High-Quality Orthopedic Research Is Having an Impact

To the Editor:

The review article by Nwachukwu et al. 1 provided interesting documentation of orthopedic studies in 5 high-impact general medical journals. However, the study was methodologically flawed and had unduly negative conclusions.

First, we contend that the publication between 2005 and April 2015 of 39 orthopedic studies, particularly the 16 randomized controlled trials (RCTs), in these high-impact journals should be viewed as good news. The collective endeavors of many in the orthopedic community, including during the Bone and Joint Decade, have helped raise research aspirations and standards such that these top-quality studies tackling priority treatment questions have been able to make a bigger, more general impact.

Second, we suggest that the finding that none of the 57 editorial board members (of 4 journals) had musculoskeletal specialty training or affiliation should serve as a prompt for key players in orthopedics to remedy this deficiency. However, the deficiency itself is not a basis for judging editorial decisions or the quality and rigor of the peer review process, which of course involved input from content specialists.

The primary target of the article by Nwachukwu et al. is the 15 RCTs that compared surgical with nonsurgical care, 8 of which concluded that “nonoperative management is preferred.” The authors treat this finding as suspect, and they put forward various non-evidenced and mistaken claims of reporting and publication biases in favor of non-operative treatment. Notably, the publication of these definitive mostly publicly funded trials contradicts their suspicion of publication bias; typically, this bias applies to the non-publication of small underpowered trials. The assessment by Nwachukwu et al of the quality of the RCTs is also flawed. This includes their use of the overly simplistic Jadad scale, which crucially fails to rate allocation concealment. More problematic is their zealous focus on crossovers and as-treated analysis, incidentally incorrectly defined in their article. Nwachukwu et al acknowledge the “methodologic advantages of an intention-to-treat analysis” but fail to appreciate just how critical intention-to-treat analysis is in avoiding bias, including a presumption in favor of surgery. For as-treated analysis to be valid, the participants who crossover have to be a random sample of all of those participants who were offered treatment. However, this is rarely, if ever, true in medical research. Hence, such analyses will lead to bias. 2

Finally, it is helpful to realize that orthopedic-specialist input would have occurred throughout the life of each RCT. As members of the trial management team of one of the RCTs, 3 we would like to place on record the active and independent oversight of our trial by methodologists, orthopedic specialists, and other stakeholders that ensured the trial design, conduct, and analysis would yield reliable evidence. Publication is the last part of this process. We attest that the editorial process at JAMA was exhaustive in its rigor and in ensuring that our conclusions were evidence based.

We hope this letter helps to redress the unwarranted conclusions of the study by Nwachukwu et al. 1 We also hope that the orthopedic community will continue the momentum shown by these important trials in obtaining the best evidence to inform practice.

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REFERENCES


Reply:

We thank Dr Handoll and colleagues for their letter regarding our article. 1 In this response, we address the points they have raised.

First, we agree that the collective endeavors of many in the orthopedic community to produce high-quality randomized controlled trials (RCTs) should be commended. Although our
review raises concern about possible sources of bias in these publications, we do not intend to detract from the accomplishments of the authors of these studies.

Second, we agree that the lack of representation of musculoskeletal specialty training or affiliation on the editorial boards of the included journals does not negate the rigorous peer review process of the individual journals. However, we do contend that the lack of musculoskeletal representation at high-impact general medical journals is troubling. Concern for general medical journal bias against musculoskeletal procedures and practitioners has been previously expressed. Dr Handoll and colleagues may want to consider how journal editorial staff and intrinsic reviewer biases may influence the publication process.

Regarding our discussion of study crossover and intention-to-treat analysis, Dr Handoll and colleagues assert that the “zealous focus on crossovers” in our review was problematic. We would like to refer Dr Handoll and colleagues to an editorial by the editors of Arthroscopy, who adopt a similar approach to highlighting the potential for significant bias and confounding associated with one-way crossover and intention-to-treat analyses applied to surgical RCTs. We implore Dr Handoll and colleagues as well as other investigators performing RCTs for invasive procedures to take a more nuanced approach to intention-to-treat analyses. In medical trials, intention to treat has a benefit for mitigating factors that may lead to noncompliance and noncompletion of assigned protocols. However, when surgical treatments are being compared with nonoperative treatment, crossover is inherently only one way. To simplify, a patient who is assigned to nonoperative treatment can crossover to receive surgery, but a patient who has undergone surgery cannot then undo the surgery and undergo nonoperative treatment. In our review, we found that 33.2% of all patients in surgical RCTs crossover from nonoperative care to surgery. This finding itself is remarkable in that only two-thirds of patients assigned to undergo nonoperative treatment actually do so. Although as-treated analysis may have its limitations, intention-to-treat analysis alone is also flawed in a surgical population and especially when there is such a large degree of crossover. Thus, as mentioned in our review, we believe that there is a role for performing both intention-to-treat analysis and as-treated analysis in surgical RCTs. In our opinion, this would represent the highest level of statistical rigor and would alleviate any concern for study bias.

We commend Dr Handoll and colleagues on the work they have put forth in providing the orthopedic community with RCT evidence. We hope that our review and subsequent discourse will encourage others to continue to improve the reporting of and mitigate any biases present in orthopedic RCTs published in general medical journals.

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