Helping users to make sense of the ever increasing volume and complexity of evidence: the KSR Evidence database of systematic reviews

Jos Kleijnen, MD, PhD
Director, Kleijnen Systematic Reviews Ltd, York, UK
&
Professor of Systematic Reviews in Health Care, Maastricht University, NL
Sources of evidence from systematic reviews: 16,000 systematic reviews published each year in health care literature

- Cochrane Library
- DARE database
- JBI reviews
- Epistemonikos
- HTA agencies
- Guidelines

- New: KSR Evidence
**News**

**DARE and NHS EED archives secure on CRD website until at least 2021**

CRD would like to reassure our many thousands of users that we are committed to maintaining archive versions of DARE and NHS EED until at least 2021 (the point to which we have funds to support maintenance). [Bibliographic records were published on DARE and NHS EED until 31st March 2015. Searches of MEDLINE, Embase, CINAHL, PsycINFO and PubMed were continued until the end of 2014.]

We know the databases remain a valuable resource to those seeking to find out if reviews and economic evaluations have already been done before embarking on new projects, and in providing brief critical reviews and bottom line statements of these.

CRD will continue to maintain and add records to the HTA database until 31st March 2018 at which point a decision about future production will be taken in partnership with INAHTA.

**Most shared**

- Effect of long-acting beta-agonists on the frequency of COPD exacerbations: a meta-analysis
- Effects of the Finnish Alzheimer Disease Exercise Trial (FINALEX): a randomized controlled trial
- A systematic review and meta-analysis of yoga for low back pain
- A comparison of the clinical effectiveness and cost-effectiveness of treatments for moderate to severe psoriasis
- Radiation-induced cardiac toxicity after therapy for breast cancer: interaction between treatment era and follow-up duration
- Efficacy of complementary and alternative medicine therapies in relieving cancer pain: a systematic review
- Continuous passive motion following primary total knee arthroplasty: short- and long-term effects on range of motion
- Role of acupuncture in the treatment of insomnia: a
Intra-articular and soft tissue injections, a systematic review of relative efficacy of various corticosteroids

Garg N, Perry L, Deodhar A

CRD summary
This review concluded that there was insufficient evidence on the comparative efficacy of different corticosteroid injections. A few trials favoured triamcinolone hexacetonide over the other corticosteroids. These conclusions reflect the evidence presented and appear to be reliable.

Authors' objectives
To determine the comparative efficacy of corticosteroid injections for intra-articular or periaricular soft tissue injections.

Searching
MEDLINE, Cochrane Database of Systematic Reviews, DARE, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched in October or November 2013, for articles in English. Search terms and a search strategy were reported. Citation tracking and manual searches of bibliographies of relevant publications were conducted.

Study selection
Double-blind randomised controlled trials (RCTs) comparing corticosteroid injections, administered to peripheral joints or periaricular soft tissues, were eligible for inclusion. Trials had to include adults or children diagnosed with inflammatory arthritis, osteoarthritis, or a periaricular regional pain syndrome. Trials of spinal injections were excluded.

The included trials were published between 1979 and 2009. The most commonly evaluated corticosteroids were methylprednisolone acetate, triamcinolone, and betamethasone. Most injections were administered to the knees or shoulders. Patient characteristics and outcome measures varied across the trials.
Intra-articular and soft tissue injections, a systematic review of relative efficacy of various corticosteroids

Two reviewers independently selected trials for inclusion. Any discrepancies were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed trial quality by assigning yes or no ratings for: specific inclusion and exclusion criteria; valid patient randomisation; blinding of patients; blinding of injectors; blinding of assessors; and power analysis. The thresholds used to define the quality of the trials were not reported.

Data extraction
The outcomes were extracted independently by two reviewers. None of the outcomes were specified before study selection and data extraction.

Methods of synthesis
The data were synthesised in a narrative.

Results of the review
Seven RCTs were included, with 306 patients (range 23 to 85). All seven RCTs were rated as high quality. One did not report blinding of assessors, and one did not report a power analysis. Two trials did not report blinding of the injector. Follow-up ranged from two weeks to 24 months.

