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: 23 December 2012

Reviewer: Erik Grove

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The topic of this study is very important, because the study results may affect clinical practise. Aspirin, the most frequently used drug worldwide, remains a cornerstone in the management of cardiovascular disease, which has been estimated by the World Health Organization to remain the most frequent cause of death in the Western world for many years. Most previous studies in this field have focused on ADP-receptor blockers in patients with acute cardiovascular events, but most of the time, patients with cardiovascular disease are treated with aspirin mono therapy.

The study protocol provides a discussion of previous meta-analysis in the field and comments on how the present study will stand out from previous ones. The authors should be complicated for preparing a detailed study protocol and for addressing important topics that were not adequately dealt with in previous studies, such as compliance and the acuteness of cardiovascular disease.

Minor Revisions:

It has previously been shown that the timing between pill ingestion and blood sampling to a large extent affects the number of “aspirin resistant” individuals. Including this factor in the analyses is perhaps not important, but the authors may wish to include this parameter in tables (in the article) summarizing previous studies.

Discretionary Revisions:

A few comments on the reference list – of course these are merely suggestions.

1) The authors state that "Several factors may influence the response of platelets to antiplatelet therapy” and could support this statement by citing e.g.: Interindividual variability in the efficacy of oral antiplatelet drugs: definitions, mechanisms and clinical importance by Würtz et al; Curr Pharm Des. 2012;18(33):5344-61.


3) In the discussion of platelet function tests (second paragraph of Background), the slightly old reviews (2003-4) included in the reference list may be
supplemented by newer ones, e.g. Platelet function testing in atherothrombotic disease; Curr Pharm Des. 2012;18(33):5379-91.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

Erik Lerkevang Grove has received lecture fees from AstraZeneca, Bayer, Boehringer Ingelheim, and Pfizer, and serves on the advisory board for AstraZeneca and Bristol-Myers Squibb.