Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease (Review)

Jacobs W, Willems PC, van Limbeek J, Bartels R, Pavlov P, Anderson PG, Oner FC

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2011, Issue 3

http://www.thecochranelibrary.com

TABLE OF CONTENTS

[Intervention Review]

Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Wilco Jacobs[1], Paul C Willems[2], Jacques van Limbeek[3], Ronald Bartels[4], Paul Pavlov[5], Patricia G Anderson[3], F Cumhur Oner[6]

[1]Department of Neurosurgery, Leiden University Medical Center, Leiden, Netherlands. [2]Department of Orthopaedics, Maastricht University Medical Centre, Maastricht, Netherlands. [3]Department of Research, Development and Education, Sint Maartenskliniek, Nijmegen, Netherlands. [4]Department of Neurosurgery, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands. [5]Department of Orthopedics, Sint Maartenskliniek, Nijmegen, Netherlands. [6]Department of Orthopedics, University Medical Center Utrecht, Utrecht, Netherlands

Contact address: Wilco Jacobs, Department of Neurosurgery, Leiden University Medical Center, PO Box 9600, Leiden, 2300 RC, Netherlands. w.c.h.jacobs@lumc.nl.

Editorial group: Cochrane Back Group.
Publication status and date: Edited (no change to conclusions), published in Issue 3, 2011.
Review content assessed as up-to-date: 14 November 2009.

Citation: Jacobs W, Willems PC, van Limbeek J, Bartels R, Pavlov P, Anderson PG, Oner FC. Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease. *Cochrane Database of Systematic Reviews* 2011, Issue 1. Art. No.: CD004958. DOI: 10.1002/14651858.CD004958.pub2.

ABSTRACT

Background

The number of surgical techniques for decompression and solid interbody fusion as treatment for cervical spondylosis has increased rapidly, but the rationale for the choice between different techniques remains unclear.

Objectives

To determine which technique of anterior interbody fusion gives the best clinical and radiological outcomes in patients with single- or double-level degenerative disc disease of the cervical spine.

Search methods

We searched CENTRAL (*The Cochrane Library* 2009, issue 1), MEDLINE (1966 to May 2009), EMBASE (1980 to May 2009), BIOSIS (2004 to May 2009), and references of selected articles.

Selection criteria

Randomised comparative studies that compared anterior cervical decompression and interbody fusion techniques for participants with chronic degenerative disc disease.

Data collection and analysis

Two review authors independently assessed risk of bias using the Cochrane Back Review Group criteria. Data on demographics, intervention details and outcome measures were extracted onto a pre-tested data extraction form.

Main results

Thirty-three small studies (2267 patients) compared different fusion techniques. The major treatments were discectomy alone, addition of an interbody fusion procedure (autograft, allograft, cement, or cage), and addition of anterior plates. Eight studies had a low risk of bias. Few studies reported on pain, therefore, at best, there was very low quality evidence of little or no difference in pain relief between the different techniques. We found moderate quality evidence for these secondary outcomes: no statistically significant difference in Odom's criteria between iliac crest autograft and a metal cage (6 studies, RR 1.11 (95% CI 0.99 to1.24)); bone graft produced more effective fusion than discectomy alone (5 studies, RR 0.22 (95% CI 0.17 to 0.48)); no statistically significant difference in complication rates between discectomy alone and iliac crest autograft (7 studies, RR 1.56 (95% CI 0.71 to 3.43)); and low quality evidence that iliac crest autograft results in better fusion than a cage (5 studies, RR 1.87 (95% CI 1.10 to 3.17)); but more complications (7 studies, RR 0.33 (95% CI 0.12 to 0.92)).

Authors' conclusions

When the working mechanism for pain relief and functional improvement is fusion of the motion segment, there is low quality evidence that iliac crest autograft appears to be the better technique. When ignoring fusion rates and looking at complication rates, a cage has a weak evidence base over iliac crest autograft, but not over discectomy alone. Future research should compare additional instrumentation such as screws, plates, and cages against discectomy with or without autograft.

PLAIN LANGUAGE SUMMARY

Fusion techniques for degenerative disc disease

Degenerative disc disease is part of the natural aging process of the human spine and can cause complications stemming from the nerve root or spinal cord. Degenerative disc disease of the spine can result in significant pain, instability, disturbances with the nerve roots or spinal cord, or a combination of symptoms. The cause of these symptoms comes from compression of the nerves.

When symptoms do not respond to conservative treatment, surgical treatment is considered. The goals of surgical treatment should be to remove pressure from the nerves, restore the alignment of the vertebrae and stabilize the spine. The common surgical technique to treat cervical disc disease is removal of the damaged disc with or without fusing the two adjacent vertebral bodies. Bone grafts (harvesting bone from other sites of the body) are usually used to stimulate the fusion process.

This review of 33 small studies (2267 participants) evaluated fusion techniques used to treat degenerative disc disease. The major treatments were discectomy (removal of the damaged disc) alone, addition of a fusion procedure (bone transplanted from another part of the body, cement, or cage), and addition of a plate.

None of the evidence from this systematic review indicates that one technique is better than another for clinically significant pain relief for patients with chronic cervical degenerative disc disease or disc herniation. The choice for a specific technique cannot be made on the most important aspect, pain relief, which was the primary outcome parameter in our review. There is moderate quality evidence that there was little or no difference in Odom's criteria (a tool that measures the success of the surgery at relieving the symptoms that were troublesome prior to the surgery) between those who received a bone transplant from the hip and a metal cage to help with fusion.

There is moderate quality evidence that the use of a bone graft (bone transplanted from another part of the body) is more effective than discectomy alone in achieving fusion. There is low quality evidence that transplanting bone from the iliac crest is more effective in achieving fusion than using a cage, while cages are more effective in preventing complications.

Further research is very likely to have an important impact on the results and our confidence in them.

BACKGROUND

Degenerative disc disease is part of the natural aging process of the human spine and can cause complaints stemming from the nerve root (radiculopathy) or spinal cord (myelopathy). Radiculopathy affects, on average, 83 in 100,000 patients each year (Radhakrishnan 1994) with a prevalence of 35 per 100 patients (Salemi 1996). Degenerative disc disease of the cervical spine can result in significant pain, instability, radiculopathy, myelopathy or a combination of symptoms (Grob 1998). The cause of these symptoms can be loss of disc space height, loss of foraminal area, disc bulging or protruding osteophytes causing neural compression. See Table 1 for definitions.

When symptoms are refractory to conservative treatment, surgical treatment is considered. The goals of surgical treatment should be decompression, restoration of alignment, and stability. Decompression involves removal of the soft disc or osteolytic structures from the compressed neural elements so they no longer impinge on the nerves. Restoration of alignment involves restoration of the disc space height and neural foraminal height as well as the normal angle between the vertebrae. Stability involves elimination of motion of the motion segment. Therefore, a fusion technique can be used, provided it incorporates a structural support to replace the disc, and that a stable fusion of the vertebrae is acquired. The treatment of degenerative disc disease can be divided into posterior procedures (entering through the back of the neck and spine), anterior procedures (entering through the front of the neck and spine) or a combination of these. The popularity of the anterior approach for discectomy and fusion has increased because this approach avoids exposure of the spinal canal (Fraser 1995) and results in less soft tissue damage. Structural support is provided by using an autograft or allograft bone with a cage filled with autologous bone graft or artificial bone and/or an anterior plate.

The common surgical technique to treat cervical degenerative disc disease is discectomy (removal of damaged disc) with or without fusing the two adjacent vertebral bodies. Discectomy without fusion will lead to a spontaneous fusion in 70% to 80% of the cases. Bone grafts are usually used for stimulating the fusion of the two vertebrae. These bone grafts are harvested from other sites in the body during surgery, usually from the iliac crest. The bone graft stimulates the bones in the spine to generate new bone, results in reliable rates of fusion, and generally maintains its structural integrity. The most frequently cited technique for anterior discectomy and fusion is the one described by Smith and Robinson (Emery 1994). This technique uses a left anterior approach, with a longitudinal incision along the anterior border of the sternocleidomastoid muscle. By dissecting the superficial cervical fascia and passing medially from the carotid sheath and laterally from the oesophagus and trachea, the anterior aspect of the cervical spine can be reached. After identification of the correct level, preferably on fluoroscopy, the anterior longitudinal ligament is explored and cut, then the disc is excised, leaving the anterior bony aspects in place. The endplate is removed from the cartilage to induce union (fusion) with the bone graft. The tricortical bone graft is harvested from the iliac crest and inserted into the disc space. The Smith and Robinson technique, as cited in the literature, can refer to either the discectomy procedure alone, or the additional fusion using an iliac crest autograft. Some modifications have been made to the original technique (Emery 1994). The Cloward technique (Cloward 1956) is used for discectomy and fusion with a round bone dowel taken from the iliac crest. In contrast to the Smith and Robinson technique, the anterior vertebral bone structure is drilled into the shape of the bone dowel. See Espine Website 2010 for a description of the procedure.

The harvesting from the iliac crest can be associated with short- and long-term morbidity in up to 22% of the cases (McConnel 2003). Most frequently reported problems include postoperative pain, wound hematoma, infection, pelvic fracture, nerve palsy, and chronic donor site pain that is reported by an average of 2.4% of the patients in studies that report this complication (McConnel 2003). In a study that specifically looked at donor site pain, no less than 90% of patients complained of donor site pain (Heneghan 2009). This donor site morbidity has fuelled the search for various forms of allograft materials as alternatives for cervical interbody fusion (Vaccaro 2003). Interbody cages provide initial stability, and by filling the disc space, require less structural bone graft. Despite its potential to yield outcomes similar to those of autograft bone, allograft is expensive to produce, incorporates more slowly, carries the potential risk of disease transmission and is not universally available. In addition, it is only osteo-conductive and does not contain the same osteo-inductive elements as autologous grafts. Examples are fibular allograft (Young 1993) and Surgibone® (Savolainen 1994). Anterior cervical plating can provide immediate stability to the segment of the spine to which it is applied, maintain spinal alignment, prevent graft dislodgement and collapse, enhance fusion rates, and eliminate the need for external immobilisation.

The choice of technique to be used should ideally be based on the best evidence available in the literature (Blettner 1999; Greenhalgh 1999; Offringa 1999). Apart from the last version of this review (Jacobs 2004) and a few in-depth narrative reviews (Floyd 2000; Theodore 2000; Whitecloud 1999; Wigfield 2001), we could not identify any systematic reviews on the anterior approach for cervical interbody fusion. The goal of this systematic review is to determine which technique of interbody fusion, using the anterior approach, gives the best clinical and radiological outcomes for patients with single or double-level degenerative disc diseases of the cervical spine.

This review updates and expands the original review (van Limbeek 2000) and subsequent Cochrane review (Jacobs 2004) comparing anterior cervical fusion options. This expansion of the review from the first publication reflects the availability of new trials comparing treatments for cervical degenerative disc disease.

OBJECTIVES

The goal of this updated review was to determine which technique of anterior interbody fusion gives the best clinical and radiological outcomes in patients with single- or double-level degenerative disc disease of the cervical spine.

METHODS

Criteria for considering studies for this review

Types of studies

In search of the best treatment for cervical degenerative disc disease, we only included randomised controlled trials (RCTs). We excluded articles that used 'quasi' randomisation techniques such as alternate appointments or birth dates to assign patients to experimental groups.

Types of participants

We included trials that included patients scheduled for surgery for chronic degenerative disc disease at one or two cervical levels, or for chronic manifestation of disc herniation, where patients suffered from complaints for at least 12 weeks. We made no exclusions for age or gender of the populations, or type, location or duration of symptoms. Trials including patients with fractures, tumours or disorders at more than two levels were excluded.

Types of interventions

The interventions evaluated in the trials were single- or double-level anterior discectomies and interbody fusion compared with other anterior fusion techniques for cervical degenerative disc disease. Discectomy alone was regarded as a technique that most frequently results in spontaneous fusion and as such, was also included in this study. Cervical interbody fusion techniques often use some kind of bone graft with or without cages, and additional instrumentation such as plates, so were also included. Disc arthroplasty was excluded because by definition, it is not a fusion procedure and because it is already covered by the review protocol on cervical disc arthroplasty by Boselie 2010.

Types of outcome measures

The outcome parameters in the studies were clinical, functional, or radiological. The primary outcome variable was pain. Below is an indication of the expected outcome measures, but we made no exclusions on the type of outcome measure. The minimal duration of follow-up was six months.

Primary outcomes

Clinical outcome measures

- Arm Pain
- Neck Pain

Secondary outcomes

Clinical outcome measures

- Dichotomised success (for example Odom's Criteria (4-level assessment of success of surgery in relieving pre-operative symptoms. Symptoms are not limited to pain, but also include other discomforts and sensations). We dichotomised the scale, combining "Excellent/Good" and "Moderate/Poor".
- Quality of Life (for example SF-36 (36-Item Short-Form Survey - quality of life))
- Disability (for example Neck Disability index)
- Motor function
- Sensory function
- Daily tasks
- Work status

Radiological outcome measures

- Kyphosis on normal lateral radiograph
- Mobility on flexion-extension radiographs
- Fusion
- Radiolucency

Serious complications

- Related deaths
- Re-operation related to primary surgery
- Incapacitating neurological damage (permanent or temporary), Horner syndrome (sympathic nerve damage)
- Pseudoarhrosis
- Hardware failure with clinical implication
- Postoperative deep infection
- Thrombosis

Search methods for identification of studies

Electronic searches

The Cochrane Back Review Group (CBRG) Trials Search Co-ordinator conducted the literature search and one reviewer (WJ) retrieved the references to be evaluated. The following databases were searched:

- CENTRAL (*The Cochrane Library* 2009, Issue 1)

- MEDLINE (1966 to May 2009)
- EMBASE (1980 to May 2009)
- BIOSIS (2004 to May 2009), Including earlier Current contents till 2004.

The search strategies were adapted for the different databases. We made no restrictions on language or date of publication. The search strategies are given in Appendix 3.

Searching other resources

We screened the references of the included studies, and with citation tracking, we searched references that cited the included articles.

Data collection and analysis

Selection of studies

Two review authors (WJ, PW) independently selected the trials from the list of titles and abstracts of identified references and met to reach consensus. For the last version of this review, the search and selection was performed by the two reviewers. For this update, the CBRG Trials Search Co-ordinator (RC) performed a pre-screening of the references and the final selection was performed by the two review authors. If relevance could not be ascertained on the basis of the abstract, the complete article was retrieved. When consensus could not be reached, a third reviewer (PA) was consulted to resolve the disagreement.
Articles were selected in two steps. In the first step, articles were excluded when it was apparent from either the title or abstract that the study did not meet the criteria mentioned in Criteria for considering studies for this review. In the second step, articles were excluded when it was apparent from a quick scan of the full text of the article that it failed to meet the same inclusion criteria. When the same population was described in more than one study, all studies were used, but the studies were grouped and analysed as one population. The reason for exclusion was documented for each reference.

Data extraction and management

Details of randomisation, blinding and exclusions from the analyses were recorded onto separate, pre-developed forms. From each study, basic information was gathered concerning authors (affiliation, sponsoring), methods (study design, sample size), patients (selection criteria and diagnoses, age, sex), treatments (instrumentation, bone and bone substitutes), and outcome variables with results. Data were extracted and entered into RevMan 5.0.22 by one author (WJ) and checked by another author (PW). Publications were managed with the aid of Reference Manager®. In addition, relevant information was recorded pertaining to database source, reason for exclusion and consensus of authors.

Assessment of risk of bias in included studies

Risk of bias of RCTs was assessed with the 12 criteria recommended by the Cochrane Back Review Group (Furlan 2009). Criteria and operationalisation are given in Appendix 1. The items were scored with 'yes', 'no', or 'unsure'. Studies were categorized as having a "low risk of bias" when at least six of the 12 criteria were met and the study had no serious methodological flaws (randomisation and allocation concealment techniques were valid).
The risk of bias was assessed independently by two review authors (WJ, PW), who again met to reach consensus. As before, if consensus could not be reached, a third review author (PA) was consulted to resolve the disagreement.
The potential to pool results was dependent on the comparability of the individual studies, i.e. identical treatments and outcome measures were used, sufficient detail was given to describe the selection criteria and other external validity criteria.

Measures of treatment effect

For dichotomous outcomes, we calculated risk ratios (RR). For continuous outcomes, we calculated a mean difference (MD). For each outcome, a 95% confidence interval (95% CI) was computed. We used a random-effects model in all our comparisons as differences between studies will always be present. Clinical relevance was assessed by the five questions recommended by Furlan 2009 (see Appendix 2). Clinically important change was evaluated against the guideline given by Ostelo 2008, where a minimal important change of 30% for Visual Analogue Scale (VAS), Numerical Rating Scale (NRS), Roland Morris Disability Questionnaire (RDQ), Oswestry Disability Index (ODI), and Quebec Back Pain Disability Questionnaire (QBPQ) was proposed in consensus.

Dealing with missing data

Missing clinical data in trials were accepted when they were less than 20%, otherwise, the trial was excluded from the specific analysis. Missing information about parameter variability was estimated from ranges if provided or estimated from comparable trials.

Assessment of heterogeneity

Heterogeneity between RCTs was first assessed clinically and then statistically. Clinical heterogeneity was evaluated for study design, (allocation concealment, outcome assessor blinding, patient blinding), patient characteristics (pain location, levels involved, age, gender), treatment characteristics (discectomy alone, use of cages, use of graft, different types of graft) variability. When studies were judged to be clinically homogeneous, homogeneity was also tested with a I^2-test.

Data synthesis

We pooled the results from individual studies when the studies were judged to be sufficiently homogeneous (Clinical and statistical).

The quality of evidence for all primary outcome parameters, regardless of quantitative analysis, was evaluated using the GRADE approach (GRADE Working Group 2004 - Atkins 2004) and GRADE Profiler software, version 3.2.2, 2004-2007). In short, the quality of evidence was judged with the following criteria (adapted from Furlan 2009 and Atkins 2004):

- 75% of studies have a low risk of bias (6 or more items met, including valid randomisation and treatment allocation techniques)
- Included studies have consistent findings
- Included population adequately reflects selection criteria of review
- Results are based on direct comparison
- Estimate of effect is sufficiently precise (confidence interval narrow and conclusive)
- Analysis is free of publication bias (more than 75% of studies contributing to analysis)

Depending on how many domains were met, the quality of evidence was judged to be 'High', 'Moderate', 'Low' or 'Very Low'. Important outcomes for which there were no trials were considered to have 'no evidence'. An outcome with only one trial was automatically low quality and if it also had a high ROB, it dropped to very low quality

High quality evidence = all domains met; further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality evidence = all but one domain met; further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality evidence = all but two domains met; further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality evidence = all but three domains met; there is great uncertainty about the estimate of effect.

No evidence = no RCTs were identified that addressed this outcome

The clinical relevance of the review results was assessed with the five questions given in Appendix 2. The results of this assessment were used to inform the discussion of the final results and conclusions. Statistical analyses were conducted using Review Manager (RevMan) software 5.0.22.

Subgroup analysis and investigation of heterogeneity

We had planned to complete subgroup analyses to assess the effects of age, gender, disease severity, one or two-level procedures, and length of follow-up time on the outcomes. However, sufficient data were not available.

Sensitivity analysis

We had planned to complete sensitivity analyses to assess the effect of risk of bias (high or low) on outcomes. The use of a funnel plot was planned to identify publication bias. However, sufficient data were not available.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification.

The results of the search and selection are from the current update. The results from the current update are further presented and analysed in addition to the previous results. For search and selection methods of the previous version we refer to Appendix 4.

Search

Electronic searches of the databases identified 2129 references, minus duplicates: 225 from CENTRAL, 660 from MEDLINE, 1400 from EMBASE, 244 from Current Contents (till May 2009) and 293 from BIOSIS (2004 to May 2009). The Trials Search Co-ordinator excluded 1999 references because the topic was not related to the topic of this review.

Selection

A total of 130 references appeared to be relevant and were further screened by the review authors (WJ, PW). After screening the titles and abstracts, we excluded 92 references. We excluded a further 21 references after screening the full text of the article, including fifteen randomised studies on disc arthroplasty initially included by one reviewer, but then excluded after consensus since disc arthroplasty was not included in this review. Neglecting the disc arthroplasty studies, the inter-rater kappa was 0.75. See Characteristics of excluded studies for further details. Screening the reference lists of the new studies yielded 36 new references, one of which could be included. Citation tracing yielded 213 new references, and also resulted in one new inclusion. One study (Lofgren 2010) was encountered and included alongside the search through a journal issue alert, this study referenced several included studies, but apparently this article was not (yet) indexed in Web of Science citation tracking.

Finally, 20 articles were included describing 19 new studies. One article presented further results for Vavruch 2002. Wigfield 2003 was in the *Studies awaiting classification* section and has now been excluded. Together with the 20 articles describing 14 studies from the previous review, a total of 40 articles describing 33 studies were included in this review.

Ten articles described three studies: four articles for Zoega 2000, two articles for Hacker 2000 and four articles for Vavruch 2002. Only one article was identified as the primary data source, although additional data were extracted from the other studies as indicated.

Comparisons

The comparisons made in the trials evaluated a range of anterior fusion techniques. Because of clinical heterogeneity, we grouped these comparisons into:

1. Discectomy alone versus human bone graft
2. Discectomy alone versus cages or cement
3. Discectomy alone versus iliac crest autograft with plates
4. Iliac crest autograft versus human allograft or bone substitute
5. Iliac crest autograft versus cages
6. Iliac crest autograft versus iliac crest autograft with plates
7. Different types of autograft
8. Allograft versus cages
9. Comparisons between different types of instrumentation

Although there are still some variations between treatments within these comparisons, we felt that these categories were based on basic differences between treatment options. This decision was made after selection of the studies.

Sponsorship

The studies that explicitly reported to have received no funds were Fernandez-Fairen 2008; Hauerberg 2008. The studies that explicitly declared no conflict of interest were Celik 2007; Nunley 2009; Thome 2006.

Lofgren 2000 received support from the County Council of Jonkøping. Zoega 2000 received grants from the Gothenburg Medical Society, Greta and Einers Foundation, and Gothenburg University. Dai 2008 was supported by Shanghai Natural Science Foundation. Peolsson 2003 and Peolsson 2007 (Secondary studies for Vavruch 2002) received support from Linkøping University and FORSS research council.

There was no mention of sponsorship in most of the trials (Abd-Alrahman 1999; Barlocher 2002; Dowd 1999; Lind 2007; Madawi 1996; Martins 1976; McConnel 2003; McGuire 1994; Nabhan 2007; Oktenoglu 2007; Pan 2005; Porras-Estrada 2004; Rosenorn 1983; Ruetten 2009; Ryu 2006; Savolainen 1998; Schroder 2007; van den Bent 1996; Vavruch 2002; Xie 2007).

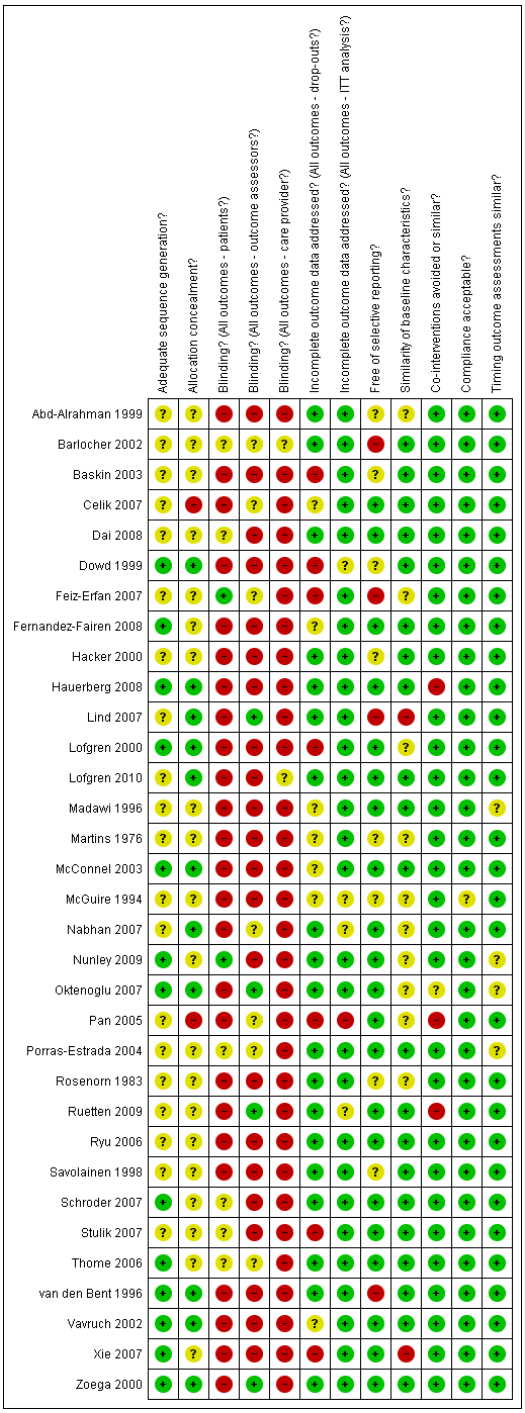
Baskin 2003 mentioned Corporate and industry funds, which were directed to a research fund, foundation, educational institution or other nonprofit organization.

The study of Feiz-Erfan 2007 was sponsored by DePuy, Johnson& Johnson. One of the authors of Hacker 2000 was employed by Sulzer Spine tech. One of the authors of Stulik 2007 is a consultant to Aesculap. The study of Lofgren 2010 was in part supported by a research grant from Zimmer.

Risk of bias in included studies

The risk of bias in the studies was variable, but often high, especially concerning randomisation, allocation concealment and blinding. This might have been the result of either poor methodology or poor reporting. Blinding is rarely used in orthopedic surgical trials, as is confirmed by the studies found in this review. No study used surgeon blinding. Two studies used patient blinding and four studies used outcome assessor blinding. The randomisation technique was mentioned in 13 of the 33 trials and valid allocation concealment in 11 of the 33 studies. Eight studies used both valid randomisation and allocation concealment techniques. The risk of bias summary of the trials is shown in Figure 1. Clinical relevance assessment of the studies is given in Table 2. Results were not sufficiently reported for one- or two-level procedures to produce a reliable subgroup analysis.

Figure 1. Summary of risks of bias



Effects of interventions

Analysis

When aggregate, pooled estimates were statistically heterogeneous, we did not produce a forest plot, except for homogeneous subgroups. When only one study with a high risk of bias was found, the data were entered into the data and analyses section, but no forest plot was made and the result was not discussed in a quantitative analysis. When only one study with a low risk of bias was found, the data were entered into the data and analyses section and the effect was depicted in a singular forest plot of the primary outcome parameter, and the result was analysed in a quantitative analysis.

Group sizes are given in number of patients, unless otherwise specified. In the comparisons and tables, the results are listed for each outcome variable for each comparison. Custom-made scoring systems are not reproduced as these cannot be pooled. Data from all studies were entered into the data and analyses section.

1. Discectomy alone versus human bone graft

Seven small studies with 487 patients were found that compared discectomy alone (N = 220) with bone graft (N = 267). Apart from Martins 1976 (graft not mentioned) and Rosenorn 1983 (freeze dried bone graft), all studies used iliac crest autograft.

Abd-Alrahman 1999 compared discectomy alone with fusion (Smith and Robinson technique) using autologous iliac crest graft (N = 90). Dowd 1999 compared discectomy alone with fusion using autologous iliac crest graft (Cloward technique) (N = 84). Martins 1976 compared discectomy alone with fusion (Cloward technique) (N = 51). Rosenorn 1983 compared discectomy alone with fusion with freeze dried bone grafts (Cloward technique) (N = 63). van den Bent 1996 compared discectomy alone with fusion with polymethyl methacrylate (PMMA) (N = 81). Savolainen 1998 compared discectomy alone with fusion with iliac crest autograft (Smith and Robinson) (N = 61). Xie 2007 compared discectomy alone with iliac crest autograft (N = 30). Barlocher 2002 compared microdiscectomy only with iliac crest autograft (N = 63).

Abd-Alrahman 1999 and Savolainen 1998 concluded that there was no difference between the two techniques. Dowd 1999 concluded that the addition of a fusion procedure was not absolutely necessary. Martins 1976 found no difference between the groups, but preferred discectomy for soft disc herniations and fusion for patients with advanced spondylosis. Xie 2007 found no difference in clinical results, but concluded that discectomy alone resulted in segmental kyphosis compared with fusion with autograft or fusion with autograft and anterior plate. Rosenorn 1983 concluded that for soft disc herniation, discectomy was an easier procedure and resulted in a shorter hospital stay and sick leave. Barlocher 2002 did not draw any definite conclusions on this specific comparison. Only Dowd 1999 was assessed as having a low risk of bias.

There are nine outcome measures reported in the six studies evaluating this comparison. Xie 2007 reported arm pain, neck pain and McGill Pain Scale scores in figures only, which did not allow data extraction. Barlocher 2002 only reported percentage of improvement for arm and neck pain. Operation time, hospital stay and blood loss were additional parameters, the results for which can be found in the Data and analyses section.