Compared with methylprednisolone or prednisolone-t-butyl acetate, for rheumatoid arthritis of the knee, triamcinolone hexacetonide demonstrated statistically significantly faster pain relief at day seven (one RCT; 30 patients). A similar result was shown when triamcinolone hexacetonide for knee osteoarthritis was compared with methylprednisolone at week three (one RCT; 57 patients). Another trial (24 patients) demonstrated significantly faster pain relief with methylprednisolone for rotator cuff tendonitis, compared with triamcinolone hexacetonide, at two weeks. All three trials demonstrated similar long-term efficacy of the corticosteroids for pain relief.

In trials of patients with knee arthritis, triamcinolone hexacetonide was found to have significantly better efficacy for pain relief than triamcinolone acetonide at 24 months (one RCT; 43 patients), and betamethasone at day 42 (one RCT; 23 patients). Occasional injection site pain, skin atrophy, and rise in blood glucose were the only adverse effects reported. Further results were reported.

Authors’ conclusions
There was insufficient evidence on the comparative efficacy of different corticosteroid injections; a few trials favoured triamcinolone hexacetonide over other corticosteroids.

CRD commentary
The review question and inclusion criteria were clear. Various relevant databases were searched, but the English-language restriction means that some trials may have been missed. All the review processes were duplicated, reducing the risk of reviewer error and bias. The quality assessment criteria were relevant for RCTs, but some important issues were not considered, such as completeness of outcome data and potential for bias to have compromised the quality of the results.
Intra-articular and soft tissue injections, a systematic review of relative efficacy of various corticosteroids

Betamethasone at day 42 (one RCT; 23 patients). Occasional injection site pain, skin atrophy, and rise in blood glucose were the only adverse effects reported. Further results were reported.

Authors' conclusions
There was insufficient evidence on the comparative efficacy of different corticosteroid injections; a few trials favoured triamcinolone hexacetonide over other corticosteroids.

CRD commentary
The review question and inclusion criteria were clear. Various relevant databases were searched, but the English-language restriction means that some trials may have been missed. All the review processes were duplicated, reducing the risk of reviewer error and bias. The quality assessment criteria were relevant for RCTs, but some important issues were not considered, such as completeness of outcome data and comparability of groups at the start. Thus, there was potential for bias to have compromised the quality of the data. The differences between the trials meant that a narrative synthesis was appropriate.

The authors' conclusions reflect the evidence presented and appear to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for clinical practice.
Research: The authors stated that trials were needed to investigate the comparative efficacy of the different corticosteroid injections for articular and periartricular pain. These trials should have specific outcome measures to facilitate evidence-based practice. Further systematic reviews were recommended to assess the adverse effects of different corticosteroid injections in specific populations, such as pregnant patients, patients with diabetes, and immune-compromised patients.

Funding
Funding received from American Regent.

Bibliographic details
Garg N, Perry L, Deodhar A. Intra-articular and soft tissue injections, a systematic review of relative efficacy of various corticosteroids. Clinical Rheumatology 2014: epub

PubMedID
24651914

DOI
10.1007/s10067-014-2572-B

Indexing Status
Subject indexing assigned by NLM

MeSH
Adrenal Cortex Hormones (administration & therapy); Betamethasone (administration & therapy); Joint Diseases/Drug Therapy; Methylprednisolone (administration & therapy); Osteoarthritis/Drug Therapy; Periarthritis/Drug Therapy; Tendinopathy/Drug Therapy; Triamcinolone Acetonide
ROBIS: A new tool to assess risk of bias in systematic reviews was developed

Penny Whiting\textsuperscript{a,b,c,*}, Jelena Savovic\textsuperscript{a,b}, Julian P.T. Higgins\textsuperscript{a,d}, Deborah M. Caldwell\textsuperscript{a}, Barnaby C. Reeves\textsuperscript{e}, Beverley Shea\textsuperscript{f}, Philippa Davies\textsuperscript{a,b}, Jos Kleijnen\textsuperscript{c,g}, Rachel Churchill\textsuperscript{a}, the ROBIS group

