush fracture syndrome	Insufficient data
Riggs 1996	Drug therapy for vertebral fractures in osteoporosis: evidence that decreases in bone turnover and increases in bone mass both determine antifracture efficacy	Does not investigate efficacy of treatment
Riggs 1980	Treatment of primary osteoporosis with fluoride and calcium. Clinical tolerance and fracture occurrence	Not best available evidence
Ringe 2009	Absolute risk reduction in osteoporosis: assessing treatment efficacy by number needed to treat	Narrative review, bibliography screened
Ringe 2009	Sustained efficacy of risedronate in men with primary and secondary osteoporosis: results of a 2-year study	Not specific to fracture patients
Ringe 2009	Potential of alfacalcidol for reducing increased risk of falls and fractures	Narrative review, bibliography screened
Ringe 2006	Efficacy of risedronate in men with primary and secondary osteoporosis: results of a 1-year study	Not specific to fracture patients
Ringe 2005	Alfacalcidol versus plain vitamin D in the treatment of glucocorticoid/inflammation-induced osteoporosis	Narrative review, bibliography screened
Ringe 2004	Alendronate treatment of established primary osteoporosis in men: 3-year results of a prospective, comparative, two-arm study	Not specific to fracture patients
Ringe 2002	Transdermal fentanyl for the treatment of back pain caused by vertebral osteoporosis	Not best available evidence
Ringe 2002	Treatment of male osteoporosis: recent advances with alendronate	Narrative review, bibliography screened
Ringe 2002	Monofluorophosphate combined with hormone replacement therapy in postmenopausal osteoporosis. An open-label pilot efficacy and safety study	Not best available evidence
Ringe 2001	Alendronate treatment of established primary osteoporosis in men: results of a 2-year prospective study	Not specific to fracture patients
Ringe 2001	Treatment of osteoporosis in men with fluoride alone or in combination with bisphosphonates	Incorrect patient population
Rizzoli 2007	Long-term strategy in the management of postmenopausal osteoporosis	Commentary
Rizzoli 2007	Osteoporosis: non-hormonal treatment	Commentary
Rizzoli 2006	Long-term outcome of weekly bisphosphonates	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Rizzoli 2002	Two-year results of once-weekly administration of alendronate 70 mg for the treatment of postmenopausal osteoporosis	Not specific to fracture patients
Rodriguez 2004	Kyphoplasty for the management of osteoporotic and malignant fractures of the spine	Retrospective case series
Rohlmann 2006	Spinal loads after osteoporotic vertebral fractures treated by vertebroplasty or kyphoplasty	Biomechanical study
Rosen 2005	The role of parathyroid hormone in the management of osteoporosis	Narrative review, bibliography screened
Rosenfeld 2000	Can the prophylactic use of raloxifene, a selective estrogen-receptor modulator, prevent bone mineral loss and fractures in women with diagnosed osteoporosis or vertebral fractures?	Commentary
Rossini 2009	Once-monthly oral ibandronate in postmenopausal osteoporosis: translation and updated review	Systematic review, bibliography screened
Rousing 2009	Percutaneous vertebroplasty compared to conservative treatment in patients with painful acute or subacute osteoporotic vertebral fractures: three-months follow-up in a clinical randomized study	Not best available evidence
Roux 2008	Prevalence of risk factors for referring post-menopausal women for bone densitometry. The INSTANT study	Does not investigate efficacy of treatment
Roux 2008	Strontium ranelate reduces the risk of vertebral fracture in young postmenopausal women with severe osteoporosis	Post hoc subgroup analysis
Rovetta 2000	Intravenous clodronate for acute pain induced by osteoporotic vertebral fracture	Treatment comparison not relevant
Ryan 2000	Intermittent oral disodium pamidronate in established osteoporosis: A 2 year double-masked placebo-controlled study of efficacy and safety	Not specific to fracture patients
Ryu 2007	Single balloon kyphoplasty using far-lateral extrapedicular approach: technical note and preliminary results	Not best available evidence
Saag 2007	Teriparatide or alendronate in glucocorticoid-induced osteoporosis	Not specific to fracture patients
Sahota 2000	A comparison of continuous alendronate, cyclical alendronate and cyclical etidronate with calcitriol in the treatment of postmenopausal vertebral osteoporosis: a randomized controlled trial	Does not report relevant outcome
Sakaino 2008	Percutaneous vertebroplasty performed by the isocenter puncture method	Not specific to fracture patients
Sakuma 2008	Incidence and outcome of osteoporotic fractures in 2004 in Sado City, Niigata Prefecture, Japan	Does not investigate efficacy of treatment
