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Interventions for managing temporomandibular joint osteoarthritis (Review)

de Souza RF, Lovato da Silva CH, Nasser M, Fedorowicz Z, Al-Muharraqi MA

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[Intervention Review]

Interventions for managing temporomandibular joint osteoarthritis

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ABSTRACT

Background

Osteoarthritis (OA) is the most common form of arthritis of the temporomandibular joint (TMJ), and can often lead to severe pain in the orofacial region. Management options for TMJ OA include reassurance, occlusal appliances, physical therapy, medication in addition to several surgical modalities.

Objectives

To investigate the effects of different surgical and non-surgical therapeutic options for the management of TMJ OA in adult patients.

Search methods

We searched the following databases: Cochrane Oral Health's Trials Register (to 26 September 2011); CENTRAL (*The Cochrane Library* 2011, Issue 3); MEDLINE via Ovid (1950 to 26 September 2011); Embase via Ovid (1980 to 26 September 2011); and PEDro (1929 to 26 September 2011). There were no language restrictions.

Selection criteria

Randomised controlled trials (RCTs) comparing any form of non-surgical or surgical therapy for TMJ OA in adults over the age of 18 with clinical and/or radiological diagnosis of TMJ OA according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) guideline or compatible criteria.

Primary outcomes considered were pain/tenderness/discomfort in the TMJs or jaw muscles, self assessed range of mandibular movement and TMJ sounds. Secondary outcomes included the measurement of quality of life or patient satisfaction evaluated with a validated questionnaire, morphological changes of the TMJs assessed by imaging, TMJ sounds assessed by auscultation and any adverse effects.

Data collection and analysis

Two review authors screened and extracted information and data from, and independently assessed the risk of bias in the included trials.

Main results

Although three RCTs were included in this review, pooling of data in a meta-analysis was not possible due to wide clinical diversity between the studies. The reports indicate a not dissimilar degree of effectiveness with intra-articular injections consisting of either sodium hyaluronate or corticosteroid preparations, and an equivalent pain reduction with diclofenac sodium as compared with occlusal splints. Glucosamine appeared to be just as effective as ibuprofen for the management of TMJ OA.

Interventions for managing temporomandibular joint osteoarthritis (Review)

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Authors' conclusions

In view of the paucity of high level evidence for the effectiveness of interventions for the management of TMJ OA, small parallel group RCTs which include participants with a clear diagnosis of TMJ OA should be encouraged and especially studies evaluating some of the possible surgical interventions.

PLAIN LANGUAGE SUMMARY

Interventions for managing osteoarthritis in the temporomandibular joint

Review question

We conducted this review to assess different interventions for managing osteoarthritis in the temporomandibular joint.

Background

The temporomandibular joint (TMJ) or jaw joint is located in front of the ear on either side of the face. However, it is the only joint that the dentists and maxillofacial surgeons predominantly have to deal with. As with many of the other joints, the TMJ can be affected by osteoarthritis (OA). This is characterized by progressive destruction of the internal surfaces of the joint which can result in debilitating pain and joint noises. Several disorders other than OA may affect the TMJ and the correct diagnosis is important such that it can be matched with appropriate therapy.

A range of therapeutic options are available for TMJ OA, which include non-surgical modalities such as control of contributory factors, occlusal appliances, cold or warm packs applied to the joint, pharmacological interventions as well as physiotherapy. Surgical treatment options include intra-articular injections, arthrocentesis (lavage of the joint) as well as attempts at repair or replacement of portions of the TMJ.

Study characteristics

Authors working with Cochrane Oral Health carried out this review of existing studies, which includes evidence current up to 26 September 2011. This review includes three studies: two conducted in Europe and one in North America. All participants (114) were recruited in university clinics. One study compared intra-articular injections of sodium hyaluronate (a natural constituent of cartilage) with corticosteroids (betamethasone (an anti-inflammatory steroid)); the second study compared diclofenac sodium (a non-steroid anti-inflammatory drug) with occlusal splint therapy; and the third study compared glucosamine sulfate or ibuprofen (a non-steroid anti-inflammatory).

Key results and quality of the evidence

This review found weak evidence indicating that intra-articular injections of sodium hyaluronate and betamethasone had equivalent effectiveness in reducing pain and discomfort. Occlusal appliances when compared with diclofenac sodium showed a similar pain reduction, as did a comparison between the food supplement glucosamine and ibuprofen.

Future studies should aim to provide reliable information about which therapeutic modality is likely to be more effective for the reduction of pain and other symptoms (e.g. joint sounds) of TMJ OA. Moreover, because the limited evidence available only covers a restricted number of interventions, comparisons with other therapeutic modalities should be encouraged. One of the authors' concerns was the large number of trials which included mixed groups of participants diagnosed with TMJ OA, in addition to other disorders of the TMJ, which could not be considered in this review.

BACKGROUND

Osteoarthritis (OA) is a chronic degenerative condition that often affects the hands and the large weight-bearing joints like feet or spine. However, any other joint can also be affected. It is characterized by progressive destruction and loss of the articular cartilage which becomes soft, frayed and thinned (Mercuri 2008; Milam 2006). It also results in a decrease in the synovial fluid that lubricates those joints and can result in severe and debilitating pain (Israel 1997) and loss of joint function. The word OA is derived from the Greek 'osteo', meaning 'of the bone', 'arthro', meaning 'joint', and 'itis', meaning 'inflammation', which is the classical name of the disease. OA has been defined as a 'low-inflammatory arthritic condition' as opposed to a 'high-inflammatory arthritic condition' such as rheumatoid arthritis and gout. It is either primary or secondary to trauma or other acute or chronic overload situations (Mercuri 2008; Milam 2006).

The synonym of OA, 'osteoarthrosis', emphasizes the degenerative nature of the disease, but OA draws attention to the secondary inflammatory changes that are superimposed on this degenerative process. The term 'osteoarthrosis' in the medical orthopaedic literature is identified with any low-inflammatory arthritic condition that results in similar degenerative changes as in OA (Mercuri 2008). In the dental literature, however, osteoarthrosis has also come to be identified with disc displacement or unsuccessful adaptation of the temporomandibular joint (TMJ) to the mechanical forces placed on it with disc derangement or disc interference disorders (Mercuri 2008; Stegenga 2006). Because the basic aetiology and management involved are the same, the terms OA and osteoarthrosis will be used synonymously in this review.

Temporomandibular joint (TMJ) OA is the most common form of arthritis occurring in the TMJs, and the main symptom is pain. Crepitus (joint noise) during functions like chewing is often present. Clinical signs include joint tenderness, crepitus, radiographic bony changes, and joint space narrowing (Kang 2007).

Aetiology and prevalence

Some of the circumstances that are suggested to lead to TMJ OA are as follow: functional overload and parafunction (like tooth grinding during sleeping), unstable occlusion (for example due to a too high restored teeth that does not interact properly with the others) or trauma (microtrauma and macrotrauma). It could also be a consequence of a dysfunctional articular remodeling due to a decreased adaptive capacity of the articulating structures of the joint (Arnett 1996; Nitzan 2001a; Stegenga 1989).

Depending on the diagnostic method used, the prevalence of degenerative TMJ diseases can vary from 1% to 84%. The wide discrepancy illustrates that diagnosis is frequently guided by the presence or absence of rather non-specific signs and symptoms (Haskin 1995). The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) guidelines have been shown to be valuable in assessing the prevalence of signs and symptoms and in classifying patients with temporomandibular joint disorders (TMDs) (Dworkin 1992). Therefore, we would use this diagnostic criteria in this review.

Diagnosis

Clinical diagnosis of OA is based on the presence of a number of signs and symptoms: pain (most commonly described as a

deep ache) in the pre-auricular area with or without associated earache, coarse crepitus in the joint with or without clicking, pain in one or both joints during palpation; and usually complemented with radiological evidence of arthrosis (Manfredini 2006). The RDC/TMD guideline (Dworkin 1992) can be a useful aid to diagnosis and is capable of discriminating TMD-related diagnoses. However, reliability is not good for TMJ OA when compared with other diagnoses (John 2005).

Although panoramic radiographs are a simple and low-cost method often used for diagnosis of TMJ lesions (Epstein 2001), they do provide little information that influences the diagnosis or management for TMJ OA at early stages (Huomonen 2007), because dramatic changes are only seen in advanced disease. A history of joint overload because of habits (e.g. excessive gum chewing) or parafunction (e.g. bruxism) and clinical examination are extremely important in early manifestations. Because of the lack of correlation between the signs and symptoms and the history and physical findings, however, the most helpful approach to diagnosis may be derived from information provided by appropriate imaging (Mercuri 2008). The characteristic imaging features of low-inflammation osteoarthritis in which normal joint mechanics have been disrupted (e.g. disc derangement, disc interference) are focal degeneration and the appearance of osteophytes. The image may be characterized by hypertrophic changes about the affected joint rather than atrophic changes seen in high-inflammatory types of arthritis. Subchondral focal degeneration, the so-called 'Eli cyst' may be seen in low-inflammatory arthritis (Mercuri 2008). Radiological examination might also include tomograms or computerised tomography (CT) scan (Dimitroulis 2005), and magnetic resonance imaging (MRI) scans in specific cases. MRIs are useful in detecting changes not readily revealed by clinical examination or other imaging techniques (Larheim 2005). In the near future, sophisticated image methods may become indicated more frequently for the diagnosis of TMJ degeneration due to the recent development of cone beam CT scans and digital volume tomography. This new technique produces the same type of image as CT for a very much reduced X-ray dose, and at low cost (Rouas 2006). Diagnostic arthroscopic surgery can also provide great insight into the potential problems causing pain to the TMJ at the same time providing treatment (Israel 1998).

Therapeutic options

A TMJ with progressive OA that is clinical detectable cannot be restored in its original structure. Therefore the management strategy either aims to decrease symptoms, stop the progress of the disease or restore the functions:

- (a) non-invasive,
- (b) minimally invasive,
- (c) invasive or surgical modalities
- (d) salvage modalities (Mercuri 2008; Tanaka 2008).

The decision for surgical management of TMJ OA is based on evaluation of the individuals response to non-invasive management, mandibular form and function, and the effect the condition has on the individuals quality of life (Mercuri 2006). The management goals in TMJ OA are: to (1) decrease joint pain, swelling, and reflex masticatory muscle spasm/pain; (2) increase joint function; (3) prevent further joint damage; and (4) disability and disease-related morbidity (Tanaka 2008).

Non-invasive modalities

Non-surgical management is one of the potential approaches in the therapy of TMJ OA and has been recommended as a first choice approach (de Leeuw 1995). Management should include reassurance, and emphasize rest and clear instructions to avoid loading of the joint as well as the control of contributing factors such as parafunction (de Bont 1997).

Occlusal appliances (e.g. stabilization splint (relaxation splint)) have been shown to be beneficial (Ismail 2007). Full coverage soft occlusal splints have also been suggested for the protection of TMJ from involuntary overloading, and for the reduction of the muscle hyperactivity and articular strain due to bruxism (Tanaka 2008). A controlled study on the effects of occlusal splint therapy in individuals with severe TMJ OA indicated a reduction of clinical signs and symptoms (Kuttilla 2002). However, the clinical effectiveness of splints in relieving pain seems modest when compared with that of pain management methods in general (Forsell 2004; Mercuri 2008). None of the occlusal adjustment studies provided evidence supporting the use of this therapeutic method. In terms of medications, non-steroidal anti-inflammatory agents, such as ibuprofen, should be used on a time contingent basis to take advantage of their pharmacokinetics. Muscle relaxants may be helpful in controlling the reflex masticatory muscle spasm/pain (Dionne 2006). Oral orthotics, while assisting in the control of parafunctional habits in many persons, can also provide relief from masticatory muscle spasm/pain and, along with a soft diet, will decrease the loads delivered across the TMJ under function. Reconstruction of the occlusion to provide bilateral occlusal stability, temporarily during the early stages of management, may also decrease the potential for unilateral joint overload (Clark 1984).

Physical therapeutic modalities act as counter-irritants to reduce inflammation and pain. Superficial warm and moist heat or localized cold may relieve pain sufficiently to permit exercise. Therapeutic exercises are designed to increase muscle strength, reduce joint contractures, and maintain a functional range of motion. Ultrasound, electrogalvanic stimulation, and massage techniques may also be helpful in reducing inflammation and pain (De Laat 2003). Active and passive jaw movements, manual therapy techniques, and relaxation techniques were used in the management of 20 consecutive persons with TMJ OA. After intervention (mean 46 days), pain at rest was reduced 80%, and there was no impairment in 37% (Nicolakis 2001).

Minimally invasive modalities

The effectiveness of intra-articular injections of hyaluronic acid (linear glycosaminoglycan) has been examined in other body joints, but no significant differences were noted in radiographic progression of the disease (Lohmander 1996). Moreover, to date hyaluronic acid has not been approved by the United States Food and Drug Administration as a safe and effective medication in the management of arthritic disease in the TMJ (Tanaka 2008).

Intra-articular injections of corticosteroids appear to have limited benefit in other joints of the body (Gray 1983). The main limitations of repeated intra-articular steroid injections are the risks of infection and the destruction of articular cartilage. Repeated intra-articular corticosteroid injections have been implicated in what is described as the 'chemical condylectomy' phenomenon in the TMJ (Toller 1977).

Arthrocentesis and arthroscopy have also been used as part of the management strategy of TMJ OA. Nitzan and Price presented a 20-month follow-up study of 36 persons with 38 dysfunctional joints that had not responded to non-surgical management, to determine the efficacy of arthrocentesis in restoring functional capacity to the osteoarthrosis joints (Nitzan 2001b). They concluded that arthrocentesis is a rapid and safe procedure that may result in the TMJ OA returning to a 'functional state'.

The value of TMJ arthroscopy may be in the early diagnosis and management of arthritic processes affecting the TMJ, especially early-stage arthritic disease, to avoid the complications of open bite and ankylosis (Holmlund 1986).

Invasive (surgical) modalities

While the majority of individuals with TMJ OA can be successfully managed with non-invasive/minimally invasive procedures, there is a small group with OA (< 20%) who have such severe pathology, pain, and dysfunction that invasive surgical management must be considered (Mercuri 2006).

Arthroplasty (reshaping the articular surfaces to eliminate osteophytes, erosions, and irregularities) found in osteoarthritis refractory to other therapeutic modalities was described in 1966 by Dingman and Grabb (Dingman 1966). While this technique reportedly provided pain relief, concerns about the resultant mandibular dysfunctions, dental malocclusions, facial asymmetries, and the potential for development of further bony articular degeneration, disc disorders or loss, and ankylosis led to the development of techniques for interposing autogenous tissues and alloplastic materials (e.g. the vascularized local temporalis muscle flap appears to present the most applicable data for the management of the arthritic TMJ) (Feinberg 1989).

Individuals with active TMJ OA and either concomitant or resultant maxillofacial skeletal discrepancies, and treated only with orthognathic surgery, often have poor outcomes and significant relapse (Wolford 2003).

Distraction osteogenesis may make its own contribution to TMJ OA in the future (van Strijen 2001).

Salvage modalities

Total joint replacement by grafts or implants, also denominated as salvage modalities, have been recommended for severe TMJ OA (Mercuri 2008). In a 'growing person' affected by either low-inflammatory or high-inflammatory arthritic disease, the costochondral graft has been the autogenous bone most frequently recommended for the reconstruction of the TMJ (MacIntosh 2000). However, orthopedists recommend alloplastic reconstruction when total joint replacement is required for the management of a 'non-growing person' affected by TMJ OA (Chapman 2001).

In the TMJ, alloplastic reconstruction has been discussed at length (McBride 1994; Mercuri 1998; Mercuri 1999). All of these authors agree that when the mandibular condyle is extensively damaged, degenerated, or lost, as in arthritic conditions, replacement with either autogenous graft or alloplastic implant is an acceptable approach to achieve optimal symptomatic and functional improvement (Mercuri 2008; Tanaka 2008).

OBJECTIVES

To investigate the effects of different surgical and non-surgical therapeutic options for the management of TMJ OA in adult patients.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) were considered in this review.

Types of participants

Adult patients over the age of 18 with clinical and/or radiological diagnosis of temporomandibular joint osteoarthritis (TMJ OA) according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) guideline were considered. Trials in which the inclusion criteria were compatible with the RDC/TMD diagnosis for OA were also considered. Complementary assessments by means of arthroscopy, computerised tomography (CT) scan or magnetic resonance imaging (MRI) were not a prerequisite for inclusion. We excluded studies which had been conducted on people with polyarthropathies.

We considered studies which included participants with two or more types of TMD only if separate data were provided for patients with TMJ OA.

Types of interventions

Any forms of non-surgical or surgical therapy for TMJ OA were considered. Studies that evaluated those interventions against each other, placebo or no therapy were included. Trials which permitted any analgesics to be administered as concomitant therapy, provided they were distributed similarly between the two groups, were also considered for inclusion.

