Reviewer's report

Title: First results of the PROSPER/PHASE study, a testing frame for pharmacogenetics of statins in the elderly

Version: 1 Date: 27 August 2011

Reviewer: Michael Vaclav Holmes

Reviewer's report:

Major Compulsory Revisions

Please provide the replication beta, SE and P value from both WOSCOPS and CARE in Table 2. It would also be helpful to add a column that describes which other studies have reported these hits (for general interest). Are the associations directionally concordant (i.e. same minor allele show increase/decrease with LDL)?

Please provide information on genomic inflation (QQ, quantile-quantile plot)

Minor Essential Revisions

Title "First results of the PROSPER/PHASE study, a testing frame for pharmacogenetics of statins in the elderly" - the title suggests that the manuscript will present some pharmacogenetic data, however this really is a replication paper - perhaps a better title would be "Replication of LDL GWAs hits in PROSPER/PHASE as validation for future pharmacogenetic analysis"

Title/Abstract "in the elderly" - why is the distinction of age made - do the authors think that the genetic contribution to drug response should change with age?

In the Discussion, please provide references for the statement "however these loci were repeatedly found to be associated with LDL cholesterol levels in various other studies with large number of participants."

In the conclusions, when you make the statement "Moreover, we can also conclude that the PROSPER/PHASE study is likely to have sufficient power to detect genome-wide significant hits for other quantitative traits." The 95 loci paper required a sample size of >100,0000 (PMID 20686565) - can one ever have sufficient power to detect all hits? Perhaps this needs to be more cautiously worded.

"Therefore, we lack of replication of these loci in WOSCOPS and CARE as most likely due to lack of statistical power."

change to

"Therefore, the lack of replication of these loci in WOSCOPS and CARE
was most likely due to lack of statistical power."

Table 2: "Genomic loci with a genome wide significant p-value < 5.0e-08" please change < to <= as the P value for rs602633 =5.0e-08

Discretionary Revisions
* none

**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 am currently collaborating with PROSPER study investigators (including S Trompet and JW Jukema) on several Mendelian randomisation projects, which are unrelated to the present article.