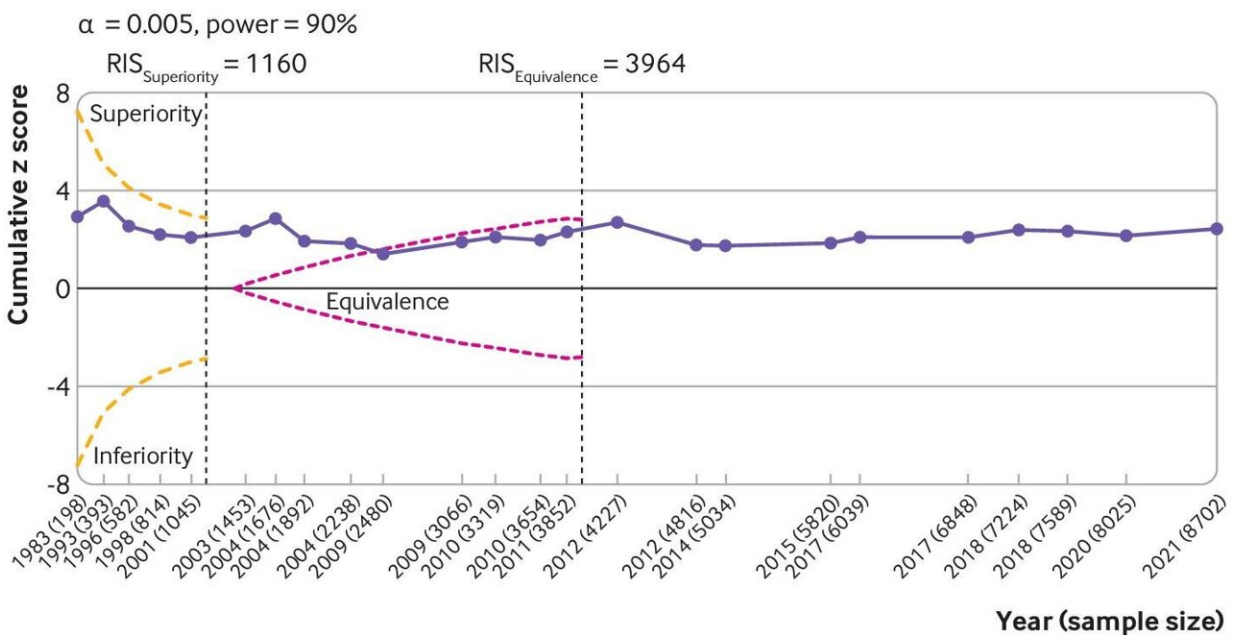


Scant evidence to recommend use of hyaluronic acid injections for knee osteoarthritis

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Trial sequential analysis for pain. Results are based on 24 large, placebo controlled trials (8997 randomized participants). Cumulative z scores were calculated under a random effects model. RIS (required information size; vertical lines) detects a minimal clinically important difference of -0.37 with 90% of power at α level of 0.005. O'Brien-Fleming monitoring boundaries are represented by dashed orange lines. The inner wedges (futility boundaries) are shown in pink and represent limits to the equivalence region considering the 0.2 equivalence margin. Circles denote cumulative z score for each additional trial added to the analysis. Between trial variation was accounted for using diversity (D^2) index adjusted sample sizes. A D^2 of 50% was assumed. Number of

participants analyzed (shown by year) might be smaller than number of randomized participants. Credit: *BMJ* (2022). DOI: 10.1136/bmj-2022-069722

Injections of hyaluronic acid (known as viscosupplementation) to treat knee osteoarthritis make almost no difference to pain and might raise risk of adverse events, suggests research published by *The BMJ* today.

Viscosupplementation has been used to treat [knee osteoarthritis](#) since the 1970s, but its effectiveness and safety has been questioned for some time.

Knee osteoarthritis is a chronic disease that involves inflammation and structural changes of the joints, resulting in [joint pain](#) and limitations to physical movement. It is a leading cause of disability among [older people](#), with an estimated 560 million people living with the condition globally.

National and international guidelines vary in their recommendations, but most advise against the use of viscosupplementation. In England, National Institute for Health and Care Excellence (NICE) guidelines recommend against its use, but health care systems in other countries including the U.S. still offer it to patients.

An international team of researchers therefore set out to review existing studies on the subject carried out during the past 50 years to evaluate just how effective and safe viscosupplementation is for pain and function in patients with knee osteoarthritis.

They identified 169 trials involving 21,163 patients with knee osteoarthritis that compared viscosupplementation with [placebo](#) (dummy) treatment or no treatment.

The main analysis of this review, which included a subset of 24 large trials of higher methodological quality involving 8,997 randomized patients, found that viscosupplementation was associated with a small reduction in pain compared with placebo, but the difference was tiny and was described as "clinically irrelevant."

Their analysis showed that since 2009, there has been conclusive evidence that viscosupplementation and placebo treatment have led to the same clinical result in terms of pain reduction, meaning there is no point to having the injections.

They also found from 15 large trials on 6,462 randomized participants that viscosupplementation was linked to a 49% higher risk of serious adverse events than placebo.

The authors say that based on their analysis of the studies between 2009 and 2021 alone, more than 12,000 patients were arguably unnecessarily subjected to these injections in viscosupplementation trials, which raises ethical concerns.

The study has some limitations in that it represents summary estimates and does not necessarily exclude the possibility that selected patient populations could benefit from viscosupplementation. Also, the researchers looked at adverse events that emerged rather than adverse events directly and clearly related to treatment.

However, strengths include the fact that this is the largest collection of randomized trials on viscosupplementation reported to date, which significantly decreases the risk of bias influencing the results.

As such, the authors conclude: "There is strong, conclusive evidence that among patients with knee osteoarthritis, viscosupplementation, compared with placebo, is associated with a clinically irrelevant

reduction in [pain](#) intensity and with an increased risk of serious adverse events.

"The findings do not support broad use of viscosupplementation for the treatment of [knee osteoarthritis](#)."

More information: Tiago V Pereira et al, Viscosupplementation for knee osteoarthritis: systematic review and meta-analysis, *BMJ* (2022). [DOI: 10.1136/bmj-2022-069722](https://doi.org/10.1136/bmj-2022-069722)

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