Types of outcome measures

Primary outcomes

1. Pain/tenderness/discomfort (associated with the TMJs or jaw muscles): patient-assessed using any recognized validated pain scale.
2. Extent of mandibular movement (maximum jaw opening, lateral movement and protrusion): this could be assessed by a ruler, calliper, kinesiograph either actively (the patients open their jaw themselves) or passively (the clinician opens the jaw of the patient).
3. Subjective TMJ sounds, as perceived by the patients (if present, attenuated or absent).

Secondary outcomes

1. Any self assessed quality of life or patient satisfaction evaluated with a validated questionnaire (e.g. Short Form-36 Health Survey (SF-36) or Oral Health Impact Profile (OHIP)).
2. Morphological changes (change in shape) of the TMJs as assessed by imaging (standard radiography, CT or MRI).
3. TMJ sounds as assessed by auscultation (if present, attenuated or absent).

4. Number of visits.
5. Number of days absent from work.
6. In studies including surgical intervention, we will also consider mean operating time and duration of hospital admission (number of days).

Adverse events

We considered any complications that occurred during or after the therapy. If the report provided any data about the severity of complications this was also recorded.

Costs

Direct costs of therapy and hospital bed.

Search methods for identification of studies

Electronic searches

For the identification of studies included or considered for this review, detailed search strategies were developed for each database to be searched. These were based on the search strategy developed for MEDLINE (Ovid) but revised appropriately for each database.

For the MEDLINE search, the subject search was run with the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials in MEDLINE: sensitivity maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0 (updated March 2011) ([Higgins 2011](#)).

The following databases were searched:

- Cochrane Oral Health's Trials Register (to 26 September 2011) ([Appendix 1](#))
- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 3) ([Appendix 2](#))
- MEDLINE via Ovid (1950 to 26 September 2011) ([Appendix 3](#))
- Embase via Ovid (1980 to 26 September 2011) ([Appendix 4](#))
- PEDro (1929 to 26 September 2011) ([Appendix 5](#)).

There was no language restriction on included studies and we arranged for translation of any relevant papers not in the English language.

Searching other resources

We confirmed from Cochrane Oral Health which journals had already been handsearched as part of the Cochrane worldwide handsearching programme (see the [Masterlist](#) of journals searched to date) and handsearched the following journals:

- *Cranio: the Journal of Craniomandibular Practice* (from 1997 to 26 September 2011)
- *Journal of Orofacial Pain* (from 1993 to 26 September 2011)
- *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics* (from 2003 to 26 September 2011).

The reference lists of any clinical trials that were identified were cross-checked for additional trials.

We contacted the investigators of the included studies by electronic mail to ask for additional details of their trials and for any

information they may have about any further published and unpublished trials.

Data collection and analysis

Selection of studies

Two review authors (Raphael Freitas de Souza (RFS) and Claudia Helena Lovato da Silva (CLS)) independently assessed the abstracts of studies resulting from the searches. Full copies of all relevant and potentially relevant studies, i.e. those appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, were obtained. The full text papers were assessed independently and in duplicate by two review authors and any disagreement on the eligibility of included studies was resolved through discussion and consensus or if necessary through a third party (Mona Nasser (MN)). All irrelevant records were excluded; details of the studies and the reasons for their exclusion were noted in the [Characteristics of excluded studies](#) table in Review Manager 5.1 ([RevMan 2011](#)).

Data extraction and management

Study details were entered into the [Characteristics of included studies](#) table in RevMan 5.1. The review authors collected outcomes data using a pre-determined form designed for this purpose. Data were extracted independently and in duplicate by two review authors (Zbys Fedorowicz (ZF) and MN). The review authors only included data if there was an independently reached consensus; any disagreements were resolved by consulting with a third review author (RFS).

The following details were extracted:

- (1) Trial methods
 - (a) method of allocation
 - (b) masking of participants and outcomes (if feasible)
 - (c) exclusion of participants after randomisation and proportion of losses at follow-up.
- (2) Participants
 - (a) demographic characteristics including symptoms of temporomandibular joint disorders (TMDs)
 - (b) source of recruitment
 - (c) country of origin
 - (d) sample size
 - (e) age
 - (f) sex
 - (g) inclusion and exclusion criteria as described in the [Criteria for considering studies for this review](#) section
 - (h) presence of co-morbidities such as fibromyalgia, irritable bowel syndrome, headache, and mitral valve prolapse.
- (3) Intervention
 - (a) type, dose and frequency of the intervention, type of surgical procedure
 - (b) duration and length of follow-up.
- (4) Control
 - (a) type, dose and frequency of the control or placebo or no therapeutic modality
 - (b) duration and length of follow-up.
- (5) Outcomes
 - (a) primary and secondary outcomes as described in the [Types of outcome measures](#) section.

If stated, the sources of funding of any of the included studies were recorded. The review authors used this information to help them assess heterogeneity and the external validity of the trials.

Assessment of risk of bias in included studies

Each of two review authors (ZF and MN) graded the selected trials using a simple contingency form and followed the domain-based evaluation described in the *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0 ([Higgins 2011](#)). The evaluations were compared and any inconsistencies between the review authors were discussed and resolved.

The following domains were assessed as at low risk of bias, unclear risk of bias or high risk of bias:

1. random sequence generation (selection bias);
2. allocation concealment (selection bias);
3. blinding (performance bias and detection bias);
4. incomplete outcome data (attrition bias);
5. selective reporting (reporting bias);
6. other bias.

Overall risk of bias in any included study was categorised according to the following:

- low risk of bias (plausible bias unlikely to seriously alter the results) if all key domains were assessed as at low risk of bias;
- unclear risk of bias (plausible bias that raises some doubt about the results) if one or more key domains were assessed as at unclear risk of bias; or
- high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more key domains were assessed as at high risk of bias.

These assessments are reported in the [Risk of bias in included studies](#) table.

Measures of treatment effect

Data were analysed by RFS and ZF using RevMan 5.1 and reported according to the criteria described in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0 ([Higgins 2011](#)).

For dichotomous data, the estimates of effect of an intervention were expressed as risk ratios together with 95% confidence intervals. For continuous outcomes, mean differences and 95% confidence intervals were used to summarise the data for each group where the mean difference and standard deviations were calculable from the data presented.

Assessment of heterogeneity

The review authors assessed clinical heterogeneity by examining the characteristics of the included studies. This included differences between the types of participants, the interventions and the outcomes across the trials. We planned to assess statistical heterogeneity using a Chi² test in addition to the I² statistic, where I² values over 50% indicate moderate to high heterogeneity ([Higgins 2003](#)). However, we were not able to do that due to the limited number of included studies.

Assessment of reporting biases

If we had identified a sufficient number of included studies considering similar interventions and outcomes, we would have attempted to assess publication bias using a funnel plot (Egger 1997).

Data synthesis

Due to the significant clinical heterogeneity between the included studies in terms of the interventions used we were unable to combine the results in a meta-analysis and therefore present data for individual outcomes and comparisons together with a descriptive analysis as appropriate.

If studies of similar comparisons reporting the same outcome variables are available in future updates, we will use the fixed-effect and random-effects models as appropriate for the synthesis and meta-analysis of any quantitative data. We will use the fixed-effect model if we establish that the each study is estimating the same quantity, otherwise we will use the random-effects model. If we establish that there is heterogeneity between the studies, we may use a random-effects model, but if the heterogeneity between the studies is significant or the studies are too clinically diverse, we will not undertake a meta-analysis.

Subgroup analysis and investigation of heterogeneity

In future updates if sufficient data are available, we will conduct a subgroup analysis according to age, gender and the degree of severity of OA.

Sensitivity analysis

If there are sufficient included trials in future updates, the review authors plan to conduct sensitivity analyses to assess the robustness of their review results by repeating the analysis after exclusion of lower quality trials. In addition, the authors will undertake sensitivity analyses to examine the effect of allocation concealment, blinded outcome assessment and completeness of follow-up.

RESULTS

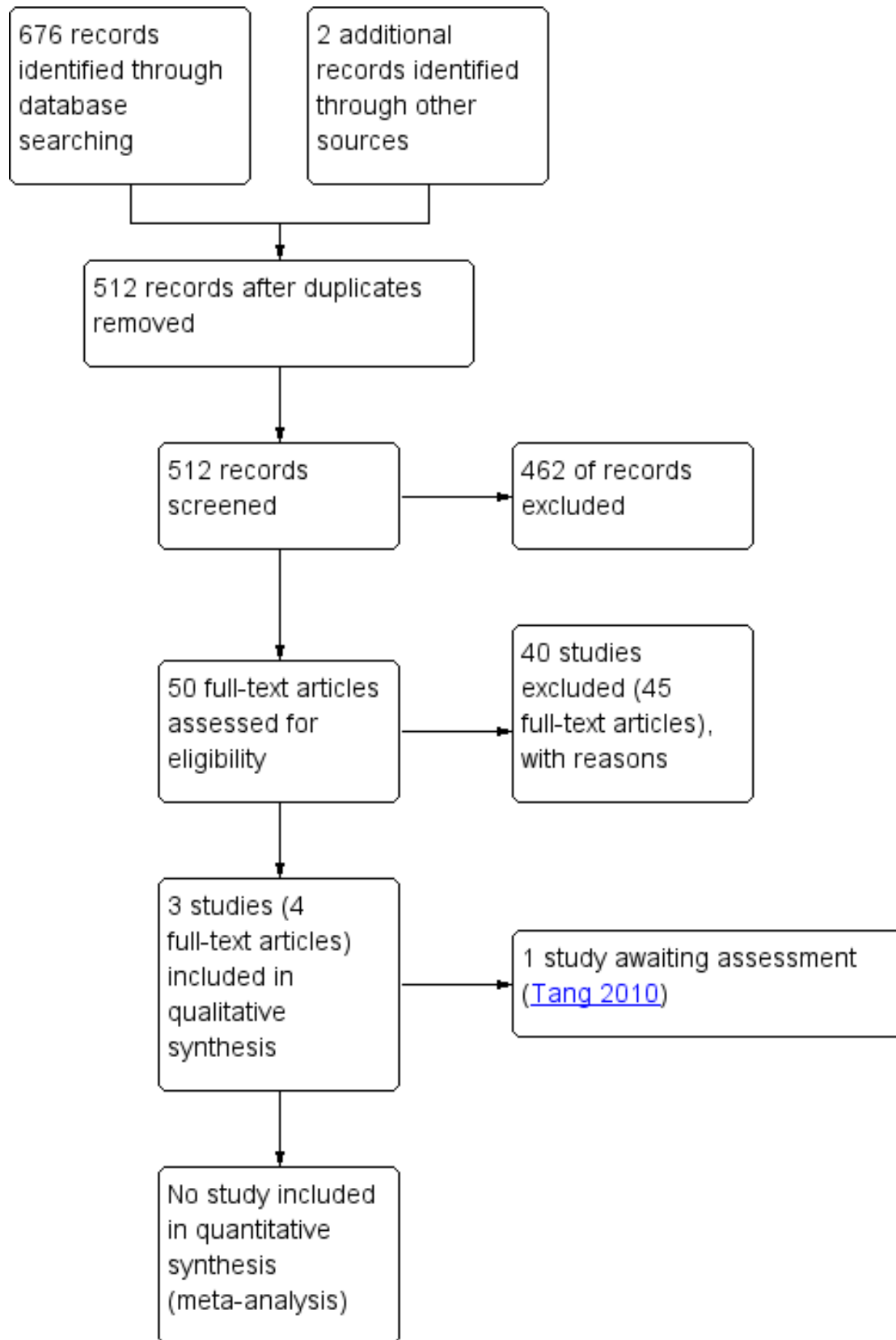
Description of studies

Results of the search

The search strategy retrieved 676 (42 Cochrane Oral Health's Trials Register, 69 CENTRAL, 396 MEDLINE, 81 Embase, 88 PEDro) references to studies and two additional reports were obtained through other sources, which after de-duplication resulted in 512 potentially eligible studies. After examination of the titles and abstracts of these references, all but 50 were eliminated and excluded from further assessment. Full text copies of these potentially relevant studies were obtained. Only three of the studies matched our inclusion criteria.

See the study flow diagram for further details (Figure 1).

Figure 1. Study flow diagram.



Included studies

We have identified three studies that matched our inclusion criteria (Bjørnland 2007; Mejersjö 2008; Thie 2001). Bjørnland 2007 (Norway) and Mejersjö 2008 (Sweden) were conducted in Europe and Thie 2001 (Canada) was conducted in North America. Two of the included trials recruited participants according to the RDC/TMD guideline (Bjørnland 2007; Mejersjö 2008) and one recruited those according to criteria compatible with the RDC/TMD diagnosis for osteoarthritis (OA) (Thie 2001). Of the three included trials all participants underwent complementary assessment by means of CT scan.

All participants of the three included trials were recruited in university clinics.

Bjørnland 2007 compared intra-articular injections of sodium hyaluronate with corticosteroids. Mejersjö 2008 compared diclofenac sodium with occlusal splint therapy. Thie 2001 compared glucosamine sulfate or ibuprofen.

All included trials considered pain or tenderness of the temporomandibular joint (TMJ) and masticatory muscles, as well as measures of mandibular movement, as outcomes. Adverse effects or post-surgical complications were also reported by the three included studies. Less frequent outcome measures were TMJ sounds (Bjørnland 2007) and morphological changes as assessed by CT scans (Mejersjö 2008).

More details are stated in the Characteristics of included studies table.

Excluded studies

All 40 studies which did not match our inclusion criteria were excluded and the reasons for their exclusion were noted in the Characteristics of excluded studies table.

The principal reasons for exclusion of many of the studies were related to the characteristics of the enrolled participants.

- Other TMJ disorders than OA (Al-Badawi 2004; Bertolucci 1995; Di Rienzo Businco 2004; Ekberg 1996; Ekberg 1998; Ekberg 2002; Emshoff 2008; Fikáčková 2007; Funch 1984; Ismail 2007; Kopp 1985; Kulekcioglu 2003; Maloney 2002; Maluf 2010; Nguyen 2001; Okeson 1983; Shi 2001; Stegenga 1993; Stowell 2007; Turk 1993; Winocur 2000), whereas a few excluded participants with signs of TMJ OA (Ayesh 2008; Schmid-Schwab 2006; Truelove 2006).
- Use of the RDC/TMD or compatible criteria but the participants were diagnosed with two or more TMDs and did not provide separate data for participants with TMJ OA (Bertolami 1993; List 2001; Marini 2010; Nilsson 2009; Peroz 2004; Reid 1994; Turner 2006).
- Study designs that were not eligible for this review (Bjørnland 1995; Haddad 2000; Israel 2010; Jones 2011; Kurita 2007; Machon 2011; Ohnuki 2006).
- Incomplete data and poor quality (Guarda Nardini 2004).
- Protocol violation (Guarda Nardini 2005).