Saltari 2007	The management of pain from collapse of osteoporotic vertebrae with continuous intrathecal morphine infusion	Not best available evidence
Sarkar 2002	Relationships between bone mineral density and incident vertebral fracture risk with raloxifene therapy	Does not investigate efficacy of treatment

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Sato 2008	Longterm effect of intermittent cyclical etidronate therapy on corticosteroid-induced osteoporosis in Japanese patients with connective tissue disease: 7-year followup	Incorrect patient population
Satre 2006	Clinical inquiries. Who should receive vertebroplasty?	Commentary
Sawka 2004	Are there differences between men and women prescribed bisphosphonate therapy in canadian subspecialty osteoporosis practices?	Does not investigate efficacy of treatment
Schnitzer 2000	Therapeutic equivalence of alendronate 70 mg once-weekly and alendronate 10 mg daily in the treatment of osteoporosis. Alendronate Once-Weekly Study Group	Not specific to fracture patients
Schnitzler 1990	Bone fragility of the peripheral skeleton during fluoride therapy for osteoporosis	Not best available evidence
Schnitzler 1987	Radiographic features of the spine in fluoride therapy for osteoporosis	Not best available evidence
Schousboe 2005	Cost-effectiveness of alendronate therapy for osteopenic postmenopausal women	Cost-effectiveness study
Seeman 2008	Strontium ranelate reduces the risk of vertebral fractures in patients with osteopenia	Post hoc subgroup analysis
Seibel 2004	Relationship between pretreatment bone resorption and vertebral fracture incidence in postmenopausal osteoporotic women treated with risedronate	Post hoc subgroup analysis
Serin 2004	Effects of two-levels, four-levels, and four-levels plus offset-hook posterior fixation techniques on protecting the surgical correction of unstable thoracolumbar vertebral fractures: A clinical study	Incorrect patient population
Serra 2007	Vertebroplasty in the treatment of osteoporotic vertebral fractures: results and functional outcome in a series of 175 consecutive patients	Not best available evidence
Seybold 1999	Functional outcome of low lumbar burst fractures. A multicenter review of operative and nonoperative treatment of L3-L5	Incorrect patient population
Shaladi 2007	Continuous intrathecal morphine infusion in patients with vertebral fractures due to osteoporosis	Not best available evidence
Shane 2004	Alendronate versus calcitriol for the prevention of bone loss after cardiac transplantation	Not specific to fracture patients
Shen 2007	Osteoporotic vertebral compression fractures: a review of current surgical management techniques	Narrative review, bibliography screened
Shen 2006	Vertebroplasty and kyphoplasty: treatment techniques for managing osteoporotic vertebral compression fractures	Narrative review, bibliography screened
Shields 1976	Late instability in cervical spine fractures secondary to laminectomy	Incorrect patient population
Shikari 1996	Effects of 2 years' treatment of osteoporosis with 1 alpha-hydroxy vitamin D3 on bone mineral density and incidence of fracture: a placebo-controlled, double-blind prospective study	Not specific to fracture patients
Shiota 1998	Evaluation of the drug therapy for established osteoporosis by dual-energy x-ray absorptiometry	Not specific to fracture patients
Shiraki 1999	A double-masked multicenter comparative study between alendronate and alfacalcidol in Japanese patients with osteoporosis. The Alendronate Phase III Osteoporosis Treatment Research Group	Not specific to fracture patients

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Silverman 2008	Efficacy of bazedoxifene in reducing new vertebral fracture risk in postmenopausal women with osteoporosis: results from a 3-year, randomized, placebo-, and active-controlled clinical trial	Insufficient data
Silverman 2004	Comparison of fracture, cardiovascular event, and breast cancer rates at 3 years in postmenopausal women with osteoporosis	Does not investigate efficacy of treatment
Silverman 2002	The analgesic role of calcitonin following osteoporotic fracture	Narrative review, bibliography screened
Silverman 2001	The relationship of health-related quality of life to prevalent and incident vertebral fractures in postmenopausal women with osteoporosis: results from the Multiple Outcomes of Raloxifene Evaluation Study	Does not investigate efficacy of treatment
Siminoski 1996	Prevention and management of osteoporosis: consensus statements from the Scientific Advisory Board of the Osteoporosis Society of Canada. 9. Calcitonin in the treatment of osteoporosis	Narrative review, bibliography screened
