2017 Vertebroplasty, Kyphoplasty, Sacroplasty Assessing Signals for Update: Risk of Bias Supplement

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Summary:

- The Buchbinder 2015 Cochrane Review was considered to be of high quality (low risk of bias) based on the validated AMSTAR assessment tool (Table 1). This systematic review included two trials (Buchbinder and Kallmes) comparing percutaneous vertebroplasty (PV) with sham (placebo) intervention.
- The Clark 2016 RCT comparing PV with sham was considered to be a moderately good quality RCT (moderately low risk of bias)
- From the 2010 WA HTAP report, the two trials (Buchbinder and Kallmes) which also compared PV to sham were considered to be moderately good quality RCTs (moderately low risk of bias) (Table 3)
- Our risk of bias evaluations below do ***not*** apply GRADE to specific outcomes for assessment of the overall strength (quality) of evidence across the studies of PV vs. sham.

Table 1. AMSTAR evaluation of Buchbinder 2015 Cochrane Review

	AMSTAR Checklist (each criteria 1 point)	Yes	No	N/A	Notes
1	Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review.	1			
2	Was there duplicate study selection and data extraction? Were there at least two independent data extractors and a consensus procedure for disagreements?	1			
3	Was a comprehensive literature search performed? Were at least two electronic sources searched? Were search dates included? Were key words/MeSH terms stated?	1			EMBASE, Medline, the Cochrane library, CINAHL, Web of Science, clinicaltrials.gov, clinical trial register of the WHO
4	Was the status of publication (i.e. grey literature) used as an inclusion criterion? Did authors state they searched for reports regardless of publication type? Did they explicitly state what reports	1			"RCTs of any design (e.g. parallel, cross-over, factorial) and controlled clinical trials using a

	AMSTAR Checklist (each criteria 1 point)	Yes	No	N/A	Notes
	were excluded based on publication status, language, etc?				quasi-randomised method of allocation, such as by alternation or date of birth. Reports of trials were eligible regardless of the language or date of publication. Only trials published as full articles or available as a full trial report were considered for inclusion."
	Was a list of studies (included and excluded) provided? Is a complete list of both included/excluded studies provided (likely as a table)?	1			Table listing and summarizing all included studies; Tables listing studies excluded at FT and studies awaiting assessment; also included and excluded studies were described in the text
6	Were the characteristics of the included studies provided? Does an aggregated form such as a table exist to provide data from original studies based on participants, interventions and outcomes? Some range of characteristics included might be age, race, sex, etc.	1			
7	Was the scientific quality of the included studies assessed and documented? Did authors state take into account study type and design (e.g. randomization, blinding, placebo controlled studies)?	1			At least two review authors (JH, AJ, RJ) in various combinations independently assessed the risk of selection, performance, detection, attrition and reporting biases for all included RCTs by evaluating the following domains: random sequence generation, allocation concealment, blinding of participants, care provider, and outcome assessor for each outcome measure, incomplete outcome data and other biases, conforming to the methods recommended by The Cochrane Collaboration (Higgins 2011). Each criterion was rated as low risk of bias, high risk of bias or unclear risk (either lack of information or uncertainty over the potential for bias). Disagreements among the review

	AMSTAR Checklist (each criteria 1 point)	Yes	No	N/A	Notes
					authors were discussed and resolved.
	Was the scientific quality of the included studies used appropriately in formulating conclusions?				
8	Did authors discuss the scientific quality of their included studies in their conclusions?	1			Authors used GRADE, which takes into account various factors including the risk of bias of the individual studies
	Were the methods used to combine the findings of studies appropriate?				
9	Did authors assess homogeniety (i.e. Chi-squared test), and take appropriate meta-analyses based on such?	1			
	Was the likelihood of publication bias assessed?				
10	Did authors include graphical (e.g. funnel plot) and/or statistical tests (e.g. Egger regression test) to evaluate included study biases?	1			To assess publication bias, we planned to generate funnel plots if at least 10 trials examining the same intervention comparison were included in the review, and comment on whether any asymmetry in the funnel plot was due to publication bias, or methodological or clinical heterogeneity of the trials; **Appraisal note:** there were too few studies to generate plots for publication bias assessment for any outcome
	Was the conflict of interest stated?				
11	Did authors explicitly state any possible conflicting sources of support from included studies?	1			
	Total Score	**11**	**out of**	**11**	