Risk of bias in included studies

Of the three included studies, two were judged as at unclear risk of bias (Bjørnland 2007; Thie 2001) and one as high risk (Mejersjö 2008). Please see Figure 2 and Figure 3 for a summary assessment and the risk of bias tables (Characteristics of included studies) for the judgement of each study.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

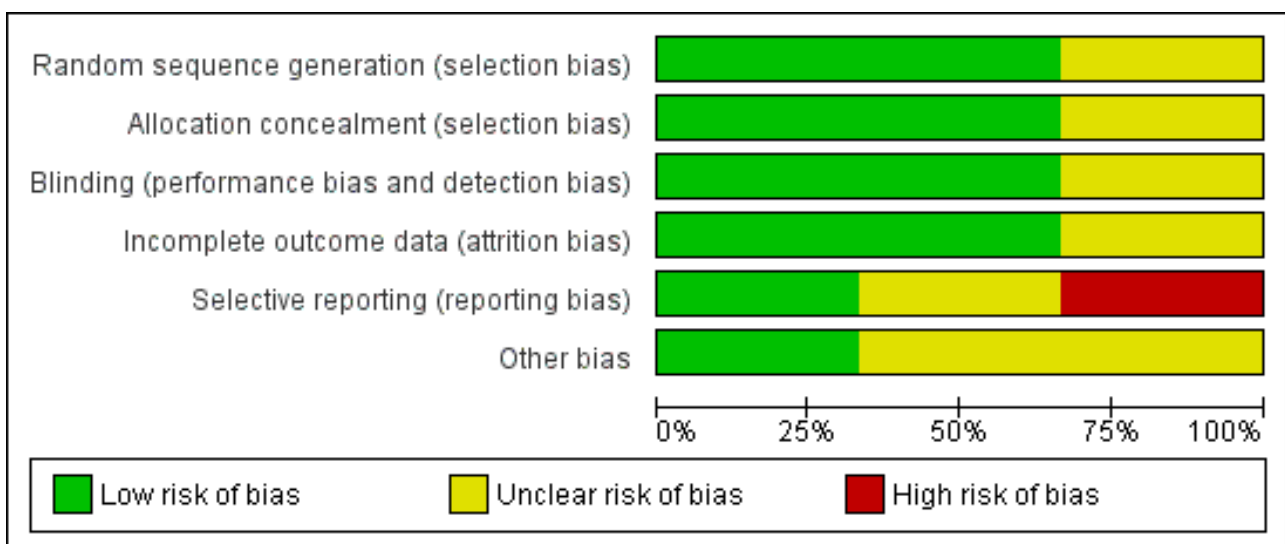
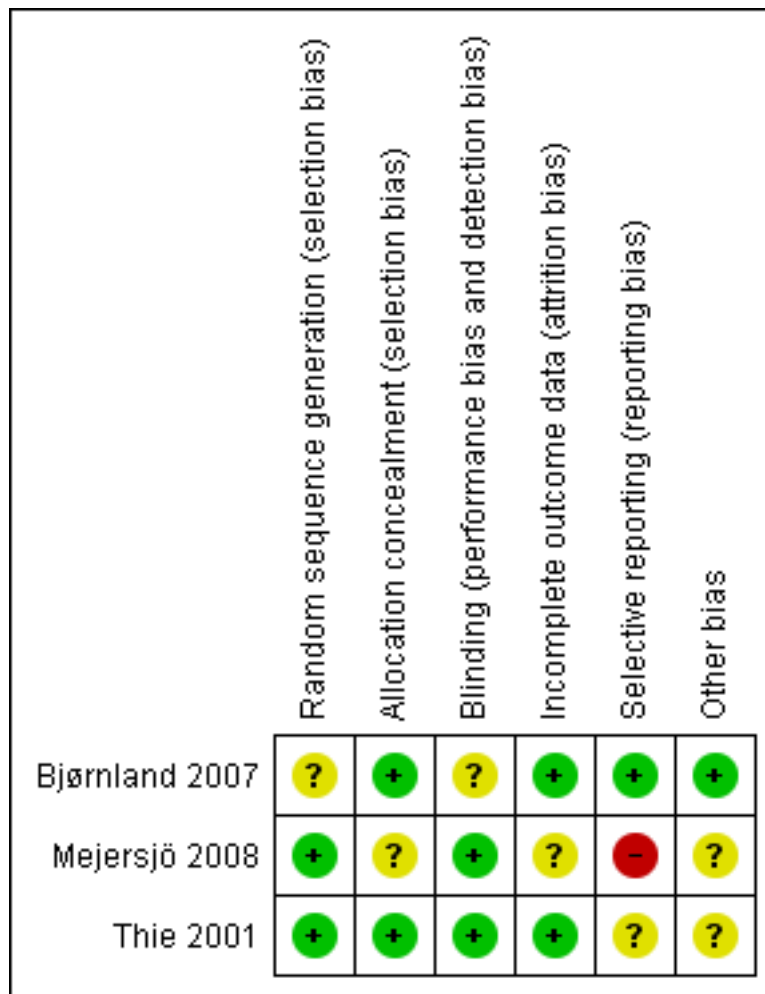


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Effects of interventions

Comparison 1. Sodium hyaluronate versus corticosteroids

Only Bjørnland 2007 compared these two interventions (40 participants).

Mean differences for reported pain on a VAS were -14.00 mm (95% confidence interval (CI): -30.80 to 2.80) at 14 days after the first injection (Analysis 1.1), and -10.00 mm (95% CI: -26.56 to 6.56)

after 1 month (Analysis 1.2). After 6 months, both interventions showed significant mean difference (-17.00, 95% CI: -32.60 to -1.40), with lower pain observed after injections with sodium hyaluronate (Analysis 1.3; Figure 4). Among the two groups, pain on palpation of the affected and contralateral TMJ and masticatory muscles presented similar frequencies regardless of the time (Analysis 1.4; Analysis 1.5; Analysis 1.6; Analysis 1.7; Analysis 1.8; Analysis 1.9; Analysis 1.10; Analysis 1.11; Analysis 1.12; Figure 5; Figure 6; Figure 7).

Figure 4. Forest plot of Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1.3. Reported pain (mm on VAS), 6 months.

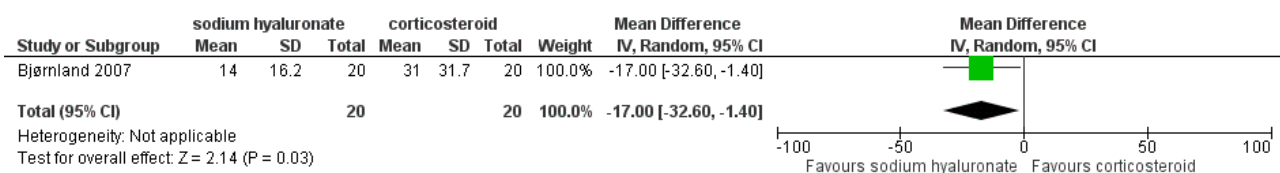


Figure 5. Forest plot of Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1.6. Pain on palpation of the affected TMJ, after 6 months.

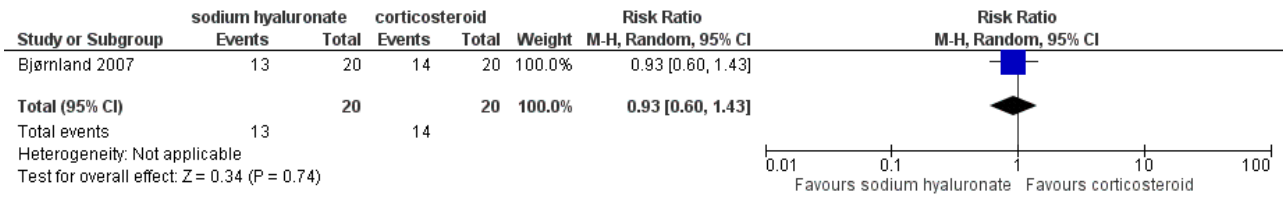


Figure 6. Forest plot of Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1.9. Pain on palpation of the contralateral TMJ, after 6 months.

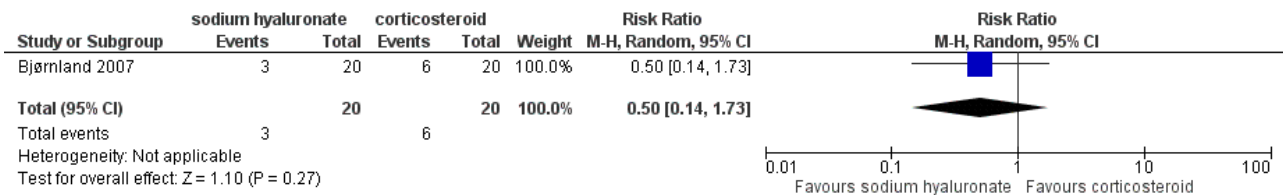
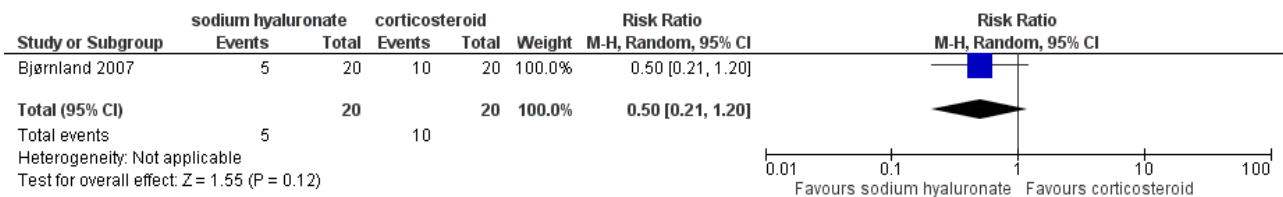


Figure 7. Forest plot of Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1.12. Pain on palpation of the masticatory muscles, after 6 months.



The study found lower frequency of TMJ sounds among the participants receiving sodium hyaluronate after 14 days (risk ratio: 0.59, 95% CI: 0.37 to 0.95) (Analysis 1.13). However, risk ratios at 1 and 6 months of follow-up are not significant (0.83, 95% CI: 0.47 to 1.47, and 0.55, 95% CI: 0.16 to 1.91, respectively) (Analysis 1.14; Analysis 1.15).

None of the mean differences between interventions for the measures of jaw movements showed significance (Analysis 1.16; Analysis 1.17; Analysis 1.18; Analysis 1.19; Analysis 1.20; Analysis 1.21; Analysis 1.22; Analysis 1.23; Analysis 1.24; Analysis 1.25; Analysis 1.26; Analysis 1.27; Figure 8; Figure 9; Figure 10; Figure 11).

Figure 8. Forest plot of Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1.18. Maximum jaw opening (mm), 6 months.

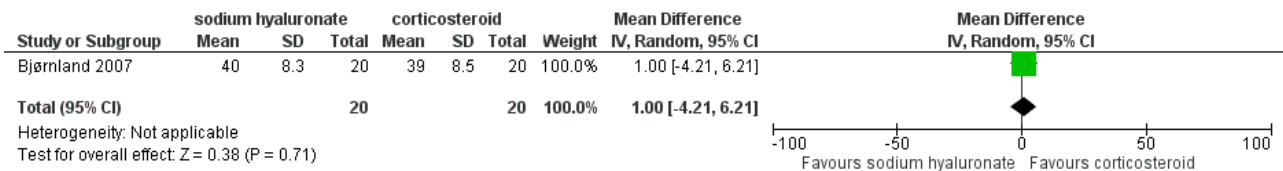


Figure 9. Forest plot of Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1.21. Lateral movement to affected side (mm), 6 months.

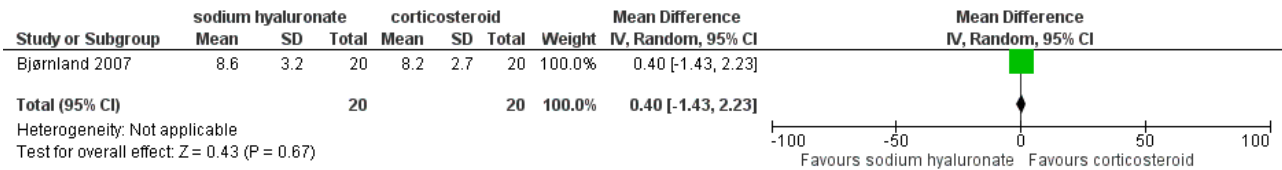


Figure 10. Forest plot of Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1.24. Contralateral movement (mm), 6 months.

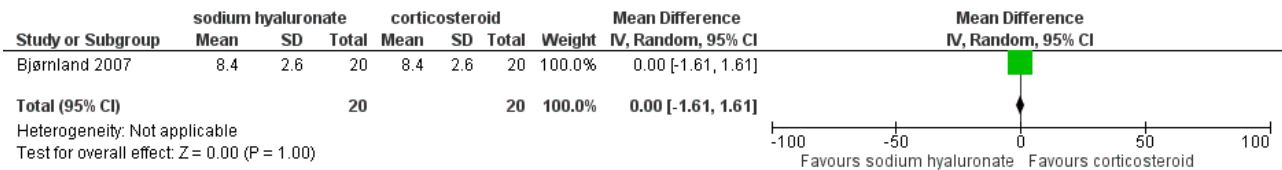
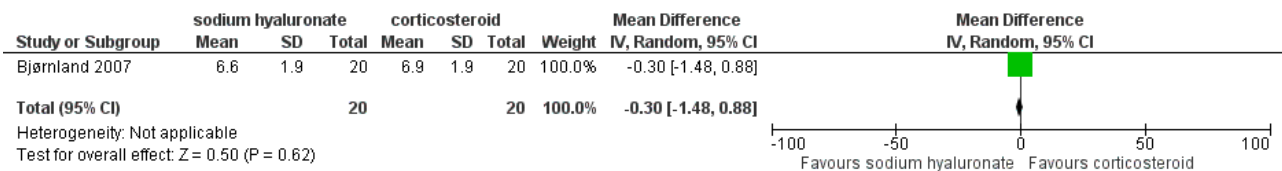


Figure 11. Forest plot of Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1.27. Jaw protrusion (mm), 6 months.



The risk ratio for complications was 1.20 (95% CI: 0.44 to 3.30), which discloses no difference between the interventions (Analysis 1.28).

Comparison 2. Diclofenac sodium versus occlusal splint

Only the Mejersjö 2008 trial compared these interventions (29 participants).

Data for pain on movement or pain on palpation of the affected TMJ (both after 1 week and 3 months) could not be extracted, as long as they are described as percentages of an unclear total number. The study reports morphological changes assessed by CT for the entire sample without distinction of group, so extraction was not possible.

The frequency of complications was similar for both groups (risk ratio: 1.07, 95% CI: 0.50 to 2.28) (Analysis 2.1), although their nature differed drastically (diclofenac sodium: gastrointestinal problems 3, sleepiness 3, dizziness 1; occlusal splint: sleeping problems 2, pressure or friction of teeth 3, increased decreased saliva 2).

Comparison 3. Glucosamine sulfate versus ibuprofen

The Thie 2001 study compared intraoral medication with glucosamine sulfate or ibuprofen (45 participants).

The researchers found that six participants in Group 1 did not experience significant improvement in TMJ pain compared to seven in Group 2 (Analysis 3.1) (Fisher's exact test, P = 0.73, according to the authors). The results for the other variables are described according to the changes from baseline after 90 days of

intervention. Mean difference for reported pain on a VAS was -4.57 mm (95% CI: -9.91 to 0.77) (Analysis 3.2).

Maximum jaw opening was similar for the tested interventions, both in its pain-free range (1.75, 95% CI: -4.10 to 7.60) and at its maximum voluntary movement (3.08, 95% CI: -0.97 to 7.13) (Analysis 3.3; Analysis 3.4).

BPI scores were similar for both groups, with no difference for the 'pain intensity' and the 'pain interference' domain either (-2.69, 95% CI: -7.38 to 2.00, and -6.74, 95% CI: -14.70 to 1.22, respectively) (Analysis 3.5; Analysis 3.6). Mean difference for the number of extraoral masticatory muscle tenderness was 0.38 (95% CI: -2.30 to 3.06) (Analysis 3.7). After 90 days, the use of acetaminophen was the same for both groups (t test; P = 0.11).

DISCUSSION

Summary of main results

Despite the wide range of therapeutic options available for the management of temporomandibular joint osteoarthritis (TMJ OA), this review included only a few trials which provided data for three comparisons for non-surgical and minimally invasive surgical modalities.

Intra-articular injections with sodium hyaluronate appear to be as effective as other modalities. One of the trials (Bjørnland 2007) found that intra-articular injections of both sodium hyaluronate or corticosteroids have similar effectiveness over several parameters.

However, TMJ pain seems to be slightly less after 6 months following injections of sodium hyaluronate, as well as TMJ sounds immediately after treatment.

Comparisons among non-surgical modalities showed no important differences either. Although diclofenac sodium showed similar benefits when compared with occlusal splints in terms of pain and complications at 3 months (Mejersjö 2008), symptoms were less intense at the 1 month follow-up for participants medicated with diclofenac sodium. Despite the similar number of complications for both interventions, the nature of these varies quite widely and these should be discussed with patients. Glucosamine was as effective as ibuprofen in terms of pain, discomfort and jaw movements, according to one of the trials (Thie 2001).

Overall completeness and applicability of evidence

The trials in general enrolled participants that were representative of the average TMJ OA patient with respect to gender and age (Kino 2005). However, any result should be interpreted with caution, as long as all comparisons are based on single studies. The external validity of these trials would be further enhanced by involving participants from other nationalities. Moreover, all participants were recruited from specialized university clinics; this way, it is likely that most were referred patients. Other settings such as general practice or emergency facilities may provide participants with different therapeutic responsiveness. Although some of the trials considered a wide range of outcomes, an aspect that should be encouraged, data extraction was not always feasible.

The scarcity of comparative evidence for intra-articular injections, occlusal splints and pharmacological agents is somewhat disappointing. However, even more important is the noticeable absence for other interventions, i.e. reassurance, physiotherapy, short-wave diathermy, ultrasound, iontophoretically applied corticosteroids, laser therapy and open surgery. The lack of data from randomised controlled trials (RCTs) makes decision making about the management of TMJ OA strongly dependent on consumers' preferences and clinical expertise.

Quality of the evidence

The review only found three unclear-high risk of bias studies with a small sample size. Two of the reports did not provide adequate information about important methodological aspects such as sequence generation, allocation concealment or blinding, despite the recommendations of guidelines such as CONSORT. A critical aspect in terms of quality of the studies is selective reporting. One of the included studies did not provide extractable results, possibly because they were not considered as the most relevant by authors or journal or both (Furukawa 2007).

As we had only one study for each comparison and outcome, we were not able to judge about consistency between study results.

We only had three included studies, therefore, we were not able to assess publication bias.