Sing 2006	Kyphoplasty and functional outcomes in patients with osteoporotic fractures: Commentary	Commentary
Singh 2006	Osteoporotic compression fractures: outcomes after single- versus multiple-level percutaneous vertebroplasty	Not best available evidence
Siris 2008	Effects of risedronate on fracture risk in postmenopausal women with osteopenia	Not specific to fracture patients
Siris 2002	Effects of raloxifene on fracture severity in postmenopausal women with osteoporosis: results from the MORE study. Multiple Outcomes of Raloxifene Evaluation	follow up analysis of included RCT
Siris 2000	Alendronate in the treatment of osteoporosis: a review of the clinical trials	Narrative review, bibliography screened
Sorensen 2003	Long-term efficacy of risedronate: a 5-year placebo-controlled clinical experience	Less than 50% follow-up
Sosa 2002	Effect of two forms of alendronate administration upon bone mass after two years of treatment	Not specific to fracture patients
Sran 2005	Physiotherapy and osteoporosis: practice behaviors and clinicians' perceptions--a survey	Does not investigate efficacy of treatment
Stadhouder 2009	Nonoperative treatment of thoracic and lumbar spine fractures: a prospective randomized study of different treatment options	Incorrect patient population
Stakkestad 2008	Monthly oral ibandronate is effective and well tolerated after 3 years: the MOBILE long-term extension	Does not investigate efficacy of treatment
Steiniche 1989	A randomized study on the effects of estrogen/gestagen or high dose oral calcium on trabecular bone remodeling in postmenopausal osteoporosis	Does not report patient oriented outcomes
Ste Marie 2004	Five years of treatment with risedronate and its effects on bone safety in women with postmenopausal osteoporosis	Not best available evidence

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Stoffel 2007	Treatment of painful osteoporotic compression and burst fractures using kyphoplasty: a prospective observational design	Not best available evidence
Storm 1996	Five years of clinical experience with intermittent cyclical etidronate for postmenopausal osteoporosis	Not best available evidence
Storm 1990	Effect of intermittent cyclical etidronate therapy on bone mass and fracture rate in women with postmenopausal osteoporosis	Insufficient data
Strom 2009	Cost-effectiveness of balloon kyphoplasty in patients with symptomatic vertebral compression fractures in a UK setting	Cost-effectiveness study
Studd 1998	A randomized study of tibolone on bone mineral density in osteoporotic postmenopausal women with previous fractures	Not specific to fracture patients
Syed 2006	Vertebroplasty: The alternative treatment for osteoporotic vertebral compression fractures in the elderly	Retrospective case series
Szucs 1992	Three-year calcitonin combination therapy for postmenopausal osteoporosis with crush fractures of the spine	Insufficient data
Takahashi 2001	Effect of vitamin K and/or D on undercarboxylated and intact osteocalcin in osteoporotic patients with vertebral or hip fractures	Does not report patient oriented outcomes
Takata 2007	Differences of therapeutic effects on regional bone mineral density and markers of bone mineral metabolism between alendronate and alfacalcidol in Japanese osteoporotic women	Incorrect patient population
Tanigawa 2007	Relationship between cement distribution pattern and new compression fracture after percutaneous vertebroplasty	Not best available evidence
Tanner 2003	Back pain, vertebroplasty, and kyphoplasty: Treatment of osteoporotic vertebral compression fractures	Narrative review, bibliography screened
Taylor 2007	Balloon kyphoplasty in the management of vertebral compression fractures: an updated systematic review and meta-analysis	Systematic review, bibliography screened
Taylor 2006	Balloon kyphoplasty and vertebroplasty for vertebral compression fractures: a comparative systematic review of efficacy and safety	Systematic review, bibliography screened
Teng 2006	Follow-up on percutaneous vertebroplasty using PMMA in osteoporotic patients	Retrospective case series
Teng 2005	A simplified method of opacifying and mixing acrylic cement for percutaneous vertebroplasty: a clinical and in vitro study	Not best available evidence
Teng 2003	Kyphosis correction and height restoration effects of percutaneous vertebroplasty	Retrospective case series
Tezeren 2009	Long segment instrumentation of thoracolumbar burst fracture: Fusion versus nonfusion	Not relevant, comparison not considered for this guideline

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Tezeren 2005	Posterior fixation of thoracolumbar burst fracture: short-segment pedicle fixation versus long-segment instrumentation	Incorrect patient population
