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Editorial

OARSI recommendations for the management of hip and knee osteoarthritis: the semantics of differences and changes

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The Osteoarthritis Research Society International (OARSI) is committed to developing consensus-driven OA treatment guidelines predicated on a continually updated database of the research evidence. This commitment extends beyond production of the first set of guidelines and endeavors to keep the database current by incorporating new research evidence into periodic updates of the consensus statements. This process can be viewed a cycle of activities that break down into (1) evidence synthesis (2) a consensus process and (3) surveillance of the database for changes in evidence that should initiate revision of the consensus statement. While methodologies are established for first two undertakings, the initiative to test an updated dataset for pivotal changes is novel. Inherent to this process are a number of methodological and logistical challenges that include the approach to layering new data on top of the old and the formulation of decision rules to define pivotal change. For these reasons, and especially because of intrigue about what lines of evidence might have changed, I was greatly interested to review the OARSI Treatment Guidelines Committee's recent report of their surveillance of the updated data[1].

Just to digress for a moment, I would point out that the first two reports from the OA Treatment Guidelines Committee rank first and second in the ranks for the number of downloads from the Osteoarthritis and Cartilage during 2009[2,3], indicating an intense level of interest. This is notable because OA treatment guidelines have also recently been developed by a number of other groups including the National Institute of Clinical Excellence (NICE), the European League Against Rheumatism (EULAR), the Orthopedic Research Society (ORS) and the American College of Rheumatology (ACR)[4–8]. We might infer from these two sets of observations that the motivation for different groups to produce their own version of OA guidelines will continue, perhaps to allow for application of contrasting methodologies and to serve differing constituencies. Nevertheless, inherent in all this parallel activity must be some duplication of effort, especially in relation to derivation of the primary database. In this respect, the OARSI endeavor could serve the broader community through sharing their current evidence repository. Of course, this will be contingent on many factors not least an acceptance of its methodological rigor and data quality, and a willingness to share.

So how do Zhang *et al.* overcome the methodological challenges of identifying important changes in research evidence between 2006 and 2009? This is a task of almost insurmountable magnitude that requires summarizing current evidence from heterogeneous evidence sources across the spectrum of OA treatments. Zhang *et al.* accomplish this by sifting and ranking research reports, using the highest level evidence, and, where possible, performing their own pooled analyses of trial results. Where a typical meta-analysis would devote an entire manuscript to assessment of a single intervention, this report considers many treatments in one document. The trade-off of this approach is a loss of transparency and detail. On the other hand, it is important to appreciate that their task was not to revise the recommendations but to determine whether changes have occurred that should prompt such revisions. As the authors point out, this is not a restatement of the guidelines and should not be interpreted as such. One lingering concern, however, is the lack of any process or algorithm to identify significant changes in the dataset.

So what has changed in the evidence base? There are now positive results for exercise (hip OA), aquatic therapy, rosehip supplements and avocado soybean unsaponifiables. New meta-analyses of weight reduction now show statistical significance around modest benefits for pain and physical function in knee OA. On the other hand, electromagnetic field therapy, which had positive results in 2006 is now viewed as ineffective based on analysis of pooled trial data; and trials of glucosamine hydrochloride (as opposed to sulfate) have also been conclusively negative.

Zhang *et al.* exert a higher level of scrutiny on subtle changes in the pooled evidence when these might impact consensus. The most prominent of these relates to acetaminophen, formerly a core recommendation for OA, for which they now infer little or no efficacy, and which has been impugned in two observational studies for associations with gastrointestinal and renal adverse effects (even thought these are highly confounded by indication). However, when we independently examined the data sources of