Potential biases in the review process

Before undertaking this review, one of our main concerns was the possible differences in the diagnosis of TMJ disorders between studies. The inclusion of participants with a generic diagnosis (e.g. painful TMJ) might well reduce the validity of our results regarding

our clinical question. Moreover, different diagnostic approaches for TMJ OA would insert non-comparable data in our review. Thus, we considered the RDC/TMD as a standard approach, due to its comprehensiveness and wide use for research about disorders of the TMJ. Although RDC/TMD may not be highly reliable for TMJ OA (John 2005), it provides a list of criteria which can be promptly compared among different studies (Laskin 2007) and is likely to be the best alternative to date (Hasanain 2009).

We employed a search in several databases and without any language restriction, in an attempt to include all eligible studies. A successful attempt to translate non-English studies (e.g. Shi 2001) was conducted in order to minimize language bias. However, we still had a low number of included studies, which are most likely linked to the restrictive inclusion criteria used.

One of the limitations of our review was the bad reporting of the trial publications. We attempted to contact the authors of the included studies for clarification regarding unclear aspects and missing data in order to minimize this condition, but were not successful. Therefore, some criteria from the risk of bias table remained unclear. Moreover, there were a number of studies that included also other patients in the trial and did not provide separate data for patients with TMJ OA and therefore, we had to exclude those studies too.

Agreements and disagreements with other studies or reviews

The results of this and other published reviews reinforce the idea that we have a restricted number of RCTs about the management of TMJ disorders. A systematic review of surgical therapy of the TMJ classified 3 out of 22 included studies as RCT, and none of the trials included participants with TMJ OA (Reston 2003). The number of studies included in other Cochrane reviews investigating TMJ disorders was not dissimilar and ranged from two to seven (Guo 2009; Koh 2003; Shi 2003).

AUTHORS' CONCLUSIONS

Implications for practice

The available evidence regarding the management of temporomandibular joint osteoarthritis (TMJ OA) continues to present challenges to clinical decision making. The scarce evidence available suggests that certain non-surgical and minimally invasive interventions might be equally effective, but any finding should be interpreted with caution.

Implications for research

In light of the paucity of evidence for the effectiveness of interventions for the management of TMJ OA, further parallel group randomised controlled trials (RCTs) comparing different interventions may provide useful data. The characteristics of participants is of concern, as long as several excluded studies did not classify TMJ problems according to their different clinical forms (e.g. TMJ OA), thus the use of RDC/TMD should be encouraged as a tool that can be used in the comparison of different trials. RCTs investigating modalities of open surgery for treating TMJ OA would provide valuable data for both clinicians and consumers. Placebo or sham interventions as comparators should provide valuable information about the effectiveness of management methods for TMJ OA as well. Future studies on the management of TMJ OA

should consider a comprehensive set of outcomes in addition to a longer follow-up period.

For more information as to the detailed design of research recommended please see Additional [Table 1](#).

ACKNOWLEDGEMENTS

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES
Characteristics of included studies [ordered by study ID]
Bjørnland 2007

Methods	<p>Parallel group trial in Norway, which compared sodium hyaluronate (S) and corticosteroids (C) for intra-articular injections in TMJ OA patients.</p> <p>No information about sequence generation methods. Reports cite sealed envelopes with codes, opened after confirming participants' eligibility and informed consent.</p> <p>Unawareness of participants and outcome assessors about the drug used.</p> <p>Participants were 40 out of 52 TMJ patients (12 presented no radiographic evidence of OA and were excluded before allocation). No drop-outs for the study (clinical assessment at follow-up), although a few participants did not return for radiographic examination (Group S: n = 3; Group C: n = 1).</p>
Participants	<p>40 patients of the Department of Oral Surgery and Oral Medicine, University of Oslo, divided into two groups (n = 20 each). All fulfilled the RDC/TMD criteria for TMJ OA.</p> <p>Group S: 19 women and 1 man, mean age (\pmSD): 53.4\pm12.9 years, mean duration of TMJ symptoms: 5.9\pm7.7 years.</p> <p>Group C: 15 women and 5 men, mean age (\pmSD): 50.0\pm13.3 years; mean duration of TMJ symptoms: 5.8\pm10.7 years.</p> <p>Inclusion criteria: (1) reported TMJ pain at function and rest form >1 year; (2) restricted mandibular function; (3) evidences of TMJ OA by CT scan, i.e. erosions, flattening and sclerosis/osteophytes of the condyle or articular fossa; (4) previous attempt of non-surgical treatment without success; (5) age >20 years.</p> <p>Exclusion criteria: (1) injections of corticosteroids or hyaluronate preparation within the previous 12 months; (2) history of general arthritis or other connective tissue disease; (3) known hypersensitivity to chicken, eggs or other avian products; (4) other systemic conditions (treatment with immunosuppressive drugs, general infection, and pregnant or breastfeeding women).</p>
Interventions	<p>Sodium hyaluronate (S) compared with a betamethasone sodium phosphate/betamethasone acetate combination (C).</p> <p>Two intra-articular injections (0.7-1.0 mL), 14 days apart. Follow-up: 14 days (before the 2nd injection), 1 month and 6 months.</p>
Outcomes	<p>(a) Pain on palpation of the affected and contralateral TMJ and masticatory muscles (VAS values and yes/no).</p> <p>(b) Extent of active mandibular movement (maximum jaw opening, lateral movement and protrusion).</p> <p>(c) TMJ sounds (crepitation and clicking) assessed by clinical exam.</p> <p>(d) Post-surgical complications.</p>

Bjørnland 2007 (Continued)

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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated into two groups". Comment: No clear description provided.
Allocation concealment (selection bias)	Low risk	Quote: "Forty sealed envelopes contained the code for participation in the two treatment groups, and the envelopes were not opened before it was determined the patient was eligible for study inclusion". Comment: Participants and investigators enrolling participants were unable to foresee the assignment.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	(a) Participants: Quote: "The patients were given information about the two drugs to be used for this study, without knowledge of which they were given". Comment: Yes. (b) Researcher: Unclear. (c) Outcome assessor: Unclear. (d) Data analyst: Unclear.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: ".there were no drop-outs for the clinical re-examinations". Comment: All outcome data appeared to be completely addressed.
Selective reporting (reporting bias)	Low risk	Quote: ".the aim of the present study was, therefore, to compare the efficacy and the complications of intra-articular injections of corticosteroids and sodium hyaluronate. We tested the hypothesis that there were no significant differences between intra-articular injections of the two drugs in terms of pain relief, joint sounds, function and complications". Comment: The stated objectives matched the listed outcomes.
Other bias	Low risk	The study appeared to be free of other sources of bias.

Mejersjö 2008

Methods	<p>Parallel group RCT in Sweden, which compared oral medication (diclofenac sodium - DS) versus occlusal splints (OS).</p> <p>Sequence generated according to computer generated tables and stratified according to the duration of symptoms (two strata: <6 months or >6 months). No information about allocation concealment was provided. The study employed blinded outcome assessors.</p> <p>Eligible participants were 29 out of 1417 orofacial pain patients. Reasons for exclusion were: did not fulfil inclusion criteria (n = 1373); refused to participate before or after randomisation (n = 11 and 3, respectively).</p> <p>Four participants (1 in DS and 3 in OS) stopped the treatment before 3 months.</p>
Participants	<p>29 TMJ OA patients referred to the Department of Stomatognathic Physiology of the University of Göteborg (27 women and 2 men; mean age: 62 years, range: 39-76 years). All had unilateral TMJ OA (right TMJ: 16; left TMJ: 13). 2/3 of the participants had some general pharmacological treatment, often related to circulatory disorders.</p>

Mejersjö 2008 (Continued)

Inclusion criteria: TMJ OA diagnosis according to the RDC/TMD.

Exclusion criteria: systemic joint disease, known sensitivity to acetylsalicylic acid, impaired coagulation, gastric ulcers, kidney or liver problems, and any previous treatment for the TMJ (except analgesics).

Group DS: n = 15; group OS: n = 14; instructions to take paracetamol tablets if additional analgesics were needed.

Interventions	<p>Group DS: diclofenac sodium 50 mg, 3 times daily.</p> <p>Group OS: acrylic flat occlusal splint covering all the upper teeth. The report does not clarify the regimen of use (e.g. continuous or during sleep only).</p> <p>The period of intervention for both groups was 3 months.</p>
Outcomes	<p>(a) Pain on movement and palpation.</p> <p>(b) Morphological changes of the TMJs as assessed by CT scans.</p> <p>(c) Adverse effects.</p>
Notes	<p>We considered the 3 months follow-up for this review, which coincides with the duration of interventions. The 1 year follow-up had several disagreements with the protocol and a large amount of drop-outs.</p> <p>No funding reported.</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The mode of treatment was decided according to two computer generated tables randomly produced in advance depending on whether the duration of symptoms was acute (<6 months) or chronic (>6 months)..."
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit a clear judgement.
Blinding (performance bias and detection bias) All outcomes	Low risk	<p>(a) Participants: N/A.</p> <p>(b) Researcher: N/A.</p> <p>(c) Outcome assessor: Yes.</p> <p>(d) Data analyst: Unclear.</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The report describes the frequency of drop-outs but not their reasons.
Selective reporting (reporting bias)	High risk	The study assessed a comprehensive set of outcomes; however, they were incompletely reported.
Other bias	Unclear risk	Participants were allowed to take paracetamol during the trial in order to achieve additional analgesia. However, the quantity and doses used by each group were unreported.

Thie 2001

Methods	<p>Parallel group trial in Canada about oral medications, with a 7 days run-in period. Several aspects associated with control of bias are well described.</p> <p>Sequence generated by means of block randomisation by a statistician. Identical clear capsules prepared and coded by a pharmacist. Neither participants nor researchers knew the administered medication before the end of the study.</p> <p>Eligible participants: 45 out of 176 interviewed volunteers. Reasons for exclusion were: no radiographic evidence of TMJ OA (n = 45); low pain levels (n = 33); allergy to NSAID (n = 12); participant did not proceed to radiographic assessment (n = 31).</p> <p>Withdrawals and losses:</p> <ul style="list-style-type: none"> • Group 1: three drop outs caused by stomach upset and one due to inadequate pain control. • Group 2: one caused by stomach upset and one by dizziness.
Participants	<p>45 orofacial pain patients of the University of Alberta or respondents to advertisement in the Edmonton area (40 women and 5 men).</p> <p>Inclusion criteria:</p> <ol style="list-style-type: none"> 1. Diagnosis of DJD of one or both TMJs according to the criteria of the American Board of Orofacial Pain. 2. Radiographic evidences of DJD (by CT scan). 3. Presence of moderate or worse TMJ pain on function. 4. Age >18 years. 5. Not pregnant. 6. OA was not a result of acute trauma, infection or systemic disease. 7. No history of intra-articular TMJ injections. 8. No previous use of glucosamine and/or chondroitin sulfate. 9. No history of congestive heart failure, renal or hepatic disease, hypersensitivity to NSAID, peptic ulceration, gastrointestinal bleeding, or coagulation disorder. 10.No active oral disease. 11.If using antidepressant or anxiolytic medication it must have been for at least 6 months. 12.If using an occlusal splint it must have been for at least 3 months. <p>Mean age (SD): Group 1 (n = 21): 36.6 (10.3); Group 2 (n = 18): 38.7 (13.3).</p>
Interventions	<p>Glucosamine sulfate 500 mg (Group 1) compared with ibuprofen 400 mg (Group 2).</p> <p>Participants used both medications 3 times daily, during 90 days.</p>
Outcomes	<p>Primary outcome: reduction of 20% or more in joint pain during function, assessed by a VAS.</p> <p>Secondary outcomes: (1) pain free and voluntary maximum incisal opening; (2) the Brief Pain Inventory (BPI) questionnaire; (3) extraoral masticatory muscle tenderness on 14 sites (= number of tender sites/14).</p> <p>Frequency of adverse effects.</p>
Notes	<p>Medications were donated by private companies.</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A statistician generated the randomisation sequence.

Thie 2001 (Continued)

Allocation concealment (selection bias)	Low risk	Medications were prepared and coded as identical clear capsules by a pharmacist. Investigators did not know which of the two medications was administered until the end of the trial.
Blinding (performance bias and detection bias) All outcomes	Low risk	(a) Participants: Yes. (b) Researcher: Yes. (c) Outcome assessor: Yes. (d) Data analyst: Unclear.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The report describes the frequency of drop-outs and their reasons. Although some missing participants reported gastric problems (expected in association with NSAID), the reasons were balanced across groups.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit a clear judgement.
Other bias	Unclear risk	It is unclear how the sponsorship of this study could have influenced results. Although the study used block randomisation, blinding was adequate and the report states that assignments were revealed after the end of the trial. Thus, it is unlikely that assignments were predictable.

DJD = degenerative joint disease; RCT = randomised controlled trial; RDC/TMD = Research Diagnostic Criteria for Temporomandibular Disorders; SD = standard deviation; TMJ OA = temporomandibular joint osteoarthritis.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Al-Badawi 2004	Participants presented arthralgia according to the RDC/TMD.
Ayesh 2008	Participants with TMJ OA were excluded.
Bertolami 1993	No separate data provided for patients with TMJ OA.
Bertolucci 1995	Participants were not diagnosed according to criteria compatible with RDC/TMD, and presented with disk displacement without reduction.
Bjørnland 1995	Non-RCT.
Di Rienzo Businco 2004	Participants received no specific diagnosis for TMJ pain.
Ekberg 1996	Participants received no specific diagnosis for TMJ pain.
Ekberg 1998	Participants received no specific diagnosis for TMJ pain.
Ekberg 2002	Participants received no specific diagnosis for TMJ pain.
Emshoff 2008	Participants with TMJ disorders according to the RDC/TMD were excluded.
Fikácková 2007	Participants with TMJ OA were excluded.
Funch 1984	Participants received no specific diagnosis of TMJ pain.
Guarda Nardini 2004	Incomplete data on the allocation of participants and masking of investigators.

Study	Reason for exclusion
	<p>Important imbalance in group size in addition to differences in the frequency of delivery of intervention and comparator.</p> <p>Very limited information about the characteristics of the participants and no usable data in the report.</p>
Guarda Nardini 2005	<p>Lack of detail about the inclusion criteria or the characteristics of participants and interventions and the overall conduct of the trial.</p> <p>Parallel arms study (intra-articular injections of sodium hyaluronate versus occlusal splints) with a third group consisting of participants who had refused any therapy for TMJ OA.</p>
Haddad 2000	Non-RCT.
Ismail 2007	No separate data provided for patients with TMJ OA.
Israel 2010	Non-RCT.
Jones 2011	Non-RCT.
Kopp 1985	Participants received no specific diagnosis for TMJ pain.
Kulekcioglu 2003	Diagnostic criteria not compatible with the RDC/TMD, no separate data provided for patients with TMJ OA.
Kurita 2007	Non-RCT.
List 2001	No separate data provided for patients with TMJ OA.
Machon 2011	Non-RCT.
Maloney 2002	No separate data provided for patients with TMJ OA.
Maluf 2010	Participants received no specific diagnosis for TMJ pain.
Marini 2010	No separate data provided for patients with TMJ OA.
Nguyen 2001	Participants received no specific diagnosis for TMJ pain.
Nilsson 2009	No separate data provided for patients with TMJ OA.
Ohnuki 2006	Non-RCT..
Okeson 1983	Participants received no specific diagnosis for TMJ pain.
Peroz 2004	No separate data provided for patients with TMJ OA.
Reid 1994	No separate data provided for patients with TMJ OA.
Schmid-Schwab 2006	Participants received no specific diagnosis for TMJ pain.
Shi 2001	Diagnostic criteria not compatible with the RDC/TMD, no separate data provided for patients with TMJ OA.
Stegenga 1993	Diagnostic criteria not compatible with the RDC/TMD, no separate data provided for patients with TMJ OA.

Study	Reason for exclusion
Stowell 2007	Participants received no specific diagnosis for TMJ pain.
Truelove 2006	Participants with TMJ OA were excluded.
Turk 1993	Participants received no specific diagnosis for TMJ pain.
Turner 2006	No separate data provided for patients with TMJ OA.
Winocur 2000	Participants received no specific diagnosis for TMJ pain.

RCT = randomised controlled trial; RDC/TMD = Research Diagnostic Criteria for Temporomandibular Disorders; TMJ OA = temporomandibular joint osteoarthritis.

