

## Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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# Are intraarticular steroids effective for knee osteoarthritis?

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### Abstract

Knee osteoarthritis is a chronic disabling condition that is both progressive and irreversible. Intraarticular steroids are commonly used to reduce osteoarthritis symptoms and to minimize the need for surgery. Nevertheless, debate still exists regarding the efficacy and safety of steroids. To address this point, we searched Epistemonikos database which is maintained by screening 30 separate databases and identified 12 systematic reviews including 41 studies addressing steroids use in knee osteoarthritis. Of these, 40 were randomized trials. The evidence from these studies was combined using meta-analysis, and a summary of findings table was constructed following the GRADE approach. We concluded intraarticular steroid use slightly decreases short-term pain, makes little or no difference in the mid-term, and may have no effects in the long-term.

### Problem

Knee osteoarthritis is one of the main causes of knee pain in the general population, affecting over 250 million people globally [1]. Some studies show that up to 10% of patients over 55 have some degree of disabling osteoarthritis, and one quarter of these patients could be severely disabled [2]. This is particularly relevant when considering the chronic and irreversible evolution of this disease, which progresses 4% annually and presents a symptomatic conversion of 1% per year [3]. Treatment for this disease is focused on pain management and maintaining patient functionality. Since knee osteoarthritis originates from degenerative and inflammatory mechanisms [4], it is widely held that intraarticular steroid administration would decrease the inflammatory response associated with this disease.

### Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

#### Key messages

- It is probable that intraarticular steroids slightly decrease pain and improve function in the short-term, but make little or no difference in the mid-term.
- Intraarticular corticosteroids may have no long-term effects, but the certainty of the evidence for this conclusion is low.
- Intraarticular steroid injection does not appear to have major associated complications, but the certainty of the evidence for this conclusion is low.

## About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We found 12 systematic reviews [5],[6],[7],[8],[9],[10],[11],[12],[13],[14],[15],[16], which included 41 primary studies [17],[18],[19],[20],[21],[22],[23],[24],[25],[26],[27],[28],[29],[30],[31],[32],[33],[34],[35],[36],[37],[38],[39],[40],[41],[42],[43],[44],[45],[46],[47],[48],[49],[50],[51],[52],[53],[54],[55],[56],[57]. All of these primary studies [42], except one, were randomized controlled trials.</p> <p>Of the primary studies, 14 randomized trials specifically addressed the topic of the present report. These 14 trials were used to create this summary [17],[18],[19],[20],[21],[22],[23],[24],[25],[26],[27],[28],[29],[30].</p>
<p>What types of patients were included</p>	<p>All of the studies included patients diagnosed with symptomatic knee osteoarthritis and with symptoms (i.e. pain) lasting more than six months. On average, patients had between 55 and 70 years-old, were mostly women (61-93%), and included patients with grade II-IV Kellgren-Lawrence osteoarthritis.</p>
<p>What types of interventions were included</p>	<p>Three studies used prednisolone acetate [24],[25],[38], seven used triamcinolone hexacetonide [17],[18],[19],[20],[23],[26],[30], three used hydrocortisone [20],[21], [27], two used methylprednisolone [18], [21], one used betamethasone [18], and one used cortivazol [22].</p>
<p>What types of outcomes were measured</p>	<p>The evaluated outcomes were pain within the first 2 weeks, 4-6 weeks, 3 months, and 6 months. Additionally, functionality was evaluated using the Western Ontario and McMaster Universities Arthritis Index (WOMAC). The different studies evaluated WOMAC outcomes between 9 and 34 weeks post-treatment. Other evaluated outcomes included severe complications and treatment discontinuation due to adverse effects.</p>

## Summary of findings

The effects of intraarticular steroids were determined based on 14 randomized, controlled trials that, in total, included 810 patients [17],[18],[19],[20],[21],[22],[23],[24],[25],[26],[27],[28],[29],[30]. Nine trials (591 patients) measured pain after 1 or 2 weeks [17],[18],[19],[20],[22],[25],[26],[28],[30]; eight trials (539 patients) measured pain after 3 months [17],[18],[22],[23],[25],[28],[29],[30]; three trials (271 patients) measured pain after 6 months [22],[27],[28]; eight trials (568 patients) reported functionality [18],[19],[20], [22],[23],[28],[29],[30]; and three trials (218 patients) reported severe adverse events [22],[28],[29].