\textsuperscript{a}School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol BS8 2PS, UK
\textsuperscript{b}The National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care West at University Hospitals Bristol NHS Foundation Trust, 9th Floor, Whitefriars, Lewins Mead, Bristol BS1 2NT
\textsuperscript{c}Kleijnen Systematic Reviews Ltd, Unit 6, Escrick Business Park, Riccall Road, Escrick, York YO19 6FD, UK
\textsuperscript{d}Centre for Reviews and Dissemination, University of York, York YO10 5DD, UK
\textsuperscript{e}School of Clinical Sciences, University of Bristol, Bristol Royal Infirmary, Level Queen’s Building, 69 St Michael’s Hill, Bristol BS2 8DZ, UK
\textsuperscript{f}Community Information and Epidemiological Technologies Institute of Population Health, 1 Stewart Street, Room 319, Ottawa, Ontario, K1N 6N5, Canada
\textsuperscript{g}School for Public Health and Primary Care (CAPHRI), Maastricht University, PO Box 616, 6200 MD, Maastricht, The Netherlands
<table>
<thead>
<tr>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Study eligibility criteria</strong></td>
<td><strong>2. Identification and selection of studies</strong></td>
</tr>
<tr>
<td><strong>Signaling questions</strong></td>
<td><strong>1.1 Did the review adhere to predefined objectives and eligibility criteria?</strong></td>
</tr>
<tr>
<td></td>
<td><strong>1.2 Were the eligibility criteria appropriate for the review question?</strong></td>
</tr>
<tr>
<td></td>
<td><strong>1.3 Were eligibility criteria unambiguous?</strong></td>
</tr>
<tr>
<td></td>
<td><strong>1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate?</strong></td>
</tr>
<tr>
<td></td>
<td><strong>1.5 Were any restrictions in eligibility criteria based on sources of information appropriate?</strong></td>
</tr>
<tr>
<td><strong>Judgment</strong></td>
<td><strong>Concerns regarding specification of study eligibility criteria</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Risk of bias in the review</strong></td>
</tr>
</tbody>
</table>
AMSTAR 2 provides a broad assessment of quality, including flaws that may have arisen through poor conduct of the review (with uncertain impact on findings). In this respect it differs from another instrument, the Risk Of Bias In Systematic reviews (ROBIS).

ROBIS is a sophisticated three phase instrument that focuses specifically on the risk of bias introduced by the conduct of the review. It covers most types of research question, including diagnosis, prognosis, and aetiology.

In contrast, AMSTAR 2 is intended to be used for reviews of healthcare interventions. Inevitably there is overlap in the items considered by ROBIS and AMSTAR 2; indeed, two investigators (BCR, BJS) were involved in the development of both.
KSR Evidence provides a user-friendly, time-efficient way to access systematic reviews in health care. KSR Evidence includes all systematic reviews and meta-analyses published since 2015 and for many reviews provides a critical appraisal and a short, accessible bottom line.
Newly added KSR Critical Appraisals

Trigonal versus extratrigonal botulinum toxin-A: a systematic review and meta-analysis of efficacy and adverse events

Davis, N. F.; Burke, J. P.; Redmond, E. J.; Elamin, S.; Brady, C. M.; Flood, H. D.

Bottom line The currently available evidence suggests that there is no significant difference in terms of frequency of adverse events and short-term efficacy rates between trigonal and extratrigonal injections. As the number of reviewers involved in the data extraction was not reported, reviewer error and bias could not be ruled out. As methodological quality assessment of the included studies was not performed, one may question the reliability of the findings. The findings should be reviewed with caution because of the relatively small number of studies included in the review and some outcomes were poorly defined in some studies, which may limit standardised comparisons between studies. Full details of the search strategy were not reported, so it was not possible to judge if this was appropriate. The ideal site for administering intravesical botulinum toxin-A remains controversial and more high-quality trials are required to establish the most effective site of injection for intravesical botulinum toxin-A.