Characteristics of studies awaiting assessment [ordered by study ID]

Tang 2010

Methods	<p>Parallel group trial in China: intra-articular injections of sodium hyaluronate versus placebo. Very limited information about trial conduct.</p> <p>No information about how the generation of allocation sequence (Quote: "Forty OA patients were randomly divided into groups").</p> <p>The report cites blinding of both patients and researchers ("operator"), but gives no further information about blinding or allocation concealment, i.e. delivery of unidentified vials with the tested substances. No reference made to the exclusion of participants after sequence generation.</p>
Participants	<p>40 participants, divided into two groups (n = 20 each). All were patients of the West China Hospital of Stomatology and presented TMJ OA from 1/2 to 1 year.</p> <p>Group 1: 11 women and 9 men, mean age: 43 years, range: 28-57 years.</p> <p>Group 2: 10 women and 10 men, mean age: 44 years, range: 25-63 years.</p> <p>Inclusion criteria: TMJ OA diagnosis according to the RDC/TMD, history of unsuccessful treatment by non-surgical therapy (jaw exercises, physiotherapy and occlusal splints).</p> <p>Exclusion criteria: systemic joint disease, treatment with immunosuppressive drugs, any organ disease, general infection or trauma-induced joint disorder.</p>
Interventions	<p>Group 1: intra-articular injections of sodium hyaluronate (1 mL, molecular weight: 1,500 - 2,500 kDa).</p> <p>Group 2: intra-articular injections of physiologic saline solution.</p> <p>Both groups received five injections (1/week for 5 weeks). Follow-up: 1 week.</p>
Outcomes	TMJ pain (VAS value, 0 to 10).
Notes	We contacted the authors in order to check if they employed any form of randomisation.

RDC/TMD = Research Diagnostic Criteria for Temporomandibular Disorders; TMJ OA = temporomandibular joint osteoarthritis.

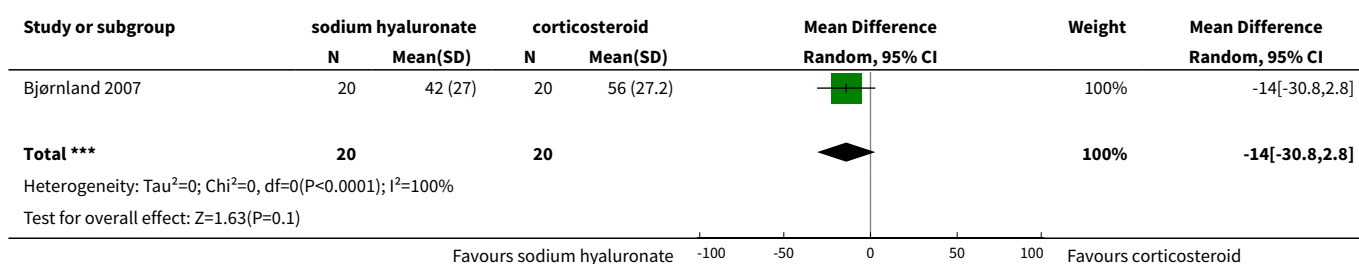
DATA AND ANALYSES

Comparison 1. Comparison 1. Sodium hyaluronate versus corticosteroids

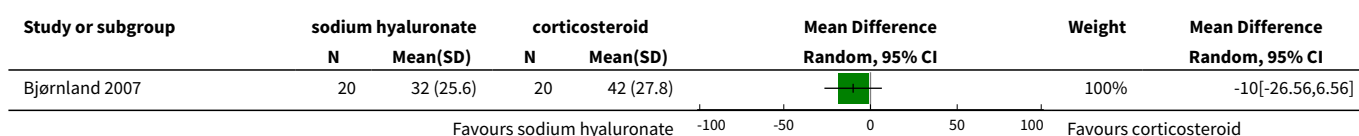
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Reported pain (mm on VAS), 14 days	1	40	Mean Difference (IV, Random, 95% CI)	-12.00 [-30.80, 2.80]
2 Reported pain (mm on VAS), 1 month	1	40	Mean Difference (IV, Random, 95% CI)	-10.0 [-26.56, 6.56]
3 Reported pain (mm on VAS), 6 months	1	40	Mean Difference (IV, Random, 95% CI)	-17.0 [-32.60, -1.40]
4 Pain on palpation of the affected TMJ, after 14 days	1	40	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.64, 1.02]
5 Pain on palpation of the affected TMJ, after 1 month	1	40	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.68, 1.16]
6 Pain on palpation of the affected TMJ, after 6 months	1	40	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.60, 1.43]
7 Pain on palpation of the contralateral TMJ, after 14 days	1	40	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.18, 1.40]
8 Pain on palpation of the contralateral TMJ, after 1 month	1	40	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.14, 1.73]
9 Pain on palpation of the contralateral TMJ, after 6 months	1	40	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.14, 1.73]
10 Pain on palpation of the masticatory muscles, after 14 days	1	40	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.35, 1.27]
11 Pain on palpation of the masticatory muscles, after 1 month	1	40	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.23, 1.07]
12 Pain on palpation of the masticatory muscles, after 6 months	1	40	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.21, 1.20]
13 Presence of TMJ sounds, after 14 days	1	40	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.37, 0.95]
14 Presence of TMJ sounds, after 1 month	1	40	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.47, 1.47]
15 Presence of TMJ sounds, after 6 months	1	40	Odds Ratio (M-H, Random, 95% CI)	0.55 [0.16, 1.91]
16 Maximum jaw opening (mm), 14 days	1	40	Mean Difference (IV, Random, 95% CI)	-1.80 [-7.10, 3.50]
17 Maximum jaw opening (mm), 1 month	1	40	Mean Difference (IV, Random, 95% CI)	-2.60 [-7.84, 2.64]
18 Maximum jaw opening (mm), 6 months	1	40	Mean Difference (IV, Random, 95% CI)	1.0 [-4.21, 6.21]

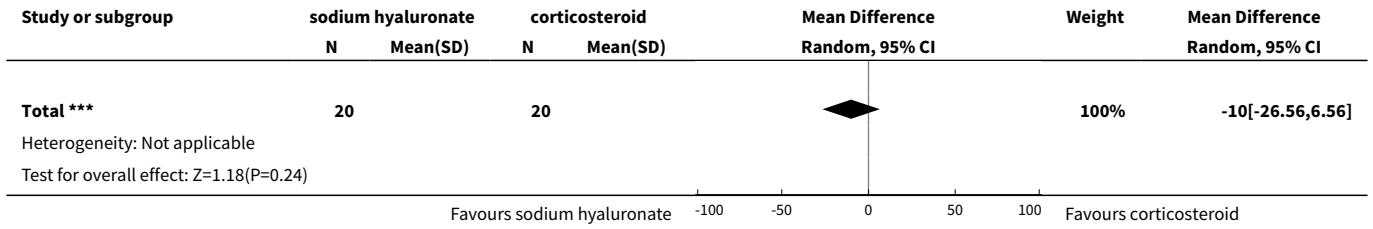
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
19 Lateral movement to affected side (mm), 14 days	1	40	Mean Difference (IV, Random, 95% CI)	-0.80 [-2.47, 0.87]
20 Lateral movement to affected side (mm), 1 month	1	40	Mean Difference (IV, Random, 95% CI)	1.10 [-0.71, 2.91]
21 Lateral movement to affected side (mm), 6 months	1	40	Mean Difference (IV, Random, 95% CI)	0.40 [-1.43, 2.23]
22 Contralateral movement (mm), 14 days	1	40	Mean Difference (IV, Random, 95% CI)	-0.30 [-2.01, 1.41]
23 Contralateral movement (mm), 1 month	1	40	Mean Difference (IV, Random, 95% CI)	0.60 [-1.32, 2.52]
24 Contralateral movement (mm), 6 months	1	40	Mean Difference (IV, Random, 95% CI)	0.0 [-1.61, 1.61]
25 Jaw protrusion (mm), 14 days	1	40	Mean Difference (IV, Random, 95% CI)	-0.40 [-1.67, 0.87]
26 Jaw protrusion (mm), 1 month	1	40	Mean Difference (IV, Random, 95% CI)	0.20 [-1.08, 1.48]
27 Jaw protrusion (mm), 6 months	1	40	Mean Difference (IV, Random, 95% CI)	-0.30 [-1.48, 0.88]
28 Post-surgical complications	1	40	Risk Ratio (M-H, Random, 95% CI)	1.2 [0.44, 3.30]

Analysis 1.1. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 1 Reported pain (mm on VAS), 14 days.

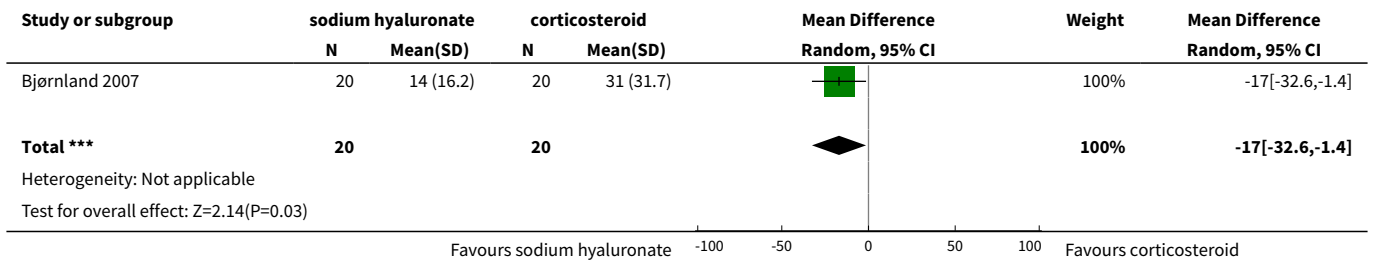


Analysis 1.2. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 2 Reported pain (mm on VAS), 1 month.

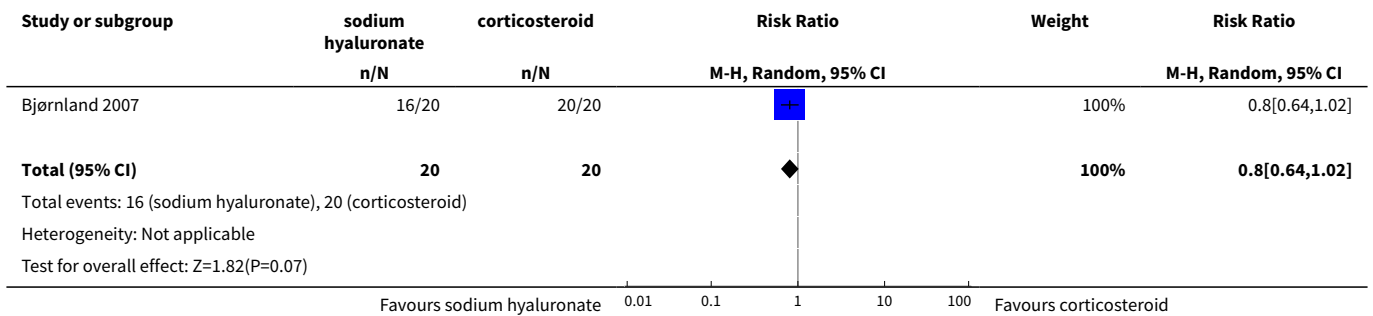




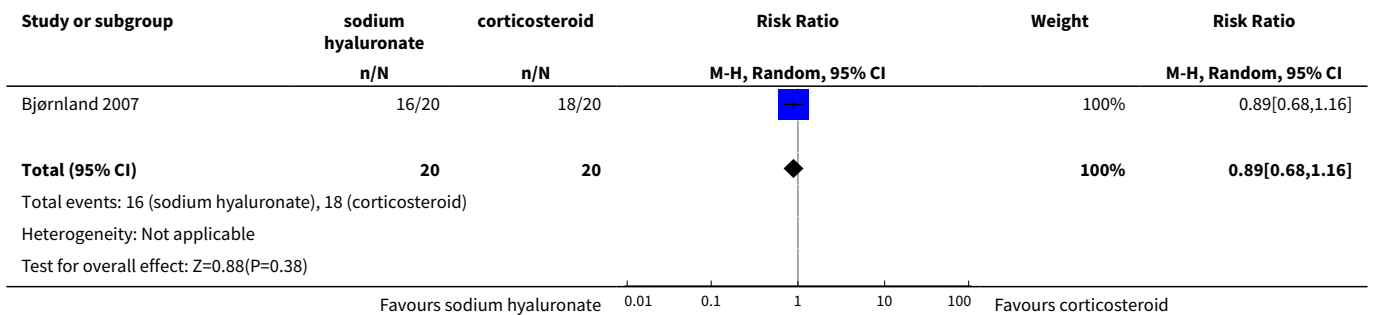
Analysis 1.3. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 3 Reported pain (mm on VAS), 6 months.



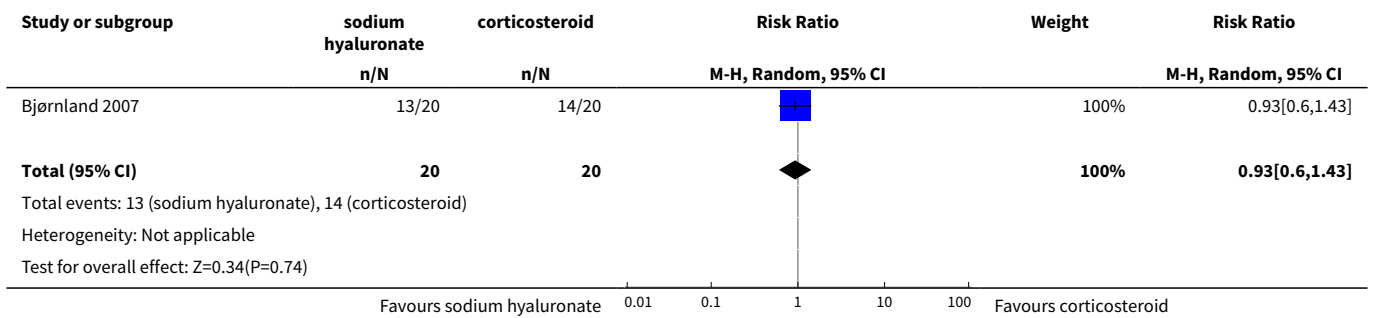
Analysis 1.4. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 4 Pain on palpation of the affected TMJ, after 14 days.



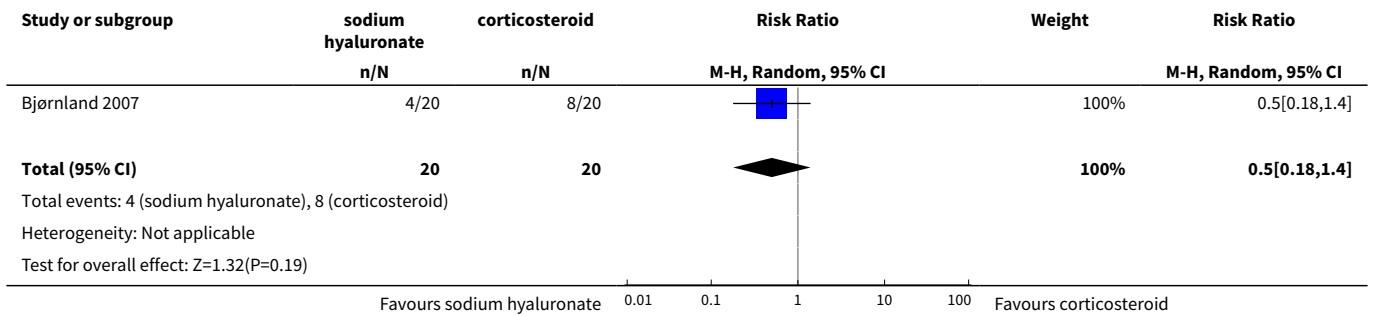
Analysis 1.5. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 5 Pain on palpation of the affected TMJ, after 1 month.



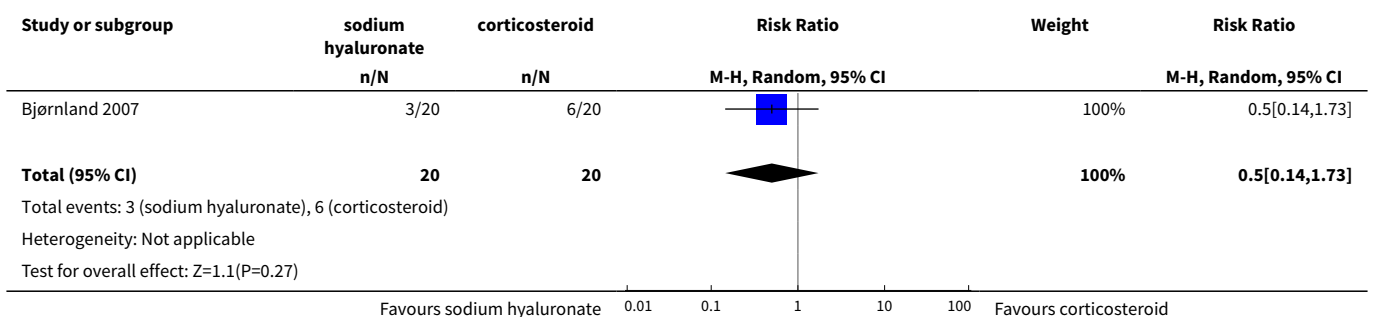
Analysis 1.6. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 6 Pain on palpation of the affected TMJ, after 6 months.