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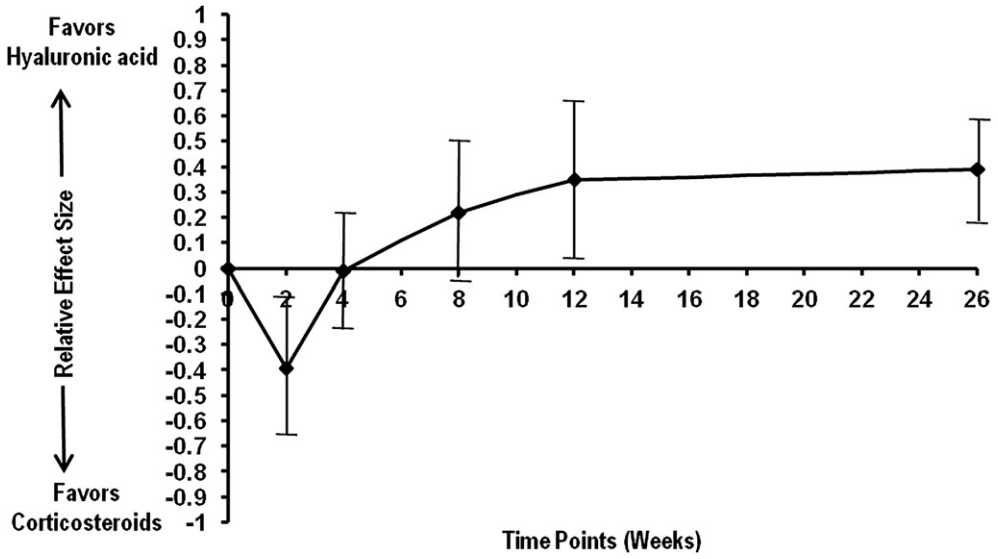

Fig. 1. Graph depicting time-dependent trajectory of the therapeutic effect of IAHA when compared with intra-articular corticosteroids. Note: Adapted from "Relative efficacy of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: Meta-analysis" by RR Bannuru, NS Natov, IE Obadan, CH Schmid, TE McAlindon, 2009, Osteoarthritis & Cartilage, 17(supplement), p. S269. Copyright 2009 OARSI by Elsevier Ltd. Adapted with permission.

these pooled analyses[9,10], we found evidence that this apparent change was, at least in part, attributable to a change in the statistical methodology used between the first and second meta-analysis. This does not necessarily invalidate the suggestion that there has been a change in the evidence, but it does highlight how the trade-off between scale and granularity could lead to erroneous interpretations.

Another situation that illustrates this semantic difference between detecting a *difference in interpretation* vs an actual *change* in the research evidence is the analysis of intra-articular hyaluronic acid (IAHA). It turns out that IAHA, based on two careful recent meta-analyses, has a time-dependent trajectory of therapeutic effect (Fig. 1)[11,12]. Thus, the time point at which its outcome is assessed will influence its apparent effectiveness. This may explain the apparent differences between 2006 and 2009 because the meta-analysis which provided the 2006 estimate of efficacy was measured 2–3 months post-intervention[13], whereas the 2009 values originate from a 1–4 week time point.

Therefore, it may be more appropriate to view varying effect sizes from separate analyses as differences in interpretation rather than a change in measured efficacy. These differences are still important, though, as signals that the evidence may need to be re-evaluated.

Ultimately, if we wish to track changes in the apparent effectiveness of an intervention over time, we will need a frequently (or continually) updated repository of high-quality data in a formulation that permits serial effect size computations and pooled analysis using a variety of approaches. These characteristics would make this database a valuable resource that could benefit other organizations and investigators. Synergy among groups will help develop more encompassing techniques, such as *network meta-analysis*, that would allow us to compare data from multiple intervention types and rank their relative efficacy. The field of evidence synthesis is exciting and developing, and one to which OARSI is making commendable contributions.

Author contributions

All authors were involved in drafting the article and revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. McAlindon had full access to all of the data in the article and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Article conception and design: McAlindon, Bannuru.
Acquisition of data: McAlindon, Bannuru.
Analysis and interpretation of data: McAlindon, Bannuru.

Conflict of interest

Dr. McAlindon has received consulting fees from Stryker Biotech, NiCox, Gelita and GlaxoSmithKline and currently has grant funding from the National Institutes of Health.

Dr. Bannuru: none.

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