Response to Letter by Kerr and Nasco

Response:

Kerr and Nasco advocate the use of an End Point Adjudication Committee in every large-scale trial and propose a number of plausible hypotheses for taking this position. Although their arguments are at face value appealing, a sounder basis for the use of an End Point Adjudication Committee would be clear evidence of added scientific value. Just as we seek to base our clinical practice in evidence, so too should our research endeavors be done on this basis.

In undertaking our investigation of the impact of end point adjudication in the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) trial, we sought to move from the “experience” of Kerr and Nasco to the evidence provided by the data. That evidence provides no strong scientific rationale for end point adjudication in a setting such as the PROGRESS trial and we would be remiss to ignore this. Furthermore, since the publication of our data, Pogue et al have reported very similar findings for 10 other masked and unmasked trials done in different settings addressing a range of therapeutic questions. Randomized trials are a fundamentally robust design and it seems that the conclusions we drew from our investigation may well be more broadly generalizable. In the trial setting, objective outcomes such as stroke, heart attack, and death can probably be adequately defined by site investigators with limited additional value provided by third party adjudication.

This is not to say that end point adjudication will never be of value. There are doubtless situations in which adjudication of softer end points that are more difficult to define will be important. However, rather than the blanket application of end point adjudication to every large-scale trial, we should use the evidence we have to apply it where it is required. Over the last few decades, the monitoring of clinical trial processes has spiraled out of control, driven in large part by the clinical research industry, mostly in the absence of clear quantitative evidence of efficacy.

Finally, Although 1% or 2% of the total cost of a trial for end point adjudication may appear a small proportion, it can easily be several million dollars in total. This is too much money to be spending without an objectively defined good cause. The end point adjudication process has become a standard part of clinical trials and is now an important part of the perceived validity of trial results. However, there are probably better and more efficient ways of assuring regulators and physicians of the strength of trial findings and we should endeavor to identify and implement those strategies.

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Disclosures

None.

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