Int Urogynecol J 2015;26(3):313-9
Search results

489 results for pneumonia

Subglottic secretion drainage and objective outcomes: a systematic review and meta-analysis
Caroff, D. A.; Li, L.; Muscedere, J.; Klompas, M.

**Bottom line** The available evidence suggests that subglottic secretion drainage may be associated with a significant reduction in ventilator-associated pneumonia in adult intensive care unit patients, compared to standard endotracheal tubes. However, subglottic secretion drainage had no significant effect on any of the other outcomes assessed (length of stay at intensive care unit, duration of mechanical ventilation, the length of stay in hospital or mortality rates, stridor after extubation and reintubation). Information about the study identification was incomplete and no information was provided about the number of authors involved in the study selection and risk of bias assessment, hence the overall risk of bias for this review is unclear.


Chinese herbal extractions for relieving radiation induced lung injury: a systematic review and meta-analysis
Deng, B.; Deng, C.; Cheng, Z.

**Bottom line** Available on request.
Evid Based Complement Alternat Med 2017;();

Effectiveness of MF59-adjuvanted seasonal influenza vaccine in the elderly: a systematic review and meta-analysis

Risk of Bias Assessment: Not yet rated
Details unavailable at this time.
Systematic review of the effectiveness of strategies to encourage patients to remind healthcare professionals about their hand hygiene

Davis, R. Parand, A. Pinto, A. Buetow, S.
J Hosp Infect 2015;89(3):141-62
Publication year: 2015 • Added to database: 16/05/2017

Bottom Line

The currently available evidence suggests that patients reminding healthcare professionals about their hand hygiene, combined with other approaches can increase both actual behaviour and intentions to participate in hand hygiene. However, a restriction to English language studies means that some relevant studies may have been missed. As methodological quality assessment of included studies was performed inappropriately, one may question the reliability of the findings. Full details of the search strategy were not reported, so it was not possible to judge if this was appropriate. Further high-quality studies and more robust outcome measures should be carried out to evaluate why some strategies are more successful than others.
KSR Evidence

Bottom Line

The currently available evidence suggests that patients reminding healthcare professionals about their hand hygiene, combined with other approaches can increase both actual behaviour and intentions to participate in hand hygiene. However, a restriction to English language studies means that some relevant studies may have been missed. As methodological quality assessment of included studies was performed inappropriately, one may question the reliability of the findings. Full details of the search strategy were not reported, so it was not possible to judge if this was appropriate. Further high-quality studies and more robust outcome measures should be carried out to evaluate why some strategies are more successful than others.

Risk of Bias Assessment

Overall summary
High risk of bias in the review

Only English language studies were considered for inclusion in the review. Full details of the search strategy were not reported, so it was not possible to judge if this was appropriate. The methodological quality of included studies was assessed, but the criteria considered were not appropriate. No information was provided on the number of reviewers involved in the risk of bias assessment.

A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? Probably no
B. Was the relevance of identified studies to the review's research question appropriately considered? Probably yes
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? Probably yes

Risk of bias in the review
High
## Details of Review

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>28</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>Unclear</td>
</tr>
<tr>
<td>Last search date</td>
<td>August 2013</td>
</tr>
<tr>
<td>Review type</td>
<td>Intervention</td>
</tr>
<tr>
<td>Objective</td>
<td>To evaluate the effectiveness of strategies aimed at increasing patient involvement in reminding healthcare professionals about their hand hygiene.</td>
</tr>
<tr>
<td>Population</td>
<td>Healthcare professionals and patients (the term ‘patient’ was used broadly to encompass patients and members of the public that were being asked their views from the position of being a patient in hospital). Both ‘lay’ and ‘expert’ patients (defined as patients that worked in a clinical profession) were included.</td>
</tr>
<tr>
<td>Interventions</td>
<td>Strategies that had been developed and been implemented and tested on hospital wards.</td>
</tr>
<tr>
<td>Comparator</td>
<td>NA.</td>
</tr>
<tr>
<td>Outcome</td>
<td>Increasing both actual behaviour and intentions to participate in hand hygiene.</td>
</tr>
<tr>
<td>Study design</td>
<td>Empirical studies (randomised controlled trials, cohort and case-control studies). Dissertations and doctoral theses, books, book reviews, conference posters and presentations, editorials and commentaries were excluded.</td>
</tr>
</tbody>
</table>
Results

