Reviewer's report

**Title:** Between-centre differences and treatment effects in randomized controlled trials: A case study in traumatic brain injury

**Version:** 2  **Date:** 16 May 2011

**Reviewer:** James Torner

**Reviewer's report:**

This article provides useful information of the effect of center and country differences on clinical trial results. The results demonstrate the stability of the treatment effect given the variation in center response.

Minor Essential Revisions
Page 3 "filed" should be "field"

While imbalances do occur, i.e. by center, the goal of randomization is eliminate selection and prognostic biases. The authors should address whether there were imbalances in randomization. Did analysis of the center effect eliminate imbalances?

For the discussion, would the authors consider that analysis by center a standard or optional?

Would the effect by different for procedural trials or for those with substantial treatment effect?

Discretionary Revisions

Did center effect modify the covariate effect on outcome or did the covariate modify the center effect?

Do the authors know the reasons for the center variability on outcome, patient or center level variables?

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

No to the above