In summary, between those who received discectomy and those who received iliac crest autograft, there is low quality evidence that there was no significant difference in short-term pain relief (1 RCT, 84 participants, RR 0.82; 95% CI 0.20 to 3.46) and very low quality evidence that there was no significant difference in Odom's criteria (2 RCTs, 149 participants, RR 0.95; 95% CI 0.82 to 1.10); short-term return-to-work (2 RCTs, 144 participants, RR 1.26; 95% CI 1.02 to 1.54); or intermediate-term return-to-work (2 RCTs, 70 participants, RR 1.44; 95% CI 0.77 to 2.69). There is moderate quality evidence that bone graft was more effective than discectomy alone in achieving fusion (5 RCTs, 303 participants, RR 0.22; 95% CI 0.17 to 0.48) and very low quality evidence that there was no significant difference in alignment (2 RCTs, 75 participants, RR 0.34; 95% CI 0.07 to 1.56). There is moderate quality evidence that there was no significant difference in complication rates (7 RCTs, 487 participants, OR 1.56; 95% CI 0.71 to 3.43). Future research is very likely to change the results and our confidence in them.

Pain

- There is low quality evidence (suspected publication bias, imprecise estimate), from one study (Dowd 1999; N = 84) that the difference in short-term (5 weeks) pain relief between the groups who received discectomy and those who received iliac crest autograft is not statistically significant (RR 0.82; 95% CI 0.20 to 3.46).

Other clinical outcome

- There is very low quality evidence (high risk of bias, imprecise estimate, suspected publication bias) from two studies (Abd-Alrahman 1999; Barlocher 2002; N =149) that there is no statistically significant difference in Odom's criteria between the groups that received discectomy and those who received iliac crest autograft (RR 0.95; 95% CI 0.82 to 1.10; P = 0.47).
- There is very low quality evidence (high risk of bias, imprecise estimate, suspected publication bias) from two studies (Dowd 1999; Rosenorn 1983; N = 144) that discectomy is more

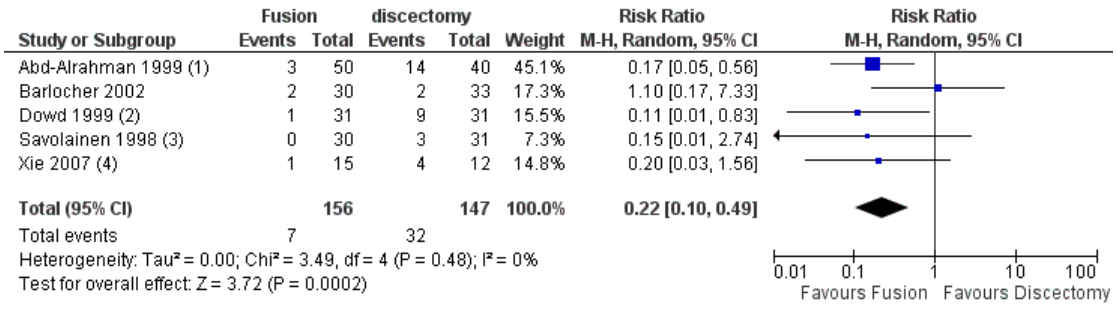
effective than autograft in improving return-to-work at five weeks (RR 1.26; 95% CI 1.02 to 1.54; P = 0.03).

- There is very low quality evidence (high risk of bias, imprecise estimate, suspected publication bias) from two studies (Dowd 1999; Rosenorn 1983; N = 70) that there is no statistically significant difference in return-to-work at 10 weeks between discectomy and autograft (RR 1.44; 95% CI 0.77 to 2.69; P = 0.25).

Radiological

- There is moderate quality evidence (high risk of bias) from five studies (Abd-Alrahman 1999; Barlocher 2002; Dowd 1999;Savolainen 1998; Xie 2007; N = 303) that bone graft is more effective than discectomy alone in achieving fusion. (RR 0.22; 95% CI 0.10 to 0.49; P = 0.0002; see Figure 2).

Figure 2. Forest plot of comparison: 1 Discectomy alone vs bone graft, outcome: 1.8 No Fusion.

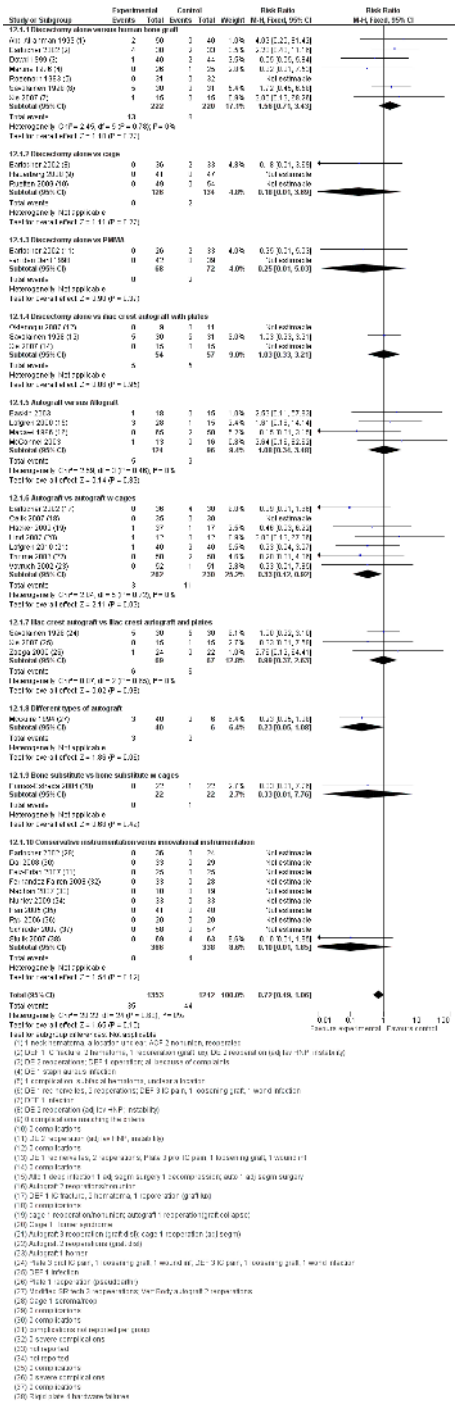


- There is very low quality evidence (high risk of bias, imprecision, suspected publication bias) from two studies (Martins 1976; Xie 2007; N = 75) that there is no statistically significant difference between discectomy alone and human bone graft in achieving a fair or poor alignment (RR 0.34; 95% CI 0.07 to 1.56).

Complications

- There is moderate quality evidence (high risk of bias) from seven studies (Abd-Alrahman 1999; Barlocher 2002; Dowd 1999; Martins 1976; Rosenorn 1983; Savolainen 1998; Xie 2007; N = 487) that the difference in complication rate between discectomy alone and iliac crest autograft is not statistically significant (OR 1.56; 95% CI 0.71 to 3.43; P = 0.27; see Figure 3). In the discectomy group, eight complications were reported (6 re-operations, 1 nerve lesion, 1 staphylococcus aureus infection); in the human bone graft group, thirteen complications (4 re-operations, 2 infection, 2 hematoma, 1 graft loosening, 1 iliac crest pain, 1 iliac crest fracture) were reported.

Figure 3. Forest plot of comparison: 12.1 complications.



2. Discectomy alone vs cages or cement

Four small studies compared discectomy alone with a cage or with intervertebral cement. Two studies used a cage, one used cement, and one used both. The studies were clinically too heterogeneous to be analysed together.

Three studies (Barlocher 2002; Hauerberg 2008; Ruetten 2009) with 277 patients compared discectomy alone (N = 140) with a cage (N = 137). Hauerberg 2008 compared discectomy alone with cages (N = 88). Ruetten 2009 compared full-endoscopic anterior decompression with conventional anterior decompression with a PEEK cage (N = 120). Barlocher 2002 compared discectomy alone with BAK/C® cage filled with Tutoplast (N = 69).

Hauerberg 2008 and Ruetten 2009 found no difference between discectomy alone and the use of titanium or PEEK cages. Barlocher 2002 concluded that the cage yields a significantly better short- and intermediate-term outcome in terms of radicular pain, Odom's criteria; return-to-work, and earlier fusion.

Only Hauerberg 2008 was assessed as having a low risk of bias.

Hauerberg 2008 reported arm and neck pain, recovery, operation time, blood loss, and fusion at 24 months. Ruetten 2009 reported VAS arm pain, VAS neck pain, NASS (North America Spine Society Instrument), operation time, blood loss, Hilibrand criteria and MRI/CT outcome. Only final, 24-month follow-up could be used, because it was unclear when patients were lost to follow-up. Furthermore, VAS and NASS score variance could not be estimated due to lack of additional studies providing this information. Also, fusion was poorly reported and could not be used. Barlocher 2002 reported VAS pain (only percentage change), Odom's criteria, hospital stay, operation time, blood loss and fusion. Operation time was reported in three studies, but showed considerable heterogeneity, probably due to differences in reporting (mean versus median) and could not be further analysed. Ruetten 2009 reported VAS arm pain, VAS neck pain, and NASS pain and neurology (at 24 months) but SD was not reported and could not be inferred from other studies in this comparison.

In summary, between those who received discectomy alone and those who received a cage, there was no evidence for pain relief, and very low quality evidence that there was no significant difference in recovery (1 RCT, 64 participants, RR 1.12; 95% CI 0.91 to 1.38), or preventing non-fusion (3 RCTs, 250 participants, RR 0.65; 95% CI 0.09 to 4.42). There was moderate quality evidence that there were no significant differences in complication rates (3 RCTs, 260 participants).

Pain

- There were no RCTs comparing discectomy alone with a cage that adequately reported the effect on pain.

Other clinical outcome

- There is very low quality evidence (imprecise estimate, non-generalisable, suspicion of publication bias) from one study (Hauerberg 2008; N = 64) that there is no statistically significant difference in recovery between discectomy alone and cages (RR 1.12; 95% CI 0.91 to 1.38; P = 0.28).

Radiological

- There is low quality evidence (high risk of bias, imprecision) from three studies (Barlocher 2002; Hauerberg 2008; Ruetten 2009; N=250) that there is no statistically significant difference between discectomy and a cage in preventing non-fusion (RR 0.65; 95% CI 0.09 to 4.42; P = 0.66).

Complications

- There is moderate quality evidence (high risk of bias) from three studies (Barlocher 2002; Hauerberg 2008; Ruetten 2009; N = 260) that the difference in complication rate between discectomy alone and a cage is not statistically significant. There were only two re-operations in one study in the discectomy group.

Two small studies (Barlocher 2002; van den Bent 1996) with 140 patients compared discectomy alone (N = 72) with polymethyl methacrylate (PMMA) (N = 68). van den Bent 1996 compared discectomy alone with PMMA (N = 81). Barlocher 2002 compared discectomy alone with PMMA (N = 59).

van den Bent 1996 found no difference and concluded that the addition of PMMA was not recommended for herniated intervertebral discs. Barlocher 2002 found a lack of fusion in the PMMA group, but concluded that PMMA was a good alternative to a fusion cage.

One study with a low risk of bias (van den Bent 1996, met 7 of 12 items; with adequate randomisation and allocation concealment) and one study with high risk of bias (Barlocher 2002, met 6 of 12 items, no adequate randomisation or allocation concealment) were included in this comparison. From the studies, the following quantitative analysis could be performed.

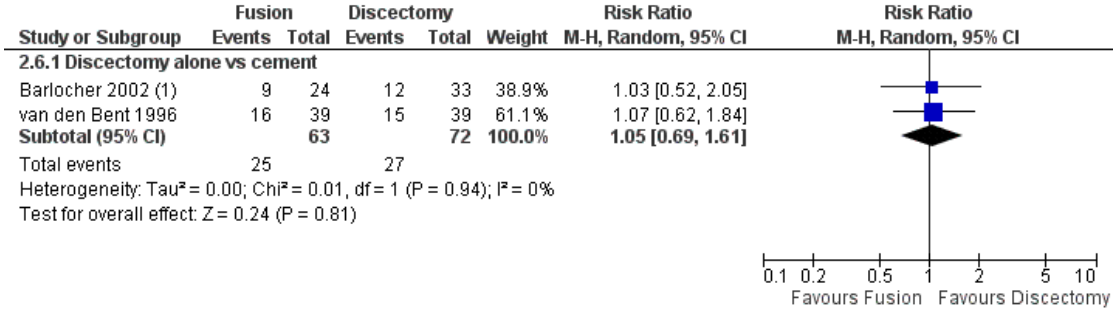
In summary, between those who received discectomy alone and those who received a bone substitute (PMMA cement) there was low quality evidence that there is no statistically significant difference for "Pain not relieved at 6 weeks" (2 RCT, 140 participants, RR 0.75; 95% CI 0.21 to 2.66) and no evidence for other clinical outcomes or complications. There was moderate quality evidence

that there is no significant difference for "Pain not relieved at 1 to 2 years" (2 RCT, 140 participants, RR 1.05; 95% CI 0.69 to 1.61). There were no RCTs comparing discectomy alone and use of PMMA that reported clinical outcomes.

Pain

- There is low quality (high risk of bias, imprecision) evidence from two studies (Barlocher 2002;van den Bent 1996; N = 140) that there is no statistically significant difference between discectomy alone and a bone substitute (PMMA) for "Pain not relieved at 6 weeks" (RR 0.75; 95% CI 0.21 to 2.66; P = 0.66).
- There is moderate quality evidence (high risk of bias) from two studies (Barlocher 2002;van den Bent 1996; N = 140) that there is no statistically significant difference between discectomy alone and a bone substitute (PMMA) for "Pain not relieved at 1 to 2 years" (RR 1.05; 95% CI 0.69 to 1.61; P = 0.81; see Figure 4).

Figure 4. Forest plot of comparison: 2 Discectomy alone vs cage, outcome: 2.6 Pain not relieved at 2 years.



Other clinical outcome

- There were no RCTs comparing discectomy alone and use of PMMA that reported clinical outcomes.

Radiological

- Fusion was reported in two studies (Barlocher 2002; van den Bent 1996; N = 140). The pooled result showed significant heterogeneity, so this comparison could not be further analysed.

Complications

- Serious complications were not reported in one study (van den Bent 1996) and there were two serious complications (re-operations) in the discectomy group in one study (Barlocher 2002).

3. Discectomy alone vs human bone graft with plates

Three small studies (Oktenoglu 2007; Savolainen 1998; Xie 2007; N = 111) compared discectomy alone (N = 57) with human bone graft and anterior plates (N = 54).

Xie 2007 compared discectomy alone with discectomy and fusion with iliac crest autograft and an Codman anterior cervical plate (N = 30). Savolainen 1998 compared discectomy alone with discectomy and fusion with iliac crest autograft and anterior Caspar plate (N = 61). Oktenoglu 2007 compared anterior cervical discectomy with complementary fusion with Tutoplast (Tutogen) allograft with semirigid anterior screw plate (Tnipsan) (N = 20).

Xie 2007 concluded that there were no significant differences between the groups, apart from segmental kyphosis in the discectomy alone group. Savolainen 1998 found no significant differences in clinical outcome and a slightly better fusion rate for the plate group. Oktenoglu 2007 concluded there were no significant differences between the groups except for a smaller decrease of disc height for the plate group.

One study (Oktenoglu 2007, met 7 of 12 items) met more than 50% of the risk of bias assessment criteria, with proper randomisation and allocation concealment and can be regarded as having a low risk of bias. The other two studies (Savolainen 1998; Xie 2007) met 50% or more of the criteria, but only Xie 2007 used a

proper randomisation technique.
There were 12 outcome parameters reported in the three studies evaluating this comparison. Xie 2007 reported arm pain, neck pain, American Spinal Injury Association score, SF-36, McGill Pain Scale score and segmental alignment in figures only, which did not allow data extraction, leaving alignment and fusion. Adjacent segment parameters (Oktenoglu 2007) were not included in this analysis. Kyphosis reported in Savolainen 1998 could not be included because it failed a definition of kyphosis.
In summary, between those who received discectomy alone and those who received anterior plating, there was very low quality evidence that there was no significant difference for VAS arm pain (1 trial, 2 participants, MD -0.16; 95% CI -0.85 to 0.53) or Odom's criteria (1 RCT, 61 participants, RR 0.96; 95% CI 0.71 to 1.28). There was very low quality evidence that bone graft with anterior plating results in better neck pain relief than discectomy alone (1 trial, 20 participants, MD 0.81 favouring plating 95% CI 0.20 to 1.42). There was very low quality evidence that there was no statistically significant difference in achieving fusion (2 RCT, 91 participants, RR 1.10; 95% CI 0.96 to 1.27).

Pain

- There is very low quality evidence (suspected publication bias, non-generalisable, imprecision) from one study (Oktenoglu 2007; N = 20) that there is no statistically significant difference between discectomy alone and anterior plating for VAS arm pain (MD -0.16; 95% CI -0.85 to 0.53; P = 0.65).
- There is very low quality evidence (suspected publication bias, non-generalisable, imprecision) from one study (Oktenoglu 2007; N = 20) that bone graft with anterior plating results in better neck pain relief than discectomy alone (MD 0.81 favouring plating 95% CI 0.20 to 1.42; P = 0.009).

Other clinical outcome

- There is very low quality evidence (high risk of bias, non-generalisable, imprecision, suspected publication bias) from one study (Savolainen 1998; N = 61) that there is no statistically significant difference between discectomy alone and graft with an anterior plate in Odom's criteria (RR 0.96; 95% CI 0.71 to 1.28; P = 0.77).

Radiological

- There is very low quality evidence (high risk of bias, imprecision, suspected publication bias) from two studies (Savolainen 1998; Xie 2007; N = 91) that there is no statistically significant difference between discectomy alone and graft with anterior plate in achieving fusion (RR 1.10; 95% CI 0.96 to 1.27; P = 0.15).

Complications

- Complications were reported in all three studies. Two studies reported no serious complications, one study reported five complications in each group. The conclusion is that the difference in complication rate between the two groups is not clinically significant.

4. Iliac crest autograft vs human allograft or bone substitute

Four small studies with 220 patients compared fusion with autograft (N = 96) versus any kind of allograft (N = 124). Lofgren 2000 compared autograft, human allograft, and bovine allograft (N = 41). Madawi 1996 compared autograft with biocompatible osteo conductive polymer (BOP) graft (N = 115). Baskin 2003 compared autograft with recombinant human bone morphogenetic protein-2 (rhBMP-2)-laden collagen carrier (N = 33) as a filler for fibular allograft. McConnel 2003 compared autograft with ProOsteon® 200 hydroxyapatite (N = 29).
Lofgren 2000 found no difference between any grafts, except autograft resulted in better pain reduction than bovine allograft. Madawi 1996 concluded that there was no difference between biocompatible osteo conductive polymer (BOP) and autograft. Baskin 2003 concluded that recombinant human bone morphogenetic protein-2 (rh-BMP-2) was a safe replacement for iliac crest autograft. The Neck Disability Index and arm pain were favourable for the rh-BMP group at 24 months. McConnel 2003 concluded that the integrity of the ProOsteon® blocks was not sufficient. Differences were not found at the final follow-up, because the trial was terminated due to radiographic fragmentation and collapse of the ProOsteon® graft. The risk of bias of these studies was high.
The treatments examined in this comparison were too clinically heterogeneous to combine any of the results in a meta-analysis. This comparison is therefore not used further in a meta-analysis. Primary outcomes of the two studies with low risk of bias were pain (total, arm and neck) for Lofgren 2000, and SF-36 and fusion for McConnel 2003, but the latter did not report any usable information. Lofgren 2000 only reported change scores for arm pain and neck pain, so these also could not be analysed.

5. Iliac crest autograft vs cage

Seven small studies (Barlocher 2002; Celik 2007; Hacker 2000; Lind 2007; Lofgren 2010; Thome 2006; Vavruch 2002) with 889 patients compared iliac crest autograft (N = 355) versus a cage (N = 534). Generally, the cages were either not filled or were filled with local autograft or bone substitute, all autograft groups received iliac crest autograft. Barlocher 2002 also compared iliac crest autograft with PMMA spacer (N = 56).
Hacker et al (Hacker 2000) compared autograft with BAK-C® cage filled with local bone reamings (N = 54). This study is a subgroup of a larger study; data of this larger study could not be included because of the limited percentage of patients with

follow-up data. Vavruch et al (Vavruch 2002) compared autograft with CIFC cage® filled with iliac crest autograft (N = 89). Celik 2007 compared autograft with PEEK cage filled with local bone graft (N = 65). Lofgren 2010 compared iliac crest autograft with a Trabecular Metal (TM) cage; the cage was not filled with bone graft (N = 80). Thome 2006 compared iliac crest autograft with RABEA titanium cages, not filled with bone graft (N = 100). Lind 2007 compared Smith and Robinson iliac crest autograft with BAK-C® cylindrical threaded titanium cage filled with local bone graft (N = 83). Barlocher 2002 compared microdiscectomy alone with a BAK-C® threaded titanium cage filled with Tutoplast bone substitute (N = 69).

Celik 2007 concluded that foraminal height was better preserved in the cage group, but there was no difference between the groups on clinical aspects. Vavruch 2002 concluded that lordotic alignment and disc height increased but with more pseudoarthrosis for the cage group and with less donor site pain, but there were no further clinical differences. Lind 2007 concluded that neck and arm pain and Odom's criteria after two years were better for the cage group, but there were no radiological differences. Thome 2006 concluded that overall pain relief was better in the cage group, but there were also no radiological differences between the groups. Hacker 2000 found no clinical differences, except more complications in the autograft group, and concluded that the cage was 'safe and effective'. Lofgren 2010 concluded that there were no clinical differences, apart from a shorter operation time with Trabecular Metal(TM) implants.

Only Vavruch 2002 had a valid randomisation technique and allocation concealment. Thus, one study with low risk of bias (Vavruch 2002) and six studies with high risk of bias (Barlocher 2002; Celik 2007; Hacker 2000; Lind 2007; Lofgren 2010; Thome 2006) compared iliac crest autograft with a cage.

There were 15 outcome parameters reported in the studies. Celik 2007 only reported postoperative values for VAS arm, VAS neck pain and JOA averaged for all postoperative assessments, therefore these data could not be included in the analyses. Lind 2007 only reported VAS arm and VAS neck in graphs, which prohibited us from extracting reliable data. Hacker 2000 only reported clinical outcomes in a subgroup analysis in a separate publication and only reported SF-36 in graphs, which did not permit data extraction. The results of the subgroup analysis are included in this analysis. Barlocher 2002 only reported percentage of improvement for arm and neck pain.

In summary, between those who received iliac crest autograft and those who received a cage, there is very low quality evidence that the difference in VAS arm pain is not statistically significant (2 RCT, 180 participants, MD -0.29; 95% CI -0.90 to 0.33). There is moderate quality evidence that the difference in Odom's criteria is not statistically significant (6 RCT, 412 participants, RR 1.11; 95% CI 0.99 to 1.24). There is low quality evidence that iliac crest autograft is more effective in achieving fusion than a cage (5 RCT, 424 participants, OR 1.87; 95% CI 1.10 to 3.17). There is low quality evidence that cages are more effective in preventing complications than iliac crest autograft (7 RCT, 889 participants, OR 0.32; 95% CI 0.11 to 0.92).

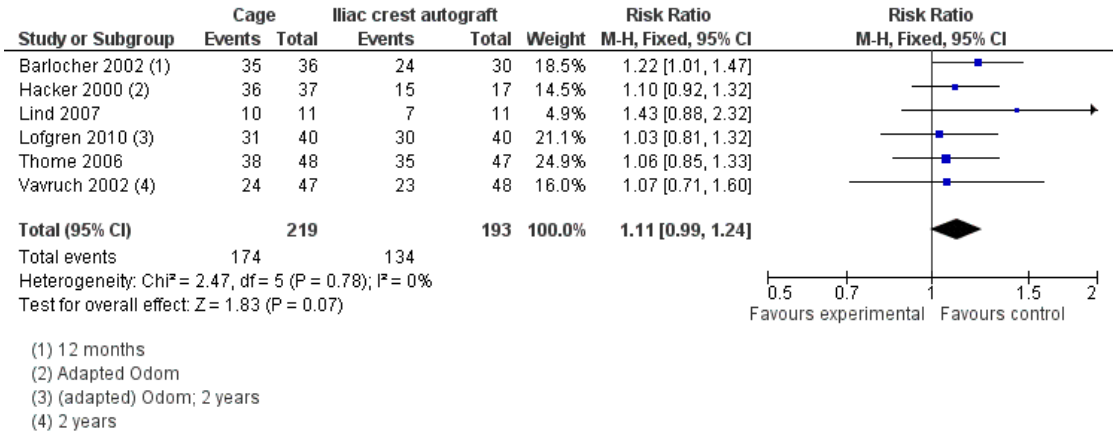
Pain

- There is very low quality evidence (high risk of bias, imprecision, suspected publication bias) from two studies (Lofgren 2010; Thome 2006; N = 180) that the difference in VAS arm pain between iliac crest autograft and a cage is not statistically significant (MD -0.29; 95% CI -0.90 to 0.33).
- VAS neck pain was reported in three studies (Lofgren 2010; Thome 2006; Vavruch 2002; N = 269). The pooled result was highly heterogeneous, so this comparison could not be further analysed.

Other clinical outcome

- There is moderate quality evidence (high risk of bias) from six studies (Barlocher 2002; Hacker 2000; Lind 2007; Lofgren 2010; Thome 2006; Vavruch 2002; N = 412) that the difference in Odom's criteria between iliac crest autograft and a metal cage is not statistically significant (RR 1.11; 95% CI 0.99 to 1.24; P = 0.07; see Figure 5).

Figure 5. Forest plot of comparison: 5 Iliac crest autograft vs cage, outcome: 5.8 Odom's criteria.



- Neck Disability Index was reported in two studies (Lofgren 2010; Vavruch 2002; N = 145). The pooled result showed significant heterogeneity, so this comparison could not be further analysed.

Radiological

- There is low quality evidence (high risk of bias, imprecision) from five studies (Barlocher 2002; Hacker 2000; Lofgren 2010; Thome 2006; Vavruch 2002; N = 424) that iliac crest autograft is more effective in achieving fusion than a cage (OR 1.87; 95% CI 1.10 to 3.17; P = 0.02).

Complications

- There is low quality evidence (high risk of bias, imprecision) from seven studies (Barlocher 2002; Celik 2007; Hacker 2000; Lind 2007; Lofgren 2010; Thome 2006; Vavruch 2002; N = 889) that cages are more effective in preventing complications than iliac crest autograft (OR 0.32; 95% CI 0.11 to 0.92; P = 0.03; see Figure 3). In the iliac crest autograft group, there were 11 complications (7 re-operations, 2 hematoma, 1 iliac crest fracture, 1 Horner syndrome) and in the cage group, there were three complications (2 re-operations, 1 Horner syndrome).

6. Iliac crest autograft vs iliac crest autograft with plates

Three small studies (Savolainen 1998; Xie 2007; Zoega 2000; N = 136) compared autograft (N = 67) with autograft and anterior plating (N = 69).

Savolainen 1998 compared fusion with autograft with or without (N = 60) additional plating. Zoega 2000 compared fusion with autograft with or without (N = 46) additional plate fixation. Xie 2007 compared iliac crest autograft with or without an anterior plate (N = 30).

Zoega 2000 concluded that the clinical benefits of plate fixation were minimal, although they found more improvement in arm pain in patients with two-level degeneration treated with a plate than in those treated without a plate. Xie 2007 did not conclude there was any difference between iliac crest autograft and anterior plating, but their study was more focused on the comparison with the discectomy group.

Two studiesmet 50% of the risk of bias assessment criteria (Savolainen 1998; Xie 2007); but only Xie 2007 used a valid randomisation technique. Both studies are regarded as having high risk of bias. Zoega 2000 met 10 of 12 items and included a valid randomisation technique and allocation concealment and could be regarded as a study with low risk of bias.

Xie 2007 reported SF-36 and McGill Pain Scale scores in graphs, which did not permit data extraction. Zoega 2000 reported pain scores, but we were unable to calculate an overall pain score because only median scores were given for subgroups.

In summary, between those who received iliac crest autograft and those who received iliac crest autograft with a plate, there is very low quality evidence that the difference in clinical outcomes is not statistically significant (2 RCT, 106 participants, RR 1.14; 95% CI 0.91 to 1.41). There is low quality evidence from two studies N = 90) that the difference in fusion is not statistically significant (2 RCT, 90 participants, RR 0.99; 95% CI 0.92 to 1.07). There is moderate quality evidence that the difference in complication rate is not statistically significant (3 RCT, 136 participants).

Pain

- There were no studies that compared iliac crest autograft with iliac crest autograft and anterior plates that adequately reported pain.

Other clinical outcome

- There is very low quality evidence (high risk of bias, imprecision, suspected publication bias) from two studies (Savolainen 1998; Zoega 2000; N = 106) that the difference in clinical outcomes between iliac crest autograft and iliac crest autograft with an anterior plate are not statistically significant (RR 1.14; 95% CI 0.91 to 1.41; P = 0.25).

Radiological

- There is low quality evidence (high risk of bias, suspected publication bias) from two studies (Savolainen 1998; Xie 2007; N = 90) that the difference in fusion between iliac crest autograft and iliac crest autograft with an anterior plate is not statistically significant (RR 0.99; 95% CI 0.92 to 1.07; P = 0.76).

Complications

- There is moderate quality evidence (high risk of bias) from three studies (Savolainen 1998; Xie 2007; Zoega 2000; N = 136) that the difference in complication rate between iliac crest autograft and iliac crest autograft with plates is not statistically significant (see Figure 3). There were six complications in each group. In the plate group, there was 1 reoperation, 3 prolonged iliac crest pain, 1 loosening graft and 1 wound infection; in the discectomy group, there were 3 patients with iliac crest pain, 1 loosening graft and 2 infections.

