Corticosteroids are potent anti-inflammatory agents with longstanding use in osteoarthritis treatment, but their effectiveness and safety are unclear. This article summarizes the results of a recent Cochrane review\(^1\) that evaluated the association of intra-articular corticosteroids with benefits and harms compared with sham injection or no intervention in patients with knee osteoarthritis.

**Summary of Findings**

Use of intra-articular corticosteroids was associated with a larger pain reduction than control (standardized mean difference [SMD], \(-0.40\) [95% CI, \(-0.58\) to \(-0.22\)]), which corresponds to a difference in pain scores of 1.0 cm on a 10-cm visual analog scale between corticosteroids and control. This effect size corresponds to a number needed to treat of 8 (95% CI, 6 to 13), meaning that for every 8 patients treated with corticosteroids rather than sham injection or no intervention, 1 patient will respond to treatment. The Figure shows random-effects meta-analyses by follow-up time and trial size.

Overall, corticosteroids were associated with a moderate benefit at 1 to 2 weeks after treatment (SMD, \(-0.48\) [95% CI, \(-0.70\) to \(-0.27\)]). The magnitude of this beneficial association decreased with increasing length of follow-up. There was no association of intra-articular steroids with benefit at 6-month follow-up (SMD, \(-0.07\) [95% CI, \(-0.25\) to 0.11]). When the meta-analysis was stratified by trial size, results from small trials were similar to the overall analysis. However, associations of intra-articular steroids with benefit were less strong in the 3 moderate to large trials that included 50 patients or more per trial group.

A test for interaction between trial size and treatment effect was positive (\(\text{P} = .01\)), suggesting small study effects. Findings were similar for physical function. Only 1 of these moderate to large trials that included a total of 100 patients reported adequate concealment of allocation, adequate measures to blind patients, and an intention-to-treat analysis.\(^2\) This trial\(^2\) included exercise therapy as a concomitant treatment in all patients, compared corticosteroid injection with sham injection, included only patients with local signs of inflammation, and used ultrasound guidance to ensure adequate intra-articular placement of needles when injecting a single dose of 40 mg of methylprednisolone acetate.

This trial did not find evidence that corticosteroids were associated with clinical benefits after follow-up of 2 weeks, 3 months, and 6 months.\(^2\) The other 2 moderate to large trials compared corticosteroids plus viscosupplementation vs viscosupplementation only or corticosteroids plus joint lavage vs joint lavage only.\(^1\)

Only 2 trials contributed to the random-effects meta-analyses of adverse events, withdrawal due to adverse events, and serious adverse events. There was no association of corticosteroids with adverse events; however, the 95% CIs were wide and could not exclude the possibility of harm. One small trial found no evidence that intra-articular corticosteroids were associated with joint space narrowing.\(^1\)

**Discussion**

Intra-articular corticosteroids may be associated with moderate improvement in pain and a small improvement in physical function up to 6 weeks after injection. However, the quality of the evidence is low.

**Limitations**

First, the quality of the evidence was generally low, there was considerable heterogeneity among trials, and there was evidence of small study effects. Heterogeneity estimates and associations with benefit decreased when analyses were restricted to trials with appropriate concealment of allocation, nonindustry funding, moderate to large sample sizes, and large effect sizes. Similar heterogeneity was found in a previous Cochrane review.\(^1\) Differences in outcome assessment may have contributed to these findings. It is not clear whether patients with knee pain are a homogenous group, and included studies were conducted in a diverse range of countries, cultures, and surgeons, which may have contributed to differences in outcomes. This may be due to differences in pain assessment, examples of different clinical populations with knee pain, or different effectiveness of corticosteroids in different populations. It was apparent from the meta-analysis that the beneficial association decreased over time, which may reflect the duration of benefit produced by the corticosteroids. A test for interaction between trial size and treatment effect was positive (\(\text{P} = .01\)), suggesting small study effects. Findings were similar for physical function. Only 1 of these moderate to large trials that included a total of 100 patients reported adequate concealment of allocation, adequate measures to blind patients, and an intention-to-treat analysis.\(^2\) This trial included exercise therapy as a concomitant treatment in all patients, compared corticosteroid injection with sham injection, included only patients with local signs of inflammation, and used ultrasound guidance to ensure adequate intra-articular placement of needles when injecting a single dose of 40 mg of methylprednisolone acetate.

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sizes, or use of viscosupplementation or joint lavage as cointerventions in both groups. Findings were similar for physical function. Second, point estimates were imprecise and we cannot exclude an association between corticosteroids and clinically relevant benefits or harm. Third, none of the included trials focused on patients with intermittent osteoarthritic flares, and only 2 trials had eligibility criteria compatible with the predominant inclusion of patients with acute or subacute exacerbations of symptoms. Therefore, it is not possible to draw conclusions about the association of corticosteroids with benefit in patients with acute or subacute worsening of symptoms after minor trauma or physical activity with signs of local inflammation, effusion, or both.

Comparison of Findings With Current Guidelines
The findings are consistent with the 2013 guidelines of the American Academy of Orthopaedic Surgeons, which did not provide any recommendations for or against the use of intra-articular corticosteroids because the evidence was inconclusive. The 2012 guidelines of the American College of Rheumatology conditionally recommend intra-articular steroids for knee osteoarthritis. The 2014 National Institute for Health and Care Excellence guidelines recommend that clinicians consider the use of corticosteroids as an adjunct to core treatments. Our findings are formally consistent with these recommendations. The 2014 Osteoarthritis Research Society International guidelines state that intra-articular corticosteroids are appropriate for knee osteoarthritis, which somewhat differs from our conclusion.

Areas in Need of Future Study
Adequately powered trials are needed to confirm or refute clinically relevant short- to midterm benefits of intra-articular corticosteroids in patients with stable disease, and in patients with intermittent exacerbations of their osteoarthritic symptoms. The trials should have a sham injection control group, and use ultrasound guidance to ensure accurate intra-articular needle placement.

ARTICLE INFORMATION
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