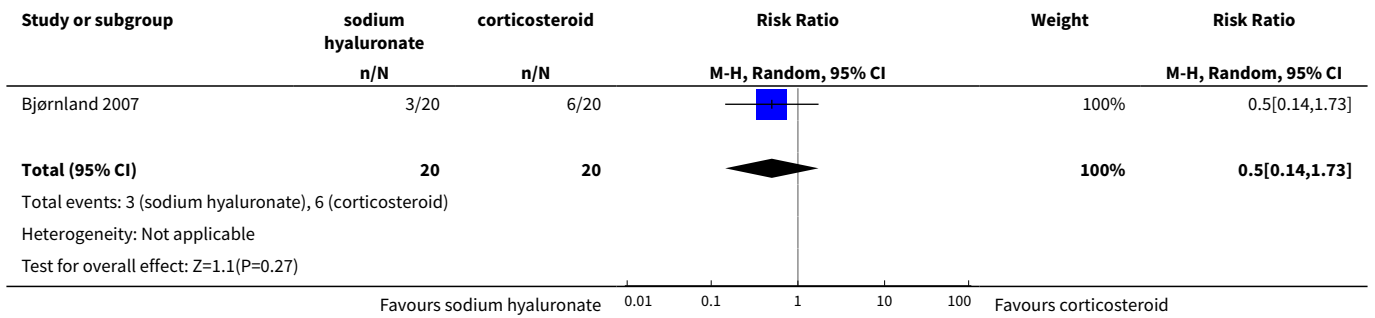
Analysis 1.7. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 7 Pain on palpation of the contralateral TMJ, after 14 days.



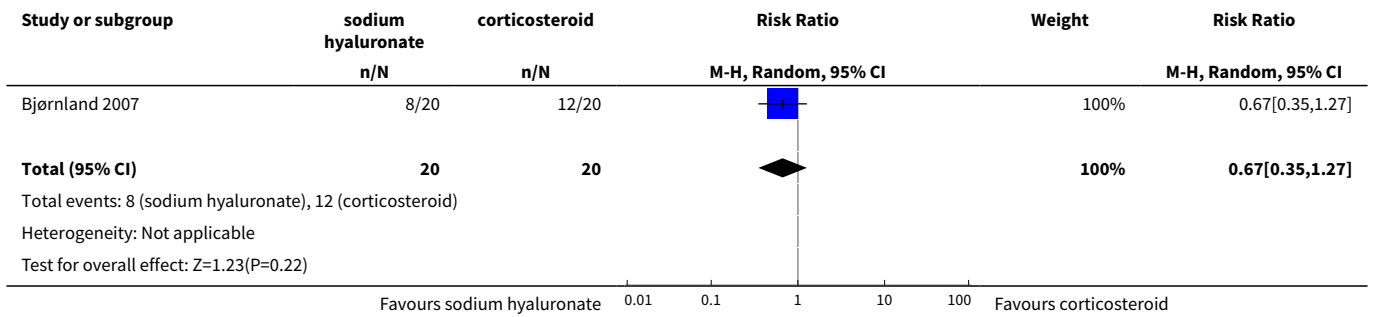
Analysis 1.8. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 8 Pain on palpation of the contralateral TMJ, after 1 month.



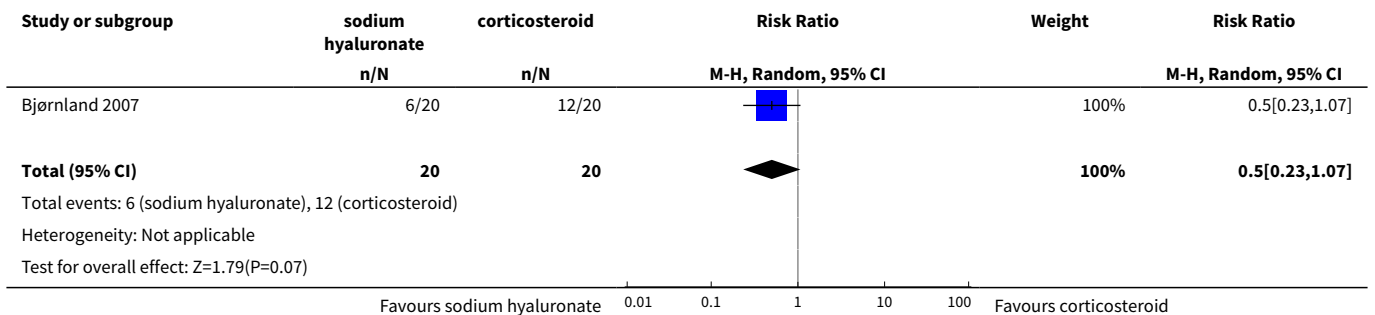
Analysis 1.9. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 9 Pain on palpation of the contralateral TMJ, after 6 months.



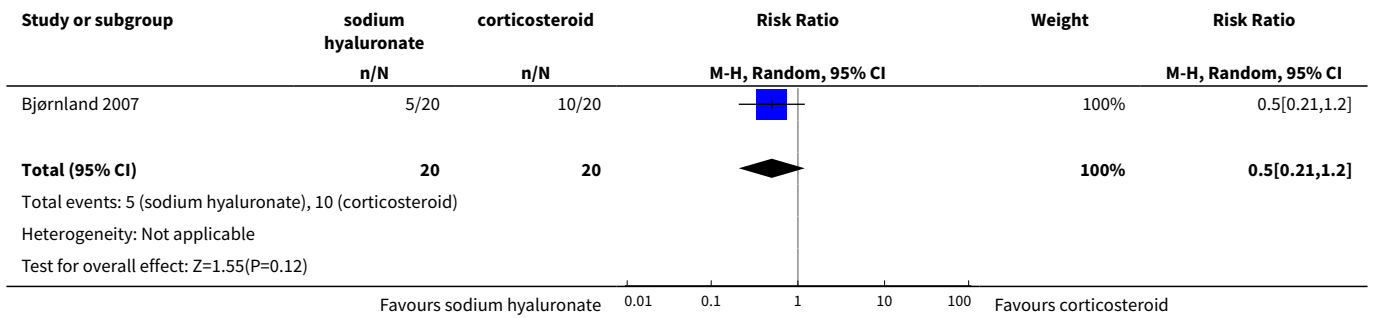
Analysis 1.10. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 10 Pain on palpation of the masticatory muscles, after 14 days.



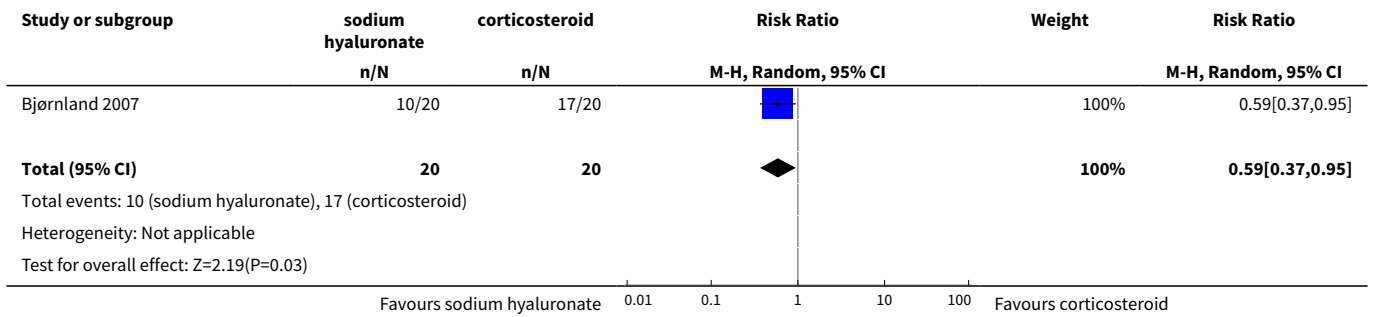
Analysis 1.11. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 11 Pain on palpation of the masticatory muscles, after 1 month.



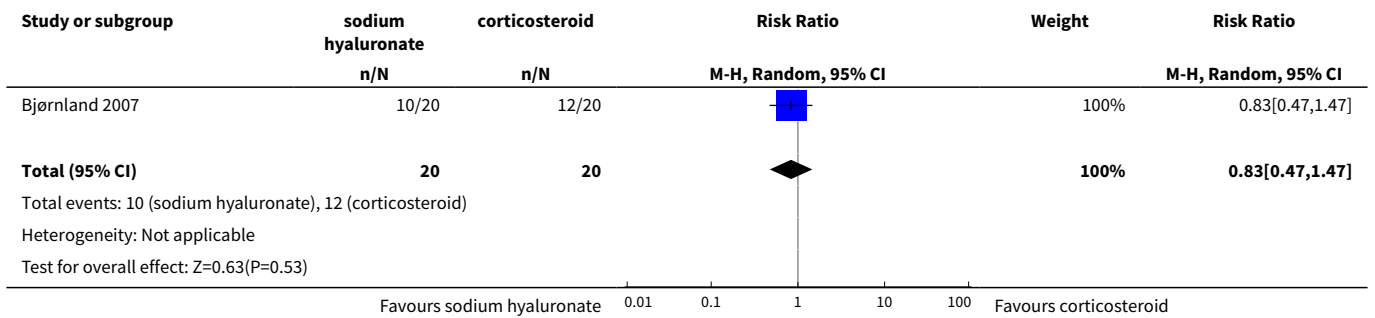
Analysis 1.12. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 12 Pain on palpation of the masticatory muscles, after 6 months.



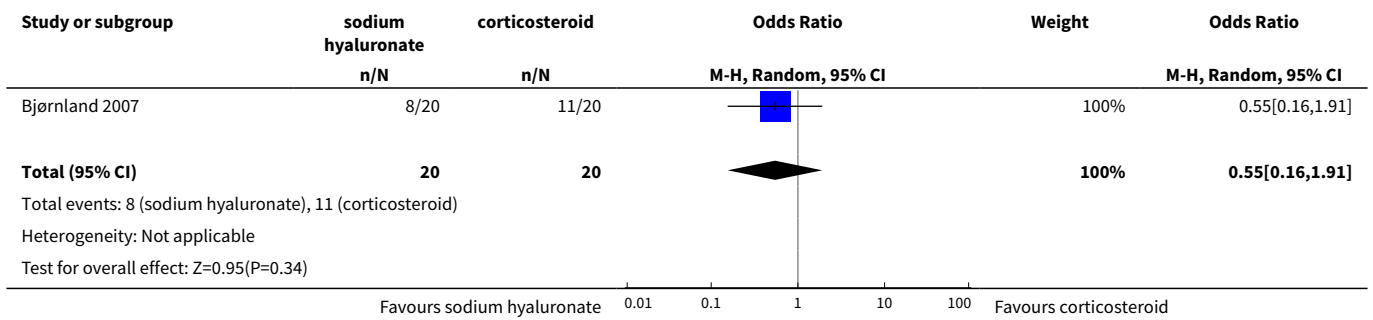
Analysis 1.13. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 13 Presence of TMJ sounds, after 14 days.



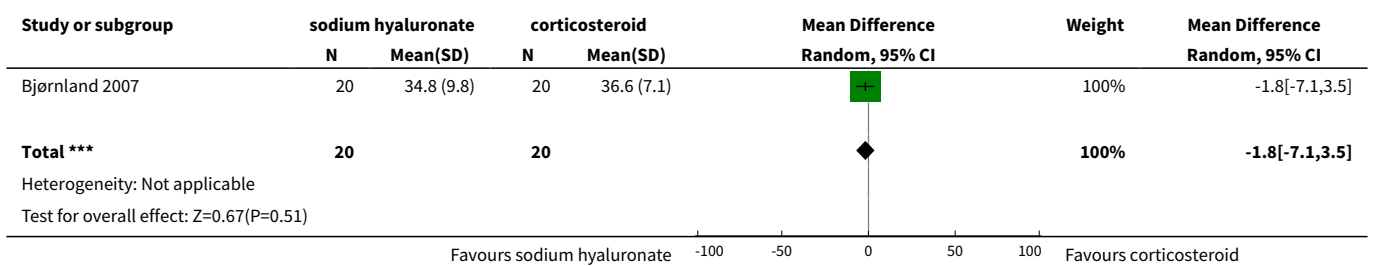
Analysis 1.14. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 14 Presence of TMJ sounds, after 1 month.



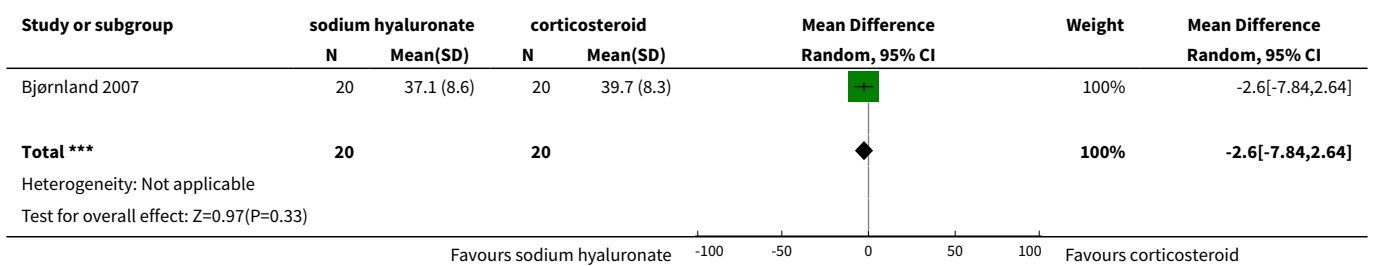
Analysis 1.15. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 15 Presence of TMJ sounds, after 6 months.



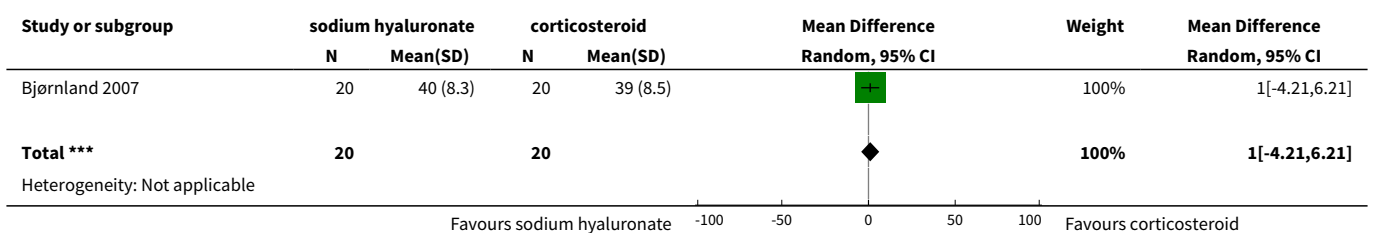
Analysis 1.16. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 16 Maximum jaw opening (mm), 14 days.

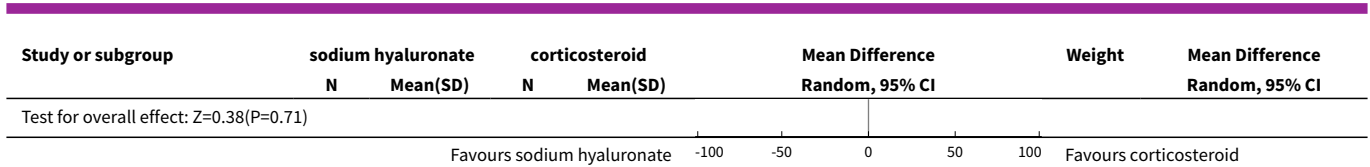


Analysis 1.17. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 17 Maximum jaw opening (mm), 1 month.

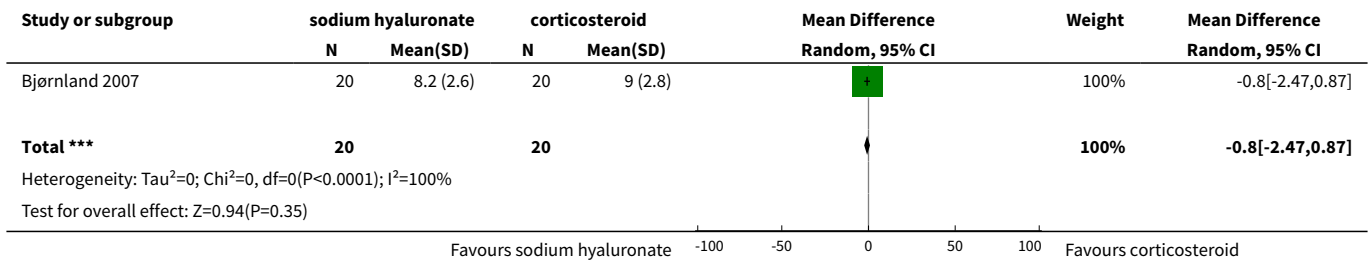


Analysis 1.18. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 18 Maximum jaw opening (mm), 6 months.

