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Rapid Responses to:

Reviews:

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Stephan Reichenbach, Rebekka Sterchi, Martin Scherer, Sven Trelle, Elizabeth Bürgi, Ulrich Bürgi, Paul A. Dieppe, and Peter Jüni

Meta-analysis: Chondroitin for Osteoarthritis of the Knee or Hip Ann Intern Med 2007; 146: 580-590 [Abstract] [Full text] [PDF]

Electronic letters published:

Interpretation of chondroitin meta-analysis

Harley A Goldberg, Andrew L Avins, MD (23 April 2007)

Clinical usefulness of chondroitin sulfate

Patrick du Souich (19 April 2007)

Interpretation of chondroitin meta-analysis

23 April 2007

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Harley A Goldberg, DO *Kaiser Permanente, Northern California,* Andrew L Avins, MD Send rapid

response to journal: <u>Re:</u> <u>Interpretation of</u> <u>chondroitin</u> <u>meta-analysis</u>

Email Harley A Goldberg, et al.

Interpretation of chondroitin meta-analysis The meta-analysis by Reichenbach and colleagues(1) is both timely and important. However, we are concerned that the authors' sweeping conclusions are not well grounded in their methodology. Based on data extraction and synthesis, the overall effect size of chondroitin is large (Figure 2, Forest plot) p<0.001, though this conclusion is limited by the presence of heterogeneity among trials (I2=92%). Using metaregression, the authors identified a subset of trials that provide homogeneity, and stronger methodology, suggesting no effect on pain. The authors accurately state that a meta-regression analysis "should be viewed as hypothesis-generating" and is "observational in nature" yet it is the results of the meta-regression that forms the cornerstone of the article's conclusion. But this conclusion makes no mention of the overall meta- analytic result or limitations, nor the limitations of the meta- regression. The pre-specified "large trial" cut off of 200 participants included five trials, with a summary small-to-moderate effect size of borderline significance. But the authors based their conclusions of "no effect" on only three of these trials (citing, additionally, reporting of intention- to-treat analyses), circumventing the single most important benefit of systematic reviews which discourages a focus on a selective subset of studies. It is of great concern that the author's choice to base their conclusions on only these three studies was almost certainly made without being blinded to these studies' results (since the authors read all of the papers at the outset). Although, in the end, the conclusion that "use of chondroitin in routine clinical practice should therefore be discouraged" may eventually turn out to be true, it is not sufficiently supported by the methodology used here. The data provided by the authors show: a meta-analysis demonstrates large effect size, but is limited by heterogeneity between trials; meta- regression identifying the better trials suggests little or no effect, raising concerns about study quality; these results apply to pain only, and do not address disease progression, which also deserves further study (though the clinical significance of joint-space narrowing is unknown (2)(3). This important analysis needs to be added to the growing evidence on the effect of chondroitin for pain in osteoarthritis, but interpretation of the results should not go beyond what the results themselves allow.

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3. Spector TD, Dacre JE, Harris PA, Huskisson EC. Radiological progression of osteoarthritis: an 11 year follow up study of the knee. Ann Rheum Dis. 1992 Oct;51(10):1107–1110.

Conflict of Interest:

None declared

Clinical usefulness of chondroitin sulfate

Patrick du Souich, MD, PhD University of Montreal

Send rapid response to journal: <u>Re: Clinical</u> <u>usefulness of</u> <u>chondroitin</u> <u>sulfate</u>

Email Patrick du Souich

TO THE EDITOR, The report of Reichenbach et al. [1] raises several points. In first place, it confirms that chondroitin sulfate is not an analgesic. As a matter of fact, glycosaminoglycans are not analgesics. In second place, this meta-analysis strongly supports several trials demonstrating that chondroitin sulfate reduces the rate of knee joint space narrowing [2,3]. Finally, this meta-analysis confirms that the incidence of adverse effects caused by chondroitin sulfate is similar to that produced by placebo. Keeping in mind that several double blinded randomized placebo-controlled trials have demonstrated that chondroitin sulfate is superior to placebo for most end-points assessed, that treatment with chondroitin sulfate is associated with a significant decrease in the incidence of joint swelling, effusion, or both [4], and that patients treated with chondroitin sulfate appear to use less NSAIDs [5], the conclusions reached by the authors may not be fully justified. In view of the potential beneficial effects of chondroitin sulfate on joint swelling and space, of its safety and absence of drugdrug interactions, and the lack of safe alternatives for patients multimedicated for osteoarthritis and other accompanying diseases, e.g. diabetes, hypertension, hyperlipidemia, etc, further studies are warranted before reaching the conclusion that the use of chondroitin in routine clinical practice should be discouraged. 1. Reichenbach S, Sterchi R, Scherer M, Trelle S, Burgi E, Burgi U, et al. Meta-analysis: chondroitin for osteoarthritis of the knee or hip. Ann Intern Med. 2007:146:580-90, 2. Michel BA, Stucki G, Frey D, De Vathaire F, Vignon E, Bruehlmann P, Uebelhart D. Chondroitins 4 and 6 sulfate in osteoarthritis of the knee: a randomized, controlled trial. Arthritis Rheum. 2005;52:779-86. 3. Uebelhart D, Malaise M, Marcolongo R, DeVathaire F, Piperno M, Mailleux E, et al. Intermittent treatment of knee osteoarthritis with oral chondroitin sulfate: a one-year, randomized, double-blind, multicenter study versus placebo. Osteoarthritis Cartilage. 2004;12:269-76. 4. Clegg DO, Reda DJ, Harris CL, Klein MA, O'Dell JR, Hooper MM, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. N Engl J Med. 2006;354:795-808. 5. Lagnaoui R, Baumevielle M, Begaud B, Pouyanne P, Maurice G, Depont F, Moore N. Less use of NSAIDs in long-term than in recent chondroitin sulphate users in osteoarthritis: a pharmacy-based observational study in France. Therapie. 2006;61 :341-6.

19 April 2007 🔳

Conflict of Interest:

Research Grant from Bioibérica S.A. No conflict of interest

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