Reviewer's report

Title: Protocol for a systematic review of the diagnostic and prognostic utility of tests currently available for the detection of aspirin resistance in patients with established cardiovascular or cerebrovascular disease

Version: 2 Date: 8 January 2013

Reviewer: Devan Kansagara

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1) Page 6 (i) "diagnostic/prognostic utility..." - how will you define "sufficient" prognostic utility? This seems like a potentially arbitrary designation - are there well agreed-upon cut-offs that you could cite as a guide?

2) Page 7, top - cost-effectiveness analysis - this seems out of scope for this review and could risk stretching the data further than it really should go. I would think that in order to truly determine cost-effectiveness you’d first have to find evidence of effectiveness. In other words, find "test-treat" studies as you suggest on page 15. Platelet function assays could be shown in the review to have excellent prognostic ability, but that doesn't necessarily mean treating patients with alternate or additional anti-platelet therapies will change clinical outcomes. I would suggest either reconsidering the inclusion of the cost-effectiveness study, or, if you do want to include, describe the types of studies you would need to find in order to conduct such analyses in the section describing study selection.

3) To be useful, it seems that these assays would have to provide incrementally more diagnostic/prognostic information than currently available information such as risk scores, or inflammatory markers like CRP. The described meta-regression and subgroup analyses may provide some information. Studies evaluating the additive contributions of assays to risk prediction would also be useful. It might be useful to frame the choice of study and analysis to more clearly address this issue of incremental value. It may very well be that you find few studies able to answer this question, but framing it in such a way would allow you to more clearly identify an important gap in evidence.