7. Different types of autograft

One small study with high risk of bias (McGuire 1994, met two of 12 items; did not report adequate randomisation or allocation concealment) with 46 patients was found that evaluated different types of autograft. This study concluded that vertebral body graft was not superior to iliac crest autograft. This comparison could not be included in a quantitative analysis.

8. Allograft vs cages

One small study with a high risk of bias (Porras-Estrada 2004) compared cylindrical allograft bone (N = 22) with a titanium implant (BAK-C®). This study concluded that there were no clinical differences between titanium cage and cylindrical bone, but that the cylindrical titanium cage provided better interspace height, interspace angulation and fusion rate. The study met six items during the risk of bias assessment, but did not report a valid randomisation technique or allocation concealment. The study is thus regarded as high risk of bias. This comparison could not be included in a quantitative analysis.

9. Other comparisons between different types of instrumentation

Nine small studies compared different types of instrumentation. Two small studies with high risk of bias (inadequate randomisation or allocation concealment; N = 101) compared allograft with plate (N = 53) versus cage (N = 48). Fernandez-Fairen 2008 compared a porous Trabecular Metal interbody cage with a semiconstrained rotational plate (Alpha plate, N = 61). Ryu 2006 compared an anterior plate (DOC™ or PEAK™ Poyaxial) with a cervical I/F cage (N = 40). Fernandez-Fairen 2008 concluded that there were no clinical differences, but that the cage prevented donor site harvesting and plate complications. Ryu 2006 concluded that there were no differences between the two treatment options with regard to clinical outcome or complications. Both studies met seven of 12 items; only Fernandez-Fairen 2008 applied a valid randomisation technique, but neither concealed the allocation. Therefore, both studies had high risk of bias. Ryu 2006 had more than 20% missing data for all parameters on all follow-up moments, so these data were not included. The study also only reported SF-36 results in graphs, which did not permit data extraction. This left only one study with a high risk of bias in the comparison; therefore, this comparison could not be included in a quantitative analysis.

Two small studies with high risk of bias compared PMMA versus a cage (N = 169). Barlocher 2002 compared PMMA with Bak/C® with Tutuoplast (N = 62). Schroder 2007 compared PMMA (Palacos(R)) with Intromed ZWE intervertebral spacer (N = 107). Barlocher 2002 concluded that PMMA is a good alternative for an interbody fusion cage, but is hindered by the absence of immediate fusion. Schroder 2007 concluded that there were no clinical differences, but that a titanium cage provided a better fusion rate than PMMA bone cement. Both studies met six or seven items on the risk of bias assessment, but only Schroder 2007 had a valid randomisation technique. Therefore, both studies have high risk of bias. Barlocher 2002 only reported percentage of improvement for arm and neck pain.

In summary, between those who received PMMA cement and those who received a cage, there is low quality evidence that the difference in improving Odom's criteria is not statistically significant (2 RCT, 169 participants, RR 1.00; 95% CI 0.85 to 1.19).

Pain

- There were no RCTs comparing PMMA with cage that adequately reported pain.

Other clinical outcome

- There is low quality evidence (high risk of bias, imprecision) from two studies (Barlocher 2002; Schroder 2007; N = 169) that the difference between PMMA and cage in improving Odom's criteria is not statistically significant (RR 1.00; 95% CI 0.85 to 1.19; P = 0.96).

Radiological

- 'No fusion' was reported in both studies, but showed significant heterogeneity and could not be further analysed.

Complications

- There were no serious complications reported in both studies.

Two small studies with high risk of bias (Nunley 2009; Stulik 2007; N = 198) compared dynamic anterior plates (N = 102) with static anterior plates (N = 96). Nunley 2009 compared a dynamic with a static (N = 66) CTEK plate. Stulik 2007 compared a dynamic ABC plate with a rigid CSLP plate (N = 132). Nunley 2009 concluded that there were no significant differences for single-level fusions, but that multi-level fusions had a better clinical outcome with dynamic plates. Stulik 2007 concluded that dynamic plates resulted in faster fusion with fewer complications. Only Nunley 2009 used a valid randomisation technique, but no allocation concealment. Therefore, both studies have a high risk of bias. Stulik 2007 had more than 20% loss of follow-up and could not be included further in the analysis. This left only one study with a high risk of bias in the comparison and therefore, this comparison could not be included in a quantitative analysis.
One small study with high risk of bias (N = 50) compared the use of platelet versus no platelet (N = 50); Feiz-Erfan 2007 concluded that there was no difference between the two treatments. This comparison could not be included in a quantitative analysis.
Two small studies with high risk of bias (Dai 2008; Nabhan 2007) compared a cage versus cage and plate. Dai 2008 compared PEEK or a carbon fibre cage with or without additional plate fixation (N = 62). Nabhan 2007 compared Solis cage with Solis cage and Caspar plate (N = 37). Dai 2008 compared carbon fibre or PEEK cage with cage and plate (N = 62). Nabhan 2007 concluded that there were no significant differences between the two groups. Dai 2008 concluded that there were no clinical differences, but that the fusion rate in the plate group was faster. Dai 2008 only reported arm and neck pain in graphs, which did not permit data extraction.
In summary, between those who received a cage and those who received a cage with additional anterior plate, there was very low quality evidence that there was no statistically significant difference in post-operative JOA score (1 RCT, 62 participants, MD 0.50; 95% CI -0.65 to 1.65) or segmental lordosis (1 RCT, 62 participants, MD -0.60; 95% CI -2.95 to 1.75; P = 0.62).

Pain

- There is very low quality evidence (high risk of bias, non-generalisable, suspected publication bias) from one study (Nabhan 2007) that plates are more effective for arm pain relief at 24 months. The authors did not find a significant difference in their analyses, probably because they could control for other variables in their own data set. Therefore, re-analysis of these data is not indicated.
- There is very low quality evidence (high risk of bias, non-generalisable, suspected publication bias) from one study (Nabhan 2007) that cages are more effective for neck pain relief at 24 months. The authors did not find a significant difference in their analyses, probably because they could control for other variables in their own data set. Therefore, re-analysis of these data is not indicated.

Other clinical outcome

- There is very low quality evidence (high risk of bias, non-generalisable, suspected publication bias) from one study with high risk of bias (Dai 2008), that the difference in postoperative JOA score between cages and cages with an additional plate is not statistically significant (MD 0.50; 95% CI -0.65 to 1.65; P = 0.39).

Radiological

- There is very low quality evidence (high risk of bias, non-generalisable, suspected publication bias) from one study with high risk of bias (Dai 2008), that the difference in segmental lordosis between cages and cages with an additional plate is not statistically significant (MD -0.60; 95% CI -2.95 to 1.75; P = 0.62).

Complications

- There were no serious complications reported in either studies.

One small study with high risk of bias (Pan 2005) compared screws and graft with anterior plate. This study concluded that an anterior plate provides a better outcome. This study had more than 20% loss to follow-up and poor data presentation, so this study could not be further included in the analysis.

DISCUSSION

Update

This update included 19 new studies. Remarkably, all new studies evaluated the use of instrumentation such as anterior plates for fusion. In this update, we adapted the Cochrane Back Review group recommendations for risk of bias in a trial, which is based on a trial meeting a minimal of 50% of the risk of bias items. This differs from our previous criteria for a study with high internal validity, when only valid randomisation and allocation concealment techniques were required. In this update, we combined the two criteria, so studies had to meet 50% of the criteria, including a positive

score on the items for randomisation and allocation concealment. With the new criteria, fewer studies have a low risk of bias.

Clinical

None of the evidence from this systematic review indicates that any technique results in (clinically relevant) better pain relief for patients with chronic cervical degenerative disc disease or disc herniation compared to another technique. The choice for a specific technique cannot be made on the most important aspect, pain relief, which was the primary outcome parameter in our review. This is in agreement with Carragee 2008, who could not find scientific support for invasive interventions in patients with isolated neck pain. For patients with radiculopathy, they found no treatment to be superior. Other important considerations in the choice for surgical technique are complication rate, other clinical outcomes and fusion rate.

When looking at complications, cages perform better than iliac crest graphs. The difference is clinically significant. Other comparisons between complication rates did not show statistically significant differences. However, we must be aware that these trials are not powered to identify a difference in the occurrence of complication rates, which have a low incidence. Also, the aggregate of studies might still fall short of adequate power.

When looking at other clinical outcomes, discectomy was more effective than human bone graft in improving return-to-work at five weeks, but the effect was small and unstable and at 10 weeks the difference was not statistically significant. For all other analyses of clinical parameters, none of the evidence from this review indicates that there is a statistical difference between any of the techniques.

Fusion rate is important because it is the key in the working mechanism of many of the surgical techniques. When looking at fusion rates, iliac crest autograft is the best treatment for preventing non-fusion, as it performs better (clinically and statistically) than discectomy alone and cages. As for the other surgical techniques, we could not find any differences of fusion rates between discectomy plus cages or PMMA, discectomy alone, iliac crest autograft plus an anterior plate or iliac crest autograft. This is in contradiction to the meta-analysis by Fraser 2007, who found better fusion rates for anterior plates. The meta-analysis included retrospective, non-controlled, studies, which may be prone to bias. As for discectomy, the intended working mechanism does not involve fusion of the motion segment, so lower fusion rates compared to iliac crest autograft may have no clinical implications.

Methodology

The small sample sizes of the studies make it hard to draw conclusions about the absence of differences, especially when only one study is found or when combined studies have a wide range of uncertainty.

To be regarded as a randomised controlled trial, the randomisation technique should be valid, applied just before the treatment is given and have an unpredictable allocation. There are several techniques to keep the allocation unpredictable, such as sealed envelopes or a telephone call to the research centre. Invalid randomisation procedures will produce unbalanced groups by confounding by indication. We excluded studies based only on randomisation technique when it was apparent that the technique used was not valid and could introduce confounding by indication. When in doubt, we kept the trial in the review, which was the case in seven of the 17 trials. These trials might have used an invalid method of randomisation that could have distorted our results. A sensitivity analysis was not possible because of the limited number of comparable outcome parameters.

Blinding is hard to achieve in orthopedic surgical trials, especially for the surgeon. However, for the outcome assessor, it is possible to use independent observers who have no knowledge of the applied treatment. Blinding of the outcome assessor was only used in three studies.

There appears to be a range of outcome scores considered relevant in the assessment of the results of cervical interbody fusion. In essence, this may be true for each separate trial, but comparison among trials is not possible if each trial uses a different score. Therefore, in the setup of a trial it is essential to go beyond the question at hand and also look at the wider picture. There appears to be little consensus on the use of specific outcome parameters in orthopedic surgery. If inferences are wanted from separate studies published in the literature, guidelines for the use of standard scales have to be developed by the orthopedic community (Pietrobon 2002). Therefore, the use of standard scales has been promoted (Pietrobon 2002) and includes patient disability and impairment scores such as the SF-36 and Neck Disability Index. In our opinion, study-specific outcome parameters should be accompanied by general global patient parameters in each dimension of outcome, i.e. pain (VAS neck and VAS arm), functional (WOMAC, NDI), societal (satisfaction/Odom's criteria, working capacities, SF-36), radiological (fusion), and complications. Outcomes should also be reported at standard outcome intervals.

Reporting

An in-depth and systematic review of the published literature requires this literature to be complete and consistent with the presentation of its data. This is certainly not the case in the studies found for this review. For the primary outcome parameter, pain, results were reported either as mean, mean improvement or percentage of the patients that showed a specific improvement. Further, the description of the methodology could be improved. A mention of allocation concealment in the randomisation technique is essential.

A second issue is the formation of homogeneous groups. In this review, it was very difficult to find comparable patient groups across

studies. Many groups differed in diagnosis because of different selection criteria. Another essential element when identifying specific subgroups, is to also provide separate data and analyses for each group. This can be applied to different diagnostic groups, such as, patients with radiculopathy, myelopathy, etc and also for different treatment groups such as single- or double-level surgery. From that aspect, we should mention that the goal of this review was changed from single-level to single- and double-level procedures, because of the limited number of studies that included only single-level procedures.

AUTHORS' CONCLUSIONS

Implications for practice

For reduction of pain in patients with cervical degenerative disc disease or disc herniation, we found no superior treatment. The literature is hampered by few studies, small studies, and generally poor research design. Consequently, it is unclear what patients, if any, benefit from cervical fusion as opposed to discectomy alone. In most studies and for most outcomes, discectomy was not statistically different from fusion by any technique, and there are no clear differences among fusion techniques. This review showed that the only evidence-based choice is between iliac crest autograft and cages for chronic cervical degenerative disc disease. This choice depends on balancing the importance of improved fusion rates with autograft versus improved complication rate with cages. As the relationship between clinical parameters and fusion rates remains weak, cages are a valid alternative for iliac crest autograft, although the working mechanism of fusion might not apply for isolated nerve root compression. The results are likely to be influenced by future research.

Implications for research

More methodologically rigorous studies are needed In the field of surgical treatment of cervical degenerative disc disease before evidence-based recommendations on this topic can be made. The methodological quality of the design of the studies would be improved by standardizing the outcome parameters and follow-up time-points. Also, more long-term outcome data (i.e. 10 years) are needed. Presentation of the data could be improved by describing the randomisation technique, the selection criteria, the population and study participants. Results should be given for every identifiable subgroup, with appropriate identification of variation. These implications have improved slightly since our previous version of this review, but still need attention. Additional instrumentation such as screws, plates, and cages should be compared against discectomy with or without autograft before any other comparisons are undertaken.

ACKNOWLEDGEMENTS

We would like to thank the Cochrane Back Review Group for their help in the literature search, the pre-selection by Rachel Couban (RC), and their help during the review process. Thanks to Miao Fang for the assessment of one Chinese article (Pan 2005) and to Tomasz Kotwicki for assessment of one Polish article (Pasciak 2005).

REFERENCES

References to studies included in this review

Abd-Alrahman 1999 *{published data only}*

* Abd-Alrahman N, Dokmak AS, Abou-Madawi A. Anterior cervical discectomy (ACD) versus anterior cervical fusion (ACF), clinical and radiological outcome study. *Acta Neurochirgica (Wien)* 1999;**141**(10):1089–92.

Barlocher 2002 *{published data only}*

Barlocher CB, Barth A, Krauss JK, Binggeli R, Seiler RW. Comparative evaluation of microdiscectomy only, autograft fusion, polymethyl-methacrylate interposition, and threaded titanium cage fusion for treatment of single-level cervical disc disease: a prospective randomized study in 125 patients. *Neurosurgical Focus* 2002;**12**(1):E4.

Baskin 2003 *{published data only}*

* Baskin DS, Ryan P, Sonntag V, Westmark R, Widmayer MA. A prospective, randomized, controlled cervical fusion study using recombinant human bone morphogenetic protein-2 with the CORNERSTONE-SR allograft ring and the ATLANTIS anterior cervical plate. *Spine* 2003;**28**(12):1219–25.

Celik 2007 *{published data only}*

* Celik SE, Kara A, Celik S. A comparison of changes over time in cervical foraminal height after tricortical iliac graft or polyetheretherketone cage placement following anterior discectomy. *Journal of Neurosurgery: Spine* 2007;**6**(1):10–6.

Dai 2008 *{published data only}*

* Dai LY, Jiang LS. Anterior cervical fusion with interbody cage containing beta-tricalcium phosphate augmented with plate fixation: A prospective randomized study with 2-year follow-up. *European Spine Journal* 2008;**17**(5):698–705.

Dowd 1999 *{published data only}*

* Dowd GC, Wirth FP. Anterior cervical discectomy: Is fusion necessary?. *Journal of Neurosurgery* 1999;**90**(1):8–12.

Feiz-Erfan 2007 *{published data only}*

* Feiz-Erfan I, Harrigan M, Sonntag VK, Harrington TR. Effect of autologous platelet gel on early and late graft fusion in anterior cervical spine surgery. *Journal of Neurosurgery: Spine* 2007;**7**(5):496–502.

Fernandez-Fairen 2008 *{published data only}*

* Fernandez-Fairen M, Sala P, Dufoo M Jr, Ballester J, Murcia A, Merzthal L. Anterior cervical fusion with tantalum implant: a prospective randomized controlled study. *Spine* 2008;**33**(5):465–72.

Hacker 2000 *{published data only}*

* Hacker RJ. A randomized prospective study of an anterior cervical interbody fusion device with a minimum of 2 years of follow-up results. *Journal of Neurosurgery* 2000;**93**(2 Suppl):222–6.

Hacker RJ. Threaded cages for degenerative cervical disease. *Clinical Orthopaedics and Related Research* 2002;**394**:39–46.

Hauerberg 2008 *{published data only}*

* Hauerberg J, Kosteljanetz M, Boge-Rasmussen T, Dons K, Gideon P, Springborg JB, et al.Anterior cervical discectomy with or without fusion with ray titanium cage: a prospective randomized clinical study. *Spine* 2008;**33**(5):458–64.

Lind 2007 *{published data only}*

* Lind BI, Zoega B, Rosen H. Autograft versus interbody fusion cage without plate fixation in the cervical spine: a randomized clinical study using radiostereometry. *European Spine Journal* 2007;**16**(8):1251–6.

Lofgren 2000 *{published data only}*

* Lofgren H, Johannsson V, Olsson T, Ryd L, Levander B. Rigid fusion after Cloward operation for cervical disc disease using autograft, allograft, or xenograft: A randomized study with radiostereometric and clinical follow-up assessment. *Spine* 2000;**25**(15):1908–16.

Lofgren 2010 *{published data only}*

Lofgren H, Engquist M, Hoffmann P, Sigstedt B, Vavruch L. Clinical and radiological evaluation of Trabecular Metal and the Smith-Robinson technique in anterior cervical fusion for degenerative disease: a prospective, randomized, controlled study with 2-year follow-up. *European Spine Journal* 2010;**19**(3):464–73.

Madawi 1996 *{published data only}*

* Madawi AA, Powell M, Crockard HA. Biocompatible osteoconductive polymer versus iliac graft. A prospective comparative study for the evaluation of fusion pattern after anterior cervical discectomy. *Spine* 1996;**21**(18):2123–9.

Martins 1976 *{published data only}*

* Martins AN. Anterior cervical discectomy with and without interbody bone graft. *Journal of Neurosurgery* 1976; **44**(3):290–5.

McConnel 2003 *{published data only}*

* McConnell JR, Freeman BJ, Debnath UK, Grevitt MP, Prince HG, Webb JK. A prospective randomized comparison of coralline hydroxyapatite with autograft in cervical interbody fusion. *Spine* 2003;**28**(4):317–23.

McGuire 1994 *{published data only}*

* McGuire RA, St. John K. Comparison of anterior cervical fusions using autogenous bone graft obtained from the cervical vertebrae to the modified Smith-Robinson technique. *Journal of Spinal Disorders* 1994;**7**(6):499–503.

Nabhan 2007 *{published data only}*

* Nabhan A, Pape D, Pitzen T, Steudel WI, Bachelier F, Jung J, et al.Radiographic analysis of fusion progression following one-level cervical fusion with or without plate fixation. *Zentralblatt fur Neurochirurgie* 2007;**68**(3):133–8.

Nunley 2009 *{published data only}*

* Nunley PD, Jawahar A, Kerr EJ III, Cavanaugh DA, Howard C, Brandao SM. Choice of plate may affect outcomes for single versus multilevel ACDF: results of a prospective randomized single-blind trial.. *Spine Journal* 2009;**9**(2):121–7.

Oktenoglu 2007 *{published data only}*

* Oktenoglu T, Cosar M, Ozer AF, Iplikcioglu C, Sasani M, Canbulat N, et al.Anterior cervical microdiscectomy with or without fusion. *Journal of Spinal Disorders & Techniques* 2007;**20**(5):361–8.

Pan 2005 *{published data only}*

* Pan SF, Li M, Wang SB, Zhang FS, Sun Y. [A prospective randomized comparison between with or without instrumentation in short-level anterior discectomy and autograft bone fusion]. [Chinese]. *Chung-Hua Wai Ko Tsa Chih [Chinese Journal of Surgery]* 2005;**43**(4):218–20.

Porras-Estrada 2004 *{published data only}*

* Porras-Estrada LF, Ugarriza-Echebarrieta LF, Lorenzana-Honrado L, Rodriguez-Sanchez JA, Garcia-Yague LM, Fernandez-Portales I, et al.[Anterior cervical interbody fusion with treated cylindrical bone versus BAK-C® cage: a comparative study]. [Spanish]. *Neurocirugia (Asturias, Spain)* 2004;**15**(3):270–8.

Rosenorn 1983 *{published data only}*

* Rosenorn J, Hansen EB, Rosenorn MA. Anterior cervical discectomy with and without fusion: A prospective study. *Journal of Neurosurgery* 1983;**59**(2):252–5.

Ruetten 2009 *{published data only}*

Ruetten S, Komp M, Merk H. Full-endoscopic anterior decompression versus conventional anterior decompression and fusion in cervical disc herniations. *International Orthopaedics* 2009;**33**:1677–82.

Ryu 2006 *{published data only}*

* Ryu SI, Mitchell M, Kim DH. A prospective randomized study comparing a cervical carbon fiber cage to the Smith-Robinson technique with allograft and plating: Up to 24 months follow-up. *European Spine Journal* 2006;**15**(2): 157–64.

Savolainen 1998 *{published data only}*

* Savolainen S, Rinne J, Hernesniemi J. A prospective randomized study of anterior single-level cervical disc operations with long-term follow-up: Surgical fusion is unnecessary. *Neurosurgery* 1998;**43**(1):51–5.

Schroder 2007 *{published data only}*

* Schroder J, Grosse-Dresselhaus F, Schul C, Wassmann H. PMMA versus titanium cage after anterior cervical discectomy - a prospective randomized trial. *Zentralblatt fur Neurochirurgie* 2007;**68**(1):2–7.

Stulik 2007 *{published data only}*

* Stulik J, Pitzen TR, Chrobok J, Ruffing S, Drumm J, Sova L, et al.Fusion and failure following anterior cervical plating with dynamic or rigid plates: 6-months results of a multi-centric, prospective, randomized, controlled study. *European Spine Journal* 2007;**16**(10):1689–94.

Thome 2006 *{published data only}*

* Thome C, Leheta O, Krauss JK, Zevgaridis D. A prospective randomized comparison of rectangular titanium cage fusion and iliac crest autograft fusion in patients undergoing anterior cervical discectomy. *Journal of Neurosurgery: Spine* 2006;**4**(1):1–9.

van den Bent 1996 *{published data only}*

* van den Bent MJ, Oosting J, Wouda EJ, van Acker EH, Ansink BJ, Braakman R. Anterior cervical discectomy with or without fusion with acrylate: A randomized trial. *Spine* 1996;**21**(7):834–9.

Vavruch 2002 *{published data only}*

Peolsson A, Hedlund R, Vavruch L. Prediction of fusion and importance of radiological variables for the outcome of anterior cervical decompression and fusion. *European Spine Journal* 2004;**13**(3):229–34.

Peolsson A, Hedlund R, Vavruch L, Oberg B. Predictive factors for the outcome of anterior cervical decompression and fusion. *European Spine Journal* 2003;**12**(3):274–80.

Peolsson A, Vavruch L, Hedlund R. Long-term randomised comparison between a carbon fibre cage and the Cloward procedure in the cervical spine. *European Spine Journal* 2007;**16**(2):173–8.

* Vavruch L, Hedlund R, Javid D, Leszniewski W, Shalabi A. A prospective randomized comparison between the Cloward procedure and a carbon fiber cage in the cervical spine: A clinical and radiologic study. *Spine* 2002;**27**(16): 1694–701.

Xie 2007 *{published data only}*

* Xie JC, Hurlbert RJ. Discectomy versus discectomy with fusion versus discectomy with fusion and instrumentation: a prospective randomized study. *Neurosurgery* 2007;**61**(1): 107–16.

Zoega 2000 *{published data only}*

Zoega B, Karrholm J, Lind B. One-level cervical spine fusion. A randomized study, with or without plate fixation, using radiostereometry in 27 patients. *Acta Orthopaedica Scandinavica* 1998;**69**(4):363–8.

* Zoega B, Karrholm J, Lind B. Outcome scores in degenerative cervical disc surgery. *European Spine Journal* 2000;**9**(2):137–43.

Zoega B, Karrholm J, Lind B. Plate fixation adds stability to two-level anterior fusion in the cervical spine: A randomized study using radiostereometry. *European Spine Journal* 1998; **7**(4):302–7.

Zoega B, Rosen H, Lind B. Anterior cervical discectomy and fusion with or without plate fixation: A prospective and randomized study. *Neuro-Orthopedics* 2000;**28**(1):39–51.

References to studies excluded from this review

An 1995 *{published data only}*

An HS, Simpson JM, Glover JM, Stephany J. Comparison between allograft plus demineralized bone matrix versus autograft in anterior cervical fusion. A prospective multicenter study. *Spine* 1995;**20**(20):2211–16.

Barlocher 2000 *{published data only}*

Barlocher C, Barth A, Binggeli R, Krauss J, Seiler R. Prospective comparative study between no fusion and three spondylodesis methods after cervical discectomy. *European Spine Journal* 2000;**4**:299.

Bishop 1996 *{published data only}*

Bishop RC, Moore KA, Hadley MN. Anterior cervical interbody fusion using autogeneic and allogeneic bone graft substrate: A prospective comparative analysis. *Journal of Neurosurgery* 1996;**85**(2):206–10.

Bolesta 2002 *{published data only}*

Bolesta MJ, Rechtine GR, Chrin AM. One and two-level anterior cervical discectomy and fusion: The effect of plate fixation. *Spine Journal* 2002;**2**(3):197–203.

Brown 1976 *{published data only}*

Brown MD, Malinin TI, Davis PB. A roentgenographic evaluation of frozen allografts versus autografts in anterior cervical spine fusions. *Clinical Orthopaedics and Related Research* 1976;**119**:231–6.

Chen 2001 *{published data only}*

Chen BH, Natarajan RN, An HS, Andersson GB. Comparison of biomechanical response to surgical procedures used for cervical radiculopathy: Posterior keyhole foraminotomy versus anterior foraminotomy and discectomy versus anterior discectomy with fusion. *Journal of Spinal Disorders & techniques* 2001;**14**(1):17–20.

Dunsker 1977 *{published data only}*

Dunsker SB. Anterior cervical discectomy with and without fusion. *Clinical Neurosurgery* 1977;**24**:516–21.

Emery 1976 *{published data only}*

Emery SE, Bolesta MJ, Banks MA, Jones PK. Robinson anterior cervical fusion comparison of the standard and modified techniques. *Spine* 1976;**19**(6):660–3.

Espersen 1984 *{published data only}*

Espersen JO, Buhl M, Eriksen EF, Fode K, Klaerke A, Kroyer L, et al.Treatment of cervical disc disease using Cloward's technique. I. General results, effect of different operative methods and complications in 1,106 patients. *Acta Neurochirurgica (Wien)* 1984;**70**(1-2):97–114.

Grob 2001 *{published data only}*

Grob D, Peyer JV, Dvorak J. The use of plate fixation in anterior surgery of the degenerative cervical spine: A

comparative prospective clinical study. *Spine* 2001;**10**(5): 408–13.

Hedlund 2001 ***{published data only}***
Hedlund R, Vavruch L, Shalabi A, Javid D, Leszniewski W. Low fusion rate with the Brantigan cage in the cervical spine: A prospective randomized study. *European Spine Journal* 2001;**7**:S16.

Herkowitz 1990 ***{published data only}***
Herkowitz, N, Kurz LT, Overholt DP. Surgical management of cervical soft disc herniation. A comparison between the anterior and posterior approach. *Spine* 1990;**15**(10): 1026–30.

Iseda 2000 ***{published data only}***
Iseda T, Nakano S, Suzuki Y, Miyahara D, Uchinokura S, Moriyama T, et al.Radiographic and scintigraphic courses of union in cervical interbody fusion: Hydroxyapatite grafts versus iliac bone autografts. *Journal of Nuclear Medicine* 2000;**41**:1642–5.

Iseda 2001 ***{published data only}***
Iseda T, Goya T, Nakano S, Kodama T, Moriyama T, Wakisaka S. Serial changes in signal intensities of the adjacent discs on T2-weighted sagittal images after surgical treatment of cervical spondylosis: Anterior interbody fusion versus expansive laminoplasty. *Acta Neurochirurgica (Wien)* 2001;**143**(7):707–10.

Jenis 2000 ***{published data only}***
Jenis LG, An HS, Simpson JM. A prospective comparison of the standard and reverse Robinson cervical grafting techniques: Radiographic and clinical analyses. *Journal of Spinal Disorders* 2000;**13**(5):369–73.

Jollenbeck 2001 ***{published data only}***
Jollenbeck B, Fernandez N, Firsching R. Titanium or polymethylmethacrylate in cervical disc surgery? A prospective study. *Zentralblatt fur Neurochirurgie* 2001;**62** (4):200–2.

Kadanka 2000 ***{published data only}***
Kadanka Z, Bednarik J, Vohanka S, Vlach O, Stejskal L, Chaloupka R, et al.Conservative treatment versus surgery in spondylotic cervical myelopathy: A prospective randomised study. *European Spine Journal* 2000;**9**(6):538–44.

Lopez-Olivia 1998 ***{published data only}***
* Lopez-Oliva Munoz F, Garcia de las Heras B, Concejero Lopez V, Asenjo Siguero JJ. Comparison of three techniques of anterior fusion in single-level cervical disc herniation. *European Spine Journal* 1998;**7**(6):512–6.