The findings can be summarized as follows:

- Intraarticular steroid injection probably lead to a slight, short-term reduction in pain. The certainty of this evidence is moderate.
- Intraarticular steroid injection probably insignificantly decrease pain in the mid-term. The certainty of this evidence is moderate.
- Intraarticular steroid injection might not make any difference in long-term pain. The certainty of this evidence is low.
- Intraarticular steroid injection probably insignificantly improve functionality. The certainty of this evidence is moderate.
- Intraarticular steroid injection might have no relevant complications. The certainty of this evidence is low.

Intraarticular steroids for knee osteoarthritis				
<b>Patients</b>	Knee osteoarthritis			
<b>Intervention</b>	Intraarticular steroids			
<b>Comparison</b>	Placebo (saline solution)			
Outcomes	Absolute effect*		Relative Effect (IC 95%)	Certainty of evidence (GRADE)
	WITHOUT Intraarticular steroids	WITH Intraarticular steroids		
Pain: 1-2 weeks 10 cm VAS †	6.1 cm	4.6 cm	SMD -0.61 (-0.78 a -0.43)	⊕⊕⊕○ <sup>1</sup> Moderate
	Difference: 1.5 cm better on VAS (Margin of error: 1.9 to 1.1 cm better)			
Pain: 3 months (VAS) †	6.1 cm	5.3 cm	SMD -0.33 (-0.51 to -0.14)	⊕⊕⊕○ <sup>1</sup> Moderate
	Difference: 0.8 cm better on VAS (Margin of error: 0.03 to 1.3 cm better)			
Pain: 6 months (VAS) †	6.1 cm	6 cm	SMD -0.03 (-0.3 to 0.24)	⊕⊕○○ <sup>1, 2</sup> Low
	Difference: 0,1 cm better on VAS (Margin of error: 0.8 cm better to 0.6 cm worse)			
Functionality (WOMAC)	-1.2 WOMAC	-1.85 WOMAC	SMD -0.31 (-0.48 to -0.14)	⊕⊕⊕○ <sup>1</sup> Moderate
	Difference: 0.65 better in WOMAC (Margin of error: 1.0 cm to 0.3 cm better)			
Severe adverse event ✓	30 per 1000	10 per 1000	RR 0.33 (0.03 to 2.98)	⊕⊕○○ <sup>1, 2</sup> Low
	Difference: 20 fewer patients per 1000 (Margin of error: 29 fewer to 60 more)			

Margin of error = 95% confidence interval.  
SMD: Standard mean difference.  
RR: Relative risk.  
VAS: Visual analog scale.  
WOMAC: Western Ontario and McMaster Universities Arthritis Index.  
GRADE: Evidence grades of the GRADE Working Group (See later in this article).

\* The risks **WITHOUT intraarticular steroids** are based on the risk in the control group of studies. The risk **WITH intraarticular steroids** (and its margin of error) is calculated from the relative effect (and its margin of error).

† Calculated on the basis of a median pooled SD of 2.5 cm, found in large-scale osteoarthritis trials that assessed pain using a 10-cm VAS, SMDs of -0.20 corresponding to approximate differences of 0.5 cm between experimental and control groups, -0.50 of 1.25 cm, and -0.80 of 2 cm. [58]. WOMAC SMDs were back-transformed on the basis of a pooled SD of 2.1 in trials that assessed function using WOMAC. SD unit reduction of 0.68 and 0.58 was assumed for pain and WOMAC, respectively, as seen in the included systematic reviews [5],[60]. For differences, a baseline VAS of 6.1 was used based on large-scale osteoarthritis trials [59].

✓ Serious adverse event: any undesired event not produced by the use of any medical product when the outcome includes: death, life-threatening hospitalization (initial or extended), disability or permanent injury, congenital anomaly or birth defect, required intervention to prevent damage or disability [61].

1 We downgraded the certainty of the evidence for risk of bias, since many studies have limitations in this domain.  
2 We downgraded the certainty of the evidence for imprecision as the confidence interval is wide.