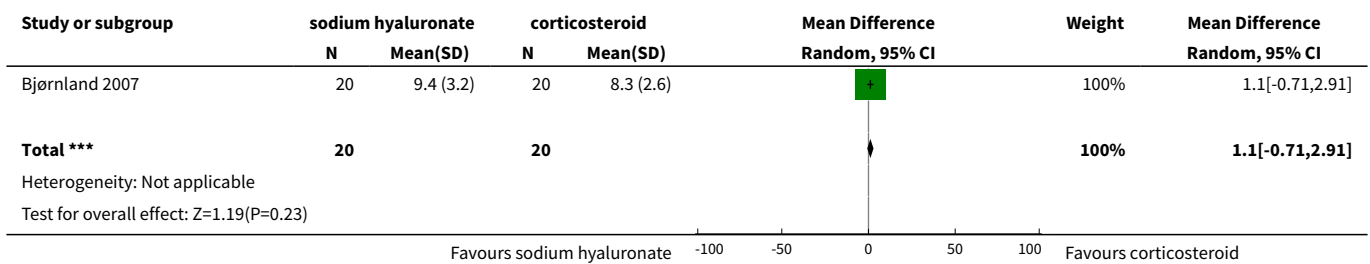




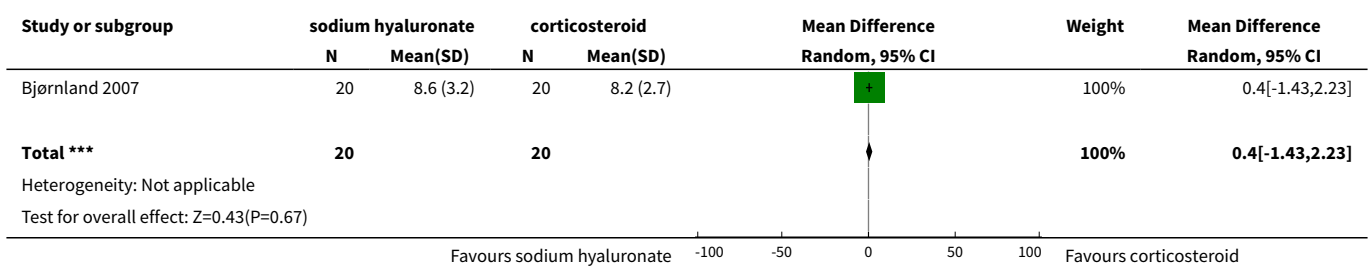
Analysis 1.19. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 19 Lateral movement to affected side (mm), 14 days.



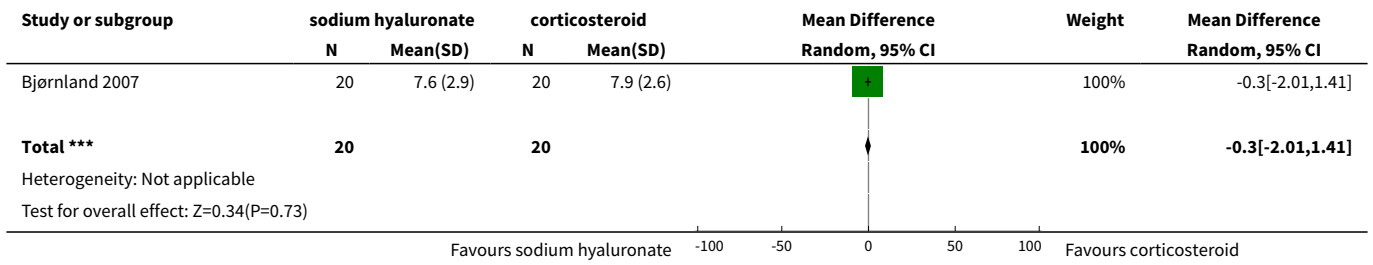
Analysis 1.20. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 20 Lateral movement to affected side (mm), 1 month.



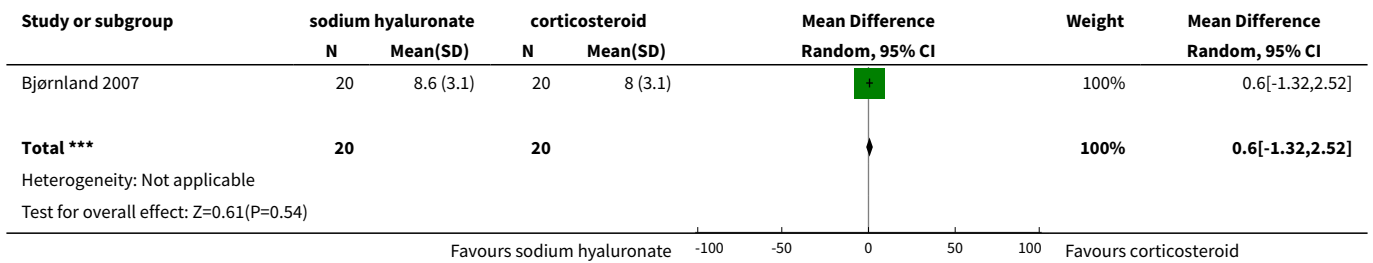
Analysis 1.21. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 21 Lateral movement to affected side (mm), 6 months.



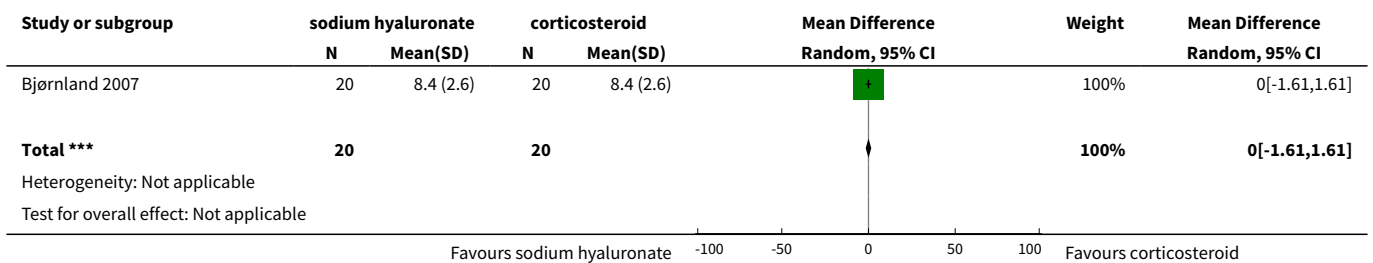
Analysis 1.22. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 22 Contralateral movement (mm), 14 days.



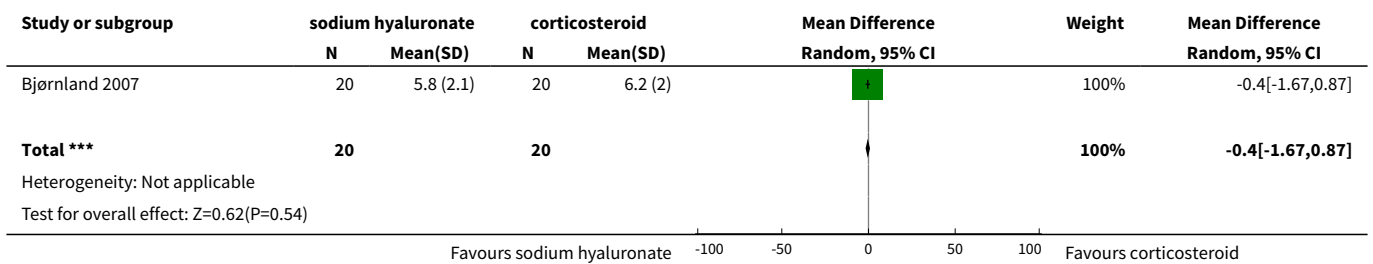
Analysis 1.23. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 23 Contralateral movement (mm), 1 month.



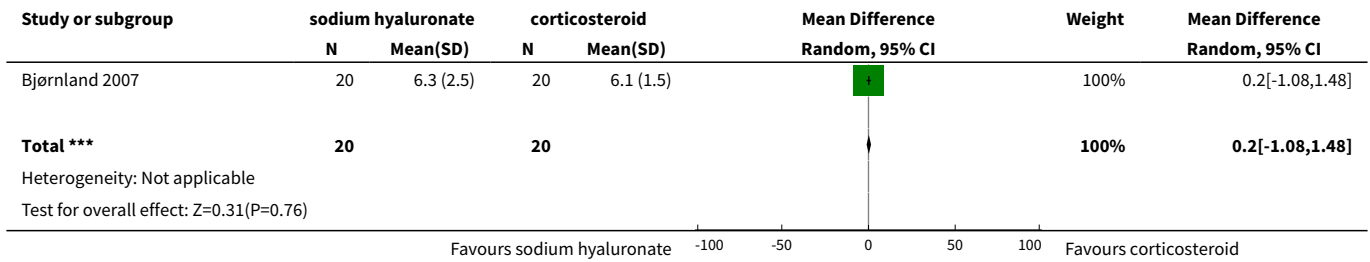
Analysis 1.24. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 24 Contralateral movement (mm), 6 months.



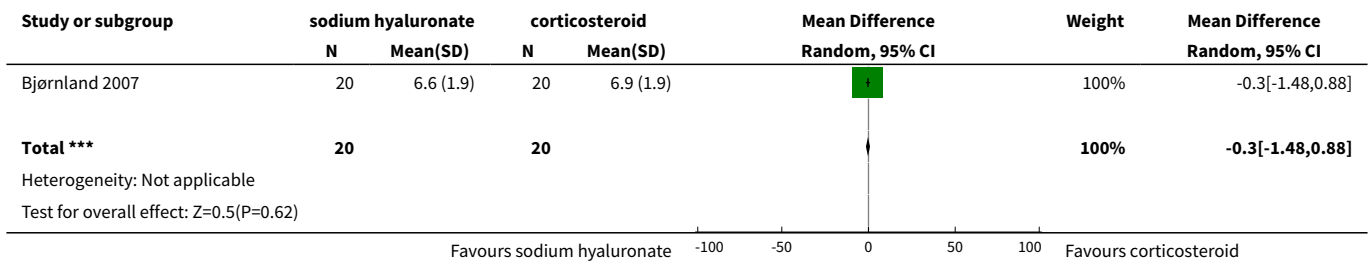
Analysis 1.25. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 25 Jaw protrusion (mm), 14 days.



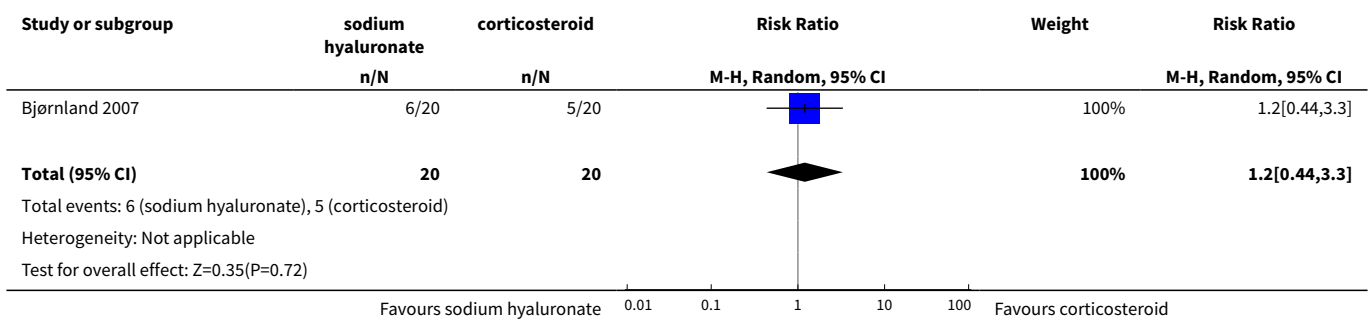
Analysis 1.26. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 26 Jaw protrusion (mm), 1 month.



Analysis 1.27. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 27 Jaw protrusion (mm), 6 months.



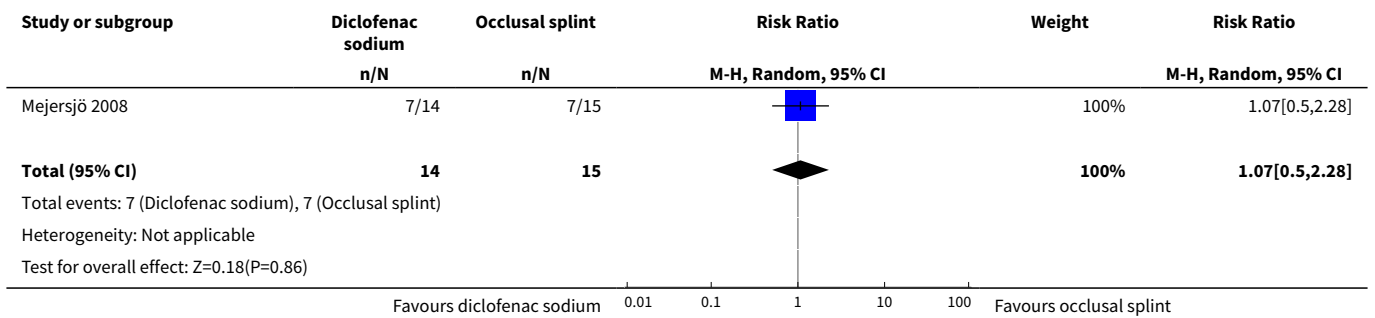
Analysis 1.28. Comparison 1 Comparison 1. Sodium hyaluronate versus corticosteroids, Outcome 28 Post-surgical complications.



Comparison 2. Comparison 2. Diclofenac sodium versus occlusal splint

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Post-surgical complications	1	29	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.50, 2.28]

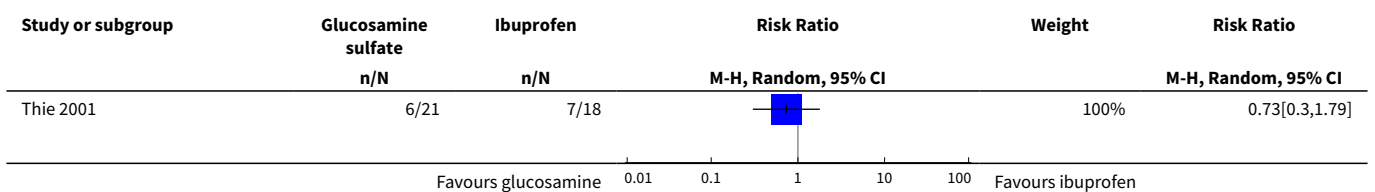
Analysis 2.1. Comparison 2 Comparison 2. Diclofenac sodium versus occlusal splint, Outcome 1 Post-surgical complications.

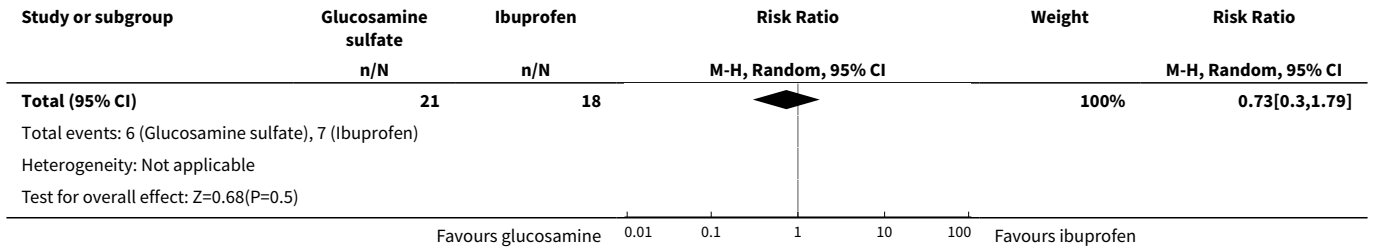


Comparison 3. Comparison 3. Glucosamine sulfate versus ibuprofen

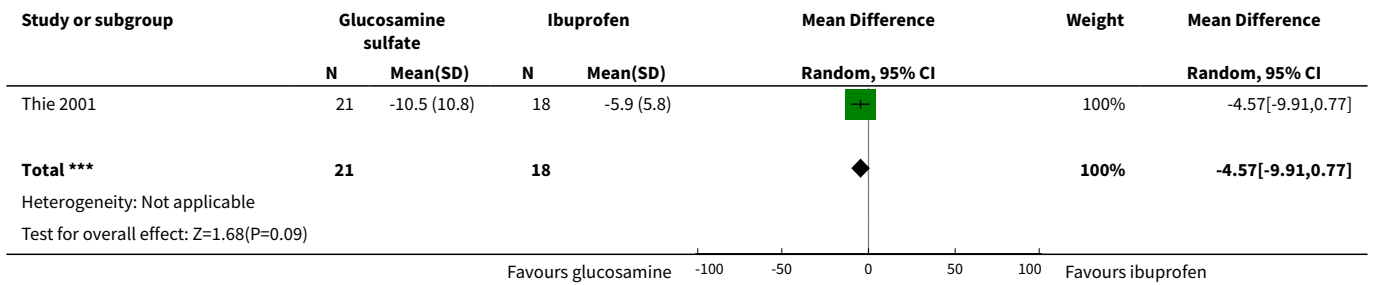
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain during function, after 90 days	1	39	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.30, 1.79]
2 Reported pain (mm on VAS), change from baseline at 90 days	1	39	Mean Difference (IV, Random, 95% CI)	-4.57 [-9.91, 0.77]
3 Pain-free maximum jaw opening (mm), change from baseline at 90 days	1	39	Mean Difference (IV, Random, 95% CI)	1.75 [-4.10, 7.60]
4 Maximum jaw opening (mm), change from baseline at 90 days	1	39	Mean Difference (IV, Random, 95% CI)	3.08 [-0.97, 7.13]
5 BPI questionnaire - pain intensity (VAS), change from baseline at 90 days	1	39	Mean Difference (IV, Random, 95% CI)	-2.69 [-7.38, 2.00]
6 BPI questionnaire - pain interference (VAS), change from baseline at 90 days	1	39	Mean Difference (IV, Random, 95% CI)	-6.74 [-14.70, 1.22]
7 Masticatory muscle tenderness (= number of tender sites/14), change from baseline at 90 days	1	39	Mean Difference (IV, Random, 95% CI)	0.38 [-2.30, 3.06]

Analysis 3.1. Comparison 3 Comparison 3. Glucosamine sulfate versus ibuprofen, Outcome 1 Pain during function, after 90 days.