Marks 1998 ***{published data only}***
Marks SM. Cervical degenerative disease: discectomy or fusion?. *British Journal of Neurosurgery* 1998;**12**(2):109–12.

Mayer 1998 ***{published data only}***
Mayer T, McMahon MJ, Gatchel RJ, Sparks B, Wright A, Pegues P. Socioeconomic outcomes of combined spine surgery and functional restoration in workers' compensation spinal disorders with matched controls. *Spine* 1998;**23**(5): 598–605.

Murphy 1994 ***{published data only}***
Murphy MA, Trimble MB, Piedmonte MR, Kalfas IH. Changes in the cervical foraminal area after anterior discectomy with and without a graft. *Neurosurgery* 1994;**34** (1):93–6.

Pasciak 2005 ***{published data only}***
Pasciak M, Grzywocz J, Widuchowski J, Koczy B, Wadek T, Werner K. [Assessment of radiological results of anterior cervical discectomy with different fusion cages]. [Polish]. *Chirurgia Narzadow Ruchu i Ortopedia Polska* 2005;**70**(5): 347–51.

Persson 1997 ***{published data only}***
Persson LC, Carlsson CA, Carlsson JY. Long-lasting cervical radicular pain managed with surgery, physiotherapy, or a cervical collar. A prospective, randomized study. *Spine* 1997;**22**(7):751–8.

Persson 2001 ***{published data only}***
Persson LC, Lilja A. Pain, coping, emotional state and physical function in patients with chronic radicular neck pain. A comparison between patients treated with surgery, physiotherapy or neck collar - a blinded, prospective randomized study. *Disability and Rehabilitation* 2001;**23** (8):325–35.

Rawlinson 1994 ***{published data only}***
Rawlinson JN. Morbidity after anterior cervical decompression and fusion. The influence of the donor site on recovery, and the results of a trial of surgibone compared to autologous bone. *Acta Neurochirurgica (Wien)* 1994;**131** (1-2):106–18.

Rish 1976 ***{published data only}***
Rish BL, McFadden JT, Penix JO. Anterior cervical fusion using homologous bone grafts: a comparative study. *Surgical Neurology* 1976;**5**(2):119–21.

Shapiro 2001 ***{published data only}***
Shapiro S, Connolly P, Donnaldson J, Abel T. Cadaveric fibula, locking plate, and allogeneic bone matrix for anterior cervical fusions after cervical discectomy for radiculopathy or myelopathy. *Journal of Neurosurgery* 2001;**95**(1 Supp): 43–50.

Shin 2007 ***{published data only}***
Shin SH, Lee WJ, Eun JP, Choi HY, Lee JC. Clinical and radiologic assessment for anterior cervical interbody fusion with synthetic cages. *Journal of Korean Neurosurgical Society* 2007;**41**(2):105–10.

Siddiqui 2003 ***{published data only}***
Siddiqui AA, Jackowski A. Cage versus tricortical graft for cervical interbody fusion. A prospective randomised study. *Journal of Bone and Joint Surgery (Br)* 2003;**85**(7):1019–25.

Suchomel 2004 ***{published data only}***
Suchomel P, Barsa P, Buchvald P, Svobodnik A, Vanickova E. Autologous versus allogenic bone grafts in instrumented anterior cervical discectomy and fusion: a prospective study with respect to bone union pattern. *European Spine Journal* 2004;**13**(6):510–5.

Theodore 2000 *{published data only}*
Theodore N, Sonntag VKH. Spinal surgery: The past century and the next. *Neurosurgery* 2000;**46**(4):767–77.

Watters 1994 *{published data only}*
Watters 3rd WC, Levinthal R. Anterior cervical discectomy with and without fusion. Results, complications, and long-term follow-up. *Spine* 1994;**19**(20):2343–7.

Wigfield 2001 *{published data only}*
Wigfield CC, Nelson RJ. Nonautologous interbody fusion materials in cervical spine surgery: How strong is the evidence to justify their use?. *Spine* 2001;**26**(6):687–694.

Wigfield 2002 *{published data only}*
Wigfield C, Gill S, Nelson R, Langdon I, Metcalf N, Robertson J. Influence of an artificial cervical joint compared with fusion on adjacent-level motion in the treatment of degenerative cervical disc disease. *Journal of Neurosurgery* 2002;**96**(1 Supp):17–21.

Wigfield 2003 *{published data only}*
Wigfield C, Robertson J, Gill S, Nelson R. Clinical experience with porous tantalum cervical interbody implants in a prospective randomized controlled trial. *Brittish Journal of Neurosurgery* 2003;**17**(5):418–25.

Wirth 2000 *{published data only}*
Wirth FP, Dowd GC, Sanders HF, Wirth C. Cervical discectomy. A prospective analysis of three operative techniques. *Surgical Neurology* 2000;**53**:340–6.

Yamamoto 1978 *{published data only}*
Yamamoto I, Kurokawa K, Tew, M, Dunsker SB, Mayfield FH. Anterior cervical discectomy with and without fusion - clinical and experimental study. *No Shinkei Geka* 1978;**6**(8):781–7.

References to studies awaiting assessment

Nabhan 2009 *{published data only}*
Nabhan A, Ishak B, Steimer O, Zimmer A, Pitzen T, Steudel WI, et al.Comparison of bioresorbable and titanium plates in cervical spinal fusion: early radiologic and clinical results. *Journal of Spinal Disorders & Techniques* 2009;**22**(3):155–61.

Pitzen 2009 *{published data only}*
Pitzen TR, Chrobok J, Stulik J, Ruffing S, Drumm J, Sova L, et al.Implant complications, fusion, loss of lordosis, and outcome after anterior cervical plating with dynamic or rigid plates: two-year results of a multi-centric, randomized, controlled study. *Spine* 2009;**34**(7):641–6.

Additional references

Atkins 2004
Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, GRADE Working Group. Grading quality of evidence and strength of recommendations. *British Medical Journal* 2004;**328**(7454):1490.

Blettner 1999
Blettner M, Sauerbrei W, Schlehofer B, Scheuchenpflug T, Friedenreich C. Traditional reviews, meta-analyses and pooled analyses in epidemiology. *International Journal of Epidemiology* 1999;**28**(1):1–9.

Boselie 2010
Boselie A, van Mameren H, de Bie R, Benzel EC, Willems PC. Fusion versus arthroplasty in single level cervical degenerative disc disease. *Cochrane Database of Systematic Reviews* 2011, Issue (in editorial process).

Carragee 2008
Carragee EJ, Hurwitz EL, Cheng I, Carroll LJ, Nordin M, Guzman J, et al.Treatment of neck pain: injections and surgical interventions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine* 2008;**33**(4 Suppl):S153–69.

Cloward 1956
Cloward RB. The anterior approach for removal of ruptured cervical disks. The anterior approach for removal of ruptured cervical disks. *Journal of Neurosurgery* 1956;**15**(6):602–17.

Emery 1994
Emery SE, Bolesta MJ, Banks MA, Jones PK. Robinson anterior cervical fusion comparison of the standard and modified techniques. *Spine* 1994;**19**(6):660–3.

Espine Website 2010
Pashman R. E-Spine; Anterior Cervical Fusion. http://www.espine.com/anterior-cervical-fusion.htm [Accessed May 10, 2010].

Floyd 2000
Floyd T, Ohnmeiss D. A meta-analysis of autograft versus allograft in anterior cervical fusion. *Europan Spine Journal* 2000;**9**(5):398–403.

Fraser 1995
Fraser RD. Interbody, posterior, and combined lumbar fusions. *Spine* 1995;**20**(24 Suppl):167S–177S.

Fraser 2007
Fraser JF, Härtl R. Anterior approaches to fusion of the cervical spine: a meta-analysis of fusion rates. *Journal of Neurosurgery: Spine* 2007;**6**(4):298–303.

Furlan 2009
Furlan A, Pennick V, Bombardier C, van Tulder M. 2009 Updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine 2009; Vol. 34, issue 18:1929–41.

Greenhalgh 1999
Greenhalgh T. *How to read a paper. The basics of evidence based medicine*. London: BMJ Publishing group, 1999.

Grob 1998
Grob D. Surgery in the degenerative cervical spine. *Spine* 1998;**23**(24):2674–83.

Heneghan 2009
Heneghan HM, McCabe JP. Use of autologous bone graft in anterior cervical decompression: morbidity & quality of life analysis. *BMC Musculoskeletal Disorders* 2009;**10**:158.

Offringa 1999
Offringa M, de Craen AJ. De praktijk van systematische reviews. I. Inleiding. *Nederlands Tijdschrift voor Geneeskunde* 1999;**143**(13):653–6.

Ostelo 2008
Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, et al.Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. *Spine* 2008;**33**(1):90–4.

Pietrobon 2002
Pietrobon R, Coeytaux RR, Carey TS, Richardson WJ, DeVellis RF. Standard scales for measurement of functional outcome for cervical pain or dysfunction: A systematic review. *Spine* 2002;**27**(5):515–22.

Radhakrishnan 1994
Radhakrishnan K, Litchy WJ, O'Fallon WM, Kurland LT. Epidemiology of cervical radiculopathy. A population-based study from Rochester, Minnesota, 1976 through 1990. *Brain* 1994;**117**:325–35.

Salemi 1996
Salemi G, Savettieri G, Meneghini F, Di Benedetto ME, Ragonese P, Morgante L, et al.Prevalence of cervical spondylotic radiculopathy: a door-to-door survey in a Sicilian municipality. *Acta Neurologica Scandinavica* 1996; **93**(2-3):184–8.

Savolainen 1994
Savolainen S, Usenius JP, Hernesniemi J. Iliac crest versus artificial bone grafts in 250 cervical fusions. *Acta Neurochirgica (Wien)* 1994;**129**(1-2):54–7.

Vaccaro 2003
Vaccaro AR, Singh K, Haid R, Kitchel S, Wuisman P, Taylor W, et al.The use of bio-absorbable implants in the spine. *Spine Journal* 2003;**3**(3):227–37.

Whitecloud 1999
Whitecloud III TS. Modern alternatives and techniques for one-level discectomy and fusion. *Clinical Orthopaedics and Related Research* 1999;**359**:67–76.

Young 1993
Young WF, Rosenwasser RH. An early comparative analysis of the use of fibular allograft versus autologous iliac crest graft for interbody fusion after anterior cervical discectomy. *Spine* 1993;**18**(9):1123–4.

References to other published versions of this review

Jacobs 2004
Jacobs WCH, Anderson PG, Limbeek J, Willems PC, Pavlov P. Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease. *Cochrane Database of Systematic Reviews* 2004, Issue 4. [DOI: 10.1002/14651858.CD004958]

van Limbeek 2000
van Limbeek J, Jacobs WC, Anderson PG, Pavlov PW. A systematic literature review to identify the best method for a single level anterior cervical interbody fusion. *European Spine Journal* 2000;**9**(2):129–36.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abd-Alrahman 1999

Methods	RCT, method unclear
Participants	1 or 2 level symptomatic disc disease refractory to conservative treatment Exclusion: multilevel disease, PLL ossification, re-operations, requiring instrumentation
Interventions	1: Discectomy with Smith and Robinson 2: Discectomy with Smith and Robinson and fusion with iliac crest autograft
Outcomes	Radiological: Kyphose Clinical: VAS - neck, arm, iliac crest donor site pain
Notes	Diagnosis DD: Spondylosis (narrow disc space, sclerosed disc margins, osteophytes) on plain Radiograph Cause of pain: radiculopathy, myelopathy Levels: 70/90 (78%) one level; 20/90 (22%) two level

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	The randomisation technique was not described.
Allocation concealment?	Unclear	not described
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Unclear	Results for arm and neck pain with VAS scores are not presented. The results are not split for one or two level procedures
Similarity of baseline characteristics?	Unclear	Unclear from text

Abd-Alrahman 1999 (*Continued*)

Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Barlocher 2002

Methods	RCT, Method unclear
Participants	Inclusion: Cervicobrachialgia, Single level disc disease C3-T1, Radiculopathy d/t HNP/ osteophytes Exclusion: Vertebral instability, Myelopathy, Systemic infection or metabolic disease, Active malignancy, Symptomatic DDD 2> segments, Acute trauma, RA
Interventions	1: Discectomy alone 2: Iliac crest autograft
Outcomes	Radiological: Flexion extension radiographs, CT Clinical: VAS, Op time, Blood loss, Odom Functional: -
Notes	Diagnosis DD: MRI Cause of pain: Radiculopathy Levels: 125 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	not described
Blinding? All outcomes - patients?	Unclear	not possible
Blinding? All outcomes - outcome assessors?	Unclear	not mentioned
Blinding? All outcomes - care provider?	Unclear	not possible
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	2 missed to follow up

Barlocher 2002 (*Continued*)

Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	implant present, no crossovers
Free of selective reporting?	No	Only change percentages reported
Similarity of baseline characteristics?	Yes	ok
Co-interventions avoided or similar?	Yes	ok
Compliance acceptable?	Yes	implants or material inside
Timing outcome assessments similar?	Yes	similar

Baskin 2003

Methods	RCT, method unclear
Participants	1 or 2 level cervical disc disease, radiculopathy, myelopathy or both
Interventions	Discectomy and fusion with allograft ring and anterior plate 1: Allograft ring filled with iliac crest Autograft 2: Allograft ring filled with rhBMP-2
Outcomes	Radiological: Flexion-extension X-rays, CT Clinical: neurologic status, neck, arm, and donor site pain Functional: Neck Disability index, SF-36, patient satisfaction
Notes	Diagnosis DD: imaging studies: herniated disc and/or osteophyte Cause of pain: radiculopathy, myelopathy or both Levels: 18/33 (55%) one level; 15/33 (45%) two level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	The randomisation technique was not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures

Baskin 2003 (*Continued*)

Incomplete outcome data addressed? All outcomes - drop-outs?	No	there is considerable lost to follow-up at 12 and 24 months.
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Unclear	results of One and two-level surgeries were combined
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Celik 2007

Methods	RCT, methods unclear
Participants	Severe radiculopathy Physiotherapy or analgesics failed
Interventions	1: Discectomy and fusion with PEEK cage 2: Discectomy and fusion with Smith and Robinson Iliac crest autograft
Outcomes	Radiological: Foraminal height, Interspace height, Cobb angle Clinical: VAS arm, VAS neck Functional: JOA
Notes	Diagnosis DD: Radiculopathy Cause of pain: Radiculopathy levels: 43/65 (66%) one level; 22 (34%) two level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	"The groups were matched" "... randomised by the first author on a 1:1 ratio.."
Allocation concealment?	No	"Patients in the FBG group were told about postoperative donor site complications"
Blinding? All outcomes - patients?	No	"patients in the FBG group were told about donor site complications"

Celik 2007 (*Continued*)

Blinding? All outcomes - outcome assessors?	Unclear	Not mentioned
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Unclear	No mention at all
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Dai 2008

Methods	RCT, Method not described
Participants	Progressive upper extremity radicular symptoms and/or myelopathy Soft disc herniation or spondylosis Exclusion: 2 levels, ossification posterior longitudinal ligament, prior cervical surgery, significant co-morbidities
Interventions	1: Carbon fibre OR PEEK cage filled with granulated beta-TCP and plate 2: Carbon fibre OR PEEK cage filled with granulated beta-TCP
Outcomes	Radiological: Fusion, Cobb angle Clinical: VAS arm, VAS neck Functional: JOA
Notes	Diagnosis DD: Conventional x-ray, MRI Cause of pain: Radiculopathy, myelopathy, disc herniation/spondylosis Levels: 25/62 (40%) one level; 37 (60%) two level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described

Dai 2008 (*Continued*)

Allocation concealment?	Unclear	Not described
Blinding? All outcomes - patients?	Unclear	Not described
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Dowd 1999

Methods	RCT, closed envelopes
Participants	1 or 2 level spondylosis, radiculopathy, radiculo-myelopathy
Interventions	1: Discectomy with Smith and Robinson 2: Discectomy with Smith and Robinson and fusion with Cloward using iliac crest autograft
Outcomes	Radiological: Lateral cervical spine X-ray Clinical: Complications, pain Functional: Return to work
Notes	No exclusion criteria; Diagnosis DD; Cause of pain: radiculopathy, radiculo-myelopathy Levels: 46/84 (55%) one level; 38 (45%) two level
Risk of bias	

Dowd 1999 (*Continued*)

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	The randomisation technique is valid
Allocation concealment?	Yes	
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	No	The percentage lost to follow-up at 4.5 years was larger than 20%
Incomplete outcome data addressed? All outcomes - ITT analysis?	Unclear	Unclear from text
Free of selective reporting?	Unclear	Outcome parameters not mentioned
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Feiz-Erfan 2007

Methods	RCT, Method unclear
Participants	Inclusion: Neurological deficit appropriate for level; MRI or CT confirmed; Failure non-surgical treatment; Change activity, Use of cervical collar and steroids
Interventions	1: Anterior Plate (Slimloc, Depuy) with VG2 allograft with platelet 2: Anterior Plate (Slimloc, Depuy) with VG2 allograft without platelet
Outcomes	Radiological: Fusion on Ap/lateral and Flexion/extension X rays Clinical: VAS Functional: Sf36, NDI, Prolo
Notes	Diagnosis DD: MRI, CT Cause of pain: DDD or Herniated disc

Feiz-Erfan 2007 (*Continued*)

	Levels: 19/50 (38%) one level; 31 (62%) two level

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"Randomised" "on a blinded 1:1 basis"
Allocation concealment?	Unclear	not mentioned
Blinding? All outcomes - patients?	Yes	
Blinding? All outcomes - outcome assessors?	Unclear	Not mentioned
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	No	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	No	
Similarity of baseline characteristics?	Unclear	Information on platelet groups is missing
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Fernandez-Fairen 2008

Methods	RCT, Computer generated random list
Participants	Inclusion: Neck pain, brachialgia, nerve root comparison/ herniated disc or spondylosis, 1 level c3-c7, MRI confirmed, Conservative treatment, No surgical previous intervention, age 18-65 Exclusion: Other cervical spine conditions, Myeolpathy, Ostopenia, osteoporosis, osteomalacia, metabolic bone diseases, Local infection, tumour, Smokers, drug abuse, alcohol, Work related conditions
Interventions	1: Anterior plate (alpha plate Stryker), IIiac crest Autograft 2: Tantalum cervical fusion cage (Zimmer)

Fernandez-Fairen 2008 (*Continued*)

Outcomes	Radiological: fusion on Ap/lateral and Flexion/extension X-rays Clinical: VAS, Duration of surgery, Blood loss, Hospital stay Functional: Odom, NDI, Zung
Notes	Diagnosis DD: MRI Cause of pain: nerve root comparison/ herniated disc or spondylosis Levels: 61 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated random list
Allocation concealment?	Unclear	Not described
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Unclear	No mention of drop-outs and no description of N for outcome parameters
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Hacker 2000

Methods	RCT, method unclear
Participants	Radiculopathy due to soft disc herniation or osteophytes, 1 or 2 levels, C3-C7 Exclusion: myelopathy, previous surgery at cervical levels
Interventions	1: Discectomy and fusion with iliac crest autograft 2: Discectomy and fusion with cage with Hydroxyapatite coating 3: Discectomy and fusion with cage without Hydroxyapatite coating
Outcomes	Radiological: Flexion-extension radiographs Clinical: VAS pain Functional: SF-36, Work, Daily function
Notes	Diagnosis DD: imaging Cause of pain: Radiculopathy Levels: 54/64 (84%) one level; 10 (16%) two level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Randomisation procedure is not clear
Allocation concealment?	Unclear	B - Unclear
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Unclear	No description of planned outcomes
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	

Hacker 2000 (*Continued*)

Timing outcome assessments similar?	Yes	

Hauerberg 2008

Methods	RCT, Computer generated list, Opaque envelopes
Participants	Inclusion: Anterior approach, Cervical root compression, 1 level c4-t1, root compression at max 2 levels, symptoms > 6 weeks, age 18-70 years Exclusion: Spinal cord compression, History of spine surgery, Neurological disease / condition
Interventions	1: Ray fusion cage 2: Discectomy alone
Outcomes	Radiological: Fusion Clinical: Pain Functional: Recovery, employment status
Notes	Diagnosis DD: radiological Cause of pain: cervical root compression Levels: 86 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated list
Allocation concealment?	Yes	Opaque envelopes
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	

Hauerberg 2008 (*Continued*)

Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	No	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Lind 2007

Methods	RCT, method unclear, Sealed envelopes
Participants	Inclusion: Radiculopathy, MRI verified disc herniation/spondylosis, 1 level, c4-c7 Exclusion: Myelopathy
Interventions	1:Threaded titanium (Centrepulse) 2: Iliac crest autograft
Outcomes	Radiological: Migration (RSA) Clinical: VAS Functional: ODOM
Notes	Diagnosis DD: MRI Cause of pain: Radiculopathy, disc herniation/spondylosis levels: 24 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not mentioned
Allocation concealment?	Yes	Sealed envelopes
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	Yes	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	

Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	No	
Similarity of baseline characteristics?	No	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Lofgren 2000

Methods	RCT, sealed envelopes
Participants	Cervical disc protrusion, stenosis or both
Interventions	Discectomy and fusion with Cloward with: 1: iliac crest autograft 2: Femoral head allograft 3: Bovine Xenograft
Outcomes	Radiological: RSA, conventional for bone bridging, flexion extension views Clinical: VAS pain Functional: muscle force, sensory function. Observers assessment
Notes	No exclusion criteria; Diagnosis DD ? Cause of pain: spondylosis, disc herniation Levels: 43 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	good description of the randomisation
Allocation concealment?	Yes	
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	

Lofgren 2000 (*Continued*)

Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	No	high lost to follow-up for the RSA measurements
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Unclear	Unclear from text
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Lofgren 2010

Methods	RCT, Method unclear
Participants	Inclusion: Radiculopathy, Degenerative disc disease (HNP/spondylosis), Compatible MRI/ clinic Exclusion: Previous cervical spine surgery, Postraumatic, Inflammatory systemic disease, Neurological disease, Drug/alcohol abuse
Interventions	1: Iliac crest autograft 2: Trabecular metal cage
Outcomes	Radiological: - Clinical: Operation time, Blood loss, VAS neck, VAS arm Functional: NDI, Patient global assessment
Notes	Diagnosis DD: MRI Cause of pain: Radiculopathy Levels: 80 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Procedure not described
Allocation concealment?	Yes	closed envelopes

Lofgren 2010 (*Continued*)

Blinding? All outcomes - patients?	No	Not possible (iliac crest scar)
Blinding? All outcomes - outcome assessors?	No	observer unbiased, blinding not mentioned
Blinding? All outcomes - care provider?	Unclear	not possible
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	no lost to follow-up
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	no cross over
Free of selective reporting?	Yes	All outcomes accounted for
Similarity of baseline characteristics?	Yes	As far as reported similar
Co-interventions avoided or similar?	Yes	not extensively described
Compliance acceptable?	Yes	implant present
Timing outcome assessments similar?	Yes	similar

Madawi 1996

Methods	RCT, method unclear
Participants	Fresh, 1 or 2 level symptomatic cervical disc disease (radiculopathy, myelopathy, radiculomyelopathy) Exclusion: Multilevel, OSS, PLL, malalignment, sepsis, re-operations, instrumented stabilisation
Interventions	Discectomy with Smith and Robinson or Cloward with 1: Biocompatible osteo-conductive polymer 2: Iliac crest autograft
Outcomes	Radiological: Radiograph/CT/MRI Clinical: Odom's criteria, VAS
Notes	Diagnosis DD: Clinical and radiological examination, no imaging for diagnosis Cause of pain: Radiculopathy, myelopathy, Radiculomyelopathy Levels: 82/115 (71%) one level; 33 (29%) two level
Risk of bias	

Madawi 1996 (*Continued*)

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	The randomisation technique was not described
Allocation concealment?	Unclear	Unclear
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Unclear	Unclear from text
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Unclear	timing of the follow-up is questionable

Martins 1976

Methods	RCT, method unclear
Participants	- Refractory signs and symptoms of cervical disc disease and radiculopathy - 1 or 2 levels - Abnormalities of cervical spine radiographs correlated with the clinical picture
Interventions	1: Discectomy 2: Discectomy and fusion according to the Cloward procedure
Outcomes	Radiological: Flexion-extension X-rays Clinical: Custom criteria
Notes	Diagnosis DD: Radiograph/Myelogram Cause of pain: Cervical disc disease and radiculopathy

Martins 1976 (*Continued*)

	Levels: 16/51 (31%) one level; 35 (69%) two level

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	The randomisation technique was not described (lottery style)
Allocation concealment?	Unclear	B - Unclear
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Unclear	Unclear from text
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Unclear	Outcome parameters not clearly described prospectively
Similarity of baseline characteristics?	Unclear	Unclear from text
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

McConnel 2003

Methods	RCT, sealed envelopes
Participants	Radiculopathy, myelopathy, discogenic pain, spondylosis, segmental instability, foraminal stenosis
Interventions	Discectomy with Smith and Robinson and fusion with anterior plate and with: 1: Iliac crest autograft 2: ProOsteon 200 Block

Outcomes	Radiological: fragmentation, graft height, angular alignment, plate complications Clinical: - ? Functional: SF-36, Oswestry disability index,
Notes	Diagnosis DD Cause of pain: Radiculopathy, myelopathy, discogenic pain, spondylosis, segmental instability, foraminal stenosis Levels: 18/29 (62%) one level; 9/29 (31%) two level; 2/29 (7%) Three level

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	The randomisation technique used sealed envelopes.
Allocation concealment?	Yes	
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Unclear	drop-out percentage is moderate
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

McGuire 1994

Methods	RCT, method unclear
Participants	Radiculopathy with motor and sensory deficits and associated neck pain Failing to conservative treatment. Exclusion: Informed consent failure
Interventions	1: Discectomy and fusion (Williams) with vertebral body autograft 2: Discectomy and fusion (S+R) with Iliac crest autograft
Outcomes	Radiological: Disc height and sagittal rotation Clinical: Custom criteria
Notes	Diagnosis DD: Radiographic/MRI/CT Cause of pain: Radiculopathy Levels: 42/46 (91%) one level; 4 (9%) two level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	The randomisation technique was not described which makes the study suspicious because of the unequal group sizes
Allocation concealment?	Unclear	Unclear
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Unclear	Unclear from text
Incomplete outcome data addressed? All outcomes - ITT analysis?	Unclear	Unclear from text
Free of selective reporting?	Unclear	Incomplete description of outcome parameters
Similarity of baseline characteristics?	Unclear	Unclear from text
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Unclear	Unclear from text

McGuire 1994 (*Continued*)

Timing outcome assessments similar?	Yes	

Nabhan 2007

Methods	RCT, Method unclear, Sealed envelopes
Participants	Inclusion: Degenerative disc disease, Radiculopath or myelopathy, Unresponsive to Conservative therapy Exclusion: no criteria
Interventions	1: Solis Peek cage (Stryker) 2: Solis Peek cage (Stryker) with Caspar plate
Outcomes	Radiological: Migration (RSA) Clinical: VAS Functional: none
Notes	Diagnosis DD: confirmatory imaging studies Cause of pain: Degenerative disc disease, Radiculopath or myelopathy Levels: 37 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not reported
Allocation concealment?	Yes	Sealed envelopes
Blinding? All outcomes - patients?	No	Not mentioned, result can be easily identified on Rx
Blinding? All outcomes - outcome assessors?	Unclear	Not described
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Unclear	Not mentioned
Free of selective reporting?	Yes	All parameters accounted for
Similarity of baseline characteristics?	Unclear	Not reported

Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Nunley 2009

Methods	RCT, Method Computer generated block randomised list
Participants	Inclusion: age 18-75, symptomatic DDD, 1-3 levels, c3-c7, radiological evidence of compressed cervical nerve/cord by bone/hernia, radiculopathy, fusion candidates Exclusion: Acute trauma, Severe myelopathy, Cervical instability, Severe facet disease, Posterior augmentation, Revision, Previous surgery at level
Interventions	1: Ctek (Biomet spine) static plate with Allograft 2: Ctek (Biomet spine) dynamic plate with Allograft
Outcomes	Radiological: Fusion at Flexion/Extension Clinical: VAS Functional: NDI
Notes	Diagnosis DD: radiological Cause of pain: compressed cervical nerve/cord by bone/hernia, radiculopathy Levels: 28/66 (42%) one level; 38/66 (58%) two or three level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated block randomised list
Allocation concealment?	Unclear	Not described
Blinding? All outcomes - patients?	Yes	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	

Nunley 2009 (*Continued*)

Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Unclear	Not described per group
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Unclear	Follow up varies, unclear per group

Oktenoglu 2007

Methods	RCT, Method: Heads or tails for each patient before the operation
Participants	Inclusion: No previous cervical surgery, Radiculopathy, MRI confirmed, Single level, 2 weeks conservative treatment Exclusion: Significant degenerative spinal disorder
Interventions	1: Discectomy alone 2: Plate (Tnipsan), iliac crest allograft (Tutoplast, Tutogen)
Outcomes	Radiological: Disc height, Foramen height Clinical: VAS Functional: none
Notes	Diagnosis DD: MRI Cause of pain: Radiculopathy Levels: 20 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Heads or tails
Allocation concealment?	Yes	
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	Yes	

Oktenoglu 2007 (*Continued*)

Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Unclear	Not enough information
Co-interventions avoided or similar?	Unclear	Not described
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Unclear	Follow up varies, not given per group

Pan 2005

Methods	RCT, Method unclear
Participants	Inclusion: Patients who underwent one- and two level anterior cervical discectomy and fusion Exclusion: -
Interventions	1: Caspar titanium Plate, Screws Graft 2: Screws Graft
Outcomes	Radiological: Fusion, Disc Height, cervical lordotic alignment Clinical: JOA Functional: Improvement
Notes	Diagnosis DD: ? Cause of pain: ? Levels: ?