Theodorou 2002	Percutaneous balloon kyphoplasty for the correction of spinal deformity in painful vertebral body compression fractures	Not best available evidence
Thomas 1999	Recurrence of vertebral fracture with cyclical etidronate therapy in osteoporosis: histomorphometry and X-Ray microanalysis evaluation	Not best available evidence
Tikiz 2005	Effects of simvastatin on bone mineral density and remodeling parameters in postmenopausal osteopenic subjects: 1-year follow-up study	Incorrect patient population
Tilyard 1994	1,25-dihydroxyvitamin D3 (calcitriol) in the treatment of postmenopausal osteoporosis	Insufficient data, n per group not reported
Tosteson 2008	Therapies for treatment of osteoporosis in US women: cost-effectiveness and budget impact considerations	Cost-effectiveness study
Tournis 2007	Improvement in bone strength parameters. The role of strontium ranelate	Commentary
Trout 2006	Does vertebroplasty cause incident vertebral fractures? A review of available data	Systematic review, bibliography screened
Trout 2006	New fractures after vertebroplasty: adjacent fractures occur significantly sooner	Retrospective case series
Trout 2006	Subsequent vertebral fractures after vertebroplasty: association with intraosseous clefts	Retrospective case series
Trovas 2002	A randomized trial of nasal spray salmon calcitonin in men with idiopathic osteoporosis: Effects on bone mineral density and bone markers	Not specific to fracture patients
Tsai 1999	The effectiveness of cyclic and continuous oral clodronate therapy on bone density and markers in osteopenic postmenopausal women	Not specific to fracture patients
Tseng 2006	Effects of alendronate combined with hormone replacement therapy on osteoporotic postmenopausal Chinese women	Incorrect patient population
Tsiridis 2006	Sacral insufficiency fractures: current concepts of management	Narrative review, bibliography screened
Tsou 2002	Percutaneous vertebroplasty in the management of osteoporotic vertebral compression fractures: initial experience	Not best available evidence
Ulivieri 2007	Back pain treatment in post-menopausal osteoporosis with vertebral fractures	Commentary
Uppin 2003	Occurrence of new vertebral body fracture after percutaneous vertebroplasty in patients with osteoporosis	Retrospective case series

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Valimaki 2007	Effects of risedronate 5 mg/d on bone mineral density and bone turnover markers in late-postmenopausal women with osteopenia: a multinational, 24-month, randomized, double-blind, placebo-controlled, parallel-group, phase III trial	Not specific to fracture patients
Vallejo 2006	Percutaneous cement injection into a created cavity for the treatment of vertebral body fracture: preliminary results of a new vertebroplasty technique	Retrospective case series
van 2007	The cost-effectiveness of bisphosphonates in postmenopausal women based on individual long-term fracture risks	Cost-effectiveness study
Vasconcelos 2002	Is percutaneous vertebroplasty without pretreatment venography safe? Evaluation of 205 consecutives procedures	Not best available evidence
Vavken 2008	Sacral fractures after multi-segmental lumbosacral fusion: a series of four cases and systematic review of literature	Case report
Verlaan 2006	Anterior spinal column augmentation with injectable bone cements	Narrative review, bibliography screened
Verlaan 2005	Balloon vertebroplasty in combination with pedicle screw instrumentation: a novel technique to treat thoracic and lumbar burst fractures	Incorrect patient population
Vieweg 2007	Vertebral body replacement system Synex in unstable burst fractures of the thoracic and lumbar spine	Incorrect patient population
Vogl 2006	CT-guided percutaneous vertebroplasty in the therapy of vertebral compression fractures	Retrospective case series
Vogt 2008	Postural correction by osteoporosis orthosis (Osteo-med): A randomized, placebo-controlled trial	Not specific to fracture patients
Voormolen 2006	The risk of new osteoporotic vertebral compression fractures in the year after percutaneous vertebroplasty	Not best available evidence
Voormolen 2006	Prospective clinical follow-up after percutaneous vertebroplasty in patients with painful osteoporotic vertebral compression fractures	Not best available evidence
Voormolen 2006	Pain response in the first trimester after percutaneous vertebroplasty in patients with osteoporotic vertebral compression fractures with or without bone marrow edema	Not best available evidence
Wagner 2005	Vertebroplasty and the randomized study: Where science and ethics collide	Commentary