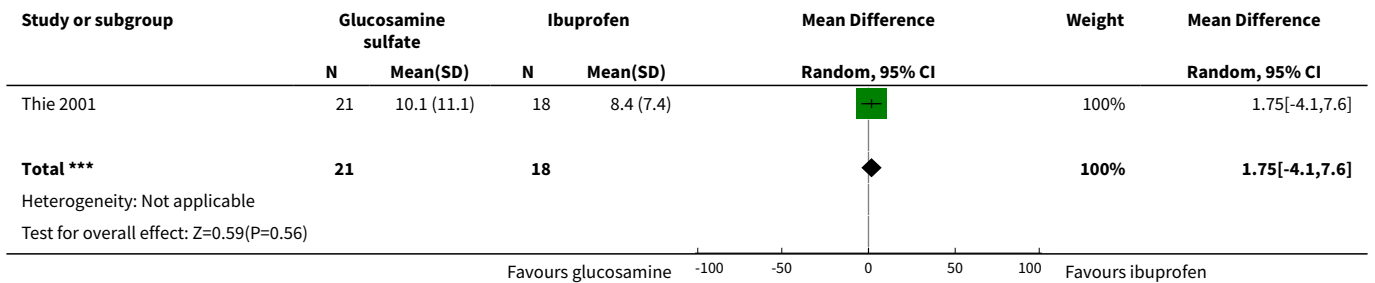




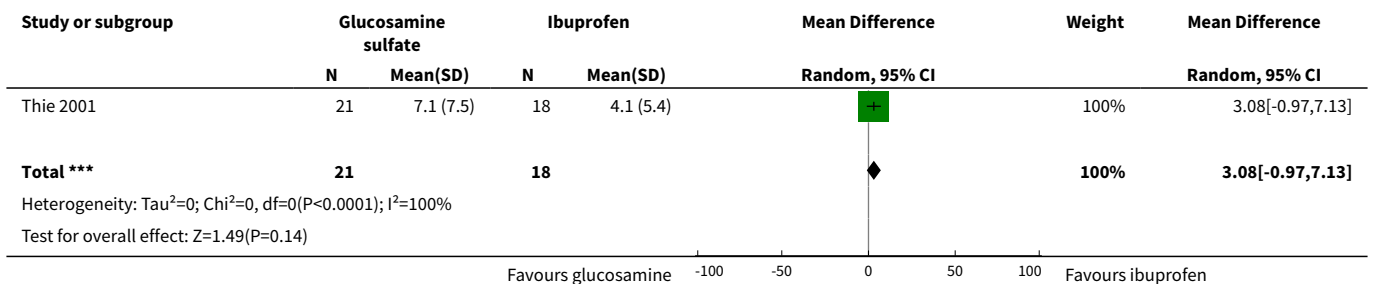
Analysis 3.2. Comparison 3 Comparison 3. Glucosamine sulfate versus ibuprofen, Outcome 2 Reported pain (mm on VAS), change from baseline at 90 days.



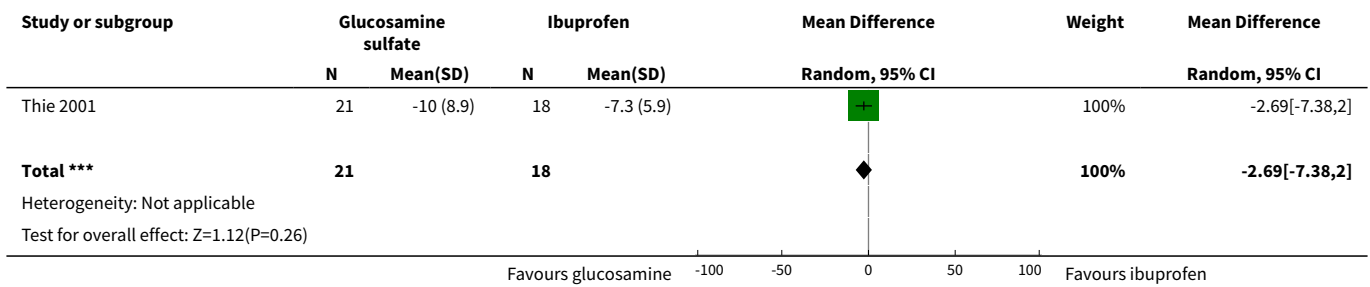
Analysis 3.3. Comparison 3 Comparison 3. Glucosamine sulfate versus ibuprofen, Outcome 3 Pain-free maximum jaw opening (mm), change from baseline at 90 days.



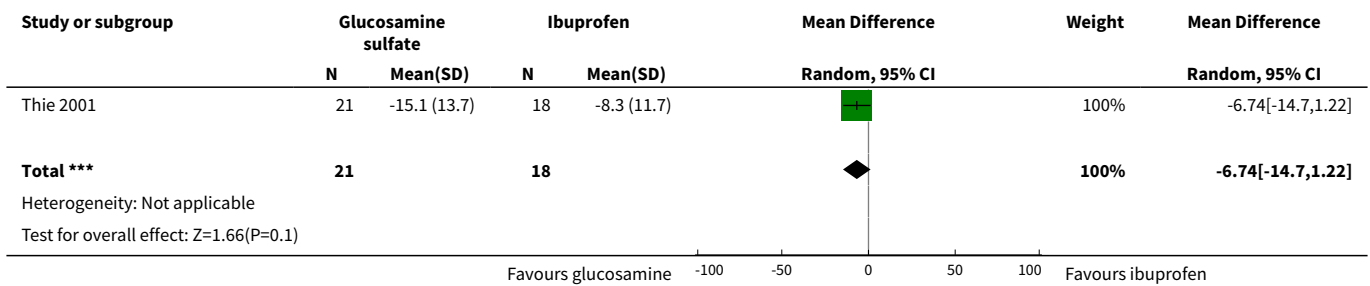
Analysis 3.4. Comparison 3 Comparison 3. Glucosamine sulfate versus ibuprofen, Outcome 4 Maximum jaw opening (mm), change from baseline at 90 days.



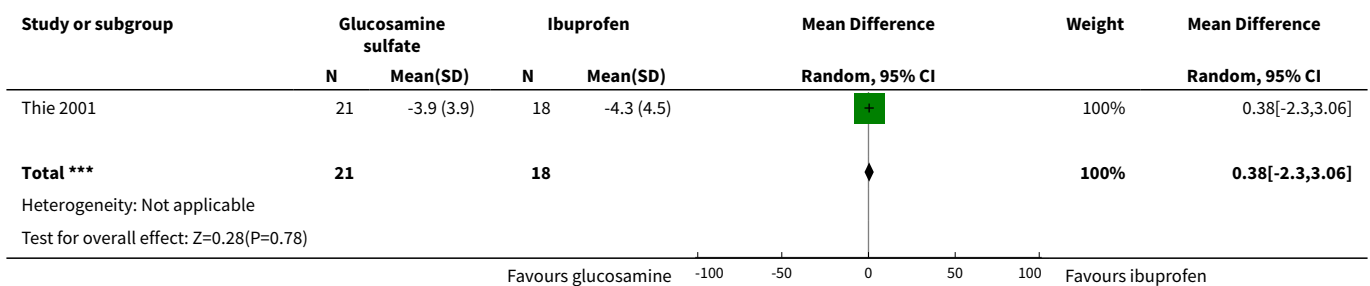
Analysis 3.5. Comparison 3 Comparison 3. Glucosamine sulfate versus ibuprofen, Outcome 5 BPI questionnaire - pain intensity (VAS), change from baseline at 90 days.



Analysis 3.6. Comparison 3 Comparison 3. Glucosamine sulfate versus ibuprofen, Outcome 6 BPI questionnaire - pain interference (VAS), change from baseline at 90 days.



Analysis 3.7. Comparison 3 Comparison 3. Glucosamine sulfate versus ibuprofen, Outcome 7 Masticatory muscle tenderness (= number of tender sites/14), change from baseline at 90 days.



ADDITIONAL TABLES

Table 1. Research recommendations based on a gap in the management of temporomandibular joint osteoarthritis

Core elements	Issues to consider	Status of research for this review
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Table 1. Research recommendations based on a gap in the management of temporomandibular joint

osteoarthritis (Continued) Evidence (E)	What is the current state of evidence?	A systematic review identified three RCTs which matched the eligibility criteria, but two were inadequately reported and assessed as 'unclear risk of bias'
Population (P)	Diagnosis, disease stage, comorbidity, risk factor, sex, age, ethnic group, specific inclusion or exclusion criteria, clinical setting	Adult patients of any gender or age, diagnosed with TMJ OA according to RDC/TMD or compatible criteria. Pain or tenderness of masticatory muscles should be considered as an important comorbidity
Intervention (I)	Type, frequency, dose, duration, prognostic factor	Any non-surgical or surgical therapy for TMJ OA. No study evaluated open surgery or arthrocentesis, which should be explored in future trials
Comparison (C)	Type, frequency, dose, duration, prognostic factor	Placebo/sham or other therapeutic modality with frequency, dose and duration comparable to the intervention. Comparison with any inactive treatment to be compared in future trials
Outcome (O)	Which clinical or patient related outcomes will the researcher need to measure, improve, influence or accomplish? Which methods of measurement should be used?	Pain/tenderness/discomfort in TMJs or jaw muscles (VAS) Extent of mandibular movement TMJ sounds (as perceived by the patients or auscultation) Health-related quality of life or patient satisfaction Morphological changes of the TMJs Number of visits or days absent from work Adverse events Costs
Time stamp (T)	Date of literature search or recommendation	March 2010
Study type	What is the most appropriate study design to address the proposed question?	Randomised controlled trial Methods: concealment of allocation sequence Blinding: participants, researchers, outcomes assessors, data analysts Setting: primary care and orofacial pain clinics

RCTs = randomised controlled trials; RDC/TMD = Research Diagnostic Criteria for Temporomandibular Disorders; TMJ OA = temporomandibular joint osteoarthritis.

APPENDICES

Appendix 1. Cochrane Oral Health's Trials Register search strategy

```
((osteoarthritis* OR arthrit* OR arthralgi* OR "degenerative disorder*" OR "degenerative condition*") AND (temporomandibular* OR "myofacial pain" OR craniomandibular OR (#4 CONTAINS TMJ) OR (#43 CONTAINS TMJ) OR (#4 CONTAINS CMD) OR (#43 CONTAINS CMD) OR (#4 CONTAINS TMD) OR (#43 CONTAINS TMD) OR "temporo mandibular" OR temporo-mandibular OR "cranio mandibular" OR craniomandibular OR "joint diseases"))
```

(#4 relates to the Title field within the Cochrane Oral Health Group Trials Register. #43 relates to the abstract field)

Appendix 2. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1 OSTEARTHRTIS Single MeSH term

#2 osteoarthriti*

#3 (arthrit* OR arthralgi* OR (degenerative near/6 disorder*) OR (degenerative* near/6 condition*))

#4 TEMPOROMANDIBULAR JOINT Exploded MeSH term

#5 TEMPOROMANDIBULAR JOINT DISORDERS Exploded MeSH term

- #6 (temporomandibular OR temporo-mandibular)
- #7 ("TMJ" in Title, Abstract or Keywords or "TMD" in Title, Abstract or Keywords or "CMD" in Title, Abstract or Keywords)
- #8 (#1 or #2 or #3)
- #9 (#4 or #5 or #6 or #7)
- #10 (#8 and #9)

Appendix 3. MEDLINE (Ovid) search strategy

1. Osteoarthritis/
2. osteoarthritis\$.mp.
3. (arthritis\$ or arthralgi\$ or (degenerative adj6 disorder\$) or (degenerative\$ adj6 condition\$)).mp.
4. exp Temporomandibular Joint/
5. exp Temporomandibular Joint Disorders/
6. (temporomandibular or temporo-mandibular).ab,sh,ti.
7. ("TMJ" or "TMD" or "CMD").ab,sh,ti.
8. or/1-3
9. or/4-7
10. 8 and 9

The above subject search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials (RCTs) in MEDLINE: sensitivity maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the *Cochrane Handbook for Systematic Reviews of Interventions* version 5.1.0 (updated March 2011).

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp animals/ not humans.sh.
11. 9 not 10

Appendix 4. Embase (Ovid) search strategy

1. Osteoarthritis/
2. osteoarthritis\$.mp.
3. (arthritis\$ or arthralgi\$ or (degenerative adj6 disorder\$) or (degenerative\$ adj6 condition\$)).mp.
4. exp Temporomandibular Joint/
5. exp Temporomandibular Joint Disorders/
6. (temporomandibular or temporo-mandibular).ab,sh,ti.
7. ("TMJ" or "TMD" or "CMD").ab,sh,ti.
8. or/1-3
9. or/4-7
10. 8 and 9

The above subject search was linked to Cochrane Oral Health filter for identifying RCTs in EMBASE via OVID:

1. random\$.ti,ab.
2. factorial\$.ti,ab.
3. (crossover\$ or cross over\$ or cross-over\$).ti,ab.
4. placebo\$.ti,ab.
5. (doubl\$ adj blind\$).ti,ab.
6. (singl\$ adj blind\$).ti,ab.
7. assign\$.ti,ab.
8. allocat\$.ti,ab.
9. volunteer\$.ti,ab.
10. CROSSOVER PROCEDURE.sh.
11. DOUBLE-BLIND PROCEDURE.sh.
12. RANDOMIZED CONTROLLED TRIAL.sh.
13. SINGLE BLIND PROCEDURE.sh.
14. or/1-13

15. ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/
16. HUMAN/
17. 16 and 15
18. 15 not 17
19. 14 not 18

Appendix 5. PEDro search strategy

The Physiotherapy Evidence Database (PEDro) was searched via the Internet: <http://search.pedro.org.au/>:

temporomandibular AND osteoarthritis

WHAT'S NEW

Date	Event	Description
18 June 2018	Review declared as stable	This review has had low usage and is not a priority for updating.

CONTRIBUTIONS OF AUTHORS

Raphael Freitas de Souza (RFS), Zbys Fedorowicz (ZF), Mona Nasser (MN) and Claudia Helena Lovato da Silva (CLS) were responsible for designing and co-ordinating the review.

RFS and CLS organised the retrieval of papers.

RFS, CLS and MN were responsible for: writing to authors of papers for additional information; screening search results; screening retrieved papers against inclusion criteria; appraising the quality of papers; data collection for the review; and obtaining and screening data on unpublished studies.

ZF and MN were responsible for: obtaining copies of trials; extracting data from papers; and entering the data into Review Manager.

All review authors contributed to analysis and interpretation of the data, and to writing the review.

DECLARATIONS OF INTEREST

There are no financial conflicts of interest and the review authors declare that they do not have any associations with any parties who may have vested interests in the results of this review.

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NOTES

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INDEX TERMS**Medical Subject Headings (MeSH)**

Anti-Inflammatory Agents [administration & dosage]; Betamethasone [administration & dosage]; Diclofenac [administration & dosage]; Glucosamine [administration & dosage]; Hyaluronic Acid [administration & dosage]; Ibuprofen [administration & dosage]; Occlusal Splints; Osteoarthritis [*therapy]; Randomized Controlled Trials as Topic; Temporomandibular Joint Disorders [*therapy]; Viscosupplements [administration & dosage]

MeSH check words

Humans