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	They did not discuss the method, just say 'they were randomised'
Allocation concealment?	No	

Pan 2005 (*Continued*)

Blinding? All outcomes - patients?	No	not mentioned
Blinding? All outcomes - outcome assessors?	Unclear	not mentioned
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	No	32% drop out, not discussed
Incomplete outcome data addressed? All outcomes - ITT analysis?	No	26 patients were not followed up, but no explanation was given
Free of selective reporting?	Yes	All result of outcomes were clearly reported for each group. There is no sign of selective outcome reporting from the article
Similarity of baseline characteristics?	Unclear	not mentioned
Co-interventions avoided or similar?	No	After surgery, patients in instrumented group wear cervical collar for 6 weeks while patients in non-instrumented group wear cervical collar for 3 months
Compliance acceptable?	Yes	Surgery
Timing outcome assessments similar?	Yes	e.g. JOA and improving rate were assessed before and after surgery for each group. Fusion rate was measured at 3-6 months after surgery for each group. Disc height and cervical lordotic alignment were assessed at last visit (10-28 months) for each group

Porras-Estrada 2004

Methods	RCT, Method unclear
Participants	Inclusion: Myelopathy and radiculopathy Exclusion: -
Interventions	1: Threaded cylindrical Bovine allograft 2: BAK-C cage
Outcomes	Radiological: Subsidence, angulation, fusion, pseudoarthrosis Clinical: Categorical, Good, average, bad Functional: -

Porras-Estrada 2004 (*Continued*)

Notes	Diagnosis DD: MRI Cause of pain: Myelopathy and radiculopathy Levels: 34/44 (77%) one level; 10 (23%) two level

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method not specified
Allocation concealment?	Unclear	Not mentioned
Blinding? All outcomes - patients?	Unclear	Not mentioned
Blinding? All outcomes - outcome assessors?	Unclear	Not mentioned
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	No lost to follow-up
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	All patients analysed in randomised group
Free of selective reporting?	Yes	All preoperative outcomes presented
Similarity of baseline characteristics?	Yes	All patients tabulated and groups comparable
Co-interventions avoided or similar?	Yes	No co-interventions
Compliance acceptable?	Yes	All treatments remained in place
Timing outcome assessments similar?	Unclear	Follow-up ranges from 2 to 5 years, no further information given

Rosenorn 1983

Methods	RCT, method unclear
Participants	Herniated cervical discs, age from 20-70 years. Exclusion: fractures, dislocations, Osteochondrosis with narrowing of foramina
Interventions	1: Discectomy according to Hirsh 2: Discectomy and fusion according to Cloward with freeze dried bone grafts

Rosenorn 1983 (*Continued*)

Outcomes	Radiological: - Clinical: custom criteria Functional: Occupation
Notes	5 surgeons Diagnosis DD: Myelography with Pantopoqaque Cause of pain: Herniated disc Levels: 40/63 (64%) one level; 23 (36%) two level

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	The randomisation technique was not described
Allocation concealment?	Unclear	B - Unclear
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Unclear	Outcome parameters not clearly described prospectively
Similarity of baseline characteristics?	Unclear	Unclear from text
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Ruetten 2009

Methods	RCT, Method unclear
Participants	Inclusion: Unilateral radiculopathy with arm pain, MRI/CT mediolateral HNP, C2/3 to c7/th1, Ventral >4mm disc height Exclusion: Foramnial HNP, Craniocaudal sequestration >1/2 vertebral body, instabilities /deformities, Isolated neck pain, Foraminal stenosis without HNP, Previous operation same segment
Interventions	1: Peek cage with Microsurgical decompression 2: Full endoscopic anterior decompression
Outcomes	Radiological: MRI/CT Clinical: VAS arm neck, Hilbrand, NASS, Blood loss, Oper time Functional: -
Notes	Diagnosis DD: MRI/CT Cause of pain: Radiculopathy Levels: 120 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Block randomisation, but procedure not mentioned
Allocation concealment?	Unclear	Allocation disclosure not mentioned
Blinding? All outcomes - patients?	No	Not possible due to different surgical technique
Blinding? All outcomes - outcome assessors?	Yes	Unclear, statement: "later examiners were not informed about which operation procedure was used"
Blinding? All outcomes - care provider?	No	Not possible
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	LTF = 17%
Incomplete outcome data addressed? All outcomes - ITT analysis?	Unclear	Not stated where 3 patients from FACD receiving ACDF were analysed
Free of selective reporting?	Yes	all parameters accounted for
Similarity of baseline characteristics?	Yes	similar
Co-interventions avoided or similar?	No	cage used in one group, ignored in comparison evaluation

Compliance acceptable?	Yes	implant present
Timing outcome assessments similar?	Yes	clear time-points

Ryu 2006

Methods	RCT, Method unclear
Participants	Inclusion: age 18-70, DDD, 1 or 2 levels, 6 weeks conservative treatment, cervicalgia/ radiculopathy Exclusion: Prior cervical spine surgery, Instability secondary to trauma, Lumbar Spine disability, History of disc/spine infection, Spine tumour, Osteoporosis/metabolic bone disease, Pregnancy, Significant illness, Psychological disturbance
Interventions	1: DOC (Depuy) or PEAK (DePuy), Allograft 2: I/F cage (DePuy), IC autograft
Outcomes	Radiological: Fusion AP, Instability F/E Clinical: pain Functional: NDI, Satisfaction, SF36
Notes	Diagnosis DD: MRI Cause of pain: Radiculopathy Levels: 21/40 (53%) one level; 19 (47%) two level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	

Ryu 2006 (*Continued*)

Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Savolainen 1998

Methods	RCT, method unclear
Participants	Single level cervical disc disease, radicular symptoms, evidenced by radiological study, long lasting severe radicular pain
Interventions	1: Discectomy 2: Discectomy and fusion (S+R) 3: Discectomy and fusion (Plating)
Outcomes	Radiological: Kyphosis, fusion Clinical: Custom: good/fair/poor
Notes	No exclusion criteria Diagnosis DD: Myelograph, MRI Cause of pain: nerve root compression Levels: 91 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	The randomisation technique is not clear.
Allocation concealment?	Unclear	Not described
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures

Savolainen 1998 (*Continued*)

Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Unclear	Outcome parameters not described clearly prospectively
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Schroder 2007

Methods	RCT, Method Block randomisation
Participants	Inclusion: age 18-65, monoradicular syndrome, herniated cervical disc Exclusion: Excessive osteophytes, Adjacent level degeneration, Myelopathy
Interventions	1: PMMA (Palacos) 2: Cage (Intromed intervertebral spacer, Intromed)
Outcomes	Radiological: Fusion, alignment Clinical: Duration procedure, Neurological impairment Functional: Odom
Notes	Level: 115 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Block randomisation
Allocation concealment?	Unclear	Not described
Blinding? All outcomes - patients?	Unclear	Not described
Blinding? All outcomes - outcome assessors?	No	

Schroder 2007 (*Continued*)

Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Stulik 2007

Methods	RCT, Method
Participants	Inclusion: Sympt DDD, 1-2 levels, traumatic disco-ligamentous injuries, no previous cervical spine surgery, not pregnant, age 21-80, informed consent Exclusion: Previous cervical spine surgery, Additional cervical spine surgery, Infection, AIDS, Hepatitis C, Osteoporosis, Malignancy, Mental disease, Sensititvity to materials, Continuous use of steroids
Interventions	1: Dynamic plate (ABC plate & screws, Aesculaep), autograft 2: Static plate (CSLP, Synthes), autograft
Outcomes	Radiological: Fusion Clinical: None Functional: None
Notes	Diagnosis DD: Unclear Cause of pain: DDD Levels: 91/132 (69%) one level; 41 (31%) two level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	Not described

Stulik 2007 (*Continued*)

Blinding? All outcomes - patients?	Unclear	Not described
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	No	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Thome 2006

Methods	RCT, computer generated
Participants	Inclusion: Spondylosis, Herniated cervical disc, Conservative treatment Exclusion: Ossification PLL, History of Cervical disc surgery, Spinal instability
Interventions	1: Iliac crest autograft 2: Rabea Cage (Signus)
Outcomes	Radiological: - Clinical: VAS, Neurological status, Functional: JOA, SF-36, Odom, PSI
Notes	Diagnosis DD: ? Cause of pain: Spondylosis / Herniated disc Levels: 73/100 (73%) one level; 27 (27%) two level

Risk of bias

Item	**Authors' judgement**	**Description**

Thome 2006 (*Continued*)

Adequate sequence generation?	Yes	
Allocation concealment?	Unclear	Not described, Not sure what is meant by "concealed randomisation"
Blinding? All outcomes - patients?	Unclear	Not described
Blinding? All outcomes - outcome assessors?	Unclear	Not described
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

van den Bent 1996

Methods	RCT, block randomised with sealed envelopes
Participants	Cervical radicular syndrome caused by a herniated disc; Failing to respond to conservative treatment Exclusion: Disease interfering with follow-up, signs and symptoms of spinal cord compression (GrII Nurick)
Interventions	1: Discectomy (S+R) 2: Discectomy (S+R) and fusion with PMMA
Outcomes	Radiological: Bony union, radiolucency Clinical: Odom's criteria, neck pain and arm pain
Notes	Diagnosis DD: Myelograph, CT with intrathecal contrast Cause of pain: Herniated intervertebral disc

van den Bent 1996 (*Continued*)

	Levels: 71/81 (88%) one level; 10 (12%) two level

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	
Allocation concealment?	Yes	
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	No	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Vavruch 2002

Methods	RCT, notes
Participants	More than 6 months of neck pain, radiculopathy of degenerative origin, compatible MRI and clinical findings Exclusion: Myelopathy, psychiatric disturbances, drug abuse, previous spine surgery
Interventions	Discectomy and fusion with iliac crest autograft 1: with Cloward technique 2: with S+R technique with Carbon fibre cage

Vavruch 2002 (*Continued*)

Outcomes	Radiological: Fusion Clinical: Odom, VAS-pain Functional: Neck Disability index, Cervical spine function score, Workstatus
Notes	Diagnosis DD: MRI Cause of pain: degenerative origin Levels: 58/89 (65%) one level; 27/89 (30%) two level; 4/89 (5%) three level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	The randomisation technique is adequate
Allocation concealment?	Yes	
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Unclear	Unclear from text
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Xie 2007

Methods	RCT, Method Computer generated randomisation matrix
Participants	Inclusion: Cervical radiculopathy, Single level, Degenerative disc disease, >18 years, English speaking Exclusion: Myelopathy, Multi level, Resection adjacent vertebral bodies, Posterior degenerative changes, Comorbidity requiring narcotic analgesic
Interventions	1: Discectomy alone 2: Iliac crest autograft 3: Codman plate (J&J) with Iliac crest autograft
Outcomes	Radiological: Fusion, Alignment, Adjacent segment degeneration Clinical: Mcgill pain Functional: Sf 36, American spinal injury scale
Notes	Diagnosis DD: MRI, Radiology Cause of pain: Radiculopathy/ DDD Level: 42 (100%) one level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated randomisation matrix
Allocation concealment?	Unclear	Not described
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	No	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	No	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	
Similarity of baseline characteristics?	No	
Co-interventions avoided or similar?	Yes	

Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

Zoega 2000

Methods	RCT, Sealed envelopes, day before
Participants	Herniated disc or spondylosis at 1 or 2 levels
Interventions	Discectomy and fusion (S+R) with iliac crest autograft 1: with CSLP plate 2: Without plate
Outcomes	Radiological: Clinical: VAS neck and arm pain, Odom's criteria Functional: Million index, Oswestry indexZung depression scale
Notes	No exclusion criteria Diagnosis DD: MRI Cause of pain: Radiculopathy Levels: 27/46 (59%) one level; 19 (41%) two level

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	The randomisation technique is valid
Allocation concealment?	Yes	
Blinding? All outcomes - patients?	No	
Blinding? All outcomes - outcome assessors?	Yes	
Blinding? All outcomes - care provider?	No	Not possible in surgical procedures
Incomplete outcome data addressed? All outcomes - drop-outs?	Yes	
Incomplete outcome data addressed? All outcomes - ITT analysis?	Yes	
Free of selective reporting?	Yes	

Zoega 2000 (*Continued*)

Similarity of baseline characteristics?	Yes	
Co-interventions avoided or similar?	Yes	
Compliance acceptable?	Yes	
Timing outcome assessments similar?	Yes	

RCT=Randomised Clinical Trial
S+R = Smith and Robinson procedure
VAS=Visual analogue scale
DD: Degenerative disc

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
An 1995	Quasi RCT with patient preferences
Barlocher 2000	Conference proceeding, Journal version included
Bishop 1996	Quasi RCT; Alternating
Bolesta 2002	Not randomised
Brown 1976	Retrospective study
Chen 2001	Biomechanical Model
Dunsker 1977	Retrospective study
Emery 1976	not randomised
Espersen 1984	Retrospective study
Grob 2001	Quasi RCT; chronological
Hedlund 2001	Conference proceeding
Herkowitz 1990	Other comparison
Iseda 2000	Outcome parameter

(*Continued*)

Iseda 2001	Outcome parameter
Jenis 2000	Quasi RCT; alternating
Jollenbeck 2001	not randomised
Kadanka 2000	Other treatment comparison
Lopez-Olivia 1998	Retrospective
Marks 1998	Editorial
Mayer 1998	Matched comparison
Murphy 1994	Not randomised
Pasciak 2005	Not randomised, retrospective
Persson 1997	Other treatment comparison
Persson 2001	Other treatment comparison
Rawlinson 1994	quasi RCT; hospital file number
Rish 1976	Not randomised
Shapiro 2001	Not randomised
Shin 2007	not randomised
Siddiqui 2003	quasi RCT; Date of birth randomisation
Suchomel 2004	Patient preference allocation
Theodore 2000	Review
Watters 1994	Retrospective study
Wigfield 2001	Review
Wigfield 2002	Other treatment comparison
Wigfield 2003	"pre-randomisation" not allowed
Wirth 2000	Acute herniated discs: other indication
Yamamoto 1978	Not randomised

Characteristics of studies awaiting assessment *[ordered by study ID]*

Nabhan 2009

Methods	RCT, method unclear. Allocation concealment by sealed envelopes. Blinding not mentioned
Participants	Single level, C3-C7, Soft or hard disc herniation, Symptomatic degenerative disc disease with radiculopathy not responding to conservative therapy. Age 20-60 Excluision: osteoporosis, infection, spondylodiscitis, malignancies, Hepatitis, HIV, AIDS, allergies, Spine injury, pregnancy
Interventions	Peek Cage 1: Dynamic titanium plate 2: Biodegradable plate
Outcomes	Radiological: RSA motion Clinical: VAS arm pain, NDI neck pain Functional: -
Notes	Levels: 40 (100%) single level

Pitzen 2009

Methods	RCT,
Participants	Type A fractures, Symptomatic degenerative disc disease in 1 or 2 levels, Traumatic disco-ligamentous injuries, 21-80 years Exclusion: Previous C-spine surgery, Additional C-spine surgery (i.e., posterior approach), Active and suspected infection, AIDS, Hepatitis C, Pregnancy, Severe osteoporosis, Known malignancy, Mental disease, Sensitivity to one of the device materials, Continuous use of steroids
Interventions	Anterior discectomy with iliac crest autograft 1: Dynamic plate 2: Rigid plate
Outcomes	Preoperative, 3, 6 months, 2 years Raiological: Motion on Flexion-Extension Clinical: Implant complication Functional: -
Notes	Levels: /132 (%) one level

DATA AND ANALYSES

Comparison 1. Discectomy alone vs human bone graft

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Hospital stay	4	300	Std. Mean Difference (IV, Random, 95% CI)	-0.48 [-1.01, 0.05]
2 Operation time	3	237	Mean Difference (IV, Random, 95% CI)	-23.71 [-33.21, -14.21]
3 Blood loss	1	63	Mean Difference (IV, Random, 95% CI)	-21.0 [-28.68, -13.32]
4 Pain not relieved at 5 weeks	1	84	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.20, 3.46]
5 Odom's criteria	2	149	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.82, 1.10]
6 Not Returned to work at 5 weeks	2	144	Risk Ratio (M-H, Random, 95% CI)	1.26 [1.02, 1.54]
7 Not Returned to work at 10 weeks	2	128	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.77, 2.69]
8 No Fusion	5	303	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.10, 0.49]
9 Alignment	2	75	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.07, 1.56]

Comparison 2. Discectomy alone vs cage or cement

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Operation time	3	334	Mean Difference (IV, Random, 95% CI)	8.74 [-8.21, 25.69]
1.1 Discectomy alone vs cage	3	275	Mean Difference (IV, Random, 95% CI)	9.49 [-13.66, 32.64]
1.2 Discectomy alone vs PMMA	1	59	Mean Difference (IV, Random, 95% CI)	6.40 [0.53, 12.27]
2 Blood loss	1	128	Mean Difference (IV, Random, 95% CI)	11.32 [6.27, 16.36]
2.1 Discectomy alone vs cage	1	69	Mean Difference (IV, Random, 95% CI)	13.10 [6.61, 19.59]
2.2 Discectomy alone vs PMMA	1	59	Mean Difference (IV, Random, 95% CI)	8.60 [0.58, 16.62]
3 Length of stay	1	118	Mean Difference (IV, Random, 95% CI)	-0.70 [-1.30, -0.09]
3.1 Discectomy alone vs cage	1	59	Mean Difference (IV, Random, 95% CI)	-0.60 [-1.43, 0.23]
3.2 Discectomy alone vs PMMA	1	59	Mean Difference (IV, Random, 95% CI)	-0.80 [-1.67, 0.07]
4 Recovery	1	79	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.91, 1.38]
4.1 Discectomy alone vs cages	1	79	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.91, 1.38]
5 Neck pain not relieved at 6 weeks	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 Discectomy alone vs cement	2	140	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.21, 2.66]
6 Neck pain not relieved at 2 years	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Discectomy alone vs cement	2	135	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.69, 1.61]
7 VAS Arm pain 24 months	1	103	Mean Difference (IV, Random, 95% CI)	Not estimable

7.1 Discectomy alone versus cage	1	103	Mean Difference (IV, Random, 95% CI)	Not estimable
8 VAS Neck pain 24 months	1	103	Mean Difference (IV, Random, 95% CI)	Not estimable
8.1 Discectomy alone versus cage	1	103	Mean Difference (IV, Random, 95% CI)	Not estimable
9 NASS pain 24 months	1	103	Mean Difference (IV, Random, 95% CI)	Not estimable
9.1 Discectomy alone vs cage	1	103	Mean Difference (IV, Random, 95% CI)	Not estimable
10 NASS neurology 24 months	1	103	Mean Difference (IV, Random, 95% CI)	Not estimable
10.1 Discectomy alone versus cage	1	103	Mean Difference (IV, Random, 95% CI)	Not estimable
11 No Fusion	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
11.1 Discectomy alone vs cement	2	131	Risk Ratio (M-H, Random, 95% CI)	4.75 [0.58, 38.67]
11.2 Discectomy alone vs cage	3	250	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.09, 4.42]
12 Odom's criteria			Other data	No numeric data
12.1 Discectomy alone vs cage			Other data	No numeric data
12.2 Discectomy alone vs PMMA			Other data	No numeric data

Comparison 3. Discectomy alone vs human bone graft with plates

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 VAS Arm pain	1	20	Mean Difference (IV, Random, 95% CI)	-0.16 [-0.85, 0.53]
2 VAS neck pain	1	20	Mean Difference (IV, Random, 95% CI)	-0.81 [-1.42, -0.20]
3 Disc height	1	20	Mean Difference (IV, Random, 95% CI)	1.33 [0.57, 2.09]
4 Odoms criteria	1	60	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.71, 1.28]
5 Fusion	2	76	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.96, 1.27]

Comparison 4. Iliac crest autograft vs human allograft or bone substitute

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 headache	1	27	Mean Difference (IV, Random, 95% CI)	18.0 [4.77, 31.23]
2 Sensory function	1	27	Mean Difference (IV, Random, 95% CI)	15.0 [2.07, 27.93]
3 Muscle power	1	27	Mean Difference (IV, Random, 95% CI)	27.0 [11.48, 42.52]
4 Odoms criteria	1	115	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.77, 1.15]

Comparison 5. Iliac crest autograft vs cage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Operation time	3	200	Mean Difference (IV, Random, 95% CI)	-13.21 [-29.99, 3. 57]
2 Blood loss	2	120	Mean Difference (IV, Random, 95% CI)	-8.05 [-15.30, -0.79]
3 Hospital stay	3	211	Mean Difference (IV, Random, 95% CI)	-0.42 [-0.84, 0.01]
4 VAS Neck Pain	3	275	Mean Difference (IV, Random, 95% CI)	0.40 [-0.94, 1.73]
5 VAS Arm pain	2	180	Mean Difference (IV, Random, 95% CI)	-0.29 [-0.90, 0.33]
6 Neck Disability Index (NDI)	2	175	Mean Difference (IV, Random, 95% CI)	1.47 [-5.39, 8.33]
7 JOA	1	100	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.79, 0.59]
8 Odom's criteria	6	412	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.99, 1.24]
9 SF-36 Physical	1	54	Mean Difference (IV, Fixed, 95% CI)	2.30 [-4.57, 9.17]
10 SF-36 Mental	1	54	Mean Difference (IV, Random, 95% CI)	5.80 [-1.32, 12.92]
11 Satisfaction	1	488	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.88, 1.08]
12 Foraminal height	1	65	Mean Difference (IV, Random, 95% CI)	1.5 [0.83, 2.17]
13 Interspace height	1	65	Mean Difference (IV, Random, 95% CI)	1.9 [1.17, 2.63]
14 Cobb angle	1	65	Mean Difference (IV, Random, 95% CI)	0.80 [-0.92, 2.52]
15 No Fusion	5	424	Risk Ratio (M-H, Random, 95% CI)	1.87 [1.10, 3.17]

Comparison 6. Iliac crest autograft vs iliac crest autograft with plates

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical outcome	2	104	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.91, 1.41]
2 No Fusion	2	76	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.92, 1.07]

Comparison 7. Different types of autograft

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Fusion	1	50	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.32, 1.17]

Comparison 9. Other comparisons between different types of instrumentation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Odom's criteria	1	107	Risk Ratio (M-H, Random, 95% CI)	1.09 [0.91, 1.31]

Comparison 10. PMMA vs cage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Operation time	2	169	Mean Difference (IV, Random, 95% CI)	13.49 [8.23, 18.75]
2 Odoms criteria	2	167	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.85, 1.19]
3 No Fusion	2	167	Risk Ratio (M-H, Random, 95% CI)	7.25 [0.70, 74.75]

Comparison 11. Cage vs cage and plate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Neck pain	1	37	Mean Difference (IV, Random, 95% CI)	0.30 [0.03, 0.57]
2 Arm pain	1	37	Mean Difference (IV, Random, 95% CI)	-0.60 [-0.80, -0.40]
3 JOA	1	62	Mean Difference (IV, Random, 95% CI)	0.5 [-0.65, 1.65]
4 Segmental lordosis	1	62	Mean Difference (IV, Random, 95% CI)	-0.60 [-2.95, 1.75]

Comparison 12. Complications

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 complications	33	2595	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.49, 1.06]
1.1 Discectomy alone versus human bone graft	7	442	Risk Ratio (M-H, Fixed, 95% CI)	1.56 [0.71, 3.43]
1.2 Discectomy alone vs cage	3	260	Risk Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 3.69]
1.3 Discectomy alone vs PMMA	2	140	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.01, 5.03]
1.4 Discectomy alone vs iliac crest autograft with plates	3	111	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.33, 3.21]
1.5 Autograft versus Allograft	4	220	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.34, 3.48]
1.6 Autograft vs autograft w cages	7	492	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.12, 0.92]

1.7 Iliac crest autograft vs iliac crest autograft and plates	3	136	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.37, 2.63]
1.8 Different types of autograft	1	46	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.05, 1.08]
1.9 Bone substitute vs bone substitute w cages	1	44	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 7.76]
1.10 Conservative instrumentation verus innovational instrumentation	10	704	Risk Ratio (M-H, Fixed, 95% CI)	0.10 [0.01, 1.85]

Analysis 1.1. Comparison 1 Discectomy alone vs human bone graft, Outcome 1 Hospital stay.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

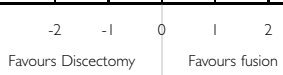
Comparison: 1 Discectomy alone vs human bone graft

Outcome: 1 Hospital stay

Study or subgroup	Discectomy N	Mean(SD)	Fusion N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Abd-Alrahman 1999	40	4.2 (0.8)	50	4.8 (1.4)		26.0 %	-0.51 [-0.93, -0.08]
Barlocher 2002	33	7.2 (2.1)	30	7.5 (1.8)		24.5 %	-0.15 [-0.65, 0.34]
Dowd 1999	44	3.6 (0.8)	40	5 (1.4)		25.0 %	-1.23 [-1.70, -0.76]
Rosenorn 1983	32	6 (2)	31	6 (6)		24.5 %	0.0 [-0.49, 0.49]
Total (95% CI)	**149**		**151**			**100.0 %**	**-0.48 [-1.01, 0.05]**

Heterogeneity: Tau² = 0.23; Chi² = 15.21, df = 3 (P = 0.002); I² =80%

Test for overall effect: Z = 1.77 (P = 0.076)



Analysis 1.2. Comparison 1 Discectomy alone vs human bone graft, Outcome 2 Operation time.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 1 Discectomy alone vs human bone graft

Outcome: 2 Operation time

Study or subgroup	Discectomy N	Mean(SD)	fusion N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Abd-Alrahman 1999	40	110 (29)	50	140 (34)		27.0 %	-30.00 [-43.02, -16.98]
Barlocher 2002	33	82.6 (11.2)	30	99.8 (9.8)		47.1 %	-17.20 [-22.39, -12.01]
Dowd 1999	44	102 (29)	40	131 (34)		25.9 %	-29.00 [-42.58, -15.42]
Total (95% CI)	**117**		**120**			**100.0 %**	**-23.71 [-33.21, -14.21]**

Heterogeneity: Tau² = 42.81; Chi² = 5.07, df = 2 (P = 0.08); I² =61%

Test for overall effect: Z = 4.89 (P < 0.00001)

Analysis 1.3. Comparison 1 Discectomy alone vs human bone graft, Outcome 3 Blood loss.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 1 Discectomy alone vs human bone graft

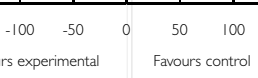
Outcome: 3 Blood loss

Study or subgroup	Discectomy N	Mean(SD)	Fusion N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Barlocher 2002	33	49.7 (12.6)	30	70.7 (17.8)		100.0 %	-21.00 [-28.68, -13.32]
Total (95% CI)	**33**		**30**			**100.0 %**	**-21.00 [-28.68, -13.32]**

Heterogeneity: not applicable

Test for overall effect: Z = 5.36 (P < 0.00001)

Test for subgroup differences: Not applicable

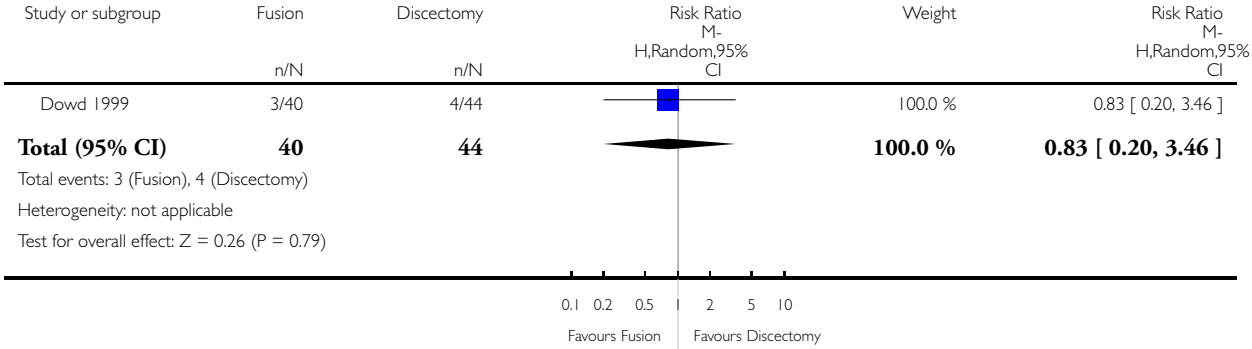


Analysis 1.4. Comparison 1 Discectomy alone vs human bone graft, Outcome 4 Pain not relieved at 5 weeks.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 1 Discectomy alone vs human bone graft