N/A: not applicable

Table 2. Risk of bias assessment for Clark RCT comparing PV with sham reflecting Spectrum's current risk of bias assessment (See appendix)

Methodological Principle	Clark 2016
Study design Randomized controlled trial Prospective cohort study Retrospective cohort study Case-control Case-series	■
Random sequence generation*	Yes
Concealed allocation*	Yes
Intention to treat*	Yes‡
Independent or blind assessment	Yes
Co-interventions applied equally	Unclear§
Complete follow-up of ≥80%	Yes**
<10% difference in follow-up between groups	Yes**
Controlling for possible confounding†	Yes
Risk of Bias	**Moderately Low**

*Applies to randomized controlled trials only.

†Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

‡61 were assigned to PV, 59 to placebo; all received intervention. By 6 months 5 patients in each group withdrew (no reason provided)

§Co-interventions: authors state that patients in the placebo group received "usual medical care" following the procedure as directed by their physicians; no similar statement is made regarding the PV group

**6 month f/u: PV 51/61 (83.6%), Placebo 51/59 (86.4%)

Table 3. Risk of bias assessment of RCTs comparing PV vs. Sham as reported in the 2010 HTA
Methodological quality of RCTs comparing PV with sham surgery

Methodological Principle	Buchbinder	Kallmes
Study design Randomized controlled trial Cohort Study Case-series	√	√
Statement of concealed allocation	√	√
Intention to treat	√	√
Independent or blind assessment	√	√
Co-interventions applied equally		
Complete follow-up of ≥85%	√	√
Adequate sample size	√	√
Controlling for possible confounding	√	√
Evidence Level	**II**	**II**

Blank cells for methodological principles indicates criterion unclear or not reported

The Buchbinder and Kallmes RCTs were considered to be moderate quality RCTs ,i.e. at moderately low risk of bias (based on Spectrum's current risk of bias assessment – see appendix)

References:

Buchbinder R, Golmohammadi K, Johnston RV, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev 2015;4:CD006349.
Clark W, Bird P, Gonski P, et al. Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet 2016;388:1408-16

From 2010 HTA Report

Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. N Engl J Med 2009;361:557-68.
Kallmes DF, Comstock BA, Heagerty PJ, et al. A randomized trial of vertebroplasty for osteoporotic spinal fractures. N Engl J Med 2009;361:569-79.

APPENDIX A. Risk of bias assessment for individual studies of therapy

Risk of bias assessment criteria and interpretation

Risk of Bias Description	Studies of Therapy	
	Study design	**Criteria**
Low risk: Study adheres to commonly held tenets of high quality design, execution and avoidance of bias	Good quality RCT	• Random sequence generation • Allocation concealment • Intent-to-treat analysis • Blind or independent assessment for author's primary important outcomes* • Co-interventions applied equally • F/U rate of 80%+ and<10% difference in follow-up between groups • Controlling for possible confounding†
Moderately low risk: Study has potential for some bias; study does not meet all criteria for a good quality RCT, but deficiencies not likely to invalidate results or introduce significant bias	Moderate quality RCT	• Violation of one or two of the criteria for good quality RCT
	Good quality cohort	• Blind or independent assessment in a prospective study, or use of reliable data‡ in a retrospective study • Co-interventions applied equally • F/U rate of 80%+ and<10% difference in follow-up between groups • Controlling for possible confounding†
Moderately High risk: Study has significant flaws in design and/or execution that increase potential for bias that may invalidate study results	Poor quality RCT	• Violation of three or more of the criteria for a good quality RCT
	Moderate or poor quality cohort	• Violation of any of the criteria for good quality cohort
	Case-control	• Any case-control design
High risk: Study has significant potential for bias; lack of comparison group precludes direct assessment of important outcomes	Case series	• Any case series design

* Outcome assessment is independent of healthcare personnel, investigator or patient judgment.

† Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups. RCTs get credit if there is a similar distribution of baseline characteristics between groupsbut must also control for confounding if distribution is not similar.

‡Reliable data are data such as mortality or re-operation