Single component strategies were examined in 16 articles. Six articles examined the use of a video and almost all the articles reported the use of a video has encouraged intentions to participate and actual behaviour. Eight studies reported that patients intentions to participate increased after healthcare professionals (HCP) encouragement and three studies reported that patients intentions to participate increased after reading the leaflets. Twelve studies reported that multi-modal approach (e.g. a combination of leaflets and videos) increased both actual behaviour and intentions to participate in hand hygiene (HH). Three of the six studies that measured patient behaviour, reported between 90% and 100% of patients asking nurses about their HH during the intervention compared to 32% to 40% of doctors. Three out of seven studies examined how HCP HH compliance increased by the use of HH products and reported a significant increase in HCP compliance.

Full Risk of Bias Assessment

Domain 1: Study Eligibility Criteria
High
The research objective was clearly stated and appropriate inclusion criteria were defined. No restrictions were applied in the eligibility criteria based on study characteristics. Only English language studies were considered for inclusion in the review.

1.1 Did the review adhere to pre-defined objectives and eligibility criteria?  
   - Probably yes

1.2 Were the eligibility criteria appropriate for the review question?  
   - Probably yes

1.3 Were eligibility criteria unambiguous?  
   - Probably yes

1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?  
   - Probably yes

1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)?  
   - Probably no

Concerns regarding specification of study eligibility criteria

---

Domain 2: Identification and Selection of Studies

Unclear
Domain 2: Identification and Selection of Studies

Unclear

EMBASE, MEDLINE and PsycINFO were searched for relevant literature. In addition, forward and backward citation searching and handsearching of key behavioural science and patient safety journals were performed to minimise the likelihood of missing relevant papers. Full details of the search strategy were not reported, so it was not possible to judge if this was appropriate. The search strategy was not restricted to the date, publication type or any language. Two reviewers independently judged the study eligibility and disagreements were resolved by consensus.

2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? Probably yes
2.2 Were methods additional to database searching used to identify relevant reports? Probably yes
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? No information
2.4 Were restrictions based on date, publication format, or language appropriate? Probably yes
2.5 Were efforts made to minimise error in selection of studies? Probably yes

Concerns regarding methods used to identify and/or select studies Unclear
Domain 4: Synthesis and Findings

High

All studies included in the review contributed to the synthesis. Analyses were explained specifically in the methods section and results were reported for defined outcomes. Due to wide heterogeneity in study methodologies, meta-analysis was not possible, so a narrative synthesis was performed to summarise the findings. The methodological quality of included studies was assessed, but the criteria considered were not appropriate.

4.1 Did the synthesis include all studies that it should? 
4.2 Were all pre-defined analyses reported or departures explained?
4.3 Was the synthesis appropriate given the degree of similarity in the research questions, study designs and outcomes across included studies?
4.4 Was between-study variation minimal or addressed in the synthesis?
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?
4.6 Were biases in primary studies minimal or addressed in the synthesis?

Concerns regarding synthesis and findings

High

Keywords
- Hand Hygiene
- Health Personnel
- Infection Control
- Infectious Disease Transmission, Professional-to-Patient
- Patient Participation
- Reminder Systems
KSR Evidence

- Includes all systematic reviews in health care
- Not only intervention reviews but also diagnosis, prognosis, aetiology
- Also includes appraisals of Cochrane Reviews
- Aims to add references to all systematic reviews, and approximately 4,000 appraisals per year
- Higher impact reviews prioritised for full appraisal (but we have an in-house true random sample of 1,000 appraisals per year for methodological research)
- User request appraisals option for €25 admin fee → Guideline developers!

- Subscription based, starting January 2018
- Until then free login with username/email: ksrevidence and password: evidence

www.ksrevidence.com