Outcome: 4 Pain not relieved at 5 weeks

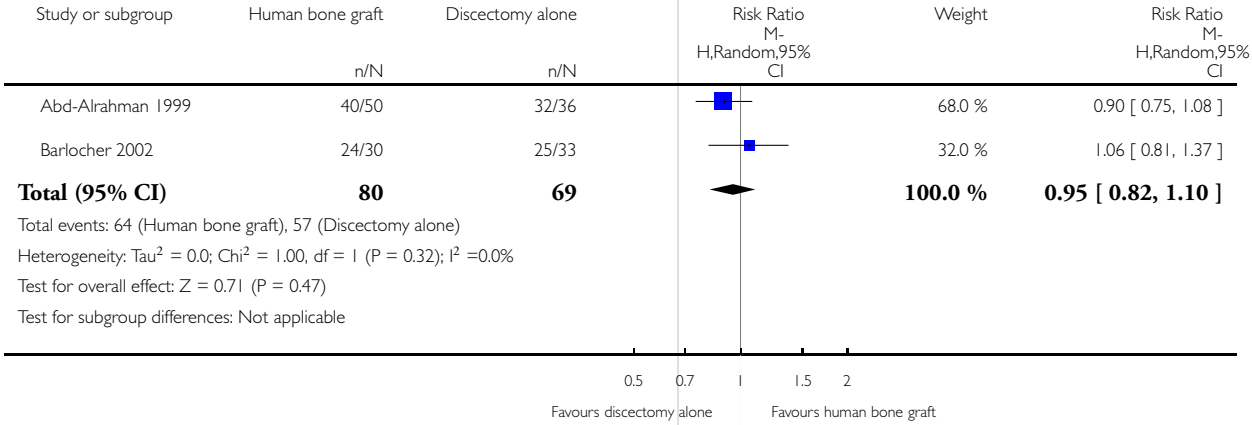


Analysis 1.5. Comparison 1 Discectomy alone vs human bone graft, Outcome 5 Odom's criteria.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 1 Discectomy alone vs human bone graft

Outcome: 5 Odom's criteria



Analysis 1.6. Comparison 1 Discectomy alone vs human bone graft, Outcome 6 Not Returned to work at 5 weeks.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 1 Discectomy alone vs human bone graft

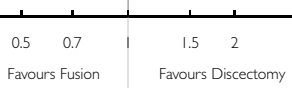
Outcome: 6 Not Returned to work at 5 weeks

Study or subgroup	Fusion n/N	Discectomy n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Dowd 1999	33/37	34/44		59.4 %	1.15 [0.95, 1.40]
Rosenorn 1983	29/31	21/32		40.6 %	1.43 [1.09, 1.86]
Total (95% CI)	**68**	**76**		**100.0 %**	**1.26 [1.02, 1.54]**

Total events: 62 (Fusion), 55 (Discectomy)

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 1.60$, df = 1 (P = 0.21); $I^2 = 38\%$

Test for overall effect: Z = 2.18 (P = 0.029)



Analysis 1.7. Comparison 1 Discectomy alone vs human bone graft, Outcome 7 Not Returned to work at 10 weeks.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 1 Discectomy alone vs human bone graft

Outcome: 7 Not Returned to work at 10 weeks

Study or subgroup	Fusion n/N	Discectomy n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Dowd 1999	23/33	20/32		58.5 %	1.12 [0.79, 1.58]
Rosenorn 1983	18/31	9/32		41.5 %	2.06 [1.10, 3.87]
Total (95% CI)	**64**	**64**		**100.0 %**	**1.44 [0.77, 2.69]**

Total events: 41 (Fusion), 29 (Discectomy)

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 3.10$, df = 1 (P = 0.08); $I^2 = 68\%$

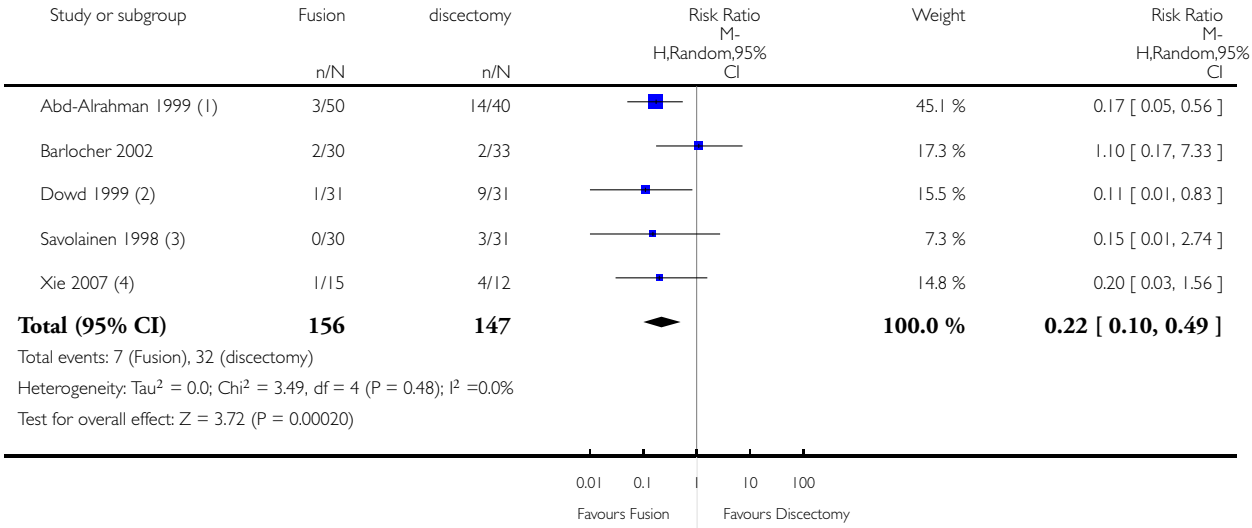
Test for overall effect: Z = 1.14 (P = 0.25)

Analysis 1.8. Comparison 1 Discectomy alone vs human bone graft, Outcome 8 No Fusion.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 1 Discectomy alone vs human bone graft

Outcome: 8 No Fusion



(1) 2 years

(2) 3 years

(3) 6 months

(4) 2 years

Analysis 1.9. Comparison 1 Discectomy alone vs human bone graft, Outcome 9 Alignment.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 1 Discectomy alone vs human bone graft

Outcome: 9 Alignment

Study or subgroup	Human bone graft n/N	Discectomy alone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Martins 1976	1/25	3/26		48.2 %	0.35 [0.04, 3.11]
Xie 2007	1/12	3/12		51.8 %	0.33 [0.04, 2.77]
Total (95% CI)	**37**	**38**		**100.0 %**	**0.34 [0.07, 1.56]**

Total events: 2 (Human bone graft), 6 (Discectomy alone)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 0.98); $I^2 = 0.0\%$

Test for overall effect: Z = 1.39 (P = 0.16)

Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 Discectomy alone vs cage or cement, Outcome 1 Operation time.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

Outcome: 1 Operation time

Study or subgroup	Cage or cement N	Mean(SD)	discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Discectomy alone vs cage							
Barlocher 2002	36	75.8 (14.8)	33	82.6 (11.2)		24.9 %	-6.80 [-12.96, -0.64]
Hauerberg 2008 (1)	40	60 (15)	46	55 (15)		24.8 %	5.00 [-1.36, 11.36]
Ruetten 2009 (2)	60	62 (15)	60	32 (8)		25.3 %	30.00 [25.70, 34.30]
Subtotal (95% CI)	**136**		**139**			**75.0 %**	**9.49 [-13.66, 32.64]**
Heterogeneity: $Tau^2 = 410.14$; $Chi^2 = 104.29$, df = 2 (P<0.00001); $I^2 = 98\%$							
Test for overall effect: Z = 0.80 (P = 0.42)							
2 Discectomy alone vs PMMA							
Barlocher 2002	26	89 (11.6)	33	82.6 (11.2)		25.0 %	6.40 [0.53, 12.27]
Subtotal (95% CI)	**26**		**33**			**25.0 %**	**6.40 [0.53, 12.27]**
(2) mean							

(*Continued . . .*)

(. . . *Continued*)

Study or subgroup	Cage or cement N	Mean(SD)	discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Heterogeneity: not applicable							
Test for overall effect: Z = 2.14 (P = 0.033)							
Total (95% CI)	**162**		**172**			**100.0 %**	**8.74 [-8.21, 25.69]**
Heterogeneity: Tau² = 290.70; Chi² = 110.59, df = 3 (P<0.00001); I² =97%							
Test for overall effect: Z = 1.01 (P = 0.31)							

-100 -50 0 50 100

Favours experimental Favours control

(1) Median

(2) mean

Analysis 2.2. Comparison 2 Discectomy alone vs cage or cement, Outcome 2 Blood loss.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

Outcome: 2 Blood loss

Study or subgroup	Solid spacer N	Mean(SD)	Discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Discectomy alone vs cage							
Barlocher 2002	36	62.8 (14.9)	33	49.7 (12.6)		60.4 %	13.10 [6.61, 19.59]
Subtotal (95% CI)	**36**		**33**			**60.4 %**	**13.10 [6.61, 19.59]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.95 (P = 0.000077)							
2 Discectomy alone vs PMMA							
Barlocher 2002	26	58.3 (17.6)	33	49.7 (12.6)		39.6 %	8.60 [0.58, 16.62]
Subtotal (95% CI)	**26**		**33**			**39.6 %**	**8.60 [0.58, 16.62]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.10 (P = 0.035)							
Total (95% CI)	**62**		**66**			**100.0 %**	**11.32 [6.27, 16.36]**
Heterogeneity: Tau² = 0.0; Chi² = 0.73, df = 1 (P = 0.39); I² =0.0%							
Test for overall effect: Z = 4.40 (P = 0.000011)							
Test for subgroup differences: Chi² = 0.73, df = 1 (P = 0.39), I² =0.0%							

-100 -50 0 50 100

Favours experimental Favours control

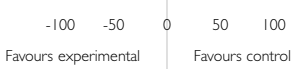
Analysis 2.3. Comparison 2 Discectomy alone vs cage or cement, Outcome 3 Length of stay.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

Outcome: 3 Length of stay

Study or subgroup	Solid spacer N	Mean(SD)	Discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Discectomy alone vs cage							
Barlocher 2002	26	7 (1.1)	33	7.6 (2.1)		52.4 %	-0.60 [-1.43, 0.23]
Subtotal (95% CI)	**26**		**33**			**52.4 %**	**-0.60 [-1.43, 0.23]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.41 (P = 0.16)							
2 Discectomy alone vs PMMA							
Barlocher 2002	26	6.8 (1.3)	33	7.6 (2.1)		47.6 %	-0.80 [-1.67, 0.07]
Subtotal (95% CI)	**26**		**33**			**47.6 %**	**-0.80 [-1.67, 0.07]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.79 (P = 0.073)							
Total (95% CI)	**52**		**66**			**100.0 %**	**-0.70 [-1.30, -0.09]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.11, df = 1 (P = 0.75); I^2 =0.0%							
Test for overall effect: Z = 2.26 (P = 0.024)							
Test for subgroup differences: Chi^2 = 0.11, df = 1 (P = 0.75), I^2 =0.0%							

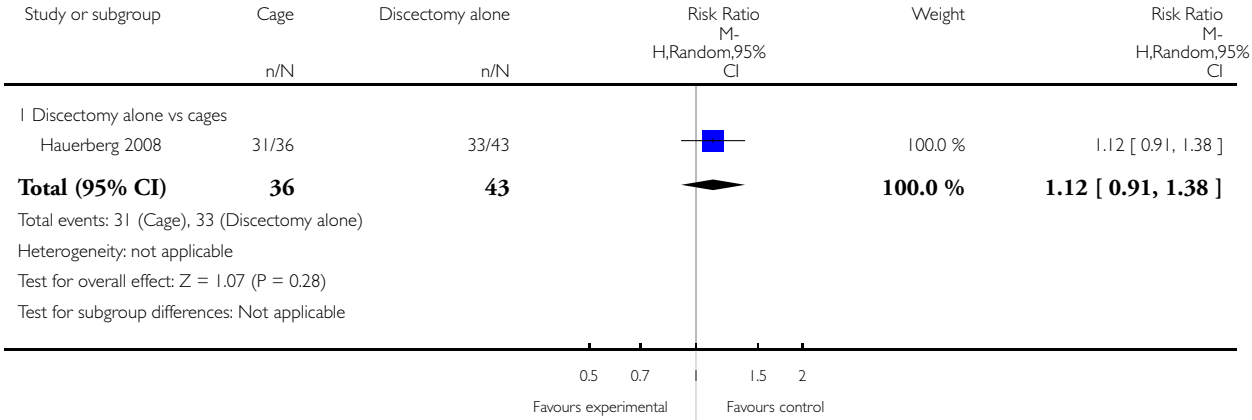


Analysis 2.4. Comparison 2 Discectomy alone vs cage or cement, Outcome 4 Recovery.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

Outcome: 4 Recovery

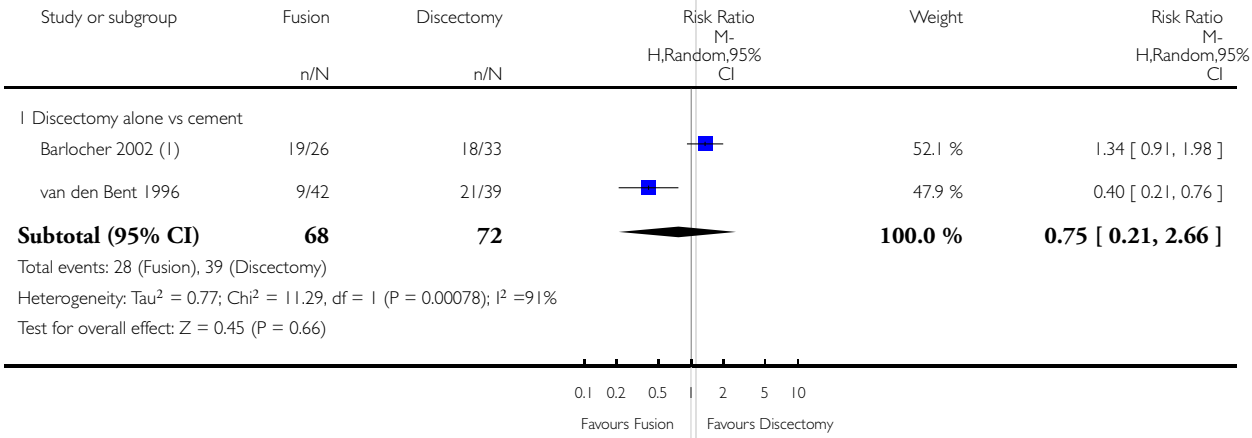


Analysis 2.5. Comparison 2 Discectomy alone vs cage or cement, Outcome 5 Neck pain not relieved at 6 weeks.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

Outcome: 5 Neck pain not relieved at 6 weeks



(1) 2 months

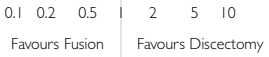
Analysis 2.6. Comparison 2 Discectomy alone vs cage or cement, Outcome 6 Neck pain not relieved at 2 years.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

Outcome: 6 Neck pain not relieved at 2 years

Study or subgroup	Fusion n/N	Discectomy n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Discectomy alone vs cement					
Barlocher 2002 (1)	9/24	12/33		38.9 %	1.03 [0.52, 2.05]
van den Bent 1996	16/39	15/39		61.1 %	1.07 [0.62, 1.84]
Subtotal (95% CI)	**63**	**72**		**100.0 %**	**1.05 [0.69, 1.61]**
Total events: 25 (Fusion), 27 (Discectomy)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.01$, df = 1 (P = 0.94); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.24 (P = 0.81)					



(1) 12 months

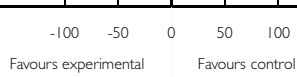
Analysis 2.7. Comparison 2 Discectomy alone vs cage or cement, Outcome 7 VAS Arm pain 24 months.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

Outcome: 7 VAS Arm pain 24 months

Study or subgroup	Cage N	Mean(SD)	Discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
1 Discectomy alone versus cage						
Ruetten 2009	49	10 (0)	54	8 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**49**		**54**			**0.0 [0.0, 0.0]**
Heterogeneity: not applicable						
Test for overall effect: Z = 0.0 (P < 0.00001)						
Test for subgroup differences: $Chi^2 = 0.0$, df = -1 (P = 0.0), $I^2 = 0.0\%$						



Analysis 2.8. Comparison 2 Discectomy alone vs cage or cement, Outcome 8 VAS Neck pain 24 months.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

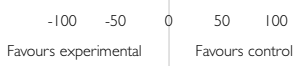
Outcome: 8 VAS Neck pain 24 months

Study or subgroup	solid spacer N	Mean(SD)	Discectomy N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
1 Discectomy alone versus cage						
Ruetten 2009	49	14 (0)	54	15 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**49**		**54**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Chi^2 = 0.0, df = -1 (P = 0.0), I^2 =0.0%



Analysis 2.9. Comparison 2 Discectomy alone vs cage or cement, Outcome 9 NASS pain 24 months.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

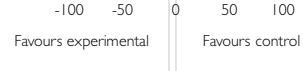
Outcome: 9 NASS pain 24 months

Study or subgroup	Solid spacer N	Mean(SD)	discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
1 Discectomy alone vs cage						
Ruetten 2009	49	1.6 (0)	54	1.5 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**49**		**54**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Chi^2 = 0.0, df = -1 (P = 0.0), I^2 =0.0%



Analysis 2.10. Comparison 2 Discectomy alone vs cage or cement, Outcome 10 NASS neurology 24 months.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 2 Discectomy alone vs cage or cement

Outcome: 10 NASS neurology 24 months

Study or subgroup	Solid spacer N	Mean(SD)	Discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
1 Discectomy alone versus cage						
Ruetten 2009	49	1.6 (0)	54	1.8 (0)		0.0 [0.0, 0.0]
Total (95% CI)	**49**		**54**			**0.0 [0.0, 0.0]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Chi^2 = 0.0, df = -1 (P = 0.0), I^2 =0.0%

Analysis 2.11. Comparison 2 Discectomy alone vs cage or cement, Outcome 11 No Fusion.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

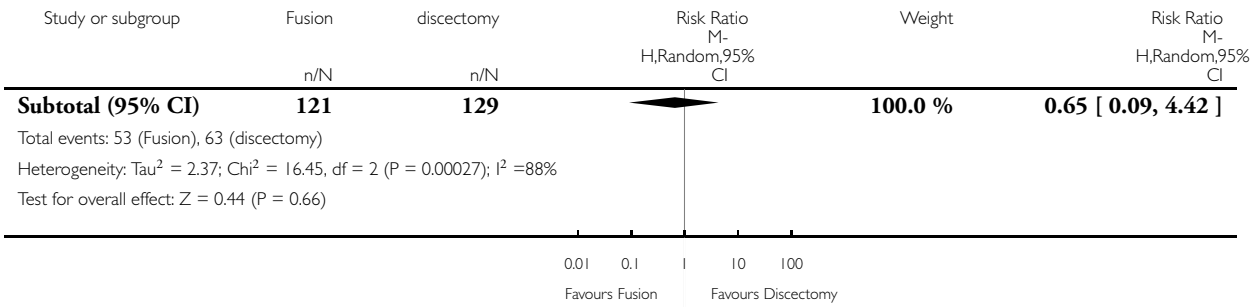
Comparison: 2 Discectomy alone vs cage or cement

Outcome: 11 No Fusion

Study or subgroup	Fusion n/N	discectomy n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Discectomy alone vs cement					
Barlocher 2002 (1)	24/24	2/33		46.6 %	13.33 [4.04, 44.01]
van den Bent 1996 (2)	28/39	13/35		53.4 %	1.93 [1.20, 3.10]
Subtotal (95% CI)	**63**	**68**		**100.0 %**	**4.75 [0.58, 38.67]**
Total events: 52 (Fusion), 15 (discectomy)					
Heterogeneity: Tau^2 = 2.08; Chi^2 = 10.69, df = 1 (P = 0.001); I^2 =91%					
Test for overall effect: Z = 1.46 (P = 0.15)					
2 Discectomy alone vs cage					
Barlocher 2002 (3)	1/36	2/33		25.2 %	0.46 [0.04, 4.82]
Hauerberg 2008 (4)	3/36	7/42		34.3 %	0.50 [0.14, 1.79]
Ruetten 2009 (5)	49/49	54/54		40.5 %	1.00 [0.96, 1.04]
(5) 121 months					

(*Continued* . . .)

(. . . *Continued*)



(1) 12 months

(2) 2 years, PMMA

(3) 12 months

(4) 2 years

(5) 121 months

Analysis 2.12. Comparison 2 Discectomy alone vs cage or cement, Outcome 12 Odom's criteria.

Odom's criteria

Study	Group	Excellent	Good	Fair	Poor
Discectomy alone vs cage					
Barlocher 2002	Discectomy	25			8
Barlocher 2002	Cage	34			2
Discectomy alone vs PMMA					
Barlocher 2002	Discectomy	25			8
Barlocher 2002	PMMA	21			3

Analysis 3.1. Comparison 3 Discectomy alone vs human bone graft with plates, Outcome 1 VAS Arm pain.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 3 Discectomy alone vs human bone graft with plates

Outcome: 1 VAS Arm pain

Study or subgroup	Bone graft with plates N	Mean(SD)	Discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Oktenoglu 2007	9	3.11 (0.78)	11	3.27 (0.79)		100.0 %	-0.16 [-0.85, 0.53]
Total (95% CI)	**9**		**11**			**100.0 %**	**-0.16 [-0.85, 0.53]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.45 (P = 0.65)

Test for subgroup differences: Not applicable

Analysis 3.2. Comparison 3 Discectomy alone vs human bone graft with plates, Outcome 2 VAS neck pain.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 3 Discectomy alone vs human bone graft with plates

Outcome: 2 VAS neck pain

Study or subgroup	Bone graft with plates N	Mean(SD)	Discectomy alone N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Oktenoglu 2007	9	2 (0.5)	11	2.81 (0.87)		100.0 %	-0.81 [-1.42, -0.20]
Total (95% CI)	**9**		**11**			**100.0 %**	**-0.81 [-1.42, -0.20]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.61 (P = 0.0092)

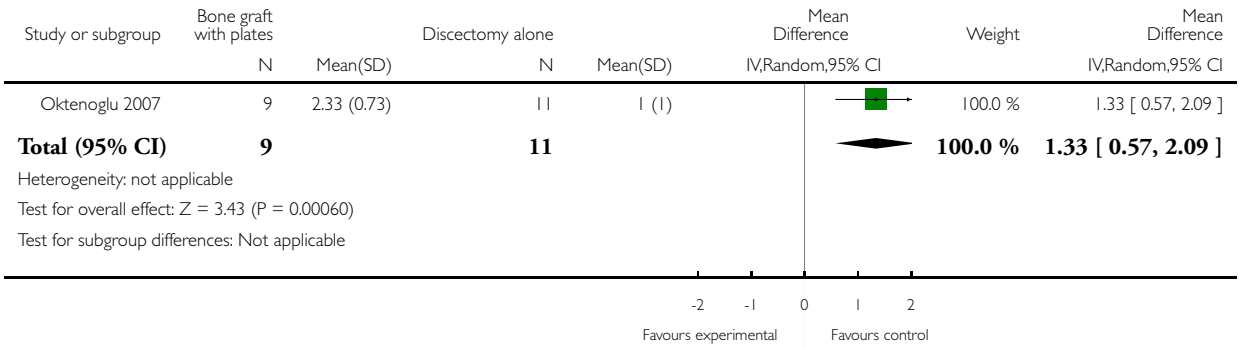
Test for subgroup differences: Not applicable

Analysis 3.3. Comparison 3 Discectomy alone vs human bone graft with plates, Outcome 3 Disc height.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 3 Discectomy alone vs human bone graft with plates

Outcome: 3 Disc height

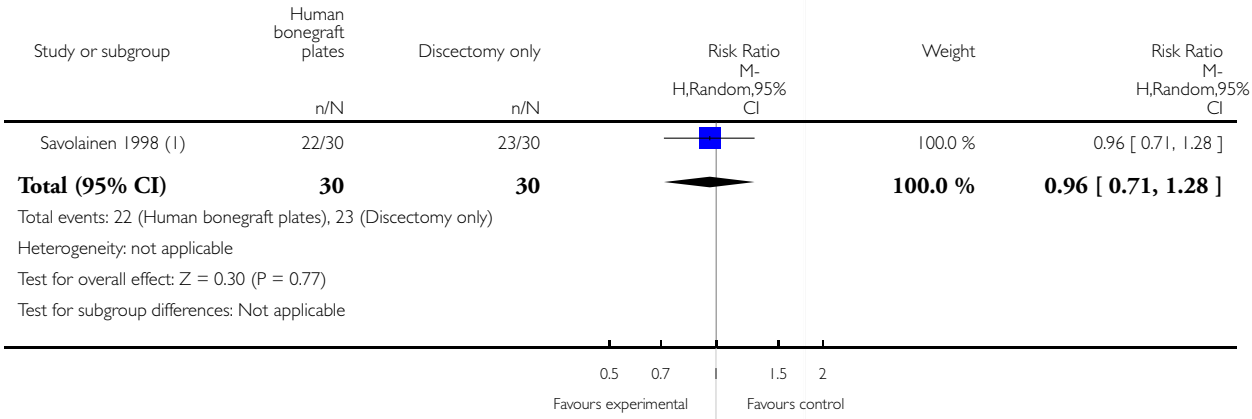


Analysis 3.4. Comparison 3 Discectomy alone vs human bone graft with plates, Outcome 4 Odoms criteria.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 3 Discectomy alone vs human bone graft with plates

Outcome: 4 Odoms criteria



(1) 4 years

Analysis 3.5. Comparison 3 Discectomy alone vs human bone graft with plates, Outcome 5 Fusion.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 3 Discectomy alone vs human bone graft with plates

Outcome: 5 Fusion

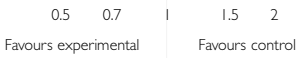
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Savolainen 1998 (1)	25/25	24/24		73.8 %	1.00 [0.93, 1.08]
Xie 2007 (2)	14/15	8/12		26.2 %	1.40 [0.92, 2.14]
Total (95% CI)	**40**	**36**		**100.0 %**	**1.10 [0.96, 1.27]**

Total events: 39 (Experimental), 32 (Control)

Heterogeneity: $Chi^2 = 7.55$, df = 1 (P = 0.01); $I^2 = 87\%$

Test for overall effect: Z = 1.44 (P = 0.15)

Test for subgroup differences: Not applicable



(1) 4 years

(2) 24 months

Analysis 4.1. Comparison 4 Iliac crest autograft vs human allograft or bone substitute, Outcome 1 headache.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 4 Iliac crest autograft vs human allograft or bone substitute

Outcome: 1 headache

Study or subgroup	Autograft N	Mean(SD)	Allograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Lofgren 2000	13	74 (18)	14	56 (17)		100.0 %	18.00 [4.77, 31.23]
Total (95% CI)	**13**		**14**			**100.0 %**	**18.00 [4.77, 31.23]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.67 (P = 0.0077)

Analysis 4.2. Comparison 4 Iliac crest autograft vs human allograft or bone substitute, Outcome 2 Sensory function.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 4 Iliac crest autograft vs human allograft or bone substitute

Outcome: 2 Sensory function

Study or subgroup	Autograft N	Mean(SD)	Allograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Lofgren 2000	13	87 (12.5)	14	72 (21)		100.0 %	15.00 [2.07, 27.93]
Total (95% CI)	**13**		**14**			**100.0 %**	**15.00 [2.07, 27.93]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.27 (P = 0.023)

Analysis 4.3. Comparison 4 Iliac crest autograft vs human allograft or bone substitute, Outcome 3 Muscle power.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 4 Iliac crest autograft vs human allograft or bone substitute

Outcome: 3 Muscle power

Study or subgroup	Autograft N	Mean(SD)	Allograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Lofgren 2000	13	83 (18)	14	56 (23)		100.0 %	27.00 [11.48, 42.52]
Total (95% CI)	**13**		**14**			**100.0 %**	**27.00 [11.48, 42.52]**

Heterogeneity: not applicable

Test for overall effect: Z = 3.41 (P = 0.00065)

Analysis 4.4. Comparison 4 Iliac crest autograft vs human allograft or bone substitute, Outcome 4 Odoms criteria.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 4 Iliac crest autograft vs human allograft or bone substitute

Outcome: 4 Odoms criteria

Study or subgroup	BOP n/N	Autograft n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Madawi 1996	49/65	40/50		100.0 %	0.94 [0.77, 1.15]
Total (95% CI)	**65**	**50**		**100.0 %**	**0.94 [0.77, 1.15]**

Total events: 49 (BOP), 40 (Autograft)

Heterogeneity: not applicable

Test for overall effect: Z = 0.59 (P = 0.55)

Analysis 5.1. Comparison 5 Iliac crest autograft vs cage, Outcome 1 Operation time.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

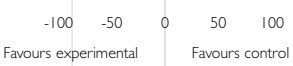
Comparison: 5 Iliac crest autograft vs cage

Outcome: 1 Operation time

Study or subgroup	Cage N	Cage Mean(SD)	Iliac crest autograft N	Iliac crest autograft Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Barlocher 2002	36	75.8 (14.8)	30	99.8 (9.8)		34.1 %	-24.00 [-29.97, -18.03]
Hacker 2000	37	58.1 (15.3)	17	55.7 (10.8)		33.5 %	2.40 [-4.72, 9.52]
Lofgren 2010	40	100 (18)	40	118 (23)		32.3 %	-18.00 [-27.05, -8.95]
Total (95% CI)	**113**		**87**			**100.0 %**	**-13.21 [-29.99, 3.57]**

Heterogeneity: $Tau^2 = 205.47$; $Chi^2 = 31.91$, df = 2 (P<0.00001); $I^2 = 94\%$

Test for overall effect: Z = 1.54 (P = 0.12)



Analysis 5.2. Comparison 5 Iliac crest autograft vs cage, Outcome 2 Blood loss.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

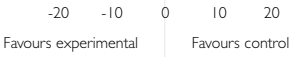
Outcome: 2 Blood loss

Study or subgroup	cage		Iliac crest autograft		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Barlocher 2002	36	62.8 (14.9)	30	70.7 (17.8)		81.9 %	-7.90 [-15.92, 0.12]
Hacker 2000	37	70.7 (30.2)	17	79.4 (29.4)		18.1 %	-8.70 [-25.73, 8.33]
Total (95% CI)	**73**		**47**			**100.0 %**	**-8.05 [-15.30, -0.79]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.01$, df = 1 (P = 0.93); $I^2 = 0.0\%$

Test for overall effect: Z = 2.17 (P = 0.030)

Test for subgroup differences: Not applicable



Analysis 5.3. Comparison 5 Iliac crest autograft vs cage, Outcome 3 Hospital stay.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

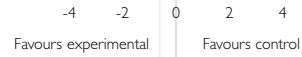
Outcome: 3 Hospital stay

Study or subgroup	Cage		Iliac crest autograft		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Barlocher 2002	36	7 (1.1)	30	7.5 (1.8)		33.4 %	-0.50 [-1.24, 0.24]
Celik 2007	35	2.3 (1.7)	30	2.4 (2.1)		20.6 %	-0.10 [-1.04, 0.84]
Lofgren 2010	40	3.6 (1.1)	40	4.1 (1.7)		46.1 %	-0.50 [-1.13, 0.13]
Total (95% CI)	**111**		**100**			**100.0 %**	**-0.42 [-0.84, 0.01]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.55$, df = 2 (P = 0.76); $I^2 = 0.0\%$

Test for overall effect: Z = 1.92 (P = 0.055)

Test for subgroup differences: Not applicable



Analysis 5.4. Comparison 5 Iliac crest autograft vs cage, Outcome 4 VAS Neck Pain.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

Outcome: 4 VAS Neck Pain

Study or subgroup	Cage N	Mean(SD)	Iliac crest autograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Lofgren 2010 (1)	40	4.1 (2)	40	2.4 (2.2)		32.7 %	1.70 [0.78, 2.62]
Thome 2006 (2)	50	1.9 (2.1)	50	2.7 (2.5)		32.9 %	-0.80 [-1.70, 0.10]
Vavruch 2002 (3)	47	3.9 (1.9)	48	3.6 (1.9)		34.4 %	0.30 [-0.46, 1.06]
Total (95% CI)	**137**		**138**			**100.0 %**	**0.40 [-0.94, 1.73]**

Heterogeneity: Tau² = 1.20; Chi² = 14.46, df = 2 (P = 0.00073); I² =86%

Test for overall effect: Z = 0.58 (P = 0.56)

Test for subgroup differences: Not applicable

(1) Median, sd estimated from other studies, 2 years

(2) 12 months

(3) pain right now, SD estimated from other studies, 2 years

Analysis 5.5. Comparison 5 Iliac crest autograft vs cage, Outcome 5 VAS Arm pain.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

Outcome: 5 VAS Arm pain

Study or subgroup	Cage N	Mean(SD)	Iliac crest autograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Lofgren 2010 (1)	40	2.4 (2)	40	2.8 (2.2)		44.4 %	-0.40 [-1.32, 0.52]
Thome 2006	50	1.1 (2)	50	1.3 (2.2)		55.6 %	-0.20 [-1.02, 0.62]
Total (95% CI)	**90**		**90**			**100.0 %**	**-0.29 [-0.90, 0.33]**

Heterogeneity: Tau² = 0.0; Chi² = 0.10, df = 1 (P = 0.75); I² =0.0%

Test for overall effect: Z = 0.92 (P = 0.36)

Test for subgroup differences: Not applicable

(1) 2 years, sd estimated from Thome

Analysis 5.6. Comparison 5 Iliac crest autograft vs cage, Outcome 6 Neck Disability Index (NDI).