## About the certainty of the evidence (GRADE)\*

⊕⊕⊕⊕

**High:** This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

**Moderate:** This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

**Low:** This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

**Very low:** This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

\*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.

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## Other considerations for decision-making

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### To whom this evidence does and does not apply

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- The evidence presented in this summary is applicable to all patients with knee pain secondary to osteoarthritis of the knee.
  - The presented evidence is not applicable to acute or chronic knee pain from other causes or osteoarthritis pain in other joints, even with similar characteristics.
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### About the outcomes included in this summary

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- The outcomes included in this summary correspond to pain at 1-2 weeks, 3 months, and 6 months. Additionally, functionality and serious adverse effects were evaluated. These outcomes are relevant when taking a clinical decision. The effectiveness of these outcomes has been previously evaluated in other meta-analyses.
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### Balance between benefits and risks, and certainty of the evidence

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- This intervention probably has a small short-term benefit, with a similarly low risk of complications. The benefit/risk balance is rather neutral.
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### What would patients and their doctors think about this intervention

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- Variability between patients and clinicians should be expected. Most people faced with little benefit should be inclined against using the intervention. However, patients placing greater value on a slight benefit, especially when other treatment options are not being considered, might opt for the intervention.
  - The rather favorable recommendations might tip the balance towards the use of intervention by many clinicians.
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### Resource considerations

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- While the direct cost of intervention is relatively low, since the benefits are slight, cost can be a key factor for decision-making, especially in settings where resources are constrained.
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### Differences between this summary and other sources

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- The conclusions presented in this summary are consistent with the identified systematic reviews [5],[6],[7],[8].
  - Conventional indications in this area present differing standpoints. The findings of this summary are partially consistent with recommendations made by the American Academy of Orthopedic Surgeons [65], which states there is insufficient evidence to support or refute the use of intraarticular steroids in knee osteoarthritis. In contrast, the International Osteoarthritis Research Society [66] recommends steroid use based on the short-term, beneficial effects.
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### Could this evidence change in the future?

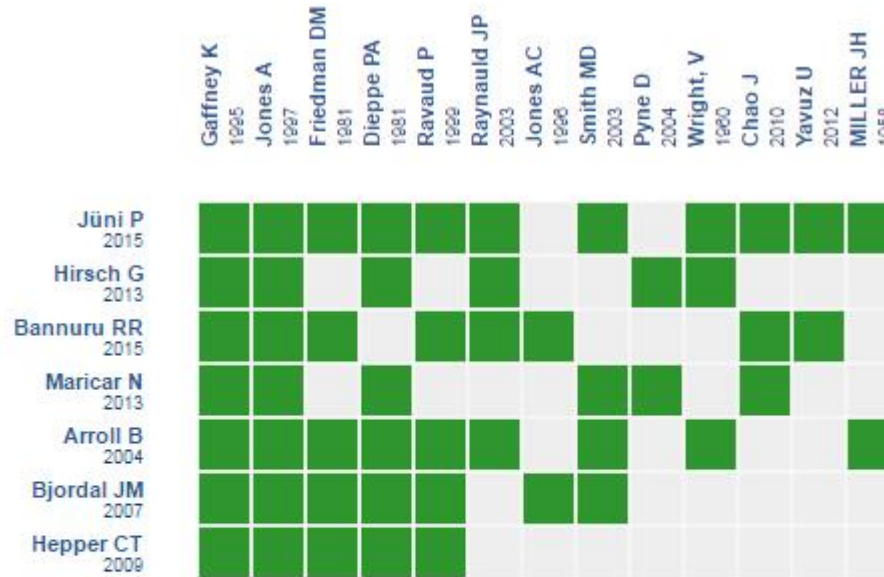
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- The probability of future evidence changing the information presented in this summary is low due to the certainty of the evidence.
  - There are no ongoing trials regarding this line of study, so it is unlikely that new information will appear in the short-term.
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## How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.

The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.

The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.

The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Intraarticular corticosteroids for knee osteoarthritis](#)

## Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here <http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-

makers with technology. Its main development is Epistemonikos database ([www.epistemonikos.org](http://www.epistemonikos.org)).

These summaries follow a rigorous process of internal peer review.

## Conflicts of interest

The authors do not have relevant interests to declare.

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