Watts 2004	Relationship between changes in bone mineral density and vertebral fracture risk associated with risedronate: greater increases in bone mineral density do not relate to greater decreases in fracture risk	Does not investigate efficacy of treatment
Watts 2003	Risedronate prevents new vertebral fractures in postmenopausal women at high risk	Post hoc subgroup analysis of included RCT's
Watts 2003	Use of matched historical controls to evaluate the anti-fracture efficacy of once-a-week risedronate	Not specific to fracture patients
Watts 2001	Risedronate for the prevention and treatment of postmenopausal osteoporosis: results from recent clinical trials	Narrative review, bibliography screened

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Watts 2001	Treatment of painful osteoporotic vertebral fractures with percutaneous vertebroplasty or kyphoplasty	Systematic review, bibliography screened
Watts 1999	The clinical tolerability profile of alendronate	Narrative review, bibliography screened
WCB Evidence Based Practice Group 2003	Percutaneous vertebroplasty for pain relief in the management of compressive vertebral fractures (Structured abstract)	Systematic review, bibliography screened
Wenger 1999	Surgically controlled, transpedicular methyl methacrylate vertebroplasty with fluoroscopic guidance	Not best available evidence
Whitlow 2007	Sacroplasty versus vertebroplasty: comparable clinical outcomes for the treatment of fracture-related pain	Retrospective case series
Wilkes 2009	Bisphosphonates and osteoporotic fractures: a cross-design synthesis of results among compliant/persistent postmenopausal women in clinical practice versus randomized controlled trials	Systematic review, bibliography screened
Wimalawansa 2000	Prevention and treatment of osteoporosis: efficacy of combination of hormone replacement therapy with other antiresorptive agents	Narrative review, bibliography screened
Winking 2004	Treatment of pain from osteoporotic vertebral collapse by percutaneous PMMA vertebroplasty	Not best available evidence
Wiseman 2003	Anterior versus posterior surgical treatment for traumatic cervical spine dislocation	Commentary
Xenodemetropoulos 2004	The impact of fragility fracture on health-related quality of life : the importance of antifracture therapy	Narrative review, bibliography screened
Xia 2009	The efficacy and safety of calcitriol and/or Caltrate D in elderly Chinese women with low bone mass	Not specific to fracture patients
Yan 2009	The efficacy and tolerability of once-weekly alendronate 70 mg on bone mineral density and bone turnover markers in postmenopausal Chinese women with osteoporosis	Not specific to fracture patients
Yee 2007	Osteoporosis management in prostate cancer patients treated with androgen deprivation therapy	Does not investigate efficacy of treatment
Yi 2007	Efficacy and safety of balloon kyphoplasty in the treatment of osteoporotic vertebral body compression fractres: Compared with vertebroplasty	Not best available evidence
Yi 2006	Operative versus non-operative treatment for thoracolumbar burst fractures without neurological deficit	Systematic review, bibliography screened
Yoh 2005	Health-related quality of life (HRQOL) in Japanese osteoporotic patients and its improvement by elcatonin treatment	Not best available evidence
Youssef 2003	Management of painful osteoporotic vertebral compression fractures: Vertebroplasty and kyphoplasty	Narrative review, bibliography screened
Yuan 1988	Early clinical experience with the Syracuse I-Plate: an anterior spinal fixation device	Retrospective case series

Table 96 Excluded Articles and Reason for Exclusion

Author	Title	Reason for Exclusion
Zanchetta 2003	Effects of teriparatide [recombinant human parathyroid hormone (1-34)] on cortical bone in postmenopausal women with osteoporosis	Does not report patient oriented outcomes
Zegels 2001	Effect of high doses of oral risedronate (20 mg/day) on serum parathyroid hormone levels and urinary collagen cross-link excretion in postmenopausal women with spinal osteoporosis	Less than 10 patients per group
Zhang 2005	A clinical study of Yigu capsule in treating postmenopausal osteoporosis	Not specific to fracture patients
Zhu 2004	Effects of combined treatment of Rocaltrol, Etidronate and Sisterly on bone pain and bone mineral density in osteoporosis patients with vertebral fracture	Not best available evidence
Zizic 2004	Pharmacologic prevention of osteoporotic fractures	Narrative review, bibliography screened
Zoarski 2002	Percutaneous vertebroplasty for osteoporotic compression fractures: quantitative prospective evaluation of long-term outcomes	Not best available evidence