Reviewer’s report

Title: Statistical design of personalized medicine interventions: The Clarification of Optimal Anticoagulation through Genetics (COAG) trial

Version: 5 Date: 28 October 2010

Reviewer: Garnet Anderson

Reviewer's report:

The authors have given a thoughtful response to each of my questions and suggestions. The motivation and the trial design at this point. The trial is an unusual one and it certainly warrants description in the literature. The re-calculation of a minimal detectable difference is not novel—this type of calculation has been done to address traditional subgroup affects and even post-randomization issues (projected lack of adherence) but its use in this context is a useful example.

I appreciate the fuller description of the sample size calculations—I learned something. I have always adjusted for the projected fraction with missing data by dividing by (1-q) where q is the proportion missing (Meinert, Clinical Trials). I didn’t know anyone used (1-q)^2 to adjust for simple MAR outcome data. I must admit I think this adjustment is overly conservative but at least it is now clear to the reader. Perhaps the authors could indicate why such a conservative adjustment is needed.

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:

I declare that I have no competing interests.