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

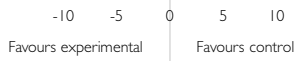
Outcome: 6 Neck Disability Index (NDI)

Study or subgroup	Cage		Iliac crest autograft		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Lofgren 2010 (1)	40	30 (6.75)	40	25 (6.75)		49.6 %	5.00 [2.04, 7.96]
Vavruch 2002 (2)	47	27 (6.75)	48	29 (6.75)		50.4 %	-2.00 [-4.71, 0.71]
Total (95% CI)	**87**		**88**			**100.0 %**	**1.47 [-5.39, 8.33]**

Heterogeneity: $Tau^2 = 22.40$; $Chi^2 = 11.68$, df = 1 (P = 0.00063); $I^2 = 91\%$

Test for overall effect: Z = 0.42 (P = 0.67)

Test for subgroup differences: Not applicable



(1) 2 years, sd estimated from Vavruch

(2) 2 years, SD estimated from other study

Analysis 5.7. Comparison 5 Iliac crest autograft vs cage, Outcome 7 JOA.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

Outcome: 7 JOA

Study or subgroup	Cage		Iliac crest autograft		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Thome 2006	50	15.7 (1.6)	50	15.8 (1.9)		100.0 %	-0.10 [-0.79, 0.59]
Total (95% CI)	**50**		**50**			**100.0 %**	**-0.10 [-0.79, 0.59]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.28 (P = 0.78)

Test for subgroup differences: Not applicable

Analysis 5.8. Comparison 5 Iliac crest autograft vs cage, Outcome 8 Odom's criteria.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

Outcome: 8 Odom's criteria

Study or subgroup	Cage n/N	Iliac crest autograft n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Barlocher 2002 (1)	35/36	24/30		18.5 %	1.22 [1.01, 1.47]
Hacker 2000 (2)	36/37	15/17		14.5 %	1.10 [0.92, 1.32]
Lind 2007	10/11	7/11		4.9 %	1.43 [0.88, 2.32]
Lofgren 2010 (3)	31/40	30/40		21.1 %	1.03 [0.81, 1.32]
Thome 2006	38/48	35/47		24.9 %	1.06 [0.85, 1.33]
Vavruch 2002 (4)	24/47	23/48		16.0 %	1.07 [0.71, 1.60]
Total (95% CI)	**219**	**193**		**100.0 %**	**1.11 [0.99, 1.24]**

Total events: 174 (Cage), 134 (Iliac crest autograft)

Heterogeneity: Chi^2 = 2.47, df = 5 (P = 0.78); I^2 =0.0%

Test for overall effect: Z = 1.83 (P = 0.067)

Test for subgroup differences: Not applicable

(1) 12 months

(2) Adapted Odom

(3) (adapted) Odom; 2 years

(4) 2 years

Analysis 5.9. Comparison 5 Iliac crest autograft vs cage, Outcome 9 SF-36 Physical.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

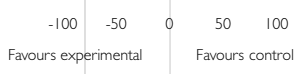
Outcome: 9 SF-36 Physical

Study or subgroup	Cage N	Mean(SD)	Iliac crest autograft N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hacker 2000	37	45.2 (12.1)	17	42.9 (11.9)		100.0 %	2.30 [-4.57, 9.17]
Total (95% CI)	**37**		**17**			**100.0 %**	**2.30 [-4.57, 9.17]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.66 (P = 0.51)

Test for subgroup differences: Not applicable



Analysis 5.10. Comparison 5 Iliac crest autograft vs cage, Outcome 10 SF-36 Mental.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

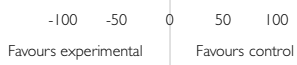
Outcome: 10 SF-36 Mental

Study or subgroup	Cage N	Mean(SD)	Iliac crest autograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Hacker 2000	37	51.7 (8.6)	17	45.9 (13.8)		100.0 %	5.80 [-1.32, 12.92]
Total (95% CI)	**37**		**17**			**100.0 %**	**5.80 [-1.32, 12.92]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.60 (P = 0.11)

Test for subgroup differences: Not applicable



Analysis 5.11. Comparison 5 Iliac crest autograft vs cage, Outcome 11 Satisfaction.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

Outcome: 11 Satisfaction

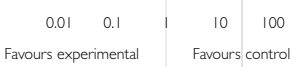
Study or subgroup	Cage n/N	Iliac crest autograft n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Hacker 2000	271/346	114/142		100.0 %	0.98 [0.88, 1.08]
Total (95% CI)	**346**	**142**		**100.0 %**	**0.98 [0.88, 1.08]**

Total events: 271 (Cage), 114 (Iliac crest autograft)

Heterogeneity: not applicable

Test for overall effect: Z = 0.49 (P = 0.62)

Test for subgroup differences: Not applicable



Analysis 5.12. Comparison 5 Iliac crest autograft vs cage, Outcome 12 Foraminal height.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

Outcome: 12 Foraminal height

Study or subgroup	Cage N	Mean(SD)	Autograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Celik 2007 (1)	35	9.6 (1.2)	30	8.1 (1.5)		100.0 %	1.50 [0.83, 2.17]
Total (95% CI)	**35**		**30**			**100.0 %**	**1.50 [0.83, 2.17]**

Heterogeneity: not applicable

Test for overall effect: Z = 4.40 (P = 0.000011)

Test for subgroup differences: Not applicable

(1) 18 months

Analysis 5.13. Comparison 5 Iliac crest autograft vs cage, Outcome 13 Interspace height.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

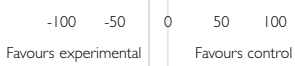
Outcome: 13 Interspace height

Study or subgroup	Cage N	Mean(SD)	Iliac crest autograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Celik 2007	35	4.5 (1.2)	30	2.6 (1.7)		100.0 %	1.90 [1.17, 2.63]
Total (95% CI)	**35**		**30**			**100.0 %**	**1.90 [1.17, 2.63]**

Heterogeneity: not applicable

Test for overall effect: Z = 5.12 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 5.14. Comparison 5 Iliac crest autograft vs cage, Outcome 14 Cobb angle.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

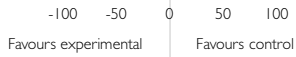
Outcome: 14 Cobb angle

Study or subgroup	Cage N	Mean(SD)	Iliac crest autograft N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Celik 2007 (1)	35	12.6 (3.2)	30	11.8 (3.8)		100.0 %	0.80 [-0.92, 2.52]
Total (95% CI)	**35**		**30**			**100.0 %**	**0.80 [-0.92, 2.52]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.91 (P = 0.36)

Test for subgroup differences: Not applicable



(1) 18 months

Analysis 5.15. Comparison 5 Iliac crest autograft vs cage, Outcome 15 No Fusion.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 5 Iliac crest autograft vs cage

Outcome: 15 No Fusion

Study or subgroup	Cage n/N	Iliac crest autograft n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Barlocher 2002 (1)	1/36	2/30		4.9 %	0.42 [0.04, 4.37]
Hacker 2000 (2)	3/45	1/19		5.5 %	1.27 [0.14, 11.42]
Lofgren 2010 (3)	12/39	3/39		17.2 %	4.00 [1.22, 13.08]
Thome 2006 (4)	16/63	12/64		41.7 %	1.35 [0.70, 2.63]
Vavruch 2002 (5)	18/48	6/41		30.7 %	2.56 [1.12, 5.84]
Total (95% CI)	**231**	**193**		**100.0 %**	**1.87 [1.10, 3.17]**

Total events: 50 (Cage), 24 (Iliac crest autograft)

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 4.75$, df = 4 (P = 0.31); $I^2 = 16\%$

Test for overall effect: Z = 2.31 (P = 0.021)

(1) 12 months

(2) 24 months

(3) 24 months

(4) 12 months

(5) 36 months, unclear if this concerns levels or patients

Analysis 6.1. Comparison 6 Iliac crest autograft vs iliac crest autograft with plates, Outcome 1 Clinical outcome.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 6 Iliac crest autograft vs iliac crest autograft with plates

Outcome: 1 Clinical outcome

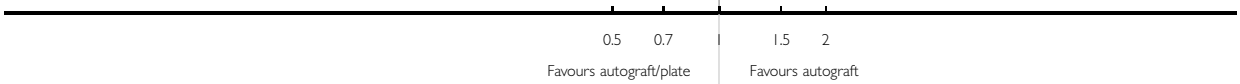
Study or subgroup	Autograft n/N	Autograft with Plate n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Savolainen 1998 (1)	23/28	22/30		57.6 %	1.12 [0.85, 1.48]
Zoega 2000 (2)	19/24	15/22		42.4 %	1.16 [0.82, 1.65]
Total (95% CI)	**52**	**52**		**100.0 %**	**1.14 [0.91, 1.41]**

Total events: 42 (Autograft), 37 (Autograft with Plate)

Heterogeneity: $Chi^2 = 0.03$, df = 1 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 1.16 (P = 0.25)

Test for subgroup differences: Not applicable



(1) 4 years

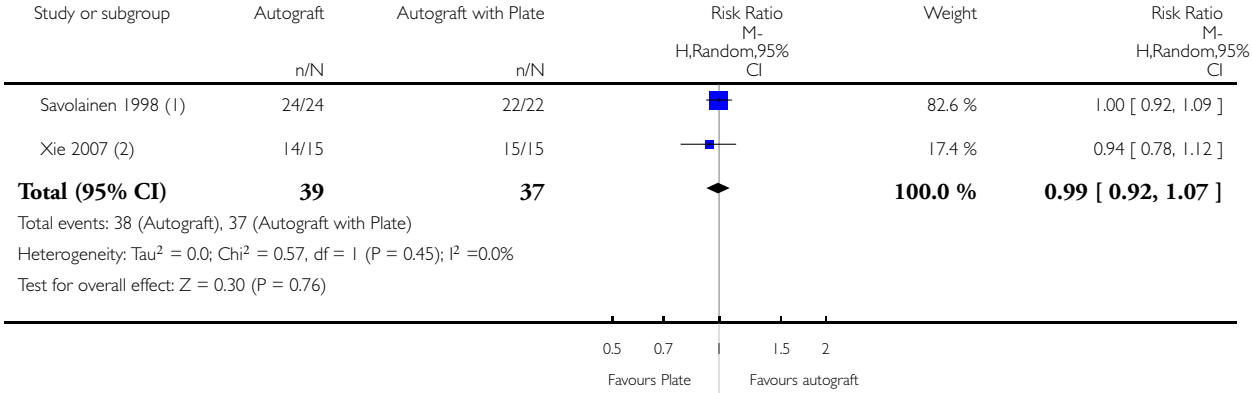
(2) Odoms criteria

Analysis 6.2. Comparison 6 Iliac crest autograft vs iliac crest autograft with plates, Outcome 2 No Fusion.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 6 Iliac crest autograft vs iliac crest autograft with plates

Outcome: 2 No Fusion



(1) 4 years

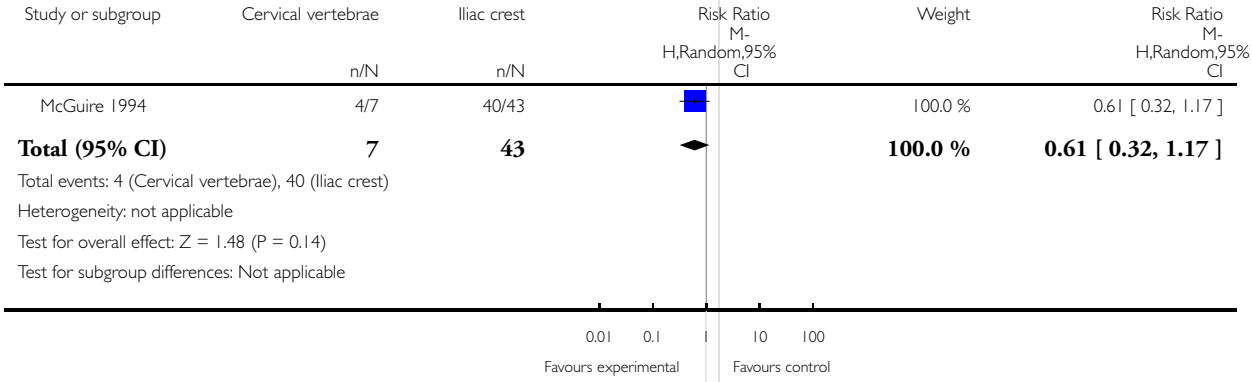
(2) 2 years

Analysis 7.1. Comparison 7 Different types of autograft, Outcome 1 Fusion.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 7 Different types of autograft

Outcome: 1 Fusion

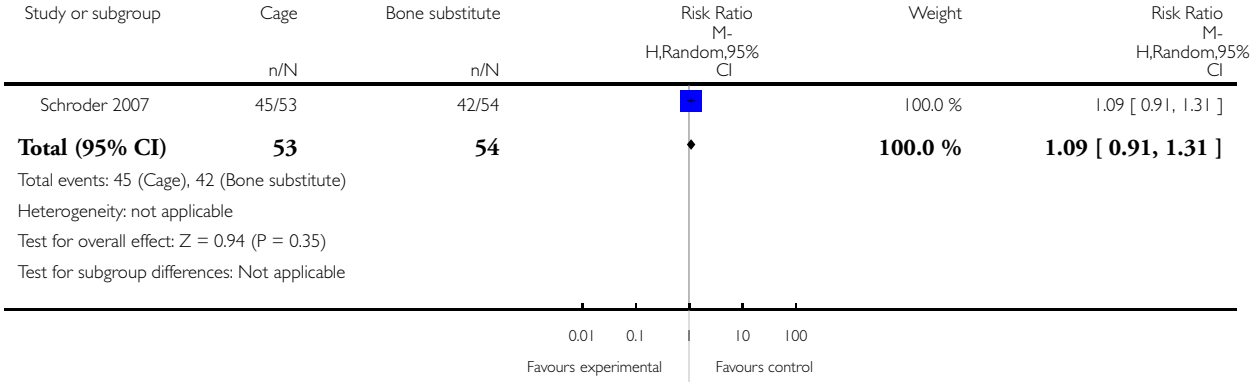


Analysis 9.1. Comparison 9 Other comparisons between different types of instrumentation, Outcome 1 Odom's criteria.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 9 Other comparisons between different types of instrumentation

Outcome: 1 Odom's criteria

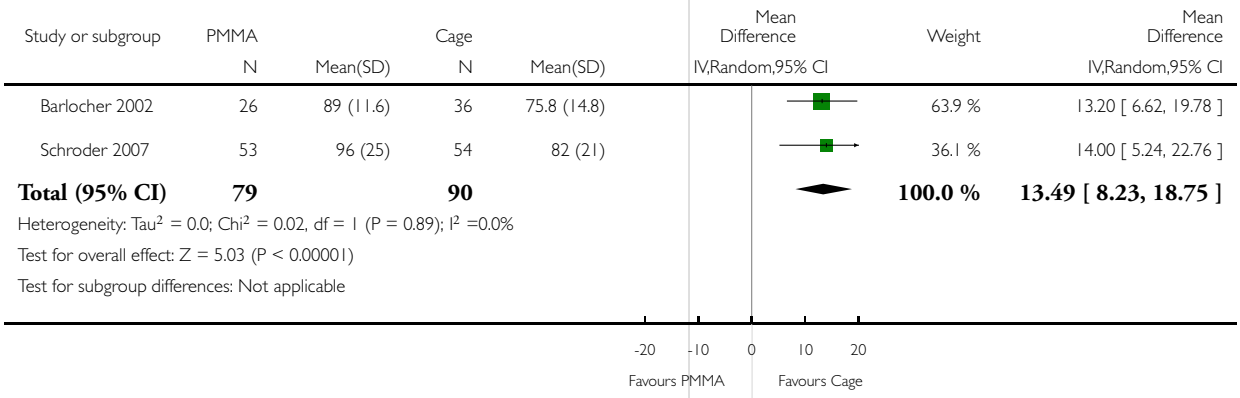


Analysis 10.1. Comparison 10 PMMA vs cage, Outcome 1 Operation time.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 10 PMMA vs cage

Outcome: 1 Operation time

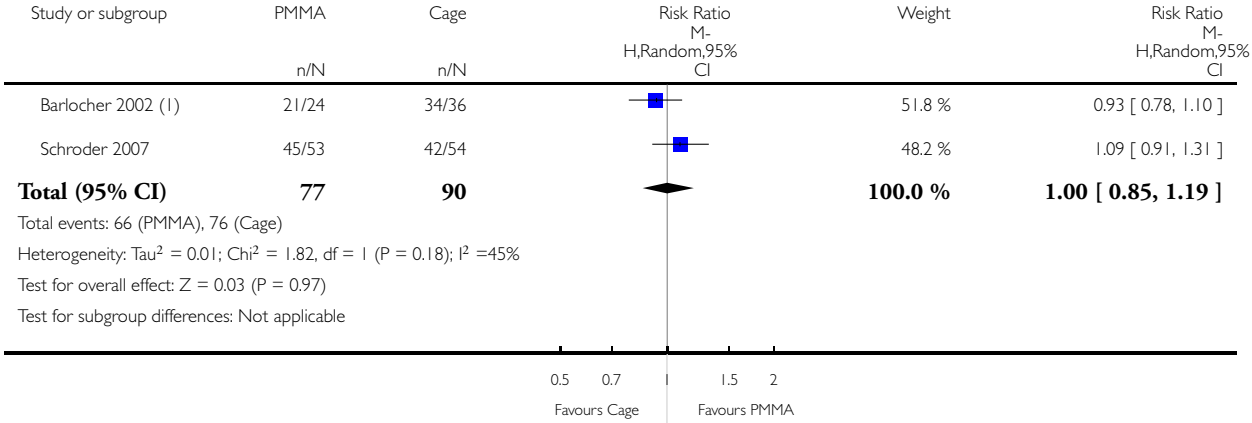


Analysis 10.2. Comparison 10 PMMA vs cage, Outcome 2 Odoms criteria.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 10 PMMA vs cage

Outcome: 2 Odoms criteria



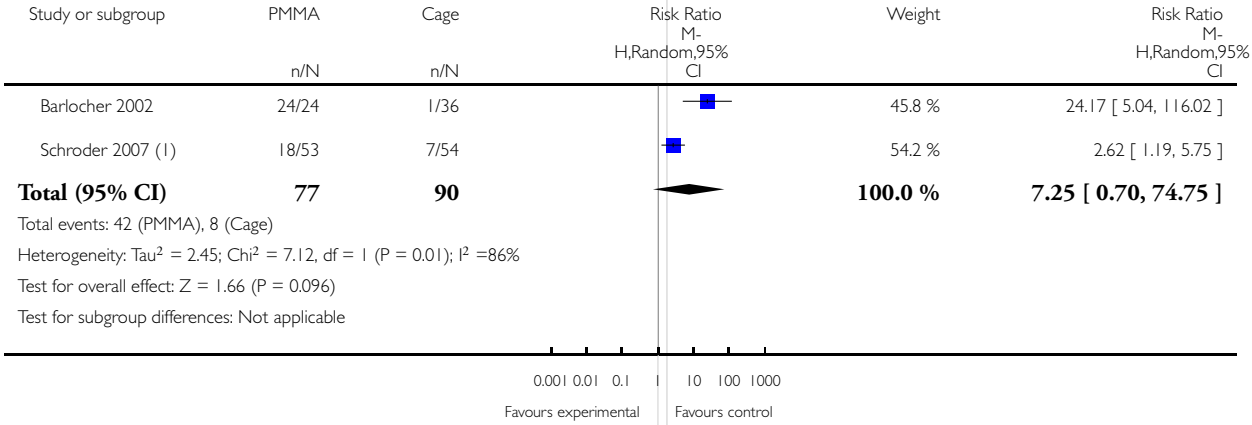
(1) 12 months

Analysis 10.3. Comparison 10 PMMA vs cage, Outcome 3 No Fusion.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 10 PMMA vs cage

Outcome: 3 No Fusion



(1) 24 months

Analysis 11.1. Comparison 11 Cage vs cage and plate, Outcome 1 Neck pain.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 11 Cage vs cage and plate

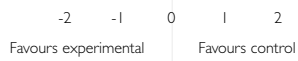
Outcome: 1 Neck pain

Study or subgroup	Cage and plate N	Mean(SD)	Cage N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Nabhan 2007 (1)	18	2 (0.5)	19	1.7 (0.3)		100.0 %	0.30 [0.03, 0.57]
Total (95% CI)	**18**		**19**			**100.0 %**	**0.30 [0.03, 0.57]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.20 (P = 0.028)

Test for subgroup differences: Not applicable



(1) 24 months

Analysis 11.2. Comparison 11 Cage vs cage and plate, Outcome 2 Arm pain.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 11 Cage vs cage and plate

Outcome: 2 Arm pain

Study or subgroup	Plate N	Mean(SD)	cage N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Nabhan 2007 (1)	18	1.5 (0.2)	19	2.1 (0.4)		100.0 %	-0.60 [-0.80, -0.40]
Total (95% CI)	**18**		**19**			**100.0 %**	**-0.60 [-0.80, -0.40]**

Heterogeneity: not applicable

Test for overall effect: Z = 5.82 (P < 0.00001)

Test for subgroup differences: Not applicable

(1) 2 years

Analysis 11.3. Comparison 11 Cage vs cage and plate, Outcome 3 JOA.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 11 Cage vs cage and plate

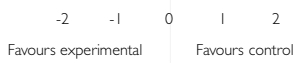
Outcome: 3 JOA

Study or subgroup	cage and Plate N	Mean(SD)	Cage N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Dai 2008	33	14.3 (2.7)	29	13.8 (1.9)		100.0 %	0.50 [-0.65, 1.65]
Total (95% CI)	**33**		**29**			**100.0 %**	**0.50 [-0.65, 1.65]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.85 (P = 0.39)

Test for subgroup differences: Not applicable



Analysis 11.4. Comparison 11 Cage vs cage and plate, Outcome 4 Segmental lordosis.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 11 Cage vs cage and plate

Outcome: 4 Segmental lordosis

Study or subgroup	Cage and plate N	Mean(SD)	cage N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Dai 2008	33	3.2 (4.6)	29	3.8 (4.8)		100.0 %	-0.60 [-2.95, 1.75]
Total (95% CI)	**33**		**29**			**100.0 %**	**-0.60 [-2.95, 1.75]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.50 (P = 0.62)

Test for subgroup differences: Not applicable

Analysis 12.1. Comparison 12 Complications, Outcome 1 complications.

