LETTERS TO THE EDITOR

Systematic reviews in endodontics

Dear Dr. Spångberg,

Your recent editorial ("Systematic reviews in endodontics—examples of GIGO?" Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:723-4) was very thought provoking. The editorial was highly critical of 3 recent systematic reviews, but also of the "poorly designed research" that characterizes much of the clinical endodontic literature. Since all of the reviews were published in peer-reviewed journals (as were most of the papers included in the meta-analyses), surely part of the blame lies with reviewers, and with the editors who oversee acceptance and publication of such papers?

Our recent systematic review[1] enjoys the dubious distinction of first place in your honor roll of "garbage in, garbage out (?)." Our review considered the evidence for a difference in healing frequency following root canal treatment in one versus multiple visits, and concluded that "current best available evidence failed to demonstrate a difference between the 2 treatment regimens." We share your concern that biased analysis will confuse the uninformed reader. To that end, we wish to address a number of the points you have raised in your editorial.

1. Publication bias. The editorial correctly noted the risk that "uninteresting" conclusions tend not to be published, which may bias available data toward a particular outcome. Statistical techniques are available to test for publication bias, but the number of studies in our review was too small for such analysis. We addressed this issue in the Discussion. In any case, all 3 of our included studies showed no statistically significant differences in healing between single- and multiple-visit treatment. As also noted in our review, of the remaining 5 papers[2-6] comparing clinical outcomes of the 2 treatment approaches (which we excluded because they were not randomized), not one reported a significant difference in outcomes. Friedman et al.[5] came closest to statistical significance ($P = .05$), with better healing after single-visit treatment. It is difficult to believe that a significantly better outcome of either single- or multiple-visit treatment would be considered "uninteresting" and not worthy of publication.
2. Our paper was cited as an example of biased sampling, with excessively narrow inclusion criteria that limited the analysis to only 3 published studies. The implication is that we omitted relevant papers. The contention that "the only factors connecting the 3 studies were the words 'single' and 'two visits' in the title" is incorrect. The initial search strategy was based on key words that included "single," "one," "two," and "multiple" "visits" or "appointments" anywhere in the Medline indexing information, which includes the title, abstract, MeSH terms, and so forth. Our paper also clearly states that subsequent search methods included scanning the reference lists of identified articles, forward searches in 3 databases for related papers, and a search of Science Citation Index for papers that had quoted the identified articles. We would be very appreciative (although somewhat chagrined) if you could kindly identify papers that we overlooked in our review. All we ask is that any such papers compare healing following single- and multiple-visit treatment in the same study.
3. Randomization. It is a misstatement that "only one study[7] is somewhat demonstrably randomized." The dynamic balance technique known as "minimization" used by Weiger et al.[8] is a widely accepted randomization technique.[9,10] In the third study,[11] subjects were alternately allocated to 1- or 2-visit treatment. All 3 studies were prospective in design, and none could be construed to be biased in patient allocation to a particular treatment protocol.
4. The "vastly different criteria" for outcome assessments among the 3 papers were in fact all based on healing of apical periodontitis as assessed by clinical and radiographic criteria. One study used the PAI for radiographic assessment while the other 2 used conventional criteria. "*Vastly* different"??? Importantly, all studies applied the same criteria to both treatment groups within the study.
5. The statement that Trope et al.[7] did not use calcium hydroxide as an intracanal medicament in their 2-visit treatment group is incorrect. Their study included 1 multi-visit group with and 1 without an intracanal medicament. Our analysis included only the group medicated with calcium hydroxide.
6. We are puzzled by the statement that sample size in both component studies as well as the final cohort "are all too small for the conclusions that there was no significant difference between 1- or 2-visit treatment protocols." A statistically significant level of difference is achievable regardless of sample size

above a certain minimum, depending on the magnitude of the difference between groups; conversely, lack of significance can occur regardless of sample size if the difference is too small. An *n* of approximately 20 per group (as in 2 of the included studies) or 67 to 79 per group (in the pooled data) is more than sufficient to demonstrate statistical significance or its absence, depending on the difference. The real issue—whether lack of statistical significance means that there is genuinely no difference in healing or whether the sample size is too small to demonstrate a small difference if it existed—was addressed in considerable detail in our Discussion.

7. The risk that less informed readers will draw "erroneous conclusions" is largely beyond our control. Our role is to assess current information on the extent of available evidence, the strength of that evidence, and the conclusions that can reasonably be drawn from the evidence. All of these have been clearly addressed in the paper, including explicit statements such as "only 3 RCTs were identified"; "the level of evidence is weak"; "the difference in healing rate between these 2 treatment regimens was not statistically significant." The only possible alternative conclusion to be drawn from the available evidence (unless we have overlooked any relevant papers) is that there is insufficient evidence to draw *any* conclusion. That would require a denial of the outcomes of 3 peer-reviewed prospective studies by highly respected endodontists.

Discerning readers may wish to contrast your comments with a more rigorous analysis[12] of our paper.

The need for good clinical studies in endodontics, and for their careful analysis and interpretation, is great. As editor of 1 of 3 leading endodontic journals, you have the opportunity, indeed the obligation, to promote the highest standards of clinical research. The *International Endodontic Journal* committed itself 3 years ago to requiring conformity to CONSORT guidelines for clinical studies reported in the journal[10,13]; *Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontics* could do the same. Experts could be invited to provide definitive guidelines for future clinical studies in relation to particular topics of interest, with the guidelines published in *Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontics*. Endodontics would benefit enormously from such positive leadership.

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In reply:

To Drs. Sathorn, Parashos, and Messer

I am glad that my editorial was thought-provoking, because thinking often helps in arriving at a better understanding of issues at hand.

I first notice that you like to assign some of the responsibility for my concerns about endodontic meta-analysis on editors and reviewers. I gladly take the responsibility for my errors of judgment, but I cannot believe that you, as scientists, accept all printed material at face value. Even publications by "highly respected endodontists" must not be beyond careful critical analysis. Therefore, it is reasonable to expect that the authors of a meta-analysis are predominantly responsible for the content.