Review: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease

Comparison: 12 Complications

Outcome: 1 complications

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Discectomy alone versus human bone graft				
Abd-Alrahman 1999 (1)	2/50	0/40		4.02 [0.20, 81.42]
Barlocher 2002 (2)	4/30	2/33		2.20 [0.43, 11.16]
Dowd 1999 (3)	1/40	2/44		0.55 [0.05, 5.84]
Martins 1976 (4)	0/26	1/25		0.32 [0.01, 7.53]
Rosenorn 1983 (5)	0/31	0/32		0.0 [0.0, 0.0]
Savolainen 1998 (6)	5/30	3/31		1.72 [0.45, 6.58]
Xie 2007 (7)	1/15	0/15		3.00 [0.13, 68.26]
Subtotal (95% CI)	**222**	**220**		**1.56 [0.71, 3.43]**
Total events: 13 (Experimental), 8 (Control)				
Heterogeneity: Chi^2 = 2.45, df = 5 (P = 0.78); I^2 =0.0%				
Test for overall effect: Z = 1.10 (P = 0.27)				
2 Discectomy alone vs cage				
Barlocher 2002 (8)	0/36	2/33		0.18 [0.01, 3.69]
Hauerberg 2008 (9)	0/41	0/47		0.0 [0.0, 0.0]
Ruetten 2009 (10)	0/49	0/54		0.0 [0.0, 0.0]
Subtotal (95% CI)	**126**	**134**		**0.18 [0.01, 3.69]**
Total events: 0 (Experimental), 2 (Control)				
Heterogeneity: Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 1.11 (P = 0.27)				
3 Discectomy alone vs PMMA				
Barlocher 2002 (11)	0/26	2/33		0.25 [0.01, 5.03]
van den Bent 1996	0/42	0/39		0.0 [0.0, 0.0]
Subtotal (95% CI)	**68**	**72**		**0.25 [0.01, 5.03]**
Total events: 0 (Experimental), 2 (Control)				
Heterogeneity: Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 0.90 (P = 0.37)				
4 Discectomy alone vs iliac crest autograft with plates				
Oktenoglu 2007 (12)	0/9	0/11		0.0 [0.0, 0.0]
Savolainen 1998 (13)	5/30	5/31		1.03 [0.33, 3.21]
Xie 2007 (14)	0/15	0/15		0.0 [0.0, 0.0]
Subtotal (95% CI)	**54**	**57**		**1.03 [0.33, 3.21]**
Total events: 5 (Experimental), 5 (Control)				
(38) Rigid plate 4 hardware failures				

(*Continued . . .*)

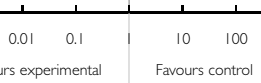
(. . . *Continued*)

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Heterogeneity: Chi² = 0.0, df = 0 (P = 1.00); I² =0.0%				
Test for overall effect: Z = 0.06 (P = 0.95)				
5 Autograft versus Allograft				
Baskin 2003	1/18	0/15		2.53 [0.11, 57.83]
Lofgren 2000 (15)	3/28	1/15		1.61 [0.18, 14.14]
Madawi 1996 (16)	0/65	2/50		0.15 [0.01, 3.15]
McConnel 2003	1/13	0/16		3.64 [0.16, 82.62]
Subtotal (95% CI)	**124**	**96**		**1.08 [0.34, 3.48]**
Total events: 5 (Experimental), 3 (Control)				
Heterogeneity: Chi² = 2.59, df = 3 (P = 0.46); I² =0.0%				
Test for overall effect: Z = 0.14 (P = 0.89)				
6 Autograft vs autograft w cages				
Barlocher 2002 (17)	0/36	4/30		0.09 [0.01, 1.66]
Celik 2007 (18)	0/35	0/30		0.0 [0.0, 0.0]
Hacker 2000 (19)	1/37	1/17		0.46 [0.03, 6.92]
Lind 2007 (20)	1/12	0/12		3.00 [0.13, 67.06]
Lofgren 2010 (21)	1/40	3/40		0.33 [0.04, 3.07]
Thome 2006 (22)	0/50	2/50		0.20 [0.01, 4.06]
Vavruch 2002 (23)	0/52	1/51		0.33 [0.01, 7.85]
Subtotal (95% CI)	**262**	**230**		**0.33 [0.12, 0.92]**
Total events: 3 (Experimental), 11 (Control)				
Heterogeneity: Chi² = 2.84, df = 5 (P = 0.72); I² =0.0%				
Test for overall effect: Z = 2.11 (P = 0.035)				
7 Iliac crest autograft vs iliac crest autograft and plates				
Savolainen 1998 (24)	5/30	5/30		1.00 [0.32, 3.10]
Xie 2007 (25)	0/15	1/15		0.33 [0.01, 7.58]
Zoega 2000 (26)	1/24	0/22		2.76 [0.12, 64.41]
Subtotal (95% CI)	**69**	**67**		**0.99 [0.37, 2.63]**
Total events: 6 (Experimental), 6 (Control)				
Heterogeneity: Chi² = 0.87, df = 2 (P = 0.65); I² =0.0%				
Test for overall effect: Z = 0.02 (P = 0.98)				
8 Different types of autograft				
McGuire 1994 (27)	3/40	2/6		0.23 [0.05, 1.08]
Subtotal (95% CI)	**40**	**6**		**0.23 [0.05, 1.08]**
Total events: 3 (Experimental), 2 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.86 (P = 0.063)				
9 Bone substitute vs bone substitute w cages				
Porras-Estrada 2004 (28)	0/22	1/22		0.33 [0.01, 7.76]
Subtotal (95% CI)	**22**	**22**		**0.33 [0.01, 7.76]**
(38) Rigid plate 4 hardware failures				

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Total events: 0 (Experimental), 1 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.68 (P = 0.49)				
10 Conservative instrumentation verus innovational instrumentation				
Barlocher 2002 (29)	0/36	0/24		0.0 [0.0, 0.0]
Dai 2008 (30)	0/33	0/29		0.0 [0.0, 0.0]
Feiz-Erfan 2007 (31)	0/25	0/25		0.0 [0.0, 0.0]
Fernandez-Fairen 2008 (32)	0/33	0/28		0.0 [0.0, 0.0]
Nabhan 2007 (33)	0/18	0/19		0.0 [0.0, 0.0]
Nunley 2009 (34)	0/33	0/33		0.0 [0.0, 0.0]
Pan 2005 (35)	0/41	0/40		0.0 [0.0, 0.0]
Ryu 2006 (36)	0/20	0/20		0.0 [0.0, 0.0]
Schroder 2007 (37)	0/58	0/57		0.0 [0.0, 0.0]
Stulik 2007 (38)	0/69	4/63		0.10 [0.01, 1.85]
Subtotal (95% CI)	**366**	**338**		**0.10 [0.01, 1.85]**
Total events: 0 (Experimental), 4 (Control)				
Heterogeneity: Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 1.54 (P = 0.12)				
Total (95% CI)	**1353**	**1242**		**0.72 [0.49, 1.06]**
Total events: 35 (Experimental), 44 (Control)				
Heterogeneity: Chi^2 = 20.22, df = 24 (P = 0.68); I^2 =0.0%				
Test for overall effect: Z = 1.65 (P = 0.099)				
Test for subgroup differences: Chi^2 = 0.0, df = 9 (P = 0.0), I^2 =0.0%				



(1) 1 neck hematoma, allocation unclear; ACF 2 nonunion, reoperated
(2) DEF 1 IC fracture, 2 hematoma, 1 reporeration (graft lux); DE 2 reoperation (adj lev HNP; instability)
(3) DE 2 reoperations; DEF 1 operation; all because of complaints
(4) DE 1 staph aureus infection
(5) 1 complication; subfacial hematoma, unclear allocation
(6) DE 1 rec nerve les, 2 reoperations; DEF 3 IC pain, 1 loosening graft, 1 wond infection
(7) DEF 1 infection
(8) DE 2 reoperation (adj lev HNP; instability)
(9) 0 complications matching the criteria
(10) 0 complications
(11) DE 2 reoperation (adj lev HNP; instability)
(12) 0 complications
(13) DE 1 rec nerve les, 2 reoperations; Plate 3 prol IC pain, 1 loosening graft, 1 wound inf
(14) 0 complications
(15) Allo 1 deep infection 1 adj segm surgery 1 decompression; auto 1 adj segm surgery
(16) Autograft 2 reoprations/nonunion
(38) Rigid plate 4 hardware failures

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
(17) DEF 1 IC fracture, 2 hematoma, 1 reporeration (graft lux)				
(18) 0 complications				
(19) cage 1 reoperation/nonunion; autograft 1 reoperation(graft collapse)				
(20) Cage 1 Horner syndrome				
(21) Autograft 3 reoperation (graft disl); cage 1 reoperation (adj segm)				
(22) Autograft 2 reoperations (graft disl)				
(23) Autograft 1 horner				
(24) Plate 3 prol IC pain, 1 loosening graft, 1 wound inf; DEF 3 IC pain, 1 loosening graft, 1 wond infection				
(25) DEF 1 infection				
(26) Plate 1 reoperation (pseudoarthr)				
(27) Modified SR tech 3 reopeerations; Vert Body autograft 2 reoperations				
(28) Cage 1 seroma/reop				
(29) 0 complications				
(30) 0 complications				
(31) complications not reported per group				
(32) 0 severe complications				
(33) not reported				
(34) not reported				
(35) 0 complications				
(36) 0 severe complications				
(37) 0 complications				
(38) Rigid plate 4 hardware failures				

ADDITIONAL TABLES

Table 1. Definitions

Term	Definition
Spondylosis	Degenerative disease of the spine associated with degeneration of the intervertebral discs and bone deformations
Radiculopathy	Symptoms, like pain and muscle weakness, arising from compression of the nerve roots
Myelopathy	Symptoms, like difficulty in walking, muscle weakness, imbalance, arising from compression of the spinal cord
Herniated disc	Bulging of the intervertebral disc, often causing pressure on the nerves that have their origin in the spinal canal
Spondylotic myelopathy	Dysfunction of the spinal cord due to direct compression by, for example, decreased size of the spinal canal, disc herniation or bone deformations
Autograft	Implant material derived from the same individual, usually from the iliac crest, where a piece of bone cn be excised with cortical bone on three sides. Another option is to use bone from the vertebral bodies

Table 1. Definitions (*Continued*)

Allograft	Implant material from any other source than the same individual, usually obtained from another human and stored and treated in a bone bank. For example, a ring from a femoral bone can be used

Table 2. Assessment of clinical relevance

Study	Clinical relevance	Patient description	Intervention description	Outcome measures	Effect size	Benefits/harms
Abd-Alrahman 1999		Yes	Yes	No	No	Unsure
Barlocher 2002	Yes	Unsure	Yes	Yes	No	Yes
Baskin 2003		Yes	Unsure	Yes	Unsure	Unsure
Celik 2007	No	No	No	No	No	No
Dai 2008	Unsure	Yes	Yes	Yes	No	No
Dowd 1999		No	Yes	Yes	Unsure	Unsure
Feiz-Erfan 2007	No	No	No	Yes	Yes	Unsure
Fernandez-Fairen 2008	Yes	Yes	Yes	Yes	Yes	No
Hacker 2000		Yes	Yes	Yes	No	Unsure
Hauerberg 2008	Yes	Yes	Yes	No	No	No
Lind 2007	No	No	No	No	No	No
Lofgren 2000		Yes	Yes	Yes	No	Unsure
Lofgren 2010	Yes	Yes	Yes	Yes	No	No
Madawi 1996		Unsure	Unsure	No	No	Unsure
Martins 1976		Yes	Yes	No	No	Unsure
McConnel 2003		Unsure	Yes	No	No	Unsure
McGuire 1994		Yes	Unsure	No	Unsure	No
Nabhan 2007	No	No	Yes	No	No	No
Nunley 2009	Yes	Yes	Yes	No	No	No

Table 2. Assessment of clinical relevance (*Continued*)

Oktenoglu 2007	No	Yes	yes	No	No	No
Pan 2005	Unsure	Yes	Yes	Yes	Unsure	Yes
Porras-Estrada 2004	No	Yes	Yes	No	Yes	Unsure
Rosenorn 1983		Yes	Yes	No	Yes	Yes
Ruetten 2009	Yes	Yes	Yes	Yes	No	No
Ryu 2006	Yes	Yes	Yes	Yes	No	No
Savolainen 1998		Yes	Yes	No	No	Unsure
Schroder 2007	No	No	No	No	Yes	Yes
Stulik 2007	No	Yes	No	No	No	Unsure
Thome 2006	Yes	No	Yes	Yes	Unsure	Unsure
van den Bent 1996		Yes	Yes	No	No	No
Vavruch 2002		Yes	Yes	Yes	No	Unsure
Xie 2007	No	Yes	Yes	Yes	No	No
Zoega 2000		Yes	Yes	Yes	No	Unsure

APPENDICES

Appendix 1. Criteria and operationalisation for Risk of Bias Assessment - RCTs and CCTs

1. Was the method of randomisation adequate? A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with two groups), rolling a dice (for studies with two or more groups), drawing of balls of different colours, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, pre-ordered sealed envelops, sequentially-ordered vials, telephone call to a central office, and pre-ordered list of treatment assignments

Examples of inadequate methods are: alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number

2. Was the treatment allocation concealed? Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.

Was knowledge of the allocated interventions adequately prevented during the study?

3. Was the patient blinded to the intervention?

This item should be scored "yes" if the index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.

4. Was the care provider blinded to the intervention? This item should be scored "yes" if the index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful

5. Was the outcome assessor blinded to the intervention? Adequacy of blinding should be assessed for the primary outcomes. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or:

- **for patient-reported outcomes** in which the patient is the outcome assessor (e.g., pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored "yes"

- **for outcome criteria assessed during scheduled visit and that supposes a contact between participants and outcome assessors** (e.g., clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination

- **for outcome criteria that do not suppose a contact with participants** (e.g., radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome

- **for outcome criteria that are clinical or therapeutic events** that will be determined by the interaction between patients and care providers (e.g., co-interventions, hospitalisation length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if the item for 'caregivers' is scored "yes"

- **for outcome criteria that are assessed from data of the medical forms**: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data

Were incomplete outcome data adequately addressed?

6. Was the drop-out rate described and acceptable? The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a 'yes' is scored. (N.B. these percentages are arbitrary, not supported by literature).

7. Were all randomised participants analysed in the group to which they were allocated? All randomised patients are reported/ analysed in the group they were allocated to by randomisation for the most important moments of effect measurement (minus missing values) irrespective of non-compliance and co-interventions.

8. Are reports of the study free of suggestion of selective outcome reporting? In order to receive a 'yes', the review author determines if all the results from all pre-specified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment.

Other sources of potential bias:

9. Were the groups similar at baseline regarding the most important prognostic indicators? In order to receive a "yes", groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurological symptoms, and value of main outcome measure(s).

10. Were co-interventions avoided or similar? This item should be scored "yes" if there were no co-interventions or they were similar between the index and control groups.

11. Was the compliance acceptable in all groups? The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered over several sessions; therefore it is necessary to assess how many sessions each patient attended. For single-session interventions (for ex: surgery), this item is irrelevant.

12. Was the timing of the outcome assessment similar in all groups? Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.

Appendix 2. Assessment of Clinial Relevance

Based on the data provided, can you determine if the results will be clinically relevant?

1. *Patient description*: Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?
2. *Intervention description*: Are the interventions and treatment settings described well enough so that you can provide the same for your patients?
3. *Outcome measures*: Were all clinically relevant outcomes measured and reported?
4. *Effect size*: Is the size of the effect clinically important?
5. *Benefits/Harms*: Are the likely treatment benefits worth the potential harms?

Appendix 3. Search Strategies

MEDLINE

1 randomized controlled trial.pt.
2 controlled clinical trial.pt.
3 randomized.ab.
4 placebo.ab,ti.
5 drug therapy.fs.
6 randomly.ab,ti.
7 trial.ab,ti.
8 groups.ab,ti.
9 or/1-8
10 (animals not (humans and animals)).sh.
11 9 not 10
12 exp Cervical Vertebrae/
13 cervical.mp.
14 degenerative.mp.
15 or/12-13
16 fusion.mp.
17 exp Spinal Fusion/
18 interbody.mp.
19 Spondylodes*.mp.
20 or/16-19
21 11 and 20 and 15
22 limit 21 to yr="2004 - 2009"

EMBASE

1 Clinical Article/
2 exp Clinical Study/
3 Clinical Trial/
4 Controlled Study/
5 Randomized Controlled Trial/
6 Major Clinical Study/
7 Double Blind Procedure/
8 Multicenter Study/
9 Single Blind Procedure/
10 Phase 3 Clinical Trial/
11 Phase 4 Clinical Trial/
12 crossover procedure/
13 placebo/
14 or/1-13
15 allocat$.mp.
16 assign$.mp.

17 blind$.mp.
18 (clinic$ adj25 (study or trial)).mp.
19 compar$.mp.
20 control$.mp.
21 cross?over.mp.
22 factorial$.mp.
23 follow?up.mp.
24 placebo$.mp.
25 prospectiv$.mp.
26 random$.mp.
27 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).mp.
28 trial.mp.
29 (versus or vs).mp.
30 or/15-29
31 14 and 30
32 human/
33 Nonhuman/
34 exp ANIMAL/
35 Animal Experiment/
36 33 or 34 or 35
37 32 not 36
38 31 not 36
39 37 and 38
40 38 or 39
41 exp Cervical Spine/
42 cervical.mp.
43 degenerative.mp.
44 or/41-43
45 fusion.mp.
46 exp Spine Fusion/
47 interbody.mp.
48 Spondylodes*.mp.
49 or/45-48
50 49 and 40 and 44
51 limit 50 to yr="2004 - 2009"

CENTRAL

#1 (cervical)
#2 MeSH descriptor Cervical Vertebrae explode all trees
#3 degenerative
#4 (#1 OR #2 OR #3)
#5 (fusion)
#6 MeSH descriptor Spinal Fusion explode all trees
#7 (Interbody)
#8 (Spondylodesis) or (Spondylodeses)
#9 (#5 OR #6 OR #7 OR #8)
#10 (#4 AND #9)
#11 (#10), from 2004 to 2009

BIOSIS

#10 #9 Timespan=2004-2009
9 #8 AND #5
8 #7 OR #6
7 Topic=(random*) OR Topic=(clinical trial) OR Topic=(controlled trial) OR Topic=(prospective*)
6 Topic=(human) NOT Topic=(animal)

5 #4 AND #3
4 Topic=(fusion) OR Topic=(spinal) OR Topic=(interbody) OR Topic=(Spondylodes*)
3 #2 OR #1
2 Topic=(degenerative disc) OR Topic=(degenerative disk)
1 Topic=(cervical vertebrae)

Appendix 4. Methods from *The Cochrane Library* 2004, issue 4 version of review

Search methods for identification of studies

We electronically searched the most common databases:

- the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 1, 2004)
- MEDLINE (Through PubMed; 1966 to February 2004)
- EMBASE (Ovid online; 1980 to 2004 week 11)
- Current Contents (1996 to February 2004)

The search strings are given in Table 2. The strings in the second column are used and connected with OR within the cells, and with AND between the cells. The search strategy was adapted for the different databases. We made no restrictions on language or date of publication. We screened the references of the included studies, and with citation tracking, we screened references from the articles that cited the included articles.

Data collection and analysis

One author (WJ) conducted the literature search and retrieved the references to be evaluated. Two authors (WJ, PW) independently selected the trials to be included in the review and met to reach consensus. When consensus could not be reached, a third author (PA) was consulted to resolve the disagreement. The methodological quality of the trials was assessed independently by two authors (WJ, PW), with the van Tulder checklist (van Tulder 2003), who again met to reach consensus. As before, if consensus could not be reached, a third author (PA) was consulted to resolve the disagreement. Details of randomisation, blinding and exclusions from the analyses were recorded. Data were extracted and entered into RevMan 4.2.3 by one author (WJ) and checked by another author (PW).
Statistical analyses were conducted using Review Manager (RevMan) software 4.2.3. Publications were managed with the aid of Reference Manager®. In addition, relevant information was recorded pertaining to database source, reason for exclusion and consensus of authors.

Selection

Articles were selected in two steps. In the first step, articles were excluded when it was apparent from either the title or abstract that the study did not meet the following criteria:

- The study was a randomised controlled trial.
- The interventions evaluated in the trials were comparisons of different techniques for anterior cervical interbody fusion
- The indication for the patients to receive the intervention was chronic (longer than 12 weeks) degenerative disc disease of the cervical spine

The outcome parameters in the studies were clinical, functional, or radiological measures. The minimal length of follow-up was six months.
In the second step, articles were excluded when it was apparent from a quick scan of the full text of the article that it failed to meet the same inclusion criteria. When the same population was described in more than one study, all studies were used, but only the most informative was used as the primary reference. The reason for exclusion was documented for each reference.

Methodological quality assessment

With the aid of a checklist, articles that met all the inclusion criteria were evaluated on meeting methodological requirements and objectives. We used the criteria recommended by the Back Group (van Tulder 2003) and. We regrouped these criteria into risk of bias (Table 3), external validity, and data presentation and statistical analysis (Table 4). Each item was scored good (+), questionable (+/-

), poor (-), unsure (?), or 'not applicable'. We added a question on group and subgroup homogeneity, because heterogeneity is often encountered and accounts for the lack of power seen in orthopedic surgical trials. We also added a question on the description and validity of the statistical analyses used.

Risk of bias was assessed by considering randomisation, blinding, proper assessments and appropriateness of outcome measures, and comparability of groups. Randomisation with envelopes was allowed, but not date of admission, birth date, alternating schemes, or other comparable techniques. When studies used these techniques, it was regarded as a concurrently controlled trial and analysed as such. If in doubt, the decision was made on the information provided by the authors. Blinding of surgeon cannot usually be achieved in orthopedic surgery, so this is generally not met. Prognostic factors considered were: one or two-level surgery, clinical diagnosis (radiculopathy, radiculomyelopathy, herniated disc), and treatments applied. Loss to follow-up was graded as 'good' if it was less than 10%, 'questionable' if less than 20% and 'poor' if greater than 20%.

External validity was assessed by considering the completeness of the description of selection criteria, the treatment methods used, and the timing of follow-up. Short-term follow-up was considered to be follow-up that was shorter than five years.

Data presentation and statistical analyses were rated according to the availability of data describing the sizes of the groups and/or subgroups, means, proportions, or other relevant point estimates and their precision. When heterogeneity of the intervention groups was observed, data (point estimates and precision) were required for the subgroups identified. In addition, the description and appropriateness of the statistical methods were rated.

The final judgement on the quality of the studies was based on a pre-set cut-off point. We decided that internal validity was the primary indicator for the quality of a study. When the evaluation of internal validity suggested a low potential for bias, the study was considered a high quality study. Minimal requirements were a concealed allocation procedure, drop out of less than 20%, and homogeneous (sub) groups.

The final judgement on the strength of the evidence on each comparison was based on the Back Group's recommendations on Levels of Evidence (van Tulder 2003):

- Strong - consistent findings among multiple high quality RCTs
- Moderate - consistent findings among multiple low quality RCTs and/or one high quality RCT
- Limited - one low quality RCT
- Conflicting - inconsistent findings among multiple RCTs
- No evidence from trials - no RCTs

The potential to pool results was dependent on the comparability of the individual studies, i.e. identical treatments and outcome measures were used, sufficient detail was given to describe the selection criteria and other external validity criteria.

Analysis

For dichotomous outcomes, we calculated relative risks (RR). For continuous outcomes, we calculated a weighted mean difference (WMD). If sufficient data were available, subgroup analyses were planned to assess the effects of age, gender, disease severity, one or two-level procedures, and length of follow-up time on the outcomes. Sensitivity analyses were planned to assess the effect of methodological quality (high or low) on outcomes. The use of a funnel plot was planned to identify publication bias. Heterogeneity was tested with a Q-test. When heterogeneity existed, post-hoc subgroup analyses and sensitivity analyses were planned to explore the reason for heterogeneity.

FEEDBACK

from Ronald Bartels, MD PhD, Nov 2004

Summary

With great interest we've read the excellent review of Jacobs et al.(5). Although we agree with the conclusions, we want to address some points:

1) the results of a study by Barlocher were excluded, because they were presented in a Conference Proceeding. However, in 2002 they were also published in Neurosurgical Focus(2), an official peer - reviewed journal. Therefore, it is not correct to exclude the study from this review.

2) Neither is the study by de la Torre et al.(3) mentioned. Although only an abstract of a presentation at a meeting is provided, the reviewers should have attempted to contact the authors to get the original data. This procedure is also advocated in the Cochrane Handbook 4.1.

3) Most articles comparing cervical discectomy with and without fusion used Odom's criteria for assessing outcome. Some authors did not explicitly mention that they used Odom's criteria, whereas it is perfectly clear from the description. A common estimated outcome can be calculated using a larger number of studies. In this way, the articles from Bärlocher et al., van de Bent et al., Abd-Alrahman et al., Martins, Rosenørn et al., and Savolainen et al.(1;2;6-9), could be used to estimate a common odds ratio. If good (including excellent) is used for clinical outcome versus the rest (fair, poor), the estimated common odds ratio (Mantel-Haenszel) is 0,89 with a 95% CL of 0.60 to 1.32 comparing non - fusion with fusion. The data of the study of Dowd(4) were not included, since follow - up was only 1 day! However, this calculation does confirm, that there does not exist any difference in clinical outcome between patients treated by cervical anterior discectomy with or without fusion.

4) The conclusion of the reviewers is correct. However, it could be formulated more explicit. Since the complication rate is higher with fusion with autologous material or more expensive in case of the use of alternatives to autologous bone, fusion should offer at least minimal advantages on the long term. These are only theoretical. Therefore, we would suggest that based on the results of this review hard evidence to perform a fusion after cervical discectomy does not exist. This has great impact since many studies are ongoing comparing arthroplasty and fusion (as the golden (?) standard).

Finally, we want to congratulate the authors with their major effort and results.

Sincerely,

R.H.M.A. Bartels, M.D., Ph.D.(1)
Gert Jan van der Wilt, M.D., Ph.D.(2)
University Medical Center St. Radboud
R. Postlaan 4
6500 HB Nijmegen
The Netherlands
(1)Department of Neurosurgery; (2) Medical Technology Assessment

References

1. Abd-Alrahman N, Dokmak AS, and Abou-Madawi A: Anterior cervical discectomy (ACD) versus anterior cervical fusion (ACF), clinical and radiological outcome study. Acta Neurochir (Wien) 141:1089-1092, 1999.

2. Bärlocher CB, Barth A, Krauss JK, Binggeli R, and Seiler RW: Comparative evaluation of microdiscectomy only, autograft fusion, polymethylacrylate interposition, and threaded titanium cage fusion for treatment of single-level cervical disc disease: a prospective randomized study in 125 patients. Neurosurg Focus 12 January:1-12, 2002.

3. de la Torre M, Martinez-Quinones JV, Isla A, Argüello C, Bendala A, Casado J, and Blazquez MG: Anterior cervical diskectomy with and without bone grafting. Multicentric comparative study. J Bone Joint Surg Br 77B (Suppl I):24, 1995.

4. Dowd GC and Wirth FP: Anterior cervical discectomy: is fusion necessary? J Neurosurg 90:8-12, 1999.

5. Jacobs WCH, Anderson PG, Limbeek J, and Pavlov P: Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease. The Cochrane Database of Systematic Reviews 2004 (3) Art. No.: CD004958. DOI: 10.1002/14651858.CD004958.

6. Martins AN: Anterior cervical discectomy with and without interbody bone graft. J Neurosurg 44:290-295, 1976.

7. Rosenorn J, Bech Hansen E, and Rosenorn M-A: Anterior cervical discectomy with and without fusion. A prospective study. J Neurosurg 59:252-255, 1983.

8. Savolainen S, Rinne J, and Hernesniemi J: A prospective randomized study of anterior single-level cervical disc operations with long-term follow-up: surgical fusion is unnecessary. Neurosurgery 43:51-55, 1998.

9. van den Bent MJ, Oosting J, Wouda EJ, van Acker EH, Ansink BJ, and Braakman R: Anterior cervical discectomy with or without fusion with acrylate. A randomized trial. Spine 21:834-839, 1996.

Reply

Many thanks for your interest in our review and well thought criticism.
The study results by Barlocher et al were not included in the review because it was not found in our search in the databases as a peer reviewed article. It was also not referenced by the other trials published after 2002; Baskin et al and McConnel et al. We are grateful for pointing to this additional study and it will of course be included in the future update. The search strategy remains a potential source of bias in any systematic review, which needs careful attention. Possible solutions could be to contact authors of conference proceedings to ask for (pending) publications and to hand search more journal contents not included in Medline and other databases.
The study by de la Torre et al was not included because including conference proceedings and contacting authors for original data was not in the protocol for the review. The authors are right in pointing to the need to contact authors for original data, but this requires additional effort, which we hope we can address in the next update.
Regarding the third point: we feel that the studies mentioned cannot be combined in a meta-analysis on the outcome parameter suggested because the definition of the score differs among the studies. Savolainen only uses three categories where the others use four. Rosenorn relies heavily on occupation where others do less. The difference between the definition between fair and good (the critical definition when good is the threshold) is not uniquely defined. We present the definitions used by the studies below. We therefore suggest strongly to the orthopedic society to come to more agreement on the outcome parameters to be used in clinical evaluations. An example could be taken from the OMERACT initiative used for rheumatoid arthritis research.
Finally, our approach was to present the evidence and draw conclusions to the extent of explicitness we feel funded by the studies found. We feel that we have not yet enough power to show equivalence, certainly as we did not perform meta-analysis on the selected studies with regard to complications. None of the studies aimed at identifying non-inferiority of discectomy. We agree with the authors that there is no established gold standard for cervical degenerative disc disease and this is supported by our results.
We hope continuously to improve our review methodology and appreciate very much these constructive remarks.

Contributors

1st author, Wilco Jacobs, MD

WHAT'S NEW

Last assessed as up-to-date: 14 November 2009.

Date	Event	Description
14 February 2011	Amended	corrected typo in Plain Language Summary; 'patents' to 'patients'

HISTORY

Protocol first published: Issue 4, 2004

Review first published: Issue 4, 2004

Date	Event	Description
23 June 2010	New search has been performed	Updated review with 19 new studies

(*Continued*)

23 June 2010	New citation required and conclusions have changed	conclusions changed due to more studies and updated methodology
17 November 2004	Feedback has been incorporated	Feedback added: 06/11/04 Response to feedback added: 17/11/04 See Feeback section.
28 February 2004	New search has been performed	This review updates the systematic review published in 2001: van Limbeek J, Jacobs WC, Anderson PG, Pavlov PW. A systematic literature review to identify the best method for a single level anterior cervical interbody fusion. Eur Spine J 2000; 9(2): 129-36. This review includes 14 studies, six more than in the 2001 review. One additional study was identified, but the authors are still waiting for the full text of the article. If it meets the inclusion criteria, it will be included in the next update

CONTRIBUTIONS OF AUTHORS

Wilco Jacobs (WJ): Protocol, Trial selection, Risk of bias assessments, Data extraction, Report, Coordination

Paul Willems (PW): Protocol, Trial selection, Risk of bias assessment, Data extraction, Draft review

Patricia Anderson (PA): Third reviewer consultation, Draft review

Jacques van Limbeek (JvL): Consultant

Ronald Bartels (RB): Clinical interpretation, Draft review

Paul Pavlov (PP): Clinical interpretation, Draft review

Cumhur Oner (CO): Draft review

DECLARATIONS OF INTEREST

none

SOURCES OF SUPPORT

Internal sources

- Sint Maartenskliniek Nijmegen, Netherlands.

LUMC provided for time and material resources.

- Leiden university Medical Center, Netherlands.

LUMC provided for time and material resources.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This updated review has some changes from the initial protocol and review.

- The methodological quality evaluation was simplified and adheres to The Cochrane Collaboration and Cochrane Back Review Group's new recommendations to use Risk of Bias tables. Tables with in- and external quality have been replaced by these tables. This standard of including text for Risk of Bias assessment was new, and only added for the newly included trials. This was also the case with the first question of the clinical relevance assessment.
- We adopted the GRADE approach to grade the quality of the evidence.
- Definition of complications were added after selection of studies, but before data extraction.

INDEX TERMS

Medical Subject Headings (MeSH)

*Intervertebral Disc [surgery]; Cervical Vertebrae [*surgery]; Diskectomy; Ilium [transplantation]; Intervertebral Disc Displacement [surgery]; Randomized Controlled Trials as Topic; Spinal Fusion [*methods]; Spondylosis [*surgery]

MeSH check words

Humans